Environmental Research 195 (2021) 110795

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Per- and polyfluoroalkyl substances in serum and associations with food consumption and use of personal care products in the Norwegian biomonitoring study from the EU project EuroMix

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ARTICLE INFO

Keywords:
Perfluoroalkyl
Polyfluoroalkyl
Biomonitoring
Food
Personal care products
Serum

ABSTRACT

Background: Human exposure to chemicals through the oral, dermal, or inhalation routes is significant. To assess this exposure, a human biomonitoring study was conducted in Norway to examine the plausibility of source-to-dose calculations for chemical mixtures. Per- and polyfluoroalkyl substances (PFASs) are man-made compounds used for their surfactant properties, and several are persistent and bioaccumulative. Some PFASs are toxic and are regarded as endocrine disruptors and have been shown to suppress immune function and affect cholesterol homeostasis. Using the participants from the EuroMix BM study, we set out to describe PFAS concentrations and to evaluate associations with diet and use of personal care products (PCPs).

Methods: Participants (44 males and 100 females) kept detailed diaries on their food consumption and their PCP use for two non-consecutive days. All urine (24 h) and blood samples were collected at the end of each study day. Levels of 25 PFASs were analysed in serum from study day 1 using a high throughput online solid phase extraction ultra-high-performance liquid chromatography tandem mass spectrometry method. Multivariable linear regressions were performed between each food and PCP category and each chemical and were sex-stratified when the consumption of food or use of PCPs was significantly different between men and women.

Results: Eight PFASs were detected in all analysed samples (PFHxS, PFHpS, PFOS, PFOA, PFNA, PFDA, PFUnDA and PFDoDA), and four PFASs were below the limit of detection (PFOPA, PFDPA, PFHxA, and EtFOSA). Several PFASs were found to be positively associated with fish consumption (PFOS, PFNA, PFUnDA, PFDoDA, PFDA, PFDS and PFTrDA). Sunscreen, mouthwash, and lip gloss/lip balm were found to be positively associated with PFASs (PFOA, PFTrDA, and PFOSA).

Conclusion: The participants in the EuroMix study were exposed to PFASs through their diet and PCP use. Several foods and PCPs were found to be potential sources of exposure to PFASs.

1. Introduction

The human population is constantly being exposed to a mixture of man-made chemicals due to their widespread presence in the environment. Human biomonitoring (BM) studies allow us to measure the internal exposure to these chemicals in biological samples from the participants. These measurements reflect the daily exposure of the participants, aggregating all routes of exposure such as oral, dermal, and inhalation (Gurusankar et al., 2017).

The goal of the EuroMix project was to develop a tiered mechanism-

Abbreviations: (as footnote): LOD, limit of detection; LOQ, limit of quantification; FFQ, food frequency questionnaire; MLR, multivariable linear regression; PCPs, personal care products; PFBS, perfluorobutanesulfonate; PFHxS, perfluorohexanesulfonate; PFHpS, perfluoroheptanesulfonate; PFOS, perfluorooctanesulfonate; PFDS, perfluorodecanesulfonate; PFPeA, perfluoropentanoate; PFHxA, perfluorohexanoate; PFHpA, perfluoroheptanoate; PFOA, perfluorooctanoate; PFNA, perfluorononanoate; PFDA, perfluorodecanote; PFUnDA, perfluoroundecanoate; PFDoDA, perfluorododecanoate; PFTrDA, perfluorotridecanoate; PFTeDA, perfluorotetradecanoate; PFHxPA, perfluorohexylphosphonate; PFOPA, perfluorooctylphosphonate; PFDPA, perfluorodecylphosphonate; PFOSA, perfluorooctanesulfonamide; MeFOSA, N-methyl perfluorooctanesulfonamide; EtFOSA, N-ethyl perfluorooctanesulfonamide; 6:2PAP, 6:2 polyfluoroalkyl phosphate monoester; 8:2PAP, 8:2 polyfluoroalkyl phosphate monoester; 6:2diPAP, 6:2 polyfluoroalkyl phosphate diester; 8:2diPAP, 8:2 polyfluoroalkyl phosphate diester.

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https://doi.org/10.1016/j.envres.2021.110795
Received 19 October 2020; Received in revised form 19 January 2021; Accepted 20 January 2021
Available online 30 January 2021

based testing strategy for refining the risk assessment of combined exposures to different chemicals using both in-silico and in-vitro tools. The Norwegian BM study aimed to assess the aggregated exposures to chemical mixtures present in food and personal care products (PCPs) (Husoy et al., 2019).

Poly- and perfluoroalkyl substances (PFASs) are synthetic organic compounds that have been used since the 1950s for their surfactant and protective properties in coatings for different fabrics and food contact paper due to their grease and water-repellent properties, as well as in aviation hydraulic fluids, fire-fighting foams, and paints (Jian et al., 2018). These molecules are widely studied because of their presence and persistence in the environment. Some PFASs bioaccumulate in wildlife and humans, and due to their persistent, bio-accumulative, and toxic properties some of the PFASs are regarded as substances of very high concern (EFSA, 2020; Sunderland et al., 2019). Among the negative health effects of PFASs in humans are immune effects, thyroid effects, and metabolic disturbances (Sunderland et al., 2019). Recently, their immunotoxic properties were defined as the critical effect for the establishment of a tolerable weekly intake (TWI) for four PFASs by the European Food Safety Authority (EFSA) (EFSA, 2020).

According to the EFSA, many food categories contribute to the exposure to PFASs, including fish, meat, fruits, and eggs. Food and drinking water are the main sources of exposure, but air, dust, and products containing PFASs that come in contact with the skin like PCPs can also contribute to this exposure (Poothong et al., 2020; Sunderland et al., 2019). The aim of this paper is to present the observed concentrations of PFASs in serum from participants in the EuroMix BM study and to describe the associations between sources of exposure such as food consumption and the use of PCPs.

2. Materials and methods

2.1. EuroMix study

The Norwegian EuroMix BM study was a part of the "European Test and Risk Assessment Strategies for Mixtures" project (EuroMix, 633172–2), which was funded by the Horizon 2020 (H2020) programme. The study was previously described in detail in the paper by Husoy et al. (2019).

In short, the EuroMix BM study investigated the exposure to chemical mixtures from foods and PCPs for two non-consecutive days (with a 2–3 week interval between days). The study recruited 144 participants, including 44 men (aged 25–72 years old) and 100 women (aged 24–72 years old). Participants were recruited from governmental institutes, authorities, and universities in the counties of Oslo and Akershus in Norway between September 2016 and November 2017. All of the participants completed the first day of the study, and 140 participants completed the second day (43 men and 97 women). Participants recorded their food consumption and their use of PCPs for the two days in a diary. They also completed a food frequency questionnaire (FFQ) and a questionnaire for socio-demographic and lifestyle characteristics such as gender, education, age, weight, height, and smoking habits. The FFQ and the weighted diaries of the food consumption were registered and coded by a dietician into the food and nutrient calculation system (KBS) at the University of Oslo. For the use of PCPs, participants had to record the type of products, the brand names, and the time of use of these products. Participants collected all urine voids in separate containers and marked these with the time and date during the 24 h recording period. Blood (in total 70 mL per participant per study day) was collected at the end of each 24 h period at the Norwegian Institute of Public Health. Serum, plasma, white and red blood cells, and RNA/DNA were prepared from the blood samples, which were all stored at −80 °C. Two subjects did not give blood samples on day 1, and one subject did not give a blood sample on day 2. The study was approved by the Regional Committees for Medical and Health Research Ethics (REK ID no 2015/1868), and all participants provided their written informed consent.

2.2. Determination of PFASs in serum

In total, 25 different PFASs (6:2PAP, 8:2PAP, 6:2diPAP, 8:2diPAP, PFHxPA, PFOPA, PFDPA, PFBS, PFHxS, PFHpS, PFOS, PFDS, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, PFTeDA, PFOSA, MeFOSA and EtFOSA) were quantified in the 142 serum samples from study day 1.

The simultaneous determination of these PFASs in serum was performed using a high throughput online solid phase extraction ultra-high-performance liquid chromatography tandem mass spectrometry (UHPLC–MS/MS) method as described by Poothong et al. (2017a). Briefly, 50 μL of blood (serum, plasma, or whole blood) was added to a 2 mL centrifuge tube, and then 90 μL of a 5 ng/mL internal standard solution and 90 μL of methanol were added. To precipitate the proteins, the sample tubes were mixed on a whirl mixer and centrifuged for 40 min at 14,000 rpm at 20 °C. The supernatant was transferred to a 250 μL polypropylene vial, and then 80 μL of the sample was analysed by high throughput online solid phase extraction and UHPLC–MS/MS. Finally, PFASs were detected by negative electrospray ionization. A summary of detection frequencies is shown in Table 1 and Table S1.

The limits of detection (LODs) were between 0.002 ng/mL and 0.090 ng/mL, and the limits of quantification (LOQs) were between 0.006 ng/mL and 0.30 ng/mL. The accuracy of the method ranged between 90% and 114% (Poothong et al., 2017a).

2.3. Statistical analysis

The PFAS concentrations in serum were only measured on study day 1. Due to the long half-lives of PFASs in humans, it is assumed that the levels of PFASs on study day 1 and 2 would be very similar. Measurements below the LOD were replaced by the LOD for each compound. Some compounds (PFOPA, PFDPA, PFHxA, MeFOSA, and EtFOSA) were barely detected or were not detected at all, so they were excluded from the statistical analyses in this paper (fewer than 10% of the samples were above the LOD). Concentrations were also reported below the LOQ whenever a signal was observed in the instrument. For concentrations between the LOD and LOQ, the values calculated by the instrument were used.

