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# PFAS levels in Europeans

## An exploratory study

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**DISCLAIMER:** VUA can not be held responsible for the design and execution of the study, nor for the analysis of the PFAS levels.

## Summary and main conclusions

This study with 110 volunteers was performed to assess the extent and potential health risk of PFAS exposure among Europeans. It included the analysis of four long-chain PFAS (PFOS, PFOA, PFHxS and PFNA, also called EFSA-4) and five ultrashort-chain PFAS (TFMS, TFA, PFEtS, PFPrA and PFPrS). Of the 110 participants, 79 filled out a questionnaire that addressed potential predictors of PFAS exposure. The main findings of this study are listed below:

### Occurrence

- All participants had long-chain PFAS PFOS, PFOA, PFHxS and PFNA in their serum. The patterns were in line with what is generally observed in human biomonitoring studies among the general population.
- Of the ultrashort-chain PFAS analysed, only TFA and PFPrA were detected (in 100% and 23% of the participants, respectively). PFPrA levels were relatively low. In contrast, TFA concentrations in this study were roughly 4–5 times higher than the summed four long-chain PFAS. The median TFA serum levels in present study are the highest reported in humans thus far.

### Predictors of PFAS exposure

- No clear differences in PFAS levels between participants from different European countries were observed. However, this could not be reliably tested due to the low number of participants per country and the limited contrast in PFAS levels between participants.
- Long-chain PFAS levels increased with age in men, but not in women. This is in line with what is seen in other biomonitoring studies. There were no clear differences in TFA levels between men and women.
- Self-reported dietary habits were associated with PFAS levels: as expected, long-chain PFAS levels increased with fish/seafood and meat intake. TFA levels appeared to be lower with increased meat intake (no association with fish/seafood), although limited dietary information from the questionnaires precluded conclusions about the dietary patterns or sources underlying this association.
- No clear patterns with PFAS levels were observed for the other predictors (BMI, statin use, blood-donation frequency, menopausal status, non-stick cookware use, take-away food frequency, water source (bottled or tap water), and self-reported residential proximity to industrial or other point sources, occupation), when analysed alone or in combination. This may be due to the study design.

### Health risks

- The levels of the sum of the four long-chain PFAS ( $\Sigma\text{EFSA-4} = \text{PFOS} + \text{PFOA} + \text{PFHxS} + \text{PFNA}$ ) exceeded the threshold of what is considered safe by EFSA in 27 of the 110 participants (25%). While the exceedance was relatively modest, with the top 5% highest exposed participants exceeding the threshold level at least 1.7 times, it exceeds what is considered to be safe and health effects cannot be excluded. This is particularly concerning for women of reproductive age (4 of whom exceeded the threshold in this study), given the possible adverse effects on the developing immune system of their (future) children.
- For TFA, no suitable health-based guidance value is currently available to assess the health risk of TFA levels in serum. However, European Agencies have recently agreed on a classification of TFA as reproductive toxicant (“may cause harm to the unborn child” and “is suspected of damaging fertility”) and lowered the acceptable daily intake to 0.014 mg/kilogram bodyweight per day, stressing the increasing concern for human health impact by TFA.

Given the design of this study, the findings in the present report should be interpreted with caution. Nevertheless, they support the urgency to continue efforts to reduce PFAS exposure and highlight the need for inclusion of ultrashort-chain PFAS such as TFA in future human health impact and biomonitoring studies.

## Table of Contents

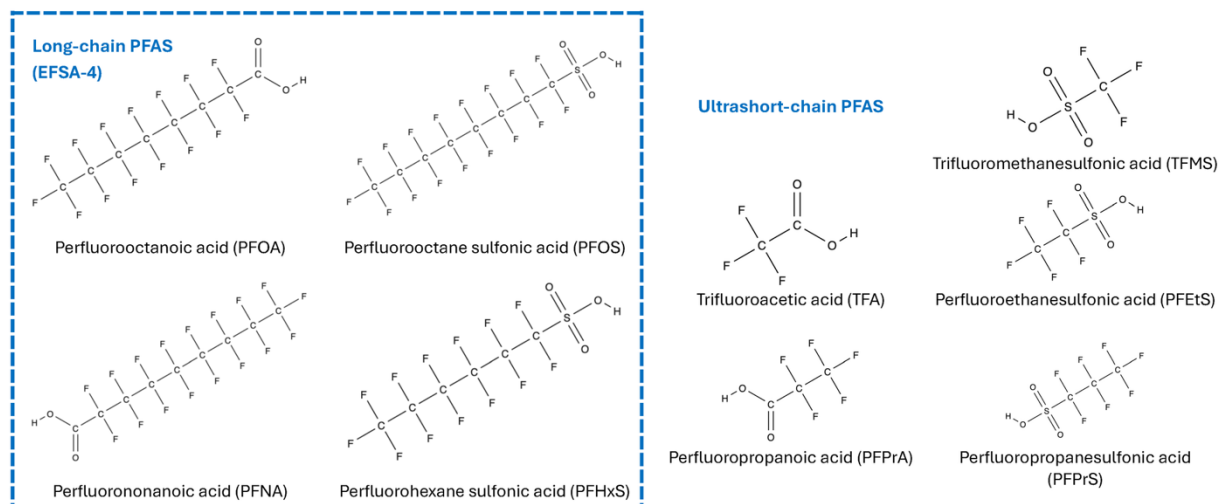
|                                                                                       |           |
|---------------------------------------------------------------------------------------|-----------|
| <b>Summary and main conclusions .....</b>                                             | <b>1</b>  |
| <b>1. Introduction.....</b>                                                           | <b>3</b>  |
| <b>1.1 Study design .....</b>                                                         | <b>3</b>  |
| <b>1.2 Data analysis .....</b>                                                        | <b>4</b>  |
| 1.2.1 PFAS in serum.....                                                              | 4         |
| 1.2.2 Participants .....                                                              | 4         |
| 1.2.3 Health-based guidance value for PFAS in human serum.....                        | 5         |
| 1.2.4 Data analysis .....                                                             | 5         |
| <b>2. Results evaluation and discussion.....</b>                                      | <b>7</b>  |
| <b>2.1 Serum PFAS levels.....</b>                                                     | <b>7</b>  |
| <b>2.2 Predictors of PFAS serum levels.....</b>                                       | <b>9</b>  |
| 2.2.1 Country .....                                                                   | 9         |
| 2.2.2 Sex and age.....                                                                | 10        |
| 2.2.3 Diet .....                                                                      | 11        |
| 2.2.4 Other predictors.....                                                           | 12        |
| <b>3. Risk assessment: comparison of PFAS levels with EFSA threshold values .....</b> | <b>13</b> |
| <b>4. Considerations .....</b>                                                        | <b>15</b> |
| <b>5. Conclusion .....</b>                                                            | <b>15</b> |
| <b>Glossary .....</b>                                                                 | <b>17</b> |
| <b>References .....</b>                                                               | <b>18</b> |
| <b>Supplementary information .....</b>                                                | <b>20</b> |

## 1. Introduction

Per- and polyfluoroalkyl substances (PFAS) are a large group of human-made chemicals known as "forever chemicals" because they do not break down easily in the environment. As a result, humans are continuously exposed to PFAS throughout their lives. PFAS exposure can come from various sources, including contaminated drinking water and food.

Most available studies on the health effects of PFAS focus on long-chain PFAS, such as PFOS and PFOA (**Figure 1**). It is clear that these PFAS can interact with biological processes in the human body and that high exposure may lead to harmful health effects. Scientific evidence shows that PFAS can suppress immune function and the ability to fight off infections. Some PFAS are also linked to elevated blood cholesterol levels, fertility problems in males and females, and to kidney and testicular cancer. As a result, several international agencies have established various safe (or threshold) levels to protect human health.

In recent years, PFAS with much shorter fluorinated carbon chains, such as TFA and PFPrA, have gained increasing attention. TFA levels have rapidly increased over the past years and are currently the most abundant PFAS in the environment. Studies addressing the potential harmful health effects of these ultrashort-chain PFAS remain limited in comparison with studies on long-chain PFAS. Still, TFA exposure has been linked to harmful effects on reproduction and development.



**Figure 1. Chemical structures of long-chain PFAS and ultrashort-chain PFAS investigated in present study.** PFOS, PFOA, PFHxS and PFNA are considered long-chain PFAS, having a chain length consisting of 6 or more fluorinated (F) carbons (C), while ultrashort-chain PFAS have 3 or fewer fluorinated carbons. The long-chain PFAS PFOS, PFOA, PFHxS and PFNA are considered in the health-based guidance value of EFSA (see 1.2.3) and are called EFSA-4 in this report. *Chemical structures are obtained with MolView v2.4.*

### 1.1 Study design

In this study, 110 European citizens volunteered to donate a blood sample in the summer of 2026. The serum samples were analysed for nine individual PFAS at the Institute for Occupational and Maritime Medicine (ZfAM), University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany (**Table S1**).

Around the time of blood sampling, 79 participants also completed a questionnaire on potential predictors of PFAS body burden, including personal characteristics and dietary patterns.

The anonymized PFAS serum levels and questionnaire data were sent to the Vrije Universiteit Amsterdam (VUA) for interpretation, with the aim to assess PFAS exposure, potential predictors and/or health risk in European citizens. The results of this interpretation are described in the present report.

## 1.2 Data analysis

### 1.2.1 PFAS in serum

All four long-chain PFAS included in the analyses were detected in the serum of all participants. The levels of PFOS, PFOA and PFHxS were all above the limit of quantification (LOQs, given in **Table S1**); three PFNA values out of the 110 serum samples fell below the LOQ.

Of the ultrashort-chain PFAS, TFA was quantified in every serum sample of every participant (100% detection frequency). PFPrA was detected above LOQ in 25 of the 110 samples (22.7% detection frequency). TFMS, PFEtS and PFPrS could not be detected above the LOQ in any of the serum samples.

### 1.2.2 Participants

Information regarding sex, parity, living area type, and country of residence were retrieved from the questionnaires, as reported. In addition, age (in years) and body mass index (BMI, kg/m<sup>2</sup>) were calculated based on the self-reported date of birth, and height and weight, respectively. Participants were a median age of 40 years (range 12–78) and 50 (64%) were female (see **Table 1**). Participants were resident in nine European countries, with Italy (n=29), Belgium (n=15), France (n=12) contributing the most participants.

**Table 1. Study participant characteristics** based on self-reported information in a questionnaire (n=79).

| Characteristic                            | N <sup>a</sup> | Value                         |
|-------------------------------------------|----------------|-------------------------------|
| <b>Age, years</b>                         | 75             | Median 40 (range 12–78)       |
| <b>BMI, kg/m<sup>2</sup></b>              | 71             | Median 24.3 (range 15.3–43.4) |
| Normal (<25)                              | 43             | 61%                           |
| Overweight (25-30)                        | 21             | 30%                           |
| Obese (>=30)                              | 7              | 10%                           |
| <b>Sex</b>                                | <b>78</b>      |                               |
| Female                                    | 50             | 64%                           |
| Male                                      | 28             | 36%                           |
| <b>Parity (≥1 pregnancy in last 10 y)</b> | <b>77</b>      |                               |
| Yes (≥1)                                  | 26             | 34%                           |
| None                                      | 51             | 66%                           |
| <b>Area type</b>                          | <b>77</b>      |                               |
| Urban                                     | 38             | 49%                           |
| Suburban                                  | 21             | 27%                           |
| Rural                                     | 18             | 23%                           |
| <b>Country</b>                            | <b>79</b>      |                               |
| Italy                                     | 29             | 37%                           |
| Belgium                                   | 15             | 19%                           |
| France                                    | 12             | 15%                           |
| Croatia                                   | 10             | 13%                           |
| Germany                                   | 8              | 10%                           |
| Luxembourg                                | 2              | 2%                            |
| Spain                                     | 1              | 1%                            |
| Denmark                                   | 1              | 1%                            |
| Finland                                   | 1              | 1%                            |

<sup>a</sup> Where N < 79, the difference reflects missing values for that characteristic; percentages are calculated using the number of participants with available data (the N shown).

