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A randomized controlled trial of a housing intervention to reduce endocrine disrupting chemical exposures in children

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A B S T R A C T

Few studies have considered household interventions for reducing endocrine disrupting chemical (EDC) exposures. We conducted a secondary analysis of a randomized controlled trial, originally designed to reduce lead exposure, to evaluate if the intervention lowered EDC exposures in young children. Study participants were children from the Cincinnati, Ohio area (n = 250, HOME Study). Prenatally, families received a housing intervention that included paint stabilization and dust mitigation, or as a control, injury prevention measures. At 24-months, we measured organophosphate esters (OPEs) and phthalates or their metabolites in dust and urine. We measured perfluoroalkyl substances (PFAS) in dust and serum at 24- and 36-months, respectively. We assessed associations between dust and biomarker EDCs using Spearman correlations, characterized EDC mixtures via principal components analysis, and investigated treatment effects using linear regression. To mitigate selection bias, we fit statistical models using inverse probability of retention weights. Correlations between dust EDCs and analogous biomarkers were weak-to-moderate (ρ's $\leq$ 0.3). The intervention was associated with 23 % (95 % CI: −38, −3) lower urinary DEHP metabolites and, in a per-protocol analysis, 34 % lower (95 % CI: −55, −2) urinary MBZP. Additionally, among Black or African American children, the intervention was associated with lower serum concentrations of several PFAS (e.g., −42 %; 95 % CI: −63, −8 for PFNA). Household interventions that include paint stabilization and dust mitigation may reduce childhood exposures to some phthalates and PFAS in Blacks/African Americans. These findings highlight the need for larger studies with tailored and sustained housing interventions.

1. Introduction

Anthropogenic chemicals, including perfluoroalkyl substances (PFAS), phthalates, and flame retardants are ubiquitous in the environment.(Kato, Wong, et al., 2011; World Health Organization, 2017) As such, human exposure to these compounds is widespread and, in some cases, nearly universal.(National Center for Environmental Health (U. S.), 2022; Wang et al., 2019) Many of these compounds can interfere with endocrine system development and functioning. For example, PFAS are known to activate human PPARα,(Evans et al., 2022) a transcription factor involved in lipid metabolism that plays a role in a variety of human diseases.(Lin et al., 2022) Phthalates can perturb endocrine systems through direct activation of estrogen receptors, inhibition of androgen production, and thyroid stimulating hormone receptor disruption.(Engel et al., 2017; Huang et al., 2022) Exposure to these endocrine distributing chemicals (EDCs) in early life has been associated with numerous adverse health outcomes including immune system dysfunction, adverse reproductive outcomes, behavioral problems, cognitive decrements, and obesity.(Braun, 2017; Ghassabian et al., 2022).

Despite substantial scientific evidence of their harmful health effects, the regulatory landscape for EDCs remains a patchwork of limited federal and state-level policies that are often circumvented through the use of under-studied, structurally similar replacements.(Brennan et al., 2021; Kamrin, 2009) This necessitates the identification of effective interventions to reduce exposure. This is particularly true for infants and children as they experience more exposure to EDCs compared to adults on a body weight basis,(Ghassabian et al., 2022) and early life is a

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critical time of endocrine mediated development that is highly susceptible to EDC toxicity (Gore et al., n.d.).

Pathways through which children are exposed to EDCs in their homes are numerous and diverse. Consumption of contaminated food and water, direct ingestion or dermal absorption, personal care product use, and ingestion or inhalation of contaminated dust are all considered major routes.(Bearer, 1995; Gore et al., n.d.) The importance of specific exposure pathways depends on both the chemical class and specific species in question. For example, household dust is considered a major exposure source for phthalates which are ubiquitous in personal care products and building materials.(Authority (EFSA), 2005; Hammel et al., 2019) For more volatile organophosphate esters (OPE) used as flame retardants and plasticizers in many household furnishings, direct dermal absorption and hand-to-mouth ingestion is likely a more important exposure pathway than dust.(Phillips et al., 2018) In contrast, ingestion of contaminated food and water is considered the primary exposure route for environmentally persistent PFAS; however, dust ingestion and inhalation may be an important route when textiles coated with PFAS are present.(Agency for Toxic Substances and Disease Registry, 2021; Hall et al., 2023; Hepburn et al., 2019) As such, wholistic housing interventions that target multiple childhood EDC exposure pathways could be vital to reduce the public health burden of EDCs.

Most interventions to reduce EDC exposures have been dietary or educational, but sometimes involve replacing traditional consumer products with healthier alternatives.(Martin et al., 2022) To our knowledge, a study by Sears et al. is the only published work that examined a housing intervention that includes dust mitigation and paint stabilization and EDC body burden in children. Both household dust and deteriorating paint being potential sources of EDC exposures as household dust contains a mixture of EDCs that can be ingested or inhaled by humans (Mitro et al., 2016; Zhu et al., 2023) and some EDCs have been used in paint manufacturing.(Fan et al., 2024; Glüge et al., 2020) The Sears et al. study investigated whether an intervention originally designed to reduce lead exposure lowered phthalate exposure among young children. That study found the intervention significantly lowered Di(2-ethylhexyl)phthalate (DEHP) metabolites in urine from 12- to 36-months of age.(Sears et al., 2020) Our study was designed to expand on the Sears et al. work by exploring whether the same randomized intervention lowered not just exposure to phthalates but also OPEs and PFAS as measured by levels in household dust and children's biomarkers.

2. Methods

2.1. Study participants and intervention assignment

We used data from The Health Outcomes and Measures of the Environment (HOME) Study, an ongoing cohort of maternal-child pairs. Between March 2003 and January 2006, the HOME Study enrolled 468 pregnant women from five counties in the greater Cincinnati metropolitan area. Enrolled women were, on average, 29 years old, mostly white (62 %), well-educated, married (64 %), and did not report tobacco use (88 %). Through 2019, mothers and children in this cohort completed up to three prenatal visits (16-, 20-, and 26-weeks gestation) and up to nine postnatal visits (delivery, four weeks, and one, two, three, four, five, eight, and twelve years) at study clinics and their homes. The HOME Study was approved by institutional review boards at Cincinnati Children's Hospital Medical Center and affiliated hospitals. Mothers provided informed consent at enrollment. We refer the reader to Braun et al. 2016 (Braun et al., 2016) and Braun et al. 2020 (Braun et al., 2020) for more detailed descriptions of this cohort's characteristics, enrollment, and follow-up.

Nested within this observational study was a randomized controlled trial of a housing intervention designed to reduce child lead exposure. (Braun et al., 2018) During pregnancy, 355 pregnant women were randomized into one of two housing interventions. The control group received injury prevention measures and the intervention group received household modifications to mitigate household lead. Randomization was conducted using random number generation and research assistants were blinded to the intervention status of participants. We limited this analysis to 250 children whose households were randomized to one of the intervention groups and had a dust sample available from the 24-month at home follow-up visit (Fig. 1). In cases where twin pairs were eligible for our study, we randomly selected one twin to be included in our analysis.

2.2. Intervention

Trained contractors carried out a housing intervention to mitigate child lead exposure for participants assigned to the intervention group. This intervention was specific to the lead hazards of the home.(Braun et al., 2018; Sears et al., 2020) The intervention involved removing and repainting surfaces with peeling, cracked or otherwise deteriorating paint; complete replacement of windows with lead paint in poor condition; installation of window trough liners; making floors smooth and easily cleanable by replacing broken floor tiles and refinishing hardwood floors; and extensive cleaning and dust elimination following the intervention. We hypothesized these steps would lower child EDC exposures by reducing contamination of household dust via EDCs in household paint, ingestion of paint fragments, and ingestion or inhalation of contaminated household dust. The intervention was completed by 32-weeks gestation and before birth. If mothers and children moved within 23 months of birth, the intervention was attempted at their new home. The control group had injury prevention devices installed (e.g., stair gates) and other household modifications performed to improve safety (e.g., lowering tap water temperature, securing rugs, and covering electrical sockets). However, we anticipate these measures had no effect on child EDC exposure.

2.3. EDC in dust, urine, and serum

During 24-month home visits, trained study staff used the high-volume surface sampler, HVS3,(Colt et al., 2008) to collect household dust from main activity rooms and child bedrooms. Dust collected from each room was pooled into a single sample. These samples were stored between −20 and −80℃ and passed through a 300 μm sieve before being analyzed.(Mendy et al., 2023) We focused our analysis on OPEs and phthalates whose metabolites were also measured in urine at 24-months and on PFAS that were also measured in serum at 36-months (Table 1). For OPEs, this included tris (2-chloroethyl) phosphate (TCEP), tris (1,3-dichloroisopropyl) phosphate (TDCPP), and triphenyl phosphate (TPP). For phthalates, benzylbutyl phthalate (BBzP), di-n-octyl phthalate (DNOP), bis(2-ethylhexyl) phthalate (DEHP), and diethyl phthalate (DEP) were analyzed. For PFAS, we considered perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorononanoic acid (PFNA), perfluorohexane sulfonate (PFHxS), as well as perfluorooctanesulfonamide (PFOSA) and 2-(N-ethyl-perfluorooctanesulfonamido) acetic acid (NEtFOSAA), which are two potential precursors of PFOS.

We measured OPE dust concentrations using ultra-high performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS).(La Guardia & Hale, 2015; Percy et al., 2020) To measure dust phthalate concentrations we used gas chromatography (GC) paired with high resolution MS. We measured dust PFAS concentrations using LC paired with high resolution MS. The methods used to measure dust concentrations of phthalates and PFAS in this study have not been published so we provided additional details on the analytical methods in the Supplemental material (sTables 1-5 and sFigures 1 and 2). For each analyte, we calculated dust loadings as: dust concentration (ng/g) × sieved weight of dust sample (g) × sample area $(m^2)^{-1}$. We focused our analysis on dust loadings as opposed to concentrations, because the former is considered a better indicator of human exposure to dust contaminants.

