LIVSMEDELS VERKET

NATUR VÅRDS VERKET
SWEDISH ENVIRONMENTAL PROTECTION AGENCY

NATIONAL ENVIRONMENTAL MONITORING COMMISSIONED BY THE SWEDISH EPA

Report to the Swedish EPA (the Health-Related Environmental Monitoring Program)

Contract no. 215 1214

Temporal trends of perfluoroalkyl substances in pooled serum samples from first-time mothers in Uppsala 1997-2014

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2015-09-07

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Rapporttitel Temporal trends of poly- and perfluoroalkyl substances in pooled serum samples from first-time mothers in Uppsala 1996-2014	**Beställare** Naturvårdsverket 106 48 Stockholm **Finansiering** Nationell hälsorelaterad miljöövervakning
Nyckelord för plats Uppsala	
Nyckelord för ämne Perfluorerade alkylsyror, PFCA, PFSA, blodserum, tidstrend, kvinnor	
Tidpunkt för insamling av underlagsdata 1996-2014	

Sammanfattning

Sedan 1996 har Livsmedelsverket regelbundet samlat in prover från förstföderskor i Uppsala för analys av persistenta halogenerade organiska miljöföroreningar (POP). I följande rapport redovisas halterna av perfluorerade alkylsyror (PFAA) i blodserum insamlade 3 veckor efter förlossningen 2007, 2009, 2011, 2013 och 2014. Prover från ungefär 30 kvinnor per år delades upp i 3 samlingsprover per provtagningsår (9-10 prover per samlingsprov) och perfluoralkyl sulfonsyror (PFSA) och perfluoralkyl karboxylsyror (PFCA) analyserades. Resultaten slogs ihop med resultat från en tidigare publicerad studie av PFAA i samlingsprover från 1997, 1998, 2000, 2002, 2004, 2006, 2008, 2010 och 2012, som finansierats av FORMAS. Samma analysmetod användes. Halten av karboxylsyror med 8-11 kol i den perfluorerade kolkedjan (PFNA, PFDA, PFUnDA och PFDoDA) ökade med runt 3 % per år. En liknande ökning antyddes även för PFTrDA (12 kol), även om ökningen inte var statistiskt signifikant. För alla dessa substanser tycks ökningen i halter plana ut i slutet av undersökningsperioden, vilket antyder att exponeringen av Sveriges befolkning för dessa substanser inte längre ökar. Resultaten måste dock följas upp i framtiden för att bekräfta detta. Befolkningen i Uppsala utsattes fram till 2012 för förhöjda halter av den mycket bioackumulerbara sulfonsyran PFHxS i dricksvattnet. Detta har resulterat i ökade blodhalter hos förstföderskor under studieperioden (ca 6 % per år), men liksom för de långkedjiga PFCA så tycks ökningen plana ut efter 2010. Även här krävs en uppföljning framöver för att säkerställa att den minskade exponeringen från dricksvatten efter 2012 verkligen har resulterat i sänkta blodhalter av PFHxS. Tillverkningen av sulfonsyran PFOS, och liknande substanser, i världen upphörde i stort sett runt 2002. Detta har resulterat i sjunkande halter av substansen (ca 8 % per år). Tillverkningen av en karboxylsyra kallad PFOA har minskat, men inte ännu fasats ut helt, och minskningen av denna substans i kvinnornas blod går därför långsammare (ca 3 % per år).

Temporal trends of perfluoroalkyl substances in pooled serum samples from first-time mothers in Uppsala 1997-2014

Background

Perfluoroalkyl substances (PFAS) are highly fluorinated organic compounds that have been manufactured for over five decades. PFAS are used in industrial processes (for instance production of fluoropolymers) and in products such as water and stain proofing agents, lubricants, paints and fire-fighting foams (Kissa 2001; Prevedouros et al. 2006). Some PFAS, such as perfluoroalkyl acids (PFAA), are environmentally persistent and have been found globally in wildlife and in humans (Giesy and Kannan 2001; Kissa 2001; Kannan et al. 2004; Houde et al. 2006).

In 2002 the chemical manufacturer 3M completed the phase out of perfluorooctane sulfonic acid (PFOS) and related compounds. Perfluorobutane sulfonic acid (PFBS) was launched as a replacement for PFOS (3M, 2002; Olsen et al. 2008). A few years later eight major manufacturers of perfluorooctane acid (PFOA) agreed with the US EPA to reduce emissions and product content of PFOA by 95% by 2010, and to work towards eliminating emissions and content by 2015 (US EPA 2015).

