



Locally caught freshwater fish across the United States are likely a significant source of exposure to PFOS and other perfluorinated compounds

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ABSTRACT

Per- and polyfluoroalkyl substances, or PFAS, gained significant public and regulatory attention due to widespread contamination and health harms associated with exposure. Ingestion of PFAS from contaminated food and water results in the accumulation of PFAS in the body and is considered a key route of human exposure. Here we calculate the potential contribution of PFOS from consumption of locally caught freshwater fish to serum levels. We analyzed data for over 500 composite samples of fish filets collected across the United States from 2013 to 2015 under the U.S. EPA's monitoring programs, the National Rivers and Streams Assessment and the Great Lakes Human Health Fish Fillet Tissue Study. The two datasets indicate that an individual's consumption of freshwater fish is potentially a significant source of exposure to perfluorinated compounds. The median level of total targeted PFAS in fish filets from rivers and streams across the United States was 9,500 ng/kg, with a median level of 11,800 ng/kg in the Great Lakes. PFOS was the largest contributor to total PFAS levels, averaging 74% of the total. The median levels of total detected PFAS in freshwater fish across the United States were 278 times higher than levels in commercially relevant fish tested by the U.S. Food and Drug Administration in 2019–2022. Exposure assessment suggests that a single serving of freshwater fish per year with the median level of PFAS as detected by the U.S. EPA monitoring programs translates into a significant increase of PFOS levels in blood serum. The exposure to chemical pollutants in freshwater fish across the United States is a case of environmental injustice that especially affects communities that depend on fishing for sustenance and for traditional cultural practices. Identifying and reducing sources of PFAS exposure is an urgent public health priority.

1. Introduction

Per- and polyfluoroalkyl substances (PFAS), previously referred to as “perfluorinated compounds”, are a class of manufactured chemicals that have been detected in nearly all sampling of geographic locations and environmental matrices worldwide, including sites that had no nearby manufacture or use of PFAS (Cousins et al., 2022; Evich et al., 2022). PFAS are used in hundreds of industrial and consumer products including food packaging and waterproof/stain resistant fabrics (Gluge et al., 2020). Their strong carbon-fluorine bonds provide both hydrophobic and oleophobic properties, which make these chemicals extremely persistent in the environment. The class of PFAS includes tens of thousands of potential environmental contaminants (Wang et al., 2021) including over one thousand chemicals previously or currently approved for use in the U.S. (U.S. EPA, 2021).

Identifying and eliminating sources of human exposure to PFAS has

become a priority for public health (National Academies of Sciences, 2022; U.S. EPA, 2022). PFAS exposure from contaminated drinking water is widespread in the United States (Andrews, 2018) and likely world-wide, particularly for people living near areas where soil and groundwater are highly contaminated with PFAS (Sunderland et al., 2019; U.S. EPA, 2022). Further, dietary intake is considered a major source of exposure to these contaminants. The European Food Safety Authority (EFSA) states that diet is the primary source of PFAS exposure for most people, with fish, meat, fruit, and eggs as significant contributors (European Food Safety Authority, 2020). Finally, inhalation of dust contaminated with PFAS from everyday consumer products, as well as direct and indirect contact with PFAS-containing products, also contributes to overall PFAS exposure (Gustafsson, 2022).

Tens of thousands of manufacturing facilities, municipal landfills and wastewater treatment plants, airports, and sites where PFAS-containing fire-fighting foams (aqueous film-forming foam or AFFF) have been used are potential sources of PFAS discharges into surface water (Andrews

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Abbreviations

AFFF	aqueous film-forming foam
BMDL5	Benchmark Dose lower limit for the 95% confidence interval for a 5% response
GenX	hexafluoropropylene oxide dimer acid and its ammonium salt
NHANES	National Health and Nutrition Examination Survey
ppt	parts per trillion
PFBS	perfluorobutane sulfonate, perfluorobutane sulfonic acid
PFDA	perfluorodecanoate, perfluorodecanoic acid
PFDoA	perfluorododecanoate, perfluorododecanoic acid
PFUnDA	perfluoroundecanoate, perfluoroundecanoic acid
PFOS	perfluorooctane sulfonate, perfluorooctane sulfonic acid
PFOA	perfluorooctanoate, perfluorooctanoic acid, perfluorooctane carboxylate
PFNA	perfluorononanoate, perfluorononanoic acid
U.S. EPA	United States Environmental Protection Agency
U.S. FDA	United States Food and Drug Administration

et al., 2021; Hu et al., 2016; Zhang et al., 2016). This contamination of water has spread PFAS to soil (Lindstrom et al., 2011), crops (Blaine et al., 2014), wildlife including fish (Giesy and Kannan, 2001; Vendl et al., 2021), and humans (Centers for Disease Control and Prevention U.S., 2022b).

Analysis of environmental and biological samples such as human serum is typically limited to a specific group of PFAS based on currently available methods (Centers for Disease Control and Prevention U.S., 2022b; Evich et al., 2022). For PFAS measured at concentrations already found in the general population, exposure may suppress the immune system (Grandjean and Clapp, 2015; NTP, 2016). Additionally, exposure to PFAS, with most studies on PFOA and PFOS, has been associated with many health harms, including an increased risk of cancer (Barry et al., 2013; Bartell and Vieira, 2021; Temkin et al., 2020), high cholesterol (Nelson et al., 2010), thyroid disease (Melzer et al., 2010), and reproductive and developmental harms (Fenton et al., 2021).

The U.S. EPA's interim updated lifetime drinking water health advisories for PFOA, at 0.004 ppt, and PFOS, at 0.020 ppt, are calculated from human serum levels associated with harm to the immune system, specifically reduced antibody response to vaccination (Grandjean, 2018) with an additional 10-fold safety factor to account for individual variation between people (U.S. EPA, 2022). The drinking water values are based on the 90th percentile water consumption rate and a default relative source contribution that attributes 80% of exposure from non-drinking water sources. The interim updated health advisory is based on a reference dose or tolerable daily intake of 7.9×10^{-9} mg/kg-bw/day for PFOS (U.S. EPA, 2022).

In human studies, fish consumption has been observed as an indicator of PFAS, specifically PFOS, exposure (von Stackelberg et al., 2017). In 1979, sampling by 3M chemical company near their manufacturing facility along the Tennessee River documented levels of more than 16,000,000 ng/kg of total organic fluoride in channel catfish (3m, 1979). Recent monitoring in the United States indicates that sportfish caught from the Great Lakes or fish caught near PFAS-contaminated areas have much higher PFAS than commercially-sold fish (Ruffle et al., 2020; Young et al., 2022). A biomonitoring study of anglers near Onondaga Lake in central New York state (northeastern United States) found the most frequent consumers of freshwater fish had median levels of PFOS and perfluorodecanoic acid (PFDA) in their blood at 9.5 and 26.9 times the general U.S. median (Wattigney et al., 2022). In the Great Lakes region in the U.S., licensed anglers and, specifically, anglers from the

Burmese immigrant community had median PFOS levels that respectively ranged two and six times the U.S. population average (Liu et al., 2022).

