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Assessing exposure of young children to common endocrine-disrupting chemicals in the home environment: a review and commentary of the questionnaire-based approach

Abstract

Background: Although infants and young children are particularly vulnerable to endocrine disrupting chemical (EDC) exposure, there is an absence of comprehensive exposure data for this age group. As young children spend the majority of their time indoors, improved methods of exposure assessment are needed to characterise the health risks from exposures in the home environment. Biologic assessment, which has been considered the gold standard for exposure assessment in recent years, is difficult to conduct in young children. Questionnaires are an alternative and indirect method of predicting exposure, which may overcome some of the limitations of direct exposure assessment.
Research problem: The feasibility of using a questionnaire-based approach to predict exposure of young children to EDCs in the home has yet to be comprehensively reviewed. Moreover, there is no one questionnaire that has been validated for predicting the exposure of infants to common EDCs in the home.
Aims and objectives: The aim of this review is to discuss the use and validation of the questionnaire-based approach to predict exposure of children to chemicals from three common classes of EDCs in the home, namely, plasticisers, flame retardants, and insecticides. We discuss the strengths and weaknesses of the questionnaire-based approach as well as the important pathways of exposure in the home environment, by which to guide the design and validation of future exposure questionnaires.
Results: The findings from our review indicate that the questionnaire-based approach is a valuable tool in the prediction of exposure to persistent organic pollutants, as well as to toxicants that have consistent patterns of exposure. With improvements to the design and validation process, the questionnaire-based approach may also prove to be a reliable instrument in predicting exposure to EDCs with short-half lives, including bisphenol A, phthalates, and pyrethroid and organophosphate insecticides.

Keywords: behaviour; BPA; diet; dust; hand-to-mouth behaviour; lifestyle; organophosphate; phthalates; pyrethroids; survey.

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Introduction

Normal childhood growth and development is sensitive to and affected by the environment in which we live. Early life adversity is widely believed to be a major contributor to health and wellbeing across the lifespan; a concept commonly referred to as the developmental origins of disease hypothesis (1). Of particular concern to human health are the group of chemical pollutants known collectively as endocrine disrupting chemicals (EDCs). EDCs are defined as a chemical or mixture of chemicals that 'alters function(s) of the endocrine system and consequently cause adverse health effects in an intact organism, or its progeny, or (sub) populations' (2). Thus, exposure of young children to EDCs in the home is increasingly becoming a global public health concern.

EDCs are extremely diverse; they comprise of a number of chemicals used extensively in the production of industrial solvents, polymers, resins, and insecticides (3). Several classes of household chemicals are also known or suspected EDCs, including organophosphate and pyrethroid insecticides, plasticisers including

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bisphenol A (BPA), and phthalates and polybrominated diphenyl ether (PBDE) flame retardants (3). These substances are common additives to household insect repellents, food packaging materials, food storage containers, children's toys, electronics and electric equipment, building and construction materials, paints, furniture, carpets, mattresses, textiles, and personal care products, as shown in Table 1 (4, 5). Numerous studies have observed that chemicals contained within household items are released over time into the home environment, and are subsequently detectable in household dust, food and indoor air samples, thus constituting multiple possible pathways of exposure of young children to these chemicals, as described below (4, 6, 7).

The widespread occurrence of PBDEs in the environment implies that the exposure of children and adults to PBDEs (flame retardants) is ubiquitous (8). The major pathway of human exposure to PBDEs is via ingestion, including ingestion of food and, particularly for children, ingestion of dust contaminated with PBDEs (8, 9). PBDEs disperse into dust following release from sources, primarily through off-gassing (release of volatilised PDBEs) and physical abrasion (7, 10, 11). Given that PBDEs are persistent and lipophilic, they have a tendency to partition readily into breast milk, making breast milk another major pathway of exposure of young children to PBDEs (9). Organophosphate and pyrethroid insecticides are semi-volatile; thus, they also disperse into dust and settle onto other surfaces, following release from their sources (12, 13). Exposure of young children to insecticides occurs via dermal, inhalation and dietary/non-dietary ingestion routes, although the relative contribution of each depends on the direct availability of the insecticide in the local environment and its residues in food, which may vary markedly by region (14). The major exposure pathway of children to the high molecular weight phthalate diethylhexyl phthalate (DEHP) and BPA is through dietary ingestion, whereas children are exposed to lower molecular weight phthalates through multiple pathways, including dietary and non-dietary ingestion (i.e., dust), dermal and inhalation (15). Dietary sources of plasticisers are from foods and drinks contaminated with epoxy resins, polycarbonate and other plastics, and paper containing BPA and phthalates (16).

Table 1 Sources of EDCs in the home.

Classes(s) of endocrine-disrupting chemicals	Sources in the home
Pyrethroids and organophosphates	Aerosol sprays, automatic dispensers, termite control, lawn/garden treatments, animal flea/tick treatments, head lice and scabies treatment, food, breast milk
BPA and phthalates	Canned food, fresh food, drinking water, bottles, plastic storage containers, plastic food wrap, plastic dishware and utensils, personal care products, thermal receipts, toys, dental sealants, textiles, leather, epoxy resin, inks, home décor, food, breast milk
Polybrominated diphenyl ethers	Textiles, foam, electronics, food, breast milk

Despite the widespread occurrence of these chemicals in the home environment, our understanding of the extent of the exposure as well as the magnitude and breadth of potential health outcomes is still limited by insufficient data on exposure patterns in early childhood, and on the temporal association between such exposures and development of childhood chronic disease. In the last decade, an increasing number of longitudinal prospective cohort studies were undertaken to address this knowledge gap on the association between EDC exposure and child health outcomes; including studies into asthma, neurobehavioral problems, thyroid dysfunction and obesity (17–20). Given that epidemiologic studies depend upon appropriate and accurate measurement of EDC exposure, there has been increasing discussion regarding the design and use of various exposure assessment methods for these studies, particularly those that are appropriate for use in children (21, 22).

Human bio-monitoring through biologic sampling has, in recent years, come to be considered as a 'gold standard' for exposure assessment, as it may give a direct measure of an individual's cumulative exposure to a toxicant, or toxicants, of interest (23). However, collecting and processing human biologic samples is costly and invasive (24). In infants, there may be the added practical issues involved in obtaining some biologic samples. Furthermore, multiple samples may be required to accurately classify long-term exposure to EDCs, which have a short half-life in humans or for which exposure is variable (25). The widespread occurrence of plasticisers and flame retardants within standard laboratory equipment and materials used in sample collection also poses a significant risk of sample contamination (26, 27).

In relation to the above, a questionnaire-based data collection method approach offers a cost-efficient and less cumbersome assessment of current and long-term EDC exposure (28, 29). Well designed questionnaires can capture exposure data that can inform every stage of the exposure pathway. This information includes potential

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sources of EDCs in the home and factors that modify their distribution in the home environment, as well as personal characteristics and behaviours that may act as drivers and modifiers of exposure and may also affect health outcomes (21). Despite the lack of a standardised validated questionnaire available for EDC exposure assessment, questionnaires have been used extensively in both epidemiologic and exposure assessment studies. A standardised validated questionnaire for EDC exposure would provide researchers with a tool that can support exposure estimation in study populations as well as compare/contrast exposure patterns among populations (30).

The design of an exposure assessment questionnaire and its validation can be described in three steps as follows: 1) initial questionnaire design, 2) questionnaire pre-testing and revisions and, 3) questionnaire validation. In the following discussion, we provide a brief overview of these steps. For a comprehensive discussion of this process, we refer the reader to White et al. (31). In the first step, the hazard(s) is initially identified, and the subsequent pathways of exposure relevant to the hazard(s) are analysed. This step is important to ensure the content validity of the questionnaire, that is, all hazards and their relevant pathways of exposure are identified and accounted for. This analysis informs development of indicators to be measured and then the questions to inform the indicators, with subsequent development of the questionnaire as a whole following. For a comprehensive description of question design and holistic design of questionnaires, we refer the reader to Dillman et al. (32). The next crucial step in questionnaire design is pre-testing; this process may involve methods like administering the questionnaire to focus groups or to volunteers under cognitive interviewing conditions. The aim of this step is to ensure that measurement error attributable to issues (e.g., question misinterpretation and recall error) are minimised. Finally, the validity of the exposure questionnaire, which is its ability to measure the true underlying exposure, is then determined by comparison to a gold standard or benchmark method, where it exists (31).

