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Two-year follow-up biomonitoring pilot study of residents' and controls' PFC plasma levels after PFOA reduction in public water system in Arnsberg, Germany

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ABSTRACT

Residents in Arnsberg, Germany, had been supplied by drinking water contaminated with perfluorooctanoate (PFOA). Biomonitoring data from 2006 evidenced that plasma PFOA concentrations of residents from Arnsberg were 4.5–8.3 times higher than those in reference groups. The introduction of charcoal filtration in July 2006 distinctly reduced PFOA concentrations in drinking water. Our one-year follow-up study showed a 10–20% reduction of PFOA plasma levels in residents from Arnsberg. Here we report the first results of the two-year follow-up study Arnsberg 2008. Additionally, the results of the two-year follow-up examination of the reference group are included. Paired plasma samples of 138 study participants (45 children, 46 mothers and 47 men) collected in 2006 and 2008 were considered in the statistical analyses. Within the two years plasma concentrations of PFOA, perfluorooctanesulfonate (PFOS) and perfluorohexanesulfonate (PFHxS) decreased in residents from Arnsberg and in control groups. The geometric means of PFOA plasma levels declined by 39% (children and mothers) and 26% (men) in Arnsberg and by 13–15% in the corresponding subgroups from the reference areas. For the population from Arnsberg a geometric mean plasma PFOA half-life of 3.26 years (range 1.03–14.67 years) was calculated. Our results confirm an ongoing reduction of the PFOA load in residents from Arnsberg. The decline of PFC levels in plasma of participants from the reference areas reflects the general decrease of human PFC exposure during the very recent years.

Introduction

Perfluorinated compounds (PFCs) are extensively used since the 1950s. They can be found worldwide in different environmental matrices, in wildlife and in humans. Long human plasma half-lives of some PFCs, like perfluorooctanoate (PFOA) and perfluorooctanesulfonate (PFOS), have been observed. Health concern is raised due to effects observed in animal studies, namely hepatotoxicity, carcinogenicity, reproductive and developmental toxicity (Lau et al., 2007). There are indications that a human PFC exposure may influence pregnancy outcome, however the results are inconsistent (Fei et al., 2007, 2008; Nolan et al., 2009). Existing information on the sources of the background exposure of the general population indicates a major role of dietary intake (Fromme et al., 2009). Additional exposure to PFOA via considerably contaminated drinking water has been observed in water districts near a chemical plant in Little Hocking, Ohio, USA (Emmett et al., 2006), in Arnsberg, Germany (Hölzer et al., 2008) and in Minnesota, USA (MDH, 2009). In Little Hocking and Arnsberg, biomonitoring studies showed a high internal PFOA load of residents, which was clearly related to the drinking water contamination (Emmett et al., 2006; Hölzer et al., 2008). In both locations, follow-up biomonitoring studies are ongoing to examine the trend of PFC concentrations in plasma, to calculate half-life elimination rates and to find out if the high PFOA exposure may cause health effects in the affected residents (Hölzer et al., 2009; Frisbee et al., 2009; Steenland et al., 2009; Bartell et al., 2010).

The drinking water contamination in Arnsberg was detected by Skutlarek et al. (2006). They reported high levels of PFOA in the rivers Rhine, Ruhr and Moehne (confluent of the river Ruhr, PFOA levels of up to 7070 ng/l), as well as in nearby public water supplies using river water to produce drinking water (500–640 ng/l). This environmental pollution was mainly caused by a so called soil improver mixed with industrial waste that was applied on agricultural areas on the upper reaches of the river Moehne (Skutlarek et al., 2006). 40,000 residents living in certain districts of Arnsberg

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had been constantly supplied by tap water that was markedly contaminated with PFOA. In July 2006, activated charcoal filters were installed that efficiently decreased PFOA concentrations in drinking water to levels predominantly under the limit of quantification (LOQ). More details on assessment and management of the PFC contamination in Arnsberg and the affected areas downstream have been summarized previously (Wilhelm et al., 2008).

