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Dietary patterns and exposure to non-persistent endocrine-disrupting chemicals during pregnancy

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ABSTRACT

Background: Exposure to non-persistent endocrine disrupting chemicals (EDCs) is widespread, causing various adverse health effects, especially during pregnancy. Diet is a major source of EDCs and the identification of dietary patterns that give rise to higher exposure levels is crucial. We aimed to explore the relationship between dietary patterns during pregnancy and exposure to non-persistent EDCs.

Methods: We included 640 pregnant women from the Barcelona Life Study Cohort (BiSC), Spain. Using food frequency questionnaires (2nd trimester), we estimated ultraprocessed food (UPF) consumption and Mediterranean diet adherence, and derived data-driven dietary patterns. Metabolites of phthalates, 1,2-cyclohexane dicarboxylic acid di(isononyl) ester (DINCH), chlorpyrifos and pyrethroid, polycyclic aromatic hydrocarbons (PAHs, including phenanthrenes), and organophosphates, and parent compounds of phenols and parabens were

Abbreviations: BPA, Bisphenol A; BPS, Bisphenol S; BMI, Body mass index; CI, Confidence interval; EDCs, Endocrine disrupting chemicals; ETPA, Ethyl paraben; DEP, Diethylphosphate; DEHP, Di(2-ethylhexyl) phthalates; DINCH, 1,2-Cyclohexane dicarboxylic acid di(isononyl) ester; DiNP, Di-*iso*-nonyl phthalates; DMTP, Dimethylthiophosphate; DPHP, Diphenylphosphate; FFQ, Food frequency questionnaires; GMR, Geometric Mean Ratio; LOD, Limit of detection; LOQ, Limit of quantification; MEPA, Methyl paraben; MEP, Monoethyl phthalate; MiBP, Mono-*iso*-butyl phthalate; MnBP, Mono-n-butyl phthalate; MBzP, Mono benzyl phthalate; oh-MPHP, 6-Hydroxy Monopropylheptylphthalate; MEHP, Mono-(2-ethyl)-hexyl phthalate; MEHHP, Mono-(2-ethyl-5-hydroxyhexyl) phthalate; MEOHP, Mono (2-ethyl-5-oxohexyl) phthalate; MECPP, Mono-2-ethyl-5-carboxypentyl phthalate; oxo-MiNCH, 2-(((4-Methyl-7-oxyooctyl)oxy)carbonyl)cyclohexanecarboxylic acid; oh-MiNCH, 2-(((Hydroxy-4-methyloctyl)oxy)carbonyl)cyclohexanecarboxylic acid; mL, Mililiter; ng, Nanogram; 2-NAOL, 2-Hydroxynaphthalene; OCPs, Organochlorine pesticides; 1-OH-PYR, 1-Hydroxypyrene; OXBE, Oxybenzone; PAHs, Polycyclic aromatic hydrocarbons; 3-PBA, 3-Phenoxybenzoic acid; PCBs, Polychlorinated biphenyls; PFAS, Per- and polyfluoroalkyl substances; 3-PHOL+2-PHOL, Sum of 2-Hydroxyphenanthrene and 3-Hydroxyphenanthrene; 9-PHOL+1-PHOL, Sum of 1-Hydroxyphenanthrene and 9-Hydroxyphenanthrene; PRPA, Propyl paraben; KMO, Kaiser-Meyer-Olkin; rMED, Relative Mediterranean Diet Score; SD, Standard deviation; TRCS, Triclosan; TCPy, 3,5,6-Trichloro-2-pyridinol; UPF, Ultra-processed food.

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measured in weekly urine pools (3rd trimester). Associations between dietary patterns and EDCs were evaluated through multivariable linear regressions.
Results: Higher compliance with a "Vegetarian" pattern or the Mediterranean diet was associated with lower levels of some of the phthalate metabolites (e.g., di-*iso*-nonyl phthalates [Geometric mean ratio (GMR) per unit increases in the "Vegetarian" score = 0.97, 95 %CI 0.95, 1.00]). Conversely, "Western" and "Animal protein" patterns, and UPF intake were associated with higher PAHs (e.g., "Western" and 2-Hydroxynaphthalene [GMR (95 %CI) 1.07(1.01, 1.13)]), pesticides (e.g., "Animal protein" and 3-Phenoxybenzoic acid [1.15(1.01, 1.32]), and phthalates metabolites levels (e.g., UPF and Monoethyl phthalate [1.05(1.01, 1.09)]). No association remained significant after correcting for multiple testing.
Conclusions: Following a plant-based diet may help reduce the exposure to certain phthalate and organophosphate metabolites, whereas higher consumption of foods from animal origin and high in fat/sugar/salt may increase exposure to PAHs, pesticides, and phthalates metabolites in pregnancy.

1. Introduction

Millions of tons of synthetic chemicals are produced and consumed every year in Europe (Eurostat, 2021), and it is estimated that about a thousand of manufactured chemicals (individual or classes of chemicals) may have endocrine-disrupting properties (Yilmaz et al., 2020). Human exposure to endocrine disrupting chemicals (EDCs) is widespread with most being detected in more than 90 % of pregnant women body fluids (Dereumeaux et al., 2017; Haug et al., 2018). Additionally, current European Union (EU) regulations on the registration, evaluation, authorization and restriction of chemicals do not cover all EDCs. Recently, stricter regulations in the EU have been implemented for some EDCs, such as bisphenol A and some phthalates, such as di(2-ethylhexyl) phthalate (DEHP) and diisononyl phthalate (DINP). These chemicals have been replaced by newer agents, such as bisphenol S and F (Liu et al., 2024) and 1,2-cyclohexane dicarboxylic acid di(isononyl) ester (DINCH) (Ketema et al., 2023). Studies have, however, demonstrated that some phthalate and bisphenol replacements may have similar adverse health impacts as the original chemicals (Abrantes-Soares et al., 2022; Svensson et al., 2021; Yland et al., 2022), and this may be due to their endocrine disrupting properties.

Epidemiological studies have shown that prenatal exposure to non-persistent EDCs, such as phthalates, bisphenols and most pesticides, have been associated with adverse outcomes during pregnancy (including negative effects on maternal gut microbiota homeostasis, damage to the placenta (Zha et al., 2024), and fetal growth restriction (Svensson et al., 2021)), at birth (such as decreased birth weight (Woods et al., 2017), preterm birth (Yland et al., 2022), and risk of being born small for gestational age (Trasande et al., 2024)), and during childhood (e.g. behavioral problems and cognitive decrements in childhood (Braun, 2017; Van Den Dries et al., 2020) and slower infancy weight gain (Svensson et al., 2021)). Exposure during pregnancy plays an important role in fetal programming, given the transfer of these chemicals from the mother to the fetus through the placenta (Zha et al., 2024) and offspring's greater sensitivity (Yang et al., 2019). EDCs can also potentially interact with genes, lifestyle behaviors, and other environmental exposures (Trasande et al., 2009). The presence of EDCs in human samples has been documented in many pregnancy and birth cohort studies, although most studies cover periods of one or two decades ago, and only a few studies measure exposure levels of currently-used chemicals (Abrantes-Soares et al., 2022; Buckley et al., 2019; Ketema et al., 2023; Liu et al., 2024; Pacyga et al., 2024; Philips et al., 2018; Steele et al., 2020; Yland et al., 2022).