### 1.2.3 Health-based guidance value for PFAS in human serum

The European Food Safety Authority (EFSA) established a health-based guidance value (HBGV) for the sum of four PFAS ( $\Sigma$ EFSA-4 = PFOS + PFOA + PFNA + PFHxS).<sup>1</sup> The EFSA Panel calculated a tolerable weekly intake (TWI) of 4.4 ng/kg body weight (bw)/week. The TWI was derived from a study showing reduced antibody response after vaccination in children. This reduced antibody response was calculated to occur above serum levels of 17.5 ng/mL for  $\Sigma$ EFSA-4 in 1-year old breastfed children. Using physiology-based pharmacokinetic modeling and assuming 12 months of breastfeeding, EFSA estimated that the serum concentration of 17.5 ng/mL in 1-year old children corresponds to serum concentration of 6.9 ng  $\Sigma$ EFSA-4/mL in women at age 35. This serum level in adults corresponds to a long-term intake of 4.4 ng/kg bw/week from an early age (see **Figure 2**). Hence, the serum level of 6.9 ng  $\Sigma$ EFSA-4/mL in women can be considered a threshold level above which a reduced vaccination response in young children who were breastfed for one year by this woman cannot be excluded.

For the ultrashort-chain PFAS, currently no serum-based HBGVs exist. However, the Risk Assessment Committee of the European Chemicals Agency (ECHA) recently recommended to classify TFA as a category 1B reproductive toxicant (“may cause harm to the unborn child” and “is suspected of damaging fertility”) by).<sup>2</sup> In July 2026, EFSA published its scientific opinion to lower the acceptable daily intake level for TFA from 0.05 mg/kg bw/day (which dated from 2017) to 0.014 mg TFA/kg bw/day based on changes in thyroid hormone levels in a rat study.<sup>3</sup>

### 1.2.4 Data analysis

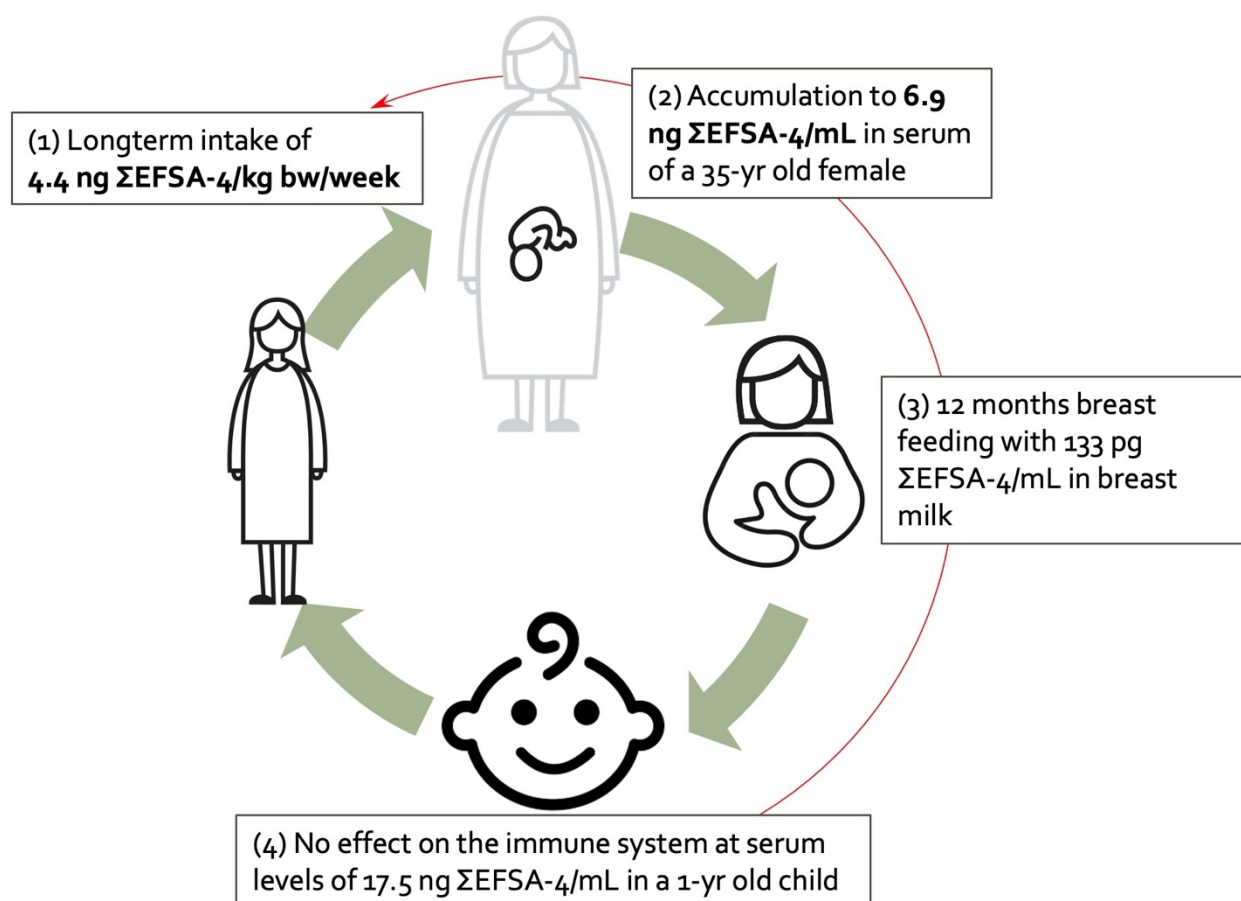
To assess if the measured long-chain PFAS levels in this study exceeded the EFSA threshold for serum, we summed the serum levels of PFOS, PFOA, PFNA and PFHxS to calculate  $\Sigma$ EFSA-4 (see 2.2.3). The three PFNA levels that were below the LOQ were assigned a value of LOQ/2. Descriptive statistics were applied to describe the quartiles, i.e. 25<sup>th</sup>, 50<sup>th</sup> (median) and 75<sup>th</sup> percentile of the PFAS levels in serum.

We then compared the  $\Sigma$ EFSA-4 levels that were measured in this study with the threshold level for PFAS in serum, for the whole study group (n=110). Any measured  $\Sigma$ EFSA-4 level that was higher than 6.89 ng/mL was considered to be higher than the threshold. This is a very conservative approach, as it considers the threshold as hard cut-off.

Next, we used the data from the questionnaire and regression modeling to assess associations between  $\Sigma$ EFSA-4 levels with known and suspected factors that may influence these levels. We also used models that included several factors at the same time (i.e., multivariable regression models). This allowed us to assess the association of each factor with  $\Sigma$ EFSA-4 concentrations, while taking the other factors into account. Because not every participant filled out a questionnaire, and some questionnaires were incomplete, the number of participants that could be included for each calculation varied between 70 and 110 (exact numbers are indicated in the text and/or in the table or figure legends).

For the ultrashort-chain PFAS, we did similar calculations as for the long-chain PFAS, i.e. associations per factor (country, sex, etc.) and multivariable regression modeling.

As there is no HBGV for TFA in serum, we could not assess a possible increased health risk based on existing guidance values. However, we used very simple, one-compartment toxicokinetic modeling to roughly estimate the serum levels that would be expected upon daily intake of the ADI established by EFSA. We used the limited and highly uncertain information available about the toxicokinetics of TFA. The calculations and assumptions we made to perform the modeling exercise are explained in the Supplementary information.

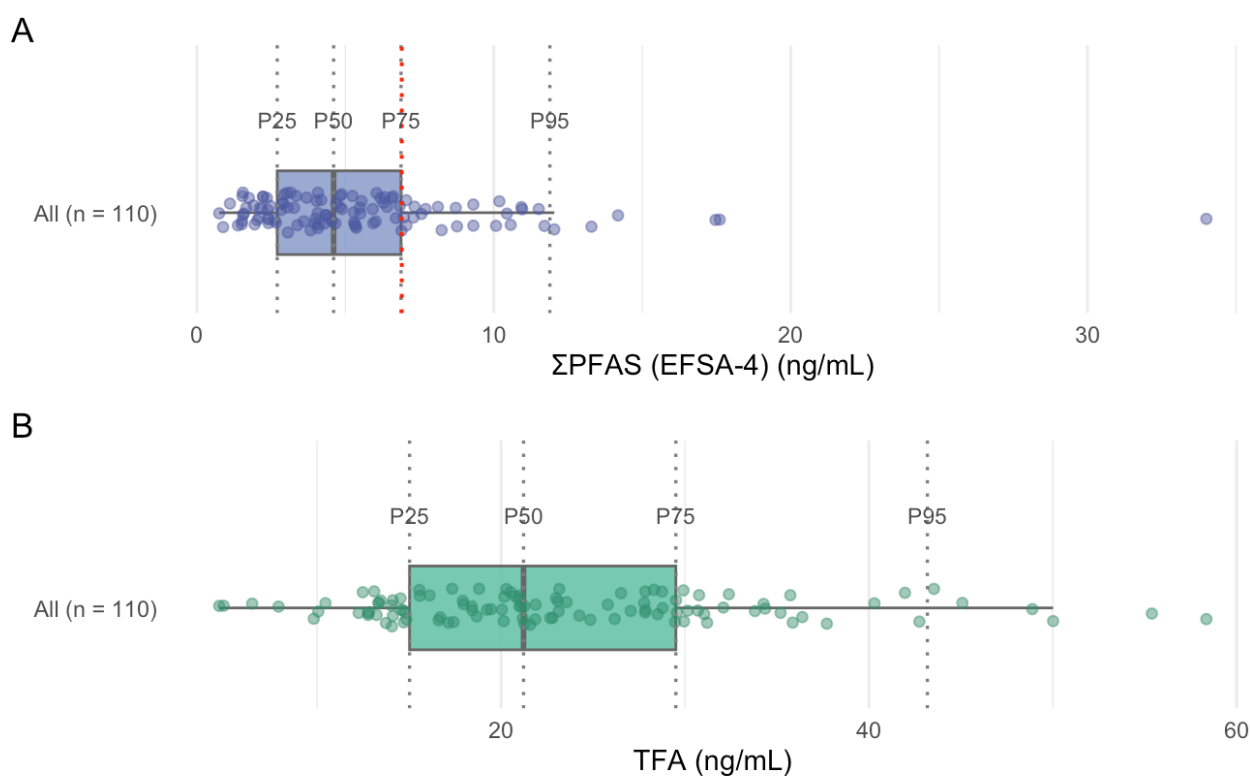


**Figure 2. Schematic overview of the derivation of the Tolerable Weekly Intake (TWI) for the sum of 4 PFAS (ΣEFSA-4 = PFOS + PFOA + PFHxS + PFNA) by EFSA:** (1) long-term intake of 4.4 ng ΣEFSA-4 per kilogram bodyweight per week leads to (2) maximal 6.9 ng ΣEFSA-4/mL serum in a 35-year old woman, so that she transfers maximal 133 pg ΣEFSA-4/mL in breast milk to her child during one year of breastfeeding, which leads to (4) maximal 17.5 ng ΣEFSA-4/mL in the child's serum at the age of 1 year, above which a reduced response to vaccination cannot be excluded. The red arrow indicates the calculations performed by EFSA, using serum levels in a 1-year-old child as the starting point to calculate the long-term intake level (TWI) of 4.4 ng ΣEFSA-4/kg bw/week.<sup>1</sup>

