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Supplemental Material

Associations of Prenatal Chemical and Nonchemical Stressors with Early-Adulthood Anxiety and Depressive Symptoms

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Table S1. List of psychotropic medications that New Bedford Cohort young adult participants reported taking on a regular basis on the early adult visit questionnaire

Medication names ^a
Alpeazolam, Xanax
Buspirone
Citalopram
Duloxetine
Fluoxetine, Prozac
Fluvoxamine
Klonopin
Lamotrigine
Lithium
Lexapro
Lorazepam, Ativan
Nortriptyline
Paroxetine
Remeron
Risperidone
Sertraline, Zoloft
Trazodone
Trileptal
Venlafaxine
Wellbutrin

^a Medications were reported on a free-response question; in cases where participants used different brand names for the same drug, we have grouped those together in this table

Table S2. Concordance between the race/ethnicity, prenatal social disadvantage index (PNSDI) score, and quality of childhood home environment groups, among 209 New Bedford Cohort young adult participants included in at least one complete case analysis

Sociodemographic or non-chemical stressor group	N (%)^a	N (%)^a
	Low PNSDI	High PNSDI
Non-Hispanic White	119 (84)	39 (57)
Underrepresented race/ethnicity ^b	22 (16)	29 (43)
High HOME score	101 (72)	15 (22)
Low HOME score	40 (28)	53 (78)
Sociodemographic or non-chemical stressor group	N (%)^a	N (%)^a
	High HOME score	Low HOME score
Non-Hispanic White	96 (83)	62 (67)
Underrepresented race/ethnicity ^b	20 (17)	31 (33)
Low PNSDI	101 (87)	40 (43)
High PNSDI	15 (13)	53 (57)
Sociodemographic or non-chemical stressor group	N (%)^a	N (%)^a
	Non-Hispanic White	Underrepresented race/ethnicity group
High HOME score	96 (61)	20 (39)
Low HOME score	62 (39)	31 (61)
Low PNSDI score	119 (75)	22 (43)
High PNSDI score	39 (25)	29 (57)

Abbreviation: HOME: Home Observation for Measurement of the Environment; PNSDI: prenatal social disadvantage index

^a Percent for the column

^b Of the 51 participants in the underrepresented racial/ethnic group, they were categorized as: 20 Cape Verdean, 18 Hispanic, 6 Black or African American, 4 Native American, 3 Asian American, and 2 Other race/ethnicity

Table S3. Sociodemographic, exposure, and outcome characteristics of New Bedford Cohort participants who completed the Generalized Anxiety Disorder Scale (GAD-7) and/or Patient Health Questionnaire (PHQ-8) at the early adult visit, and that were included versus excluded in the complete case analytic cohort

	Completed GAD-7 and/or PHQ-8 (n=240)		Included in any complete case analysis (n=209)		Excluded from any complete case analysis (n=579)	
	Mean \pm SD or N (%)	N	Mean \pm SD or N (%)	N	Mean \pm SD or N (%)	N
Parental and household characteristics						
High PNSDI (≥ 3 on 0-5 scale)	81 ^a (34)	235	68 ^a (33)	209	237 (47)	503
Maternal age at child's birth <20 years ^a	28 (12)	240	24 (11)	209	82 (14)	579
Maternal high school graduate or less ^a	119 (51)	235	101 (49)	208	320 (61)	523
Paternal high school graduate or less ^a	150 (64)	234	131 (63)	207	381 (74)	513
Annual household income <\$20,000 ^a	74 (31)	237	64 (31)	209	201 (39)	515
Not married at birth ^a	84 (35)	237	68 (33)	209	263 (50)	524
Maternal prenatal smoking	60 (26)	227	53 (25)	209	151 (32)	477
Low HOME score [<median (45) on 0-60 scale]	100 ^b (46)	218	93 ^b (45)	209	172 (58)	298
Obstetrical risk score	14.8 \pm 10.2	240	14.6 \pm 10.1	209	15.8 \pm 10.8	579
Participant characteristics						
Age at GAD-7 and PHQ-8 assessment	22.1 \pm 1.6	240	22.1 \pm 1.5	209		
Female	160 (67)	240	139 (67)	209	241 (42)	579
Underrepresented racial/ethnic group	62 (26)	240	51 (24)	209	204 (35)	577
Birth weight (grams)	3396 \pm 414	240	3417 \pm 415	209	3383 \pm 468	578
Gestational age at birth (weeks)	39.6 \pm 1.1	239	39.6 \pm 1.1	208	39.6 \pm 1.2	579
Chemical biomarker levels						
Cord serum HCB (ng/g)	0.03 \pm 0.02	234	0.03 \pm 0.02	204	0.03 \pm 0.04	547
Cord serum p,p'-DDE (ng/g)	0.46 \pm 0.73	234	0.48 \pm 0.77	204	0.48 \pm 0.99	547
Cord serum Σ PCB ₄ (ng/g)	0.27 \pm 0.38	234	0.28 \pm 0.40	204	0.24 \pm 0.24	547
Cord blood Pb (μ g/dL)	1.54 \pm 1.58	228	1.43 \pm 1.12	198	1.57 \pm 1.46	550
Peak early childhood Pb (μ g/dL) ^c	6.60 \pm 3.76	206	6.56 \pm 3.79	193	6.92 \pm 4.01	383
Cord blood Mn (μ g/dL)	4.36 \pm 1.82	220	4.30 \pm 1.67	193	4.24 \pm 1.86	516

Early adulthood internalizing outcomes						
GAD-7 score (0-21)	5.8 ± 4.1	239	5.6 ± 4.1	208	7.1 ± 3.9	31
PHQ-8 score (0-24)	6.4 ± 5.7	239	6.4 ± 5.7	209	6.6 ± 5.6	30
Moderately elevated GAD-7 symptoms (≥10)	50 (21)	239	40 (19)	208	10 (32)	31
Moderately elevated PHQ-8 symptoms (≥10)	58 (24)	239	51 (24)	209	7 (23)	30
Psychotropic medication use	20 (11)	188	15 (9)	164	6 (11)	57
Diagnosis of an anxiety disorder	56 (28)	199	42 (25)	172	18 (27)	66
Diagnosis of depression	44 (22)	199	36 (21)	172	13 (20)	66

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Mn: manganese; Pb: lead; Σ PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; p,p'-DDE: dichlorodiphenyldichloroethylene; PNSDI: prenatal social disadvantage index; SD: standard deviation

^a These parental and household characteristics contribute towards the total score for the prenatal social disadvantage index (PNSDI); for 3 participants (in complete case analysis) who were missing one of the parental and household characteristics, the PNSDI score was weighted (i.e., multiplied by 5/4)

^b For 16 participants (in the complete case analysis) who were missing the HOME score at the 15-year assessment, the HOME score from the 8-year assessment was used

^c Peak early childhood blood lead levels from ages 12 to 36 months

Table S4. Overall and strata-specific sample sizes and prevalence of moderately elevated anxiety symptoms [Generalized Anxiety Disorder scale (GAD-7)] and depressive symptoms [Patient Health Questionnaire (PHQ-8)] in complete case single-chemical models

Internalizing symptoms GAD-7 (Anxiety)	Organochlorines (HCB, p,p'-DDE, Σ PCB ₄)		Pb		Mn	
	N (%)	N (%) ^a Cases	N (%)	N (%) ^a Cases	N (%)	N (%) ^a Cases
Total	203	39 (19)	197	37 (19)	192	36 (19)
Sex-stratified						
Female	134 (66)	29 (22)	132 (67)	28 (21)	129 (67)	28 (22)
Male	69 (34)	10 (14)	65 (33)	9 (14)	63 (33)	8 (13)
Race/ethnicity-stratified						
Underrepresented group	50 (25)	15 (30)	48 (24)	15 (31)	47 (24)	14 (30)
Non-Hispanic White	153 (75)	24 (16)	149 (76)	22 (15)	145 (76)	22 (15)
PNSDI-stratified						
High (≥ 3)	65 (32)	20 (31)	66 (34)	21 (32)	66 (34)	21 (32)
Low (<3)	138 (68)	19 (14)	131 (67)	16 (12)	126 (66)	15 (12)
HOME-stratified						
Low (<45)	91 (45)	23 (25)	88 (45)	24 (27)	86 (45)	23 (27)
High (≥ 45)	112 (55)	16 (14)	109 (55)	13 (12)	106 (55)	13 (12)
PHQ-8 (Depressive)	Organochlorines (HCB, p,p'-DDE, Σ PCB ₄)		Pb		Mn	
	N (%)	N (%) ^a Cases	N (%)	N (%) ^a Cases	N (%)	N (%) ^a Cases
Total	204	49 (24)	198	48 (24)	193	47 (24)
Sex-stratified						
Female	135 (66)	36 (27)	133 (67)	36 (27)	130 (67)	36 (28)
Male	69 (34)	13 (19)	65 (33)	12 (18)	63 (33)	11 (17)
Race/ethnicity-stratified						
Underrepresented group	51 (25)	17 (33)	49 (25)	16 (33)	48 (25)	15 (31)
Non-Hispanic White	153 (75)	32 (21)	149 (75)	32 (21)	145 (75)	32 (22)
PNSDI-stratified						
High (≥ 3)	66 (32)	25 (38)	67 (34)	26 (39)	67 (35)	26 (39)
Low (<3)	138 (68)	24 (17)	131 (66)	22 (17)	126 (65)	21 (17)
HOME-stratified						
Low (<45)	92 (45)	32 (35)	89 (45)	31 (35)	87 (45)	30 (34)
High (≥ 45)	112 (55)	17 (15)	109 (55)	17 (16)	106 (55)	17 (16)

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Mn: manganese; Pb: lead; Σ PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; p,p'-DDE: dichlorodiphenyldichloroethylene; PNSDI: prenatal social disadvantage index

^a Percent of elevated symptom cases in specific strata (by row)

Table S5. Concordance between 1) elevated anxiety symptoms identified on the Generalized Anxiety Disorder scale (GAD-7) and elevated depressive symptoms identified on the Patient Health Questionnaire (PHQ-8); and 2) self-report physician diagnosed (in the past 10 years) anxiety or depression, among young adult New Bedford Cohort participants included in at least one complete case analysis ^{a, b, c}

	N (%)^d	N (%)^d	
	GAD-7 score <10	GAD-7 score ≥10	Total
PHQ-8 score <10	150 (89)	7 (18)	157 (75)
PHQ-8 score ≥10	18 (11)	33 (83)	51 (25)
Total	168	40	208 ^a
	N (%)^d	N (%)^d	
	GAD-7 score <10	GAD-7 score ≥10	Total
No self-reported diagnosed anxiety disorder	115 (83)	13 (39)	128 (75)
Self-reported diagnosed anxiety disorder	23 (17)	20 (61)	43 (25)
Total	138	33	171 ^{b, c}
	N (%)^d	N (%)^d	
	PHQ-8 score <10	PHQ-8 score ≥10	Total
No self-reported diagnosed depression	115 (88)	21 (50)	136 (79)
Self-reported diagnosed depression	15 (12)	21 (50)	36 (21)
Total	130	42	172 ^b

