challenges

MDPI

Article

Relationships of First-Trimester Body Mass Index and Weight Change with Persistent Organic Pollutant Concentrations in Pregnant Canadian Individuals

Marianne Levesque [1,2,3,†], Mariame Ouedraogo [1,2,4,†], Romina Fakhraei [1,2], Alysha Dingwall Harvey [2], Elizabeth Bratton [1], Mark Walker [1,2], Linda Dodds [3] and Laura Gaudet [1,2,5,*]

1 Faculty of Medicine, University of Ottawa, Ottawa, ON K1H 8M5, Canada
2 OMNI Research Group, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, ON K1H 8L6, Canada
3 Department of Obstetrics and Gynecology, Dalhousie University, Halifax, NS B3K 6R8, Canada
4 Dalla Lana School of Public Health, University of Toronto, Toronto, ON M5T 3M7, Canada
5 Department of Obstetrics and Gynecology, Queen's University, Kingston, ON K7L 2V7, Canada
* Correspondence: laura.gaudet@kingstonhsc.ca
† These authors contributed equally to this work.

Abstract: Persistent organic pollutants (POPs) are toxic chemicals with demonstrable effects on pregnancy and neonatal outcomes. The associations of early pregnancy body mass index (BMI) and antenatal weight changes with circulating POP concentrations are poorly understood in the Canadian context. The aim of this study was to explore the relationship between maternal BMI in the first trimester, weight change from pre-pregnancy to 6–13 weeks of pregnancy, and first-trimester plasma POP concentrations among Canadian pregnant women. We analyzed data collected as part of the Maternal-Infant Research on Environmental Chemicals (MIREC) study and evaluated POP concentrations based on first-trimester BMI and early gestational weight change categories. We tested for overall differences using Kruskal-Wallis tests. The associations between first-trimester maternal BMI, weight change, and plasma concentrations of 41 POPs were evaluated using censored regression models. After controlling for potential confounders, first-trimester plasma levels of multiple POPs differed significantly across BMI categories, with the highest concentrations in underweight/normal-weight individuals and the lowest in class III obese individuals. Our findings provide preliminary evidence of higher circulating POP levels in individuals with obesity and align with previous findings of an inverse relationship between circulating POP concentrations and BMI in pregnancy. Future studies should prospectively evaluate the interplay between weight change and POP concentrations throughout pregnancy to inform gestational weight gain recommendations for pregnant individuals with obesity.

Keywords: maternal obesity; early gestational weight changes; persistent organic pollutants; maternal health; fetal health

Citation: Levesque, M.; Ouedraogo, M.; Fakhraei, R.; Dingwall Harvey, A.; Bratton, E.; Walker, M.; Dodds, L.; Gaudet, L. Relationships of First-Trimester Body Mass Index and Weight Change with Persistent Organic Pollutant Concentrations in Pregnant Canadian Individuals. *Challenges* **2023**, *14*, 13. https://doi.org/10.3390/challe14010013

Academic Editor: Susan Prescott

Received: 13 January 2023
Revised: 10 February 2023
Accepted: 14 February 2023
Published: 16 February 2023

1. Introduction

Obesity is a major health concern, particularly during pregnancy. Pregnant patients with obesity have higher rates of adverse obstetrical complications such as gestational diabetes, gestational hypertension, pre-eclampsia and thromboembolic events [1–3]. Obesity in pregnancy is also associated with an increased risk of stillbirth, early pregnancy loss, preterm birth, fetal macrosomia and fetal anomalies [1,2]. In addition to these immediate consequences, maternal pre- or early-pregnancy obesity has been shown to have long-term impacts, increasing the risk of obesity among children born to these mothers [4,5].

Gestational weight gain (GWG)—irrespective of pre-pregnancy weight class—may affect pregnancy outcomes. Excessive or inadequate GWG has been associated with

detrimental effects on maternal and fetal outcomes [6]. Health organizations across the world have established healthy GWG recommendations based on pre-pregnancy maternal body mass index (BMI) in attempts to mitigate pregnancy risks. For individuals with obesity (BMI $\geq$ 30 kg/m^2), Canadian recommendations include pre-conception weight loss whenever possible and a total GWG of 5.0–9.0 kg [7]. In contrast, normal-weight individuals (BMI 18.5–24.9 kg/m^2) in Canada are recommended to gain between 11.5–16 kg during pregnancy [8]. In a Canadian study using the Nova Scotia Atlee Perinatal Database, GWG was reported to be inadequate in 15.8% and excessive in 57.9% of patients [9].

Based on current evidence, weight changes in non-pregnant individuals are suspected of promoting the mobilization of lipophilic environmental toxins referred to as persistent organic pollutants (POPs) [10–12]. Given their widespread occurrence, resistance to environmental degradation and implications on human health, POPs have generated research and public health interest across the world. Typically, POPs are polyhalogenated organic compounds that are highly lipid soluble, enabling accumulation and biomagnification along food chains [13]. Increased agricultural activities and accompanying pesticide use, along with rapidly developing industrial sectors, led to large concentrations of POPs being released into the environment [14]. Aside from their bioaccumulation capabilities, POPs have long-range transport potential, easily traveling through soil, water, and air [13]. Many POPs have been banned or restricted for use; however, residues remain in the environment due to the persistent nature of these chemicals [14]. Further, some lower-income countries have continued to use these banned chemicals due to the lack of international monitoring and enforcement [14]. Human exposure may occur through inhalation, dermal absorption, and dietary consumption of contaminated food [13–15].

POPs are measurable in the tissues of pregnant individuals and their offspring [16–20] with demonstrable effects on pregnancy and long-term pediatric outcomes [21,22]. Neonates are easily susceptible to the toxic effects of environmental pollutants due to their unique body composition, immature organ systems, limited metabolism and elimination processes and rapid development [23]. Understanding the relationship between maternal BMI and weight changes and plasma concentrations of POPs is essential for reducing exposure to toxic chemicals and improving health outcomes.

Because of the inherent characteristics of POPs, it has been hypothesized that weight stability, particularly in overweight or obese individuals who are likely to have a greater body burden of POPs, is protective against the release of toxic lipophilic chemicals through their sequestration in the adipose compartment [10]. Investigations of POP burden relative to weight change in pregnancy have been limited, particularly in North America. In 2016, Fisher and colleagues reported significantly higher concentrations of plasma POPs in individuals with a normal pre-pregnancy BMI compared to individuals with higher BMIs participating in a large pregnancy cohort [24]; however, the relationship between first-trimester BMI and weight fluctuations was not evaluated. Given the negative effects of POPs on pregnancy and neonatal outcomes, it is crucial to understand the associations between maternal BMI, weight changes, and POP concentrations. This information can be used to inform public health policies and interventions aimed at reducing exposure to toxic chemicals and improving health outcomes for mothers and their infants.

In the present study, we aimed to assess the association between gestational weight change in early pregnancy with maternal POP plasma concentrations using data from the Maternal-Infant Research on Environmental Chemicals (MIREC) study. We hypothesize that individuals experiencing weight loss in early pregnancy, particularly those with a BMI $\geq$ 30 kg/m^2, would have higher plasma levels of POPs.

