

CORRESPONDENCE

Response to the comment on: Prenatal exposure to acid-suppressive drugs and the risk of allergic disease in the offspring: a cohort study

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Petrus and colleagues commented on our study [1] making a case for the application of internationally accepted clinical guidelines for the diagnosis of atopic diseases, notably asthma in children. Indeed, the identification of children with asthma in our pharmacy-based retrospective cohort study was based on respiratory prescriptions for inhaled corticosteroids rather than clinical symptoms or diagnoses. In the discussion, we have acknowledged that this is a limitation of our data. However, according to the primary care guidelines, asthma (like) symptoms should be treated preferably with bronchodilators and only the severe cases should receive corticosteroids. So, we limited our outcome definition to the more severe cases of asthma to increase specificity. High specificity is needed for causal research, but the downside is that we will have missed potential asthma cases. Consequently, asthma definitions used in causal research differ from the circumscription of asthma in clinical practice. In addition, diagnosing asthma in young children in Dutch primary care is rarely carried out by golden standard diagnostics such as lung function measurements as suggested by Petrus and colleagues which when included in the case definition would have led to serious selection bias. Further, we believe that misclassification of asthma, if present, is most likely random between mothers who did or did not use acid-suppressive drugs during pregnancy which would have biased our findings towards a null finding.

Of note, results of the current study by Mulder et al. [1] were comparable to that of Hak et al. [2] using a complete different database with primary care diagnoses (CPRD) in which the same relation was studied and children were defined as having asthma based on both clinical diagnoses and anti-asthma prescriptions. We agree with Petrus et al. that the peak percentage of asthma in this study lies at an earlier age than presented by Barnetson and Rogers [3]. This may well be explained by differences in outcome definitions. We therefore additionally examined the subgroup of children that were prescribed two inhaled corticosteroids after the age of 5 years. Results of this subanalysis yielded even higher risks for the development of childhood asthma after prenatal exposure to acid-suppressive drugs [aHR 2.59 95% CI (1.69–3.95)].

We agree with Petrus and colleagues that the identification of childhood asthma with the aid of prescription data is not ideal. However, we believe that the relation between prenatal exposure to acid-suppressive drugs and the development of childhood asthma is confirmed by our study due to additional information of the subgroup analysis and the concordance of our results with the results of the study of Hak et al. [2]. More prospective studies including preferably unselected asthma cases are needed to confirm findings from our and other groups.

References

- 1 Mulder B, Schuiling-Veninga CCM, Bos HJ, De Vries TW, Jick SS, Hak E. Prenatal exposure to acid-suppressive drugs and the risk of allergic diseases in the offspring: a cohort study. *Clin Exp Allergy* 2014; 44:261–9.
- 2 Hak E, Mulder B, Schuiling-Veninga CCM, Bos JH, De Vries TW, Jick SS. Use of acid-suppressive drugs in pregnancy and the risk of childhood asthma: bidirectional case-crossover study using the General Practice Research Database. *Drug Saf* 2013; 36:1097–104.
- 3 Barnetson RS, Rogers M. Childhood atopic eczema. *BMJ* 2002; 324:1376–9.

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