The measured concentration of PFASs in serum were not normally distributed. A Wilcoxon rank-sum test was performed to test the statistical significance of PFAS serum concentrations between genders. Spearman's rank correlation coefficient was used to evaluate the correlation between PFASs in order to create a heatmap. Multiple comparisons were performed using the Sidak correction $1-(1-\alpha)^{1/n}$, where n is the number of chemicals multiplied by gender, leading to a significance level of $P \leq 0.002$.

Multivariable linear regressions (MLRs) were performed between the PFASs and the different categories of food and PCPs in order to identify exposure sources for these chemicals. Two separate MLR analyses were performed for the food categories, one based on the information from the FFQ (Table 3) and the other based on the information from the day-1 food diary (Table S2). Food and PCP categories with fewer than 10% of the consumers/users were excluded from the MLR analyses. Only PFASs with serum concentrations above their LODs for more than 50% of the samples were included in the MLR (6:2PAP, 8:2PAP, PFPeA, and PFTeDA were excluded). Fifteen different food groups were included for both men and women, namely, bread, grains, cakes, potatoes, vegetables, fruits and berries, meat, fish, eggs, dairy, cheese, butter and oil, sweets, beverages, and other foods. For both genders combined, the 17 independent PCPs were shower gel, shampoo, conditioner, deodorant, facial cleanser, facial moisturiser, body lotion, mouthwash, toothpaste, perfume, lip gloss/lip balm, foundation, hand cream, hair styling, eye makeup, rouge powder, and hand soap. Nineteen independent PCP variables were taken into account for women, including shower gel,

Table 1
Summary data of the detection frequencies of PFASs in serum in ng/mL.

Group	PFAS	Name	LOD	LOQ	% > LOD	LOD < % < LOQ	% > LOQ
PAPs	6:2PAP	6:2 polyfluoroalkyl phosphate monoester	0.09	0.30	15	15	0
	8:2PAP	8:2 polyfluoroalkyl phosphate monoester	0.045	0.15	10	2	8
	6:2diPAP	6:2 polyfluoroalkyl phosphate diester	0.018	0.06	75	47	28
	8:2diPAP	8:2 polyfluoroalkyl phosphate diester	0.009	0.03	55	17	38
PFPAs	PFHxPA	Perfluorohexylphosphonate	0.045	0.15	52	52	0
	PFOPA	Perfluorooctylphosphonate	0.009	0.03	0	0	0
	PFDPA	Perfluorodecylphosphonate	0.009	0.03	0	0	0
PFSAs	PFBS	Perfluorobutanesulfonate	0.009	0.03	68	0	68
	PFHxS	Perfluorohexanesulfonate	0.004	0.012	100	0	100
	PFHpS	Perfluoroheptanesulfonate	0.004	0.012	100	0	100
	PFOS	Perfluorooctanesulfonate	0.009	0.03	100	0	100
	PFDS	Perfluorodecanesulfonate	0.002	0.006	90	0	90
PFCAs	PFPeA	Perfluoropentanoate	0.09	0.30	19	18	1
	PFHxA	Perfluorohexanoate	0.045	0.15	0	0	0
	PFHpA	Perfluoroheptanoate	0.045	0.15	59	1	58
	PFOA	Perfluorooctanoate	0.018	0.06	100	0	100
	PFNA	Perfluorononanoate	0.009	0.03	100	0	100
	PFDA	Perfluorodecanoate	0.045	0.15	100	2	99
	PFUnDA	Perfluoroundecanoate	0.009	0.03	100	0	100
	PFDoDA	Perfluorododecanoate	0.004	0.012	100	0	100
	PFTrDA	Perfluorotridecanoate	0.018	0.06	82	11	71
	PFTeDA	Perfluorotetradecanoate	0.009	0.03	29	1	27
FOSAs	PFOSA	Perfluorooctanesulfonamide	0.002	0.006	66	10	55
	MeFOSA	N-methyl perfluorooctanesulfonamide	0.045	0.15	3	3	0
	EtFOSA	N-ethyl perfluorooctanesulfonamide	0.045	0.15	0	0	0

Table 2
Demographic characteristics of the participants in the EuroMix study presented in Husoy et al. (2019).

Basic characteristics		Males (n = 44)	Females (n = 100)
Age (years, mean ± SD)		43.4 ± 11.7	42.2 ± 12.3
Weight (kg, mean ± SD)		82.0 ± 8.5	65.2 ± 8.9
Height (m, mean ± SD)		1.81 ± 0.06	1.68 ± 0.06
BMI (kg/m^2, mean ± SD)		25.0 ± 2.34	22.8 ± 3.78
Smoking status (n)	Non-smokers	26	64
	Ex-smokers	11	24
	Occasional smokers	7	12
Education (n)	University/college up to 4 years	8	22
	University/college > 4 years	36	78
Women with children (n)	No children	–	45
	1 child	–	19
	2 children	–	26
	3–4 children	–	10

shampoo, conditioner, deodorant, facial cleanser, facial moisturiser, body lotion, anti-wrinkle cream, sunscreen, mouthwash, toothpaste, perfume, lip gloss/lip balm, foundation, hand cream, hair styling products, eye makeup, rouge/powder, and hand soap. Finally, 11 independent PCP variables were taken into account for men, namely shower gel, shampoo, conditioner, deodorant, facial moisturiser, mouthwash, toothpaste, perfume, hair styling products, shaving products, and hand soap. The intake of foods and PCP use were used as categorical variables with 2 or 3 groups (categories) depending on the distribution of each variable. The lowest food intake or PCP use category was used as the reference category in the MLR analyses.

A three-step approach was used for the MLR (Fig. 1). Step 1) A linear regression was performed between each PFAS as the dependent variable and each food or PCP group, age, gender, and education of the participants as independent variables to determine if there was a significant difference ($P < 0.05$) in consumption or use between males and females. The outcome decided if the MLR should be performed separately for males and females. Step 2) A second linear regression between each PFAS as a dependent variable and each food or PCP group as the independent variable was performed to establish if the targeted food or PCP group was contributing to the exposure of the targeted PFAS. Age, gender, and education were included as covariates. The food and PCP groups from these linear regressions with a P-value < 0.2 were included in the final MLR models for each chemical. Step 3) The MLR was performed for each chemical including the independent categorical variables with a P-value below 0.2 from step 2. Males and females were analysed separately if the outcome of step 1 for a food or PCP category was significant and if one of these categories had a P-value below 0.2 for step 2. The results of these MLRs are presented in Tables 3 and 4. Each association between the chemical and the food or PCP group was regarded as significant when the P-value was below 0.05. The serum concentrations of PFASs were log-transformed to approach a normal distribution. Hence, the beta coefficients from all models were exponentiated (base 10) to produce the ratio of the geometrical mean (GM) of contaminant concentration of each category with respect to the GM of the reference category (Barrera-Gomez and Basagana, 2015). R version 3.6.2 was used for the statistical analyses and figures.

3. Results

3.1. Descriptive data

The demographic characteristics of the participants are presented in Table 2 (Husoy et al., 2019). The study participants were recruited from governmental institutes and universities near Oslo, and almost 80% of them had a university degree. More than 60% of the participants never smoked, 24% had quit smoking, and 13% smoked occasionally. The age of the participants was 25–72 years for men and 24–72 years for women.

3.1.1. Diet from the weighed food record and the FFQ

The food groups with the highest absolute intake in grams per day were beverages, fruits and berries, dairy products, vegetables, bread, and grains. There were no significant differences between genders regarding the intake of these food groups, but the energy intake and intake of several micronutrients showed a significant difference between males and females (Husoy et al., 2019) with men having a higher energy

Table 3
Multivariable linear regression analysis showing the association between the concentration of PFASs in serum (log transformed) and the main categorical food variables from the FFQ.