In Europe, published reports indicate that consuming freshwater fish just a few times a year was found to be an important annual source of PFAS exposure (Augustsson et al., 2021; Richterova et al., 2022). A study in Sweden also found that freshwater fish from contaminated areas contributed significantly to dietary PFOS exposure (Berger et al., 2009). Another study of nearly 500 anglers in France found higher serum levels of PFOS in the 75th and 95th percentiles compared to the general population (Denys et al., 2014). Levels in the angler population were similar to levels in the general population with the similarly attributed to low fish consumption rates among anglers (Denys et al., 2014).

The U.S. EPA recognizes that eating locally caught freshwater fish is a significant source of exposure to PFOS, yet there are no current federal policies or regulations providing guidance on fish consumption specific to PFOS or other PFAS. There are an estimated 17.6 million high-frequency consumers of fish in the U.S. over age 18, with the highest mean consumption attributed to the Black, non-Hispanic population (von Stackelberg et al., 2017). For most populations of individuals who catch fish for dietary consumption, there is a lack of consistent national guidance with respect to how much fish can be safely eaten.

A closer evaluation of PFAS as a source of dietary exposure from fish, specifically freshwater fish, is urgently needed. Towards this goal, the present study provides the first analysis to estimate the relationship between fish consumption and PFAS in serum in the U.S. population and to compare PFAS in freshwater fish with commercial seafood samples in the U.S.

2. Methods

2.1. Datasets

Multiple datasets were aggregated and analyzed to evaluate the concentrations of PFAS in locally caught freshwater fish and commercially caught fish sold in grocery stores and supermarkets. The datasets on freshwater fish were generated by the U.S. EPA. For this study, we downloaded the datasets directly from the program-associated websites; the National Rivers and Streams Assessment (NRSA), available at <https://www.epa.gov/national-aquatic-resource-surveys/nrsa> and the National Coastal Condition Assessment's Great Lakes Human Health Fish Tissue Studies available at <https://www.epa.gov/fish-tech/national-coastal-condition-assessment-great-lakes-human-health-fish-tissue-studies>. Testing data on retail fish from multiple U.S. FDA datasets within the Total Diet Study sampling from 2019 to 2021 and a specific sampling of seafood conducted in 2022, were compared to the U.S. EPA's results on freshwater fish testing. The National Health and Nutrition Examination Survey (NHANES) data from 2017 to 2018 was used to calculate serum concentrations of PFAS in the general U.S. population.

2.1.1. National Rivers and Streams Assessment and the National Coastal Conditions Assessment's Great Lakes Human Health Fish Fillet Tissue Study

The National Rivers and Streams Assessment, is a collaborative survey of perennial rivers and streams throughout the conterminous United States (U.S. Environmental Protection Agency, 2020). Every 5 years, the U.S. EPA works with state, tribal, and federal partners to collect biological, chemical, and physical indicators of stream quality, including samples of fish filets. The 2013–2014 dataset includes 353 composited results from fish filets from sites across all 48 continental U.S. states. All PFAS concentrations are reported for wet weight of fish tissue. Samples were tested for 13 different PFAS with detection limits varying between 43 and 110 ng/kg, with 77 ng/kg for PFOS, as detailed in Table S1.

As part of the U.S. EPA National Coastal Conditions Assessment Studies, samples of fish filets from the nearshore freshwater

environment of the Great Lakes are tested for PFAS. In the present study, we evaluated the 2015 Great Lakes Human Health Fish Fillet Tissue Study (U.S. Environmental Protection Agency, 2021). Approximately 30 sampling sites were selected per lake, 152 sites in total. The criteria for collecting fish were the same as for the National Rivers and Streams Assessment, with composites containing 1 to 10 fish each. The PFAS concentrations were also reported for wet weight of fish tissue. The results included the same 13 PFAS assessed in the National Rivers and Streams Assessment, but with higher detection limits that varied between 90 and 630 ng/kg, with 520 ng/kg for PFOS, as detailed in Table S1.

Across both U.S. EPA sampling programs, a total of 501 composites, aggregated samples of the same fish species at the same location, corresponding to 1968 individual fish, were analyzed for the 13 PFAS compounds. Composited samples of fish are henceforth referred to simply as fish samples. Fish samples include 44 different species, with channel catfish (*Ictalurus punctatus*), smallmouth bass (*Micropterus dolomieu*), largemouth bass (*Micropterus salmoides*), yellow perch (*Perca flavescens*), and walleye (*Sander vitreus*) as the most frequently measured species. All PFAS results with values below the limit of detection were treated as zero.

2.1.2. Total Diet Study

To test for PFAS in the general food supply, the Federal Food and Drug Administration (U.S. FDA) has included this analysis within the Total Diet Study since 2019. Samples are collected either regionally or nationally from grocery stores. The U.S. FDA's previous testing has monitored between 16 and 20 different PFAS. All PFAS included the U.S. EPA's testing, except perfluorooctane sulfonamide (PFOSA), were included in the U.S. FDA's results.

In 2022, the U.S. FDA published results from testing a larger sample of retail seafood samples (U.S. Food and Drug Administration, 2022; Young et al., 2022). Eighty-one samples, including approximately 10 samples each of clams, crab, shrimp, cod, tilapia, salmon, pollock, and tuna, were evaluated for 20 different PFAS. In the present study, all of the U.S. FDA's results were combined based on their broad category of fish type (e.g. tuna, cod, catfish, etc.) to provide a reference for levels of PFAS measured in commercially sourced seafood in the U.S. A comparison of the detection limits within the U.S. EPA National Rivers and Streams Assessment, the U.S. EPA Great Lakes Human Health Fish Fillet Tissue Study, and the U.S. FDA's surveys is included in Supporting Information Table S11.

2.1.3. State fish advisories in the United States

To compile U.S. state fish advisories, we first utilized the U.S. EPA web resource (available at <https://fishadvisoryonline.epa.gov/Contacts.aspx>) that lists state, tribe, and territory fish advisory websites. States with at least one official fish consumption advisory based on PFAS concentrations measured in fish tissue were identified. Additionally, we required the advisory to be presented alongside other formal fish consumption advisories for the state. Along with identifying state-level consumption advisories, we reviewed the methodologies used in different advisories to determine if a state calculated a health-based exposure threshold for PFAS in fish. When identified, these threshold values for PFAS concentrations in fish were recorded, along with the reference dose used to calculate the values. Supporting Information Table S12 provides a table of U.S. state fish consumption advisories for PFOS.

2.2. Characterization of exposure

To model PFOS in serum levels after consumption of PFOS-contaminated fish we assumed: (1) steady-state fish consumption where consumption is equivalent to elimination; (2) consumption of any freshwater fish results in additional exposure above baseline, a median of PFOS in the U.S. population from NHANES; (3) no PFOS is removed

through cooking; and (4) one hundred percent of PFOS in fish tissue is absorbed. To calculate dose in nanograms per kilogram of body weight (ng/kg bw) we incorporated additional parameters commonly used by states when calculating fish consumption advisory thresholds: an average body weight of 70 kg and one fish meal constitutes 227 g of fish according to food portion recommendations established by the U.S. FDA.