Benchmark methods used to characterise exposure to individual chemicals include for instance biomonitoring. These methods might vary according to several factors, like chemical exposure patterns, the exposure period under investigation, toxicokinetics (including the distribution, metabolism and route of elimination from the body), as well as the practicalities of obtaining and analysing biologic media (33). Although biomonitoring may be conducted just once to reliably classify long-term (weeks, months, and years as opposed to days) exposure to persistent pollutants, multiple samples are required to reliably characterise exposure to chemicals that are non-persistent in the human body (e.g., phthalates, BPA, and organophosphate and pyrethroid insecticides), particularly if they have variable exposure patterns (25, 34). The criteria for what constitutes a validated exposure assessment questionnaire have not been formally defined. We propose that validation of the questionnaire by benchmarking methods of exposure assessment constitutes the major criterion (35). Additional criteria would include elements common to all epidemiologic study design, including considerations like sampling size, representativeness of the population, as well as variations in and prevalence of specific exposure patterns in the population (31).

In this review, we provide an overview of studies, in which the questionnaire-based approach has been used in combination with at least one biologic sample to assess exposure of children to common EDCs found in the domestic environment. We limit our discussion to questionnaires that have been used to assess exposure of children to three chemical groups, which have endocrine disrupting properties, including 1) the plasticisers BPA and phthalates, 2) the PBDE flame retardants, and 3) insecticides containing organophosphates and pyrethroids. The chemicals chosen for this review are not inclusive of all EDCs found in the household. Numerous studies have found that a very large number of chemicals exhibit endocrine disrupting properties. EDCs may even be found in products that have been engineered to specifically limit the content of certain EDCs, like BPA-free water bottles (36). The EDCs selected for inclusion in this review are found in a wide array of sources in the home environment; they exist along a broad spectrum of physical and chemical properties, and encompass a broad array of unique exposure pathways. Therefore, an in-depth assessment of the questionnaire-based approach for these specific chemicals may also be informative for the development and validation of questionnaires, in order to assess exposure to other EDCs.

Materials and methods

The aim of our literature search was to locate studies that assessed exposure of children to at least one of the toxicants of interest and collected questionnaire data. We conducted three separate searches via PubMed and Web of Knowledge for each of the three groups of toxicants. The primary terms were the toxicant(s) of interest, including 'BPA', 'bisphenol A', 'phthalate', 'plasticiser', 'polybrominated diphenyl ether(s)', 'PBDE', 'polybrominated biphenyl ether(s)', 'brominated flame retardant', 'pyrethrins', 'pyrethroid', 'organophosphates', 'insecticides'. Secondary terms included terms relating to children, behaviour, questionnaire, biomonitoring, the home environment and potential sources of exposure in the home. The inclusion criteria were as follows: 1) primary scientific reports from peer-reviewed journals; 2) sample group including children under

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the age 10 years of age; 3) exposure assessment to at least one of the toxicants of interest through the use of biomonitoring; and 4) at least one question pertaining to possible exposure through the home environment. Some studies that assessed human exposure pathways to the toxicants of interest, but not necessarily in children <10 years of age or in the home environment were also included. Studies were excluded if they only assessed human health, were animal studies, or did not address any of the toxicants of interest mentioned above.

Results

We were unable to perform a systematic search of the literature using 'questionnaire' or 'survey' as keywords, as most of the relevant studies that reported on questionnaire data did not list these as keywords nor discuss the use of questionnaires within the abstract. In other cases, the administration of a questionnaire was discussed, but no findings or results from questionnaire data were reported. Therefore, we conducted a broad search of full text articles and assessed the reference list of studies to ensure that we identified as many relevant studies as possible. We assessed over 3000 reports in total. A total of eight papers for PBDEs, 13 papers for phthalates and BPA, and 16 papers for pesticides were assessed as highly relevant. These reports are found in Tables 2–4.

There is increasing recognition of the fact that in real life, humans are exposed not to individual chemicals but to mixtures of chemicals. Therefore, we present results from the identified studies in scenarios of common sources and modifiers of exposure, including diet, general features of the home and goods in the home, product use, and consumer application behaviour.

Diet

Dietary diaries, recalls, and food frequency questionnaires (FFQs) have the potential to provide a wealth of data on dietary exposures in epidemiologic studies. The less-varied diet of young children – compared with adults and older children – and their relatively larger food intake may lead to greater or different EDC exposures (77, 78). In infants, their diet is even more restricted, often to a singular source. Numerous EDCs have been detected in both breast milk and infant formula samples; thus, dietary sources of exposure would be expected to be an important exposure pathway (8, 79–83). If the primary dietary source is contaminated, this may result in increased exposure in infants. However, when considering EDCs, food-preparation practices that may increase or decrease the risk of chemical contamination need to be considered. In the following section we review the use of the questionnaire-based approach in assessing exposure of young children to BPA and phthalates, PBDEs, and organophosphate, and pyrethroid insecticides.

More than ten studies have reported associations between dietary habits, including consumption of particular foods or liquids (including breast milk and formula) and consumption of foods that come into contact with plastic materials containing BPA and phthalates, as shown in Table 3 (45–49, 51–57). Trasande et al., controlling only for urinary creatinine, reported a positive association between total dietary energy intake and exposure to the high-molecular weight phthalate DEHP, recorded in a 24-h dietary recall from children enrolled in the United States National Health and nutrition examination survey (NHANES) 2003–2008 (56). Positive associations between phthalate exposure and increasing consumption of vegetables, dairy, and poultry were reported. In contrast, consumption of fruit and grains were negatively associated with exposure to low-molecular weight phthalates, whereas consumption of soy was negatively associated with exposure to DEHP. LaKind et al. reported that frequency of soda consumption was significantly associated with exposure of children to BPA, as measured through the NHANES questionnaires (51). Meanwhile, consumption of canned foods has been found to significantly increase exposure of adults to BPA, but this association has not been adequately investigated in children (51, 84–86). A Spanish cohort of 4-year-old children, assessed through an FFQ, showed that consumption of canned fish and canned beverages correlated with higher levels of BPA measured in spot urine samples, although the association was not statistically significant (48). The lack of significance may be partly explained by exposure misclassification from collecting only one spot urine sample, as well as the lack of accounting for recent dietary exposure and the time of day at which the sample was collected.

Due to the short half-lives of BPA and phthalates, spot samples reflect only very recent exposure, which is not readily captured by an FFQ designed to assess longer term exposure. In this scenario, it may be easier to validate a 24-h recall or a prospective food diary to assess short-term exposure of children to plasticisers. If an FFQ is being designed for use to assess long-term exposure to plasticisers in epidemiologic studies, it would be necessary to first validate the FFQ against regular biologic samples throughout the time period to be assessed.

