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Maternal dietary patterns during pregnancy and exposure to persistent endocrine disrupting chemicals in two European birth cohorts

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Abstract

Food consumption, particularly of animal-based products, is considered the most important contributor to persistent endocrine disrupting chemical (EDC) exposure. This study aims to describe the association between maternal diet during pregnancy and exposure to persistent EDCs

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Declarations of interest:

None

Disclosures

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention (CDC). Use of trade names is for identification only and does not imply endorsement by the CDC, the Public Health Service, or the U.S. Department of Health and Human Services.

Data Statement

The informed consent obtained from ALSPAC participants does not allow the data to be made freely available through any third party maintained public repository. However, data used for this submission can be made available on request to the ALSPAC Executive. The ALSPAC data management plan describes in detail the policy regarding data sharing, which is through a system of managed open access. Full instructions for applying for data access can be found here: <http://www.bristol.ac.uk/alspac/researchers/access/>. The ALSPAC study website contains details of all the data that are available (<http://www.bristol.ac.uk/alspac/researchers/our-data/>). The consent given by the MoBa participants does not allow for storage of data on an individual level in repositories or journals. Researchers who want access to data sets for replication should submit an application to www.helsedata.no. Access to data sets requires approval from The Regional Committee for Medical and Health Research Ethics in Norway and an agreement with MoBa.

using dietary pattern analysis. This study is based on subsamples of the Avon Longitudinal Study of Parents and Children (ALSPAC) (N=422) and the Norwegian Mother, Father, and Child Cohort Study (MoBa) (N=276) which uses data from the Medical Birth Registry of Norway (MBRN). Women in both studies completed food frequency questionnaires (FFQs) during pregnancy, from which consumption data were categorized into 38 aggregated food groups. Maternal blood samples were collected during pregnancy and concentrations of perfluoroalkyl substances (PFAS), polychlorinated biphenyls (PCBs), and organochlorine pesticides (OCPs) in serum/plasma were measured. Dietary patterns were identified using reduced rank regression, with blood EDC concentrations as response variables. Within ALSPAC, all patterns (PFAS, PCB, and OCP) were characterized by high consumption of meat, poultry, white fish, and biscuits. In MoBa, high consumption of sausages and burgers (representing processed meats), pasta, and chocolate bars characterized PCB and OCP dietary patterns, while high consumption of cheese characterized the PFAS pattern. Across both cohorts, PFAS patterns were characterized by high consumption of cheese, PCB patterns by high consumption of rice, and OCP patterns by poultry. Dietary patterns explained between 8 and 20% of the variation in serum EDC concentrations, with explained variance being the highest for PCBs in both cohorts. In conclusion, dietary patterns high in animal-based products appear to be associated with persistent EDC concentrations among pregnant women. Diet explains more variation in PCB concentrations than for other persistent EDC classes.

Keywords

ALSPAC; MoBa; MBRN; endocrine disrupting chemical; dietary pattern; pregnancy

1. Introduction

An endocrine disrupting chemical (EDC) is a chemical that may interfere with the body's endocrine system, potentially producing adverse developmental, reproductive, neurological, and immune effects (NIEHS, 2019). Persistent EDCs, such as organochlorine pesticides (OCPs), polychlorinated biphenyls (PCBs), and perfluoroalkyl substances (PFAS), have been used throughout the 20th and 21st centuries for a variety of purposes. These chemicals are typically highly resistant to degradation and tend to bioaccumulate in animals and humans (ATSDR, 2000, 2002, 2009). Exposure levels have declined in the general population following many countries banning or severely restricting the production, handling, and disposal of several OCPs and PCBs, as well as certain PFAS. Still, almost all humans have detectable levels of most of these persistent chemicals in their blood (CDC, 2021a, 2021b, Schoeters et al., 2017). Moreover, during pregnancy, most EDCs can cross the placental barrier, allowing for fetal exposure, and the amount of EDCs found in cord serum may be substantial in relation to a developing fetus's size (Inoue et al., 2004, Jacobson et al., 1984, Kezios et al., 2012, Sala et al., 2001).

Contaminated air and soil are potential routes of exposure to persistent EDCs, but food and drinks (including water) may be the most important routes (Caspersen et al., 2013, Darnerud et al., 2006, Haug et al., 2010, Kvale et al., 2009, Schrenk et al., 2020, Scientific Committee on Food, 2000). Diet accounts for up to 90% of exposure to persistent organic

pollutants like PCBs and OCPs (Malisch and Kotz, 2014). Diet is also the main source of PFAS exposure in the general population. Contaminated drinking water can be the predominant source of PFAS exposure for populations living near sources of contamination such as industrial sites and military bases and other sites where firefighting foam has been sprayed, causing groundwater contamination (Hu et al., 2016, Sunderland et al., 2019). Contaminants in foods may come from the application of pesticides to crops, the transport of industrial chemicals in the environment, and chemicals used in food packaging products (EPA, 2013). Many persistent environmental contaminants tend to accumulate in animals through bioaccumulation and biomagnification, and may commonly be found in meat, poultry, fish, and dairy products (Caspersen et al., 2013, Ericson et al., 2008, Haug et al., 2010, Schecter et al., 2010, Tittlemier et al., 2007). Other contaminants, such as a variety of pesticides, are often found in fruits, vegetables, and other agricultural commodities (Chiu et al., 2018, Hu et al., 2016).

Several previous studies have assessed levels of exposure to persistent EDCs through food by comparing a population's intake to tolerable daily intakes, such as Haug et al. (2010) and Caspersen et al. (2013) (Caspersen et al., 2013, Haug et al., 2010). Other studies have examined associations between consumption of specific foods, such as fish, and EDC blood concentrations (Berg et al., 2014, Cao et al., 2011, Christensen et al., 2017, Lin et al., 2020, Manzano-Salgado et al., 2016, Singh et al., 2019). While such studies are critical, there is also the need to better understand exposure patterns. Dietary pattern analysis allows for the examination of overall diet, as opposed to single foods (Hu, 2002), which shows a more complete picture of human exposure because humans do not consume individual foods or nutrients in isolation. Data-driven dietary pattern analysis (e.g., principal component analysis, factor analysis) extracts patterns from the population under study using a statistical tool and leads to identification of pattern(s) specific to that population. Reduced rank regression is a method that identifies dietary patterns associated with selected response variables (e.g., biomarkers of EDC exposure) (Hoffmann et al., 2004, Weikert and Schulze, 2016).

