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Article

Human Exposure to Chlorinated Paraffins via Inhalation and Dust Ingestion in a Norwegian Cohort

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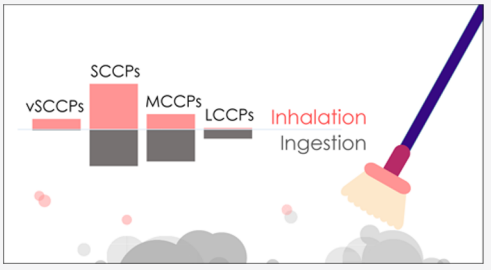
ABSTRACT: Very-short- (vSCCPs, C_{6-9}), short- (SCCPs, C_{10-13}), medium- (MCCPs, C_{14-17}), and long-chain chlorinated paraffins (LCCPs, $C_{>17}$) were analyzed in indoor air and dust collected from the living rooms and personal 24 h air of 61 adults from a Norwegian cohort. Relatively volatile CPs, i.e., vSCCPs and SCCPs, showed a greater tendency to partition from settled indoor dust to paired stationary indoor air from the same living rooms than MCCPs and LCCPs, with median logarithmic dust−air partition ratios of 1.3, 2.9, 4.1, and 5.4, respectively. Using the stationary indoor air and settled indoor dust concentrations, the combined median daily exposures to vSCCPs, SCCPs, MCCPs, and LCCPs were estimated to be 0.074, 2.7, 0.93, and 0.095 ng/kg bw/d, respectively. Inhalation was the predominant exposure pathway for vSCCPs (median 99%) and SCCPs (59%), while dust ingestion was the predominant exposure pathway for MCCPs (75%) and LCCPs (95%). The estimated inhalation exposure to total CPs was ∼ 5 times higher when the personal 24 h air results were used rather than the corresponding stationary indoor air results in 13 paired samples, indicating that exposure situations other than living rooms contributed significantly to the overall personal exposure. The 95th percentile exposure for CPs did not exceed the reference dose.



INTRODUCTION

The majority of people spend more than 20 h per day indoors,[1−5] which is further lengthened in the COVID-19 pandemic situation.[6,7] The indoor environment is thus particularly pertinent to near-field human exposure to semivolatile organic compounds (SVOCs) with significant indoor uses, e.g., as flame retardants and plasticizers.[8,9] Evaporation, abrasion, and direct transfer of SVOCs from consumer products can result in considerable contamination in indoor environment.[10,11] For example, concentrations of polybrominated diphenyl ethers (PBDEs) in indoor air have been found to be several orders of magnitude higher than in outdoor air.[12,13] Inhalation and ingestion of contaminated air and dust are two major exposure pathways for SVOCs,[14−17] leading to elevated body burden and potential adverse health effects[18,19] including immunosuppression,[20] diabetes,[21] and asthma.[22]

Inhalation and ingestion exposure to SVOCs are affected by partitioning behaviors of SVOCs between air and indoor dust[11] as well as their bioaccessibility.[23] For a comprehensive indoor exposure assessment of potential hazardous SVOCs, many studies have used concentrations of paired indoor air and dust collected from the same indoor spaces. Inhalation was found to contribute more to the exposure of relatively volatile SVOCs such as 2-bromoallyl 2,4,6-tribromophenyl ether (BATE)[24] and tri-*n*-butyl phosphate (TNBP),[25] while dust ingestion was found to be the main route of exposure to the less volatile SVOCs such as BDE-209,[10] hexabromocyclododecanes (HBCDs), and tetrabromobisphenol-A (TBBPA).[26] Exposure assessment using paired air and dust can be particularly important for chlorinated paraffins (CPs), which represent a large family of potential hazardous SVOCs with a wide range of volatilities.[27]

CPs are polychlorinated straight alkane chain mixtures (chemical formula: $C_nH_{2n+2-m}Cl_m$) with carbon chain lengths $n \geq 6$ and with variable numbers of substituted chlorines.[28] Their estimated log K_{OA} values range from 7[29] to higher than 15.[27] Currently, every year, ∼1 million metric tons of CPs are produced and used as flame retardants, lubricants, plasticizers, and fat liquors of leather.[30] They can be categorized on the basis of carbon-chain-length ranges as very-short-chain (vSCCPs, $C_{<10}$), short-chain (SCCPs, C_{10-13}), medium-chain (MCCPs, C_{14-17}), and long-chain mixtures (LCCPs, $C_{>17}$).[31]

Hazardous concerns about CPs have been raised since the 1980s,[32] but relevant research and hazard assessments were hindered by the complex compositions and extremely challenging analysis of CPs.[33] To date, only SCCPs have

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been listed for global bans by the UN Stockholm Convention on Persistent Organic Pollutants (POPs) in 2017.[34] With recent methodological achievements,[35] studies have shown that the other CP mixtures also exhibit POP characteristics or other hazardous properties. CPs, from vSCCPs to LCCPs, have been found to be persistent,[36,37] bioaccumulative in humans,[38,39] and shown to biomagnify in food chains.[40] SCCPs are legally classified as category 2 carcinogens according to Annex VI of the European Union (EU) Classification and Labeling (CLP) Regulation.[41] Although still limited, increasing research has begun to focus on the toxicity of the other CPs in recent years. Subacute exposure to a mixture of vSCCPs and SCCPs showed immunomodulatory effects in mice.[42] A cytotoxic study[43] reported significant metabolic perturbation of SCCPs, MCCPs, and LCCPs in HepG2 cell cultures. Compared to SCCPs and MCCPs, the LCCPs produced a stronger suppressive effect on amino acid transport across the cell membrane and caused a decrease in purine metabolism. These research findings highlight the need to characterize health risks associated with all CPs as one class of chemicals.

