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Full length article

Pre- and post-natal exposure of children to organophosphate flame retardants: A nationwide survey in France

Z. Chupeau^a, F. Mercier^a, E. Rouxel^a, B. Le Bot^a, G. Chauvet^b, T. Siméon^c, N. Bonvallot^a, C. Zaros^c, C. Chevrier^a, P. Glorennec^{a,*}

^a Univ Rennes, EHESP, Inserm, Irset (Institut de recherche en santé, environnement et travail) - UMR_S 1085, F-35000 Rennes, France

^b Ensai (Irmar), Campus de Ker Lann, Bruz, France

^c UM Ined-Inserm-EFS, France



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ABSTRACT

The use of organophosphate flame retardants (OPFRs) has been on the rise ever since many brominated flame retardants were banned, back in the 2000 s. The objectives of this study are to describe the pre- and post-natal exposure of children to OPFRs, and to explore their possible determinants. A total of 259 children aged 3.5 years and 388 mothers from the French ELFE mother–child cohort were included. Both pre- and post-natal exposure to OPFRs were assessed, using OPFR concentrations in the hair of pregnant women (in 2011) and their 3.5-year-old children (in 2014–2015) for 15 OPFRs, of which 9 were detected in > 20 % hair samples. The highest geometric means for pre-natal exposure were 272 ng/g for tris(1-chloro-2-propyl) phosphate (TCPP), 69.7 ng/g for ng/g for triphenyl phosphate (TPP) and 54.4 ng/g for tris(1,3-dichloro-2-propyl) phosphate (TDCPP). The highest geometric means for post-natal exposure were 249.6 ng/g for TCPP, 85.3 ng/g for TDCPP and 83.8 ng/g for 2-ethyl-hexyl diphenyl phosphate (EHDPP). Correlations were found between both pre-natal exposures, and between pre-and post-natal exposures. No correlation was however found between pre-and post-natal exposures for any given OPFR. Pre-natal exposure to the 9 OPFRs was associated with pre-natal exposure to polybrominated diphenyl ethers 209 (BDE₂₀₉), and 47 (BDE₄₇). Maternal BMI was associated with pre-natal exposure to OPFRs other than TBEP. Home renovation work prior to birth was also associated with pre-natal exposure to OPFRs, with the exception of EHDPP, tris(2-butoxyethyl) phosphate (TBEP) and triethyl phosphate (TEP). Determinants of post-natal exposure appeared more disparate across OPFRs; although both the type of flooring in children's rooms and pre-natal exposure to polybrominated diphenyl ethers seem to be associated with post-natal exposure. Lastly, higher socioeconomic status appeared to be associated with lower exposure for several (though not all) OPFRs.

The high prevalence of exposure to OPFRs suggests the need for studies to assess the health effects of OPFRs exposure, particularly on children.

1. Introduction

Organophosphorus flame retardants (OPFRs) are chemical compounds belonging to the organophosphate esters (OPE) chemical class that are added to many consumer products during the manufacturing process (Kemmllein et al., 2003; Van der Veen and de Boer, 2012). In 1992, worldwide usage of flame retardants was estimated at 600,000 t, of which 102,000 t (or about 17 %) were organophosphate-based (Hartmann et al., 2004). Since the 2000 s, these have increasingly been used to replace polybrominated diphenyl ethers (PBDE), a family

of brominated flame retardants classified under the Stockholm Convention as persistent organic pollutants (POPs), and gradually banned (Blum et al., 2019; Chupeau et al., 2020; Stapleton et al., 2012). In 2019, worldwide consumption of flame retardants amounted to >2.39 million tons, 18 % of which were organophosphorous (www.flame-retardants-online.com, 2022). OPFRs were already widely used, (even before the BFR restrictions) and their applications go beyond those of the flame retardants (e.g., as plasticizers) that contribute to the ubiquity of organophosphate esters in products and materials (Hartmann et al., 2004; Patisaul et al., 2021; Sheldon and Hites, 1978; Staaf and Östman,

* Corresponding author

E-mail address: philippe.glorennec@ehesp.fr (P. Glorennec).

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2005). Halogenated OPFRs are mostly used as flame retardants, with the intention of either minimizing the risk of a fire starting, or reducing the spread of fire (European Flame Retardants Van der Veen and de Boer, 2012; European Flame Retardant Association, 2007), while non-halogenated OPFRs are mostly used as plasticizers. OPFRs are widely used in cars, electronics, construction materials, furniture, nail polishes, and textiles (Andresen et al., 2004; Blum et al., 2019; Patisaul et al., 2021; Stapleton et al., 2009; Van der Veen and de Boer, 2012). OPFRs are not chemically bound in products and can be released into the environment via volatilisation, leaching and/or abrasion. Thus, they can be found in biota, sediment, soil and water, as well as in indoor environments (especially dwellings), where people spend the vast majority of their time (Chupeau et al., 2020; Pantelaki and Voutsas, 2021; Van der Veen and de Boer, 2012; Wei et al., 2015). A large prevalence of exposure to OPFRs can thus be expected, including among pregnant women and children. Since OPFRs are semi-volatile, they are regularly found in household air and dust, especially in Europe (Ballesteros-Gómez et al., 2016; Bergh et al., 2011; Björnsdotter et al., 2018; Cequier et al., 2014a; Chupeau et al., 2020; Coelho et al., 2016; Harrad et al., 2016; Langer et al., 2016; Persson et al., 2018; Sugeng et al., 2017; Vykoukalová et al., 2017; Wong et al., 2018; Zhou et al., 2017), and people can thus be exposed by inhalation, skin contact, or dust ingestion (Cequier et al., 2015; Hoffman et al., 2015). Studies on rodents have found that OPFRs are neurotoxic via non-cholinergic pathways, including disruption of both glutamate and gamma-aminobutyric acid (GABA) and of the endocrine system, whereas organophosphorus pesticides do seem to be neurotoxic via cholinergic pathways (Patisaul et al., 2021). Because they may be exposed to OPFRs during a critical period of development (such as in utero and during the first years of life, as reviewed by Chupeau et al., 2020), this raises the question of the health effects of OPFRs on children. Thanks to recent analytic progress and its advantages in considering all sources and routes of exposure, chemical measurement of human biological samples is an increasingly popular tool used in assessing human exposure. Previous European studies have found OPFRs and their metabolites in human biological matrices such as: breast milk (Beser et al., 2019; Sundkvist et al., 2010), urine (Cequier et al., 2015, 2014b; Fromme et al., 2014; Reemtsma et al., 2011; Schindler et al., 2009; Van den Eede et al., 2013; Völkel et al., 2018) and hair (Kucharska et al., 2015a). Human hair analysis is both non-invasive and has the advantages of offering simple and cost-effective sampling, transport and storage as well as sample stability, access to temporal exposure patterns by segmental analysis, and information on short- to long-term exposure to several environmental contaminants (Esteban and Castaño, 2009). Because the hair root is irrigated with blood vessels, chemical contaminants present in the blood stream are incorporated into the internal structure of hair during hair synthesis in the scalp. Exposure information stored in hair is thus very stable over time, and analysis of a 1 cm length of hair is enough to assess average exposure over a 1-month period (Hajeb et al., 2022). Hair is a promising biological matrix for assessing chronic exposure, and thanks to the increased sensitivity provided by the newest analytical systems (Kucharska et al., 2015a, 2015b; Martinez et al., 2021; Peng et al., 2021; Tang et al., 2021; Zhao et al., 2021), is now accessible for organic contaminants (including OPFRs). Hair is thus beginning to be used in epidemiologic surveys, especially for flame retardants (Poon et al., 2018). Because of the relatively short biological half-lives of organophosphate esters, their urinary metabolite concentrations reflect short-term exposure, while OPE levels in hair better reflect long-term exposure because of the low metabolic activities of organophosphate esters in these matrices (Yang et al., 2022).

