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Time trends in per- and polyfluoroalkyl substances (PFAS) concentrations in the Danish population: a review based on published and newly analyzed data

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Abbreviations: PFAS, per- and polyfluoroalkyl substances; PFOS, perfluorooctane sulfonic acid; PFOA, perfluorooctanoic acid; ENFORCE, National Cohort Study of Effectiveness and Safety of SARS-CoV-2 vaccines; DNBC, Danish National Birth Cohort; PFNA, perfluorononanoic acid; PFDA, perfluorodecanoic acid; PFHxS, perfluorohexane sulfonic acid; PFHpS, perfluoroheptane sulfonate; PFHpA, perfluoroheptanoic acid; POPs, Persistent Organic Pollutants; REACH, Regulation on the registration, evaluation, authorization and restriction of chemicals; US EPA, U.S. Environmental Protection Agency.

Abstract

Introduction: Per- and polyfluoroalkyl substances (PFAS) are persistent chemicals used in many industries and everyday consumer products and exposure has been linked to several adverse health outcomes. Currently, no systematic monitoring of PFAS levels in the general Danish population has been conducted.

Objective: To study temporal trends of PFAS concentrations in the Danish population.

Materials and methods: In August 2023, we performed a search for original peer-reviewed reports in PubMed using combinations of search terms for PFAS and Denmark. Reports were included if they comprised a Danish study population and direct measurements of PFAS in serum or plasma samples. Scatter plots of medians presented in the reports were used to visualize time-trends of PFAS concentrations among Danish individuals.

Results: We included 29 reports based on a total of 18,231 individuals from 19 Danish study populations. A total of 24 PFAS measured in serum or plasma were presented in the reports, the most frequent being PFOS, PFOA, PFDA, PFNA, PFHpA, PFHpS, and PFHxS. Median concentrations of PFOS ranged from 4.0 ng/mL to 44.5 ng/mL, PFOA ranged from 0.8 ng/mL to 9.7 ng/mL, while lower concentrations were presented for the other PFAS. Median concentrations of PFOS and PFOA increased from 1988 until the late 1990s followed by a decrease until 2021. A less clear time-trend were observed for the other PFAS.

Conclusion: Blood concentrations of PFOS and PFOA in the Danish population have declined substantially from the late 1990s until 2021 reflecting a phase-out of the production and regulation of the use of these PFAS. Time-trends for PFDA, PFNA, PFHpA, PFHpS, and PFHxS were less evident, yet a tendency toward a decline was observed. As only some of the compounds are measured, it is not possible to determine if the decrease in some PFAS is outweighed by an increase in others.

Key words: Denmark; PFAS; Per- and polyfluoroalkyl substances; Review; Short communication.

Introduction

The so called "forever chemicals"[1], per- and polyfluoroalkyl substances (PFAS), are a group of chemicals ubiquitously distributed in wildlife and human populations[2]. PFAS were first introduced in the 1940s and their unique water- and oil-repellent properties have made them popular in a wide range of products. Today, more than 9000 individual compounds are categorized as PFAS and used in consumer products such as coated cookware, stain- and water-resistant textiles and carpets, but also in industrial goods and firefighting foams[2–4]. Their carbon-fluorine bonds make them highly resistant to degradation and thus so extremely persistent in the environment that they can be detected in water, soil, animals, food, drinking water, and human serum globally[2].

The primary exposure route for humans is ingestion of contaminated food and drinking water followed by inhalation of e.g. dust and airborne volatiles, and with minor contributions from dermal absorption[2,5,6]. Once in the body, the most common PFAS are not metabolized and elimination is slow with half-lives largely dependent on the length of the carbon chain of the specific PFAS (e.g. 4.8 years and 3.5 years for perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) respectively[7,8]). Although the toxicity of PFAS is still under investigation, some compounds, such as PFOA and PFOS, have been linked to adverse health effects, including higher cholesterol levels, lower birth weight, lower vaccine response, and kidney cancer[2,5,9–11].

