

# Extractable Organofluorine (EOF) in Serum from Norwegian Participants in the EuroMix Study and the Role of Fluorinated Pharmaceuticals to EOF Results

Welmoed Nauta<sup>1</sup>, Enmiao Jiao<sup>1</sup>, Trine Husøy<sup>2</sup>, Dorte Herzke<sup>2</sup>, Line Småstuen Haug<sup>2</sup>, Monica Andreassen<sup>2</sup>, Hubert Dirven<sup>2</sup>, Leo Yeung<sup>1</sup>

<sup>1</sup>MTM Research Centre, Örebro University, Fakultsgatan 1, Örebro, 701 82, Sweden

<sup>2</sup>Norwegian Institute of Public Health, Division for Climate and Environmental Health, Lovisenberggata 8, 0456, Oslo, Norway

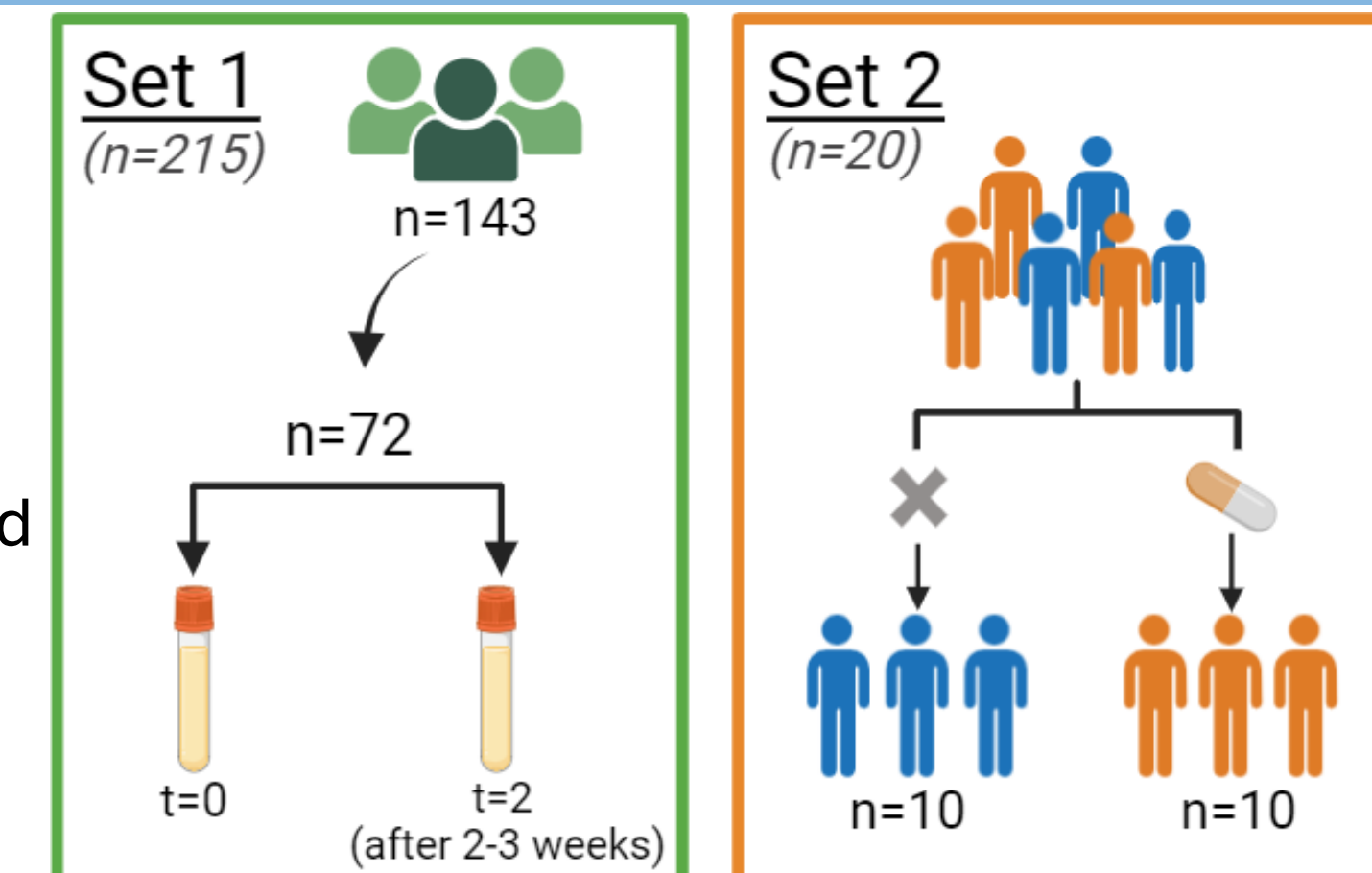
## Challenges

- Only a limited set of PFAS are included in human biomonitoring studies, leaving the full extent of exposure unknown.
- Extractable organofluorine (EOF) has been proposed as a screening tool.<sup>1</sup>
- EOF has been used as a proxy to measure PFAS total
- Evaluate changes in **PFAS exposure** across **two to three weeks** using the **EOF approach (research question #1)**.
- Recent studies have shown that the concentration of the legacy compounds (e.g. PFOS and PFOA) has been decreasing, and the unidentified organofluorine (UOF) fraction has been increasing.<sup>2,3</sup>
- A recent publication<sup>4</sup> confirmed the amount of UOF is related to the increasing number of fluorinated pharmaceuticals on the market.<sup>5</sup>
- Investigate how **fluorinated pharmaceuticals** impact **EOF levels in human serum (research question #2)**.

## Materials and Methods

### Samples

- Set 1 (provided by NIPH, Euromix study)
  - 100 females (age: 24 - 74, median 40)
  - 44 male (age: 25 - 72, median 43)
  - For t=2 (after 2-3 weeks), 72 pairs selected
    - 35 females (age: 24 - 67, median 40)
    - 37 males (age: 25 - 72, median 44)
- Set 2 (purchased commercially from BioIVT)
  - 10 subjects had records of using fluorinated pharmaceuticals (ie. fluoxetine)
  - 10 subjects did not have records of using any medications



### Extractable organofluorine analysis (EOF)

Sample set 1: Extracted using the ion pair extraction method without adjusting the pH (~4).  
Sample set 2: Extracted first at pH 4, followed by extraction at pH 11.

