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Exposure to organophosphate and polybrominated diphenyl ether flame retardants via indoor dust and childhood asthma

Abstract Although the ubiquitous detection of polybrominated diphenyl ether (PBDE) and organophosphate flame retardants (PFRs) in indoor dust has raised health concerns, only very few epidemiological studies have assessed their impact on human health. Inhalation of dust is one of the exposure routes of FRs, especially in children and can be hazardous for the respiratory health. Moreover, PFRs are structurally similar to organophosphate pesticides, which have been associated with allergic asthma. Thus, we investigated whether the concentrations of PFRs and PBDEs in indoor dust are associated with the development of childhood asthma. We selected 110 children who developed asthma at 4 or at 8 years old and 110 matched controls from a large prospective birth cohort (BAMSE – Barn, Allergy, Milieu Stockholm Epidemiology). We analyzed the concentrations of 7 PFRs and 21 PBDEs in dust collected around 2 months after birth from the mother's mattress. The abundance rank in dust was as follows: TBOEP≫TPHP>mmp-TMPP>EHDPHP~TDCIPP>TCEP ~TCIPP~BDE-209≫BDE-99>BDE-47>BDE-153>BDE-183>BDE-100. There was no positive association between the FRs in mattress dust and the development of childhood asthma. In contrast, dust collected from mattresses of the mothers of children who would develop asthma contained significant lower levels of TPHP and mmp-TMPP. This study provides data on a wide range of PFRs and PBDEs in dust samples and development of asthma in children.

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Practical Implications

Although many studies have raised health concerns about exposure to PFR and PBDE flame retardants via indoor dust only a very limited number of studies have investigated health effects. This is one of the few studies to investigate a relationship between the concentration of FRs in dust and development of (childhood) asthma. In this nested case–control study with 110 asthmatic children no association was observed between the development of childhood asthma and higher concentrations of PFRs or PBDEs in mother's mattress dust. However this study provides data about the concentrations of the most environmentally abundant PFRs and PBDEs in 220 mattress dust samples. Mattress dust has been scarcely studied until now but can be an important source for indoor exposure to FRs.

Introduction

Many studies have tried to find explanations for the increase in the incidence of asthma since the 1960s (Devereux, 2006; Ding et al., 2014). Indoor pollution has been recognized as a risk factor for the development of asthma (Hulin et al., 2012). Exposure to indoor pollutants has changed tremendously since the 1950s, both in kind as in concentrations (Weschler, 2009). Flame retardants have become widespread environmental pollutants. Its use has increased greatly since the 1960s to meet fire safety legislation to delay flammability of consumer goods. Penta- and octa-polybrominated diphenylethers (PBDEs) were precautionarily banned by the European Union in 2004, as they raised health concerns because of their persistence and bio-accumulation in both animals and humans (Ali et al., 2012; Frederiksen et al., 2009; van der Veen and de Boer, 2012). The global use of organophosphate flame retardants (PFRs) is rapidly increasing as these compounds are often proposed as alternatives for the banned PBDEs (Dodson et al., 2012; Marklund et al., 2005). Remarkably, few epidemiology studies have investigated the health effects of exposure to PBDEs and PFRs (Alcock and Busby, 2006; Araki et al., 2014; Harley et al., 2010; Meeker and Stapleton, 2010; Meeker et al., 2013; van der Veen and de Boer, 2012).

Flame retardants are frequently present as additives rather than chemically bound to diverse materials resulting in an easy release to environmental matrices such as house dust. Inhalation of house dust is one of the routes of human exposure to PBDEs and PFRs and raises concerns for respiratory health (Dirtu et al., 2012; Domingo, 2012; Hulin et al., 2012; Jones-Otazo et al., 2005; Wei et al., 2015). PFRs are structurally similar to organophosphate pesticides which have been associated with developing or exacerbating asthma (Hernandez et al., 2011; Hoppin et al., 2009). Prevalence of asthma is higher among children compared with adults. It is estimated that toddlers have a higher exposure to PFRs and PBDEs via dust compared to adults because of their increased contact with dust, by crawling over the floor and by mouth–hand-object contact (Jones-Otazo et al., 2005; Marklund et al., 2005; Wei et al., 2015). A recent cross-sectional study in 182 homes in Japan found increased odds ratios for increased concentrations of PFR 'tributyl phosphate' and 'tris (1,3-dichloroisopropyl) phosphate' (TDCIPP) in house dust with allergic disorders such as asthma, allergic rhinitis and atopic dermatitis of the inhabitants of the houses in which the dust was collected (Araki et al., 2014). The scarce studies investigating the health effects of PBDE exposure have been focused mainly on their potential endocrine-disrupting effects and on developmental neurotoxicity rather than on respiratory health effects.

In a longitudinal nested case–control study, we determined the levels and profiles of PFR and PBDE flame retardants in mother's mattress dust and investigated the relationship with the development of childhood asthma. We selected a subset of 110 children who developed asthma at 4 or at 8 years old from a large prospective birth cohort [Barn, Allergy, Milieu Stockholm Epidemiology (BAMSE)] in Sweden and matched controls on sex, atopic background of parents and socio-economic status (Wickman et al., 2002). In mother's mattress dust, which was collected 2 months after birth, the levels of seven commonly used PFRs and 21 PBDEs were examined.

Materials and methods

Study population

The details of the birth cohort have been reported previously (Almqvist et al., 2003). Briefly, from February 1994 until November 1996, 4089 newborn children (2065 boys and 2024 girls) in pre-defined areas of Stockholm were included in a prospective study. Data on background characteristics of the parents, housing and mattress characteristics were requested in questionnaires filled out by the parents when the child was around 2 months old (median age). At that time, mother's mattress dust was collected. Asthma at 4 or 8 years was defined based on at least two of the following three criteria: (i) >1 episode of wheeze in the last 12 months; (ii) a doctor's diagnosis of asthma; (iii) asthma medicine prescribed occasionally or regularly over the last 12 months (Lodrup Carlsen et al., 2012). Asthmatic children from whom dust samples were available were included in this study. Controls were matched on sex, atopic background of the parents and socio-economic status. Atopic background was defined as mother and/or father with doctor's diagnosis of asthma and asthma medication and/or doctor diagnosed hay fever in combination with furred pets allergy and/or pollen allergy at the time of questionnaire. Socio-economic status was defined according to dominance order in three classes; 'Blue-collar worker' or 'White-collar worker' (incl. liberal professional practician with university graduate jobs) or 'Other' (student, housewife/man, unemployed). The asthmatic children and their matched controls did not differ significantly from each other or from the BAMSE cohort for background characteristics such as sex, age of the mother (<25 years), any parent born outside Sweden, atopic background parents, socio-economic status or smoking at baseline (Table S1). However, children in this study cohort tended to receive more often exclusive breastfeeding for at least 4 months compared to the complete cohort (83.6% vs. 79.5%, $P = 0.027$), but cases and controls were not different (Table S1). Mothers of

asthmatic children smoked more often during pregnancy compared with the controls (16.2% vs. 6.3%, $P = 0.032$). At the age of 4 and 8 years, sensitization (≥0.35 kU/l serum) to common allergens was determined [Phadiatop: cat, dog, horse, timothy, birch, mite, mugwort, mold (Cladosporium)]. Controls were selected as never asthmatic and not sensitized at 4 and 8 years. Children with asthma at 4 years but not at 8 years old who were not sensitized to any of the common allergens were excluded from the study to limit the number of children that were misdiagnosed as asthmatic during a viral infection (Table 1).