Various efforts have been made to regulate the production and use of certain PFAS since the early 2000s[12]. In the same period, many novel PFAS have emerged as alternatives and may increasingly be present in humans[13]. Although PFAS have never been produced in Denmark, they have been imported from other countries to a variety of industries and used in manufacturing facilities of consumer products and in firefighting foam. In 2021, a discovery of excessive PFAS levels in the blood of individuals living close to a firefighting training facility in the municipality of Korsoer, raised concerns about the magnitude of PFAS exposure in Denmark. Following this finding, hundreds of potential contamination sites distributed throughout the country were identified, including firefighting training facilities and industrial sites using PFAS. This sparked a public movement pushing for a global ban on PFAS and access to blood tests to determine individual exposure. However, the PFAS concentrations in the general Danish population are largely unknown making it difficult to determine whether individuals are highly exposed and to determine potential effects of regulation.

Given the importance of assessing human exposure to PFAS for targeted prevention and risk communication strategies, a mapping of measured concentrations in the Danish population is warranted. Considering the complexity, cost, and high time consumption of setting up a human biomonitoring program, we make use of the vast existing data summarizing human measurements of PFAS in Denmark.

Materials and methods

In August 2023, we performed a literature search to identify available original peer-reviewed reports of PFAS concentrations measured in biological specimens of the Danish population. The search was conducted in PubMed using combinations of MeSH and free text search terms for PFAS and Denmark (supplementary, Table S1). A filter was applied in the search to only identify reports based on humans. No restrictions on language or year were applied. Two authors (LD and SDH) performed the search and selected relevant reports eligible for full-text reading based on a screening of titles and abstracts. When study populations with measurements of PFAS in biological specimens were identified, we performed an additional search in PubMed for reports using data from these populations. We also cross-checked reference lists to identify relevant reports that did not appear in the PubMed searches. Lastly, we reached out to our research network asking to share recently analyzed unpublished data. We included reports with PFAS concentrations measured in any type of biological specimen (e.g., plasma, serum, urine, seminal fluid, amniotic fluid, breast milk, placenta, or adipose tissue), and we had no restrictions regarding study population e.g., pregnant women, children, adolescents, adults, and occupationally exposed workers, or the type of PFAS compound reported. We excluded reports from Greenland and the Faroe Islands, as the distribution of PFAS in the Arctic regions is distinctly different with populations being exposed through a high intake of local animals, mainly seafood[14,15]. Reviews, meta-analyses, and reports that did not present a median concentration of PFAS were also excluded. If more than one report presented concentrations of PFAS for the same study population, the report with the largest study population was chosen unless the measurements in the smaller study population could provide information on additional compounds. For each selected report, we extracted the specific PFAS reported, year of sample retrieval, biological specimen, sample size, median concentration of PFAS, and characteristics of the study population such as age, sex, and whether the study population was a sub-population of a larger population (**Table 1**).

To visualize time-trends of PFAS concentration in the Danish population, we plotted median concentrations according to year of sample retrieval in a scatter plot and stratified on pregnant women, children, and adults. For reports carried out over a longer period, we used the middle year of sample retrieval. All PFAS with a sufficient number of datapoints to visualize a time-trend were plotted.

Results

Study selection

We identified 87 reports that presented concentrations of PFAS measured in biological specimens in the Danish population. After full-text reading, we excluded 55 reports due to overlapping populations and two reports that did not present median concentrations of PFAS. Since only three reports presented PFAS measured in amniotic fluid, cord blood, or breast milk, we excluded these to assess only comparable measures of PFAS. Thus, we selected 27 reports that all presented PFAS concentrations measured in blood samples (serum or plasma)[16,17,26–35,18,36–42,19–25]. We further included recently analyzed unpublished data from the National Cohort Study of Effectiveness and Safety of SARS-CoV-2 vaccines (ENFORCE) and Odense Child Cohort. An overview of the study selection resulting in 29 reports is shown in **Figure S1**.

Study characteristics

Characteristics of the 29 reports are presented in **Table 1**. The included reports were based on a total of 18,231 individuals from 19 study populations, of which four were sub-populations of the Danish National Birth Cohort (DNBC). We did not identify any occupationally exposed study populations. The reports were published between 2008 and 2022, and biological specimens were collected between 1988 and 2021. PFAS were measured in plasma (61%) or serum (39%). Most of the included individuals were pregnant women (58%), but infants, children, and adults were also represented (age 18 months to 90 years). Median concentrations of 24 different PFAS were presented in the reports of which we visualized the seven most frequently presented. Concentrations of PFOS and PFOA were measured in all study populations, while PFDA, PFNA, PFHpA, PFHpS, and PFHxS were measured in 20, 22, 9, 9, and 20 study populations, respectively.