## 2. Results evaluation and discussion

### 2.1 Serum PFAS levels

In the whole study group of 110 participants, the median  $\Sigma$ EFSA-4 in serum was 4.6 ng/mL, with 50% of the participants falling within the 25–75th percentiles of 2.7–6.9 ng/mL (**Figure 3**). In the present study, PFOS made the largest relative contribution to the  $\Sigma$ EFSA-4 (PFOS 57% > PFOA 21% > PFHxS 16% > PFNA 5%) based on median serum levels (**Table S2**). This is in line with what is observed in most general population studies. EFSA reported based on studies from 2007-2018 that in adults the most prominent PFAS was PFOS (64%) followed by PFOA (16%), PFHxS (5.6%) and PFNA (5.1%), with median levels being 7.7, 1.9, 0.67 and 0.61 ng/mL, respectively.<sup>1</sup> These relative contributions are dependent on the year of sampling. The four PFAS that make up the EFSA-4 are considered so-called legacy PFAS. These are long-chain PFAS with half-lives up to several years in the human body.<sup>4</sup> Following restrictions on their production and use, absolute and relative serum concentrations of these legacy PFAS have changed in European populations. Generally, a decline in PFOS and PFOA has been observed after the year 2000, while studies found that concentrations of PFHxS and PFNA may have declined, remained stable or increased.<sup>5,6</sup>

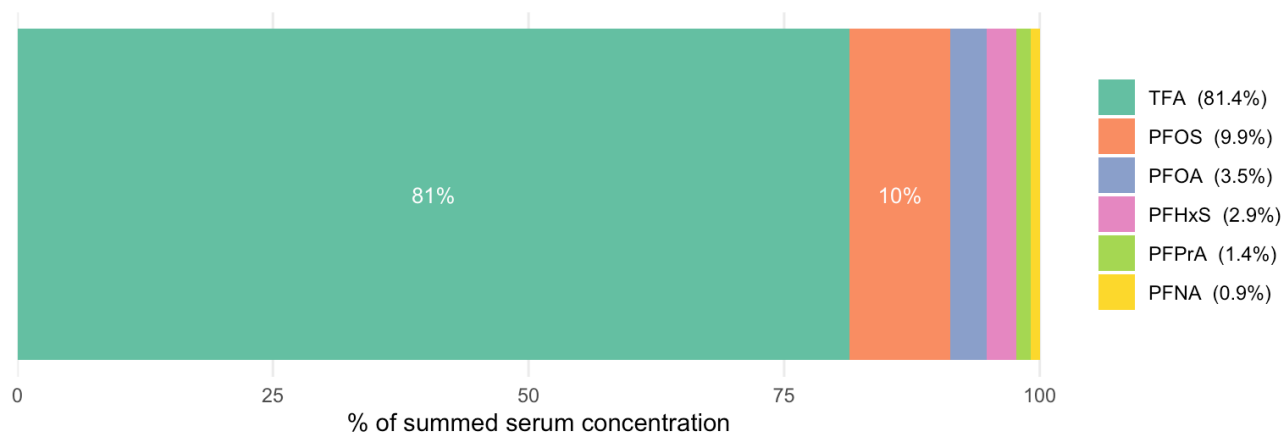


**Figure 3. Sum of serum levels of long-chain EFSA-4 PFAS ( $\Sigma$ EFSA-4 = PFOS + PFOA + PFHxS + PFNA, in ng/mL; A) and TFA (B) in all study participants (n=110).** The  $\Sigma$ EFSA-4 or TFA levels were divided into quartiles (P25, P50, P75), where P50 represents the median levels, meaning that half of the measured PFAS levels are lower and half are higher. P95 represents the 95<sup>th</sup> percentile, which is often used in human studies to indicate extreme values, highly exposed subgroups, or worst-case scenarios. Each dot represents one participant in this study. The red dotted line represents the EFSA threshold value for serum (6.9 ng  $\Sigma$ EFSA-4 /mL; see 1.2.3). Please note the difference in scale of the X-axis: for  $\Sigma$ EFSA-4 levels (A) the maximum level was 34 ng/mL and for TFA the maximum measured level was 58 ng/mL.

At the same time, levels of some shorter-chain replacement PFAS, such as GenX (not included in this study), or PFAS breakdown products, such as TFA and PFPrA, have started to emerge in the environment. However, human biomonitoring data regarding their presence in human serum remains limited. In the present study, the median TFA concentration in serum was 21.22 ng/mL (range 4.67–58.35 ng/mL), see **Figure 3**. The median PFPrA concentration was 1.13 ng/mL among the 25 of 110 samples in which PFPrA was detected (range 0.79–3.01 ng/mL; **Figure S1**).

The TFA serum levels that were measured in the present study are higher than those reported in the few other studies available (**Table S3**). The only other study among Europeans concerned a study among 143 Norwegian adults sampled blood in 2016–2017, in which TFA was detected in all serum samples and was the most abundant of the PFAS analysed.<sup>7</sup> One study reported a maximum level of 590 ng TFA/mL serum, though this study was performed among US residents living in an area with drinking water that was highly polluted with PFAS, where high and extreme levels are to be expected.<sup>8</sup> PFPrA was also detected in that study and contributed 5.4% to the total mass of PFAS in serum.<sup>8</sup> The detection frequency of PFPrA in present study is similar to the Norwegian study, but lower than that reported in the two Chinese<sup>9,10</sup> and two US studies.<sup>8,11</sup> A recent study of PFAS in urine of German adults detected TFA in all samples, no PFPrA, but, for the first time, also reported TFMS in human urine.<sup>12</sup>

In the present study, TFA contributed 81% and PFPrA 1.4% to the total mass of the PFAS (PFOS + PFOA + PFHxS + PFNA + TFA + PFPrA) (**Figure 4**). This is relatively high compared to the few other studies available. However, the other studies included more PFAS in their analyses, which logically reduces the relative contribution of TFA to the total mass of PFAS. In almost every participant in present study, TFA made up the greater part of the combined TFA +  $\Sigma$ EFSA-4 levels in (**Figure S2**), showing that this high relative contribution of TFA is the typical pattern, not just the result of a few people with high TFA levels. On average, the TFA levels were 4.6 times higher than the summed four long-chain PFAS (medians 21.2 versus 4.6 ng/mL). These TFA serum levels are among the highest levels reported in humans thus far.



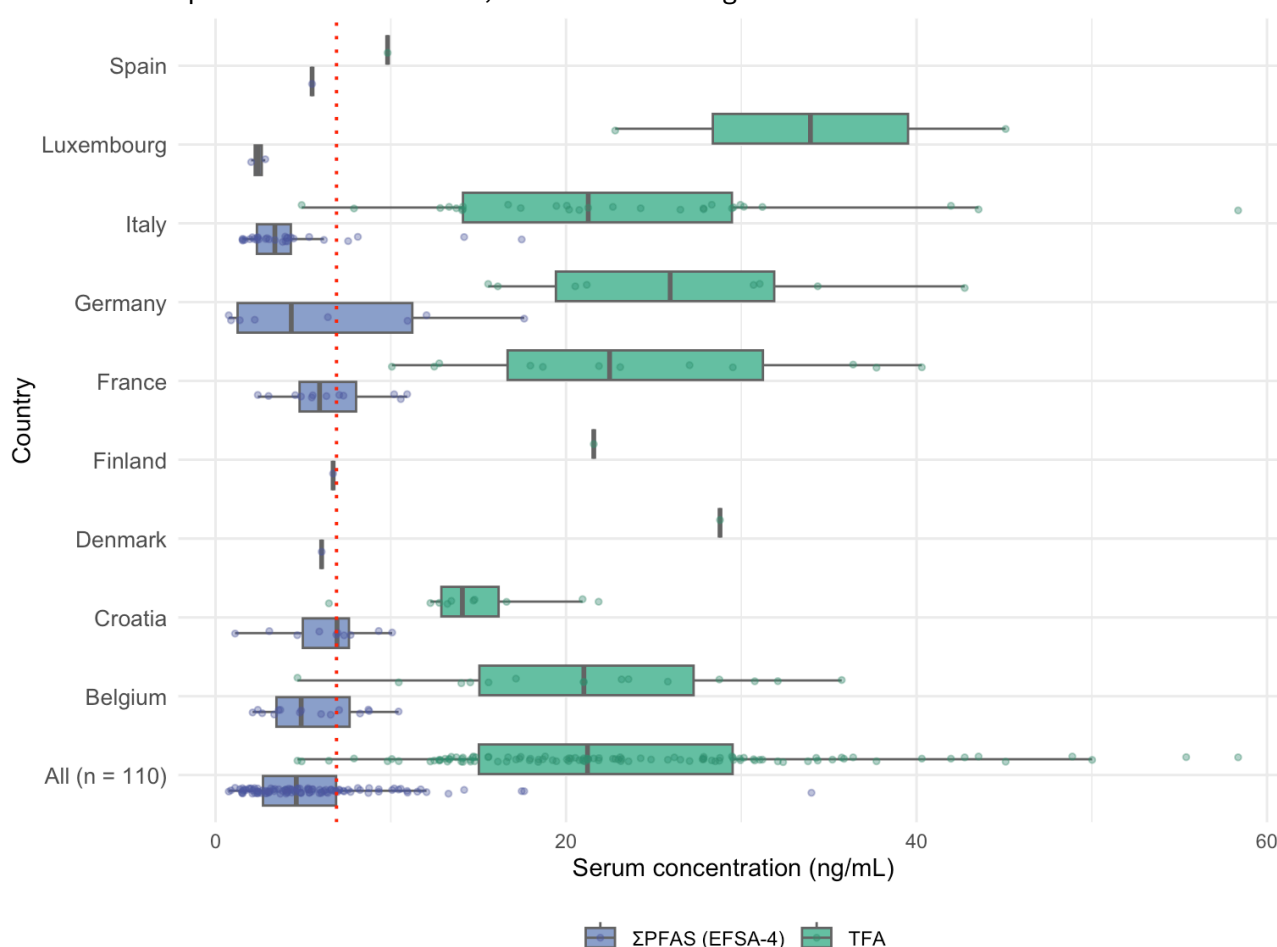
**Figure 4. Relative contribution of each individual PFAS (long-chain EFSA-4 + ultrashort-chain TFA + PFPrA) to the total PFAS concentration measured in serum (n=110).** For each participant, the concentration of each PFAS was expressed as a percentage of the summed concentration of the six PFAS that were detected; the figure shows the median within-person contribution of each PFAS across participants, rescaled to 100%, with the 85 of 110 PFPrA values below the LOQ imputed at LOQ/2. TFA accounted for the largest share (81.4%), followed by PFOS (9.9%); each of the other PFAS contributed <4% (PFPrA 1.4%). Please note that the number of detects for PFPrA are small. However, results were robust to both the summary method (median vs. mean) and the handling of PFPrA non-detects (using LOQ/2 vs 0).

All four long-chain PFAS included in this study were positively correlated with one another (**Figure S3**). This means that participants with higher levels of one of the EFSA-4 PFAS generally also tended to have higher levels of the other three. This is consistent with the results from larger human biomonitoring studies.<sup>13,14</sup> The ultrashort-chain PFAS TFA and PFPrA were moderately positively correlated with each other, meaning that participants with higher TFA levels also tended to have higher PFPrA levels, suggesting a similar route of exposure. TFA was weakly correlated with PFOA, but showed little or no correlation with the other long-chain PFAS. The weak positive correlation between TFA and PFOA may reflect some overlap in exposure sources or determinants, although the low correlation suggests that their exposure patterns are largely distinct.