Chemical	Food variable	Gender	Category 1				Category 2			
			GM ratio	95% CI		P-value	GM ratio	95% CI		P-value
6:2diPAP	Potatoes	M	1.40	0.74	2.63	0.29	1.22	0.57	2.48	0.57
	Eggs	F	1.25	0.79	1.98	0.34	1.52	0.09	2.46	0.09
	Dairy	F	0.67	0.42	1.06	0.09	0.73	0.20	1.19	0.20
	Butter and oil	M	0.89	0.45	1.75	0.73	2.03	0.04	4.01	0.04
		F	1.16	0.73	1.83	0.53	1.23	0.41	2.04	0.41
	Sweets	F	1.11	0.69	1.77	0.67	1.38	0.18	2.23	0.18
	Beverages	F	0.97	0.61	1.53	0.88	1.33	0.22	2.11	0.22
	Other foods	F	1.22	0.76	1.96	0.40	0.86	0.57	1.43	0.57
8:2diPAP	Bread	M	1.22	0.67	2.21	0.51	1.48	0.22	2.81	0.22
	Vegetables	M	0.72	0.35	1.45	0.34	0.58	0.09	1.10	0.09
		F	0.98	0.65	1.48	0.93	1.47	0.07	2.23	0.07
	Meat	M	1.13	0.59	2.18	0.70	0.86	0.64	1.67	0.64
	Eggs	M	1.01	0.55	1.84	0.98	0.71	0.27	1.32	0.27
	Cheese	F	1.31	0.84	2.02	0.23	1.15	0.53	1.77	0.53
	Butter and oil	M	0.73	0.37	1.44	0.36	1.02	0.95	1.98	0.95
		F	1.12	0.74	1.70	0.59	1.02	0.92	1.61	0.92
	Sweets	F	0.94	0.62	1.43	0.78	1.32	0.19	1.99	0.19
	Beverages	M	0.58	0.31	1.09	0.09	0.82	0.54	1.60	0.54
PFHxPA	Bread	M	1.13	1.01	1.27	0.04	1.07	0.26	1.22	0.26
	Grain	M	1.04	0.92	1.19	0.50	1.07	0.40	1.28	0.40
		F	0.97	0.87	1.07	0.52	0.87	0.01	0.97	0.01
	Cakes	F	0.95	0.86	1.05	0.28	0.98	0.65	1.09	0.65
	Vegetables	F	1.03	0.93	1.14	0.62	0.84	0.00*	0.94	0.00*
	Meat	M	1.13	1.00	1.28	0.04	1.01	0.92	1.14	0.92
	Fish	F	0.91	0.82	1.01	0.06	0.92	0.13	1.02	0.13
	Eggs	F	1.02	0.91	1.14	0.69	1.11	0.06	1.24	0.06
	Dairy	M	1.04	0.89	1.22	0.60	1.07	0.34	1.23	0.34
	Butter and oil	M	0.95	0.83	1.08	0.44	0.85	0.02	0.77	0.02
	Dressing	M	0.89	0.78	1.02	0.08	0.98	0.72	1.11	0.72
	Beverages	M	0.99	0.87	1.12	0.81	0.95	0.44	1.08	0.44
	Other foods	F	0.91	0.82	1.01	0.08	1.01	0.88	1.13	0.88
PFBS	Bread	M	0.37	0.13	1.04	0.06	0.50	0.25	1.67	0.25
	Grain	M	2.30	0.83	6.41	0.11	3.61	0.03	11.81	0.03
		F	0.93	0.41	2.09	0.85	1.82	0.15	4.11	0.15
	Vegetables	F	0.86	0.38	1.98	0.73	2.94	0.02	7.22	0.02
	Eggs	F	0.61	0.25	1.48	0.27	1.10	0.83	2.67	0.83
	Cheese	M	0.31	0.08	1.21	0.09	0.41	0.27	2.09	0.27
	Butter and oil	M	0.93	0.28	3.06	0.90	3.54	0.06	13.43	0.06
		F	1.71	0.68	4.29	0.25	1.36	0.57	3.99	0.57
	Dressing	M	1.24	0.45	3.41	0.66	0.31	0.04	0.95	0.04
		F	0.91	0.38	2.19	0.83	0.98	0.97	2.76	0.97
	Other foods	F	1.46	0.65	3.29	0.36	1.09	0.84	2.63	0.84
PFDS	Bread	F	0.60	0.34	1.06	0.08	0.90	0.71	1.57	0.71
	Grain	F	1.39	0.79	2.46	0.25	0.51	0.02	0.90	0.02
	Cakes	M	0.65	0.38	1.12	0.12	0.64	0.13	1.14	0.13
	Potatoes	M	0.57	0.32	1.04	0.06	0.67	0.17	1.19	0.17
	Vegetables	F	1.51	0.85	2.67	0.16	0.98	0.95	1.81	0.95
	Fish	F	1.61	0.91	2.84	0.10	2.43	0.00	4.43	0.00
	Eggs	M	1.23	0.71	2.14	0.44	1.25	0.37	2.06	0.37
		F	0.42	0.22	0.79	0.01	0.67	0.17	1.19	0.17
	Dairy	F	1.24	0.70	2.20	0.45	1.31	0.41	2.51	0.41
	Dressing	M	1.43	0.85	2.42	0.17	1.41	0.23	2.48	0.23
		F	0.85	0.49	1.46	0.54	0.57	0.06	1.02	0.06
	Beverages	M	1.81	1.06	3.08	0.03	2.06	0.02	3.66	0.02
PFHxS	Grain	MF	1.08	0.86	1.35	0.00	0.85	0.53	1.07	0.53
	Eggs	MF	0.88	0.71	1.10	0.26	0.87	0.13	1.04	0.13
	Cheese	MF	0.89	0.70	1.13	0.32	0.95	0.67	1.20	0.67
	Dressing	MF	0.86	0.68	1.08	0.20	1.02	0.88	1.30	0.88
	Beverages	MF	1.32	1.03	1.68	0.03	1.09	0.46	1.39	0.46
	Other foods	MF	0.95	0.76	1.20	0.69	0.80	0.08	1.03	0.08
PFHpS	Grain	MF	0.93	0.77	1.12	0.44	0.80	0.03	0.98	0.03
	Fruits and berries	MF	0.90	0.75	1.09	0.30	0.90	0.30	1.10	0.30
	Eggs	MF	1.10	0.86	1.39	0.45	1.11	0.27	1.34	0.27
	Dairy	MF	0.90	0.74	1.08	0.25	1.08	0.44	1.32	0.44
	Dressing	MF	0.91	0.76	1.10	0.33	1.17	0.10	1.42	0.10
	Beverages	MF	1.13	0.94	1.37	0.20	1.01	0.96	1.21	0.96
	Other foods	MF	0.88	0.73	1.05	0.15	0.74	0.00	0.90	0.00
PFOS	Grain	MF	0.93	0.74	1.16	0.50	0.76	0.02	0.96	0.02
	Potatoes	MF	0.83	0.66	1.05	0.12	0.77	0.03	0.97	0.03
	Fruits and berries	MF	0.96	0.76	1.21	0.71	0.86	0.21	1.09	0.21
	Fish	MF	1.42	1.13	1.77	0.00	1.32	0.02	1.66	0.02
	Other foods	MF	1.02	0.82	1.28	0.84	0.90	0.38	1.14	0.38

(*continued on next page*)

Table 3 (*continued*)

Chemical	Food variable	Gender	Category 1				Category 2			
			GM ratio	95% CI		P-value	GM ratio	95% CI		P-value
PFHpA	Bread	M	1.99	1.09	3.61	0.03	1.43	0.31	2.90	0.31
	Potatoes	F	0.73	0.48	1.13	0.16	0.81	0.35	1.26	0.35
	Fruits and berries	F	1.29	0.84	1.98	0.23	0.74	0.18	1.15	0.18
	Fish	M	0.84	0.44	1.58	0.57	1.17	0.57	2.02	0.57
	Eggs	M	1.54	0.84	2.82	0.16	1.04	0.89	1.84	0.89
	Dairy	F	0.64	0.42	0.98	0.04	0.81	0.36	0.24	0.36
	Cheese	M	0.81	0.42	1.55	0.51	0.86	0.73	2.12	0.73
	Dressing	M	1.56	0.84	2.92	0.15	0.65	0.20	1.27	0.20
	Sweets	M	0.98	0.44	2.16	0.96	1.63	0.14	3.16	0.14
	Other foods	M	0.63	0.32	1.24	0.17	0.63	0.19	1.27	0.19
PFOA	Grain	M	0.84	0.58	1.22	0.36	0.94	0.73	1.36	0.73
		F	0.97	0.75	1.27	0.85	0.96	0.78	1.27	0.78
	Vegetables	M	0.95	0.65	1.40	0.79	1.00	0.98	1.49	0.98
	Fruits and berries	F	0.97	0.74	1.27	0.84	0.85	0.24	1.12	0.24
	Meat	M	0.88	0.61	1.27	0.48	0.82	0.30	1.21	0.30
	Eggs	F	0.86	0.65	1.12	0.26	1.04	0.79	1.38	0.79
	Butter and oil	F	0.87	0.64	1.18	0.37	0.91	0.59	1.29	0.59
	Dressing	M	0.77	0.52	1.12	0.16	0.77	0.12	1.08	0.12
		F	0.95	0.71	1.26	0.72	1.09	0.63	1.52	0.63
	Sweets	M	1.28	0.84	1.97	0.24	1.11	0.62	1.68	0.62
	Other foods	M	0.96	0.66	1.39	0.82	0.75	0.19	1.15	0.19
		F	0.95	0.72	1.24	0.63	0.80	0.68	1.08	0.68
PFNA	Grain	MF	1.00	0.84	1.19	1.00	0.89	0.19	1.06	0.19
	Potatoes	MF	0.86	0.72	1.03	0.10	0.81	0.02	0.96	0.02
	Fruits and berries	MF	0.97	0.81	1.16	0.73	0.89	0.19	1.06	0.19
	Fish	MF	1.27	1.07	1.50	0.01	1.21	0.04	1.44	0.04
	Dairy	MF	0.86	0.72	1.02	0.08	0.96	0.67	1.16	0.67
	Beverages	MF	1.11	0.93	1.32	0.24	1.09	0.30	1.30	0.30
	Other foods	MF	0.96	0.81	1.13	0.60	0.84	0.06	1.11	0.06
PFDA	Grain	M	0.82	0.59	1.15	0.24	0.83	0.38	1.27	0.38
	Potatoes	F	0.95	0.79	1.12	0.52	0.89	0.19	1.06	0.19
	Fruits and berries	F	0.93	0.79	1.11	0.44	0.79	0.01	0.94	0.01
	Fish	M	1.41	1.01	1.97	0.04	1.28	0.11	1.75	0.11
		F	1.28	1.08	1.51	0.00	1.31	0.00	1.57	0.00
	Eggs	M	0.91	0.66	1.26	0.57	1.25	0.16	1.70	0.16
	Dairy	M	0.77	0.52	1.14	0.19	0.99	0.96	1.44	0.96
	Butter and oil	F	1.22	1.01	1.47	0.04	1.21	0.08	1.50	0.08
	Dressing	F	1.02	0.85	1.23	0.81	1.05	0.62	1.30	0.62
	Beverages	M	1.20	0.85	1.67	0.29	1.19	0.30	1.68	0.30
	Other foods	F	0.85	0.71	1.01	0.06	0.82	0.05	1.00	0.05
PFUnDA	Grain	M	0.86	0.54	1.38	0.53	0.76	0.36	1.39	0.36
	Potatoes	F	0.66	0.50	0.87	0.00	0.60	0.00*	0.79	0.00*
	Fish	M	1.67	1.03	2.69	0.04	1.35	0.16	2.08	0.16
		F	1.69	1.29	2.22	0.00*	1.69	0.00*	2.24	0.00*
	Dairy	M	0.81	0.47	1.39	0.43	0.95	0.86	1.62	0.86
	Butter and oil	M	1.12	0.68	1.83	0.65	1.33	0.22	2.13	0.22
		F	1.27	0.93	1.72	0.13	1.04	0.83	1.47	0.83
	Dressing	F	1.17	0.70	1.29	0.76	1.19	0.56	1.57	0.56
	Beverages	M	1.32	0.82	2.14	0.24	1.33	0.25	2.17	0.25
		F	0.96	0.73	1.27	0.78	1.15	0.34	1.52	0.34
PFDoDA	Grain	MF	1.02	0.88	1.18	0.83	0.89	0.12	1.03	0.12
	Potatoes	MF	0.88	0.76	1.02	0.10	0.86	0.05	1.00	0.05
	Fish	MF	1.30	1.13	1.50	0.00*	1.27	0.00*	1.47	0.00*
	Dairy	MF	0.83	0.71	0.96	0.01	0.93	0.35	1.09	0.35
	Beverages	MF	1.09	0.94	1.26	0.26	1.21	0.01	1.40	0.01
	Other foods	MF	0.89	0.77	1.02	0.10	0.94	0.42	1.09	0.42
PFTrDA	Grain	MF	0.79	0.57	1.07	0.13	0.77	0.10	1.05	0.10
	Potatoes	MF	0.84	0.61	1.17	0.30	0.70	0.03	0.97	0.03
	Fish	MF	1.36	1.00	1.86	0.05	1.24	0.18	1.71	0.18
	Dressing	MF	1.40	1.02	1.91	0.04	1.32	0.08	1.82	0.08
	Other foods	MF	1.41	1.02	1.96	0.04	1.24	0.19	1.72	0.19
PFOSA	Bread	F	1.49	0.91	2.43	0.11	1.28	0.33	2.14	0.33
	Cakes	F	1.27	0.77	2.12	0.34	1.51	0.15	2.60	0.15
	Potatoes	F	0.62	0.37	1.03	0.07	0.75	0.29	1.28	0.29
	Meat	F	0.67	0.41	1.08	0.10	1.01	0.97	1.70	0.97
	Fish	M	0.70	0.31	1.57	0.37	0.68	0.31	1.46	0.31
	Eggs	F	1.45	0.86	2.45	0.16	0.77	0.31	1.29	0.31
	Dairy	F	1.39	0.84	2.30	0.20	1.11	0.68	1.86	0.68
	Cheese	M	0.65	0.27	1.58	0.33	0.51	0.16	1.31	0.16
	Butter and oil	F	1.06	0.66	1.71	0.81	0.85	0.55	1.47	0.55
	Dressing	M	1.80	0.79	4.11	0.16	1.58	0.35	4.19	0.35
	Sweets	F	1.24	0.77	1.99	0.36	0.91	0.72	1.57	0.72
	Other foods	F	1.15	0.69	1.92	0.58	0.65	0.12	1.12	0.12