As for several other SVOCs, levels of CPs in the indoor environment were higher than in the outdoors[44] and varied with the types of buildings based on studies of both indoor and outdoor window films and air samples.[45,46] Concentrations of total CPs as high as mg/g have been reported for indoor dust from several countries worldwide (Table S1),[45,47−49] and CP concentrations exceeded those for the other flame retardants analyzed in the same dust samples.[47,50,51] Published data for CPs in indoor air (Table S1) are primarily only available for SCCPs and MCCPs, with only one reported study for vSCCPs,[29] and none for LCCPs. There is a lack of data for CP concentrations in paired indoor air and indoor dust from the same microenvironment, and partitioning behavior of CPs between air and indoor dust thus remains unclear. The lack of data on indoor concentrations of different CP groups in air and dust from the same microenvironments also hinders exposure assessments for these compounds, particularly for vSCCPs or LCCPs. In addition, large differences in air concentrations of CPs were found between apartments of the same building.[51] Therefore, the existing studies, which only extrapolated the human inhalation exposure from stationary air data, may not comprehensively reflect people's residential and occupational settings.[24,52]

Recently, we found complex mixtures of vSCCPs, SCCPs, MCCPs, and LCCPs in the hand wipes of a Norwegian cohort, which suggested significant near-field human exposure to these CPs.[53] We hypothesized that air inhalation is an important source of exposure to relatively volatile CPs and dust ingestion to CPs with low volatilities. Therefore, in the present study, vSCCPs, SCCPs, MCCPs, and LCCPs were analyzed in indoor air and dust in the same cohort, and exposures from inhalation and dust ingestion were assessed. The results from paired indoor stationary air and settled dust were used to determine partitioning coefficients. Personal air was also sampled simultaneously in a subsample of the participants, which enabled comparisons of CP levels in indoor stationary air in a room in the home with personal air for the first time.

MATERIALS AND METHODS

Sample Collection. The study cohort consisted of 61 adult participants from Oslo, Norway (45 women and 16 men, with ages of 20−66). Stationary air, settled dust, and floor dust samples were collected from the living room of households between November 2013 and April 2014. Personal air samples were collected from the participants residing in these homes, as well as air and dust field blanks. Approximately 17 m^3 stationary air was collected using a low-volume active air pump (Leland Legacy, SKC Inc., Eighty Four, PA) with four sampling trains in parallel, each containing two polyurethane foam (PUF) plugs and one glass fiber filter (GFF) run for 24 h. About 1.4 m^3 personal air was collected with a low-volume active air pump (SKC pump 224-PCMTX4, SKC Inc., Eighty Four, PA) with one sampling train containing two PUF plugs and a GFF run for 24 h. Thirteen personal air samples were available for this study, as the other personal air samples went to studies of other SVOCs elsewhere. Field blanks of the air samples were collected by installing the PUF plug and GFF on the sampler for a few seconds without turning on the pump. After the air sampling, dust samples were collected in the same living room area using a vacuum cleaner connected with a cellulose dust sampling filter (KTN AB, Bålsta, Sweden). Settled dust was collected from all elevated surfaces at least 0.5 m above the floor such as tables, bookshelves, and window sills, while floor dust was collected from the entire floor surface of the living room. Dust field blanks were collected by installing the filter on the vacuum cleaner without turning on the cleaner. Dust samples were not sieved but hair and food particles were removed using steel tweezers and a spatula.[54]

The air samples and the field blanks were wrapped in aluminum foil and stored in ziplock plastic bags. The dust samples and the field blanks were stored in amber glass containers. All of the samples were stored at −20 °C until analysis. Since CPs are chemically stable under general environmental conditions,[36,37] the storage strategies are considered to be able to minimize potential degradation of CPs. The participants also answered a questionnaire regarding their daily time spent indoors and the characteristics of their home, such as information on the number of pieces of electronic equipment and built year of homes. Detailed sampling procedures are described in Papadopoulou et al.[54] and also given in the Supporting Information (SI).

Analysis of CPs. CPs were analyzed in the settled indoor dust and stationary indoor air samples from all of the 61 homes, as well as in personal air from the 13 participants. In addition, CPs were analyzed in five floor dust samples chosen at random, the CP concentrations of which were then compared to those in paired settled dust from the same household. Ultrasonic extraction and multilayer SPE clean-up methods for all of the samples have been previously published[24,55] and are also described in the SI.

A total of 675 CP homologues (denoted as C_nCl_m, n = 6−48, $m \geq 2$) were measured using UPLC-APCI-Orbitrap-HRMS (Q Exactive, Thermo Fisher Scientific, San Jose) in full-scan mode (m/z 250−2000) with a resolution of 120 000 full width at half-maximum (FWHM). An ACQUITY UPLC BEH C18 column (1.7 μm, 2.1 × 50 mm^2, Waters, Manchester, U.K.) was maintained at 40 °C, the injection volume was 3 μL, and the flow rate was 0.4 mL/min. The mobile phases consisted of water (A) and methanol (B). The gradient elution started from 10% B for 0.5 min, ramped to 100% by 2.5 min, held for 2.5 min, ramped to 10% by 5.1 min, and finally held for 1 min. Dichloromethane (DCM) was introduced into the mobile phase at a flow rate of 0.028 mL/min between the UPLC column and the ion source using a syringe pump. The settings of the MS can be found in the SI.

