# CONTAMINATION LEVELS AND DISTRIBUTION OF PERSISTENT AND NON-PERSISTENT POLLUTANTS IN PAIRED HAIR, URINE AND SERUM SAMPLES FROM A BELGIAN NON-OCCUPATIONALLY EXPOSED POPULATION

Julien Claessens[a,b], Patrice Dufour[a,b], Nadia Dardenne[c], Corinne Charlier[a,b], and Catherine Pirard[a,b]

[a]*Department of Clinical, Forensic, Environmental, and Industrial Toxicology, University Hospital of Liege, Liege, Belgium;*
[b]*Center For Interdisciplinary Research on Medicines (C.I.R.M), University of Liege, Liege, Belgium;*
[c]*University and Hospital Biostatistics Center (B-STAT), Faculty of Medicine, University of Liège, Liège, Belgium*

**KEYWORDS** : Biomonitoring ; contamination levels ; hair ; serum ; urine ; paired samples

## ABSTRACT

Designing ideal human biomonitoring studies involves the selection of reliable markers of exposure in adequate biological matrix. Besides conventional matrices such as blood or urine, hair has been increasingly investigated as a promising noninvasive alternative. However, understanding the pollutant distribution between differing biological compartments is essential for reliable interpretation of data collected. Therefore, the contamination levels and the distribution of some persistent (8 perfluoroalkyl substances – PFAS – and 6 polychlorobiphenyls – PCBs) and non-persistent pollutants (2 bisphenols and 3 parabens) were investigated in paired serum and hair samples, or paired spot urine and hair samples obtained from 30 Belgian non-occupationally exposed individuals. The levels measured were close to those reported in recent larger-scale studies. PFAS, PCB and bisphenol distributions largely differed depending upon the matrix and within the same chemical family depending upon the congener. The correlation and agreement between pollutant levels in differing matrices demonstrated that the information provided is comparable only for highly chlorinated PCBs and parabens, while the classification of exposure for bisphenols was substantially different according to the matrix. The selection of the human matrix thus remains complex and might markedly bias the results obtained, especially when assessing the health risk related to chemical exposure.

# Introduction

The presence of chemical products in our environment is ubiquitous, and thus, continuous exposure to cocktails of substances occurs (Naidu et al. 2021; UNEP 2019). To accurately assess human exposure to environmental pollutants, human biomonitoring (HBM), consisting of the measurement of chemicals and pollutants in biological matrices, has been demonstrated to be an efficient tool since it accounts for all routes and sources of exposure (Shilnikova et al. 2025; Vorkamp et al. 2021). Several biological matrices, such as blood, urine, fat tissues, and maternal milk have been used depending upon the target chemicals and their toxicokinetic (Shilnikova et al. 2025). For persistent organic pollutants (POPs), which are known to be stable and accumulate in living organisms, blood has traditionally been the preferred matrix. In fact, blood might effectively reflect internal dosing due to its contact with the whole organism. Further, for some lipophilic compounds such as PCBs, lipid adjustment of the chemical concentration enables their levels to be reflected in the lipid compartment where these compounds accumulate (Schettgen et al. 2015; Vorkamp et al. 2021). For non- persistent chemicals that are rapidly metabolized and excreted, urine samples are usually collected for the measurement of the chemical itself or its metabolites (Roggeman et al. 2022). Both conventional sample types suffer from several drawbacks, mainly the invasiveness of the sampling for blood and the high intra-individual variability for urine spot samples. Therefore, the use of alternative matrices like nails, saliva, or hair has been increasingly investigated (Alves et al. 2014; Appenzeller and Tsatsakis 2012; Jian et al. 2018). While hair has been predominantly employed for many years within the field of forensic or clinical toxicology because of the incorporation of chemicals from blood into hair roots, the interest in its use to monitor environmental pollutants is more recent. The key advantages of this method come from the simplicity and affordability of the sampling procedure, the non-critical storage conditions required, and its particular suitability for vulnerable populations including infants, children or elderly (Alves et al. 2014; Appenzeller 2015; Appenzeller and Tsatsakis 2012; Schramm 2008). Despite the increasing number of investigations focusing on environmental pollutants in hair, levels of these pollutants in the general population using a hair matrix are not as well documented compared to traditional matrices. This might be due to (1) analytical challenges of reaching appropriate sensitivity, (2) difficulties in differentiating internal from external contamination, (3) lack of reference materials, or (4) questionable representativeness of the body burden (Junaid et al. 2024; Vorkamp et al. 2021). Nevertheless, hair still constitutes a promising alternative matrix, and a rising number of studies were conducted on hair contamination of several chemical classes aiming to investigate the reliability of hair for assessing human exposure (Junaid et al. 2024; Lallmahomed et al. 2024). Weak or missing correlations between contaminant levels in conventional matrices and hair were frequently observed indicating that the information provided by the different matrices may vary (Faÿs et al. 2021; Hardy et al. 2021; Hernández et al. 2019; Kim, Lee, and Oh 2019; N. Li et al. 2021; Wang et al. 2018). Indeed blood, urine and hair chemical levels are related to different time windows of exposure: (1) blood is usually considered to accurately measure medium- to long-term exposure to POPs, (2) urine provides information on very recent exposure, from a few hours to a few days, to rapidly metabolized chemicals (Calafat et al. 2016; Engel et al. 2014; LaKind et al. 2019; Roggeman et al. 2022) and (3) hair might encompass an extended window of detection depending upon the strand length analyzed, ranging from few weeks to few months (considering a mean of 1 cm/month of growth). The mechanisms of chemical incorporation into hair are still not fully elucidated and external contamination might not be excluded (Alves et al. 2014; Appenzeller 2015; Appenzeller and Tsatsakis 2012; Schramm 2008). Although data gathered from these matrices may be complementary, the adequate selection of biomarkers and matrices for designing biomonitoring, as well as reliable interpretation of data collected, are substantial and further investigations are needed to improve knowledge and understanding of the pollutant distribution between the different biological compartments (Lallmahomed et al. 2024; Vorkamp et al. 2021). Studies examining contamination levels in different paired sample types remain scarce, usually focusing either on hair-blood or hair-urine paired samples and rarely on more than two biological matrices. Further, few investigations cover a wide range of different chemical classes of substances. Wang et al. (2018) compared the results obtained in paired serum, urine, hair and nail samples but only for 8 perfluoroalkyl substances (PFAS), while Faÿs et al. (2021) noted the levels for a total of 29 chemically closed substances including phthalates, bisphenols, or pesticides. Hardy et al. (2021) examined a larger number of different pesticides (orga- nochlorines, organophosphates, pyrethroids, and carbamates) but only in hair and urine samples. However, the distribution of chemicals between different body compartments and thus between varying available biological matrices needs to be at least partly determined by their physicochemical properties (Chata et al. 2016), which might differ widely depending upon the targeted chemical family and sometimes even within the same chemical class.

To fill this gap, the aim of this study was to examine the contamination levels and distribution of some persistent and non-persistent pollutants between different biological matrices. For these purposes, 8 PFAS including perfluoropentanoic acid (PFPeA), perfluorohexanoic acid, (PFHxA), perfluoroheptanoic acid (PFHpA), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), perfluorohexanesulfonate (PFHxS), and linear perfluorooctanesulfonate (PFOS), 6 polychlorobiphenyls (PCB-28, -52, -101, -138, -153, and -180), three parabens (methyl-, ethyl- and propylparaben), and two bisphenols (BPA and BPS) were measured in paired serum and hair samples, or paired spot urine and hair samples from 30 Belgian non-occupationally exposed individuals. These target chemicals were selected to cover different elimination and persistence profiles. The levels measured are discussed as follows (1) in light of available literature, (2) occur-rence and distribution between matrices, and (3) factors influencing the incorporation rate of chemicals in hair. This short preliminary study was initially aimed to help in the selection of the most suitable markers in the perspective of an upcoming epidemiological study assessing the relationship between persistent and non-persistent pollutant exposure and diabetes pathologies.

# Material and method

## POPULATION AND SAMPLE COLLECTION

A subgroup of 30 individuals was selected among a larger sample of healthy volunteers recruited within the frame of a future study approved by the Hospital Faculty Ethics Committee of the University of Liege (N°2016–296), predominantly through the Belgian Red Cross blood donation centers from the Province of Liege (Belgium), and to a lesser extent from the staff of the University and the University Hospital of Liege. A blood sample, a single spot urine sample and strand of hair was obtained from all 30 volunteers in the present study. Participants were aged from 22 to 60 years old (average of 30.5 years) and included 12 men and 18 women without known occupational exposure to the targeted environmental pollutants.

Hair samples (0.5–1 g) were cut near the scalp at the occipital cranial region and were directly stored in paper envelope in dark room at ambient temperature until analysis. Analyses were performed on the two first proximal centimeters (oriented from the scalp). To remove the external contamination, hair was washed successively in water, sodium dodecyl sulfate in water (0.1% m/v) and two times again in water (Claessens, Pirard, and Charlier 2022).

Urine samples were collected in 100 ml polypropylene vessels, whereas blood samples were collected in clot activator tubes (without gel) and centrifuged to collect serum. Both urine and serum samples were stored at -20°C until analysis.

