Hand wipes: a useful tool for assessing human exposure to poly- and perfluoroalkyl substances (PFASs) through hand-to-mouth and dermal contacts

Somrutai Poothong, [1, 2*] Juan Antonio Padilla-Sánchez,[1] Eleni Papadopoulou,[1] Georgios Giovanoulis,[3] Cathrine Thomsen,[1] Line Småstuen Haug[1]

[1]Department of Environmental Exposure and Epidemiology, Norwegian Institute of Public Health, P.O. Box 4404, Nydalen, NO-0403 Oslo, Norway.

[2]Department of Chemistry, University of Oslo, P.O. Box 1033, Blindern, NO-0315 Oslo, Norway.

[3]IVL Swedish Environmental Research Institute, SE-10031 Stockholm, Sweden

*__Corresponding author:__ Somrutai Poothong

Department of Environmental Exposure and Epidemiology, Norwegian Institute of Public Health, P.O. Box 4404, Nydalen, NO-0403 Oslo, Norway

E-mail: somrutai.poothong@fhi.no

Abstract

The indoor environment contribute considerably to human exposure to poly- and perfluoroalkyl substances (PFASs). This study estimated the human exposure to PFASs from the indoor environment through hand-to-mouth and dermal contacts using hand wipes. An analytical method was developed to determine 25 PFASs in hand wipe samples collected as a composite sample from both hands of 60 adults. Polyfluoroalkyl phosphate esters (PAPs) were the predominant PFASs in the hand wipe samples (medians between 0.21 and 0.54 ng per sample). Positive and significant correlations were observed between PAPs, perfluorooctanesulfonate (PFOS), and perfluorooctanoate (PFOA) in hand wipes. Low frequency of daily hand washing ($\leq$8 times day^{-1}) was associated with 30–50% higher concentrations of PFOS, PFOA, and 8:2diPAP in hand wipes. Further, significant correlations between paired hand wipes and house dust samples were observed for PFOS, PFOA, and 6:2diPAP. Also, a significant correlation between PFOS in hand wipes and EtFOSE in indoor air was found. This finding indicates either a common source of exposure or a transformation of EtFOSE to PFOS in the environment or on the hands. The contributions of direct and indirect exposure to perfluoroalkyl acids (PFAAs) showed that PFOA contributed the highest exposure to adults via hand-to-mouth and dermal contacts, followed by PFOS. The median of estimated daily intakes via hand-to-mouth and dermal contacts (for hands only) for PFOA were 0.83 and 0.50 pg·kg bw^{-1}·day^{-1}, respectively. This study gives a first indication that PFAS concentrations in hand wipes can be used as a proxy for the exposure to PFASs from indoor environments, but further studies are needed to confirm this.

Introduction

Poly- and perfluoroalkyl substances (PFASs, C_nF_{2n+1} −R) comprise a large group of synthetic organic chemicals.[1] Their ubiquitous contamination of the global environment has led to concern on their effects in humans and animals.[2] Exposure to PFASs has become an emerging public health issue due to their persistence, bioaccumulation potential, and associations with adverse health outcomes in epidemiological studies.[3-5] Furthermore, a range of adverse effects have also been reported in animal studies.[6-7]

PFASs have been detected in numerous consumer products including carpets, clothes,[8] cosmetics, food packaging paper,[9-10] and waterproofing agents.[8, 11] Recently, a range of PFASs have been found in various personal care products.[12] The frequently reported sources of human exposure to PFAS are food, drinking water, house dust, and indoor air.[13-14] Dermal absorption is considered a likely route of exposure for humans, particularly for chemicals found in personal care products and the indoor environment (dust and air).[15] Thus, dermal absorption might also be a route of exposure to PFASs. Also, hand-to-mouth contact has been reported as an exposure pathway for environmental contaminants. Adults can be exposed directly from hand-to-mouth contact through nail biting, smoking, and consumption of finger foods. Currently, little is known about the sources and magnitude of exposure to PFASs via hand-to-mouth and dermal contacts. To perform a thorough evaluation of human exposure to PFASs through hand-to-mouth contact and dermal absorption, extensive knowledge and information is required, such as concentrations of PFASs in exposure media (e.g. house dust, indoor air, and personal care products), the duration of exposure, and existence of accurate transfer rates from the medias to the skin surface. Several of the above-mentioned key elements are presently unknown. Hand wipes are expected to be suitable for assessing exposure to PFASs through both hand-to-mouth and dermal contacts.

However, hand wipes is a complex matrix, as it does not only consist of the wipe material but it also contains residues from hands (e.g. fat after wiping). Thus, a selective and robust method is needed for determination of environmental pollutants in hand wipe samples. To our knowledge, there are no previous reports on concentrations of PFASs in hand wipes, and estimating the corresponding exposure from hand-to-mouth and dermal contacts.

The study aimed to develop a method to determine 25 PFASs in 60 hand wipe samples from Norwegian adults, and estimate the human exposure to PFASs through hand-to-mouth and dermal contacts. Also, relationships and comparability between PFAS concentrations found in hand wipes, dust and air samples collected from the participant's house were assessed. Moreover, the impact of individual characteristics, behaviors, and living conditions on PFAS concentrations measured in hand wipes, was evaluated.