In September and October 2006, our first biomonitoring study was accomplished to examine 90 children, 164 women and 101 men from Arnsberg who had been supplied by contaminated drinking water (Hölzer et al., 2008). The control group comprised 80 children, 153 mothers and 103 men from the neighboring towns Siegen and Brilon who received water with PFOA levels below the LOQ. In both locations, school beginners and their mothers were asked to participate. For the recruitment of male adults randomly selected residents were interviewed concerning their habits of drinking water consumption and those with highest intake were selected to participate. Geometric mean levels of PFOA plasma concentration of children, women and men from Arnsberg were 22.1 μg/l, 23.4 μg/l and 25.3 μg/l, respectively. They were increased 4.5–8.3 fold in comparison to PFOA levels in the control population. Consumption of PFC-contaminated tap water was a significant predictor of PFOA plasma concentrations (Hölzer et al., 2008). Our one-year follow-up examination conducted in Arnsberg in 2007 revealed a PFOA reduction of 10% (men), 17% (mothers) and 20% (children) during the first year (Hölzer et al., 2009).

Here we report the first results of the two-year follow-up study. Since PFC concentrations have been found to be declining in the general population in recent years (Olsen et al., 2008; Haug et al., 2009), we additionally included residents from the reference areas in the investigation. Moreover, we tried to identify factors influencing the amount of the decline of PFOA plasma concentrations.

Population, methods

Participants

The present survey is a follow-up examination of 138 individuals who already participated in the biomonitoring study in 2006. We considered data of 20–25 children, mothers and men each, from the target area and the reference areas, respectively. In Arnsberg, another analysis of plasma concentrations was offered to all 355 study participants from 2006. Those in each subgroup who first answered the invitation and agreed to a certain appointment were selected and taken in the pilot study group. For the recruitment of participants from the reference groups all 80 children and 80 mothers examined in 2006 were invited. Randomly selected, half of the men ($N = 50$) who took part in the study in 2006 were asked to participate again. All invitees from the control areas who agreed to join the examination were included in the pilot study.

The study was approved by the ethical commission of the Ruhr-University of Bochum and was conducted in accordance with the ethical principles for medical research involving human subjects as defined by the Declaration of Helsinki. Written informed consent was obtained from each subject or parent in the case of children. Information on demographic and occupational characteristics as well as health conditions and drinking water and food consumption had been surveyed during the first biomonitoring study. Within the follow-up study mail questionnaires for self-completion at home elicited information about actual body weight and body height, smoking and drinking habits, smoking exposure, actual drug intake and newly diagnosed diseases since the last study. On the day of the blood withdrawal trained interviewers accomplished a standardized questionnaire on drinking water consumption and food consumption habits since the last study and asked for acute diseases and drug consumption.

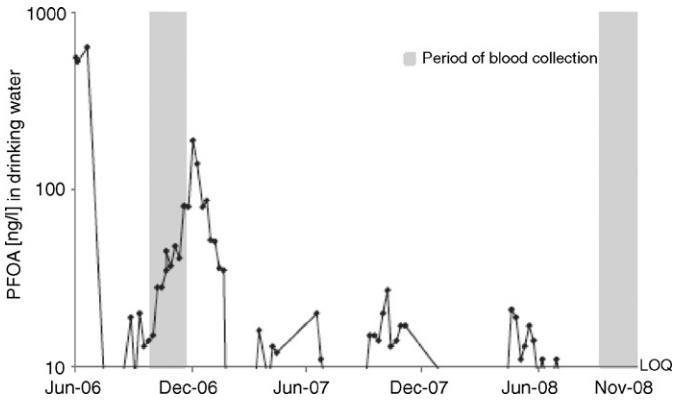

Fig. 1. PFOA concentrations in drinking water (frequency of analysis: weekly) in the waterworks Möhnebogen between May 2006 and November 2008 as published by the North Rhine-Westphalia State Agency for Nature, Environment and Consumer Protection, Germany (http://www.pft.lua.nrw.de/owl/GIS/exhibit/pft_tw.php?exhibit-use-local-resources; retrieved 1st December 2009). Measurement results below the limit of quantification (LOQ) of 10 ng/l are not drawn in the graph.

Sampling and chemical analysis

Blood samples were taken between 14 October and 11 November 2008. All materials used for venipuncture and processing had been tested for PFC contamination on the occasion of the first study without any findings. For PFC determinations 4.9 ml of blood were drawn into an EDTA tube and centrifuged the same day. The resulting plasma was stored at −20 °C and transported to the analytical laboratories in Erlangen, Germany, where analyses for PFOA, PFOS, perfluorohexanesulfonate (PFHxS), perfluorobutanesulfonate (PFBS), perfluorohexanoate (PFHxA) and perfluoropentanoic acid (PFPA) were performed using HPLC/tandem mass spectrometry. Handling of samples, assay procedure and quality control have been performed in the same way as in 2006 (Hölzer et al., 2008).