2. Materials and Methods

2.1. Study Population

Our study cohort was assembled using data collected from the MIREC Study, a multisite Canadian prospective cohort study that aimed to examine the potential adverse health effects of prenatal exposure to environmental chemicals on pregnancy and infant health. Spe-

cific details regarding the MIREC study have been previously described [25] and are briefly indicated here. Between 2008 and 2011, a total of 2001 pregnant people were recruited from 10 cities across Canada during their first trimester of pregnancy (6–13 completed gestational weeks) and were followed through delivery. The study exclusion criteria included: an inability to communicate in English or French, under 18 years of age, above 14 weeks gestation at the time of recruitment, the presence of a known fetal anomaly in the current pregnancy, or a history of maternal medical complications. The MIREC database contains information collected at study visits during pregnancy and post-delivery. In addition to the MIREC questionnaire information, this database is supplemented by maternal and infant data collected through medical chart extraction. For the present study, the population was restricted to MIREC mothers with measured first-trimester POP concentration data.

2.2. Data and Sample Collection

The outcome variables of interest in this study were POP plasma concentrations. Data on 41 different POPs measured from first-trimester maternal blood plasma were used. These included 24 polychlorinated biphenyls (PCB 28, 66, 74, 99, 101, 105, 118, 128, 138, 146, 153, 156, 163, 167, 170, 178, 180, 183, 187, 194, 201, 203 and 206 and Aroclor 1260), 10 organochlorinated pesticides (beta-hexachlorocyclohexane [β-HCH], hexachlorobenzene, cis-nonachlor, trans-nonachlor, oxychlordane, dichlorodiphenyldichloroethylene [DDE], p, p'-dichlorodiphenyltrichloroethane [DDT], Mirex, Parlar 26 and 50), 6 polybrominated diphenyl ethers (PBDE 28, 33, 47, 99, 100, 153) and hexabromobiphenyl (PBB 153). As previously described [24], the POP concentrations were measured and analyzed by the Centre de Toxicologie du Québec of the Institut National de Santé Publique du Québec, which holds accreditation from the Standards Council of Canada and is regularly evaluated for accuracy and precision through external quality assessment programs. To ensure the quality of the analysis, the laboratory used certified reference materials such as SRM-1958 from the National Institute of Standards and Technology (NIST), reference materials from the Arctic Monitoring and Assessment Program (AMAP), and in-house reference materials for PFASs. The laboratory's performance was monitored through participation in interlaboratory programs like AMAP and the German External Quality Assessment Scheme. We considered all POPs measured in first-trimester maternal plasma for the analysis.

The main explanatory variables were first-trimester BMI and early weight change during pregnancy. First-trimester BMI was determined from maternal height and weight measurements taken during the first MIREC visit, which took place between weeks 6 and 13 of pregnancy. Participants' BMI was categorized into underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), obese class I & II (30.0–39.9 kg/m^2), and obese class III ($\geq$40.0 kg/m^2). We estimated early pregnancy weight changes as the percentage change in weight recorded at the time of the first MIREC visit from the self-report pre-pregnancy weight. First-trimester weight change was dichotomized into first-trimester "weight loss" (if the participant had a weight loss of $\geq$2% of their total body weight early in pregnancy) and "weight neutral or gain" (if the participant had a weight loss of <2% of their total body weight or any weight gain reported early in pregnancy). We could not find a percent weight change cut-off for pregnant people in their first trimester in the literature. We, therefore, relied on clinical expertise and relevance to set the cut-off of 2%.

2.3. Statistical Analysis

All statistical analyses were conducted using SAS/STAT® software, version 9.4 of the SAS system (SAS Institute, Cary, NC, USA). Only 11 out of the 41 POPs were analyzed, as sample plasma concentrations were below the laboratory level of detection (LOD) for the majority of POPs. As a result, censoring techniques were used to generate descriptive statistics. All POPs were expressed in micrograms per kilogram of serum lipid, as previously done [24]. Concentration ranges were determined where possible, and the geometric means and medians with 95% confidence intervals were obtained using Maximum Likelihood

Estimate (MLE) and Kaplan–Meier (KM) methods, respectively. Analyses were performed only on the 11 POPs with concentrations above the laboratory level of detection for at least 50% of the sample.

We adjusted the relationship between explanatory variables and POP concentrations for several confounders, which were selected based on a review of related studies [20,24,26] and directed acyclic graphs [27]. Confounders included gestational age, parity, maternal age, education, smoking status, place of birth, and self-reported pre-pregnancy BMI.

We estimated lipid-adjusted POP concentrations by first-trimester BMI category for the eleven POPs with less than 50% censored data. The normal weight category included underweight individuals (N = 25), as there were too few to be analyzed separately. Kruskal–Wallis tests were used to assess the relationship between first-trimester BMI and plasma lipid-adjusted POP concentrations, as the assumption of normality did not hold [28]. The overall difference in lipid-adjusted POP concentrations was considered significant at a level of 5%.

To analyze the relationship between first-trimester BMI and lipid-adjusted POP concentrations, censored regression models were applied, assuming a lognormal distribution of the POP concentrations. Both unadjusted and adjusted models were used to estimate the beta coefficients and 95% confidence intervals. The adjusted models accounted for the confounding variables identified. The same process was used to analyze the relationship between weight change and lipid-adjusted POP concentrations.

3. Ethical Approval

This study was approved by the Ottawa Health Science Network Research Ethics Board (Approval number: 20140736). Applications were also filled in to access the MIREC Study data. All participating individuals provided informed consent.

4. Results

4.1. Characteristics of Study Participants

The baseline characteristics of the MIREC study participants are presented in Table 1. Plasma POP data were collected at the first-trimester visit for 1983 pregnant people with a mean gestational age of 11.6 weeks (SD = 1.58 weeks). The majority of participating individuals were older than 30 years (69.8%), were married or in union (95.3%), had completed at least an undergraduate degree (62.3%) and had a combined household income surpassing $50,000 (77.8%).

Self-reported pre-pregnancy BMI was missing for 146 participants (approximately 7.4% of the cohort). About 60% of the individuals were classified as being of normal weight (18.5–<25.0 kg/m^2) based on their pre-pregnancy weight. Close to 15% of study participants had obesity prior to pregnancy. The proportion of individuals with obesity at the time of the first-trimester visit was 19.3%. Of these individuals, 15.7% had class III obesity (≥40.0 kg/m^2). First-trimester BMI measurements were missing for 71 participants (3.5%). According to our weight change classification, 3.9% had experienced weight loss during their first trimester.

Table 1. Descriptive characteristics of participants in the Maternal-Infant Research on Environmental Chemicals (MIREC) Study, N = 1983 pregnant women.

Characteristic	N	%
Maternal age		
<25	139	7.01
25–29	459	23.15
30–34	709	35.75
35+	676	34.09
Maternal education [a]		
High school or less	175	8.83
Some college or college degree	572	28.87

Table 1. *Cont.*

Characteristic	N	%
Undergraduate degree or higher	1234	62.29
Marital status		
Married or common law	1889	95.26
Other	94	4.74
Maternal race		
Caucasian	1661	83.76
Not Caucasian	322	16.24
Place of birth		
Canada	1612	81.29
Other	371	18.71
Income		
<$50,000	347	17.5
$50,001–$100,000	786	39.64
>$100,000	757	38.17
Missing	93	4.69
Smoking status [b]		
Current	237	11.96
Former [c]	542	27.36
Never	1202	60.68
Pre-pregnancy BMI [d]		
Underweight (<18.5 kg/m^2)	52	2.83
Normal weight (18.5–<25.0 kg/m^2)	1106	60.21
Overweight (25.0–<30.0 kg/m^2)	404	21.99
Obese (≥30.0 kg/m^2)	275	14.97
First-trimester BMI [e]		
Underweight/Normal weight (<18.5–<25.0 kg/m^2)	1013	52.98
Overweight (25.0–<30.0 kg/m^2)	530	27.72
Class I & II obese (30.0–<40.0 kg/m^2)	311	16.27
Class III obese (≥40.0 kg/m^2)	58	3.03
Weight change category [f]		
Weight loss	72	3.93
Weight neutral or gain	1760	96.07
Parity		
0	876	44.18
1	800	40.34
2	231	11.65
3+	76	3.83
Fasting status		
No	1914	98.00
Yes	39	2.00
Season of blood collection (first trimester)		
Spring	448	22.92
Summer	464	23.73
Fall	575	29.41
Winter	468	23.94
Gestational age at first-trimester visit (mean ± SD; wks)	11.56 (1.58)	

[a] Education level missing for two participants; [b] Smoking status missing for 2 participants; [c] Includes women who quit smoking during pregnancy; [d] Self-reported pre-pregnancy BMI missing for 146 participants; [e] First-trimester BMI missing for 71 participants; [f] Weight change missing for 151 participants. Abbreviations: BMI—Body Mass Index; SD—Standard Deviation.