Materials and methods

Study population

Samples were collected from participants of the Advanced Tools for Exposure Assessment and Biomonitoring (A-TEAM) project. This well-characterized study group of 60 women and men from the general adult population living in the Oslo area, in Norway, has been used to enhance the knowledge of a variety of aspects related to internal and external exposure to selected consumer chemicals. The sampling campaign was conducted during the winter season between November 2013–April 2014, and several indoor environment samples, dietary, and biological samples were collected from the participants and their households.[16] It should be noted that the potential seasonal variation has not been assessed, and the exposure factors do not reflect this. The Regional Committees for Medical and Health Research Ethics in Norway approved this study (2013/1269) before conducting the sampling campaign. Participants completed a written consent form before participating.

Measurement of PFASs in hand wipes

Hand wipes collection

All hand wipe samples were self-collected. The participant received a written sampling procedure, and the researcher demonstrated the self-sampling with the participant during a home visit. The participants were advised to keep their hands unwashed at least 60 min before collecting the hand wipes, and the sample reserved for PFAS analysis was collected in the evening before going to bed. One sterile gauze pad (Sterile Gauze Pads, 3x3 inches, Swift First Aid Inc. Valencia, CA, USA) was applied to each hand after being immersed in 3 mL isopropyl alcohol (reagent grade). The hand was wiped on both sides from the wrist to the fingertips, including the sides of the hand and the fingers. The two gauze pad samples were stored together in a polypropylene bottle and kept at -20ºC until analysis. Field blanks were collected when the researchers visited the participant's house. A total of 60 hand wipe samples and 15 field blanks were collected from 60 participants (age: 20–66; median age 41; gender: 45 women and 15 men) for PFASs analysis. Details on the target PFASs are provided in **Table S1 of the supporting information (SI)**.

Hand wipes extraction

Several stages of method development and validation experiments were conducted before the extraction of the real samples. An internal standard mixture (containing 2.7 ng of each of the PFAS internal standards) was added to the bottle containing the hand wipe sample and dried at room temperature, and then 50 mL methanol was added. The sample bottles were shaken, and sonicated in an ultrasonic bath for 30 min. Then the extraction solvent was transferred to a new centrifuge tube, and the solvent was evaporated to approximately 500 μL using a RapidVap (Labconco, MO, USA) adjusted to 180 mbar and 40°C. After this, the sample was transferred into a 2 mL centrifuge tube containing a total amount of 10 mg of mixed sorbents (primary-secondary amine : C_{18} : activated carbon, 1:1:1, by weight). The tubes were shaken and centrifuged for 10 min at 14000 rpm, and then the supernatant was transferred into a polypropylene injection vial.

Instrumental analysis

The instrumental analysis was performed on an online solid phase extraction, ultra-high performance liquid chromatography coupled with tandem mass spectrometry (online-SPE-UHPLC-MS/MS) system. The instrument was operated in negative electrospray ionization (-ESI) mode, and the method was based on an established analytical method for analysis of PFASs in serum, plasma, and whole blood as described by Poothong et al.[17] The instrumentation consisted of a column switching system coupled to an Agilent 1290 UHPLC, interfaced to an Agilent 6490 Triple Quadrupole mass spectrometer equipped with Agilent Jet-Stream electrospray ionization (Agilent Technologies, Palo Alto, CA, USA).

Analytes were quantified with appropriate internal standards, which were selected based on retention time and accuracy obtained in the spiking experiment. The calibration curves used for quantification were based on matrix-matched calibration solutions (using gauze pads) which were prepared using the same procedure as real samples, but spiked with the 25 native PFASs in 11 different concentrations in the range of 0.003–22.5 ng per sample.

Validation and QA/QC

The hand wipe method was validated using spiked samples. Initially, method recovery was evaluated by the analysis of both spiked blank gauze pads and a hand wipe sample containing a commercial hand cream product and 1.2 ng internal standard mixture in order to simulate a real hand wipe sample. Method recoveries in spiked blank gauze pads were 60–90% while in spiked gauze pads with a commercial hand cream the recovery of internal standards ranged between 50–75%.

Details on the accuracy and repeatability of the method are presented in **SI Table S2**. Briefly, the method accuracy was obtained from five spiking levels of PFASs (n=5) at 0.0225, 0.09, 0.45, 3.0, and 15 ng per sample. An average method accuracy ((the obtained concentration in the spiked sample / the nominal concentration) *100) of 98±12% was obtained, including all spiking levels for all compounds. The repeatability of the method was given as the coefficients of variation (CV) using the same samples as was used to evaluate the accuracy. The average repeatability was calculated to be 12%. In order to assess the method intermediate precision, new sets of calibration standards and spiked hand wipes (n=5) at 0.45 and 3.0 ng were analyzed. The intermediate precision was obtained by calculating the CVs of both the samples used to evaluate the repeatability and the new samples analyzed to evaluate the intermediate precision (n=10). The average intermediate precision was 11±6%. Differences in the accuracy between the two sets of spiked samples were also evaluated, obtaining an average difference of 10±8% (**Table S3**).

Procedure blanks (i.e., a solvent with ISs, n=3) and zero blank samples (i.e., gauze pads with ISs, n=3) were included in the validation series. Method quantification limits (MQLs) were obtained from the lowest calibration point for each analyte (S/N > 10), and method detection limits (MDLs) were set to 3/10 of the MQLs. The method detection limits (MDLs) ranged from

0.0045–0.09 ng. Method quantification limits (MQLs) were 0.015–0.3 ng (**Table S4**). No PFASs levels in blank samples were above the MDLs. Field blank samples (n=5) were included in the analysis of hand wipe samples. PAPs were detected in levels (i.e. 0.009–0.066 ng) slightly above their MDLs (i.e. 0.009–0.045 ng). These concentrations were subtracted from the determined concentrations in the real hand wipe samples.