Dietary intake is a major source of these chemicals in humans, due to the contact of food with packaging materials, such as phthalates in plastic containers (Vieyra et al., 2023), bisphenols in canned foods, beverage containers, plastic dinnerware, etc. (Pacyga et al., 2019), as well as pesticides in fruits, grains, meat (Liu et al., 2021), animal feed, fertilizers, and contaminated groundwater (Rashid et al., 2020). Although regulations on the use of certain EDCs on food packaging materials exist for decades in the EU (European Commission, 2024; European Parliament, 2004), these are still widely detected in urine samples. Since most EDCs enter food through contamination, they are not declared in the ingredient labels (except parabens), increasing difficulty for consumers to assess or modify their dietary exposure (Melough et al., 2022). Besides, individuals do not consume foods in isolation, but as complex combinations of different foods. The identification of dietary patterns related to chemical exposure is important to assist the design and delivery of effective dietary guidelines, which need to balance the health risks related to dietary exposure and the health benefits of important foods and nutrients, especially in susceptible periods of life, such as pregnancy (Papadopoulou et al., 2019). Here, an approach aimed at identifying dietary patterns may be more useful than focusing on individual food groups, since it includes the overall diet, and achieves a resemblance of real life (Schulz et al., 2021).

A few studies have investigated the association of dietary patterns and EDCs exposure in pregnancy. One recent study using maternal *a priori* dietary patterns (Mediterranean diet score, Healthy Eating Index) in the US described that higher adherence to a healthy diet was associated with higher organochlorine pesticide (OCP) concentrations, besides higher levels of a variety of persistent organic chemicals, such as PFAS (per- and polyfluoroalkyl substances) and PCBs (polychlorinated biphenyls) (Yu et al., 2024). Another study in China, using data-driven dietary patterns, showed that those with greater adherence to the fruit-nut-vegetable dietary pattern had lower urinary phthalates and polycyclic aromatic hydrocarbons (PAHs) concentrations, while higher levels of these chemicals were observed in the egg-dairy products, whole grain-tuber crop, and meat-aquatic dietary patterns (Luo et al., 2022). In the US, Baker et al. described that among a sample of pregnant participants, a 10 % increase in ultra-processed food (UPF) consumption, which are typically high-energy-dense products, high in sugar, unhealthy fats and salt (Monteiro et al., 2019), was associated with 13.1 % higher molar sum concentrations of phthalates; the opposite was found for minimally processed food intake and phthalate exposure (Baker et al., 2024). Lastly, another study with two European birth cohorts (Marks et al., 2021) found that pregnant women consumed three distinct dietary patterns that contributed to exposure to persistent EDCs (PFAS, PCBs) and OCPs. All patterns were characterized by high consumption of meat, poultry, white fish, and biscuits in the British cohort ALSPAC; in the Norwegian cohort MoBa, high consumption of processed meat, pasta, and chocolate characterized the PCB and OCP dietary patterns, while high consumption of cheese characterized the PFAS pattern. It is worth mentioning that this study examined exposure to persistent chemicals only, which are reflective of long-term exposure and are, therefore, not fully summarized by the use of Food Frequency Questionnaires (FFQ) (Marks et al., 2021).

Studies with pregnant women have mainly focused on single food groups (Casas et al., 2013; Gardener et al., 2022; Mariscal-Arcas et al., 2009; Papadopoulou et al., 2019; Sugeng et al., 2020), rather than dietary patterns. In addition, more recent substitutes of non-persistent chemicals have been less studied (Abrantes-Soares et al., 2022; Pacyga et al., 2024; Philips et al., 2018; Steele et al., 2020; Yland et al., 2022). Also, existing studies assessing *in utero* exposure to non-persistent chemicals rely on one or a few spot urine samples (Baker et al., 2024;

Casas et al., 2013; Gardener et al., 2022; Luo et al., 2022; Papadopoulou et al., 2019; Santos et al., 2021; Wu et al., 2020), giving rise to high levels of exposure misclassification (Perrier et al., 2016), since exposure to these short-lived chemicals is highly variable over time (Sugeng et al., 2020). To overcome these research gaps, we aimed to explore the relationship between dietary patterns during pregnancy and exposure to a wide range of non-persistent EDCs (i.e., metabolites of phthalates and DINCH, metabolites of chlorpyrifos and pyrethroid, PAHs (including phenanthrenes), and organophosphates (OP), and parent compounds of phenols and parabens measured in weekly urine pools in a recent birth cohort in Barcelona, Spain.

2. Materials and methods

2.1. Participants and study design

This study used data from the birth cohort "Barcelona Life Study Cohort – BiSC" (https://www.projectebisc.org (Dadvand et al., 2024)). BiSC is being conducted in Barcelona, Spain, and includes three of city's major hospitals. Its primary goal is to identify early environmental and genetic causes of normal and abnormal growth, development and health from fetal life until young adulthood. Pregnant women were recruited in their 1st trimester, with recruitment taking place between October 2018 and March 2021, using the following inclusion criteria: singleton pregnancy, aged between 18–45 years, within weeks 11–15 of pregnancy, being able to communicate in Spanish/Catalan, resident in the catchment area of the hospitals, and planning to give birth in one of the BiSC recruiting hospitals. Women were followed-up in the 1st (week 12), 2nd (week 20) and 3rd trimester (week 32) of pregnancy. A total of 1080 pregnant women were followed throughout the whole pregnancy. In the current study, 255 participants had missing data on dietary intake in the 2nd trimester and 4 had implausible daily energy intakes (<500Kcal or ≥ 5000Kcal per day) (Marks et al., 2021). A total of 755 women had measurements of non-persistent EDCs in 3rd trimester urine samples. Including women with data on both diet and non-persistent EDCs exposures, our final sample size was 640 pregnant women (see study population flowchart in Fig. 1).

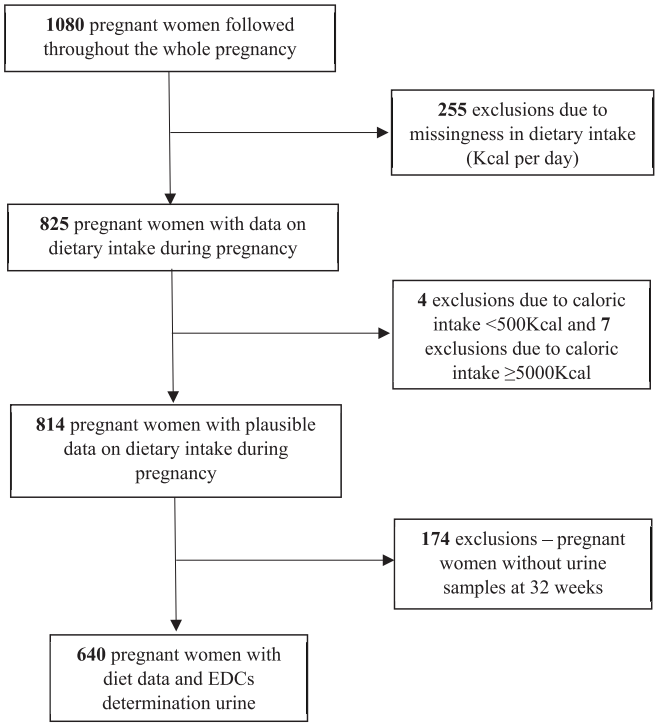


Fig. 1. Study population flowchart.

