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Obesity in relation to serum persistent organic pollutant concentrations in CHAMACOS women

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Background: Environmental exposure to endocrine-disrupting chemicals (EDCs), including persistent organic pollutants (POPs), has been hypothesized to increase risk of obesity. Using data from the Center for Health Assessment of Mothers and Children of Salinas (CHAMACOS) study, we examined the longitudinal relationship between serum concentrations of a POPs mixture and several obesity measures.

Methods: Concentrations of 17 POPs were measured in serum collected in 2009–2011 from 468 CHAMACOS women. Anthropometry measurements and personal interviews were completed at up to three study visits between 2009 and 2014. We assessed the relationship of serum POPs concentrations with adiposity measures longitudinally using generalized estimation equation (GEE) models. We implemented Bayesian Kernel Machine Regression (BKMR) to elucidate the effects of joint exposure to the POPs mixture.

Results: In GEE models, positive associations with body mass index were found for dichlorodiphenyltrichloroethane (Q4 vs. Q1: adjusted $\beta = 3.2\,kg/m^2$; 95% CI = 1.5, 4.9), β-hexachlorocyclohexane (Q4 vs. Q1: adjusted $\beta = 3.6\,kg/m^2$; 95% CI = 2.0, 5.2), and polybrominated diphenyl ether (PBDE)-47 (Q4 vs. Q1: adjusted $\beta = 1.9\,kg/m^2$; 95% CI = 0.3, 3.5), while PBDE-153 was inversely associated (Q4 vs. Q1: adjusted $\beta = -2.8\,kg/m^2$; 95% CI = –4.4, –1.2). BKMR results, while largely consistent with single pollutant models, revealed the shape and direction of the exposure–response relationships, as well as interactions among pollutants within the mixture, that could not be discovered by single-pollutant models.

Conclusion: In summary, we found significant associations of serum POPs with several adiposity measures using both conventional regressions and BKMR. Our results provide support for the chemical obesogen hypothesis, that exposure to EDCs may alter risk for later obesity.

The increasing prevalence of obesity worldwide is a major public health concern, associated with significant morbidity and mortality.[1–3] Among the most common and costly chronic disorders worldwide, obesity affects more than one-third of adults in the United States and accounts for an estimated 20% of total mortality.[2,4] In the United States, the prevalence of obesity and related morbidities varies among ethnic/racial groups,[4–7] with a higher prevalence in Hispanic women.

Although excess caloric consumption and physical inactivity are well-recognized risk factors for obesity, increasing evidence suggests these factors alone do not fully explain the observed increase in prevalence.[8] Environmental exposure to endocrine-disrupting chemicals (EDCs), including persistent organic pollutants (POPs), has been hypothesized to play a role in promoting obesity by disrupting normal homeostatic controls over adipogenesis and energy balance.[9,10] POPs, including organochlorine (OC) pesticides, polychlorinated biphenyls (PCBs), and polybrominated diphenyl ether (PBDE) flame retardants, are a class of xenobiotic chemicals that are persistent in the environment, highly lipophilic, and bioaccumulate with relatively long half-lives in humans.[11,12] These compounds have been used as insecticides (dichlorodiphenyltrichloroethane [*p,p′*-DDT], β-hexachlorocyclohexane [β-HCH]), fungicides (hexachlorobenzene [HCB]), heat exchange fluids in electrical transformers

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What this study adds

This study employs modern methods of assessing the relationship between persistent organic pollutants and obesity, specifically the use of Bayesian Kernel Machine Regression to examine mixture effects. As pollutants can be highly correlated, the exclusive use of single-pollutant models may produce biased results, and this study presents an example of how mixture and nonlinear effects can be evaluated. In addition, the present study takes advantage of a wealth of data from a well-established longitudinal cohort study, allowing longitudinal analyses, but from a population within the study that has been seldom studied (the Center for Health Assessment of Mothers and Children of Salinas [CHAMACOS] mothers).

and capacitors (PCBs), and additive flame retardants (PBDEs). Under the Stockholm Convention on POPs, production and use of PCBs, PBDEs, and several OC pesticides have been eliminated, while use of DDT has been restricted to disease vector control.[13] Despite being banned decades ago, their persistence and bioaccumulation has led to continued low-level human exposure worldwide. For example, the OC pesticide, DDT, has not been sprayed in the United States since 1972; nonetheless, most US residents still have detectable levels of the primary metabolite, *p,p′*-dichlorodiphenyldichloroethylene (*p,p′*-DDE).[14] Although pentaBDE was phased out in 2004, its primary congeners (PBDE-47, PBDE-99, PBDE-100, PBDE-153) are commonly found in serum in the US population.[15]

In experimental studies, several of the above-mentioned POPs are associated with adipose dysfunction, including visceral obesity, insulin resistance, and glucose intolerance.[9,10,16,17] Epidemiologic studies, however, are less consistent. Positive associations between individual serum POP concentrations, including *p,p′*-DDT, *p,p′*-DDE, HCB, β-HCH, PCB-118, and PBDE-47, and body mass index (BMI) have been inconsistently reported in cross-sectional studies in the United States,[18,19] Belgium,[20,21] and Spain.[22] Inverse associations have been reported for PCB-180 and PBDE-153 in some,[20,23] but not all, cross-sectional studies.[19,22] However, longitudinal studies of POPs exposure and obesity are limited.[24,25] Serum *p,p′*-DDT and *p,p′*-DDE were significantly positively associated with BMI 20 years later in a sample of 90 participants.[25] However, among participants in the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study, no association was found between serum levels of *p,p′*-DDE, HCB, or PBDE-47 and abdominal obesity 5 years later.[24] Additionally, previous epidemiologic studies of POPs and obesity have only considered exposure to a single chemical at a time, which may not address the true effect of chemical mixtures on obesity.[26]

The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS) study, initiated in 1999, is a well-established longitudinal birth cohort of low-income, Mexican-American mother–child dyads living in an agricultural community in California.[27] Although we have previously examined the relationship of chemical exposures with obesity in CHAMACOS children,[28–32] we have not investigated their effects in the mothers. Here, we examine the longitudinal relationship between serum concentrations of a POPs mixture, including OC pesticides, PCBs, and PBDEs, and risk of obesity in CHAMACOS women, with individual POP exposures as well as the effects of joint exposure to the POPs mixture on BMI using Bayesian Kernel Machine Regression (BKMR) methods.[33]

Methods

Study participants

Details of the CHAMACOS study have been presented elsewhere.[27,34] Briefly, between October 1999 and October 2000, the first cohort (CHAM1) of women was recruited from prenatal clinics serving the farmworker population in the Salinas Valley, California. Eligible women were at least 18 years of age, less than 20 weeks gestation, English- or Spanish-speakers, qualified for government-sponsored health insurance, and planned to deliver at the county hospital. A total of 601 pregnant women enrolled and 531 remained in the study at the time of delivery. A second cohort of 309 mothers of 9-year-old children (CHAM2) was recruited to join the study between January 2010 and September 2011 when the children of CHAM1 women were 9 years old. Eligibility criteria for CHAM1 and CHAM2 were similar to ensure that participants were from the same underlying population.