Data-driven pattern analyses have been used in several previous studies among various populations to identify dietary patterns that contribute to exposure to persistent EDCs, most often dioxins and PCBs (Arisawa et al., 2011, Arrebola et al., 2018, Boada et al., 2014, Eguchi et al., 2017, Kvaalem et al., 2009, Lee et al., 2018, Papadopoulou et al., 2019, Papadopoulou et al., 2014, Ravenscroft and Schell, 2018). Previous studies in pregnant women have identified positive associations of fish (Eguchi et al., 2017, Papadopoulou et al., 2019, Papadopoulou et al., 2014), eggs (Eguchi et al., 2017), red and white meat (Papadopoulou et al., 2014), and low-fat dairy (Papadopoulou et al., 2014) with higher concentrations of persistent EDCs. Existing research shows diets characterized by high intakes of certain animal-based products are associated with greater serum concentrations of persistent EDCs (Arisawa et al., 2011, Arrebola et al., 2018, Boada et al., 2014, Eguchi et al., 2017, Kvaalem et al., 2009, Lee et al., 2018, Papadopoulou et al., 2019, Papadopoulou et al., 2014, Ravenscroft and Schell, 2018).

Given increasing evidence of adverse health outcomes related to EDC exposure (Diamanti-Kandarakis et al., 2009), especially in early life, it is important to identify major sources

of exposure, such as dietary sources. This study aims to identify dietary patterns that contribute to exposure to persistent EDCs (PFAS, PCBs, and OCPs) as measured serum/plasma concentrations in two European pregnant populations.

2. Methods

2.1. Study populations

2.1.1. The Avon Longitudinal Study of Parents and Children (ALSPAC)—The Avon Longitudinal Study of Parents and Children (ALSPAC) is an ongoing prospective birth cohort of 14,541 pregnancies. ALSPAC enrolled pregnant women with an expected delivery date between 1 April 1991 and 31 December 1992 from three health districts in the former county of Avon, in South West England. Information has been collected on these parents and children through clinic visits, interviews, and mailed questionnaires. Details on ALSPAC recruitment and study methods have been described elsewhere (Boyd et al., 2013, Fraser et al., 2013). A sub-study (case-control study) was conducted within ALSPAC to examine prenatal maternal serum concentrations of various EDCs in relation to daughters' age at menarche among 448 mothers. Details of the sub-study are described elsewhere (Christensen et al., 2011).

The study website contains details of all the data that are available through a fully searchable data dictionary and variable search tool (<http://www.bris.ac.uk/alspac/researchers/our-data/>). We obtained ethical approval for the study from the ALSPAC Ethics and Law Committee, the Local Research Ethics Committees, and the Centers for Disease Control and Prevention (CDC) Institutional Review Board. Mothers provided written informed consent for participation in the study. Consent for biological samples was collected in accordance with the Human Tissue Act (2004). Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee.

2.1.2. The Norwegian Mother, Father, and Child Cohort Study (MoBa)—The Norwegian Mother, Father, and Child Cohort Study (MoBa) is a population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health (NIPH) (Magnus et al., 2016). Participants were recruited from all over Norway between 1999 and 2008. The participation rate was 41%. The cohort includes 114,500 children, 95,200 mothers and 75,200 fathers. The current study is based on version 12 of the quality-assured data files released for research in January 2019. The establishment of MoBa and initial data collection was based on a license from the Norwegian Data protection agency and approval from The Regional Committees for Medical and Health Research Ethics. The MoBa cohort is currently based on regulations related to the Norwegian Health Registry Act. The current study was approved by The Regional Committees for Medical and Health Research Ethics (reference number: 2019/864). Some of the study data come from linkage with the Medical Birth Registry (MBRN), which is a national health registry containing information about all births in Norway (Irgens, 2000). As part of MoBa, blood samples were obtained from both parents during pregnancy and from mothers and children (umbilical cord) at birth (Paltiel

et al., 2014). Mothers received three questionnaires during pregnancy (including a food frequency questionnaire (FFQ)), and additional questionnaires after delivery.

A subsample (n=278) of the MoBa cohort mothers had EDCs measured through the European Union's Human Early Life Exposome (HELIX) initiative (Maitre et al., 2018). The aim of the HELIX study was to measure and describe multiple environmental exposures during early life (pregnancy and childhood) in a prospective cohort and associate these exposures with molecular omics signatures and child health outcomes. The HELIX study represents a collaborative project across six established and ongoing longitudinal population-based birth cohort studies in six European countries (France, Greece, Lithuania, Norway, Spain, and the United Kingdom). In order to have access to detailed dietary data, only the subsample of MoBa mothers was used for this study. Though MoBa is a nation-wide birth cohort, the included sample of pregnant women were all from Oslo, the country's capital.

2.2. Dietary assessment

Analyses were restricted to mothers who completed an FFQ during pregnancy with plausible average energy intake and had measured biomarkers of persistent EDC exposure. No mothers in ALSPAC had implausible energy intakes (defined as <500 or >5000 kcal/day) and two mothers in MoBa reported >5000 kcal/day and were, therefore, excluded. Mothers were also excluded if they did not respond to the FFQ. In the ALSPAC sample, we excluded 26 mothers, and in the MoBa sample, we did not exclude any mothers for this reason. In total, there were 422 ALSPAC mothers and 276 MoBa mothers included in the analyses. Pooling the ALSPAC and MoBa data was not possible due to terms of data use agreements.

In ALSPAC, maternal diet was assessed using a non-quantitative FFQ completed by the women at 32 weeks of gestation (Supplemental Table 1) (Rogers and Emmett, 1998). The FFQ contained questions about the weekly frequency of consumption of 43 different foods and food groups. The women were asked to tick one of the following options for each item as consumed "nowadays": never or rarely, once in 2 weeks, 1–3 times per week, 4–7 times per week, more than once a day. The FFQ provides frequency of consumption for foods; total energy intake and macro- and micronutrients were estimated from the FFQ using standard portion sizes (The Royal Society of Chemistry and MAFF, 1991) (more detailed information on the methodology is published elsewhere (Rogers and Emmett, 1998)).

Similarly, maternal diet was assessed using a semi-quantitative validated FFQ completed by the women at 22 weeks of gestation in the MoBa study (Supplemental Table 2) (Meltzer et al., 2008). The FFQ asked about the intake of 255 food items and was designed to capture dietary habits and intake of dietary supplements. Respondents were asked to fill in the usual intake of the food items eaten since becoming pregnant. The frequency intervals ranged from never to more than eight times per day. The MoBa FFQ was validated in a subsample of MoBa participants (n=119) using 4-day weighed food diaries and biological markers as reference methods. Compared with food diaries, the FFQ produced reasonably valid intake estimates and ranks of pregnant women according to low and high intakes of energy, nutrients, and foods (Brantsaeter et al., 2008). Validation study participants were

correctly classified into the same or adjacent quintiles 75%, 59%, and 73% of the time for dairy foods, meats (e.g., beef, pork), and fish/seafood, respectively (Brantsaeter et al., 2008).