From pregnancy up to 18 months visits were approved by the Clinical Research Ethics Committee of the Parc de Salut Mar project (2018/8050/I), Medical Research Committee of the Fundació de Gestió Sanitària del Hospital de la Santa Creu i Sant Pau de Barcelona (EC/18/206/5272), and Ethics Committee of the Fundació Sant Joan de Déu (PIC-27–18).

Before joining the cohort during their regular 1st trimester hospital visit, participants were informed by a BiSC midwife or nurse about the study's details, duration, and their option to withdraw without penalty. If they agreed to take part, they signed consent forms permitting the collection of biological samples and genetic studies, receiving a copy for themselves. Parents or legal guardians of children also provided informed consent before any study procedures commenced.

2.2. Dietary intake

Dietary data were collected in the 2nd trimester of pregnancy using a semi-quantitative and validated 114-item FFQ (Vioque et al., 2013). All items included a description of standardized food/beverages servings and referred the usual food intake during pregnancy, without specifying a specific duration. Possible answers were given in nine categories ("Never or < 1 month", "1–3 per month", "1 per week", "2–4 per week", "5–6 per week", "1 per day", "2–3 per day", "4–5 per day", "6 + per day"). Responses were transformed in grams/day of intake and food items were grouped into food groups, as described in Supplementary Table 1.

Dietary patterns were described through two main methods: data-driven and *a priori*. Regarding *a priori* dietary patterns, we considered maternal adherence to Mediterranean diet (rMED). Intake in 9 food groups were energy adjusted (converted in grams per 1,000 kcal/day) and divided into tertiles. A value of 0, 1, and 2 was assigned to the 1st, 2nd, and 3rd tertiles of intake, respectively, for fruit (excluding fruit juices), nuts, vegetables (excluding potatoes), legumes, cereals (including whole-grain and refined flour, pasta, rice, other grains, and bread), fish (including seafood), and olive oil. The scoring was reversed for two components: meat (including processed meat) and dairy (including low-fat and high-fat milk, yogurt, cheese, cream desserts, and dairy and non-dairy creams). We did not include the consumption of alcohol, so 8 components were used and summed to give a total rMED ranging from 0 (minimal adherence) to 16 (maximum adherence). A rMED score of 0–6 was labeled "low adherence", 7–10 as "medium adherence", and > 10 as "high adherence". Regarding food processing, every food item was classified into 4 groups according to the NOVA scheme (Monteiro et al., 2019): group 1, unprocessed or minimally processed foods (e.g., fresh, dry or frozen fruits or vegetables), group 2, processed culinary ingredients (e.g., sugar, salt, oil), group 3, processed foods (e.g., canned food, cheese), and group 4, UPF (e.g., soft drinks, sweet and savory packaged snacks). We categorized the intake of UPF into tertiles (grams/day). The classification of certain FFQ items using the NOVA scheme may be complex, due to limited detail regarding food ingredients, processing methods or preparation techniques. In this study, when a FFQ food item could correspond to foods from different NOVA groups, we classified it under the more processed group (group 4). This approach was taken to minimize the risk of underestimating UPF intake, which is central to our study objectives.

To derive the data-driven dietary patterns, we used information obtained from the FFQ and estimated dietary patterns using exploratory factor analyses with orthogonal varimax rotation. We did not include the consumption of water and alcohol, resulting in the inclusion of 15 food groups (Meat (white and red), eggs, dairy, fish and seafood, vegetables, legumes, fruits, cereals, potatoes, oils, solid fats, bakery products, juices, sugar-sweetened beverages, nuts). The Kaiser-Meyer-Olkin (KMO) and Bartlett's sphericity tests was applied and confirmed data adequacy for factor analysis in the current sample. The number of factors to be retained was selected considering: (i) eigenvalues using the Kaiser criterion (eigenvalues > 1), (ii) inflection point of the scree plot of

eigenvalues, and (iii) interpretability of the factor solution. After rotation, loading cut-offs were applied to select the food groups in each pattern (≥ 0.25 and ≤ -0.25) (Castro et al., 2015; Jayedi et al., 2023; Shin et al., 2013). Each woman was then given scores for each factor (i.e., pattern), by multiplying the most relevant factor loadings ($\geq$0.25 and $\leq$ -0.25) by the corresponding food group daily intake and by summing all these items. Greater scores indicate a higher consumption of foods/drinks in these patterns, and lower scores indicate a lower consumption (Englund-Ögge et al., 2019). For each pattern, tertiles of adherence were calculated to define low, medium and high adherence.

In this study, we assumed that participant's diet did not change dramatically from the 2nd to the 3rd trimester (assessment of EDCs exposure). Previous studies have reported that dietary patterns throughout pregnancy to not change significantly over time (Crozier et al., 2009; Cucó et al., 2006; McGowan and McAuliffe, 2013; Rifas-Shiman et al., 2006). Therefore, food intake information obtained at one time point of pregnancy may provide reliable information on dietary pattern throughout pregnancy (Cucó et al., 2006).

2.3. Assessment of exposure to non-persistent endocrine disrupting chemicals (EDCs)

Non-persistent EDCs were measured in weekly pools of urine samples collected in the 3rd trimester visit (mean gestational age was 34.7 weeks). Women collected the first morning and bedtime urine voids during 6 consecutive days (day 2 to day 7) using 70 ml polypropylene containers, and stored them in their freezers (around −20 °C) at home. In total, each participant collected 10–12 urine samples (first morning and last evening voids per day, for 6 days). Samples were then collected on day 8 by fieldworkers and within-subject pools of all urines collected in a week were made by taking 0.5 ml from each collected sample. Target biomonitoring assays for the measurement of chemicals in biospecimens were performed at the Department of Food Safety at the Norwegian Institute of Public Health. BiSC participants included in the urinary chemical analyses were those who (i) had at least 10 voids at the collection time point, (ii) did not experience termination of the pregnancy; and (iii) were still retained in the study at birth of the child.