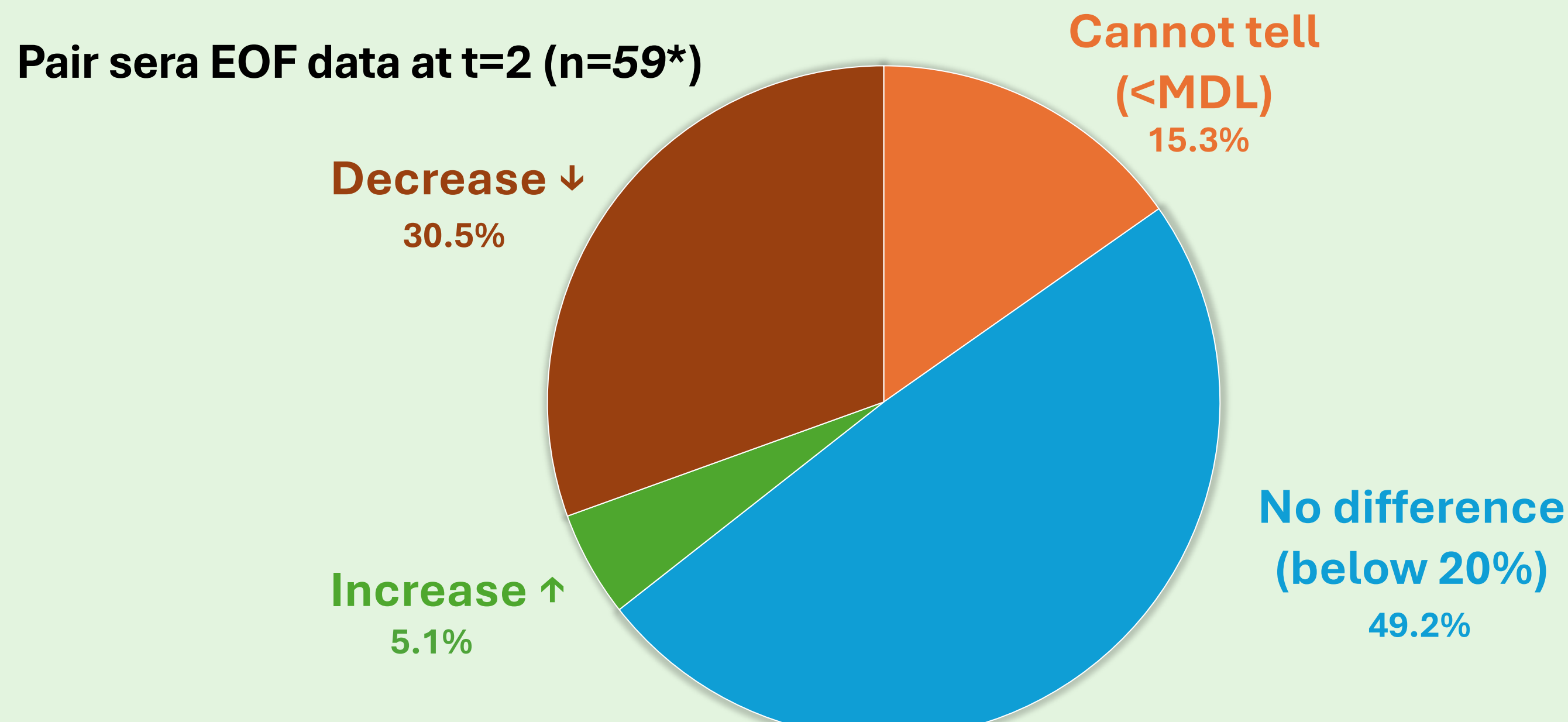
- Analysis using Combustion Ion Chromatography (CIC)
- Each batch contained procedural blanks, calf serum, and NIST SRM 1957

### Target analysis

- Analysis using SFC-MS/MS (for C2-C3 compounds) and LC-MS/MS (for ≥C4 compounds)
- Target 64 PFAS, seproxetine and fluoxetine
- The reported PFAS concentrations are not recovery corrected

## Research question #1: Any changes in PFAS levels between two/three weeks of sample collection using the EOF-CIC approach in humans? Sample set 1