Dust samples

Dust samples were collected as described previously (Almqvist et al., 2003). Briefly, dust samples have been collected when the children were about 2 months old. The parents were asked to vacuum the mattress of the mother's bed with their own vacuum cleaner for 2.5 min in a standardized way. They were requested not to vacuum clean the bed for 14 days before collection. A small disposable filter bag (Allergy Control Products Inc., Ridgefield, CT, USA) was inserted at the front hose of the vacuum cleaner, before attaching the nozzle for vacuuming textiles. After collection, the filter bags were sealed in plastic bags and stored at −20°C until extracted, and the levels of TCEP, TCIPP, TDCIPP, TBOEP, TPHP, EHDPHP, mmp-TMPP and PBDE-28, -47, -49, -66, -71, -77, -85, -99, -100, -119, -126, -138, -153, -154, -156, -183, -184, -191, -196, -197 and -209 were determined (see Table 2 for acronyms and applications).

Table 1 Characteristics of the study population selected from the BAMSE (Barn, Allergy, Milieu Stockholm Epidemiology) cohort

	Never asthma (n = 100)	Transient asthma (0–4 years)	Late asthma (4–8 years)	Persistent asthma (0–8 years)	Total asthma (n = 110)
Sex					
Female	48	11	18	19	48
Male	62	20	28	14	62
Parental atopy					
No	63	15	28	20	63
Yes	47	16	18	13	47
Socio-economic status[a]					
Blue-collar	21	2	10	9	21
White-collar	89	29	36	24	89
Sensitized at 4 years					
No	88	11	30	26	67
(missing values)	(22)	(8)	(5)	(1)	
Yes	0	12	11	6	29
Sensitized at 8 years					
No	99	1	25	24	50
(missing values)	(11)	(1)			
Yes	0	29	21	9	59

[a]Blue-collar worker, white-collar worker (incl. liberal professional practician with university graduate jobs) or other (student, house wife/man, unemployed) (Almqvist et al., 2005).

Table 2 Acronyms and applications (Wei et al., 2015) of the studied FRs

TCEP	Tris(2-chloro-ethyl) phosphate	FR, plasticizer, lacquer, glue, industrial processes
TCIPP	Tris(1-chloro-2 propyl) phosphate	FR, plasticizer
TDCIPP	Tris(1,3-dichloroisopropyl) phosphate	FR, plasticizer, lacquer, paint, glue
TBOEP	Tris(2-butoxyethyl) phosphate	FR, plasticizer, floor finish, wax, lacquer, paint, glue, antifoam agent
TPHP	Triphenylphosphate	FR, plasticizer, hydraulic fluids, lacquer, paint
EHDPHP	2-Ethylhexyldiphenyl phosphate	Plasticizer, hydraulic fluids
mmp-TMPP	Meta, meta, para-tricresyl phosphate	TMMP: plasticizer, polyvinylchloride, hydraulic fluids, cellulose, cutting oils, transmission fluids
PBDE	Polybrominated diphenyl ether	FRs in textiles, polyurethane foam and various plastic polymers, etc.

Measurement of indoor PFR levels

Briefly, the collected dust was placed in glass containers that had been pre-cleaned with acetone (Baker, ultra-resi). Contaminants such as visible fibers, feathers, hair and sand were removed from dust samples with tweezers. Approximately 50 mg of each dust sample was weighed in an acetone-rinsed and air-dried glass tube and internal standards (TPHP-d15, BDE-58 and ^{13}C-BDE-209 (Sigma-Aldrich Chemie B.V., Zwijndrecht, The Netherlands) were added, followed by 5 ml of acetone. Samples were vortexed for 1 min followed by ultrasonification for 15 min. The organic phase was transferred to a new, acetone-rinsed, glass tube. The dust samples were re-extracted by adding 5 ml toluene (Fisher Chemicals, analytical reagent grade), vortexed for 1 min, followed by 15-min ultrasonification. The toluene fraction was combined with the acetone fraction. This organic fraction was evaporated under a gentle stream of nitrogen in a water bath (±35°C) until 1 ml. The sample was quantitatively transferred on a Na_2SO_4 column to remove any co-extracted particles. This column was pre-washed with 6 ml acetone/toluene (1:1 v/v). The PFRs were eluted from the column with 8 ml of acetone/toluene (1:1 v/v). The volume was reduced to 1 ml under nitrogen evaporation in a water bath before analyzing with GC-EI-MS. After GC-EI-MS analysis of the PFRs, the sample was cleaned over a silica-impregnated H_2SO_4 column (40% concentrated H_2SO_4 w/w) by 13 ml dichloromethane:hexane (1:3 v/v). The volume was reduced to 0.1 ml under nitrogen evaporation in a water bath (±35°C) before analyzing with GC-EI-MS. Gas chromatography methods and quality assurance have been described elsewhere (Brandsma et al., 2014).

Quality control

Two control dust samples (50 mg of reference dust, SRM 2585; NIST, Gaithersburg, MD, USA) and two laboratory blanks were included in each batch of 20 samples. In the blanks, TCEP, TCIPP, TDCIPP,

TBOEP, TPHP, EHDPHP, mmp-TMPP and all PBDEs were below detection limits (PFRs detected < 1.7 ng/g dust, PBDEs detected < 0.24 ng/g dust). In two batches (of 12), the BDE-209 analyses of the 20 corresponding case–control pairs were omitted from the study because a high background level of BDE-209 was found in the blanks. Each asthmatic case and matched control dust sample was analyzed in the same batch to prevent variation due to between-batch variation. The coefficient of variation of the 25 reference dust samples measured in 12 independent batches ranged on average from 6.5% to 18% for the individual PFRs. The coefficient of variation for the individual PBDEs ranged on average from 11.0% to 26% (based on 24 reference dust samples in 12 batches). Analyzed values below the detection limits were replaced by 0.5× limit of detection (LOD) for the purpose of statistics. The LOD was adapted on the amount of analyzed dust per sample because in some cases, less than 50 mg was available (<45 mg: $n = 15/220$). Average LODs are provided in Tables 3, 4 and S4.

Levels of PFRs and PBDEs flame retardants in standard reference material 2585 (Organic contaminants in House Dust-SRM2585) have been analyzed. Our results showed similar levels as reported in other studies and for certified levels for PBDEs (difference ranged from 2.1% to 37.6%) (Tables S2A,B).