Questionnaires

PFAS concentrations in hand wipes and information from a questionnaire completed by the participants were evaluated. The questionnaire comprised information on participant habits and activity, and characteristic of their houses including age and gender of participants, hand washing frequency, years of living in the house, the use of hand cream, and age of the building.

Measurement of PFASs in house dust and indoor air

The methods used for the analysis of house dust[18] and indoor air[19] has been described in details elsewhere including information on quality assurance. In brief, floor dust samples and elevated surface dust from >0.5 m above the floor were collected separately from the living room using a vacuum cleaner equipped with a nozzle and a weighted cellulose paper filter fixed in a housing. Also, vacuum cleaner bags were collected from the participants, and the content was sieved using a 500 mm sieve. A 0.1 g of dust was analysed using solid-liquid extraction with methanol, and then clean-up by activated carbon before analysis on an online solid phase extraction-ultrahigh performance liquid chromatography-time-of-flight-mass spectrometry instrument (online SPE-UHPLC-TOF-MS).

Indoor air samples were collected in the participants living room for 24 hours using a SKC Leland Legacy pump (SKC Inc., PA, USA) connected to four SPE cartridges in parallel

(200mg, 6mL, Biotage, Uppsala, Sweden). For the chemical analysis, the cartridges were eluted using methanol, and then the extract was gently evaporated under nitrogen steam before analysis using a gas chromatography-mass spectrometry instrument (GC-MS).

Data analysis

The data were analyzed statistically using the SPSS software version 23 (SPSS IBM Statistics). PFAS concentrations below the MDLs were replaced with their MDLs divided by the square root of 2 (MDL/√2).[20] Non-parametric statistical analyses were performed due to non-normally distributed PFAS concentrations as tested by the Shapiro–Wilk test of normality. Correlations between the different PFASs in hand wipes were examined using Spearman's rank correlation coefficient (*rho*). Correlations between PFAS concentrations in hand wipes and indoor environments (house dust and indoor air) were also evaluated using Spearman's rank correlation coefficient (*rho*). A Mann-Whitney U-test was used to assess significant differences of PFAS concentrations in hand wipes between two groups of population characteristics. A significance level of 0.05 was used, and *p*-values lower than that level were considered statistically significant.

PFAS exposure assessments from hand wipes

Exposure to PFASs through hand-to-mouth contact

Individual daily intakes of PFAS (pg·kg bw^{-1}·day^{-1}) via hand-to-mouth contact was estimated based on the concentration found in the hand wipe samples. The estimated daily intakes of each participant were determined with the following equation:

$$EDI_{htm} = \frac{Q_{hw} \times TF_{htm} \times H_{contact\ area} \times f_{htm} \times t_{exp} \times F_{uptake-GIT}}{BW}$$

where EDI_{htm} is the estimated daily exposure to the target PFAS via hand-to-mouth contact (pg·kg bw^{-1}·day^{-1}), Q_{hw} is the total PFAS mass present on the hands based on the concentrations in the hand wipes (pg), TF_{htm} is the efficiency of the PFAS mass transferr at each contact from hand to mouth (%), $H_{contact\text{-}area}$ is the proportion of the hand contact area in each event (%), f_{htm} is the frequency of hand-to-mouth events (events hour $^{-1}$), t_{exp} is the time exposed (hour day^{-1}), $F_{uptake\text{-}GIT}$ is the uptake fraction of PFASs via the gastrointestinal tract (GIT) (unitless), BW is the individual body weight (kg).

The individual daily intakes via hand-to-mouth contact can be estimated from the PFAS concentrations measured in hand wipe samples. A transfer fraction from hand to mouth of 50%, similar to what has previously been reported for pesticide control products, has been assumed.[21] It is likely that the entire hands are not in contact with the mouth, and thus a contact surface area of 5% was used.[22] The frequency of hand-to-mouth events for adults was set to 2 events per hour in this study.[23] The number of times exposed to PFASs via hand-to-mouth contact was limited to the active hours (hours not asleep) which were assumed to be two-thirds of a day (16 hours). Further, it was assumed that the total PFAS mass on the hands was constant, and the uptake fraction of PFASs via the gastrointestinal tract was assumed to be complete (i.e., 100%), similar to other human exposure studies.[24-25]

Exposure to PFASs through dermal absorption

Exposure to the studied PFASs via dermal absorption was estimated using the following equation:

$$EDI_{dermal} = \frac{Q_{hw} \times t_{exp} \times F_{uptake-dermal}}{BW}$$

where EDI_{dermal} is the estimated daily exposure to the target PFAS via dermal absorption (pg·kg bw^{-1}·day^{-1}), Q_{hw} is the total PFAS mass present on the hands based on the concentrations in hand wipes (pg), t_{exp} is the time exposed (hour day^{-1}), F_{dermal} is the uptake fraction of PFASs absorbed through the skin (%), BW is the individual body weight (kg).

It was assumed that the total PFAS mass on the hands was constant. The exposure duration in a day was set to 24 hours. The absorption factor for PFASs through the skin was adopted from an *in vitro* study[26] that reported that 48% of the applied dose of PFOA was transferred through the human epidermis in 24 hours.