There were 38 food groups included in the analysis (Table 3), selected from the ALSPAC FFQ items that were frequently consumed (>25% of the population with any consumption) (Supplemental Table 1). The unit used was frequency of intake in times/week. Comparing across the two FFQs required condensing foods in the MoBa FFQ (255 items) to be aligned with the 38 food groups (Supplemental Table 2); this was done in consultation with nutritional epidemiologists from both cohorts (KN from ALSPAC and ALB from MoBa). For example, the ALSPAC FFQ lists “Sweets (peppermints, boiled sweets, toffees)” as one item, whereas the MoBa FFQ lists individual varieties separately. In the MoBa FFQ, caramel, candies, licorice; jelly sweets and marshmallow; pastille (regular and sugar-free); and marzipan each have their own category and, therefore, were combined for comparability.

2.3. EDC assessment

Maternal fasting blood samples were collected during pregnancy at enrollment in ALSPAC during 1991–1992 at a median of 15 (interquartile range (IQR): 10–28) weeks gestation and processed and frozen for later analysis. Maternal serum samples were held in storage facilities at the University of Bristol until they were transferred under controlled conditions and analyzed at the CDC’s National Center for Environmental Health (Atlanta, GA). Laboratory analyses included low- and high-concentration pooled quality control materials, standards, reagent blanks, and study samples.

Within MoBa, non-fasting maternal plasma samples were collected during pregnancy at a mean of 18 (standard deviation: 0.9) weeks gestation during 1999–2008 and stored in the cohort’s biobank (Magnus et al., 2006, Paltiel et al., 2014, Ronningen et al., 2006). Samples were analyzed for EDCs as part of the HELIX initiative in women with infants born in 2005–2007. Chemical assays were conducted in the laboratory at the Department of Environmental Exposure and Epidemiology at the NIPH (Haug et al., 2018).

Maternal serum/plasma concentrations were used as a surrogate for exposure. Concentrations below the limit of detection (LOD) were imputed by dividing the LOD by the square root of 2 prior to statistical analysis (Hornung and Reed, 1990). PCB and OCP concentrations were lipid-adjusted.

2.3.1. Perfluoroalkyl substances—The following PFAS were measured in both cohorts: perfluorooctanoate (PFOA), perfluorooctane sulfonate (PFOS), perfluorohexane sulfonate (PFHxS), and perfluorononanoate (PFNA). In ALSPAC, PFAS were measured in serum via on-line solid-phase extraction coupled to isotope dilution high-performance liquid chromatography-tandem mass spectrometry (Kuklennyik et al., 2005). Limits of detection (LODs) were 0.082 ng/mL (PFNA), 0.10 ng/mL (PFHxS, PFOA) and 0.20 ng/mL (PFOS). In MoBa, PFAS were measured in plasma using online column switching liquid chromatography coupled to a triple quadrupole mass spectrometer (MS) (Haug et al., 2009). LODs were 0.02 ng/mL for all PFAS under study.

2.3.2. Organochlorine pesticides and polychlorinated biphenyls—

The following OCPs were measured: hexachlorobenzene (HCB), dichlorodiphenyldichloroethylene (DDE), and dichlorodiphenyltrichloroethane (DDT). Five PCB congeners were measured: PCB118, PCB138, PCB153, PCB170, and PCB180. In ALSPAC, OCPs and PCBs were measured in serum using gas chromatography isotope dilution high resolution mass spectrometry (Sjödin et al., 2004). PCB congeners 138 and 158 could not be separated and were quantified as a summed concentration hereafter referred to as PCB138. Within ALSPAC, LODs for PCBs and OCPs are dependent on the size of the sample available. Thus, an individual LOD was reported for each individual result rather than an overall LOD. In MoBa, OCPs and PCBs were measured in plasma using solid-phase extraction and gas chromatography-tandem mass spectrometry as described by Haug et al (2018) (Haug et al., 2018). LODs were 0.3 pg/g (DDT, PCB118), 0.61 pg/g (DDE, PCB138, PCB153, PCB170), 0.91 pg/g (PCB180), and 1.52 pg/g (HCB).

2.4. Covariates

In both cohorts, covariate information was collected by clinical staff (e.g., gestational age at biological sample collection) or through self-report on questionnaires completed by the mother during or immediately after pregnancy (e.g., maternal education, maternal race); in MoBa, some covariate information comes from the MBRN. Covariates were selected based on previous knowledge and by taking into consideration the associations of maternal diet and persistent EDCs with maternal characteristics. Covariates included maternal age (years), maternal pre-pregnancy body mass index (BMI) (kg/m^2), maternal race or nativity (white/nonwhite in ALSPAC, Norwegian-born/not Norwegian-born in MoBa), maternal education (classified as <O-level [ordinary level: required, completed at age 16], O-level, or > O-level in ALSPAC; no higher education, 1–4 years higher education, or >4 years higher education in MoBa), parity (nulliparous/multiparous), smoking during pregnancy (any/none), gestational age at biological sample collection (weeks; ALSPAC only), and infant sex (male/female; MoBa only).

2.5. Statistical analyses

Within ALSPAC, each food item was coded according to the frequency of weekly consumption as 0, 0.5, 2, 5.5, or 10 (for no consumption, consumption once every two weeks, 1–3 times/week, 4–7 times/week, or more than once/day, respectively). Within MoBa, mothers could report their frequency of intake by day, week, or month. We converted all frequencies to weekly frequencies by multiplying daily intake by 7; and coding monthly intake as 0 for 0 times per month, 0.25 for once/month, 0.5 for twice/month, and 0.75 for three times/month. The aggregated food groups were analyzed both as absolute frequency of consumption and in relation to total energy intake. For the latter, we adjusted the weekly frequency of consumption variables for intake of total energy (kilocalories) using the residual method (Willett et al., 1997).

Reduced rank regression (RRR) is a statistical method that determines linear functions of predictors (e.g., foods) by maximizing the explained variation in response variables (e.g., disease-related biomarkers) (Hoffmann et al., 2004). RRR was applied to extract dietary patterns from 38 food groups, specifying measured concentrations of persistent EDCs in

blood as the response variables, which were grouped by class (PFAS, PCBs, and OCPs). EDCs under study include those that were measured in both ALSPAC and MoBa: the PFAS pattern specified PFOA, PFOS, PFHxS, and PFNA as response variables; the PCB pattern used PCB118, PCB138, PCB153, PCB170, and PCB180 as response variables; and the OCP pattern used DDE, DDT, and HCB as response variables. RRR derives the same number of dietary patterns as response variables (e.g., for the PFAS class, there are four response variables and thus four derived patterns), though typically only the first pattern (explaining the greatest variation) is used, as was done here. Food groups with factor loading values 0.2 or -0.2 were considered the principal contributors to each derived dietary pattern; a high absolute value of a factor loading indicates higher contribution of that food group to the dietary pattern. We were unable to weight RRR analyses in the ALSPAC nested case-control study back to the full cohort due to limitations of the software.

