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Current Breast Milk PFAS Levels in the United States and Canada: After All This Time, Why Don't We Know More?

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Background: Despite 20 y of biomonitoring studies of per- and polyfluoroalkyl substances (PFAS) in both serum and urine, we have an extremely limited understanding of PFAS concentrations in breast milk of women from the United States and Canada. The lack of robust information on PFAS concentrations in breast milk and implications for breastfed infants and their families were brought to the forefront by communities impacted by PFAS contamination.

Objectives: The objectives of this work are to: *a*) document published PFAS breast milk concentrations in the United States and Canada; *b*) estimate breast milk PFAS levels from maternal serum concentrations in national surveys and communities impacted by PFAS; and *c*) compare measured/estimated milk PFAS concentrations to screening values.

Methods: We used three studies reporting breast milk concentrations in the United States and Canada We also estimated breast milk PFAS concentrations by multiplying publicly available serum concentrations by milk:serum partitioning ratios for perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), perfluorohexane sulfonate (PFHxS), and perfluorononanoic acid (PFNA). Measured and estimated breast milk concentrations were compared to children's drinking water screening values.

Discussion: Geometric means of estimated breast milk concentrations ranged over approximately two orders of magnitude for the different surveys/communities. All geometric mean and mean estimated and measured breast milk PFOA and PFOS concentrations exceeded drinking water screening values for children, sometimes by more than two orders of magnitude. For PFHxS and PFNA, all measured breast milk levels were below the drinking water screening values for children; the geometric mean estimated breast milk concentrations were close to—or exceeded—the children's drinking water screening values for certain communities. Exceeding a children's drinking water screening value does not indicate that adverse health effects will occur and should not be interpreted as a reason to not breastfeed; it indicates that the situation should be further evaluated. It is past time to have a better understanding of environmental chemical transfer to—and concentrations in—an exceptional source of infant nutrition. https://doi.org/10.1289/EHP10359

Introduction

In 1984, former Surgeon General of the United States C. Everett Koop, MD, stated that "We need to identify and reduce the barriers that interfere with breastfeeding. . .." (Koop 2009; U.S. Department of Health and Human Services 1984). Seventeen years later, in 2001, a call was made for a national breast milk monitoring program in the United States (LaKind et al. 2001). Various features for such a program that would assist in understanding women's and infants' exposures to environmental chemicals were described, but overall, the goal of such a program was to ". . .provide the information needed to assess infant exposures during breast-feeding and develop scientifically sound information on benefits and risks of breast-feeding in the United States" (LaKind et al. 2001).

Since that time, the environmental health community has taken notice of a class of chemicals called per- and polyfluoroalkyl substances or PFAS. PFAS are a large class of more than 9,000 structurally different compounds, many of which have been used in industry and consumer products since the 1950s (Glüge et al. 2020). Members of the class are "defined as fluorinated substances that contain at least one fully fluorinated methyl or methylene carbon atom (without any H/Cl/Br/I atom attached to it)" (OECD 2021). PFAS do not occur naturally, are widespread and persistent in the environment, and have been detected in people, wildlife, and fish all over the world (Brase et al. 2021; Domingo and Nadal 2017; Routti et al. 2019). Although these chemicals began to be produced in the 1940s (U.S. EPA 2021a), several PFAS were measured in serum in the Centers for Disease Control and Prevention's (CDC) National Health and Nutrition Examination Survey (NHANES) in 1999–2000, and it quickly became clear that some PFAS were measurable in the serum of at least 95% of the adolescent and adult U.S. population (Calafat et al. 2007; CDC 2020a). Although serum concentrations of some PFAS have decreased in the general population over the last 20 y, there is still widespread exposure to PFAS. This widespread exposure is true even years after the primary U.S. manufacturer of perfluorooctane sulfonate (PFOS) voluntarily phased out its production in 2002, and eight major companies in the PFAS industry in the United States voluntarily agreed to phase

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out production of perfluorooctanoic acid (PFOA) and PFOA-related chemicals by 2015 (U.S. EPA 2017a; Ye et al. 2018).

Despite 20 y of biomonitoring studies of these chemicals in both serum and urine, and the availability of several studies of breast milk PFAS levels outside North America (CDC 2020a; Llorca et al. 2010; Macheka-Tendenguwo et al. 2018), we have an extremely limited understanding of PFAS concentrations in breast milk of American and Canadian women.

Concerns regarding the lack of robust information on PFAS concentrations in breast milk and the implications for both breastfed infants and their families were recently voiced by individuals raising their children in communities impacted by PFAS contamination, such as those living in proximity to industries producing PFAS, airports, military bases, and landfills (Hurtes 2021; NASEM 2021). Among concerns, parents have described the dilemma faced by their families in trying to understand the implications of a mother's PFAS exposure for exposure to her infant and what PFAS in breast milk may mean for their children's health.