Phthalate and DINCH metabolites were determined according to (Sabaredzovic et al., 2015): MEP, MiBP, MnBP, MBzP, MnPeP, MEHP, MCHP, MnOP, MEHHP, MEOHP, MECPP, oh-MiNP, oxo-MiNP, cx-MiNP, oh-MPHP, oh-MINCH, oxo-MINCH. Parabens, phenols, PAHs metabolites and other pesticide metabolites were determined by using a modified method of (Sakhi et al., 2018): Parabens (MEPA, ETPA, PRPA, BUPA), phenols (BPA, BPS, BPF, OXBE, TRCS), PAHs metabolites (2-NAOL, 2-OHFLU + 3-OHFLU, 1-OH-PYR, 3-OH-CRY, 3-PHOL + 2-PHOL, 9-PHOL + 1-PHOL, 4-PHOL). Metabolites of chlorpyrifos and pyrethroid (2–4-D, TCPy, 3-PBA) and organophosphates (DPHP, DMP, DMTP, DMDTP, and DEP) were determined by (Cequier et al., 2016; Cequier et al., 2014). A detailed description of chemicals abbreviations and raw concentrations, limit of detection (LOD) and limit of quantification (LOQ) values are in Supplementary Table 2. For some phthalate and DINCH (sum_DEHP, sum_DiNP, sum_DINCH), and PAHs metabolites (sum_PHOL), the molar sums were calculated and used in the current analyses, instead using single metabolites, since they originate from the same parent compound (Supplementary Table 2). Some EDCs showed high proportion of values below the LOD (so less than 50 % was detected), thus being excluded from the present analysis (MnPeP – 97.2 %, MCHP – 98.5 %, MnOP – 94.6 %, BPF – 88.4 %, BUPA – 83.7 %, 2–4-D – 56.5 %, 2-OHFLU + 3-OHFLU – 96.7 %, 4-PHOL – 80.3 %, 3-OH-CRY – 99.5 %, DMP – 55.3 %, DMDTP – 79.4 %, and DETP – 79.0 %), resulting in 23 chemicals analyzed (Supplementary Table 2).

To ensure high quality of non-persistent EDCs data, internal quality control samples were analyzed with each sample batch and results were plotted in quality control charts by contaminant. Concentrations between the LOD and the LOQ were reported for each chemical, and empty cells represented the occurrence of either lack of signal from the machine or concentrations below the LOD. For samples in which no concentrations were detected, defined as below LOD, values were singly, left-censored, imputed. Imputations were based on the underlying distribution of the specific chemical compound, using quantile regression approach implemented in the *fill_in* function of the NADA2 R package (Julian, 2024) based on Helsel (1990). Because we relied on pooled samples, correction for creatinine was not applied (Philippat and Calafat, 2021).

After close examination of the variation across batches and the influence of other technical variables, we determined that none of these factors influenced the measurement of chemicals, thus no batch correction was applied in the current analyses. Lastly, log-2 transformation was applied aiming to achieve normal distribution in all included EDCs. For descriptive proposes, the non-imputed and non-log2-transformed values were used, while for statistical analyses, the imputed, log2-transformed values were used. The geometric mean (GM), median and interquartile range were used to describe their distributions.

2.4. Covariates

At each follow-up, participants answered to online questionnaires and face-to-face interviews. In the 1st trimester we collected information on a variety of sociodemographic information, including maternal age (in years), parity (number of previous times the participant gave birth at $>$ 22 weeks of gestational age – 0 = nulliparous; $\geq$1 = multiparous), ethnic origin (European; Other (Arabic, East Asian, Iranian, Latin American, and South Asian)), and educational level (no studies or incomplete primary education studies; Primary education (EGB; Primary; ESO); secondary studies or professional formation (BUP; COO; FP; High School); university studies (Degree; etc); postgraduate studies (Master; PhD; MIR; etc); Don't know / Rather not answer; and Other), which were grouped into three categories: primary of less, secondary, and university. In the 1st trimester, pregnant participants were physically examined by trained researchers. Weight (in kg) and height (in cm) were measured three times and an average was coded for each woman. Body mass index (BMI) was then calculated as weight (kg)/height^2. For descriptive purposes, weight status categories were defined as: underweight: $<$18.5 kg/m^2, healthy weight: 18.5–24.99 kg/m^2, overweight: 25–29.99 kg/m^2, and obesity $\geq$ 30 kg/m^2 (World Health Organization, 1995). In the 3rd trimester, pregnant participants responded again to various questionnaires on lifestyle behaviors, including any smoking habits during pregnancy (smoker; non-smoker), which was included as a confounder in the current analyses. Also, since participants recruitment occurred during the COVID-19 pandemic, we included a variable describing whether the mother underwent strict confinement during or before/after the pregnancy (coded as Yes; Not during pregnancy, respectively) (see the study DAG in Supplementary Fig. 1).

2.5. Statistical analyses

To avoid loss of statistical power, we imputed missing values in covariate data by performing multiple imputations by chained equations. Twenty datasets were generated using the "mice" package in RStudio (van Buuren and Groothuis-Oudshoorn, 2011), which assumes that data are missing at random. Results from use of the imputed data sets were combined using Rubiń's combination rules (more detail on the covariate imputation procedures can be found in Supplementary Text 1).

Multivariable linear regression analysis was performed to examine the association between the data-driven and *a priori* dietary patterns during pregnancy (2nd trimester) and concentrations of each EDCs in the 3rd trimester. Main models included data-driven dietary patterns as continuous variables (scores) or UPF consumption (grams/day) or score (rMED) as independent variables. In secondary analyses, we explored associations between levels of adherence to each dietary pattern (highest tertile adherence *vs.* lowest tertile adherence as the reference

category) and EDCs exposure in the 3rd trimester. In the multivariable models, covariates were included *a priori* based on reported associations with environmental contaminant concentrations and dietary patterns in the literature (Baker et al., 2024; Englund-Ögge et al., 2019; Liu et al., 2024; Luo et al., 2022; Trasande et al., 2009). Models included maternal ethnicity, age, education, parity, BMI at baseline (1st trimester), smoking during pregnancy (3rd trimester), and COVID-19 confinement. Geometric Mean Ratios (GMR) were derived by exponentiating the β coefficients obtained from linear regression analysis. Generalized linear regression assumption checks were performed through visualization of residual checks and QQ plots.

As a sensitivity analysis we analyzed the association between specific food groups included in statistically significant associations between dietary patterns and non-persistent EDCs, aiming to better understand which were the main drivers for the associations with EDCs concentrations in the 3rd trimester. The food groups analyzed were: fish and seafood, meat, dairy, eggs, fruits and vegetables (as number of servings/day), and this choice was based on prior studies (Luo et al., 2022; Pacyga et al., 2019; Papadopoulou et al., 2019).

In order to control for family-wise error rate (FWER), we used a multiple testing correction method based on the effective number of tests (Li et al., 2012), which takes into account the correlation structure of the data. In this study, the corrected level of significance was 0.0008. All analyses were conducted in R version 2023.03.1 Build 446 (R Core Team, Vienna, Austria).

3. Results

3.1. Characteristics of the study population

Women were, on average, 34.5 years old at baseline, almost 80 % were European, highly educated (76 % with a university degree), and with mean 1st trimester BMI of 23.9 kg/m^2 (30 % with overweight or obesity). Almost one fourth of the sample (24.5 %) experienced strict COVID-19 confinement during pregnancy. On average, 3 servings/day of vegetables and 2.5 servings/day of fruits were consumed, and legumes were consumed less frequently (0.3 servings/day). Meat (white and red) was consumed, on average, once per day (1 serving), and fish and seafood, 0.7 serving/day (Table 1). Regarding non-persistent EDCs in our study (Supplementary Fig. 2 and 3), we found that MEP showed the highest concentrations (median 38.13 μg/mL) compared to the other phthalate metabolites. Phenol compounds that showed the highest concentrations were MEPA (median 17.85 μg/mL), highest concentrations, among the PAHs metabolites, were seen for 2-NAOL (median 11.41 μg/mL), and concentrations of the measured organophosphates and metabolites of chlorpyrifos and pyrethroid were similar among included participants (organophosphates ranging from 0.81 μg/mL (DPHP) to 2.34 μg/mL (DMTP) and metabolites of chlorpyrifos and pyrethroid ranging from 1.10 μg/mL (TCPy) to 1.16 μg/mL (3-PBA) (Supplementary Table 2).