In infants, the mode and delivery of feeding appears to be an important cause of plasticiser exposure. Infants who are not exclusively breast fed have higher concentrations of

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Table 2 Association between questionnaire responses and biomonitoring estimates of internal exposure of young children (<10 years) to PBDEs,

References	Media	Study name and location[a]	Age (years)	N[b]	Units	Features of the home	Consumer goods	Diet and breast feeding	Behaviour/time activity
Bradman et al. (37)	Blood	CHAMACOS USA	7	272	ng/g lipid;	Number of rooms with wall-to-wall carpeting in the home and ΣBDE[c] (β: 1.07, p value 0.16), BDE-47 (β: 1.10, p value 0.11)	NA[d] number of TVs	NA daily servings of dairy or meat, total daily fat intake or fish consumption at 5 years and internal exposure at 7 years Duration of exclusive breastfeeding and ΣBDE[c] **(β: 1.05, p value 0.04),** BDE-47 **(β: 1.06, p value 0.03),** BDE-153 (β: 1.03, 0.11)	Lack of safe places to play in neighbourhood and ΣBDE[c] **(β: 1.42, p value 0.003),** BDE-47 **(β: 1.44, p value 0.005),** BDE-153 **(β: 1.34, 0.006)**
Carrizo et al. (38)	Blood	Spain	4	244				Average concentration of PBDE congeners and breastfeeding vs. formula feeding; BDE-47 **(3.4, 0.73, p value <0.01)**, BDE-99 **(1.4, 0.26, p value <0.01),** ΣBDE[e] **(3.6, 1.30, p value <0.05)**	
Eskenazi et al. (39)	Blood	Proyecto Mariposa, Mexico	5	283	–			Percent change in PBDE congener concentration per month breast feeding; BDE-47 (0.5%, p value 0.62), BDE-99 (0.8%, p value 0.42), BDE-100 (0.7%, p value 0.41), BDE-153 **(2.0%, p value 0.004)**	
Link et al. (40)	Blood	Germany	9–11	1537 (divided into 66 pooled samples)				NA breast feeding and PBDEs	
Lunder et al. (41)	Blood	USA	1.5–4	20	–	NR[f]			

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(**Table 2** Continued)

References	Media	Study name and location[a]	Age (years)	N[b]	Units	Features of the home	Consumer goods	Diet and breast feeding	Behaviour/time activity
Rose et al. (42)	Blood	CHARGE, USA	2–5	94	pmol/g lipid;	Home size (m^2) and ΣBDE-197-209 (β: −0.18, p value: 0.11) Carpet or upholstered furniture and ΣBDE NR	Purchase of a new mattress or upholstered furniture and ΣBDE-197-209 **(β:0.20, p value: 0.05)** NA number of electronics in the home	Frequency of pork consumption per week and **ΣBDE-197-209 (β: 0.25, p value: 0.02);** Frequency of poultry consumption per week and ΣBDE-28-153 (β: 0.10, p value: 0.06), Frequency of processed meat consumption per week and ΣBDE-28-153 (β: 0.06, p value: 0.39) ΣBDE 28–153 concentrations and age in breast fed children (β: 0.20, p value: 0.14)	NA age of car and time spent in cars
Stapleton et al. (43)	Blood	USA	1–3	83	ng/g			Months of breast-feeding Σ-BDE-47,-49 and -100 (β: 0.99 p value: 0.41); **BDE-153 (β: 1.07, p value: <0.0001)**	Hours away from home each week and Σ-BDE-47,-49 and -100 (β: 1.00, p value 0.50), BDE-153 (β: 1.00, p value 0.95)
Windham et al. (44)	Blood	BCERC, USA	6–9	599				NA breast feeding and PBDEs	

Significant findings ($p<0.05$) in bold.

[a]CHAMACOS (The Center for the Health Assessment of Mothers and Children of Salinas), CHARGE (Childhood Autism Risks from Genetics and the Environment), BCERC (Breast Cancer and the Environment Research Centers); [b]n, Number of participants; [c]ΣBDE-17, -47, -66, -85, -99, -100, -153, -154, -183; [d]NA, No Association; [e]ΣBDE-17, -28, -47, -66, -71, -85, -99, -100, -138, -153, -154, -183, -190; [f]NR, Not Reported.

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Table 3 Association between questionnaire responses and biomonitoring estimates of internal exposure of young children (<10 years) to BPA and phthalates.

References	Media	Study name[a] and location	Age (years)	N[b]	Units	Features of the home	Consumer goods and personal care products (PCP)	Behaviour/time activity	Diet and breast feeding
Becker et al. (45)	Morning urine sample	GerES IV, Germany	3–14	254	–	NA[c]plastic/vinyl home décor or furniture and DEHP		NA time spent playing on the floor and DEHP NA time spent indoors and DEHP NA time spent in cars and DEHP	NA consumption of meat, milk products, and fish and DEHP
Brock et al. (46)	Two spot urine samples	USA	1–1.5	19	–		NA plastic toy use and MEP, MEHP, MBzP and MBP NA Primary caregiver's PCP use and MEP, MEHP, MBzP and MBP in children		NA consumption of solid food and MEP, MEHP, MBzP and MBP NA breast feeding and MEP, MEHP, MBzP and MBP
Carlstedt et al. (47)	Overnight urine sample	Sweden	0–1	83	ng/mol; creatinine adjusted	NA size of the home and DEHP, BBzP, DBP and DEP vinyl flooring in infants room (presence vs. absence) and MBzP **(GM: 10.3, 6.0, p value <0.01)** vinyl flooring in parents room (presence vs. absence) and MBzP **(GM: 10., 6.0, p value <0.01)** Single family home vs. apartment and MBzP **(GM: 5.9, 6.4, p value < 0.05)**			Formula fed (yes vs. no) and MEHHP **(5.6, 2.4, p value <0.001)** MEOHP **(7.7, 3.8, p value <0.001)**
Casas et al. (48)	Spot urine sample	Sabadell birth cohort, Spain	4	130					NA consumption of meals stored in plastic containers, canned food and food in plastic containers and BPA
Hoepner et al. (49)	Spot urine sample	CCCEH, USA	3–7	306–398	–				NA breastfeeding and BPA
Koch et al. (50)	First morning void urine sample	Germany	2.6–6.5	36	µg/L		Skin/body care product use (often or occasional use vs. seldom or never used) and MnBP **(182, 89.7, p value 0.047)** NA MBzP	NA mouthing behaviour and MnBP or MBzP	

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(**Table 3** Continued)

References	Media	Study name[a] and location	Age (years)	N[b]	Units	Features of the home	Consumer goods and personal care products (PCP)	Behaviour/time activity	Diet and breast feeding
Lakind and Naiman (51)	Spot urine sample	NHANES 2005–2006, US	8–18	1054					Frequency of consumption of school lunches significantly positively associated with BPA exposure **(CC[d] not reported)** Frequency of consumption of soda significantly positively associated with BPA exposure **(CC not reported)** NA canned tuna consumption and BPA NA primary water source (tap water, bottled water, purified, other) and BPA or phthalates NA consuming food microwaved on or in plastic containers or wrappers and phthalates or BPA NA consumption of canned food and beverages and BPA or phthalates
Lewis et al. (52)	Spot urine sample	ELEMENT, Mexico	8–13	108	ng/mL	NA plastic/vinyl floor and BPA or phthalates	NA reported PCP use in previous 48 h and BPA or MBzP Median concentrations (use vs. non use) in the previous 48 h with reported PCP use: Boys; cologne and MEP **(135, 49.5, p value 0.007)**, MCPP **(2.6, 1.7, p value 0.009)**, MEHHP **(57.1, 38.4, p value 0.03)**, MEOHP **(25.7, 16.5, p value 0.01)** Boys, lotion and MEHP **(9.8, 6.7, p value 0.02)** Girls; colored cosmetics and MBP **(246, 101, p value 0.02)**, MEHP **(17.3, 7.2, p value 0.001)**, MEHHP **(102, 46.0, p value 0.005)**, MEOHP **(40.0, 21.9, p value 0.01)**, MECPP **(141, 71.9, p value 0.009)** Girls; conditioner and MEP **(276, 51.8, p value 0.001)** Girls, deodorant and MEP **(147, 46.4, p value 0.003)** Girls and other hair products and MBP **(293, 101, p value 0.02)**, MIBP **(22.0, 12.0, p value 0.008)**, MCPP **(4.5, 2.3, p value 0.03)**		

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(**Table 3** Continued)