Biotransformation from PAPs → FTOHs → PFCAs was expected,[27-28] and a complete biotransformation of PAPs to FTOHs was assumed. Biotransformation of FTOHs to odd chain length PFCAs is slower than for the even chain length PFCAs,[27] therefore, one order of magnitude lower biotransformation rates were assumed. A biotransformation rate of 0.003 was used for 6:2PAP to PFHxA and 8:2PAP to PFOA, and a biotransformation rate of 0.0003 was used for 6:2PAP to PFHpA and 8:2PAP to PFNA. As each mole of diPAP degrade to two moles of the respective monoPAP, the same biotransformation was used, but a factor of two was multiplied for 6:2diPAP and 8:2diPAP to PFCAs.

Results and discussion

Levels and profiles of PFASs in hand wipes

The developed analytical method was applied to 60 hand wipe samples. Twenty of the twenty-five PFASs were detected in hand wipe samples. **Table 1** presents the concentrations of PFASs determined in hand wipe samples.

Table 1. Descriptive statistics for PFASs measured in the hand wipes (ng) from both hands for adult participants (n=60)

	n>MDL (%) [a]	MDL<n<MQL (%)	Mean (ng) [b]	Median (ng) [b]	25^{th} percentile (ng)	75^{th} percentile (ng)	Maximum (ng)
6:2 PAP	93	33	0.77	0.21	0.09	0.39	16
8:2 PAP	100	10	1.3	0.23	0.12	0.39	44
6:2 diPAP	98	3	3.3	0.54	0.28	1.0	87
8:2 diPAP	100	0	4.7	0.41	0.20	0.80	213
PFHxPA	2	2	<MDL	<MDL	<MDL	<MDL	0.01
PFDPA	3	0	0.01	<MDL	<MDL	<MDL	0.10
PFBS	25	3	0.01	<MDL	<MDL	0.01	0.05
PFHxS	45	22	0.04	<MDL	<MDL	0.01	1.5
PFHpS	78	17	0.56	0.02	0.01	0.35	6.5
PFOS	98	23	0.04	0.03	0.02	0.04	0.56
PFDS	45	12	0.02	<MDL	<MDL	0.02	0.45
PFHxA	7	3	0.05	<MDL	<MDL	<MDL	0.61
PFHpA	2	0	0.13	<MDL	<MDL	<MDL	5.7
PFOA	80	7	0.18	0.07	0.01	0.14	2.8
PFNA	47	5	0.05	<MDL	<MDL	0.06	0.36
PFDA	20	5	0.04	<MDL	<MDL	<MDL	0.61
PFUnDA	30	3	0.03	<MDL	<MDL	0.04	0.19
PFDoDA	10	2	0.02	<MDL	<MDL	<MDL	0.51
PFTrDA	2	0	0.05	<MDL	<MDL	<MDL	0.95
PFTeDA	7	2	0.06	<MDL	<MDL	<MDL	0.62

[a] % detection frequency was calculated from the number of sample above their MDLs. [b] For values below MDL, the MDLs divided by the square root of two was used. [c] No sample had PFOPA, PFPeA, PFOSA, MeFOSA, and EtFOSA levels above their respective MDLs (0.009–0.09 ng).

Interestingly, the PFAA precursors 8:2PAP and 8:2diPAP were detected in 100% and 6:2PAP and 6:2diPAP were detected in more than 93% of the samples. Detection frequencies of PFHpS, PFOS, and PFOA were equal to or higher than80%. Approximately half of the samples had detectable levels of PFHxS, PFDS, and PFNA while the other PFSAs and PFCAs, PFHxPA, and PFDPA were less frequently detected (<30%). No samples had PFOPA, PFPeA, PFOSA, MeFOSA, and EtFOSA levels above their respective MDLs (0.009–0.09 ng).

PAPs were the most prominent compounds found in the hand wipe samples. The median concentrations of PAPs ranged from 0.21 to 0.54 ng per sample, which was 3 to 27 times higher than median concentrations of PFOS (0.03 ng per sample) and PFOA (0.07 ng per sample) (**Table 1**). The highest median concentration was observed for 6:2diPAP being 0.54 ng per sample, while the median concentrations of 6:2PAP, 8:2PAP, and 8:2diPAP were 0.21, 0.23, and 0.41 ng per sample, respectively. A few samples had a considerably higher amount of the PAPs than the other samples. PFAS concentrations on a molar basis can be seen in **Table S5**, which molar sum of PAPs ranged from <1–433 pgM. This finding suggests that an individual can be exposed to different levels of PFASs. The relatively high concentrations and detection frequencies of PAPs in hand wipes indicate widespread use of these PFASs in consumer products.[11] The relative contribution of PAPs in hand wipe samples were approximately 20–100% of the total PFASs (**Figure 1**). This finding is in accordance with previous findings in the indoor dust where PAPs were found to dominate.[29-30]