3.2. Data-driven dietary patterns

Three data-driven dietary patterns were identified (Supplementary Fig. 4), with a total explained cumulative variance of 24 %. Dietary patterns were named according to their predominant factor loadings: the "Animal protein pattern", with meat, eggs, fish and seafood, and juices, the "Vegetarian pattern", with vegetables, legumes, fruits, oils, dried fruits, juices and potatoes, and the "Western pattern", with oils, bakery products, dairy, cereals and solid fats. A correlation plot between the data-driven dietary patterns, the rMED pattern and UPF consumption is displayed in Supplementary Fig. 5.

There were differences with regards to maternal BMI (higher BMI in the higher UPF intake group and in the "Animal protein" high adherence group), education (lower education associated with higher UPF intake and lower Mediterranean diet adherence), and smoking during pregnancy (more common in high adherence to Western diet and high UPF intake groups) (Supplementary Table 3).

Table 1
Maternal sociodemographic characteristics and food intake during pregnancy (n = 640).

	Sample (n = 640)
Age (years) – Mean (SD)	34.5 (4.35)
Ethnicity – n (%)	
European	510 (79.7)
Other[a]	130 (20.3)
Educational level – n (%)	
Primary or less	19 (3.0)
Secondary	134 (20.9)
University	487 (76.1)
Smoking during pregnancy – n (%)	
Smoker	47 (7.3)
Non-smoker	593 (92.7)
Parity – n (%)	
Multiparous	272 (42.5)
Nulliparous	368 (57.5)
BMI (kg/m^2) – Mean (SD)	23.9 (4.10)
Weight status[b] – n (%)	
Underweight (< 18.5 kg/m^2)	19 (3.0)
Healthy weight (18.5–24.99 kg/m^2)	426 (66.6)
Overweight (25–29.99 kg/m^2)	146 (22.8)
Obesity (≥ 30 kg/m^2)	49 (7.7)
COVID-19 pandemic confinement – n (%)	
Yes	157 (24.5)
Not during pregnancy	483 (75.5)
Daily food group intake (2nd trimester, servings/day) – Mean (SD)	
Vegetables	3.15 (2.08)
Potatoes	0.99 (0.66)
Legumes	0.29 (0.33)
Cereals	1.49 (0.84)
Fruits	2.49 (1.55)
Dried fruits	1.00 (0.84)
Juices	0.61 (0.55)
Meat (white and red)	1.07 (0.76)
Dairy	2.40 (1.50)
Eggs	0.39 (0.25)
Fish and seafood	0.71 (0.44)
Oils	1.46 (1.06)
Solid fats	0.46 (0.96)
Bakery products	1.15 (1.05)
Sugar-sweetened beverages	0.17 (0.37)

BMI: Body Mass Index; SD: Standard deviation. [a]Other ethnicities included Arabic, East Asian, Iranian, Latin American, and South Asian; [b]Maternal weight status defined according to the World Health Organization (World Health Organization, 1995).

3.3. Dietary patterns and EDCs concentrations

Higher adherence to the "Vegetarian pattern" showed an association with lower levels of some of the phthalate metabolites (sum_DiNP [Geometric mean ratio (GMR) per unit increases in the score/pattern = 0.97, 95 %CI 0.95, 1.00, p-value 0.047], oh-MPHP [GMR = 0.97; 95 %CI 0.94, 1.00, p-value 0.035]), and the organophosphate metabolite DPHP [GMR = 0.96; 95 %CI 0.93, 0.99, p-value 0.012] (Fig. 2). In the analyses treating the dietary patterns as high *vs.* low adherence to the "Vegetarian pattern" was associated with higher levels of MBzP (phthalate metabolite) [GMR = 1.29; 95 %CI 1.05, 1.58, p-value 0.014] and lower levels of DPHP (organophosphate metabolite) [GMR = 0.76; 95 %CI 0.62, 0.94, p-value 0.011] (Supplementary Fig. 6).

Increased consumption in the "Western pattern" was associated with a 7 % GMR increase per unit in the score [95 %CI 1.01, 1.13, p-value 0.018] of the PAHs metabolite 2-NAOL (Fig. 2). This association was also observed when comparing high *vs.* low adherence to the "Western pattern", with a 22 % increase of the PAHs metabolite 2-NAOL [95 %CI = 1.03, 1.46, p-value 0.025]. Further, high *vs.* low adherence to the "Western pattern" was associated with lower levels of BPS (phenol)