## 2.2 Predictors of PFAS serum levels

### 2.2.1 Country

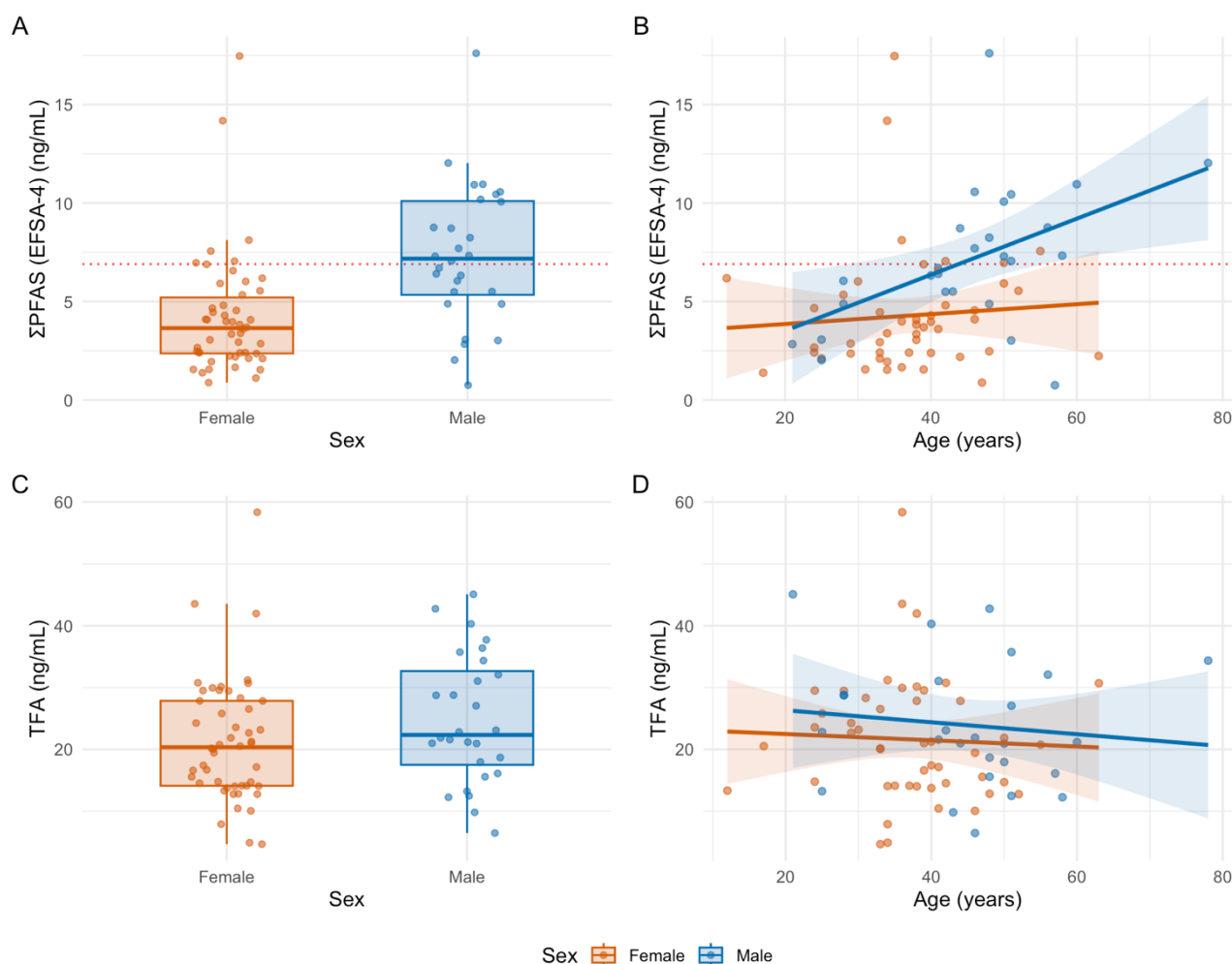
There were no apparent differences in  $\Sigma$ EFSA-4 or TFA levels between countries (**Figure 5** and **Figure S4** for individual PFAS), although the small and unequal numbers per country preclude meaningful statistical comparison. In all countries, TFA levels were higher than the  $\Sigma$ EFSA-4 levels.



**Figure 5. Distribution of the summed EFSA-4 PFAS ( $\Sigma$ EFSA-4; PFOS + PFOA + PFNA + PFHxS) and TFA levels in serum, by country, and in all participants.** Boxes represent the interquartile range (25th–75th percentiles), with the median shown by the horizontal line (half the levels lie below this line and half above). The whiskers extend to the lowest and highest values within 1.5 times the interquartile range (IQR), and each dot indicates an individual participant. The red dotted line indicates the EFSA serum threshold value of 6.9 ng  $\Sigma$ EFSA-4/mL. The box for “All” includes all participants, including those without questionnaire data (n=110), whereas country-specific results are shown for participants who completed the questionnaire (n=79; specific number of participants per country are indicated in Table 1). PFPrA serum levels per country are shown in Figure S1 and S4.

### 2.2.2 Sex and age

The most important predictors of long-chain  $\Sigma$ EFSA-4 in this study were sex and age. On average, male participants had higher levels than female participants (median 7.3 ng/mL in men vs 3.7 ng/mL in women; **Figure 6A**). The  $\Sigma$ EFSA-4 levels increased with age in men, but not in women (**Figure 6B**). This sex difference is well-established in other studies and is partly due to elimination of PFAS in women via menstruation<sup>15</sup> and breastfeeding<sup>16</sup>. There was no significant association between  $\Sigma$ EFSA-4 serum levels and body mass index (BMI) after adjustment for age, sex and parity. These findings are broadly in line with other human biomonitoring studies.<sup>17</sup> In multivariable regression models that assessed multiple predictors simultaneously, age and sex remained the most important predictors of PFAS serum levels.



**Figure 6.  $\Sigma$ EFSA-4 and TFA concentrations in serum by age and sex.** The upper panels show the sum of the four long-chain EFSA PFAS (PFOS, PFOA, PFNA and PFHxS; A and B), and the lower panels show TFA (C, D). Each point represents one participant. Panels A and C show concentrations by sex, unadjusted for other factors ( $n=78$ ; sex was missing for one questionnaire participant). Each box spans the 25<sup>th</sup> to 75<sup>th</sup> percentile; the line represents the median; whiskers extend to 1.5×IQR; and points represent individual participants. Panels B and D show concentrations by age separately for women and men; lines show the linear trend estimated by regression models and shaded areas indicate the 95% confidence intervals. The red dotted line marks the EFSA-derived reference value concentration of 6.9 ng/mL for  $\Sigma$ EFSA-4.  $\Sigma$ EFSA-4 concentrations were higher in men than in women, and tended to increase with age in men, while little age-related pattern was apparent in women. No statistically significant difference in TFA concentrations was observed between men and women. No clear age-related pattern was observed for TFA in men or women.

The TFA levels did not differ between men and women when considered separately from other factors (median 22.34 ng/mL in men and 20.35 ng/mL in women), nor were TFA levels associated with age (**Figure 6C,D**). The study with Chinese volunteers<sup>9</sup> reported an increase in TFA levels with age, but no differences between levels in males and females. Data from animal studies do not indicate a sex-related difference in kinetics ('what the body does to a chemical'), though specific data addressing this is limited.<sup>3</sup> Unlike the long-chain PFAS, TFA has a reported elimination half-time of about 16-60 hours<sup>18</sup>, meaning that it does not remain in the body for long. Animal studies also indicate that TFA does not progressively accumulate in the body upon repeated exposure (the levels plateau after some time upon repeated exposure).<sup>3</sup> This indicates that the TFA levels measured in serum in present study are likely the result of frequent exposure of significant amounts of TFA in daily life.

### 2.2.3 Diet

Participants reporting mostly meat- or fish-based diets had higher  $\Sigma$ EFSA-4 levels than participants who indicated to be vegetarian or vegan (**Figure 7A**). When looking more closely at fish or meat intake, higher fish/seafood and higher meat intake showed associations with higher  $\Sigma$ EFSA-4 levels (**Figure 7C**). Fish and seafood are known to contain high levels of PFAS, and prior evidence supports that fish/seafood is the most important dietary source of PFAS exposure.<sup>1</sup>

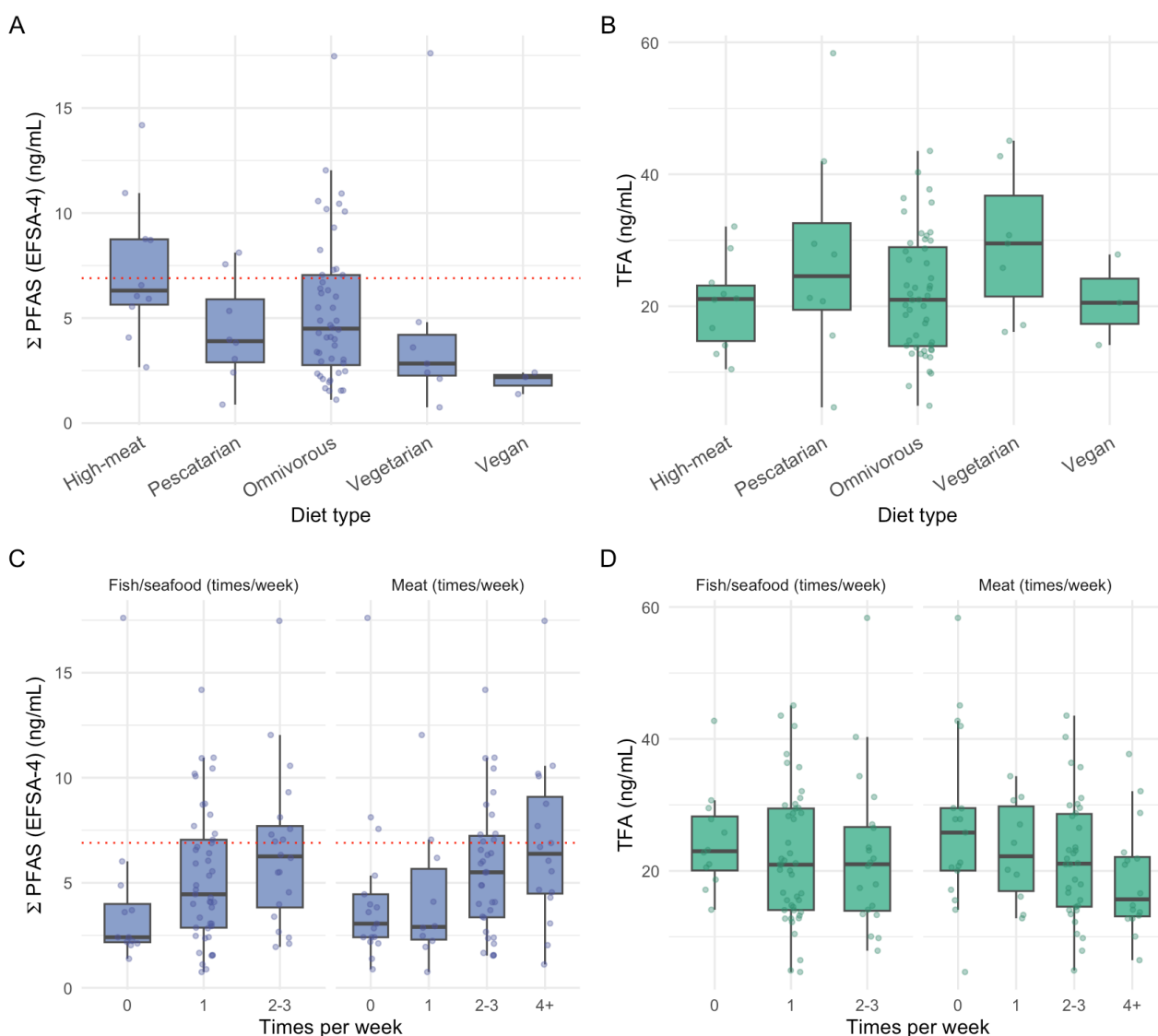


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**Figure 7. Serum PFAS concentrations according to diet type and fish/seafood and meat intake.** Serum concentrations of  $\Sigma$ EFSA-4 (PFOS + PFOA + PFNA + PFHxS) and TFA are shown according to diet type (A–B) and frequency of fish/seafood and meat consumption (C–D) (n=76 participants with data on diet type and 77 with data on fish/seafood/meat intake). Each box spans the 25th to 75th percentile (the interquartile range (IQR)), the line represents the median; whiskers extend to 1.5×IQR of the box, and points represent individual participants. The red dotted line in panels A and C marks the EFSA-derived reference value concentration of 6.9 ng/mL for  $\Sigma$ EFSA-4. Diet type was associated with  $\Sigma$ EFSA-4 concentrations (high-meat > pescatarian > omnivore > vegetarian > vegan) but not TFA, although data were limited for most diet types. Higher meat intake, and less clearly higher fish/seafood intake, was associated with higher levels of  $\Sigma$ EFSA-4; higher meat intake was associated with lower TFA levels, whereas fish/seafood intake was not associated with TFA. These trends for  $\Sigma$ EFSA-4 and TFA remained significant in multivariable regression analyses accounting for other predictors.