Statistical analysis

Conditions for a normal distribution were not met for the concentrations of PFRs and PBDEs in mattress dust. Therefore, nonparametric tests were applied for univariate analysis of the data (Wilcoxon signed rank test for matched pairs for comparison of FR levels between asthmatics and healthy controls). Mann–Whitney *U*-test was used to compare the FR levels between different housing, mattress and population background characteristics. Bivariate correlations between concentrations of individual FRs in dust were determined by Spearman's rho correlation coefficient. Distribution of background, housing and mattress characteristics of asthmatic and control children was compared by chi-squared test. FR profiles in dust were determined by multivariate analysis by K-means cluster analysis on log-transformed concentrations of PFR, PBDE or FR (PFR + PBDE). The distribution of these profiles in the asthmatic and control groups were analyzed by the chi-squared test. Multivariate linear regression analysis of log-transformed FR concentrations was used to adjust for housing, mattress or

Table 3 Concentrations organophosphate flame retardants (PFRs) in mother's mattress dust (ng/g) collected of asthmatic children and controls

		House dust from asthmatic children						House dust from matched controls						
PFR (ng/g dust)	LOD	>LOD (%)	Min	25th	Median	75th	Max	>LOD (%)	Min	25th	Median	75th	Max	*P*
TCEP	20	93.6	<LOD	49	102	263	>330 000	98.2	<LOD	52	107	207	>320 000	0.096
TCIPP	20	95.5	<LOD	60	116	243	>250 000	94.5	<LOD	44	96	362	>720 000	0.810
TDCIPP	40	93.6	<LOD	85	141	427	>610 000	89.1	<LOD	88	162	374	>200 000	0.722
TBOEP	400	90.9	<LOD	1082	3138	5593	>43 000	93.6	<LOD	1434	3723	7069	>95 000	0.737
TPHP	20	100	109	271	419	774	>13 000	100	96	308	631	1493	>95 000	**0.007**
EHDPHP	20	100	27	107	163	276	>15 000	100	23	111	172	421	>7300	0.139
mmp-TMPP	40	81.8	<LOD	90	192	437	>5400	84.5	<LOD	102	288	790	>42 000	**0.026**
∑PFRs			959	3718	6449	12 865	>660 000		822	3575	6795	13 000	>740 000	0.817
Dust (mg)			5	115	260	469	>9800		9	123	326	437	>8700	0.401

P-values were calculated using the Wilcoxon paired rank test.
Significant differences are depicted in bold (P value < 0.05).

Table 4 Concentrations polybrominated diphenyl ethers in mother's mattress dust (ng/g) of asthmatic children and healthy controls

		Asthmatic children						Healthy matched controls						
BDE (ng/g dust)	LOD	>LOD (%)	Min	25th	Median	75th	Max	>LOD (%)	Min	25th	Median	75th	Max	*P*
-47	2	96.4	1	6	11	24	>2200	95.5	1	7	11	24	>52 000	0.776
-99	1	92.7	1	7	14	36	>4100	97.3	1	8	13	34	>74 000	0.833
-100	3	90.0	0	1	2	5	>600	91.8	0	2	3	6	>16 000	0.802
-153	2	88.2	1	3	7	20	>500	88.2	1	3	6	16	>9200	0.391
-183	2	62.7	1	1	3	9	>500	68.2	1	1	3	10	198	0.904
-209	11	98.9	11	49	118	306	>29 000	93.3	5	36	122	389	>41 000	0.770
∑BDEs			21	107	259	498	>29 000		23	91	239	791	>150 000	0.801

P-values were calculated using the Wilcoxon paired rank test.

background characteristics for the comparison of FR concentrations between the two study groups. IBM SPPS Statistics version 20 (IBM, Armonk, NY, USA) was used. P values <0.05 were considered to be significant.

Results

Comparison of FR levels in dust between asthmatic children and matched controls

In a large prospective birth cohort study, dust was collected from the mother's mattress around 2 months after birth. Children who would develop childhood asthma and matched controls were selected from this cohort. As higher amounts of collected dust have been negatively associated with the development of allergic sensitization (Gehring et al., 2007), the amount of dust collected in both groups was compared, but no significant difference was observed (Table 3). We determined the concentrations of PFRs and PBDEs in these dust samples (Tables 3 and 4). All seven PFRs were detectable in at least 81.8% of the dust samples. The abundance rank order was as follows: TBOEP>TPHP>mmp-TMPP>EHDPHP~TDCIPP>TCEP~TCIPP. In comparison with the dust collected in the control group, the concentrations of the two most abundant PFRs besides TBOEP, TPHP (419 ng/g dust vs. 613 ng/g dust, $P = 0.007$) and mmp-TMPP (192 vs. 288 ng/g dust, $P = 0.026$) were significantly lower in the asthma group. There was no difference found in total amount of these seven flame retardants in dust collected in the asthmatic group and in the healthy control group. Further analysis in subgroups of our population based on sex, duration and period of childhood asthma and sensitization to allergens revealed a lower concentration of TPHP and mmp-TMPP in the group of sensitized asthmatic children ($n = 61$) but not in non-sensitized asthmatic children ($n = 49$) (Table S3). The sample size of the subgroups might not have been sufficient to draw firm conclusions, but analysis of subgroups did not show an association with higher levels of FRs and development of childhood asthma.

Twenty-one PBDE congeners were compared in mother's mattress dust between the asthmatic group and the control group. Only six PBDEs, namely BDE-47, -99, -100, -153, -183 and -209 were above the LOD in a considerable amount (62.7–98.9%) of dust samples. BDE-28, -66, -77, -119, -126, -138, -156, -184, -191 were detected in less than 5% of all dust samples; BDE-49, -71, -196 in less than 15%; and -85, -154, -197 were below the LOD in 25% (Table S4). The determined concentrations of PBDEs are presented in Table 4, with the abundance rank order as follows: BDE-209>BDE-99>BDE-47>BDE-153>BDE-183>BDE-100. There were no significant differences in the concentrations of PBDEs between dust samples collected in the asthmatic group in comparison with their matched healthy controls. Analysis of PBDE concentrations in subgroups as performed for PFRs (Table S3) did not yield any significant differences (data not shown).

Tables S5–7 show correlations between individual FRs in mattress dust samples which were collected before the use of some PBDEs were restricted. Strong correlations were only found between major components of the Penta-BDE formulation (at that time not banned); BDE-47, -99 and -100. The Rho correlation coefficient was >0.902 for any of the three combinations with a $P < 0.01$. All significant correlations between PFRs and/or remaining PBDEs were low (ρ: 0.15–0.25) to moderate (ρ: 0.25–0.4). Significant but moderate correlations were observed for TCIPP and TDCIPP and BDE-47, -99, -100 ($\rho > 0.301$–0.368,

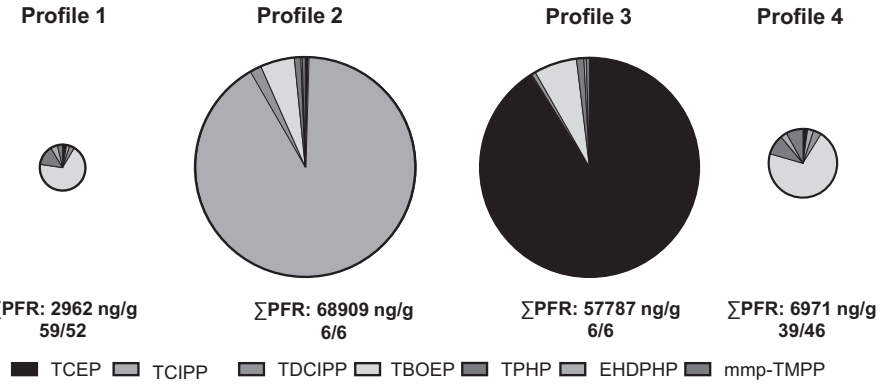

Fig. 1 Distribution of identified PFR profiles in mother's mattress dust samples of 110 children who developed childhood asthma and 110 matched healthy controls. Pie charts depict the relative proportion of each PFR within each profile (concentration levels visualized by different surface areas of pie charts). Below each pie chart, the frequency of the number of dust samples of each study group showing the corresponding profile is depicted: number of dust samples of asthmatic children vs. number of dust samples of healthy controls. For this analysis, 220 samples were included (distribution PFR profiles: chi-squared test: $P = 0.797$)

$P < 0.01$), while only TDCIPP was moderately correlated with the concentration of BDE-153 (ρ: 0.297, $P < 0.01$).