# Analytical procedure

## SERUM PFAS

PFAS were extracted from serum samples following the procedure previously described in Dufour et al. (2018). In brief, 1 ml sample was acidified with formic acid before being extracted by solid phase extraction using Oasis WAX cartridge (Waters). After the elution using 2 × 2 ml $NH_4OH$ in methanol (MeOH) (2%), extracts were evaporated until dryness and reconstituted in 80 µl mixture of ammonium acetate in water (2 mm) and in acetonitrile (2 mm) in proportion 8/2 (v/v). Samples were analyzed using Ultra-High Performance Liquid Chromatography (UHPLC) coupled to tandem mass spectrometer (MS/MS). Limits of quantification (LOQs) are gathered in supplementary material (Table S1). Each sequence consisted, in addition to unknown samples, in one procedural blank and two reference materials from the Arctic Monitoring and Assessment Program (AMAP) ring test for organic pollutants organized by the Institut National de Santé Publique du Québec (INSPQ) to ensure the accuracy of the analyses. The sequence was validated if the levels of the reference materials measured were included in the tolerable ranges provided by the ring test organizers.

## SERUM PCBS

PCBs in serum were measured using the method previously described by Cirello et al. (2024). Briefly, after the addition of internal standard, the serum sample (1 ml) was treated with 0.3 ml acetic acid before a double liquid-liquid extraction using 4 ml hexane/acetone mixture (95/5 v/ v). The combined organic layers were evaporated until 500 µl eluted on a PHREE cartridge, and concentrated at room temperature in 50 µl nonane as keeper. The final determination was performed by gas chromatography (GC) coupled to MS/MS. The analytical method and conditions are fully detailed in supplementary materials, as well as the LOQs (Table S1). Each sequence consisted, in addition to unknown samples, in one procedural blank and two reference materials from the AMAP ring test for organic pollutants (INSPQ) to ensure the accuracy of the analyses. The sequence was validated if the levels of the reference materials measured were included in the tolerable ranges provided by the ring test organizers.

## PFAS, PARABENS, AND BISPHENOLS IN HAIR

Hair samples were treated for PFAS, paraben, and bisphenol determination as already reported by Claessens, Pirard, and Charlier (2022). Briefly, washed hair samples were cut into 1–2 mm segments using stainless steel scissors. Fifty mg washed hair were weighed and introduced into clean glass tubes, spiked with 10 µl isotopically mass-labeled internal standard (0.1 µg/ml for PFAS and 5 µg/ml for all other compounds) and let equilibrate at ambient temperature for one hr. Two ml MeOH/acetic acid mixture (85/15 v/v) were then added, and tubes were incubated at 38°C overnight. After incubation, samples were sonicated for 15 min with 2 × 2 ml acetone and centrifuged for 10 min. Supernatants were collected and evaporated to dryness at 30°C under a nitrogen flow. Extracts were finally reconstituted with 100 µl ammonium acetate 2 mm in water and MeOH (70/30 v/v) and transferred into vials for further analysis by UHPLC-MS/MS. LOQs are gathered in supplementary material (Table S1). Procedural blank and home-made QC (spiked at 100 and 1000 pg/mg for BPA, PrP, MeP and PFOS, 20 and 200 pg/mg for BPS and EtP, and 2 and 20 pg/mg for the other PFCs) were added to the unknown sample series to ensure accuracy of *the method*.

## HAIR PCBS

The hair samples previously washed and cut in small pieces (50 mg) were hydrolyzed by ultra-sonication with 1 ml NaOH 5 M until total dissolution. Then the hydrolyzate was extracted similarly to acidified serum samples and analyzed using the same GC-MS/MS method. The analytical method and conditions are fully detailed in supplementary materials, as well as the LOQs (Table S1).

## URINE BISPHENOLS

Bisphenol (namely BPA and BPS) analysis was previously described (Pirard and Charlier 2022). Briefly, 3 ml urine were initially enzymatically hydrolyzed using β glucuronidase and sulfatase in 750 µl sodium acetate buffer (pH 5) for 30 min at 40°C. Samples were then extracted by solid phase extraction on Oasis HLB SPE Cartridge (Waters), followed by a liquid/liquid extraction using 3 ml ethyl acetate, and then derivatized using (N-methyl-N-(trimethylsilyl))trifluoroacetamide. The determination was performed using GC-MS /MS. LOQs are gathered in supplementary material (Table S1). Each sequence consisted, in addition to unknown samples, in one procedural blank and two reference material samples: one from the German External Quality Assessment Scheme for Analysis in Biological Materials (G-EQUAS; material 14/15) and another from the External Quality Assessment Scheme for Organic Substances in Urine (OSEQUAS) provided by the INSPQ. The sequence was validated if the levels of the reference materials measured were included in the tolerable ranges provided by the ring test organizers.

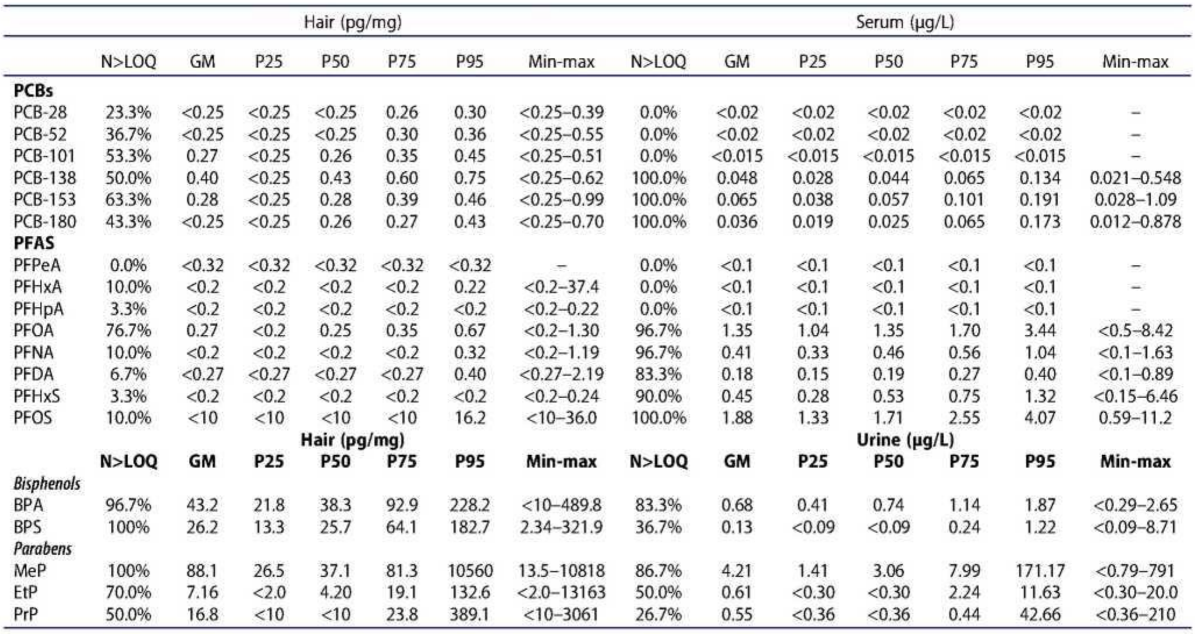
## URINE PARABENS

The extraction and determination of parabens (namely methylparaben (MeP), ethylparaben (EtP) and propylparaben (PrP)) were carried out following the method previously developed and validated by Dewalque et al. (2014). The extraction consisted in the enzymatic hydrolysis of 3 ml urine sample using β glucuronidase followed by a solid phase extraction on Bond Elut certify LRC car-tridge. The analysis was performed using UHPLC- MS/MS. LOQs are gathered in supplementary material (Table S1).

## STATISTICAL ANALYSIS

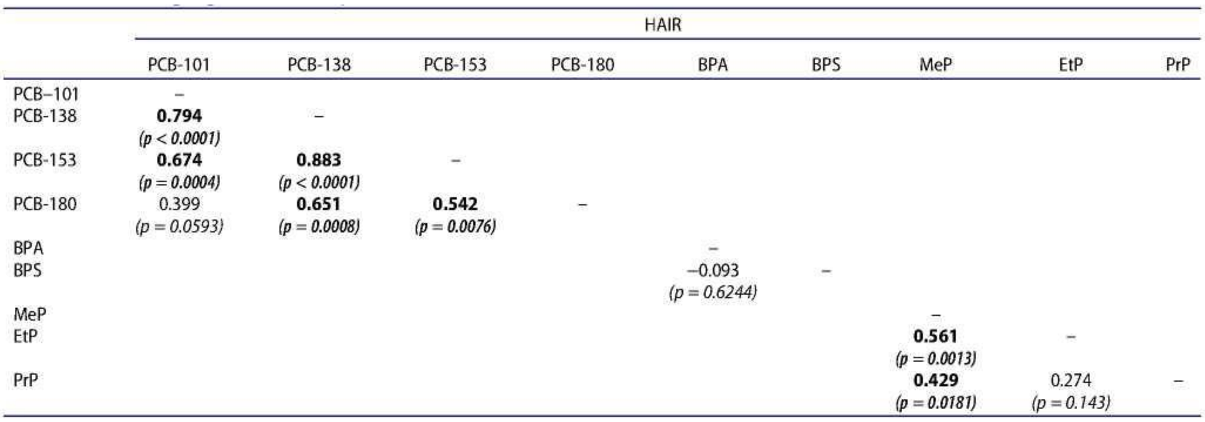
Statistical analyses were performed using R (version 4.0.3) with packages VCD and irr and Excel (Microsoft office 2013). Results below LOQ were replaced by LOQ/$\sqrt{2}$ (Sun et al. 2018). The normality of data distribution was assessed by a Shapiro Wilk's test. Because all distributions were highly skewed, non-parametric test was used (Spearman correlation). All statistical analyses were performed for chemicals showing a detection frequency (DF) above 50%, using the significance threshold set at the 5% critical level ($p < 0.05$). Correlations between pollutant concentrations within the matrices were assessed by Spearman's correlation test to highlight potential common sources of exposure. Comparisons intermatrices were carried out using Spearman's correlation coefficient, weighted Cohen's kappa coefficient ($\kappa$) and two-way fixed Intraclass Correlation Coefficients (ICC (A, 1) with 95 CI%. Weighted Cohen's kappa coefficient was calculated to evaluate the concordance of the classification of the contamination levels between the different matrices (McHugh 2012). Contamination values were converted into categorical variables by classifying obtained results between cutoffs for each matrix. The cutoffs were determined based on the percentile values previously reported in other biomonitoring studies selected to provide the more recent and as similar as possible monitoring data in terms of biological matrix and populations. These data and references are reported in supplementary materials (Table S2). Cutoffs, attributed classifications and weights used for each chemical depending on the matrix are presented in supplementary materials (Tables S3–S4). Cohen's kappa concordance value > 0.90 was interpreted as almost perfect agreement, value between 0.80 and 0.89 as strong, value between 0.60 and 0.79 as moderate value between 0.40 and 0.59 as weak, value between 0.20 and 0.39 as minimal, and value < 0.20 means no agreement (McHugh 2012). The two-way fixed ICC reflects the degree of correlation but also the agreement between measurements (Koo and Li 2016) and were calculated using standardized concentrations by mean and standard deviation (Bro and Smilde 2003). Concentrations were log-transformed to approximate a normal distribution. Reliability values of ICC range between 0 and 1, with 1 meaning strongest reliability or agreement (Koo and Li 2016).