The aims of this study are to estimate both prevalence and levels of pre- and post-natal exposure to OPFRs in children in France, using OPFR concentrations found in the hair of pregnant women and their 3.5-year-old children respectively, and to explore the role of sociodemographic characteristics, residential building characteristics, and co-exposures to PBDEs as determinants of exposure.

2. Material and methods

2.1. Population

ELFE (Etude longitudinale française depuis l'enfance) is a French national birth cohort. Its objective is to study determinants of the development, health and socialisation of children from birth to adulthood, using a multidisciplinary approach. A total of 349 maternity units (from private or public hospitals) were randomly selected from across metropolitan France, and the children were recruited at birth from the 320 maternity units that agreed to participate. Recruitment took place during 25 days in 2011, grouped into four periods over the year (April 1 – April 4, June 27 – July 4, September 27 – October 4 and November 28 – December 5). Inclusion criteria were single or twin live births at ≥ 33 weeks of gestation, mother ≥ 18 years old with no plans to leave metropolitan France within 3 years, and informed consent signed by either both parents or just the mother, with the father being informed of his right to deny consent for participation (Charles et al., 2020). A total of 18,329 mother-child pairs were recruited.

Biological samples, including hair, were collected from women at birth, at a subsample of 154 maternity units (of 211 that were eligible). These maternity units were selected for their expected number of deliveries (average > 500 deliveries per year) and their proximity (< 150 km) to the biological treatment and storage units made available by the French blood agency. Biological samples were available for women included during the last three periods of recruitment (from June to December in 2011). 2,956 maternal hair samples were collected. These hair samples were cut with scissors in the occipital region (behind the head), at the hairline. The hair strand was attached by paper clip to a cardboard sheet placed in an envelope at room temperature. Data concerning socio-demographic status, family life, parental health, behaviour and life values were collected in the course of a face-to-face interview at birth (Charles et al., 2020).

When the children were 3.5 years old, data concerning day care and school as well as child environmental exposures were collected via telephone interview. For 9,293 children, home visits were specifically organised at this stage of follow-up, to assess the children's cognitive function. Non-invasive biological samples (including hair) were collected from 2,044 children for whom maternal biological samples had already been collected at birth. In families for which both maternal urine and hair samples at inclusion were available, we also obtained a home dust sample (Charles et al., 2020). A total of 74 dust samples were available for our analyses.

Hair strands from mothers and children were cut as close as possible to the scalp, using an identical procedure, before being placed in individual envelopes and shipped to the biobank for storage at ambient temperature (Béranger et al., 2018).

Assuming a hair growth rate of 1 cm per month, we selected all women who had a length of hair strand > 7 cm and a mass of hair strand greater than or equal to 25 mg to ensure detection, and where a British Ability Scale (BAS) Picture Similarities test was available for her child ($n = 397$), in anticipation of a future epidemiological study. OPFR concentration in the first 7 cm (proximal) from maternal hair samples allowed estimation of integrated exposure during the 7 months of pregnancy known as pre-natal exposure. Their children were included if the child's hair strand was greater than or equal to 25 mg ($n = 265$). Post-natal exposure was estimated by the OPFR concentration measured from these hair samples. We excluded seven mothers and three children for whom there was no concentration available for at least one chemical. We also excluded 2 mothers and three children for whom statistical weight was not available at birth and at 3.5 years, respectively. In the end, our sample comprised 388 mothers and 259 children (Fig. 1). During the home visit at 3.5 years dust samples were collected by the investigator (from the vacuum cleaner and the floor of the room where the child played most often). These were placed in a zipped bag and then in a black bag for protection from light (Blanchard et al., 2014; Charles

