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COMPARISON OF THE TRENDS IN PFAS CONCENTRATIONS OBTAINED FROM A 10 YEAR LONGITUDINAL COHORT INVESTIGATION TO GENERAL CROSS-SECTIONAL AND RETROSPECTIVE POPULATION BASED STUDIES

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Introduction

Poly- and perfluoroalkyl substances (PFASs) have been used as surfactants and processing aids in a broad range of commercial applications since the 1950s. A group of PFASs called perfluoroalkyl acids (PFAAs) can be formed as breakdown products of other PFASs or as residual by-products in PFAS production. Due to their chemical stability, PFASs are resistant to breakdown and thus reside for many years in our environment and between 2 to 29 years in our bodies, depending on the length of the carbon chain (1). The increased levels of PFASs in humans and recent association of background PFAS levels and negative health effects has resulted in a shift in PFAS production in order to limit human exposure. Several restrictions were placed on the use of some PFASs, including the addition of PFOS and like compounds produced from perfluorooctane sulfonyl fluoride to the Stockholm Convention in 2009.

Biomonitoring studies have been carried out in order to observe how the implemented restrictions in PFAS use has affected human concentrations and to assess the change in PFAS concentrations among general populations over time. Usually biomonitoring studies provide cross-sectional or retrospective trends, where either new test subjects are sampled at each investigation or previously collected samples from random individuals are re-analyzed to assess a change in a chemical of interest over time. However, when compared to a longitudinal investigation, these sampling techniques may not account for the variation associated with sampling a continuously changing test population. For example, in other general trend studies, the sampling population changes over time, but in this study, the same individuals were repeatedly sampled over time. Therefore, we can assess each individual's change in concentration, which may provide a more accurate portrayal of the temporal trend in PFAS concentration that is occurring.

This is the first known study to evaluate the longitudinal trend for a range of PFAS concentrations in a large background-level exposed population of men and women known as the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) cohort. The PIVUS cohort includes individuals with the same age and location who were repeatedly sampled at three different time points between 2001 and 2014. We present what we believe are the most recent trends of eight PFAS concentrations in humans, a comparison of the longitudinal trends of PFAS concentrations analyzed from the PIVUS cohort to results from general population studies and a brief assessment of gender dependent changes in PFAS concentrations over time.

Methods

Serum samples were collected from the PIVUS cohort (n=1,016 of which about 50% women) when they turned 70 (2001-2004), 75 (2006-2009) and 80 (2011-2014) years old, with 579 participant's serum present in all three collections. Each of the participant's PFAS concentrations were individually determined at ages 70, 75 and 80, followed by an individual-based assessment of the change in each PFAS concentration over time. The levels obtained from the first sampling investigation (2001-2004) were used as a baseline comparison to assess the change in median PFAS concentrations in subsequent sampling investigations (2006-2009 and 2011-2014). The median change in PFAS concentration was used for comparison to other general trend studies. The changes in the concentrations of PFASs over time were tested using random effects (mixed) model analysis. Also mixed models were used to assess if the changes in PFASs over time were sex-dependent. A $p<0.05$ was regarded as significant.

The sample preparation included solvent protein precipitation and sample filtration using 96-well plates. The samples were analyzed using an Acquity UPLC- Quattro Premier XE MS/MS system (Waters Corporation) operating in negative ionization mode. Fourteen target PFASs were quantified via a matrix matched calibration curve and isotope dilution, however only the eight (C6-11) PFASs that were detected in the majority of individuals were included in the statistical assessment. The eight PFASs include: perfluoroheptanoic acid (PFHpA), perfluorohexane sulfonic acid (PFHxS), PFOA (perfluorooctanoic acid), perfluorooctane sulfonic acid (PFOS), perfluorooctane sulfonamide (FOSA), perfluorononanoic acid (PFNA), perfluorodecanoic acid (PFDA), and perfluoroundecanoic acid (PFUnDA).

Results and Discussion

The median concentrations of the eight PFASs tested in the PIVUS cohort are similar to the levels reported in other background-level exposed populations (Table 1). From 2001-2004 and 2006-2009, the greatest increase in PFAS concentrations was observed in the PIVUS cohort. Only median PFOS (-6%) and FOSA (-40%) concentrations significantly decreased, while the remaining six PFASs: PFHpA, PFHxS, PFOA, PFNA, PFDA, and PFUnDA significantly increased (14% to 59%). These results indicate that the implemented restrictions on PFAS production and use positively influenced the PIVUS cohort's PFOS and FOSA levels, but did not show the same effect in other PFASs analyzed. However, from 2006-2009 and 2011-2014, all median PFAS levels significantly decreased (-20% to -64%), which suggests that in general PFAS restrictions had a positive influence on decreasing PFAS levels during this time.