The goals of this work were to: *a*) document published PFAS breast milk concentrations in the United States and Canada; *b*) estimate breast milk PFAS levels from maternal serum concentrations in national surveys and communities impacted by PFAS; and *c*) compare measured/estimated milk PFAS concentrations to screening values. In doing so, we hope to bring attention to the need for more information on PFAS in breast milk, especially for families living in communities with drinking water contaminated with PFAS.

Methods

Data Sources

We searched for papers reporting PFAS concentrations in breast milk in the United States and Canada with PubMed using combinations of the following single search terms: "PFAS," "PFC," "PFOA," "PFOS," "PFHxS," "PFNA," ("and") "breast milk." Searches were conducted in September 2021 and again in January 2022. Our focus in this paper was on the PFAS for which there were *a*) breast milk data, *b*) serum or plasma data, *c*) at least two reports of milk:serum ratios, and *d*) health-based screening values.

Measured breast milk PFAS concentrations. In pursuit of our objective to document published PFAS breast milk concentrations in the United States and Canada, we identified only three publications that included measured PFAS concentrations in breast milk in the United States (Tao et al. 2008; von Ehrenstein et al. 2009; Zheng et al. 2021). Although von Ehrenstein et al. (2009) obtained serum and milk samples from breastfeeding women in North Carolina, we could not use the data because PFAS concentrations in milk were all below the analytical limit of quantitation (LOQ) (Armbruster and Pry 2008) [150–600 pg per milliliter (pg/mL)] (pg/mL = ng/L). Of note, the LOQs reported in von Ehrenstein et al. (2009), using previously established methods (Kuklenyik et al. 2004), were an order of magnitude above the LOQ for Tao et al. (2008) (5.2–32 pg/mL).

Tao et al. (2008) measured PFOS, PFOA, PFHxS, and PFNA in breast milk from 45 primiparous and multiparous women. The women were from Massachusetts; more specific information was not given. Mean (maximum) concentrations were: PFOS: 131 pg/mL (617 pg/mL); PFOA: 43.8 pg/mL (161 pg/mL); PFHxS: 14.5 pg/mL (63.8 pg/mL); and PFNA: 7.26 pg/mL (18.4 pg/mL).

Zheng et al. (2021) measured 39 PFAS in the breast milk of 50 women from Washington State. Median (maximum) levels were: PFOS: 30.4 pg/mL (187 pg/mL); PFOA: 13.9 pg/mL (50.7 pg/mL); PFHxS: 6.55 pg/mL (16.7 pg/mL); and PFNA: 5.98 pg/mL (36.3 pg/mL).

One paper reported breast milk PFOA data for Ontario, Canada (Kubwabo et al. 2013) [breast milk was also analyzed for PFOS, PFHxS, and PFNA, but all were below the limit of detection (LOD)]. Samples, collected during 2003–2004, were from 13 women. PFOA concentrations ranged from <LOD to 520 pg/mL, with a mean concentration of 250 pg/mL. The LODs (nanograms per milliliter) reported for this study were: PFOS, 0.416; PFHxS, 0.416; and PFNA, 0.208.

Measured serum and plasma PFAS concentrations. To estimate nationally representative breast milk concentrations for the United States, we used the most recent available serum PFOS, PFOA, PFHxS, and PFNA data (nanograms per milliliter) from the NHANES for women of childbearing age (18–44 y of age). The individual, publicly available data were from survey years 2017–2018 (Table 1) (CDC 2020a). Detection frequencies for PFOS, PFOA, and PFHxS were >99% and 85% for PFNA. All nondetect observations were substituted with a value equal to the LOD divided by the square root of 2 prior to geometric mean and 95th percentile calculations. NHANES 2-y weights were provided along with the NHANES PFAS data (CDC 2020a). Weights, created by the CDC, account for the complex survey design of NHANES (including oversampling), survey nonresponse, and poststratification adjustment to match total population counts from the U.S. Census Bureau; weight-adjusted data are designed to be representative of the U.S. population. Following NHANES guidelines (CDC n.d.), we calculated weighted averages of raw concentrations or in the case of geometric means, exponentially transformed weighted averages of log raw concentrations. Calculations of weighted percentiles were carried out using Hmisc: Harrell Miscellaneous package in R (version 4.5-0; R Project).

Nationally representative plasma data were also available from the Canadian Health Measures Survey (CHMS) from 2016 to 2017 (Cycle 5) for Canadian females 20–79 y old (PFOA, PFOS, PFHxS) or 12–79 y old (PFNA) (Health Canada 2019). Data for individuals in the CHMS are not readily accessible, so we used summary data from the latest report and were not able to select relevant ages (Table 1). Detection frequencies ranged from 98.2% to 100%. CHMS substituted all nondetect observations with a value equal to the LOD divided by 2 prior to geometric mean and 95th percentile calculations. Concentrations from the CHMS accounted for sampling weights.