Data for the current analysis are from three study visits (1, 2, and 3) completed about 1 and a half years apart between April 2009 and August 2014 and timed to coincide with the cohort child's age of 9 (visit 1: April 2009–September 2011), 10 and half (visit 2: October 2010–March 2013), and 12 (visit 3: March 2012–August 2014) years. In total, 643 CHAMACOS women participated in visit 1, of whom 593 underwent a fasting blood draw; concentrations of POPs were measured in serum for 471 (79% of eligible) women. We excluded three women who were missing all anthropometry measurements, leaving a final analysis sample of 468 women with anthropometry measurements from at least one study visit (visit 1: n = 459; visit 2: n = 428; visit 3: n = 418). All study activities were approved by the Institutional Review Boards at participating institutions; written informed consent was obtained from all participants prior to participation.

Procedure

Women underwent a fasting blood draw at visit 1 (2009–2011). At each of the three study visits, women underwent anthropometric measurements and were interviewed in English or Spanish using structured questionnaires. During each interview, we collected information about family sociodemographics, maternal characteristics, pregnancy, and medical histories. Anthropometric measurements, including height (cm), weight (kg), and waist circumference (cm), were measured at each study visit; triplicate measures were made for height and waist circumference and averaged for analysis. Barefoot standing height was measured to the nearest 0.1 cm using a stadiometer. Weight was measured to the nearest 0.1 kg using a bioimpedance scale (Tanita TBF-300A Body Composition Analyzer, Tanita Corporation of America, Inc. Arlington Heights, IL) that also provided a measure percentage of body fat by "foot-to-foot" bio-electrical impedance analysis. Waist circumference was measured to the nearest 0.1 cm by placing a tape measure around the abdomen parallel to the ground at the level of the iliac crest. We calculated BMI (kg/m^2) and classified women as "overweight" or "obese" if they had a BMI ≥ 25 and <30 kg/m^2 or ≥ 30 kg/m^2, respectively.[35]

Measurement of POPs in serum

Serum from fasting blood was stored at −80°C until shipment to the Centers for Disease Control and Prevention (Atlanta, GA), where specimens were analyzed for 9 persistent pesticides (*p,p′*-DDT, *o,p′*-DDT, *p,p′*-DDE, HCB, β-HCH, γ-hexachlorocyclohexane, mirex, trans-nonachlor, oxychlordane), 10 PBDE congeners (PBDE-17, -28, -47, -66, -85, -99, -100, -153, -154, -183), and 35 PCB congeners (International Union for Pure and Applied Chemistry numbers 28, 44, 49, 52, 66, 74, 87, 99, 101, 105, 110, 118, 128, 138/158, 146, 149, 151, 153, 156, 157,167, 170, 172, 177, 178, 180, 183, 187, 189, 194, 195, 196/203, 199, 206, 209) by gas chromatography isotope dilution high-resolution mass spectrometry (GC-IDHRMS).[15] Total lipid content of each serum specimen was estimated using a "summation" method,[36] and analytical results were reported on a lipid-adjusted basis in units of nanograms per gram lipid. The limits of detection (LOD) were 1.9–29.95 ng/g lipid for HCB, 0.6–9.5 ng/g lipid for all other persistent pesticides, 0.7–5.5 ng/g lipid for PBDE-47, 0.2–2.9 ng/g lipid for all other PBDE congeners, 0.4–10.7 ng/g lipid for PCB-28, and 0.1–3.6 ng/g lipid for all other PCB congeners. Each analytic run included laboratory quality control and method blank samples.

Quantifiable results less than the detection limits were reported when observed. For results below the LOD, a value was imputed based on a log-normal probability distribution via maximum likelihood estimation.[37] Analysis was restricted to PBDE and PCB congeners with detection frequencies >75% and pesticides with detection frequencies >50% (to include *p,p′*-DDT). Thus, *p,p′*-DDT, *p,p′*-DDE, HCB, β-HCH, trans-nonachlor, PBDE-47, PBDE-99, PBDE-100, PBDE-153, PCB-28,

PCB-74, PCB-99, PCB-118, PCB-138/158, PCB-153, PCB-170, and PCB-180 were included in the analysis.

Statistical analysis

All exposure variables were initially $\log_{10}$-transformed to more closely approximate a normal distribution. Generalized additive models (GAM), using 3-degree-of-freedom cubic splines, identified departures from linearity in several cases. As a result, the primary analysis modeled exposures as categorical (quartile) variables.

Based on our review of the obesity literature, variables considered as potential confounders included age, country of origin, years of residence in the United States prior to cohort birth, primary language (Spanish or English), education level, marital and employment status, household income, smoking status, alcohol consumption, household food insecurity, parity, and lactation. Age, household income, and household food insecurity were assessed at each visit (see Table 1). The final set of covariates was determined using a Directed Acyclic Graph (see eFigure 1; http://links.lww.com/EE/A24) and included age (continuous variable), household income (categorical variable, below or equal to poverty versus above the poverty line), and years of residence in the United States prior to cohort birth (categorical variable, ≤1, 2–5, 6–10, ≥11, entire life).

The primary analysis assessed the relationship between exposures and obesity outcomes longitudinally using generalized estimation equation (GEE) models. Continuous outcomes included BMI (kg/m^2), waist circumference (cm), and body fat percent; obesity status (BMI ≥30 versus <30) was treated as a binary outcome, using a Poisson GEE model with a log-link function to estimate the relative risk (RR). In sensitivity analyses, we examined cross-sectional models at each of the visit points to assess differences in associations over time. Robust standard errors were estimated for all models using the Huber-White sandwich estimator.[38,39]

In addition to the single-pollutant exposure models, we implemented BKMR on continuous outcomes to elucidate the effects of joint exposure to all 17 POPs. BKMR models the outcome as a flexible kernel function of the exposure variables, adjusted for covariates and fit with a random effect for subject to account for repeat measures.[33] BKMR models also accommodate the examination of both individual and joint effects within a mixture of exposures (see eTable 1; http://links.lww.com/EE/A24). Specifically, BKMR allows the analyst to "group" highly correlated exposures such that only a single component within a group enters into the model at a time.[33] Since these complex mixtures consist of highly correlated classes of POPs, we used BKMR's hierarchical (or grouped) variable selection option. Variable selection is a key aspect to BKMR because it computes a posterior inclusion probability (PIP) to indicate the probability that a specific exposure (or group of exposures in the case of group PIPs) was selected into a model across the entire set of possible models. Therefore, we obtained the group PIP, which is the posterior mean of the indicator variable for inclusion in the given iteration of the model,[40] and we consider a group PIP of 0.50 or greater as indicative of exposure-group importance.[41] BKMR also computes conditional PIPs within the three groups of OC pesticides, PBDEs, and PCBs, indicating the relative ranking of individual chemicals when a particular chemical group is selected across model iterations. We evaluated the shape and direction of the exposure–response relationship for each POP by visual inspection of graphical output from BKMR. This entailed plotting exposure–response relationships for each POP when holding all other exposure variables at specified values (e.g., 25th, 50th, and 75th percentiles). While we present the BKMR results for each of the continuous outcomes, for the sake of brevity we focus on BMI. Given the high prevalence of obesity in the study population, we were not able to use BKMR for the binary outcome.