Using RRR, a pattern score for each dietary pattern was calculated as a continuous measure for each individual; the pattern score is the sum of the products of food group consumption and the corresponding factor loading. Therefore, a higher pattern score indicates a greater degree of adherence to that dietary pattern. Spearman correlation coefficients (r_s) were estimated between the dietary pattern scores and measured concentrations of each EDC in blood. To assess how well the dietary pattern(s) reflect maternal blood EDC concentrations, we performed multiple linear regression analysis, adjusting for maternal race/nativity, maternal age, maternal education, pre-pregnancy body mass index, parity, smoking during pregnancy, gestational age at sample collection, and total energy intake. Outcomes of these models included blood concentrations of individual EDCs and totals by class (PFAS, PCBs, and OCPs), calculated as the summed total of Z scores within a class. SAS software 9.4 (Cary, NC) was used for all analyses.

3. Results

Most ALSPAC pregnant women were white (98.1%), well-educated (81.7% ordinary level or above), and younger than 30 years old (56.9%) (Table 1). The majority of women entered pregnancy at a normal or low BMI (77.8%) and half were nulliparous (49.9%). Few women smoked during pregnancy (18.2%). Similarly, 86.6% of MoBa women received higher education, 82.2% entered pregnancy at a normal or low weight, and half (48.9%) were nulliparous. Compared to ALSPAC, MoBa women were older (85.1% were 30 years or older) and less likely to smoke (2.6%).

Within the classes of PFAS, PCBs, and OCPs, median concentrations were highest in both cohorts for PFOS, PCB153, and DDE, respectively (Table 2). Concentrations were consistently higher in ALSPAC than MoBa with the exception of PFNA, for which concentrations were similar. PCBs and OCPs showed high correlation within and between the two classes (Supplemental Figure 1). There were also strong within-class correlations for PFAS in both cohorts.

Median daily total energy intake was 1730 Calories/day (IQR: 1389, 2082) among ALSPAC mothers and 2148 Calories/day (IQR: 1809, 2555) among MoBa mothers (Table 3). The frequency of consumption for the 38 food groups is presented in Table 3. Among both

ALSPAC and MoBa mothers, fresh fruit was the most frequently consumed food group. Other frequently consumed food groups within ALSPAC included cheese, pure juice, boiled potatoes, and biscuits (sweet, like cookies). Within MoBa, cheese, mixed vegetables (peas, sweet corn, broad beans), crispbreads, and sausages and burgers (representing processed meats) were frequently consumed.

The PFAS dietary pattern was characterized by high consumption of meat, pasta, and biscuits in ALSPAC; and cheese, pure juice, pulses, and sweets in MoBa (factor loadings 0.20) (Table 4). In ALSPAC and MoBa, the PFAS patterns explained just under 10% of the variation in serum PFAS concentrations. The PCB dietary pattern in ALSPAC was characterized by high consumption of poultry, white fish, cheese, other green vegetables, cakes or buns, and biscuits; while sausages and burgers (representing processed meats), rice, pasta, pure juice, chocolate bars, and sweets loaded highly in MoBa. These patterns explained 20.3% and 13.8% of the variation in PCB concentrations in ALSPAC and MoBa, respectively. The OCP dietary pattern was characterized by high consumption of meat, poultry, white fish, other fish, rice, and other green vegetables in ALSPAC; sausages and burgers (representing processed meats), poultry, pasta, salad, oat cereals, and chocolate bars loaded highly in MoBa. In ALSPAC, the OCP pattern explained 16.0% of the variation in OCP concentrations, while in MoBa, the OCP pattern explained 8.1% of the variation. Findings were similar for absolute (unadjusted for energy) dietary pattern factor loadings (Supplemental Table 3).

Within ALSPAC, all patterns (PFAS, PCB, and OCP) were characterized by high consumption of meat, poultry, white fish, and biscuits (factor loadings ranging from 0.16 to 0.31) (Table 4). Within MoBa, high consumption of sausages and burgers (representing processed meats), pasta, and chocolate bars characterized PCB and OCP dietary patterns (factor loadings: 0.29 to 0.35), while high consumption of cheese (factor loading: 0.38) characterized the PFAS pattern. Across both cohorts, PFAS patterns were characterized by high consumption of cheese (factor loadings: 0.19 and 0.38 for ALSPAC and MoBa, respectively), PCB patterns by high consumption of rice (factor loadings: 0.17 and 0.37), and OCP patterns by poultry (factor loadings: 0.29 and 0.21). Detailed results using MoBa's 255 food groups and intake data can be seen in Supplemental Table 4.

EDC concentrations increased linearly with higher dietary pattern scores in ALSPAC and MoBa. The associations of dietary pattern scores and EDC concentrations (summed total of Z scores across class) controlling for covariates are shown in Table 5. In ALSPAC, the PCB dietary pattern, in combination with covariates, explained the most variance (38.4%) out of the three patterns. Across all three EDC classes in ALSPAC, dietary pattern score, maternal age, and parity were important contributors in predicting EDC concentration. In MoBa, the PFAS dietary pattern along with covariates explained the most variance (16.4%) out of the three patterns. The dietary pattern score was the only important contributor in predicting EDC concentrations within MoBa.

Spearman correlation coefficients provide some information on the relationship between the identified dietary patterns and EDC concentrations in the blood; correlation coefficients ranged from 0.22–0.48 for EDC concentrations and their respective patterns (Supplemental

Table 5). While the three PFAS, PCB, and OCP dietary patterns were derived for their respective chemical class, dietary patterns correlated with many chemicals under study. For example, PCB and OCP patterns were significantly correlated with chemicals of both classes.

4. Discussion

Using data from two population-based pregnancy cohorts, we identified dietary patterns associated with exposure to classes of persistent EDCs in pregnancy. PFAS, PCB, and OCP patterns in ALSPAC were all characterized by high consumption of meat, poultry, white fish, and biscuits. Within MoBa, dietary patterns with high consumption of sausages and burgers, pasta, and chocolate bars were associated with PCBs and OCPs, and cheese was most strongly associated with PFAS. While patterns were not necessarily similar across cohorts, some similarities existed; the PFAS patterns in both studies were characterized by high consumption of cheese, the PCB patterns were characterized by high consumption of rice, and the OCP patterns were characterized by high consumption of poultry.