Using the NHANES median value as a baseline allowed for calculating potential serum levels for those who consume locally caught fish. In France and in the U.S., locally caught freshwater fish consumption is uncommon for a majority of the population (Denys et al., 2014; U.S. Environmental Protection Agency, 2014). NHANES is a representative study of the U.S. population; the sample of participants from the 2017–2018 data contained 1929 individuals ages 12 and older. All sampled individuals had detectable concentrations of PFOS, which is reported as the sum of linear and branched PFOS isomers.

The potential impact of increasing PFAS in serum levels through consuming fish for the general population was calculated for various consumption rates: one meal per week, one meal per month, one meal per three months, and one meal per year. These consumption rates were chosen to reflect fish consumption advisory recommendations as well as to provide a clear differentiation on the variation of increasing PFAS in serum with different fish-eating habits.

Impacts on serum concentration are calculated using a first order, one-compartment pharmacokinetic model dependent on dose, clearance factor, and volume of distribution (Thompson et al., 2010; U.S. EPA, 2016; U.S. EPA, 2022). At steady state the PFOS concentration from fish intake will equal the elimination from the body (U.S. EPA, 2016). In equation (1) the PFOS clearance factor of 8.1×10^{-5} L/kg/day is calculated using a half-life of 5.4 years and a volume of distribution of 0.23 L/kg as published by the U.S. EPA and the New Jersey Drinking Water Quality Institute (New Jersey Drinking Water Quality Institute, Health Effects Subcommittee, 2018; U.S. EPA, 2016).

$$\text{clearance factor} = Vd * \frac{\ln 2}{t_{1/2}} = 8.1 \times 10^{-5} \text{ L/kg/day} \quad (1)$$

where:

Vd = volume of distribution = 0.23 L/kg (relates dose to plasma concentration).

$T_{1/2}$ = half-life = 1971 days (5.4 years).

The increase in serum concentration is then calculated, as shown in equation (2), as the daily dose divided by the daily PFOS clearance factor. Consistent with a first order pharmacokinetic model the elimination of PFOS is proportional to the concentration.

$$\text{increase in serum level} = \text{PFOS dose} / \text{clearance factor} \quad (2)$$

3. Results

3.1. Analysis of the U.S. EPA National Rivers and Streams Assessment and the Great Lakes Human Health Fish Fillet Tissue Study

Fish with detectable levels of PFAS were found in all 48 continental U.S. states. Of the 349 samples analyzed in the 2013–2014 National Rivers and Streams Assessment, just one sample contained no detectable PFAS. All 152 fish samples tested within the 2015 Great Lakes Human Health Fish Fillet Tissue Study had detectable PFAS. The total PFAS concentration for each sample was calculated as the sum of individual PFAS detected above the limit of detection. The geographic distribution of composite samples can be seen in Fig. 1, with total PFAS concentration in tissue displayed for four concentration-based groups. Most fish samples had concentrations of total PFAS between 1000–10,000 ng/kg (44%) and 10,000–50,000 ng/kg (45%). Within the National Rivers and Streams Assessment, the U.S. EPA categorizes streams as urban (91 samples) or non-urban (258 samples). Median levels of PFOS and total PFAS were both 2.7 times higher in the urban locations compared to the

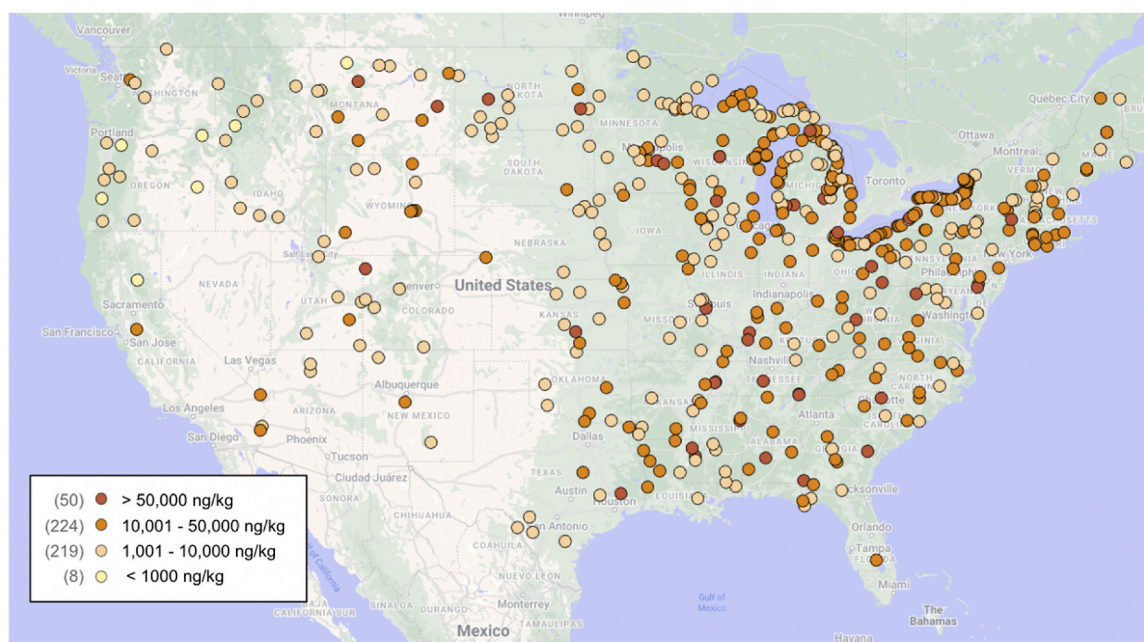


Fig. 1. Total quantifiable PFAS in freshwater fish in the continental United States (2013–2015). Dots depict sample locations from the National Rivers and Streams Assessment and the Great Lakes Human Health Fish Fillet Tissue Study. The dots are divided into four color-coded groups based on the composite sample's concentration of total PFAS. There are 349 sampling locations from the National Rivers and Streams Assessment and 152 sampling locations from the Great Lakes Human Health Fish Fillet Tissue Study, for a total of 501 sampling locations. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

non-urban locations. Average PFOS and total PFAS concentrations were 1.5 and 1.6 times higher in urban locations (Wathan, 2022).

Across both U.S. EPA's datasets, the lowest total PFAS was 425 ng/kg and the highest was 286,767 ng/kg. The mean total PFAS was 20,870 ng/kg and the median was 11,880 ng/kg. A summary table of the individual U.S. fish sampling results and the authors calculations are provided in Supporting Information Table SI3. Of the 13 PFAS measured, all were detected in at least one fish sample, with PFHpA detected the least often (one detection among 501 fish samples). As shown in Fig. 2, PFOS was the major compound detected, with perfluoroundecanoic acid (PFUnDA), PFDA, perfluorododecanoic acid (PFDoA) and perfluorononanoic acid (PFNA) the next largest

contributors, on average. Each of these five PFAS were detected in most samples.

It is notable that fish sampling from the Great Lakes Human Health Fish Fillet Tissue Study found overall higher levels of PFOS and total sum of detected perfluorinated compounds compared to the National Rivers and Streams Assessment, both in terms of median concentrations and interquartile ranges (Table 1). These results highlight that PFAS contamination may be of particular concern for the Great Lakes ecosystem and the health of people who depend on fishing on the Great Lakes for sustenance and cultural practices.