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; PHQ-8: Patient Health Questionnaire

^a Of the 209 participants included in the analytic cohort, 208 had both a GAD-7 and PHQ-8 score

^b When comparing GAD-7 and PHQ-8 scores with self-reported medical diagnosis on the early adult assessment, 172 participants had data available on medical diagnosis information

^c Of the 172 participants who have self-reported medical diagnosis information, only 171 individuals had corresponding data for the GAD-7

^d Percent for the column

Table S6. Adjusted ^a overall and stratified ^b risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of chemical in single-exposure models, among New Bedford Cohort participants

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling chemical level				
	GAD-7 (Anxiety)	HCB (n=203)	p,p'-DDE (n=203)	∑PCB₄ (n=203)	Pb (n=197)
Total	1.31 (0.89, 1.92)	1.19 (0.89, 1.59)	0.97 (0.76, 1.24)	1.41 (1.03, 1.94)	0.99 (0.58, 1.71)
Sex-stratified					
Female	1.31 (0.89, 1.94)	1.20 (0.84, 1.71)	1.01 (0.76, 1.34)	1.24 (0.86, 1.78)	1.11 (0.59, 2.07)
Male	1.30 (0.53, 3.18)	1.17 (0.76, 1.80)	0.83 (0.53, 1.31)	2.22 (1.18, 4.16)	0.71 (0.25, 2.04)
p _{interaction}	0.99	0.94	0.49	0.09	0.49
Race/ethnicity-stratified					
Underrepresented group	1.86 (1.18, 2.95)	1.39 (0.97, 1.97)	1.03 (0.69, 1.53)	1.47 (0.86, 2.50)	0.96 (0.48, 1.90)
Non-Hispanic White	1.07 (0.66, 1.72)	1.04 (0.63, 1.73)	0.93 (0.68, 1.27)	1.37 (0.97, 1.96)	1.03 (0.45, 2.37)
p _{interaction}	0.10	0.36	0.69	0.83	0.89
PNSDI-stratified					
High (≥3)	1.22 (0.69, 2.16)	0.93 (0.59, 1.47)	0.62 (0.43, 0.91)	1.24 (0.84, 1.83)	1.16 (0.61, 2.22)
Low (<3)	1.42 (0.88, 2.31)	1.35 (0.98, 1.86)	1.33 (0.92, 1.91)	1.88 (1.14, 3.10)	0.66 (0.23, 1.84)
p _{interaction}	0.69	0.19	0.004	0.18	0.37
HOME-stratified					
Low (<45)	1.32 (0.75, 2.33)	0.77 (0.51, 1.16)	0.78 (0.58, 1.05)	1.30 (0.89, 1.90)	1.00 (0.54, 1.84)
High (≥45)	1.28 (0.81, 2.03)	1.54 (1.20, 1.99)	1.23 (0.80, 1.90)	1.78 (1.07, 2.94)	0.99 (0.31, 3.19)
p _{interaction}	0.94	0.01	0.09	0.31	0.99
PHQ-8 (Depressive)	HCB (n=204)	p,p'-DDE (n=204)	∑PCB₄ (n=204)	Pb (n=198)	Mn (n=193)
Total	1.10 (0.84, 1.45)	1.08 (0.83, 1.39)	0.93 (0.76, 1.14)	1.18 (0.91, 1.53)	0.82 (0.52, 1.32)
Sex-stratified					
Female	1.21 (0.88, 1.65)	1.03 (0.73, 1.46)	0.95 (0.75, 1.20)	1.17 (0.88, 1.56)	0.95 (0.55, 1.64)
Male	0.94 (0.64, 1.38)	1.19 (0.84, 1.69)	0.88 (0.59, 1.30)	1.21 (0.68, 2.14)	0.53 (0.21, 1.34)
p _{interaction}	0.31	0.58	0.75	0.92	0.29
Race/ethnicity-stratified					
Underrepresented group	1.26 (0.81, 1.97)	1.12 (0.80, 1.57)	0.96 (0.66, 1.38)	1.14 (0.71, 1.85)	0.70 (0.36, 1.36)
Non-Hispanic White	1.04 (0.75, 1.43)	1.06 (0.73, 1.52)	0.91 (0.71, 1.17)	1.20 (0.90, 1.59)	0.93 (0.48, 1.80)
p _{interaction}	0.49	0.85	0.85	0.87	0.56
PNSDI-stratified					
High (≥3)	0.97 (0.70, 1.35)	0.76 (0.53, 1.10)	0.64 (0.46, 0.90)	0.85 (0.58, 1.25)	0.78 (0.46, 1.33)
Low (<3)	1.29 (0.89, 1.88)	1.30 (0.99, 1.70)	1.20 (0.90, 1.61)	1.99 (1.34, 2.98)	0.93 (0.36, 2.43)
p _{interaction}	0.26	0.02	0.01	0.002	0.75
HOME-stratified					
Low (<45)	1.03 (0.73, 1.45)	0.92 (0.66, 1.29)	0.85 (0.67, 1.09)	0.96 (0.68, 1.37)	0.79 (0.48, 1.29)
High (≥45)	1.27 (0.84, 1.89)	1.25 (0.92, 1.70)	1.04 (0.71, 1.53)	1.85 (1.22, 2.81)	0.93 (0.32, 2.67)
p _{interaction}	0.44	0.20	0.40	0.02	0.79

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Mn: manganese; Pb: lead; Σ PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; $p_{\text{interaction}}$: p-value for interaction term between prenatal chemical biomarker and sociodemographic/non-chemical stressor; p,p'-DDE: dichlorodipenyldichloroethylene; PNSDI: prenatal social disadvantage index

^a Adjusted for parental and household characteristics (prenatal social disadvantage index, maternal smoking during pregnancy, Home Observation for Measurement of the Environment score) and participant characteristics (sex, race/ethnicity, age at assessment)

^b For each outcome and chemical, risk ratios were estimated from five models: one with no interaction term and four including a product interaction term between the chemical and each of the four specified other stressors

Table S7. Unadjusted overall risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of chemical in single-exposure models, among New Bedford Cohort participants

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling chemical level				
	HCB (<i>n</i> =203)	p,p'-DDE (<i>n</i> =203)	∑PCB ₄ (<i>n</i> =203)	Pb (<i>n</i> =197)	Mn (<i>n</i> =192)
GAD-7 (Anxiety)	1.17 (0.80, 1.71)	1.13 (0.85, 1.50)	0.94 (0.73, 1.22)	1.51 (1.14, 2.01)	1.30 (0.72, 2.33)
PHQ-8 (Depressive)	1.01 (0.76, 1.34)	1.01 (0.79, 1.30)	0.91 (0.74, 1.12)	1.30 (1.01, 1.68)	1.05 (0.63, 1.73)

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; Mn: manganese; Pb: lead; ∑PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; p,p'-DDE: dichlorodipenyldichloroethylene

Table S8. Adjusted ^a strata-specific (calculated by running models in stratified datasets) ^b risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of chemical in single-exposure models, among New Bedford Cohort participants

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling chemical level				
	HCB	p,p'-DDE	∑PCB ₄	Pb	Mn
GAD-7 (Anxiety)					
Sex-stratified					
Female	1.21 (0.84, 1.75)	1.20 (0.83, 1.76)	0.98 (0.75, 1.29)	1.33 (0.96, 1.85)	1.21 (0.65, 2.25)
Male	1.30 (0.59, 2.85)	1.17 (0.76, 1.81)	0.85 (0.58, 1.25)	2.38 (1.32, 4.29)	0.75 (0.32, 1.75)
Race/ethnicity-stratified					
Underrepresented group	1.56 (1.06, 2.31)	1.22 (0.87, 1.71)	1.02 (0.68, 1.53)	1.39 (0.85, 2.29)	1.00 (0.47, 2.10)
Non-Hispanic White	1.04 (0.64, 1.69)	1.07 (0.62, 1.85)	0.94 (0.67, 1.30)	1.37 (1.01, 1.85)	0.94 (0.41, 2.19)
PNSDI-stratified					
High (≥3)	1.19 (0.74, 1.92)	0.93 (0.60, 1.45)	0.63 (0.43, 0.91)	1.27 (0.86, 1.87)	1.20 (0.61, 2.33)
Low (<3)	1.40 (0.86, 2.28)	1.34 (0.95, 1.91)	1.31 (0.92, 1.87)	2.14 (1.21, 3.77)	0.68 (0.21, 2.22)
HOME-stratified					
Low (<45)	1.26 (0.74, 2.17)	0.76 (0.51, 1.15)	0.79 (0.58, 1.07)	1.31 (0.91, 1.87)	1.04 (0.55, 1.97)
High (≥45)	1.31 (0.83, 2.09)	1.50 (1.11, 2.02)	1.27 (0.86, 1.86)	1.94 (1.10, 3.45)	0.77 (0.23, 2.56)
PHQ-8 (Depressive)					
Sex-stratified					
Female	1.18 (0.87, 1.61)	1.03 (0.72, 1.48)	0.94 (0.75, 1.17)	1.27 (0.97, 1.65)	1.00 (0.59, 1.70)
Male	0.91 (0.63, 1.32)	1.26 (0.87, 1.81)	0.79 (0.54, 1.15)	1.17 (0.71, 1.91)	0.62 (0.24, 1.61)
Race/ethnicity-stratified					
Underrepresented group	1.01 (0.61, 1.65)	0.95 (0.70, 1.31)	0.87 (0.61, 1.24)	1.02 (0.67, 1.56)	0.65 (0.32, 1.31)
Non-Hispanic White	1.05 (0.75, 1.47)	1.09 (0.74, 1.61)	0.94 (0.72, 1.22)	1.22 (0.94, 1.58)	0.86 (0.44, 1.67)
PNSDI-stratified					
High (≥3)	0.94 (0.69, 1.29)	0.74 (0.50, 1.10)	0.66 (0.45, 0.95)	0.85 (0.59, 1.23)	0.75 (0.45, 1.26)
Low (<3)	1.31 (0.88, 1.94)	1.23 (0.94, 1.62)	1.24 (0.92, 1.66)	2.14 (1.38, 3.32)	0.89 (0.32, 2.48)
HOME-stratified					
Low (<45)	1.03 (0.74, 1.41)	0.94 (0.66, 1.34)	0.87 (0.68, 1.12)	0.97 (0.70, 1.36)	0.78 (0.48, 1.26)
High (≥45)	1.26 (0.84, 1.87)	1.15 (0.84, 1.57)	1.03 (0.74, 1.44)	2.12 (1.36, 3.32)	0.82 (0.26, 2.53)