References	Media	Study name[a] and location	Age (years)	N[b]	Units	Features of the home	Consumer goods and personal care products (PCP)	Behaviour/time activity	Diet and breast feeding
Li et al. (53)	Morning urine sample	China	3–24	287	ug/L				Reported preferred use of plastic versus ceramic drinking vessel associated with significantly higher BPA concentration **(p value 0.037)**
Mendonca et al. (54)	Urine sample collected from wet diaper	EARtH, USA	0.25–1.5	31	–				NA breastfeeding or formula consumption and BPA
Sathyanarayana et al. (55)	Urine sample collected from wet diaper	SFFI, USA	<2.5	163	Adjusted for square root creatinine		NA time spent playing with a plastic toy and phthalates[a,c] Ratio of phthalate metabolite concentrations (use vs. non use in the previous 24 h): Baby lotion and MEP **(1.8, p value <0.05),** MMP **(1.4, p value <0.05)** Baby shampoo and MMP **(1.4, p value <0.05)** Baby powder and MiBP **(1.6, p value <0.05)** NA use of the above Personal care products and other phthalates[e] NA diaper cream or baby wipes and phthalates[e]		
Trasande et al. (56)	Spot urine	NHANES 2003–2008, USA	6–19	2743					Percent change in phthalate concentration with each additional unit reported consumed via 24-h dietary recall: kcal and DEHP **(+0.007%, p value <0.05);** g grain intake and low-molecular weight phthalates[f] **(–0.04%, p value <0.05),**

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(**Table 3** Continued)

References	Media	Study name[a] and location	Age (years)	N[b]	Units	Features of the home	Consumer goods and personal care products (PCP)	Behaviour/time activity	Diet and breast feeding
									g fruit intake and low-molecular weight phthalates[f] **(−0.02%, p value <0.05)**; g vegetable intake **(0.01%, p value <0.05);** g non-whole grain and DEHP **(0.08%, p value <0.05),** g dairy intake and DEHP **(0.02%, p value <0.05),** g poultry and DEHP **(0.22%, p value <0.05),** g soy and DEHP **(−0.37%, p value <0.05)**
Volkel et al. (57)	Urine collected in urine bags	Germany	0–0.5	47	µg/L				Median BPA concentration and reported use of baby bottle vs. non use (2.11, 0.81)

Significant findings ($p<0.05$) in bold.

[a]GerES IV (German Environmental Survey on Children 2001/2002), CCCEH (Columbia Centre for Children's Environmental Health), NHANES (National Health and Nutrition Examination Survey), ELEMENT (Early Life Exposure in Mexico to Environmental Toxicants), EARtH (Environment and Reproductive Health); SSFI (Study for Future Families); [b]n, number of participants; [c]NA, No Association; [d]CC, Correlation Coefficient; [e]BBzP, DBP, DEP, DEHP, DnOP, DMP; [f]DEP, DBP, DnOP, DiBP.

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Table 4 Association between questionnaire responses and biomonitoring estimates of internal exposure of young children (<10 years) to organophosphate and pyrethroid insecticides.

References	Media	Study name[a] and location	Age (years)	Units	N[b]	Diet	Insecticide use in the home	Behaviour/time activity	Other
Aprea et al. (58)	Spot urine sample	Italy	6–7	nmol/g creatinine	195	Consumption of meals at the school cafeteria (yes vs. no) and concentration of Σ organophosphate metabolites[c] (376.9, 327.3, p value>0.05)	Use of pesticides in the home (yes vs. no) and concentration of Σ organophosphate metabolites[c] **(451.0, 329.0, p value<0.05)**		Presence of a vegetable garden at the home (yes vs. no) and concentration of Σ organophosphate metabolites[c] (362.1, 321.4, p value>0.05) Presence of domestic animals at the residence (yes vs. no) and concentration of Σ organophosphate metabolites[c] (301.9, 359.3, p value>0.05)
Babina et al. (59)	First morning void urine	Australia	2.5–6		340		NR[c]		
Becker et al. (60)	First morning void urine	GerES IV, Germany,	2–5	µg/g	60	Consumption of fruit juice[d] and DMP **(β: 0.14. p value 0.011),** DMTP **(β: 0.11, p value 0.029),** DEP **(β: 0.16, p value 0.004),** NA[e] DETP Consumption of fresh fruit per day[f] and DETP **(β: 0.20. p value<0.001),** NA DMP, DMTP or DEP Consumption of boiled vegetables[g] and 3-PBA **(β: 0.16 p value 0.023),** *Cis*-DCCA **(β: 0.11 p value 0.043),** *Trans*-DCCA **(β: 0.15 p value 0.004)**	Use of biocides indoors at home (vs. no use) and exposure to pyrethroids; *Cis*-DCCA **(β: 0.10 p value 0.049),** *Trans*-DCCA **(β: 0.10 p value 0.040),** NA 3-PBA		NA presence of garden at homes of children and exposure to organophosphates
Bradman et al. (61)	Spot urine sample	CHAMACOS (rural population)	0.5–2	Log	~400	Daily servings of fruits and vegetables (more than one or one or less) and organophosphate metabolites; Σ DMAP metabolites[h] **(β: 1.60. p value <0.05),** Σ DEAP[i] (β: 1.25, p value >0.05)	NA use of insecticides in the home and organophosphate metabolites[j]	NA time spent mouthing fingers and toes and organophosphate metabolites[j]	NA any dogs and cats in the home and organophosphate metabolites[j]
Bradman et al. (62)	Spot and overnight urine samples	Planning for the NCS, USA	0.5–1 and 2		20	NR	NR		

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(**Table 4** Continued)

References	Media	Study name[a] and location	Age (years)	Units	N[b]	Diet	Insecticide use in the home	Behaviour/time activity	Other
Lu et al. (63, 64)	Daily first morning voids for 15 days	CPES-WA 2003, USA	3–11	µg/L	23		Residential Pesticide Use (yes vs no) and DVWA[k] 3-PBA **(1.84, 0.94, p value <0.001),** *trans*-DCCA **(1.91, 0.94, p value <0.001)**		
Morgan and Jones (65)	Up to six spot urine samples over 48 h	CTEPP NC and OH, USA	2–5	ng/mL	135	Food type consumption (low vs. high) and TCP; apples **(5.76, 9.40, p value 0.04),** fruit juice **(8.41, 4.11, p value 0.040),** NA other food types Food type consumption (low vs. high) and 3-PBA; chicken/turkey **(0.7, 0.41, p value 0.013)**	NR		
Morgan et al. (66)	Urine	CTEPP-OH 2000–2001, USA	1.7–5.6		127		NR		
Munoz-Quezada et al. (67)	Two spot urine samples, one in summer and one in autumn	Chile	6–12		190	Consumption of foods found to typically contain residues of the organophosphate phosmet and Σ DMAP[h] metabolites **(β:4.12 p value <0.0001)**	Use of the organophosphate pesticide fenitrothion at the home and Σ DMAP[h] metabolites **(β:1.44 p value 0.009)**		
Naeher et al. (68)	Urine; baseline and following head lice treatment	USA	6–10	µg/g creatinine	78				Permethrin exposure significantly higher following self-reported head lice treatment (CC[l] not reported)
Naeher et al. (69), Tulve et al. (70), Tulve et al. (71)	Spot urine	JAX-EXP	4–6	µg/g creatinine	203		Insecticide use in the home in the last 4 weeks (yes vs. no) and 3-PBA **(4.1, 2.8, p value<0.05),** *cis*-DCCA **(1.6, 1.0, p value<0.05),** *trans*-DCCA **(2.7, 1.7, p value<0.05);** DMP (3.9, 5.6, p value>0.1), DMTP (5.2, 7.7, p value>0.1), DMDTP (0.8, 1.2, p value<0.1), DEP (4.8, 5.3, p value>0.1) DETP (1.0, 1.0, p value>0.1), DEDTP (0.2, 0.2, p value>0.1)		

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(**Table 4** Continued)