The overall medians for both PFOS and PFAS were higher for the EPA's Great Lakes data compared to the EPA's national stream data, as

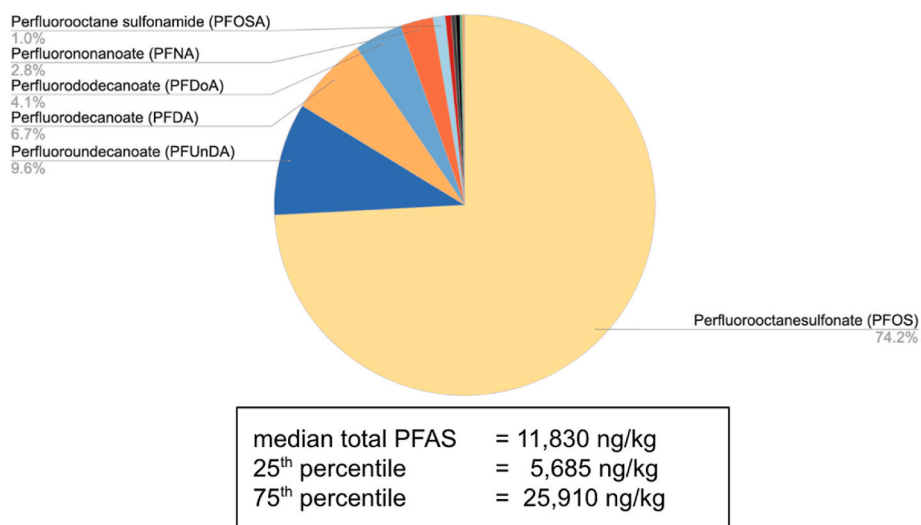


Fig. 2. Average individual PFAS contribution to total PFAS across all fish samples with detections (n = 500). The remaining 1.6% was comprised of Perfluorohexanoate (PFHxA), Perfluorobutanoate (PFBA), Perfluorohexane sulfonate (PFHxS), Perfluoropentanoate (PFPeA), Perfluorooctanoate (PFOA), Perfluorobutane sulfonate (PFBS), Perfluoroheptanoate (PFHpA) in descending order of average contribution to total PFAS.

Table 1

Summary of U.S. EPA freshwater fish sampling from the National Rivers and Streams Assessment and the Great Lakes Human Health Fish Fillet Tissue Study.

Testing program	Sampling year (s)	Number of fish samples	Median PFOS (ng/kg)	Median total PFAS (ng/kg)	25-75th percentile total PFAS (ng/kg)
U.S. EPA National Rivers and Streams Assessment	2013–2015	349	6,600	9,510	5,034–24,844
U.S. EPA Great Lakes Human Health Fish Fillet Tissue Study	2015	152	12,350	17,765	8,478–27,360

shown in Table 1. Further information on detection limits for individual PFAS in these two U.S. EPA testing programs is included in Supporting Information Table S11. The most commonly sampled fish and freshwater fish species frequently consumed in the United States across both of U.S. EPA's datasets are shown in Fig. 3. The ten species shown in Fig. 3 represent 286 samples or 57% of the total. For the three most sampled species, median and interquartile range values for total PFAS are: channel catfish median total PFAS of 8,575 ng/kg (5,447–17,628 ng/kg), smallmouth bass 18,780 ng/kg (7,763–28,227 ng/kg) and largemouth bass 21,460 ng/kg (9,397–41,219 ng/kg).

3.2. Modeled contribution of PFOS from dietary fish consumption to total serum levels

The estimated increases of PFOS in serum based on the contribution of fish meals at different frequencies were calculated (Fig. 4). These calculations are based on the median PFOS levels in fish tissue documented in the National Rivers and Streams Assessment and the Great Lakes Human Health Fish Fillet Tissue Study.

From the 2017–2018 NHANES dataset the median PFOS level was 4.35 ng/mL and the 95th percentile serum concentration was 14.6 ng/mL (Centers for Disease Control and Prevention U.S., 2022b). A serving of fish with median PFOS levels was calculated to increase serum levels 0.92 ng/mL if consumed once a year, 3.69 ng/mL if consumed four times a year, 11.07 ng/mL if consumed monthly, and 47.96 ng/mL if consumed weekly. For a person with a median PFOS serum level, our model indicates that consuming freshwater fish 12 times per year would

more than triple PFOS serum levels and result in exposure similar to the 95th percentile in the population. For those more reliant on freshwater fish consumption for sustenance, the model shows that average consumption of one meal per week results in serum levels over 50 ng/mL. Fish from waterbodies impacted by PFOS would likely lead to significantly higher serum levels.

With PFOS in serum levels above public health goal values, comparing contributions from different exposure routes is necessary to prioritize actions for individuals, policy makers, and regulators. To relate PFOS exposure from drinking water to contaminated fish we have calculated equivalent oral doses as shown in Table 2. We calculated the equivalent PFOS dose in one month of drinking water to five fish tissue concentrations: the average from U.S. FDA's data, the median from U.S. EPA's data, the 90th percentile from U.S. EPA's data, an intermediate value between the U.S. FDA's testing data, and the U.S. EPA's human health fish tissue benchmark from 2020.

We calculated equivalent drinking water levels according to the EPA's interim drinking water health advisory value for PFOS, which assumes that 80% of exposure is coming from non-drinking water sources. Drinking water intake was assumed to be 44 ounces a day, the mean value measured during 2015–2018 in the U.S. (Centers for Disease Control and Prevention U.S., 2022a, Centers for Disease Control and Prevention U.S., 2022b). The mean PFOS concentration in fish sampled by the U.S. FDA was 20 ng/kg, equivalent to water with 0.1 ppt of PFOS ingested for a month. A serving of fish at this concentration would exceed the U.S. EPA's interim health advisory value of 0.02 ppt for PFOS in drinking water. For persons consuming freshwater fish with PFOS