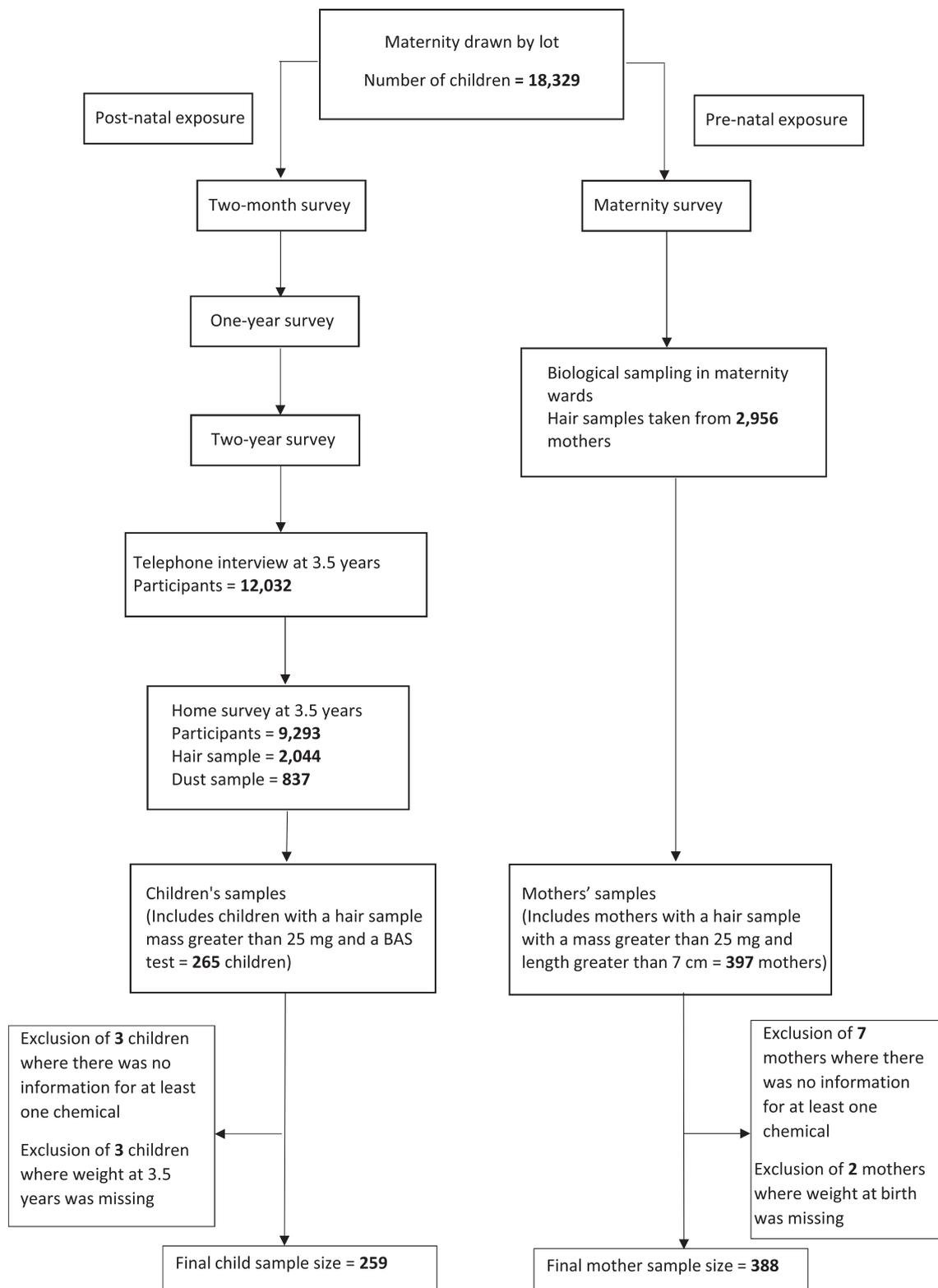


Fig. 1. Mother and child recruitment in the ELFE cohort, for evaluation of pre- and post-natal exposure.

et al., 2020). Of the 74 dust samples available for our study participants, 50 were randomly selected.

2.2. Choice of OPFRs of interest and choice of other flame retardants

The OPFRs were prioritised according to European production (or import tonnage) and their chemical properties facilitating exposure; of

the top-ranking chemicals (Niang et al., 2019), fifteen were measured simultaneously: diethyl ethyl phosphonate (DEEP), ethylhexyl diphenyl phosphate (EHDPP), tris(2-butoxyethyl) phosphate (TBEP), tri-*n*-butyl phosphate (TBP), tris(2-chloroethyl) phosphate (TCEP), tris(2-chloropropyl) phosphate (TCPP), tris(1,3-dichloro-2-propyl) phosphate (TDCPP), tris(2-ethylhexyl) phosphate (TEHP), triethyl phosphate (TEP), tri-*m*-cresyl phosphate (TMCP), trimethyl phosphate (TMP), tri-

o-cresyl phosphate (TOCP), tri-isopropyl phosphate (TIPP), triphenyl phosphate (TPP) and trixylenyl phosphate (TXP). To study potential co-exposures to other flame retardants, eight PBDEs (BDE 28, 47, 85, 99, 100, 119, 153 and 154) were also measured in these same hair samples from mothers and children, as well as in dust. BDE₂₀₉ was also measured in maternal hair samples, though not (for economic reasons) in children's hair samples.

2.3. Chemical analyses

Hair and dust samples were analysed by the LERES (Laboratory for Study and Research into the Environment and Health) at the French School of Public Health (EHESP, Rennes, France). A detailed description of the analytical methods used (including quality assurance and quality control) is available elsewhere (Yon et al., 2022) and is briefly described below.

Approximately 30 to 50 mg of each (unwashed) hair sample was accurately weighed and transferred to a 5 mL stainless steel grinding jar, using one 10 mm ball per jar. Grinding was performed in the mixer mill MM400 (Retsch GmbH, Haan, Germany) for 10 min at 25 Hz. The resulting hair powder was transferred into an amber glass vial, which was then sealed and stored at $-18\text{ }^{\circ}\text{C}$ until the time of chemical analysis.

Dust was passed through a pre-cleaned (dichloromethane) 250 μm stainless steel sieve using a Retsch AS 200 vibratory sieve shaker (Retsch GmbH, Haan, Germany) to remove coarse material (cotton and debris). The sieved dust was then stored at $-18\text{ }^{\circ}\text{C}$ in a hermetically sealed 20 mL amber glass flask until the time of chemical analysis.

Target chemicals were extracted from the hair and settled dust samples using a pressurised liquid extractor (PLE) ASE (Accelerated Solvent Extractor) 350 (Dionex Corporation, Sunnyvale, USA). This procedure was adapted from a previous study (Mercier et al., 2014). Briefly, 20–25 mg of hair powder or settled dust was accurately weighed and mixed with 2.4 g of pre-conditioned Celite® 545. The mixture was then loaded into a 5 mL stainless steel extraction cell. After the addition of internal standards (ISTDs), the extraction process was performed with dichloromethane, then repeated once using fresh solvent. The two organic extracts were combined, transferred into clean glass tubes and concentrated to 0.5 mL at $30\text{ }^{\circ}\text{C}$ under a nitrogen stream, using a N-EVAP 111 Organomation Nitrogen Evaporators. Concentrated extracts were transferred into 1.5 mL amber glass vials (with aluminium caps fitted) with a PTFE/silicon/PTFE septum, and stored at $-18\text{ }^{\circ}\text{C}$ prior to analysis by GC/MS/MS. Analyses were performed using a 7890B GC system coupled to a 7010B GC/MS Triple Quad (Agilent Technologies, Santa Clara, California, United States) operated in electron impact ionization (EI) mode (70 eV). The GC system was equipped with a 7693 Autosampler and a split/splitless (SSL) injector fitted with a 4.0-mm I.D. single taper borosilicate glass liner with deactivated wool (Siltek deactivation) supplied by Restek Corporation (Bellefonte, Pennsylvania, United States). Calibration samples and sample extracts were injected (1 μL) in the splitless mode ($250\text{ }^{\circ}\text{C}$). Helium was used as the column carrier gas, at a constant flow rate of 1.0 mL/min. Chromatographic separation was performed on an Rtx®-PCB capillary column (30 m length \times 0.25 mm I.D., 0.25 μm film thickness) supplied by Restek Corporation (Bellefonte, Pennsylvania, United States), using the following oven temperature programme: $37\text{ }^{\circ}\text{C}$ (hold 1.85 min), first ramp at $30\text{ }^{\circ}\text{C}/\text{min}$ to $250\text{ }^{\circ}\text{C}$ (hold 8.5 min), second ramp at $20\text{ }^{\circ}\text{C}/\text{min}$ to $320\text{ }^{\circ}\text{C}$ (hold 8 min to reach an analysis time of 28.95 min). The MSD transfer line, ion sources and quadrupole temperatures were fixed at 315, 270 and $150\text{ }^{\circ}\text{C}$, respectively. The mass spectrometer (triple quadrupole) was operated in multiple reaction monitoring (MRM) mode. The two most intense and specific MRM transitions of each compound (quantifier and qualifier transitions) were monitored for identification, confirmation and quantification.