Different PFR and PBDE flame retardant profiles in dust

We investigated whether different PFR and PBDE profiles in dust could be associated with the development of childhood asthma. A K-means cluster analysis was performed to cluster dust samples based on similarities in concentrations for individual FRs. K-means cluster analysis based on PFR concentrations identified four different PFR profiles (Figure 1 and Table S8). The majority of the dust samples ($n = 196$) could be clustered into two similar profiles with a relative low total amount of PFRs with TBOEP being the most abundant one, followed by TPHP and either mmp-TMPP (profile 4, $n = 85$) or EHDPHP (profile 1, $n = 111$). Two profiles with a higher total amount of PFRs were found in only 24 samples with either TCIPP or TCEP being the most abundant PFR followed by TBOEP and TPHP. However, comparison of profiles observed in the asthmatic group in comparison with the control group did not reveal an overrepresentation of a certain cluster in one group ($P = 0.797$ according to Pearson's chi-squared test on distribution frequency of profiles over cases and controls). As expected, dust in the asthmatic group showed a trend to match more often profile 1 (59 vs. 52), while profile 4 was less prominent (39 vs. 46) compared with matched controls. This is in accordance with the analysis based on the individual concentrations of PFRs as profile 1 has lower concentrations of TPHP and mmp-TMPP in comparison with profile 4 (Table S8).

K-means cluster analysis based on concentrations of BDE-47, -99, -100, -153, -183 and -209 identified four PBDE profiles (Figure 2, please note that median concentrations can be deducted from the sum PBDEs and the relative distribution of each PBDE depicted under each chart pie). Likewise to PFR, in the majority (88%) of the samples, a low level of PBDEs was detected (profiles 2 and 3) and no differences were observed in the distribution of the different profiles over the two groups (Chi Square test: $P = 0.733$). Likewise, a K-means cluster analysis based on both PFRs and PBDE concentrations did not show a different distribution over the asthmatic group or control group (Table S9, Pearson's chi-squared test $P = 0.800$).

Relationship between FR concentrations and housing or mattress characteristics

Analysis of associations between housing and mattress characteristics and FR concentrations in all mother's mattress dust samples is represented in Tables 5 (PFRs) and 6 (PBDEs). No significant differences in FR levels were found when comparing houses on forced ventilation, airing routines, air intake/draught in master bedroom or formation of condensation (as

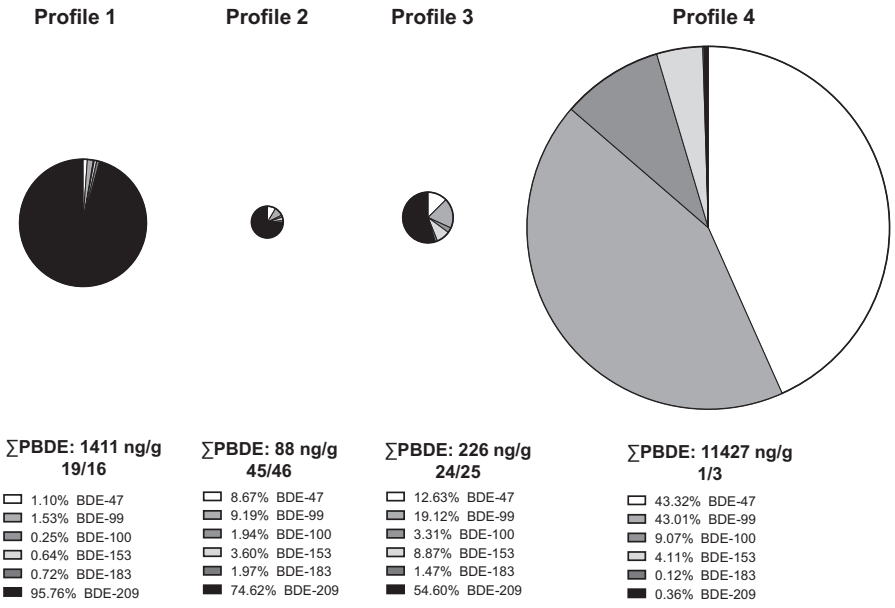

Fig. 2 Distribution of identified PBDE profiles in mother's mattress dust samples of 110 children who developed childhood asthma and 110 matched healthy controls. Pie charts depict the relative proportion of each PBDE within each profile (concentration levels visualized by different surface areas of pie charts). Below each pie chart, the frequency of the number of dust samples of each study group showing this profile is depicted: number of dust samples of asthmatic children vs. number of dust samples of healthy controls. For this analysis, 40 samples had to be excluded because BDE-209 concentrations were missing (distribution PBDE profiles: chi-squared test: $P = 0.733$)

Table 5 Relationship between housing and mattress characteristics and median concentrations of organophosphate flame retardants (ng/g dust)

	n	TCEP	TCIPP	TDCIPP	TBOEP	TPHP	EHDPHP	mmp-TMPP
Construction house								
Before 1960	107	94	115	139	3386	529	168	403
After 1960	112	113 (*0.477*)	115 (*0.776*)	157 (*0.237*)	3475 (*0.885*)	487 (*0.711*)	180 (*0.64*)	157 **(<0.0001)**
Daily airing of residence in wintertime								
Yes	149	96	112	160	3743	544	189	238
No	71	108 (*0.632*)	125 (*0.073*)	140 (*0.943*)	2998 (*0.112*)	479 (*0.855*)	154 (*0.21*)	259 (*0.831*)
Air intake/draught in master bedroom								
Yes	113	124	112	160	3054	470	167	273
No	97	95 (*0.233*)	1152 (*0.536*)	140 (*0.223*)	3747 (*0.875*)	549 (*0.305*)	169 (*0.439*)	229 (*0.300*)
Condensation in the master bedroom in winter								
Yes	27	95	161	170	3910	473	143	233
No	187	107 (*0.815*)	98 (*0.62*)	151 (*0.558*)	3372 (*0.43*)	491 (*0.234*)	168 (*0.703*)	244 (*0.785*)
Frequency of vacuum cleaning per month								
≤10 times	194	99	118	151	3318	487	166	261
>10	25	174 (*0.096*)	87 (*0.60*)	239 (*0.135*)	4341 (*0.339*)	566 (*0.953*)	204 (*0.224*)	125 **(0.030)**
Forced ventilation								
Yes	81	107	111	168	3329	479	173	184
No	98	112 (*0.592*)	115 (*0.871*)	134 (*0.224*)	3240 (*0.928*)	478 (*0.308*)	159 (*0.529*)	266 (*0.342*)
Type of bed								
Foam/box spring	205	104	114	156	3415	491	165	244
Waterbed	13	101 (*0.840*)	138 (*0.328*)	141 (*0.854*)	2667 (*0.434*)	529 (*0.618*)	346 (*0.02*)	229 (*0.71*)
Age of mattress								
≤5 years	158	113.5	119	153	3333	499	173	274
>5 years	60	92.5 (*0.592*)	108 (*0.148*)	160 (*0.754*)	3588 (*0.641*)	481 (*0.632*)	142 (*0.087*)	193 (*0.203*)

P values were calculated using Mann-Whitney U-test and represented in italics.
Bold numbers represent significant differences between the two groups (*P* value < 0.05).

an indicator of insufficient ventilation). A higher frequency of vacuum cleaning (>10 per month) significantly decreased mmp-TMPP but not for other analyzed FRs. A significantly higher concentration of mmp-TMPP was observed in houses built before 1960. Significantly lower levels of the Penta-BDE formulation BDE-47, -99 and -100 were found in older mattresses (>5 years). Comparison of housing and mattress characteristics between asthmatic and control children showed that more control children lived in an older house (built before 1960) and had less forced ventilation (Table S10). After adjustment for the age of the house, no significant difference was observed anymore for mmp-TMPP between the asthmatic and control group. Adjustment for the housing or mattress characteristics in the statistical analysis of observed FR concentrations between the two study groups did not change the outcome for the remaining FRs. TPHP was still higher in mother's mattress dust of controls, while no differences were observed for the remaining PFRs and PBDEs.