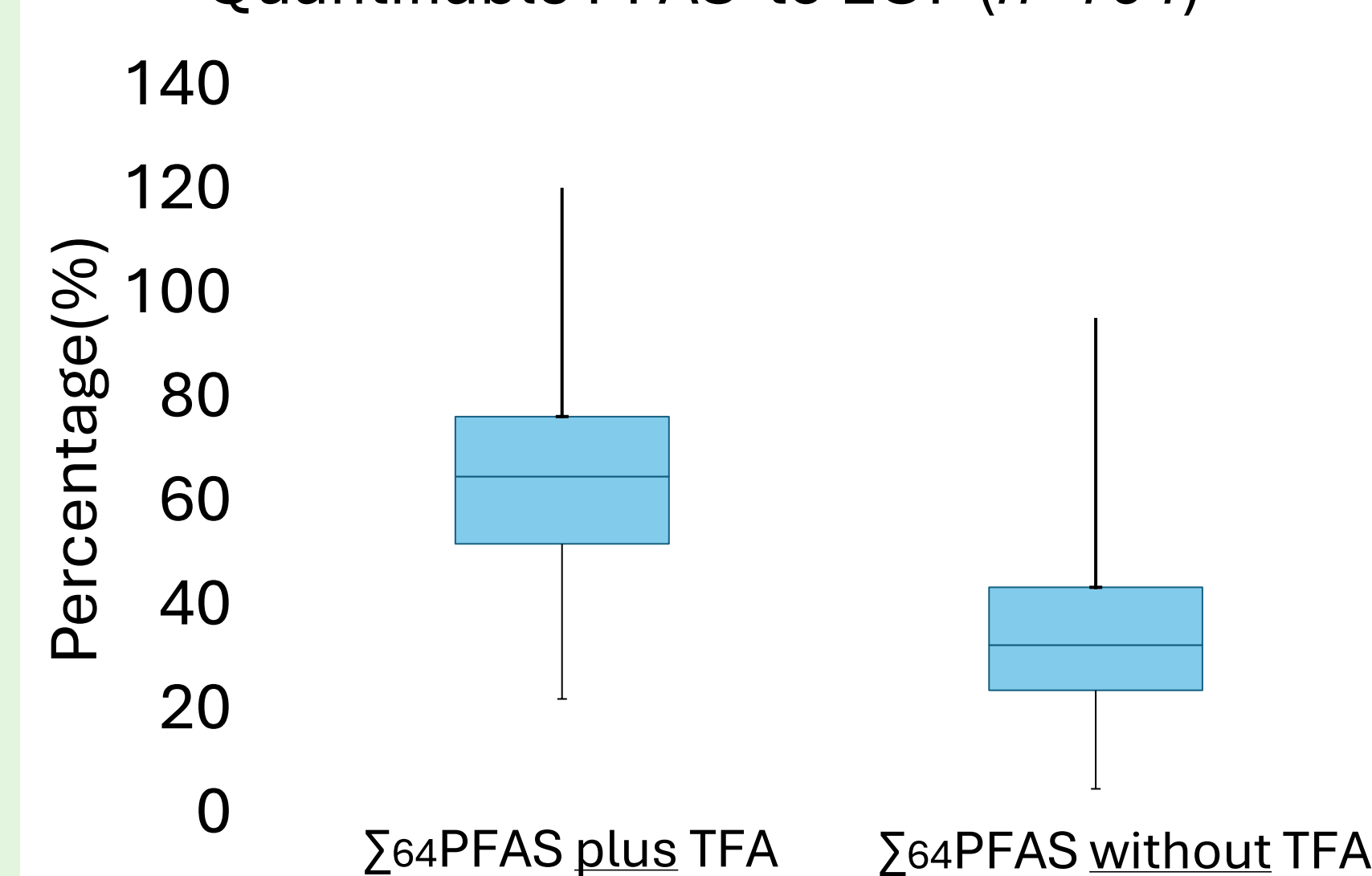
- Samples above MDL (n=164) ranging from 7.6 to 32 ng F/mL with a median of 14.6 ng F/mL
- PFOA, PFNA, PFDA, PFHxS, PFHpS, PFOS and TFA were detected in all samples
- PFOS and PFOA data between t=0 and t=2
  - Should not vary much given that the half-life is 4.3 - 8.2 years and 8.2 - 14.5 years



\*13 pair samples were removed because the differences of PFOS showed a variation >20%

- Not show any observable changes (>20%) within three weeks → suggesting fluctuations of EOF → ie. reactive or fast-eliminating PFAS or OF

