The Authors Reply

We thank Drs. Fei and Olsen for their comments (1) on our paper (2). They mention several study limitations that we acknowledged in our paper. First, the C8 Health Project was a cross-sectional study with exposure and outcome measured concurrently, thus calling for cautious interpretation. Second, the frequencies of most self-reported pregnancy outcomes (miscarriage, preterm birth, preeclampsia, birth defects) were higher than expected. We attributed the higher frequencies to the limited quality of self-reported data as opposed to reflecting a higher background risk in this population. With the data currently available, we are unable to fully address this concern, but we are in the process of linking pregnancy information from the C8 Health Project to birth certificates from Ohio and West Virginia that will provide reliable data on gestational age and birth weight.

Third, Fei and Olsen (1) question the inclusion of pregnancies up to 5 years prior to exposure measurement. Half-life estimates are approximately 4 years for perfluorooctanoic acid (PFOA) and 5 years for perfluorooctane sulfonate (PFOS) (3). As described in our paper (2), in this population, the strongest predictor of PFOA serum level was current residence in a contaminated water district, with distance to the plant directly affecting PFOA levels (4). By restricting the PFOA analyses to women who lived in the same water district from the approximate start of pregnancy through the time of exposure measurement, we ensured that even if individual exposure varied over the 5 years, position within the distribution of PFOA levels likely remained constant. PFOS exposure was not determined by residence in a PFOA-contaminated water district, so it was not subject to the same inclusion restrictions.

Nationally, PFOS levels are dropping (5), and it is possible that PFOS levels during pregnancy were higher than at the time of measurement. As we reported (2), we also conducted analyses restricted to pregnancies within the 3 years prior to measurement, presumably generating values with more concordance between the measurement and the exposure at the time of the pregnancy. Results for PFOA and PFOS were similar to those observed for the 5-year period, but less precise. We are developing exposure reconstruction models that will enable us to refine exposure estimates in future analyses. Fei and Olsen measured PFOA and PFOS levels during pregnancy, a notable strength of their study (6).

Fei and Olsen (1) also question the results we selected to highlight in our paper’s abstract and conclusion (2). In judging whether a given association was worthy of mention, we considered magnitude, precision, dose-response gradient, and the results for both continuous and categorical measures. There is inherent subjectivity in which results are emphasized; however, all results, including the suggestion of an association between PFOS and preterm birth for exposures above the 90th percentile, were presented in the text and tables.

Lastly, we appreciate Fei and Olsen’s discussion (1) about why we may be observing divergent results for PFOA and PFOS exposure, particularly given the unusually high PFOA serum levels in this population. To address their concern that the effect of PFOA may plateau at an exposure level below the upper limit of our original reference category (<50th percentile), we reran the analyses by categorizing serum PFOA level into quintiles. These results did not alter our interpretations. We agree that the inconsistencies across epidemiologic investigations of perfluorinated compound exposure and reproductive health warrant continued exploration as well as an improved understanding of the correlation across perfluorinated compounds and the similarities and differences in their reproductive toxicities.

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References


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