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Environ. Sci. Technol. 2021, 55, 1145−1154

Table 1. Descriptive Statistics for CPs Measured in Settled Dust, Stationary Air, and Personal Air Samples[a]

CP category	vSCCPs	SCCPs	MCCPs	LCCPs	sumCP
Settled Dust Concentration (μg/g, n = 61)					
geometric mean	0.0085	6.7	22	8.5	40
median	0.0040	5.8	21	8.1	37
range	<0.0038-0.19	0.76−460	2.3−840	0.66−340	4.7−1400
chlorine content (% Cl)	61	58	54	47	53
DF (%)	56	100	100	100	100
Stationary Air Concentration (ng/m^3, n = 61)					
geometric mean	0.37	8.9	1.4	0.031	11
median	0.42	9.6	1.2	0.020	13
range	0.044−7.1	1.7−54	<0.35−13	<0.0063−1.1	2.0−61
chlorine content (% Cl)	60	55	48	45	52
DF (%)	100	100	95	79	100
Personal air concentration (ng/m^3, n = 13)					
geometric mean	2.2	38	6.7	0.58	50
median	2.1	33	4.5	0.58	50
range	0.37−11	8.3−97	<1.8−59	<0.087−4.1	10−170
chlorine content (% Cl)	59	54	48	43	52
DF (%)	100	100	92	85	100

[a]The sum of CPs (sumCPs) were calculated from individual results. The detection frequency (DF) is the percentage of samples with a mass above the MDLs; chlorine content: w/w, geometric mean.

Quantification of vSCCPs, SCCPs, MCCPs, and LCCPs was made on the basis of a C_nCl_m-profile reconstruction method[56] and has been introduced in detail in Du et al.[40] CP profile of each sample was reconstructed by linearly superimposing the profiles of several CP reference standards. Four single-chain-length and 19 mixed-chain-length CP standards and commercial mixtures were used for quantification (Tables S2 and S3).

QA/QC. The resolution of MS was sufficient to resolve C_nCl_m from the mass interference of C_nCl_{m+1}[57] and chlorinated alkenes.[58] The performance of quantification was evaluated with the goodness-of-fit R^2 between the measured C_nCl_m profile and the linearly superimposed one. The single-chain-length standards were used to improve the performance of profile reconstruction[59,60] and the comparability of CP concentrations with different instrumental setups and quantification methods.[61] Quantification of S/M/LCCPs of all samples fulfilled the criterion of $R^2 \geq 0.50$ (Table S2),[56] which suggested a mean deviation of concentration less than 40%.[53] The results with $R^2 < 0.5$ were reported as tentative values.[48] For quantification of vSCCPs, the R^2 ranged from 0.16 to 0.99 (median: 0.72; Table S3). The mean recoveries (±SD) of ^{13}C-labeled CP internal standard ($^{13}C_{10}$-1,5,5,6,6,10-hexachlorodecane) in the dust, stationary air, and personal air samples were 83 ± 24, 85 ± 29, and 88 ± 14%, respectively.

The sampling trains were precleaned ultrasonically in methanol and water (30:70, v/v) and air-dried, PUF plugs by Soxhlet extraction for 24 h in DCM and 24 h in acetone and GFFs by heat-cleaning in a furnace at 450 °C for 24 h before use. Field blanks were collected together with the dust, stationary air, and personal air samples (SI). Method detection limits (MDLs) and method quantification limits (MQLs) were calculated based on previous studies on SVOCs in air and dust samples.[24,62,63] The MDLs and MQLs were defined as mean field blank values plus 3 and 5 times the standard deviation (SD), respectively. The MDLs and the MQLs for the vS/S/M/LCCPs in the different sample matrices are given in Table S4.

Statistical Analysis. CP concentrations below the MDL were replaced with MDL/$\sqrt{2}$, and those above the MDL but below MQL were replaced with MQL/$\sqrt{2}$. Since the distributions of CPs in dust and air samples were highly skewed, the Mann−Whitney U and Kruskal−Wallis tests were used to explore differences between CP concentrations in all of the matrices (with >75% detection frequency) and categorical indoor environment variables. Spearman's rank correlation was used to calculate correlations between CP categories and different sample types. The level of significance was set at α = 0.05 for all of the statistical analyses.

Inhalation and Dust Ingestion Exposure Calculation. The calculation of daily intake [ng/kg body weight (bw)/d] was performed individually for each participant according to eqs 1 and 2 from the U.S. EPA Exposure Factors Handbook[64]

$$\text{inhalation exposure} = \frac{C_{air} \times IR \times ED \times AF_{inhalation}}{BW} \quad (1)$$

$$\text{dust ingestion exposure} = \frac{C_{dust} \times DI \times AF_{ingestion}}{BW} \quad (2)$$

where C_{air} and C_{dust} are the concentrations of CPs in air (ng/m^3) and dust (ng/g), respectively. IR is the inhalation rate (m^3/day), which was assigned on the basis of body weight (BW, range: 52−125 kg), gender, and age of each participant (Table S5) according to the U.S. EPA Exposure Factors Handbook.[64] In this study, the assigned IRs ranged from 11.93 to 20.39 m^3/day. ED is the exposure duration as a time fraction of the 24 h. Using stationary air, the ED is calculated based on average hours spent indoors per day (range: 18−23.8 h) as assessed by questionnaires, which ranges from 0.75 to 0.99. Using personal air, the ED is 24/24 h = 1. $AF_{inhalation}$ and $AF_{ingestion}$ are the absorption fraction of inhalation (assumed to be 100% bioavailable) and ingestion (Table S6), respectively. $AF_{ingestion}$ values were estimated to be 33, 21, 7.9, and 3% bioavailable for vSCCPs, SCCPs, MCCPs, and LCCPs, respectively. DI is the mean daily dust intake (30 mg/d for adults[64]).