Table 1

Select characteristics of women, CHAMACOS Study, Salinas, CA, 2000–2014

Characteristic	n (%)
Total	468 (100.0)
Country of birth	
Mexico	410 (87.6)
United States	54 (11.5)
Other	4 (0.9)
Race/ethnicity	
Latina	451 (96.4)
Non-Latina	17 (3.6)
Year of cohort birth	
2000	115 (24.6)
2001	196 (41.9)
2002	157 (33.6)
Years of residence in United States at time of cohort birth	
≤1	84 (18.0)
2–5	128 (27.4)
6–10	119 (25.4)
≥11	97 (20.7)
Entire life	40 (8.5)
Primary language	
Spanish	421 (90.0)
English	47 (10.0)
Education	
≤6th grade	196 (41.9)
7th–12th grade	155 (33.1)
High school graduate or higher	117 (25.0)
Marital status at visit 1[a]	
Not married	125 (26.8)
Married/living as married	341 (73.2)
Age at visit 1 (years)	
27–32	115 (24.6)
32–36	119 (25.4)
36–40	114 (24.4)
40+	120 (25.6)
Household income status at visit 1	
At or below the poverty level	352 (75.2)
Above the poverty level	116 (24.8)
Parity at visit 1[a]	
1	25 (5.4)
2	111 (23.8)
3	169 (36.2)
4+	162 (34.7)
Current smoking status at visit 1[a]	
No	458 (98.1)
Yes	9 (1.9)
Household food insecurity at visit 1	
Food secure	274 (58.6)
Low food security	136 (29.1)
Very low food security	58 (12.4)

[a]Missing data (marital status, n = 2; smoking, n = 1; parity, n = 1).
CHAMACOS indicates Center for Health Assessment of Mothers and Children of Salinas.

Statistical analyses were performed using STATA, version 13.1 (Stata Corporation, College Station, TX). The BKMR analysis was performed using R, version 3.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Table 1 presents select characteristics of the CHAMACOS women. Almost all of the 468 women identified as Latina (96.4%) and were born in Mexico (87.6%), with almost half residing in the United States for 5 years or less at the time of the cohort pregnancy. The majority of women had not completed high school and were living at or below the poverty level at each visit. At the time of the blood draw, women were an average of 36.4 (±5.4; range 27–54) years. The mean BMI at each visit was around 31 kg/m^2, with over half of women classified as obese

Table 2

Summary of obesity outcome measures for women at each of the study visits,[a] CHAMACOS Study, Salinas, CA, 2009–2014.

	Visit 1	Visit 2	Visit 3
N	459	428	418
Body mass index (kg/m^2), mean (SD)	31.2 (6.4)	31.6 (6.7)	31.5 (6.3)
Categorical BMI, n (%)			
Normal	59 (12.9)	49 (12.0)	46 (11.3)
Overweight	163 (35.8)	138 (33.9)	140 (34.5)
Obese	234 (51.3)	221 (54.1)	220 (54.2)
Waist circumference (cm), mean (SD)	100.3 (15.6)	101.5 (15.6)	102.3 (15.9)
Body fat percent, mean (SD)	37.8 (7.7)	38.2 (7.5)	38.5 (7.1)

[a]Visit 1 (April 2009 to September 2011), Visit 2 (October 2010 to March 2013), Visit 3 (March 2012 to August 2014).
CHAMACOS indicates Center for Health Assessment of Mothers and Children of Salinas.

(BMI ≥ 30 kg/m^2; see Table 2). Waist circumference and body fat percent averaged around 101 cm and 38%, respectively. The intraclass correlation coefficients (ICC) are 0.93 for BMI, 0.83 for waist circumference, and 0.83 for body fat percent.

POP concentrations measured in serum of CHAMACOS women are summarized in Table 3. Geometric mean concentrations of *p,p′*-DDT and *p,p′*-DDE were 4.7 and 291.2 ng/g lipid, respectively, with *p,p′*-DDE detected in all samples. PBDEs were almost universally detected; total concentrations were dominated by PBDE-47 (GM = 17.1 ng/g lipid), followed by comparable levels of PBDE-99, -100, and -153. The PCBs were dominated by PCB-28 (GM = 11.8 ng/g lipid), with several other congeners (PCB-118, PCB-138/158, PCB-153, PCB-180) detected in over 95% of samples.

Results of GEE models by quartiles of POPs exposure concentrations are presented in Table 4. Compared to the lowest quartile, *p,p′*-DDT concentrations were positively associated with BMI (Q2: adjusted-β = 2.00 [95% CI = 0.45, 3.55]; Q3: adjusted-β = 2.81 [95% CI = 1.21, 4.40]; Q4: adjusted-β = 3.19 [95% CI = 1.51, 4.86]; *P* trend <0.01; Table 4). β-HCH was also positively associated with BMI in quartile models. No associations were found for *p,p′*-DDE, HCB, or trans-nonachlor. PBDE-47 was positively associated with BMI (Q4: adjusted-β = 1.89 [95% CI = 0.26, 3.52]; *P* trend =0.02), while PBDE-153 was inversely associated with BMI (Q3: adjusted-β = −1.98 [95% CI = −3.39, −0.57]; Q4: adjusted-β = −2.78 [95% CI = −4.39, −1.18]; *P* trend <0.01). Several PCBs (PCB-74 and PCB-99) were associated with increased BMI; conversely, PCB-180 was inversely associated with BMI.

GEE models for waist circumference showed similar results to the BMI models; positive associations were found for *p,p′*-DDT, β-HCH, PBDE-47, PCB-74, and PCB-99, and inverse associations were found for PBDE-153 and PCB-180 (Table 4). GEE models for body fat percent were generally consistent with the other outcomes; however, PBDE-47 was not associated, and additional positive associations were found for PCB-118 and PCB-138/158 (Table 4).

Results of GEE models for risk of obesity by quartiles of POPs exposure concentrations are presented in Table 5. Consistent with the continuous-outcome models, we observed a significant increasing trend in risk of obesity for *p,p′*-DDT (Q2: adjusted-RR = 1.38 [95% CI = 1.08, 1.76]; Q3: adjusted-RR = 1.45 [95% CI = 1.13, 1.85]; Q4: adjusted-RR = 1.48 [95% CI = 1.16, 1.89]; *P* trend <0.01) and β-HCH (*P* trend <0.01). Associations were positive for PBDE-47 (Q4: adjusted-RR = 1.29 [95% CI = 1.03, 1.60]; *P* trend = 0.02) but inverse for PBDE-153 (Q4: adjusted-RR = 0.70 [95% CI = 0.56, 0.88]; *P* trend <0.01). Higher concentrations of PCB-99 were associated with increased risk of obesity (*P* trend <0.01), while a significant decreasing trend was observed for PCB-180 (*P* trend = 0.03). These findings are consistent with the continuous BMI-outcome models presented above.