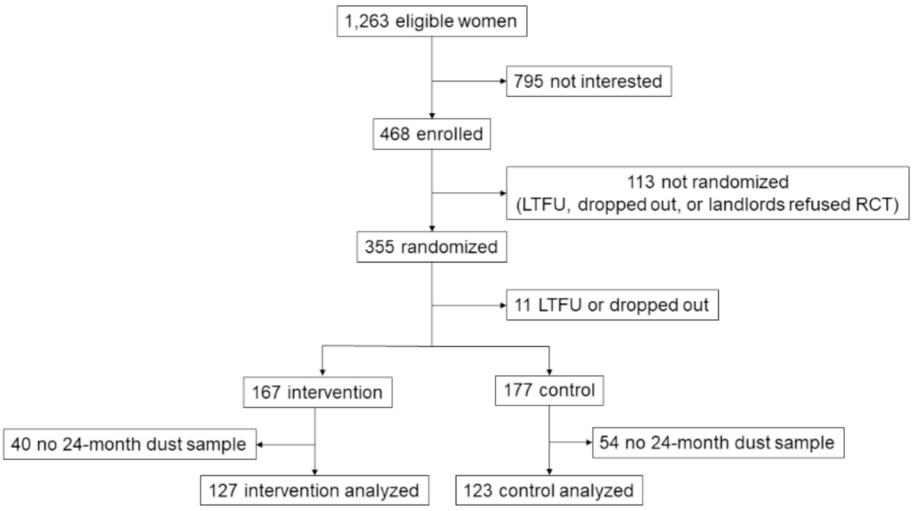

Fig. 1. Flowchart describing derivation of analytic sample.

Table 1
EDCs and EDC metabolites measured in dust, urine, and serum in the HOME Study at child ages 24- or 36-months.

Class	Dust	Urine	Serum
OPEs	Tris (2-chloroethyl) phosphate (TCEP)	Bis(2-chloroethly) phosphate (BCEtP)	N/A
	Tris (1,3-dichloroisopropyl) phosphate (TDCPP)	Bis(1,3-dichloroisopropyl) phosphate (BDCPP)	N/A
	Triphenyl phosphate (TPP)	Diphenyl phosphate (DPHP)	N/A
PFAS[†]	N-Ethyl-N-[(heptadecafluorooctyl)sulphonyl]glycine (NEtFOSAA)	N/A	*
	Perfluorooctanesulfonamide (PFOSA)	N/A	*
	Perfluorohexanesulphonic acid (PFHxS)	N/A	Perfluorohexanesulphonic acid (PFHxS)
	Perfluorononanoic acid (PFNA)	N/A	Perfluorononanoic acid (PFNA)
	Perfluorooctanoic acid (PFOA)	N/A	Perfluorooctanoic acid (PFOA)
	Perfluorooctane sulfonic acid (PFOS)	N/A	Perfluorooctane sulfonic acid (PFOS)
Phthalates	Benzylbutyl phthalate (BzBP)	Monobenzylphthalate (MBZP)	N/A
	Di-n-octyl phthalate (DNOP)	Mono(3-carboxypropyl) phthalate (MCPP)	N/A
	Diethyl phthalate (DEP)	Monoethyl phthalate (MEP)	N/A
	Di(2-ethylhexyl) phthalate (DEHP)	Mono(2-ethyl-5-carboxypentyl) phthalate (MECPP) [‡]	N/A
		Mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) [‡]	
		Mono(2-ethyl-5-oxohexyl) phthalate (MEOHP) [‡]	

[*] NEtFOSAA and PFOSA can degrade to PFOS in the environment.
[†] PFAS measured in serum at 36-months.
[‡] These three DEHP metabolites were combined as a molar sum in our analysis. Another metabolite of DEHP, mono(2-ethylhexyl) phthalate, was excluded because of contamination of diaper inserts used in urine sample collection.

(Bevington et al., 2021) To determine whether the intervention lowered total household dust at 24-months, we also considered total dust loading as: sieved weight of dust sample (g) × sample area $(m^2)^{-1}$.

During clinic visits, we measured concentrations of metabolites of four OPEs and six phthalates in urine at 24-months and six PFAS in serum at 36-months. Urine samples were collected using diaper inserts or taken from training potties lined with diaper inserts. Prior to analysis, urine and serum samples were stored at −20 and −80℃ respectively. To quantify urinary OPEs and phthalates and serum PFAS, trained technicians at the Centers for Disease Control and Prevention used UHPLC-MS. (Jayatilaka et al., 2017, 2019; Kato, Basden, et al., 2011; Silva et al., 2007) We creatinine standardized urinary metabolites of OPEs and phthalates to account for urine dilution. We combined three metabolites of DEHP, mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP); mono(2-ethyl-5-oxohexyl) phthalate (MEHOP); and mono(2-ethyl-5-carboxypentyl) phthalate (MECPP), as a molar sum (ΣDEHP) by multiplying the creatinine standardized urinary concentration of by their respective molar masses and taking the sum. Diaper inserts used for urine sample collection were contaminated with di-n-butyl phthalate, di-*iso*-butyl phthalate, and one metabolite of DEHP, mono(2-ethylhexyl) phthalate, so the latter was not included in the sum of DEHP metabolites.

2.4. Statistical analysis

We initially examined descriptive statistics of baseline participant characteristics overall and stratified by intervention group. We also compared baseline characteristics between randomized participants who were included and excluded from our analysis based on whether they had a 24-month house dust sample collected. We imputed all analyte concentrations in dust, urine, and serum that were non-detectable as LOD ÷ $\sqrt{2}$.(Hornung & Reed, 1990) To describe dust, urine, and serum EDC measures, we calculated geometric means, 25th and 75th percentiles, and %<LOD for each analyte. To assess bivariate associations between biomarker and dust EDCs we used Spearman correlations and created a chord diagram.

To adjust for potential selection bias due to attrition, we constructed inverse probability of retention weights (IPRWs). Using logistic regression, we estimated the probability that a participant was included in our analysis conditional on baseline characteristics: maternal and child race (White/Black/other) and Hispanic ethnicity, maternal age at delivery (years), household income ($ per year), maternal education (<HS/HS or GED/some college/college or higher), breastfeeding (any/none), housing type (single family/other), cleanliness (appears clean/no or some cleaning), clutter (high/low or moderate), and intervention group (lead/

injury). We took the inverse of these predicted probabilities and used them as frequency weights in all statistical models. We assessed the effectiveness of our IPRWs by calculating the weighted and unweighted standardized difference ($(\mu_{included}-\mu_{excluded})/\sigma_{included}$) in baseline characteristics between included and excluded participants. We considered a standardized difference threshold of ≤ 0.2 as adequate balance.(Zhang et al., 2019).

To characterize EDC mixtures in dust or biomarkers, we used principal components analysis (PCA). We fit separate PCA models for each matrix-chemical class combination (e.g., dust OPEs, urinary OPE metabolites, dust PFAS, serum PFAS etc.). Ln-transformed dust loadings and metabolite concentrations were mean-centered and scaled to the standard deviation prior to fitting PCA models. All principal component scores were coded such that they were positively correlated with analyte loadings or concentrations.

Our primary examination of treatment effects was carried out as an intention-to-treat analysis, including all eligible participants regardless of whether they had relocated since randomization. To quantify the intervention effect, we used linear regression, regressing each ln-transformed EDC biomarker concentration, ln-transformed dust loading, or component score on intervention status. We expressed regression coefficients for intervention status as a percent change using the control group as a reference category calculated as $(e^{\beta}-1) \times 100$ % for dust and biomarker concentrations. Negative values for percent differences indicate lower loadings or concentrations for the intervention group. We considered effect estimates with confidence intervals that did not contain zero as statistically significant.

For sensitivity analysis, we conducted a per-protocol analysis of treatment effects using only participants who, at 24-months, had not relocated since randomization (n = 154). For our per-protocol analysis, we recalculated IPRWs using the same procedure described above. Second, since ingestion is a primary route of exposure to EDCs in dust, (Zhu et al., 2023) we conducted a stratified analysis of urine and serum analytes by maternal report of toy mouthing frequency at 24-months old (daily/<daily). Additionally, Braun et al. previously reported that the same lead reduction intervention reduced blood-lead concentration only in non-Hispanic black children.(Braun et al., 2018) As such, we conducted a stratified analysis of urine and serum analytes by child race (White/Black or African American) excluding those who reported being "other/multiracial" due to small sample size. We also stratified our analysis based on whether a child was breastfed ≥ 14 weeks, the median length of breastfeeding among children in the HOME cohort. We considered effect modification to be statistically significant if the p-value for a likelihood ratio test comparing nested models with and without an interaction term between intervention group and effect modifier was < 0.05. Lastly, in an attempt gain statistical precision, we refit our primary statistical models including precision variables. These precision variables were selected using backwards model selection based on AIC with a starting saturated model containing intervention status along with maternal age at delivery (years), income ($ per year), maternal education (<HS/HS or GED/some college/college or higher), age at 24-month visit (years), sex, child race (White/Black/other), housing type (single family or other), and breastfeeding (<14 or $\geq$ 14 weeks). Intervention status was forced into the final selected model.

3. Results

The 250 children eligible for our study were about half female (52 %), mostly White (74 %), largely non-Hispanic (97 %), and 87 % had been fed at least some human milk. Their mothers were on average aged 30 years at delivery, 62 % had a bachelor's degree or higher, and had an average annual household income of $67,570. Most homes were single family (80 %), had low to moderate clutter (96 %), and were carpeted (85 %). Baseline characteristics were similar between the intervention and control groups. Importantly, median PFAS concentrations in cord serum were similar, suggesting prenatal EDC exposure did not confound our effect estimates (Table 2).

We observed notable differences in baseline characteristics between randomized participants with a dust sample available and those without. Specifically, those included in our analysis were more likely to be White (74 vs. 55 %), have a mother with a college degree (62 vs. 40 %), live in a single-family home (80 vs. 66 %), and have a higher annual household income (sTable 6). Our IPRWs were effective in balancing baseline characteristics between these two groups, as all standardized differences in participant characteristics were ≤ 0.2 (Fig. 2). The same was true for balancing baseline characteristics in our per-protocol analysis

Table 2
Baseline participant characteristics by intervention group in the HOME Study (2003–2006).