2.4. Selection of potential exposure determinants

Potential determinants of OPFRs exposure were chosen, a priori, on the basis of the literature. Some are related to socioeconomic and health status: parental education level, household income, BMI (Doherty et al., 2019), number of people living in the dwelling (Percy et al., 2020). Some are related to the building, such as construction date (Canbaz et al., 2016), flooring material and aeration (Araki et al., 2014). A further criterion was data availability in the ELFE survey. (Araki et al., 2014; Brommer et al., 2012; Canbaz et al., 2016; Carignan et al., 2018; Castorina et al., 2017; Cequier et al., 2015; Coelho et al., 2016; Deziel et al., 2018; Hoffman et al., 2017; Larsson et al., 2018; Meeker et al., 2013; Soubry et al., 2017; Sugeng et al., 2017; Wong et al., 2018; Zheng et al., 2017). Finally, concerning potential sources of OPFRs exposure and co-exposures, six variables were built: renovation work in dwelling in the past year for pre- and post-natal exposure (from either the maternity survey or the 3.5 years survey, respectively), construction year of home, type of floor in child's room and duration of breastfeeding for post-natal exposure, and BDE₄₇, BDE₂₀₉, exposure for pre- and post-natal exposure (BDE₄₇ only). Concerning the potential health and socio-demographic determinants for both pre- and post-natal exposures, we used maternal education level, household income, number of persons living in the home and pre-pregnancy maternal BMI. For post-natal exposure, we were also able to consider lifestyle determinants and housing characteristics: time spent outside by the child, time spent by the child using electronic devices, number of windows in the child's room, ventilation in the child's room. We also considered season of sampling.

2.5. Statistical analyses

The ELFE cohort is based on a two-stage random stratified sampling design (stratified for maternity units and for selected days). Initial weights from ELFE cohort sampling and correction for unit non-response at baseline were available for both the maternity surveys (pre-natal exposures) and the 3.5 year surveys (post-natal exposures).

The weighting process comprised three steps. First, we created Response Homogeneity Groups (RHGs) to reduce non-response bias. We obtained each participant's probability of inclusion in our study. The inverse of this probability was then multiplied by the initial weight from ELFE cohort sampling. These weights were calibrated to reduce the variance of estimators. Second with respect to the French population, using the margins of the National Perinatal Survey (Blondel and Kermarrec, 2011). All of the following results were weighted, with the exception of correlations between OPFR levels in children's hair and house dust. The number of dust samples was too small to compute weighted correlations and obtain results for the French population. The unweighted results are available in the [supplementary materials](#).

Potential determinants had low missing data, with the exception of year of house construction information (collected at the maternity survey, for pre-natal exposure) which had $>95\%$ of missing data and was therefore not included in our analyses. The type of flooring in the child's room was the variable with the highest percentage of missing data (8%). Variables with $<5\%$ of missing data were imputed by the mode. Variables (maternal education level, household income, construction year of house (collected at 3.5 years), type of floor in the child's room) with missing data $>5\%$ and $<8\%$ were imputed using prediction via logistic regression with the two most-correlated other variables.

Left-censored OPFR concentrations measured in dust and hair samples (up to 80 % of censored data) were imputed (Helsel, 2011); those with $>80\%$ of censored data were considered for data description only, rather than for correlations nor determinants analysis. For each chemical, we used the maximum-likelihood estimation method (MLE) to estimate parameters of lognormal probability distribution (Helsel, 2011). Then, for each LOD in each chemical, censored data were imputed by random values between 0 and the LOD from this estimated distribution

(Jin et al., 2011). This method allowed us to take into account the presence of multiple LODs in each chemical.

The geometric mean and geometric standard deviation and median (2nd quartile), 1st and 3rd quartile were calculated. Since these were not (according to the Shapiro-wilk test) distributed normally, OPFR concentrations in hair and dust were log-transformed to ensure normality. Correlations between OPFR concentrations in each population and between mother-child pair levels were assessed using Pearson's correlation matrices. Correlations between OPFR concentrations in children's hair and house dust were also analysed using Pearson's correlation.

Linear associations between log-transformed hair concentrations and potential determinants were tested using univariate analysis.

SAS software 9.4 was used to impute censored data and describe OPFR concentrations. The CALMAR macro available in SAS software 9.4 was used for calibration (Deville et al., 1993). Weighted results were calculated using the SURVEY package from R software V4.0.

2.6. Ethical issues

Ethical approvals for data collection in maternity units, and for each data collection wave during follow-up, were obtained from the French national advisory committee on information processing in health research (CCTIRS: Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé), the French national data protection authority (CNIL: Commission Nationale Informatique et Liberté) and, in the case of invasive data collection (such as biological sampling) the committee for the protection of persons engaged in research (CPP: Comité de Protection des Personnes). The ELFE study was also approved by the national committee for statistical information (CNIS: Conseil National de l'Information Statistique) (Charles et al., 2020).

Table 1

Characteristics of pregnant women and children included in our study, and in the French population in 2011*.

Determinants	Modalities	Study sample (unweighted results) (%)		France (weighted results) (%)	
		Mother-child pairs (n = 259)	Mothers (n = 388)	Mother-child pairs	Population of Mothers
Sex of child^b	Boy	40.9	53.6	44.1	49.8
	Girl	59.1	46.4	55.9	50.2
Mother's age^{a b}	NA (%)	1.1	0	1.1	0
	25–30	18.5	43.5	24.8	45.8
	31–35	38.7	34.8	40.1	34.0
	36–40	30.1	17.8	24.2	15.6
	>40	12.7	3.9	10.9	4.6
	NA (%)	0.8	0	0.7	0
Mother's BMI^b	<18.5	6.9	8.2	4.4	8.9
	18.5 - < 25	70.7	69.1	69.1	62.0
		15.1	14.7	12.5	12.7
	25 - < 30	7.3	8.0	14.0	16.3
	30 or more	0.8	1	0.7	1
	NA (%)				
Mother's education level^{a b}	<= BAC	23.6	26.5	44.3	46.1
	BAC + 2	23.1	26.3	16.6	18.8
	> BAC + 2	53.3	47.2	39.1	35.1
	NA (%)	0.8	0.8	0.7	0.8
Father's education level^{a b}	<= BAC	42.5	43.5	61.6	58.0
	BAC + 2	20.8	20.4	16.7	15.7
	> BAC + 2	36.7	36.1	21.7	26.3
	NA (%)	3.1	5	3	5
Monthly household Income (euros)^{a b}	<=2,999	22.8	33.5	39.0	52.9
	[3,000; 3,999]	27.4	31.2	27.3	22.7
	>= 4,000	49.8	35.3	33.7	24.1
	NA (%)	4.5	5.5	4.6	5.5
Smoking status during pregnancy^b	Not a smoker	80.7	82.2	75.9	78.8
	Smoker	19.3	17.8	24.1	21.2
	NA (%)	0.3	0.8	0.7	0.8
Alcohol consumption during pregnancy^b	No	72.9	75.3	80.0	79.1
	Yes	27.1	24.7	20.0	20.9
	NA (%)	0.8	0.3	0.3	0.3
Duration of breastfeeding (months)^a	<= 1	37	X	36.8	X
] 1; 4]	30.9		27.7	
	>4	32.1		35.5	
	NA (%)	0.08		0.1	
Season when hair was collected^{ab}	Summer	0	31.44	0	31.9
	Autumn	33.2	68.6	37.7	68.1
	Winter	66.8	0	62.3	0
	Spring	0	0	0	0
	NA (%)	1.9	3.4	1.9	3.4
Number of people in household^{ab}	<= 3 people	24.3	44.3	27.7	45.7
	4 people	48.6	37.4	41.6	36.2
	>5 people	27.1	18.3	30.7	18.1
	NA (%)	0.08	3.4	0.1	3.4

*: Excluding French overseas territories.