Opposite to the long-chain  $\Sigma$ EFSA-4 PFAS, TFA levels did not show an association with diet type (mostly meat, pescatarian, omnivore, vegetarian or vegan; **Figure 7B**). Fish/seafood intake was not associated with TFA levels and increased meat intake was associated with lower TFA levels (**Figure 7D**). This association remained when adjusting for other predictors (data not shown). Rather than a direct effect of meat intake on TFA levels, this inverse relationship may reflect dietary patterns among lower-meat consumers, for example a greater intake of plant-based food and beverages<sup>19</sup>. However, the limited dietary information collected (see Section 4) did not allow us to evaluate dietary patterns in detail.

#### 2.2.4 Other predictors

The questionnaire addressed several factors that have been shown to influence PFAS levels in other studies. Besides age, sex and some dietary factors (described above), no other variables were significantly associated with  $\Sigma$ EFSA-4 levels, including BMI, statin use, blood-donation frequency, menopausal status, non-stick cookware use, take-away food frequency, water source (bottled or tap water), and self-reported residential proximity to industrial or other point sources. The lack of associations in this study may reflect the small number of participants and/or the limited contrast in PFAS levels between the groups.

People working with PFAS (e.g. firefighters or fluorochemical workers) or living in communities with contaminated drinking water or next to a fluorochemical plant often show higher and different patterns of PFAS levels in their blood than is observed in the general population, such as higher PFHxS or PFOA levels than PFOS. Among all participants, five participants had PFOA levels that were 1.6 to 4.5-fold higher than PFOS. However, their total  $\Sigma$ EFSA-4 was between 0.7–8.1 ng/mL, which does not point to extreme exposure scenarios. In this study population, fourteen participants indicated to work or have worked as firefighter or in fluorochemical industry. The median  $\Sigma$ EFSA-4 level in these participants was not different from the other participants when corrected for sex, age and diet. Of these 14 participants, one had a deviating pattern in PFAS levels, with PFHxS being higher than PFOS. The other 13 participants showed no clear deviations from what is expected in the general study population in terms of absolute or relative PFAS levels. One participant had a high PFOS level (of 29.6 ng/mL) and a  $\Sigma$ EFSA-4 level of 34.0, but no questionnaire information was available for this participant to indicate a potential source of exposure.

The sources for TFA and PFPrA are less well-defined. Both TFA and PFPrA are breakdown products of various chemicals, including fluorinated refrigerants, pharmaceuticals, some active substances used in plant protection products and PFAS. It is well-known that TFA can accumulate in water resources and in plants, including crops used for consumption.<sup>20</sup> In the present study, there were no clear predictors of TFA levels based on the information that was obtained through questionnaires. We did not assess predictors of PFPrA given the low detection rate and small sample size (PFPrA was detected in 25 of the 110 serum samples).

### 3. Risk assessment: comparison of PFAS levels with EFSA threshold values

All EFSA-4 PFAS, i.e. PFOS, PFOA, PFHxS and PFNA, were detected in serum samples of every participant, though PFNA levels were below LOQ in three participants. To assess potential health risks, the levels of PFOS, PFOA, PFHxS and PFNA were summed and compared to the serum threshold levels determined by EFSA (see 1.2.3). Of the 110 participants, 27 (25%) exceeded the EFSA serum threshold of 6.9  $\Sigma$ EFSA-4/mL. At the 95<sup>th</sup> percentile of the observed  $\Sigma$ EFSA-4 levels, this exceedance was 1.7-fold (**Table 3**). This means that at the highest 5% exposure level (11.9 ng/mL), PFAS levels are 1.7 times higher than the EFSA serum reference value. When only looking at women of reproductive age ( $\leq 49$  years; n=46), the range of  $\Sigma$ EFSA-4 levels was 0.88–17.5 ng/mL, with 4 of the 46 women exceeding the EFSA threshold value (1.1-fold at the 95<sup>th</sup> percentile; individual exceedances were 2.5-, 2.1-, 1.2- and 1.0-fold; see 1.2.4).

For comparison, aligned studies that were performed within the European Human Biomonitoring project HBM4EU<sup>5</sup>, PFAS serum levels were measured in teenagers (n=1,957; ages 12–18) from nine European countries, sampled between 2014 and 2021. Of these teenagers, 14% exceeded the  $\Sigma$ EFSA-4 threshold value for serum.<sup>21</sup> Higher PFAS concentrations were observed in teenagers in countries from the North and West of Europe, of which 24% exceeded the EFSA threshold<sup>22</sup>, compared with the South and East. The present study did not have sufficient participants per country (i.e., statistical power) to assess differences in levels between regions. In another study, the  $\Sigma$ EFSA-4 levels in serum exceeded the EFSA threshold in 71% of adults (n=1254, sampled in the Netherlands between 2016-2017) by 1.4-fold at P50 and 4.2-fold at P95.<sup>23</sup> In that study, 42% of the women of reproductive age (18-45, n=378) exceeded the threshold by 1.9-fold at the 95<sup>th</sup> percentile (0.9-fold at P50). This difference in exceedance of the EFSA threshold among women of reproductive age (42% in the Netherlands versus 9% in present study) may reflect the changes over time in long-chain PFAS levels (2016/2017 versus 2026), a slightly different age window (18-45 years versus  $\leq 49$  years), or could be due to the small sample size in present study.

**Table 3. Summed EFSA-4 PFAS ( $\Sigma$ EFSA-4 = PFOS + PFOA + PFNA + PFHxS) in serum relative to the EFSA serum threshold value (n = 110).**

|                                                         | Serum levels (ng/mL) |      | % above EFSA threshold | Ratio of measured $\Sigma$ EFSA-4 divided by EFSA serum value (6.9 ng/mL) <sup>c</sup> |     |
|---------------------------------------------------------|----------------------|------|------------------------|----------------------------------------------------------------------------------------|-----|
|                                                         | P50                  | P95  |                        | P50                                                                                    | P95 |
| <b>Sum EFSA-4 PFAS (all; n=110)<sup>a</sup></b>         | 4.6                  | 11.9 | 25% (27 of 110)        | 0.7                                                                                    | 1.7 |
| <b>Women (<math>\leq 49</math>yr; n=46)<sup>b</sup></b> | 3.4                  | 7.8  | 9% (4 of 46)           | 0.5                                                                                    | 1.1 |

<sup>a</sup>Serum concentrations of PFOS, PFOA, PFNA and PFHxS at the 50<sup>th</sup> and 95<sup>th</sup> percentile (P50 and P95, respectively); <sup>b</sup>Women of reproductive age ( $\leq 49$  years) in line with the World Health Organisation age categorical cut-off; <sup>c</sup>The measured  $\Sigma$ EFSA-4 serum concentrations divided by the EFSA serum threshold value 6.9 ng/mL. It represents a fold-exceedance of the reference value and should not be interpreted as a proportional increase in the probability or risk of an adverse health outcome.

A health-based guidance value (HBGV) is typically based on the most sensitive effect that is observed in experimental animal studies and/or human epidemiological studies. For PFAS, the effect seen at the lowest exposure was suppression of the immune system in young children. PFAS levels in young children mainly result from transfer from mother to child during pregnancy and breastfeeding. Therefore, EFSA calculated a long-term intake that would result in a maximal body burden in women of reproductive age that would not lead to immune effects in children (see **Figure 2**). In present study, 6 of the 50 participating women (12%) exceeded the EFSA threshold. Of these women, 4 were  $\leq 49$  years old,

which is considered the reproductive age by the World Health Organisation (WHO)<sup>24</sup>. This does not mean that their (future) children are at immediate higher risk for infections; how one's immune system functions is also dependent on other factors, such as sex, genetics, obesity, and general well-being.

More than half of the male participants exceeded the EFSA threshold (15 of the 28 males; 54%). In these fifteen males, the exceedance of the EFSA threshold was 2.0-fold at P95 exposure. PFAS exposure is also associated with other health effects, such as increased cholesterol, fertility problems and certain types of cancer.<sup>1,25</sup> The HBGV for ΣEFSA-4 PFAS should in principle also be protective against these effects, in both males and females. While the exceedance of the EFSA threshold is relatively modest (1.7-fold in the whole study group at P95), the fact that these PFAS were detected in all participants and the clear trend of increasing PFAS levels with age in men shows that the long-chain 'legacy' PFAS are still ubiquitous in the environment and that exposure is still prevalent throughout a person's life-time.

In July 2026, EFSA published an updated HBGV for TFA: the acceptable daily intake (ADI) that was established in 2017 for TFA was lowered 3.5 times to 0.014 mg/kg bw/day.<sup>3</sup> Studies in rats have shown that the target organs for TFA are thyroid, liver and fetal development. The effects seen at the lowest doses TFA involve the thyroid (lower thyroid hormone levels), and this effect was used to calculate the HBGV for TFA. EFSA concluded that the ADI of 0.014 mg/kg bw/day would also be sufficiently protective against other reported effects in animal studies. However, it was also noted that many uncertainties remain regarding the health effects of TFA. The types of effect seen with TFA are similar as what is observed with long-chain PFAS. However, the effects of TFA on the immune system, which is considered the most sensitive effect of long-chain PFAS, are not well studied for TFA. Also, there are no studies addressing the potential carcinogenicity of TFA, while this is an established effect of long-chain PFAS.