References	Media	Study name[a] and location	Age (years)	Units	N[b]	Diet	Insecticide use in the home	Behaviour/time activity	Other
Riederer et al. (72)	Spot urine	NHANES 1999–2002, USA	6–10		179	3-PBA concentrations and consumption of food types (by bootstrap analysis); ground beef **(3.3×10^{-2}, p value <0.0001)**, toasted white bread **(2.4×10^{-2}, p value 0.0332)**, ice cream **(6.6×10^{-3}, p value 0.0288),** tortilla chips **(-2.1×10^{-2}, p value 0.0158)**, cheese **(–2.5×10–2, p value 0.0154)** and cookies**(-3.4×10^{-2}, p value 0.0046),** NA other foods and 3-PBA	NA reported domestic insecticide use and 3-PBA	NA time spent playing games and pyrethroid metabolites[m]	
Sexton et al. (73)	Three first morning void urine samples over one week	MNCPES, USA	3–13		102		Malathion exposure given insecticide use reported in the home vs. insecticide use not reported in the home (Odds Ratio: 0.550, p value >0.05)		
Trunnelle et al. (74)	End of day spot urine sample	SUPERB, USA	2–8		83	NR	NR		
Trunnelle et al. (75)	End of day spot urine sample	MICASA, USA	2–8		103	Consumption of food items (yes vs. no) in the previous 24 h and 3-PBA; apple (t value: –1.5, p value 0.13), milk total (t value –1.2, p value 0.22), all meat total (1.7, 0.1), cereal total (t value –1.7, p value 0.08)	Outdoor spray use and 3-PBA (t value 1.8, p value 0.10)		Home Disrepair Score (water damage, water leaks, carpet damage, counter damage and rotten wood) and 3-PBA (t value 1.7, p value 0.10)
Wilson et al. (76)	First morning urine void	PEPCOT, USA	0–6		100		NR		

Significant findings ($p<0.05$) in bold.

[a]GerES IV (German Environmental Survey on Children 2001/2002, planning for NCS (National Children's Study), CPES (Children's Pesticide Exposure Study), CHAMACOS (Center for the Health Assessment of Mothers and Children of Salinas Quantitative Exposure Assessment Study), CTEPP (Children's Total Exposure to Persistent Pesticides and Other Persistent Organic Pollutants), JAX-EXP (Biological and Environmental Monitoring for Organophosphate and Pyrethroid Pesticide Exposures in Children Living in Jacksonville, Florida Study), NHANES (National Health and Nutritional Examination Survey), MNCPES (Minnesota Children's Pesticide Exposure Study), SUPERB (Study of Use of Products and Exposure Related Behavior), MICASA (Mexican Immigration to California: Agricultural Safety and Acculturation Study), PEPCOT (Pesticide Exposure of Preschool Children Over Time); [b]n, number; [c]N, Not Reported; [d]less than one glass-one glass-more than one glass; [e]NA, No Association; [f]>once day – once per day – less than once per day; [g]once a week or less frequently–several times a week – daily; [h]Dimethyl alkyl phosphate metabolites (DMAP): DMP, DMTP, DMDTP; [i]Diethyl alkyl phosphate metabolites (DEAP): DEP, DEDTP, DETP; [j]DMP, DMTP, DMDTP, DEP, DEDTP, DETP; [k]DVWA (Daily Volume Weighted Average); [l]CC, correlation coefficient; [m]3-PBA, *trans*-DCCA, *cis*-DCCA.

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DEHP metabolites in their urine than those who are exclusively breastfed, which may indicate either contamination of infant formula or leaching of phthalates from baby bottles used to administer the infant formula (47). Several studies have reported varying concentrations of BPA and phthalates in infant formula; hence, a questionnaire-based approach may be useful because it can capture information about factors that may indicate the presence and concentration of EDCs in infant formula (87, 88). These may include the brand of infant formula used, the water supply used to prepare the formula, the brand of baby bottle, and the length of time the formula is stored in a plastic bottle prior to administration, and whether formula is heated in the bottle or whether hot liquid is poured into the plastic bottle. The way the bottle is cleaned between uses may also influence contaminant levels in the formula.

A limited number of studies have assessed whether breastfeeding is associated with exposure of young children to BPA or phthalates, of which none reported any significant associations (46, 49, 54). Although BPA and phthalates partition into breast milk, unlike PBDEs they do not accumulate in breast milk (9, 54, 89). Therefore, concentrations of plasticisers in breast-milk are generally low and may vary according to recent maternal exposure. More studies are required to understand how recent maternal exposure influences the variability of BPA and phthalate breast milk concentrations, as well as the relative contribution of breast milk to total body burden in infants. However, it is reasonable to expect that a questionnaire-based approach attempting to predict infant exposure to plasticisers through breast-milk should account for maternal exposure, as well as any plastic-based aides used in the collection and storage of breast milk, including breast pumps, baby bottles, or plastic freezer storage containers.

In school-aged children, the frequency of consumption of school lunches outside of the home, which may be a proxy for consumption of food prepared or stored in packaging, has also been found to be associated with BPA exposure (51). The leaching of plasticisers from food-contact materials is facilitated under several conditions, including heating, exposure to alkaline conditions (i.e., dishwashing soap), and exposure to lipid-rich foods (90). Therefore, when assessing exposure to plasticisers from food contact material using a questionnaire-based approach, it is important to consider the conditions that the food contact materials are subject to and whether the materials come into contact with fatty foods in particular.

The persistent, lipophilic properties of PBDEs enable them to bioaccumulate and biomagnify in the food web. Thus, lipid-rich foods and foods that originate from higher trophic levels contain the highest concentrations of PBDEs (8). PBDEs also persist in humans. Owing to this property, unlike plasticisers, validation of an FFQ assessing average PBDE dietary intake over a given developmental period may be successfully achieved by conducting comparison with spot-samples.

Only two studies, both from the US, have assessed whether the results of FFQs can be used to predict dietary exposure of young children to PBDEs, see Table 2 (37, 42). Rose et al. found that the consumption of poultry, pork, and processed meat is positively associated with PBDE concentrations in serum from children (42). Neither study found an association between children's consumption of dairy products or fish and PBDE body burden (37, 42). PBDEs are known to vary greatly between different food items, which may be attributable to differences in lipid content or trophic levels. Therefore, the lack of association may be a result of collecting insufficiently detailed data regarding consumption of specific types of fish or dairy (8). Given this marked variation in concentrations and the long half-lives of PBDEs, the FFQ has advantages over a 2-day diary or 24-h recall study approach in assessing cumulative exposure of children to PBDEs. This is because the FFQ can capture rare events, which may contribute significantly to dietary exposure. Such events may otherwise be missed with a 2-day diary, including consumption of seafood, which may only occur rarely in some populations.

Breastfeeding duration, as assessed through questionnaires, is a significant predictor of increased exposure of infants and toddlers to PBDEs (Table 2). The strength of the association tends to decrease with time since weaning and the association with specific PBDEs may vary according to maternal exposure, maternal age, and the half-life of the specific BDE congener (37–39, 41–44).

The impact of diet on children's exposure to insecticides has been assessed through more than half a dozen studies that used both questionnaires and biomonitoring (Table 4). As assessed through questionnaires, frequency of consumption of fruit, fruit juice, chicken/turkey, ground beef, toasted white bread, ice cream, tortilla chips, cheese, cookies and boiled vegetables has been found to modify exposure to insecticides; moreover, consumption of fruit (as a broad category and also the sub-category of apples) is a consistent significant predictor of increased organophosphate, but not pyrethroid, exposure (60, 61, 65, 67, 72). A longitudinal intervention study also observed that switching to an organic diet significantly reduced organophosphate exposure, although the impact of consuming an organic diet on insecticide exposure has not been adequately investigated through the questionnaire-based approach (58, 63, 64). Insecticide residues may vary

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greatly in concentration between regions and between seasons (91). Therefore, insecticide exposure questionnaires designed to predict dietary exposure must be specifically validated for each region that they are to be used in, across seasons and also for other factors that may modify exposure like washing or peeling fruits and vegetables prior to consumption.