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Mn: manganese; Pb: lead; ∑PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; p,p'-DDE: dichlorodiphenyldichloroethylene; PNSDI: prenatal social disadvantage index

^a Adjusted for parental and household characteristics (prenatal social disadvantage index, maternal smoking during pregnancy, Home Observation for Measurement of the Environment score) and participant characteristics (sex, race/ethnicity, age at assessment)

^b Main effect estimates from models run in datasets stratified by specific dichotomized sociodemographic/non-chemical stressor

Table S9. Adjusted ^a overall and stratified ^b risk ratios (95% confidence intervals) for self-report physician diagnosed (in the past 10 years) anxiety or depression at the early adult assessment associated with a doubling of chemical in single-exposure models among New Bedford Cohort participants (*n*=161-167)

Diagnosis in past 10 years	Risk ratio (95% confidence interval) per doubling chemical level				
	HCB (<i>n</i>=167)	p,p'-DDE (<i>n</i>=167)	∑PCB₄ (<i>n</i>=167)	Pb (<i>n</i>=163)	Mn (<i>n</i>=161)
Anxiety disorder					
Total	1.01 (0.72, 1.43)	1.15 (0.93, 1.43)	0.99 (0.81, 1.21)	1.20 (0.90, 1.61)	1.14 (0.69, 1.88)
Sex-stratified					
Female	1.02 (0.74, 1.42)	1.14 (0.88, 1.48)	0.97 (0.78, 1.21)	1.11 (0.81, 1.51)	1.14 (0.66, 1.96)
Male	0.98 (0.35, 2.73)	1.18 (0.78, 1.80)	1.07 (0.59, 1.93)	1.78 (0.98, 3.24)	1.13 (0.33, 3.87)
p _{interaction}	0.93	0.90	0.77	0.15	1.00
Race/ethnicity-stratified					
Underrepresented group	1.36 (0.90, 2.07)	1.27 (1.01, 1.60)	0.98 (0.77, 1.26)	1.22 (0.80, 1.85)	0.71 (0.35, 1.40)
Non-Hispanic White	0.83 (0.55, 1.26)	0.99 (0.64, 1.53)	0.99 (0.73, 1.36)	1.20 (0.81, 1.76)	1.69 (0.82, 3.50)
p _{interaction}	0.10	0.32	0.96	0.95	0.09
PNSDI-stratified					
High (≥3)	0.97 (0.49, 1.92)	1.02 (0.62, 1.67)	0.75 (0.51, 1.09)	1.12 (0.71, 1.77)	1.10 (0.51, 2.35)
Low (<3)	1.04 (0.73, 1.48)	1.20 (0.95, 1.53)	1.11 (0.87, 1.42)	1.28 (0.89, 1.86)	1.18 (0.60, 2.30)
p _{interaction}	0.87	0.55	0.09	0.65	0.89
HOME-stratified					
Low (<45)	0.94 (0.52, 1.69)	0.77 (0.53, 1.10)	0.75 (0.55, 1.01)	1.07 (0.66, 1.73)	0.91 (0.44, 1.87)
High (≥45)	1.07 (0.73, 1.58)	1.38 (1.07, 1.78)	1.19 (0.90, 1.57)	1.34 (0.93, 1.93)	1.50 (0.75, 3.02)
p _{interaction}	0.71	0.01	0.02	0.47	0.32
Depression					
Total	0.95 (0.65, 1.40)	1.13 (0.85, 1.50)	1.02 (0.79, 1.31)	1.15 (0.82, 1.62)	0.81 (0.46, 1.44)
Sex-stratified					
Female	0.98 (0.67, 1.45)	1.18 (0.83, 1.66)	1.02 (0.77, 1.34)	1.03 (0.70, 1.51)	0.84 (0.44, 1.62)
Male	0.87 (0.38, 1.99)	1.02 (0.61, 1.68)	1.04 (0.56, 1.92)	1.94 (0.98, 3.85)	0.71 (0.21, 2.36)
p _{interaction}	0.80	0.64	0.95	0.11	0.81
Race/ethnicity-stratified					
Underrepresented group	1.16 (0.67, 2.02)	1.30 (0.93, 1.80)	0.98 (0.68, 1.41)	1.05 (0.62, 1.80)	0.45 (0.18, 1.13)
Non-Hispanic White	0.85 (0.55, 1.33)	0.92 (0.56, 1.53)	1.06 (0.73, 1.53)	1.22 (0.80, 1.87)	1.20 (0.54, 2.68)
p _{interaction}	0.38	0.26	0.77	0.67	0.12
PNSDI-stratified					
High (≥3)	1.00 (0.52, 1.93)	0.93 (0.52, 1.67)	0.70 (0.46, 1.05)	0.96 (0.57, 1.62)	1.13 (0.52, 2.45)
Low (<3)	0.91 (0.57, 1.44)	1.24 (0.89, 1.72)	1.26 (0.89, 1.77)	1.41 (0.86, 2.32)	0.53 (0.23, 1.21)
p _{interaction}	0.82	0.41	0.03	0.29	0.20
HOME-stratified					
Low (<45)	0.92 (0.53, 1.60)	0.67 (0.45, 1.00)	0.71 (0.51, 1.00)	0.86 (0.48, 1.55)	0.77 (0.35, 1.69)
High (≥45)	0.99 (0.59, 1.65)	1.51 (1.08, 2.11)	1.42 (0.95, 2.12)	1.58 (0.96, 2.62)	0.87 (0.36, 2.11)
p _{interaction}	0.85	0.002	0.01	0.12	0.84

Abbreviations: HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Mn: manganese; Pb: lead; \sum PCB₄: sum of four polychlorinated biphenyl congeners; $p_{\text{interaction}}$: p-value for interaction term between prenatal chemical biomarker and sociodemographic/non-chemical stressor; p,p'-DDE: dichlorodiphenyldichloroethylene; PNSDI: prenatal social disadvantage index

^a Adjusted for parental and household characteristics (prenatal social disadvantage index, maternal smoking during pregnancy, Home Observation for Measurement of the Environment score) and participant characteristics (sex and race/ethnicity)

^b For each outcome and chemical, risk ratios were estimated from five models: one with no interaction term and four including a product interaction term between the chemical and each of the four specified other stressors

Table S10. Inverse probability of censoring weighted (IPCW) ^a adjusted ^b overall and stratified ^c risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of chemical in single-exposure models, among New Bedford Cohort participants

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling chemical level				
GAD-7 (Anxiety)	HCB (n=189)	p,p'-DDE (n=189)	∑PCB₄ (n=189)	Pb (n=189)	Mn (n=184)
Total	1.43 (0.91, 2.23)	1.14 (0.88, 1.47)	0.89 (0.70, 1.13)	1.45 (1.05, 2.01)	0.92 (0.55, 1.55)
Sex-stratified					
Female	1.32 (0.87, 2.01)	0.94 (0.59, 1.50)	0.88 (0.66, 1.19)	1.04 (0.67, 1.62)	0.96 (0.49, 1.88)
Male	1.51 (0.69, 3.33)	1.32 (0.98, 1.78)	0.90 (0.60, 1.34)	2.03 (1.22, 3.38)	0.89 (0.37, 2.16)
p _{interaction}	0.78	0.23	0.95	0.03	0.90
Race/ethnicity-stratified					
Underrepresented group	2.18 (1.49, 3.18)	1.34 (0.98, 1.84)	0.99 (0.69, 1.42)	1.67 (1.04, 2.67)	0.93 (0.49, 1.78)
Non-Hispanic White	0.94 (0.58, 1.54)	0.82 (0.51, 1.33)	0.78 (0.57, 1.06)	1.14 (0.73, 1.78)	0.91 (0.38, 2.17)
p _{interaction}	0.01	0.10	0.35	0.21	0.96
PNSDI-stratified					
High (≥3)	1.35 (0.77, 2.38)	1.19 (0.85, 1.67)	0.73 (0.51, 1.03)	1.26 (0.84, 1.88)	1.01 (0.55, 1.85)
Low (<3)	1.65 (0.96, 2.85)	1.08 (0.73, 1.59)	1.15 (0.76, 1.72)	2.05 (1.24, 3.39)	0.62 (0.24, 1.60)
p _{interaction}	0.62	0.72	0.08	0.12	0.40
HOME-stratified					
Low (<45)	1.37 (0.74, 2.54)	0.89 (0.61, 1.30)	0.82 (0.61, 1.11)	1.27 (0.84, 1.91)	0.85 (0.48, 1.51)
High (≥45)	1.56 (1.00, 2.45)	1.44 (1.08, 1.92)	1.00 (0.65, 1.55)	1.97 (1.22, 3.17)	1.21 (0.38, 3.85)
p _{interaction}	0.74	0.05	0.47	0.16	0.59
PHQ-8 (Depressive)	HCB (n=190)	p,p'-DDE (n=190)	∑PCB₄ (n=190)	Pb (n=190)	Mn (n=185)
Total	1.12 (0.83, 1.52)	1.04 (0.83, 1.32)	0.86 (0.70, 1.07)	1.06 (0.80, 1.41)	0.77 (0.48, 1.23)
Sex-stratified					
Female	1.23 (0.89, 1.72)	0.89 (0.61, 1.28)	0.86 (0.66, 1.12)	1.01 (0.70, 1.44)	0.95 (0.52, 1.71)
Male	1.05 (0.70, 1.59)	1.20 (0.89, 1.63)	0.86 (0.61, 1.23)	1.12 (0.70, 1.78)	0.60 (0.27, 1.34)
p _{interaction}	0.56	0.22	0.98	0.74	0.38
Race/ethnicity-stratified					
Underrepresented group	1.45 (0.94, 2.24)	1.17 (0.85, 1.62)	0.93 (0.63, 1.37)	1.14 (0.73, 1.78)	0.63 (0.33, 1.21)
Non-Hispanic White	0.95 (0.71, 1.29)	0.91 (0.65, 1.27)	0.81 (0.62, 1.06)	0.98 (0.68, 1.40)	0.95 (0.45, 2.01)
p _{interaction}	0.14	0.28	0.60	0.61	0.43
PNSDI-stratified					
High (≥3)	1.04 (0.73, 1.48)	0.88 (0.61, 1.27)	0.63 (0.43, 0.93)	0.66 (0.44, 1.00)	0.71 (0.41, 1.24)
Low (<3)	1.33 (0.89, 1.98)	1.20 (0.91, 1.58)	1.14 (0.84, 1.56)	2.01 (1.34, 3.01)	0.95 (0.37, 2.43)
p _{interaction}	0.37	0.19	0.02	0.0002	0.61
HOME-stratified					
Low (<45)	1.10 (0.75, 1.62)	1.04 (0.74, 1.46)	0.83 (0.64, 1.09)	0.86 (0.58, 1.26)	0.74 (0.45, 1.22)
High (≥45)	1.18 (0.80, 1.74)	1.05 (0.76, 1.45)	0.91 (0.62, 1.33)	1.62 (1.01, 2.61)	0.88 (0.27, 2.89)
p _{interaction}	0.82	0.96	0.73	0.05	0.79