Concentrations of PFOS and PFOA

Concentrations of PFOS and PFOA have been measured in plasma and serum samples since 1988 and up to 2021. The median concentrations of PFOS ranged from 4.0 ng/mL to 44.5 ng/mL with the lowest concentration measured in serum between 2016 and 2019 among children and adults from Odense Child Cohort (unpublished data). The highest median concentration was measured in plasma

of randomly selected 9-year-old school boys from the Odense municipality in 1997[36]. Median concentrations of PFOS appeared to increase from 1988 to the late 1990s and then decrease until 2021 with a substantial drop after the EU regulation of PFOS in 2006 (**Figure 1A**)[12]. The median blood concentrations of PFOA were generally lower than PFOS and ranged from 0.8 ng/mL to 9.7 ng/mL but followed the same time-trend (**Figure 1B**). The lowest median PFOA concentration was measured in serum samples of adults participating in the ENFORCE study in 2020 (unpublished data). The highest median concentration was measured in plasma of randomly selected 9-year-old school boys from the Odense municipality in 1997[36]. Similar time-trends were observed for pregnant women, children, and adults.

Other frequently reported PFAS

From 1988 to 2021, PFDA, PFNA, PFHpA, PFHpS, and PFHxS have been measured in plasma and serum samples. Median blood concentrations ranged from 0.02 ng/mL for PFHpA measured in serum in 2021 to 6.6 ng/mL for PFHxS measured in serum from 2003. The median concentration of PFNA appeared to increase from 1988 until the late 2000s followed by a slight decrease while concentrations of PFHxS seemed to have slightly decreased since the mid-1990s except for one report that measured high concentrations in 105 young men at conscription in 2003[19] (**Figure S2**). The reported median concentrations of PFDA, PFHpA, and PFHpS appeared to be stable over time (**Figure S2**). Similar time-trends were observed when stratifying on pregnant women, children, and adults.

Discussion

In this first-ever mapping of PFAS exposure over time in the Danish population, we observed indications of an overall trend of an increase of PFAS from 1988 until late 1990s followed by a decrease until 2021. The most pronounced decline was observed for PFOS and PFOA, whereas a less clear time trend was observed for PFDA, PFNA, PFHpA, PFHpS, and PFHxS.

The highest median concentrations in the Danish population were reported for PFOS and PFOA. This is similar to reports from other European countries[43–47]. An increasing trend in PFOS and PFOA concentrations up until the late 1990s followed by a decrease in the last two decades have also consistently been observed in other European populations[43,44,46,48–50]. The strong decline since around year 2000 in Denmark and other European countries likely reflects the phase-out of PFOS and PFOA initiated by the worldwide manufacturer 3M in 2002[51]. In 2006, the European Union further restricted the use of PFOS, and in 2009 PFOS was added to the Stockholm Convention on Persistent Organic

Pollutants (POPs)[12]. PFOA was included in the Stockholm convention in 2019 and has been regulated by the EU REACH regulation of chemicals since 2020[12]. With only one datapoint after 2019 it is not possible to conclude if this has had an impact on human exposure.

For PFDA, PFNA, PFHpA, PFHpS, and PFHxS we observed lower median concentrations and less clear time-trends. A small decreasing trend was observed for PFHxS already from the first measurement in the mid-1990s. In several other European countries an increasing trend was observed up until around the year 2000, whereafter a decrease was observed in most countries[43,44,46,48,50]. Since the main producer of PFHxS took actions to phase out the production of this PFAS in 2000-2002[52], we expected a more pronounced decrease in the years to follow in Denmark. We cannot explain the discrepancy between Danish and other European measurements before year 2000. However, the initial lower values of PFHxS in Denmark may have diminished the effect of the discontinuation of PFHxS production. A similar trend as for PFOS and PFOA, although less pronounced, was observed for PFNA, however with the highest median concentrations measured in 2009. This is in accordance with reports from Germany[46], Norway[48], and Sweden[43] showing a decrease starting around 2006 and 2009, although no significant declining trends of PFNA were observed in a review of global human data published up until 2015[53]. The decline observed in some countries, including Denmark, coincides with the voluntary agreement between the US EPA and several large manufactures to phase out PFNA. For PFHpS, PFDA, and PFHpA, the concentrations appeared stable over time. This differs from findings of three Norwegian reports that showed increasing concentrations of PFHpS in serum from adult men and women until around year 2000 whereafter the concentrations started to decrease[48,54,55]. For PFDA, increasing concentrations were observed up until 2007 and 2010 in Norwegian adults and Swedish primiparous women, respectively[44,49]. Similarly, an increasing trend between 2000 and 2009 followed by a decrease from 2009 to 2017 was observed in Swedish adolescents[43]. A review of published data up until 2015 concluded that no significant declining trend in PFDA was observed in human samples[53].