To estimate milk concentrations in communities with a known history of PFAS drinking water contamination, geometric mean serum concentrations measured as part of the Agency for Toxic Substances and Disease Registry (ATSDR) PFAS Exposure Assessments (https://www.atsdr.cdc.gov/pfas/activities/assessments.html) were used (note that these data are not publicly available). As part of these investigations, blood samples were collected in 2019 and 2020 from participants living in communities near current or former military bases that were known to have had PFAS in their drinking water in the past (Table 1). We estimated milk concentrations for eight different communities across the United States (referred to as "ATSDR location A–H"). The serum data for these communities were for all genders and ages. For PFOA, PFOS, PFHxS, and PFNA, more than 95% of serum samples were above the LOD (except for PFNA at ATSDR location A, with 77% of samples above the LOD). ATSDR substituted all nondetect observations with a value equal to the LOD divided by the square root of 2 prior to geometric mean and 95th percentile calculations.

We also used publicly available data from the New York State Department of Health for information on the Hoosick Falls and Petersburgh areas. Participant blood samples were collected

Table 1. Characteristics of data sets used to estimate breast milk concentrations. Serum or plasma PFAS concentrations (in nanograms per milliliter) and the number of participants in each cohort (n) are shown.

		PFOA (ng/mL)		PFOS (ng/mL)		PFHxS (ng/mL)		PFNA (ng/mL)	
Population[a]	n	GM	95th percentile	GM	95th percentile	GM	95th percentile	GM	95th percentile
ATSDR Location A	214	2.2	13.2	4.2	20.6	6	80.7	0.2	0.573
ATSDR Location B	333	9.7	40.4	42.4	192	72.9	415	0.7	2.4
ATSDR Location C	214	5	15.7	21.5	128	20.1	152	1	2.6
ATSDR Location D	275	1.5	3.2	5.1	16.6	2.9	15.2	0.4	1.1
ATSDR Location E	459	1.9	4.9	5.9	18.6	4.7	24.9	0.4	1.1
ATSDR Location F	88	2.1	8.7	18.3	146	11.7	115	0.3	0.8
ATSDR Location G	346	2.1	6.4	6.2	23.8	10.6	55.9	0.3	0.9
ATSDRLocation H	59	2.0	4.9	10.6	32.1	8.3	30.8	0.5	1.2
Hoosick Falls, NY	685	37.5	166	4.8	14.4	1.1	3	0.6	1.4
CHMS (2016–2017)	530–742[b]	1.1	3	2.7	10[c]	0.65	3.8	0.49	1.7[b]
NHANES (2017–2018)[d]	363	0.879	2.5	1.786	5.3	0.606	2.9	0.259	0.9

Note: ATSDR, Agency for Toxic Substances and Disease Registry; CHMS, Canadian Health Measures Survey; GM, geometric mean; NHANES, National Health and Nutrition Examination Survey; PFAS, polyfluoroalkyl substances; PFHxS, perfluorohexane sulfonate; PFNA, perfluorononanoic acid; PFOA, perfluorooctanoic acid; PFOS, perfluorooctane sulfonate.
[a]ATSDR data are not publicly available.
[b]CHMS report N of 530 for PFOA, 532 for PFOS and PFHxS, and 742 for PFNA.
[c]The CHMS report warns that this value should be used with caution.
[d]The NHANES data shown is for women of childbearing age (18–44 y of age only). Geometric means (nanograms per milliliter) for all women in the 2017–2018 NHANES are as follows: PFOA, 1.26; PFOS, 3.42; PFHxS, 0.805; PFNA, 0.384.

between June 2018 and March 2019 and took place about 2.5 y after most exposures to PFOA from drinking water had ended (NYS DOH 2019). The serum data were for both genders and all ages becaue the subset of data for women of childbearing age was not publicly available (Table 1). For PFOA and PFOS, 99% of the samples were above the LOD. For PFHxS and PFNA, 88% and 61%, respectively, were above the LOD. All nondetect observations were substituted with a value equal to the LOD divided by the square root of 2 prior to geometric mean and 95th percentile calculations. The LODs reported for this study were 0.5 ng/mL for all PFAS.

Calculations and Assumptions

Breast milk:serum partitioning values. Because data on breast milk concentrations in the United States and Canada were extremely limited, we chose to estimate breast milk concentrations based on serum or plasma concentrations reported for women in national surveys and communities with known PFAS drinking water contamination. This approach for estimating breast milk concentrations is supported by correlations between maternal serum and breast milk PFAS concentrations: Correlation coefficients range between 0.36 and 0.88, with most values above 0.6 for predominant PFAS (Cariou et al. 2015; Kärrman et al. 2007; Kim et al. 2011; Liu et al. 2011). This approach has also been successfully used and validated for other environmental contaminants, such as polybrominated diphenyl ethers (Marchitti et al. 2017).