Calculation of PFOA intake via drinking water

The North Rhine-Westphalia State Agency for Nature, Environment and Consumer Protection, Germany, accomplished weekly analyses of PFOA concentration in drinking water in Arnsberg since May 2006 (Fig. 1). Each study participant's PFOA intake via drinking water between October 2006 and October 2008 was calculated. For each month in this period, arithmetic mean results of the PFOA levels in tap water (usually 4 measurements per month) were multiplied with the amount of individual drinking water consumption, which had been examined in detail in the interviews. For PFOA concentrations below the limit of quantification (LOQ) of 10 ng/l, a value of 5 ng/l was used in the calculations. In contrast to the weekly PFOA-analyses in Arnsberg's drinking water, the PFOA levels in drinking water in Siegen and Brilon have only been measured during each study period. PFOA has not been detected in any of the samples. To calculate the daily total PFOA exposure from all sources, the PFOA intake via drinking water was added to the amount of background exposure of the general population (1.6 ng/kg$_{\text{body weight}}$) as it was evaluated by Fromme et al. (2009).

Statistical analysis

All statistical analyses were carried out with SAS 9.2 (SAS Institute Inc., Cary, NC). A $p < 0.05$ was considered statistically significant. Plasma levels of fluorochemicals below the limit of

Table 1
Characteristics of study groups in target and reference areas in 2008. For age, body mass index (BMI) and daily drinking water consumption arithmetic means (AM), standard deviation (SD) and range are given. The drinking water consumption refers to the time period between October 2006 and October 2008.

	Children		Mothers		Men	
	Arnsberg	Siegen	Arnsberg	Siegen	Arnsberg	Brilon
N	20	25	22	24	23	24
Male [%]	45	52				
Age [years]						
AM ± SD	7.9 ± 0.3	7.8 ± 0.4	38.1 ± 4.7	40.1 ± 3.7	55.2 ± 13.1	52.6 ± 13.9
Range	7.4–8.3	7.3–8.6	27–49	34–47	32–71	23–71
BMI [kg/m^2]						
AM ± SD	16.6 ± 1.2	16.0 ± 1.6	25.1 ± 5.4	24.1 ± 4.5	26.1 ± 3.4	26.5 ± 5.7
Range	14–18	13–20	19–39	20–41	19–33	20–40
Drinking water consumption [l/day]						
AM ± SD	0.3 ± 0.2	0.7 ± 0.5	0.8 ± 0.6	1.6 ± 0.8	1.4 ± 0.8	1.8 ± 0.7
Range	0.0–0.9	0.2–2.2	0–2.8	0.4–2.9	0.5–3.6	1.0–4.1

detection (LOD) (0.1 μg/l for PFOA, PFOS, PFHxS and PFBS; 1.0 μg/l for PFPA, PFHxA) were assigned the midpoint between zero and the LOD. Normality assumptions were tested. The common log transformation resulted in improved distributions of PFC concentrations and was chosen in statistical hypothesis tests. Mean values of demographic characteristics and PFC concentrations in Arnsberg and reference areas were compared using two sample *t*-test. Differences in PFC concentrations between the two examination dates were evaluated with paired two sample *t*-test. Relative reduction of PFC plasma concentrations was calculated as the percentual reduction of the initially measured PFC load within the period from October 2006 to October 2008.

Table 2
Descriptive statistics for PFOA, PFOS and PFHxS plasma concentrations of children, mothers and men from Arnsberg and reference areas in 2006 and 2008.