	Control (n = 123)	Intervention (n = 127)	Total (n = 250)
Maternal age at delivery (years)	30.3 (5.3)	30.5 (5.3)	30.4 (5.3)
Maternal race			
White or Caucasian	96 (78.0)	95 (74.8)	191 (76.4)
Black or African American	22 (17.9)	26 (20.5)	48 (19.2)
Other/Multiracial	5 (4.1)	6 (4.7)	11 (4.4)
Maternal ethnicity			
Not Hispanic	121 (98.4)	124 (97.6)	245 (98.0)
Hispanic	2 (1.6)	3 (2.4)	5 (2.0)
Maternal education			
< High school	5 (4.1)	10 (7.9)	15 (6.0)
High school or GED	10 (8.1)	11 (8.7)	21 (8.4)
Some college or trade school	32 (26.0)	27 (21.3)	59 (23.6)
Bachelor's or higher	76 (61.8)	79 (62.2)	155 (62.0)
Annual household income ($)	67,195.1 (38,564.9)	67,933.1 (42,117.9)	67,570 (40,329.6)
Child sex			
Male	53 (43.1)	66 (52.0)	119 (47.6)
Female	70 (56.9)	61 (48.0)	131 (52.4)
Child race			
White or Caucasian	95 (77.2)	90 (70.9)	185 (74.0)
Black or African American	20 (16.3)	24 (18.9)	44 (17.6)
Other/Multiracial	8 (6.5)	13 (10.2)	21 (8.4)
Child ethnicity			
Not Hispanic	121 (98.4)	122 (96.1)	243 (97.2)
Hispanic	2 (1.6)	5 (3.9)	7 (2.8)
Housing type			
Single family house	102 (82.9)	98 (77.2)	200 (80.0)
Other	21 (17.1)	29 (22.8)	50 (20.0)
Cleanliness			
Appears clean	78 (63.4)	82 (64.6)	160 (64.0)
No/Some cleaning	45 (36.6)	45 (35.4)	90 (36.0)
Clutter			
Low/moderate clutter	116 (94.3)	124 (97.6)	240 (96.0)
High clutter	7 (5.7)	3 (2.4)	10 (4.0)
Flooring type			
Carpet	103 (84.4)	107 (85.6)	210 (85.0)
Wood or linoleum/vinyl	19 (15.6)	18 (14.4)	37 (15.0)
missing	1	2	3
Cohabitation			
Cohabitating (married or unmarried)	108 (87.8)	105 (82.7)	213 (85.2)
Living alone	15 (12.2)	22 (17.3)	37 (14.8)
Breastfeeding Hx			
No breastfeeding	14 (11.4)	19 (15.0)	33 (13.2)
At least some breastfeeding	109 (88.6)	108 (85.0)	217 (86.8)
PFHxS cord blood (ng/mL)	0.7 [0.5, 1.2]	0.7 [0.4, 1.1]	0.7 [0.5, 1.2]
missing	51	57	108
PFNA cord blood (ng/mL)	0.4 [0.3, 0.6]	0.5 [0.4, 0.6]	0.4 [0.3, 0.6]
missing	51	57	108
PFOA cord blood (ng/mL)	3.4 [2.6, 5.0]	3.5 [2.5, 4.7]	3.4 [2.5, 4.8]
missing	51	57	108
PFOS cord blood (ng/mL)	4.1 [2.9, 6.1]	4.9 [3.4, 6.4]	4.4 [3.2, 6.4]
missing	51	57	108

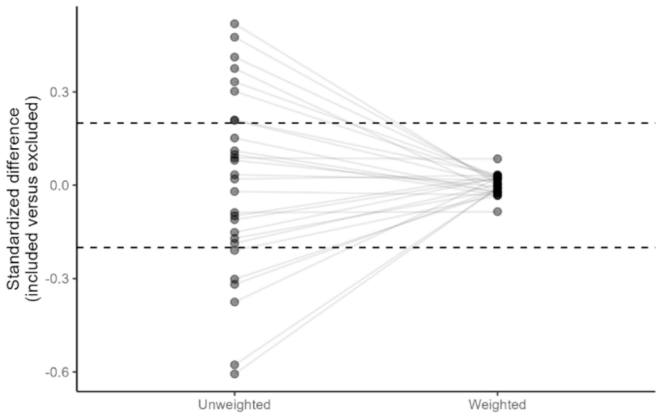

Fig. 2. IPRW weighted and unweighted standardized differences in baseline characteristics, maternal and child race (White/Black/other) and Hispanic ethnicity, maternal age at delivery (years), household income ($ per year), maternal education (<HS/HS or GED/some college/college or higher), breast-feeding (any/none), housing type (single family/other), cleanliness (appears clean/no or some cleaning), clutter (high/low or moderate), and intervention group (lead/injury) between included and excluded participants. Dashed lines have y-intercepts at −0.2 and 0.2.

(sFigure 3).

The geometric mean of total dust loading was 0.3 g of dust/m^2. OPEs measured in dust were detected in ≥ 93 % of samples. Detection frequencies for the six PFAS measured in dust ranged from 74 % (PFOSA) to 100 % (PFHxS). Four of the five phthalates measured in dust were detected in ≥ 98 % of samples while DNOP was detected in 66 %. On average, dust loadings were highest for phthalates followed by OPEs and then PFAS. DEHP had the highest geometric mean dust loading (GM: 100,239 ng/m^2) and PFOSA had the lowest (GM: 0.1 ng/m^2). Several EDCs measured in dust had a relatively high proportion of values < LOD. Namely, PFOS (23 %), PFOSA (27 %), and DNOP (34 %). Phthalate and OPE metabolites measured in urine were detected in > 93 % of samples, except BCEtP (87 %). Geometric mean urinary phthalate metabolite concentrations exceeded that of OPE metabolites. The four PFAS measured in serum were nearly universally detected. Serum concentrations were highest for PFOS (GM: 7.2 ng/mL) and lowest for PFNA (GM: 1.4 ng/mL) (Table 3).

In general, EDCs were most correlated within chemical class and within biological matrix (urine or serum) (Fig. 3). Correlations between EDCs in dust with their analogs measured in urine or serum were in the weak-to-moderate range (ρ's ≤ 0.3). Dust PFAS and phthalates were more correlated with their serum or urinary analogs when compared to OPEs. Dust DEP and urinary MEP was the most correlated pair (ρ: 0.3) (sFigure 4-6).

The first principal component from each matrix-class specific PCA explained 74, 50, and 68 % of the variance in OPE, PFAS, and phthalate dust loadings, respectively; and 55, 53, and 54 % of the variance in urinary OPE metabolite, serum PFAS, and urinary phthalate metabolite concentrations, respectively. Given the importance of the first component score from each principal component model, we used it as a summary measure for that matrix-chemical class.

In our primary, intention-to-treat analysis, there was little evidence that the intervention was associated with differences in 24-month dust loadings for any of the EDCs considered. Point estimates for intervention effects on 24-month dust loadings ranged from −41 % (95 % CI: −71, 19) for PFOA to 73 % (95 % CI: −25, 298) for PFOS (Table 4). With respect to biomarker EDC concentrations, the intervention was most strongly associated with lower urinary DEHP (ΣDEHP) metabolites (percent difference: –22; 95 % CI: −38, −3) but again, there was little evidence that the intervention lowered biomarker concentrations of other EDCs. Point estimates for intervention effects on EDC biomarker concentrations other than ΣDEHP ranged from −20 % (95 % CI: −41, 9) for BDCPP to 1 % (95 % CI: −29, 42) for MEP (Fig. 4 and Table 4). Results from models regressing matrix-class-specific principal component scores on intervention status echoed the results from our analysis of individual analytes (Fig. 5).

Our per-protocol analysis suggested the intervention group had lower urinary MBZP concentrations (percent difference: −34; 95 % CI: −55, −2). Additionally, point estimates for OPE and phthalate dust loadings were attenuated or reversed in direction. Lastly, point estimates

Table 3
Descriptive statistics for EDCs measured in dust, urine, and serum in the HOME Study (2003–2006).

Class	Analyte	Matrix	Age (months)	n	Geometric mean	25th	75th	% <LOD	Unit
	Total dust load	Dust	24	215	0.3	0.1	0.6	NA	g/m^2
OPEs	TCEP	Dust	24	215	150	32	878	6.5	ng/m^2
	TDCPP	Dust	24	215	528	163	2,397	6.5	ng/m^2
	TPP	Dust	24	215	577	208	1,570	3.3	ng/m^2
PFAS	NEtFOSAA	Dust	24	162	2.7	0.8	10	12	ng/m^2
	PFHxS	Dust	24	162	9.3	1.8	41	0	ng/m^2
	PFNA	Dust	24	162	1	0.3	2.8	6.2	ng/m^2
	PFOA	Dust	24	162	6.3	1.3	25	17	ng/m^2
	PFOS	Dust	24	162	5.4	1.1	36	23	ng/m^2
	PFOSA	Dust	24	162	0.1	0	1	27	ng/m^2
Phthalates	BzBP	Dust	24	167	8,579	3,191	28,945	1.8	ng/m^2
	DEHP	Dust	24	167	100,239	47,465	221,585	0	ng/m^2
	DNOP	Dust	24	167	1,295	88	11,335	34	ng/m^2
	DBP	Dust	24	167	6,929	3,044	16,553	0	ng/m^2
	DEP	Dust	24	167	689	264	1,878	0	ng/m^2
OPE metabolites*	BCEtP	Urine	24	190	2.9	1.6	5.4	13	μg/g
	BDCPP	Urine	24	196	5.9	2.9	11	2	μg/g
	DPhP	Urine	24	196	8.5	4.7	13	0	μg/g
PFAS	PFHXS	Serum	36	170	2.2	1.2	3.5	0	ng/mL
	PFNA	Serum	36	170	1.4	1	1.8	0	ng/mL
	PFOA	Serum	36	170	5.9	4	7.9	0	ng/mL
	PFOS	Serum	36	170	7.2	5	11	0	ng/mL
Phthalate metabolites*	MBZP	Urine	24	205	38	21	64	0.5	μg/g
	MCPP	Urine	24	205	14	9.4	22	0	μg/g
	MECPP	Urine	24	205	138	81	216	0	μg/g
	ΣDEHP†	Urine	24	205	0.8	0.5	1.4	6.5	μmol/g

* Creatinine standardized by dividing urinary concentration (μg/L) by creatinine concentration (g/L).
† Molar sum of MECPP, MEHHP, and MEOHP.