4.2. First-Trimester POP Levels

The levels of 30 POPs were below their respective LOD in more than 50% of participants (Table 2). Descriptive statistics are provided for the remaining 11 POPs that had detectable concentrations in more than 50% of participants. The KM and MLE approaches used to calculate the KM medians and geometric means, respectively, provided comparable results. DDE and Aroclor 1260, which were detected in more than 95% of the

sample, exhibited the highest lipid-adjusted geometric mean levels, with concentrations of 56.01μg/kg serum lipid (95% CI: 54.02–58.07) and 60.00 μg/kg serum lipid (95% CI: 58.11–61.95), respectively. A maximum DDE concentration of 5306.12 μg/kg serum lipid was noted. PCB170 was the least abundant POP with a concentration of 1.67 μg/kg serum lipid (95% CI: 1.58–1.75) and was observed in 53.2% of the MIREC study participants.

Table 2. Distribution of persistent organic pollutant (POP) concentrations (μg per kg serum lipid) in maternal blood plasma in 1983 pregnant women participating in the MIREC Study.

POP	LOD	% <LOD	Maximum Value	KM Median (95% CI)	GM (95% CI)
Polychlorinated biphenyl (PCB)					
PCB28	0.05	99.74	260.00	NE	NE
PCB66	0.03	99.28	28.00	NE	NE
PCB74	0.03	96.54	18.40	NE	NE
PCB99	0.03	97.16	12.93	NE	NE
PCB101	0.03	99.90	12.06	NE	NE
PCB105	0.01	95.71	13.62	NE	NE
PCB118	0.01	26.61	37.93	2.30 (2.23, 2.38)	2.35 (2.29, 2.43)
PCB128	0.01	99.79	5.00	NE	NE
PCB138	0.01	7.03	71.66	4.01 (3.92, 4.21)	4.21 (4.08, 4.37)
PCB146	0.01	85.43	16.00	NE	NE
PCB153	0.01	1.29	155.00	7.00 (6.72, 7.29)	7.30 (7.06, 7.54)
PCB156	0.01	79.07	17.46	NE	NE
PCB163	0.01	68.11	23.81	NE	NE
PCB167	0.01	98.41	4.48	NE	NE
PCB170	0.01	46.82	71.66	1.55 (1.29, 1.67)	1.67 (1.58, 1.75)
PCB178	0.01	95.71	9.02	NE	NE
PCB180	0.01	7.39	183.33	4.72 (4.52, 4.90)	4.87 (4.70, 5.05)
PCB183	0.01	91.21	23.33	NE	NE
PCB187	0.01	57.21	45.00	NE	NE
PCB194	0.01	81.17	30.00	NE	NE
PCB203	0.01	89.35	14.16	NE	NE
PCB201	0.01	83.72	20.00	NE	NE
PCB206	0.01	97.67	6.61	NE	NE
Aroclor 1260	0.1	2.69	1183.33	57.45 (55.29, 59.65)	60.00 (58.11, 61.95)
Organochlorines					
Beta-HCH	0.01	31.88	1108.11	2.24 (2.16, 2.31)	2.32 (2.19, 2.46)
Cis-nonachlor	0.005	88.31	3.91	NE	NE
DDE	0.09	1.03	5306.12	48.33 (46.67, 50.00)	56.01 (54.02, 58.07)
DDT	0.05	96.28	175.44	NE	NE
HCB	0.04	69.54	101.66	NE	NE
Mirex	0.01	91.83	38.03	NE	NE
Oxychlordane	0.005	7.81	17.50	2.09 (2.00, 2.15)	2.00 (1.95, 2.05)
Parlar26	0.005	97.47	3.64	NE	NE
Parlar50	0.005	87.28	5.00	NE	NE
Transnonachlor	0.01	15.87	34.33	2.89 (2.69, 3.02)	2.90 (2.82, 2.98)
Polybrominated diphenyl ethers (PBDE) & Hexabromobiphenyl (PBB)					
PBB153	0.02	99.48	13.61	NE	NE
PBDE100	0.02	78.46	327.27	NE	NE
PBDE153	0.02	55.60	527.27	NE	NE
PBDE28	0.03	99.07	27.14	NE	NE
PBDE33	0.03	99.90	6.28	NE	NE
PBDE47	0.03	34.28	727.27	6.97 (6.55, 7.31)	7.02 (6.68, 7.38)
PBDE99	0.02	80.85	169.09	NE	NE

Abbreviations: LOD—Limit of Detection; NE—Not Estimated; MIREC—Maternal-Infant Research on Environmental Chemicals; POP—persistent organic pollutant; KM—Kaplan Meier; GM—Geometric Mean.

4.3. POP Levels and First-Trimester BMI

Figure 1 depicts the lipid-adjusted geometric means, and 95% CIs for the 11 detected POPs, stratified by first-trimester BMI category. For nine of the POPs, the mean lipid-adjusted serum concentration was highest among pregnant individuals of the underweight/normal weight category (<18.5 to <25.0 kg/m^2) and the lowest in pregnant people with class III obesity. The reverse pattern was observed for PBDE47, whereby mean concentration levels were higher among those classified in the higher BMI categories. The observed distribution of geometric means for Beta-HCH did not vary by the first trimester. Kruskal–Wallis tests provided *p*-values of <0.0001 for all POPs except Beta-HCH (which had a *p*-value = 0.1195).