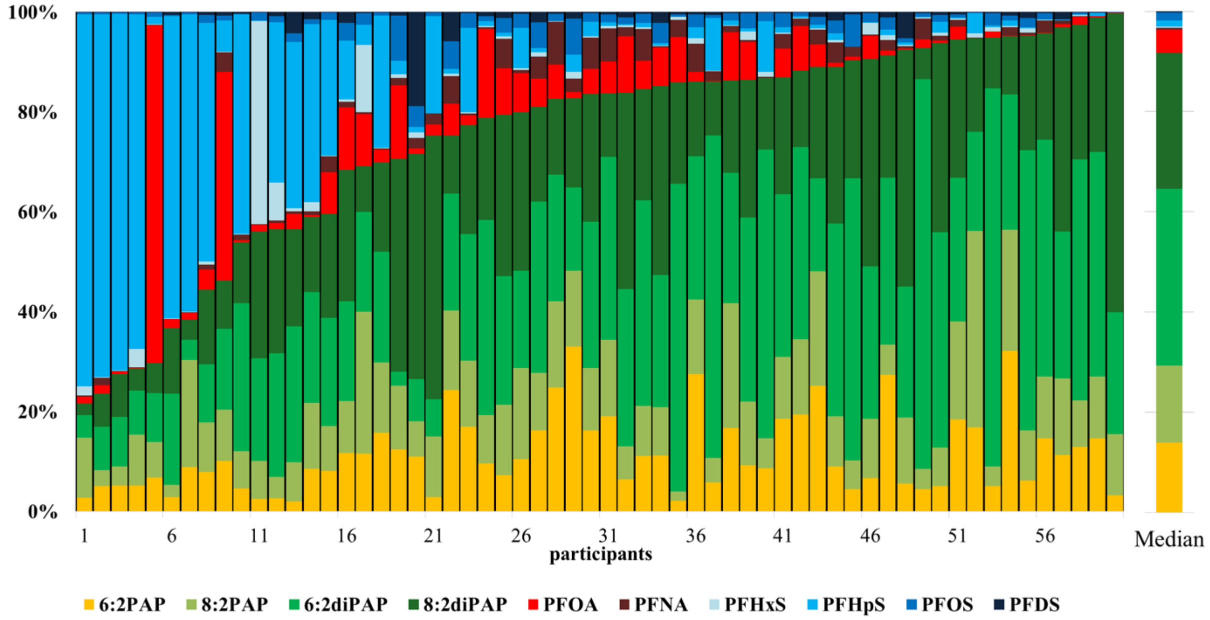

Figure 1. Individual and median relative profiles of PFASs with detection frequency above 45% in hand wipe samples (n=60).

Intra correlations between PFASs in hand wipes

Intra correlations between the different PFASs (with >80% detection frequency) were evaluated based on Spearman's rank correlation coefficients, and are presented in **Figure 2**. PAPs, PFOS, and PFOA were positive and significantly correlated with each other ($p<0.01$). Some were moderately correlated (r_s range: 0.39–0.70) while others were strongly correlated ($r_s>0.70$) with each other. Among PAPs, the highest correlations were observed between 6:2PAP and 8:2PAP ($r_s=0.84$) and between 6:2diPAP and 8:2diPAP ($r_s=0.80$), suggesting common sources of exposure. Moderate correlations were observed between PAPs and PFOA as well as PFOS (r_s range: 0.39–0.49). A significant correlation of 0.58 was also found between PFOS and PFOA, indicating common sources of exposure from the indoor environment for PAPs and perfluoroalkyl acids (PFAAs).

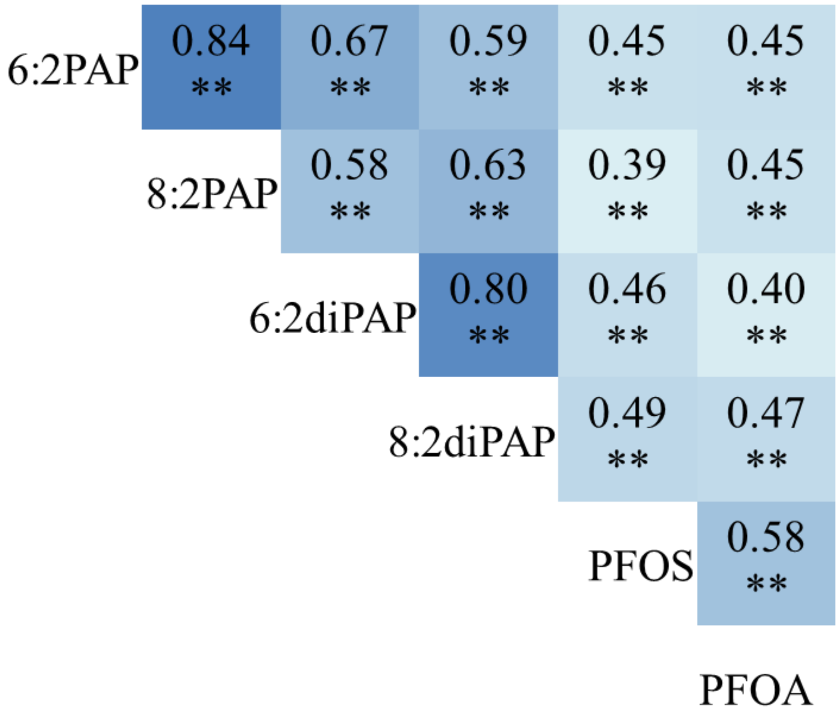

Figure 2. Correlation matrix (Spearman's rank) for PFAS concentrations in hand wipes (>80% detection frequency). ** Significant correlation (p<0.01).