***Table 1**. Detection Frequencies (N>loq), Geometric Mean (GM), Percentiles and Minimal and Maximal Concentrations Measured in the 30 Paired Hair and Urine Samples, and Hair and Serum Samples*



| | Hair (pg/mg) | | | | | | | Serum (µg/L) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N>LOQ | GM | P25 | P50 | P75 | P95 | Min-max | N>LOQ | GM | P25 | P50 | P75 | P95 | Min-max |
| **PCBs** | | | | | | | | | | | | | | |
| PCB-28 | 23.3% | <0.25 | <0.25 | <0.25 | 0.26 | 0.30 | <0.25–0.39 | 0.0% | <0.02 | <0.02 | <0.02 | <0.02 | <0.02 | – |
| PCB-52 | 36.7% | <0.25 | <0.25 | <0.25 | 0.30 | 0.36 | <0.25–0.55 | 0.0% | <0.02 | <0.02 | <0.02 | <0.02 | <0.02 | – |
| PCB-101 | 53.3% | 0.27 | <0.25 | 0.26 | 0.35 | 0.45 | <0.25–0.51 | 0.0% | <0.015 | <0.015 | <0.015 | <0.015 | <0.015 | – |
| PCB-138 | 50.0% | 0.40 | <0.25 | 0.43 | 0.60 | 0.75 | <0.25–0.62 | 100.0% | 0.048 | 0.028 | 0.044 | 0.065 | 0.134 | 0.021–0.548 |
| PCB-153 | 63.3% | 0.28 | <0.25 | 0.28 | 0.39 | 0.46 | <0.25–0.99 | 100.0% | 0.065 | 0.038 | 0.057 | 0.101 | 0.191 | 0.028–1.09 |
| PCB-180 | 43.3% | <0.25 | <0.25 | 0.26 | 0.27 | 0.43 | <0.25–0.70 | 100.0% | 0.036 | 0.019 | 0.025 | 0.065 | 0.173 | 0.012–0.878 |
| **PFAS** | | | | | | | | | | | | | | |
| PFPeA | 0.0% | <0.32 | <0.32 | <0.32 | <0.32 | <0.32 | – | 0.0% | <0.1 | <0.1 | <0.1 | <0.1 | <0.1 | – |
| PFHxA | 10.0% | <0.2 | <0.2 | <0.2 | <0.2 | 0.22 | <0.2–37.4 | 0.0% | <0.1 | <0.1 | <0.1 | <0.1 | <0.1 | – |
| PFHpA | 3.3% | <0.2 | <0.2 | <0.2 | <0.2 | <0.2 | <0.2–0.22 | 0.0% | <0.1 | <0.1 | <0.1 | <0.1 | <0.1 | – |
| PFOA | 76.7% | 0.27 | <0.2 | 0.25 | 0.35 | 0.67 | <0.2–1.30 | 96.7% | 1.35 | 1.04 | 1.35 | 1.70 | 3.44 | <0.5–8.42 |
| PFNA | 10.0% | <0.2 | <0.2 | <0.2 | <0.2 | 0.32 | <0.2–1.19 | 96.7% | 0.41 | 0.33 | 0.46 | 0.56 | 1.04 | <0.1–1.63 |
| PFDA | 6.7% | <0.27 | <0.27 | <0.27 | <0.27 | 0.40 | <0.27–2.19 | 83.3% | 0.18 | 0.15 | 0.19 | 0.27 | 0.40 | <0.1–0.89 |
| PFHxS | 3.3% | <0.2 | <0.2 | <0.2 | <0.2 | <0.2 | <0.2–0.24 | 90.0% | 0.45 | 0.28 | 0.53 | 0.75 | 1.32 | <0.15–6.46 |
| PFOS | 10.0% | <10 | <10 | <10 | <10 | 16.2 | <10–36.0 | 100.0% | 1.88 | 1.33 | 1.71 | 2.55 | 4.07 | 0.59–11.2 |
| | **Hair (pg/mg)** | | | | | | | **Urine (µg/L)** | | | | | | |
| | **N>LOQ** | **GM** | **P25** | **P50** | **P75** | **P95** | **Min-max** | **N>LOQ** | **GM** | **P25** | **P50** | **P75** | **P95** | **Min-max** |
| ***Bisphenols*** | | | | | | | | | | | | | | |
| BPA | 96.7% | 43.2 | 21.8 | 38.3 | 92.9 | 228.2 | <10–489.8 | 83.3% | 0.68 | 0.41 | 0.74 | 1.14 | 1.87 | <0.29–2.65 |
| BPS | 100% | 26.2 | 13.3 | 25.7 | 64.1 | 182.7 | 2.34–321.9 | 36.7% | 0.13 | <0.09 | <0.09 | 0.24 | 1.22 | <0.09–8.71 |
| ***Parabens*** | | | | | | | | | | | | | | |
| MeP | 100% | 88.1 | 26.5 | 37.1 | 81.3 | 10560 | 13.5–10818 | 86.7% | 4.21 | 1.41 | 3.06 | 7.99 | 171.17 | <0.79–791 |
| EtP | 70.0% | 7.16 | <2.0 | 4.20 | 19.1 | 132.6 | <2.0–13163 | 50.0% | 0.61 | <0.30 | <0.30 | 2.24 | 11.63 | <0.30–20.0 |
| PrP | 50.0% | 16.8 | <10 | <10 | 23.8 | 389.1 | <10–3061 | 26.7% | 0.55 | <0.36 | <0.36 | 0.44 | 42.66 | <0.36–210 |

***Table 2**. Spearman Correlation Coefficients Between Chemical Levels Measured in Hair (p-value in Parentheses). Significant Correlations are Highlighted in Bold (p < 0.05)*



| | HAIR | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | PCB-101 | PCB-138 | PCB-153 | PCB-180 | BPA | BPS | MeP | EtP | PrP |
| PCB–101 | – | | | | | | | | |
| PCB-138 | **0.794**<br>*(p < 0.0001)* | – | | | | | | | |
| PCB-153 | **0.674**<br>*(p = 0.0004)* | **0.883**<br>*(p < 0.0001)* | – | | | | | | |
| PCB-180 | 0.399<br>*(p = 0.0593)* | **0.651**<br>*(p = 0.0008)* | **0.542**<br>*(p = 0.0076)* | – | | | | | |
| BPA | | | | | – | | | | |
| BPS | | | | | −0.093<br>*(p = 0.6244)* | – | | | |
| MeP | | | | | | | – | | |
| EtP | | | | | | | **0.561**<br>*(p = 0.0013)* | – | |
| PrP | | | | | | | **0.429**<br>*(p = 0.0181)* | 0.274<br>*(p = 0.143)* | – |

# Results and discussion

Descriptive statistics are reported in Table 1, which includes the detection frequencies (DF), geometric means (GM), percentiles and concentration ranges measured according to the matrix. PCBs and PFAS were not measured in urine samples because of the poor urinary excretion of these substances and, subsequently, the expected low urinary levels and detection frequencies (Genuis, Beesoon, and Birkholz 2013; G. Zheng, Eick, and Salamova 2023). Similarly, even if it was previously successfully measured in blood in previous studies, bisphenols and parabens were not measured in the present serum samples due of the higher concentration of these compounds and their metabolites observed in urine (LaKind et al. 2019; Vorkamp et al. 2021) and the limited literature reporting serum levels for comparison (Vorkamp et al. 2021). Spearman's correlations between pollutants within each matrix were reported in Tables 2–4, whereas the results of the inter-matrix comparisons (Spearman correlation, weighted Cohen's kappa and ICC) were gathered in Table 5.