Environmental tobacco smoke is a risk factor for the development of asthma. Although there was no difference at smoking by either the father and/or mother at the time of birth, asthmatic children had significant more mothers who smoked during pregnancy (Table S1). However, adjustment for this in a multivariate linear regression analysis did not affect the outcomes seen in Tables 3 and 4 (data not shown).

Discussion

This study investigated the possible association between increased concentrations of PFRs and PBDE flame retardants in mother's mattress dust and the development of childhood asthma. All seven analyzed PFRs could be detected in at least 81–100% of the 220 dust samples, while only 6 (of 21) PBDE congeners could be detected in 62.7–98.9% of the samples with the abundance rank as follows: TBOEP≫TPHP>mmp-TMPP>EHDPHP~TDCIPP>TCEP~TCIPP~BDE-209≫BDE-99>BDE-47>BDE-153>BDE-183>BDE-100. Dust samples of the asthmatic group contained lower concentrations of TPHP and mmp-TMPP compared with samples of the matched control group, while no differences could be observed for the other analyzed FRs.

Only scarce data are available to compare PFR and PBDE levels in mattress dust observed in the present study, but levels in floor dust have been reported for several countries. In support for comparison with floor dust samples, a study in New Zealand showed a similar PFR profile in mattress dust with corresponding floor dust samples and similar concentrations of TPHP, TMPP and TCIPP. TBOEP, TCEP and TDCIPP concentrations were different, but a positive correlation was found for TBOEP. These results might indicate that certain PFRs have an uniform occurrence, similar sources and behavior in the indoor environment (Ali

Table 6 Relationship between housing and mattress characteristics and median polybrominated diphenyl ether levels (ng/g dust)

	n	BDE-47	BDE-99	BDE-100	BDE-153	BDE-183	BDE-209
Construction house							
Before 1960	107	11	13	2	7	3	151
After 1960	112	12 (*0.309*)	14 (*0.716*)	3 (*0.333*)	6 (*0.451*)	3 (*0.549*)	100 (*0.11*)
Daily airing of residence in wintertime							
Yes	149	11	13	3	7	3	122
No	71	12 (*0.344*)	15 (*0.135*)	3 (*0.364*)	6 (*0.536*)	5 **(0.019)**	117 (*0.816*)
Air intake/draught in master bedroom							
Yes	113	11	13	3	7	3	100
No	97	12 (*0.870*)	14 (*0.925*)	3 (*0.998*)	7 (*0.792*)	2 (*0.051*)	126 (*0.61*)
Condensation in the master bedroom in winter							
Yes	27	13	15	3	10	3	157
No	187	11 (*0.998*)	13 (*0.477*)	2 (*0.771*)	6 (*0.091*)	3 (*0.975*)	118 (*0.898*)
Frequency of vacuum cleaning per month							
≤10 times	194	12	14	3	6	3	128
>10	25	10 (*0.779*)	15 (*0.968*)	2 (*0.931*)	9 (*0.195*)	3 (*0.566*)	77 (*0.127*)
Forced ventilation							
Yes	81	12	13	3	6	3	105
No	98	11 (*0.653*)	13 (*0.939*)	2 (*0.576*)	7 (*0.444*)	3 (*0.823*)	145 (*0.125*)
Type of bed							
Foam/box spring	205	11	13	2	6	3	118
Waterbed	13	20 (*0.065*)	22 (*0.225*)	4 (*0.146*)	8 (*0.948*)	9 (*0.065*)	197 (*0.250*)
Age of mattress							
≤5 years	158	14	15	3	7	3	142
>5 years	60	9 **(0.008)**	12 **(0.013)**	2 **(0.023)**	5 (*0.168*)	3 (*0.077*)	90 (*0.201*)

P values were calculated using Mann-Whitney U-test and represented in italics.
Bold numbers represent significant differences between the two groups (*P* value < 0.05).

et al., 2012) and that mattress dust might reflect indoor contamination for at least certain PFRs. This relationship will have to be confirmed in other countries. The PFR levels found in mattress dust in the present study were comparable to the reported levels in mattress dust in New Zealand and to the concentrations reported in floor dust collected in Belgium and eastern Romania (except for higher levels of TCIPP in both countries) (Dirtu et al., 2012; Van Den Eede et al., 2011). However, much higher levels of PFRs are reported in floor dust samples especially in Japan (Araki et al., 2014; Kanazawa et al., 2010; Mizouchi et al., 2015; Tajima et al., 2014) but also in the USA, Spain, Germany and for settled dust in Sweden (Ingerowski et al., 2001; Ali et al., 2012; Bergh et al., 2011; Garcia et al., 2007; Stapleton et al., 2009) (Table S11). PBDE levels found in this study were similar to the reported levels in floor dust collected in Denmark (Frederiksen et al., 2010) and Kuwait (Ali et al., 2013) and settled dust in Sweden (Newton et al., 2015) but lower compared with dust collected in Germany, USA, Canada and for floor/furniture dust in Sweden (Karlsson et al., 2007; Stapleton et al., 2005; Wilford et al., 2005) (Table S12). The higher FR concentrations in indoor dust samples reported before in Sweden in comparison with our study might be related to the source of dust. Investigating the risk of exposure to FRs for development of childhood asthma might have a different outcome in countries with a higher FR level in dust. However, our PFR results seem to be in line with the study by Araki et al. (2014), which observed an association with TNBP in dust and asthma in Japan but not for the other analyzed PFRs.

Evaluation of mattress characteristics but also several housing characteristics revealed a relation between the age of the house and frequency of vacuum cleaning with the level of mmp-TMPP, and the age of the mattress was negatively related to the concentration of the Penta-BDE mix components BDE-47, 99 and 100. Houses which were daily aired showed lower levels of BDE-183. As Penta-BDE mix is mainly used in flexible polyurethane foam in mattresses, it is not surprising that the age of the mattress showed a negative correlation with the concentration of components of the at-that-time not-banned Penta-BDE mix BDE-47, BDE-99 and BDE-100, but remarkably none of the other FR concentrations were correlated. These Penta-BDE components were also the only FRs which were strongly correlated in mattress dust. All other significant correlations between the analyzed FRs were weak to moderate, indicating a different behavior of these FRs, contamination of different sources and/or variable use of individual FRs added to mattress foam and/or mattress fabrics.

In two Japanese studies, it was observed that ventilation equipment use increased TBOEP concentrations in indoor dust (Araki et al., 2014; Tajima et al., 2014). In our study, FR levels (except for BDE-183) were not significantly different for houses with different ventilation regimes- or ventilation-related characteristics.

After the adjustment for living in a house built before 1960, the level of mmp-TMPP was no longer significantly increased in the control group but the level of TPHP remained higher. Adjustment for several housing and mattress characteristics did not change the outcome for the comparison of FR (except for mmp-TMPP) concentrations between the asthmatic and control group (data not shown). It is unlikely that the higher levels of TPHP relate to behavior of the parents of asthmatic children in relation to dust management because controls were matched for atopic background of the parents and there was no significant difference in the amount of dust collected or in ventilation regime/vacuum cleaning frequency between the asthmatic group and the control group.