Despite of governmental regulation of manufacture and use of certain PFAS within the last 20 years, the environmental persistence of PFAS means that existing contamination will remain a concern for years to come. At the same time, many novel PFAS are emerging as alternatives to the regulated compounds and could also be present in humans, but these have yet to be included in standard laboratory analyses. The decrease in PFOS, PFOA, and PFHxS after year 2000 suggest that the voluntary and regulatory actions taken to mitigate exposure have had an impact on the exposure to long-chained PFAS in the Danish population. The fact that PFAS is a large, heterogenous group of

fluorinated compounds, where new types continuously enter the market, complicates the process of mapping out human exposure. Consequently, only a small fraction of the entire PFAS group is presented in this review. Some reports measured more PFAS than those presented in their study. For instance, Hærvig et al., 2022, measured 15 different PFAS, but as eight were below the limit of detection in most samples these were not included in the results of the report.

During the last five years, the highest median concentration of PFAS in the Danish population was 5.9 ng/mL for PFOS in 2021 in a population of adults mainly aged above 50 years and being either healthcare workers, individuals with increased risk of disease, or the general population[56]. This concentration is much lower than recent findings of PFOS concentrations among individuals living near a confirmed pollution hotspot in the municipality of Korsoer in Denmark. Here the mean concentration of PFOS measured in serum was 43.0 ng/mL[57,58] indicating that the hotspot has indeed increased human exposure.

Methodological considerations

The reports included in this paper comprise different study populations within all age groups with the majority being pregnant women. Comparability may be limited for some reports because individual factors like age, sex, parity, and educational level are determinants of body burden of PFAS[45,59,60]. We did, however, observe the same time-trends when stratifying on pregnant women, children, and adults. In many cases, participants were selected with a specific study objective in mind and may therefore not be representative of the general population. For example, in one report of the association between prenatal PFAS exposure and attention deficit/hyperactivity disorder (ADHD) and autism in childhood, women were selected based on the children's diagnoses (cases and controls)[34]. If PFAS is in fact associated with ADHD or autism, we would expect this sample to have a higher median concentration than an unselected sample. The included reports measured PFAS in both plasma and serum samples. Since concentrations of PFOS, PFOA, and PFHxS have previously been reported to be comparable in serum and plasma with a ratio of 1:1 independent of the level of concentrations measured[61], we do not expect this to affect the results. As PFAS bind to serum and/or plasma proteins[62], they accumulate predominately in blood and concentrations measured here may not be comparable to those measured in other tissues. Searching only one database, we may have overlooked some reports. To minimize this risk, we also cross-checked reference lists to identify relevant reports that did not appear in the PubMed searches. Further, differences in the sample collection and laboratory analytical methods may account for some of the differences in trends across reports. Since the analytical methods have improved over time, a larger variation likely existed in the earlier

samples. However, as the majority of samples were analyzed in the same three laboratories and previous studies in general have demonstrated strong agreement between different laboratories[63–65], we do not believe that the clear time-trends observed can be solely explained by interlaboratory variation. Lastly, we cannot rule out that some individuals may have been included more than once as some of the included reports are based on sub-samples from the DNBC[28–35]. However, since the DNBC comprises 101,041 pregnancies[32], and the sub-samples were constructed with different research aims and inclusion criteria, we expect only a minor overlap.

Conclusion

Blood concentrations of PFOS and PFOA in the Danish population have declined substantially from the late 1990s until 2021 indicating a clear impact of the regulation of the use of these PFAS. Concentrations of PFNA and PFHxS have slightly declined while PFDA, PFHpA, and PFHpS appear stable. Reports have generally focused on a limited number of PFAS but are increasingly expanding the number of PFAS analyzed. Still, it is only a fraction of the thousands of PFAS compounds that are measured. It is therefore not possible to conclude if a decrease in one type of PFAS is outweighed by an increase in others. By aggregating individual-level data from the study populations included, we can achieve a more comprehensive analysis over time and across various population strata in Denmark, thus providing a more accurate depiction of the levels in general population and identification of susceptible groups.

