THE AUTHORS REPLY

We thank Olsen and Zhu for their observations (1). We have reanalyzed our data (2) in light of Olsen and Zhu’s suggestion that parental age discrepancy may have confounded the association we reported between parental age at delivery and risk of autism. We found the following.

First, there were notable associations between advancing maternal and paternal age, on the one hand, and average parental age discrepancy (number of years older 1 parent was than the other parent; note that this is a negative number for a parent who is younger than the other parent) on the other hand. As Figure 1 shows, mothers tended to be younger than their partners before age 40 years, and the age discrepancy with their partners decreased, on average, with advancing maternal age. For fathers, there was little discrepancy in partner ages until after age 30 years, when the average age discrepancy increased steeply with paternal age.

Second, we found a weak positive association between parental age discrepancy and the risk of autism spectrum disorder in offspring. A 5-year parental age discrepancy was associated with a 20% increase in autism risk (unadjusted odds ratio = 1.2, 95% confidence interval: 1.1, 1.4).

Third, there was no significant effect of parental age discrepancy when it was included in our adjusted model (for a 5-year parental age discrepancy, adjusted odds ratio = 1.1, 95% confidence interval: 1.0, 1.3). Inclusion of parental age discrepancy in the model did not affect the point estimates for or significance of the maternal and paternal age effects that we reported earlier (2) and did not improve the model fit as measured by log-likelihood tests.

Fourth, since the relation between parental age and parental age discrepancy was not linear—particularly in the older age ranges—we also stratified our results by 5-year age category for fathers and mothers. After adjustment for the other covariates, the odds ratios for age discrepancy (whether treated as a continuous variable or as a dichotomous variable) were not significantly different from 1.0 in any age-parent category.

On the basis of these results, we conclude that the effects of parental age on autism risk are best accounted for by the age of each parent rather than by parental age discrepancy. In addition, our finding that autism risk was higher when both parents were older than when only 1 parent was older is not consistent with Olsen and Zhu’s age discrepancy hypothesis. We cannot comment on the assertion that parental age discrepancy is associated with a “fetotoxic lifestyle,” as we have not seen any evidence pertaining to this.

Olsen and Zhu also point out a possible explanation for the inverse association we reported between birth order and risk of autism spectrum disorder—namely, that reduced
fecundity is likely to be associated with advanced parental age at first birth and therefore may partially explain the birth order effect (1). This is a logical suggestion but, unfortunately, it is not one we can examine, as the data available for our cohort did not include markers of fecundity or information on specific disorders associated with reduced fecundity. This hypothesis, along with others mentioned in our original report (2), merits further study.

Finally, we would like to correct the statement made by Olsen and Zhu that our data showed the parental age effects to be especially strong for firstborn children (1). In fact, we found no interaction between parental age and birth order in the effects of these factors on autism risk. The increased risk with parental age was present for firstborn as well as later-born children. However, because the effects of each parent’s age and birth order were independent of each other, the highest risk group included firstborn children with parents who were both older.

ACKNOWLEDGMENTS

Conflict of interest: none declared.

REFERENCES


Maureen S. Durkin1, Matthew J. Maenner1, Christopher M. Cunniff2, Laura A. Schieve3, and Mark A. Albanese1 (e-mail: mdurkin@wisc.edu)
1 Department of Population Health Sciences, School of Medicine and Public Health, University of Wisconsin–Madison, Madison, WI 53726
2 Department of Pediatrics, College of Medicine, University of Arizona, Tucson, AZ 85724
3 National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA 30333

DOI: 10.1093/aje/kwp063; Advance Access publication April 24, 2009

Figure 1. Average parental age discrepancy for mothers and fathers, by parental age, in a 1994 birth cohort representing 10 study sites from the Centers for Disease Control and Prevention’s Autism and Developmental Disabilities Monitoring Network (n = 253,347 births with complete parental age information).