In our study, there was no association between development of childhood asthma and higher levels of FR in mattress dust. It is important to note that the contribution of exposure to FRs via mother's mattress dust to the total exposure to FRs is not known in this study and no reports are available to make a valid estimation. To provide a gross indicative value for exposure to the most abundant PFR, TBOEP, found in this study, ingestion of mattress dust in a high dust ingestion scenario (200 mg/day) for a 12-kg toddler (Ali et al., 2012) would be 52.3 ng/kg bw/day. This is based on 100% absorption of ingested mother's mattress dust but is still much lower compared to the RfD value of 15 μg/kg bw/day (as proposed by Ali et al. by dividing the chronic NOAEL by a factor of 1000 (Ali et al., 2012)). Children have been exposed via many more sources of FR (indoor and outdoor environment) and routes (air, skin and diet) which might have dominated the contribution via exposure to mattress dust (Gehring et al., 2008; Schram-Bijkerk et al., 2005). In addition, dust contains a complex mixture of chemicals, such as phthalates, but also potential allergens and endotoxins which can all be associated with the development of asthma (Ege et al., 2011; Hulin et al., 2012). These and other factors in dust might have influenced the analysis of the effect of FR exposure and could not be adjusted for in our study.

One could argue whether another source of dust would have been more relevant to study early exposure of FRs of children. Firstly, only mother's mattress dust was collected around time of birth within the longitudinal birth cohort 'BAMSE', being the only available source of indoor dust at this time point. Secondly, there is some evidence, albeit limited, that concentrations of certain PFRs and BDE-209 in mattress dust correlate with levels in corresponding floor dust samples (Ali et al., 2012; Coakley et al., 2013). However, we were not able to investigate these correlations in our study cohort, and in addition, there are no reports investigating the consistency of these correlations over time. Thirdly, the observed PFR profile (TBOEP>TPHP>mmp-TMPP>EHDPHP~TDCIPP>TCEP~TCIPP) seems to be similar to reported values for floor dust in several countries which is in support of the found correlation between floor dust and mattress dust (Table S11).

In conclusion, our study found a broad range of PFRs and PBDEs in 220 mother's mattress dust samples which may be an important source for indoor exposure to FRs. No associations were found between higher levels of FRs in dust and the development of childhood asthma. In contrast, mmp-TMPP (related to age of the house) and TPHP were found in lower concentrations in mother's mattress dust of children who would develop childhood asthma in comparison with matched controls.

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Author contributions

Conception, design, writing of manuscript: DC, LvR, RvR, PL, MW, AZ; acquisition of data: DC, LvR, MvV, EH, MW.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Distribution of background characteristics of the study population in comparison to the birth cohort (p value).

Table S2. (A,B) Analysis of PFRs (A) and PBDEs (B) in SRM 2585 reference dust material in mg/kg based upon 12 independent measurements in replicate in comparison with other studies and certified values for PBDEs.

Table S3. Median difference between case and controls in concentrations of PFRs in house dust in subgroups of the study population and p value.

Table S4. Comparison of less abundant PBDEs (found in less than 25% of total dust samples) between dust collected in homes of children who would develop asthma and in healthy controls.

Table S5. Correlations between individual PFR concentrations (ng/g) in mattress dust.

Table S6. Correlations between individual PBDE concentrations (ng/g) in mattress dust.

Table S7. Correlations between individual PFR and PBDE concentrations (ng/g) in mattress dust.

Table S8. Profiles of PFRs in dust samples; relative distributions of individual PFRs and median PFR concentration in ng/g dust.

Table S9. Relative distribution (%) and median ng/g dust concentration of both PFRs and PBDEs in 4 different profiles identified by K-means cluster analysis and the distribution of the different profiles in the asthmatic group in comparison to the control group.

Table S10. Comparison of housing and mattress characteristics between asthmatics and controls.

Table S11. Comparison of median concentrations of PFRs studied in indoor dust (ng/g dust).

Table S12. Comparison of median concentrations of PBDEs studied in indoor dust (ng/g dust).

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Exposure to organophosphate and polybrominated diphenyl ether flame retardants via indoor dust and childhood asthma

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Table S11: Comparison of median concentrations of PFRs studied in indoor dust (ng/g dust)

Table S12: Comparison of median concentrations of PBDEs studied in indoor dust (ng/g dust)

Table S1: Distribution of background characteristics in study population compared to the birth cohort (Absolute number, percentage and p value)

Factor	**BAMSE cohort (n=4089) vs study cohort (n=222)**	**Asthmatic children in BAMSE cohort (n=672) vs study cohort (n=111)**	**Asthmatic children (n=111) vs healthy controls (n=111) in study cohort**
Sex (Male)	2065 (50.5%) vs 126 (56.8%) *0.081*	389 (57.9%) vs 63 (56.8%) *0.905*	63 (56.8%) vs 63 (56.8%) *n.a.*
Socioeconomic status (Low)	695 (17.3%) vs 44 (19.8%) *0.319*	137 (20.8%) vs 22 (19.8%) *0.991*	22 (19.8%) vs 22 (19.8%) *n.a.*
Parental history of allergic disease (Yes)	1200 (29.7%) vs 94 (42.3%) ***<0.001***	281 (42.4%) vs 47 (42.3%) *0.140*	47 (42.3%) vs 47 (42.3%) *n.a.*
Mother's age (<25 years)	319 (7.8%) vs 16 (7.2%) *0.847*	75 (11.2%) vs 10 (9.0%) *0.610*	10 (9.0%) vs 6 (5.4%) *0.436*
Any parent born outside Sweden (Yes)	718 (21.1%) vs 35 (15.8%) *0.552*	115 (19.0%) vs 15 (13.5%) *0.420*	15 (13.5%) vs 20 (18.0) *0.461*
Smoking at baseline (Yes)	855 (21.0%) vs 52 (23.4%) *0.418*	175 (26.2%) vs 32 (28.8%) *0.617*	32 (28.8%) vs 20 (18.0%) *0.081*
Smoking mother during pregnancy	506 (13.1%) vs 25 (11.1%) *0.474*	121 (18.0%) vs 18 (16.2%) *0.685*	18 (16.2%) vs 7 (6.3%) ***0.032***
Breast feeding, excl (4 months or more)	3116 (79.5%) vs 184 (83.6%) ***0.027***	498 (75.9%) vs 93 (84.6%) ***0.038***	93 (83.8%) vs 91 (82.0%) *0.859*

p-Values were calculated using the Chi-Square test. N.a.: not applicable, matched for this variable.

Table S2A: Concentrations of PFRs in SRM 2585 reference dust material (mg/kg as received) based upon 12 independent measurements in duplo.

	This study (n=25)	Fromme et al.(Fromme et. al. , 2014) (n=3)	Bergh et al.(Bergh et. al. , 2012) (n=7)	Ali et al.(Ali et. al., 2012) (n=6)	Van den Eede et al.(Van den Eede et. al., 2011) (n=11)
TCEP	0.8	0.7	0.8	0.8	0.7
TCIPP	0.8	1.0	0.9	0.8	0.8
TDCIPP	2.5	2.2	2.3	1.9	2.0
TBOEP	117	71	82	40	49
TPHP	0.9	0.7	1.1	1.1	1.0
EHDPHP	0.9				
mmp-TMPP	1.1				

Table S2B: Concentrations of PBDEs in SRM 2585 reference dust material (µg/kg as received) based upon 12 independent measurements in duplo.