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Author contribution

Sidsel Dan Hull: Conceptualization, Methodology, Formal analysis, Investigation, Writing - Original Draft, Writing - Review & Editing, Visualization. **Laura Deen**: Conceptualization, Methodology, Formal analysis, Investigation, Writing - Original Draft, Writing - Review & Editing, Visualization. **Kajsa Ugelvig Petersen**: Conceptualization, Writing - Review & Editing, Funding acquisition. **Tina Kold Jensen**: Conceptualization, Resources, Writing - Review & Editing, Funding acquisition **Paula Hammer**: Conceptualization, Writing - Review & Editing. **Regitze Sølling Wils**: Conceptualization, Writing - Review & Editing. **Hannah Nørtoft Frankel**: Conceptualization, Methodology, Writing - Review & Editing. **Sisse Rye Ostrowski**: Conceptualization, Resources, Writing - Review & Editing. **Sandra Søgaard Tøttenborg**: Conceptualization, Methodology, Supervision, Writing - Review & Editing, Visualization, Funding acquisition, Project administration. All authors made a final approvement of the version to be published.

Figures and tables

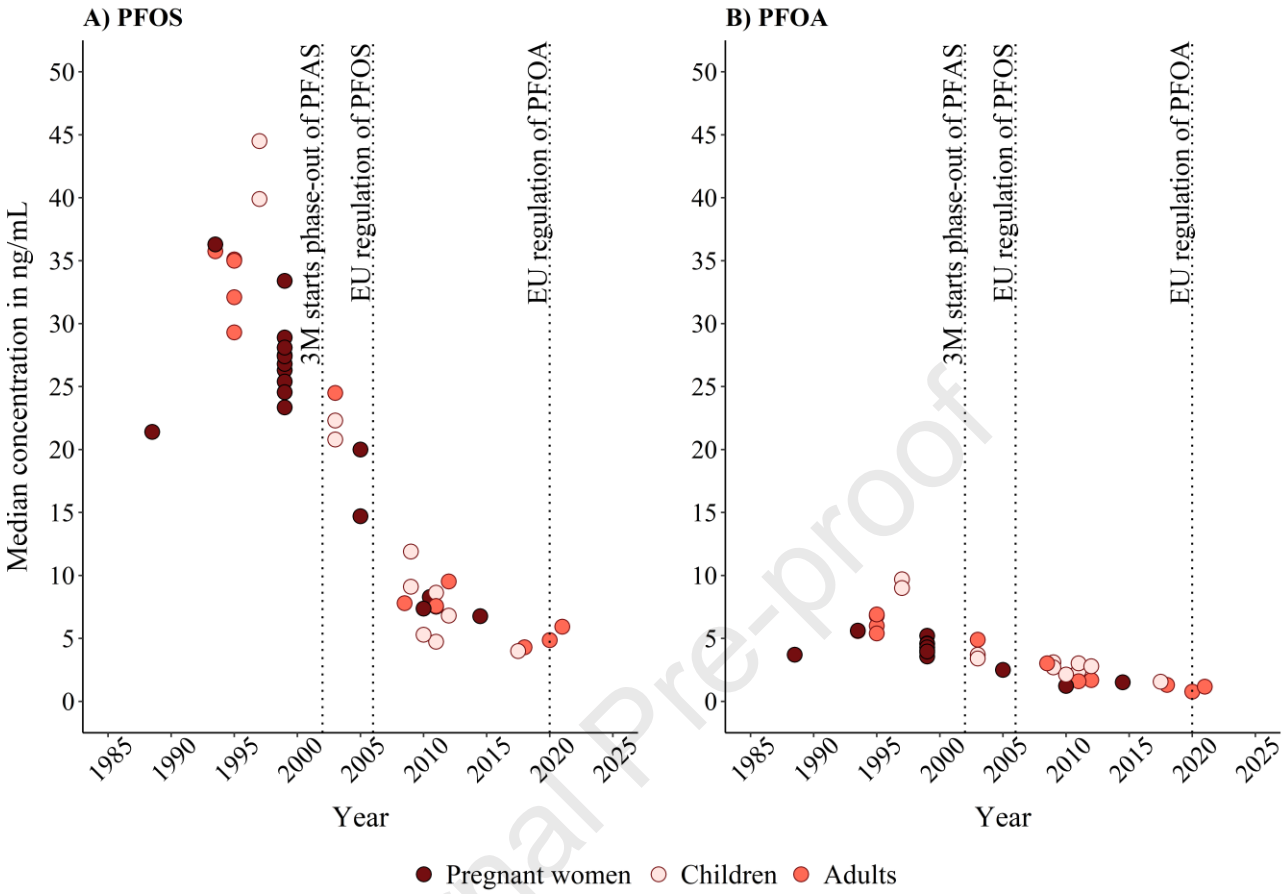

Figure 1. Median concentration of PFOS and PFOA in ng/mL measured in the Danish population, 1988-2021.

Table 1. Study characteristics (n=29).

Name of study population	Reports identified in PubMed	Reports included	Author, year	Specimen	Year for sample of specimen	Type of PFAS reported (median [ng/mL])	Population (age)	N
Aarhus Birth Cohort	9	2	Bjerregaard-Olesen et al., 2016[16]	Serum	2008-2013	PFOS (8.3), PFOA (2.0), PFDA (0.3), PFNA (0.8), PFHpS (0.2), PFHxS (0.5), PFUnA (0.3)	Pregnant women (29y)[1]	1533
		2	Bonefeld-Jørgensen et al., 2023[17]	Serum	2011-2013	PFOS (6.9), PFOA (1.6), PFDA (0.3), PFNA (0.7), PFHpS (0.1), PFHxS (0.4), PFUnA (0.3), PFHpA (0.03)	Pregnant woman (29y)[1]	800[7]
Aarhus University Hospital	1	1	Bach et al., 2015[18]	Plasma	2005	PFOS (20), PFOA (2.5), PFDA (0.5), PFNA (0.8), PFHpS (0.3), PFHxS (0.6), PFUnA (1.1), PFHpA (0.1)	Pregnant women (winter samples)[2]	36