### Quantifiable PFAS to EOF (n=164)



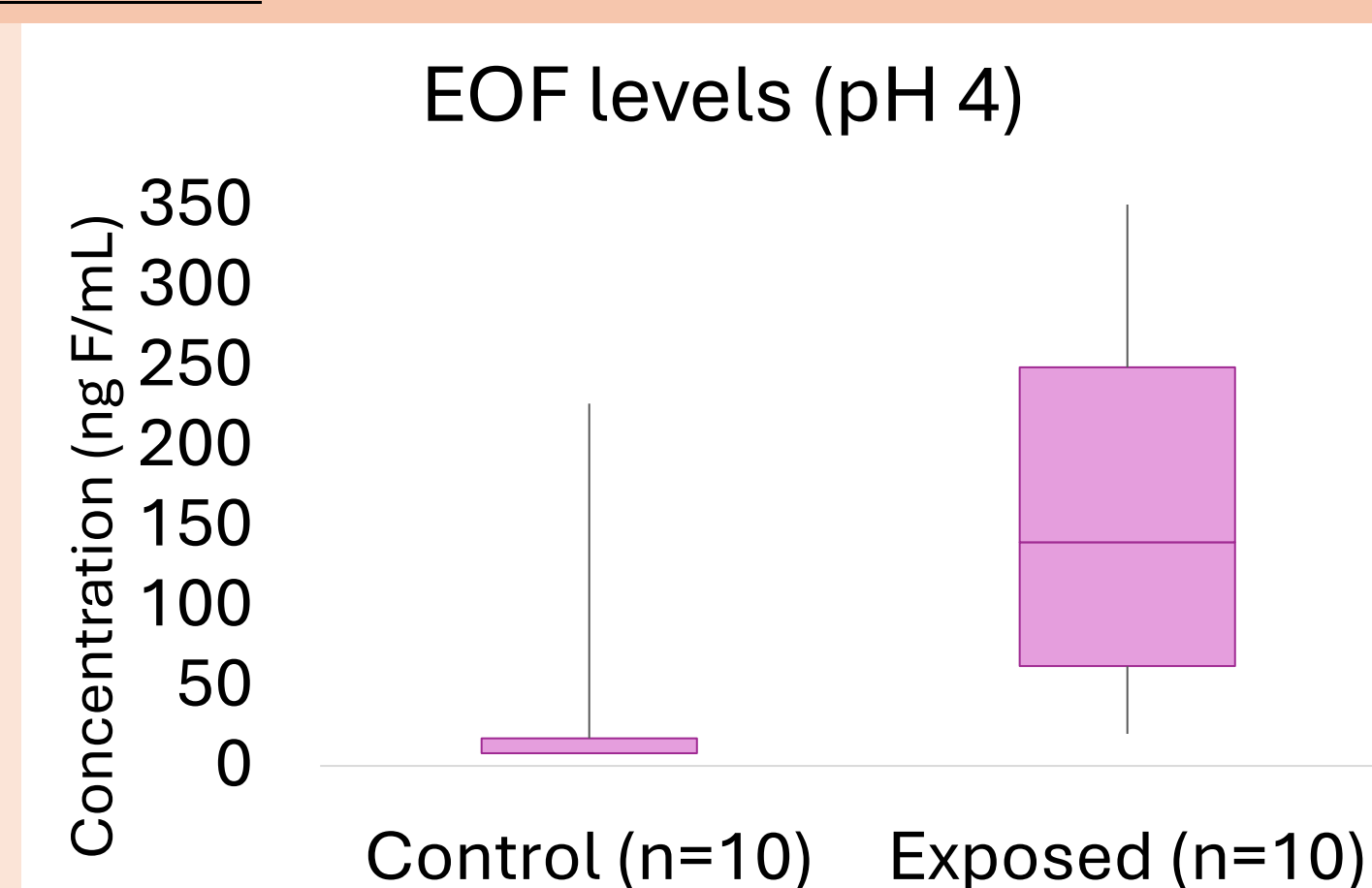
\*The PFAS data have been converted into F-equivalent concentration

Whiskers: min/max, horizontal line: median, lower and upper borders of box: value of 1st and 3rd quartile

- TFA accounted for 30% of the Σ<sub>64</sub>PFAS concentration
- Σ<sub>64</sub>PFAS concentration overall was higher for men than for women