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; IPCW: inverse probability of censoring weighting; Mn: manganese; Pb: lead; \sum PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; $p_{\text{interaction}}$: p-value for interaction term between prenatal chemical biomarker and sociodemographic/non-chemical stressor; p,p'-DDE: dichlorodiphenyldichloroethylene; PNSDI: prenatal social disadvantage index

^a Weights calculated from 622 participants with full data on prenatal chemical concentrations (HCB, p,p'-DDE, \sum PCB₄, and Pb); parental and household characteristics (maternal age, education, marital status, household income, smoking during pregnancy, obstetrical risk score; paternal education); and participant characteristics (sex, race/ethnicity); sample sizes differ from complete case single-chemical analyses because 1) participants with weighted PNSDI scores (i.e., missing data on one of the five variables used to derive the PNSDI) were not included in any IPCW analysis and 2) participants who were missing a measure of cord blood lead were not included in IPCW analyses for organochlorine and manganese exposures

^b Adjusted for parental and household characteristics (prenatal social disadvantage index, prenatal smoking, Home Observation for Measurement of the Environment score at 15-year assessment) and participant characteristics (sex, race/ethnicity, age at assessment)

^c For each outcome and chemical, risk ratios were estimated from five models: one with no interaction term and four including a product interaction term between the chemical and each of the four specified other stressors

Table S11. Adjusted ^a overall and stratified ^b risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of hexachlorobenzene (HCB) in single-exposure models among New Bedford Cohort participants, when excluding the minimum outlier HCB value

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling HCB level	<i>p</i> _{interaction}
GAD-7 (n=202)		
Total	1.50 (1.09, 2.07)	
Sex-stratified		0.06
Female	1.31 (0.89, 1.93)	
Male	2.32 (1.49, 3.61)	
Race/ethnicity-stratified		0.27
Underrepresented group	1.88 (1.17, 3.00)	
Non-Hispanic White	1.30 (0.85, 2.00)	
PNSDI-stratified		0.73
High (≥3)	1.58 (1.03, 2.44)	
Low (<3)	1.41 (0.87, 2.29)	
HOME-stratified		0.40
Low (<45)	1.66 (1.10, 2.51)	
High (≥45)	1.28 (0.81, 2.03)	
PHQ-8 (n=203)		
Total	1.20 (0.93, 1.56)	
Sex-stratified		0.96
Female	1.21 (0.89, 1.65)	
Male	1.19 (0.75, 1.89)	
Race/ethnicity-stratified		0.78
Underrepresented group	1.27 (0.81, 1.99)	
Non-Hispanic White	1.17 (0.85, 1.61)	
PNSDI-stratified		0.60
High (≥3)	1.12 (0.78, 1.61)	
Low (<3)	1.29 (0.89, 1.87)	
HOME-stratified		0.77
Low (<45)	1.17 (0.82, 1.65)	
High (≥45)	1.26 (0.84, 1.89)	

Abbreviation: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; *p*_{interaction}: p-value for interaction term between prenatal chemical biomarker and sociodemographic/non-chemical stressor; PHQ-8: Patient Health Questionnaire; PNSDI: prenatal social disadvantage index

^a Adjusted for parental and household characteristics (prenatal social disadvantage index, maternal smoking during pregnancy, Home Observation for Measurement of the Environment score) and participant characteristics (sex, race/ethnicity, age at assessment)

^b For each outcome, risk ratios were estimated from five models: one with no interaction term and four including a product interaction term between HCB and each of the four specified other stressors

Table S12. Adjusted ^a overall and stratified ^b risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of chemical in five-exposure models, among New Bedford Cohort participants

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling chemical level				
	GAD-7 (n=187)	HCB	p,p'-DDE	∑PCB₄	Pb
Total	1.41 (0.89, 2.23)	1.28 (0.84, 1.94)	0.72 (0.52, 1.02)	1.47 (1.04, 2.09)	0.78 (0.43, 1.44)
Sex-stratified					
Female	1.48 (0.96, 2.28)	1.26 (0.71, 2.23)	0.78 (0.52, 1.17)	1.34 (0.89, 2.02)	0.97 (0.50, 1.88)
Male	1.32 (0.37, 4.67)	1.29 (0.83, 2.01)	0.66 (0.41, 1.04)	1.82 (1.08, 3.09)	0.46 (0.14, 1.50)
p _{interaction}	0.87	0.95	0.56	0.30	0.27
Race/ethnicity-stratified					
Underrepresented group	1.71 (0.99, 2.97)	1.56 (0.87, 2.80)	0.71 (0.41, 1.25)	1.35 (0.87, 2.10)	0.75 (0.30, 1.86)
Non-Hispanic White	1.19 (0.68, 2.07)	1.06 (0.50, 2.25)	0.77 (0.47, 1.24)	1.46 (1.01, 2.10)	0.69 (0.29, 1.62)
p _{interaction}	0.36	0.42	0.84	0.79	0.89
PNSDI-stratified					
High (≥3)	1.36 (0.69, 2.69)	1.41 (0.79, 2.52)	0.45 (0.24, 0.84)	1.36 (0.89, 2.06)	1.10 (0.52, 2.37)
Low (<3)	1.36 (0.71, 2.61)	1.24 (0.81, 1.91)	1.01 (0.65, 1.59)	1.71 (1.04, 2.83)	0.69 (0.27, 1.73)
p _{interaction}	1.00	0.72	0.03	0.44	0.41
HOME-stratified					
Low (<45)	1.47 (0.77, 2.81)	0.89 (0.53, 1.48)	0.72 (0.46, 1.11)	1.41 (0.94, 2.12)	0.96 (0.44, 2.10)
High (≥45)	1.01 (0.53, 1.91)	1.68 (1.19, 2.37)	0.80 (0.49, 1.31)	1.70 (1.05, 2.76)	0.78 (0.25, 2.43)
p _{interaction}	0.40	0.04	0.73	0.54	0.76
PHQ-8 (n=188)	HCB	p,p'-DDE	∑PCB₄	Pb	Mn
Total	1.16 (0.85, 1.60)	1.15 (0.83, 1.59)	0.80 (0.62, 1.05)	1.20 (0.90, 1.59)	0.77 (0.46, 1.29)
Sex-stratified					
Female	1.32 (0.94, 1.86)	1.07 (0.69, 1.67)	0.84 (0.60, 1.17)	1.20 (0.86, 1.69)	0.93 (0.51, 1.71)
Male	0.95 (0.58, 1.55)	1.49 (0.95, 2.32)	0.74 (0.47, 1.17)	1.06 (0.64, 1.75)	0.45 (0.14, 1.42)
p _{interaction}	0.27	0.31	0.67	0.67	0.27
Race/ethnicity-stratified					
Underrepresented group	1.26 (0.74, 2.15)	1.28 (0.77, 2.12)	0.82 (0.48, 1.39)	1.11 (0.66, 1.89)	0.65 (0.26, 1.60)
Non-Hispanic White	1.12 (0.77, 1.61)	1.08 (0.69, 1.71)	0.82 (0.58, 1.16)	1.21 (0.89, 1.66)	0.81 (0.40, 1.64)
p _{interaction}	0.72	0.63	1.00	0.78	0.70
PNSDI-stratified					
High (≥3)	0.98 (0.67, 1.43)	1.37 (0.81, 2.31)	0.54 (0.33, 0.90)	0.87 (0.56, 1.33)	1.00 (0.52, 1.94)
Low (<3)	1.15 (0.74, 1.79)	1.24 (0.87, 1.76)	0.99 (0.71, 1.38)	1.91 (1.23, 2.98)	0.99 (0.40, 2.49)
p _{interaction}	0.66	0.89	0.07	0.01	0.89
HOME-stratified					
Low (<45)	1.08 (0.71, 1.64)	1.11 (0.60, 2.05)	0.79 (0.51, 1.22)	0.96 (0.63, 1.45)	0.88 (0.50, 1.55)
High (≥45)	1.13 (0.68, 1.87)	1.20 (0.78, 1.84)	0.88 (0.59, 1.33)	1.76 (1.15, 2.67)	0.90 (0.30, 2.70)
p _{interaction}	0.90	0.85	0.72	0.03	0.97

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Mn: manganese; Pb: lead; \sum PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; $p_{\text{interaction}}$: p-value for interaction term between prenatal chemical biomarker and sociodemographic/non-chemical stressor; p,p'-DDE: dichlorodiphenyldichloroethylene; PNSDI: prenatal social disadvantage index

^a Adjusted for parental and household characteristics (prenatal social disadvantage index, maternal smoking during pregnancy, Home Observation for Measurement of the Environment score), participant characteristics (sex, race/ethnicity, age at assessment), and other biomarkers of prenatal chemical exposures

^b For each outcome, risk ratios were estimated from five models: one with no interaction term(s) and four including five product interaction terms between each chemical and each of the four specified other stressors

Table S13. Adjusted ^a overall and stratified ^b risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of organochlorine exposure in single-exposure models additionally adjusted for prenatal consumption of seafood and local produce, among New Bedford Cohort participants