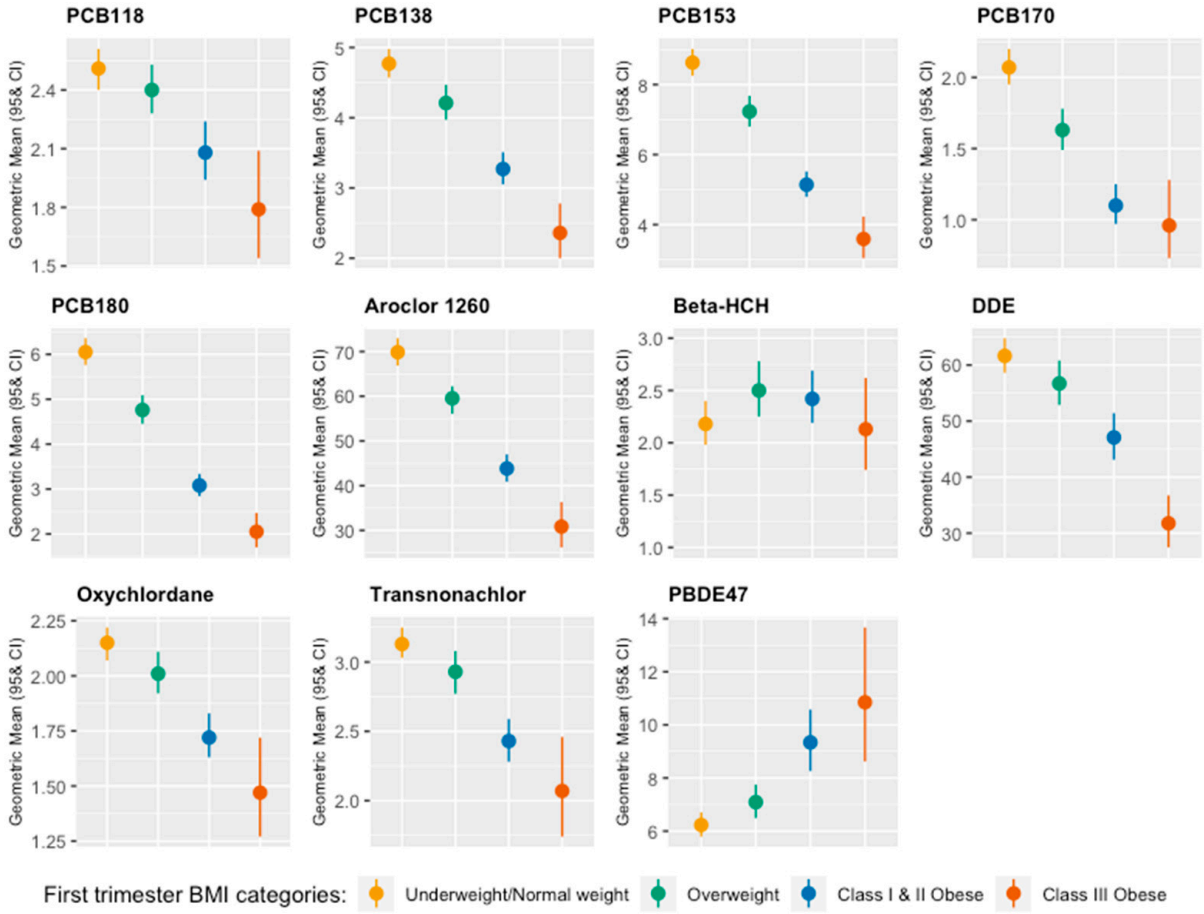

Figure 1. Geometric means and 95% confidence intervals (CI) of eleven POP concentrations by first-trimester BMI categories (colors illustrate BMI categories). N = 1912 pregnant people, MIREC Study.

Similar trends to those depicted in Figure 1 were observed in the unadjusted censored regression models (Table 3). The exponentiated β coefficients represent the ratio of the expected geometric means for overweight, class I & II obese, and class III obese compared with that of the underweight/normal (reference) category. For instance, for PCB118, the adjusted ratios comparing underweight/normal-weight individuals with overweight, class I & II obese, and class III obese are 0.96, 0.92, and 0.83, respectively. These can be interpreted as adjusted geometric means (or concentrations on the log scale) in overweight, class I & II obese, and class III obese pregnant individuals being approximately 4%, 8%, and 17%, respectively, lower than the concentration in underweight/normal-weight pregnant individuals.

The association between first-trimester BMI and most POPs remained after adjustment for the main confounders (parity, maternal age, maternal education, maternal smoking

status, and mother's place of birth). In both univariate and multivariable models, there was no clear evidence that the Beta-HCH concentrations of overweight, class I & II obese, and class III obese study participants were significantly different than the concentration reported in underweight/normal-weight pregnant individuals.

Table 3. Unadjusted and adjusted [a] associations [β (95%CI)] between first-trimester body mass index (BMI) category and lipid-adjusted persistent organic pollutant (POP) concentrations detected in at least 50% of the sample, MIREC Study [b].

POP	Overweight		Class I & II Obese		Class III Obese	
	Unadjusted	**Adjusted**	**Unadjusted**	**Adjusted**	**Unadjusted**	**Adjusted**
PCB118	−0.058 (−0.127, 0.011)	−0.045 (−0.108, 0.018)	**−0.199 (−0.282, −0.115)**	**−0.083 (−0.162, −0.003)**	**−0.371 (−0.548, −0.195)**	**−0.181 (−0.347, −0.014)**
PCB138	**−0.124 (−0.196, −0.052)**	**−0.106 (−0.169, −0.044)**	**−0.381 (−0.469, −0.293)**	**−0.253 (−0.331, −0.174)**	**−0.716 (−0.900, −0.531)**	**−0.475 (−0.638, −0.311)**
PCB153	**−0.176 (−0.251, −0.102)**	**−0.157 (−0.219, −0.095)**	**−0.518 (−0.608, −0.427)**	**−0.379 (−0.456, −0.303)**	**−0.881 (−1.068, −0.695)**	**−0.640 (−0.800, −0.481)**
PCB170	**−0.241 (−0.340, −0.142)**	**−0.223 (−0.309, −0.137)**	**−0.721 (−0.852, −0.589)**	**−0.557 (−0.674, −0.439)**	**−1.137 (−1.452, −0.821)**	**−0.835 (−1.117, −0.553)**
PCB180	**−0.241 (−0.323, −0.158)**	**−0.228 (−0.295, −0.161)**	**−0.683 (−0.783, −0.582)**	**−0.544 (−0.629, −0.459)**	**−1.114 (−1.328, −0.899)**	**−0.885 (−1.068, −0.702)**
Aroclor 1260	**−0.160 (−0.233, −0.087)**	**−0.141 (−0.202, −0.079)**	**−0.468 (−0.557, −0.379)**	**−0.333 (−0.410, −0.256)**	**−0.825 (−1.009, −0.640)**	**−0.583 (−0.743, −0.423)**
Beta-HCH	0.065 (−0.070, 0.201)	0.101 (−0.006, 0.209)	−0.026 (−0.187, 0.138)	0.225 (−0.092, 0.359)	−0.221 (−0.565, 0.123)	0.296 (−0.019, 0.574)
DDE	−0.083 (−0.168, 0.002)	−0.053 (−0.124, 0.018)	**−0.269 (−0.372, −0.167)**	**−0.118 (−0.206, −0.030)**	**−0.672 (−0.884, −0.459)**	**−0.368 (−0.549, −0.187)**
Oxychlordane	**−0.064 (−0.122, −0.006)**	**−0.062 (−0.115, −0.010)**	**−0.219 (−0.289, −0.149)**	**−0.163 (−0.228, −0.097)**	**−0.373 (−0.519, −0.226)**	**−0.261 (−0.397, −0.125)**
Transnonachlor	**−0.064 (−0.126, −0.002)**	**−0.066 (−0.122, −0.010)**	**−0.258 (−0.334, −0.182)**	**−0.191 (−0.261, −0.122)**	**−0.403 (−0.561, −0.244)**	**−0.282 (−0.428, −0.136)**
PBDE47	0.103 (−0.011, 0.217)	0.086 (−0.029, 0.201)	**0.402 (0.266, 0.537)**	**0.362 (0.222, 0.502)**	**0.528 (0.254, 0.802)**	**0.460 (0.177, 0.743)**

Statistically significant results are highlighted in bold; [a] Adjusted for gestational age, maternal age, parity, maternal education, smoking status, and place of birth; [b] Underweight/Normal weight is the reference category; Abbreviations: CI—Confidence Interval, MIREC—Maternal-Infant Research on Environmental Chemicals; PCB—Polychlorinated biphenyl, DDE—Dichlorodiphenyldichloroethylene; PBDE—Polybrominated diphenyl ethers; HCH—Hexachlorocyclohexane.