We present the continuous models ($\log_{10}$-transformed) as a sensitivity analysis (eTable 2; http://links.lww.com/EE/A24): results were largely consistent with the quartile models. When examining cross-sectional models at each of the three study visits, the results were unchanged and consistent across the individual visits (eTable 2; http://links.lww.com/EE/A24).

Table 6 presents the group and conditional PIPs derived from the BKMR models for BMI. All three chemical exposure groups (OC pesticides, PBDEs, PCBs) were associated with BMI (each group PIP was >0.5). Within the pesticide group, β-HCH had the highest conditional PIP (93%), but *p,p′*-DDT was also associated with the outcome (6%). Within the PBDEs, PBDE-153 had the highest conditional PIP (51%), followed by PBDE-47 (23%). Within the PCBs, PCB-99 had the highest conditional PIP (52%), followed by PCB-180 (28%).

Figure 1 shows plots of the univariate exposure–response relationships from the BKMR analyses for BMI when all other chemical exposures in the mixture are held at their median values. For many chemicals, including positive associations with *p,p′*-DDT, PCB-74, and PCB-99 and inverse associations with PBDE-153 and PCB-180, the direction of the exposure–response curve was consistent with the results from single-pollutant models. However, some chemicals show different exposure–response

Table 3

Summary of persistent organic pollutant concentrations (ng/g lipid) measured in serum, CHAMACOS Study, Salinas, CA, 2009–2011.

Exposure	n	% Detect	% Quant.	Min	25%	Med	75%	Max	GM
p,p′-DDT	468	57.5	99.4	0.6	1.9	3.2	7.2	5,276.5	4.7
p,p′-DDE	467	100.0	100.0	5.8	128.8	229.6	519.8	55,836.0	291.2
HCB	467	64.0	99.8	1.2	7.2	9.8	14.4	121.4	10.1
B-HCH	466	63.7	76.3	0.1	2.1	5.2	13.5	764.6	5.3
Trans-nonachlor	467	69.8	99.8	0.6	2.5	3.9	6.7	263.4	4.1
PBDE-47	467	99.2	100.0	0.3	9.3	17.6	31.2	185.9	17.1
PBDE-99	467	93.4	98.9	0.2	1.7	3.2	6.4	119.9	3.3
PBDE-100	467	97.4	98.1	0.2	2.0	3.3	5.5	82.5	3.3
PBDE-153	467	99.4	99.6	0.3	2.4	3.7	5.8	124.8	3.9
PCB-28	462	96.1	99.4	0.2	7.0	12.7	22.2	163.3	11.8
PCB-74	456	76.1	92.3	0.2	0.5	0.8	1.1	7.6	0.8
PCB-99	463	81.0	96.8	0.1	0.6	0.9	1.3	4.7	0.9
PCB-118	461	95.7	99.6	0.3	0.9	1.3	2.0	18.5	1.4
PCB-138/158	463	97.4	98.7	0.4	1.4	2.2	3.3	15.5	2.2
PCB-153	462	98.9	100.0	0.4	1.9	3.0	4.6	26.1	3.0
PCB-170	462	82.5	94.8	0.2	0.6	0.9	1.5	10.2	1.0
PCB-180	462	98.7	100.0	0.3	1.4	2.2	3.5	25.2	2.3

β-HCH indicates β-hexachlorocyclohexane; CHAMACOS, Center for Health Assessment of Mothers and Children of Salinas; *p,p′*-DDE, *p,p′*-dichlorodiphenyldichloroethylene; *p,p′*-DDT, *p,p′*-dichlorodiphenyltrichloroethane; HCB, hexachlorobenzene; Max, maximum; Med, median; Min, minimum; PBDEs, polybrominated diphenyl ethers; PCBs, polychlorinated biphenyls.

Table 4

Results of generalized estimating equation models[a] for change in body mass index, waist circumference, and body fat percent by quartiles of persistent organic pollutant exposure concentrations, CHAMACOS Study, Salinas, CA, 2009–2014.