	This study (n=25)	Certified NIST (dry-mass basis)[(a)]	(Stapleton et. al. , 2006) (n=6)	(Ali et. al., 2012)(n=6)
BDE-28	37.8±6.6	46.9±4.4	47.2	38.5
BDE-47	417.1±49.1	497±46	539	412
BDE-49	33.4±4.0	53.5±4.2	49.3	NM
BDE-66	<25.3	29.5±6.2	32.3	NM
BDE-71	<3.7	<0.2	<9.2	NM
BDE-77	<2.2		NM	NM
BDE-85	34.2±4.6	43.8±1.6	44.4	NM
BDE-99	717.7±94.9	892±53	920	665
BDE-100	118.5±16.3	145±11	153	130
BDE-119	6.7±0.5	<0.2	<10.9	NM
BDE-126	2.9±0.4		NM	NM
BDE-138	11.2±2.2	15.2±2.0	14.0	NM
BDE-153	127.0±22.8	119±1	117	114
BDE-154	59.4±9.5	83.5±2.0	82.1	95.0
BDE-156	<2.7	<0.2	<9.7	NM
BDE-183	42.1±11.4	43.0±3.5	44.1	33.5
BDE-184	<2.3		NM	NM
BDE-191	<3.4	<0.3	<8.94	NM
BDE-196	23.0±5.2		NM	24.0
BDE-197	18.4±6.0		NM	17.5
BDE-209	2771. ±6	2510±190	2380	2260

(a)According to Certificate of Analysis by NIST: material contained approximately 2.1% moisture.

Table S3: Median difference (ng/g) between case and matched control in concentrations of PFRs in mattress dust in subgroups of the study population and p value

Sub groups (n)	TCEP	TCIPP	TDCIPP	TBOEP	TPHP	EHDPHP	mmp-TMPP
Asthma in males N=62 pairs	12.0 0.208	31.5 0.648	-59.0 0.145	-450.0 0.611	-143.5 **0.046**	8.5 0.321	49.5 0.088
Asthma in females N=48 pairs	-43.5 0.158	22.5 0.364	14.5 0.285	247.0 0.926	-163.0 0.071	-25.0 0.270	-16.0 0.147
Sensitized N=61	14.0 0.144	41.0 0.138	0.0 0.941	12.0 0.695	-192.0 **0.009**	7.0 0.154	-55.0 **0.022**
Non-sensitized N=49	-25.0 0.137	-110.0 0.066	-40.0 0.534	-702 0.332	-125 0.238	-16.0 0.561	-13.0 0.436
Transient asthma N=31	10.0 0.456	38.0 0.845	8.0 0.984	720.0 0.308	-390.0 **0.011**	-30.0 0.075	-256.0 **0.008**
Late onset asthma N=46	7.0 0.533	6.5 0.658	-27.5 0.413	-6.5 0.747	-147.0 **0.05**	26.5 0.694	80.0 0.619
Persistent asthma N=33	-27.0 0.174	17.0 0.933	14.0 0.688	-1164.0 0.288	92.0 0.993	-29.0 0.662	-86.0 **0.037**

p-Values were calculated using Mann-Whitney U test.

Table S4: Concentrations (ng/g dust) of less frequently found PBDEs

		Mother's mattress dust from asthmatic children						**Mother's mattress dust from matched controls**	***P***					
BDE	**LOD**	**>LOD (%)**	**Min**	**25th**	**median**	**75th**	**Max**	**>LOD (%)**	**min**	**25th**	**median**	**75th**	**Max**	
-28	4	**3.6**	1	2	2	2	18	**3.6**	2	2	2	2	117	**0.045**
-49	3	6.4	1	1	1	1	46	8.2	1	1	1	1	524	0.207
-66	29	0.9	6	12	13	13	141	1.8	11	12	12	13	420	0.062
-71	3	12.7	1	1	1	1	255	13.6	1	1	1	1	190	0.272
-77	3	0.0	1	1	1	1	14	0.9	1	1	1	1	9	0.035
-85	2	17.3	1	1	1	1	118	17.3	1	1	1	1	2317	0.455
-119	8	0.0	2	3	3	3	37	0.9	3	3	3	3	64	0.066
-126	2	2.7	0	1	1	1	11	3.6	1	1	1	1	255	0.076
-138	3	0.9	1	1	1	1	65	3.6	1	1	1	1	586	0.195
-154	4	18.2	1	2	2	2	290	16.4	1	1	1	1	7720	0.257
-156	4	**0.0**	1	1	2	2	17	**0.0**	1	1	1	1	12	**0.026**
-184	3	**0.9**	1	1	1	1	14	**0.9**	1	1	1	1	26	**0.024**
-191	4	**0.0**	2	2	2	2	22	**0.0**	2	2	2	2	15	**0.026**
-196	5	9.1	1	2	2	2	83	15.5	2	2	2	2	66	0.814
-197	5	25.5	1	2	2	5	390	22.7	2	2	2	4	61	0.287

p-Values were calculated using Mann-Whitney U test.

Table S5: Correlations between individual PFR concentrations (ng/g) in mattress dust

PFR	TCEP	TCIPP	TDCIPP	TBOEP	TPHP	EHDPHP	mmp-TMPP
TCEP	1	0.186**	0.298**	0.240**	0.106	0.143*	0.120
TCIPP		1	0.296**	0.048	0.079	0.065	0.201**
TDCIPP			1	0.184**	0.142**	0.113	0.160*
TBOEP				1	0.206**	0.192**	0.147*
TPHP					1	0.335**	0.134*
EHDPHP						1	0.148*
mmp-TMPP							1

Correlation coefficient values were calculated with Spearman's rho, *P<0.05, **P<0.01.

Table S6: Correlations between individual PBDE concentrations (ng/g) in mattress dust

PBDE	**-47**	**-99**	**-100**	**-153**	**-183**	**-209**
-47	1.000	**0.902****	**0.950****	0.373**	0.294**	0.137
-99		1.000	**0.940****	0.397**	0.328**	0.213**
-100			1.000	0.395**	0.287**	0.154*
-153				1.000	0.334**	0.209**
-183					1.000	0.182*
-209						1.000

Correlation coefficient values were calculated with Spearman's rho, *P<0.05, **P<0.01.

Table S7: Correlations between individual PFR and PBDE concentrations (ng/g) in mattress dust

PFR	TCEP	TCIPP	TDCIPP	TBOEP	TPHP	EHDPHP	mmp-TMPP
BDE-47	0.145*	0.307**	0.305**	0.118	0.193**	0.244**	0.115
BDE-99	0.160*	0.301**	0.368**	0.156*	0.183**	0.223**	0.111
BDE-100	0.188**	0.308**	0.360**	0.163*	0.187**	0.198**	0.143*
BDE-153	0.179**	0.116	0.297**	0.217**	0.156*	0.113	0.163*
BDE-183	0.149**	0.110	0.198**	0.092	0.155*	0.178**	0.116
BDE-209	0.086	0.111	0.156*	0.160*	0.05	0.064	0.159*

Correlation coefficient values were calculated with Spearman's rho, *P<0.05, **P<0.01.