		N	*N* < LOD	Min	P50	P90	P95	Max	GM	95% CI GM
PFOA (μg/l)										
Children	Arnsberg 2006	20	0	9.6	22.4	37.3	45.7	53.6	23.4	19.2–28.5
	Arnsberg 2008	20	0	7.9	13.0	19.9	24.0	26.6	13.2	11.4–15.4
	Siegen 2006	25	0	2.3	5.9	8.0	10.1	11.5	5.5	4.6–6.5
	Siegen 2008	25	0	2.0	4.9	6.8	7.2	8.3	4.5	3.8–5.2
Mothers	Arnsberg 2006	22	0	6.4	25.1	41.9	53.5	54.8	23.6	19.2–29.0
	Arnsberg 2008	22	0	3.5	14.4	21.9	23.0	38.4	13.3	10.6–16.7
	Siegen 2006	24	0	0.8	3.8	5.8	5.9	8.3	3.2	2.5–4.1
	Siegen 2008	24	0	0.8	2.8	5.0	5.8	7.9	2.6	2.0–3.3
Men	Arnsberg 2006	23	0	15.1	32.8	44.3	49.2	77.5	30.3	25.3–36.3
	Arnsberg 2008	23	0	8.4	22.6	38.8	43.9	52.3	21.7	17.7–26.6
	Brilon 2006	24	0	2.8	7.2	10.9	12.4	15.3	6.9	5.7–8.3
	Brilon 2008	24	0	2.5	5.5	9.3	11.4	13.9	5.7	4.7–7.0
PFOS (μg/l)										
Children	Arnsberg 2006	20	0	2.6	5.1	9.2	15.0	20.6	5.1	4.1–6.4
	Arnsberg 2008	20	0	2.4	3.6	6.0	12.4	18.7	4.1	3.4–5.1
	Siegen 2006	25	0	2.6	5.2	10.5	12.2	12.7	5.3	4.5–6.3
	Siegen 2008	25	0	1.8	3.8	6.4	7.0	9.1	3.9	3.4–4.6
Mothers	Arnsberg 2006	22	0	2.7	5.5	10.4	12.3	12.7	5.7	4.7–6.8
	Arnsberg 2008	22	0	2.1	4.0	9.2	9.5	10.5	4.3	3.6–5.2
	Siegen 2006	24	0	1.8	5.7	11.8	13.5	21.5	5.6	4.4–7.3
	Siegen 2008	24	0	1.8	4.1	8.7	9.1	15.0	4.3	3.4–5.4
Men	Arnsberg 2006	23	0	5.2	12.7	24.3	30.2	33.3	12.7	10.3–15.7
	Arnsberg 2008	23	0	4.1	9.7	19.1	19.8	23.5	9.3	7.5–11.4
	Brilon 2006	24	0	3.4	9.2	25.3	25.6	26.4	10.4	8.1–13.3
	Brilon 2008	24	0	2.5	8.0	14.9	16.9	21.1	8.0	6.3–10.1
PFHxS (μg/l)										
Children	Arnsberg 2006	20	0	0.5	1.2	1.9	7.7	13.4	1.3	0.9–1.7
	Arnsberg 2008	20	0	0.5	0.7	1.6	7.0	11.8	1.0	0.7–1.3
	Siegen 2006	25	0	0.4	0.9	2.7	2.8	9.1	1.0	0.8–1.4
	Siegen 2008	25	4	<0.1	0.5	1.4	1.9	4.2	0.5	0.3–0.9
Mothers	Arnsberg 2006	22	1	<0.1	1.0	1.5	1.5	1.9	0.9	0.7–1.2
	Arnsberg 2008	22	0	0.4	0.8	1.0	1.6	1.9	0.8	0.7–0.9
	Siegen 2006	24	1	<0.1	0.7	1.5	1.8	2.1	0.6	0.4–0.9
	Siegen 2008	24	11	<0.1	0.5	1.1	1.3	1.8	0.2	0.1–0.4
Men	Arnsberg 2006	23	0	1.6	2.9	3.6	4.0	4.5	2.7	2.4–3.0
	Arnsberg 2008	23	0	1.3	2.3	3.2	3.3	3.7	2.3	2.1–2.6
	Brilon 2006	24	0	1.0	2.1	3.7	4.4	5.4	2.2	1.8–2.6
	Brilon 2008	24	0	0.5	1.4	3.0	4.1	4.1	1.6	1.2–2.0

Abbreviations: LOD = limit of detection (LOD = 0.1); Min = minimum; P50, P90, P95 = 50th, 90th, 95th percentile; Max = maximum; GM = geometric mean; 95% CI = 95% confidence interval of the geometric mean.