						PFOS (14.7), PFOA (2.5), PFDA (0.3), PFNA (0.7), PFHpS (0.2), PFHxS (0.6), PFUnA (0.3), PFHpA (0.1)	Pregnant women (summer samples)[2]	52
Conscription register	2	2	Joensen et al., 2009[19]	Serum	2003	PFOS (24.5), PFOA (4.9), PFDA (0.9), PFNA (0.8), PFHpA (0.2), PFHxS (6.6), PFTrA (0.00), PFDoA (0.1), PFUnA (0.1), PFOSA (0.1)	Men (19y)	105
			Joensen et al., 2013[20]	Serum	2008-2009	PFOS (7.8), PFOA (3.0), PFDA (0.4), PFNA (1.1), PFHpS (0.3), PFHxS (0.7)	Men (19y)	247
Copenhagen mother-child cohort	3	1	Thomsen et al., 2021[21]	Serum	2012	PFOS (6.8), PFOA (2.8), PFDA (0.3), PFNA (0.9), PFHxS (0.5)	Children (12.6y)	109
COPSAC	2	1	Sevelsted et al., 2022[22]	Plasma	2009-2011	PFOS (7.4), PFOA (1.2)	Pregnant women (32y)[3]	727
				Plasma	2009-2011	PFOS (5.3), PFOA (2.1)	Children (18mth)	606
Danish Cohort of Covid-19 patients	1	1	Grandjean et al., 2020[23]	Plasma	2020	PFOS (4.9), PFOA (0.8), PFNA (0.4), PFHxS (0.5), PFBA (<LOD)*	Men and women (30 to 70y)	323
Danish Diet, Cancer, and Health Cohort	3	1	Eriksen et al., 2009[24]	Plasma	1993-1997	PFOS (35.1), PFOA (6.8)	Cancer group of men (50 to 65y)	1111
						PFOS (35.0), PFOA (6.9)	Comparison group of men (50 to 65y)	680
						PFOS (32.1), PFOA (6.0)	Cancer group of women (50 to 65y)	129
						PFOS (29.3), PFOA (5.4)	Comparison group of women (50 to 65y)	92
Danish Fetal Origins 1988 cohort	5	2	Halldorsson et al., 2012[25]	Serum	1988-1989	PFOS (21.5)*, PFOA (3.7)*, PFNA (0.3), PFOSA (1.1)	Pregnant women (29y)[4]	423[8]
			Strøm et al., 2014[26]	Serum	1988-1989	PFOS (21.4), PFOA (3.7)	Pregnant women (29y)[4]	876
DEMOCOPHES	1	1	Mørck et al., 2015[27]	Plasma	2011	PFOS (7.6), PFOA (1.6), PFDA (0.3), PFNA (0.6), PFHxS (0.3)	Women (41y)	143
				Plasma	2011	PFOS (8.6), PFOA (3.0), PFDA (0.3), PFNA (0.8), PFHxS (0.3)	Children (6 to 11y)	116
DNBC FEPOS	3	3	Hærvig et al., 2020[28]	Plasma	1996-2002	PFOS (26.3), PFOA (4.6)	Pregnant women (31y)[5]	1057
				Plasma	2017-2019	PFOS (4.3), PFOA (1.3)	Men (19 to 21y)	1058