Overall, the change in PFAS concentrations over time was similar to general test populations from biomonitoring studies conducted in the U.S. (NHANES) (2), Norway (3), Germany (4), and Australia (5). However, unlike these studies, which showed an overall decrease in PFHxS concentrations, the median level of PFHxS in the PIVUS cohort had an overall significant increase of 34% from 2001 to 2014, indicating that our cohort experienced an additional exposure to PFHxS compared to other background-level exposed populations. In 2012, a pilot study that tested drinking water in Uppsala, Sweden found high concentrations of PFHxS and PFBS, which is believed to be due to the leaching of aqueous firefighting foams (AFFFs) from a military airport that used PFOS and PFAS AFFFs until 2003 into a nearby water production well (6). A separate study which tested the temporal trend of PFAS concentrations in primiparous Uppsala women from 1996 to 2012 also found an increasing trend of PFHxS and PFBS, but decreasing trend in FOSA, PFOS, PFDS and PFOA after 2000 (7). The dramatic difference between the overall increase of PFHxS concentrations in the PIVUS cohort and other general population trend studies from other countries is seen in Figure 1.

In general, the change in PFAS concentrations between men and women of the PIVUS cohort were similar over the ten year period, with the exception of PFHxS and PFHpA. PFHxS concentrations significantly increased more so in women over time, while PFHpA concentrations significantly decreased more so in men over time. Our results differ compared to studies which include younger age groups. However, another study that compares the temporal trend in PFAS concentration versus gender in a 60+ aged study group showed similar results to the PIVUS cohort (8). The similarity between these two studies and dissimilarity among studies which include younger age groups may suggest that PFAS concentration is influenced by both age and gender.

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Table 1: A comparison of the range in median PFAS levels detected in the PIVUS cohort to other background level general trend studies.

PFAS	PIVUS (2001-2014)	The U.S.(1) (2003-2012)	Germany(2) (2001-2010)	Australia(3) (2002-2011)	Norway(4) (2001-2007)
	Range of median concentrations (ng/mL)				
PFHpA	**0.03-0.07**	**<LOD**	**N/A**	**N/A**	**0.1-0.1**
PFOA	**2.5-4.0**	**2.16-4.3**	**3.2-5.2**	**4.3-9.7**	**3.1-4.2**
L-PFOS	**7.6-14**	**N/A**	**N/A**	**N/A**	**23-30**
PFNA	**0.73-0.87**	**0.89-1.23**	**N/A**	**N/A**	**1.1-1.5**
PFDA	**0.32-0.34**	**<LOD-0.300**	**N/A**	**N/A**	**0.7-0.8**
PFUnDA	**0.30-0.45**	**<LOD-0.200**	**N/A**	**N/A**	**1.1-1.3**
FOSA	**0.02-0.11**	**<LOD-0.100**	**N/A**	**N/A**	**0.2-1.0**
PFHxS	**2.2-3.5**	**1.28-1.90**	**0.86-1.87**	**N/A**	**1.9-2.0**

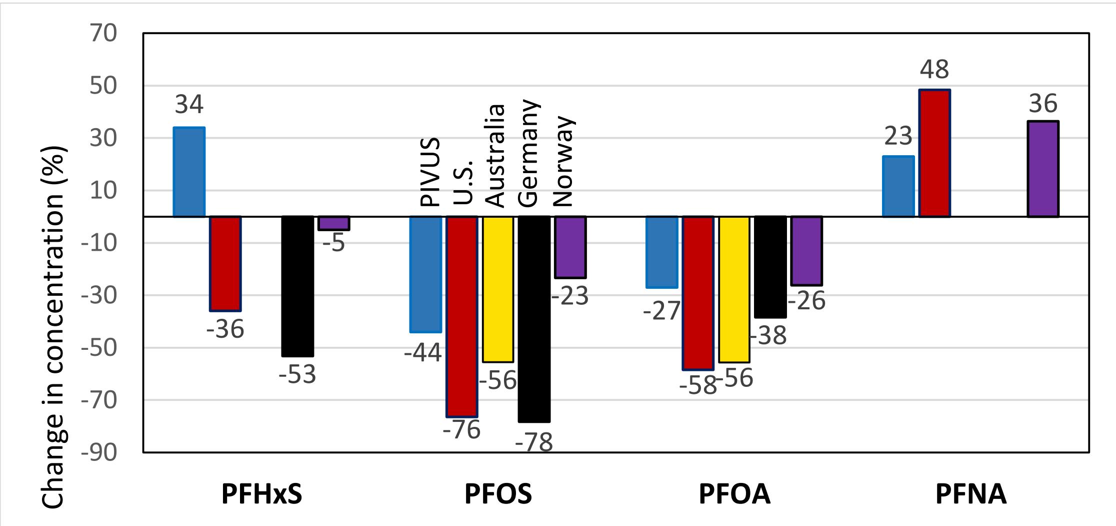

Figure 1: A comparison of the longitudinal change in concentration of four PFASs detected in the PIVUS cohort to the results obtained from cross-sectional and retrospective trend studies conducted in the U.S. (1), Australia (3), Germany (2)and Norway (4).