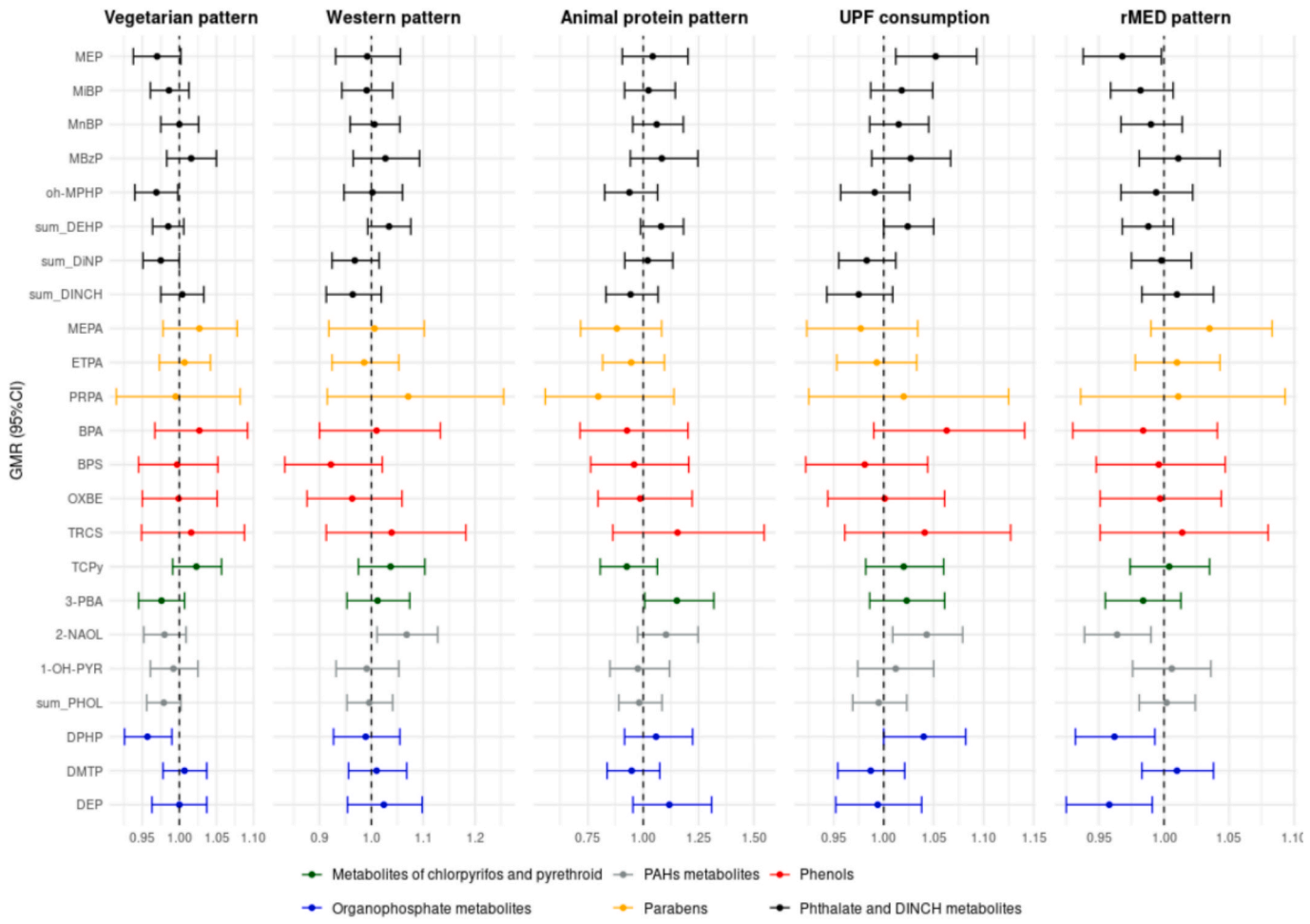


Fig. 2. Associations (Geometric Mean Ratio (GMR) (95 %CI)) between continuous data-driven and *a priori* dietary patterns and concentrations of non-persistent EDCs from linear regression models, using log2-transformed EDCs concentrations. Models adjusted for maternal ethnicity, age, education, pre-pregnancy body mass index, parity, smoking during pregnancy, and COVID-19 confinement. GMR < 1 signify lower exposure and GMR > 1 signify higher exposure. rMED: relative Mediterranean Diet Score; UPF: Ultraprocessed food.

[GMR = 0.69; 95 %CI 0.49, 0.96, p-value 0.026] (Supplementary Fig. 6).

GMR per unit increase in the score of "Animal protein pattern" was associated with a 15 % increase of 3-PBA (chlorpyrifos and pyrethroid metabolite) [95 %CI 1.01, 1.32, p-value 0.04] (Fig. 2). High *vs.* low adherence to the "Animal protein pattern" was associated with a 15 % increase of the sum_DEHP phthalate metabolites [95 %CI 1.01, 1.31, p-value 0.03] (Supplementary Fig. 6).

Increased consumption of UPFs showed associations with greater levels of the phthalate metabolite MEP [GMR per unit increase in the UPF daily consumption = 1.05; 95 %CI 1.01, 1.09, p-value 0.01] and the PAHs metabolite 2-NAOL [GMR = 1.04; 95 %CI 1.01, 1.08, p-value 0.014] (Fig. 2). High *vs.* low adherence to UPF was also associated with a 30 % increase of phthalate metabolite MEP [95 %CI 1.06, 1.59, p-value 0.01], and lower levels of the DINCH metabolite sum_DINCH [GMR = 0.84; 95 %CI 0.70, 1.00, p-value 0.049] (Supplementary Fig. 6).

Lastly, the Mediterranean diet pattern was associated with significantly lower levels of the PAHs metabolite 2-NAOL [GMR = 0.96; 95 % CI 0.94, 0.99, p-value 0.007], the phthalate metabolite MEP [GMR = 0.97; 95 %CI 0.94, 1.00, p-value 0.036], and organophosphate metabolite (DPHP [GMR = 0.96; 95 %CI 0.93, 0.99, p-value 0.016] and DEP [GMR = 0.96; 95 %CI 0.93, 0.99, p-value 0.014]) (Fig. 2). High *vs.* low adherence to Mediterranean diet was associated with lower levels of phthalate metabolites (sum_DEHP [GMR = 0.85; 95 %CI 0.73, 0.99, p-value 0.042], MiBP [GMR = 0.79; 95 %CI 0.66, 0.96, p-value 0.018]), organophosphate metabolites (DPHP [GMR = 0.73; 95 %CI 0.57, 0.93, p-value 0.013], DEP [GMR = 0.72; 95 %CI 0.55, 0.95, p-value 0.019]) and 2-NAOL (PAHs metabolite) [GMR = 0.78; 95 %CI 0.63, 0.96, p-value 0.019] (Supplementary Fig. 6).

However, after applying a correction for multiple testing (p = 0.0008), none of the above-mentioned associations between the data-driven dietary patterns, rMED pattern and UPF consumption and non-persistent EDCs remained statistically significant.

In the sensitivity analysis, we explored the association between the consumption of specific food groups in the 2nd trimester and levels of chemicals in the 3rd trimester (Supplementary Fig. 7). Higher daily consumption of dairy showed to be significantly negatively associated with levels of sum_PHOL (PAHs metabolite) [GMR = 0.96; 95 %CI 0.92, 1.00, p-value 0.027], while also being associated with an increase of both 2-NAOL [GMR = 1.07, 95 %CI 1.02, 1.12, p-value 0.009] and the organophosphate metabolite DEP [GMR = 1.07, 95 %CI 1.01, 1.14, p-value 0.033]. Higher daily consumption of eggs showed to be negatively associated with a wide range of phthalate metabolites (MEP, MiBP, MnBP, oh-MPHP and sum_DiNP), and the metabolite of chlorpyrifos and pyrethroid TCPy [GMR = 0.67; 95 %CI 0.48, 0.92, p-value 0.013]. Higher meat intake showed to be negatively associated with the PRPA (paraben) [GMR = 0.75; 95 %CI 0.57, 0.98, p-value 0.035]. Fish and seafood intake was associated with a 67 % [95 %CI 1.04, 2.69, p-value 0.035] increase of PRPA (paraben) and a 22 % [95 %CI 1.02, 1.47, p-value 0.028] increase of 3-PBA (metabolite of chlorpyrifos and pyrethroid). Vegetable intake was associated with lower levels of the

phthalate metabolite oh-MPHP [GMR = 0.95; 95 %CI 0.92, 0.99, p-value 0.008]. Finally, higher fruits intake was associated with lower levels of the organophosphate metabolite DPHP [GMR = 0.91; 95 %CI 0.86, 0.96, p-value 0.001], only.

As seen for the main analyses, none of the above-mentioned significant associations between all the food groups and non-persistent EDCs were retained after correcting for multiple testing (p = 0.0008).

4. Discussion

In this population-based cohort study of pregnant women, we found that dietary patterns related to the higher consumption of plant-based foods were associated with lower urinary levels of EDCs, mainly phthalate and organophosphate metabolites. On the other hand, dietary patterns characterized by higher consumption of foods from animal origin and high in fat, sugar and/or salt were associated with higher levels of PAHs metabolites, such as 2-NAOL, metabolites of chlorpyrifos and pyrethroid, such as 3-PBA, and phthalate metabolites. Animal products, namely meat, fish and seafood were associated with higher levels of parabens, such as PRPA, and metabolites of chlorpyrifos and pyrethroid, such as 3-PBA, whilst vegetables and fruits intake were associated with lower levels of metabolites of phthalates, PAHs, and organophosphates. However, it is important to highlight that these associations did not remain significant after correcting for multiple testing. In this study we opted to describe the results using a more holistic approach, taking into account the directions of associations.