N: number; SD: standard deviation; NA: percentage of missing data for 383 mothers and 259 children; ^a variables present in the 3.5-year questionnaire; ^b variables present in the maternity questionnaire or in the two-month questionnaire; x: data not collected in either the maternity survey or the 2-month survey; the percentages of the modalities exclude NA.

3. Results

3.1. Population

Characteristics of mothers (for pre-natal exposures) and children (for post-natal exposures) are presented in [Table 1](#), with unweighted and weighted estimations. Unweighted results describe the participants included in our analyses (388 mothers and 259 children). Weighted results describe the entire population of women who gave birth in France in 2011, and their children at 3.5 years. The population of mothers and the population of mother–child dyads differed in terms of several sociodemographic characteristics: mothers among the population of the mother–child dyads were older and better-educated than the population of mothers. The population of the mother–child dyads group was also characterized by higher household income per month and a higher number of persons in the household. For other characteristics listed in [Table 1](#), differences were fewer. In the population of mothers, mean age at inclusion was 31 years (standard deviation: 0.5). During pregnancy, 79 % of French mothers did not smoke, 79 % did not drink alcohol and 16 % were obese (BMI ≥ 30 kg/m²) before the pregnancy in question. For more than half of the fathers, educational attainment was below degree level, and for 53 % of families, monthly household income was <2,999 euros. A slightly higher proportion of girls was observed (50.2 % vs 49.8 %) among the children.

3.2. Pre- and post-natal exposure to OPFRs

Pre- and post-natal exposure to OPFRs are presented in [Table 2](#), while unweighted results are presented in [Table S2](#). For pre-natal exposure, TMP was not detected. Five OPFRs (DEEP, TEHP, TiPP, TOCP and TXP) were detected in < 5 % of hair samples. EHDPP, TBEP, TBP, TCEP, TCPP, TDCPP, TEP, TMCP and TPP were detected in > 20 % of hair samples. For post-natal exposure, TXP was not detected, five OPFRs (DEEP, TEHP, TiPP, TOCP and TMP) were detected in < 5 % of

hair samples. EHDPP, TBEP, TBP, TCEP, TCPP, TDCPP, TEP, TMCP and TPP were detected in > 20 % of hair samples; their concentrations were imputed and used in later analyses. The highest geometric mean was measured for TCPP in both pre-natal (geometric mean: 272 ng/g, IC95%: 269; 274) and post-natal (geometric mean: 250 ng/g; IC 95 %: 247; 252) exposure. The highest concentration was observed for TCPP with P₉₅: 822 and 631 ng/g for pre- and post-natal exposures, respectively. There is no clear pattern between post-natal and pre-natal exposures, post-natal being higher for half of the OPFRs (EHDPP, TBEP, TCEP, TDCPP and TPP), and lower for others. Pre- and post-natal PBDE exposures are available in the [supplementary material](#) (Tables S7-8) as well as PCB exposures (Tables S7-8) and correlations ([Fig S8–11](#)).

3.3. Correlations of children's exposure to OPFRs, and OPFR concentration in house dust

[Figs. S1 and S2](#) in the [supplementary material](#) show correlation matrices for OPFRs with a detection rate > 20 % (9 OPFR for pre- and post-natal exposure). Many positive correlations can be observed in the pre-natal correlation matrix. Correlation coefficients range from −0.1 (between TCEP and TEP) to 0.5 (between EHDPP and TPP). Many positive significant (p < 0.5) correlations can be observed for post-natal exposure, with no negative correlations, up to 0.45 (between TCPP and TPP). [Fig. S3](#) presents OPFR correlations between pre- and post-natal exposure. Some weak correlations were observed (from −0.2 for TBP to 0.26 for TCPP). As displayed in [Fig. S7](#), the only post-natal exposure significantly correlated to OPFR dust concentration was TEP, with very weak association (r = −0.02, p.value < 0.05).

3.4. OPFR exposure determinants

The associations between children's pre- and post-natal exposure to OPFRs, and their potential determinants, are shown in [Table 3](#) and [Table 4](#). Relationships (β) are for (log)transformed concentrations.

Table 2

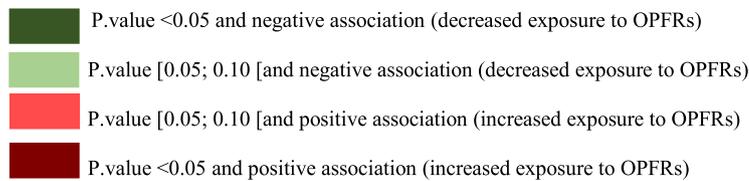
Pre- and post-natal exposure of children to OPFR, measured by concentrations (ng/g) in mothers' hair at birth in 2011 and in the hair of children aged 3.5 years old in 2014–2015, in France.

OPFR	CAS number	Populations	% > LOD	Min	P25	P50	P75	P95	Max	Geometric mean [IC95%]
EHDPP	1241-94-7	Children	95	11	40	73	204	244	4,423	83.7 [81.6; 85.9]
		Mothers	92.2	0.7	22	35	58	182	51,204	39.1 [37.; 41.2]
DEEP	78-38-6	Children	1.9	–	–	–	–	–	–	–
		Mothers	2.9	–	–	–	–	–	–	–
TBEP	78-51-3	Children	49.8	0.8	24	53	116	281	2,082	53.7 [51.5; 56.0]
		Mothers	25.3	31	34	35	37	225	2,034	46.2 [44.6; 48.8]
TBP	126-73-8	Children	45.9	4.5	15	20	26	33	89	20.4 [18.3; 22.4]
		Mothers	92.7	9.5	27	35	45	61	84	34.5 [32.4; 36.5]
TCEP	115-96-8	Children	68.3	0.9	9.2	15	28	49	623	15.6 [13.4; 17.8]
		Mothers	61.3	0.2	7.1	13	23	102	939	14.2 [12; 16.4]
TCPP	13674-84-5	Children	66.4	37	159	246	399	631	11,848	250 [247; 252]
		Mothers	74.7	14	203	260	401	822	3,155	272 [269; 274]
TDCPP	13674-87-8	Children	97.3	3.0	32	79	161	542	2,343	85.3 [83.0; 87.5]
		Mothers	95.3	2.4	23	47	109	456	16,689	54.4 [52.2; 56.6]
TEHP	78-42-2	Children	1.1	–	–	–	–	–	–	–
		Mothers	1.3	–	–	–	–	–	–	–
TEP	78-40-0	Children	67.9	2.3	9.2	13	18	34	153	13.5 [11.4; 15.6]
		Mothers	95.3	4.0	22	49	77	130	238	42.4 [40.3; 44.5]
TiPP	513-02-0	Children	0.4	–	–	–	–	–	–	–
		Mothers	0.5	–	–	–	–	–	–	–
TMCP	563-04-2	Children	38.2	0.1	1.0	3.5	4.4	29	1,229	2.9 [0.6; 5.2]
		Mothers	78.3	0.1	5	10	27	205	18,194	12.8 [10.5; 15.1]
TMP	512-56-1	Children	0.39	–	–	–	–	–	–	–
		Mothers	0	–	–	–	–	–	–	–
TOCP	78-30-8	Children	1.16	–	–	–	–	–	–	–
		Mothers	0.8	–	–	–	–	–	–	–
TPP	115-86-6	Children	100	8.0	44	76	143	242	1,874	77.5 [75.2; 79.5]
		Mothers	99.5	5.4	35	61	106	793	8,621	69.7 [67.5; 71.9]
TXP	25155-23-1	Children	0	–	–	–	–	–	–	–
		Mothers	0.5	–	–	–	–	–	–	–

N.B: Displayed concentrations were imputed when % > LOD was > 20 %.