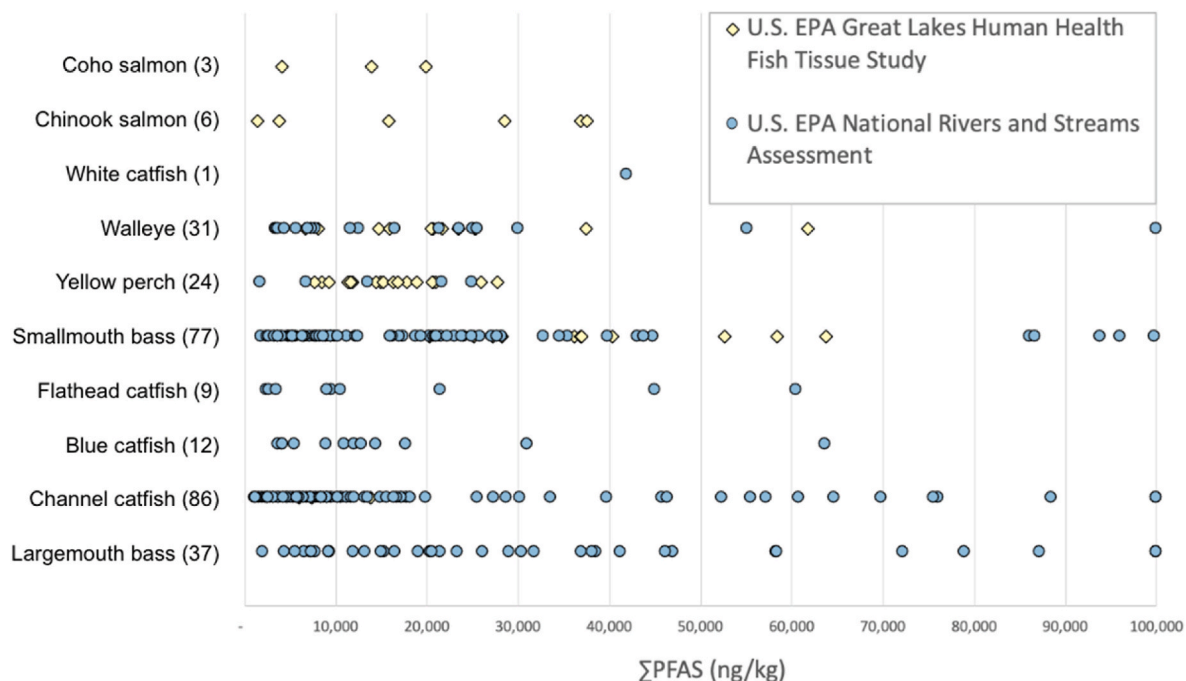


Fig. 3. Sum of PFAS for commonly sampled fish species from the U.S. EPA National Rivers and Streams Assessment and the U.S. EPA Great Lakes Human Health Fish Fillet Tissue Study. The five most sampled freshwater fish species were included along with all catfish and salmon. Five samples from the National Rivers and Streams Assessment were greater than 100,000 ng/kg (112,488 ng/kg, 145,250 ng/kg, 146,130 ng/kg, 192,030 ng/kg, and 286,767 ng/kg) and rounded down to 100,000 ng/kg to show the variation in lower concentration samples.

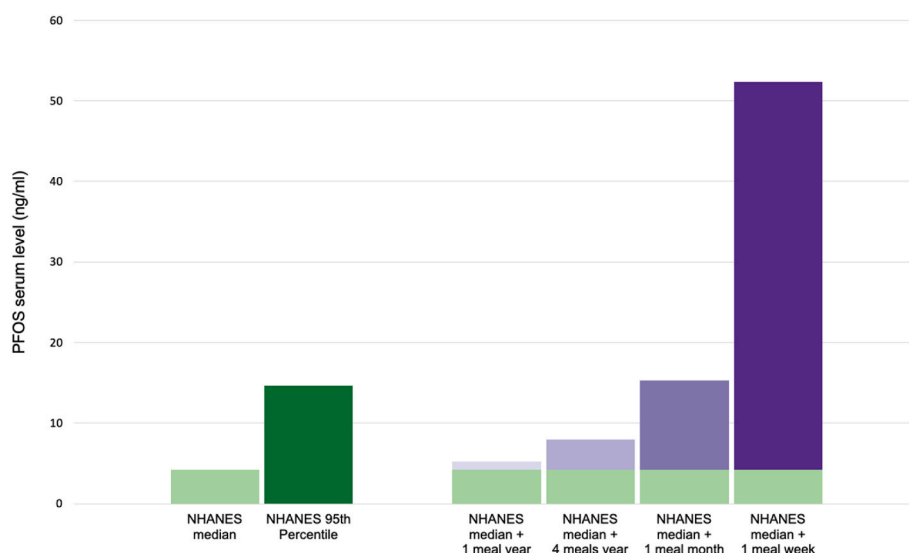


Fig. 4. The right-side panel shows the modeled average increase of PFOS in serum based on different freshwater fish consumption rates using a PFOS level of 8,410 ng/kg (median of 501 samples) in fish. PFOS exposure from fish is added to the NHANES median PFOS level. The left-side panel shows the mean and 95th percentile PFOS in serum from the 2017–2018 NHANES representative sample of PFOS in blood serum among the U.S. population.

Table 2

Concentrations of PFOS in fish expressed as an equivalent concentration of PFOS in one month's drinking water (assumed adult consumption of 39.6 L of water based on national survey data from CDC).

Eating one 8 ounce serving of fish at	20 ng/kg PFOS (average PFOS level in fish from FDA testing with non-detects set at 0 ng/kg)	is equivalent to consuming one month of drinking water at	0.1 ppt. (5.7 times the interim U.S. EPA health advisory)
	1000 ng/kg PFOS (Concentration between the U.S. FDA results and the EPA results)		6 ppt. (290 times the interim U.S. EPA health advisory)
	8410 ng/kg PFOS (Median PFOS level in freshwater fish in U.S. EPA testing from 2013 to 2015)		48 ppt. (2400 times the interim U.S. EPA health advisory)
	41,400 ng/kg PFOS (90th percentile PFOS level in freshwater fish from U.S. EPA testing from 2013 to 2015)		237 ppt. (11,854 times the interim U.S. EPA health advisory)
	68,000 ng/kg PFOS (EPA human health fish tissue benchmark from 2020)		389 ppt. (19,470 times the interim U.S. EPA health advisory)

contamination at the levels reported in this study, even occasional consumption of several fish meals a year would likely translate into PFOS exposure from fish significantly greater than exposure from drinking water.

4. Discussion

4.1. Comparison of U.S. EPA datasets with other published studies

4.1.1. International studies of PFAS in freshwater fish

Freshwater fish are impacted by PFAS contamination on a global scale, especially in industrialized regions and near pollution discharge sources, as documented in studies in the ten different countries compiled in Table 3. Overall median total PFAS and PFOS values for the U.S. EPA data were within the range of values observed in other countries. The

sampling campaigns reported by Roscales et al. in Spain, and Valsecchi et al. in Italy, France, and Switzerland reported mean and median PFOS values approximately thirty five percent lower than the U.S. EPA sampling analyzed here. The mean and median for U.S. EPA data were similar to data collected for South Korea's Asan Lake reported by Lee et al. (2020). Studies with reported mean and/or median freshwater fish PFOS levels are compared to the U.S. EPA data in Supporting Information Fig. S2.

4.1.2. Comparison of freshwater and marine fish

The results presented within this manuscript are specific to freshwater caught fish in the U.S. and do not provide insight into potential exposure to PFAS from fish caught in marine environments. According to the U.S. National Oceanic and Atmospheric Administration, marine anglers in the U.S. took 187 million fishing trips in 2019 and harvested 350 million pounds of fish, or just under 5% of American's seafood consumption (National Marine Fisheries Service, 2021).