In 2012 the Swedish National Food Agency and the Department of Environmental Science and Analytical Chemistry (ACES; formerly the Department of Applied Environmental Sciences [ITM]), Stockholm University, published a study on PFAS temporal trends in blood serum from first-time mothers in Uppsala County (1996-2010), with financial support from the Swedish EPA (Glynn et al. 2012). It was shown that the levels of PFOS and PFOA had declined during the study period with a faster decline of PFOS (8% per year) than of PFOA (3% per year). However, levels of the shorter-chained PFAS, PFBS and perfluorohexane sulfonic acid (PFHxS), had instead increased around 10% per year, while the longer-chained PFAS perfluorononane acid (PFNA) and perfluorodecane acid (PFDA) had increased around 4% per year (Glynn et al. 2012). In a following study of PFAS temporal trends using an improved analytical method, it was shown that levels of the long-chained perfluoroundecane acid (PFUnDA), perfluorododecane acid (PFDoDA) and perfluoorotridecane acid (PFTrDA) also increased at a similar rate as PFNA and PFDA (Gebbink et al. 2015).

Here we present updated PFAS data from Uppsala first-time mothers for the period 1997-2014, expanding on the previous temporal trend study by Gebbink et al. (2015) covering the period 1997-2012. The study period has been extended with measurements of samples from 2013 and 2014, and additional analyses of samples from 2007, 2009 and 2011 have been included to improve the statistical power in the trend analyses.

Material and methods

Recruitment and sampling

In the POPUP study (Persistent Organic Pollutants in Uppsala Primiparas), first-time mothers from the general population living in Uppsala County were recruited between 1996 and 2014 as described in Glynn et al. (2012). The participants donated a blood sample 3 weeks after delivery. Blood sampling was carried out using 9 ml Vacutainer® or Vacuette® serum tubes, and serum was stored at -20°C. The study was approved by the local ethics committee of Uppsala University, and the participating women gave informed consent prior to the inclusion in the study.

Table 1. Composition of the pooled serum samples used for analyses of PFAS. Samples analyzed in the present study in bold.

Sampling year	No of pools	N in each pool	Age (yrs) range
1997	3	10	21-33
1998	3	10	22-34
2000	3	10	21-37
2002	3	10	24-37
2004	3	10	21-34
2006	3	10	19-40
2007	**3**	**9-10**	**21-39**
2008	3	10	20-35
2009	**3**	**10**	**22-39**
2010	3	10	20-41
2011	**3**	**9-10**	**21-37**
2012	3	10	20-38
2013	**3**	**10**	**22-39**
2014	**3**	**10**	**20-38**

In the present study we used banked pooled serum samples from 2007, 2009, 201, 2013 and 2014 for analysis of PFAS. For each year of recruitment 3 pooled serum samples were prepared, with serum from 9-10 individual mothers in each pool (Table 1). In contrast to the study by Glynn et al. (2012), data for 1996 are not available in the present study due to lack of serum samples from this year.

PFAS analyses

In Table 2, the analyzed PFAS are listed. Precursors of PFAA were also analyzed in the present study. The results of these analyses will be reported in 2017, according to EPA contract no. 2215-15-001, when results from 2015 and 2016 are available.

PFAS were analyzed as described in Gebbink et al. (2015). Briefly, serum samples (1 g) were spiked with 50µL of a solution containing isotopically-labeled internal standards. Following addition of 3mL of acetonitrile, samples were vortex-mixed, sonicated for 15min, and then centrifuged for 10min at 3000 rpm. The organic phase was transferred to a separate tube and the extraction procedure was repeated twice. The combined sample extracts were reduced to ~1ml under a stream of nitrogen, fortified with 10mL of water, and then loaded onto weak anion exchange (WAX) cartridges (Waters, 150mg, 6mL) which had been pre-conditioned with 6mL each of 2% NH_4OH in methanol, methanol, and water. The cartridges were rinsed with 1mL of 1% formic acid in water and 2mL of water, and then dried under vacuum. Neutral PFAS were subsequently eluted with 1mL methanol (fraction 1). Cartridges were rinsed with an additional 2mL of MeOH which was discarded. Ionic PFAS were subsequently eluted with 4mL of 2% ammonium hydroxide in methanol (fraction 2). Fraction 1 was filtered and then transferred to a microvial containing 50 µl recovery standards ($^{13}C_8$-PFOS and $^{13}C_8$-PFOA). Fraction 2 was evaporated to dryness under nitrogen, re-dissolved in methanol, and then filtered, prior to transferring to a microvial containing 50 µl recovery standards ($^{13}C_8$-PFOS and $^{13}C_8$-PFOA).