4.4. POP Levels and Early Pregnancy Weight Change

The unadjusted concentrations of most analyzed POPs tended to be slightly higher in individuals who were classified in the weight-neutral/gain group (Figure 2). Kruskal-Wallis tests returned *p*-values greater than 0.05 for all POPs (values not shown).

In the unadjusted analyses, the plasma concentrations of POPs were not significantly different between individuals who lost weight and those who gained weight or remained weight neutral during their first trimester (Table 4). After controlling for the confounders (parity, maternal age, maternal education, maternal smoking status, mother's place of birth and pre-pregnancy BMI), the β coefficients for many POPs were positive, suggesting that, compared to the weight neutral/gain category, the concentrations of circulating POPs were higher among individuals who had a first-trimester weight loss of at least 2% of their total body weight. None of these estimates were statistically significant, as the 95% confidence intervals included the null value of zero.

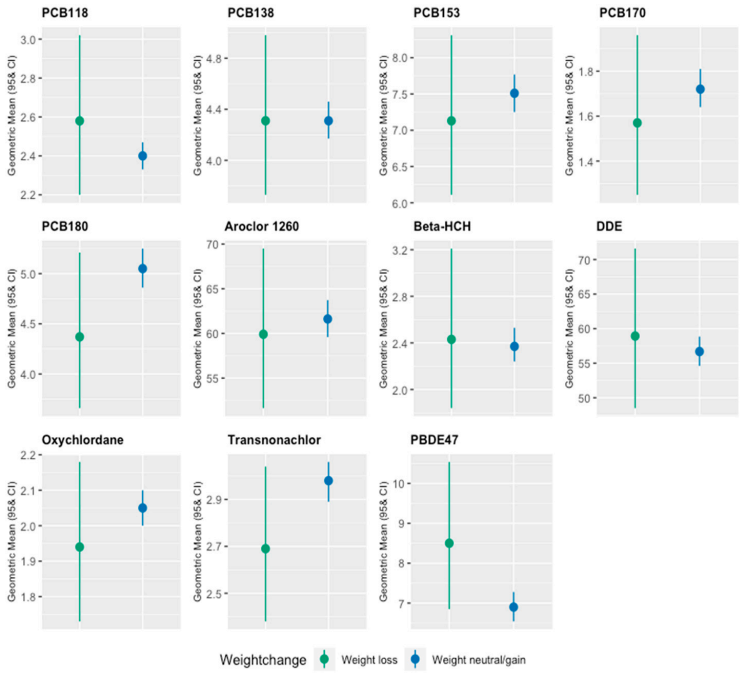

Figure 2. Geometric means and 95% confidence intervals (CI) of eleven POP concentrations by early gestational weight change categories (colors illustrate the weight change categories). N = 1832 pregnant individuals, MIREC Study.

Table 4. Unadjusted and adjusted [a] associations [β (95%CI)] between first-trimester weight change (BMI) and lipid-adjusted persistent organic pollutants (POPs) concentrations detected in at least 50% of the samples, MIREC Study [b].

	Weight Loss	
	Unadjusted	**Adjusted**
PCB118	0.075 (−0.080, 0.230)	0.144 (−0.003, 0.291)
PCB138	−0.002 (−0.168, 0.164)	0.146 (0.0003, 0.292)
PCB153	−0.052 (−0.226, 0.121)	0.143 (−0.001, 0.288)
PCB170	−0.152 (−0.391, 0.087)	0.112 (−0.098, 0.323)
PCB180	−0.148 (−0.343, 0.045)	0.134 (−0.024, 0.293)
Aroclor 1260	−0.028 (−0.198, 0.141)	0.148 (0.004, 0.292)
Beta-HCH	−0.008 (−0.314, 0.297)	0.019 (−0.226, 0.254)
DDE	0.039 (−0.152, 0.229)	0.123 (−0.038, 0.285)
Oxychlordane	−0.056 (−0.187, 0.074)	0.031 (−0.091, 0.152)
Transnonachlor	−0.112 (−0.254, 0.029)	0.015 (−0.115, 0.144)
PBDE47	0.172 (−0.083, 0.426)	−0.008 (−0.273, 0.258)

[a] Adjusted for gestational age, maternal age, parity, pre-pregnancy BMI, maternal education, smoking status, and place of birth; [b] Weight neutral/gain is the reference category; Abbreviations: CI—Confidence Interval, MIREC—Maternal-Infant Research on Environmental Chemicals; PCB—Polychlorinated biphenyl, DDE—Dichlorodiphenyldichloroethylene; PBDE—Polybrominated diphenyl ethers; HCH—Hexachlorocyclohexane.

5. Discussion

5.1. Summary of Findings and Clinical Significance of the Findings

Thirty of the 41 POPs collected in the MIREC Study were below their respective LOD in over 50% of the participants. Population-based national surveys from Canada [29] and the United States [30], as well as observational studies from Canada [16], Mexico [16], Greece [31], and Lebanon [18], suggest relatively low levels of exposure to circulating POPs in general and obstetrical populations. As described previously, individuals participating in the MIREC study had lower plasma concentrations of Aroclor 1260 and DDE than individuals of an equivalent age (20–39 years of age) participating in the 2012–2013 Canadian Health Measures Survey report on Human Biomonitoring of Environmental Chemicals in Canada [29] and those surveyed in the Fourth National Report on Human Exposure to Environmental Chemicals of the Centre for Disease Control [30]. The most dominant compounds in the MIREC study were Aroclor 1260 and DDE. DDE was also the dominant contaminant in a number of other maternal-newborn cohorts [16,32,33]. Aroclor 1260 is a PCB mixture that was commonly used in electrical equipment and other industrial applications. PCBs are persistent in the environment and have been linked to a range of toxic effects in humans, including reproductive and developmental problems, immune system dysfunction, and an increased risk of cancer. DDE is a byproduct of the insecticide DDT and is known to have toxic effects, including hormonal disruption, reproductive and developmental problems, immune system dysfunction, and an increased risk of cancer. The toxicity implications of these compounds are significant and underscore the importance of reducing exposure to POPs in order to protect human health and the environment. Further research is needed to fully understand the toxic effects of these compounds and develop strategies to minimize exposure and mitigate their impacts.

This study underscores the original findings from the MIREC study cohort that environmental and chemical contaminants are quantifiable in the plasma of Canadian pregnant individuals [24] and provides further insight into the relative body burden of POPs among pregnant women across categories of first-trimester BMI and early pregnancy weight changes. We expanded on previous findings to demonstrate that first-trimester plasma levels of multiple POPs differed significantly across categories of first-trimester BMI. Oxychlordane, Aroclor 1260, transnonachlor, PCB 170, 180, 118, 138 and 153 and DDE plasma levels were negatively associated with first-trimester BMI. Put simply, the highest POP concentrations were found in underweight and normal-weight individuals and the lowest in individuals with class III obesity. Inverse relationships between circulating concentrations of POPs and BMI in pregnancy have been previously reported in previous studies [17,20,34]. Our results are also in line with other Canadian studies that focused specifically on pre-pregnancy BMI [33]. Further, a study by Vizcaino et al. (2014) found cord serum concentrations of POPs to be inversely associated with GWG, suggesting that GWG influences the accumulation of POPs among newborns [19].

