and may be biased for the exposure effect at a specific time. We tested the proportionality assumption by examining the odds of becoming pregnant in each discrete month when no contraception was used. Although the magnitude of the association was slightly less in the first month of follow-up compared with later months, we found that higher PBDE concentration was associated with decreased fecundability in every month.

Goodman et al. were also concerned about uncontrolled confounding. Although it is true that many factors affect the timing of pregnancy, confounding is present only when these factors are associated with the exposure as well as the outcome. We have no reason to believe that the factors mentioned by Goodman et al. would be associated with PBDE levels, other than by chance. We did evaluate many of the factors they listed (i.e., frequency of intercourse, alcohol consumption, smoking, and drug use) and reported that they did not confound our results. Although we agree that one can never control for all possible confounding factors in an observational study—this is an inherent limitation of epidemiology—we have taken care to minimize confounding as much as possible.

Finally, Goodman et al. argue that limiting the study to pregnant women could bias results away from the null. We cannot think of a circumstance in which this would be true. The inherent selection bias of retrospective studies in pregnant populations is that infertile couples are excluded and subfertile couples are underrepresented. Thus, if there is a true association between PBDEs and time to pregnancy, then limiting the study to the most fertile couples will reduce statistical power and lead to an underestimation of the effect. However, if there is no association between PBDEs and time to pregnancy, then we would expect the fOR to be 1.0 among all women. Overrepresenting the most fertile couples would continue to show a null effect. We fail to see how excluding subfertile women would bias findings away from the null or show a spurious association.

Time-to-pregnancy studies are methodologically complicated, and both prospective and retrospective studies have their limitations. For a detailed discussion of the biases in retrospective study designs, as well as a discussion of how to minimize them, see Joffe et al. (2005). A strength of our study is that we undertook multiple sensitivity analyses to investigate the extent that our findings changed when inclusion criteria or details of the analytic methods were altered. Our findings remained largely unchanged in all these sensitivity analyses. In summary, the limitations pointed out by Goodman et al. would serve to underestimate our estimate of effect, not inflate it. However, since this is the first study of PBDE exposure and time to pregnancy, our findings need to be replicated in other populations.

The authors declare they have no competing financial interests.

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Probabilistic Modeling of Dietary Arsenic Exposure

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We read with interest the article "Probabilistic Modeling of Dietary Arsenic Exposure and Dose and Evaluation with 2003–2004 NHANES Data," by Xue et al. (2010). We are concerned that the article misrepresented our earlier article on a similar topic (Petito Boyce et al. 2008) and that, by doing so, Xue et al. failed to appreciate the consistency of their estimates of arsenic intake from food and water with ours. Specifically, Xue et al. (2010) stated, "A recent publication [i.e., Petito Boyce et al. (2008)] concluded that typical and high-end background exposures to iAs [inorganic arsenic] in the U.S. population do not present elevated risks of carcinogenicity." However, they then seemed to call into question our conclusion and to suggest that our analysis either underestimated or failed to include consideration of dietary intake of iAs, citing work by others indicating that iAs intake from food has been estimated to be on the order of several micrograms per day. This suggestion does not accurately reflect our analysis. In fact, our estimates of background exposures to iAs include dietary intake estimates similar to those noted by Xue et al. (2010), and both studies used some of the same data sources.

In our study (Petito Boyce et al. 2008), we conducted a probabilistic analysis using Monte Carlo analysis with Crystal Ball software, incorporating 10,000 iterations, whereas Xue et al. (2010) used the SHEDS model. Table 1 demonstrates the remarkable similarity between the iAs intake estimates from dietary and drinking water sources reported by Xue et al. (2010) and our 2008 intake estimates (Petito Boyce et al. 2008). Our analysis also included estimates of iAs intake from soil, as well as total iAs intake.

A key element of our conclusion (Petito Boyce et al. 2008) regarding the lack of carcinogenic risk was the use of a margin-of-exposure model for iAs, which was applied using an epidemiologically derived no observable adverse effect level. We chose this model based on an analysis of arsenic's mode of action, from which we concluded that all plausible modes of action were supportive of a nonlinear dose response. Our conclusion was not based on a lower iAs intake estimate, as implied by Xue et al. (2010).

We believe that the analysis by Xue et al. (2010) is important and provides additional understanding of the significance of background exposures to iAs, particularly via ingestion of food. However, by not providing an accurate representation of our work, the authors missed an opportunity to provide additional support for their overall conclusions.

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Table 1. Comparison of iAs intake estimates.

Study	iAs intake from food (μg/kg/day)			iAs intake from drinking water (μg/kg/day)		
	Mean	50th percentile	95th percentile	Mean	50th percentile	95th percentile
Petito Boyce et al. 2008	0.061	0.048	0.14	0.034	0.001	0.12
Xue et al. 2010	0.05	0.02	0.19	0.025	0.002	0.11

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Xue J, Zartarian V, Wang S-W, Liu SV, Georgopoulos P. 2010. Probabilistic modeling of dietary arsenic exposure and dose and evaluation with 2003–2004 NHANES data. Environ Health Perspect 118:345–350.

Dietary Arsenic Exposure: Xue et al. Respond

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In our article (Xue et al. 2010), we cited Petito Boyce et al. (2008) based on their major conclusion stated at the end of their abstract that, "typical and high-end background exposures to inorganic arsenic in U.S. populations do not present elevated risks of carcinogenicity." We agree with Petito Boyce et al. that we "missed an opportunity to provide additional support for" our overall conclusions, and very much appreciate that they have offered this detailed comparison showing the agreement between our modeling results.

Our discussion of Petito Boyce et al. (2008)'s conclusions was intended to bolster the need to develop a more comprehensive analysis of the sources of inorganic arsenic exposure, not to suggest that their exposure analysis was incomplete or inaccurate.

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