Table 3
Determinants of children’s pre-natal exposure to OPFR, France (2011).

Determinants	Modalities	EHDPP	TBEP	TBP	TCEP	TCPP	TDCPP	TEP	TMCP	TPP
Home renovation work before birth	No (ref)									
	Yes									
Maternal BDE ₄₇ concentration at birth (ng/g)	≤ 0.43 ng/g (ref)									
]0.43; 1.23]									
	>1.23									
Maternal BDE ₂₀₉ concentration at birth (ng/g)	≤ 5.4 ng/g (ref)									
]5.4; 11.8]									
	>11.8									
Maternal education level at birth	≤ BAC (ref)									
	BAC +2									
	> BAC+2									
Monthly household income at birth (euros)	≤ 2,999 € (ref)									
]3,000; 3,999] €									
	>=4,000 €									
Number of persons in the household at birth	≤ 3 people (ref)									
	4 people									
	>=5 people									
Pre-pregnancy BMI	18.5; 25] (ref)									
	< 18.5									
]25; 30 [
	>30									
Season of maternal hair sampling	Autumn (ref)									
	Summer									



With regard to potential sources of OPFR exposure and co-exposures, renovation work undertaken in the home during the year before birth was associated with a p-value < 5 % and higher pre-natal exposure to TBP ($\beta = 0.08 [0.00; 0.16]$), TCEP ($\beta = 0.37 [0.13; 0.60]$), TCPP ($\beta = 0.15 [0.01; 0.29]$), TDCPP ($\beta = 0.53 [0.26; 0.79]$), TMCP ($\beta = 0.43 [0.09; 0.77]$) and TPP ($\beta = 0.43 [0.22; 0.65]$). This trend was observed for post-natal exposure for TCEP and TDCPP, though without statistical significance. The presence of lino (for TBEP and TPP), carpet (TCEP) or parquet (TBEP, TCPP and TPP) in the child’s room was significantly associated with higher post-natal exposure to some OPFRs (TBEP, TCEP, TCPP and TPP), in comparison with tiles. Year of home construction was not associated with post-natal exposure to OPFRs. Children breastfed for >4 months had lower exposure to TEP ($\beta = -0.26 [-0.47; -0.06]$) than children breastfed for <1 month. Pre-natal exposure to BDE₄₇ (3rd tertile > 1.23 ng/g, vs 1st tertile) was associated with higher pre-natal exposure to TBP ($\beta = 0.18 [0.08; 0.29]$), TCEP ($\beta = 0.42 [0.09; 0.76]$), TCPP ($\beta = 0.43 [0.24; 0.62]$), TEP ($\beta = 0.30 [0.04; 0.50]$), TMCP ($\beta = 1.26 [0.80; 1.72]$) and TPP ($\beta = 0.32 [0.02; 0.63]$). Post-natal exposure to BDE₄₇ (3rd tertile > 1.23 ng/g) was also associated with post-natal exposure to TBP ($\beta = 0.13 [0.01; 0.26]$) and TCPP ($\beta = 0.46 [0.22; 0.71]$), as well as to EHDPP ($\beta = 0.36 [0.03; 0.70]$). Higher pre-natal exposure to BDE₂₀₉ concentration (3rd tertile > 11.8 ng/g, vs 1st tertile) was significantly associated with an increase in all OPFR pre-natal exposure (p.value < 0.05), with the exception of TCPP and TEP.

The highest maternal education level (>high school) was significantly associated with lower pre-natal exposure to EHDPP ($\beta = -0.27 [-0.47; -0.07]$) and post-natal exposure to TDCPP ($\beta = -0.43 [-0.76; -0.10]$) and TEP ($\beta = -0.21 [-0.40; -0.01]$) and with higher pre-natal exposure to TCPP ($\beta = 0.19 [0.03; 0.35]$). The highest household income

(3rd tertile: > 4,000 euros per month) was associated with lower pre-natal exposure to EHDPP ($\beta = -0.40 [-0.60; -0.17]$), TEP ($\beta = -0.36 [-0.56; -0.16]$) and TMCP ($\beta = -0.64 [-1.05; -0.22]$) and lower post-natal exposure to TBP ($\beta = -0.20 [-0.32; -0.09]$), TDCPP ($\beta = -0.49 [-0.84; -0.14]$) and TEP ($\beta = -0.34 [-0.54; -0.13]$). Living in a home with five persons or more was associated with lower pre-natal exposure to TBP ($\beta = -0.19 [-0.29; -0.08]$) but higher EHDPP ($\beta = 0.27 [0.03; 0.52]$) and TBEP ($\beta = 0.20 [0.001; 0.40]$) and lower post-natal exposure to TMCP ($\beta = -0.66 [-1.19; -0.12]$) compared to homes with three persons or less. Pre-pregnancy obesity (vs normality) was significantly associated with higher pre-natal exposure to all OPFRs, though not with TBEP. No such association was observed for post-natal OPFR exposure, other than for TBEP, for which exposure was lower ($\beta = -0.74 [-1.17; -0.31]$).

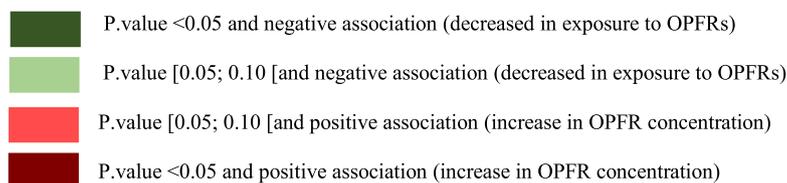
When considering lifestyle determinants and housing characteristics as potential determinants of post-natal exposure, we observed that children spending >4.5 h per week outdoors had higher exposure to TDCPP ($\beta = 0.54 [0.19; 0.90]$) and children using electronic devices between 2 and 4 h per week had lower exposure to TBEP ($\beta = -0.45 [-0.85; -0.04]$), TCEP ($\beta = -0.45 [-0.77; -0.13]$), TDCPP ($\beta = -0.53 [-0.91; -0.15]$) and TPP ($\beta = -0.34 [-0.63; -0.04]$) compared with children spending <2 h per week using electronics devices. This lower exposure to TPP was also observed for children using electronic devices >4 h per week ($\beta = -0.30 [-0.57; -0.04]$).

The presence of two windows (vs one) in the child’s bedroom was associated with higher exposure to TCEP ($\beta = 0.38 [0.03; 0.74]$), as well as presence (vs absence) of ventilation in the bedroom, with higher exposure to TDCPP ($\beta = 0.36 [0.03; 0.69]$).

The summer season (compared to the autumn season) was associated

Table 4
Determinants of children’s post-natal exposure to OPFR, France (2014–2015).