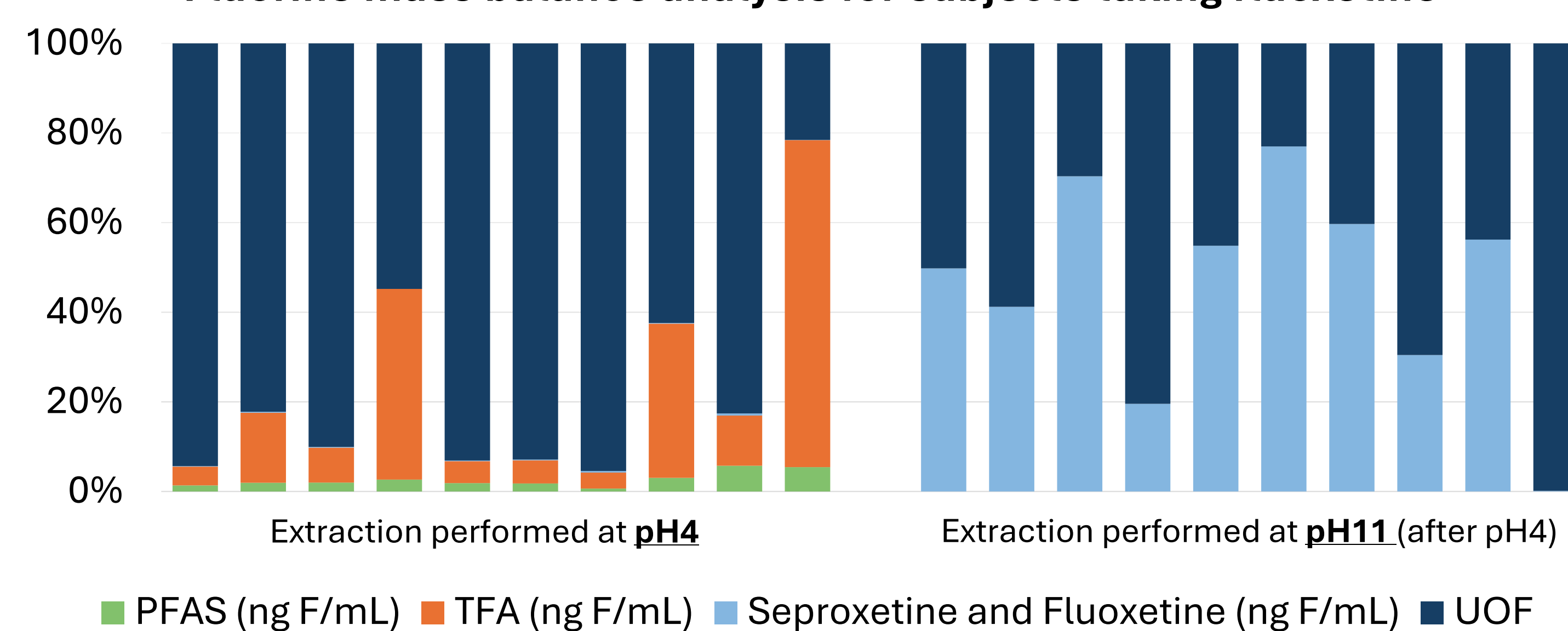
## Research question #2: How fluorinated pharmaceuticals may affect EOF levels in human serum? Sample set 2

- Higher concentrations for seproxetine and fluoxetine were found for subjects taking fluoxetine at higher doses
- TFA mostly found in samples extracted with a pH of 4
- Sproxetine and fluoxetine mostly found in samples extracted with a pH of 11