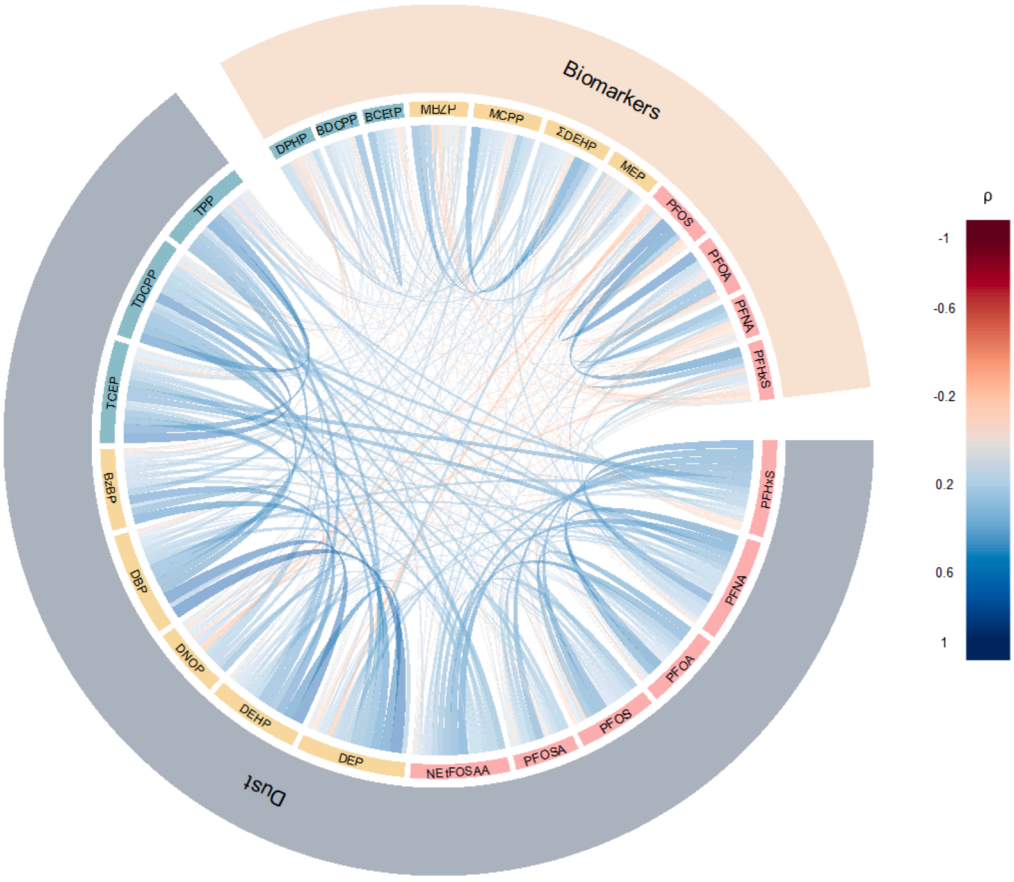

Fig. 3. Spearman correlations for EDCs and EDC metabolites measured in dust, urine, and serum in the HOME Study (2003–2006). Both the width of the band and the intensity of the color correspond to the strength of the association.

for PFAS dust loadings in the per-protocol analysis were notably stronger compared to our intention-to-treat analysis, but otherwise results were similar (Table 4).

We observed no convincing evidence of effect modification of treatment effects for biomarker EDCs by mouthing behaviors or length of breastfeeding (Fig. 6 and sTable 8). However, when we stratified our analysis by child race, we found that for Black or African American children, serum concentrations of PFNA (percent difference: −42; 95 % CI: −63, −8), PFOA (percent difference: −21; 95 % CI: −38, −1), and PFOS (percent difference: −38; 95 % CI: −56, −13) were lower in the intervention as compared to the control group. Although, we found statistically significant effect modification of the intervention effect by race for PFNA only (p-value for interaction: 0.033). Results from our models including precision variables were comparable to results from our primary analysis with some modest gains in precision for some biomarkers (sFigure 7). The optimal model based on backwards selection was slightly different for each dependent variable but generally contained ≤ four precision variables. Maternal age at delivery, maternal education, income, age at 24-month visit, race, and breast feeding were frequently retained.

4. Discussion

In our secondary analysis of a randomized controlled trial, we found that an intervention (originally designed to lower child lead exposure via dust control, paint stabilization, cleaning, and other housing renovations) may have reduced child exposure to some EDCs, especially PFAS for Black or African American children. This study, which expands on previous work by Sears et al., is, to our knowledge, one of the only published studies examining whether such a housing intervention reduced EDCs in children's biomarkers and household dust.

Our study's novelty makes comparing it with existing literature difficult. We replicated the Sears et al. finding demonstrating that this intervention may have lowered urinary DEHP metabolites although their estimated effect size was smaller (percent difference: −12; 95 % CI: −23, 1). This is likely due to differences in study design and statistical analysis.(Sears et al., 2020) The effects we observed were smaller than those observed in studies of dietary interventions to reduce phthalate exposures. For example, Rudel et al. found that a diet with fewer packaged foods reduced urinary DEHP metabolites by 53–56 %.(Rudel et al., 2011) However, the efficacy of our housing intervention may be on par with interventions targeting personal care products (PCPs) as a source of EDC exposures. For example, Harley et al. reported an intervention promoting PCPs labeled free of several EDCs reduced concentrations of some phthalate metabolites between 11 and 27 % among adolescent girls.(Harley et al., 2016) Although, as expected, that study only observed reductions in metabolites of low molecular weight phthalates used in PCPs, whereas we observed reductions primarily in metabolites of high molecular weight phthalates used as plasticizers, in electronics, and flooring. The clinical significance of the observed reductions in urinary phthalate metabolites is unclear. For example, in our per-protocol analysis, geometric mean urinary concentrations for MBZP for the intervention (29.4 μg/g) and control (36.8 μg/g) groups was above the NHANES 75th percentile for children ages 6–11 in 2009–2010 (29.3 μg/g).(National Center for Environmental Health (U.S.), 2022).

One of the more notable findings of our study was that the intervention reduced serum PFAS concentrations among Black or African American children. It is unclear why, especially since household dust, a focus for this intervention, is not generally considered a major source of PFAS exposure.(Mitro et al., 2016; Zhu et al., 2023) The paint

Table 4
Percent difference (±95 % CI) in 24-month EDC dust loadings, 24-month urinary OPE and phthalate metabolite concentrations, and 36-month PFAS serum concentrations comparing intervention to control group (The HOME Study, 2003–2006): Intention-to-treat vs. per-protocol analysis.

Matrix	Class	Analyte	Percent difference (±95 % CI)	
			Intention-to-treat	Per-protocol
Dust loadings	NA	Total load	20 (−16, 73)	24 (−41, 158)
Dust loadings	OPEs	TCEP	16 (−38, 116)	−35 (−74, 65)
Dust loadings	OPEs	TDCPP	45 (−20, 165)	–23 (−68, 88)
Dust loadings	OPEs	TPP	60 (−4, 167)	33 (−43, 214)
Dust loadings	PFAS	NEtFOSAA	–32 (−62, 21)	−50 (−77, 8)
Dust loadings	PFAS	PFOSA	−9 (−62, 115)	−69 (−92, 23)
Dust loadings	PFAS	PFHxS	−29 (−63, 38)	−48 (−80, 36)
Dust loadings	PFAS	PFNA	−36 (−67, 21)	−52 (−81, 23)
Dust loadings	PFAS	PFOA	−41 (−71, 19)	−62 (−88, 18)
Dust loadings	PFAS	PFOS	73 (−25, 298)	56 (−52, 404)
Dust loadings	Phthalates	BzBP	1 (−49, 97)	−2 (−69, 210)
Dust loadings	Phthalates	DBP	2 (−34, 58)	−28 (−61, 36)
Dust loadings	Phthalates	DNOP	30 (−45, 212)	−4 (−82, 409)
Dust loadings	Phthalates	DEP	37 (−17, 126)	−2 (−58, 128)
Dust loadings	Phthalates	DEHP	3 (–32, 57)	−30 (−67, 48)
Urine	OPEs	BCEtP	−16 (−41, 19)	0 (−34, 50)
Urine	OPEs	BDCPP	−20 (−41, 9)	−8 (−43, 48)
Urine	OPEs	DPhP	−6 (−25, 16)	11 (−14, 44)
Serum	PFAS	PFHxS	−4 (−28, 29)	33 (−36, 180)
Serum	PFAS	PFNA	−5 (−21, 15)	−5 (−27, 25)
Serum	PFAS	PFOA	−8 (−21, 9)	−14 (−39, 21)
Serum	PFAS	PFOS	−10 (−26, 10)	−6 (−34, 33)
Urine	Phthalates	MBZP	−16 (−36, 11)	−34 (−55, −2)
Urine	Phthalates	MCPP	−15 (−29, 2)	−11 (−29, 11)
Urine	Phthalates	MEP	1 (−29, 42)	−28 (−55, 16)
Urine	Phthalates	ΣDEHP	–22 (−38, −3)	−14 (−37, 17)

Note: Percent difference (±95 % CI) in EDC dust loadings, 24-month urinary OPE and phthalate metabolite concentrations, and 36-month PFAS serum concentrations comparing intervention to control group. Estimates from linear model regressing ln-transformed loadings and concentrations on intervention status weighted using IPRW. Percent difference calculated as exp(βintervention) x100%. Positive values indicate higher loadings or concentrations in the intervention group. ΣDEHP is the molar sum of urinary MEHHP, MEOHP, and MECOO. Intent-to-treat analysis includes all eligible participants. Per-protocol analysis includes only participants who, at 24-months, still lived in the home where the intervention was performed. Sample sizes for each model stratified by intervention group can be found in sTable 7.

stabilization aspect of this intervention could be important here as PFAS have been used extensively in paint manufacturing(Glüge et al., 2020) and Black or African American children are more likely to live in housing with deteriorating paint.(Lanphear et al., 1996; Yeter et al., 2020) One comparable intervention study by Morgan et al. showed a lifestyle intervention designed to reduce dietary lipids significantly lowered circulating PFAS by as much as 20 %, similar to our findings.(Morgan et al., 2023) There is also reason to believe that the differences in serum PFAS associated with the intervention among Black or African American children are clinically meaningful, at least for PFOS, where the geometric mean serum concentration in the intervention group (4.1 ng/mL) but not the control group (6.2 ng/mL) was lower than the established German human biomonitoring (HBM-I) value.(Hölzer et al., 2021).

