Supplemental Material

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

Lisa B. Rokoff, Brent A. Coull, Michelle Bosquet Enlow, and Susan A. Korrick

Table of Contents

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.

Table S8. Adjusted strata-specific (calculated by running models in stratified datasets) 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.

Table S9. Adjusted overall and stratified 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).

Table S10. Inverse probability of censoring weighted (IPCW) adjusted overall and stratified 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.

Table S11. Adjusted overall and stratified 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.

Table S12. Adjusted overall and stratified 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.

Table S13. Adjusted overall and stratified 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.

Table S14. Adjusted overall and stratified 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).

Table S15. Adjusted overall and stratified 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).

Table S16. Adjusted overall and stratified 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.

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; $\sum PCB_4$, 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.

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).