Sampling of marine fish from the Charleston Harbor and tributaries in South Carolina along with San Francisco Bay indicate that in some locations marine fish may have levels of PFAS similar to those detected in freshwater fish analyzed in our study (Buzby et al., 2021; Fair et al., 2019). International sampling of fish has reported significantly lower levels of PFAS in farmed fish compared to marine fish (Zafeiraki et al., 2019), and higher levels in the vicinity of military bases (Langberg et al., 2022). In a large study of hundreds of fish composite samples in French rivers and metropolitan coastal areas, the mean sum PFAS levels were 18 times lower in marine fish compared to freshwater fish (Yamada et al., 2014). Considering PFAS contamination of marine fish and the exposure to recreational marine anglers, providing fish consumption guidance for marine fish should be advanced alongside guidance for freshwater fish consumption.

4.1.3. Commercial fish sampling by the U.S. FDA

The total PFAS concentrations in the U.S. EPA's datasets were significantly higher compared to commercial fish testing results from the U.S. FDA testing (Fig. 5). A summary of the U.S. FDA finfish results is provided in Supporting Information Table S14 and Table S15. The U.S. EPA's study assessed PFAS in freshwater fish across the U.S. and in fish within the Great Lakes, while the U.S. FDA's testing was focused on the retail seafood purchased by consumers in grocery stores. The U.S. FDA included the most commonly consumed fish and seafood in the U.S. in its

Table 3

International studies published in 2019–2022 measuring PFAS in freshwater fish.

Country (reference)	Sampling years	Fish species	PFAS range, mean, (median), ng/kg wet weight
Vietnam (Hoa et al., 2022)	2016	bighead carp (<i>Hypophthalmichthys nobilis</i>), common carp (<i>Cyprinus carpio</i>), rohu (<i>Labeo rohita</i>), and tilapia (<i>Oreochromis niloticus</i>)	Total PFAS: 510–2,600, (1000)
Norway (Langberg et al., 2022)	2009–2019	arctic Char (<i>Salvelinus alpinus</i>), bream (<i>Abramis brama</i>), brown trout (<i>Salmo trutta</i>), European smelt (<i>Osmerus eperlanus</i>), perch (<i>Perca fluviatilis</i>), pike (<i>Esox lucius</i>), roach (<i>Rutilus rutilus</i>), european chub (<i>Squalius cephalus</i>), vendace (<i>Coregonus albula</i>), whitefish (<i>Coregonus lavaretus</i>), and zander (<i>Sander lucioperca</i>)	Range of mean concentration of the sum of seven PFAS in individual species: 1,200–271,000
Canada (Munoz et al., 2022)	2019	sand shiner/mimic shiner (<i>Notropis stramineus</i>), Notropis volucellus, sicklefin redbone (<i>Moxostoma</i> spp.), bluntnose minnow (<i>Pimephales notatus</i>), emerald shiner (<i>Notropis atherinoides</i>), white sucker (<i>Catostomus commersoni</i>), gold shiner (<i>Notemigonus crysoleucas</i>), rock bass (<i>Ambloplites rupestris</i>), pumpkinseed (<i>Lepomis gibbosus</i>), yellow perch (<i>Perca flavescens</i>), northern pike (<i>Esox lucius</i>), and smallmouth bass (<i>Micropterus dolomieu</i>).	PFOS: 12,000–140,000 Total PFAS: 13,300–179,800
Spain (Roscales et al., 2022)	2018	Iberian gudgeon (<i>Gobio lozanoi</i>), Iberian barbel (<i>Luciobarbus bocagei</i>), zander (<i>Sander lucioperca</i>) common bleak (<i>Alburnus</i>), pumpkinseed (<i>Lepomis gibbosus</i>), river trout (<i>Salmo trutta fario</i>), northern pike (<i>Esox lucius</i>), European eel (<i>Anguilla</i>), Ebro nase (<i>Parachondrostoma miegii</i>), River trout (<i>Salmo trutta fario</i>), gold fish (<i>Carassius auratus</i>), black bullhead catfish (<i>Ameiurus melas</i>), common carp (<i>Cyprinus carpio</i>), eastern mosquitofish (<i>Gambusia holbrooki</i>), common chub (<i>Squalius cephalus</i>), common rudd (<i>Scardinius erythrophthalmus</i>).	PFOS: LOQ-55,000, 10,000, (4700) Total PFAS: 610–68,000, 15,000 (8700)
Germany (Rüdel et al., 2022)	2016, 2017	chub (<i>Squalius cephalus</i>), roach (<i>Rutilus rutilus</i>), bream (<i>Abramis</i>	PFOS: 545–16,000, 5030 C8–C14:

Table 3 (continued)

Country (reference)	Sampling years	Fish species	PFAS range, mean, (median), ng/kg wet weight
South Korea (Lee et al., 2020)	2017–2018	<i>brama</i>), perch (<i>Perca fluviatilis</i>), and whitefish (<i>Coregonus renke</i>) crucian carp (<i>Carassius carassius</i>), skygager (<i>Notropis uranoscopus</i>), bluegill (<i>Lepomis macrochirus</i>), bass (<i>Micropterus salmoides</i>), barbel steed (<i>Hemibarbus labeo</i>), and common carp (<i>Cyprinus carpio</i>), shad (<i>Alosa agone</i>), European whitefish (<i>Coregonus lavaretus</i>), burbot (<i>Lota</i>), rainbow trout (<i>Oncorhynchus mykiss</i>), European perch (<i>Perca fluviatilis</i>), roach (<i>Rutilus rutilus</i>), brown trout (<i>Salmo trutta</i>), Arctic char (<i>Salvelinus alpinus</i>)	14,938–29,626, 9453 PFOS: ND-119,000, 18,600, (13,900) Total PFAS: ND-197,000, 30,700, (22,700)
Italy, France, Switzerland (Valsecchi et al., 2021)	2015–2019	Ten edible fresh water fish species (n = 186 individuals) including crucian carp (<i>Carassius auratus</i>), catfish (<i>Silurus asotus</i>), common carp (<i>Cyprinus carpio</i>), northern snakehead (<i>Channa argus</i>), skygager (<i>Erythroculter erythropterus</i>), Korea piscivorous chub (<i>Opsariichthys uncirostris</i>), barbel steed (<i>Hemibarbus labeo</i>), blue gill (<i>Lepomis macrochirus</i>), mandarin fish (<i>Siniperca scherzeri</i>), bass (<i>Micropterus salmoides</i>)	PFOS: 200–50,500, 9,800, (6000) Total PFAS: 350–60,400, 13,000 (8500)
South Korea (Hung et al., 2019)	2013, 2014	European perch (<i>Perca fluviatilis</i>)	PFOS: <110–71,700, 5,150, (1140) Total PFAS: 220–129,000, 8,420, (2940)
Finland (Junttila et al., 2019)	2014–2016		PFOS: max 18,000, 3400 Total PFAS: 980–31,000

testing, such as frozen cod fillets and canned tuna (NOAA Fisheries, 2022) (Young et al., 2022). The U.S. FDA reported significantly lower mean and median concentrations of PFAS compared to the freshwater fish samples collected and analyzed by the U.S. EPA. Twenty-two commercial finfish samples tested by the U.S. FDA did not have any PFAS identified above the limit of reporting for that study. Among the finfish samples with detectable PFAS, total concentrations ranged from 20 to 1,748 ng/kg. The median PFOS level in finfish was below the limit of detection. To estimate potential impact of commercial fish consumption on PFOS blood serum levels we used 41 ng/kg or one half the highest limits of detection reported by U.S. FDA. Weekly consumption at this level would add 0.23 ng/mL or 5% to the general population median reported in NHANES 2017–2018 testing. Weekly commercial fish consumption would impact serum levels approximately half as much as a single freshwater fish serving per year, based on the U.S. EPA results as shown in Fig. 4.