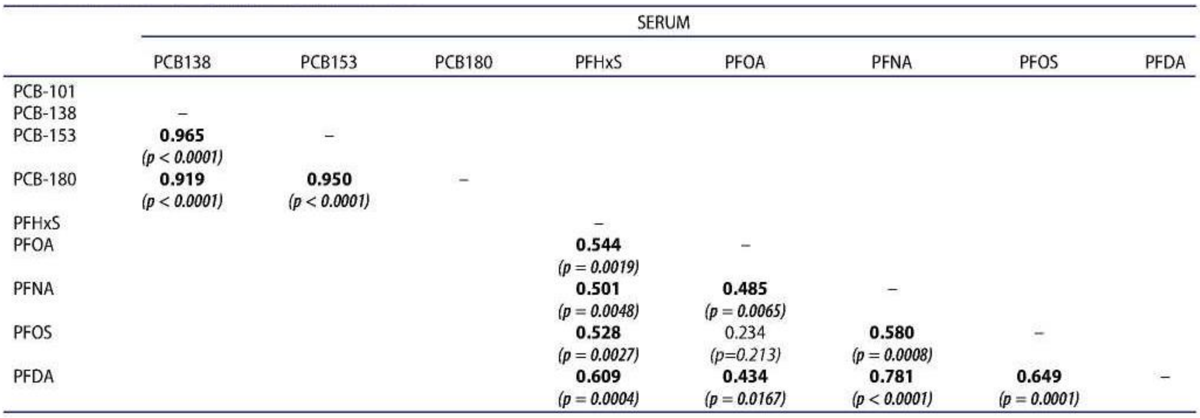
## PCBS LEVELS IN HAIR AND SERUM

As expected, PCB-28, -52 and -101 were not detected in serum samples based on our LOQs (from 0.015 to 0.020 µg/L), while the most abundant was PCB-153 accounting for 42% of the sum of PCBs, followed by PCB-138 and PCB-180. These levels are far lower than those reported from a study on Walloon adults recruited in 2015 (Pirard et al. 2018), from the French ESTEBAN study conducted between 2014 and 2016 (Balestier et al. 2021), or from the German general population within 2010 and 2014 (Schettgen et al. 2015). This is in agreement with the declining trends observed these last decades due to the strict regulations concerning their uses and disposals established at the end of 1980's, and the creation of the "dirty dozen" blacklist within the Stockholm Convention (EU, 1996 ; Pirard et al. 2018; Schettgen et al. 2015). A similar profile was found in hair samples for higher chlorinated congeners, with PCB-153 being the congener detected the most frequently and in the highest concentration levels (DF: 82.6%; P50: 0.43 pg/mg). On the other hand, lower chlorinated PCBs seemed to be present in higher proportions in hair compared to serum. Comparisons between both matrices are difficult for these congeners due to the inability to detect them in serum. Therefore, it was not possible to determine if this trend is driven by the higher sensitivity of the analytical method developed for hair (and thus its greater suitability), or if the profiles of PCBs in serum and hair are actually different regarding the chlorination degree of congeners. According to J. Zheng et al. (2016), within an occupational context (Chinese e-waste recycling facility), air would be the primary source of PCB contamination in hair predominantly through external deposition, especially for lower chlorinated congeners, while blood contribution (and thus internal exposure) would be lower. Even if markedly lower air contribution might occur during environmental exposure, this pathway should not be neglected, and differentiation between internal and external contamination sources is still a hindrance to the use of hair in biomonitoring studies. Although few studies reported PCB levels in hair from European populations, concentrations measured are in the same range as those previously reported from French populations (Iglesias-González, Hardy, and Appenzeller 2020; Peng et al. 2020) and lower than hair results observed in Luxembourg (Peng et al.

2021). In serum as well as in hair, PCB-138, -153 and -180 levels were significantly correlated (Tables 2 and 3), suggesting common sources of exposure.

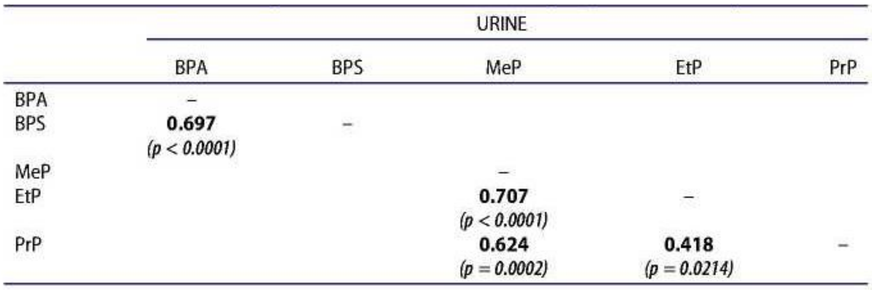
The results of the inter-matrix correlations (Table 5) show significant Spearman's coefficient and ICC for PCB-180, and the agreement between matrices according to Cohen's kappa was found as "minimal." This indicates that levels in hair and serum might present a similar reliability for the PCB-180 exposure assessment even if the agreement is poor according to Cohen's kappa value. For PCB-138 and -153, ICC were significant but lower than for PCB-180, while no significant correlation nor agreement were observed between both matrices (for PCB-153 only, Cohen's kappa could not be evaluated for PCB-138 due to the low detection frequencies observed in the reference population used for the cutoff determination). Even with the use of three different statistical meth-ods to compare concentrations obtained in different matrices enabling a more reliable and cautious interpretation of correlation results, these conclusions are globally consistent with previous findings reporting positive correlations between hair and serum concentrations for some PCBs (Barmpas et al. 2020; J. Zheng et al. 2016). These correlations or agreements between matrices support the hypothesis of an effective transfer from blood circulation to hair, enhanced by the high lipophilicity of these substances which facilitates their diffusion across cell membranes and incorporation into a lipid-rich matrix such as hair (containing 3.5–4% of lipids vs 0.2–1% for blood) (Cone 1996; Hsu et al. 2022; Junaid et al. 2024).

***Table 3**. Spearman Correlation Coefficients Between Chemical Levels Measured in Serum (p-value in Parentheses). Significant Correlations are Highlighted in Bold (p < 005)*



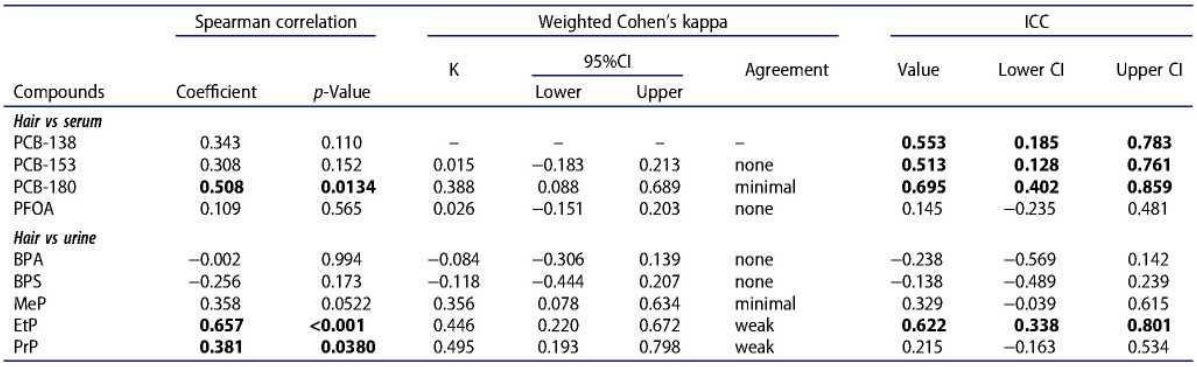
| | SERUM | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | PCB138 | PCB153 | PCB180 | PFHxS | PFOA | PFNA | PFOS | PFDA |
| PCB-101 | | | | | | | | |
| PCB-138 | – | | | | | | | |
| PCB-153 | **0.965**<br>*($p < 0.0001$)* | – | | | | | | |
| PCB-180 | **0.919**<br>*($p < 0.0001$)* | **0.950**<br>*($p < 0.0001$)* | – | | | | | |
| PFHxS | | | | – | | | | |
| PFOA | | | | **0.544**<br>*($p = 0.0019$)* | – | | | |
| PFNA | | | | **0.501**<br>*($p = 0.0048$)* | **0.485**<br>*($p = 0.0065$)* | – | | |
| PFOS | | | | **0.528**<br>*($p = 0.0027$)* | 0.234<br>*($p=0.213$)* | **0.580**<br>*($p = 0.0008$)* | – | |
| PFDA | | | | **0.609**<br>*($p = 0.0004$)* | **0.434**<br>*($p = 0.0167$)* | **0.781**<br>*($p < 0.0001$)* | **0.649**<br>*($p = 0.0001$)* | – |

***Table 4**. Spearman Correlation Coefficients Between Chemical Levels Measured in Urine (p-value in Parentheses). Significant Correlations are Highlighted in Bold (p < 0.05)*



| | URINE | | | | |
|---|---|---|---|---|---|
| | BPA | BPS | MeP | EtP | PrP |
| BPA | – | | | | |
| BPS | **0.697**<br>*($p < 0.0001$)* | – | | | |
| MeP | | | – | | |
| EtP | | | **0.707**<br>*($p < 0.0001$)* | – | |
| PrP | | | **0.624**<br>*($p = 0.0002$)* | **0.418**<br>*($p = 0.0214$)* | – |