As the HBGV for TFA is based on external intake (via ingestion), it could not be used to compare with the TFA levels measured in the serum of the participants in this study and determine a health risk. For that, we would need a serum-based threshold or HBGV. Nevertheless, the median TFA levels in present study are the highest reported in serum of humans thus far, which deserves some preliminary risk assessment. Using very simplified (one-compartment) toxicokinetic modeling with multiple crude assumptions (see **Supplementary information**), we estimated that TFA consumption similar to the EFSA ADI of 0.014 mg/kg bw/day would lead to TFA serum levels of 0.024 mg/L (= 24 ng/mL). This very rough estimation is marginally higher than the median TFA levels that were measured in present study and may suggest that the participants had a daily intake of TFA that is approximately 90% of the EFSA ADI. However, when assuming a longer half-life of TFA (61 hours instead of 16 hours), the estimated daily intake would be around 23% of the ADI (for further explanation see Supplementary information). Based on TFA urine levels, one study estimated that adults in the general German population are exposed to quantities of TFA that are 138 times below to 11 times higher than the ADI of the EFSA.<sup>12</sup> These calculations are highly uncertain due to the lack of good toxicokinetic data for TFA in humans, and should thus be considered very preliminary. A study estimated that in 2022, a person (70 kg) would have a daily intake of 24.1 µg TFA through a typical Swedish diet<sup>26</sup>, which is 2.5% of the EFSA ADI. However, since TFA levels in the environment are rapidly rising and TFA is already ubiquitously found in drinking water and food sources<sup>20</sup>, it is conceivable that human TFA intake has increased in the last years. This study, together with the few other human studies (**Table S3**), show that TFA is commonly detected in human serum and urine and contributes significantly to the overall PFAS load in humans. The median TFA levels in present study are the highest reported in serum of humans thus far. Taken together, this stresses the need to gain better insight in human exposure levels and how TFA behaves in the human body. It is likely that when more research on the exposure levels and health impacts of TFA and other ultrashort PFAS will emerge, safety limits will be adjusted, similar to what has happened for long-chain PFAS, some of their replacements such as GenX, and recently also for TFA.

## 4. Considerations

This study was made possible by the participation of 110 volunteers across Europe. It was not designed to obtain a representative sample of the European population, nor to address a specific subgroup (e.g. occupationally exposed). Moreover, the study population was too small to reach scientifically sound conclusions for most measures. For example, to detect even a moderate difference in PFAS serum levels across nine countries, this would require at least 20–30 participants per country. Consequently, the findings described in this report should be interpreted with caution and considered indicative.

Of the 110 participants, 79 persons (partially) filled out a questionnaire that could point to known or suspected predictors of PFAS exposure. However, the questionnaire contained relatively low level of detail, was open for interpretation, and self-reporting (e.g. of dietary habits) is known to be prone to bias. Moreover, the factors that were included in the questionnaire were based on known or highly suspected predictors of long-chain PFAS. The limited number of associations with TFA levels in this study may suggest that these predictors are not relevant to predict exposure of ultrashort-chain PFAS.

As this study concerned a European focus, we compared measured PFAS serum levels to the serum threshold level for the sum of four PFAS established by EFSA. The EFSA threshold is generally used within Europe, though some countries use other and/or additional reference values for individual PFAS<sup>27</sup>, or to account for differences in potency to cause an effect.<sup>28</sup> The EFSA threshold assumes that PFOS, PFOA, PFNA and PFHxS are equally potent in causing immune suppressive effects. However, studies have shown this is not the case and that PFHxS is less potent than PFOS, PFOA and PFNA, and PFOS and PFNA are more potent than PFOA in causing immune suppression and liver effects.<sup>28</sup> Furthermore, it is well-established that humans are exposed to more PFAS than the four included by EFSA to calculate a TWI, and that those PFAS cause similar effects as the EFSA-4 PFAS. The focus on EFSA-4 in this study is thus an underestimation of the total PFAS exposure, and comparison with the EFSA threshold may represent an over- or underestimation of the risk. The WHO is currently assessing approaches to address PFAS as a mixture and inform the development of HBGVs for PFAS in food and drinking water through the joint FAO/WHO Expert Committee on Food Additives (JECFA).<sup>29</sup> It remains to be established if this is also feasible for PFAS with limited data, such as the ultrashort-chain PFAS.

The ultrashort-chain PFAS TFA was detected in all participants and occurred at considerably higher serum concentrations than the four long-chain PFAS combined. While the current safety limits for TFA preclude sound assessment of a health risk in this study (the EFSA ADI concerns oral uptake, which cannot directly be compared to serum levels and toxicokinetic human data is highly uncertain), the recent recommendation to classify TFA as reproductive toxicant by ECHA and the lowering of the HBGV by EFSA highlight the importance of including ultrashort-chain PFAS in future human biomonitoring and warrant actions to limit its production and, more importantly, of its precursors. The same rationale applies for PFPrA.

## 5. Conclusion

This exploratory study with 110 volunteers was performed to assess the extent and potential health risk of PFAS exposure among Europeans. All participants had long-chain PFAS PFOS, PFOA, PFHxS and PFNA in their serum. In 27 of the 110 participants (25%), these levels exceeded what is considered safe by current health-based guidance value established by EFSA for these four PFAS ('EFSA-4'). While this exceedance was relatively modest, there were clear increasing trends in EFSA-4 PFAS levels with increasing age in males and in participants who reported high fish/seafood or meat intake. Of the ultrashort chain PFAS, TFA and PFPrA were detected in 100% and 23% of the participants, respectively. Notably, the TFA levels were 4-5 times higher than that of the sum of EFSA-4 PFAS on a mass base. No clear trends in TFA were found with known and suspected predictors of PFAS exposure, based on the information that was provided by the participants (e.g. sex, diet). A very preliminary, worst-case risk assessment suggests that current intake levels of TFA may approach the acceptable daily intake of TFA

that was derived by EFSA. This warrants close monitoring of TFA levels, considering the rapidly rising levels of TFA in the environment, including in drinking water and crops for consumption. Additional studies are highly needed to better understand the sources of TFA and its levels in humans as well as to reduce uncertainties regarding human health impact.

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## Glossary

| Term                                              | Definition                                                                                                                                                                                                                                                                                                                                                                                          |
|---------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Acceptable Daily Intake (ADI)</b>              | The amount of a substance that can be consumed every day over a lifetime without an appreciable health risk. Usually expressed per kilogram of body weight per day. An ADI is commonly used for compounds that tend to remain a relatively short time in the body.                                                                                                                                  |
| <b>Health-based guidance value (HBGV)</b>         | A general term for a level of exposure considered unlikely to pose an appreciable health risk. ADIs and TWIs are examples of HBGVs.                                                                                                                                                                                                                                                                 |
| <b>Limit of Quantification (LOQ)</b>              | The lowest concentration of a substance that can be reliably measured and quantified with acceptable accuracy and precision. The LOQ is dependent on the analytical techniques used to measure a compound.                                                                                                                                                                                          |
| <b>Long-chain PFAS</b>                            | PFAS with longer carbon chains: perfluoroalkyl sulfonic acids with six or more carbons and perfluoroalkyl carboxylic acids with seven or more carbons. Examples are PFOS, PFOA, PFNA and PFHxS (the four PFAS in $\Sigma$ EFSA-4). They are the more extensively studied, "legacy" PFAS and tend to accumulate in the body.                                                                         |
| <b>Per- and polyfluoroalkyl substances (PFAS)</b> | A large group (estimates range from 10 000 to several million) of human-made fluorinated chemicals that are highly persistent in the environment. That is why they are sometimes referred to as "forever chemicals".                                                                                                                                                                                |
| <b>Tolerable Weekly Intake (TWI)</b>              | The amount of a substance that can be consumed each week over a lifetime without an appreciable health risk. Usually expressed per kilogram of body weight per week. A TWI is usually derived for compounds that are not easily eliminated from the body and accumulate over time with repeated exposure.                                                                                           |
| <b>Toxicokinetics</b>                             | Toxicokinetics is the quantitative study of the movement of an exogenous chemical from its entry into the body, through its distribution to organs and tissues via the blood circulation, and to its final disposition by way of biotransformation and excretion. Or simply stated: what the body does to a chemical.                                                                               |
| <b>Ultrashort-chain PFAS</b>                      | Ultrashort-chain PFAS have short carbon chains (three or fewer carbon atoms). They are highly persistent and mobile in the environment. In the human body, they tend to be excreted more quickly than long-chain PFAS (i.e., a shorter biological half-life). Examples are trifluoroacetic acid (TFA) and perfluoropropionic acid (PFPrA).                                                          |
| <b><math>\Sigma</math>EFSA-4</b>                  | The sum of the serum concentrations of the four PFAS included in EFSA's TWI: PFOS, PFOA, PFNA and PFHxS (all long-chain PFAS). EFSA (European Food Safety Authority) is the European agency that provides independent scientific advice on risks associated with the food chain. In 2020, EFSA established the health-based guidance value for the sum of four PFAS, which was used in this report. |

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## Supplementary information

**Table S1.** PFAS analysed in serum samples in this study and their limits of quantification.

| PFAS class       | Carbon chain length | Abbreviation      | Full Name                     | Chemical Formula <sup>a</sup> | LOQ <sup>b</sup> (ng/mL) |
|------------------|---------------------|-------------------|-------------------------------|-------------------------------|--------------------------|
| Ultrashort-chain | 1                   | TFMS              | Trifluoromethanesulfonic acid | CHF3O3S                       | 0.05                     |
|                  | 2                   | TFA               | Trifluoroacetic acid          | C2HF3O2                       | 1.00                     |
|                  | 2                   | PFEtS             | Perfluoroethanesulfonic acid  | C2HF5O3S                      | 0.05                     |
|                  | 3                   | PFPrA             | Perfluoropropanoic acid       | C3HF5O2                       | 0.60                     |
|                  | 3                   | PFPrS             | Perfluoropropanesulfonic acid | C3HF7O3S                      | 0.05                     |
| Long-chain       | 6                   | PFHxS             | Perfluorohexanesulfonic acid  | C6HF13O3S                     | 0.04                     |
|                  | 8                   | PFOA              | Perfluorooctanoic acid        | C8HF15O2                      | 0.04                     |
|                  | 8                   | PFOS <sup>c</sup> | Perfluorooctanesulfonic acid  | C8HF17O3S                     | 0.10                     |
|                  | 9                   | PFNA              | Perfluorononanoic acid        | C9HF17O2                      | 0.05                     |

<sup>a</sup>Chemical structures are shown in **Figure 1**; <sup>b</sup>LOQ, limit of quantification; <sup>c</sup> Sum of branched and linear iso-forms.

**Table S2.** Serum concentrations (ng/mL) of measured PFAS analytes in the present study (n = 110 European citizens sampled in 2026).