Figure SI 2 provides a plot of the individual composite fish sample results in the U.S. EPA and U.S. FDA testing, including results for U.S. FDA clams, crabs and shrimp testing. In the sampled clams, the mean ΣPFAS of 10,273 ng/kg predominantly due to the presence of PFOA.

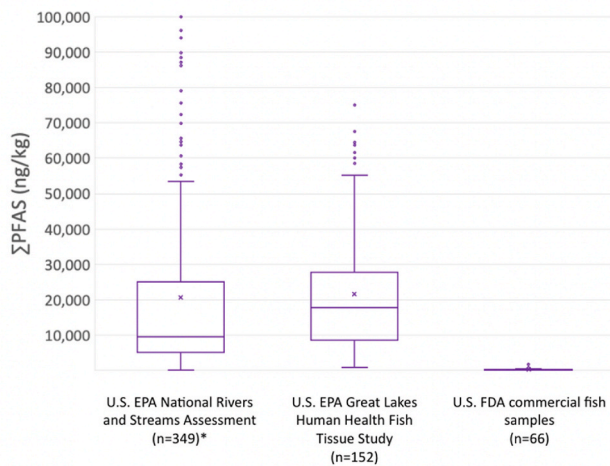


Fig. 5. Comparison of total PFAS concentrations in the U.S. EPA's freshwater fish studies data and the U.S. FDA's testing of commercially sold fish. The box represents the 25th–75th percentile of results, the line within the box is the median and the x represents the mean. Outlier points shown are more than 1.5 times the interquartile range above the 75th percentile. *Five samples with concentrations over 100,000 ng/kg not shown.

These PFOA results led to product recalls (U.S. FDA, 2022a; U.S. FDA, 2022b).

4.2. PFAS contamination of fish: an environmental injustice issue

Anglers, along with their families, often eat locally caught fish. For many communities across North America, including indigenous Tribal Nations, catching fish is an important way of life and cultural identity. Catching and consuming fish remains an essential social practice and source of economic sustenance for many communities across the U.S. (Aboii, 2021). Catching and eating fish is a sovereign right for the Tribal Nations and a cultural and traditional practice that must be honored and respected (Cantzler and Huynh, 2015). Further, for many communities and families that experience economic difficulties, eating locally caught fish can be an essential source of protein in their diet (Quimby et al., 2020).

Eating contaminated fish from local rivers and lakes can result in exposure to not only PFAS, but to other toxic environmental contaminants, such as mercury and polychlorinated biphenyls (PCBs). Many people who consume fish regularly from freshwater sources come from communities that have been marginalized by historical discrimination and mistreated by inequitable government policies (Cantzler and Huynh, 2015), making the presence of industrial pollutants in fish a social justice issue. In a study of two higher-fish consumption populations in New York State, licensed anglers and anglers from the Burmese immigrant community, both groups had greater levels of PFOS in serum compared to the general population, with the Burmese refugee and immigrant population having the greatest exposure (Liu et al., 2022). In the Burmese population, the four PFAS detected at the highest concentrations relative to the median in the general population were PFUnDA, PFDA, PFOS and PFNA (Liu et al., 2022). As shown in Fig. 2, these four PFAS contributed the most to tissue PFAS levels in fish.

While levels of PFAS in serum exceed the benchmark doses associated with adverse health impacts, reducing PFAS exposure should remain a public health priority. Federal and state efforts should focus on eliminating PFAS releases into the environment and identifying those who face the greatest risk of exposure to PFAS from fish consumption. Environmental restoration and stopping PFAS pollution so that fish can be safely consumed are urgently needed to ensure environmental justice and to protect the health of people and communities that rely on fish and

local ecosystems for material and cultural sustenance (Hoover, 2013).

4.3. Exposure assumptions and uncertainties

PFOS levels in fish, dietary intake, cooking and the modeled transfer of PFOS from consumed fish tissue to serum are sources of uncertainty in calculations of increased PFOS in serum concentrations from dietary exposure to PFOS in fish.

4.3.1. Variability in detected PFOS in fish

The results of nationwide sampling analyzed here show significant variability in both PFOS and total PFAS in freshwater fish. Correspondingly, serum levels will vary significantly based on the localized contamination (Hansen et al., 2016). However, frequent freshwater fish consumers are unlikely to be consuming fish from many different water bodies. The use of the median value was chosen to provide a conservative estimate of the impact on frequent fish consumers and not focus on highly contaminated areas.

The fish samples analyzed here were collected from 2013 to 2015 making many of the samples nearly 10 years old. Compared to data collected by the U.S. EPA in 2008–2009, median PFOS levels decreased by 30 percent in the present data set collected just 5 years later. With decreasing use of PFOS in commerce, it is possible that PFOS levels in fish have continued to decrease, and our modeled serum impacts are an overestimate of the current median level of exposure. Updating sampling results including the anticipated U.S. EPA 2018–2019 dataset from the National Rivers and Stream Assessment should provide more insight on trends in PFOS levels in freshwater fish. Increased sampling of ponds and lakes where water has a longer residence time may provide additional insights into PFAS contamination of locally caught fish that are consumed.

4.3.2. Dietary intake

Within the U.S. population there is significant variability with respect to dietary fish intake. The CDC has found that the general population consumes about 18 g/day of fish, with greater fish consumption among men and adults between 31 and 50 years old (Love et al., 2020). High fish consumption is considered eating one fish meal a week or more. This designation often includes anglers, individuals living along the coast or along lakes, immigrant communities coming from high fish consumption nations, and communities where fishing is a large part of the culture.

Based on the present analysis, the impact on serum from exposure to PFAS from dietary fish consumption may depend on how much one eats fish that are commercially sourced versus locally caught. High frequency fish consumers may source as much as 90% of their fish locally, while many individuals do not consume any locally caught fish (Burger, 2000; von Stackelberg et al., 2017). A recent analysis of seafood consumption amount adults in the U.S. within NHANES reported just 5% of fish consumed are locally caught (Love et al., 2020). Further research is necessary to provide a more detailed understanding of the patterns of public exposure to PFAS from fish and to determine potential differences between PFAS exposure from freshwater, coastal, and deep-sea caught fish.

4.3.3. Model uncertainty and comparison of modeled PFOS serum levels and measured values

While no direct measurements of PFOS absorption through the gastrointestinal tract have been conducted in humans (Agency for Toxic Substances and Disease Registry, 2021), there has been extensive study of serum half-life in response to oral exposure through contaminated drinking water (U.S. EPA, 2016).