Instrumental analysis was carried out by ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) using a BEH C18 (50×2.1 mm, 1.7 µm particle size, Waters) analytical column operated under gradient elution conditions. Mobile phases consisted of 95 % water and 5 % methanol (solvent A) and 75 % methanol, 20 % acetonitrile, and 5 % water (solvent B). Both mobile phases contained 2 mM ammonium acetate and 5 mM 1-methyl piperidine. The column temperature was maintained at 40 °C, and the injection volume was 5 µl. The mass spectrometer was operated in negative ion electrospray ionization (ESI−) mode.

Quantification was performed using an internal standard approach. For each compound a nine point calibration curve was prepared, which was linear over the entire concentration range (r values greater than 0.99) for all compounds. The linear isomer and the sum of branched isomers of PFHxS, PFOS and PFOA were chromatographically separated and quantified individually. Branched isomers were quantified using the linear isomer calibration curve. For quantification of the sum of branched PFOS isomers an average of the response obtained with the product ions m/z 80 and 99 was used.

In each batch of samples three method blanks were included to monitor for background contamination. For compounds where blank contamination was observed the method quantification limits (MQLs) were determined as the mean plus three times the standard deviation of the quantified procedural blank signals. A blank correction was performed by subtracting the average quantified concentration in the blanks from PFAS concentrations in the samples. For other compounds the MQL was determined as the concentration in a serum sample giving a peak with a signal-to-noise ratio of 10. Recoveries of the labeled internal standards in the serum samples ranged between 40% and 92%. Together with the serum samples, a NIST standard reference material (SRM 1957) was analyzed in each batch. Concentrations obtained for several PFAAs in SRM 1957 were lower compared to the certified values, however, they were in agreement with reported concentrations in other studies. Relative standard deviations (RSDs) for quantified concentrations in SRM 1957 (n=9) were <20% for PFAAs (with the exception of PFTrDA), Duplicate analyses of the pooled serum samples revealed <10% deviation for PFHxS, PFOS, and C8-C12 PFCAs, and <25% deviation for PFBS, PFDS, PFHpA and PFTrDA. Larger variations were occasionally observed for compounds detected close to their respective MQLs.

Table 2. PFAS included in the study.

Substance	No of carbons in fluorinated chain	Abbreviation
Perfluoroalkyl sulfonic acids (PFSA)		
Perfluorobutane sulfonic acid	4	PFBS
Perfluorohexane sulfonic acid[a]	6	PFHxS
Perfluorooctane sulfonic acid[a]	8	PFOS
Perfluorodecane sulfonic acid	10	PFDS
Perfluoroalkyl carboxylic acids (PFCA)		
Perfluorobutanoic acid	3	PFBA
Perfluoropentanoic acid	4	PFPeA
Perfluorohexanoic acid	5	PFHxA
Perfluoroheptanoic acid	6	PFHpA
Perfluorooctanoic acid	7	PFOA
Perfluorononanoic acid	8	PFNA
Perfluorodecanoic acid	9	PFDA
Perfluoroundecanoic acid	10	PFUnDA
Perfluorododecanoic acid	11	PFDoDA
Perfluorotridecanoic acid	12	PFTrDA
Perfluorotetradecanoic acid	13	PFTeDA

[a]Branced and linear isomers

[b]Linear isomer

Calculations and statistics

To test for significant changes in the individual PFAS concentrations over time, log-linear regression analyses were carried out. In cases of levels <MQL the level was set to LOQ (upper-bound).