To make these calculations, human milk:serum ratios were necessary. Human milk:serum ratios have been calculated only for a small number of PFAS; therefore, we restricted our analyses to those PFAS with the most documented human milk:serum ratios—namely, PFOA, PFOS, PFHxS, and PFNA. Central tendency values (mean or median) for milk:serum ratios were taken from four international studies to enhance the accuracy of our calculations (Cariou et al. 2015; Kärrman et al. 2007; Kim et al. 2011; Liu et al. 2011), and values were averaged. The published milk:serum concentration ratios used in the analysis, including sample sizes, are available in Table 2. For Cariou et al. (2015) and Kärrman et al. (2007), values were extracted from the study's supplemental material. The milk:serum ratios used in our analyses were 0.073 for PFOA, 0.013 for PFOS, 0.0133 for PFHxS, and 0.03 for PFNA. We assumed that serum and plasma levels for those PFAS were equivalent (Ehresman et al. 2007).

Measured serum/plasma concentrations in national surveys and communities impacted by PFAS were multiplied by milk:serum ratios to estimate breast milk PFAS levels. We derived geometric mean and 95th percentile estimates for PFOS, PFOA, PFHxS, and PFNA concentrations in breast milk. Geometric means of estimated breast milk concentrations ranged over approximately 2 orders of magnitude for the different surveys/communities. Concentrations ranged from 64 to 2,738 pg/mL for PFOA, 22 to 530 pg/mL for PFOS, 8 to 972 pg/mL for PFHxS, and 6 to 29 pg/mL for PFNA (data are shown in Table S1). Estimated breast milk levels were highest in Hoosick Falls, New York, for PFOA, ATSDR Site B for PFOS and PFHxS, and ATSDR Site C for PFNA. Figure 1 shows the results for each data set.

Screening values. As used here, health "guidance values" are defined as concentrations or dose levels that are not anticipated to result in adverse health effects. Examples of health guidance values include reference doses and concentrations as well as tolerable daily and weekly intakes and minimal risk levels (MRLs) (ATSDR 2018). These values include a margin of safety and are used by public health professionals to make decisions about which exposures might require closer evaluation. There are currently no existing guidance values for PFAS in breast milk. We evaluated different approaches to place measured and estimated breast milk PFAS levels into context, and although no approach

Table 2. Published milk:serum concentration ratios for PFOA, PFOS, PFHxS, and PFNA.

Study	Country	PFOA	PFOS	PFHxS	PFNA
Cariou et al. 2015	France	0.038 ($n=10$)	0.011 ($n=19$)	0.012 ($n=8$)	—
Kärrman et al. 2007	Sweden	0.12 ($n=1$)	0.01 ($n=12$)	0.02 ($n=12$)	0.01 ($n=2$)
Kim et al. 2011	Korea	0.025 ($n=17$)	0.011 ($n=17$)	0.008 ($n=17$)	—
Liu et al. 2011	China	0.11 ($n=50$)	0.02 ($n=50$)	—	0.05 ($n=50$)
Mean		0.0733	0.0130	0.0133	0.030

Note: n = number of samples with measured milk and serum concentrations within individual studies. —, no data; PFHxS, perfluorohexane sulfonate; PFNA, perfluorononanoic acid; PFOA, perfluorooctanoic acid; PFOS, perfluorooctane sulfonate.

