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Letter to the Editor

Paracetamol use for non-respiratory indications and subsequent asthma: a valuable way to eliminate confounding by respiratory infections

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Rusconi *et al*.[1] report an interesting analysis of the data arising out of SIDRIA-2 (Italian Studies of Respiratory Disorders in Childhood and the Environment phase 2), the Italian arm of phase two of the International Study of Asthma and Allergies in Childhood (ISAAC). Using directed acyclic graph (DAG) and logistic regression analysis, the authors conclude that the association between paracetamol consumption in early life and childhood asthma 'might fully or in part, be due to confounding'. The use of age of onset of symptoms is innovative and useful, and we appreciate the more comprehensive analysis of ISAAC data relating to this question than has been previously reported.[2,3] Whereas we agree with the authors' overall conclusion, we feel that one of the issues raised within this paper needs further discussion to put the results in the context of all the available evidence.

The authors state that 'It is well known that wheeze, especially in the first years of life, is chiefly triggered in susceptible individuals by viral infections for which paracetamol (owing to accompanying fever) and antibiotics (owing to a difficult differential diagnosis with bacterial infections) are often prescribed'. Although paracetamol is commonly used for the management of fever, it is also often used as an analgesic in young children. In the Melbourne Atopy Cohort Study (MACS), a birth cohort of 620 children with a family history of allergic disease, we found that 94% of children had received paracetamol for various forms of physical injury, or for the management of immunization-related pain, by 2 years of age.[4] Examining the impact of paracetamol treatment for non-respiratory causes on subsequent asthma is not confounded by respiratory infections, and allows us to see the direct effect of paracetamol exposure on risk of allergic disease. Such an approach is valuable in disentangling the effect of paracetamol and respiratory tract infections on subsequent risk of asthma. Unfortunately, the indication for use of paracetamol was not collected within the ISAAC study.

In the MACS, we found that, although total use of paracetamol was associated with increased risk of childhood asthma (at 6–7 years of age), paracetamol for non-respiratory tract indications was not associated with any allergic disease outcome, including asthma.[4] This provides further evidence that the association between paracetamol intake in early life and childhood asthma is more likely to be due to confounding, rather than a causal relationship.

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