***TABLE 5****. Results of the Inter-Matrix Correlations Using Spearman Correlation, Weighted Cohen's Kappa and Two-Way Fixed Intraclass Correlation*



| | Spearman correlation | | Weighted Cohen's kappa | | | | ICC | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | K | 95%CI | | Agreement | Value | Lower CI | Upper CI |
| Compounds | Coefficient | *p*-Value | | Lower | Upper | | | | |
| ***Hair vs serum*** | | | | | | | | | |
| PCB-138 | 0.343 | 0.110 | – | – | – | – | **0.553** | **0.185** | **0.783** |
| PCB-153 | 0.308 | 0.152 | 0.015 | −0.183 | 0.213 | none | **0.513** | **0.128** | **0.761** |
| PCB-180 | **0.508** | **0.0134** | 0.388 | 0.088 | 0.689 | minimal | **0.695** | **0.402** | **0.859** |
| PFOA | 0.109 | 0.565 | 0.026 | −0.151 | 0.203 | none | 0.145 | −0.235 | 0.481 |
| ***Hair vs urine*** | | | | | | | | | |
| BPA | −0.002 | 0.994 | −0.084 | −0.306 | 0.139 | none | −0.238 | −0.569 | 0.142 |
| BPS | −0.256 | 0.173 | −0.118 | −0.444 | 0.207 | none | −0.138 | −0.489 | 0.239 |
| MeP | 0.358 | 0.0522 | 0.356 | 0.078 | 0.634 | minimal | 0.329 | −0.039 | 0.615 |
| EtP | **0.657** | **<0.001** | 0.446 | 0.220 | 0.672 | weak | **0.622** | **0.338** | **0.801** |
| PrP | **0.381** | **0.0380** | 0.495 | 0.193 | 0.798 | weak | 0.215 | −0.163 | 0.534 |

## PFAS LEVELS IN HAIR AND SERUM

PFPeA, PFHxA and PFHpA were detected in few hair samples (respectively 0%, 10% and 3.3%) and in none of the serum samples. For all other PFAS, serum was widely contaminated (more than 80% of the samples measured), while hair contamination was mainly dominated by PFOA, the other PFAS being positively measured in less than 10% of the samples. These low detection frequencies for PFAS other than PFOA were previously reported by Claessens, Pirard, and Charlier (2022), indicating the poorer suitability of PFAS hair measurements compared to serum measurements and/or the low sensitivity of the analytical method used compared to the low levels to detect.

The serum PFAS levels are consistent with those observed in populations from Wallonia and with levels measured in Germany and France (Fillol et al. 2021; Göckener et al. 2020; Pirard, Dufour, and Charlier 2020) but lower than those observed in a Flemish population (Colles et al. 2020). The latter were collected from an older population recruited a decade ago, confirming either the worldwide temporal decline trend and/or the regional difference in exposure previously observed for PFAS in Belgium (Dufour et al. 2018; Pirard, Dufour, and Charlier 2020). The levels measured in hair were in the same range as those noted in the literature (Claessens, Pirard, and Charlier 2022; Kim, Lee, and Oh 2019; Martín et al. 2019). These comparisons demonstrated that despite the small sample size of the present population, the participants recruited experienced usual background exposure.

Correlation was not performed between PFAS in hair because of the low DF. All PFAS (except PFOS and PFOA) levels were significantly correlated in serum (Table 3) suggesting that common exposure sources are occurring, rather through the environmental accumulation of these "forever" chemicals than through their individual uses in consumer products (De Silva et al. 2021; Glüge et al. 2020).

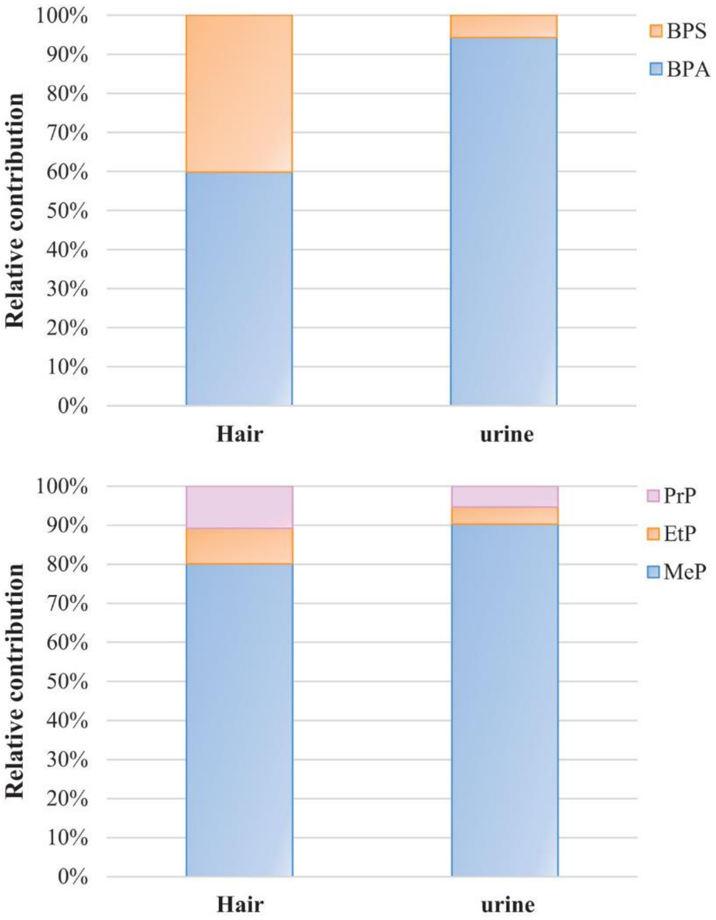
Despite the statistical test carried out (Table 5), no significant correlation nor agreement was found for PFOA concentrations between serum and hair. The results of association between hair and serum levels of PFAS reported in the literature have been inconsistent. While few investigators found significant asso-ciation between hair and serum levels of PFOS or PFOA (Kim, Lee, and Oh 2019; J. Li et al. 2013), others did not report any correlation between both matrices (J. Li et al. 2013; Liu et al. 2020; Wang et al. 2018). This lack of correlation between serum and hair PFAS levels was not expected for such persistent compounds. Indeed, the incorporation of chemicals is thought to occur into the hair root follicles from the surrounding blood capillaries and mainly influenced by blood concentration and contact time (Chata et al. 2016; Junaid et al. 2024). Therefore, since, like PCBs, PFAS are known to be poorly metabolized and eliminated from the organism, leading to their blood levels being relatively constant (Knutsen et al. 2018; LaKind et al. 2019; Schettgen et al. 2015), correlations between serum and hair levels might be expected to compare to those observed for some PCBs. On the other hand, the incorporation rate into the hair matrix may also be influenced by the affinity of the compound for hair components (i.e. proteins, melanin, lipids) and the affinity for blood proteins (Carnevale et al. 2014; Cone 1996; Lallmahomed et al. 2024) which might limit the transfer from blood for PFAS, known to be strongly bound to serum albumin (Fischer et al. 2024). These differences in matrix affinity between PFAS and PCBs resulting in a lower hair incorporation rate for PFAS are also suggested by their comparable or even lower hair levels compared to PCBs, whereas PFAS serum concentrations were roughly 100-fold higher than PCB levels.

## BISPHENOL LEVELS IN HAIR AND URINE

The urinary and hair levels of bisphenols measured in the present study are similar to those reported in previous Belgian studies on a larger population(Claessens, Pirard, and Charlier 2022; Pirard and Charlier 2022). Bisphenol A was the predominant bisphenol in urine and hair, with a median value of 0.74 µg/L (DF: 97%) and 38.3 pg/mg (DF: 83%), respectively. BPS was detected in less than 40% of the urine samples despite the lower LOQ (vs BPA), and all hair strands presented quantifiable levels close to those measured for BPA. Although having similar chemical structures, the additional sulfur atom in BPS may impact its binding to hair keratin (Cao et al. 2024) and/or its metabolism and renal excretion, and therefore might explain at least partly, the different distribution between urine and hair observed for BPA and BPS, as highlighted in Figure 1. The correlation between BPA and BPS hair levels on one hand, and the lack of significant correlation in urine (Tables 2 and 4) on the other confirm the different behavior of both bisphenols within both matrices.