MF: males and females; M: males; F: females.

*-significant correlation after multiple comparison using the Sidak correction ($P \leq 0.002$).

Models are adjusted for age, gender, and education.
Categories for each food variable (grams of food for the reference category, category 1, and category 2): All participants – bread: 0–99, n = 47; 99.1–180, n = 47; 180.1–668, n = 47, grains: 23.2–100, n = 47; 100.1–179, n = 47; 179.1–529, n = 47, cakes: 0–11, n = 47; 11.1–19.3, n = 48; 19.4–114, n = 46, potatoes: 0–37.8, n = 49; 37.9–57.9, n = 46; 58–143, n = 46, vegetables: 59.6–195, n = 47; 195.1–303, n = 47; 303.1–630, n = 47, fruits and berries: 15.8–255, n = 47; 255.1–404, n = 47; 404.1–1470, n = 47, meat: 0.38–157, n = 47; 157.1–253, n = 47; 253.1–653, n = 47, fish: 0–69.2, n = 47; 69.3–120, n = 47; 120.1–368, n = 47, eggs: 0–11.6, n = 60; 11.7–27, n = 43; 27.1–107, n = 38, dairy: 0–177, n = 47; 177.1–333, n = 47; 333.1–4870, n = 47, cheese: 0.45–24, n = 47; 24.1–40.7, n = 47; 40.8–137, n = 47, butter and oil: 1.3–28.1, n = 47; 28.2–46.3, n = 47; 46.4–146, n = 47, dressing: 0–6, n = 47; 6.1–14.3, n = 47; 14.4–71, n = 47, sweets: 0–14.2, n = 47; 14.3–29.6, n = 48; 29.7–136, n = 46, beverages: 598–1580, n = 47; 1580.1–2000, n = 47; 2000.1–4580, n = 47, other foods: 0–9.5, n = 47; 9.6–20.6, n = 48; 20.7–148, n = 46.
Males – bread: 0–121, n = 15; 121.1–239, n = 14; 239.1–668, n = 15, grains: 23.2–88.2, n = 15; 88.3–163, n = 14; 163.1–529, n = 15, cakes: 0–12.1, n = 15; 12.2–24.7, n = 14; 24.8–78.4, n = 15, potatoes: 0–34.5, n = 16; 34.6–66.2, n = 14; 66.3–124, n = 14, vegetables: 59.6–152, n = 15; 152.1–274, n = 14; 274.1–605, n = 15, fruits and berries: 15.8–237, n = 15; 237.1–408, n = 14; 408.1–859, n = 15, meat: 1.5–180, n = 15; 180.1–272, n = 14; 272.1–653, n = 15, fish: 4.5–78.4, n = 15; 78.5–128, n = 14; 128.1–329, n = 15, eggs: 0.468–11.6, n = 17; 11.7–26.5, n = 13; 26.6–53.8, n = 14, dairy: 8.5–184, n = 15; 184.1–350, n = 14; 350.1–2020, n = 15, cheese: 2–22, n = 15; 22.1–41.3, n = 14; 41.4–137, n = 15, butter and oil: 9.8–35, n = 15; 35.1–56.3, n = 14; 56.4–146, n = 15, dressing: 0–6.7, n = 15; 6.8–14, n = 14; 14.1–71, n = 15, sweets: 1.5–19.5, n = 15; 19.6–32, n = 14; 32.1–111, n = 15, beverages: 857–1640, n = 15; 1640.1–1950, n = 14; 1950.1–4580, n = 15, other foods: 0–8.1, n = 15; 8.2–18.7, n = 14; 18.8–102, n = 15.
Females – bread: 11.3–84.5, n = 33; 84.6–154, n = 32; 154.1–542, n = 32, grains: 32.6–104, n = 33; 104.1–194, n = 32; 194.1–369, n = 32, cakes: 0–10.8, n = 33; 10.9–17.9, n = 32; 18–114, n = 32, potatoes: 5.4–41.9, n = 38; 42–54.6, n = 29; 54.7–143, n = 30, vegetables: 73.4–217, n = 33; 217.1–325, n = 32; 325.1–360, n = 32, fruits and berries: 26.4–258, n = 33; 258.1–403, n = 32; 403.1–1470, n = 32, meat: 0.38–136, n = 33; 136.1–240, n = 32; 240.1–469, n = 32, fish: 0–66.5, n = 33; 66.6–117, n = 32; 117.1–368, n = 32, eggs: 0–11.6, n = 43; 11.7–27, n = 26; 27.1–107, n = 28, dairy: 0–163, n = 33; 163.1–319, n = 32; 319.1–4870, n = 32, cheese: 0.45–24.3, n = 33; 24.4–40.7, n = 32; 40.8–115, n = 32, butter and oil: 1.3–26.8, n = 33; 26.9–42.4, n = 33; 42.5–123, n = 31, dressing: 0–6.1, n = 34; 6.2–14.5, n = 31; 14.6–44.5, n = 32, sweets: 0–13.1, n = 33; 13.2–25.6, n = 32; 25.7–136, n = 32, beverages: 598–1490, n = 33; 1490.1–2010, n = 32; 2010.1–3370, n = 32, other foods: 0–10.3, n = 33; 10.4–20.8, n = 32; 20.9–148, n = 32.

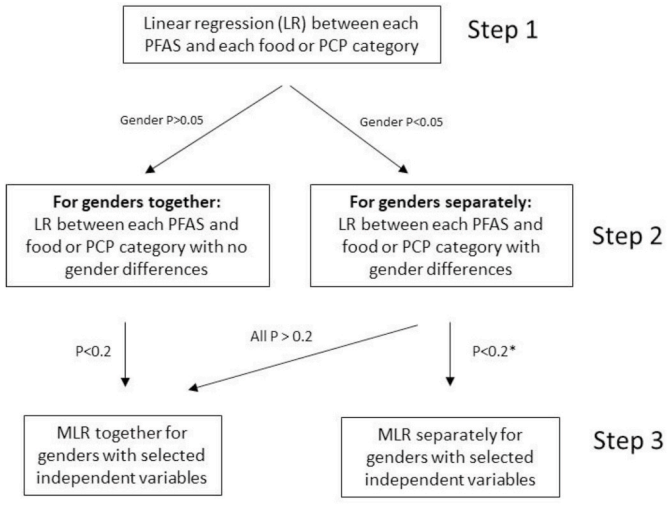

Fig. 1. Overview of the workflow of the linear regression and the final MLR. *When the outcome was different for the genders, the food category was only used in the MLR for the gender with P < 0.2.

intake than women.