With respect to EDCs in dust, similar studies found that health-conscious renovations and article substitution significantly lowered dust concentrations of several EDCs in Swedish preschools.(Giovanoulis et al., 2019; Langer et al., 2021) For example, Giovanoulis et al. found that article substitution reduced dust concentrations of two phthalates also analyzed in our study including DEHP (≈50 % reduction) and BzBP (≈25 % reduction), whereas we could not conclude that the intervention had such an effect of phthalate dust loadings.

It is also worth mentioning that 85 % of homes had carpeting in the main activity room at baseline. When it comes to lead, flooring type has been demonstrated to influence the relationship between dust lead loadings and child blood concentrations. Interestingly, Yiin et al.'s secondary analysis of a dust mitigation intervention to reduce lead exposure found that it was only effective in non-carpeted homes.(Yiin et al., 2003) As such, the efficacy of this intervention may have been curtailed by the predominance of carpet flooring in participant homes.

We suspected that the intervention would have reduced children's EDC body burden by reducing exposures via household dust. However, most correlations between EDCs in dust and their analogs in biomarkers were weak-to-moderate ($\rho \leq 0.3$) and intervention effects were often not consistent. For example, the intervention group had lower urinary DEHP metabolites (–22 %; 95 % CI: −30, −3) but not dust DEHP (3 %, 95 % CI: –32, 57). Studies of the relations between EDCs in dust and associated biomarkers exist but are relatively few, especially for PFAS.(Zhu et al., 2023) This is an important and nuanced topic that is beyond the scope of our study but warrants further investigation in the HOME cohort.

Our study has noteworthy limitations. First, given the modest sample size and some missing data, our study was underpowered to detect more subtle intervention effects. The 95 % confidence intervals around our effect estimates were relatively wide, and almost all included the null, limiting our ability to draw definitive conclusions. Second, dust samples were taken from homes at 24-month visits, perhaps not proximal enough to the intervention, especially as 38 % of eligible participants moved after randomization. We attempted to address this issue by conducting a "per-protocol" analysis of just those participants who did not relocate. However, EDCs are present in electronics and household furnishings not targeted by the intervention.(Metcalfe et al., 2022) These sources may have reintroduced non-persistent EDCs into household dust during the 24-months between the completion of the intervention and dust sampling. Relatedly, we used serum samples collected three years after the intervention to quantify PFAS body burden. Estimated human half-lives of the perfluoroalkyls considered in this study range from 2.1-10.1 years for PFOA to 4.7–35 years for PFHxS.(Agency for Toxic Substances and Disease Registry, 2021) It is possible that our ability to evaluate the effect of our intervention body burden of some PFAS could have been attenuated by their slow biological clearance. Although, it is difficult to speculate how much of an issue this is because estimates of half-lives for PFAS are based largely on adults. Third, detection frequency for PFOS, an abundant legacy PFAS, in dust was much lower than expected, likely due to peak integration interference from similar PFAS. Fourth, using dust samples from only child bedrooms and main activity rooms may have led to measurement error. Perhaps this measurement error is greater for children of higher socioeconomic status who live in larger homes with more rooms, but this is speculatory and cannot be confirmed with the data we have. Lastly, this intervention was originally designed to reduce child lead exposure. As such, the housing modifications performed did not specifically target EDC exposures and varied substantially between households based on identified sources of lead in each home.

Our study is one of the first to examine how this type of housing intervention may have reduced EDCs in children and household dust. A strength was our ability to consider different EDC chemical classes including OPEs, PFAS, and phthalates and mixtures using PCA, something seldom seen in published intervention studies. This is particularly important given the multifaceted nature of this intervention and that OPE, PFAS, and phthalate mixtures have been associated with different adverse health outcomes.(Braun, 2017) Finally, the breadth and depth of sociodemographic, behavioral, and household characteristics recorded in the HOME Study allowed us to adjust for suspected sources of selection bias and examine potentially important effect modifiers.

It is important to consider how our findings fit into an international context. EDC dust concentrations in our study were comparable to others reported in the U.S. (Mitro et al., 2016) However, in comparison to similar studies in Asia (Huang et al., 2021; Tan et al., 2024; Wang et al., 2020) and Europe,(Kolarik et al., 2008; Li et al., 2019; Weiss et al., 2021) dust concentrations of some OPEs (TDCPP and TPP), PFAS, and some phthalates (BzBP, DEP, and DNOP) were notably higher (sTable 9-11). Urinary concentrations of OPE and phthalate metabolites were

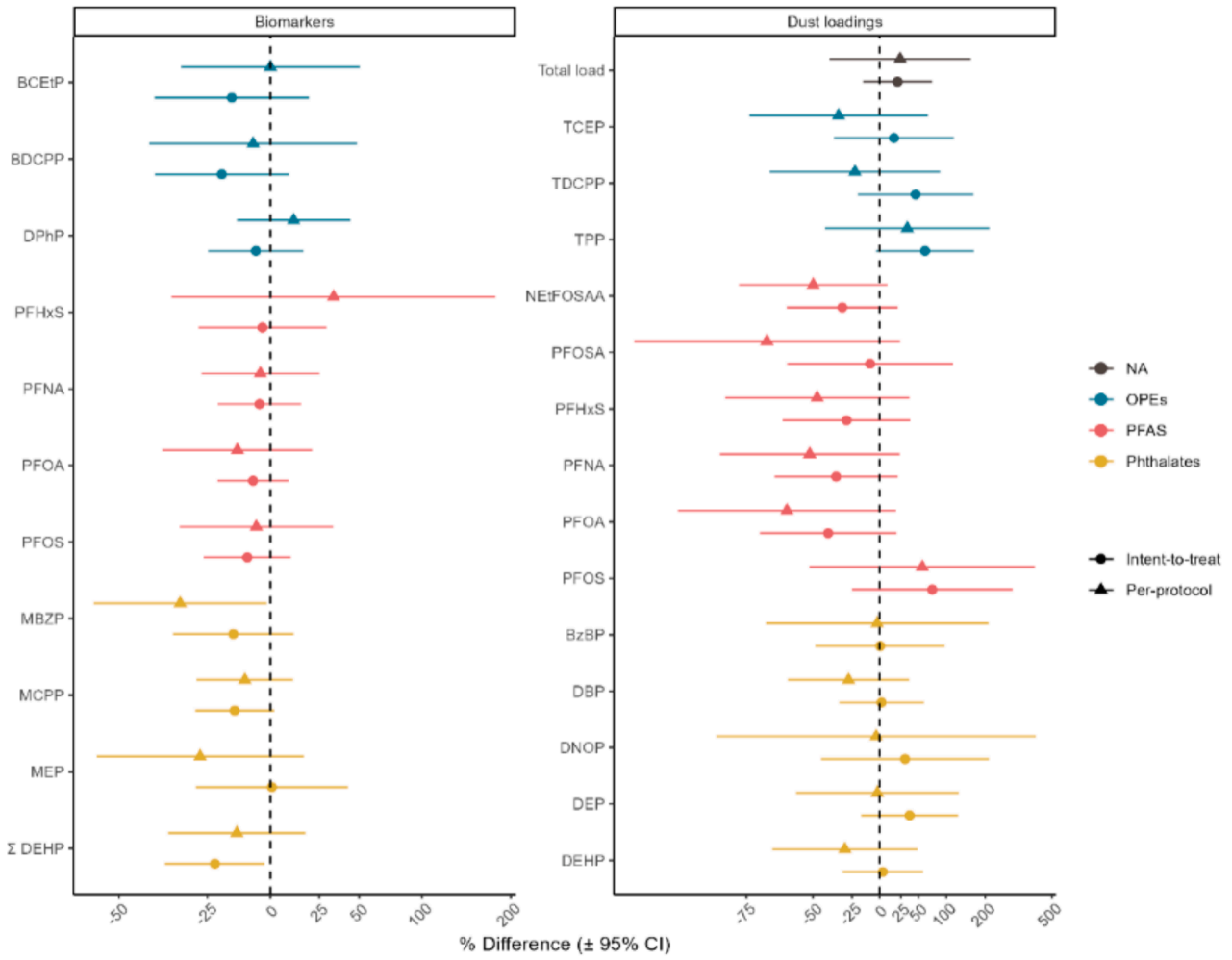

Fig. 4. Percent difference (±95 % CI) in 24-month EDC dust loadings, 24-month urinary OPE and phthalate metabolite concentrations, and 36-month PFAS serum concentrations comparing intervention to control group (The HOME Study, 2003–2006). Estimates from linear model regressing ln-transformed loadings and concentrations on intervention status weighted using IPRW. Percent difference calculated as exp(βintervention)-1x100%. Negative values indicate lower loadings or concentrations in the intervention group. ΣDEHP is the molar sum of urinary MEHHP, MEOHP, and MECPP.