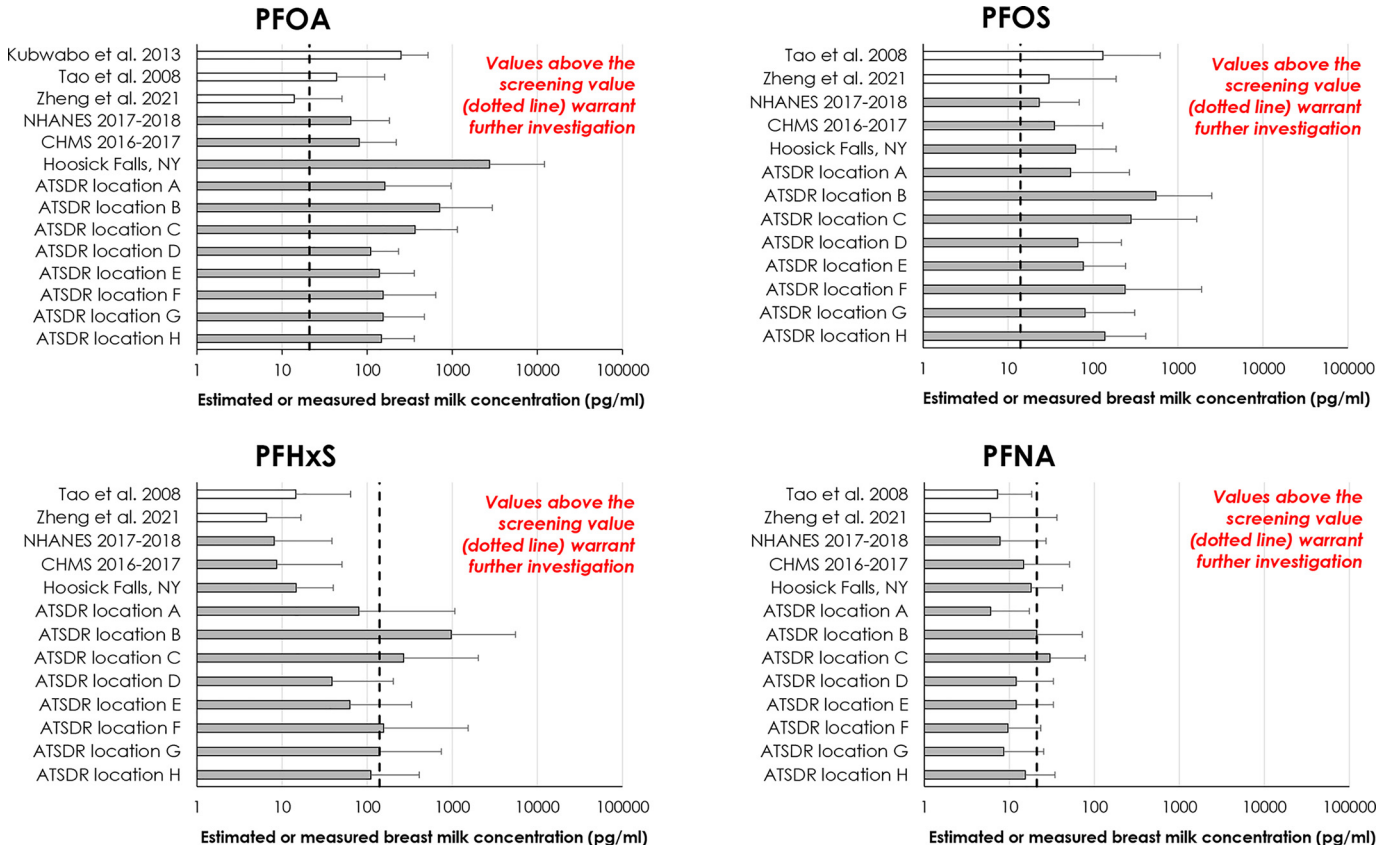

Figure 1. Measured (white bars) and estimated (gray bars) breast milk concentrations of per- and polyfluoroalkyl substances (PFAS) in the United States and Canada, in comparison with children's drinking water screening values (dotted line). Bars represent the mean measured breast milk levels for the data from Kubwabo et al. (2013) and Tao et al. (2008), the median measured breast milk levels from Zheng et al. (2021), the geometric mean estimated breast milk levels for National Health and Nutrition Evaluation Survey (NHANES), Canadian Health Measures Survey (CHMS), and PFAS-contaminated communities (as reported in Table 1). Error bars represent maximum measured concentrations in Kubwabo et al. (2013) and Tao et al. (2008), and 95th percentile of estimated concentrations for NHANES, CHMS, and PFAS-contaminated sites. Of note, PFOS, PFHxS, and PFNA were not detected in milk samples from Kubwabo et al. (2013). The *x*-axis is log-scale. *n* values are given in Table 1. Agency for Toxic Substances and Disease Registry children's drinking water screening values: PFOA (21 ppt), PFOS (14 ppt), PFHxS (140 ppt), and PFNA (21 ppt) (ATSDR 2018).

is entirely adequate, we decided to compare measured and estimated breast milk concentrations with PFAS drinking water screening values developed by ATSDR (2018). Although lifetime health advisories (HAs) for PFOA and PFOS are also available from the U.S. EPA (U.S. EPA 2016), they are based on *adult* water intake rates and incorporate a relative source contribution factor. We opted to use the ATSDR screening values because they are based on *child* intake rates and were derived more recently, integrating the results of research that was not available when the U.S. EPA's HAs were developed. In addition, ATSDR screening values are available for a wider variety of PFAS (i.e., PFHxS and PFNA in addition to PFOA and PFOS). ATSDR develops MRLs as a screening tool to identify environmental exposures that warrant further evaluation. Exposures below the MRL are not expected to result in adverse health effects. The MRLs, derived from epidemiological and toxicological data, are set "well below" a value that is likely to cause health effects (ATSDR 2021). Exceeding an MRL does not indicate that adverse health effects will occur, but it does indicate that the situation should be further evaluated.