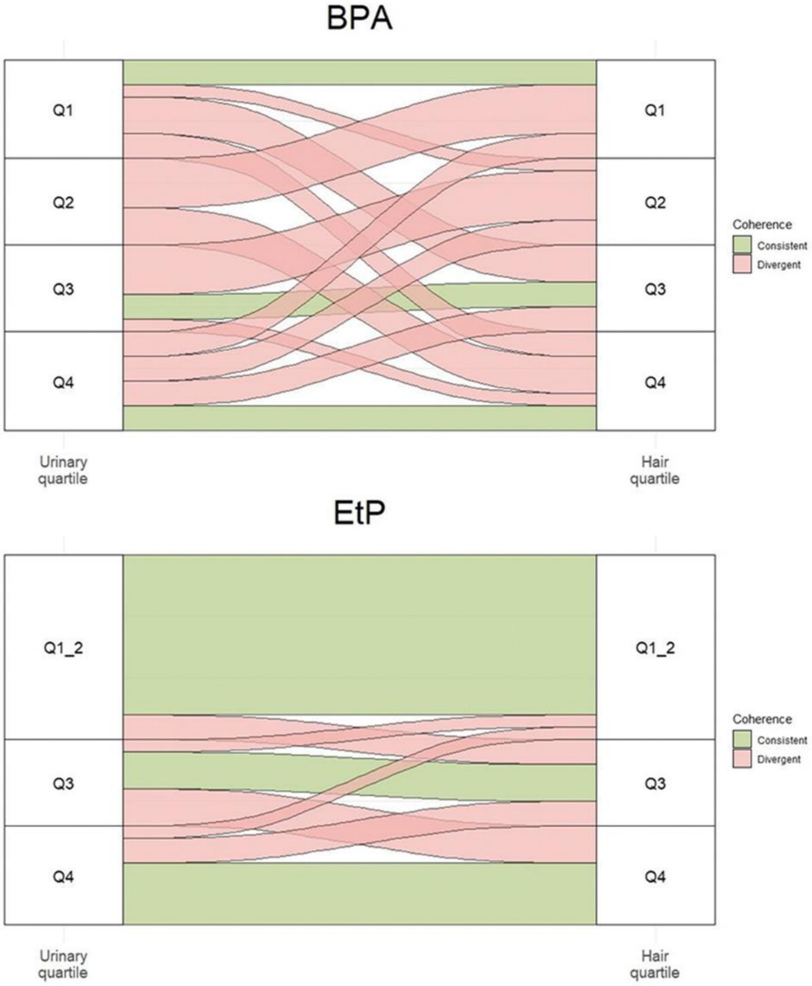
The comparison between urinary and hair levels did not highlight any correlation nor agreement between both matrices (Table 5). This lack of cor-relation was expected since bisphenol urinary levels was demonstrated to widely vary from day to day and even within a day. In fact, their high intraindividual variability, reflecting very short-term exposure (few hours), suggests a poor accuracy of a single spot urine sample in representing midterm exposure (LaKind et al. 2019; Roggeman et al. 2022). In contrast, hair has been considered to cover a wider exposure window, from a few weeks to several months depending on the strand length (Alves et al. 2014; Appenzeller 2015). In addition, the variability of bisphenol levels in hair was demonstrated to be lower compared to urine and depending on the bisphenol (higher reliability for BPS compared to BPA) (Faÿs et al. 2021). This difference in the temporal exposure window covered by the two matrices might result in different information being provided: peaks or valleys of exposure occurring within a day highlighted by the urinary levels (depending on the timing of sample collection), and levels averaged and smoothed over several weeks or months provided by hair chemical levels. Another difference between urine and hair comes from the species measured in both matrices. Because bisphenols are rapidly metabolized and eliminated in urine as conjugated compounds (sulfo- and glucuro-conjugates) (Dekant and Volkel 2008), the sum of free and conjugated bisphenols was measured in urine within the present study, while free bisphenol levels were determined using hair samples. Indeed, it was expected that mainly unconjugated bisphenols might be incorporated from blood into hair as previously observed for phthalate metabolites because highly hydrophilic and large molecules might readily penetrate biological membranes (Hsu et al. 2022). Since the unconjugated form is thought to be responsible for the endocrine disrupting properties of bisphenols (Ma et al. 2019), their measurements in hair may be relevant from a toxicological perspective. However, the information provided by hair and urinary levels is definitively different, as already suggested by Faÿs et al. (2021), making the selection of the best marker in epidemiological studies aiming to investigate associations between chemical exposure and health outcomes uncertain. Figure 2 represents the exposure classification of individuals according to the quartile of contamination in both matrices for BPA and EtP. For BPA, few participants were similarly classified using urinary or hair levels (also demonstrated by the lack of agreement according to the Cohen's kappa value), indicating that depending upon the matrix selected, the classification of the exposure level may vary thus strongly influencing the association evaluation between exposure and health outcomes.

***Figure 1**. Relative contributions of individual compound levels to the corresponding total concentrations.*



*Published in : Journal of Toxicology and Environmental Health, Part A (2025), vol. 88, n°11, pp. 447-462*
*DOI: https://doi.org/10.1080/15287394.2025.2451676*
*Status : Postprint (Author's version)*

***Figure 2**. The classification of exposure for each individual according to the quartile of contamination in both matrices for BPA and EtP. Divergent and consistent classifications are represented respectively in pink and green.*



## PARABEN LEVELS IN HAIR AND URINE

As expected, and previously reported, MeP was the most abundant paraben measured in urine and hair with a median of respectively 3.06 µg/L and 37.1 pg/mg, far higher than EtP and PrP. Once again, levels measured in the urine and hair from our small population are close to those obtained on similar larger-sized populations (Claessens, Pirard, and Charlier 2022; Pirard and Charlier 2022). These urinary levels are also similar to the results detected the French ESTEBAN study (Fillol et al. 2021), but lower than the concentrations measured in the urine of Spanish breastfeeding mothers (Sanchis et al. 2020). This might be due to different use profile of cosmetics between countries or subpopulations. Similarly, the paraben concentrations measured in hair samples were largely lower than those found in the hair of a small Spanish or Polish cohort (Martín et al. 2019; Wojtkiewicz et al. 2021). The profile of parabens observed in urine and hair does not seem to be markedly different, the contribution of PrP being lower in urine than hair (Figure 1). As previously observed MeP levels are significantly correlated with EtP and PrP in both matrices (Dewalque, Pirard, and Charlier 2014;

Tian et al. 2023) as presented in Tables 2 and 4 reflecting the combined use of parabens in their applications such as cosmetics or food (Janjua et al. 2008; Soni, Carabin, and Burdock 2005).

Significant correlations between urinary and hair levels were detected for EtP regardless of the statistical test used (significant Spearman coefficient and ICC, Cohen's kappa value representing a significant weak agreement). The consistency of the distribution within quartiles of contamination in urine and hair paired samples for EtP is also depicted in Figure 2, largely contrasting with the trend observed for BPA. PrP also showed a significant weak agreement and Spearman's coefficient, but the ICC did not indicate any correlation due to a lower detection frequency especially in urine, which decreases the statistical effectiveness of the test. These correlations and agreement between urine and hair levels were not surprising. Indeed, on one hand, the regular habits in the daily cosmetic and personal care product applications (main paraben sources of exposure) leads to a fairly reproductive day-to-day exposure. On the other hand, the specificity of dermal absorption tends to reduce peak and valley concentrations compared to oral intake (Braun et al. 2012; Philippat et al. 2015). Both of these factors might result in low intra-individual variability of urinary paraben levels and therefore a fair reliability of urine spot samples to represent mid- to long-term paraben exposure (Braun et al. 2012; Dewalque et al. 2015; LaKind et al. 2019), a time window of exposure comparable to the one covered by hair analysis. Conversely, no marked correlation was demonstrated for MeP according to Spearman and ICC, and only minimal agreement was observed between the classification in both matrices. Although Tian et al. (2023) also found a lack of correlation between hair and urine levels for several parabens, this inconsistency in the behavior of the three studied parabens was not expected, since all three demonstrated similar chemical structures. However, the different lengths of the carbon chain might influence the incorporation in the hair shaft because of the different related lipophilicity. Longer chains showing higher lipophilicity might enhance the transfer to hair. Further, the hydrolysis of parabens by human microsomes occurs more rapidly for methylparaben and the rate decreases with increasing carbon chain length (Abbas et al. 2010), likely providing less time for MeP to be incorporated into hair arguing for contact time as a contributor to the incorporation of pollutants into the hair in addition to concentration (Chata et al. 2016; Faÿs et al. 2023; Junaid et al. 2024). Finally, MeP is the most abundant paraben found in food, either occurring naturally such like in cloudberry, yellow passion fruit juice, white wine, vanilla, or added as preservatives in processed food like cakes, pastries, icings, toppings and fillings, or soft drinks (Soni, Carabin, and Burdock 2005), thus involving an additional exposure pathway besides dermal absorption. This latter assumption may be weakened by significant correlations observed between parabens in each matrix.

A last point arguing to the detriment of the hair use is the occurrence of some outlier concentrations in MeP measured in hair, more than 120-fold higher than the interquartile range (IQ) whereas urine levels are less spread. These extreme outlier values might arise from an external contamination due the participant's use of hair wax or other hair products containing MeP, which were not entirely removed despite the successive washing steps prior to hair analysis (Claessens, Pirard, and Charlier 2022).

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## Limitations of the study

The main limitation of this study was the small size and non-representativeness of the population selected, thus reducing the statistical power of the obtained results. Nevertheless, the pollutant levels measured across the matrices were similar to those reported from recent larger scale studies carried out on similar populations, validating the design of the present study and the selection of cutoff values for the Cohen's kappa determination. In addition, this study also suffers from the known limitations inherent in the matrices tested. Single spot urine samples were found to not reliably reflect exposure to some non-persistent compounds due to a high intra-individual level variability (Dewalque et al. 2015; Roggeman et al. 2022), but the collection of multiple samples or 24-hour urine samples might not significantly reduce this variability (Faÿs et al. 2021; Lassen et al. 2013). The (1) difficulty to differentiate endogenous from exogenous contaminations, (2) lack of standardized decontamination procedure and (3) limited availability of commercial quality controls diminish the usefulness of the use of hair markers (Claessens, Pirard, and Charlier 2022; Junaid et al. 2024). Nonetheless, urine spot sample remains the most used matrix for the biomo-nitoring of chemicals such as bisphenols and parabens (Vorkamp et al. 2021), and hair is undoubtedly one of the promising alternative matrices due to its non-invasiveness nature and the lower concentration variability for non- persistent compounds compared to urine (Faÿs et al. 2021). Therefore, since this investigation was intended to knowingly select matrices to be used within an epidemiological study, considering the information provided and the current advantages and disadvantages, these limitations are an integral part of the study.