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling organochlorine level		
	HCB	p,p'-DDE	∑PCB₄
GAD-7 (Anxiety) (n=182)			
Total	1.22 (0.81, 1.84)	1.20 (0.85, 1.69)	0.96 (0.73, 1.27)
Sex-stratified			
Female	1.23 (0.77, 1.95)	1.20 (0.78, 1.84)	1.03 (0.75, 1.40)
Male	1.21 (0.56, 2.63)	1.19 (0.77, 1.83)	0.77 (0.46, 1.28)
P _{interaction}	0.97	0.98	0.35
Race/ethnicity-stratified			
Underrepresented group	1.65 (0.98, 2.79)	1.52 (1.07, 2.17)	1.09 (0.72, 1.65)
Non-Hispanic White	1.04 (0.64, 1.70)	0.95 (0.46, 1.95)	0.87 (0.60, 1.25)
P _{interaction}	0.21	0.22	0.45
PNSDI-stratified			
High (≥3)	1.15 (0.70, 1.88)	0.95 (0.62, 1.45)	0.66 (0.46, 0.94)
Low (<3)	1.35 (0.72, 2.55)	1.36 (0.92, 2.03)	1.35 (0.85, 2.14)
P _{interaction}	0.68	0.22	0.01
HOME-stratified			
Low (<45)	1.19 (0.69, 2.04)	0.75 (0.49, 1.16)	0.79 (0.57, 1.09)
High (≥45)	1.28 (0.72, 2.29)	1.61 (1.21, 2.14)	1.21 (0.74, 1.98)
P _{interaction}	0.85	0.004	0.16
PHQ-8 (Depressive) (n=183)			
Total	1.08 (0.80, 1.47)	1.08 (0.82, 1.43)	1.00 (0.80, 1.26)
Sex-stratified			
Female	1.17 (0.81, 1.70)	1.06 (0.75, 1.51)	1.04 (0.80, 1.35)
Male	0.94 (0.64, 1.39)	1.13 (0.75, 1.71)	0.90 (0.59, 1.38)
P _{interaction}	0.41	0.81	0.59
Race/ethnicity-stratified			
Underrepresented group	1.34 (0.81, 2.20)	1.20 (0.83, 1.73)	1.04 (0.69, 1.56)
Non-Hispanic White	0.99 (0.70, 1.40)	1.01 (0.67, 1.53)	0.98 (0.73, 1.31)
P _{interaction}	0.34	0.54	0.82
PNSDI-stratified			
High (≥3)	1.00 (0.69, 1.43)	0.76 (0.51, 1.12)	0.67 (0.47, 0.96)
Low (<3)	1.21 (0.77, 1.90)	1.27 (0.96, 1.69)	1.34 (0.94, 1.90)
P _{interaction}	0.51	0.03	0.01
HOME-stratified			
Low (<45)	1.01 (0.69, 1.47)	0.93 (0.64, 1.34)	0.93 (0.70, 1.23)
High (≥45)	1.25 (0.77, 2.02)	1.24 (0.90, 1.71)	1.10 (0.73, 1.65)
P _{interaction}	0.50	0.25	0.52

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Σ PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; $p_{\text{interaction}}$: p-value for interaction term between prenatal chemical biomarker and sociodemographic/non-chemical stressor; p,p'-DDE: dichlorodiphenyldichloroethylene; PNSDI: prenatal social disadvantage index

^a Adjusted for parental and household characteristics (prenatal social disadvantage index, maternal smoking during pregnancy, Home Observation for Measurement of the Environment score; maternal prenatal seafood consumption, local produce consumption) and participant characteristics (sex, race/ethnicity, age at assessment)

^b For each outcome, risk ratios were estimated from five models: one with no interaction term(s) and four including five product interaction terms between each chemical and each of the four specified other stressors

Table S14. Adjusted ^a overall and stratified ^b risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of chemical in single-exposure models, among New Bedford Cohort participants who had data available on regular medication use at the early adult assessment (*n*=153-161)

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling chemical level					
	GAD-7 (Anxiety)	HCB (<i>n</i> =160)	p,p'-DDE (<i>n</i> =160)	∑PCB ₄ (<i>n</i> =160)	Pb (<i>n</i> =155)	Mn (<i>n</i> =153)
Total		1.21 (0.82, 1.80)	1.24 (0.91, 1.69)	0.89 (0.69, 1.15)	1.17 (0.82, 1.68)	1.09 (0.59, 2.01)
Sex-stratified						
Female		1.23 (0.82, 1.85)	1.27 (0.84, 1.91)	0.91 (0.67, 1.23)	1.05 (0.70, 1.58)	1.17 (0.60, 2.29)
Male		1.18 (0.48, 2.90)	1.19 (0.80, 1.77)	0.83 (0.53, 1.30)	1.97 (0.95, 4.09)	0.76 (0.18, 3.22)
P _{interaction}		0.94	0.82	0.76	0.11	0.60
Race/ethnicity-stratified						
Underrepresented group		1.94 (1.20, 3.15)	1.43 (1.01, 2.03)	1.02 (0.69, 1.50)	1.19 (0.69, 2.03)	0.90 (0.41, 1.95)
Non-Hispanic White		0.91 (0.61, 1.36)	0.99 (0.57, 1.73)	0.79 (0.59, 1.07)	1.16 (0.75, 1.80)	1.29 (0.53, 3.14)
P _{interaction}		0.02	0.26	0.33	0.95	0.54
PNSDI-stratified						
High (≥3)		1.24 (0.73, 2.09)	0.93 (0.58, 1.47)	0.66 (0.46, 0.95)	1.07 (0.69, 1.66)	1.23 (0.59, 2.57)
Low (<3)		1.17 (0.65, 2.12)	1.56 (1.06, 2.32)	1.14 (0.74, 1.76)	1.52 (0.85, 2.71)	0.77 (0.25, 2.43)
P _{interaction}		0.90	0.09	0.06	0.31	0.51
HOME-stratified						
Low (<45)		1.17 (0.67, 2.03)	0.95 (0.65, 1.41)	0.72 (0.54, 0.97)	0.98 (0.61, 1.59)	0.98 (0.47, 2.03)
High (≥45)		1.29 (0.78, 2.16)	1.49 (0.99, 2.25)	1.10 (0.68, 1.76)	1.82 (1.05, 3.16)	1.43 (0.48, 4.25)
P _{interaction}		0.79	0.12	0.14	0.07	0.57
PHQ-8 (Depressive)		HCB (<i>n</i>=161)	p,p'-DDE (<i>n</i>=161)	∑PCB₄ (<i>n</i>=161)	Pb (<i>n</i>=156)	Mn (<i>n</i>=154)
Total		1.07 (0.82, 1.40)	1.12 (0.84, 1.49)	0.88 (0.71, 1.09)	1.04 (0.79, 1.37)	0.86 (0.52, 1.44)
Sex-stratified						
Female		1.20 (0.84, 1.72)	1.07 (0.72, 1.61)	0.88 (0.68, 1.14)	1.01 (0.74, 1.38)	0.93 (0.52, 1.66)
Male		0.91 (0.69, 1.20)	1.20 (0.84, 1.69)	0.88 (0.60, 1.28)	1.19 (0.61, 2.33)	0.65 (0.22, 1.95)
P _{interaction}		0.25	0.69	1.00	0.66	0.57
Race/ethnicity-stratified						
Underrepresented group		1.33 (0.85, 2.07)	1.20 (0.84, 1.70)	0.92 (0.63, 1.35)	1.01 (0.65, 1.57)	0.71 (0.34, 1.48)
Non-Hispanic White		0.95 (0.71, 1.28)	1.02 (0.65, 1.61)	0.85 (0.65, 1.10)	1.06 (0.76, 1.48)	0.99 (0.49, 2.00)
P _{interaction}		0.24	0.59	0.73	0.91	0.52
PNSDI-stratified						
High (≥3)		1.02 (0.77, 1.35)	0.84 (0.59, 1.20)	0.66 (0.48, 0.91)	0.80 (0.55, 1.17)	0.85 (0.47, 1.51)
Low (<3)		1.22 (0.69, 2.14)	1.47 (1.00, 2.16)	1.16 (0.81, 1.65)	1.97 (1.18, 3.28)	0.91 (0.30, 2.70)
P _{interaction}		0.58	0.03	0.02	0.004	0.91
HOME-stratified						
Low (<45)		1.00 (0.75, 1.33)	1.14 (0.82, 1.60)	0.81 (0.64, 1.04)	0.80 (0.53, 1.20)	0.81 (0.47, 1.41)
High (≥45)		1.27 (0.75, 2.12)	1.09 (0.67, 1.76)	0.99 (0.63, 1.56)	1.98 (1.19, 3.30)	1.01 (0.33, 3.10)

$p_{\text{interaction}}$

0.44

0.82

0.45

0.01

0.74

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Mn: manganese; Pb: lead; Σ PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; $p_{\text{interaction}}$: p-value for interaction term between prenatal chemical biomarker and sociodemographic/non-chemical stressor; p,p'-DDE: dichlorodiphenyldichloroethylene; PNSDI: prenatal social disadvantage index

^a Adjusted for parental and household characteristics (prenatal social disadvantage index, maternal smoking during pregnancy, Home Observation for Measurement of the Environment score) and participant characteristics (sex, race/ethnicity, age at assessment)

^b For each outcome and chemical, risk ratios were estimated from five models: one with no interaction term and four including a product interaction term between the chemical and each of the four specified other stressors

Table S15. Adjusted ^a overall and stratified ^b risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of chemical in single-exposure models, among New Bedford Cohort participants who had data available on medication use at the early adult assessment and did not report regularly using psychotropic medications (*n*=139-147)