Our findings are largely in agreement with previous studies examining dietary patterns associated with persistent chemicals in various populations, including those which examined pregnant women from six European countries (Eguchi et al., 2017, Papadopoulou et al., 2019, Papadopoulou et al., 2014) and Japan (Eguchi et al., 2017, Papadopoulou et al., 2019, Papadopoulou et al., 2014). While the literature is growing, much of the previous work on dietary patterns and persistent chemicals has focused on PCBs, which makes sense in the context of our study, as diet seems to explain more variation for PCBs than other persistent EDCs (PFAS, OCPs) in both studies. Findings of previous studies have shown positive associations of PCBs with eggs (Arisawa et al., 2011, Arrebola et al., 2018, Boada et al., 2014, Eguchi et al., 2017), fish (Arisawa et al., 2011, Arrebola et al., 2018, Boada et al., 2014, Eguchi et al., 2017, Kvaem et al., 2009, Lee et al., 2018, Papadopoulou et al., 2019, Papadopoulou et al., 2014, Ravenscroft and Schell, 2018), meat (Boada et al., 2014, Papadopoulou et al., 2014), poultry (Boada et al., 2014, Papadopoulou et al., 2014), and dairy (Boada et al., 2014, Lee et al., 2018, Papadopoulou et al., 2014, Ravenscroft and Schell, 2018). Results from ALSPAC are in agreement on fish, meat, poultry, and dairy (cheese). In MoBa, there was a strong association of processed meats with PCBs. The association of PCBs with eggs was not replicated here (in ALSPAC or MoBa) nor in the only other study specifically examining European pregnant women (Papadopoulou et al., 2014).

Previous studies have identified similar positive associations of OCPs with poultry (Boada et al., 2014), fish (Arrebola et al., 2018, Lee et al., 2018), and dairy (specifically cheese) (Arrebola et al., 2018, Boada et al., 2014), and negative associations with processed meats (Boada et al., 2014, Lee et al., 2018). We found the same in ALSPAC: positive factor loadings for poultry, fish, and cheese, and a negative factor loading for processed meats (sausages, burgers). Within MoBa, we saw positive factor loadings for poultry, fish, and processed meats, but not cheese.

One previous study has examined dietary patterns and PFAS, finding positive associations with cold cuts, fish, and eggs (Arrebola et al., 2018). In ALSPAC, we found positive associations of PFAS with meat and white fish, but not other fish or eggs, which showed negative factor loadings. In MoBa, the PFAS pattern was largely characterized by a high loading of cheese, with moderate positive loadings of eggs. Overall, diet seems to explain little variation in PFAS concentrations (<10%). One possible reason for the low R^2 values for PFAS patterns in particular could be that the contribution of different food categories to the total intake varies drastically between the specific types of PFAS, indicating different dietary sources for different PFAS (Schrenk et al., 2020). Such differences by chemical could impact our ability to identify dietary patterns for PFAS as a class, as we have attempted here. Further, with PFAS especially, it is possible that there could be greater contributions from other sources.

Although our dietary patterns derived using reduced rank regression account for a reasonable proportion of the variation in EDC concentrations, and even more variation is explained when additional characteristics are included in the model, this does not account for the total variance. Given the R^2 values seen in our study, which are similar to those reported in previous studies (Lee et al., 2018, Papadopoulou et al., 2014), there are likely to be alternative routes of exposure. While ingestion of food and drinks (including water) is generally the predominant pathway, house dust ingestion and indoor air inhalation are important contributors for some individuals (Poothong et al., 2020). Furthermore, foods associated with EDCs might not have been adequately captured by these FFQs, which could have affected the results observed. Given their long half-lives, concentrations of these persistent chemicals in blood are reflective of long-term exposure, and may not be fully summarized by the FFQs, which reflect diet “nowadays.” Women often make small dietary changes, usually early in pregnancy, to reduce intake of foods for the benefit of the child’s health (e.g., caffeine, alcohol, and meats) (Forbes et al., 2018).

In this study, we attempted to compare derived dietary patterns among pregnant women from two Northern European populations using two different FFQs. Within the FFQs, there were foods unique to each population that played important roles. There were typically British foods, like pies and pasties and baked beans, that were important contributors to the ALSPAC environmental dietary patterns but were not queried in the MoBa FFQ. Similarly, the MoBa FFQ included some foods specific to the Norwegian diet, such as certain types of fish and game meat. Further, the number of food items within the two FFQs (43 in ALSPAC versus 255 in MoBa) likely explains some of the difference observed in energy intake between ALSPAC (median: 1730 Calories) and MoBa (median: 2141 Calories) women. When presented with more food items, women may tend to report eating more. A longer questionnaire might also lead to fatigue and less accurate reporting. The number of line items also relates to the comparability of the FFQs: comparing across the two FFQs required consolidating line items from the MoBa FFQ. While this was done in consultation with nutritional epidemiologists from both cohorts to the best of our knowledge, there is some subjectiveness to the process and some details from the MoBa FFQ were lost in this process. If we mis-categorized some foods from the MoBa FFQ, the comparability of results could be impacted. Detailed results using MoBa’s 255 food groups and intake data can be seen in Supplemental Table 4. There is also the issue of food groups being heterogeneous; foods

in the same group may have different relationships with the EDCs under study, potentially diluting the associations observed. Lastly, the timing of the FFQs differed, with ALSPAC women completing the FFQ at 32 weeks gestation and MoBa women completing the FFQ at 22 weeks gestation. Both FFQs were intended to capture diet over the course of the pregnancy to date and it is unlikely that maternal diet changed drastically in the second half of pregnancy.

While there were differences in diet across the two cohorts, there were also differences in concentrations of persistent EDCs. Generally, concentrations were higher in ALSPAC mothers than MoBa mothers, a pattern that fits with global trends over time. Comparing persistent EDC concentrations in ALSPAC and MoBa to present day levels using the National Health and Nutrition Examination Survey (NHANES) from the United States, we see the same pattern: concentrations decrease over time, with PFOA, PFOS, PCBs, and OCPs all being the highest in ALSPAC (1991–1992), followed by MoBa (2005–2007), and lowest in NHANES (2015–2016 for PCBs and OCPs, 2017–2018 for PFAS) (CDC, 2021a, 2021b). PFHxS and PFNA are similar across all three countries and time points.

Pregnancy is a critical period during which maternal nutrition and lifestyle choices have major influence on both mothers' and children's health. Exposure to toxic environmental chemicals during windows of vulnerability, like the prenatal period, may have lasting effects on health across the life course (The American College of Obstetricians and Gynecologists, 2013). Therefore, it is essential to identify modifiable sources of exposure, such as maternal diet to limit fetal exposure to EDCs. Because dietary patterns differ by an individual's food preferences, eating habits, age, gender, and region (Birch et al., 2007), and are shaped by cultural, environmental, ecological, and technological factors (Ezzati and Riboli, 2013), there is a need to conduct studies in various populations.