Determinants	Modalities	EHDPP	TBEP	TBP	TCEP	TCPP	TDCPP	TEP	TMCP	TPP
Home renovation work at 3.5 years of child during the year before the survey	No (ref)									
	Yes									
Residential home year construction at 3.5 years of child	> 2000 (ref)									
	[1970; 2000]									
	< 1970									
Type of floor in the children's room	Tiles (ref)									
	Lino									
	Carpet									
	Parquet									
Duration of breastfeeding	<=1 month (ref)									
] 1 ; 4] months									
	>4 months									
Children’s BDE ₄₇ concentration at 3.5 years(ng/g)	<= 0.43 ng/g (ref)									
]0.43; 1.23]									
	>1.23									
Maternal education level at 3.5 years of child	<= BAC (ref)									
	BAC +2									
	> BAC+2									
Monthly household income at 3.5 years of child (euros)	<=2,999 € (ref)									
	[3,000; 3,999] €									
	>=4,000 €									
Number of persons in the household at 3.5 years of child	<=3 people (ref)									
	4 people									
	>=5 people									
Pre-pregnancy BMI	[18.5; 25] (ref)									
	< 18.5									
	[25; 30 [
	>30									
Time spent outside by children at 3.5 years (hours/week)	<=4.5 hours (ref)									
]4.5; 7] hours									
	>7 hours									
Time spent using electronic devices by children at 3.5 years (hours/week)	<=2 hours (ref)									
]2; 4] hours									
	> 4 hours									
Number of windows in child’s room	1 window (ref)									
	2 windows									
Ventilation in child’s room	Yes (ref)									
	No									
Season of children’s hair sampling at 3.5 years	Autumn (ref)									
	Winter (child)									



with either higher pre-natal exposures for EHDPP ($\beta = 0.41$ [0.22; 0.60]), TDCPP ($\beta = 0.30$ [0.02; 0.60]), TEP ($\beta = 0.19$ [0.01; 0.36]) and TMCP ($\beta = 0.44$ [0.07; 0.80]) or with lower pre-natal exposure for TBEP ($\beta = -0.21$ [-0.36; -0.05]. The winter season (compared to the autumn season) was associated with lower post-natal exposure to TDCPP ($\beta = -0.54$ [-0.84; -0.25]) and TPP ($\beta = -0.25$ [-0.48; -0.01]).

4. Discussion

To our knowledge, this is the first study to describe pre- and post-

natal OPFRs exposure in children in France, and finds exposure to several OPFRs to be ubiquitous.

We used OPFR concentrations in the hair of pregnant women and their 3.5-year-old children to estimate exposure. This is a non-invasive matrix, quite easy to collect and store, and reflects several months of exposure, reflecting the content of blood, and thus what the foetus may be exposed to; it has thus been proposed as an indicator of exposure (Kucharska et al., 2015a). A toxicological study on rats has shown that hair can provide a relevant assessment of exposure to contaminants (Appenzeller et al., 2017); these authors demonstrated, using cross-

sectional measurements, that the concentration of pesticides, including those that are organophosphorous, and their metabolites in hair was representative of the level of exposure in the experiments. For all chemicals detected in hair, the association between exposure and concentration in hair was always significant. For most compounds (including organophosphorus pesticides) the association between exposure intensity and the concentration of chemicals in hair was stronger than (or comparable to) that found in urine and plasma (Appenzeller et al., 2017). We are not aware of the existence of such a study for OPFRs. However, certain limitations prevent the wide application of hair as a matrix for human biomonitoring to flame retardants. For instance, only a small amount of hair can be sampled per individual (normally 0.05 to 0.2 g), and in addition, participants may not wish to donate hair. Also, the number of strands and their lengths (from 2 to 10 cm) were not homogeneous between children. Consequently, the hair-measurements of the 3.5-year-old children may reflect various exposure windows from the previous several months to about one year. Furthermore, interpretation of hair levels is not without ambiguity, as they reflect both external exposure (via deposition from air and dust) and internal exposure (through contact with blood at the hair follicle/root). As there is not yet any effective procedure capable of eliminating contamination that is exclusively external (Kucharska et al., 2015a), the hair used in our study was not washed. Distinguishing between these exposure routes can be difficult, especially when hair is used as an indicator of exposure to flame retardants, where the contribution made by atmospheric deposition cannot be ignored (Hajeb et al., 2022). However, (Kucharska et al., 2015a) found very weak or no correlation of OPFR concentrations in mothers' and children's hair and estimated that it indicates that the concentrations measured in the hair of mothers and children are not driven by the (minor) amount of dust deposited onto the hair surface.

A further limitation of the present study concerns censored exposure data. Since our study was exploratory, we decided to impute OPFR concentrations with a percentage of censored data of up to 80 %. However, the weighting process enables us to take the initial (ELFE) sampling design into account. In particular, large maternity units were oversampled, which is accounted for in the initial design weights. The weighting process also enables us to correct for unit non-response at the various steps of the survey. This is performed using the Response Homogeneity Groups method, and leads to a strong reduction of the non-response bias. Lastly, the weights are calibrated on margins from the French National Perinatal survey, which results in reduced variance of estimators. In all, the weighting process is key to describing pre- and post-natal OPFR exposure precisely for the entire population of children born in 2011 in France. Because our objective was descriptive, we did not correct for multiplicity of tests, and neither did we adjust the models.

The final limitation is related to data unavailability for some determinants – because ELFE is a generalist cohort, without any specific focus on flame retardants. Some major determinants, such as number of electronic devices in the household, (Sha et al., 2018) or cleaning frequency, (Canbaz et al., 2016; Cequier et al., 2015; Larsson et al., 2018) could not be studied. Cleaning frequency data was collected, but we decided not to use it because of high levels of missing data (>80 %).

The first strength of our study is the wide exposure period covering pregnancy. The hair root is irrigated by blood vessels, and chemical contaminants present in the blood stream are incorporated into the internal structure of hair during hair synthesis in the scalp. Exposure information stored in hair is very stable over time, and analysis of 1 cm hair length is accepted to assess average exposure over a 1-month period (Hajeb et al., 2022). Considering the human hair growth rate of 1 cm per month, and with a minimal length of 7 cm, we assessed children's OPFR exposure during at least 7 months of pregnancy.

The second strength of our study is that we were able to assess exposure to a wide variety of currently-used OPFRs (nine OPFRs in both the pre-natal and post-natal periods). In a Norwegian mother-child cohort, seven OPFRs were measured in the hair samples of both mothers

(n = 48) and children (n = 54) aged 6–12 years old, (collected simultaneously) between January and mid-May 2012 (Kucharska et al., 2015a). In our study, maternal hair samples were collected in 2011, with the children's samples being collected about 3.5 years later (between 2014 and 2015). In the Norwegian mother-child cohort, the highest median concentrations in mothers were observed for TCEP (median = 72 ng/g), TBEP (median = 65 ng/g), TPP (median = 52 ng/g) and TDCPP (median = 30 ng/g) whereas, in our study, the highest median concentrations were observed for TCPP (median = 246 ng/g), TPP (median = 61 ng/g) and TEP (median = 49 ng/g). In both studies, only TPP was observed in high and similar concentrations. Among the children of the Norwegian cohort, the highest median concentrations were observed for TBEP (median = 318 ng/g), TPP (median = 63 ng/g), TCEP (median = 59 ng/g) and TDCPP (median = 31 ng/g). In our study, the highest median concentrations were observed for TCPP (median = 246.2 ng/g), TCDPP (median = 79.6 ng/g), TPP (median = 76.5 ng/g) and EHDPP (median = 73.5 ng/g). TDCPP and TPP were observed in high (though differing) concentrations in both studies. We do not have a clear explanation for these differences in countries from the same economic market and studied at roughly the same time; many factors may be involved, since these phosphorous compounds have many uses. Earlier European studies measuring OPFRs in other human matrices (such as urine and breastmilk) found that the highest median concentrations were also observed for TBEP, both in the children's urine (2 ng/mL) (Fromme et al., 2014) and in breastmilk (14.8 ng/g of lipid weight) (Beser et al., 2019).