Dust−Air Partition Ratios ($K_{dust-air}$). $K_{dust-air}$ (m^3/g) of vSCCPs, SCCPs, MCCPs, and LCCPs were calculated according to eq 3[65,66]

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Environ. Sci. Technol. 2021, 55, 1145−1154

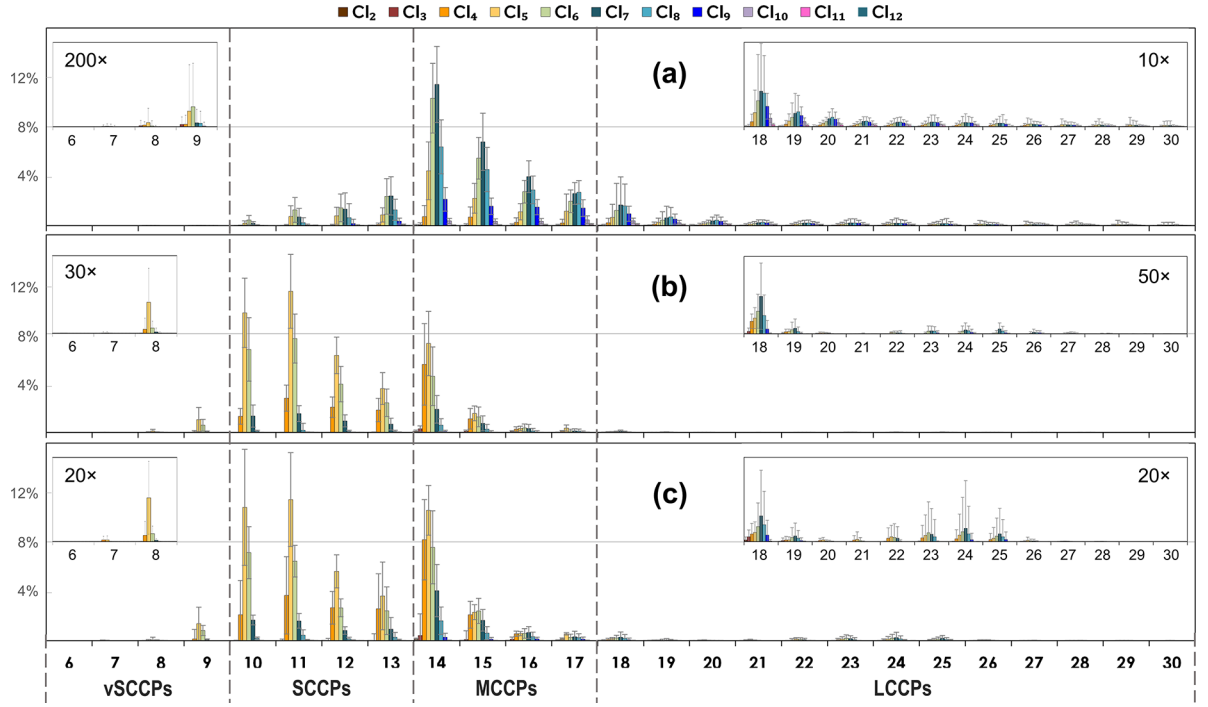

Figure 1. Mean relative abundance of CP homologues with standard deviation error bars for (a) settled dust, (b) stationary air, and (c) personal air samples of the Norwegian cohort. The horizontal axes represent carbon chain lengths. Homologue compositions from C_{31} to C_{48} are given in Figure S1.

$$K_{\text{dust-air}} = \frac{C_{\text{dust}}}{C_{\text{air}}} \quad (3)$$

where C_{air} and C_{dust} are in units of ng/m^3 and ng/g, respectively.

RESULTS AND DISCUSSION

Settled Indoor Dust. SCCPs, MCCPs, and LCCPs were detected in all of the 61 settled indoor dust samples, while concentrations of vSCCPs were above the MDL in only 56% of the samples (Table 1). C_7 to C_{44} CPs were found in the settled dust samples (Figures 1 and S1), with total CP concentrations ranging from 4.7 to 1400 μg/g dust. Mean percentage compositions of vSCCPs, SCCPs, MCCPs, and LCCPs were 0.052, 19, 56, and 25%, respectively. Concentrations of SCCPs, MCCPs, and LCCPs in house dust from international studies are summarized in Table S1 for comparison. This is the first study that has included vSCCP concentrations, so there is no data to compare with. The median concentration of SCCPs (5.8 μg/g) found in the current study was comparable to those in house dust samples from 13 cities in Canada (6.2 μg/g)[67] and Munich, Germany (6.0 μg/g),[49] and lower than from Beijing, China (98.7 μg/g),[45] and Pretoria, South Africa (16 μg/g).[48] The median concentration of MCCPs (21 μg/g) in the present study was comparable with those from the 13 Canadian cities (19 μg/g)[67] and lower than from Beijing (89.8 μg/g),[45] Munich (176 μg/g),[49] and Pretoria, South Africa (46 μg/g).[48] The median concentration of LCCPs (8.1 μg/g) was lower than from Pretoria, South Africa (11 μg/g).[48]

Several other flame retardants were reported previously in the same settled indoor dust samples (Table S7). The median total CP concentration (37 μg/g) was higher than for PBDEs (1.2 μg/g), HBCDs (0.19 μg/g), emerging brominated flame retardants (EBFRs) (0.73 μg/g),[24] and organophosphorus flame retardants (OPFRs) (33.1 μg/g).[68] Similarly, CPs were found to be the most abundant flame retardants in the hand wipes of the same cohort.[53]

Floor Dust. Concentrations and chlorine contents of CPs in the five paired floor dust and settled dust samples from the same households are shown in Table S8. The median total CP concentration in the five floor dust samples was 51 μg/g, which was slightly higher compared to the paired settled dust samples (median: 49 μg/g), but the differences were not significant ($p > 0.05$). The chlorine contents of CPs in the floor dust samples were ∼1% Cl higher than those in the settled dust samples, but this was not statistically significant ($p > 0.05$). It should be noted that only five paired samples were analyzed, and thus, the statistical power may not be high enough to detect significant differences. The homologue profiles in floor dust samples were highly comparable with those in the paired settled dust samples, with a median $R^2 = 0.96$ (range: 0.83−0.97).