Table 3. Concentrations of perfluoroalkyl sulfonic acids (PFSA) (ng/g) in pooled blood serum samples from primiparous women in Sweden.[1]

Year	PFBS	br-PFHxS	lin-PFHxS	tot-PFHxS	br-PFOS	lin-PFOS	tot-PFOS
1997	0.025	0.17	1.97	2.14	5.37	9.86	15.2
1997	0.017	0.13	1.56	1.69	6.47	12.2	18.7
1997	0.017	0.12	1.53	1.64	6.52	12.0	18.5
1998	0.024	0.16	2.15	2.31	6.94	12.4	19.3
1998	0.020	0.14	1.85	1.99	6.78	13.5	20.3
1998	<0.009[2]	0.09	1.31	1.40	5.92	11.3	17.2
2000	0.014	0.11	1.85	1.96	5.57	11.2	16.8
2000	0.029	0.21	2.30	2.51	6.63	12.4	19.0
2000	0.025	0.22	2.94	3.16	7.27	12.3	19.6
2002	<0.009	0.25	2.76	3.01	5.78	10.6	16.4
2002	<0.009	0.12	2.32	2.44	6.63	11.6	18.2
2002	<0.009	0.16	2.62	2.78	5.80	10.0	15.8
2004	0.019	0.21	2.32	2.53	4.10	7.36	11.5
2004	0.011	0.25	3.39	3.64	4.81	9.99	14.8
2004	<0.009	0.22	2.88	3.10	5.34	10.3	15.6
2006	0.058	0.47	4.15	4.62	5.35	9.62	15.0
2006	0.048	0.52	5.99	6.51	4.07	7.26	11.3
2006	0.022	0.17	2.06	2.23	3.71	6.32	10.0
2007	**0.058**	**0.52**	**5.23**	**5.75**	**4.04**	**7.06**	**12.9**
2007	**0.046**	**0.38**	**4.79**	**5.16**	**5.50**	**9.71**	**17.8**
2007	**0.041**	**0.34**	**4.05**	**4.38**	**2.89**	**8.84**	**10.0**
2008	0.056	0.43	3.90	4.33	3.21	5.30	8.51
2008	0.023	0.33	3.51	3.85	3.49	5.30	8.80
2008	0.019	0.34	4.01	4.35	3.11	5.33	8.44
2009	**0.029**	**0.36**	**3.77**	**4.13**	**2.34**	**5.05**	**8.29**
2009	**0.029**	**0.54**	**7.40**	**7.93**	**3.15**	**5.72**	**10.2**
2009	**0.041**	**0.38**	**4.36**	**4.73**	**3.02**	**5.30**	**9.60**
2010	<0.009	0.21	2.36	2.57	2.21	3.75	5.96
2010	0.038	0.58	5.94	6.52	2.69	4.73	7.41
2010	0.019	0.45	5.19	5.65	2.35	4.13	6.48
2011	**0.023**	**0.39**	**5.61**	**6.01**	**2.81**	**5.12**	**9.04**
2011	**0.058**	**0.49**	**6.30**	**6.79**	**1.99**	**4.16**	**6.98**
2011	**0.027**	**0.38**	**5.38**	**5.75**	**1.88**	**4.29**	**6.90**
2012	<0.009	0.13	1.87	2.00	1.90	3.71	5.61
2012	0.020	0.39	4.60	5.00	2.51	3.94	6.45
2012	<0.009	0.32	4.60	4.91	2.44	4.29	6.73
2013	**0.011**	**0.30**	**5.01**	**5.30**	**1.55**	**3.55**	**5.71**
2013	**0.030**	**0.34**	**5.00**	**5.34**	**1.66**	**3.10**	**5.37**
2013	**0.029**	**0.28**	**4.50**	**4.79**	**1.50**	**3.68**	**5.76**
2014	**0.024**	**0.21**	**3.41**	**3.62**	**1.31**	**2.99**	**4.89**
2014	**0.033**	**0.35**	**4.76**	**5.11**	**2.06**	**3.55**	**6.48**
2014	**<0.016**	**0.18**	**3.17**	**3.35**	**1.51**	**3.17**	**5.50**

[1]Reported concentrations are the average of duplicate analyses. Results in bold data generated in the present study. Other data from Gebbink et al. (2015).

[2] <values indicating the method quantification limit (MQL).

Table 4. Concentrations of perfluoroalkyl carboxylic acids (PFCA) (ng/g) in pooled blood serum samples from primiparous women in Sweden.[1]