ATSDR MRLs were derived based on studies of skeletal effects in mice for PFOA (Koskela et al. 2016); delayed eye opening and decreased pup weight in rats for PFOS (Luebker et al. 2005); thyroid follicular cell damage in rats for PFHxS (Butenhoff et al. 2009); and delayed eye opening, delayed pubertal development, and decreased pup weight gain in mice for PFNA (Das et al. 2015). Points of departure (PODs) from these studies based on animal serum perfluoroalkyl levels for sensitive end points were converted into human equivalent doses (HEDs) based on the assumptions that a serum concentration resulting in an effect in a laboratory animal would also result in an effect in humans and that PFAS concentrations are at steady state in humans as a result of long-term exposure. PODs for PFOA, PFOS, and PFNA are based on predicted serum levels in maternal animals associated with health effects in offspring exposed during gestation and lactation. Using these values with estimates of exposure in infants introduces some uncertainty; the potential for health risk could be over- or underestimated depending on the kinetics of intergenerational PFAS transfer in humans and animals (Kieskamp et al. 2018). MRLs were obtained by dividing the calculated HEDs by relevant uncertainty factors. Because the MRLs are determined as doses in units of milligrams per kilogram per day, these are converted to equivalent environmental concentrations (Environmental Media Evaluation Guides, or EMEGs) based on body weight and contact rate (e.g., drinking water consumption). EMEGs are not designed or intended to be used as water standards or to quantify risk, but they can provide valuable context to evaluate exposures at contaminated sites, which often include private and public water sources. For PFAS, ATSDR estimates EMEGs for children based on infants (age birth to 1 y old) weighing 7.8 kg with a drinking water intake rate of 1.113 L/day, or 143 mL/kg per day. Using this approach, ATSDR determined EMEGs for PFOA (21 ppt), PFOS (14 ppt), PFHxS (140 ppt), and PFNA (21 ppt). Although these EMEGs

are intended to evaluate drinking water concentrations, we believe they can also be used to give context to estimated breast milk concentrations because they are based on exposure factors specific to young children and assume no other sources of exposure (no relative source contribution adjustment). Breast milk may be the only source of hydration for some infants under 6 months of age. Table 15-1 of the 2011 U.S. EPA Exposure Factors Handbook (U.S. EPA 2011) recommends upper percentile intakes ranging from 220 mL/kg-d in young infants to 130 mL/kg-d in older exclusively breastfed infants. The child EMEG estimated drinking water intake rate of 143 mL/kg-d is lower than the recommended upper percentile for infants younger than 3 months of age but is similar or higher for infants older than 3 months of age. Use of the child EMEG value is a reasonable approach to evaluating the potential risk of exposure to PFAS in breast milk. For the purposes of this paper, we refer to EMEGs as "children's drinking water screening values."

When comparing measured or estimated milk PFAS concentrations to children's drinking water screening values in Figure 1, all geometric mean and mean estimated/measured breast milk PFOA and PFOS concentrations exceeded the drinking water screening values for children, sometimes by over 2 orders of magnitude. For PFHxS and PFNA, measured breast milk levels were below the drinking water screening values for children, but the geometric mean estimated breast milk concentrations from some communities with known PFAS drinking water contamination were close to—or exceeded—the children's drinking water screening values. Some of the published milk:serum ratios were based on a small number of samples; e.g., ratios reported in Kärrman et al. (2007) were based on one participant for PFOA and two participants for PFNA. When we excluded these values, results for PFOA were similar, but we observed more locations with PFNA geometric mean breast milk concentrations exceeding the ATSDR screening concentrations (Figure S1).

Discussion

The exercise undertaken in this research provides estimates of nationally representative concentrations of four PFAS in breast milk from the general population in the United States and Canada as well as concentrations estimated for several areas in the United States known to be contaminated with PFAS from industrial dumping or from aqueous film-forming foam (AFFF) used in fuel-based fire training at military bases, airports, and other areas. Importantly, estimated and measured breast milk concentrations of PFOA, PFOS, PFHxS, and PFNA ranged over several orders of magnitude and were near or—in most cases for PFOA and PFOS—exceeded the ATSDR children's drinking water screening values. Exceeding these screening values does not indicate that adverse health effects will occur and should not be interpreted as a reason to not breastfeed; it indicates that the situation should be further evaluated.

Given the uncertainty involved in making these predictions, it is reasonable to ask whether the estimates of PFAS in breast milk mirror actual concentrations in breast milk in the United States and Canada. Unfortunately, we cannot answer that question because the three available publications included small, nonrepresentative samples of women from only a few locations (Kubwabo et al. 2013; Tao et al. 2008; Zheng et al. 2021). In fact, three studies with small sample sizes (34, 45, and 50 samples) from limited geographic regions (North Carolina, Massachusetts, Washington) provide the entire database for PFAS in breast milk in the United States (Tao et al. 2008; von Ehrenstein et al. 2009; Zheng et al. 2021), and one study with 13 samples provides all the information available for Canada (Kubwabo et al. 2013). Further, we have an extremely poor understanding of how concentrations of PFAS in breast milk change over the course of lactation (and the information that is available offers conflicting information) (Lee et al. 2018; Fromme et al. 2010; Thomsen et al. 2010), which in turn limits our ability to accurately estimate infant intake of these chemicals. The fact that other countries have undertaken research on breast milk PFAS levels and paired milk and serum concentrations demonstrates that this kind of effort is feasible and produces critical information (Černá et al. 2020; Jin et al. 2020; Lamichhane et al. 2021; Macheka et al. 2022). It is not possible to draw conclusions about whether an individual should or should not breastfeed based on these estimates.