Figure 2 shows the CP profile for paired settled and floor dust samples from the household where these had the highest difference between the two ($R^2 = 0.83$). The floor dust sample was predominated by more highly chlorinated homologues of CPs (i.e., C_nCl_{n-2} to C_nCl_{n+2}). The homologue profiles also showed that the content of highly chlorinated homologues in the floor dust is much more abundant than in the paired settled dust (Figure 2b). In a previous study on Swedish coastal sediment cores, highly chlorinated SCCPs were found in a section representing the year 1942 collected nearby a steel factory,[37] while the dust result is the first observation of highly chlorinated MCCPs and LCCPs in the environment. The highly chlorinated homologues were only found in the dust samples from 1 of the 61 households, suggesting that the source for these may not be as common as for the moderately chlorinated homologues.

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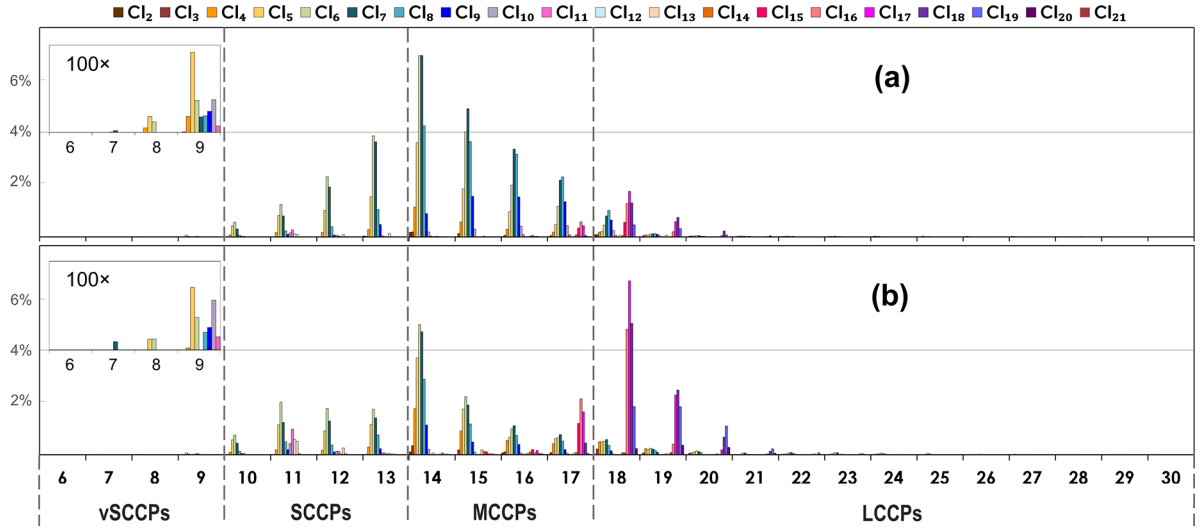

Figure 2. Relative abundance of CP homologues for (a) one paired settled dust and (b) floor dust sample from the living room of the same household of the Norwegian cohort. The horizontal axes represent carbon chain lengths.

Stationary Indoor Air. vSCCPs and SCCPs were detected in all 61 samples. Concentrations of MCCPs and LCCPs were above the MDLs in 95 and 79% of the stationary air samples, respectively (Table 1). Carbon chain lengths of CPs in the stationary air ranged from C_6 to C_{34} (Figures 1 and S1). The vSCCPs, SCCPs, MCCPs, and LCCPs contributed on average 4.1, 82, 14, and 0.58%, respectively, to the total concentrations of CPs (median: 12.6 ng/m^3). The median was higher than reported for PBDEs (0.018 ng/m^3), HBCDs (0.0004 ng/m^3), and EBFRs (0.22 ng/m^3),[24] but lower than OPFRs (163 ng/m^3)[68] in the stationary air samples from the same cohort.

Concentrations of CPs in indoor air worldwide are summarized in Table S1, and most results available were from China. The mean concentration of vSCCPs in the current study (0.37 ng/m^3) was lower than that found in indoor air from Beijing, China (C_9 CPs only, 47.4 ng/m^3).[29] The mean SCCP concentration (8.9 ng/m^3) was lower than that found in China (range of means: 13.4−368 ng/m^3).[29,45,63] Means of MCCPs (1.4 ng/m^3) were lower than reported MCCPs (range of means: 3.36 and 30.9 ng/m^3) in China.[45,63] There is a lack of data for LCCP concentrations in indoor air, and thus, no comparison was made.