These studies are strengthened by their basis in population-based birth cohorts, reliable biological measures of several persistent EDCs, and extensive covariate data. This research also has limitations. One limitation of this research is the cross-sectional nature of the environmental and dietary data. In some instances, blood samples were taken weeks before the FFQ was administered, though the different timing of dietary and environmental assessments are unlikely to meaningfully affect persistent EDC concentrations since they have long half-lives (Bu et al., 2015, Olsen et al., 2007, Wimmerova et al., 2011) and no major changes in diet would be expected. Given their long half-lives, measures of EDC concentrations collected during pregnancy reflect pre-pregnancy exposures to some extent. Further, clearance of EDCs may differ during pregnancy. Second, generalization of the results is hampered by the non-representative nature of the study populations (e.g., more educated, less likely to smoke). There are also limitations relating to the covariate data. Education was the only proxy for socioeconomic status used in ALSPAC because many women did not report income, and, therefore, it is possible that socioeconomic status was not completely assessed. Additionally, misreporting of diet is always a possibility. For example, individuals with higher true intake tend to under-report and individuals with lower true intake tend to over-report. Further, detailed information about food preparation, amounts (in ALSPAC), brands, and contextual information about intake is lacking in FFQs.

Finally, both diet and exposure to EDCs differ over time and place, which limit our ability to generalize our results.

5. Conclusions

In conclusion, our study aligns with previous work and identifies a number of animal-based foods associated with persistent EDC exposure in pregnant mothers. We attempted to identify dietary patterns that associate food groups with persistent EDCs in two European populations from the 1990s and 2000s. While we expected greater similarity between the derived patterns in terms of foods with high loadings, typical diets in the United Kingdom and Norway are quite different and sources of EDCs may be different. Regardless, this type of work is important to eventually developing locally and culturally relevant recommendations for pregnant women seeking to limit their exposure to EDCs before and during pregnancy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

ALSPAC	Avon Longitudinal Study of Parents and Children
BMI	body mass index
CDC	Centers for Disease Control and Prevention
EDCs	endocrine disrupting chemicals
FFQ	food frequency questionnaire
HELIX	Human Early Life Exposome
IQR	interquartile range
LOD	limit of detection
MoBa	Norwegian Mother, Father, and Child Cohort Study
MBRN	Medical Birth Registry of Norway
NIPH	Norwegian Institute of Public Health
OCPs	organochlorine pesticides
PCBs	polychlorinated biphenyls
PFAS	per- and polyfluoroalkyl substances
RRR	reduced rank regression

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Table 1. Characteristics of the Avon Longitudinal Study of Parents and Children (ALSPAC) (N=422) and the Norwegian Mother, Father, and Child Cohort Study (MoBa) (N=276) substudy populations.

Characteristic	ALSPAC		MoBa	
	N	%	N	%
Maternal race				
White	412	98.1	229	84.2
Non-white	8	1.9	43	15.8
Maternal education ^a				
<O-level	74	18.3	34	13.4
O-level	134	33.2	82	32.3
>O-level	196	48.5	138	54.3
Maternal pre-pregnancy BMI, kg/m ²				
<25 (under/normal weight)	302	77.8	226	82.2
>25 (overweight/obesity)	86	22.2	49	17.8
Prenatal smoking				
Any	75	18.2	7	2.6
None	337	81.8	264	97.4
Maternal age at delivery, years				
<30	240	56.9	41	14.9
>30	182	43.1	235	85.1
Child birth order				
First born	201	49.9	135	48.9
Second born or later	202	50.1	141	51.1
Child's sex				
Female	422	100.0	127	46.0
Male	0	0.0	149	54.0

Abbreviations: kg/m², kilograms per meter-squared

^a <O-level=none, Certificate of Secondary Education, and vocational education, which are equivalent to no diploma or a GED in the United States. O-levels (ordinary levels) are required and completed at the age of 16. >O-level=A-levels (advanced levels) completed at 18, which are optional, but required to get into university; and a university degree.

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No higher education=1-2 years high school, technical high school, 3-year high school general studies, junior college, 1-4 years higher education=Regional technical college, 4-year university degree
(Bachelor's degree, nurse, teacher, engineer). >4 years of higher education=University, technical college, more than 4 years (Master's degree, medical doctor, PhD).

Table 2.

Serum/plasma concentrations of persistent endocrine disrupting chemical (EDC) exposure among mothers of the Avon Longitudinal Study of Parents and Children (ALSPAC) (N=422) and the Norwegian Mother, Father, and Child Cohort Study (MoBa) (N=276) during pregnancy.

	ALSPAC			MoBa		
	Median	Q1	Q3	Median	Q1	Q3
Perfluoroalkyl substances (PFAS) (ng/mL)						
PFOA	3.8	2.9	4.8	2.1	1.4	3.0
PFOS	20.0	15.3	25.3	9.0	6.6	12.9
PFHxS	1.6	1.2	2.2	0.6	0.4	0.9
PFNA	0.49	0.41	0.66	0.50	0.36	0.66
Polychlorinated biphenyls (PCBs) (ng/g lipid)						
PCB118	15.0	10.9	20.8	7.2	5.3	9.8
PCB138 ^a	41.8	30.3	54.0	21.4	15.9	30.6
PCB153	64.8	48.3	86.2	44.6	32.9	61.2
PCB170	19.0	14.4	25.2	8.3	5.5	11.0
PCB180	45.6	33.5	60.4	24.5	15.9	32.0
Organochlorine pesticides (OCPs) (ng/g lipid)						
HCB	50.7	38.3	63.5	15.7	12.0	19.7
DDE	318.5	193.5	502.5	56.1	38.4	87.5
DDT	11.0	7.8	16.5	2.1	1.3	3.4

Abbreviations: Q1, quartile 1; Q3, quartile 3; ng/mL, nanogram per milliliter; ng/g lipid, nanogram per gram lipid

^aIn ALSPAC, PCB congeners 138 and 158 could not be separated and were quantified as a summed concentration referred to as PCB138.

Table 3.

Summary of daily intake of food groups among mothers of the Avon Longitudinal Study of Parents and Children (ALSPAC) (N=422) and the Norwegian Mother, Father, and Child Cohort Study (MoBa) (N=276) during pregnancy.