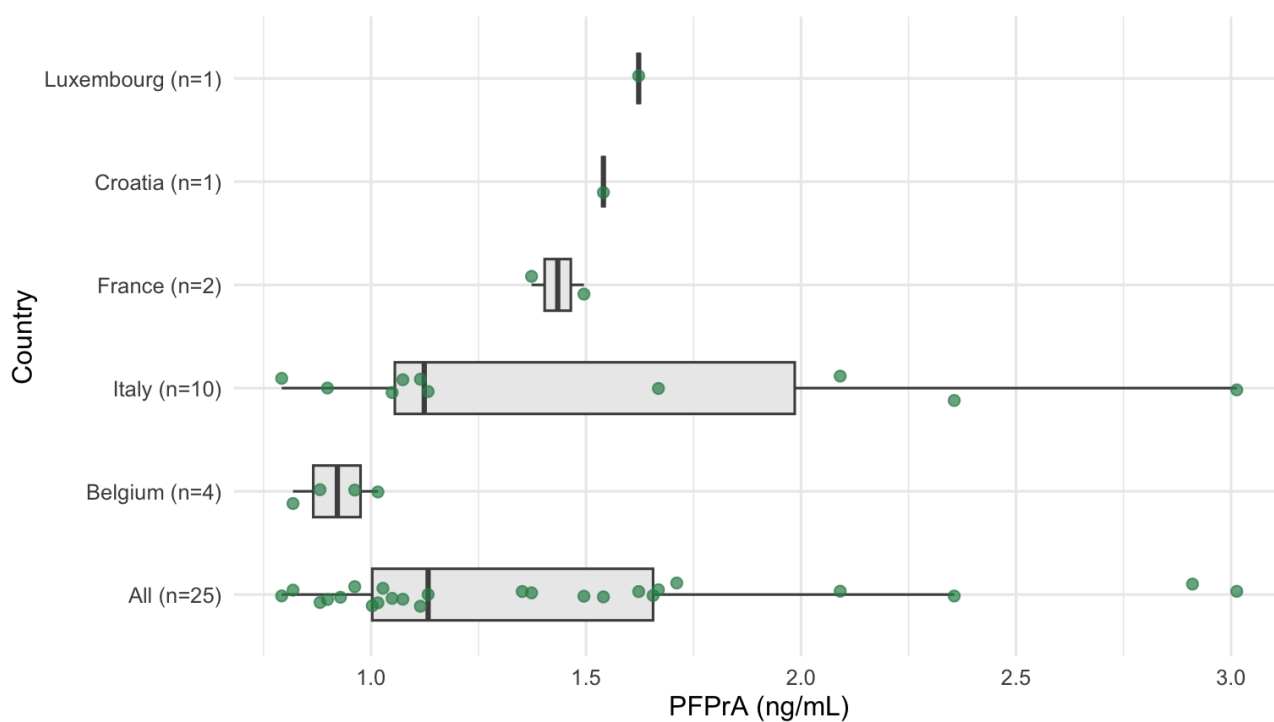
| Analyte                      | LOQ  | n > LOQ/N            | % > LOQ           | Min. | P5    | P25   | P50   | P75   | P95   | Max.  |
|------------------------------|------|----------------------|-------------------|------|-------|-------|-------|-------|-------|-------|
| <b>Long-chain PFAS</b>       |      |                      |                   |      |       |       |       |       |       |       |
| PFOS                         | 0.10 | 110/110              | 100.0             | 0.21 | 0.69  | 1.36  | 2.48  | 4.16  | 7.72  | 29.65 |
| PFOA                         | 0.04 | 110/110              | 100.0             | 0.14 | 0.34  | 0.64  | 0.92  | 1.27  | 2.44  | 5.92  |
| PFNA                         | 0.05 | 107/110 <sup>a</sup> | 97.3 <sup>a</sup> | <LOQ | 0.07  | 0.13  | 0.24  | 0.36  | 0.64  | 1.05  |
| PFHxS                        | 0.04 | 110/110              | 100.0             | 0.05 | 0.14  | 0.33  | 0.71  | 1.26  | 2.19  | 8.66  |
| ΣEFSA-4                      | —    | 110/110              | 100.0             | 0.75 | 1.53  | 2.71  | 4.60  | 6.88  | 11.89 | 34.00 |
| <b>Ultrashort-chain PFAS</b> |      |                      |                   |      |       |       |       |       |       |       |
| TFA                          | 1.0  | 110/110              | 100.0             | 4.67 | 10.24 | 15.02 | 21.22 | 29.50 | 43.18 | 58.35 |
| PFPrA                        | 0.6  | 25/110               | 22.7              | <LOQ | <LOQ  | <LOQ  | <LOQ  | <LOQ  | 1.66  | 3.01  |
| TFMS                         | 0.05 | 0/110                | 0.0               | <LOQ | <LOQ  | <LOQ  | <LOQ  | <LOQ  | <LOQ  | <LOQ  |
| PFEtS                        | 0.05 | 0/110                | 0.0               | <LOQ | <LOQ  | <LOQ  | <LOQ  | <LOQ  | <LOQ  | <LOQ  |
| PFPrS                        | 0.05 | 0/110                | 0.0               | <LOQ | <LOQ  | <LOQ  | <LOQ  | <LOQ  | <LOQ  | <LOQ  |

<sup>a</sup> For PFNA, concentrations below the LOQ (n = 3) were assigned a value of LOQ/2 for calculation of percentiles. LOQ, limit of quantification: the lowest concentration that could be reliably quantified. n > LOQ/N indicates the number of samples with concentrations above the LOQ out of the total number analysed; % > LOQ is the corresponding percentage. P5, P25, P50, P75 and P95 indicate the 5th, 25th, 50th (median), 75th and 95th percentiles, respectively. ΣEFSA-4 is the sum of PFOS, PFOA, PFNA and PFHxS. Values below the LOQ are shown as <LOQ where applicable.

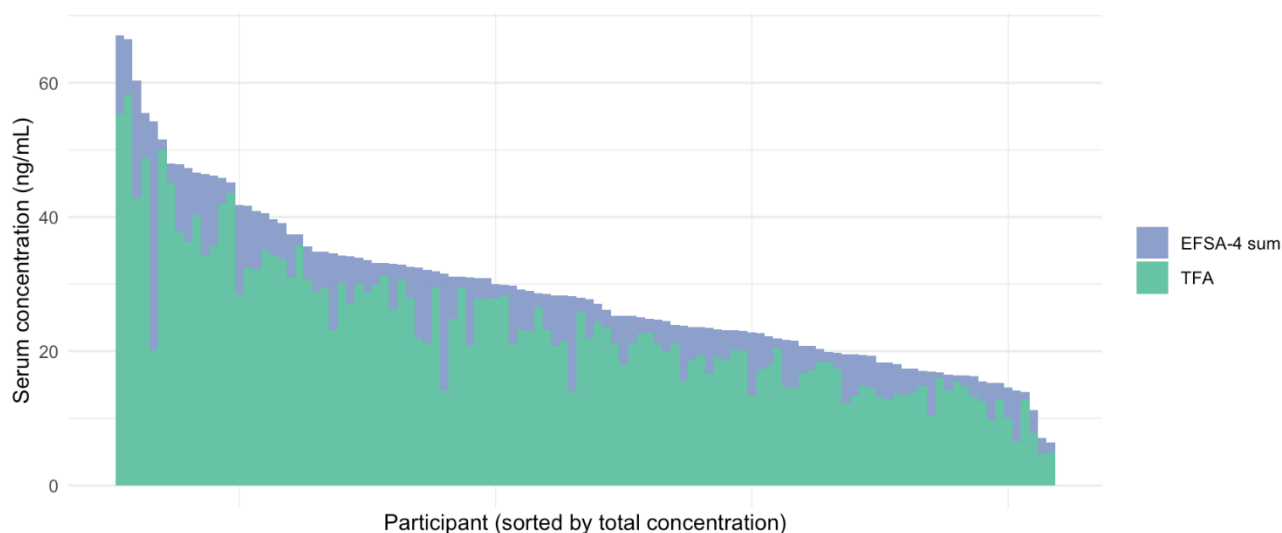
**Table S3.** Summary of human biomonitoring studies measuring TFA and PFPrA levels in serum.

|              | Country       | Number of participants | Year of sampling | Median (min-max)           | Mass contribution (number of PFAS measured <sup>\$</sup> ) | Reference            |
|--------------|---------------|------------------------|------------------|----------------------------|------------------------------------------------------------|----------------------|
| <b>TFA</b>   | <b>Europe</b> | <b>110</b>             | <b>2026</b>      | <b>21.22 (4.67, 58.35)</b> | <b>81% (6)</b>                                             | <b>Present study</b> |
|              | China         | 252                    | 2017             | 8.46 (5.36, 12.55)*        | 17.2% (21)                                                 | [9]                  |
|              | China         | 66 <sup>#</sup>        | 2022             | 0.229 (0.006, 2.476)       | 11.5% (17)                                                 | [10]                 |
|              | Norway        | 143                    | 2016-2017        | 7.04 (3.31, 16.0)          | 61% (21)                                                   | [7]                  |
|              | USA           | 81                     | 2020             | 6.0 (ND, 77)               | 57% (39)                                                   | [11]                 |
|              | USA           | 119                    | 2010-2016        | 17 (max 590)               | 17% (34)                                                   | [8]                  |
| <b>PFPrA</b> | <b>Europe</b> | <b>110</b>             | <b>2026</b>      | <b>1.13 (0.79, 3.01)</b>   | <b>1.4% (6)</b>                                            | <b>Present study</b> |
|              | China         | 252                    | 2017             | 0.48 (0.24, 0.82)*         | <10%/NS (21)                                               | [9]                  |
|              | China         | 66 <sup>#</sup>        | 2022             | 1.092 (0.002, 4.533)       | 21.4% (17)                                                 | [10]                 |
|              | Norway        | 143                    | 2016-2017        | NS (0.18, 0.59)            | NS (21)                                                    | [7]                  |
|              | USA           | 81                     | 2020             | 1.0 (0.14, 2.9)            | 9.5% (39)                                                  | [11]                 |
|              | USA           | 119                    | 2010-2016        | 5.4 (max 47)               | 5.4% (34)                                                  | [8]                  |

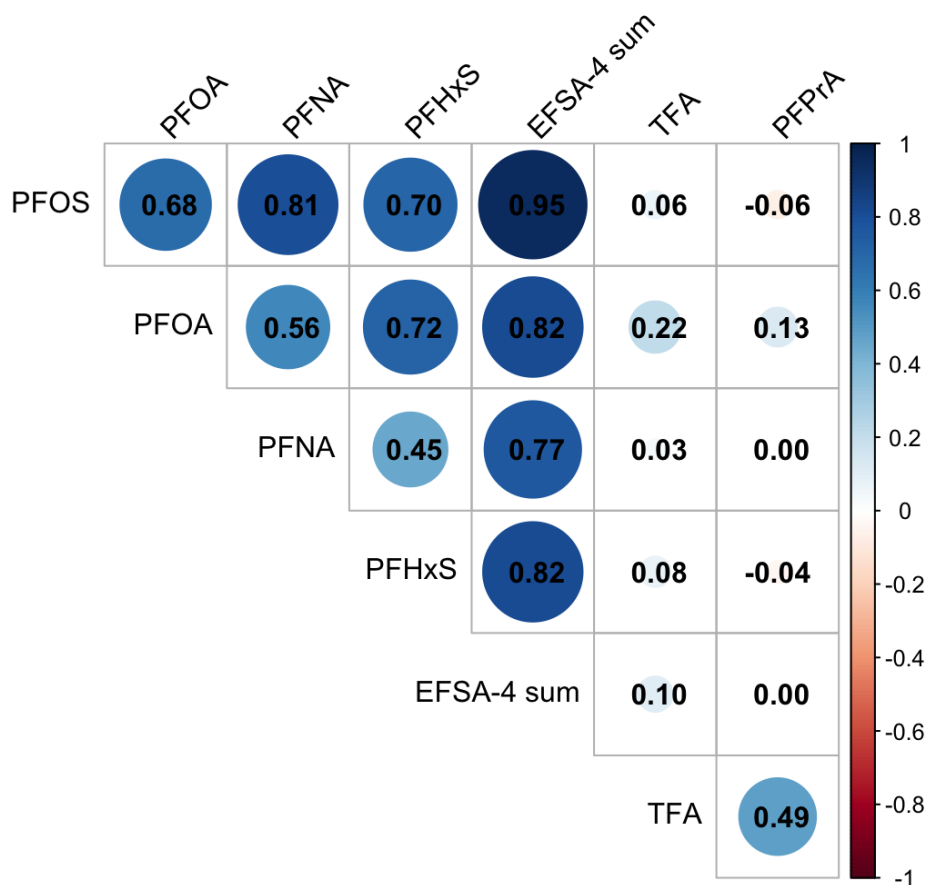
\* 25th and 75th percentiles are given; \$ number of PFAS that were detected, the study often included more PFAS in the analyses; # PFAS were measured in serum from cord blood; ND=Not detected; NS=Not specified.