The inverse relationships noted for most POPs can be explained by the known biochemistry of POPs: Lipophilic compounds that tend to be stored in the adipose tissues rather than in circulation [17]. In contrast to previous findings [17,24,35], we did not detect a positive relationship between Beta-HCH concentrations and maternal BMI, although our ability to study this association may have been limited by the low detection rate of Beta-HCH compound in our samples (approximately 32%). Interestingly, PBDE47 was the only POP that had a positive relationship with BMI. Similar findings were noted by Fisher et al. for the association between pre-pregnancy BMI and POP serum concentrations [24]. Minimal evidence is available on this POP's association with maternal BMI. As demonstrated by research studies of pregnant individuals from Denmark and Mexico [16,17], it is a POP with a low detection level. Studies from North America, where concentrations of PBDEs are known to be greater than in other parts of the world, have, however, found concentrations of various PBDEs to increase with pre-pregnancy BMI and have suggested that PBDEs may have an obesogenic effect and accelerate the proliferation of adipose cells [26,36]. It can also be noted that, compared to PCBs, PBDEs represent a "younger"

class of POPs and could therefore have a different distribution in the body than PCBs. Given the known effects of obesity on maternal and fetal health, additional research is needed to clarify the mechanisms linking PBDEs with obesity.

Weight changes are expected during pregnancy. A small number of individuals will lose weight or remain weight neutral during pregnancy. This may be achieved with or without intention. Many will become motivated to make lifestyle changes to improve overall health, such as consuming a healthier diet or engaging in more physical activity. Others may be affected with significant nausea and vomiting or worsening of pre-existing medical conditions. Our study observed slightly higher POP concentrations (after controlling for confounders) in pregnant individuals who lost weight compared to those who gained weight or remained weight neutral during the first trimester. On the premise that individuals with a higher body fat composition would have a higher POP storage capacity, weight loss, particularly among overweight and obese individuals, is typically associated with a redistribution of POPs from the adipose tissues into the bloodstream [10,11,37]. POPs have been shown to cross the placenta, and intrauterine exposure has been associated with low birth weight and prematurity [21,22,31]. Furthermore, alteration of immune system development, endocrine disruption and abnormal growth and development have been observed in children with early exposure to POPs [14,15,23,31]. The release of POPs into circulation during pregnancy in individuals who lose weight, regardless of etiology, could become of clinical importance as more evidence becomes available.

While it was beyond the current project scope, evaluation of maternal POPs serum concentration relative to maternal weight variations between pregnancy trimesters in individuals who participated in the MIREC project and other prospective cohorts will be important to carry out in future studies. POPs have previously been shown to interfere with biological systems. The first step in understanding their clinical significance in pregnancy is describing the burden of POPs and the factors that contribute to higher levels. If weight change in pregnancy (most likely weight loss) results in higher levels of circulating POPs, then studying the potential harmful impact on the mother, developing fetus, and placenta should be considered. If proven, patients and health care providers could benefit from counseling around strategies to optimize a healthy GWG and about the possible risks of higher levels of circulating POPs in pregnancy, whenever possible.

5.2. Strengths and Limitations

The study highlights the importance of considering the impact of maternal weight on toxic chemical exposure during pregnancy and contributes to the understanding of environmental health risks in the Canadian context. The strengths of this study include the use of a well-characterized cohort and concurrent sampling of first-trimester BMI and maternal plasma for POP analysis. We were also able to consider a large number of POPs in our analysis. Additionally, we included key confounding variables in our censored regression models. Still, other important variables capturing the dietary habits of the participants (e.g., fish consumption) were not considered in our analyses; this should be noted as a limitation of our study. The exclusion of key confounders may have resulted in residual confounding and biased our estimation of the associations of first-trimester BMI and early pregnancy weight change with POPs. Furthermore, this analysis relied on the MIREC Study's baseline data, which were cross-sectional, thus preventing us from clearly defining the direction of some of the associations. As reported in some prospective cohort studies, POPs may lead to low gestational weight change throughout pregnancy [14,15,23,31,38]. Other studies conducted in Canada have also shown that certain environmental chemicals may be associated with increased GWG [39].

More studies investigating the mechanisms linking maternal weight changes and POPs are required. Our findings are limited by our small sample size (N = 72 pregnant individuals experienced weight loss in the first trimester), possible inaccuracy of self-reported pre-pregnancy weight, and a short time interval between pre-pregnancy and first-trimester weight measurements. Self-reported pre-pregnancy weight may have limited the accuracy

of our weight change calculations, given the inherent potential for error and misclassification. However, it is important to note that self-reported maternal weight is commonly used in clinical practice to calculate pre-pregnancy BMI. Studies have shown a high correlation between self-reported and measured pre-pregnancy weight [40]. When discrepancies were observed between the two measurements, this generally did not misclassify BMI classes [40]. Furthermore, maternal body composition may be stable during the first trimester, and POPs may, in fact, be more strongly related to weight changes over longer time periods than that observed during pregnancy [37].

In addition, the results of this study cannot be generalized to all populations. Most participants were recruited from southern urban settings. Similarly, individuals from the MIREC study were older, less likely to smoke, more likely to be married, and to be educated than the general Canadian population giving birth in 2009 [25]. Lastly, while the majority of the POPs considered in our study (30/41) had levels below their respective LODs in more than 50% of samples, we attempted to address this by limiting our analyses to those POPs with less than 50% of samples under the LOD.

6. Conclusions

This study provides preliminary evidence that first-trimester maternal BMI may be negatively associated with first-trimester plasma concentrations of POPs, possibly suggesting that individuals with obesity may have higher POP concentrations within adipose tissues. Our findings are relevant in the wider context of environmental health and planetary health as it sheds light on the potential health risks associated with exposure to toxic chemicals during pregnancy. While the preliminary results of this study hold promise in informing future research and public health policies and interventions aimed at improving the health of mothers, infants, and the environment, it is important to exercise caution in interpreting them due to the limitations of the data used. Further research is required to understand this observed relationship and underlying mechanisms, as well as the potential implications on newborn health. Future studies should evaluate the dynamic interplay between gestational weight change and circulating POP concentrations using a prospective cohort design, including measurements across the continuum of pregnancy. This evidence would be beneficial for maternal healthcare providers to help guide and inform gestational weight gain recommendations, particularly for pregnant individuals with pre-existing obesity, who potentially may have a high body burden of POPs at the onset of pregnancy.

Author Contributions: L.G. conceived the project. L.G., E.B., M.L., L.D., M.W. and M.O. developed the protocol and the analytical plan. M.O. performed all data preparation and analyses, with L.G., M.L., R.F. and A.D.H. providing guidance on the statistical approach. M.L., M.O. and R.F. wrote the manuscript with input from all authors. All authors interpreted the findings and contributed to the writing and completion of the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: Canadian Institutes of Health Research (CIHR), Grant/Award Number: MFM-146444.

Data Availability Statement: Permission to use the data that support the findings of this study can be obtained from the MIREC Study Group upon reasonable request.