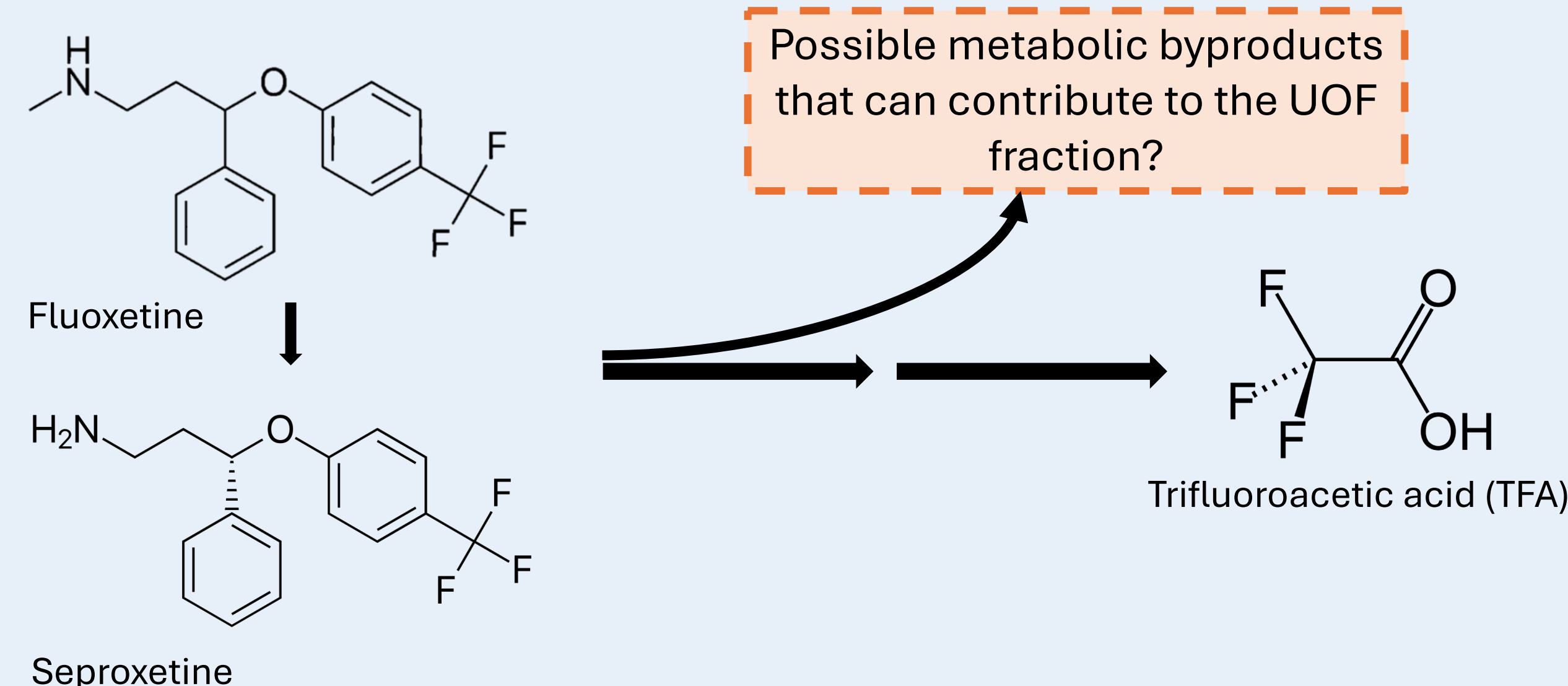


		EOF (ng F/mL)			TFA (ng F/mL)			Sproxetine and Fluoxetine (ng F/mL)		
		% above MDL	Range	Median	% above MDL	Range	Median	% above MDL	Range	Median
Fluoxetine taking group (n=10)	at pH 4	100	20 - 362	139.5	100	8.8 - 22.5	13.7	80	<0.1 - 1.3	0.4
	at pH 11	90	<17 - 91.4	26.8	0	n.d.	n.d.	90	<0.1 - 54.6	16.1
Control group (n=10)	at pH 4	40	<8 - 226	38.7	60	<2.5 - 6.2	3.1	0	n.d.	n.d.
	at pH 11	0	<17	<17	0	n.d.	n.d.	0	n.d.	n.d.

### Fluorine mass balance analysis for subjects taking fluoxetine



## Discussion points



- Addressing these unidentified substances is crucial for accurate assessments and understanding the full scope of OF exposure for potential health hazard identification.

- Further research needs to be done to understand the exposure, elimination route and effects of TFA.

- Extraction should include different pH to improve the extraction efficiency for a range of fluorinated pharmaceuticals to minimize the UOF fraction.

### References

1. Aro et al., 2021 Environmental Science & Technology, 55, 13142
2. Yeung and Mabury, 2016 Environmental Chemistry, 13, 102
3. Cioni et al., 2023 Environmental Science & Technology, 57, 14849
4. Aro et al., 2022 Environmental International 159, 107035
5. Cioni et al., 2024 Environmental Science & Technology 58, 12943

### Acknowledgements

We thank the Nordic Council of Ministers for funding the project (2023-016) and the EuroMix project for providing the samples.

QR code