			Adjusted-β (95% CI)			
Exposure	**N**	**obs**	**Quartile 2[b]**	**Quartile 3**	**Quartile 4**	***P***
Body mass index						
p,p′-DDT	467	1,271	2.00 (0.45, 3.55)[c]	2.81 (1.21, 4.40)[d]	3.19 (1.51, 4.86)[d]	<0.01
p,p′-DDE	466	1,268	–1.40 (–2.95, 0.16)	–0.19 (–1.86, 1.48)	0.41 (–1.28, 2.10)	0.35
HCB	466	1,268	0.09 (–1.46, 1.64)	–0.09 (–1.70, 1.52)	0.82 (–0.82, 2.46)	0.40
β-HCH	465	1,265	0.39 (–1.09, 1.87)	2.50 (0.98, 4.02)[d]	3.61 (1.97, 5.24)[d]	<0.01
Trans-nonachlor	466	1,268	–0.16 (–1.80, 1.47)	–0.63 (–2.27, 1.00)	0.54 (–1.22, 2.31)	0.69
PBDE-47	466	1,268	0.37 (–1.11, 1.85)	0.77 (–0.83, 2.38)	1.89 (0.26, 3.52)[c]	0.02
PBDE-99	466	1,268	–0.05 (–1.55, 1.44)	0.89 (–0.71, 2.49)	1.05 (–0.52, 2.61)	0.11
PBDE-100	466	1,268	0.75 (–0.81, 2.30)	1.57 (0.03, 3.10)[c]	1.01 (–0.57, 2.58)	0.13
PBDE-153	466	1,268	–0.37 (–1.98, 1.24)	–1.98 (–3.39, –0.57)[d]	–2.78 (–4.39, –1.18)[d]	<0.01
PCB-28	461	1,253	–1.45 (–3.02, 0.12)	–1.04 (–2.71, 0.64)	0.35 (–1.35, 2.05)	0.61
PCB-74	455	1,240	0.98 (–0.45, 2.42)	0.93 (–0.74, 2.60)	2.05 (0.42, 3.68)[c]	0.02
PCB–99	462	1,256	0.12 (–1.39, 1.63)	1.38 (–0.34, 3.10)	2.38 (0.74, 4.02)[d]	<0.01
PCB-118	460	1,252	0.98 (–0.63, 2.58)	0.76 (–0.74, 2.27)	1.62 (–0.07, 3.30)	0.09
PCB-138/158	462	1,256	0.17 (–1.35, 1.69)	0.62 (–1.04, 2.28)	1.38 (–0.29, 3.05)	0.09
PCB-153	461	1,253	–0.42 (–1.99, 1.15)	0.44 (–1.21, 2.09)	0.52 (–1.19, 2.22)	0.38
PCB-170	461	1,253	–0.09 (–1.74, 1.55)	–1.26 (–2.84, 0.32)	–0.75 (–2.44, 0.94)	0.21
PCB-180	461	1,253	–0.84 (–2.45, 0.76)	–1.75 (–3.29, –0.20)[c]	–1.45 (–3.27, 0.38)	0.06
Waist circumference						
p,p′-DDT	466	1,263	5.71 (1.77, 9.65)[d]	6.34 (2.53, 10.15)[d]	6.72 (2.75, 10.69)[d]	<0.01
p,p′-DDE	465	1,260	–3.88 (–7.50, –0.26)[c]	–1.55 (–5.56, 2.46)	–1.02 (–4.97, 2.93)	0.95
HCB	465	1,260	0.44 (–3.46, 4.33)	–0.83 (–4.56, 2.89)	1.53 (–2.31, 5.38)	0.60
β-HCH	464	1,257	0.24 (–3.48, 3.96)	6.11 (2.44, 9.78)[d]	7.13 (3.36, 10.89)[d]	<0.01
Trans-nonachlor	465	1,260	-0.27 (–4.09, 3.55)	–0.39 (–4.38, 3.61)	1.27 (–2.89, 5.42)	0.58
PBDE-47	465	1,260	0.44 (–2.82, 3.70)	1.43 (–2.34, 5.20)	4.69 (0.67, 8.70)[c]	0.02
PBDE-99	465	1,260	–0.23 (–3.43, 2.96)	2.11 (–1.55, 5.76)	3.82 (–0.15, 7.79)	0.03
PBDE-100	465	1,260	1.89 (–1.57, 5.34)	3.77 (0.07, 7.47)[c]	2.42 (–1.31, 6.15)	0.13
PBDE-153	465	1,260	–1.00 (–4.78, 2.77)	–4.58 (–7.92, –1.23)[d]	–7.12 (–10.90, –3.34)[d]	<0.01
PCB-28	460	1,245	–2.92 (–6.49, 0.65)	–0.71 (–4.68, 3.26)	0.72 (–3.20, 4.64)	0.51
PCB-74	454	1,230	1.32 (–2.02, 4.66)	1.74 (–2.33, 5.81)	4.72 (0.73, 8.71)[c]	0.02
PCB-99	461	1,248	–0.82 (–4.21, 2.57)	4.14 (0.10, 8.17)[c]	5.18 (1.24, 9.12)[d]	<0.01
PCB-118	459	1,244	1.38 (–2.37, 5.13)	1.13 (–2.31, 4.57)	4.08 (–0.03, 8.18)	0.07
PCB-138/158	461	1,248	–0.32 (–3.85, 3.22)	1.26 (–2.52, 5.04)	3.86 (–0.26, 7.98)	0.05
PCB-153	460	1,245	–0.83 (–4.50, 2.83)	1.77 (–2.05, 5.58)	1.84 (–2.18, 5.85)	0.19
PCB-170	460	1,245	–0.25 (–4.11, 3.62)	–3.43 (–7.12, 0.26)	–1.80 (–5.80, 2.19)	0.18
PCB-180	460	1,245	–1.95 (–5.69, 1.79)	–4.61 (–8.25, –0.96)[c]	–3.70 (–8.02, 0.62)	0.04
Body fat percent						
p,p′-DDT	446	1,188	2.68 (0.90, 4.46)[d]	2.94 (1.11, 4.78)[d]	2.52 (0.55, 4.49)[c]	0.01
p,p′-DDE	445	1,185	–1.18 (–2.97, 0.60)	–0.47 (–2.39, 1.44)	–0.50 (–2.59, 1.58)	0.84
HCB	445	1,185	–0.05 (–1.93, 1.83)	0.22 (–1.65, 2.09)	0.83 (–1.21, 2.87)	0.40
β-HCH	444	1,185	0.17 (–1.71, 2.06)	4.19 (2.34, 6.03)[d]	4.40 (2.59, 6.22)[d]	<0.01
Trans-nonachlor	445	1,185	0.39 (–1.54, 2.33)	0.14 (–1.83, 2.11)	1.63 (–0.46, 3.72)	0.17
PBDE-47	445	1,185	0.61 (–1.06, 2.27)	0.26 (–1.64, 2.17)	1.56 (–0.22, 3.35)	0.13
PBDE-99	445	1,185	–0.33 (–2.02, 1.35)	0.05 (–1.76, 1.85)	0.41 (–1.34, 2.17)	0.58
PBDE-100	445	1,185	0.29 (–1.42, 2.01)	0.83 (–1.04, 2.70)	0.37 (–1.40, 2.13)	0.57
PBDE-153	445	1,185	–1.84 (–3.65, –0.04)[c]	–2.57 (–4.20, –0.93)[d]	–4.27 (–6.12, –2.43)[d]	<0.01
PCB-28	440	1,171	–1.54 (–3.30, 0.23)	–1.15 (–2.98, 0.69)	0.21 (–1.64, 2.05)	0.78
PCB-74	436	1,161	0.74 (–1.08, 2.55)	0.92 (–0.94, 2.78)	2.26 (0.25, 4.27)[c]	0.03
PCB-99	441	1,174	0.90 (–0.91, 2.71)	1.74 (–0.29, 3.77)	3.19 (1.34, 5.04)[d]	<0.01
PCB-118	439	1,170	1.44 (–0.53, 3.40)	1.27 (–0.59, 3.14)	2.29 (0.27, 4.32)[c]	0.04
PCB-138/158	441	1,174	0.35 (–1.59, 2.28)	1.38 (–0.56, 3.32)	2.22 (0.26, 4.17)[c]	0.02
PCB-153	440	1,171	0.04 (–1.94, 2.01)	0.92 (–1.03, 2.88)	1.79 (–0.22, 3.80)	0.06
PCB-170	440	1,171	0.00 (–1.91, 1.92)	–1.03 (–2.99, 0.92)	–0.07 (–2.05, 1.91)	0.69
PCB-180	440	1,171	–0.55 (–2.43, 1.33)	–1.66 (–3.63, 0.32)	–0.89 (–3.01, 1.24)	0.23

[a]All models adjusted for age, household income status, and years of residence in the United States.

[b]Reference category is lowest quartile (Quartile 1).

[c]$p<0.05$;

[d]$p<0.01$.

β-HCH indicates β-hexachlorocyclohexane; CHAMACOS, Center for Health Assessment of Mothers and Children of Salinas; *p,p′*-DDE, *p,p′*-dichlorodiphenyldichloroethylene; *p,p′*-DDT, *p,p′*-dichlorodiphenyltrichloroethane; HCB, hexachlorobenzene; Max, maximum; Med, median; Min, minimum; PBDEs, polybrominated diphenyl ethers; PCBs, polychlorinated biphenyls.