The exposure to these chemicals is not unique to pregnant women in Spain, as similar or even higher concentrations of phthalates, phenols, PAHs metabolites, and pesticides have been observed among pregnant women in China (Luo et al., 2022), Mexico (Wu et al., 2020), the US (Gardener et al., 2022; Liu et al., 2021), and in other parts of Europe (Philips et al., 2018; Svensson et al., 2021). These chemicals are very common, since all of these studies, including ours, describe that most chemicals are detectable in 70–100 % of women. Consequently, the various health effects from the exposure to EDCs are a public health concern worldwide.

Phthalates are diesters of phthalic acid classified based on their molecular weights. Low-molecular-weight phthalates are usually used as solvents, fixatives and adhesives in personal care products, while high-molecular-weight phthalates are used by manufacturers to make flexible plastics for many purposes, including food processing and packaging (Giuliani et al., 2020; Pacyga et al., 2019). As whole fruits and vegetables, legumes, nuts and unsaturated fats are less likely to be processed and packed in plastic, the consumption of these may also be linked to lesser chemical exposure, as seen in the present study and in recent studies with women in China (Luo et al., 2022) and in the US (Baker et al., 2024; Pacyga et al., 2024; Vieyra et al., 2023). However, findings from other studies have been mixed. One study did not find evidence of an association between diet and EDCs and suggested that factors beyond food selection (such as production, storage, and preparation) may be stronger predictors of phthalate contamination (Melough et al., 2022). Also, the little consistencies related to specific dietary sources of phthalates (Pacyga et al., 2019) and lack of information on dietary determinants of phthalate replacements such as DINCH and DEHTP (Pacyga et al., 2024), which have also demonstrated adverse perinatal health effects, such as preterm birth (Yland et al., 2022), highlight the need for further studies.

High-fat/processed foods have been described as major sources of high molecular-weight phthalates, since these are lipophilic and tend to accumulate in fat-containing foods (Gardener et al., 2022; Giuliani et al., 2020; Vieyra et al., 2023). In our study, we observed that the higher consumption of UPF was associated with greater general urinary concentrations of both low molecular-weight and high molecular-weight phthalate metabolites. These results align with previous studies that have demonstrated associations between UPF consumption (Baker et al., 2024; Buckley et al., 2019; Steele et al., 2020) and specific ultra-processed products, such as diet soft drinks, creamers (Gardener et al., 2022), condiments, sauces, snacks, etc. (Da Costa et al., 2023), and exposure to phthalates. This may be explained especially by the long-shelf life and ready-to-eat characteristics of UPF, which enable that these substances leach into foods. Thus, reducing the consumption of packaged foods seem to be effective in reducing exposure to these compounds. As described in a fresh-food intervention study by Rudel and colleagues, urinary levels of phenols (BPA) and phthalates (DEHP) were significantly reduced (by 66 and 53–56 %, respectively) when diets were restricted to foods with limited packaging (Rudel et al., 2011).

BPA is a synthetic monomer that is a constituent of many polycarbonate plastics and consumer products, such as food containers. Studies have, however, linked the presence of this compound in humans' samples with various harmful health effects, as described in the introduction. Besides, more recent BPA analogs, as described previously, may also lead to adverse maternal and fetal health outcomes (Abrantes-Soares et al., 2022; Svensson et al., 2021). In the present study, we were not able to find significant associations between dietary intake and phenol concentrations. In our secondary analyses, however, we found that high *vs* low adherence to the "Western pattern" was associated with lower levels of BPS. In the study by Steele and colleagues, using NHANES 2009–2016 data, participants in the highest quintile of UPF consumption showed lower levels of BPS, and higher concentrations of BPF (Steele et al., 2020). Researchers discussed that BPS has been used in thermal papers in recent years, however it is not clear if it had been used as a substitute for BPA in can coatings. As described in a Canadian study, BPS was not detected in canned foods, but mainly in meat and meat products, indicating that sources of BPS other than can coatings may be possible and that the migration ability of BPS to food seems to be lower compared to BPA (Cao et al., 2019). Additionally, a recent study showed that BPS was highly present in price labels of food packages, and was not detected in food items (Cao et al., 2024). We may also speculate that BPS is a recent chemical introduced in the market (BPA concentrations are 3-fold BPS concentrations in the current sample, as described in Supplementary Table 2). Thus, more studies are necessary aiming to understand which dietary sources may increase the exposure of BPA and its most recent analogues, BPS and BPF, particularly in the coming years.

In the present study, we have measured as organophosphate compounds both pesticides and flame retardants. These chemicals are commonly used in residential and agricultural settings worldwide and, as other non-persistent chemicals, enter human organism through diet (Li and Kannan, 2018). Although organophosphate compounds are banned in many countries, their use persist, and they are still manufactured for export and are highly persistent in the environment. In the current study, DEP and DPHP exposures were lower among pregnant participants with higher consumption of Mediterranean diet and the "Vegetarian" pattern. DPHP is mostly used as a flame retardant, antifoaming agent in industries and plasticizer (Marklund et al., 2003), and foodstuff may be contaminated by its bioaccumulation in foods of animal origin and during food treatment processes and packaging. Industrially processed foods, compared to other foods, have shown higher concentrations of flame retardants in 53 food samples in Sweden, suggesting the contamination through food processing (Poma et al., 2017). As described previously, plant-based foods are less likely to be processed and packed in plastic, which might explain the association found between higher consumption of Mediterranean diet and the "Vegetarian" pattern and lower DPHP exposure. An Australian study, analyzing 87 food samples, has, however, evidenced that DPHP exposure was mainly through dietary intake, specifically vegetables and cereals, and in a lesser degree through fruits, meat and beverages (He et al., 2018). Regarding organophosphates, it was expected to find higher levels of these chemicals in plant-based foods, as a study with pregnant women in the US has shown that higher Σdialkyl phosphate metabolites levels were associated with greater fruit, grains, and meat intake. The intake of more than 2 fruits/day seemed to increase by 4.51

μg/g creatinine DMP levels in pregnancy (Papadopoulou et al., 2019). According to the latest EFSA report (European Food Safety Authority (EFSA) et al., 2023), 40 % of food samples collected in European countries contained pesticides residues not exceeding legal limits, and around 4 % of foods exceeded legal limits. Foods with higher non-compliance rates were mainly fruits and vegetables: passionfruit, granate apples/pomegranates and chili peppers. Regarding organic foods, 15.4 % of foods analyzed contained quantified pesticide residues below of at the maximum residue level, and almost 2 % exceeded residue levels above corresponding maximum residue levels (European Food Safety Authority (EFSA) et al., 2023). The consumption of organic foods has been reported to lower pesticide exposure in both pregnancy and childhood (Bradman et al., 2015; Papadopoulou et al., 2019) and to lower phthalate levels in pregnancy (Valvi et al., 2015). In another study, however, organic food consumption did not show a protective effect against exposure to phthalates and bisphenols (BPA) (Gardener et al., 2022). Organic food consumption may be efficient in reducing organophosphate exposure. However, in our study we did not have information if the plant-based foods were organic foods or not. A proxy for following organic diet could be maternal educational level, so we further examined whether there were differences in these associations among the higher educated (University degree) and less educated (Secondary degree or lower) participants. We found that higher adherence to the "Vegetarian" and Mediterranean patterns and lower levels of DPHP were statistically significant only among the less educated women (data not shown). This finding is in line with the assumption that higher educated participants, compared to less educated, tend to consume more organic foods (Andersen et al., 2022) and are, therefore, less exposed to this chemical. For DEP, on the other hand, we found that, only among the highly educated women, higher Mediterranean diet adherence was associated with lower DEP levels. Further studies are necessary aiming to investigate the link between dietary patterns, instead of single foods, organic food consumption and organophosphates.