General features of the home and goods in the home

Flooring may be a significant cause of exposure of young children to toxins in the home (92). Carlstedt et al. reported that the presence of vinyl flooring in infant's (n=88) bedrooms in Sweden, as assessed through a self-administered questionnaire completed by parents, was significantly and positively associated with exposure of infants to certain phthalates (47). In contrast, in a similar-sized cohort of children aged 8–13 years (n=108), no association was reported between the presence of vinyl flooring in the home and exposure to phthalates, as assessed through a nurse-administered questionnaire completed by the children with assistance from their parents (52). The difference in findings may be attributable to a difference in exposure risk between young children (infants) compared with older children. Phthalates in vinyl flooring can disperse into dust, which may explain the greater exposure risk posed by vinyl flooring to young children who may ingest more dust than older children (93). Moreover, these differences could be explained by the greater relative surface area of young children, the increased amount of time that they spend on the floor, and the increased amount of time they spend in the home environment.

Several studies from the US observed a weak positive association between questions relating to the presence of carpet in homes and BDE-47 (a specific PDBE congener) concentrations in children and adults, which may be explained by the foam underlay of carpets containing PBDEs, the carpet itself, or the collection of PBDE contaminated dust within the carpet (37, 94, 95). Given that young children spend more time on the floor than adults, assessing the type of flooring in homes, the time spent on flooring by children, and the frequency of floor cleaning/vacuuming are important considerations for the content validity of a comprehensive EDC exposure assessment questionnaire for children.

Based on experimental evidence, features of the home (e.g., ventilation, house size, and cleaning practises) alter the concentrations of toxins in dust, and may thus have the potential to modify exposure (96). Indeed, dust concentrations of BDE-209 are inversely correlated with house size (97). Rose et al. reported a significant negative association between the size of their homes and BDE-209 concentrations in serum of Californian children (42). In contrast, Carlstedt et al. reported no significant association between the size of the home and exposure of children to phthalates (47). PBDEs have historically been used in foam-based materials to ensure they meet fire safety standards (5). Abrasion of the foam releases foam particles containing PBDEs, which young children could ingest either directly or in dust (7). No studies have assessed whether home furniture with exposed or crumbling foam predict exposure of children to PBDEs, despite the fact that crumbling foam in the homes is positively associated with PBDE concentrations in house dust (98). Although baby-car seats and foam toys may contain PBDEs, we found no studies that assessed whether the presence or use of these products by children modifies their exposure to PBDEs (99, 100). Although the Californian study by Rose et al. did not focus on baby products per se, they did find a positive correlation between ΣBDE-197-209 in serum and the purchase of new mattresses, which in most cases, was meant for the child (42). It has been suggested that baby and toddler products are sources of exposure that are inadequately accounted for because human exposure to PBDEs peaks at approximately 3 years of age (100, 101).

The concentration of PBDEs in electronic appliances and equipment varies greatly (102, 103). This poses a significant challenge to the ability of the questionnaire-based approach to predict exposure. Two studies from California, US, used questionnaires to assess whether electronics in the home are predictive of children's exposure to PBDEs (37, 42). Neither study found a significant association between the number or hours of use of electronics in the home and the concentration of any PBDEs in children's serum (37, 42). In contrast, significant associations between the presence of electronics in the home and PBDE body burden in adults has been reported for pregnant women living in New York and North Carolina in the US (94, 104). It is possible that the difference in findings is explained by the dominance of alternative exposure pathways like breast feeding, thus attenuating any associations that may exist between the presence of electronics in the home and PBDE exposure in children.

To date, no study has yet to assess the association between reported portable electronic device use (e.g., tablets, gaming devices, and mobile phones), and exposure to PBDEs in children. With the growing use of electronic devices by children, including very young children, this is an important consideration. In cohorts of infants and toddlers, questions regarding mouthing (sucking or chewing on) of electronic devices may also need to be included.

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Plasticisers are found extensively in the home environment; thus, items containing plasticisers are of particular concern, especially because young children may suck or chew on these. Sathyanarayana found that maternally-reported time spent by infants playing with plastic toys and using dummies was not predictive of exposure to DBP, di-isobutyl phthalate (DiBP), diethyl phthalate (DEP), DEHP, di-n-octyl phthalate (DnOP) or dimethyl phthalate (DMP), as measured in urine (105). Exposure to DiNP, which may be found in these products, was not assessed. Given that the concentration of phthalates may vary between toys and the way that children play with the toys may also vary, it may be necessary to include questions that explore which toys are played with most often, and how they are played with, including whether the child sucks or chews on the toy.

Products in the home: personal care products and insecticides

Personal care products (PCPs), including shampoo, sunscreen, moisturising lotion and soap, are a major source of phthalates (55, 106, 107). Studies conducted in both the US and in Mexico have demonstrated that reported PCP use in the previous 24–48 h was associated with exposure of children to phthalates (52, 55). In particular, the total number of reported PCPs used on infants or by children is a significant predictor of DEP exposure (52, 55). To our knowledge, no questionnaire-based approach has assessed whether selecting conventional versus eco-friendly or chemical-free products modifies exposure in children. Serrano et al. found that adult women in the US who reported always purchasing eco-friendly, chemical-free, and environmentally friendly household products had lower levels of exposure to phthalates than women who reported rarely or never purchasing these types of products (108).

Questionnaires that have been used in conjunction with biomonitoring to assess children's exposure to insecticides have predominantly focused on assessing whether dietary factors or residential insecticide use modify exposure (Table 4). As reported by Trunnelle et al., exposure to insecticides is elevated in children who live in homes that are in poor condition (75). Homes that are in a poorer condition may be difficult to clean, with a higher incidence of pest infestations leading to more frequent domestic insecticide use (109).

Meanwhile, self-reported insecticide use in the home has not been consistently associated with children's exposure to insecticides when organophosphates and pyrethroids are considered together. Findings are more consistent for studies examining the association between reported use of insecticides in the home and exposure to pyrethroids. Of the four studies reporting the association between self-reported insecticide use and pyrethroid exposure, a significant positive association between self-reported insecticide use and pyrethroid exposure was reported by Becker et al. in Germany and by Lu et al. in the US; a non-significant positive association between self-reported use of outdoor spray and pyrethroid exposure was reported by Trunnelle et al., also in the US (60, 64, 72, 75). Naeher et al. reported the association between self-reported insecticide use and exposure to both pyrethroids and organophosphates in the US and found a significant association only for pyrethroids (69). It is likely that the association between domestic insecticide use and pyrethroid exposure from studies in the US is more consistent than the association with organophosphate exposure; this is because the use of pyrethroid active ingredients in domestic insecticides has increased due to the the implementation of stricter regulations on the sale of organophosphates for domestic use (76).

Of the three studies that assessed whether the presence of a vegetable garden or time reportedly spent in the garden predicts exposure to insecticides, only Aprea et al. reported a non-significant association between the presence of a vegetable garden and exposure to organophosphates in an Italian cohort of 6–7-year-old children (58, 60, 72). Both variables may act as proxies for exposure to insecticides due to their use in the garden. The strength of the association between insecticide exposure and the presence of a garden may vary according to location, due to differences in patterns of use of insecticides in the garden as well as differences in children's behaviour, including how much time they spend in the garden.

A study assessing the association between head lice treatment and exposure to insecticides found that insecticide metabolites in urine were significantly elevated in a sub-group of children following medicated treatment for head-lice (68). The children who underwent lice treatment also had higher pre-exposure concentrations of insecticide metabolites than the control children. The authors concluded that this may be due to repeat treatments that are often required for head lice; however, no data regarding the frequency of prior treatments were available.