Personal Air. The detection frequencies (DFs) of vSCCPs, SCCPs, MCCPs, and LCCPs were 100%, 100, 92, and 85%, respectively (Table 1), with carbon chain lengths ranging from C_6 to C_{32} (Figures 1 and S1). Relative to the stationary air, the personal air contained slightly higher proportions of C_{14} and C_{23-25} CPs. The vSCCPs, SCCPs, MCCPs, and LCCPs contributed on average 5.0, 78, 15, and 2.3%, respectively, to the total concentrations of CPs. The median total CP concentration in the current study (50 ng/m^3) was higher than reported for PBDEs (0.096 ng/m^3), HBCDs (0.03 ng/m^3), EBFRs (0.41 ng/m^3),[24] and OPFRs (44 ng/m^3)[68] in personal air samples from the same cohort. This indicates that exposure occurs not only in households but also in other microenvironments that the participants were present during the day such as offices.

The concentrations of vSCCPs, SCCPs, MCCPs, and LCCPs were significantly higher in personal air (medians of 2.1, 33, 4.5, and 0.58 ng/m^3, respectively) compared to those in the corresponding stationary air samples (medians of 0.46, 11, 2.0, and 0.020 ng/m^3, respectively) (Wilcoxon signed rank test, $p < 0.05$). This agrees with Barber et al., who found 1−2 orders of magnitude higher levels of SCCPs and MCCPs in the stationary air of a workshop, lab, and office than in a household in the United Kingdom (Table S1).[46] Significantly higher concentrations of BDE-209 and DBE-DBCH were also found in personal air than in stationary air from the same cohort in previous studies (Table S7), which could be due to the "personal cloud effect".[24,52] The SVOCs, especially those with large K_{OA} values, tend to partition to particles and can be resuspended to a higher degree by human activities.[52,69] This may also contribute to higher concentrations of SVOCs, including CPs, near the body and in particular near the breathing zone.

CP Partitioning between Stationary Air and Settled Dust. CP homologues with shorter-chain lengths and less substituted chlorines have higher volatilities.[70] This can be seen in Figure 1, where the stationary and personal air samples have higher abundances of shorter-chain, lower chlorinated CPs (Figure 1b,c) than the dust samples (Figure 1a). The percentage compositions of vSCCPs and SCCPs in the air samples (on average 4.1 and 82%, respectively) were both significantly higher than in the corresponding settled dust samples (which were, on average, 0.052 and 19%, respectively), while in the case of MCCPs and LCCPs, the trend was the reverse (related-sample Wilcoxon signed rank test, $p < 0.05$). The chlorine contents of CPs were 1−6% lower in the stationary air samples than in the settled dust samples (Table 1), which is equivalent to 1−2 less chlorines on the carbon chain (Figure 1).

The $\log K_{dust-air}$ values increased with the chain length ranges and the modeled K_{OA} values, the medians of which were 1.3, 2.9, 4.1, and 5.4 for vSCCPs, SCCPs, MCCPs, and LCCPs, respectively (Table 2). The $\log K_{dust-air}$ values of several other halogenated SVOCs were calculated by Wei et al.[71] and are summarized in Table 2. Compared with PCBs, the $\log K_{dust-air}$ of vSCCPs was similar to the relatively volatile SVOCs such as PCB-52 (median: 1.33), while SCCPs were similar to less volatile SVOCs such as PCB-153 (median: 2.89). The $\log K_{dust-air}$ values of MCCPs and LCCPs were comparable to those of the SVOCs with low volatilities, such as

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Environ. Sci. Technol. 2021, 55, 1145−1154

Table 2. Dust−Air Partition Ratios (log $K_{dust-air}$) of CPs and Other Halogenated SVOCs

		log $K_{dust-air}$	
chemical	log K_{OA}	median	interquartile range
vSCCPs	7.24[29]	1.3	1.1−1.8
SCCPs	9−11[27]	2.9	2.5−3.3
MCCPs	11−15[27]	4.1	3.9−4.5
LCCPs		5.4	5.1−5.8
α-HCH	7.61[72]	0.36	−0.50−0.62
γ-HCH	7.85[72]	0.81	0.63−1.08
PCB-31	7.92[73]	0.82	0.82−0.91
PCB-52	8.22[73]	1.33	1.10−1.53
PCB-101	8.80[73]	2.06	1.81−2.25
PCB-138	9.51[73]	2.76	2.28−3.23
PCB-153	9.37[73]	2.89	2.31−3.28
PCB-180	9.88[73]	3.65	2.86−4.02
BDE-28	9.11[74]	2.38	2.17−2.51
BDE-47	10.23[74]	3.30	2.94−3.41
BDE-99	11.27[74]	4.26	3.80−4.44
BDE-153	12.36[74]	5.10	4.80−5.70
BDE-209	16.54[74]	11.34	9.75−11.42

Table 3. Estimated Daily Exposure to CPs via Dust Ingestion and Air Inhalation for Adults[a]

CP category	vSCCPs	SCCPs	MCCPs	LCCPs	sumCP
Estimated Dust Ingestion Exposure for Adults (ng/kg bw/d, n = 61)					
5P	n/a	0.19	0.15	0.015	1.1
median	0.00069	1.1	0.70	0.090	5.7
95P	0.012	7.9	4.1	0.60	40
Estimated Air Inhalation Exposure for Adults (ng/kg bw/d, stationary air, n = 61)					
5P	0.0094	0.36	0.075	n/a	0.43
median	0.073	1.6	0.23	0.0046	2.0
95P	0.41	6.8	1.1	0.078	7.6
Estimated Air Inhalation Exposure for Adults (ng/kg bw/d, personal air, n = 13)					
5P	0.090	2.4	n/a	n/a	3.3
median	0.46	8.8	1.1	0.12	13
95P	2.2	21	7.2	0.65	30
Reference dose (ng/kg bw/d)					
RfD	n/a	2300	6000	71000	n/a

[a]RfD values for SCCPs, MCCPs, and LCCPs were calculated by dividing respective LOEL values (2.3,[77] 6, and 71[78] mg/kg bw/d) by a safety factor of 1000.