Associations between PFASs in hand wipes and information from questionnaires

Information on hand washing was reported in the questionnaire by choosing one of the three categories; less than 4 times day^{-1}, 4–8 times day^{-1}, and more than 8 times day^{-1}. For the statistical analyses, the information on hand washing was collapsed into two categories; less than or 8 times day^{-1} (n=32, low-frequency hand washing) and more than 8 times day^{-1} (n=28, high frequency of hand washing). Differences in PFAS levels related to the frequency of hand washing were seen for PFOS, PFOA and 8:2diPAP, but only PFOS reached formal significance ($p<0.05$, Mann-Whitney test) (**Table 2**). The median concentration of PFOS in hand wipes was 36% higher in participants who washed their hands less than 8 times day^{-1}, compared to those who washed their hands more frequently. For PFOA and 8:2diPAP, 49% and 30% higher median PFOA and 8:2diPAP concentrations in hand wipes were observed for participants who washed their hands less than 8 times day^{-1} compared to more than 8 times day^{-1}, respectively.

Table 2. Characteristic of the study group and the median concentrations of PFASs with detection frequencies above 80% measured in the hand wipes (ng)

	n	6:2PAP	8:2PAP	6:2diPAP	8:2diPAP	PFOA	PFOS
Hand washing							
≤8 times day^{-1}	32	0.22	0.24	0.53	0.48	0.08	0.03
>8 times day^{-1}	28	0.21	0.23	0.55	0.35	0.05	0.02
% median difference [a]		5	3	3	30	49	**36** [b]
Age of participants							
<41 years old	30	0.18	0.29	0.37	0.27	0.05	0.02
≥41 years old	30	0.26	0.21	0.65	0.47	0.08	0.04
% median difference [a]		36	31	**56** [b]	**52** [b]	54	**56** [b]
Years of living in the house							
≤4 years	32	0.19	0.23	0.47	0.37	0.05	0.02
>4 years	28	0.25	0.23	0.58	0.42	0.08	0.04
% median difference [a]		24	1	22	14	55	**49** [b]

[a] *PFASs median difference in concentration of two categories in %, ((A-B)/((A+B)/2))*100,*
[b] *Statistical significant difference, p-value < 0.05, Mann-Whitney test*

Other relevant information from the questionnaire was assessed to identify factors that might be associated with PFASs in the hand wipes. Only the age of participants (<40 and >40, n = 30 each) and years of living in the house (<5 and ≥ 5, n=32 and 28, respectively) had an impact on the PFAS concentrations in hand wipes (**Table 2**). Increasing concentrations of PFASs in hand wipes were observed with increasing age of participants and with an increased number of years of living in the house. No significant differences were observed between gender (45 women and 15 men), the use of hand cream (34 used and 27 never used), and age of the building (≤36 years and >36 years, n =30 each).

Associations between PFASs in hand wipes versus house dust and indoor air

Correlations between amounts of PAPs, PFOA, and PFOS in hand wipes (ng per sample) and concentrations of PAPs, PFOA, and PFOS in three types of house dust samples (ng g^{-1}) were explored (reported in Papadoupoulou et al., manuscript).[31] As can be seen from **Table 3**, significant correlations between concentrations of PFAS in hand wipes and all types of dust were observed only for PFOS. The correlations were similar for floor dust (r_s = 0.27, p<0.05), elevated surface dust (r_s = 0.28, p<0.05), and vacuum cleaner bag dust (r_s = 0.25, p<0.05). Further, significant and positive correlations between 6:2diPAP in hand wipes and the corresponding concentrations in floor dust (r_s = 0.34, p<0.01) and elevated surface dust (r_s = 0.28, p<0.05) were found. The PFOA concentrations in hand wipes were significantly correlated with the corresponding concentrations only in elevated surface dust samples (r_s = 0.33, p<0.01). PFOS concentrations in hand wipes were also correlated to PFOA concentrations in the elevated surface dust (r_s = 0.30, p<0.05).

Further, PFOA concentrations in hand wipes were significantly correlated to 8:2PAP and 8:2diPAP in floor dust (r_s range: 0.26–0.32, p<0.05) and correlations between 6:2diPAP in hand wipes and 6:2PAP in floor dust (r_s = 0.28, p<0.05) were also observed. This may indicate that PFOA, 8:2PAP and 8:2diPAP in hand wipes and house dust come from the same source. Another possible explanation for the significant correlations between PFOA in hand wipes and 8:2PAP or 8:2diPAP in floor dust samples is that PFOA found in hand wipes may have come from environmental transformation or biotransformation of 8:2PAP and 8:2diPAP on the hands.

Table 3. Correlation coefficients (Spearman's rho) between PFAS amount measured in hand wipes (ng) and PFASs concentrations measured in house dust (ng g^{-1}) or indoor air (ng m^{-3}).