Table 5

Results of generalized estimating equations models for adjusted[a] relative risk of obese status by quartiles of persistent organic pollutant exposure concentrations, CHAMACOS Study, Salinas, CA, 2009–2014.

			Adjusted-RR (95% CI)			
Exposure	**N**	**obs**	**Quartile 2[b]**	**Quartile 3**	**Quartile 4**	***P***
p,p′-DDT	467	1,271	1.38 (1.08, 1.76)[c]	1.45 (1.13, 1.85)[d]	1.48 (1.16, 1.89)[d]	<0.01
p,p′-DDE	466	1,268	0.78 (0.61, 0.99)[c]	0.92 (0.74, 1.15)	1.00 (0.80, 1.25)	0.61
HCB	466	1,268	0.96 (0.77, 1.20)	0.91 (0.72, 1.15)	1.01 (0.81, 1.26)	0.93
β-HCH	465	1,265	0.99 (0.77, 1.27)	1.43 (1.11, 1.84)[d]	1.37 (1.06, 1.77)[c]	<0.01
Trans-nonachlor	466	1,268	1.07 (0.86, 1.33)	0.87 (0.68, 1.12)	1.07 (0.85, 1.36)	0.95
PBDE-47	466	1,268	1.00 (0.79, 1.27)	1.14 (0.91, 1.44)	1.29 (1.03, 1.60)[c]	0.02
PBDE-99	466	1,268	1.06 (0.84, 1.33)	1.10 (0.87, 1.38)	1.24 (0.99, 1.55)	0.06
PBDE-100	466	1,268	1.05 (0.83, 1.34)	1.23 (0.98, 1.54)	1.21 (0.96, 1.52)	0.05
PBDE-153	466	1,268	0.88 (0.72, 1.08)	0.83 (0.67, 1.02)	0.70 (0.56, 0.88)[d]	<0.01
PCB-28	461	1,253	0.97 (0.78, 1.21)	0.94 (0.75, 1.18)	1.08 (0.87, 1.33)	0.59
PCB-74	455	1,240	0.99 (0.80, 1.22)	0.91 (0.71, 1.17)	1.06 (0.84, 1.32)	0.79
PCB-99	462	1,256	1.12 (0.88, 1.42)	1.34 (1.05, 1.70)[c]	1.34 (1.06, 1.69)[c]	<0.01
PCB-118	460	1,252	1.07 (0.84, 1.36)	1.18 (0.94, 1.48)	1.11 (0.86, 1.42)	0.28
PCB-138/158	462	1,256	1.09 (0.87, 1.38)	1.03 (0.81, 1.31)	1.15 (0.90, 1.46)	0.36
PCB-153	461	1,253	1.00 (0.79, 1.27)	1.13 (0.90, 1.41)	1.05 (0.82, 1.34)	0.51
PCB-170	461	1,253	1.04 (0.84, 1.28)	0.89 (0.72, 1.12)	0.85 (0.67, 1.09)	0.11
PCB-180	461	1,253	0.95 (0.77, 1.17)	0.83 (0.67, 1.05)	0.78 (0.60, 1.00)	0.03

[a]All models adjusted for age, household income status, and years of residence in the United States.

[b]Reference category is lowest quartile (Quartile 1).

[c]$p<0.05$;

[d]$p<0.01$.

β-HCH indicates β-hexachlorocyclohexane; CHAMACOS, Center for Health Assessment of Mothers and Children of Salinas; *p,p′*-DDE, *p,p′*-dichlorodiphenyldichloroethylene; *p,p′*-DDT, *p,p′*-dichlorodiphenyltrichloroethane; HCB, hexachlorobenzene; Max, maximum; Med, median; Min, minimum; PBDEs, polybrominated diphenyl ethers; PCBs, polychlorinated biphenyls.

Table 6

Group and conditional posterior inclusion probabilities (PIP) derived from Bayesian Kernal Machine Regression model for continuous outcomes, CHAMACOS Study, Salinas, CA, 2009–2014.

	Body mass index		Waist circumference		Body fat percent	
Exposure	**Group[a] PIP**	**Conditional[b] PIP**	**Group[a] PIP**	**Conditional[b] PIP**	**Group[a] PIP**	**Conditional[b] PIP**
OC Pesticides	0.99		0.97		1.00	
p,p′-DDT		0.063		0.024		0.000
p,p′-DDE		0.003		0.007		0.000
HCB		0.005		0.015		0.000
β-HCH		0.928		0.948		1.000
Trans-nonachlor		0.001		0.006		0.000
PBDEs	0.91		0.95		0.98	
PBDE-47		0.225		0.187		0.015
PBDE-99		0.164		0.278		0.009
PBDE-100		0.097		0.146		0.001
PBDE-153		0.514		0.389		0.976
PCBs	0.90		0.91		0.82	
PCB-28		0.027		0.012		0.035
PCB-74		0.021		0.033		0.018
PCB-99		0.519		0.270		0.696
PCB-118		0.055		0.042		0.031
PCB-138/158		0.019		0.014		0.029
PCB-153		0.027		0.033		0.021
PCB-170		0.056		0.064		0.055
PCB-180		0.275		0.532		0.115

[a]Group PIP is posterior probability that the exposure group (e.g., PBDEs) was included in the "true" model based on multiple iterations (25,000) of the MCMC sampler. For example, across all BMI models, the PBDE group was included 91% of the time.

[b]Conditional PIP is posterior probability that a particular chemical exposure (e.g., PBDE-153) *within* an exposure group (e.g., PBDEs) was included in the "true" model based on multiple iterations (25,000) of the MCMC sampler, conditional on the exposure group being included. For example, across all BMI models that included the PBDE group, PBDE-153 was included 51% of the time.

β-HCH indicates β-hexachlorocyclohexane; CHAMACOS, Center for Health Assessment of Mothers and Children of Salinas; *p,p′*-DDE, *p,p′*-dichlorodiphenyldichloroethylene; *p,p′*-DDT, *p,p′*-dichlorodiphenyltrichloroethane; HCB, hexachlorobenzene; Max, maximum; Med, median; Min, minimum; PBDEs, polybrominated diphenyl ethers; PCBs, polychlorinated biphenyls.

relationships than in the single-pollutant models. For example, PBDE-47 showed a positive association in quartile models but a negative association in BKMR results. In addition, β-HCH showed evidence of a nonlinear relationship in both the single-pollutant and BKMR models.

The BKMR models also assessed the relative exposure–response relationship with BMI when all of the pollutants in the mixture are held at specified quantities. As indicated in Figure 2, as the exposure mixture increases incrementally for all chemicals, there is an apparent nonlinear increasing trend in BMI that becomes considerably stronger above the 75th percentile of exposure, suggesting a possible synergistic interaction of exposures in the mixture. The BKMR models also suggested interactions between several exposures and the overall mixture.