3.1.2. Use of PCPs

There were significant differences between males and females regarding the frequency and type of PCPs that were used. Women used a wider variety of PCPs and had a higher frequency of use for the products used by both genders. Women had a higher frequency of use for conditioner, deodorant, facial cleanser, facial moisturiser, body lotion, and toothpaste. Most of the participants (66.2%) had taken one shower, while some had taken none (17.9%), two (7.6%), or three (1.4%) showers during the 24 h period prior to the blood sampling. The average number of hand washes was 10 ± 5.4 times per 24 h (Husoy et al., 2019).

3.2. Analysed data

3.2.1. PFASs in serum

The concentrations of PFASs in serum are presented in Fig. 2. PFHxS, PFHpS, PFOS, PFDS, PFOA, PFNA, PFDA, PFUnDA, PFDoDA, PFTrDA, and 6:2diPAP were detected in 75–100% of the serum samples. PFHxPA, 8:2diPAP, PFHxA, PFOSA, and PFBF were detected in 52–68% of the serum samples, while MeFOSA, 8:2PAP, 6:2PAP, PFPeA, and PFTeDA were detected in 3–29% of the samples. Some chemicals (PFOPA, PFDPA, PFHxA and EtFOSA) were below the LOD in all serum samples (Table 1). The percentage of the analyses between the LOD and LOQ are presented in Table 1.

Among the 25 PFASs measured, the highest concentrations in the serum samples were observed for PFOS, PFOA, PFHxS, and PFNA for both females and males. On average, they were found at 5.7, 1.7, 0.9, and 0.8 ng/mL in females and 9.3, 2.1, 1.3, and 1.1 ng/mL in males, respectively (Table S1). Five of these PFASs – PFOS ($P \leq 0.0001$), PFHxS ($P \leq 0.0001$), PFHpS ($P \leq 0.0001$), PFOA ($P \leq 0.01$), and PFNA ($P \leq 0.05$) – were significantly different between males and females, with the highest concentrations observed in males.

PFOS was detected at the highest concentrations for both genders, and 5% of male and female PFOS serum concentrations were higher than 21.15 ng/mL and 12.82 ng/mL, respectively. PFPeA, PFTeDA 6:2PAP, and 8:2PAP had low rates of detection in blood, and many of the samples were below the LOD.

3.2.2. Correlation between PFASs in serum

The heat map of the Spearman correlation (Fig. 3) represents the correlation between the presence of two PFASs in the serum of the participants. A positive correlation between PFHxS, PFHpS, PFNA, PFDA, and PFOS (r = 0.72–0.85) in serum was found. Another positive correlation was observed between PFNA, PFDA, PFUnDA, PFDoDA, and PFTrDA (r = 0.63–0.82) in serum, whereas PFHxPA was not positively correlated with any of the other PFASs studied.

3.2.3. PFAS exposure and food determinants

The MLR results between PFAS concentrations in serum and the food consumption obtained from the FFQ is shown in Table 3. Positive associations were established between many PFASs and fish for both males and females and for both categories of consumption (Category 1 and category 2 in Table 3). For seven PFASs (PFDS, PFOS, PFNA, PFDA, PFUnDA, PFDoDA, and PFTrDA) positive associations with fish consumption were observed. The highest GM ratios of 2.43 and 1.69 were found for the association between fish consumption and PFDS and PFUnDA, respectively. The serum concentration of PFBS was found to be associated with grain consumption for men, with a GM ratio of 3.61. A positive association was found in females for PFBS in serum and vegetables consumption, and 6:2diPAP was positively associated with butter and oil. Positive associations remained significant after correction for multiple comparisons between PFHxPA and vegetables, PFUnDA and potatoes and fish, and for PFDoDA and fish in both genders.

In addition, MLR was performed between PFAS serum

Table 4
Multivariable linear regression analysis showing the association between the concentrations of PFASs in serum (log transformed) and the main categorical personal care product (PCP) variables.

Chemical	PCP category	Gender	Category 1				Category 2				Category 3			
			GM ratio	95% CI		P-value	GM ratio	95% CI		P	GM ratio	95% CI		P-value
6:2diPAP	Shampoo	F	1.06	0.73	1.54	0.74	NA	NA	NA	NA	NA	NA	NA	NA
	Deodorant	M	0.61	0.34	1.09	0.09	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.11	0.74	1.66	0.62	0.73	0.40	1.33	0.30	NA	NA	NA	NA
	Body lotion	F	1.25	0.84	1.86	0.27	NA	NA	NA	NA	NA	NA	NA	NA
	Anti-wrinkle cream	F	1.29	0.70	2.38	0.40	NA	NA	NA	NA	NA	NA	NA	NA
	Sunscreen	F	2.20	1.24	3.92	0.01	NA	NA	NA	NA	NA	NA	NA	NA
	Foundation	F	1.20	0.78	1.84	0.40	NA	NA	NA	NA	NA	NA	NA	NA
	Hand cream	F	1.41	0.79	2.54	0.24	1.00	0.54	1.87	1.00	NA	NA	NA	NA
	Hair styling products	F	0.84	0.48	1.46	0.53	NA	NA	NA	NA	NA	NA	NA	NA
	Eye makeup	F	0.90	0.59	1.38	0.63	1.14	0.68	1.93	0.62	NA	NA	NA	NA
	Rouge and powder	F	1.91	1.09	3.33	0.02	NA	NA	NA	NA	NA	NA	NA	NA
	Hand soap	F	1.32	0.77	2.27	0.31	0.93	0.54	1.58	0.77	0.86	0.51	1.45	0.57
8:2diPAP	Anti-wrinkle cream	F	1.42	0.80	2.52	0.22	NA	NA	NA	NA	NA	NA	NA	NA
	Sunscreen	F	1.11	0.65	1.89	0.70	NA	NA	NA	NA	NA	NA	NA	NA
	Mouthwash	F	1.38	0.87	2.19	0.17	NA	NA	NA	NA	NA	NA	NA	NA
	Hair styling	M	0.59	0.33	1.05	0.07	NA	NA	NA	NA	NA	NA	NA	NA
	products	F	1.48	0.91	2.40	0.12	NA	NA	NA	NA	NA	NA	NA	NA
	Hand soap	M	0.74	0.39	1.41	0.35	1.67	0.91	3.04	0.09	0.66	0.36	1.21	0.17
PFHxPA	Deodorant	F	0.89	0.78	1.02	0.09	0.95	0.81	1.12	0.57	NA	NA	NA	NA
	Perfume	F	1.07	0.97	1.18	0.16	NA	NA	NA	NA	NA	NA	NA	NA
	Eye makeup	F	1.02	0.92	1.13	0.68	1.08	0.96	1.21	0.21	NA	NA	NA	NA
	Hand soap	M	1.07	0.93	1.23	0.32	1.06	0.93	1.20	0.41	1.15	1.01	1.31	0.04
PFBS	Deodorant	M	2.22	0.86	5.73	0.10	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.60	0.79	3.23	0.19	1.32	0.48	3.60	0.59	NA	NA	NA	NA
	Anti-wrinkle cream	F	1.67	0.56	5.04	0.36	NA	NA	NA	NA	NA	NA	NA	NA
	Sunscreen	F	3.19	1.16	8.81	0.03	NA	NA	NA	NA	NA	NA	NA	NA
	Mouthwash	F	1.27	0.52	3.09	0.60	NA	NA	NA	NA	NA	NA	NA	NA
	Shaving products	M	2.59	0.68	9.90	0.16	NA	NA	NA	NA	NA	NA	NA	NA
PFDS	Facial moisturiser	F	1.32	0.67	2.64	0.42	1.18	0.58	2.39	0.64	NA	NA	NA	NA
	Sunscreen	F	2.16	1.00	4.66	0.05	NA	NA	NA	NA	NA	NA	NA	NA
	Hand cream	F	0.65	0.29	1.46	0.29	2.11	0.89	5.01	0.09	NA	NA	NA	NA
	Rouge and powder	F	0.42	0.22	0.81	0.01	NA	NA	NA	NA	NA	NA	NA	NA
	Shaving products	M	1.73	0.90	3.34	0.10	NA	NA	NA	NA	NA	NA	NA	NA
	Hand soap	M	0.54	0.29	1.03	0.06	1.11	0.61	2.04	0.73	0.72	0.39	1.33	0.29
		F	1.43	0.68	3.02	0.34	1.14	0.54	2.39	0.73	1.15	0.57	2.35	0.69
PFHxS	Deodorant	M	0.77	0.58	1.03	0.07	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.29	1.00	1.67	0.05	0.98	0.63	1.40	0.90	NA	NA	NA	NA
	Mouthwash	M	0.49	0.32	0.76	0.00*	NA	NA	NA	NA	NA	NA	NA	NA
	Perfume	M	0.93	0.64	1.35	0.70	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	0.99	0.72	1.36	0.95	1.42	1.03	1.95	0.03	1.57	1.09	2.27	0.02
	Eye makeup	F	0.82	0.63	1.08	0.15	0.70	0.51	0.96	0.03	NA	NA	NA	NA
	Hand soap	F	1.25	0.88	1.78	0.21	1.14	0.80	1.62	0.46	0.99	0.72	1.37	0.97
PFHpS	Facial cleanser	F	1.37	1.06	1.78	0.02	1.00	0.69	1.46	0.99	NA	NA	NA	NA
	Rouge and powder	F	0.84	0.61	1.16	0.28	NA	NA	NA	NA	NA	NA	NA	NA
PFOS	Deodorant	M	0.76	0.54	1.07	0.11	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.16	0.89	1.50	0.27	0.88	0.61	1.27	0.50	NA	NA	NA	NA
	Sunscreen	F	1.22	0.82	1.81	0.32	NA	NA	NA	NA	NA	NA	NA	NA
	Mouthwash	M	1.24	0.88	1.73	0.21	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	1.20	0.87	1.65	0.26	1.12	0.79	1.58	0.51	1.41	0.97	2.07	0.07
	Eye makeup	F	0.84	0.64	1.11	0.23	0.80	0.58	1.09	0.16	NA	NA	NA	NA
	Hand soap	F	1.41	0.98	2.02	0.07	1.34	0.94	1.93	0.11	1.07	0.77	1.49	0.68
PFHpA	Shampoo	F	0.89	0.63	1.27	0.53	NA	NA	NA	NA	NA	NA	NA	NA
	Deodorant	M	1.24	0.71	2.17	0.45	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.41	0.96	2.05	0.08	1.21	0.71	2.06	0.47	NA	NA	NA	NA
	Sunscreen	F	0.48	0.27	0.84	0.01	NA	NA	NA	NA	NA	NA	NA	NA
	Toothpaste	M	NA	NA	NA	NA	1.53	0.91	2.57	0.10	NA	NA	NA	NA
	Perfume	M	1.74	0.86	3.50	0.12	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	1.38	0.86	2.20	0.17	1.98	1.22	3.23	0.01	1.56	0.90	2.72	0.11
	Eye makeup	F	0.94	0.63	1.40	0.75	1.01	0.63	1.61	0.97	NA	NA	NA	NA
	Hand soap	F	2.07	1.22	3.50	0.01	1.13	0.68	1.89	0.62	1.20	0.74	1.93	0.46
PFOA	Shower gel	M	0.82	0.63	1.06	0.13	NA	NA	NA	NA	NA	NA	NA	NA
	Conditioner	M	0.77	0.52	1.14	0.19	NA	NA	NA	NA	NA	NA	NA	NA
	Deodorant	M	0.90	0.69	1.18	0.44	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.10	0.88	1.38	0.41	0.81	0.59	1.11	0.19	NA	NA	NA	NA
	Facial moisturiser	M	0.84	0.60	1.18	0.31	NA	NA	NA	NA	NA	NA	NA	NA
		F	1.04	0.80	1.36	0.76	1.25	0.96	1.64	0.10	NA	NA	NA	NA
	Mouthwash	F	1.52	1.16	2.00	0.00	NA	NA	NA	NA	NA	NA	NA	NA
	Perfume	M	0.75	0.54	1.04	0.08	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	1.14	0.88	1.48	0.31	1.25	0.96	1.63	0.10	1.67	1.22	2.29	0.00*
	Rouge and powder	F	0.80	0.61	1.06	0.12	NA	NA	NA	NA	NA	NA	NA	NA