## Conclusions

This short preliminary study provides valuable data on the levels and distributions of several persistent (8 PFAS and 6 PCBs) and non-persistent pollutants (three parabens and two bisphenols) in paired serum and hair samples or paired spot urine and hair samples from 30 Belgian non-occupationally exposed individuals. The results were expected to help in the selection of the most suitable markers (and thus the most appropriate matrix) to be measured in an upcoming epidemiological study to assess the relationship between chemical exposure and diabetes.

When investigating the distribution of chemicals between the reference (serum or urine) and the alternative (hair) matrices, the first and main takeaway is that the conclusions are different according to the chemical group and even according to the targeted chemical within the same group. For PFAS, despite the invasiveness of the sampling, serum still appears to be the most suitable matrix compared to hair. This results from the low concentrations observed in hair compared to serum, resulting in a high proportion of non-detected measurements in hair samples. In addition, the unknown mechanism of incorporation into hair, the potential role of keratin and plasma proteins in PFAS distribution, the higher representativeness of internal exposure in serum compared to hair (due to the difficulty in discerning internal and external contamination of hair), and the large amount of data available on PFAS serum levels support this option. PCB results in serum and hair seemed to lead to similar interpretations for higher chlorinated congeners, while lower chlorinated ones seemed to be in higher proportion in hair and mainly undetected in serum. Data suggest hair as the preferred matrix for PCB measurement, if external contamination might be undoubtedly be excluded. For bisphenols, hair and urine levels provided different information. The classification of the levels measured in both matrices varied markedly, therefore making the selection of the matrix strongly influential on the association evaluation between exposure and health outcomes. Further, BPA and BPS seemed to behave differently during their incorporation in the hair shaft, further complicating the selection of the matrix. Finally for parabens, even if differences occurred regarding the carbon chain length of the paraben, hair or urine seemed to show similar reliability in exposure assessment. Nevertheless, a highly performant decontamination procedure needs to be performed to ensure the absence of external contamination for these chemicals used in hair care products.

The selection of markers and the human matrix to be sampled within the design of a biomonitoring or epidemiological study is both complex and critical, as it can significantly bias the results when studying health risks related to chemical exposure assessed from chemical levels in biological matrices. Further research is needed to better understand the distribution of chemicals in human biological matrices, including the mechanisms underlying the incorporation of chemicals into alternative matrices such as hair. In addition, efforts need to focus on addressing the limitations inherent to each matrix such as (1) distinguishing external from internal hair contamination (2), improving the reliability of urinary results, and (3) reducing the invasiveness of sampling procedures.

## ABBREVIATIONS

| | |
|---|---|
| HBM | Human biomonitoring |
| POPs | Persistent organic pollutants |
| PFAS | Perfluoroalkyl substances |
| PCBs | Polychlorobiphenyls |
| PFPeA | Perfluoropentanoic acid |
| PFHxA | Perfluorohexanoic acid |
| PFHpA | Perfluoroheptanoic acid |
| PFOA | Perfluorooctanoic acid |
| PFNA | Perfluorononanoic acid |
| PFDA | Perfluorodecanoic acid |
| PFHxS | Perfluorohexanesulfonate |
| PFOS | Linear perfluorooctanesulfonate |
| MeOH | Methanol |
| UHPLC | Ultra-high performance liquid chromatography |
| MS/MS | Tandem mass spectrometer |
| LOQ | Limit of quantification |
| GC | Gas chromatography |
| MeP | Methylparaben |
| EtP | Ethylparaben |
| PrP | Propylparaben |
| DF | Detection frequency |
| ICC | Intraclass correlation coefficient. |
| GM | Geometric mean |
| P25 | Percentile 25 |
| P50 | Percentile 50 |
| P75 | Percentile 75 |
| P95 | Percentile 95 |
| Min-max: | Minimum-maximum |
| CI | Confidence interval |

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# Supplementary materials

PFAS and PCB measurements in serum, bisphenol and paraben determinations in urine, and analyses of all hair markers except PCBs were previously detailed elsewhere (respectively in Dufour et al., 2018; Cirello et al., 2024; Pirard and Charlier, 2022; Dewalque et al., 2014a; Claessens et al., 2022). The PCB extraction and final determination in hair was strongly inspired from the method used for PCB analysis in serum with an additional hydrolysis step. Both are detailed below.

## PCBs analysis:

Chemicals:

Analytical grade acetone, acetic acid, and isopropanol were bought from Macron fine Chemicals (Gliwice Poland). LC/MS grade water and for Organic residues grade n-hexane were bought from JT Baker (Deventer, The Netherland). Sigma Aldrich (St Louis, MO, USA) was the supplier of $Na_2SO_4$.

### Extraction hair samples:

1) Hair hydrolysis

Twenty µL of internal standard mixture (25 $ng.mL^{-1}$) were added to 50 mg of washed cut hair with 1 mL of NaOH 5M. Mixture was ultrasonicated until total dissolution (around one hour).

2) Extraction

Four mL of n-hexane/acetone were added to sample. Samples were agitated using multitubes vortexer (VWR DVX 250) for 10 min. After agitation, tubes were centrifuged for 5 min at 5000 rpm. Organic phase was collected, and operations were repeated a second time. Organic phases were gathered and evaporated until 500 µL using Supervap$^{TM}$ (FMS concentration/Evaporation system).

Five hundred µL of organic phases were percolated on Phospholipid Removal Solution column (PHREE column, Phenomenex®) fill with approximatively 1 cm of $Na_2SO_4$.

Percolate was transferred in silanised ultra recovery vials containing 50 µL of Nonane.

Vials were let at ambient temperature to evaporate until 50 µL.

### Extraction of serum samples:

0.7 mL of $H_2O$, 0.3 mL of HAc and 20 µL of internal standard mixture (25 $ng.g^{-1}$) were added to 1 mL of sample (or standard). Samples were vortexed using multi tube vortexer (VWR DVX 250) for one hour at 2500 rpm.

Then, liquid/liquid extraction was performed: 4 mL of n-hexane/acetone were added to sample. Samples were agitated using multitubes vortexer for 10 min. After agitation, tubes were centrifuged for 5 min at 5000 rpm. Organic phase was collected, and operations were repeated a second time. Organic phases were gathered and evaporated until 500 µL using Supervap$^{TM}$ (FMS concentration/Evaporation system).

Five hundred µL of organic phases were percolated on Phospholipid removal solution column (PHREE column, Phenomenex) filled with 1 cm of $Na_2SO_4$.

Percolate was transferred in silanised ultra recovery vials containing 50µL of Nonane.

Vials were let at ambient temperature to evaporate until 50 µL.

### Gas Chromatography and mass spectrometer (GC-MS/MS) analysis for both serum and hair determination:

Final determination was realized on a GC 7890A-7000A GC/MS-MS (Agilent Technologies). Combination of Restek Rxi-17SIL (1.5 m × 0.25 mm ID × 0.25 µm) column and Rxi-XLB (30 m × 0.25 mm ID × 0.25 µm) column linked by press-fit connector (0.25 × 0.25 mm ID) was used under a constant flow of 1.4 mL.min$^{-1}$ of helium (He N60, air liquid)

GC settings:

- Injection: splitless
- Injection temperature: 300 °C
- Injected volume: 2 µL
- Transfer line temperature: 230 °C
- Temperature gradient:

| | **Gradient (°C.min$^{-1}$)** | **Temperature (°C)** | **Time of maintain (min)** |
|---|---|---|---|
| Initial temperature (°C) | | 140 | 1 |
| First ramp | 60 | 200 | 0 |
| Second ramp | 20 | 290 | 0 |
| Third ramp | 2 | 300 | 0 |

After Temperature gradient, a 325°C with reverse helium flow backflush is applied for two minutes to wash the column.

MS/MS settings*:*

- Ionization: electronic impact (EI)
- Source temperature: 230 °C
- Quadrupoles temperature: 150 °C
- Acquisition mode: MRM

| **Compounds** | **Q1 mass (m/z)** | **Q3 mass (m/z)** | **Collision energy (eV)** |
|---|---|---|---|
| PCB-28 | **257.9** | **186.0** | **30** |
| | 185.9 | 151.0 | 25 |
| PCB-28 $^{13}C_{12}$ | **267.5** | **198.1** | **30** |
| PCB-52 | **289.3** | **220.0** | **30** |
| | 291.3 | 222.0 | 25 |

| | | | |
|---|---|---|---|
| PCB-52 $^{13}C_{12}$ | **303.4** | **233.9** | **30** |
| PCB-101 | **325.3** | **256.0** | **35** |
| | 327.3 | 256.0 | 35 |
| PCB-101 $^{13}C_{12}$ | **337.3** | **267.9** | **35** |
| PCB-118 | **325.3** | **256.0** | **35** |
| | 327.3 | 256.0 | 35 |
| PCB-118 $^{13}C_{12}$ | **337.3** | **267.9** | **35** |
| PCB-138 | **359.8** | **289.9** | **35** |
| | 359.8 | 287.8 | 35 |
| PCB-138 $^{13}C_{12}$ | **371.3** | **301.9** | **35** |
| PCB-153 | **359.8** | **289.9** | **35** |
| | 359.8 | 287.8 | 35 |
| PCB-153 $^{13}C_{12}$ | **371.3** | **301.9** | **35** |
| PCB-180 | **393.3** | **323.9** | **35** |
| | 395.2 | 323.9 | 35 |
| PCB-180 $^{13}C_{12}$ | **405.4** | **335.9** | **35** |

Bold transitions are used for quantifications.