Table S8: Profiles of PFRs in mattress dust; relative distributions of individual PFRs and median PFR concentrations (ng/g dust)

Profile	% TCEP (median)	% TCIPP (median)	% TDCIPP (median)	% TBOEP (median)	% TPHP (median)	% EHDPHP (median)	% mmp-TMPP (median)
1	2.8 (83)	2.3 (68)	3.48 (103)	68.77 (2037)	13.94 (413)	5.03 (149)	3.68 (109)
2	0.45 (309)	91.25 (62882)	1.7 (1169)	5.02 (3458)	0.94 (648)	0.22 (152)	0.42 (291)
3	90.96 (52563)	0.19 (108)	0.6 (347)	6.34 (3661)	1.09 (629)	0.35 (205)	0.47 (274)
4	2.18 (152)	2.85 (199)	3.86 (269)	70.58 (4920)	9.44 (658)	3.10 (216)	7.99 (557)

Table S9: Median ng/g dust concentration and relative distribution (%) of PFRs and PBDEs in 4 determined FR profiles and frequency of profiles in the asthmatic group vs control group (n/n).

	PFR/PBDE profiles:			
	1 (46/45)	**2 (36/36)**	**3 (1/3)**	**4(6/6)**
TCEP	65 (2,0%)	167 (2.7%)	66 (0.2%)	353 (0.6%)
TCIPP	75 (2.3%)	121 (1.9%)	232 (0.5%)	49454 (90.3%)
TDCIPP	101 (3.1%)	201 (3.2%)	17079 (39.3%)	232 (0.4%)
TBOEP	2270 (68.6%)	4385 (69.7%)	6627 (15.2%)	3458 (6.3%)
TPHP	390 (11.8%)	567 (9.0%)	4074 (9.3%)	567 (1.0%)
EHDPHP	147 (4.4%)	215 (3.4%)	144 (0.3%)	213 (0.4%)
mmp-TMPP	155 (4.7%)	287 (4.6%)	3843 (8.8%)	292 (0.5%)
BDE-47	8 (0.2%)	22 (0.3%)	4950 (11.4%)	22 (0.04%)
BDE-99	8 (0.2%)	31 (0.5%)	4915 (11.3%)	25 (0.05%)
BDE-100	2 (0.1%)	6 (0.1%)	1036 (2.4%)	5 (0.01%)
BDE-153	3 (0.1%)	13 (0.2%)	470 (1.1%)	11 (0.02%)
BDE-183	2 (0.1%)	5 (0.1%)	14 (0.03%)	2 (0.00%)
BDE-209	84 (2.5%)	276 (4.4%)	42 (0.1%)	130 (0.2%)

Profiles were determined by multivariate cluster analysis by K-means on log transformed FR concentrations. No difference in frequency of profiles between the two groups: Chi square test p=0.800).

Table S10: Housing and mattress characteristics: asthmatics vs controls

Housing or mattress characteristic	**Asthmatics (n/N)**	**Controls (n/N)**	**P**
Construction house *Before 1960 (vs after 1960)*	44/109	59/105	**0.028**
Daily airing of residence in wintertime *Yes (vs no)*	76/110	72/110	1.000
Air intake/draught in master bedroom *Yes (vs no)*	57/102	55/103	0.828
Wall to wall carpeting *Yes (vs no)*	8/110	6/110	0.784
Frequency of vacuum cleaning per month *≤10 times (vs >10)*	94/110	96/104	0.132
Forced ventilation *yes (vs no)*	47/86	31/88	**0.015**
Type of bed *Foam/box spring (vs waterbed)*	105/110	95/103	0.397
Age of mattress *≤5 years (vs >5 years)*	81/109	73/104	0.542

P values were calculated by Chi square test comparing the frequency in the asthmatic group vs control.

Table S11: International comparison of median concentrations of PFRs in indoor dust (ng/g)

Country	Sample size	TCEP	TCIPP	TBOEP	TPHP	TDCIPP	TMPP	Reference
Sweden (mattress dust)	Homes n=220	102	116	3138	419	141	192	Present study
Sweden (settled dust)	Homes n=10	2100	1600	4000	1200	10000	n.a.	Bergh et al. (2011)
New Zealand (mattress dust)	Homes n=16	40	250	1550	240	110	160	Ali et al (2012)
New Zealand (floor dust)	Homes n=34	111	350	4020	600	230	120	Ali et al (2012)
Belgium (floor dust)	Homes n=33	230	1380	2030	500	360	240	Van de Eede et al. (2011)
Romania (floor dust)	Homes n=47	100	860	1500	800	80	800	Dirtu et al (2012)
Spain (floor dust)	Homes n=8	500	3800	9400	1900	120	n.a.	García et al. (2007)
Germany (floor dust)	Homes n=216(TCIPP) n=356 (TCEP)	600	400	n.a.	n.a.	n.a.	n.a.	Ingerowski et al. (2001)
USA* (floor dust)	Homes n=50	n.a.	570	n.a.	7360	1890	n.a.	Stapleton et al. (2009)
USA* (floor dust)	Homes n=30	348	3440	2730	n.a.	n.a.	n.a.	Stapleton et al. (2014)
Japan (floor dust)	Homes n=41	7500	1870	1 570 000	5400	4000	n.a.	Kanazawa et al. (2010)
Japan (floor dust)	Homes n=148	5830	8690	508 000	4510	n.a.	<MDL	Araki et al. (2014)
Japan (floor dust)	Homes n=48	<LOD	740	30 880	870	n.a.	<LOD	Tajima et al. (2014)
Japan (floor dust)	Homes n=10	2700	1700	82 000	820	2200	1200	Mizouchi et al. (2015)

MDL, method detection limit, *geometric mean values, LOD: Limit of detection. Adapted/updated from (Van den Eede et. al., 2011)

Table S12: International comparison of median concentrations of PBDEs studied in indoor dust (ng/g dust)

Country	Sample size	BDE-47	BDE-99	BDE-100	BDE-153	BDE-183	BDE-209	Reference
Sweden (mattress dust)	Homes n=220	11	14	2	7	3	118	Present study
New Zealand (mattress dust)	Homes n=16	46.3	41.8	9.8	6.7	6.3	1018	Coakley et al. (2013)
Sweden (settled dust, not from FR rich products)*	Homes n=4	18-84	10-70	1.7-22	6.3-15	14-<41	<11-140	Newton et al (2015)
Sweden** (floor/furniture)	Homes n=5	51	79	24	4.9	4.8	470	Karlsson et al. (2007)
Denmark (vacuum cleaner bags)	Homes n=50	20	16	3	3	4	407	Frederiksen et al. (2010)
Germany (floor dust)	Homes N=15-40	122	180	20.8	30.7	23.3	980	Knoth et al (2003) in Karlsson et al, 2007)
USA (floor dust)	Homes n=10	430	880	150	140	73	2000	Sjödin et al. (2004)
USA* (floor dust)	Homes n=17	1220	1700	274	181	30.7	2090	Stapleton et al. (2005)
Canada (floor dust)	Homes N=64	1100	1800	490	470	44	1100	Wilford et al. (2005)
Pakistan (floor dust)	Homes n=31	0.57	0.6	<0.2	0.24	0.75	19.7	Ali et al, 2012b
Pakistan (floor dust)	Homes n=15	1.3	1.7	0.3	0.6	1.5	138	Ali et al. (2013)
Kuwait (floor dust)	Homes n=15	9.5	12	2.3	2.4	1.9	310	Ali et al. (2013)
USA* (floor dust)	Homes n=30	452	741	98.6	40.6	1.0	1720	Stapleton et al. 2014

MDL, method detection limit, *samples range, **geometric mean values. Adapted/updated from (Karlsson et. al., 2007)

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