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling chemical level				
GAD-7 (Anxiety)	HCB (<i>n</i>=146)	p,p'-DDE (<i>n</i>=146)	∑PCB₄ (<i>n</i>=146)	Pb (<i>n</i>=141)	Mn (<i>n</i>=139)
Total	1.38 (0.97, 1.97)	1.13 (0.78, 1.63)	0.86 (0.61, 1.22)	1.10 (0.69, 1.76)	1.11 (0.50, 2.46)
Sex-stratified					
Female	1.20 (0.78, 1.86)	1.15 (0.70, 1.90)	0.88 (0.58, 1.33)	0.97 (0.60, 1.56)	1.30 (0.56, 3.04)
Male	2.24 (1.31, 3.81)	1.07 (0.71, 1.61)	0.82 (0.48, 1.42)	1.96 (0.62, 6.17)	0.50 (0.10, 2.62)
P _{interaction}	0.09	0.82	0.86	0.23	0.30
Race/ethnicity-stratified					
Underrepresented group	1.87 (1.08, 3.22)	1.46 (0.99, 2.15)	1.11 (0.72, 1.71)	1.29 (0.64, 2.61)	0.99 (0.36, 2.66)
Non-Hispanic White	1.02 (0.64, 1.63)	0.68 (0.35, 1.32)	0.70 (0.49, 1.01)	0.95 (0.58, 1.55)	1.24 (0.38, 4.00)
P _{interaction}	0.10	0.05	0.12	0.43	0.77
PNSDI-stratified					
High (≥3)	1.80 (1.22, 2.65)	0.78 (0.46, 1.34)	0.58 (0.32, 1.03)	0.95 (0.53, 1.72)	1.45 (0.55, 3.79)
Low (<3)	0.88 (0.48, 1.62)	1.38 (0.90, 2.14)	1.14 (0.66, 1.96)	1.41 (0.75, 2.64)	0.60 (0.15, 2.42)
P _{interaction}	0.05	0.10	0.09	0.33	0.31
HOME-stratified					
Low (<45)	1.67 (1.12, 2.48)	0.97 (0.62, 1.51)	0.69 (0.45, 1.05)	0.86 (0.45, 1.62)	1.04 (0.39, 2.73)
High (≥45)	1.04 (0.58, 1.86)	1.25 (0.75, 2.08)	1.04 (0.58, 1.86)	1.73 (0.90, 3.30)	1.28 (0.35, 4.74)
P _{interaction}	0.19	0.46	0.27	0.12	0.79
PHQ-8 (Depressive)	HCB (<i>n</i>=147)	p,p'-DDE (<i>n</i>=147)	∑PCB₄ (<i>n</i>=147)	Pb (<i>n</i>=142)	Mn (<i>n</i>=140)
Total	1.16 (0.85, 1.58)	1.12 (0.81, 1.54)	0.85 (0.66, 1.09)	0.98 (0.71, 1.37)	0.91 (0.49, 1.68)
Sex-stratified					
Female	1.15 (0.76, 1.74)	0.94 (0.57, 1.56)	0.82 (0.58, 1.14)	0.85 (0.59, 1.22)	0.94 (0.46, 1.91)
Male	1.17 (0.74, 1.87)	1.42 (1.02, 1.98)	0.92 (0.63, 1.36)	1.51 (0.77, 2.95)	0.83 (0.25, 2.77)
P _{interaction}	0.95	0.18	0.64	0.15	0.86
Race/ethnicity-stratified					
Underrepresented group	1.34 (0.81, 2.21)	1.33 (0.91, 1.94)	0.89 (0.56, 1.41)	1.06 (0.65, 1.71)	1.05 (0.48, 2.28)
Non-Hispanic White	1.01 (0.67, 1.54)	0.86 (0.53, 1.40)	0.83 (0.61, 1.12)	0.93 (0.60, 1.43)	0.82 (0.34, 1.98)
P _{interaction}	0.42	0.17	0.81	0.69	0.67
PNSDI-stratified					
High (≥3)	1.29 (0.92, 1.80)	0.98 (0.66, 1.48)	0.68 (0.47, 0.98)	0.75 (0.49, 1.15)	0.88 (0.43, 1.82)
Low (<3)	0.92 (0.49, 1.74)	1.25 (0.79, 1.98)	1.06 (0.69, 1.63)	1.55 (0.92, 2.60)	0.98 (0.29, 3.39)
P _{interaction}	0.36	0.42	0.13	0.03	0.89
HOME-stratified					
Low (<45)	1.13 (0.80, 1.60)	1.29 (0.91, 1.84)	0.86 (0.65, 1.12)	0.69 (0.43, 1.10)	0.71 (0.36, 1.39)
High (≥45)	1.23 (0.64, 2.33)	0.91 (0.48, 1.71)	0.85 (0.51, 1.41)	1.92 (1.14, 3.26)	1.67 (0.49, 5.67)
P _{interaction}	0.83	0.36	0.97	0.01	0.22

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Mn: manganese; Pb: lead; Σ PCB₄: sum of four polychlorinated biphenyl congeners; PHQ-8: Patient Health Questionnaire; $p_{\text{interaction}}$: p-value for interaction term between prenatal chemical biomarker and sociodemographic/non-chemical stressor; p,p'-DDE: dichlorodipenyldichloroethylene; PNSDI: prenatal social disadvantage index

^a Adjusted for parental and household characteristics (prenatal social disadvantage index, maternal smoking during pregnancy, Home Observation for Measurement of the Environment score) and participant characteristics (sex, race/ethnicity, age at assessment)

^b For each outcome and chemical, risk ratios were estimated from five models: one with no interaction term and four including a product interaction term between the chemical and each of the four specified other stressors

Table S16. Adjusted ^a overall and stratified ^b risk ratios (95% confidence intervals) for moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, associated with a doubling of prenatal and postnatal (i.e., peak early childhood) lead (Pb), among New Bedford Cohort participants

Internalizing symptoms	Risk ratio (95% confidence interval) per doubling Pb level	
	Prenatal Pb	Postnatal Pb
GAD-7 (n=197)		
Total	1.55 (1.11, 2.16)	1.04 (0.68, 1.60)
Sex-stratified		
Female	1.39 (0.96, 2.00)	0.99 (0.60, 1.63)
Male	2.16 (1.03, 4.55)	1.05 (0.41, 2.67)
P _{interaction}	0.27	0.91
Race/ethnicity-stratified		
Underrepresented group	1.37 (0.82, 2.29)	1.80 (0.91, 3.59)
Non-Hispanic White	1.70 (1.26, 2.29)	0.70 (0.41, 1.20)
P _{interaction}	0.46	0.03
PNSDI-stratified		
High (≥3)	1.40 (0.96, 2.04)	0.85 (0.46, 1.59)
Low (<3)	1.98 (1.15, 3.39)	1.23 (0.67, 2.28)
P _{interaction}	0.29	0.41
HOME-stratified		
Low (<45)	1.43 (0.98, 2.09)	1.00 (0.57, 1.75)
High (≥45)	1.98 (1.14, 3.43)	1.08 (0.54, 2.13)
P _{interaction}	0.32	0.87
PHQ-8 (n=198)		
Total	1.32 (1.00, 1.74)	0.78 (0.56, 1.08)
Sex-stratified		
Female	1.29 (0.93, 1.77)	0.88 (0.60, 1.30)
Male	1.44 (0.77, 2.71)	0.60 (0.36, 1.00)
P _{interaction}	0.75	0.24
Race/ethnicity-stratified		
Underrepresented group	1.11 (0.68, 1.81)	0.89 (0.51, 1.55)
Non-Hispanic White	1.46 (1.11, 1.93)	0.70 (0.48, 1.03)
P _{interaction}	0.33	0.48
PNSDI-stratified		
High (≥3)	0.95 (0.64, 1.41)	0.76 (0.44, 1.32)
Low (<3)	2.31 (1.52, 3.51)	0.72 (0.48, 1.07)
P _{interaction}	0.002	0.86
HOME-stratified		
Low (<45)	1.06 (0.74, 1.52)	0.86 (0.55, 1.34)
High (≥45)	2.26 (1.46, 3.50)	0.62 (0.36, 1.07)
P _{interaction}	0.01	0.36

Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HOME: Home Observation for Measurement of the Environment; Pb: leadPHQ-8: Patient Health Questionnaire; $p_{\text{interaction}}$: p-value for interaction term between chemical biomarker and sociodemographic/non-chemical stressor; PNSDI: prenatal social disadvantage index

^a Adjusted for parental and household characteristics (prenatal social disadvantage index, maternal smoking during pregnancy, Home Observation for Measurement of the Environment score) and participant characteristics (sex, race/ethnicity, age at assessment)

^b For each outcome, risk ratios were estimated from five models: one with both prenatal and postnatal Pb biomarkers and no interaction term, and four including two product interaction terms between (1) cord blood Pb and each of the four specified other stressors and (2) peak early childhood Pb and each of the four specified other stressors

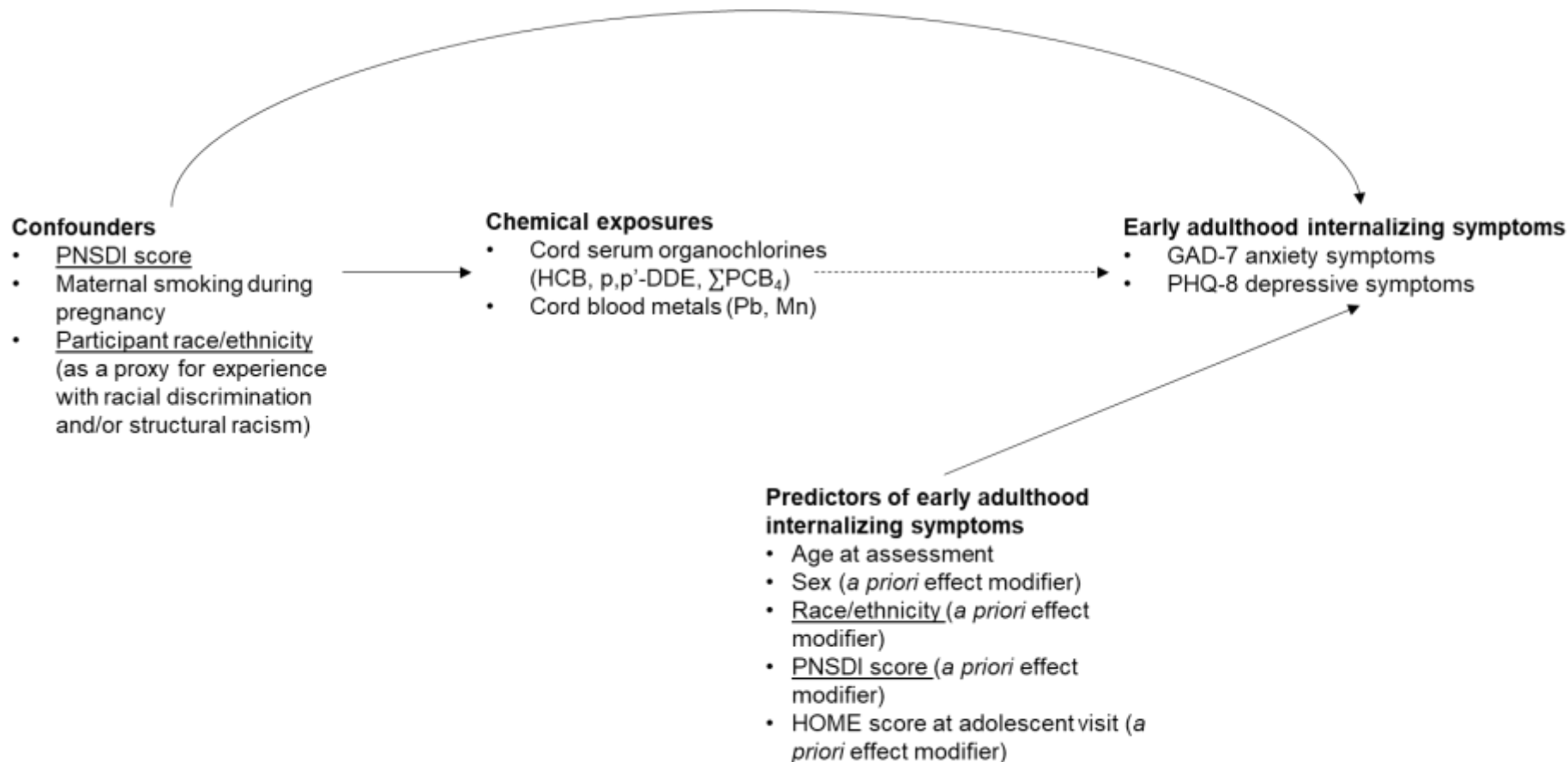
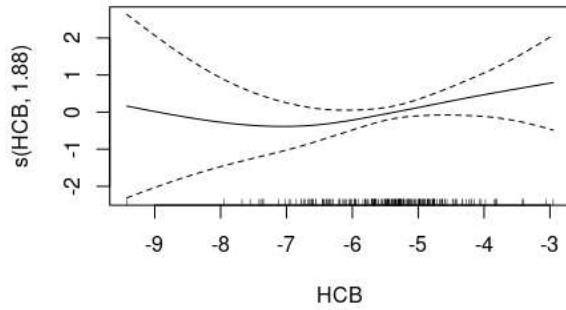