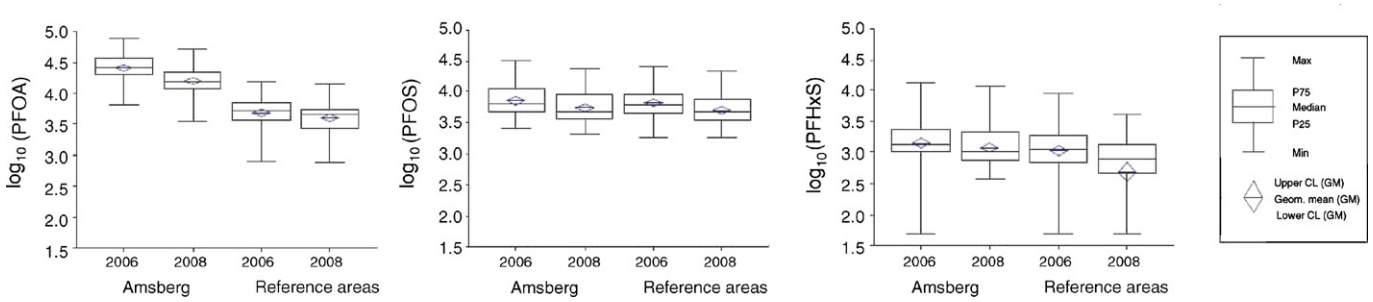

Fig. 2. Boxplots of logarithmic PFOA, PFOS and PFHxS blood plasma concentrations [ng/l] in 2006 and 2008, stratified by location. *Abbreviations*: Max = maximum; Min = minimum; P25, P75 = percentiles; GM = geometric mean; CL = 95% confidence limit of the geometric mean.

Assuming a first order elimination the plasma half-life of PFOA was calculated as follows:

$$t_{1/2} = -\log 2 \times \frac{2}{\log(\text{plasma PFOA in 2008}/\text{plasma PFOA in 2006})}$$

Multivariate linear regression was performed with the data of the adult study participants from Arnsberg and the reference areas to assess factors affecting the relative reduction of PFOA levels. Age data of one mother from Siegen was missing. Thus, 92 residents were included in the analysis. Independent variables were chosen based on bivariate calculations (inclusion if $p < 0.05$) (domicile, age, sex) and specific assumptions (estimated daily PFOA exposure in the period between the samplings, body mass index (BMI)).

Results

Concentrations of PFCs in plasma samples were available from 20 children, 22 women and 23 men living in the districts of Arnsberg, where contaminated tap water was provided until July 2006 and from 25 children, 24 women and 24 men belonging to the reference groups in Siegen and Brilon. Subgroups from target and control areas were comparable in regard to age and BMI, but residents from Arnsberg consumed significantly less drinking (tap) water in the period between October 2006 and October 2008 (Table 1).

Table 2 presents the distribution of PFOA, PFOS and PFHxS levels in 2006 and 2008 stratified by study group. PFOA and PFOS have been detected in all plasma samples. 98.6% (2006) and 89% (2008) of the PFHxS plasma concentrations were above the LOD. PFBS was only detected in 7% of the blood plasma samples in 2006 and in 0.7% in 2008. PFPA and PFHxA were not detected in any of the samples in both years.

As shown in Fig. 2, PFOA concentrations of residents markedly decreased within the two years between the blood examinations in Arnsberg as well as in the reference areas ($p < 0.001$). In 2008, mean PFOA plasma levels of residents in Arnsberg still were 2.9 (children), 5.0 (mothers) and 3.8 (men) times higher compared with the control groups. For comparison, in 2006 the PFOA-concentrations in Arnsberg were 4.5–8.3 times higher compared with controls. PFOS plasma concentrations also declined significantly in both study groups ($p < 0.001$ in each location) as well as PFHxS levels ($p = 0.002$ in Arnsberg and $p < 0.001$ in the reference areas).

Table 3 shows the geometric means of relative PFC reduction in plasma during the two years between the analyses considered. PFOA plasma concentrations in Arnsberg declined by 39% in women and children but only decreased by 26% in men. In Siegen and Brilon, the PFOA reduction was considerably lower and with 13–15% homogeneous in all study groups. PFOA levels decreased in all study participants from Arnsberg, while in the reference areas five residents had increasing PFOA concentrations. Geometric means of PFOS reduction varied from 20 to 29% in both target and reference groups. Rates of PFHxS reduction were 14–41%. In each subgroup higher PFHxS reduction was observed in the reference areas.

Apart from these group differences in relative PFOA plasma reduction other factors potentially affecting PFOA reduction were examined. A distinct positive association between PFOA plasma concentrations from the year 2006 and absolute reduction of PFOA could be observed (Fig. 3).