PFOS is readily absorbed in the gastrointestinal tract after oral exposure (European Food Safety Authority, 2020) and our assessment assumes one hundred percent absorption. To support our assumption of one hundred percent PFOS absorption, a study in sheep showed that

animals excreted just six percent of PFOS after eating PFAS-contaminated corn feed for 21 days (Kowalczyk et al., 2012).

The European Food Safety Authority compared the one-compartment model and PBPK models to estimate early life serum levels and concluded that results provide similar predictions of PFOA serum concentrations (European Food Safety Authority, 2020). The models were not compared for PFOS. Variability in clearance-rate is not considered in our study, although it could lead to additional variation. A recent research paper measured large differences in PFOS half-life in individuals with a range of 2.2–6.2 years when considering the 5th to 95th percentiles (Li et al., 2018).

The calculations within the present study and those used by states to develop fish consumption advisories assume that cooking does not materially impact PFAS and that 100% of the PFAS measured in fillets will result in exposure and subsequently impact serum levels. This could potentially overestimate exposure, especially for fish cooked in water or oil that is discarded according to a recent review that found cooking seafood on average reduces PFAS by 29% (Vendl et al., 2022).

The estimated increases in serum from fish consumption are generally consistent with serum levels of PFOS observed in other studies of freshwater fish consumers. One meal per month was calculated to increase PFOS in serum by 11.1 ng/mL, resulting in a total PFOS concentration of 15.3 ng/mL. This calculated value of PFOS in serum for a person consuming one meal of freshwater fish per month is comparable to the reported NHANES 95th percentile value of 14.6 ng/mL. The calculated value is also similar to concentrations in serum found in studies that measured PFOS in anglers and other high consumption populations who ate approximately 1 meal/month of freshwater fish (Christensen et al., 2016; Hansen et al., 2016; Holzer et al., 2011; Liu et al., 2022). A study in western New York state reported that the 90th percentile serum PFOS concentrations in 397 licensed anglers was 35.4 ng/mL; the same study also looked at PFOS in 199 anglers of Burmese origin, the group for whom 90th percentile concentration of PFOS was 95.7 ng/mL in serum (Liu et al., 2022). These body burden levels of PFOS are higher than what we calculated here for persons consuming fish once-a-week. In individuals who eat freshwater fish less frequently, approximate one meal a year, two studies found higher PFOS in serum than our estimate (Hansen et al., 2016; Holzer et al., 2011).

The U.S. EPA interim updated drinking water health advisory values are based on small changes to PFOS serum levels relative to current exposure levels. The U.S. EPA used reference serum values of 0.017 ng/mL for PFOA and 0.054 ng/mL for PFOS that were calculated from a BMDL5 value with 10-fold safety factor (U.S. EPA, 2022). This serum concentration, or point of departure, used to calculate a drinking water health advisory is significantly below the median levels of PFOA or PFOS in the general U.S. population measured in 2017–2018 (Centers for Disease Control and Prevention U.S., 2022b). Survey data from the 2017–2018 NHANES dataset show a median level of 1.42 ng/mL for PFOA and a median of 4.25 ng/mL for PFOS in serum. The median serum levels from this NHANES data exceeds the new U.S. EPA health advisory associated serum level by a factor of 84 for PFOA and by a factor of 79 for PFOS. With general population exposure above the serum levels associated with health impact, any potential source of exposure that increases serum levels is of particular concern (New Jersey Drinking Water Quality Institute, Health Effects Subcommittee, 2018).

4.4. Fish advisories published by different states in the U.S.

A fish consumption advisory can inform anglers of the risk of consuming a certain species of fish that may have chemical contaminants at concentrations harmful to human health. At the U.S. state level, these advisories are often specific to a single body of water, species of fish, and chemical of concern. We identified 14 out of 50 states that have issued a fish consumption advisory specific to PFAS in their most recent advisory reports for contaminants in fish, shown in Table SI 2. A national food exposure guideline does not exist for PFAS; however, many states

use the U.S. EPA's former 2016 reference dose for PFOA and PFOS of 2×10^{-5} mg/kg-bw/day as a basis for an advisory. However, the U.S. EPA, 2022 updated interim lifetime health advisory is based on a reference dose that is three orders of magnitude lower at 7.9×10^{-9} mg/kg-bw/day. If fish advisories were updated to reflect this interim health advisory, nearly all freshwater fish collected by the U.S. EPA from 2013 to 2015 would be considered unsafe to eat.

The lack of guidance across the country, with just 14 of 50 states issuing specific guidance, is likely contributing to excess exposure to PFAS for anglers and consumers of locally caught fish. Even a single serving of fish per year, at the median levels of PFOS observed in the National Rivers and Streams Assessment and Great Lakes surveys, would lead to a measurable increase in blood serum levels. PFOS is not the only PFAS in fish, and correspondingly exposure to other compounds also likely occurs.

Some chemical contaminants in fish have a national standard and states base their fish consumption guidelines on that value. This analysis indicates that there has likely been insufficient attention and insufficient public guidance on freshwater fish consumption. A federal consumption advisory would enable uniform PFAS fish exposure guidance from states and more importantly to anglers and their families.

4.5. Future research needs

Significant gaps remain in understanding the contribution of different exposure routes to blood serum levels, and specifically there are limited data on PFAS levels in food and locally caught fish. The freshwater fish samples collected by the U.S. EPA were primarily caught from 2013 to 2015. The National Rivers and Streams Assessment collected another round of fish samples in 2018–2019, and as of October 2022, those results were not publicly available for researchers outside of the U.S. EPA. From an initial round of sampling in 2008–2009 by the U.S. EPA, we calculated a median for PFOS that was 30% higher than data collected in 2013–2015. It is possible that PFOS in fish has continued to decrease, but additional data are needed. It is also possible the rates of declining PFOS and PFAS in freshwater fish have slowed as contaminants in some water bodies can have a long retention time, hundreds of years for the Great Lakes, and soil and sediment may serve as a long-term reservoirs (Codling et al., 2018).

5. Conclusions

Widespread PFAS contamination of freshwater fish in surface waters in the U.S. is likely a significant source of exposure to PFOS and potentially other perfluorinated compounds for all persons who consume freshwater fish, but especially for high frequency freshwater fish consumers. This is an example of a social and environmental injustice facing communities that depend on catching fish for cultural practices or economic necessity. At the general population level there are uncertainties regarding current PFOS levels in fish, consumption rates for freshwater anglers, and the overall impact on blood serum levels. Current levels of PFOS in serum exceed health guidance values indicating that identifiable sources of exposure should be reduced. National testing done by the U.S. EPA shows that nearly all fish in U.S. rivers and streams and the Great Lakes have detectable PFAS, primarily PFOS, in the $\mu\text{g/kg}$ or parts per billion range, while U.S. FDA testing shows that seafood purchased at grocery stores have significantly lower levels of PFAS. Self-caught fish are an important source of subsistence for many individuals, indicating that advisories for PFAS will disproportionately affect these individuals who cannot afford to replace self-caught fish with purchased fish. At the same time, knowing that high levels of PFOS present in freshwater fish could impact serum levels is concerning and should warrant the creation of national consumption advisories and an awareness program.

Credit author statement

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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.

Data availability

Data is publicly available and referenced.

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Appendix A. Supplementary data

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