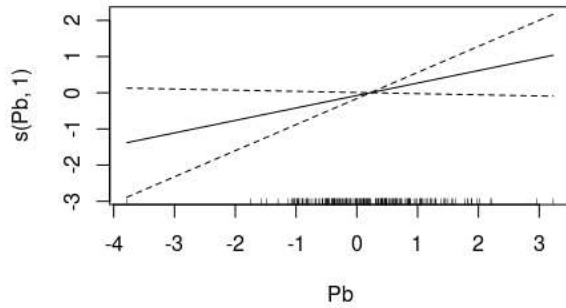
Figure S1. Directed acyclic graph identifying confounders, predictors of internalizing symptoms, and effect modifiers for inclusion in regression models. Solid lines indicate *a priori* associations and dashed lines indicate hypothesized associations; underlined text indicates covariates that were considered both confounders and effect modifiers in models. Abbreviations: GAD-7, Generalized Anxiety Disorder scale; HCB, hexachlorobenzene; HOME: Home Observation for Measurement of the Environment; Mn, manganese; Pb, lead; Σ PCB₄, sum of four polychlorinated biphenyl congeners (congeners: 118, 138, 153, 180); PHQ-8, Patient Health Questionnaire; PNSDI, prenatal social disadvantage index; p,p'-DDE, dichlorodiphenyldichloroethylene.

A) HCB and GAD-7

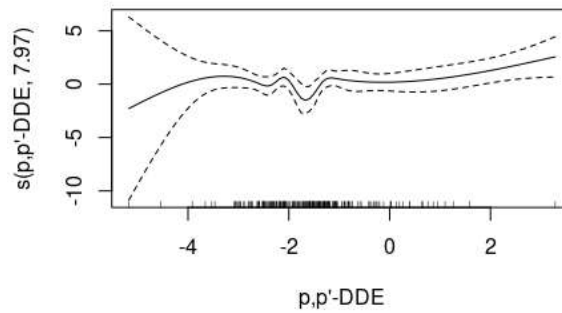


QICu for model with linear term: 210.7
 QiCu for model with linear and quadratic terms: 211.2

D) Pb and GAD-7

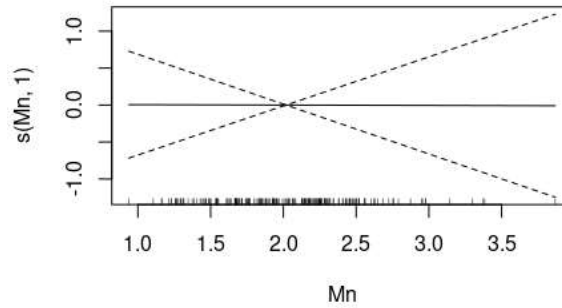


B) p, p'-DDE and GAD-7

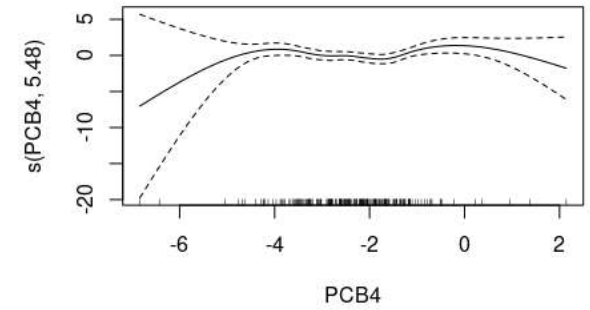


QICu for model with linear term: 211.5
 QiCu for model with linear and quadratic terms: 210.7

E) Mn and GAD-7

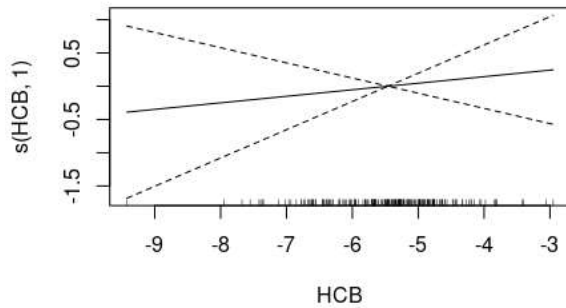


C) ΣPCB4 and GAD-7

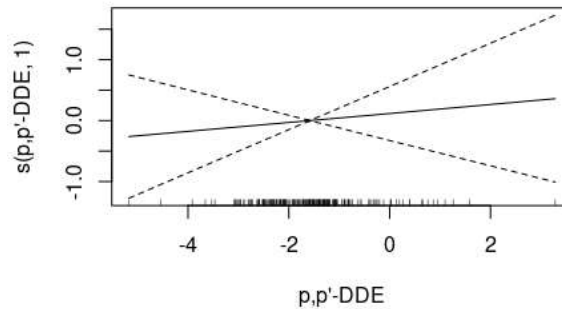


QICu for model with linear term: 212.8
 QiCu for model with linear and quadratic terms: 214.7

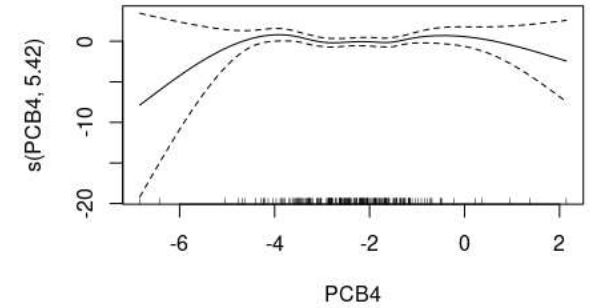
F) HCB and PHQ-8



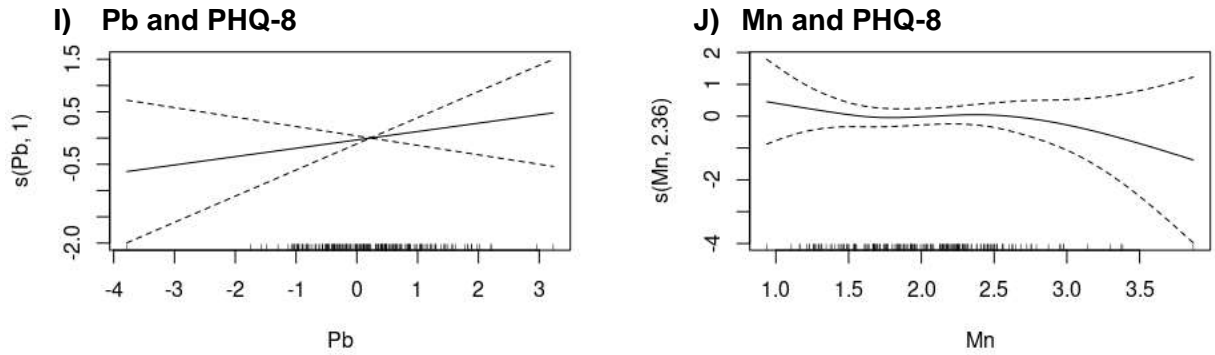
G) p, p'-DDE and PHQ-8



H) ΣPCB4 and PHQ-8



QICu for model with linear term: 239.5
 QiCu for model with linear and quadratic terms: 241.4



QICu for model with linear term: 228.2
 QiCu for model with linear and quadratic terms: 229.9

Figure S2. Covariate-adjusted associations between the log risk ratio of moderately elevated anxiety and depressive symptoms, measured via the Generalized Anxiety Disorder scale (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively, and chemical biomarkers in single-chemical generalized additive models. Notes: In cases where splines indicated possible quadratic associations, goodness of fit was evaluated with the quasi-likelihood under the independence model information criterion (QICu) to compare modified Poisson regression models including a linear term versus both linear and quadratic terms for exposures; Models were adjusted for parental and household characteristics [prenatal social disadvantage index score (PNSDI), maternal smoking during pregnancy] and participant characteristics [age at assessment, race/ethnicity sex, Home Observation for Measurement of the Environment score]. Abbreviations: GAD-7: Generalized Anxiety Disorder scale; HCB: hexachlorobenzene; Mn: manganese; Pb: lead; PCB4: sum of four polychlorinated biphenyl congeners (congeners: 118, 138, 153, 180); PHQ-8: Patient Health Questionnaire; p,p'-DDE: dichlorodiphenyldichloroethylene.