		Hand wipes					
		6:2PAP	8:2PAP	6:2diPAP	8:2diPAP	PFOA	PFOS
Floor dust	6:2PAP	0.14	0.04	**0.28***	0.10	0.21	0.04
	8:2PAP	0.17	0.10	0.20	0.14	**0.32***	0.19
	6:2diPAP	0.11	0.01	**0.34****	0.12	0.18	0.11
	8:2diPAP	0.06	0.001	0.17	0.12	**0.26***	0.16
	PFOA	0.01	-0.17	-0.06	-0.15	0.06	0.14
	PFOS	0.18	0.13	0.17	0.25	0.25	**0.27***
Elevated surface dust	6:2PAP	0.16	0.10	0.20	0.13	0.10	0.14
	8:2PAP	0.19	0.20	0.07	0.18	0.16	0.24
	6:2diPAP	0.13	0.09	**0.28***	0.15	0.03	0.16
	8:2diPAP	0.15	0.19	0.10	0.17	0.14	0.21
	PFOA	0.25	0.13	-0.02	0.05	**0.33****	**0.30***
	PFOS	0.10	0.06	0.16	0.20	0.08	**0.28***
Vacuum cleaner bag dust	6:2PAP	0.11	0.09	0.25	0.12	0.07	-0.07
	8:2PAP	0.10	0.09	0.16	0.17	0.15	0.05
	6:2diPAP	0.02	-0.04	0.18	0.04	0.05	-0.11
	8:2diPAP	0.15	0.12	0.24	0.24	0.23	0.03
	PFOA	0.13	-0.01	0.03	0.03	0.20	0.11
	PFOS	0.23	0.13	0.12	0.14	0.04	**0.25***
Indoor air	6:2FTOH	0.19	0.11	0.21	0.16	0.01	0.03
	8:2FTOH	0.23	0.13	0.18	0.13	0.12	0.13
	10:2FTOH	0.20	0.11	0.16	0.11	0.15	0.13
	MeFOSE	0.25	0.15	0.15	0.19	0.05	0.19
	EtFOSE	0.11	0.02	0.23	0.21	0.08	**0.33***

*The significance levels indicated are *(p<0.05) and ** (p<0.01). Detection frequencies of PFOS (PFOA) in floor dust, elevated surface dust, and vacuum cleaner bag dust were 62 (98), 65 (92), and 40 (74)%, respectively while PAPs were detectable >80% of all house dust samples. Detection frequencies of FTOHs, MeFOSE, and EtFOSE in indoor air were 100%, 70%, and 50%, respectively. Grey highlight; significant correlations between the concentration of corresponding PFASs in hand wipes and house dust or indoor air.*

Concentrations of FTOHs and FOSEs measured in indoor air samples (ng m^{-3}) from the living room of the participants in the present study have previously been reported.[19] In this present study, correlations between concentrations of PFAA precursors in indoor air and amounts of PFASs in hand wipes (ng per sample) were explored. Interestingly, a positive and significant correlation between PFOS in hand wipes and EtFOSE, a precursor to PFOS, in air samples (r_s = 0.33, $p<0.01$) was observed. One explanation for this may be that PFOS and EtFOSE are present in the same consumer products. Other likely possibilities are environmental transformation or biotransformation of EtFOSE to PFOS on the hands.

Participants with PFOS concentrations in house dust above the median showed a higher level of PFOS on their hand wipes than participants with PFOS concentrations in dust below the median. The PFOS concentrations in hand wipes were found to be in the range 39–50% higher in houses having elevated surface dust and vacuum cleaner bag dust concentrations above the median compared to the ones below the median (**Figure S1**). A similar pattern was found for PFOA and 6:2diPAP. The median PFOA concentration in hand wipes was 55% higher in participants that had PFOA concentrations in elevated surface dust from their house above the median. Also, the 6:2diPAP concentration in hand wipes was found to be significantly higher (43–45%) when the participant had 6:2diPAP concentrations in their floor dust and elevated surface dust above the median.

Exposure via hand-to-mouth contact and dermal absorption

One important factor when estimating individual intakes is the body weight of the exposed individual. In this study population, individual body weight information was collected (the median body weight was 69 kg). The PFAS concentrations in hand wipes and the reported individual body weight were used to estimate the PFAS exposure from hand-to-mouth and dermal contacts. Exposure to PFAAs and PFAA precursors via hand-to-mouth and dermal contacts can be seen in **Table S6** and **S7**, respectively. The contributions of direct and indirect exposure to perfluoroalkyl acids (PFAAs) showed that PFOA contributed most to the total PFAS exposure from hand-to-mouth and dermal contacts followed by PFOS > PFHpS > PFNA > PFHxS ≈ PFDS ≈ PFHxA > PFNA (**Figure 3**). The median of estimated individual daily intakes hand-to-mouth and dermal contacts were 0.83 and 0.50 pg·kg bw^{-1}·day^{-1} for PFOA, respectively. While the median estimated individual daily intake of PFOS via hand-to-mouth and dermal contacts were 0.32 and 0.19 pg·kg bw^{-1}·day^{-1}, respectively. These estimated individual daily intakes included both direct exposure to PFCAs, and indirect exposure from biotransformation of PFCA precursors. PAPs contributed to PFOA and PFNA intakes with approximately <1–80% and <1–77%, respectively (**Table S8**). PFCA precursors also contributed to indirect exposure to PFHxA and PFHpA. Hand-to-mouth behavior and dermal contacts also contributed to exposure to PFHxS and PFHpS, but only via direct exposure.

