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## Author's response

I want to thank Drs Mahut and Delclaux for their interesting letter concerning our recent paper<sup>1</sup> and would offer the following response. During acute asthma exacerbation only two of 15 patients with asthma (13%) had a combined abnormally elevated central airways nitric oxide (NO) flux and elevated peripheral airway/alveolar NO concentration after correction for NO axial back-diffusion. Central airways NO flux remained the major site of 'NO-mediated inflammation' in 13 of 15 patients with asthma since two had normal NO gas exchange despite acute exacerbation.<sup>1</sup> This latter observation needs to be further investigated since the clinical response was similar to that in patients with asthma with abnormal NO gas exchange. Many years ago we investigated the simplified detection of peripheral airway disease and showed that analyses of the distal part of the maximum expiratory flow–volume curve were helpful.<sup>2</sup> However, in a subsequent study<sup>3</sup> we reported that, if the ratio of forced expiratory volume in 1 s to forced vital capacity (FEV<sub>1</sub>/FVC) was  $\geq 75\%$ , the occurrence of an isolated abnormal mid forced expiratory flow (FEF<sub>25–75</sub>) was rare. However, if the FEV<sub>1</sub>/FVC was  $< 75\%$ , it would not be unusual to find an abnormal FEF<sub>25–75</sub>, but it would not discriminate peripheral from large central airways obstruction.<sup>3</sup> I hope these comments are helpful and appreciate their interest.

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## Definitions are important and not all wheeze is asthma

We read with great interest the paper by Moncayo *et al*<sup>1</sup> showing a predominance of non-atopic compared with atopic wheeze in children in rural Ecuador. Undoubtedly their study adds to the literature regarding the influence of environmental factors, particularly chronic helminth infections, on wheezing phenotypes. However, we feel that the interpretation and presentation of findings in this paper is open to question. This concern stems from the authors' lack of distinction between wheeze and asthma. While the analysis focused predominantly on current wheeze, subsequent discussion (and, indeed, the title) presents this as asthma.

There is good evidence for the validity of a questionnaire-based definition of asthma.<sup>2</sup> Our understanding of the definition of asthma used in this paper was of a positive response to 'wheeze in the last 12 months'. Yet wheeze may not necessarily reflect asthma, particularly in childhood where both acute infection and chronic illness might be associated with wheeze. Using only one symptom therefore runs the risk of poor discriminatory value between asthma and other causes of wheeze, making this definition of asthma potentially problematic.<sup>3</sup>

Relying on 'current wheeze' to represent asthma may also exclude a substantial proportion of 'ever wheezed' subjects, given the heterogeneous nature of childhood wheeze<sup>4</sup> and the relapsing and remitting course it may run.<sup>5</sup> There is therefore an additional risk of misclassification where subjects with asthma who were currently asymptomatic are regarded as non-asthmatic. Given that the stated principal aim of this study was to investigate risk factors for asthma/wheeze, exclusion of those without current symptoms potentially provides an incomplete picture of risk, especially when one considers that 'ever wheezing' has been shown to be a superior predictor of lifetime asthma diagnosis.<sup>5</sup>

Ultimately, asthma is a clinical diagnosis and no questionnaire-based definition can be all-encompassing. Since none of the children in this study were on regular asthma medication, perhaps combining current wheeze with the number of wheezing episodes and including a variable of 'ever wheeze' in the

diagnostic criteria might have better selected participants with a greater likelihood of asthma.

In summary, we feel that the distinction between asthma and wheeze is important to recognise and this paper fails to clearly acknowledge this. Finally, we thank the authors for describing some of our previous findings from the Isle of Wight Birth Cohort,<sup>4</sup> but wish to clarify that those findings related to atopic/non-atopic wheeze and not asthma as they suggest in the introduction to their paper.

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## Author's response

Drs Marsh and colleagues are essentially correct in saying that the word 'wheeze' rather than 'asthma' may have been more appropriate in the title of our paper. Not all wheeze is asthma but, given the lack of a widely agreed definition for asthma, we chose to use a simple but widely used definition (wheeze in the past 12 months) in this Ecuadorian study to estimate prevalence. As the authors will have seen from the abstract, the aim of the study was to investigate risk factors for atopic and non-atopic wheeze illness to understand better those that may cause or protect against asthma in the study population.<sup>1</sup>

All subjects with wheeze in the past 12 months had a history of wheeze ever. A high proportion of children in the study population had a history of wheeze ever (32.5%), most of which could be attributed