Behaviour: a major knowledge gap

Several behaviours of children lead to increased EDC exposure relative to adults (110, 111). Within the home, infants and toddlers occupy different microenvironments than

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adults, which may lead to different pathways and durations of exposure (112, 113). Young children exhibit frequent hand and object-to-mouth behaviour (78), whereas certain play activities may lead to increased non-dietary EDC exposure (12, 77, 114, 115). Toys in themselves can be an important source of exposure to some EDCs (99, 100). Collecting questionnaire data on individual behaviours in children can be particularly informational for exposure assessment because there is marked intra and inter-individual variation in these behaviours during developmental stages of childhood (116).

Questionnaires have the potential to provide valuable information on individual behaviour in children and on whether their behaviour modifies their exposure to toxicants in the home; however, this has only been tested through a limited number of studies. Bradman et al. and Koch et al. did not find any association between questionnaire-reported hand-to-mouth behaviour in children as well as exposure to organophosphate insecticides or phthalates (specifically the high molecular weight phthalate di-*n*-butylphthalate (DnBP) and the low molecular weight phthalate BBzP), respectively (50, 61). Hand-to-mouth behaviours are believed to be a major contributor to children's exposure to many chemicals; therefore, an absence of association is unexpected. However, there are multiple possible explanations for the absence of association, including the small sample size (n=36) in the study by Koch et al., the limitations of the biologic monitoring (limited numbers of samples), and attenuation due to the dominance of alternative exposure pathways, including diet (particularly for DnBP and organophosphate insecticides), personal care product use (phthalates), and inhalation (particularly for BBzP and some organophosphates) (50, 61). In contrast, hand-to-mouth behaviours in adults, as assessed through questionnaires, modify exposure to PBDEs (104, 117). Furthermore, Stapleton et al. demonstrated that reported hand-washing behaviour is associated with reduced PBDE concentrations in children's hand-wipe samples, which could lead to decreased exposure to PDBEs via non-dietary ingestion or trans-dermal absorption given that they have previously demonstrated that hand-wipe concentrations of PBDEs are correlated with PBDE body burden (118). Young children may also ingest toxicants through excess dietary exposure that occurs when toxicants transfer from their hands or other surfaces in the home to foods that they then consume (119). No studies have assessed – through questionnaires – whether exposure of children to EDCs may be modified by variables that could reduce excess dietary exposure like washing hands prior to eating.

Of the few studies that have assessed – through questionnaires – whether additional physical behaviours like crawling and playing on the floor would increase exposure, none reported any significant associations between these behaviours and exposure to EDCs; in both studies, only spot urine samples were collected (45, 72). These variables have been found to modify exposure of children to toxicants in the home through alternative assessment methods like analysing toxicant concentrations on children's clothes (62, 120). In addition, although time-and-place activity diaries have been used in conjunction with exposure assessment in young children, few studies have assessed behaviour or time-activity patterns through the questionnaire-based approach (43, 45). In one study conducted in the US, children whose mothers reported having no safe places to play in their neighbourhood as 'a big problem' had elevated PBDE body burden, presumably from spending more time indoors (37). In contrast, Stapleton et al. found no association between time spent away from the home and exposure to PBDEs (43). Thus, it may be necessary to collect more detailed time-and-place activity data than this to determine more accurately the time spent indoors, particularly in the home. Although more detailed time-activity data can be collected through 24-h recalls, including online based surveys, these recalls can be burdensome for parents of young children who may have other family and work responsibilities (121). The use of monitors like Global Positioning Systems and accelerometers provides more accurate data and may be potentially less burdensome for study participants (122, 123). However, there are also issues with this approach, including the cost, possibility of technologic issues and data analysis issues, privacy invasion, and the impracticality of having very young children wear these devices (123).

Discussion

Few questionnaires have been adequately validated as to whether they may accurately assess exposure of children to toxicants in the home. Although some studies have demonstrated that responses to some questions are predictive of exposure of children to toxicants, there is typically marked variation between the studies, which cause uncertainty in the use of this approach.

However, significant correlations have been reported for young children's exposure to specific toxicants for which the exposure is relatively consistent, including benzyl butyl phthalate (BBzP) and vinyl flooring in the home, DEP and personal care product use and PBDEs and breastfeeding (25, 37–39, 43, 47, 52, 55). The association between breastfeeding and PBDE exposure appears strong

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not only because exposure is consistent, but also because PBDEs have half-lives on the order of weeks to years compared with hours, enabling the questionnaire to be adequately validated through one biologic sample (124, 125). The ability of the questionnaire-based approach to predict exposure to toxicants, for which long-term exposure is not accurately classified through one biologic sample (e.g., exposure to phthalates, BPA, and insecticides), may currently be underestimated (25, 126).

There are two key areas that introduce error into the questionnaire-based approach. These are a) factors associated with the design of the study and questionnaire, and b) factors associated with its validation. These errors could have contributed significantly to the variation in findings by studies that have used questionnaires and biomonitoring. These sources of error must be carefully considered when designing an exposure assessment questionnaire.

Limiting error through attention to questionnaire design

Failing to account for all sources and causes of exposure can introduce error into the questionnaire (29). If all the pathways of exposure to a specific toxicant or groups of toxicants are not accounted for, the precision of the instrument will be reduced because unaccounted for exposure pathways may obscure associations. Where exposure through one pathway dominates over all others, then small but significant associations between other pathways and exposure will be obscured, particularly when these pathways are inadequately characterised. For example, the difference between the ability of questionnaires to predict adult exposure versus child exposure to PBDEs may be due to the greater contribution of non-dietary dust ingestion to children's exposure, which has been inadequately characterised through the questionnaire-based approach (127, 128). Throughout this review, we have alluded to pathways of exposure that must be considered when designing an EDC exposure assessment questionnaire for young children at home.

Failing to account for unknown pathways of exposure can also attenuate true associations. For example, although it is assumed that the majority of exposure to BPA occurs through the diet, studies on individuals who have fasted have indicated that alternative exposure routes like dermal exposure may also contribute substantially to exposure (129). Therefore, more research is needed to better characterise exposure pathways of young children to flame retardants, plastics and insecticides in the home environment, particularly for children living in domestic and other settings associated with an impoverished status in developing countries. This is because majority of the studies we have reviewed originated from developed countries. Although children in developing countries may experience some of the same exposure pathways as children in developed countries, they may well have additional and different exposure pathways. For example, a Nicaraguan study found that children aged 11–15 years who not only lived, but also worked at a waste disposal site had PBDE exposures that exceeded by 20–50 times those of a reference group of children who lived in urban Managua, away from the waste site (130). Exposure levels of the reference children were similar to exposure levels in the US and higher than those of children in Europe.

In cases where exposure pathways are known, but the EDC sources cannot be definitively identified through a questionnaire, then a questionnaire-based approach alone cannot predict exposure with limited uncertainty. For many consumer goods, companies are not required to indicate on the label whether these contain EDCs. Moreover, the concentrations may vary greatly among goods of the same type, making it difficult to identify sources of EDCs in the home environment (4, 103). Thus, additional direct or on-site observation would be required to identify goods that pose the greatest health risk though exposure.

Poor wording or phrasing of questions can also lead to misinterpretation of questions. This can lead to measurement error and obscure any true associations between questionnaire responses and exposure. In the Australian study conducted by Babina et al., many parents reported the use of 'domestic disinfectants, dishwashing detergents and even air fresheners [to the question] "Do you/your partner use pesticides in the house?' ", when the authors were really interested in the use of insecticides (59). Misinterpretation of questions may be limited by ensuring that questionnaires undergo pre-testing with a population that is representative of the study population prior to actual use (32).

Poor recall may also introduce error into the questionnaire-based approach. For example, respondents can typically only infrequently recall specific product use, particularly when the recall time frame of use is long (73, 131–133). Additional methods like visual aids accompanying each question have been used to help minimise recall error and improve comprehension (134). In addition, it is difficult, if not impossible, to assess average use of some products through questionnaires, particularly when their use is intermittent, and when the questionnaire is not answered by all adult residents in the home (135, 136). Alternative monitoring approaches (e.g., using bar-code scanners and taking an inventory) have been shown to be acceptable by participants in longitudinal studies, but require more resources and may be more intrusive (136, 137).