The relative reduction of PFOA plasma concentrations by age group and location is presented in Table 4. For all study participants, as well as the subgroups from Arnsberg and the reference areas, the highest PFOA reduction was observed in the 20–40 year old residents and declined with higher age. The reduction of PFOA in children was lower than in adults under 40 years.

Table 5 shows the results of a linear multivariate regression analysis on the relative reduction of PFOA blood plasma concentration with the data of all adult study participants. The estimated mean daily PFOA intake in the period surveyed, place of residence, age, BMI and sex were chosen as independent variables. The proportion of variance predictable with the model variables was 0.40

Table 3
Geometric mean (GM), 95% confidence intervals (95% CI) and range of the relative reduction of PFC plasma levels [%] between 2006 and 2008.

	Children		Mothers		Men	
	Arnsberg	Siegen	Arnsberg	Siegen	Arnsberg	Brilon
PFOA						
GM	39.2	13.4	39.4	15.2	25.5	13.8
95% CI	31.6–48.5	8.0–22.5	33.5–46.3	9.3–24.8	21.3–30.5	9.9–19.3
Range	9.0–58.9	0.0–34.0	13.9–73.9	−26.8 to 38.7	10.8–47.4	−9.6 to 29.6
PFOS						
GM	20.1	28.8	21.7	19.6	25.0	20.2
95% CI	14.7–27.6	24.2–34.3	16.0–29.4	14.6–26.3	21.5–29.0	14.8–27.8
Range	−26.8 to 43.0	−14.0 to 71.1	−20.6 to 53.0	2.9–48.5	13.3–46.3	−7.9 to 52.1
PFHxS						
GM	18.7	36.1	29.6	41.4	14.3	23.1
95% CI	10.4–33.7	26.9–48.4	24.7–35.4	28.4–60.3	10.4–19.7	17.4–30.8
Range	−6.0 to 43.2	−35.9 to 94.6	0.0–49.2	−16.9 to 93.8	−21.4 to 33.5	4.7–56.7

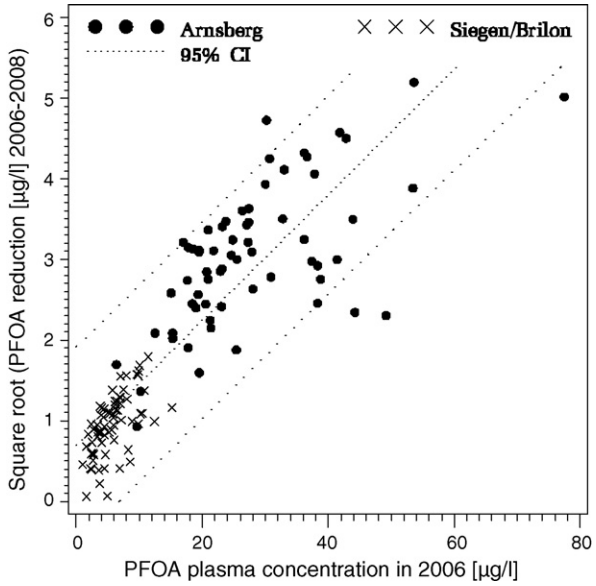

Fig. 3. Scatterplot of PFOA plasma concentrations in 2006, by PFOA reduction between 2006 and 2008 (square root transformation shown).

Table 4
Geometric mean of the relative reduction of PFOA plasma concentration [%] between 2006 and 2008 by age group [age in 2006] and location (missing age data of one mother from Siegen.).

Subgroup		Age group [years]			
		<9	20–40	40–60	>60
All	*N*	45	36	38	18
	PFOA reduction [%]	21.9	26.8	19.2	16.1
Arnsberg	*N*	20	19	16	10
	PFOA reduction [%]	39.2	41.1	28.8	22.1
References	*N*	25	17	22	8
	PFOA reduction [%]	13.4	16.6	13.9	10.2

(adjusted R^2). The regression analysis indicated statistical significance for a negative association of the relative PFOA reduction with age (younger people had higher elimination rates) and for a positive association with the domicile Arnsberg. There was no evidence of dependence between relative PFOA reduction on the one hand and sex, BMI or PFOA exposure via drinking water after 2006 on the other hand.