(*continued on next page*)

Table 4 (*continued*)

Chemical	PCP category	Gender	Category 1				Category 2				Category 3			
			GM ratio	95% CI		P-value	GM ratio	95% CI		P	GM ratio	95% CI		P-value
	Hand soap	F	1.44	1.08	1.91	0.01	0.98	0.73	1.32	0.89	1.01	0.78	1.31	0.94
PFNA	Deodorant	M	0.85	0.63	1.14	0.27	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.16	0.97	1.39	0.11	0.84	0.65	1.08	0.17	NA	NA	NA	NA
	Facial moisturiser	F	0.99	0.80	1.22	0.91	1.19	0.95	1.50	0.13	NA	NA	NA	NA
	Anti-wrinkle cream	F	1.23	0.95	1.61	0.12	NA	NA	NA	NA	NA	NA	NA	NA
	Sunscreen	F	0.84	0.64	1.11	0.22	NA	NA	NA	NA	NA	NA	NA	NA
	Mouthwash	M	0.78	0.50	1.22	0.27	NA	NA	NA	NA	NA	NA	NA	NA
		F	1.30	1.03	1.63	0.03	NA	NA	NA	NA	NA	NA	NA	NA
	Perfume	M	0.83	0.56	1.22	0.33	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	1.21	0.99	1.48	0.06	1.28	1.02	1.61	0.03	1.58	1.22	2.05	0.00*
	Hand cream	F	1.06	0.82	1.37	0.66	1.00	0.75	1.33	1.00	NA	NA	NA	NA
	Hand soap	F	1.15	0.91	1.45	0.23	1.03	0.81	1.30	0.84	1.04	0.84	1.30	0.70
PFDA	Shower gel	M	0.82	0.62	1.09	0.16	NA	NA	NA	NA	NA	NA	NA	NA
	Conditioner	F	0.93	0.80	1.08	0.33	NA	NA	NA	NA	NA	NA	NA	NA
	Deodorant	M	0.80	0.60	1.08	0.14	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.17	0.99	1.37	0.07	0.94	0.75	1.17	0.57	NA	NA	NA	NA
	Perfume	M	0.73	0.51	1.05	0.09	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	1.09	0.90	1.32	0.39	1.15	0.94	1.40	0.18	1.20	0.96	1.50	0.10
	Hand soap	F	1.02	0.82	1.27	0.88	0.95	0.76	1.19	0.66	0.86	0.70	1.06	0.15
PFUnDA	Shower gel	M	0.77	0.54	1.11	0.15	NA	NA	NA	NA	NA	NA	NA	NA
	Deodorant	M	0.84	0.56	1.23	0.36	NA	NA	NA	NA	NA	NA	NA	NA
		F	1.38	0.95	2.01	0.09	1.36	0.86	2.14	0.18	NA	NA	NA	NA
	Facial cleanser	F	1.22	0.93	1.61	0.16	0.85	0.58	1.24	0.39	NA	NA	NA	NA
	Sunscreen	F	1.17	0.78	1.76	0.43	NA	NA	NA	NA	NA	NA	NA	NA
	Perfume	M	0.72	0.45	1.16	0.17	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	1.22	0.87	1.69	0.24	1.45	1.02	2.08	0.04	1.56	1.06	2.30	0.03
	Hand soap	M	0.71	0.42	1.21	0.20	1.15	0.71	1.88	0.56	0.72	0.44	1.18	0.18
		F	0.87	0.59	1.27	0.47	0.83	0.57	1.20	0.31	0.70	0.49	1.00	0.05
PFDoDA	Shower gel	M	0.90	0.71	1.11	0.29	NA	NA	NA	NA	NA	NA	NA	NA
	Shampoo	F	0.96	0.77	1.22	0.76	NA	NA	NA	NA	NA	NA	NA	NA
	Conditioner	M	0.91	0.71	1.17	0.46	NA	NA	NA	NA	NA	NA	NA	NA
	Deodorant	M	0.87	0.69	1.11	0.26	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.15	0.96	1.37	0.13	0.92	1.40	1.17	0.48	NA	NA	NA	NA
	Facial moisturiser	F	1.04	0.85	1.28	0.69	1.17	0.94	1.45	0.15	NA	NA	NA	NA
	Perfume	M	0.80	0.60	1.08	0.14	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	1.09	0.88	1.34	0.44	1.19	0.97	1.47	0.10	1.25	0.98	1.60	0.07
	Eye makeup	F	0.96	0.81	1.15	0.66	0.84	0.67	1.06	0.14	NA	NA	NA	NA
PFTrDA	Shower gel	F	0.90	0.63	1.30	0.57	0.98	0.54	1.80	0.95	NA	NA	NA	NA
	Conditioner	F	0.87	0.60	1.25	0.45	NA	NA	NA	NA	NA	NA	NA	NA
	Facial cleanser	F	1.37	0.99	1.90	0.06	0.75	0.48	1.18	0.21	NA	NA	NA	NA
	Sunscreen	F	1.65	1.02	2.69	0.04	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	1.75	1.18	2.61	0.01	2.11	1.38	3.22	0.00*	1.88	1.16	3.03	0.01
	Eye makeup	F	0.73	0.51	1.05	0.09	0.74	0.48	1.13	0.16	NA	NA	NA	NA
	Hand soap	F	0.54	0.34	0.85	0.01	0.57	0.36	0.88	0.01	0.59	0.39	0.89	0.01
PFOSA	Mouthwash	M	3.81	1.44	10.1	0.01	NA	NA	NA	NA	NA	NA	NA	NA
	Toothpaste	F	NA	NA	NA	NA	0.68	0.40	1.13	0.14	NA	NA	NA	NA
	Perfume	F	0.68	0.45	1.04	0.07	NA	NA	NA	NA	NA	NA	NA	NA
	Lip gloss/lip balm	F	2.13	1.26	3.57	0.00	1.09	0.64	1.88	0.74	1.70	0.93	3.08	0.08
	Hand soap	M	0.72	0.31	1.68	0.44	0.37	0.16	0.88	0.03	1.10	0.49	2.48	0.81
		F	0.91	0.51	1.62	0.74	0.60	0.33	1.08	0.09	1.05	0.60	1.82	0.87

NA: not applicable. MF: males and females; M: males; F: females.

*-significant correlation after multiple comparison using the Sidak correction ($P \leq 0.002$).

All models are adjusted for age and education and including gender for models with all participants.

Categories for each PCP variable (frequency of use for reference category, category 1, and category 2): All participants – shower gel: 0, n = 44; 1–2, n = 100, deodorant: 0, n = 27; 1, n = 101; 2, n = 16, facial cleanser: 0, n = 100; 1–2, n = 44, facial moisturiser: 0, n = 57; 1, n = 47; 2, n = 40, toothpaste: 0–1, n = 40; 2–3, n = 104, perfume: 0, n = 107; 1–2, n = 37, lip gloss and balm: 0, n = 94; 1, n = 20; 2–5, n = 30, hair styling products: 0, n = 121; 1–4, n = 23, hand soap: 0–6, n = 41; 7–9, n = 45; 10–33, n = 57.

Males – shower gel: 0, n = 28; 1, n = 64; 2, n = 10, shampoo: 0, n = 27; 1, n = 17, conditioner: 0, n = 39; 1, n = 5, facial moisturiser: 0, n = 35; 1, n = 9, shaving products: 0, n = 38; 1, n = 6.

Females; shower gel: 0, n = 28; 1, n = 64; 2, n = 10, shampoo: 0, n = 51; 1–2, n = 49, conditioner: 0, n = 60; 1–2, n = 40, deodorant: 0, n = 13; 1, n = 71; 2, n = 16, facial cleanser: 0, n = 57; 1, n = 31; 2, n = 12, facial moisturiser: 0, n = 22; 1, n = 38; 2–4, n = 40, anti-wrinkle cream: 0, n = 90; 1–2, n = 10, sunscreen: 0, n = 87; 1–2, n = 12, toothpaste: 0–1, n = 19; 2–3, n = 81, perfume: 0, n = 70; 1–2, n = 30, lip gloss and balm: 0, n = 50; 1–2, n = 37; 3–5, n = 13, foundation: 0, n = 73; 1–2, n = 27, hand cream: 0, n = 79; 1, n = 11; 2–5, n = 10, hair styling products: 0, n = 85; 1–4, n = 15, eye makeup: 0, n = 49; 1, n = 29; 2–4, n = 22, rouge and powder: 0, n = 83; 1–2, n = 17, hand soap: 0–6, n = 20; 7–10, n = 40; 11–30, n = 39.

concentrations and the food consumption of the first day of the study from the diaries (Table S2). With the consumption data of the first day only, the number of positive associations were much lower than for the MLR done with the FFQ data. Some positive associations were established between vegetables and some PFASs (especially with PFDS for males and PFDoDA for both genders). Positive associations were also found between the consumption of butter and oil and PFTrDA in males. Finally, fish was also found to be positively associated with PFDoDA (for both genders) and PFUnDA (for females).

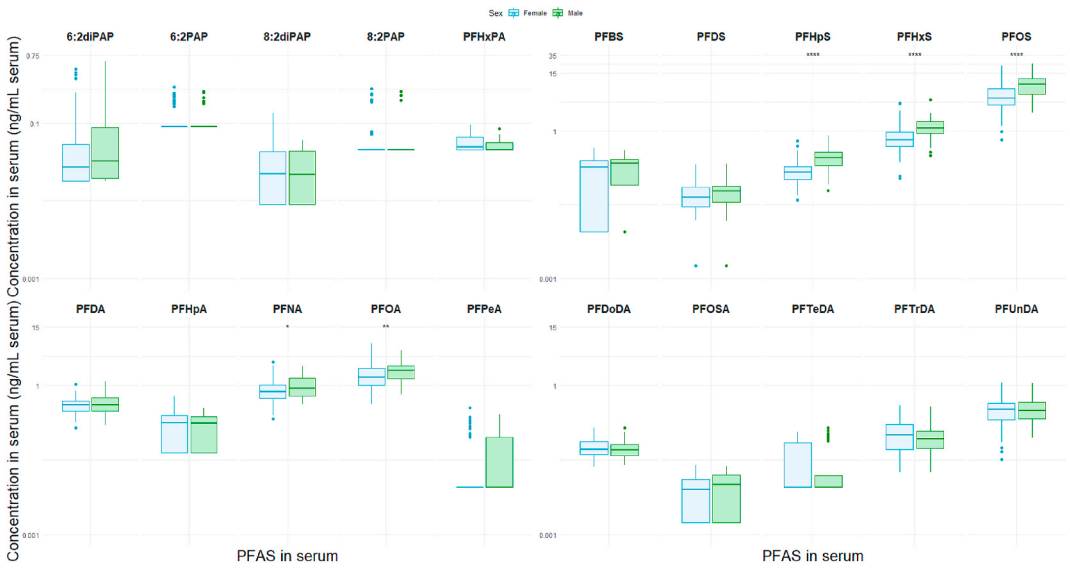

Fig. 2. Concentrations of PFASs in serum (presented on a logarithmic scale). Significant differences between males and females (* = P ≤ 0.05, ** = P ≤ 0.01, *** = P ≤ 0.001, **** = P ≤ 0.0001) were calculated using the Wilcoxon rank sum test.

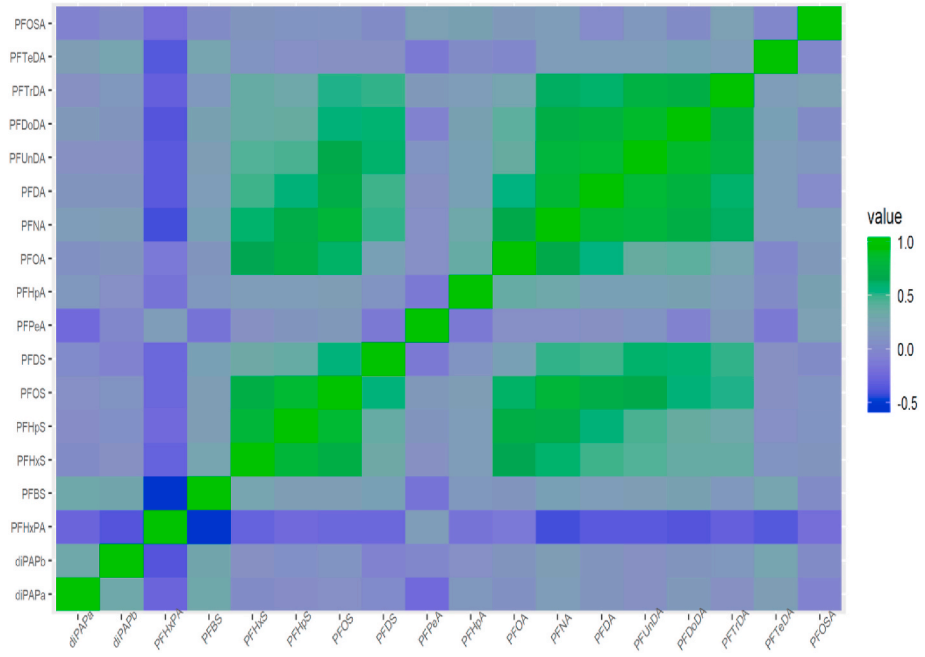

Fig. 3. Heatmap of the Spearman correlation coefficients of PFASs in serum. From blue to green shows an increased positive correlation. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

3.2.4. PFAS exposure and PCP determinants

The MLR between PFAS concentrations in serum and the use of PCPs is shown in Table 4. Many of the PCPs were only used by females. Positive associations were established between PFTrDA, 6:2diPAP, PFBS, and PFDS and sunscreen use by females. Three of the GM ratios were above 2, and the highest GM ratio of 3.19 was observed for the association between PFBS and sunscreen. For the use of mouthwash, positive associations were found for PFNA and PFOA in females and for PFOSA in men with a GM ratio of 3.81. Many PFASs showed positive associations with the use of lip gloss and lip balm for females, and for some of these stronger associations were observed with increased use (category 1, 2, and 3) such as for PFHxS, PFOA, and PFNA. PFTrDA, PFUnDA, and PFHpA were also positively associated with the use of lip gloss. The rouge and powder category showed a positive association with 6:2diPAP for females. PFTrDA showed negative associations with hand soap for the three categories of use for women. After multiple comparison, positive associations remained significant for PFHxS and mouthwash and for PFOA, PFNA, and PFTrDA and lip gloss.

4. Discussion

PFASs are persistent compounds, and they bioaccumulate in organisms due to their presence in the environment and thus are present in food and in seafood. In addition, some PFASs are used in food contact materials, which can also contribute to the presence of PFASs in food (Trier et al., 2011). Because of their presence in water and soil, PFASs can also be found in agricultural plants (Ghisi et al., 2019). The dietary intake (through water and food) seems to be the main source of exposure

to PFASs (Averina et al., 2018; Domingo and Nadal, 2017; Eriksson et al., 2013; Haug et al., 2011; Jian et al., 2018; Poothong et al., 2020), but dust and cosmetics also contribute to this exposure (Ghisi et al., 2019).

D'Hollander et al. (2015) studied the dietary intake of PFOS and PFOA in Norway, Italy, Belgium, and the Czech Republic, representing the north, south, west, and east of Europe, respectively. The dietary intake range for PFOS was from 0.27 ng/kg bodyweight (bw)/day (Norway) to 1.75 ng/kg bw/day (Belgium). For PFOA, it ranged from 0.15 ng/kg bw/day (Norway) to 0.65 ng/kg bw/day (Belgium). The concentrations were slightly lower, 0.14 and 0.051 ng/kg bw/day for PFOS and PFOA, respectively, in a more recent Norwegian study in adults (Papadopoulou et al., 2017).

4.1. Concentrations of PFASs in serum

The study of PFASs in EuroMix was performed on human serum because PFASs accumulate in serum due to their high binding affinity for serum proteins such as albumin (Bischel et al., 2010; Han et al., 2003; Jian et al., 2018). PFASs detected at the highest concentrations in the serum of the participants in the EuroMix study (PFOS, PFOA, PFHxS and PFNA) were the same PFASs that are found most often in serum in Europe (EFSA, 2020). For PFOS, PFOA, PFNA, and PFHxS, our results (PFOS: 5.19 ng/mL; PFOA: 1.60 ng/mL; PFNA: 0.79 ng/mL; PFHxS: 0.81 ng/mL) were on the same order of magnitude for both men and women as the EFSA-reported medians (PFOS: 7.7 ng/mL; PFOA: 1.9 ng/mL; PFNA: 0.61 ng/mL; PFHxS: 0.67 ng/mL).

The highest concentrations in the EuroMix study were observed for PFOS and in descending order PFOA $>$ PFNA $\approx$ PFHxS. PFOPA, PFDPA, PFHxA, and EtFOSA were not detected in any of the serum samples. PFOS is the most abundant PFAS reported in serum samples around the world (Domingo and Nadal, 2017; Jian et al., 2018; Poothong et al., 2017b; Wang et al., 2018). A Norwegian study conducted by Poothong et al. (2017a) observed the same order of PFASs concentrations. In the same study, PFHxA was detected in whole blood but was not detected in serum, which can explain the fact that PFHxA was not detected at all in our study. Polyfluoroalkyl phosphate esters (PAPs) are precursors of perfluoroalkyl carboxylates (PFCAs), and perfluoroalkyl sulfonamides (FOSAs) are precursors of perfluoroalkyl sulfonates (PFSAs), which means that, for example, the concentrations observed for PFCAs such as PFOA are a result of direct exposure to PFOA but also indirect from exposure to PAPs (Haug et al., 2011; Poothong et al., 2020).

An increase in the serum level of some PFASs (PFHpS, PFHxS, PFDA, and PFNA) was observed in Norway between 2007 and 2014, while serum levels of PFOS decreased (Poothong et al., 2017b). In the same study, median serum levels of PFASs were determined for both genders (PFOS: 5.2 ng/mL; PFOA: 1.9 ng/mL). In our study, the median male serum levels of PFOS were higher (PFOS: 9.03 ng/mL) but levels of these PFASs in females were lower in our study (PFOS: 4.71 ng/mL; PFOA: 1.50 ng/mL). In addition, PFNA serum levels were found to be lower in our study (PFNA: 0.41 ng/mL and 0.40 ng/mL for men and women, respectively) than in the study of Poothong et al. (2017) (PFNA: 0.9 ng/mL). A study conducted in northern Norway investigated PFAS levels in serum in 53 men (Nost et al., 2014). Even though PFOS and PFOA are the most commonly found PFASs, that study showed that the serum concentrations of these PFASs increased until 2001 and then decreased. However, serum levels of PFASs like PFHxS, PFNA, PFDA, and PFUnDA kept increasing between 1997 and 2007.

Serum levels of PFHpS, PFHxS, PFOS, PFNA, and PFOA were found to be significantly different between genders in the EuroMix study and were also found to be significantly different between genders in Swedish adults (Bjermo et al., 2013). In general, the PFAS serum levels in men were higher than in women, which can at least partly be explained by the excretion of PFASs through menstruations or breastfeeding (Colles et al., 2020; Park et al., 2019; Poothong et al., 2017b). Of note, PFHxPA showed a negative correlation with several of the other PFASs (Fig. 3).

4.2. Diet and association with PFAS concentration in serum

In the EuroMix study, the serum level of some of the PFASs (PFUnDA, PFOS, PFNA, and PFDoDA) were positively associated with the consumption of fish. This was expected because fish and seafood contain the highest concentrations of PFASs in Norway and in many other areas of the world (Domingo and Nadal, 2017; Fair et al., 2019; Papadopoulou et al., 2017). In general, food and drinking water are the major contributors to the exposure of PFASs (Averina et al., 2018; Fair et al., 2019; Haug et al., 2011; Poothong et al., 2020; Trudel et al., 2008; Vestergren and Cousins, 2009). Our findings are also in line with several other studies world-wide. The study by Haug et al. (2010b) demonstrated that seafood (fish and shellfish) consumption is the major dietary source of PFASs and that seafood consumption can be responsible for 93% of the total dietary intake of PFUnDA. Increases in the PFOS, PFNA, and PFHxS levels in the plasma of women who ate fish or shellfish were observed in the study by Rylander et al. (2010). A recent study including pregnant women and children from six European cohorts reported positive associations between fish consumption and levels of PFOS, PFNA, and PFUnDA in child plasma and levels of PFUnDA in maternal plasma (Papadopoulou et al., 2019). In a Norwegian study by Haug et al. (2010a), levels of PFASs were analysed in food. Their study highlighted the presence of PFASs in fish, some vegetables, meat, eggs, and drinking water. PFASs like PFDA and PFOS were mainly found in fish and some meat, whereas PFOA was not found in fish. In our study, the correlation between PFOA and fish was not significant either. The study by Averina et al. (2018) found that fatty fish, sweetened beverages, reindeer meat, and seagull eggs were positively associated with the presence of PFASs in the serum of the Norwegian participants.

4.3. The association between the use of PCPs and PFAS concentrations in serum

In the EuroMix study, sunscreen, mouthwash, and lip gloss/lip balm were found to be positively associated with concentrations of PFASs in serum. Hand soap, on the contrary, was often found to be negatively associated with PFASs in EuroMix. A Belgian study described an association between internal exposure to PFNA and the use of PCPs (Colles et al., 2020). Fluorinated compounds are added to PCPs as emulsifiers, antistatics, surfactants, stabilizers, film formers, solvents, and viscosity regulators (Schultes et al., 2018), and some studies have investigated the presence of PFASs in some PCPs (Henricsson, 2017; Miljøstyrelsen, 2018; Schultes et al., 2018). PFASs were found in 52% of the samples in the study by Schultes et al. (2018) and in 4% of the samples in the study by Henricsson (2017). Also, both studies showed the presence of PFASs in foundation, but we did not find a positive association between use of foundation and PFASs in EuroMix. In the study by Schultes et al. (2018), three samples of foundation contained up to 479 μg/g of PFASs (these PFASs were mostly PAPs). In the study by Henricsson (2017), no PFASs were found in sunscreen products, while the study by Fujii et al. (2013) reported the presence of PFASs in sunscreen (up to 6500 ng of PFHxA per gram of sunscreen), which may explain the positive association found between some PFASs and sunscreen. The negative association between hand soap and PFASs in our study may be explained by washing away the PFASs, similar to what Sakhi et al. (2018) suggested in their study on phenols. Poothong et al. (2019) also found that higher concentrations of PFOS, PFOA, and 8:2diPAP in hand wipes were associated with a low frequency of daily handwashing ($\leq$8 times a day).

4.4. Strengths and limitations

The EuroMix study is comprehensive because of all of the information that was gathered in the different questionnaires filled out by the participants. Here we used the FFQ, which is less detailed and precise than the food diaries. However, the FFQ is more relevant for studying dietary sources of accumulative compounds like PFASs because it

estimates long-term exposure. The diaries filled out for the use of PCPs, which only covered a 24 h period prior to the blood sampling, can also reflect a longer period because users tend to use the same PCPs over time. However, because the FFQ and diaries are based on self-recording, this can lead to bias in the recording (Althubaiti, 2016).

One major limitation of the EuroMix study is that the study was not representative of the Norwegian population. Most of the participants were highly educated, they had a relatively healthy diet, and most of them were non-smokers (62.5%), which does not represent the smokers in Norway (15% of the population) (Husoy et al., 2019). Another limitation of this study is its small size of only 144 participants, especially in relation to the many exposures and outcomes included in the present paper. Finally, the PFAS exposure was determined in serum, and this blood matrix might not be the more suitable for the detection of every PFAS because some of them are detected in whole blood and not serum, which can lead to an underestimation of PFAS exposure (Poothong et al., 2017b).

5. Conclusions

Eight out of the 25 PFASs analysed were found in all serum samples. Fish was found to be the major determinant for PFAS exposure from foods, while sunscreen, mouthwash, and lip gloss/lip balm were determinants of several PFASs from PCP use. The PFAS serum levels in the EuroMix participants were similar to levels in other European studies, and associations with the consumption of several types of food and use of PCPs indicate that this population is exposed to PFASs both through their diet and through their use of PCPs. Further studies are needed to explore the relative importance of these two sources of exposure.

Credit statement

Thépaut E, Formal analyses, Writing – original draft, writing– review and editing. Dirven HAAM, Conceptualisation, Resources, Writing – original draft, writing– review and editing, Haug LS, Methodology, Writing – original draft, writing– review and editing, Lindeman B: Methodology, Writing – original draft, Poothong S, Methodology, analyses, Writing – original draft, writing– review and editing, Andreassen M, Investigation, Writing – original draft, Hjertholm H, Investigation, Writing – original draft, writing– review and editing, Husøy T, Conceptualisation, Investigation, formal analyses, Resources, Writing – original draft, writing– review and editing, Project administration.

Funding

The EuroMix project was funded by the Horizon 2020 Framework Program of the European Union (Grant Agreement 633172 – EuroMix). The study was approved by the Regional Committees for Medical and Health Research Ethics (REK ID no 2015/1868), and all of the participants provided their written informed consent.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2021.110795.

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