Determination of concentration in serum of unknown samples:

Each PCB was quantified using his $^{13}C_{12}$ mass-labelled homologue as internal standard. Calibration curve was realized using nine spiked standards solution in nonane with concentrations ranging from 1-1000 ng.L$^{-1}$. Each batch included the calibration curve, one home-made quality control (serum spiked at 10 ng.L$^{-1}$), one blank serum, one chemical blank, one quality control from former external control programs (AMAP from "Institut National de Santé Publique du Québec – INSPQ") and 30 unknown serum samples.

Determination of concentration in hair samples

Each PCB is quantified using his $^{13}C_{12}$ mass-labelled homologue as internal standard. Calibration curve was realized using nine spiked standards solution in nonane with concentrations ranging from 0.25 to 50 pg.mg$^{-1}$. Each batch included the calibration curve, one home-made quality control (blank hair sample spiked at 25 pg.mg$^{-1}$), one blank hair sample, one chemical blank, one quality control from former external control programs (AMAP from "Institut National de Santé Publique du Québec – INSPQ") and 30 unknown hair samples.

Table S1: Limits of quantification (LOQs) for targeted chemicals according to the matrix analyzed.

| | **Hair (pg/mg)** | **Serum (μg/L)** |
|---|---|---|
| ***PFAS*** | | |
| PFPeA | 0.32 | 0.10 |
| PFHxA | 0.20 | 0.10 |
| PFHpA | 0.20 | 0.10 |
| PFOA | 0.20 | 0.50 |
| PFNA | 0.20 | 0.10 |
| PFDA | 0.27 | 0.10 |
| PFHxS | 0.20 | 0.15 |
| PFOS | 10 | 0.50 |
| ***PCBs*** | | |
| PCB 28 | 0.25 | 0.020 |
| PCB 52 | 0.25 | 0.020 |
| PCB 101 | 0.25 | 0.015 |
| PCB 138 | 0.25 | 0.007 |
| PCB 153 | 0.25 | 0.006 |
| PCB 180 | 0.25 | 0.005 |
| | **Hair (pg/mg)** | **Urine (μg/L)** |
| ***Bisphenols*** | | |
| BPA | 10 | 0.29 |
| BPS | 2 | 0.09 |
| ***Parabens*** | | |
| MeP | 10 | 0.79 |
| EtP | 2 | 0.30 |
| PrP | 10 | 0.36 |

Table S2: Summary of the reference studies used for the cut-off determination used in kappa Cohen’s calculation

| Compounds | Matrix | N | Min | P25 | P50 | P75 | Max | Location | Reference |
|---|---|---|---|---|---|---|---|---|---|
| Bisphenols | | | | | | | | | |
| BPA | Urine (µg/L) | 90 | <0.29 | 0.37 | 0.78 | 1.57 | 2.65 | Belgium, Wallonia | (Pirard and Charlier 2022) |
| | Hair (pg/mg) | 114 | <10.0 | 21.7 | 46.6 | 88.8 | 587 | Belgium, Wallonia | (Claessens et al. 2022) |
| BPS | Urine (µg/L) | 84 | <0.09 | <0.09 | <0.09 | 0.25 | 8.84 | Belgium, Wallonia | (Pirard and Charlier 2022) |
| | Hair (pg/mg) | 114 | <2.00 | 15.4 | 31.9 | 62.4 | 2298 | Belgium, Wallonia | (Claessens et al. 2022) |
| Parabens | | | | | | | | | |
| MeP | Urine (µg/L) | 92 | <0.79 | 1.65 | 3.55 | 11.7 | 549.2 | Belgium, Wallonia | (Pirard and Charlier 2022) |
| | Hair (pg/mg) | 114 | <10.0 | 24.1 | 58.9 | 204 | 53356 | Belgium, Wallonia | (Claessens et al. 2022) |
| EtP | Urine (µg/L) | 92 | <0.30 | <0.30 | 0.57 | 2.16 | 63.7 | Belgium, Wallonia | (Pirard and Charlier 2022) |
| | Hair (pg/mg) | 114 | <2.00 | <2.00 | 5.20 | 16.7 | 26697 | Belgium, Wallonia | (Claessens et al. 2022) |
| PrP | Urine (µg/L) | 92 | <0.30 | <0.30 | <0.3 | 0.54 | 107 | Belgium, Wallonia | (Pirard and Charlier 2022) |
| | Hair (pg/mg) | 114 | <10.0 | <10.0 | 16.4 | 61.6 | 1517 | Belgium, Wallonia | (Claessens et al. 2022) |
| PFAS | | | | | | | | | |
| PFOA | Serum (µg/L) | 242 | <0.50 | 1.25 | 1.91 | 2.86 | 6.79 | Belgium, Wallonia | (Pirard et al. 2020) |
| | Hair (pg/mg) | 114 | <0.20 | <0.20 | <0.20 | 0.30 | 3.40 | Belgium, Wallonia | (Claessens et al. 2022) |
| PCBs | | | | | | | | | |
| PCB 153 | Serum (µg/L) | 536 | <0.07 | <0.07 | 0.10 | 0.15 | 0.69 | Belgium, Wallonia | (ISSeP 2021) |
| | Hair (pg/mg) | 310 | <0.25 | <0.25 | <0.25 | 0.30 | 9.68 | France | (Peng et al. 2020) |
| PCB 180 | Serum (µg/L) | 536 | <0.05 | <0.05 | 0.07 | 0.12 | 1.41 | Belgium, Wallonia | (ISSeP 2021) |
| | Hair(pg/mg) | 310 | <0.25 | <0.25 | 0.25 | 0.45 | 6.79 | France | (Peng et al. 2020) |

Table S3: Cut-off and attributed classification used in kappa Cohen's calculation.

| Cut off and attributed classification | | | | |
|---|---|---|---|---|
| Compound | Cut off | Attributed classification | Cut off | Attributed classification |
| EtP | Hair (pg/mg) | | Urine (µg/L) | |
| | <LOQ | 1 | <LOQ | 1 |
| | LOQ<x<5.20 | 2 | LOQ<x<0.57 | 2 |
| | 5.20<x<16.7 | 3 | 0.57<x<2.16 | 3 |
| | 16.7<x | 4 | 2.16<x | 4 |
| MeP | Hair (pg/mg) | | Urine (µg/L) | |
| | <24.1 | 1 | <1.65 | 1 |
| | 24.1<x<58.9 | 2 | 1.65<x<3.55 | 2 |
| | 58.9<x<204.8 | 3 | 3.55<x<11.7 | 3 |
| | 204.8<x | 4 | 11.7<x | 4 |
| PrP | Hair (pg/mg) | | Urine (µg/L) | |
| | x<16.4 | 1 | <LOQ | 1 |
| | 16.4<x<61.6 | 2 | LOQ<x<0.54 | 2 |
| | 61.6<x | 3 | 0.54<x | 3 |
| BPS | Hair (pg/mg) | | Urine (µg/L) | |
| | x<31.9 | 1 | x<LOQ | 1 |
| | 31.9<x<62.4 | 2 | LOQ<x<0.25 | 2 |
| | 62.4<x | 3 | 0.25<x | 3 |
| BPA | Hair (pg/mg) | | Urine (µg/L) | |
| | x<21.7 | 1 | x<0.37 | 1 |
| | 21.7<x<46.6 | 2 | 0.37<x<0.78 | 2 |
| | 46.6<x<88.8 | 3 | 0.78<x<1.57 | 3 |
| | 88.8<x | 4 | 1.57<x | 4 |
| PFOA | Hair (pg/mg) | | Serum (µg/L) | |
| | x<LOQ | 1 | <1.91 | 1 |
| | LOQ<x<0.30 | 2 | 1.91<x<2.86 | 2 |
| | 0.30<x | 3 | 2.86<x | 3 |
| PCB 153 | Hair (pg/mg) | | serum (µg/L) | |
| | <LOQ | 1 | <0.070 | 1 |
| | LOQ<x<0.30 | 2 | 0.100<x<0.150 | 2 |
| | 0.30<x | 3 | 0.150<x | 3 |
| PCB 180 | Hair (pg/mg) | | Serum (µg/L) | |
| | <LOQ | 1 | <0.050 | 1 |
| | LOQ<x<0.50 | 2 | 0.050<x<0.070 | 2 |
| | 0.50<x | 3 | 0.070<x | 3 |

Table S4: Weights for Cohen’s kappa coefficients.

| BPS, PrP, PFOA, PCB153, PCB 180 | | | | | BPA, MeP, EtP | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Classification | | Hair | | | Classification | | Hair | | | |
| | | 1 | 2 | 3 | | | 1 | 2 | 3 | 4 |
| Urine/serum | 1 | 1.0 | 0.5 | 0.0 | Urine/serum | 1 | 1.00 | 0.66 | 0.33 | 0.00 |
| | 2 | 0.5 | 1.0 | 0.5 | | 2 | 0.66 | 1.00 | 0.66 | 0.33 |
| | 3 | 0.0 | 0.5 | 1.0 | | 3 | 0.33 | 0.66 | 1.00 | 0.66 |
| | | | | | | 4 | 0.00 | 0.33 | 0.66 | 1.00 |