				Hærvig et al., 2022[29]	Plasma	1996-2002	PFOS (27.6)*, PFOA (4.4)*, PFDA (0.2), PFNA (0.4), PFHpA (0.1), PFHxS (0.8), PFUnDA (0.1)	Pregnant women (31y)[5]	864[9]
				Petersen et al., 2022[30]	Plasma	2017-2019	PFOS (3.9)*, PFOA (1.2)*, PFDA (0.2), PFNA (0.5), PFHxS (0.3), PFUnDA (0.1)	Men (19 to 21y)	1041[9]
	FETOTOX	1	1	Liew et al., 2014[31]	Plasma	1996-2002	PFOS (28.9), PFOA (4.6), PFDA (0.2), PFNA (0.5), PFHpS (0.3), PFHxS (1.0)	Pregnant women (son diagnosed with congenital cerebral palsy) (≈30y)[5]	86
							PFOS (27.5), PFOA (3.9), PFDA (0.2), PFNA (0.4), PFHpS (0.3), PFHxS (0.9)	Pregnant women (daughter diagnosed with congenital cerebral palsy) (≈30y)[5]	66
	LDPS	2	1	Liew et al., 2018[32]	Plasma	1996-2002	PFOS (28.1), PFOA (4.3), PFDA (0.2), PFNA (0.5), PFHpA (0.1), PFHpS (0.4), PFHxS (1.1), PFTrA (<LLOQ), PFUnA (<LLOQ), PFDS (<LLOQ), PFOSA (2.3), PFSoA (<LLOQ)	Pregnant women (31y)[6]	1592
	DNBC	27	3	Fei et al., 2008[33]	Plasma	1996-2002	PFOS (33.4), PFOA (5.2)	Pregnant women (≈30y)[6]	1400
				Liew et al., 2015[34]	Plasma	1996-2002	PFOS (26.8), PFOA (4.1), PFDA (0.2), PFNA (0.4), PFHpS (0.3), PFHxS (0.8)	Pregnant women (child diagnosed with ADHD) (≈30y)[5]	215
							PFOS (25.4), PFOA (3.8), PFDA (0.2), PFNA (0.4), PFHpS (0.3), PFHxS (0.9)	Pregnant women (child diagnosed with autism) (≈30y)[5]	213
							PFOS (27.4), PFOA (4.0), PFDA (0.2), PFNA (0.4), PFHpS (0.3), PFHxS (0.9)	Pregnant women (controls) (≈30y)[5]	545
				Liew et al., 2020[35]	Plasma	1996-2002	PFOS (23.4), PFOA (3.6), PFDA (0.2), PFNA (0.4), PFHpA (0.1), PFHpS (0.4), PFHxS (1.1), PFTeA (<0.4), PDTrA (<0.4), PFDoA (<0.4), PFUnA (<0.2), PFDS (<0.4), PFOSA (3.7), PFHxA (<0.03), PFBS (<0.1)	Pregnant women (pregnancy ending in miscarriage) (≈30y)[6]	220
							PFOS (24.6), PFOA (4.0), PFDA (0.2), PFNA (0.4), PFHpA (0.1), PFHpS (0.4), PFHxS (1.1), PFTeA (<0.4), PDTrA (<0.4), PFDoA (<0.4), PFUnA (<0.2), PFDS (<0.4), PFOSA (3.8), PFHxA (<0.03), PFBS (<0.1)	Pregnant women (pregnancy with a singleton liveborn child) (≈30y)[6]	218
European Youth Heart Study		3	2	Domazet et al., 2016[36]	Plasma	1997-2009	PFOS (44.5), PFOA (9.7)	Boys (9y)	236
							PFOS (39.9), PFOA (9.0)	Girls (9y)	265
							PFOS (22.3), PFOA (3.7)	Boys (15y)	91[10]
							PFOS (20.8), PFOA (3.4)	Girls (15y)	110[10]
							PFOS (11.9), PFOA (3.1)	Men (21y)	92[10]
							PFOS (9.1), PFOA (2.7)	Women (21y)	110[10]