Year	lin-PFOA	tot-PFOA	PFNA	PFDA	PFUnDA	PFDoDA	PFTrDA
1997	2.25	2.30	0.29	0.14	0.14	0.026	0.038
1997	2.53	2.60	0.34	0.18	0.14	0.025	0.022
1997	2.19	2.23	0.26	0.14	0.11	0.017	0.016
1998	2.47	2.53	0.37	0.18	0.17	0.018	0.021
1998	2.58	2.62	0.39	0.23	0.21	0.031	0.028
1998	2.33	2.38	0.36	0.19	0.14	0.016	0.019
2000	2.59	2.62	0.39	0.19	0.17	0.023	0.026
2000	2.64	2.70	0.39	0.20	0.23	0.030	0.037
2000	2.54	2.59	0.31	0.17	0.16	0.020	0.027
2002	2.85	2.91	0.45	0.24	0.22	0.031	0.037
2002	2.64	2.68	0.43	0.24	0.23	0.027	0.021
2002	2.84	2.88	0.41	0.23	0.18	0.024	0.022
2004	2.31	2.35	0.38	0.20	0.18	0.026	0.030
2004	2.47	2.50	0.66	0.38	0.30	0.040	0.046
2004	2.67	2.69	0.56	0.37	0.29	0.038	0.044
2006	2.08	2.12	0.54	0.25	0.21	0.026	0.022
2006	2.18	2.22	0.52	0.29	0.25	0.034	0.045
2006	1.99	2.01	0.46	0.24	0.24	0.029	0.032
2007	**2.72**	**2.78**	**0.57**	**0.24**	**0.18**	**0.032**	**0.020**
2007	**2.67**	**2.75**	**0.75**	**0.35**	**0.26**	**0.047**	**0.027**
2007	**1.90**	**1.90**	**0.55**	**0.31**	**0.25**	**0.043**	**0.025**
2008	1.65	1.67	0.56	0.26	0.25	0.036	0.049
2008	1.82	1.84	0.51	0.28	0.24	0.031	0.039
2008	2.19	2.21	0.72	0.39	0.26	0.035	0.039
2009	**1.82**	**1.83**	**0.59**	**0.26**	**0.25**	**0.036**	**0.028**
2009	**2.27**	**2.29**	**0.63**	**0.27**	**0.26**	**0.040**	**0.032**
2009	**2.30**	**2.30**	**0.58**	**0.27**	**0.28**	**0.045**	**0.034**
2010	1.61	1.62	0.63	0.31	0.28	0.032	0.038
2010	1.93	1.95	0.75	0.38	0.31	0.040	0.047
2010	1.79	1.80	0.60	0.38	0.31	0.042	0.042
2011	**2.39**	**2.41**	**0.65**	**0.32**	**0.31**	**0.051**	**0.042**
2011	**1.61**	**1.61**	**0.53**	**0.26**	**0.30**	**0.038**	**0.038**
2011	**1.76**	**1.78**	**0.48**	**0.28**	**0.33**	**0.044**	**0.049**
2012	1.28	1.29	0.48	0.27	0.23	0.027	0.030
2012	1.71	1.73	0.56	0.27	0.25	0.031	0.030
2012	1.40	1.41	0.54	0.29	0.27	0.033	0.038
2013	**1.66**	**1.66**	**0.54**	**0.32**	**0.32**	**0.050**	**0.035**
2013	**1.87**	**1.87**	**0.50**	**0.24**	**0.20**	**0.025**	**<0.023**[2]
2013	**1.50**	**1.50**	**0.49**	**0.27**	**0.29**	**0.041**	**0.031**
2014	**1.43**	**1.43**	**0.62**	**0.35**	**0.29**	**0.042**	**0.022**
2014	**1.57**	**1.57**	**0.46**	**0.25**	**0.18**	**0.036**	**<0.023**
2014	**1.33**	**1.34**	**0.54**	**0.31**	**0.28**	**0.037**	**0.025**

[1] Reported concentrations are the average of duplicate analyses. Results in bold generated in the present study. Other data from Gebbink et al. (2015).

[2] <values indicating the method quantification limit (MQL).

Results and discussion

Concentrations of PFAS in the serum pools are shown in Tables 3 and 4, and plots of PFAS concentrations against year of sampling are shown in Fig. 1 and 2. The concentrations of PFBA, PFHxA, PFHpA are not reported, due to inconsistencies in measured levels compared to those reported by Gebbink et al. (2015). The results of these PFAA will be reported in the 2017 report. Levels were <MQL for most samples in the case of PFDS (<0.019 ng/g), PFPeA (<1.44 ng/g), br-PFOA (<0.045 ng/g) and PFTeDA (<0.18 ng/g).