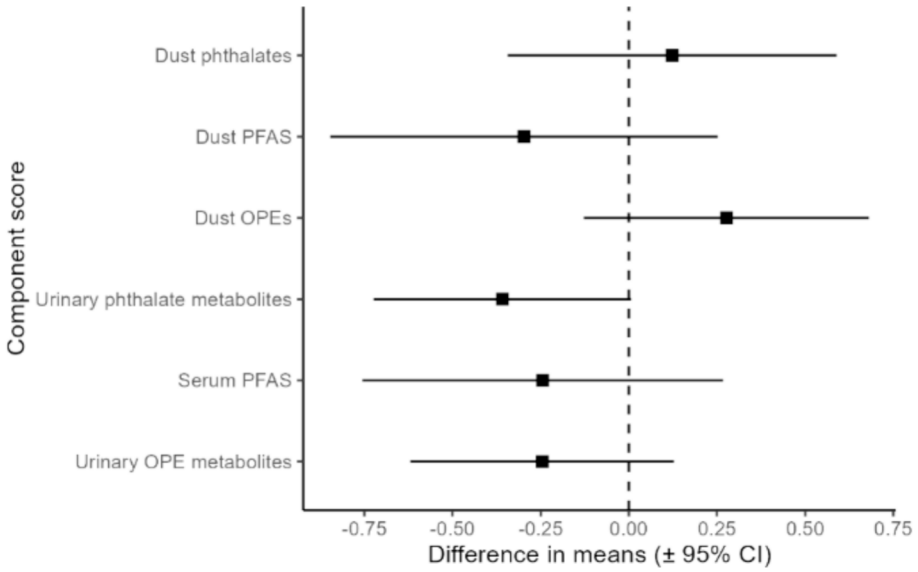

Fig. 5. Difference in means (±95 % CI) for matrix-class specific component scores comparing intervention to control group (The HOME Study, 2003–2006). Estimates from generalized linear model regressing component scores on intervention status weighted using IPRW. The control group is used as a reference category. Ln-transformed dust loadings and metabolite concentrations were mean-centered and scaled to the standard deviation prior to fitting PCA models.

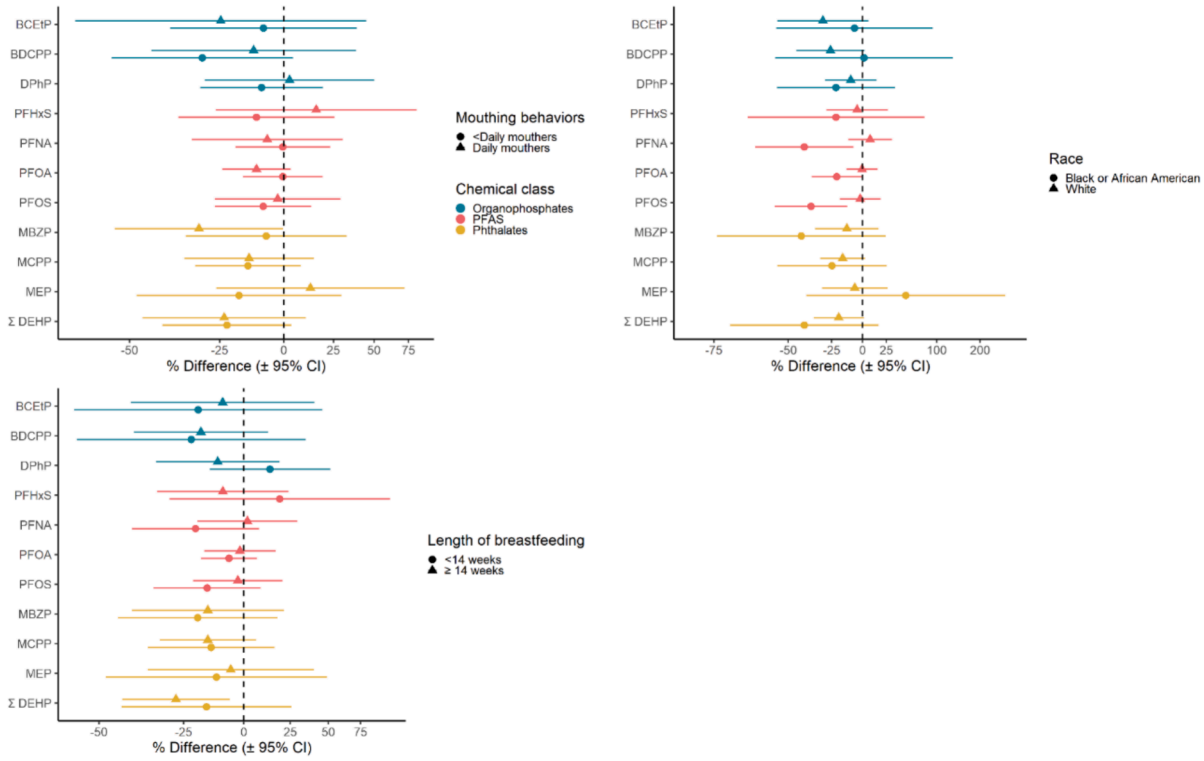

Fig. 6. Percent difference (±95 % CI) in 24-month urinary OPE and phthalate metabolite concentrations, and 36-month PFAS serum concentrations comparing intervention to control group stratified by mouthing behaviors (daily/<daily), child race (Black or African American/White), and length of breastfeeding (≥14 weeks/<14 weeks). Estimates from linear model regressing ln-transformed concentrations on intervention status. Percent difference calculated as exp(βintervention) x100%. Negative values indicate lower concentrations in the intervention group. ΣDEHP is the molar sum of urinary MEHHP, MEOHP, and MECPP. Stratified models adjusted for other effect modifiers tested.

generally higher compared to existing studies of children and adolescents in Asia,(Ding et al., 2019; Liao et al., 2021; Shi et al., 2018) Europe,(Govarts et al., 2023) and the U.S.(National Center for Environmental Health (U.S.), 2022) that report creatinine standardized concentrations. These differences could be the result of age, temporal trends, or true geographic heterogeneity (sTable 12 and 13). Serum PFAS concentrations were also high compared to similar studies in Asia, (Zhang et al., 2010) Europe,(Gyllenhammar et al., 2019) and the U.S., (Oh et al., 2024; Schecter et al., 2012) likely owing to documented industrial pollution of the Ohio river, a drinking water source for this cohort (sTable 14).(Herrick et al., 2017) It is unclear how age, temporal, and geographic differences in EDC exposures would influence the effectiveness of similar housing interventions. However, when designing and studying such interventions in an international context, factors like housing stock age and prevalent building materials warrant consideration.

Future research could tailor household interventions to reduce known sources of EDC exposures. This could include targeting household dust using both cleaning and air filtration, with the latter being a potential method to reduce indoor air phthalate and PFAS levels. (Dodson et al., 2023) Reintroduction of non-persistent of EDCs via household products and the time at which dust samples and biospecimens are collected relative to the intervention are other important considerations. To increase efficacy, future interventions may need to be sustained rather than carried out at a single timepoint as was this intervention, especially if long-term outcomes are of interest. Lastly, given frequent threats to precision including attrition, missing data, and EDC exposure variability, larger sample sizes are merited particularly in subpopulations such as Blacks or African Americans that may greatly benefit from these interventions.

5. Conclusions

Household interventions that mitigate traditional sources of lead exposure through dust mitigation, paint stabilization, cleaning, and other renovations may reduce some child EDC exposures, particularly high molecular weight phthalates, as well as PFAS in Blacks or African Americans. However, the importance of dust mitigation warrants further investigation. Larger studies of more sustained interventions specifically tailored to remove sources of EDC exposures are needed.

CRediT authorship contribution statement

Alan J. Fossa: Writing – original draft, Visualization, Software, Methodology, Formal analysis, Conceptualization. **Katherine E. Manz:** Writing – review & editing, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **George D. Papandonatos:** Writing – review & editing, Supervision, Software, Methodology, Funding acquisition, Conceptualization. **Aimin Chen:** Writing – review & editing, Resources, Methodology, Data curation. **Mark J. La Guardia:** Writing – review & editing, Resources, Investigation. **Bruce P. Lanphear:** Writing – review & editing, Supervision, Resources, Conceptualization. **Robert C.Hale:** Writing – review & editing, Resources, Methodology. **Alexandra Pagano:** Resources, Methodology, Investigation, Data curation. **Kurt D. Pennell:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Data curation. **Kimberly Yolton:** Writing – review & editing, Supervision, Resources, Investigation. **Joseph M. Braun:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2024.108994.

References

Agency for Toxic Substances and Disease Registry. (2021, May). *Toxicological Profile for Perfluoroalkyls*. U.S. Department of Health and Human Services. https://www.atsdr.cdc.gov/toxprofiles/tp200.pdf.

Authority (EFSA), E. F. S. (2005). Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) related to Bis (2-ethylhexyl)phthalate (DEHP) for use in food contact materials. *EFSA Journal*, *3* (9), 243. Doi: 10.2903/j.efsa.2005.243.

Bearer, C.F., 1995. How are children different from adults? Environmental Health Perspectives 103.

Bevington, C., Gardner, H.D., Cohen, J., Henning, C., Rasmussen, P.E., 2021. Relationship between residential dust-lead loading and dust-lead concentration across multiple North American datasets. Building and Environment 188, 107359. https://doi.org/10.1016/j.buildenv.2020.107359.

Braun, J.M., 2017. Early-life exposure to EDCs: Role in childhood obesity and neurodevelopment. Nature Reviews Endocrinology 13 (3), 161–173. https://doi.org/10.1038/nrendo.2016.186.

Braun, J.M., Kalloo, G., Chen, A., Dietrich, K.N., Liddy-Hicks, S., Morgan, S., Xu, Y., Yolton, K., Lanphear, B.P., 2016. Cohort Profile: The Health Outcomes and Measures of the Environment (HOME) study. International Journal of Epidemiology dyw006. https://doi.org/10.1093/ije/dyw006.

Braun, J.M., Hornung, R., Chen, A., Dietrich, K.N., Jacobs, D.E., Jones, R., Khoury, J.C., Liddy-Hicks, S., Morgan, S., Vanderbeek, S.B., Xu, Y., Yolton, K., Lanphear, B.P., 2018. Effect of Residential Lead-Hazard Interventions on Childhood Blood Lead Concentrations and Neurobehavioral Outcomes: A Randomized Clinical Trial. JAMA Pediatrics 172 (10), 934. https://doi.org/10.1001/jamapediatrics.2018.2382.

