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Maternal Antenatal Corticosteroid Treatment and Childhood Mental and Behavioral Disorders

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2020-10-20

Sjölander , A , Kaprio , J & Latvala , A 2020 , ' Maternal Antenatal Corticosteroid Treatment and Childhood Mental and Behavioral Disorders ' , JAMA : The Journal of the American Medical Association , vol. 324 , no. 15 , pp. 1570-1570 . <https://doi.org/10.1001/jama.2020.15452>

<http://hdl.handle.net/10138/328227>

<https://doi.org/10.1001/jama.2020.15452>

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7/11/20

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Group Title: Maternal antenatal corticosteroid treatment and childhood mental and behavioral disorders

To the Editor:

Dr Räikkönen and colleagues¹ examined the association between maternal antenatal corticosteroid treatment and mental and behavioral disorders in children. We are concerned that there may be an important statistical error in the analysis.

An essential element of the authors' conclusions was their statistical analysis of "within-sibpair comparison,s, in which they estimated differences in cumulative incidence rates and hazards ratios. The authors claimed that their analysis automatically adjusted for unmeasured familial confounding.

However, this claim is incorrect for the estimated hazard ratios, since these compared siblings *between* families with treatment and families without treatment, rather than between treated and untreated siblings *within* families, as would be expected in a *within-sibpair* comparison.

Specifically, the authors' hazards ratios compared treated siblings from treatment discordant pairs (numerator) to siblings from pairs in which both siblings were untreated (denominator).

This comparison is non-standard, and there is no reason why it would adjust for unmeasured familial confounding.

Consider the following example. Suppose that women with low socioeconomic status are at a higher risk of preterm delivery and hence also at higher probability of receiving the treatment.

Suppose also that children who are born to mothers with low socioeconomic status are at a higher risk of mental disorders. Then siblings from pairs in which one sibling is treated will more often have mothers with low socioeconomic status, and will thus more often have mental

disorders, than siblings from pairs in which both siblings are untreated. In the presence of such familial confounding, the hazard ratios estimated by Räikkönen and colleagues will be greater than 1 even in the complete absence of a treatment effect. In contrast, by comparing siblings from the same family, a correct within-sibpair comparison would, to a large extent, adjust for socioeconomic status, since this factor is fairly constant within families across time.

The within-sibling comparison is a powerful epidemiological design that, if used correctly, may adjust for a large set of unmeasured confounders. We thus encourage Räikkönen and colleagues to provide a correct within-sibpair analysis of their data, as in Sjölander et al²⁻⁴ or Allison.⁵

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Conflict of Interest Disclosures: None reported.

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