The average (geometric mean) half-life of PFOA in 65 study participants from Arnsberg was 3.26 years (range: 1.03–14.67 years). Regarding the half-lives by quartiles of initial PFOA plasma concentrations no clear differences can be observed (quartile 1 [<19.5 µg/l]: 3.32; quartile 2 [19.5–25.4 µg/l]: 3.39; quartile 3 [25.5–36.3 µg/l]: 2.51; quartile 4 [>36.3 µg/l]: 4.40 years.

Table 5
Linear multivariate regression analysis on the reduction of PFOA blood plasma concentration [%] between 2006 and 2008. Adult study participants ($N = 92$) (missing age data of one mother from Siegen). Adjusted $R^2 = 0.40$. The PFOA intake refers only to the consumption of drinking water between October 2006 and October 2008; other sources are not considered.

	Reduction of PFOA [%]			
	β	95% CI	p	SE
Male sex	−3.258	−9.936 to 3.419	0.335	−0.101
PFOA intake [ng/day]	0.140	−0.199 to 0.480	0.414	0.083
Age [years]	−0.357	−0.618 to −0.095	0.008	−0.275
Domicile Arnsberg	16.810	10.689 to 22.932	<0.0001	0.523
BMI [kg/m^2]	0.236	−0.379 to 0.851	0.448	0.065

Abbreviations: β = parameter estimate; CI = confidence interval; SE standardized estimate.

Discussion

Some differences in the characteristics of the whole study group from 2006 (Hölzer et al., 2008) and the subgroup of this pilot study could be detected. Participants of the pilot study were older and had slightly higher PFOA plasma concentrations in 2006 (geometric mean whole group: 9.93 µg/l; this study: 10.74 µg/l). These differences were accepted because comparisons in this study do not refer to the whole study group from 2006.

In 2008, 75% of the children, 73% of the mothers and 96% of the men from Arnsberg still presented PFOA plasma concentrations that exceeded the reference value of 10 µg/l set up by the German Human Biomonitoring Commission (Umweltbundesamt, 2009). However, the PFOA levels of all children and mothers and 92% of the men from the reference groups were below the PFOA reference value. In 5% of the children from Arnsberg PFOS plasma levels above the reference value of 10 µg/l were measured. All mothers presented PFOS plasma concentrations <20 µg/l (reference value for women), and PFOS levels of all men were <25 µg/l (reference value for men). The PFOS levels measured in the reference areas all fell below the respective reference values.

The decrease of PFOA plasma levels in Arnsberg seems to reflect both a general reduction of human PFOA burden and a specific decrease due to the considerable reduction of exposure via drinking water. Within two years, between October 2006 and October 2008, PFOA plasma concentrations declined significantly by 39% (mothers and children) and 26% (men) in the population that had been exposed to contaminated drinking water. The clear, but slow reduction of PFOA plasma concentrations of residents from Arnsberg has already been observed in the one-year follow-up study (Hölzer et al., 2009). In the reference groups, the decrease of PFOA plasma concentrations was lower (13–15%). The PFOS plasma concentrations declined to a similar degree (about 20%) in target and reference areas. The geometric mean rates of relative PFHxS reductions (14–41%) were comparable to the reduction rates of PFOA. This may indicate that PFHxS is also eliminated slowly from humans. This assumption is supported by a recent study on the elimination pharmacokinetics in monkeys showing half-life for PFHxS in the range of that for PFOS (Lieder et al., 2009). But relative PFHxS reductions were more pronounced in Siegen and Brilon than in Arnsberg. It has to be considered that the absolute decline was small because PFHxS levels were close to the limit of detection. Minor fluctuations can result in considerable rates of in- or decrease, as it is reflected by the wide range of the reduction rate (Table 3).

The observations in the reference groups are in accordance with time trend data from international biomonitoring studies describing declining levels of PFC in the general population since the year 2000 without examination of within-person change. A Norwegian study described an increase of PFOA and PFOS concentrations until 2000 and a subsequent decrease of the serum levels (Haug et al., 2009). A comparison of plasma samples from American blood donor centers from 2000 to 2001 with samples collected in 2006 also presented a reduction of PFOA, PFOS and PFHxS levels (Olsen et al., 2008). However, a Japanese study reported rising PFOS levels and to a greater amount increasing PFOA levels for the period of 1977 to 2003 in Miyagi; only a discrete PFOS increase could be measured in Akita (Harada et al., 2004).

