Reviewer’s report

Title: A comparison of temporal trends in United States autism prevalence to trends in suspected environmental causes.

Version: 2  Date: 7 April 2014

Reviewer: Jennie Kline

Reviewer’s report:

The purpose of this paper is to identify whether exposure levels for selected environmental agents increase over time as do the prevalence rates of diagnosed autism. The author concludes that the agents without increases in levels over time are unlikely to be “driving” the temporal increase in autism. This conclusion rests on the assumption that the increase in diagnosed autism over time is due to one (or perhaps a couple) of environmental exposures. The conclusion is not equivalent to saying that the agent is unlikely to be a cause of autism. The utility of an ecologic analysis of this type is limited. It is best suited to identifying suspect agents for further study, rather than excluding agents.

I appreciate the scholarly effort it took to describe temporal trends in selected environmental agents. While the main conclusion of the manuscript is clear (i.e., some exposures increase over time, others do not), I find the description of the analysis and interpretation unclear.

1. The terminology is unclear. What is an age-resolved snapshot? The closest I can come to a definition is on page 7 where it says Report year is held constant while age was varied from 5-17. Is this the same as the prevalence of autism at ages 5-17? In the tracking approach, “Age was held constant while Report year was varied from 1991-2010”. In Figure 1, for example, 8- and 11-year old “tracks” are provided. Are these the prevalence of autism among 8 and 11 year olds, respectively? Did the author consider using cumulative incidence to age x? I am not sure what age x should be, since there is a trade-off between the completeness of diagnosis in the birth cohort and the latest birth cohort that could be included.

2. The author states that comparison of the age-resolved snapshot with estimated changes in prevalence over time from regression analysis identifies the proportion of the change over time in autism prevalence that is “real” (e.g., page 9, 15), rather than due to “better or expanded diagnosis”. I do not understand how this comparison yields the proportion of cases that are “real”.

3. It is unclear whether this paper is looking at time trends in autistic disorder (narrowly defined) or ASD. The CDDS primarily measures autistic disorder, whereas the IDEA includes ASDs.

4. I concur that the prevalence of diagnosed AD or of ASD has increased over time. This change does not mean, however, that either the true prevalence or incidence has changed. A major limitation of the analysis is the assumption that
temporal trends reflect real changes rather than changes in diagnosis or the likelihood of ascertaining an affected child. For example, the Hertz-Picciotto and Delwiche paper (California data) suggests that 56% of the increase in rates in recent years may be due to providing services to milder cases (as compared with a 20% estimate in the current manuscript). The author considers the 56% estimate “wrong” (page 16), but I do not follow her argument.

The author refers to the “diagnosed prevalence of autism”. She means the “prevalence of diagnosed autism”.

5. The manuscript is not organized in the usual manner, making it difficult to follow. Thus, the author includes interpretation under Results (e.g., page 11 “the results indicate that the IDEA definition of ….”) and then again under Discussion (e.g., page 15 repeats the point on page 11). The discussion of the Hertz-Ricciotto and Delwiche paper (page 16) is difficult to follow without reading the previous report.

6. The discussion of reasons for temporal changes in the selected environmental exposures, while interesting, detracts from the central points of the paper. What is the rationale for including obesity (which is not on the list of 10 agents set out by Landrigan et al 2012)?

7. Throughout the discussion, the author provides references to both individual level and ecologic studies that implicate agents that do not show increases in exposure levels over time (i.e., were not similar in direction to autism time trends in the current analysis). These examples illustrate that the approach taken in this paper cannot be used to identify agents that are not causally related to autism. Conversely, other exposures which increased in frequency or level over time (e.g., folic acid, ultrasound) are not positively associated with autism; indeed, folic acid exhibits an inverse association.

8. I find the terminology “drivers of the temporal trend” confusing. Does this terminology mean the same thing as “possible causes of autism”? Page 14 states that the premise of this paper is that the 20-fold increase in autism prevalence over 35 years is due to a single exposure or “collective influence of multiple environmental exposures”. The paper does not deal with collective multiple exposures, nor can I see how it could. As far as single exposures go, if the increase in autism prevalence were really 20-fold, it seems unlikely to me that a single cause would have gone undetected for the last two decades. It is common knowledge that some of the exposures studied (e.g., lead, air pollution) have decreased over time. I do not see a reason for carrying out a time trend analysis on these exposures.

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
No competing interest.