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The Authors Respond

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To the Editor

We thank Cox¹ for his interest in our recent article.² Our aim was to get closer to the causal relationship by evaluating statistical associations while eliminating non-causal reasons for observed associations, a critical step in evidence generation. Throughout the paper we referred to associations between unconventional natural gas development and birth outcomes, except in Cox's example. Cox suggested the use of more formal causal approaches including directed acyclic graphs (DAGs), which we constructed based on prior studies and understanding of human biology (see eFigure). The Hoeting approach³ represents another way to obtain effect estimates without a DAG.

Cox's concerns regarding the unconventional natural gas development activity index may result from a misunderstanding about what we designed it to capture. It was developed to simultaneously integrate complex pathways by which unconventional natural gas development may affect birth outcomes, including social and environmental impacts (e.g., psychosocial stress, social upheaval, truck traffic, noise, air pollution) that operate at individual and community levels.^{4,5} Geology, topography, or monitoring data are thus less relevant than if we sought to characterize, for example, only air pollution. Since no single measurement could summarize our index, we could not use kriging to predict exposure, with uncertainty estimates, at unsampled locations. More practically, we could not justify the expense of more rigorous exposure assessment when ours was one of the first studies of unconventional natural gas development in relation to health.^{6–8} The imputation of well data we described in our paper is better termed extrapolation because we estimated, for example, stimulation dates, which must fall between known spud and production dates. This was done for <4% of wells.⁹ We have been unable to envision a scenario where measurement error would have been differential with respect to birth outcomes, or substantially biased our

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Conflicts of Interest:

We declare that we have no conflicts of interest.

results away from the null. Although we acknowledge that such bias is theoretically possible,¹⁰ Cox did not propose any such specific scenario.

Cox also had concerns about residual spatial confounding. We used multilevel modeling, conducted model diagnostics, and found that residuals did not exhibit spatial autocorrelation. Cox recommends that we randomly assign well locations as an exposure control. In the paper, we used a different exposure control by assigning mothers that gave birth between 2006–2008 (prior to most UNGD) the exposure they would have had, had they given birth in 2009–2012 and found no association, suggesting that time-invariant residual confounding did not account for our results. In response to Cox’s suggestion, we have utilized a negative outcome control¹¹ to assess the association between our unconventional natural gas development activity index and skin and soft tissue infections in mothers and found the expected null result.

Our observational study does not offer conclusive evidence, and like all scientific inquiry, should be weighed against alternatives and amended in light of new evidence. However, unconventional natural gas development continues to expand – 25,000–30,000 new wells were drilled each year from 2011–2014 in the United States¹² – with more women potentially exposed. Given the impossibility of randomized controlled trials, there is an urgent need for many more and more rigorous observational studies on the possible health effects of unconventional natural gas development.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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