			Domazet et al., 2020[37]	Plasma	1997	PFOS (40.8)*, PFOA (9.0)*, PFDA (0.1), PFNA (0.4), PFHxS (0.8)	Children (9y)	257[11]
First time pregnancy planners	1	1	Vestergaard et al., 2012[38]	Serum	1992-1995	PFOS (35.8), PFOA (5.6), PFDA (0.1), PFNA (0.5), PFHxS (1.1), EtFOSAA (2.1), MeFOSAA (0.5), FOSA (0.1)	Pregnancy planners (women without pregnancy) (20 to 35y)	93
				Serum	1992-1995	PFOS (36.3), PFOA (5.6), PFDA (0.1), PFNA (0.5), PFHxS (1.2), EtFOSAA (1.8), MeFOSAA (0.4), FOSA (0.1)	Pregnancy planners (women with recognized pregnancy) (20 to 35y)	129
Odense Child Cohort	19	2	Dalsager et al., 2021[39]	Serum	2010-2012	PFOS (7.5), PFOA (1.7), PFDA (0.3), PFNA (0.6), PFHxS (0.4)	Pregnant women (31y)[5]	1503
			Højsager et al., 2022[40]	Serum	2010-2012	PFOS (4.7), PFOA (2.4), PFDA (0.2), PFNA (0.6), PFHxS (0.3)	Children (18mth)	511
Pregnant women from Skejby and Randers Hospital	2	1	Mamsen et al., 2019[41]	Serum	2014-2015	PFOS (6.8), PFOA (1.5), PFDA (0.3), PFNA (1.0), PFUnA (0.4)	Pregnant women (26y)[2]	23
Staff at Rigshospitalet	1	1	Kielsen et al., 2016[42]	Serum	2012	PFOS (9.5), PFOA (1.7), PFDA (0.3), PFNA (0.7), PFHpA (0.1), PFHxS (0.4), PFDoDA (0.04), PFUnDA (0.2)	Men and women (38y)	12
Unpublished data								
ENFORCE			Sandra Søgaard Tøttenborg	Serum	2021	PFOS (5.9), PFOA (1.2), PFDA (0.2), PFNA (0.6), PFHpA (0.02), PFHpS (0.7), PFHxS (0.1), PFUnDA (0.1)	Men and women (30 to 90y)	991
Odense Child Cohort			Tina Kold Jensen	Serum	2016-2019	PFOS (4.0), PFOA (1.6), PFDA (0.2), PFNA (0.6), PFHpA (0.8), PFHpS (0.1), PFHxS (0.3), PFUdA (0.1)	Children (5y)	913

Study acronyms: COPSAC, Copenhagen Prospective Studies of Asthma in Childhood 2; DEMOCOPHES, Demonstration of a study to Coordinate and Perform Human Biomonitoring on a European Scale; DNBC, Danish National Birth Cohort; ENFORCE, National Cohort Study of Effectiveness and Safety of SARS-CoV-2 vaccines; FEPOS, Fetal Programming of Semen Quality; LDPS, Lifestyle During Pregnancy Study

[1]Blood samples in 1. and 2. trimester; [2]Blood samples in 1. and 3. Trimester; [3]Blood samples in 2. trimester; [4]Blood samples in 3. trimester; [5]Majority of blood samples in 1. trimester and some in 2. trimester; [6]Blood samples in 1. trimester

[7]Same study population as Bjerregaard-Olesen et al., 2016

[8]Same study population as Strøm et al., 2014.

[9]Same study population as Hærvig et al., 2020.

[10]Same study population delivered blood sample at age 9, 15, and 21 in the study by Domazet et al., 2016.

[11]Same study population as Domazet et al., 2016.

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Declaration of interests

☒ 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.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: