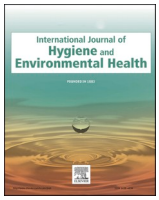
International Journal of Hygiene and Environmental Health 247 (2023) 114057

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

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



# PFAS levels and determinants of variability in exposure in European teenagers – Results from the HBM4EU aligned studies (2014–2021)

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## ARTICLE INFO

*Keywords:*
HBM4EU
Perfluoroalkyl substances
Adolescents
Exposure
Determinants
Food consumption

## ABSTRACT

*Background:* Perfluoroalkyl substances (PFAS) are man-made fluorinated chemicals, widely used in various types of consumer products, resulting in their omnipresence in human populations. The aim of this study was to describe current PFAS levels in European teenagers and to investigate the determinants of serum/plasma concentrations in this specific age group.

*Methods:* PFAS concentrations were determined in serum or plasma samples from 1957 teenagers (12–18 years) from 9 European countries as part of the HBM4EU aligned studies (2014–2021). Questionnaire data were post-harmonized by each study and quality checked centrally. Only PFAS with an overall quantification frequency of at least 60% (PFOS, PFOA, PFHxS and PFNA) were included in the analyses. Sociodemographic and lifestyle factors were analysed together with food consumption frequencies to identify determinants of PFAS exposure. The variables study, sex and the highest educational level of household were included as fixed factors in the multivariable linear regression models for all PFAS and each dietary variable was added to the fixed model one by one and for each PFAS separately.

*Results:* The European exposure values for PFAS were reported as geometric means with 95% confidence intervals (CI): PFOS [2.13 μg/L (1.63–2.78)], PFOA ([0.97 μg/L (0.75–1.26)]), PFNA [0.30 μg/L (0.19–0.45)] and PFHxS [0.41 μg/L (0.33–0.52)]. The estimated geometric mean exposure levels were significantly higher in the North and West versus the South and East of Europe. Boys had significantly higher concentrations of the four PFAS compared to girls and significantly higher PFASs concentrations were found in teenagers from households with a higher education level. Consumption of seafood and fish at least 2 times per week was significantly associated

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https://doi.org/10.1016/j.ijheh.2022.114057
Received 8 July 2022; Received in revised form 14 September 2022; Accepted 21 October 2022
Available online 31 October 2022

with 21% (95% CI: 12–31%) increase in PFOS concentrations and 20% (95% CI: 10–31%) increase in PFNA concentrations as compared to less frequent consumption of seafood and fish. The same trend was observed for PFOA and PFHxS but not statistically significant. Consumption of eggs at least 2 times per week was associated with 11% (95% CI: 2–22%) and 14% (95% CI: 2–27%) increase in PFOS and PFNA concentrations, respectively, as compared to less frequent consumption of eggs. Significantly higher PFOS concentrations were observed for participants consuming offal (14% (95% CI: 3–26%)), the same trend was observed for the other PFAS but not statistically significant. Local food consumption at least 2 times per week was associated with 40% (95% CI: 19–64%) increase in PFOS levels as compared to those consuming local food less frequently.

*Conclusion:* This work provides information about current levels of PFAS in European teenagers and potential dietary sources of exposure to PFAS in European teenagers. These results can be of use for targeted monitoring of PFAS in food.

## 1. Introduction

Perfluoroalkyl substances (PFAS) are human-made fluorinated chemical compounds, listed by Stockholm Convention (2019) as persistent organic pollutants. They are persistent in the environment, widespread and bioaccumulating in both humans and wildlife. The use of PFAS include surface coating and protectant formulations, fire-fighting foams, paper and cardboard packaging products, carpets, leather products, and water- and stain-proof textiles (ATSDR, 2018). The wide use of these chemicals resulted in their presence in the body of almost every human (Berg et al., 2014; Kato et al., 2014; Liu et al., 2011; Mørck et al., 2015; Schoeters et al., 2017). Due to its adverse health effects, perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) were phased out by major manufacturers since 2000 and 2006, respectively (Dassuncao et al., 2018; Xu et al., 2021) and have been restricted under the EU's Persistent Organic Pollutants Regulation in 2009 and 2019 (PFOS and PFOA, respectively). Another substance in PFAS group, perfluorohexane sulfonic acid (PFHxS), is under consideration for inclusion in the Stockholm Convention as well (Stockholm Convention, 2019). Despite the phase out, PFOS and PFOA were still predominant PFAS substances in European newborns years after the regulation (Cariou et al., 2015; Colles et al., 2020; Richterová et al., 2018). Besides, new substitutes of restricted PFAS are emerging, such as shorter-chain PFAS analogues (Xu et al., 2021). In the general population, exposure to PFAS can occur through contaminated air, drinking water, food, soil and dermal uptake (ATSDR, 2018; Ragnarsdóttir et al., 2022). Most of the previous studies on PFAS exposure have been done in pregnant women, newborns, or adults, however, less attention is paid to teenagers. However, some recent studies showed associations between high PFAS exposure in teenagers and higher risk of health outcomes, such as dyslipidemia, hypertension, obesity (Averina et al., 2021), asthma (Averina et al., 2019) or association with levels of reproductive hormones (Tsai et al., 2015).

Determinants of exposure to chemicals in teenagers might differ from those of children, since the typical hand-to-mouth behaviour of young children can lead to different ways of exposure. Exposure determinants of PFAS of teenagers may also differ from those of adults. Unlike teenagers, adults can be occupationally exposed to PFAS, and the use of PFAS containing products probably vary between these two age groups. Previous studies reported associations with parity, breastfeeding or educational level and PFAS levels in serum or plasma (Berg et al., 2014; Bjerregaard-Olesen et al., 2016; Kato et al., 2014; Richterová et al., 2018; Sagiv et al., 2015). However, in teenagers, these determinants most likely do not play a major role in their PFAS exposure, except of educational level of household, which could be linked to the lifestyle of members of household. Also, the shift from more parent-dependent behaviour of a child to more (but not-fully) independent behaviour of teenagers must be taken into account. Altogether, it gives a unique opportunity to explore determinants of PFAS exposure in this very specific age group in both sexes, before occupational exposure or giving birth can step in as the main determinants of PFAS concentrations.

EFSA reported detectable PFAS levels in various types of food samples obtained from 16 European countries and tolerable weekly intake (TWI) of 4.4 ng/kg body weight was derived for the sum of PFOA, PFOS, PFNA and PFHxS (EFSA, 2020). This suggests that diet can be an important source of PFAS exposure also for teenagers. In this study, we describe exposure levels of PFAS in European teenagers of the HBM4EU aligned studies (2014–2021), explore differences in exposure levels between the geographical regions (North, East, South, West) and examine the associations between sociodemographic characteristics, dietary patterns and serum/plasma PFAS levels in pooled data from 9 European countries.

## 2. Methods

### 2.1. Study population

This study was conducted as a part of the European Human Biomonitoring Initiative (HBM4EU) aligned studies. The aim of this initiative was to harmonise human biomonitoring in Europe to support policy making (Ganzleben et al., 2017). Design and general characteristics of the HBM4EU aligned studies was described elsewhere (Gilles et al., 2021, 2022). Briefly, the HBM4EU aligned studies collected comparable exposure data, questionnaire data and data on health outcomes across the European studies. The population was divided into three age groups: children (6–11 years), teenagers (12–19 years) and adults (20–39 years), and in each age group prioritized chemical substances were analysed. PFAS exposure was selected to be measured in the teenagers age group only. Blood samples were taken by clinical staff. Questionnaires were filled out by interviewer or the study participants themselves and/or their parents. 9 out of 11 European studies of teenagers included in the aligned studies determined PFAS concentrations in blood samples: ESTEBAN (Étude de santé sur l'environnement, la biosurveillance, l'activité physique et la nutrition; France; Fillol et al., 2021), GerES V-sub (German Environmental Survey, 2014–2017, unweighted subsample; Germany; Schultz et al., 2021), Riksmaten Adolescents 2016–17 (Sweden; Moraeus et al., 2018), NEBII (Norwegian Environmental Biobank II; Norway; Magnus et al., 2016), FLEHS IV (Flemish Environment and Health Study IV; Belgium; Schoeters et al., 2022), BEA (Biomonitorización en Adolescentes; Spain; Pérez-Gómez et al., 2013), SLO CRP (Exposure of children and adolescents to selected chemicals through their habitat environment; Slovenia; Stajnko et al., 2020), PCB cohort follow-up (Endocrine disruptors and health in children and teenagers in Slovakia; Slovakia; Hertz-Picciotto et al., 2003) and CROME (Cross-Mediterranean Environment and Health Network; Greece) (Table 1). All studies had obtained ethical approval and all participants or their legal guardians signed an informed consent prior to participation.

### 2.2. Exposure assessment

Blood samples of teenagers were collected and analysed in laboratories that participated and obtained successful results in the HBM4EU Quality Assurance/Quality Control (QA/QC) programme (Esteban López et al., 2021). The proficiency of laboratories for the analysis of PFAS in serum comprised one round of interlaboratory comparison

**Table 1**
Description of participating studies with PFAS concentrations data available.

| Study | Country[a] | Region | N | Sampling year | Age (years) |
|---|---|---|---|---|---|
| Riksmaten Adolescents | Sweden | North | 300 | 2016–2017 | 12–17 |
| NEB II | Norway | North | 177 | 2016–2017 | 12–14 |
| PCB cohort follow-up | Slovakia | East | 292 | 2019–2020 | 15–17 |
| BEA | Spain | South | 299 | 2017–2018 | 13–17 |
| SLO CRP | Slovenia | South | 94 | 2018 | 12–15 |
| CROME | Greece | South | 52 | 2020–2021 | 12–18 |
| ESTEBAN | France | West | 143 | 2014–2016 | 12–17 |
| GerES V-sub | Germany | West | 300 | 2014–2017 | 12–17 |
| FLEHS IV | Belgium | West | 300 | 2017–2018 | 13–16 |

[a] The HBM4EU aligned studies are not all country representative studies.

investigations (ICI) and three rounds of external quality assurance schemes (EQUAS) (Nübler et al., 2022). 21 laboratories from 12 countries achieved satisfactory results for at least six of PFAS biomarkers. ESTEBAN and GerES V-sub PFAS exposure data were generated before the HBM4EU QA/QC programme, but the laboratories successfully participated in the HBM4EU QA/QC programme, thus exposure data were deemed comparable and approved a posteriori by the HBM4EU Quality Assurance Unit (QAU) (Table S1). Data for Riksmaten Adolescents 2016-17 were generated before the HBM4EU QA/QC scheme and were evaluated as comparability not guaranteed by the HBM4EU QAU. Sensitivity analysis was performed to see if the data from Sweden affected the calculated European exposure values and geographical comparisons. Concentrations of twelve PFAS were measured in blood serum or plasma: perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonic acid (PFHxS), perfluorononanoic acid (PFNA), perfluorohexanoic acid (PFHxA), perfluoropentanoic acid (PFPeA), perfluoroheptanoic acid (PFHpA), perfluorodecanoic acid (PFDA), perfluoroundecanoic acid (PFUnDA), perfluoroheptanane sulfonic acid (PFHpS), perfluorododecanoic acid (PFDoDA) and perfluorobutane sulfonic acid (PFBS). Information with regard to biological matrix, analytical method, type of forms measured, and HBM4EU QA/QC label for each of the studies can be found in Supplementary material (Table S1). The limit of quantification (LOQ) differed across the studies, more details can be found in Supplementary material (Table S2).

### 2.3. Questionnaire data

Only few studies used the modified questionnaires developed within the HBM4EU project, other studies were already ongoing or finished, therefore different questionnaires were applied across the studies and post-harmonization was necessary. The post-harmonization process for questionnaire data was done by each study according to the HBM4EU codebook (https://doi.org/10.5281/zenodo.6598532). Data on socio-demographic and lifestyle factors were gathered for this study. The variables included sex and age of participant, degree of urbanization, the highest educational level of household, occupation of the participant (part time job relevant only for older participants), alcohol consumption and smoking of participant. A subject's living environment is classified according to the degree of urbanisation (DEGURBA) classification of Eurostat distinguishing three levels of urbanisation. i.e. densely populated area (cities), intermediate density area (towns and suburbs) and thinly populated area (rural area) (Lewis Dijkstra, 2014). Data on educational level were categorized based on The International Standard Classification of Education (ISCED, 2012): low education (ISCED 0–2), medium education (ISCED 3–4), high education (ISCED ≥5). Smoking, alcohol consumption and occupation of participant were categorized as yes or no. We also received information about recent renovation works in the residency, however variable renovation was not provided by Riksmaten Adolescents and GerES V-sub study. Data on many other variables that may be important for PFAS-exposure such as use of impregnated clothes or sport equipment, data on food packaging, popcorn consumption or use of Teflon cookware were missing in most of the studies.

Dietary factors were analysed as potential determinants of PFAS exposure. We received data on consumption of seafood, fish (including freshwater and sea fish when available), meat, offal, milk and dairy products, eggs, local food and fast food (consumption over the last year or 24 h). Frequency of food consumption for each variable was divided into 6 categories: 0 = Never, 1 = Rarely (<1x/month), 2 = Sometimes (≤1x/week but ≥1x/month), 3 = Often (2-3x/week), 4 = Very Often (4-6x/week), 5 = Everyday (≥7x/week). Since we observed low percentage of subjects in some categories of food consumption (Table 3), we decided to group some categories together based on the proportion of subjects in each category of frequency. Seafood and fish, eggs consumption and consumption of local food was dichotomised: <2x/week or ≥2x/week, meat consumption was grouped into 3 categories: ≤1x/week, 2-3x/week, ≥4x/week, offal was categorized as never or sometimes, milk and dairy consumption was categorized as <4x/week or ≥4x/week, and fast food consumption was grouped into 3 categories: <1x/month, ≥1x/month but ≤1x/week, ≥2x/week. No data on seafood consumption were available in PCB cohort follow-up. In Riksmaten Adolescents cohort, seafood and fish consumption were the only dietary variables provided. Fast food consumption was missing in FLEHS IV and data on local food consumption were provided by 4 out of 9 studies: CROME, SLO CRP, PCB cohort follow-up and FLEHS IV. Variable local food included consumption of plant-based and animal-based locally produced food in PCB cohort follow-up and plant-based local food consumption in CROME, SLO CRP and FLEHS IV. We also obtained data on type (bottled, tap, ground water or other) and source of drinking water (public, private well or both). Data on the type of drinking water consumed were missing in Riksmaten Adolescents and GerES V-sub study and source of drinking water was missing in ESTEBAN study. Overall, only 5 people responded that the source of water at home is both public and private well. The answer itself does not provide any information on the potential source of exposure, thus we decided to treat this category as missing.

### 2.4. Data management and statistical analysis

Harmonized data were uploaded to a data platform, quality checked by the central data management team (checking for outliers, coding, inconsistencies, etc.) and after that, the final dataset was provided for statistical analyses. Statistical analyses were performed using statistical programs, SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and SPSS (version 22). Concentrations below LOQ were imputed, using a truncated lognormal distribution (Lubin et al., 2004). The imputation was done per biomarker and per data collection. Random values were imputed (between 0 and the LOQ) from the lognormal distribution with the estimated mean and standard deviation. Distribution of PFAS concentrations were skewed and concentrations were ln-transformed using natural logarithm. Only PFAS with an overall quantification frequency of at least 60% were included for further analysis, and this includes PFOS, PFOA, PFHxS and PFNA.

European exposure values were derived as geometric means with their 95% confidence intervals (CIs) using the survey procedure in SAS with country as cluster to account for the complex survey design when calculating variance estimates. To look into the effect of geographical region on the estimated exposure values, region was tested in a survey regression model adjusted for sex of the participant and educational level of the household. A p-value $< 0.05$ was taken as significance level. A sensitivity analysis was performed to check the influence of the PFAS data from Sweden, for which the comparability was not guaranteed by the HBM4EU QAU, on the estimated European exposure values and geographical comparisons.

To identify possible exposure determinants, association between

each PFAS and each variable (sex, age, education, sampling year, degree of urbanisation, smoking, renovation) was examined in the individual studies and in the pooled sample of teenagers by univariate linear regression. Directed acyclic graphs were plotted to prioritize potential predictors of exposure (data not shown). The variables study, sex and the highest educational level of household were included as fixed factors in the multiple linear regression (MLR) models for all PFAS, because of their significance in the univariate analysis. Age of participants in years was not significant in the multiple regression analysis and was not included as a fixed factor in further analyses. Next, we built separate model for each dietary variable and each PFAS, adjusted for the fixed factors. Using this approach, we were able to identify dietary determinants of PFAS exposure, while taking into account important general characteristics, such as sex and educational level of household, and differences between countries (studies). Beta coefficients were exponentiated and presented are the effect estimates that represent proportional changes in PFAS concentrations in each category compared to the reference category.

As a sensitivity analysis, we included sampling year in MLR model as another potential determinant of PFAS exposure. We also compared results of MLR with/without educational level. Final MLR models used in the pooled data analysis were applied to study-by-study analysis as well.

## 3. Results

General characteristics of the teenagers (households), and their food consumption behaviour are described in Tables 2 and 3 respectively.

**Table 2**
**General characteristics of the study population** (n = 1957).

| Characteristics | n (%) or AM ± SD | Missing[a] n (%) |
|---|---|---|
| **Teenager** | | |
| **Sex** | | 0 (0) |
| Boys | 937 (48) | |
| Girls | 1020 (52) | |
| **Age (in years)** | 14.5 ± 1.4 | 4 (0) |
| **Active smoking** | | |
| Yes | 98 (7) | 572 (29) |
| No | 1287 (93) | |
| **Passive smoking** | | |
| Yes | 331 (25) | 647 (33) |
| No | 979 (75) | |
| **Alcohol** | | |
| Yes | 680 (56) | 753 (38) |
| No | 524 (44) | |
| **Occupation** | | |
| Yes | 124 (7) | 99 (5) |
| No | 1734 (93) | |
| **Household** | | |
| **Region** | | 0 (0) |
| North | 477 (24) | |
| South | 445 (23) | |
| West | 743 (38) | |
| East | 292 (15) | |
| **Educational level of household** | | 43 (2) |
| Low (ISCED 0–2) | 162 (8) | |
| Medium (ISCED 3–4) | 737 (39) | |
| High (ISCED ≥ 5) | 1015 (53) | |
| **Degree of urbanization** | | 2 (0.1) |
| Cities | 620 (32) | |
| Towns and suburbs | 750 (38) | |
| Rural areas | 585 (30) | |
| **Recent renovation** | | |
| Yes | 492 (39) | 681 (35) |
| No | 784 (61) | |

AM = arithmetic mean; SD = standard deviation.

[a] In some studies variable was not included in the questionnaire (see Supplementary Material Table S3).

**Table 3**
**Food and drinking water consumption in population of European teenagers** (n = 1957).

| | n (%) | Missing n (%)* |
|---|---|---|
| **Drinking water** | | 912 (47) |
| Bottled | 141 (13) | |
| Tap | 810 (78) | |
| Ground | 24 (2) | |
| Other | 70 (7) | |
| **Drinking water - source** | | 391 (20) |
| Public | 1488 (95) | |
| Private well | 73 (4) | |
| Both | 5 (1) | |
| **Food consumption** | | |
| **Fish** | | 131 (7) |
| never | 187 (10) | |
| <1x/month | 279 (16) | |
| ≤1x/week but ≥ 1x/month | 826 (45) | |
| 2-3x/week | 332 (18) | |
| 4-6x/week | 150 (8) | |
| ≥7x/week | 52 (3) | |
| **Seafood** | | 362 (19) |
| never | 145 (9) | |
| <1x/month | 69 (4) | |
| ≤1x/week but ≥ 1x/month | 741 (47) | |
| 2-3x/week | 416 (26) | |
| 4-6x/week | 164 (10) | |
| ≥7x/week | 60 (4) | |
| **Meat** | | 346 (18) |
| never | 19 (1) | |
| <1x/month | 91 (6) | |
| ≤1x/week but ≥ 1x/month | 332 (21) | |
| 2-3x/week | 241 (15) | |
| 4-6x/week | 394 (24) | |
| ≥7x/week | 534 (33) | |
| **Offal** | | 638 (33) |
| never | 870 (66) | |
| <1x/month | 365 (28) | |
| ≤1x/week but ≥ 1x/month | 76 (5) | |
| 2-3x/week | 8 (1) | |
| 4-6x/week | - | |
| ≥7x/week | - | |
| **Milk and dairy products** | | 344 (18) |
| never | 50 (3) | |
| <1x/month | 34 (2) | |
| ≤1x/week but ≥ 1x/month | 403 (25) | |
| 2-3x/week | 160 (10) | |
| 4-6x/week | 191 (12) | |
| ≥7x/week | 775 (48) | |
| **Eggs** | | 640 (33) |
| never | 39 (3) | |
| <1x/month | 123 (9) | |
| ≤1x/week but ≥ 1x/month | 770 (58) | |
| 2-3x/week | 311 (24) | |
| 4-6x/week | 60 (5) | |
| ≥7x/week | 14 (1) | |
| **Fast food** | | 638 (33) |
| never | 130 (10) | |
| <1x/month | 408 (31) | |
| ≤1x/week but ≥ 1x/month | 528 (40) | |
| 2-3x/week | 185 (14) | |
| 4-6x/week | 58 (4) | |
| ≥7x/week | 10 (1) | |
| **Local food** | | 1221 (62) |
| never | 193 (26) | |
| <1x/month | 226 (30) | |
| ≤1x/week but ≥ 1x/month | - | |
| 2-3x/week | 4 (1) | |
| 4-6x/week | 6 (1) | |
| ≥7x/week | 307 (42) | |

* In some studies variable was not included in the questionnaire (see Supplementary Material Table S4).

Mean age of teenagers at sampling was 14.5 (±1.4) years and 52% were girls. 7% of teenagers already had a part-time job. More than a half (56%) of the study population have ever drunk an alcoholic beverage, 7% were smokers and 25% of teenagers reported exposure to passive smoking. The largest number of participants were from Western Europe (38%), while Eastern Europe was represented only by one study (15%). More than half of the households had high educational level, only 8% of households had low educational level. 30% of teenagers was living in cities, 38% in towns or suburbs and 30% in rural areas, however, categories were not equally represented in some studies. For example, in PCB cohort follow-up, none of the participants was living in cities and in SLO CRP study, all the participants were living in rural area. On the other hand, in BEA and CROME studies, majority of participants was living in cities (86 and 73%, respectively). Recent renovation was reported by 39% of the households. The main source of drinking water was public source (95%) and the most common type of drinking water was tap water (78%). For food consumption, 10% of teenagers never ate fish and 9% never ate seafood. Fish consumption several times per week was reported by 29% of study population and even more (40%) ate seafood more than once a week. Meat was consumed everyday by 33% of teenagers, only 1% never ate meat. On the other hand, 66% of teenagers responded that they never ate offal. Almost half of the study population (48%) consumed milk and/or dairy products daily. Majority of participants (58%) consumed eggs several times per month but less than once a week. Fast food consumption several times per week was reported by 19% of teenagers, 10% never consumed fast food. 44% of teenagers consumed local food several times per week, however, data on consumption of local food was available only in 4 studies. Detailed characteristics of study participants in each study are presented in the Supplementary Tables S3 and 4.

Supplementary Table S2 gives an overview of the LOQ, percentage of samples above LOQ, and observed percentiles per compound per data collection. Only PFOS, PFOA, PFNA and PFHxS were quantified for at least 60% (PFOS 100%, PFOA 98%, PFHxS 81% and PFNA 80%) in the overall population, and were explored in further analyses.

For PFNA, GerES V-sub was excluded from the statistical analyses as only 12% of the values were quantified due to a high LOQ of 0.5 μg/L in comparison with the other LOQs (0.012–0.288 μg/L) (Table S2). For PFHxS, BEA was excluded from the statistical analyses as only 20% of the values were quantified due to a high LOQ of 0.34 μg/L in comparison with the other LOQs (0.014–0.25 μg/L) (Table S2).

PFOS is the most abundant PFAS compound, with an overall GM and 95% CI of 2.13 μg/L (95% CI: 1.63–2.78), followed by PFOA [0.97 μg/L (95% CI: 0.75–1.26)], PFHxS [0.41 μg/L (0.33–0.52)] and PFNA [0.30 μg/L (0.19–0.45)]. In the basic model adjusted for sex and educational level of the household, geographical region was a strongly influencing factor on the estimated exposure levels. Significantly higher levels were observed in the North (represented by 2 studies from NO and SE) and West (represented by 3 studies from FR, DE and BE) of Europe versus the South (represented by 3 studies from ES, EL, SI) and East (only represented by one study from SK) of Europe (Fig. 1) for all four PFASs, except for PFNA for which the observed difference between West and South was not statistically significant, while the East was significantly lower in comparison with all other regions. Excluding the data from Sweden, for which the comparability was not guaranteed by the HBM4EU QAU, did not affect the interpretation of the results (data not shown).

Detailed results of multiple linear regressions are presented in Supplementary Tables S5–8. We present results from pooled sample analysis only. Boys had significantly higher concentrations of the four PFAS compared to girls. In addition, we observed that medium and high educational level of household to be associated with increased levels of all four PFAS analysed compared to low educational level. Regarding dietary variables, we observed significant associations between PFOS and PFNA levels and consumption of seafood and fish (both $p < 0.001$), the same trend was observed for PFOA and PFHxS although not statistically significant (Fig. 2). Consumption of seafood and fish at least 2 times per week was associated with 21% (95% CI: 12–31%) increase in PFOS levels and 20% (95% CI: 10–31%) increase in PFNA levels. Consumption of eggs at least 2 times per week was associated with 11% (95% CI: 2–22%) ($p = 0.020$) and 14% (95% CI: 2–27%) ($p = 0.019$) increase in PFOS and PFNA levels, respectively. Consumption of offal was associated with 14% (95% CI: 3–26%) increase in PFOS levels ($p = 0.012$). Local food consumption at least 2 times per week was associated with 40% (95% CI: 19–64%)) increase in PFOS levels ($p < 0.001$), the same trend was observed between the other PFAS and local food consumption, although not statistically significant. We did not find any significant association between consumption of milk and dairy products or fast food consumption and PFAS levels. The observed associations between dietary determinants and PFAS concentrations were not affected by educational level in the model. As a sensitivity analysis, we included sampling year in MLR model. However, it was not significant in the MLR models. MLR models used in the pooled data analysis were applied to study-by-study analysis and we observed the same direction of the associations with dietary variables across the studies, although mostly not significant.

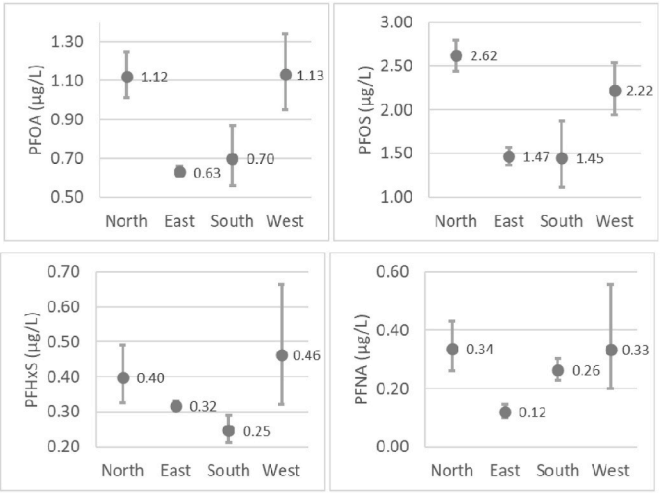


**Fig. 1.** Estimated geometric mean (GM) and 95% confidence interval (CI) for plasma/serum concentrations of PFOS, PFOA, PFHxS and PFNA by European region adjusted for sex of the participant and educational level of the household Contributing studies for Northern Europe: NEBII (Norway), Riksmaten Adolescents 2016–17 (Sweden); for Eastern Europe: PCB cohort follow-up (Slovakia); for Southern Europe: BEA (Spain), CROME (Greece), SLO CRP (Slovenia); and for Western Europe: ESTEBAN (France), GerES V-sub (Germany), FLEHS IV (Belgium).

## 4. Discussion

The HBM4EU aligned studies (2014–2021) generated PFAS exposure data for 1957 teenagers (12–19 years) from 9 European countries geographically spread over Europe. European exposure values, calculated as GM with 95% CI, were obtained for PFOS [2.13 μg/L (1.63–2.78)], PFOA ([0.97 μg/L (0.75–1.26)]), PFNA [0.30 μg/L (0.19–0.45)] and PFHxS [0.41 μg/L (0.33–0.52)]. Significantly higher concentrations were observed in the North and West of Europe versus the South and East.

These GM levels of PFOS and PFOA are comparable to data reported for Canadian teenagers for sampling in the same period (2016–2017 and 2018–2019) in a comparable age group (12–19 years) (Health Canada, 2019, 2021), and slightly lower than the levels observed in the United States (2015–2016 and 2017–2018; 12–19 years) (US-CDC, 2022). The GM levels for PFNA and PFHxS are lower than those reported from Health Canada and US-CDC. Respectively 9 and 8% of the HBM4EU participants exceeds the HBM-I values for PFOS (5 μg/L) and PFOA (2

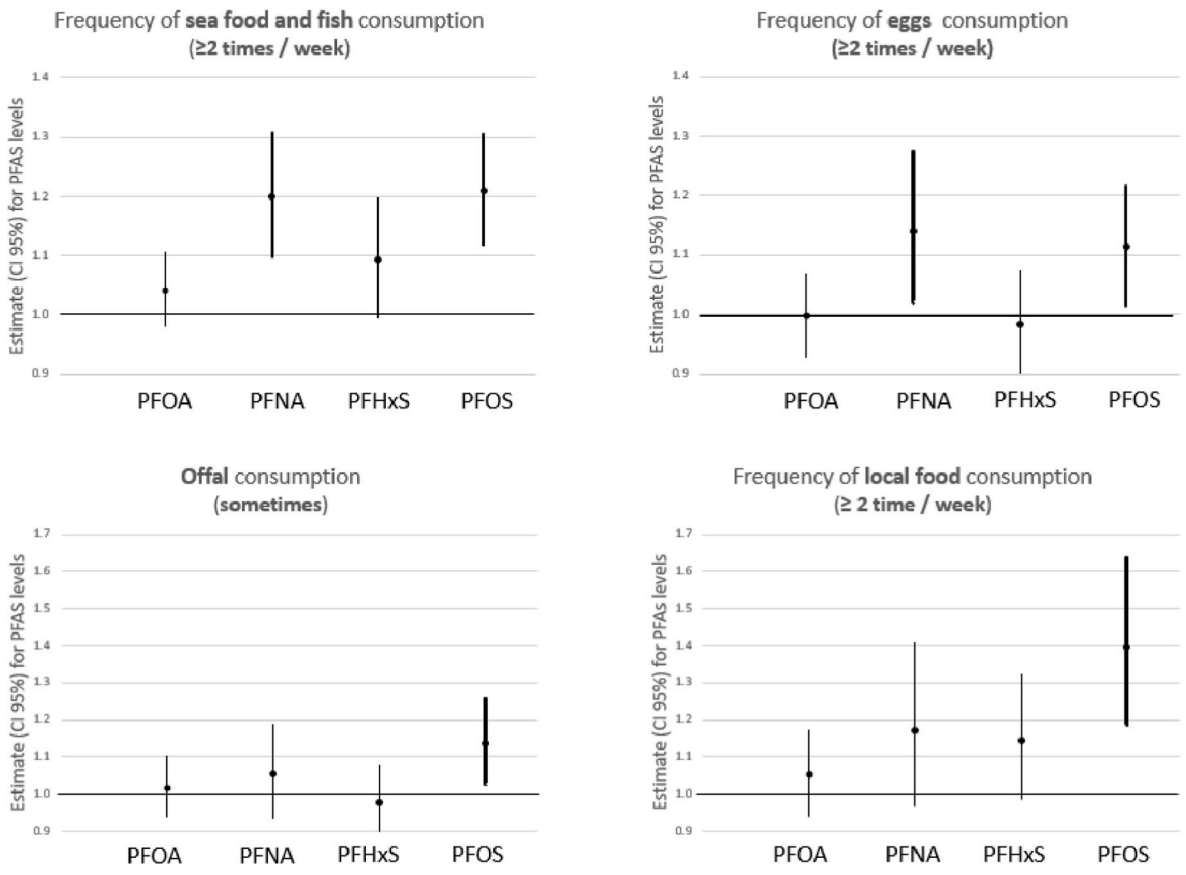


**Fig. 2.** Associations between PFAS concentrations in teenagers and food consumption
Reference category: seafood & fish consumption = <2x/week; eggs consumption = <2x/week; offal consumption = never; local food consumption = <2x/week
All models adjusted for study, sex and educational level of household.

μg/L) derived by the German HBM Commission (Apel et al., 2017). For the sum of PFOS, PFOA, PFNA and PFHxS the proportion of participants exceeding the blood serum concentration of 6.9 μg/L derived from the external Tolerable Weekly Intake established by EFSA (2020) was 14%, indicating that concerns for adverse health effects cannot be excluded (Govarts and Gilles, 2022; submitted). In the subpopulation of teenagers with high seafood & fish, offal and egg consumption, the proportion of exceedance was even elevated to 17%, 16% and 16%, respectively.

For regulated PFAS, PFOS and PFOA, time trends were previously observed indicating that sampling year might be one of the determinants of PFAS exposure (Land et al., 2018; Schoeters et al., 2017). In our study, pooled data analysis did not show significant association between sampling year and PFAS concentrations in teenagers. This could probably be explained by the short sampling time frame for the aligned studies that include samples only from 2014 until 2021, therefore the difference in sampling year between study participants is not substantial and it appears that it does not affect the PFAS levels as much as other assessed factors. Effect of sampling year can also partially be addressed by the study variable in the model and addition of sampling year together with the study variable in the model could lead to over-adjustment.

In this study, significantly higher concentrations of all four PFAS were observed in boys compared to girls. Similar results were previously observed in children and adolescents (Canova et al., 2021) as well as in adults (Calafat et al., 2007). For adolescent girls, menstruation could be an elimination pathway for PFAS, resulting in lower levels of PFAS in blood (Colles et al., 2020), however, we did not have data on menarche available in all studies. We observed association between higher PFAS concentrations and higher educational level, which was also reported in other studies in different populations (adults - Calafat et al., 2007; pregnant women - Bjerregaard-Olesen et al., 2016; newborns – Richterová et al., 2018).

We observed higher frequency of seafood and fish and eggs consumption to be significantly associated with higher levels of PFOS and PFNA in teenagers. Higher PFOS levels were significantly associated with offal consumption and higher consumption of local food. We did not find any significant association between diet and PFOA or PFHxS levels, although the same increased trend was observed with seafood and fish consumption and local food. Even though food packaging could be an important source of PFAS, fast food consumption was not associated with PFAS levels in our study population.

Associations between seafood and fish consumption and PFAS levels were reported by several studies (Haug et al., 2010; Jain, 2014; Manzano-Salgado et al., 2016; Shu et al., 2018). In the current study, not only countries with high consumption of fish and seafood (e. g. Spain or Norway) but also data from countries with low consumption of fish (e. g. Slovakia or Germany) were included in pooled analysis with similar results as previous studies. Fish and seafood consumption was identified as one of the main contributors to dietary exposure to PFAS by EFSA (2020).

We observed an association between eggs consumption at least 2 times per week and higher PFOS and PFNA levels. Similarly, PFNA levels were significantly associated with consumption of eggs more than once per week in Belgian adults (Colles et al., 2020). On the other hand, Liu et al. (2017) did not observe association between eggs consumption and PFAS blood concentrations. EFSA (2020) reported high concentrations of PFOS and PFOA in eggs and egg products, which suggests it can be an important source of exposure to PFAS for those, whose eggs consumption is high.

In our study, consumption of offal was associated with significantly

higher PFOS levels, and the same trend was observed for PFOA and PFNA, although not statistically significant. This association was observed in the study by Tian et al. (2018) as well. They observed consumption of offal at least once a week to be associated with higher PFOS and PFNA levels in pregnant women. In addition, a Belgian study observed increased PFOS, PFOA and PFNA levels in cord blood when mothers reported consumption of offal (Colles et al., 2020). PFAS are absorbed in the gastrointestinal tract of mammals, then distributed via plasma to the other parts of the body and tend to accumulate in the liver (EFSA, 2020).

We found that consumption of local food at least 2 times per week was associated with higher levels of PFOS. However, data on local food consumption were available only in 4 studies and the definitions of local food varied across the studies with different types of food included in the variable. 3 out of 4 studies (CROME, SLO CRP and FLEHS IV) included only plant-based local food, one study (PCB cohort follow-up) included both plant-based and animal-based local food. Despite these limitations, association between PFOS and local food consumption was observed in both, the pooled dataset, and each study separate (results not shown). This suggests that even in countries with no PFAS production (e. g. Slovakia), local food might be contaminated by these chemicals.

One of the limitations of this study is that we were not able to perform statistical analyses for the other eight PFAS compounds measured, due to a high LOQ in some studies and subsequent low quantification frequency. Although PFAS were measured in blood serum or plasma (Table S1), this probably does not affect the results, since 1:1 serum to plasma ratio was observed for PFHxS, PFOS, and PFOA, independently of concentrations measured (Ehresman et al., 2007). Another limitation is underrepresentation of households with lower educational level in all studies, except of BEA and SLO CRP studies. Due to missing data on use of consumer products containing PFAS, we could not investigate the association between the use of these products in the households and PFAS concentrations in teenagers. Another limitation is that not all studies measured the total PFOS levels, but only the linear isomer was measured (ESTEBAN and FLEHS IV) (Table S1). Branched PFOS may account for more than 30% of the total sum of PFAS (Schultz et al., 2020), therefore, these levels could be an underestimation of the actual exposure levels for these studies. As both studies are situated in the West of Europe, this further strengthens the observation on geographical differences, with higher values observed in the North and West of Europe.

Despite the limitations, our study has several strengths as well. One of our main advantages is the size of our study population. We analysed PFAS and questionnaire data on 1957 teenagers from 9 European countries. We had geographic coverage of all four European regions and we covered countries with different lifestyle and dietary patterns. Our study provides the most recent data on exposure as the sampling period was from 2014 to 2021. The comparability and accuracy of measured PFAS concentrations between laboratories was assured by QA/QC programme performed within HBM4EU project. Two studies in which PFAS exposure data were generated before the HBM4EU QA/QC program were deemed comparable by the HBM4EU QAU, since the laboratories successfully passed the QA/QC programme. Only for one study (Riksmaten Adolescents, 2016–17) comparability was not guaranteed by the HBM4EU QAU. Moreover, questionnaire data used in the study were harmonized, which improved results of the statistical analysis for PFAS exposure determinants.

## 5. Conclusion

This is the first study using harmonized and quality controlled comparable PFAS exposure data across Europe. Significantly higher PFAS concentrations were observed in teenagers in the North and West of Europe compared to the South and East. Some dietary factors were identified as determinants of PFAS exposure. Higher frequency of seafood and fish consumption was associated with higher levels of PFAS. Eggs consumption was associated with higher levels of PFOS and PFNA. Additionally, PFOS levels were associated with offal consumption and higher consumption of local food. These results provide information about potential sources of exposure to PFAS for targeted monitoring of PFAS in food.

## Funding

This work was supported by the European Union's Horizon 2020 research and innovation programme under Grant agreement No 733032 HBM4EU (www.HBM4EU.eu), and received co-funding from the authors' organizations:

Riksmaten Adolescents: Riksmaten Adolescents was performed by the Swedish Food Agency with financial support from the Swedish Environmental Protection Agency and the Swedish Civil Contingencies Agency.

NEB II: The Norwegian Institute of Public Health (NIPH) has contributed to funding of the Norwegian Environmental Biobank (NEB). The laboratory measurements have partly been funded by the Research Council of Norway through research projects (275903 and 268465)

PCB cohort follow-up: PCB cohort follow-up received additional funding from the Ministry of Health of the Slovak Republic, program 07B0103.

BEA: BEA study was funded by the Spanish Ministry of Agriculture, Fisheries and Food and the Instituto de Salud Carlos III (SEG 1321/15)

SLO-CRP: The Slovenian SLO-CRP study was co-financed by the Jožef Stefan Institute program P1- 0143, and a national project "Exposure of children and adolescents to selected chemicals through their habitat environment" (grant agreement No. C2715-16-634802).

CROME: CROME study was co-funded by the European Commission research funds of Horizon 2020.

ESTEBAN: ESTEBAN study was funded by Santé Publique France and the French ministries of Health and the Environment.

GerES V-sub: The funding of the German Ministry for the Environment, Nature Conservation, Nuclear Safety and Consumer Protection is gratefully acknowledged.

FLEHS IV: The Flemish Center of Expertise on Environment and Health is funded by the Government of Flanders, Department of Environment & Spatial Development.

## Acknowledgment

We are grateful to all teenagers and their families that participated in the studies.

HBM4EU is co-financed under Horizon 2020 (grant agreement No 733032).

FLEHS: We thank the field workers from the Provincial Institute of Hygiene and VITO for the sample and data collection. All collaborators of the scientific teams of the Flemish Center of Expertise on Environment and Health (https://www.milieu-en-gezondheid.be/en/about-the-center-0) and Karen Van Campenhout and Caroline Teughels from the Flemish Department of Environment & Spatial Development for their valuable input in the field work committee.

Riksmaten Adolescents: Personnel from the regional Occupational and Environmental Medicine Divisions in Gothenburg, Linköping, Lund, Stockholm, and Umeå are acknowledged for help with blood sampling. Jonathan P. Benskin and colleagues at the Department of Environmental Science and Analytical Chemistry, Stockholm University are acknowledged for the chemical analyses.

PCB cohort follow-up: We wish to thank Dana Jurečková, MD, PhD, head of Department of Pediatrics, hospital "Svet zdravia", Michalovce and her personnel for blood sampling, questionnaire administration and examination of adolescents, personnel from the laboratory of biochemistry and haematology (AlphaMedical) in Michalovce, Slovakia, for blood samples processing and colleagues from RECETOX, Masaryk University, Brno, Czech Republic, for chemical analyses.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijheh.2022.114057.

## References


Apel, P., Angerer, J., Wilhelm, M., Kolossa-Gehring, M., 2017. New HBM values for emerging substances, inventory of reference and HBM values in force, and working principles of the German Human Biomonitoring Commission. Int. J. Hyg Environ. Health 220 (2), 152–166. https://doi.org/10.1016/j.ijheh.2016.09.007.

ATSDR, 2018. Toxicological Profile for Perfluoroalkyls. U.S. Department of Health and Human Services, Public Health Service, Atlanta, GA.

Averina, M., Brox, J., Huber, S., Furberg, A.S., 2021. Exposure to perfluoroalkyl substances (PFAS) and dyslipidemia, hypertension and obesity in adolescents. The Fit Futures study. Environ. Res. 195, 110740 https://doi.org/10.1016/j.envres.2021.110740.

Averina, M., Brox, J., Huber, S., Furberg, A.S., Sørensen, M., 2019. Serum perfluoroalkyl substances (PFAS) and risk of asthma and various allergies in adolescents. The Tromsø study Fit Futures in Northern Norway. Environ. Res. 169, 114–121. https://doi.org/10.1016/j.envres.2018.11.005.

Berg, V., Nøst, T.H., Huber, S., Rylander, C., Hansen, S., Veyhe, A.S., Fuskevåg, O.M., Jø, Odland, Sandanger, T.M., 2014. Maternal serum concentrations of per- and polyfluoroalkyl substances and their predictors in years with reduced production and use. Environ. Int. 69, 58–66. https://doi.org/10.1016/j.envint.2014.04.010.

Bjerregaard-Olesen, C., Bach, C.C., Long, M., Ghisari, M., Bech, B.H., Nohr, E.A., Henriksen, T.B., Olsen, J., Bonefeld-Jørgensen, E.C., 2016. Determinants of serum levels of perfluorinated alkyl acids in Danish pregnant women. Int. J. Hyg Environ. Health 219 (8), 867–875. https://doi.org/10.1016/j.ijheh.2016.07.008.

Calafat, AM, Wong, L-Y, Kuklenyik, Z, Reidy, JA, Needham, LL, 2007. Polyfluoroalkyl chemicals in the U.S. population: Data from the National Health and Nutrition Examination Survey (NHANES) 2003–2004 and comparisons with NHANES 1999–2000. Environmental Health Perspectives 115 (11), 1596–1602. https://doi.org/10.1289/ehp.10598.

Canova, C, Di Nisio, A, Barbieri, G, Russo, F, Fletcher, T, Batzella, E, Zuanna, TD, Pitter, G, 2021. PFAS Concentrations and cardiometabolic traits in highly exposed children and adolescents. International Journal of Environmental Research and Public Health 18. https://doi.org/10.3390/ijerph182412881.

Cariou, R., Veyrand, B., Yamada, A., Berrebi, A., Zalko, D., Durand, S., Pollono, C., Marchand, P., Leblanc, J.-C., Antignac, J.-P., Le Bizec, B., 2015. Perfluoroalkyl acid (PFAA) levels and profiles in breast milk, maternal and cord serum of French women and their newborns. Environ. Int. 84, 71–81. https://doi.org/10.1016/j.envint.2015.07.014.

Centers for Disease Control and Prevention. National environmental public health Tracking Network (n.d.) Web. www.cdc.gov/ephtracking. (Accessed 6 June 2022).

Colles, A., Bruckers, L., Den Hond, E., Govarts, E., Morrens, B., Schettgen, T., Buekers, J., Coertjens, D., Nawrot, T., Loots, I., Nelen, V., De Henauw, S., Schoeters, G., Baeyens, W., van Larebeke, N., 2020. Perfluorinated substances in the Flemish population (Belgium): levels and determinants of variability in exposure. Chemosphere 242, 125250. https://doi.org/10.1016/j.chemosphere.2019.125250.

Dassuncao, C., Hu, X.C., Nielsen, F., Weihe, P., Grandjean, P., Sunderland, E.M., 2018. Shifting Global exposures to poly- and perfluoroalkyl substances (PFASs) Evident in Longitudinal birth cohorts from a seafood-consuming population. Environ. Sci. Technol. 52 (6), 3738–3747. https://doi.org/10.1021/acs.est.7b06044.

EFSA, 2020. Risk to human health related to the presence of perfluoroalkyl substances in food. EFSA J. 18 (9), 2020. ISSN 1831-4732.

Ehresman, D.J., Froehlich, J.W., Olsen, G.W., Chang, S.C., Butenhoff, J.L., 2007. Comparison of human whole blood, plasma, and serum matrices for the determination of perfluorooctanesulfonate (PFOS), perfluorooctanoate (PFOA), and other fluorochemicals. Environ. Res. 103 (2), 176–184. https://doi.org/10.1016/j.envres.2006.06.008.

Esteban López, M., Göen, T., Mol, H., Nübler, S., Haji-Abbas-Zarrabi, K., Koch, M.H., Kasper-Sonnenberg, M., Dvorakova, D., Hajslova, J., Antignac, J.P., Vaccher, V., Elbers, I., Thomsen, C., Vorkamp, K., Pedraza – Díaz, S., Kolossa-Gehring, M., Castaño, A., 2021. The European human biomonitoring platform - design and implementation of a laboratory quality assurance/quality control (QA/QC) programme for selected priority chemicals. Int. J. Hyg Environ. Health 234. https://doi.org/10.1016/j.ijheh.2021.113740.

Fillol, C., Oleko, A., Saoudi, A., Zeghnoun, A., Balicco, A., Gane, J., Rambaud, L., Leblanc, A., Gaudreau, É., Marchand, P., et al., 2021. Sébastien Denys Exposure of the French population to bisphenols, phthalates, parabens, glycol ethers, brominated flame retardants, and perfluorinated compounds in 2014–2016: results from the Esteban study. Environ. Int. 147, 106340.

Ganzleben, C., Antignac, J.P., Barouki, R., Castaño, A., Fiddicke, U., Klánová, J., Lebret, E., Olea, N., Sarigiannis, D., Schoeters, G.R., Sepai, O., Tolonen, H., Kolossa-Gehring, M., 2017. Tool to support chemicals regulation in the European Union. Int. J. Hyg Environ. Health 220, 94–97. https://doi.org/10.1016/j.ijheh.2017.01.007. Human Electronic copy available at: https://ssrn.com/abstract=408466221 biomonitoring as a.

Gilles, L., Govarts, E., Rambaud, L., Vogel, N., Castaño, A., Esteban López, M., Rodriguez Martin, L., Koppen, G., Remy, S., Vrijheid, M., Montazeri, P., Birks, L., Sepai, O., Stewart, L., Fiddicke, U., Loots, I., Knudsen, L.E., Kolossa-Gehring, M., Schoeters, G., 2021. HBM4EU combines and harmonises human biomonitoring data across the EU, building on existing capacity - the HBM4EU survey. Int. J. Hyg Environ. Health 237, 113809. https://doi.org/10.1016/j.ijheh.2021.113809.

Gilles, L., Govarts, E., Rodriguez Martin, L., Andersson, A.M., Appenzeller, B.M.R., Barbone, F., Castaño, A., Coertjens, D., Den Hond, E., Dzhedzheia, V., Eržen, I., López, M.E., Fábelová, L., Fillol, C., Franken, C., Frederiksen, H., Gabriel, C., Haug, L.S., Horvat, M., Halldórsson, T.I., Janasik, B., Holcer, N.J., Kakucs, R., Karakitsios, S., Katsonouri, A., Klánová, J., Kold-Jensen, T., Kolossa-Gehring, M., Konstantinou, C., Koponen, J., Lignell, S., Lindroos, A.K., Makris, K.C., Mazej, D., Morrens, B., Murínová, Ľ.P., Namorado, S., Pedraza-Diaz, S., Peisker, J., Probst-Hensch, N., Rambaud, L., Rosolen, V., Rucic, E., Rüther, M., Sarigiannis, D., Tratnik, J.S., Standaert, A., Stewart, L., Szigeti, T., Thomsen, C., Tolonen, H., Á, Eiríksdóttir, Van Nieuwenhuyse, A., Verheyen, V.J., Vlaanderen, J., Vogel, N., Wasowicz, W., Weber, T., Zock, J.P., Sepai, O., Schoeters, G., 2022. Harmonization of human biomonitoring studies in Europe: characteristics of the HBM4EU-aligned studies participants. Int J Environ Res Public Health 19 (11), 6787. https://doi.org/10.3390/ijerph19116787.

Govarts, E, Gilles, L, et al., 2022. Harmonized human biomonitoring in European children, teenagers and adults: Summary of Key Results of the HBM4EU Aligned Studies (2014-2021). Submitted.

Haug, L.S., Thomsen, C., Brantsaeter, A.L., Kvalem, H.E., Haugen, M., Becher, G., Alexander, J., Meltzer, H.M., Knutsen, H.K., 2010. Diet and particularly seafood are major sources of perfluorinated compounds in humans. Environ. Int. 36 (7), 772–778. https://doi.org/10.1016/j.envint.2010.05.016.

Health Canada, 2019. Fifth report on human biomonitoring of environmental chemicals in Canada - Canada.ca [WWW Document], URL. https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/fifth-report-human-biomonitoring.html.

Health Canada, 2021. Sixth report on human biomonitoring of environmental chemicals in Canada - Canada.ca [WWW Document], URL. https://www.canada.ca/en/health-canada/services/environmental-workplace-health/reports-publications/environmental-contaminants/sixth-report-human-biomonitoring.html.

Hertz-Picciotto, I., Trnovec, T., Kočan, A., Charles, M.J., Č ižnar, P., Langer, P., Sovcikova, E., James, R., 2003. PCBs and early childhood development in Slovakia: study design and background. Fresenius Environ. Bull. 12, 208–214.

ISCED. International, 2012. Standard Classification of Education - ISCED 2011. UNESCO Institute for Statistics, Montreal, Quebec, Canada, ISBN 978-92-9189-123-8.

Jain, R.B., 2014. Contribution of diet and other factors to the levels of selected polyfluorinated compounds: data from NHANES 2003-2008. Int. J. Hyg Environ. Health 217 (1), 52–61. https://doi.org/10.1016/j.ijheh.2013.03.008.

Kato, K., Wong, L.Y., Chen, A., Dunbar, C., Webster, G.M., Lanphear, B.P., Calafat, A.M., 2014. Changes in serum concentrations of maternal poly- and perfluoroalkyl substances over the course of pregnancy and predictors of exposure in a multiethnic cohort of Cincinnati, Ohio pregnant women during 2003-2006. Environ. Sci. Technol. 48 (16), 9600–9608. https://doi.org/10.1021/es501811k.

Land, M., de Wit, C.A., Bignert, A., Cousins, I.T., Herzke, D., Johansson, J.H., Martin, J. W., 2018. What is the effect of phasing out long-chain per- and polyfluoroalkyl substances on the concentrations of perfluoroalkyl acids and their precursors in the environment? A systematic review. Environ. Evid. 7 (4) https://doi.org/10.1186/s13750-017-0114-y.

Lewis Dijkstra, H.P., 2014. European Commission. Directorate-general for regional and urban policy (DG REGIO). In: A Harmonised Definition of Cities and Rural Areas: the New Degree of Urbanisation. European Commission, Brussels, Belgium.

Liu, J., Li, J., Liu, Y., Chan, H.M., Zhao, Y., Cai, Z., Wu, Y., 2011. Comparison on gestation and lactation exposure of perfluorinated compounds for newborns. Environ. Int. 37 (7), 1206–1212.

Liu, Y., Su, J., van Dam, R.M., Prem, K., JYS, Hoong, Zou, L., Lu, Y., Ong, C.N., 2017. Dietary predictors and plasma concentrations of perfluorinated alkyl acids in a Singapore population. Chemosphere 171, 617–624. https://doi.org/10.1016/j.chemosphere.2016.12.107.

Lubin, J.H., Colt, J.S., Camann, D., Davis, S., Cerhan, J.R., Severson, R.K., Bernstein, L., Hartge, P., 2004. Epidemiologic evaluation of measurement data in the presence of detection limits. Environ. Health Perspect. 112, 1691–1696. https://doi.org/10.1289/EHP.7199.

Magnus, P., Birke, C., Vejrup, K., Haugan, A., Alsaker, E., Daltveit, A.K., Handal, M., Haugen, M., Hoiseth, G., Knudsen, G.P., et al., 2016. Cohort profile Update: the Norwegian mother and child cohort study (MoBa). Int. J. Epidemiol. 45, 382–388.

Manzano-Salgado, C.B., Casas, M., Lopez-Espinosa, M.J., Ballester, F., Martinez, D., Ibarluzea, J., Santa-Marina, L., Schettgen, T., Vioque, J., Sunyer, J., Vrijheid, M., 2016. Variability of perfluoroalkyl substance concentrations in pregnant women by socio-demographic and dietary factors in a Spanish birth cohort. Environ. Int. 92–93, 357–365. https://doi.org/10.1016/j.envint.2016.04.004.

Moraeus, L., Lemming, E.W., Hursti, U.K., Arnemo, M., Sipinen, J.P., Lindroos, A.K., 2018. Riksmaten Adolescents 2016–17: a national dietary survey in Sweden—design, methods, and participation. Food Nutr. Res. 62.

Mørck, T.A., Nielsen, F., Nielsen, J.K., Siersma, V.D., Grandjean, P., Knudsen, L.E., 2015. PFAS concentrations in plasma samples from Danish school children and their mothers. Chemosphere 129, 203–209.

Nübler, S, Esteban López, M, Castano, S, Mol, H, Haji-Abbas-Zarrabi, K, Schafer, M, Muller, J, Hajslova, J, Dvorakova, D, Antignac, J-P, 2022. Interlaboratory Comparison Investigations (ICI) and External Quality Assurance Schemes (EQUAS) for Human Biomonitoring of Perfluoroalkyl Substances (PFASs) in Serum as Part of the Quality Assurance Programme Under HBM4EU.

Pérez-Gómez, B., Pastor-Barriuso, R., Cervantes-Amat, M., Esteban, M., Ruiz-Moraga, M., Aragonés, N., Pollán, M., Navarro, C., Calvo, E., Román, J., et al., 2013. BIOAMBIENT.ES study protocol: Rationale and design of a cross-sectional human biomonitoring survey in Spain. Environ. Sci. Pollut. Res. 20, 1193–1202.

Ragnarsdóttir, O., Abdallah, M.A., Harrad, S., 2022. Dermal uptake: an important pathway of human exposure to perfluoroalkyl substances? Environ. Pollut. 307, 119478 https://doi.org/10.1016/j.envpol.2022.119478.

Richterová, D., Fábelová, L., Patayová, H., Pulkrabová, J., Lanková, D., Rausová, K., Šovčíková, E., Štencl, J., Hajšlová, J., Trnovec, T., Palkovičová Murínová, Ľ., 2018. Determinants of prenatal exposure to perfluoroalkyl substances in the Slovak birth cohort. Environ. Int. 121 (Pt 2), 1304–1310. https://doi.org/10.1016/j.envint.2018.10.051.

Sagiv, S.K., Rifas-Shiman, S.L., Webster, T.F., Mora, A.M., Harris, M.H., Calafat, A.M., Ye, X., Gillman, M.W., Oken, E., 2015. Sociodemographic and Perinatal predictors of early pregnancy per- and polyfluoroalkyl substance (PFAS) concentrations. Environ. Sci. Technol. 49 (19), 11849–11858. https://doi.org/10.1021/acs.est.5b02489.

Schoeters, G., Govarts, E., Bruckers, L., Den Hond, E., Nelen, V., De Henauw, S., Sioen, I., Nawrot, T.S., Plusquin, M., Vriens, A., Covaci, A., Loots, I., Morrens, B., Coertjens, D., Van Larebeke, N., De Craemer, S., Croes, K., Lambrechts, N., Colles, A., Baeyens, W., 2017. Three cycles of human biomonitoring in Flanders–time trends observed in the Flemish Environment and Health Study. Int. J. Hyg Environ. Health 220 (2), 36–45.

Schoeters, G., Verheyen, V., Colles, A., Remy, S., Martin, L.R., Govarts, E., Nelen, V., Hond, E.D., De Decker, A., Franken, C., et al., 2022. Internal exposure of Flemish teenagers to environmental pollutants: results of the Flemish environment and health study 2016–2020 (FLEHS IV). Int. J. Hyg Environ. Health 242, 113972.

Schulz, C., Conrad, A., Rucic, E., Schwedler, G., Reiber, L., Peisker, J., Kolossa-Gehring, M., 2021. The German environmental survey for children and adolescents 2014–2017 (GerES V)—study population, response rates and representativeness. Int. J. Hyg Environ. Health 237, 113821.

Schulz, K., Silva, M.R., Klaper, R., 2020. Distribution and effects of branched versus linear isomers of PFOA, PFOS, and PFHxS: a review of recent literature. Sci. Total Environ. 733, 139186 https://doi.org/10.1016/j.scitotenv.2020.139186.

Shu, H., Lindh, C.H., Wikström, S., Bornehag, C.G., 2018. Temporal trends and predictors of perfluoroalkyl substances serum levels in Swedish pregnant women in the SELMA study. PLoS One 13 (12), e0209255. https://doi.org/10.1371/journal.pone.0209255.

Stajnko, A., Snoj Tratnik, J., Kosjek, T., Mazej, D., Jagodic, M., Erzen, I., Horvat, M., 2020. Seasonal glyphosate and AMPA levels in urine of children and adolescents living in rural regions of Northeastern Slovenia. Environ. Int. 143, 105985.

Stockholm Convention on persistent organic pollutants (POPs), 2019. Retrieved September 13, 2022, from. http://www.pops.int/TheConvention/ThePOPs/TheNewPOPs/tabid/2511/Default.aspx.

Tian, Y., Zhou, Y., Miao, M., Wang, Z., Yuan, W., Liu, X., Wang, X., Wang, Z., Wen, S., Liang, H., 2018. Determinants of plasma concentrations of perfluoroalkyl and polyfluoroalkyl substances in pregnant women from a birth cohort in Shanghai, China. Environ. Int. 119, 165–173. https://doi.org/10.1016/j.envint.2018.06.015.

Tsai, M.S., Lin, C.Y., Lin, C.C., Chen, M.H., Hsu, S.H., Chien, K.L., Sung, F.C., Chen, P.C., Su, T.C., 2015. Association between perfluoroalkyl substances and reproductive hormones in adolescents and young adults. Int. J. Hyg Environ. Health 218 (5), 437–443. https://doi.org/10.1016/j.ijheh.2015.03.008.

Xu, B., Liu, S., Zhou, J.L., Zheng, C., Weifeng, J., Chen, B., Zhang, T., Qiu, W., 2021. PFAS and their substitutes in groundwater: Occurrence, transformation and remediation. J. Hazard Mater. 412, 125159 https://doi.org/10.1016/j.jhazmat.2021.125159.