BDE-99 (median: 4.26) and BDE-153 (median: 5.10), respectively. Dust is a convenient medium that can be readily sampled and analyzed.[65] With CP concentrations in dust, the $K_{dust-air}$ values measured in the present study can be applied in indirect air-quality monitoring of CPs, especially for the time being when there are scarce experimental K_{OA} values of CPs.

CP profiles in the air samples are a reflection of the sources (e.g., dust). Three paired dust and air samples of the cohort are shown in Figure S2 as examples. When C_{14} CPs were much more abundant than C_{13} CPs in the dust samples, C_{14} CPs were more abundant than C_{13} CPs in the paired air samples (Figure S2b,c). Similarly, when a dust sample contained abundant C_{24} and C_{25} CPs, the least volatile CPs, C_{24-25} CPs were still detectable in the air sample (Figure S2c). Thus, CP profiles in the air seem to be significantly driven by the volatility of CP homologues. To explore this, log $K_{dust-air}$ were tentatively calculated for CP homologues with DFs higher than 50% in both matrices on the basis of the relative instrumental responses (Table S9). The values ranged from 0.46 to 6.1 for homologues from C_9Cl_5 to $C_{25}Cl_7$ and generally increased with the carbon chain length and chlorine numbers. Driven by the large volatility difference, C_{10}−C_{12} CPs were the most abundant CPs in the air samples even when MCCPs and LCCPs were much more abundant than SCCPs in the dust samples (Figure S2).

Estimation of Daily Intakes from Inhalation and Dust Ingestion. The partitioning tendencies of vSCCPs, SCCPs, MCCPs, and LCCPs in indoor air and dust led to different exposures from inhalation and dust ingestion for different CP groups. In this study (Table 3), median human exposure to vSCCPs via inhalation of stationary air (0.073 ng/kg bw/d) was over 100 times higher than via ingestion of settled dust (0.00069 ng/kg bw/d). Inhalation exposure to SCCPs (1.6 ng/kg bw/d) was similar to the dust ingestion exposure (1.1 ng/kg bw/d). For MCCPs and LCCPs, dust ingestion exposures (0.70 and 0.090 ng/kg bw/d, respectively) were ∼3 and ∼20 times higher than inhalation exposures (0.23 and 0.0046 ng/kg bw/d, respectively). A limitation of the exposure estimation was that the influence of particle size of samples was not considered. Particle size distribution was reported for several SVOCs,[75,76] and those bound to small inhaled particles (<10 μm) could affect inhalation exposure assessment.

Bioavailability of CPs also affects the daily exposure estimation. However, only bioaccessibility data were available for CPs via dust ingestion and thus these were used as the AFs via dust ingestion (eq 2). Du et al. evaluated bioaccessibility of indoor dust-borne SCCPs and MCCPs using an in vitro Tenax bead-assisted sorptive physiologically based method. A rapid decreasing trend in bioaccessibility of CP homologues was found with increasing carbon chain length.[79] Similarly, the bioaccessibility of phthalate ester (PEs) through lung fluid decreased with longer-chain PEs, which was primarily governed by their hydrophobicity and water solubility.[80] As a result, although LCCPs (mean 25% of the total CPs) were generally more abundant than SCCPs (mean: 19%) in the dust samples, human exposure to SCCPs via dust ingestion was the highest in the cohort, followed by MCCPs and LCCPs due to the higher estimated bioaccessibility of SCCPs.

It should be noted that exposure assessment using bioaccessibility data may not be completely accurate, given that the actual bioavailability of CPs could be lower. Therefore, it is necessary to improve models for bioavailability prediction. However, the measured bioaccessibilities of SCCPs (21.1%) and MCCPs (7.9%)[79] were both lower than the bioavailability data of the other flame retardants (25−94%) within the similar range of log K_{OW} (Table S6). Due to the lack of bioavailability data, using the measured bioaccessibility data leads to less overestimation in exposure assessment relative to using the bioavailability data of the other flame retardants. For consistency with most other SVOCs,[24] we assumed 100% absorption of air inhalation intake. Whether these assumed/estimated AFs provide realistic exposure estimates requires further validation, such as comparisons with the internal exposure results.

The comparisons between floor and settled dust indicate that the estimation of ingestion intake of CPs based on the floor dust or settled dust concentrations could be generally comparable in this cohort study. Since adults are less likely to ingest floor dust compared to toddlers, only settled dust was

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Environ. Sci. Technol. 2021, 55, 1145−1154

considered in the exposure assessment for the participants in this study.

Estimation of daily inhalation exposure to CPs using personal air showed ∼5 times higher intakes than when using the stationary air from the same participants' living rooms (Table S10). This is mainly due to higher levels of CPs in the personal air compared to those in the stationary indoor air. When estimating inhalation exposure to CPs using stationary house indoor air, the occupational exposure of participants is not taken into account. However, the participants spent 8−11 h at work during the sampling period. Moreover, any nonhouse exposure was also not included and was estimated to be 10% of exposure. In addition, when staying at home, the participants spent time not only in the living room where the sampler was placed but also in the bedroom. Therefore, using stationary air data exclusively might contribute significant bias in the assessment of inhalation exposure to CPs.

Estimation of CP inhalation and ingestion exposures has been mostly made in China, which is the largest producer and user worldwide (Table S11). The inhalation and dust ingestion exposures of the Norwegian cohort were lower than estimated for the Chinese citizens.[45,63] The risk of inhalation and dust ingestion exposure of the Norwegian cohort was estimated by comparing the estimated exposure values to the oral reference doses (RfDs) (Table 3). The results showed that even the 95th percentile daily exposure to CPs is still at least ∼ 100 folds below the RfDs.