Braun, J.M., Buckley, J.P., Cecil, K.M., Chen, A., Kalkwarf, H.J., Lanphear, B.P., Xu, Y., Woeste, A., Yolton, K., 2020. Adolescent follow-up in the Health Outcomes and Measures of the Environment (HOME) Study: Cohort profile. BMJ Open 10 (5), e034838.

Brennan, N.M., Evans, A.T., Fritz, M.K., Peak, S.A., Von Holst, H.E., 2021. Trends in the Regulation of Per- and Polyfluoroalkyl Substances (PFAS): A Scoping Review. International Journal of Environmental Research and Public Health 18 (20), 10900. https://doi.org/10.3390/ijerph182010900.

Colt, J.S., Gunier, R.B., Metayer, C., Nishioka, M.G., Bell, E.M., Reynolds, P., Buffler, P. A., Ward, M.H., 2008. Household vacuum cleaners vs. The high-volume surface sampler for collection of carpet dust samples in epidemiologic studies of children. Environmental Health 7 (1), 6. https://doi.org/10.1186/1476-069X-7-6.

Ding, J., Deng, T., Ye, X., Covaci, A., Liu, J., Yang, F., 2019. Urinary metabolites of organophosphate esters and implications for exposure pathways in adolescents from Eastern China. The Science of the Total Environment 695, 133894. https://doi.org/10.1016/j.scitotenv.2019.133894.

Dodson, R.E., Manz, K.E., Burks, S.R., Gairola, R., Lee, N.F., Liu, Y., Pennell, K.D., Walker, E.D., Braun, J.M., 2023. Does Using Corsi-Rosenthal Boxes to Mitigate COVID-19 Transmission Also Reduce Indoor Air Concentrations of PFAS and Phthalates? Environmental Science & Technology 57 (1), 415–427. https://doi.org/10.1021/acs.est.2c05169.

Engel, A., Buhrke, T., Imber, F., Jessel, S., Seidel, A., Völkel, W., Lampen, A., 2017. Agonistic and antagonistic effects of phthalates and their urinary metabolites on the steroid hormone receptors ERα, ERβ, and AR. Toxicology Letters 277, 54–63. https://doi.org/10.1016/j.toxlet.2017.05.028.

Evans, N., Conley, J.M., Cardon, M., Hartig, P., Medlock-Kakaley, E., Gray, L.E., 2022. In vitro activity of a panel of per- and polyfluoroalkyl substances (PFAS), fatty acids, and pharmaceuticals in peroxisome proliferator-activated receptor (PPAR) alpha, PPAR gamma, and estrogen receptor assays. Toxicology and Applied Pharmacology 449, 116136. https://doi.org/10.1016/j.taap.2022.116136.

Fan, Y., Song, Z., Wu, Y., Ren, X., Bi, C., Ye, W., Wei, H., Xu, Y., 2024. Chemicals of Emerging Concern in Water-Based Paint Products. Environmental Science & Technology Letters. https://doi.org/10.1021/acs.estlett.4c00052.

Ghassabian, A., Vandenberg, L., Kannan, K., Trasande, L., 2022. Endocrine-Disrupting Chemicals and Child Health. Annual Review of Pharmacology and Toxicology 62 (1), 573–594. https://doi.org/10.1146/annurev-pharmtox-021921-093352.

Giovanoulis, G., Nguyen, M.A., Arwidsson, M., Langer, S., Vestergren, R., Lagerqvist, A., 2019. Reduction of hazardous chemicals in Swedish preschool dust through article substitution actions. Environment International 130, 104921. https://doi.org/10.1016/j.envint.2019.104921.

Glüge, J., Scheringer, M., Cousins, I.T., DeWitt, J.C., Goldenman, G., Herzke, D., Lohmann, R., Ng, C.A., Trier, X., Wang, Z., 2020. An overview of the uses of per- and polyfluoroalkyl substances (PFAS). Environmental Science: Processes & Impacts 22 (12), 2345–2373. https://doi.org/10.1039/D0EM00291G.

Gore, A.C., Crews, D., Doan, L.L., Merrill, M.L., Patisaul, H., Zota, A. (n.d.). Introduction to Endocrine Disrupting Chemicals (EDCs).

Govarts, E., Gilles, L., Rodriguez Martin, L., Santonen, T., Apel, P., Alvito, P., Anastasi, E., Andersen, H.R., Andersson, A.-M., Andryskova, L., Antignac, J.-P., Appenzeller, B., Barbone, F., Barnett-Itzhaki, Z., Barouki, R., Berman, T., Bil, W., Borges, T., Buekers, J., Schoeters, G., 2023. Harmonized human biomonitoring in European children, teenagers and adults: EU-wide exposure data of 11 chemical substance groups from the HBM4EU Aligned Studies (2014–2021). International Journal of Hygiene and Environmental Health 249, 114119. https://doi.org/10.1016/j.ijheh.2023.114119.

Gyllenhammar, I., Benskin, J.P., Sandblom, O., Berger, U., Ahrens, L., Lignell, S., Wiberg, K., Glynn, A., 2019. Perfluoroalkyl Acids (PFAAs) in Children's Serum and Contribution from PFAA-Contaminated Drinking Water. Environmental Science & Technology 53 (19), 11447–11457. https://doi.org/10.1021/acs.est.9b01746.

Hall, S.M., Zhang, S., Tait, G.H., Hoffman, K., Collier, D.N., Hoppin, J.A., Stapleton, H. M., 2023. PFAS levels in paired drinking water and serum samples collected from an exposed community in Central North Carolina. Science of the Total Environment 895, 165091. https://doi.org/10.1016/j.scitotenv.2023.165091.

Hammel, S.C., Levasseur, J.L., Hoffman, K., Phillips, A.L., Lorenzo, A.M., Calafat, A.M., Webster, T.F., Stapleton, H.M., 2019. Children's exposure to phthalates and non-phthalate plasticizers in the home: The TESIE study. Environment International 132, 105061. https://doi.org/10.1016/j.envint.2019.105061.

Harley, K.G., Kogut, K., Madrigal, D.S., Cardenas, M., Vera, I.A., Meza-Alfaro, G., She, J., Gavin, Q., Zahedi, R., Bradman, A., Eskenazi, B., Parra, K.L., 2016. Reducing Phthalate, Paraben, and Phenol Exposure from Personal Care Products in Adolescent Girls: Findings from the HERMOSA Intervention Study. Environmental Health Perspectives 124 (10), 1600–1607. https://doi.org/10.1289/ehp.1510514.

Hepburn, E., Madden, C., Szabo, D., Coggan, T.L., Clarke, B., Currell, M., 2019. Contamination of groundwater with per- and polyfluoroalkyl substances (PFAS) from legacy landfills in an urban re-development precinct. Environmental Pollution 248, 101–113. https://doi.org/10.1016/j.envpol.2019.02.018.

Herrick, R.L., Buckholz, J., Biro, F.M., Calafat, A.M., Ye, X., Xie, C., Pinney, S.M., 2017. Polyfluoroalkyl substance exposure in the Mid-Ohio River Valley, 1991–2012. Environmental Pollution 228, 50–60. https://doi.org/10.1016/j.envpol.2017.04.092.

Hölzer, J., Lilienthal, H., Schümann, M., 2021. Human Biomonitoring (HBM)-I values for perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS)—Description, derivation and discussion. Regulatory Toxicology and Pharmacology 121, 104862. https://doi.org/10.1016/j.yrtph.2021.104862.

Hornung, R.W., Reed, L.D., 1990. Estimation of average concentration in the presence of nondetectable values. Applied Occupational and Environmental Hygiene 5 (1), 46–51.

Huang, H.-B., Cheng, P.-K., Siao, C.-Y., Lo, Y.-T.-C., Chou, W.-C., Huang, P.-C., 2022. Mediation effects of thyroid function in the associations between phthalate exposure and lipid metabolism in adults. Environmental Health 21 (1), 61. https://doi.org/10.1186/s12940-022-00873-9.

Huang, C., Zhang, Y.-J., Liu, L.-Y., Wang, F., Guo, Y., 2021. Exposure to phthalates and correlations with phthalates in dust and air in South China homes. Science of the Total Environment 782, 146806. https://doi.org/10.1016/j.scitotenv.2021.146806.

Jayatilaka, N.K., Restrepo, P., Williams, L., Ospina, M., Valentin-Blasini, L., Calafat, A. M., 2017. Quantification of three chlorinated dialkyl phosphates, diphenyl phosphate, 2,3,4,5-tetrabromobenzoic acid, and four other organophosphates in human urine by solid phase extraction-high performance liquid chromatography-tandem mass spectrometry. Analytical and Bioanalytical Chemistry 409 (5), 1323–1332. https://doi.org/10.1007/s00216-016-0061-4.

Jayatilaka, N.K., Restrepo, P., Davis, Z., Vidal, M., Calafat, A.M., Ospina, M., 2019. Quantification of 16 urinary biomarkers of exposure to flame retardants, plasticizers, and organophosphate insecticides for biomonitoring studies. Chemosphere 235, 481–491. https://doi.org/10.1016/j.chemosphere.2019.06.181.

Kamrin, M.A., 2009. Phthalate Risks, Phthalate Regulation, and Public Health: A Review. Journal of Toxicology and Environmental Health, Part B 12 (2), 157–174. https://doi.org/10.1080/10937400902729226.

Kato, K., Basden, B.J., Needham, L.L., Calafat, A.M., 2011a. Improved selectivity for the analysis of maternal serum and cord serum for polyfluoroalkyl chemicals. Journal of Chromatography A 1218 (15), 2133–2137. https://doi.org/10.1016/j.chroma.2010.10.051.

Kato, K., Wong, L.-Y., Jia, L.T., Kuklenyik, Z., Calafat, A.M., 2011b. Trends in Exposure to Polyfluoroalkyl Chemicals in the U.S. Population: 1999–2008. Environmental Science & Technology 45 (19), 8037–8045. https://doi.org/10.1021/es1043613.

Kolarik, B., Naydenov, K., Larsson, M., Bornehag, C.-G., Sundell, J., 2008. The Association between Phthalates in Dust and Allergic Diseases among Bulgarian Children. Environmental Health Perspectives 116 (1), 98–103. https://doi.org/10.1289/ehp.10498.