Since the time of the earliest research on environmental chemicals in breast milk (e.g., Laug et al. 1951), it has been well understood that a wide array of environmental chemicals can transfer to breast milk and that breastfeeding can serve as a major source of infant exposure to those chemicals. Further, it is well known that infancy is a susceptible life stage, and minimizing environmental chemical exposures to infants has been—and should be—a priority. Finally, the fact that PFAS can transfer to breast milk and then pass to infants through breastfeeding has been known for nearly 20 y. Specifically, biomonitoring data (Fromme et al. 2010) and modeling efforts (Goeden et al. 2019; Loccisano et al. 2013; Verner et al. 2016) have shown that children's PFAS levels can substantially increase during breastfeeding, exceeding PFAS levels in their mothers. Due to accumulated maternal levels, exposures to breastfed infants may be higher than older individuals or formula fed infants (Goeden et al. 2019). Yet, the sum total of our knowledge of PFAS concentrations in breast milk in the United States and Canada from the published literature is based on 129 samples from three states in the United States and 13 samples from one province in Canada.

The PFAS discussed in this paper (PFOA, PFOS, PFHxS, PFNA) are long-chain, highly persistent PFAS that are no longer produced in North America, but exposures continue. As noted by Awad et al. (2020), "human exposure assessments focused only on legacy substances may severely underestimate overall PFAS exposure in breastfeeding infants." For example, NHANES also reported serum concentrations for 12 other PFAS; some of these were detected at frequencies comparable to or greater than PFOA, PFOS, PFHxS, and PFNA [e.g., perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUA)]. In addition, PFAS that have not been the focus of many studies are now being observed in breast milk. For example, 9-chlorohexadecafluoro-3-oxanone-1-sulfonic acid (trade name: F53-B) was detected in breast milk sampled in Chinese cities (Awad et al. 2020), and Zheng et al. (2020) also reported on shorter-chain PFAS [e.g., perfluoro-*n*-hexanoic acid (PFHxA)] in breast milk. However, available milk:serum data for these PFAS were insufficient for inclusion in our analysis, and currently no established screening values exist for assessing the potential health impacts of these exposures alone or in combination. In our view, when considering infant PFAS exposures in the United States and Canada, it is critical that newer replacement PFAS be included in monitoring studies [e.g., emerging PFAS measured in the U.S. EPA's Fifth Unregulated Contaminant Monitoring Rule (UCMR 5) (U.S. EPA 2021b)].

Of course, the United States and Canada are not the only countries in which infant PFAS exposure is a concern, and two recent publications report PFAS contamination in breast milk on multiple continents. In a study of nationally representative pooled breast milk samples from 42 countries, PFOA was quantified in all samples, PFOS in 36, and PFHxS and PFNA in 4, with countries with the highest incomes reporting the highest breast milk PFAS measurements (Fiedler and Sadia 2021). International data on breast milk PFAS summarized by Macheka-Tendenguwo et al. (2018) and Liu et al. (2020) further indicates that countries in Europe and Asia are impacted by PFAS contamination.

We recognize the many uncertainties in this assessment. First, given the limited data [i.e., number of studies, number of participants per study ($n = 1$–50)] on milk:serum partitioning for the four PFAS included in our analyses, the estimates for breast milk concentrations contain a degree of uncertainty. In addition to variations in milk:serum values across studies, some studies (not all) reported on the variability of milk:serum partition values, with coefficients of variation ranging approximately between 30% and 60%. Because this is an exploratory analysis, we decided not to propagate uncertainty and variability in breast milk–level estimates. Consequently, the estimates presented here should not be used to draw conclusions about whether or not an individual should breastfeed.

Second, although breast milk and serum PFAS concentrations are generally correlated, the minimal amount of data on PFAS in breast milk in the United States and Canada did not permit us to evaluate the accuracy of the estimated milk concentrations. That being said, estimated breast milk levels based on the NHANES serum data approximate the levels recently reported by Zheng et al. (2021). The inferences of this analysis are intended for women of reproductive age. However, because we did not have ready access to data specifically for women of reproductive age based on publicly available data, estimates of breast milk concentrations in communities highly exposed to PFAS were based on serum concentrations from all community members who participated in blood sampling, including men and older women. Because men and older women may have higher PFAS levels than younger women (for example, due to loss of serum PFAS during menstruation), this could have resulted in an overestimation of breast milk levels in these communities.

Third, there is limited and conflicting information on how PFAS concentrations in breast milk change during a feeding and over the course of lactation (Fromme et al. 2010; Lee et al. 2018; Thomsen et al. 2010). Thus, depending on the sampling technique, the postpartum time at which the sample was collected and whether depuration impacts postpartum milk PFAS concentrations, the estimated breast milk data reported in Figure 1 may either over- or underestimate general concentrations in the United States and Canada.