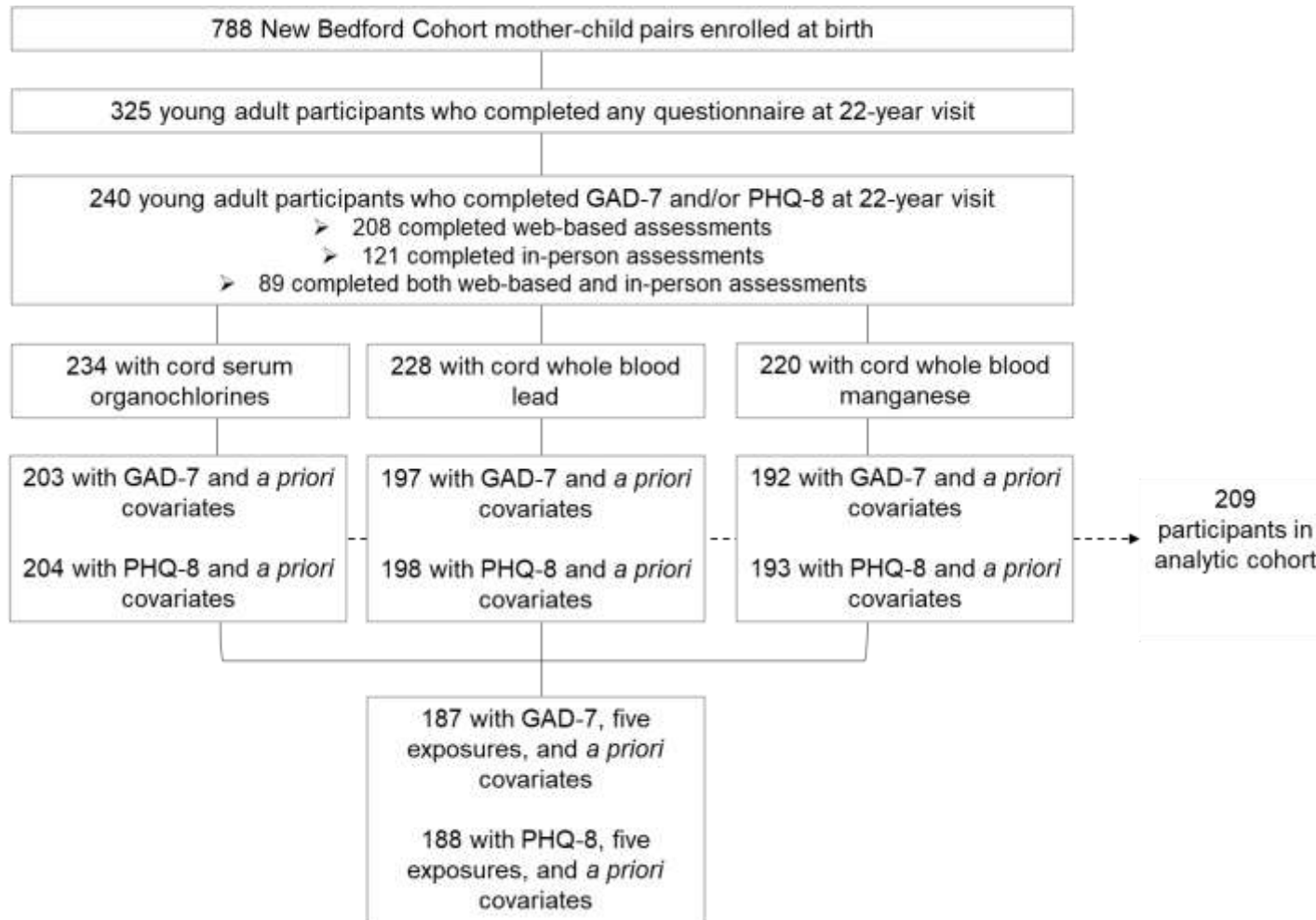


Figure S3. Study flow chart for New Bedford Cohort participants included in the analytic cohort. Abbreviations: GAD-7, Generalized Anxiety Disorder Scale; PHQ-8, Patient Health Questionnaire.

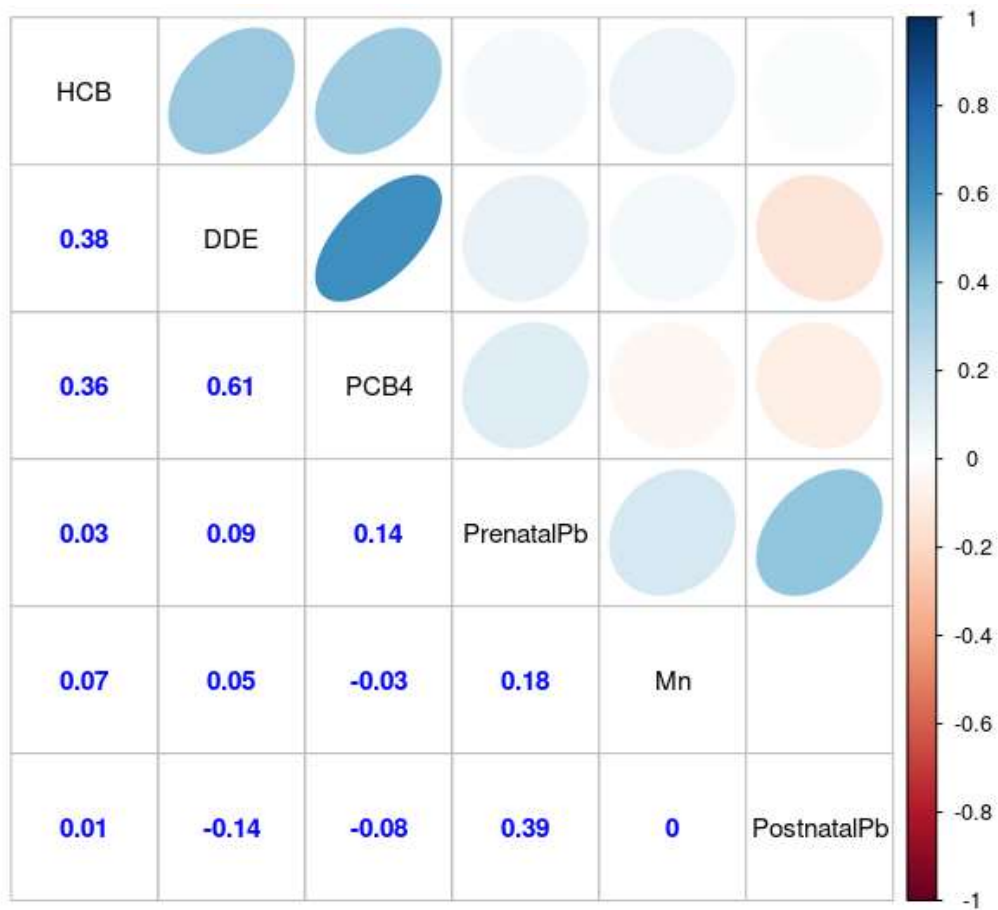


Figure S4. Spearman correlations between cord serum biomarkers of organochlorine exposure [i.e., hexachlorobenzene (HCB), dichlorodiphenyldichloroethylene (DDE), sum of four polychlorinated biphenyl congeners (PCB4; congeners: 118, 138, 153, 180)], cord blood biomarkers of metal exposure [lead (PrenatalPb), manganese (Mn)], and peak early childhood blood lead (PostnatalPb) for 209 New Bedford Cohort participants included in at least one complete case analysis.

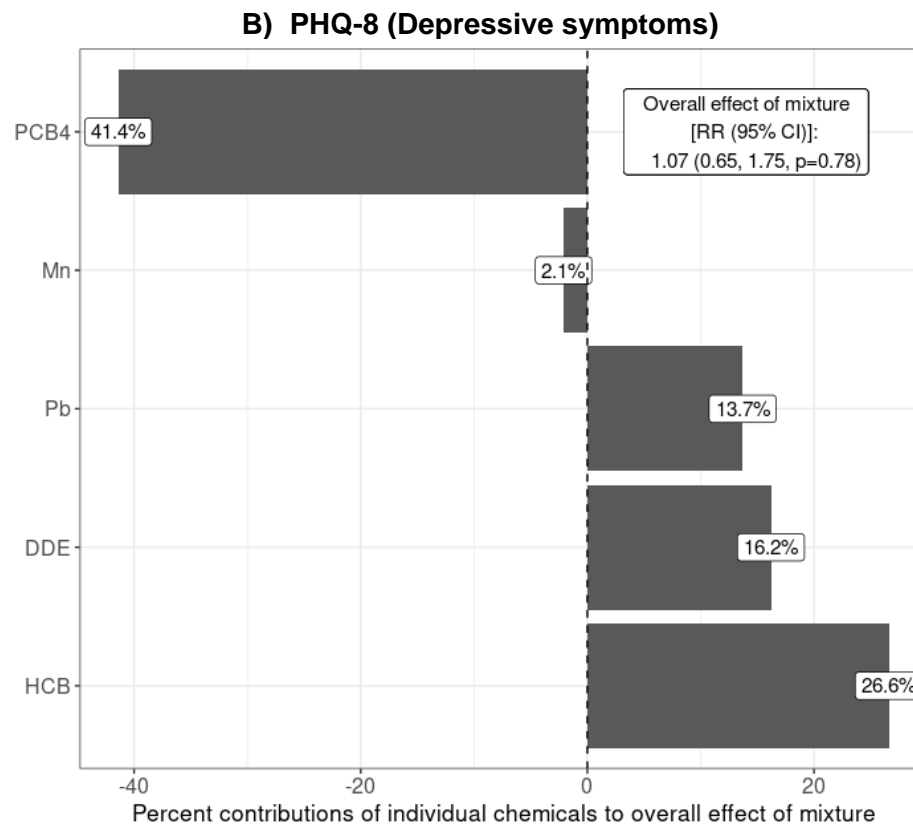
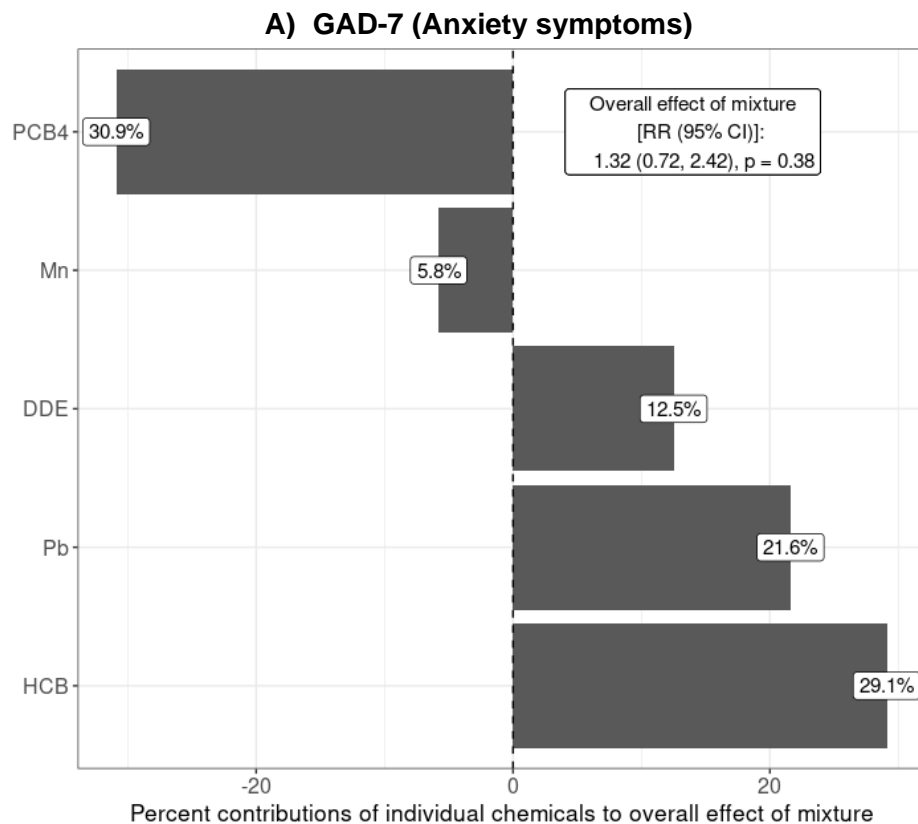


Figure S5. Quantile g-computation weights for each chemical in relation to elevated A) Generalized Anxiety Disorder scale (GAD-7) anxiety symptoms and B) Patient Health Questionnaire (PHQ-8) depressive symptoms, in the overall analytic cohort of New Bedford Cohort participants ($n=187$ for GAD-7, $n=188$ for PHQ-8). Abbreviations: DDE, dichlorodiphenyldichloroethylene; HCB, hexachlorobenzene; Mn, manganese; Pb, lead; PCB4, sum of four polychlorinated biphenyl congeners (congeners: 118, 138, 153, 180).