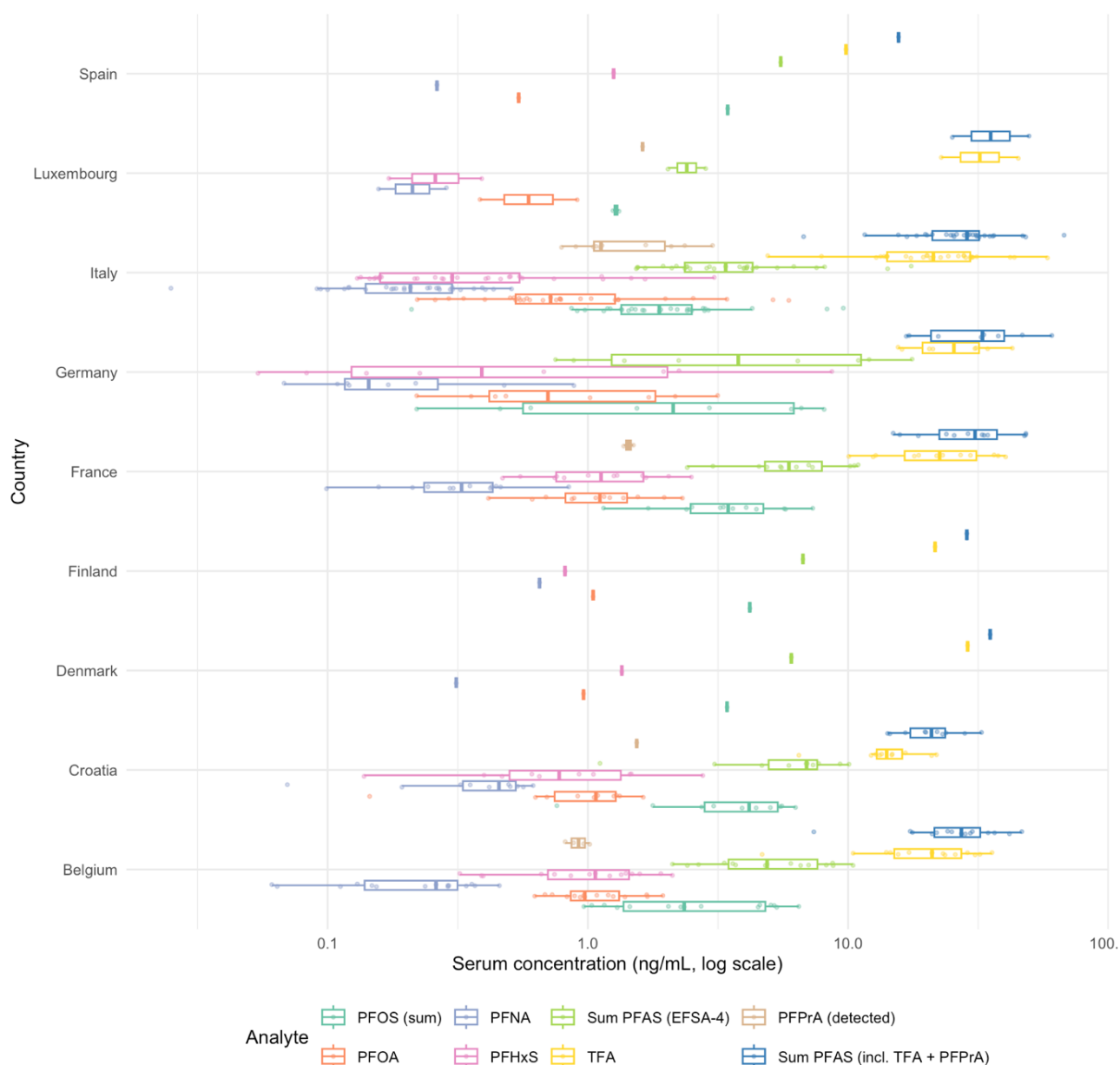
**Figure S1. Quantified serum PFPrA concentrations by country.** PFPrA was quantified above the limit of quantification (LOQ) in 25 of 110 serum samples overall (22.7%; shown as "All"). Country-specific panels show the 18 quantified samples from participants who completed a questionnaire and had a recorded country; the remaining 7 quantified samples were from participants without questionnaire data and are included only in "All." Individual points show PFPrA concentrations >LOQ; boxplots show the median and interquartile range where sufficient observations were available. Values <LOQ are not shown, and n indicates the number of participants with quantified PFPrA in each country.



**Figure S2. Within-participant serum concentrations of TFA and  $\Sigma$ EFSA-4 PFAS.** Each stacked bar represents one participant (n=110) and shows the serum concentration of TFA and the summed concentration of the four long-chain EFSA PFAS (PFOS, PFOA, PFNA, and PFHxS). Participants are ordered by the combined concentration. The predominance of TFA was observed across participants rather than being driven by a small number of participants with high TFA concentrations.



**Figure S3. Correlations between PFAS concentrations in serum.** The numbers show how closely the concentrations of each pair of PFAS were related (Spearman correlation coefficient,  $\rho$ ). Values closer to 1 indicate a stronger positive correlation, meaning that participants with higher concentrations of one PFAS also tended to have higher concentrations of the other. Values around 0 indicate little or no correlation. The four long-chain EFSA-4 PFAS were moderately to strongly correlated with each other ( $\rho = 0.5\text{--}0.8$ ). TFA was moderately correlated with PFPrA ( $\rho = 0.5$ ), weakly correlated with PFOA ( $\rho = 0.2$ ), and showed little or no correlation with the other long-chain PFAS ( $\rho < 0.1$ ).



**Figure S4. Serum concentrations of individual and summed PFAS, by country.** Boxplots show concentrations of PFOS, PFOA, PFNA, PFHxS, TFA and PFPrA, together with the sum of the four long-chain PFAS ( $\Sigma$ EFSA-4: PFOS + PFOA + PFNA + PFHxS) and the sum including TFA and PFPrA. Boxes represent the 25th–75th percentiles, lines within boxes the median, and points individual participants. Concentrations are shown on a logarithmic scale. For PFPrA, only samples with concentrations above the limit of quantification are shown (25 of 110 samples). Country-specific results should be interpreted cautiously because participant numbers were small and unequal.

## Supplemental information – estimation of plasma levels upon ingestion of TFA

We considered an exposure scenario in which the Acceptable Daily Intake (ADI, set by EFSA) of 0.014 mg/kg bodyweight (BW) per day was ingested by an adult person of 70 kg BW in 10 equal doses evenly distributed over the day. The corresponding Dose (D) was calculated as:

$$D = \frac{0.014 \frac{\text{mg TFA}}{\text{kg bw} \times \text{day}} \times 70 \text{ kg bw}}{10 \text{ doses per day}} = 0.098 \text{ mg TFA per dose}$$

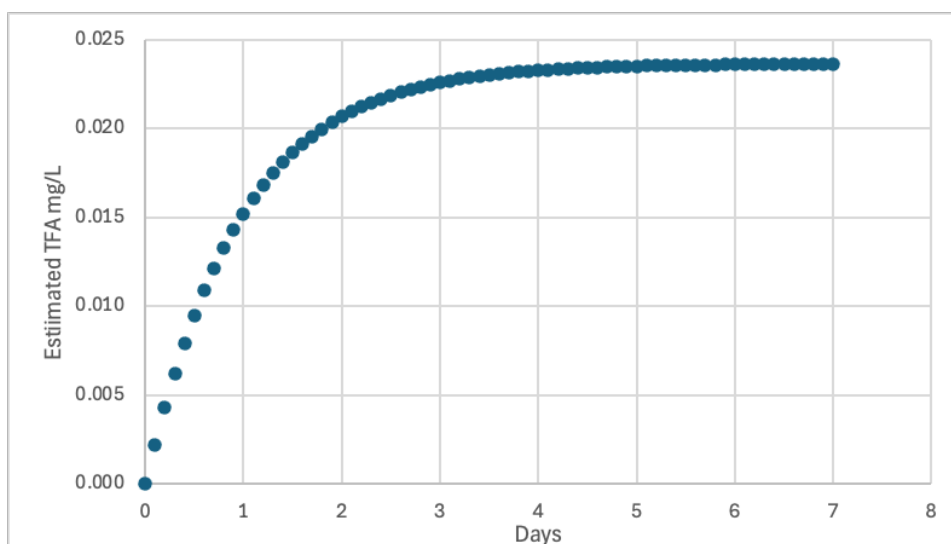
This dose was then calculated into a plasma concentration after the  $n^{\text{th}}$  dose ( $C_n$ ) using the formula:

$$C_n = \frac{F \cdot k_a \cdot D}{V_d \cdot (k_a - k_e)} \left[ \frac{1 - e^{-nk_e\tau}}{1 - e^{-k_e\tau}} e^{-k_e t} - \frac{1 - e^{-nk_a\tau}}{1 - e^{-k_a\tau}} e^{-k_a t} \right]$$

In this formula the following parameters and corresponding values were used:

| Parameter | Represents          | value | unit              | Assumption                                                                                                                   |
|-----------|---------------------|-------|-------------------|------------------------------------------------------------------------------------------------------------------------------|
| Vd        | distribution volume | 39    | liter             | TFA distributes equally in all the water in the body, basically assuming the body is 'one bag of water'                      |
| $t_{1/2}$ | half-life time      | 0.667 | day               | 16 hours, which is the lower bound of half-life time ranges in human volunteers (16-61 hours) according to reference 18      |
| ke        | elimination rate    | 1.04  | day <sup>-1</sup> | Based on a half-life time of 16 hours, see $t_{1/2}$                                                                         |
| ka        | absorption rate     | 27.1  | day <sup>-1</sup> | Based on a maximum plasma concentration in rabbits after a single dose at $t_{\text{max}}=3$ hours, according to reference 3 |
| F         | bioavailability     | 100%  |                   | All TFA that is ingested is taken up by the body                                                                             |
| D         | dose                | 0.098 | mg                | See calculation above                                                                                                        |
| n         | number of doses     | 0-70  |                   | For a seven-day period with 10 doses per day                                                                                 |
| $\tau$    | dose interval       | 0.1   | day               | Time interval between doses                                                                                                  |
| t         | time                | 0-0.1 | day               | Time elapsed after the most recent $n^{\text{th}}$ administration (so not the total time since the very first dose)          |

The calculated values for  $C_n$  converged to a steady-state plasma level of 0.024 mg TFA/L (=24 ng/mL; see **Figure S5 below**), which is marginally higher than the median TFA level of 0.021 mg TFA/L (=21 ng/mL) that was measured in present study. However, this estimation is highly sensitive to the assumptions made and toxicokinetic parameters remain poorly characterized. For example, the estimated plasma concentration after ADI ingestion would be higher if the distribution volume (Vd) is smaller. On the other hand, the estimated plasma concentration after ADI ingestion would be lower if the bioavailability (F) is less than 100%. Importantly, we used the lower bound of the reported elimination half-life (16 h). Using the upper bound (61 h) instead would raise the predicted steady-state serum concentration corresponding to the ADI from ~24 to ~92 ng/mL, in which case the measured median would represent ~23% of the ADI intake rather than ~90%. By using the shortest reported half-life (16h), the modelled serum level is a lower-bound estimate and the implied fraction of the ADI (90%) an upper-bound one; this estimation exercise should therefore be regarded as indicative only.



**Figure S5. Predicted plasma TFA levels using one-compartment toxicokinetic modeling.** Ingesting one tenth of the EFSA-ADI for TFA every day, ten times a day, by a person of 70 kg, leads to a steady-state plasma level of 0.024 mg TFA/L (=24 ng/mL).