In a first and simple calculation with the data of the study group from Arnsberg, the geometric mean half-life was 3.26 years. Some limitations of this estimation have to be considered. The number of samples ($N = 65$) is relatively small and only two blood samplings

within two years built the database. The exact amount and duration of the PFOA contamination of the drinking water are unknown and the PFOA exposure (via drinking water and other sources) after filter installation has not been estimated, so these factors were not considered in half-life calculations. With our data we were not able to estimate the PFOA background exposure of the study population. The decline of PFOA concentrations in the reference groups suggests a decrease of the PFOA background exposure. Although based on animal studies with high PFC doses multicompartment models for PFOA toxicokinetics were suggested (Tan et al., 2008), the use of a one compartment model may be appropriate in a human biomonitoring study regarding long-term PFOA plasma trends in a relatively low exposed population.

Only few data on repeated PFC analyses in humans have been published. Bartell et al. (2010) examined 197 residents with PFOA serum concentrations higher than 50 μg/l, who had been supplied by PFOA-contaminated drinking water in Little Hocking, Ohio and Lubeck, West Virginia, USA. Repeated samples were taken before and up to one year after activated carbon filtration was installed. The preliminary estimate of average PFOA serum half-life was 2.3 years (95% CI, 2.1–2.4). In a five-year follow-up study on 26 retired US fluorochemical production workers with mean PFOA serum concentrations of 691 μg/l, a geometric half-life of 3.5 years was calculated for PFOA (Olsen et al., 2007). The average half-life estimations in the three above-mentioned follow-up studies are relatively close to each other. A comparison has to consider the different sample periods and the fact that both US studies examined populations with much higher PFOA concentrations than in the group from Arnsberg. The influence of the background exposure may be greater in the study group from Arnsberg resulting in overestimated half-lives. This effect could not be discovered within the cohort from Arnsberg itself: geometric means of half-life calculations did not differ significantly in the quartiles of baseline PFOA concentrations. Obviously, PFOA levels of the exposed population were uniform enough to result in stable half-life estimations.

Supplemental explorative analyses were conducted to identify associations of elimination rates with certain covariates. These calculations have to be carefully interpreted regarding the high grade of interaction of the potential covariates. Male adult study participants were selected from all age-groups, while all female participants were mothers of pre-school children. The male subjects were selected because of their high tap water consumption, so they were higher exposed to PFOA and had higher PFOA plasma concentrations.

The geometric mean of PFOA reduction from plasma was considerably lower for males than for women and children (Table 3), but sex was no significant predictor for PFOA elimination in the multivariate regression model chosen (Table 5). This might be explained by the fact that male study participants were older than females. Age appeared to be an influencing factor in the bivariate analysis (Table 4) as well as a significant predictor in the regression.

Especially mothers and children from Arnsberg reduced their drinking water consumption since they knew about the PFOA contamination of the tap water. The low drinking water intake could be discussed as a reason why relative reduction of PFOA plasma concentrations was higher in women and children than in men. Regarding the ongoing higher tap water consumption of male study participants after the installation of filters in the waterworks (Table 1), and knowing about the low, but measurable PFOA contamination of the water in times of declining filter performance (Fig. 1), it was imaginable that drinking water still was an important source of PFOA exposure. However, in this first approach the calculated PFOA intake via tap water between 2006 and 2008 was no significant predictor on PFOA plasma reduction (Table 5). Due to low numbers of PFOA concentrations in tap water above LOQ, the calculation of PFOA intake may not reflect the true intake.

Bivariate calculations and the regression analysis identified the resident's domicile as a significant predictor for their PFOA reduction rates. The faster decrease in PFOA plasma concentrations of participants from Arnsberg seems to reflect the elimination of the additional contamination. Other variables that were associated with PFC blood concentration in earlier studies were the consumption of locally grown fruit and vegetables or locally caught fish (Hölzer et al., 2008). These variables potentially influence PFOA elimination, but were not considered because of the small number of residents consuming local products.

In conclusion, the presented study results confirm the ongoing reduction of the PFOA load in formerly exposed residents from Arnsberg. The decline of PFC levels in participants from the reference areas reflects the general decrease of human PFC exposure during the recent years.

Data of all participants of the follow-up study in Arnsberg will be analyzed to provide more reliable information on the decline and half-life of PFOA plasma concentrations in Arnsberg.

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