Lastly, PAHs enter the food supply through contamination, including food contact material, food processing, as well as environmental sources, such as fertilizers, contaminated water and/or soil (Rashid et al., 2020). These chemicals in food could also arise from roasting, smoking, frying, drying, and other food processing procedures (Hamidi et al., 2022), which might explain the previously seen associations between PAHs and the higher consumption of UPF (Kliemann et al., 2022), meats, fish, smoked products, and high-fat foods (Domingo and Nadal, 2015), and egg-dairy, meat-aquatic dietary patterns (Luo et al., 2022). Corroborating with this, in the present study we observed that higher PAHs metabolite levels (namely 2-NAOL) was linked to greater consumption of UPF, which includes ready-to-eat products. The consumption of dairy, as also seen in the current study, has also shown to be associated with greater exposure to these chemicals, and this might be explained by the heat treatment during milk processing (Santonicola et al., 2017).

This study has several strengths. The majority of studies that explored the association between dietary intake and exposure to chemicals relied on single food analyses approaches to identify those foods/food groups that contributed to EDC exposure. However, humans do not consume individual foods or nutrients in isolation (Hu, 2002). The investigation of dietary patterns, in this sense, allows the examination of the overall human diet, with multiple dietary sources, and a better picture of exposure patterns. Second, this study used data of repeated urine measures during pregnancy. Since many EDCs have short biological half-life (with some as short as 6 h), not persisting in the body for a long time, such as phthalates, BPA, and pesticides, exposure assessment requires the collection and analysis of multiple urine samples rather than one or two spot urine samples, aiming to increase the accuracy of exposure assessment (Perrier et al., 2016). Besides, multiple pathophysiological changes that occur during pregnancy (such as increased blood volume, changes to renal function, shifts in hormones) can influence the measurement of these chemicals (Kazma et al., 2020). Assessing, therefore, exposure to chemicals using only one spot urine biospecimens poorly estimates average exposure levels during the pregnancy period and may lead to misclassification (Perrier et al., 2016). Finally, this study includes a great variety of non-persistent EDCs, both well-known chemicals, such as BPA, and "next-generation" chemicals, such as DINCH and BPS. Since these replacement compounds are widely used nowadays, more studies are necessary aiming to understand their safety for human health.

This study has limitations that need to be mentioned. First, dietary intake was self-reported, which may be subject to bias due to intentional and unintentional misreporting. Second, we acknowledge the complexity of classifying UPF with certain FFQ items due to limited detail regarding food ingredients, processing methods, or preparation techniques. Thus, we employed an approach of food item classification aiming to minimize the risk of underestimating UPF intake. Third, even though we had repeated measures of urine in the present study, we assessed exposure only in the 2nd trimester, so we are unable to capture potential dietary changes throughout pregnancy. Some pregnant women may change their diet (regarding, for example, the intake of alcohol, coffee, meats, fruits, sweets and milk products) (Forbes et al., 2018) and this may lead to bias. However, as in our study we focused on dietary patterns rather than food groups consumption, we do not believe that drastically changes would have occurred, since dietary patterns are reported to remain stable throughout pregnancy (Crozier et al., 2009; Cucó et al., 2006; McGowan and McAuliffe, 2013). Fourth, we had no information on whether foods were organic or not in the BiSC cohort, limiting our ability to evaluate the link between organic food consumption and pesticide exposure. Fifth, chemicals may enter human organism through other sources, such as cosmetics and personal care products. As educational level/socioeconomic status is associated with cosmetic use (Gardener et al., 2022; Wu et al., 2020) and diet (Baker et al., 2024; Luo et al., 2022), it is reasonable to expect that phthalate concentrations may also be influenced by these exposure sources, besides dietary consumption. In our analyses, we adjust for educational level, aiming to reduce residual confounding. Sixth, the BiSC cohort was recruited within the city of Barcelona, so the generalizability of the findings may be limited to this population. Besides, the external validity may be limited, due to the high education levels of participating individuals (76 % with a university degree or above).

5. Conclusion

To our knowledge, this study was the first to evaluate both data-driven and *a priori* dietary patterns during pregnancy, using repeated urine measures and exposure to wide range of non-persistent EDCs. Although none of the associations survived multiple testing correction, results suggest that Mediterranean diet and diets rich in plant-based foods are associated with lower exposure to phthalates and organophosphates. Higher adherence to dietary patterns characterized by the greater consumption of animal products and UPF, was associated with greater exposure to EDCs, such as PAHs and phthalates. These findings underscore the importance in safety monitoring of chemicals and materials used for food production and processing, since these may have long-lasting health impacts among pregnant women and their offspring. Also, future studies are necessary aiming to develop dietary assessment tools including more information of packaging, aiming to better comprehend the exposure to different chemicals throughout the lifespan.

CRediT authorship contribution statement

Sarah Warkentin: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Formal analysis, Conceptualization. **Sandra Márquez:** Writing – review & editing, Methodology, Formal analysis. **Hana Vespalcová:** Writing – review & editing, Resources, Data curation. **Bethany Knox:** Writing – review &

editing, Resources, Data curation. **Mireia Gascon:** Writing – review & editing, Resources, Data curation. **Nuria Güil-Oumrait:** Writing – review & editing, Resources. **Sandra González-Palacios:** Writing – review & editing, Resources, Data curation. **Maria Dolores Gomez Roig:** Writing – review & editing, Resources, Data curation. **Camille Lassale:** Writing – review & editing, Resources, Data curation. **Elisa Llurba:** Writing – review & editing, Resources, Data curation. **Matthieu Rolland:** Writing – review & editing, Resources, Data curation. **Amrit K. Sakhi:** Writing – review & editing, Resources, Data curation. **Cathrine Thomsen:** Writing – review & editing, Resources, Data curation. **Jesús Vioque:** Writing – review & editing, Resources, Data curation. **Mariona Bustamante:** Writing – review & editing, Resources, Data curation. **Jordi Sunyer:** Writing – review & editing, Resources, Project administration, Funding acquisition, Data curation. **Martine Vrijheid:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Funding acquisition, Data curation, Conceptualization.

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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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2025.109612.

Data availability

Data will be made available on request.

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