As in the study by Glynn et al. (2012), covering the period 1996-2010 and using a different analytical method, levels of PFOS and PFOA decreased between 1997-2014, and levels of PFHxS, PFDA and PFNA increased (Table 5). This indicates that the two different analytical methods generated similar trend results. In the present study the MQLs for PFUnDA, PFDoDA and PFTrDA were lower and increasing temporal trends were evident also for PFUnDA and PFDoDA (Table 5). A closer look at the results (Fig. 2) suggests an increasing trend also of PFTrDA 1997-2010, and a levelling off in later years. A levelling off of the increasing trend is also suggested for PFNA, PFDA, PFUnDA and PFDoDA since 2010 (Fig. 2). The trends have to be followed-up in the future to confirm that the exposure of the population of young women to these long-chain PFCAs is levelling off, or is even decreasing.

No statistically significant temporal trend of PFBS 1997-2014 could be detected in the present study. If the statistical analysis was restricted to the period 1997-2010, an increasing temporal trend was indicated (5.6% per year, p=0.060). In Glynn et al. (2012), an increase of PFBS by 11% (p<0.001) per year was reported between 1996 and 2010. As pointed out by Gebbink et al. (2015), the differences in observed trends could be due to differences in composition of the pooled samples, since each pool from the early study period was composed of more than 10 individual samples in Glynn et al. (2012) and since the present study is lacking pools from 1996 (too few individual samples). Moreover, the analytical methods differed between the studies.

A study of differences in PFAS levels in individual serum from the Uppsala mothers between 1996-1999 and 2008-2011, with high statistical power, has shown that the population in Uppsala has experienced increased PFBS exposure since 1996 (Gyllenhammar et al. 2015). The increase in PFBS levels, as well as of PFHxS levels, during the study period is due to exposure of the study participants to these PFAA from contaminated drinking water in Uppsala (Gyllenhammar et al. 2015).

In 2012 the polluted drinking water production wells were taken out of production in Uppsala. Based on the new data from 2007, 2009, 2011, 2013 and 2014 a plateau in the PFHxS trend is indicated at the end of the study period (Fig. 1). However, the trend has to be followed-up before firm conclusion can be made weather a change in the PFHxS trend has occurred, as a result of the decreased PFAA contamination in Uppsala drinking water.

The decrease in PFOS is a reflection of the phase-out of PFOS-related production. The slower decline in PFOA levels may be due to a slower world-wide phase-out of production of PFOA and PFOA-related compounds.

Table 5. Annual change in concentrations of PFAS in blood serum 1997–2014[1].

Compound	**N**	**Change (%)** Mean (SE)	**R^2 (%)**	**p**	**Change (%)[2]** Mean
PFBS	42			ns	11
PFHxS (total)	42	5.9 (0.91)	52	<0.001	8.3
PFHxS (linear)	42	5.6 (1.1)	37	<0.001	
PFHxS (branched)	42	6.0 (0.90)	52	<0.001	
PFOS (total)	42	-7.9 (0.51)	86	<0.001	-8.4
PFOS (linear)	42	-8.4 (0.46)	86	<0.001	
PFOS (branched)	42	-8.9 (0.56)	86	<0.001	
PFOA (total)	42	-3.3 (0.43)	58	<0.001	-3.1
PFOA (linear)	42	-3.2 (0.43)	59	<0.001	
PFNA	42	3.3 (0.51)	51	<0.001	4.3
PFDA	42	3.3 (0.54)	48	<0.001	3.8
PFUnDA	42	3.6 (0.53)	53	<0.001	ns
PFDoDA	42	3.6 (0.61)	46	<0.001	nd
PFTrDA	42			ns	nd

[1]SE=standard error, ns=not significant, nd=not detected.
[2]Glynn et al. (2012)