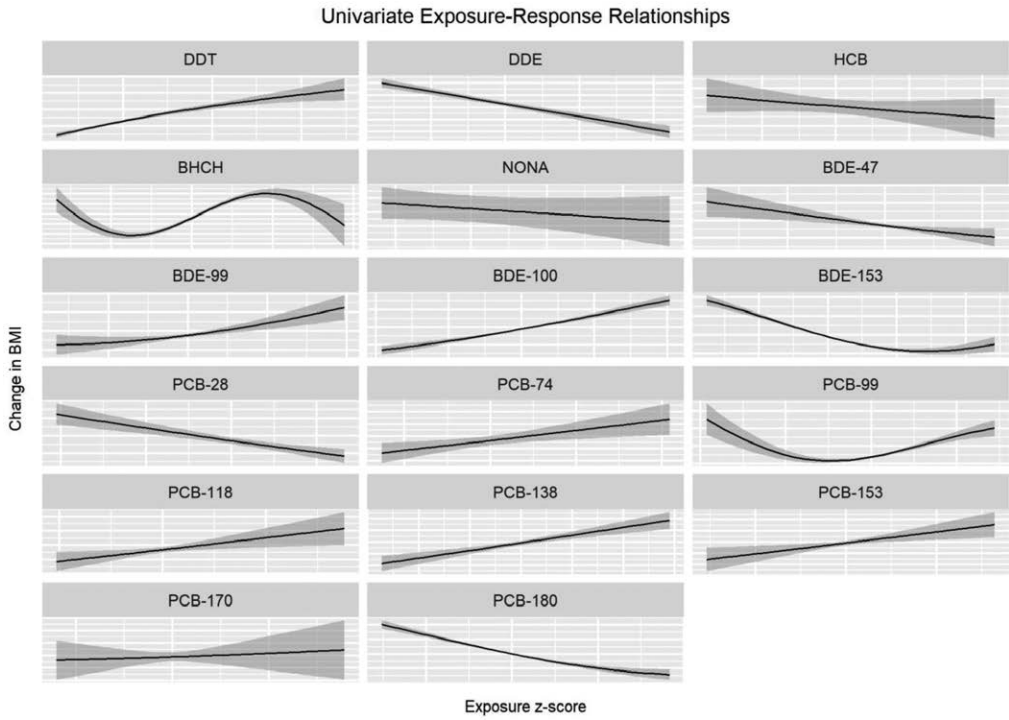

Figure 1. Plots of the univariate exposure–response relationships for chemical exposure and change in body mass index (BMI)[a] from Bayesian Kernel Machine Regression (BKMR) analyses while other chemicals are fixed at their median level, Center for Health Assessment of Mothers and Children of Salinas (CHAMACOS) Study, Salinas, CA, 2009–2014. [a]Y axis scales differ between exposures to capture the shape of each exposure–response curve.

Supplementary eFigure 2; http://links.lww.com/EE/A24 presents the change in BMI associated with an IQR change in a single chemical, while all other chemicals in the mixture are fixed at their 25th, 50th, and 75th percentiles. In particular, the inverse associations of PBDE-47 and PCB-180 with BMI were significantly stronger when the rest of the exposures were held at their 75th percentiles than at their 25th percentile. Likewise, *p,p′*-DDT appears to show no association with BMI with the mixture at low levels, but the association becomes significantly positive with the rest of the mixtures at high levels.

BKMR results for the other continuous outcomes were similar (see Table 6; eFigures 3–8; http://links.lww.com/EE/A24). Although PIPs generated for variable selection may be unstable with BKMR, we found that the relative ranking of PIPs is preserved across multiple runs of the analysis, consistent with observations previously made.[33] The BKMR results also

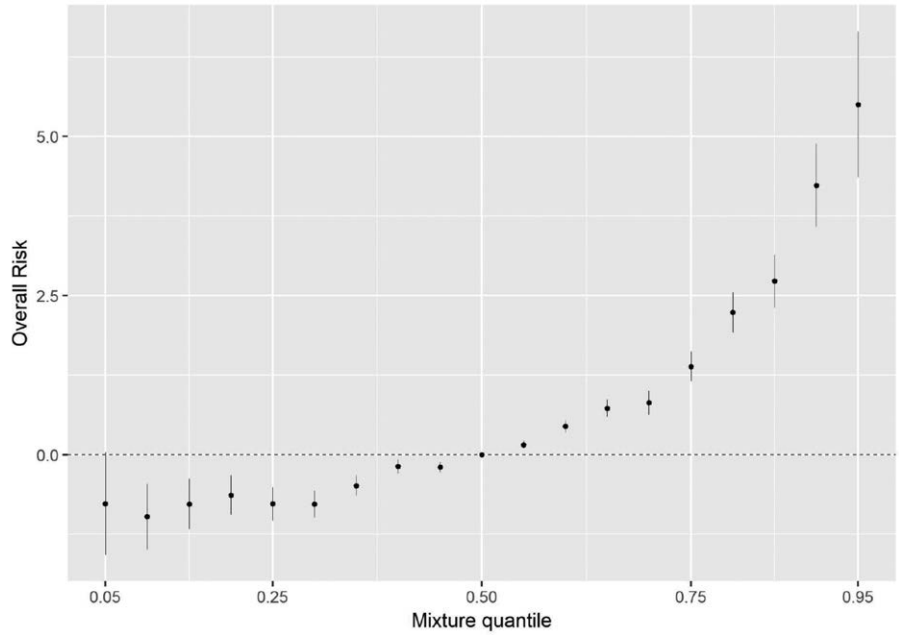

Figure 2. Overall effect of the chemical mixture (estimates and 95% credible intervals) on body mass index (BMI) estimated by Bayesian Kernel Machine Regression (BKMR). This figure plots the estimated change in BMI when chemical exposures are all at a particular percentile compared to when chemical exposures are all at the 50th percentile, Center for Health Assessment of Mothers and Children of Salinas (CHAMACOS) Study, Salinas, CA, 2009–2014.

suggested bivariate interactions between several pairs of POPs from different groups (data not shown); these interactions were not significant when examined in GEE models (data not shown).

Discussion

This study of predominantly Mexican-American women residing in a California agricultural community provides evidence that POPs exposure may alter the risk for obesity. We found significant associations of serum POPs with several measures of body weight and composition. Among OC pesticides, higher serum levels of *p,p′*-DDT and β-HCH were significantly associated with increased BMI and risk of obesity, as well as increased waist circumference and percent body fat. Among PBDEs, serum PBDE-47 concentrations were associated with increased BMI and risk of obesity, as well as waist circumference; in contrast, serum PBDE-153 concentrations were associated with decreased BMI and lower risk of obesity, decreased waist circumference, and lower body fat. Among PCBs, observed associations were more heterogeneous. Higher serum levels of PCB-180, however, were consistently associated with decreased BMI and waist circumference and lower risk of obesity.