OPFRs have been used in baby products containing polyurethane foam, such as nursing pillows and changing mats (Fang et al., 2013; Hoffman et al., 2015; Stapleton et al., 2011). A Californian study reported that the most common flame retardant detected in baby products was TDCPP (detection frequency 36 %), followed by components (including TPP) typically found in the "Firemaster 550" commercial mixture (detection frequency 17 %) (Stapleton et al., 2011). Higher TBEP exposure to among children (in comparison to mothers) can also be explained by the particular higher-frequency hand-to-mouth behaviour of children. This OPFR is specifically used in floor polishes (Van den Eede et al., 2013; Wei et al., 2015), though we did not find any correlation between TBEP concentrations in post-natal exposures and house dust concentrations.

In the present study, correlations between pre- and post-natal exposures to OPFRs were very weak, with the highest correlation being for TCPP ($r = 0.27$). This was also observed by Kucharska et al., (2015). This absence of correlations might be explained by changes to habits or lifestyle (resulting in different sources of exposure) between pregnancy and the child reaching 3.5 years of age, or by different pathways of exposure between adults and children.

As in our study, Kucharska et al., (2015) assessed correlations between post-natal exposures and OPFR concentrations in house dust for TBEP, EHDPP and TDCPP, and found a significant association for TBEP only. In our study, a higher number of correlations between hair and dust were assessed, and the only (and weak) significant association was observed for TEP ($r = -0.02$, p .value = 0.00). House dust ingestion has not appeared as the main contributor to children's exposure to OPFRs in this study, even for TBEP (sometimes referred as TBOEP) for which dust is often considered as an important pathway (Chupeau et al., 2020). One possible explanation is, as observed in Australia (He et al., 2018), food is a major pathway for several OPFRs.

With regard to potential determinants of pre-natal exposure to OPFRs in our present study, co-exposures to other flame retardants such as BDE₂₀₉ and BDE₄₇ were most consistently associated. These positive associations can be explained by common sources, the indoor persistence of BDE₂₀₉ and/or by concomitant exposure to consumer products produced before and after restrictions on PBDE use came into force, and their replacement by OPFRs (Van der Veen and de Boer, 2012). These positive associations can also be explained by a high number of electronic devices or by furniture in households. In the present study, BDE₂₀₉

could not be measured in children's hair samples. Post-natal exposure to BDE₄₇ was also associated with high post-natal exposure to 3 OPFRs (EHDPP, TBP, and TCPP).

Of the personal and socio-demographic factors, higher household income was consistently associated with lower pre- or post-natal exposure to several OPFRs (EHDPP, TEP, TMCP, TBP, TDCPP) and a similar tendency was observed with the highest level of maternal education being associated with lower OPFR exposure (EHDPP, TDCPP, TEP). This suggests that a higher socioeconomic status might be associated with lower OPFR exposure. Findings from other studies on the relationship between socioeconomic status and OPFR are both scarce and inconsistent. (Phillips et al., 2018) did not observe a significant relation between mother education and exposure of children to OPFR, while (Hammel et al., 2021) noticed an influence of socioeconomic status for some. In their review of all types of flame retardants (mainly PBDEs) (Arvaniti and Kalantzi, 2021) noticed higher exposure to flame retardants in lower-income households, influenced by quality of domestic furniture, inadequate ventilation, dietary habits (such as ingestion of highly contaminated food or malnutrition) are considered important determinants. Interestingly, pre-pregnancy BMI higher than 30 kg/m² was associated with an increase of pre-natal exposure for all studied OPFRs except TBEP, suggesting either possible physiological mechanisms or a specific lifestyle influence. (Hoffman et al., 2017) did not observe such an association for metabolites of TDCIPP and TPHP, and observations on organophosphorus insecticides reported conflicting results (Pinos et al., 2021). Breastfeeding appears not to be a major determinant of OPFR exposure observed at 3.5 years.

The present study suggests that few housing characteristics are capable of impacting OPFR exposure. Home renovation work in the past year has consistently been associated with higher OPFR exposure (TBP, TCEP, TCPP, TDCPP, TMCP and TPP), suggesting a potential release by old materials and/or new items of furniture. Such an association was observed by (Cequier et al., 2015) for one OPFR in air, though not by (Araki et al., 2014) for OPFRs in dust. The presence of parquet or lino in the child's bedroom was associated with higher post-natal exposure to TBEP, as in (Araki et al., 2014)'s study; this can be explained by the use of this particular OPFR as a floor varnish (Van der Veen and de Boer, 2012; Wei et al., 2015). We did not have information about the number of pillows in the home, and were therefore unable to assess any associations between these potential determinants and post-natal exposure to OPFRs (specifically, TDCPP and TPP) found in high concentrations in children and used in the manufacture of pillows.

5. Conclusion

This study is the first to provide representative populational assessment of exposure to OPFRs at nationwide level in France. Our results show that these children were exposed, both during pregnancy and in their early years, to a variety of OPFRs, with a high prevalence of exposure for some: for instance EHDPP, TDCPP and TPP exposures were above the limit of detection for >90 % of both pre-and post-natal exposures. In addition to exposure prevalence, recent neurotoxic studies have shown OPFRs to be neurotoxic via non-cholinergic pathways including disruption of both glutamate and gamma-aminobutyric acid (GABA) and of the endocrine system (Patisaul et al., 2021); a better understanding of the resulting health effects is called for. Because this study was not specifically designed to identify the main determinants and sources of OPFRs exposure, additional research on this issue is needed, to help with setting up public policy aimed at reducing OPFRs exposure.

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CRedit authorship contribution statement

Z. Chupeau: Methodology, Formal analysis, Data curation, Writing – original draft. **F. Mercier:** Methodology, Writing – review & editing, Supervision. **E. Rouxel:** Methodology, Formal analysis. **B. Le Bot:** Methodology, Writing – review & editing, Supervision, Funding acquisition, Project administration. **G. Chauvet:** Methodology, Writing – review & editing. **T. Siméon:** Data curation, Methodology, Writing – review & editing. **N. Bonvallot:** Methodology, Writing – review & editing. **C. Zaros:** Investigation, Writing – review & editing. **C. Chevrier:** Methodology, Writing – review & editing, Supervision. **P. Glorion:** Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The authors do not have permission to share data.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2022.107435>.

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