Food group	ALSPAC						MoBa					
	Frequency of Consumption (per day)			Frequency of Consumption (per day)			Frequency of Consumption (per day)			Frequency of Consumption (per day)		
	Median	Q1	Q3	Median	Q1	Q3	Median	Q1	Q3	Median	Q1	Q3
Total energy (Calories)	1730	1389	2082	2141	1804	2522						
Sausages, Burgers	0.07	0.00	0.07	0.91	0.46	1.79						
Pies, Pasties	0.07	0.00	0.07	N/A ^a	N/A ^a	N/A ^a						
Meat	0.29	0.29	0.29	0.43	0.29	0.64						
Poultry	0.29	0.07	0.29	0.21	0.14	0.36						
Liver	0.00	0.00	0.00	0.50	0.11	0.79						
White fish	0.07	0.07	0.29	0.32	0.21	0.50						
Other fish	0.07	0.00	0.29	0.36	0.14	0.82						
Shellfish	0.00	0.00	0.00	0.07	0.04	0.14						
Eggs, quiche	0.29	0.07	0.29	0.21	0.21	0.50						
Cheese	0.29	0.29	0.79	1.69	1.08	2.72						
Pizza	0.07	0.00	0.07	0.11	0.07	0.11						
Chips (French fries)	0.07	0.07	0.29	0.04	0.00	0.09						
Roast potatoes	0.07	0.00	0.29	0.04	0.00	0.04						
Boiled, mashed, jacket potatoes	0.29	0.29	0.79	0.21	0.09	0.50						
Rice	0.07	0.07	0.29	0.21	0.09	0.21						
Pasta	0.07	0.07	0.29	0.29	0.18	0.43						
Crisps (potato chips)	0.29	0.07	0.29	0.09	0.04	0.21						
Baked beans	0.29	0.07	0.29	N/A ^a	N/A ^a	N/A ^a						
Peas, sweet corn, broad beans	0.29	0.29	0.29	1.19	0.77	1.78						
Green leafy vegetables	0.29	0.07	0.29	0.09	0.04	0.13						
Other green vegetables	0.29	0.07	0.29	0.55	0.38	0.98						
Carrots	0.29	0.29	0.29	0.30	0.18	0.59						
Other root vegetables	0.07	0.00	0.29	0.68	0.39	1.21						

Food group	ALSPAC				MoBa				
	Frequency of Consumption (per day)		Frequency of Consumption (per day)		Frequency of Consumption (per day)		Frequency of Consumption (per day)		
	Median	Q1	Q3	Median	Q1	Q3	Median	Q1	Q3
Salad	0.29	0.07	0.79	0.88	0.46	1.35	0.88	0.46	1.35
Fresh fruit	0.79	0.79	1.43	2.46	1.58	3.54	2.46	1.58	3.54
Pure juice not in tin	0.29	0.07	0.79	0.88	0.30	1.25	0.88	0.30	1.25
Pudding	0.07	0.07	0.29	0.22	0.13	0.34	0.22	0.13	0.34
Oat cereals	0.07	0.00	0.29	0.09	0.00	0.21	0.09	0.00	0.21
Wholegrain or bran cereals	0.29	0.00	0.79	0.04	0.00	0.21	0.04	0.00	0.21
Other cereals	0.07	0.00	0.29	0.00	0.00	0.00	0.00	0.00	0.00
Cakes or buns	0.29	0.07	0.29	0.25	0.16	0.39	0.25	0.16	0.39
Crispbreads	0.00	0.00	0.07	0.93	0.21	2.00	0.93	0.21	2.00
Biscuits	0.29	0.29	0.79	0.04	0.00	0.09	0.04	0.00	0.09
Chocolate bars	0.29	0.07	0.29	0.09	0.00	0.21	0.09	0.00	0.21
Pulses (legumes)	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00
Nuts	0.00	0.00	0.07	0.09	0.04	0.21	0.09	0.04	0.21
Chocolate	0.07	0.07	0.29	0.21	0.09	0.21	0.21	0.09	0.21
Sweets	0.07	0.00	0.29	0.38	0.18	0.68	0.38	0.18	0.68

^aItem not assessed in MoBa

Factor loadings^{ab} of dietary patterns for exposure to EDCs in blood in the Avon Longitudinal Study of Parents and Children (ALSPAC) and Norwegian Mother, Father, and Child Cohort Study (MoBa) determined through reduced rank regression.

Table 4.

Food Group	Energy-adjusted dietary pattern factor loadings					
	PFAS pattern		PCB pattern		OCP pattern	
	ALSPAC	MoBa	ALSPAC	MoBa	ALSPAC	MoBa
R²	9.6%	9.7%	20.3%	13.8%	16.0%	8.1%
Sausages, Burgers		-0.21	-0.20	0.35	-0.12	0.29
Pies, Pasties		N/A ^c	-0.22	N/A ^c	-0.12	N/A ^c
Meat	0.31	-0.11	0.18	-0.15	0.30	-0.33
Poultry	0.17		0.20		0.29	0.21
Liver	-0.30	-0.17				0.17
White fish	0.16		0.24		0.27	0.13
Other fish	-0.16		0.18	-0.14	0.20	
Shellfish	0.11			-0.11	0.19	
Eggs, quiche	-0.14	0.10		-0.12		-0.23
Cheese	0.19	0.38	0.20		0.13	
Pizza	0.16	-0.13	-0.17		-0.19	-0.11
Chips (French fries)		-0.33	-0.28	-0.32	-0.22	-0.21
Roast potatoes	-0.11		-0.13		-0.13	
Boiled, mashed, jacket potatoes	-0.14	-0.16		-0.27		-0.21
Rice		0.16	0.17	0.37	0.20	
Pasta	0.22		0.10	0.30	0.12	0.30
Crisps (potato chips)		-0.26	-0.31		-0.24	
Baked beans	-0.14	N/A ^c	-0.30	N/A ^c	-0.37	N/A ^c
Peas, sweet corn, broad beans	0.10	0.18				
Green leafy vegetables					0.11	
Other green vegetables			0.22		0.27	

	Energy-adjusted dietary pattern factor loadings							
	PFAS pattern		PCB pattern		OCP pattern			
	ALSPAC	MoBa	ALSPAC	MoBa	ALSPAC	MoBa	ALSPAC	MoBa
Carrots			0.11					0.14
Other root vegetables	-0.15	0.14		0.19				
Salad	-0.15							0.25
Fresh fruit	-0.16		0.10	0.15	0.10	0.10		0.17
Pure juice not in tin	0.12	0.23		0.20				0.21
Pudding		-0.15	0.18	-0.12	0.10	0.10		-0.18
Oat cereals	-0.19	-0.23						0.20
Wholegrain or bran cereals		0.12		-0.12				
Other cereals		-0.17	-0.11					
Cakes or buns		0.25	0.10	0.15				
Crispbreads			0.10	-0.17				-0.14
Biscuits	0.27		0.22	-0.15	0.19			-0.20
Chocolate bars	0.14	-0.28		0.29				0.32
Pulses (legumes)	-0.46	0.25	0.17	-0.12	0.10	0.10		-0.12
Nuts	-0.27	-0.12	0.10		0.14	0.14		-0.16
Chocolate		-0.11		0.19	0.12			
Sweets		0.27	-0.18	0.20				-0.18

Abbreviations: PFAS, perfluoroalkyl substances; PCBs, polychlorinated biphenyls; OCPs, organochlorine pesticides.

^a Adjusted for energy intake using the residual method.

^b Only results with factor loading values $|0.1|$ are shown; bold indicates factor loading value $|0.2|$.