Acknowledgments: The MIREC Biobank is acknowledged as the source of data used in this project. The authors thank the participants and staff of the MIREC study, along with the MIREC Site Co-Investigators. We acknowledge Jillian Ashley-Martin, who reviewed this manuscript on behalf of the MIREC Study Group. We also acknowledge all members of the MIREC Study Group. The MIREC study group consists of TE Arbuckle and WD Fraser (MIREC Study Principal Investigators) and D Jin, T Rawn, B Dabeka, M Fisher, S Brooks, XL Cao, K Cockell, A Becalski, R Vincent, M Villeneuve, Z Wang, N Ratnayake (retired), G Bondy, M D'Amour, I Massarelli, A MacFarlane, N Hidiroglou (deceased), P Kumarathasan, M Legrand, S Tittlemier, D Avard (retired), JP Weber (retired), R Platt, H Weiler, A Ettinger, G Mitchell, ZC Luo, A LeBlanc, P Julien, W Foster, G Smith, M Sermer, G Ross, P Fredette, M Lawson, R Shear, W Fraser, M Helewa, S Taback, D Hemmings, J Wang, P von Dadelszen

and B Lanphear (all MIREC Study Co-investigators). The MIREC study was supported by Health Canada, the Ontario Ministry of the Environment, and the Canadian Institutes of Health Research.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

Beta-HCH	Beta-Hexachlorocyclohexane
BMI	Body Mass Index
DDE	Dichlorodiphenyldichloroethylene
DDT	Dichlorodiphenyltrichloroethane
GWG	Gestational Weight Gain
LOD	Limit of Detection
MIREC	Maternal-Infant Research on Environmental Chemicals
PBB	Polybrominated biphenyl
PBDE	Polybrominated diphenyl ether
PCB	Polychlorinated biphenyl
POP	Persistent Organic Pollutant

References

1. Arendas, K.; Qiu, Q.; Gruslin, A. Obesity in pregnancy: Pre-conceptional to postpartum consequences. *J. Obstet. Gynaecol. Can.* **2008**, *30*, 477–488. [CrossRef] [PubMed]
2. Crane, J.M.G.; Murphy, P.; Burrage, L.; Hutchens, D. Maternal and perinatal outcomes of extreme obesity in pregnancy. *J. Obstet. Gynaecol. Can.* **2013**, *35*, 606–611. [CrossRef] [PubMed]
3. Langley-Evans, S.C.; Pearce, J.; Ellis, S. Overweight, obesity and excessive weight gain in pregnancy as risk factors for adverse pregnancy outcomes: A narrative review. *J. Hum. Nutr. Diet.* **2022**, *35*, 250–264. [CrossRef] [PubMed]
4. Block, S.R.; Watkins, S.M.; Salemi, J.L.; Rutkowski, R.; Correia, J.A.; Kirby, R.S. Maternal pre-pregnancy body mass index and risk of selected birth defects: Evidence of a dose-response relationship. *Paediatr. Perinat. Epidemiol.* **2013**, *27*, 521–531. [CrossRef] [PubMed]
5. Neri, C.; Serafino, E.; Morlando, M.; Familiari, A. Microbiome and Gestational Diabetes: Interactions with Pregnancy Outcome and Long-Term Infant Health. *J. Diabetes Res.* **2021**, *2021*, 9994734. [CrossRef] [PubMed]
6. LifeCycle Project-Maternal Obesity and Childhood Outcomes Study Group; Voerman, E.; Santos, S.; Inskip, H.; Amiano, P.; Barros, H.; Charles, M.A.; Chatzi, L.; Chrousos, G.P.; Corpeleijn, E.; et al. Association of Gestational Weight Gain With Adverse Maternal and Infant Outcomes. *JAMA* **2019**, *321*, 1702–1715. [CrossRef]
7. Maxwell, C.; Gaudet, L.; Cassir, G.; Nowik, C.; McLeod, N.L.; Jacob, C.É.; Walker, M. Guideline No. 391-Pregnancy and Maternal Obesity Part 1: Pre-conception and Prenatal Care. *J. Obstet. Gynaecol. Can.* **2019**, *41*, 1623–1640. [CrossRef]
8. Health Canada. Prenatal Nutrition Guidelines for Health Professionals, Background on Canada's Food Guide. 2010. Available online: https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/fn-an/alt_formats/pdf/nutrition/prenatal/ewba-mbsa-eng.pdf (accessed on 1 November 2022).
9. Woolcott, C.; Dodds, L.; Ashley-Martin, J.; Piccinini-Vallis, H. Distribution of pregnancy-related weight measures. *Can. Fam. Phys.* **2016**, *62*, e400–e406.
10. Lim, J.S.; Son, H.K.; Park, S.K.; Jacobs, D.R.; Lee, D.H. Inverse associations between long-term weight change and serum concentrations of persistent organic pollutants. *Int. J. Obes.* **2011**, *35*, 744–747. [CrossRef]
11. Malarvannan, G.; Van Hoorenbeeck, K.; Deguchtenaere, A.; Verhulst, S.L.; Dirinck, E.; Van Gaal, L.; Jorens, P.G.; Covaci, A. Dynamics of persistent organic pollutants in obese adolescents during weight loss. *Environ. Int.* **2018**, *110*, 80–87. [CrossRef]
12. Pestana, D.; Faria, G.; Sá, C.; Fernandes, V.C.; Teixeira, D.; Norberto, S.; Faria, A.; Meireles, M.; Marques, C.; Correia-Sá, L.; et al. Persistent organic pollutant levels in human visceral and subcutaneous adipose tissue in obese individuals—Depot differences and dysmetabolism implications. *Environ. Res.* **2014**, *133*, 170–177. [CrossRef] [PubMed]
13. Hagen, P.; Walls, M.P. The Stockholm Convention on Persistent Organic Pollutants. *Nat. Resour. Environ.* **2005**, *19*, 49–52. [CrossRef]
14. Ruzzin, J. Public health concern behind the exposure to persistent organic pollutants and the risk of metabolic diseases. *BMC Public Health* **2012**, *12*, 298. [CrossRef]
15. The World Health Organization. Persistent Organic Pollutants: Impact on Child. Health. 2010. Available online: https://www.who.int/publications/i/item/persistent-organic-pollutants-impact-on-child-health (accessed on 1 November 2022).
16. Adlard, B.; Davis, K.; Liang, C.L.; Curren, M.S.; Rodríguez-Dozal, S.; Riojas-Rodríguez, H.; Hernández-Ávila, M.; Foster, W.; Needham, L.; Wong, L.Y.; et al. Persistent organic pollutants (POPs) and metals in primiparous women: A comparison from Canada and Mexico. *Sci. Total Environ.* **2014**, *500–501*, 302–313. [CrossRef] [PubMed]

