Supplemental Material

Serum Perfluorooctanoate (PFOA) and Perfluorooctane Sulfonate (PFOS) Concentrations and Liver Function Biomarkers in a Population with Elevated PFOA Exposure

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Detail of between- and within-regression models

Water district data available in the C8 Health Project questionnaire data were considered: using the geocoded locations of the address, combined with a detailed mapping of streets covered by each water districts piped water supplies, geocoded residences could be assigned a water district code. These analyses were restricted to those living in the six contaminated districts (Little Hocking Water Association of Ohio; City of Belpre, Ohio; Tupper Plains–Chester District of Ohio; Village of Pomeroy, Ohio; Lubeck Public Service District of West Virginia; Mason County Public Service District of West Virginia) at the time of the survey (*n*=26,777). For each water districts, on the ln-transformed scale, a mean PFOA value and a deviation from the mean for each individual was calculated as the difference between the individual level and the water district mean. Regression coefficients with relative standard errors (SE) and p-values were calculated for the association within water district and between water districts with both the mean ln-PFOA values, and the individual deviations, in a fully adjusted linear regression model. The significance of the difference between these within and between water district coefficients was also assessed. Models also included a random effect at the water district level.

Formal model description:

To estimate within and between water district (i=1,..., 6) coefficients relating log serum PFOA in individual j in that district ($x_{i,j}$) to numerical outcomes ($y_{i,j}$), we fit the model:

$$y_{i,j} = a + \beta_w(d_{i,j}) + \beta_b\bar{x}_i + \{\text{covariate terms}\} + \alpha_i + \varepsilon_{i,j} \quad ,$$

$$Where\ d_{i,j} = (x_{i,j} - \bar{x}_i), \alpha_i \sim N(0,\sigma_b^2), and\ \varepsilon_{i,j} \sim N(0,\sigma_w^2)$$

To test the hypothesis $\beta_w = \beta_b$, we re-parameterised this relationship writing $\beta_{diff} = \beta_w - \beta_b$, giving:

$$E(y) = a + \beta_w (x_{i,j}) + \beta_{difference} \bar{x}_i + \{\text{covariate terms}\}$$

We used the Wald test for $\beta_{diff} = 0$ as a test for $\beta_w = \beta_b$.

For dichotomous outcomes we fit analogous logistic models, except that instead of fitting a random effect at water district level, which was computationally cumbersome, we used a sandwich (Huber-White) estimator of variance clustering by water district.