Fourth, when considering infant exposure, it is worth noting that infant PFAS exposures originate *in utero* (Kang et al. 2021; Eryasa et al. 2019; Blake and Fenton 2020; Bach et al. 2015) but may also derive from food sources (typically started at or around 6 months of age) and from formula feeding and that little is known about PFAS levels in reconstituted or ready-to-use formulas in the United States and Canada (although it is clear that many U.S. drinking water supplies contain measurable amounts of PFAS) (Andrews and Naidenko 2020; U.S. EPA 2017b). Because there are multiple nutritional sources that could contribute to infant PFAS exposures, a full understanding of infant exposure potential would require exposure estimates not only from breastfeeding but also from alternative sources of nutrition, such as infant formula, that are not currently available.

Last, we recognize that comparing the current breast milk concentrations (measured and estimated) to the ATSDR screening values introduces uncertainty because the MRLs for PFOA, PFOS, and PFNA are based on maternal exposure metrics assuming concentrations are at steady state; health guidance values based on measures or estimates of offspring exposure could potentially reduce this uncertainty (Kieskamp et al. 2018), but such values are currently unavailable. The MRL for PFHxS is based on health effects observed following exposure in adult animals; as such, some uncertainty is associated with the application of this value to assess the potential for health risk in young children. Also, the MRLs used by ATSDR (3, 2, 3, and 20 ng/kg/d for PFOA, PFOS, PFNA, and PFHxS, respectively) to derive screening values were based on animal studies and are higher than the guideline value based on epidemiological studies by the European Food Safety Authority (0.63 ng/kg/d for the sum of PFOA, PFOS, PFNA, and PFHxS; EFSA 2020).

In our judgment, these important uncertainties and the reported breast milk estimates above the EMEGs indicate a critical need for more data on PFAS transfer to infants through breast milk and other nutritional sources. Because of the large number of PFAS that can potentially transfer to breast milk, we need to be able to model or estimate breast milk concentrations of these chemicals. Where measuring PFAS in breast milk is not feasible, models should be available to estimate milk concentrations from serum or plasma levels. Research is needed to answer questions such as: What factors drive partitioning of the wide spectrum of PFAS into milk? Is the process dominated by protein binding or are other factors able to modify transfer (e.g., molecule size or charge)? Modeling efforts would be facilitated by obtaining simultaneous data from the serum or plasma and breast milk of women for PFAS beyond legacy PFAS. If these kinds of models were supported by sufficient data, they could inform the complex decision-making around breastfeeding for families.

Numerous benefits to infants and mothers associated with breastfeeding have been described in the literature (AAP 2012; Global Breastfeeding Collective 2018a; Hennet and Borsig 2016; Ip et al. 2007), and breastfeeding has been recommended by numerous health organizations (WHO 2011; AAP 2012; Global Breastfeeding Collective 2018b; Kramer and Kakuma 2002). The 2020–2025 Dietary Guidelines for Americans provides the current U.S. recommendations around breastfeeding (USDA/HHS 2020). Some of the many benefits of breastfeeding for infants include a reduced risk of ear and respiratory infections, asthma, obesity, and sudden infant death syndrome. Breastfeeding can also help lower a mother's risk of high blood pressure, type 2 diabetes, and ovarian and breast cancer (AAP 2012). The benefits from breastfeeding in comparison with formula feeding have been recognized despite the presence of various environmental chemicals in breast milk (LaKind et al. 2018). Thus, we strongly remind the reader that the information in this paper is designed to highlight important data gaps in our understanding of PFAS and breast milk. It is not our intent that this information be used as a basis for deciding to wean earlier than planned (Geraghty et al. 2008), to avoid breastfeeding, or to adversely impact breastfeeding rates (CDC 2020b).

To conclude, a woman's choice to breastfeed is complex, personal, and based on many different considerations. We propose that additional breast milk monitoring data could inform one of these many considerations. Although we believe a national breast milk monitoring program is still needed in the long-term to inform scientific, clinical, and lactation experts, additional resources and data are needed in the near-term to support decision-making regarding the risks and benefits of breastfeeding. This information is also essential for public health agencies for making recommendations to individuals, clinicians, and communities.

We close with the following question: How can we improve the scientific understanding of PFAS concentrations in breast milk in the United States and Canada? Research that includes pregnant and lactating women—including biomonitoring studies—can provide the information needed to produce solutions leading to minimization of unwanted exposures to environmental chemicals such as PFAS to infants. A targeted monitoring program or several well-powered studies aimed at measurements in breast milk and maternal serum would be invaluable for contextualizing our estimates of breast milk concentrations in the United States and Canada and for validating the analysis presented in this paper. The need for such a program was recognized in recent testimonials at the National Academies of Sciences, Engineering, and Medicine's Town Hall Meeting for Guidance on PFAS Testing

and Health Outcomes (NASEM 2021). It is past time for us to have a better understanding of environmental chemical transfer to—and concentrations in—breast milk, an exceptional source of infant nutrition.

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