Our findings are consistent with some, but not all, previous epidemiologic studies of individual POPs exposure and BMI and waist circumference. For example, serum *p,p′*-DDT concentrations were significantly positively associated with BMI and waist circumference in the US National Health and Nutrition Examination Survey (NHANES)[18] and the CARDIA study after 20 years of follow-up.[25] Positive associations of serum β-HCH concentrations with BMI, waist circumference, and fat mass percent have been reported in cross-sectional studies in Belgium[20] and Spain[22] but not in the only other prospective study.[25] Serum PBDE-47 concentrations, but not PBDE-153, were positively associated with BMI in the Michigan fish eaters study.[19] In contrast, PBDE-153 was associated with decreased BMI, while PBDE-47 concentration was not associated with BMI or waist circumference in NHANES.[23] In the PIVUS study, serum PBDE-47 was not associated with waist circumference, visceral (VAT) and subcutaneous (SAT) adipose tissue, or fat mass percent in cross-sectional or after 5 years of follow-up.[24,42,43] Finally, an inverse association between serum PCB-180 and BMI and waist circumference has also been reported in cross-sectional[20,21] and prospective studies.[24,25]

We found no associations of *p,p′*-DDE concentrations with any adiposity measure. Dirinck et al[20] also reported no association of serum *p,p′*-DDE with BMI, waist circumference, or fat mass percent. However, *p,p′*-DDE was significantly positively associated with BMI in two cross-sectional studies in Flanders and Spain.[21,22] In the PIVUS study, cross-sectional analysis suggested a significant positive association of serum *p,p′*-DDE with waist circumference, VAT and SAT, and fat mass percent, that was no longer significant after 5 years of follow-up.[24,42,43] In the only study that measured both *p,p′*-DDT and *p,p′*-DDE, Lee et al. reported a positive linear association of BMI with *p,p′*-DDT but a nonmonotonic dose response of BMI with *p,p′*-DDE.[25]

Differences in results across studies could be due to the variation in POPs exposure levels among study populations. Compared to the NHANES data for women of similar age, CHAMACOS women had lower concentrations of PCBs, similar concentrations of PBDEs, and higher concentrations of *p,p′*-DDT and *p,p′*-DDE (likely due to immigration from Mexico, where DDT was used until the year 2000).[14,44] Further, in NHANES pools, PBDE-47, PCB-153, and *p,p′*-DDE were the dominant POPs among PBDE, PCB, and OC pesticide groups, respectively.[15] In CHAMACOS women, they were slightly different; dominant POPs were PBDE-47, PCB-28, and *p,p′*-DDE.

We were able to consider exposure–response relationships in the context of the exposure mixture. We applied BKMR in an effort to disentangle independent associations among several co-exposures, many of which were highly correlated, and assess their combined effects on BMI. BKMR revealed the shape and direction of the exposure–response relationships, as well as interactions with the overall mixture, that could not be discovered by single-pollutant models. For instance, for PBDE-47, we observed a change in direction for the exposure–response relationship between the single- and multi-pollutant models (from positive to inverse). Moreover, the magnitude of the inverse exposure–response relationship for PBDE-47 increases as the overall mixture increases, suggesting mixture effects. In addition, the positive exposure–response for PBDE-47 in the conventional GEE regression model may be confounded by the presence of other chemicals not controlled for but which BKMR controls for to some extent. These results imply that the mixture of exposures needs to be considered to elucidate obesogenic effects of POPs exposure. Although BKMR is an exploratory analysis, it is a flexible way of estimating joint exposures in a mixture, as it does not assume a linear dose–response function and accounts for multiple testing by penalizing credible intervals. It also has potential to identify which chemical(s) in the mixture may be driving results. We found evidence that all three POPs groups were important contributors to BMI. Within the OC pesticide group, β-HCH and *p,p′*-DDT contributed, while within PBDEs both PBDE-153 and PBDE-47 contributed the most. Within the PCBs, PCB-99 and PCB-180 contributed most. Overall, we found that the results of BKMR mostly support our inference from single pollutant models. However, PBDE-47 showed a different direction of association across the single-pollutant and BKMR models.

BKMR can also be useful to suggest interactions between several exposures within different groups, thus reducing the number of comparisons to be made and the likelihood of false positives. BKMR did suggest several such pairs of exposures; however, conventional regression models did not show interactions. This highlights the differences between the two approaches but is not necessarily a weakness in either approach.

Various mechanisms of action are involved in chemical-induced adipogenesis, and the mechanisms are likely to differ between POPs compounds.[45] Although the biologic mechanisms underlying these findings are not clear, our results are biologically plausible. Experimental studies have demonstrated associations of individual POPs, including *p,p′*-DDT and PBDE-47, with adipocyte differentiation *in vitro*.[46–48] In animal studies, exposure to low doses of DDT or PBDE-47 is associated with increased weight gain,[49,50] and exposure to technical pentaBDE is associated with metabolic obesity.[51] Our finding that PBDE-153, unlike the other PBDE congeners, was associated with lower BMI and reduced risk of obesity is puzzling. That PBDE-153 has been shown to exhibit anti-estrogenic properties while the other congeners exhibit estrogenic properties offers a possible mechanism.[52,53]

Strengths of this study include the relatively large sample size and longitudinal design with serial measures over time. CHAMACOS is a homogeneous study population with a long follow-up period, yielding considerable information about potential confounders. Unlike other studies, we were able to consider several measures of adiposity (BMI, obese status, waist circumference, percent body fat), and the results provide evidence of obesogenic effects of POPs on additional obesity phenotypes (visceral adiposity, body fat).

While this study includes a fairly short follow-up period, there is potential for additional follow-up as part of future planned CHAMACOS study visits. This study population is well-suited to examine effects of POPs exposure on related adverse metabolic outcomes, including metabolic syndrome, diabetes, and nonalcoholic fatty liver disease. Given the relatively high prevalence of overweight in the study population, our findings may not be generalizable to the wider US population. A limitation of BKMR involves the grouped exposure option for variable

selection. Although the grouping method offers the benefit of exploring the relative importance of highly correlated exposures, which is also an important strength of BKMR's variable selection approach, it precludes exploration of chemical by chemical interactions between grouped exposures and thus presents an important limitation as well. In addition, we did not vary the prior specifications within BKMR and therefore cannot substantively speak to the impact that the mixture prior specification has on our results.

We see some apparent incongruity between the single-pollutant models and BKMR. In general, we view both methods as complimentary to one-another. The BKMR results are able to showcase aspects of the mixtures effects that GEE is less equipped to address, while at the same time allowing the reader to evaluate consistencies (or lack thereof) between the methods. A lack of consistency does not necessarily entail one method is superior to another or that one method should be given more weight. Rather, we suggest that a lack of consistency is possibly driven by underlying factors of the POPs mixture, which should prompt further examination such as using all of the available information provided from this analysis.

CONCLUSION

In summary, we found significant associations of serum POPs with several measures of body weight and composition, using both conventional regressions and BKMR, which produced largely consistent results. Our results provide support for the chemical obesogen hypothesis that exposure to EDCs may alter risk for later obesity.

Conflicts of interest statement

The authors declare that they have no conflicts of interest with regard to the content of this report.

Acknowledgments

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