La Guardia, M.J., Hale, R.C., 2015. Halogenated flame-retardant concentrations in settled dust, respirable and inhalable particulates and polyurethane foam at gymnastic training facilities and residences. Environment International 79, 106–114. https://doi.org/10.1016/j.envint.2015.02.014.

Langer, S., de Wit, C.A., Giovanoulis, G., Fäldt, J., Karlson, L., 2021. The effect of reduction measures on concentrations of hazardous semivolatile organic compounds in indoor air and dust of Swedish preschools. Indoor Air 31 (5), 1673–1682.

Lanphear, B.P., Weitzman, M., Eberly, S., 1996. Racial differences in Urban children's environmental exposures to lead. American Journal of Public Health 86 (10), 1460–1463.

Li, W., Wang, Y., Asimakopoulos, A.G., Covaci, A., Gevao, B., Johnson-Restrepo, B., Kumosani, T.A., Malarvannan, G., Moon, H.-B., Nakata, H., Sinha, R.K., Tran, T.M., Kannan, K., 2019. Organophosphate esters in indoor dust from 12 countries: Concentrations, composition profiles, and human exposure. Environment International 133, 105178. https://doi.org/10.1016/j.envint.2019.105178.

Liao, K.-W., Chang, W.-H., Chou, W.-C., Huang, H.-B., Waits, A., Chen, P.-C., Huang, P.-C., 2021. Human biomonitoring reference values and characteristics of Phthalate exposure in the general population of Taiwan: Taiwan Environmental Survey for Toxicants 2013–2016. International Journal of Hygiene and Environmental Health 235, 113769. https://doi.org/10.1016/j.ijheh.2021.113769.

Lin, Y., Wang, Y., Li, P., 2022. PPARα: An emerging target of metabolic syndrome, neurodegenerative and cardiovascular diseases. Frontiers in Endocrinology 13, 1074911. https://doi.org/10.3389/fendo.2022.1074911.

Martin, L., Zhang, Y., First, O., Mustieles, V., Dodson, R., Rosa, G., Coburn-Sanderson, A., Adams, C.D., Messerlian, C., 2022. Lifestyle interventions to reduce endocrine-disrupting phthalate and phenol exposures among reproductive age men and women: A review and future steps. Environment International 170, 107576. https://doi.org/10.1016/j.envint.2022.107576.

Mendy, A., Percy, Z., Braun, J.M., Lanphear, B., La Guardia, M.J., Hale, R., Yolton, K., Chen, A., 2023. Exposure to dust organophosphate and replacement brominated flame retardants during infancy and risk of subsequent adverse respiratory outcomes. Environmental Research 235, 116560. https://doi.org/10.1016/j.envres.2023.116560.

Metcalfe, C.D., Bayen, S., Desrosiers, M., Muñoz, G., Sauvé, S., Yargeau, V., 2022. An introduction to the sources, fate, occurrence and effects of endocrine disrupting chemicals released into the environment. Environmental Research 207, 112658. https://doi.org/10.1016/j.envres.2021.112658.

Mitro, S.D., Dodson, R.E., Singla, V., Adamkiewicz, G., Elmi, A.F., Tilly, M.K., Zota, A.R., 2016. Consumer Product Chemicals in Indoor Dust: A Quantitative Meta-analysis of U.S. Studies. *Environmental Science & Technology* 50 (19), 10661–10672. https://doi.org/10.1021/acs.est.6b02023.

Morgan, S., Mottaleb, M.A., Kraemer, M.P., Moser, D.K., Worley, J., Morris, A.J., Petriello, M.C., 2023. Effect of lifestyle-based lipid lowering interventions on the relationship between circulating levels of per-and polyfluoroalkyl substances and serum cholesterol. Environmental Toxicology and Pharmacology 98, 104062. https://doi.org/10.1016/j.etap.2023.104062.

National Center for Environmental Health (U.S.) (Ed.). (2022). *National Report on Human Exposure to Environmental Chemicals* (cdc:133100). https://stacks.cdc.gov/view/cdc/133100.

Oh, J., Shin, H.-M., Kannan, K., Calafat, A.M., Schmidt, R.J., Hertz-Picciotto, I., Bennett, D.H., 2024. Per- and Polyfluoroalkyl Substances (PFAS) in Serum of 2 to 5 year-Old Children: Temporal Trends, Determinants, and Correlations with Maternal PFAS Concentrations. Environmental Science & Technology 58 (7), 3151–3162. https://doi.org/10.1021/acs.est.3c08928.

Percy, Z., La Guardia, M.J., Xu, Y., Hale, R.C., Dietrich, K.N., Lanphear, B.P., Yolton, K., Vuong, A.M., Cecil, K.M., Braun, J.M., Xie, C., Chen, A., 2020. Concentrations and loadings of organophosphate and replacement brominated flame retardants in house dust from the HOME Study during the PBDE phase-out. Chemosphere 239, 124701. https://doi.org/10.1016/j.chemosphere.2019.124701.

Phillips, A.L., Hammel, S.C., Hoffman, K., Lorenzo, A.M., Chen, A., Webster, T.F., Stapleton, H.M., 2018. Children's residential exposure to organophosphate ester flame retardants and plasticizers: Investigating exposure pathways in the TESIE study. Environment International 116, 176–185. https://doi.org/10.1016/j.envint.2018.04.013.

Rudel, R.A., Gray, J.M., Engel, C.L., Rawsthorne, T.W., Dodson, R.E., Ackerman, J.M., Rizzo, J., Nudelman, J.L., Brody, J.G., 2011. Food Packaging and Bisphenol A and Bis(2-Ethyhexyl) Phthalate Exposure: Findings from a Dietary Intervention. Environmental Health Perspectives 119 (7), 914–920. https://doi.org/10.1289/ehp.1003170.

Schecter, A., Malik-Bass, N., Calafat, A.M., Kato, K., Colacino, J.A., Gent, T.L., Hynan, L. S., Harris, T.R., Malla, S., Birnbaum, L., 2012. Polyfluoroalkyl Compounds in Texas Children from Birth through 12 Years of Age. Environmental Health Perspectives 120 (4), 590–594. https://doi.org/10.1289/ehp.1104325.

Sears, C.G., Lanphear, B.P., Calafat, A.M., Chen, A., Skarha, J., Xu, Y., Yolton, K., Braun, J.M., 2020. Lowering Urinary Phthalate Metabolite Concentrations among Children by Reducing Contaminated Dust in Housing Units: A Randomized Controlled Trial and Observational Study. Environmental Science & Technology 54 (7), 4327–4335. https://doi.org/10.1021/acs.est.9b04898.

Shi, W., Lin, Z., Liao, C., Zhang, J., Liu, W., Wang, X., Cai, J., Zou, Z., Wang, H., Norback, D., Kan, H., Huang, C., Zhao, Z., 2018. Urinary phthalate metabolites in relation to childhood asthmatic and allergic symptoms in Shanghai. Environment International 121, 276–286. https://doi.org/10.1016/j.envint.2018.08.043.

Silva, M., Samandar, E., Preaujr, J., Reidy, J., Needham, L., Calafat, A., 2007. Quantification of 22 phthalate metabolites in human urine. Journal of Chromatography B 860 (1), 106–112. https://doi.org/10.1016/j.jchromb.2007.10.023.

Tan, H., Tang, S., Yang, L., Li, J., Deng, Y., Shen, H., Dai, Q., Gao, Y., Wu, P., Zhu, L., Cai, Z., 2024. Global quantification of emerging and legacy *per-* and polyfluoroalkyl substances in indoor dust: Levels, profiles and human exposure. Science of the Total Environment 927, 172132. https://doi.org/10.1016/j.scitotenv.2024.172132.

Wang, Y., Zhu, H., Kannan, K., 2019. A Review of Biomonitoring of Phthalate Exposures. Toxics 7 (2), 21. https://doi.org/10.3390/toxics7020021.

Wang, Y., Yao, Y., Han, X., Li, W., Zhu, H., Wang, L., Sun, H., Kannan, K., 2020. Organophosphate di- and tri-esters in indoor and outdoor dust from China and its implications for human exposure. Science of the Total Environment 700, 134502. https://doi.org/10.1016/j.scitotenv.2019.134502.

Weiss, J.M., Jones, B., Koekkoek, J., Bignert, A., Lamoree, M.H., 2021. Per- and polyfluoroalkyl substances (PFASs) in Swedish household dust and exposure of pet cats. Environmental Science and Pollution Research 28 (29), 39001–39013. https://doi.org/10.1007/s11356-021-13343-5.

World Health Organization. (2017). *Inheriting a sustainable world? Atlas on children's health and the environment*. World Health Organization. https://iris.who.int/handle/10665/254677.

Yeter, D., Banks, E.C., Aschner, M., 2020. Disparity in Risk Factor Severity for Early Childhood Blood Lead among Predominantly African-American Black Children: The 1999 to 2010 US NHANES. International Journal of Environmental Research and Public Health 17 (5), 1552. https://doi.org/10.3390/ijerph17051552.

Yiin, L.-M., Lioy, P.J., Rhoads, G.G., 2003. Impact of home carpets on childhood lead intervention study. Environmental Research 92 (2), 161–165. https://doi.org/10.1016/S0013-9351(03)00014-8.

Zhang, Z., Kim, H.J., Lonjon, G., Zhu, Y., 2019. Balance diagnostics after propensity score matching. Annals of Translational Medicine 7 (1), 16. https://doi.org/10.21037/atm.2018.12.10.

Zhang, T., Wu, Q., Sun, H.W., Zhang, X.Z., Yun, S.H., Kannan, K., 2010. Perfluorinated compounds in whole blood samples from infants, children, and adults in China. Environmental Science & Technology 44 (11), 4341–4347. https://doi.org/10.1021/es1002132.

Zhu, L., Hajeb, P., Fauser, P., Vorkamp, K., 2023. Endocrine disrupting chemicals in indoor dust: A review of temporal and spatial trends, and human exposure. Science of the Total Environment 874, 162374. https://doi.org/10.1016/j.scitotenv.2023.162374.