^c Item not assessed in MoBa

Table 5.

Associations of dietary pattern scores and summed Z-scores of persistent EDCs controlling for covariates in the Avon Longitudinal Study of Parents and Children (ALSPAC) and Norwegian Mother, Father, and Child Cohort Study (MoBa) determined through multiple linear regression analysis.

	Total PFAS ^a (n=350) ^d				MoBa				Total PFAS ^a (n=231) ^d						
	β^e	SE	t-value	p-value	partial R ² (%)	β^e	SE	t-value	p-value	partial R ² (%)	β^e	SE	t-value	p-value	partial R ² (%)
Dietary pattern score	1.17	0.17	6.74	<0.01	11.5	1.39	0.23	5.99	<0.01	12.8	1.39	0.23	5.99	<0.01	12.8
Non-white race	2.94	1.94	1.52	0.13	0.4	0.02	0.58	0.03	0.98	0.0	0.02	0.58	0.03	0.98	0.0
Maternal age (years)	0.11	0.04	3.10	<0.01	1.7	0.00	0.07	-0.02	0.98	0.1	0.00	0.07	-0.02	0.98	0.1
Pre-pregnancy BMI (kg/m ²)	0.03	0.04	0.83	0.41	0.2	0.01	0.07	0.19	0.85	0.1	0.01	0.07	0.19	0.85	0.1
Multiparous	-1.52	0.33	-4.64	<0.01	6.1	0.14	0.45	0.31	0.75	0.1	0.14	0.45	0.31	0.75	0.1
> O-level education	-0.13	0.46	-0.29	0.77	0.0	-0.72	0.71	-1.01	0.31	0.5	-0.72	0.71	-1.01	0.31	0.5
O-level education	-0.21	0.47	-0.44	0.66	0.1	-1.59	0.68	-2.35	0.02	2.1	-1.59	0.68	-2.35	0.02	2.1
Smoking	-0.81	0.45	-1.81	0.07	1.0	0.20	1.45	0.14	0.89	0.0	0.20	1.45	0.14	0.89	0.0
Sample gestation (weeks)	-0.02	0.02	-1.02	0.31	0.2	0.62	0.44	1.42	0.16	0.8	0.62	0.44	1.42	0.16	0.8
Total Energy (kJ)	0.00	0.00	-1.25	0.21	0.4	0.00	0.00	-0.09	0.93	0.0	0.00	0.00	-0.09	0.93	0.0
Total R ² (%)					21.6					16.4					16.4
	Total PCBs ^b (n=336) ^d				Total PCBs ^b (n=239) ^d				Total PCBs ^b (n=239) ^d						
	β^e	SE	t-value	p-value	partial R ² (%)	β^e	SE	t-value	p-value	partial R ² (%)	β^e	SE	t-value	p-value	partial R ² (%)
Dietary pattern score	1.19	0.26	4.58	<0.01	21.1	2.07	0.36	5.71	<0.01	12.6	2.07	0.36	5.71	<0.01	12.6
Non-white race	4.86	2.58	1.89	0.06	0.4	-1.11	0.81	-1.38	0.17	0.7	-1.11	0.81	-1.38	0.17	0.7
Maternal age (years)	0.46	0.06	8.42	<0.01	13.9	-0.03	0.09	-0.35	0.73	0.0	-0.03	0.09	-0.35	0.73	0.0
Pre-pregnancy BMI (kg/m ²)	-0.08	0.05	-1.44	0.15	0.4	0.00	0.09	0.05	0.96	0.0	0.00	0.09	0.05	0.96	0.0
Multiparous	-1.20	0.46	-2.60	0.01	1.4	0.52	0.62	0.84	0.40	0.3	0.52	0.62	0.84	0.40	0.3
> O-level education	-1.02	0.64	-1.59	0.11	0.0	0.28	0.98	0.29	0.78	0.0	0.28	0.98	0.29	0.78	0.0
O-level education	-1.52	0.65	-2.32	0.02	1.0	0.39	0.93	0.42	0.68	0.1	0.39	0.93	0.42	0.68	0.1
Smoking	-0.80	0.64	-1.24	0.21	0.3	-0.47	1.87	-0.25	0.80	0.0	-0.47	1.87	-0.25	0.80	0.0
Sample gestation (weeks)	0.00	0.02	0.08	0.93	0.0	-0.14	0.60	-0.24	0.81	0.0	-0.14	0.60	-0.24	0.81	0.0
Total Energy (kJ)	0.00	0.00	-0.03	0.98	0.0	0.00	0.00	0.01	0.99	0.0	0.00	0.00	0.01	0.99	0.0

	Total OCPs ^c (n=324) ^d				Total OCPs ^c (n=226) ^d				Total R ² (%)	
	β^e	SE	t-value	p-value	partial R ² (%)	β^e	SE	t-value	p-value	partial R ² (%)
Dietary pattern score	0.40	0.11	3.60	<0.01	10.2	0.69	0.19	3.57	<0.01	5.8
Non-white race	2.27	1.08	2.10	0.04	0.1	-0.55	0.45	-1.23	0.22	0.6
Maternal age (years)	0.18	0.02	7.52	<0.01	12.3	-0.05	0.05	-0.93	0.36	0.3
Pre-pregnancy BMI (kg/m ²)	0.09	0.02	3.91	<0.01	4.1	-0.01	0.05	-0.17	0.87	0.0
Multiparous	-0.63	0.20	-3.17	<0.01	1.6	0.27	0.33	0.82	0.41	0.3
> O-level education	-1.13	0.27	-4.18	<0.01	2.5	0.07	0.54	0.14	0.89	0.0
O-level education	-0.63	0.28	-2.29	0.02	1.1	0.20	0.51	0.40	0.69	0.1
Smoking	-0.45	0.28	-1.63	0.10	0.6	0.53	0.99	0.54	0.59	0.1
Sample gestation (weeks)	0.00	0.01	-0.34	0.74	0.0	-0.25	0.32	-0.79	0.43	0.3
Total Energy (kJ)	0.00	0.00	-0.55	0.59	0.1	0.00	0.00	-0.41	0.68	0.1
Total R ² (%)					38.4					13.7
					32.6					7.6

Abbreviations: PFAS, perfluoroalkyl substances; PCBs, polychlorinated biphenyls; OCPs, organochlorine pesticides; BMI, body mass index

^aTotal PFAS=summed z-scores of PFOA, PFOS, PFHxS, and PFNA

^bTotal PCBs=summed z-scores of PCB118, PCB138, PCB153, PCB170, and PCB180

^cTotal OCPs=summed z-scores of DDT, DDE, and HCB

^dSample size varies across models due to missing data on EDCs

^eThe β represents the change in EDC z-score that would be expected with a 1-unit change in predictor variables, controlling for the other variables in the model