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Use of proxy-respondents, which is necessary when assessing young children's exposure, may introduce error into the questionnaire-based approach. For example, Riederer et al. compared the reporting of pesticide use in NHANES by self-reporting adults and those who were serving as proxy-respondents for children (72). Although the reporting of household insecticide use was the same, adults tended to under-report the use of insecticides in the yard when they were the proxy-respondent for children (16% vs. 9%).

There are also additional challenges associated with the questionnaire-based approach specific to particular exposure pathways. Investigating the contribution of diet to exposure in children is made challenging by the fact that questionnaires to collect dietary information are typically burdensome, and it is difficult to accurately portray frequency and quantity of intake of specific items. Parents in the study conducted by Rose et al. had difficulty assigning portion sizes to the foods eaten by their children (42). Therefore, the authors used only data regarding the frequency of food consumption. Frequency of food consumption is a reasonable approach in young children, for whom estimating portion sizes is also made difficult by frequent food spillages.

An additional issue that may arise when using a questionnaire-based approach to predict exposure to EDCs through the use of FFQs is that a high level of resolution, which may introduce more burden, is required to accurately determine foods that are particularly associated with increased exposure and to determine whether there are any interactions between food types (72). In children, excess dietary exposure, i.e., ingestion of toxicants that have transferred to foods from contaminated hands or surfaces, may contribute substantially to total exposure (119). Additionally, as discussed earlier, exposure through the diet to plasticisers may be modified by how plastic food contact materials are used, what foods they come into contact with and how the food is prepared. Heating foods in plastic containers may increase exposure but is rarely assessed in a FFQ. Therefore, when assessing children's exposure to EDCs through FFQs, it is necessary to also ask additional questions about factors that may modify exposure through the diet other than just frequency of intake of specific food types.

Minimising error by focusing on questionnaire validation

There are multiple sources of error that may be associated with the method of validating questionnaires, which is typically dependent on biologic assessment. The choice of sampling medium, the time of sampling, and the number of samples to be taken may affect the accuracy of exposure classification. According to Barr et al., 'differences between biomarker measurements made multiple times in the same child over a defined period or once in numerous children at approximately the same time can be because of dissimilarities in actual exposures, variations in pharmacokinetics, or both' (126). A major source of error in the validation of EDC exposure assessment questionnaire is from exposure misclassification from collecting only one spot-samples, especially when classifying exposure to toxicants with short half-lives (138). Most studies included in this review collected one biologic sample. A minority collected two or more samples (46, 64, 65, 67, 73). Therefore, the potential for exposure misclassification in the studies that have been reviewed is generally high.

The number of repeat samples that are necessary to accurately determine an individual's average exposure and to differentiate exposure levels between individuals is dependent upon the intra-class coefficient (ICC) and the intra- vs. inter-individual variations in exposure to the toxicant of exposure, respectively (25). The limited data available from studies conducted in children indicate that temporal variation in exposure to BPA may be less pronounced in children, including infants, than in adults (ICC of 0.4–0.51 in children compared with 0.1–0.4 in adults) (34, 139, 140). In adults, it has been recommended that five urine samples should be collected within one discrete sampling period (i.e., 2 days) to classify exposure with acceptable accuracy (139). Based on an ICC of 0.51 in children over a 2-day period, one-spot sample can classify an individual into their correct exposure quartile 68% of the time (34). However, more samples are needed to correctly classify exposure over a longer period of time.

The intra- vs. inter-individual variation in children's exposure to phthalates and organophosphate insecticides has been studied by Sexton et al (25). They reported that the level of inter-individual variation amongst children as a proportion of total variance was significantly greater than intra-individual variation for the metabolite of DEP, the most common and abundant phthalate in personal care products (0.77 vs. 0.70), thus indicating that differences in exposure to DEP between individuals can be accurately detected by taking limited numbers of biologic samples. In contrast, inter-individual variation was significantly less of a contributor to total variance than intra-individual variation for metabolites of DEHP, BBzP and organophosphates, thereby indicating that more samples are required for accurate exposure classification for these toxicants. However, more studies are required

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Table 5 Strengths and limitations of the questionnaire-based approach.

Strengths	Limitations
Once-off administration of a questionnaire may gather sufficient data to accurately classify long-term exposure to toxicants with short half-lives and/or variable exposure patterns	Initial validation of the questionnaires for long-term exposure to toxicants with short half-lives requires extensive, repetitive biologic monitoring which is expensive, time consuming, burdensome and biomonitoring techniques may not be available for all toxicants of concern
Relatively non-intrusive for participants	Comprehensive repetitive exposure assessment questionnaires may be time consuming for participants to complete
Collection of individual behaviour data combined with environmental data (collected through a questionnaire or alternative indirect or direct approach) may improve the precision of exposure predictions at an individual level.	Unable to directly quantify internal exposure to toxicants
Inexpensive, particularly when questionnaires are administered online	Validation needs to be repeated for each new population it is to be used with
Can be used to capture exposure events that occur too infrequently to be reliably characterised through typical biomonitoring protocols	Cannot definitively identify all potential sources of exposure to EDCs in the home as EDC content and labelling practices vary greatly between goods
May be combined with other validated questionnaires to improve health risk assessment	Some exposure pathways that have a small impact on toxicant body burden may not be detectable through the questionnaire-based approach when other exposure pathways are unaccounted for.

to characterise the ICC for phthalates and insecticides in young children, as well as to characterise the ICC over the time frame, which is typically assessed through the questionnaire-based approach (months to years as opposed to days) (34).

Strengths and applications of the questionnaire-based approach

Up to this point of the discussion, we have suggested how the limitations of the questionnaire-based approach can be addressed by close attention to questionnaire design and validation. We now address the strengths and suggest potential applications of the questionnaire based approach, as summarised in Table 5. Although the data from questionnaires cannot be used to directly determine exposure concentrations, questionnaires are usually less intrusive and less costly than direct methods, particularly when they are administered online, which may allow researchers to increase the number of study participants. Questionnaires are the 'most efficient data collection method, allowing a larger study size and greater statistical power', provided that limitations with the questionnaire-based approach can be sufficiently minimised (29). As long as the questionnaire is first validated with an appropriate biologic sampling protocol, exposure questionnaires may prove to be particularly useful when it comes to characterising long-term exposure to toxicants with short half-lives. In these cases, researchers would otherwise have to collect multiple biologic samples at several time-points throughout the period of exposure that they were trying to capture. Furthermore, data obtained from questionnaires can be used to complement direct monitoring data, which provide useful insights into the contribution of particular exposure pathways to total exposure. Exposure assessment questionnaires may also be combined with other questionnaires like the validated Home Observation for the Measurement of the Environment to assess additional impacts of the home environment that may modify the health risks associated with children's exposure to toxicants (141).

It is worth noting that an initial search strategy using the terms 'questionnaire' and 'survey' failed to detect many of the relevant articles, as those studies matching questionnaire data with bio-monitoring rarely listed 'questionnaire' as a keyword, and many studies did not mention that questionnaires were administered in the abstract. This may be an indication that the potential benefits of questionnaires as a valuable tool for exposure assessment is being under-recognised.

Conclusion

The questionnaire-based approach has the potential to predict the exposure of young children to EDCs through exposure pathways common to the domestic environment, provided that several aspects of study design, in particular sampling methods, that may affect the validation of

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questionnaires are addressed. A specific questionnaire for EDC exposure in children – properly designed and validated – is an important measurement tool for the future. Such a questionnaire can be used with parents of young children, from whom it may be difficult to collect biologic specimens. It could then be used to collect exposure data for epidemiologic studies and it could ultimately be used by public health and health care practitioners to design, monitor, and evaluate interventions towards minimising the exposure of young children to EDCs.

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