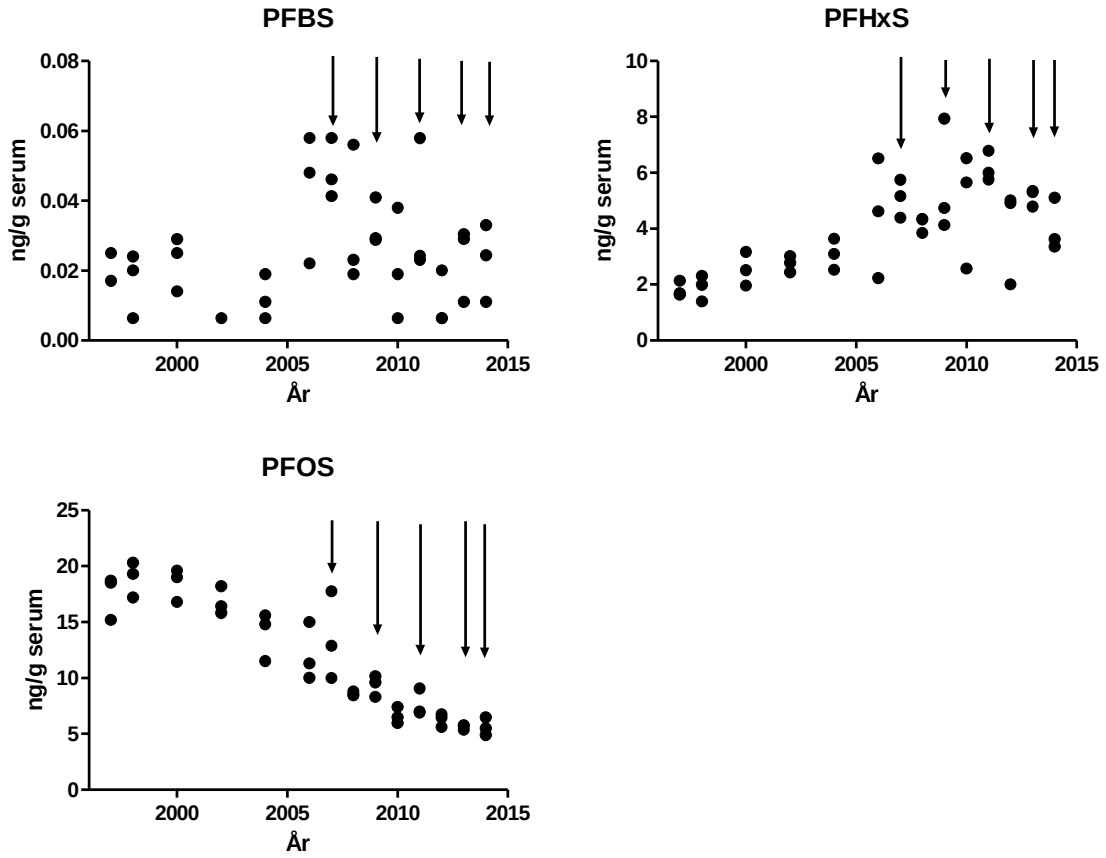

Figure 1. Concentrations of perfluoroalkyl sulfonic acids (PFSA) in pooled samples (3 pools per year, N=42 pools) of blood serum from first-time mothers in Uppsala sampled between 1997 and 2014. N= 9-10 individual samples per pool. The arrows show the data generated in the present study and the rest of the data has been reported by Gebbink et al. (2015).