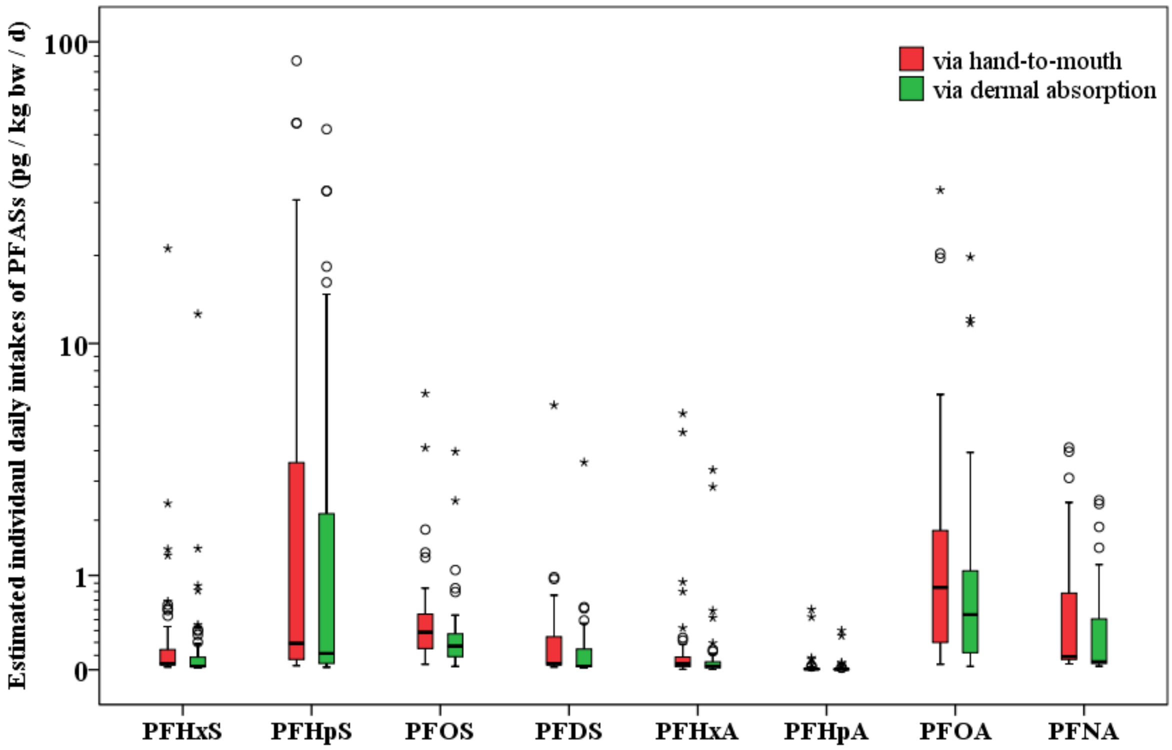

Figure 3. Estimated individual intakes of PFASs (log scale) for adults via hand-to-mouth and dermal contacts (pg·kg bw^{-1}·day^{-1}) (for hands only).

The estimated daily PFAS intakes via hand-to-mouth contact were higher than the estimated intakes from dermal absorption (both hands). However, several factors and assumptions are included in the estimations, and some of these are quite uncertain (e.g., the absorption factor). For adults, PFASs exposure may likely more frequency occur via dermal absorption than from hand-to-mouth contact. The variability in the amount of PFASs on human skin is unknown and may depend on how much of the body is covered by clothes, because clothes may limit the amount of PFASs settled on the skin but also some of them are PFAS sources by themselves.[32-33] Furthermore, as exposure has been calculated based on hand wipes collected at one time point, temporal variation such as variability between hours, days and seasons have not been taken into account. A complete assessment of dermal absorption exposure that includes the whole body results in a more considerable exposure than this hand wipe approach. However, the hand skin is likely the part of the body which is most contaminated from the indoor environment. Similar contamination and PFAS absorptions for the entire adult body (age ≥18 years old) was assumed. The median surface area is defined at 0.29 m^2 kg^{-1}, and the hand surface area is obtained from the average hand surface area of man and woman and was defined at 0.097 m^2 (USEPA Exposure Factors Handbook).[34] Thus, the median estimated daily intake via dermal absorption for the whole body would be approximately 11 pg·kg bw^{-1}·day^{-1} for PFOA (which 6% was the median indirect exposure of 8:2PAP and 8:2diPAP), and 3.6 pg·kg bw^{-1}·day^{-1} for PFOS. Currently, there are no data available on dermal absorption exposure to PFASs. However, these PFOA and PFOS intakes corresponded to less than 1% of the tolerable daily intake (TDI) derived by the European Food Safety Authority (EFSA) in 2008.[35]

It should be noted that many variables applied in the estimated daily intakes from hand-to-mouth and dermal contacts were based on PFOA studies, which adds to the uncertainty for the other PFASs explored.

Strengths and limitations

The major strength of this study is that hand wipes and samples from the indoor environment were collected at the same time from the same microenvironment (i.e., the participant's living room). One limitation of this study is that the temporal variability of PFAS concentrations on hands over time is unknown as only one hand wipe sample was analyzed per individual. Several interesting correlations were observed, but due to the limited statistical power, more and preferably larger studies are needed. This study demonstrated that PFASs deposited on the skin surface can be measured by collecting and analyzing hand wipes, however, this study only reflects intakes estimated through hands.

In conclusion, significant amounts of PFASs were found in hand wipes, and these were correlated to concentrations of PFASs in house dust and PFAS precursor in indoor air. Also, associations between PFAS concentrations in hand wipes and population characteristics and lifestyle were observed, e.g., age and gender, frequency of hand washing, and years of living in the house. To our knowledge, this is the first study to assess PFASs in hand wipes and estimating the human exposure to PFASs via hand-to-mouth and dermal contacts based on measured hand wipe concentrations. The findings of our study give some first indications that hand wipes can be used as a proxy for the exposure to PFASs from the indoor environments, but further studies to support this are required. Hand wipes may serve as an intermediate variable between the indoor environment and what is found in human body fluids, but this remains to be confirmed. Studies assessing the influence of hand-to-mouth and dermal contacts on the internal dose of PFASs are needed.

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Supporting Information Available

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