Correlations between CP Categories in the Samples. Moderately positive but statistically significant correlations (range of r = 0.39−0.55) were found between concentrations of vSCCPs and the other three CP categories in the settled indoor dust samples (Table S12), suggesting that vSCCPs were impurities/byproducts of the commercial CP mixtures containing SCCPs, MCCPs, and LCCPs.[31] High correlations (r = 0.91) were found between concentrations of SCCPs and MCCPs in the settled indoor dust, which may indicate SCCP impurities in MCCP products. The carbon chain distribution of SCCPs, with C_{13} CPs as the predominant SCCP group (Figure 1a), also supported this indication. High correlations (r = 0.81) were found between LCCPs and MCCPs in settled indoor dust samples, with a decreasing trend in the abundance of CP homologues with increasing chain length from C_{17} (the longest chain length of MCCPs), indicating that some MCCP mixtures used in products found indoors might contain LCCP components.

Moderately positive statistically significant correlations were found between paired stationary indoor air and settled indoor dust samples for vSCCPs (r = 0.30) and SCCPs (r = 0.16), while low correlations were found for MCCPs (r = 0.04). Similar correlations were found for relatively volatile compounds such as BDE-47 and DBE-DBCH in the same paired air and dust samples in a previous study.[24] Closer correlations (i.e., higher r value) were found for more volatile analytes, which may be explained by the partitioning behaviors of SVOCs between air and indoor dust, which means they have probably reached equilibrium within the indoor environment. For example, BDE-47 has a log $K_{dust-air}$ value (median: 2.94) similar to SCCPs (median: 2.9; Table 2).

No significant correlations were found between matched personal air and stationary indoor air samples, which is similar to results for the other halogenated SVOCs previously investigated in the same cohort project.[24] Additionally, we had a limited number of paired samples (n = 13) that may not be enough to detect significant differences.

Factors Influencing CP Concentrations in Settled Dust and Air. The highest concentrations of CPs were found in the settled indoor dust from the houses/apartments built between 1978 and 2002 (Kruskal−Wallis test, $p < 0.05$; Table S13). A similar trend was found in a dated Baltic Sea sediment core collected from the neighboring country of Sweden, where the highest concentrations of CPs were found in the sediment sections representing the 1990s.[37] This may reflect the trend of CP use in building materials. Norway banned the sale and use of SCCPs in consumer products from 2002.[81] This was mirrored by SCCP concentrations in the settled dust, where the lowest median levels were found in the houses/apartments built after the ban of SCCPs (Table S13).

A statistically significant difference was also found between the levels of LCCPs in the stationary indoor air samples and different heating methods of the houses/apartments (Kruskal−Wallis test, $p < 0.05$; Table S13). The living rooms with central heating showed lower levels of LCCPs in the stationary indoor air than those using electric or stove/fireplace heating methods (Mann−Whitney U test, $p < 0.05$). A significant negative correlation was observed between the levels of LCCPs in the stationary indoor air and vacuum cleaning frequency (times per month) (Kruskal−Wallis test, $p < 0.05$; Table S13). No significant correlation was found between the levels of CPs in the stationary indoor air and the size of the living room.

For participants whose personal air samples were analyzed in this study, the median times spent at home, at work, and in transportation were 14, 8, and 0.5 h, respectively. No statistically significant differences in CP concentrations were found by working hours or by hours spent at home/bedroom (Table S13), which could be due to participants having similar work/residence time durations. Statistically significantly higher levels of LCCPs were observed in the personal air samples from participants who spent longer than half an hour in transportation every day (Mann−Whitney U test, $p < 0.05$; Table S13). A statistically significant difference was also found between the levels of SCCPs and MCCPs in the personal air and different sofa materials (Kruskal−Wallis test, $p < 0.05$; Table S13). Specifically, participants who own a sofa made of synthetic material showed higher levels of CPs in the personal air than those owning wool or cotton sofas (Mann−Whitney U test, $p < 0.05$). However, caution should be used in interpreting these correlations given the small sample sizes in each comparison group.

The exposure route could affect the rates of metabolism and therefore the potential toxicity[82] of different CP categories. This study revealed different contributions of air inhalation and dust ingestion in human exposure to CPs with varying volatilities. The partitioning coefficients of CPs improved our understanding of this ubiquitous complex mixture. The elevated inhalation exposure to CPs using personal air results suggests that exposure situations other than living rooms contributed significantly to the overall personal exposure. Personal air is likely to be more representative for assessing human exposure to CPs than stationary air. However, the personal sampling is expensive and time-consuming and could be an intrusion into the participant's normal daily life. To compare the air sampling approaches, the internal exposure data from the same cohort should be evaluated.

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Environ. Sci. Technol. 2021, 55, 1145−1154

■ ASSOCIATED CONTENT

Supporting Information

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Sample collection and ethical permission; sample pretreatment; instrumental analysis; C_{31-48} homologue profiles (Figure S1); CP profiles of three samples (Figure S2); worldwide CP results (Table S1); profile reconstruction results (Tables S2 and S3); MDLs and MQLs (Table S4); inhalation rates (Table S5); AFs (Table S6); previous A-TEAM results (Table S7); floor versus settled dust (Table S8), log $K_{dust-air}$ values (Table S9); inhalation exposure estimation comparisons (Table S10); human exposure data comparison (Table S11); and statistical analyses (Tables S12 and S13) (PDF)

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Notes

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