17. Bjerregaard-Olesen, C.; Long, M.; Ghisari, M.; Bech, B.H.; Nohr, E.A.; Uldbjerg, N.; Henriksen, T.B.; Olsen, J.; Bonefeld-Jørgensen, E.C. Temporal trends of lipophilic persistent organic pollutants in serum from Danish nulliparous pregnant women 2011–2013. *Environ. Sci. Pollut. Res. Int.* **2017**, *24*, 16592–16603. [CrossRef]
18. Helou, K.; Matta, J.; Harmouche-Karaki, M.; Sayegh, N.; Younes, H.; Mahfouz, Y.; Mahfouz, M.; Karake, S.; Finan, R.; Abi-Tayeh, G.; et al. Maternal and cord serum levels of polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs) among Lebanese pregnant women and predictors of exposure. *Chemosphere* **2021**, *266*, 129211. [CrossRef] [PubMed]
19. Vizcaino, E.; Grimalt, J.O.; Glomstad, B.; Fernández-Somoano, A.; Tardón, A. Gestational weight gain and exposure of newborns to persistent organic pollutants. *Environ. Health Perspect.* **2014**, *122*, 873–879. [CrossRef]
20. Wang, R.Y.; Jain, R.B.; Wolkin, A.F.; Rubin, C.H.; Needham, L.L. Serum concentrations of selected persistent organic pollutants in a sample of pregnant females and changes in their concentrations during gestation. *Environ. Health Perspect.* **2009**, *117*, 1244–1249. [CrossRef]
21. Longnecker, M.P.; Klebanoff, M.A.; Zhou, H.; Brock, J.W. Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth. *Lancet* **2001**, *358*, 110–114. [CrossRef]
22. Nieuwenhuijsen, M.J.; Dadvand, P.; Grellier, J.; Martinez, D.; Vrijheid, M. Environmental risk factors of pregnancy outcomes: A summary of recent meta-analyses of epidemiological studies. *Environ. Health* **2013**, *12*, 6. [CrossRef]
23. World Health Organization. Principles for Evaluating Health Risks in Children Associated with Exposure to Chemicals. 2006. Available online: https://apps.who.int/iris/handle/10665/43604 (accessed on 1 August 2022).
24. Fisher, M.; Arbuckle, T.E.; Liang, C.L.; LeBlanc, A.; Gaudreau, E.; Foster, W.G.; Haines, D.; Davis, K.; Fraser, W.D. Concentrations of persistent organic pollutants in maternal and cord blood from the maternal-infant research on environmental chemicals (MIREC) cohort study. *Environ. Health A Glob. Access Sci. Source* **2016**, *15*, 1–14. [CrossRef]
25. Arbuckle, T.E.; Fraser, W.D.; Fisher, M.; Davis, K.; Liang, C.L.; Lupien, N.; Bastien, S.; Velez, M.P.; von Dadelszen, P.; Hemmings, D.G.; et al. Cohort profile: The maternal-infant research on environmental chemicals research platform. *Paediatr. Perinat. Epidemiol.* **2013**, *27*, 415–425. [CrossRef]
26. Mehta, S.S.; Applebaum, K.M.; James-Todd, T.; Coleman-Phox, K.; Adler, N.; Laraia, B.; Epel, E.; Parry, E.; Wang, M.; Park, J.S.; et al. Associations between sociodemographic characteristics and exposures to PBDEs, OH-PBDEs, PCBs, and PFASs in a diverse, overweight population of pregnant women. *J. Expo. Sci. Environ. Epidemiol.* **2020**, *30*, 42–55. [CrossRef]
27. Williamson, E.J.; Aitken, Z.; Lawrie, J.; Dharmage, S.C.; Burgess, J.A.; Forbes, A.B. Introduction to causal diagrams for confounder selection. *Respirology* **2014**, *19*, 303–311. [CrossRef] [PubMed]
28. Helsel, D.R. Chapter 13: Multivariate Methods for Censored Data. In *Statistics for Censored Environmental Data Using Minitab and R*; John Wiley & Sons: Hoboken, NJ, USA, 2011; pp. 268–296.
29. Government of Canada. Third Report on Human Biomonitoring of Environmental Chemicals in Canada. 2015. Available online: https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/ewh-semt/alt_formats/pdf/pubs/contaminants/chms-ecms-cycle3/chms-ecms-cycle3-eng.pdf (accessed on 1 November 2022).
30. Centers for Disease Control and Prevention (CDC). Fourth National Report on Human Exposure to Environmental Chemicals. 2021. Available online: https://ecologycenter.org/wp-content/uploads/2021/04/FourthReport_UpdatedTables_Volume2_Mar2021-508.pdf (accessed on 1 November 2022).
31. Vafeiadi, M.; Georgiou, V.; Chalkiadaki, G.; Rantakokko, P.; Kiviranta, H.; Karachaliou, M.; Fthenou, E.; Venihaki, M.; Sarri, K.; Vassilaki, M.; et al. Association of Prenatal Exposure to Persistent Organic Pollutants with Obesity and Cardiometabolic Traits in Early Childhood: The Rhea Mother-Child Cohort (Crete, Greece). *Environ. Health Perspect.* **2015**, *123*, 1015–1021. [CrossRef] [PubMed]
32. Adetona, O.; Horton, K.; Sjodin, A.; Jones, R.; Hall, D.B.; Aguillar-Villalobos, M.; Cassidy, B.E.; Vena, J.E.; Needham, L.L.; Naeher, L.P. Concentrations of select persistent organic pollutants across pregnancy trimesters in maternal and in cord serum in Trujillo, Peru. *Chemosphere* **2013**, *91*, 1426–1433. [CrossRef] [PubMed]
33. Foster, W.G.; Cheung, A.P.; Davis, K.; Graves, G.; Jarrell, J.; Leblanc, A.; Liang, C.L.; Leech, T.; Walker, M.; Weber, J.P.; et al. Circulating metals and persistent organic pollutant concentrations in Canadian and non-Canadian born primiparous women from five Canadian centres: Results of a pilot biomonitoring study. *Sci. Total Environ.* **2012**, *435–436*, 326–336. [CrossRef]
34. Glynn, A.; Aune, M.; Darnerud, P.O.; Cnattingius, S.; Bjerselius, R.; Becker, W.; Lignell, S. Determinants of serum concentrations of organochlorine compounds in Swedish pregnant women: A cross-sectional study. *Environ. Health* **2007**, *6*, 2. [CrossRef]
35. Dirinck, E.; Jorens, P.G.; Covaci, A.; Geens, T.; Roosens, L.; Neels, H.; Mertens, I.; Van Gaal, L. Obesity and persistent organic pollutants: Possible obesogenic effect of organochlorine pesticides and polychlorinated biphenyls. *Obes. (Silver Spring)* **2011**, *19*, 709–714. [CrossRef]
36. Vuong, A.M.; Braun, J.M.; Sjödin, A.; Webster, G.M.; Yolton, K.; Lanphear, B.P.; Chen, A. Prenatal Polybrominated Diphenyl Ether Exposure and Body Mass Index in Children Up To 8 Years of Age. *Environ. Health Perspect.* **2016**, *124*, 1891–1897. [CrossRef]
37. Jansen, A.; Lyche, J.L.; Polder, A.; Aaseth, J.; Skaug, M.A. Increased blood levels of persistent organic pollutants (POP) in obese individuals after weight loss—A review. *J. Toxicol. Environ. Health Part B Crit. Rev.* **2017**, *20*, 22–37. [CrossRef] [PubMed]
38. Jaacks, L.M.; Boyd Barr, D.; Sundaram, R.; Grewal, J.; Zhang, C.; Buck Louis, G.M. Pre-Pregnancy Maternal Exposure to Persistent Organic Pollutants and Gestational Weight Gain: A Prospective Cohort Study. *Int. J. Environ. Res. Public Health* **2016**, *13*, 905. [CrossRef] [PubMed]

39. Ashley-Martin, J.; Dodds, L.; Arbuckle, T.E.; Morisset, A.S.; Fisher, M.; Bouchard, M.F.; Shapiro, G.D.; Ettinger, A.S.; Monnier, P.; Dallaire, R.; et al. Maternal and Neonatal Levels of Perfluoroalkyl Substances in Relation to Gestational Weight Gain. *Int. J. Environ. Res. Public Health* **2016**, *13*, 146. [CrossRef] [PubMed]
40. Headen, I.; Cohen, A.K.; Mujahid, M.; Abrams, B. The accuracy of self-reported pregnancy-related weight: A systematic review. *Obes. Rev.* **2017**, *18*, 350–369. [CrossRef]