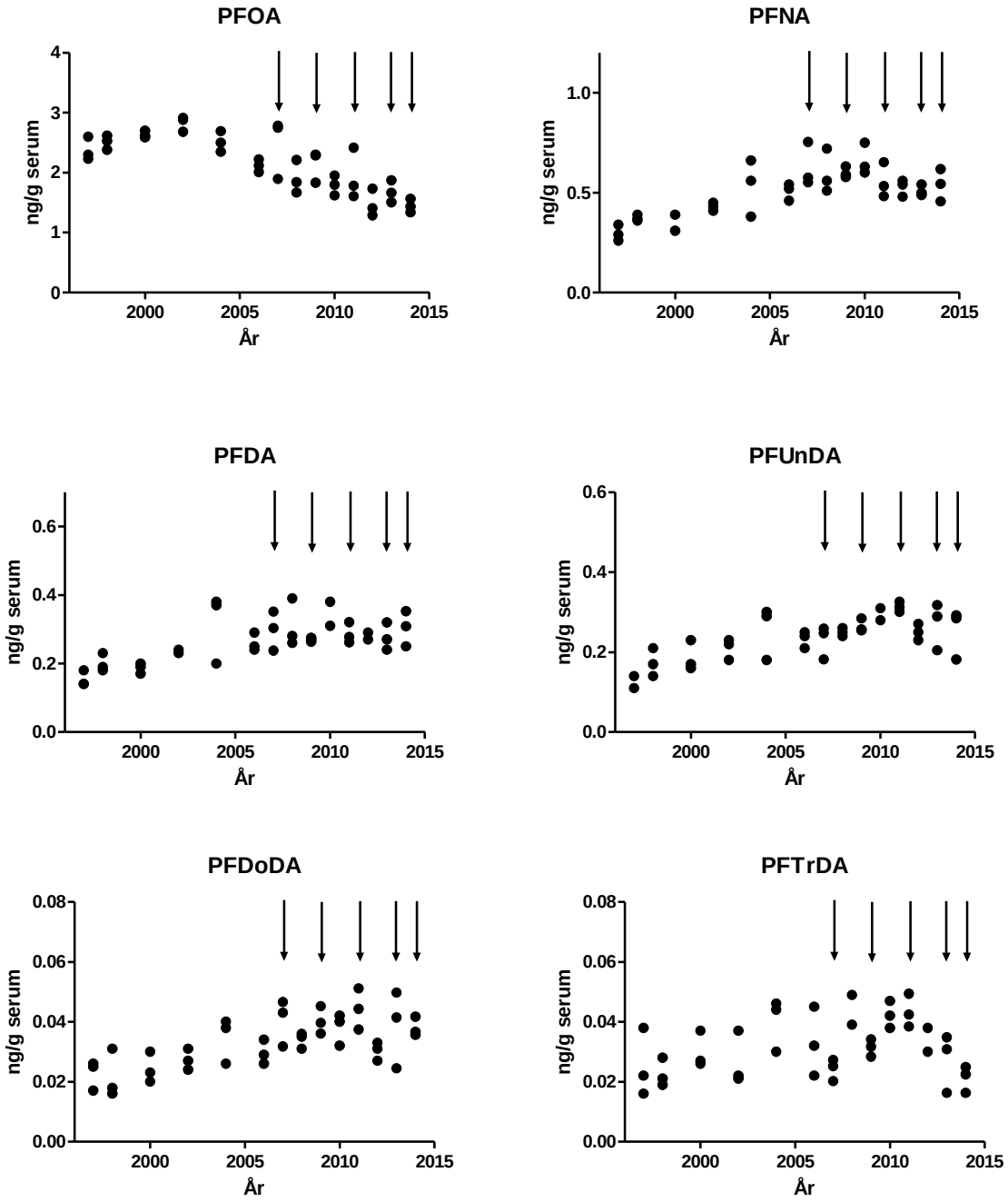

Figure 2. Concentrations of perfluoroalkyl carboxylic acids (PFCA) in pooled samples (3 pools per year, N=42 pools) of blood serum from first-time mothers in Uppsala sampled between 1997 and 2014. N= 9-10 individual samples per pool. The arrows show the data generated in the present study and the rest of the data has been reported by Gebbink et al. (2015).

References

3M (2002a). "Environmental, health, safety, and regulatory (EHSR) profile of perfluorobutane sulfonate (PFBS)." Technical Data Bulletin http://www.fluoro.co.kr/tt/site/db/board/product_05/upload/1_10000/2/%C8%AF%B0%E6%BE%C8%C0%FC%BC%BA%C0%DA%B7%E1.pdf.

3M (2002b). "Identification of fluorochemicals in human sera. III. Pediatric participants in a group A Streptococci clinical trial investigation." Final Report from the Epidemiological Department, 3M Company.

Gebbink, W.A., A. Glynn, et al. 2015. Temporal changes (1997-2012) of perfluoralkyl acids and selected precursors (including isomers) in Swedish human serum. Environ Pollut 199, 166-173.

Giesy, J. P. and K. Kannan (2001). "Global distribution of perfluorooctane sulfonate in wildlife." Environ Sci Technol 35: 1339-1342.

Glynn, A., U. Berger, A. et al. 2012. Perfluorinated alkyl acids in blood serum from primiparous women in Sweden: Serial sampling during pregnancy and nursing, and temporal trends 1996-2010. Environ Sci Technol 46, 9071-9079.

Gyllenhammar, I., U. Berger, et al. 2015. Influence of contaminated drinking water on perfluoralkyl acid levels in human serum – A case study from Uppsala, Sweden. Environ Res 140, 673-683.

Houde, M., J. W. Martin, et al. (2006). "Biological monitoring of polyfluoroalkyl substances: A review." Environ Sci Technol 40(11): 3463-3473.

Kannan, K., S. Corsolini, et al. (2004). "Perfluorooctanesulfonate and related fluorochemicals in human blood from several countries." Environ Sci Technol 38: 4489-4495.

Kissa, E. (2001). Fluorinated surfactants and repellents. New York, Marcel Dekker.

Prevedouros, K., I. T. Cousins, et al. (2006). "Sources, fate and transport of perfluorocarboxylates." Environ Sci Technol 40: 32-44.

US EPA. 2015. http://www.epa.gov/oppt/pfoa/.