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## Predicting risk of asthma in wheezing infants

Devulapalli *et al*'s paper<sup>1</sup> attempts to answer the commonly encountered clinical question, "what is the risk of asthma in this wheezy infant?" While welcoming this attempt, we wish to put this into perspective and draw comparison with our similar work on the Isle of Wight Birth Cohort published 5 years ago.<sup>2</sup>

Findings that children with asthma at 10 years often had recurrent bronchial obstruction (RBO+ve) at 2 years are not new. We previously reported that recurrent chest infections at 2 years (causing airway obstruction and wheeze) increases the risk of asthma development at 10 years by more than fourfold.<sup>3</sup> A simple risk score such as that of Devulapalli *et al*, not reliant on invasive testing, is an attractive concept. However, there are significant shortcomings in this work. For wide acceptability, the factors contributing to the risk scores should be unambiguous. The proposed risk score relies on "severity", which is difficult to define and measure in this context. Hospitalisations for wheezing in infancy do not necessarily reflect a set degree of severity. Secondly, the outcome variable of diagnosed asthma is potentially contentious given the subjective nature of that label. The reasons for not including an objective measure such as bronchial hyperresponsiveness to consolidate asthma diagnosis is not clear. Alternatively, a phenotypic analysis using "wheeze" rather than "asthma" may be less prone to subjective bias. We have demonstrated<sup>4</sup> that most childhood asthma originated in infancy as "early onset persistent wheeze". We feel that a phenotypic understanding is vital in asthma where analysis of isolated events in time could

convey a misleading snapshot of a complex disease. Finally, any case control study is prone to misclassification based on response evaluation and investigator bias. Reliance on such methodology to create a risk score could draw into question the potential validity of that tool.

The authors fail to compare their "risk score" with our published risk scores to show that theirs is indeed an improvement on what has already been known. We proposed a simple and practical risk scoring system for outcome of early life wheeze<sup>2</sup> comprising four factors (family history of asthma, recurrent chest infections at 2 years, absence of nasal symptoms in infancy and atopic sensitisation at 4 years), showing independent significance for persistence of early wheeze to age 10 years in our cohort. The presence of all four was associated with a positive predictive value of 83.3 and a negative predictive value of 63.9 for persistent disease, compared with corresponding values of 54.3 and 86.8 with the score outlined by Devulapalli and colleagues.<sup>1</sup>

The ability to accurately predict outcome of early life wheeze is clearly desirable. However, any new proposal should be considered in the context of existing work. Comparisons should be made in terms of sensitivity and specificity, and common ground should be sought to eventually develop a predictive scoring system, which is practical, valid and clinically useful. We are certainly not there, yet!

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## Authors' reply

We wish to reply to Drs Raza, Kurukulaaratchy and Arshad who commented on our recent article.<sup>1</sup> Our primary aim for making a severity score was to try to predict the prognosis of early life obstructive airways disease, independent of invasive examinations

or measurements, and easily applicable for use in other studies and in primary care. Thus it is not clear to us why Raza *et al* find the factors used in our severity score difficult to define, including our use of hospitalisations for obstructive airways disease. In our view, hospital admission because of bronchial obstruction is an objective measure of severity, which is easily verified and recorded.

They question the use of diagnosed current asthma as the outcome, suggesting that this may reduce the validity of the tool and criticise that bronchial hyperresponsiveness (BHR) was not used to consolidate the diagnosis of asthma. We disagree with both of these comments. In fact, as was clearly stated, exercise induced bronchoconstriction (EIB; a measure of BHR) is part of our well defined term "current asthma" used for the 10 year follow-up study of our birth cohort, including studies on asthma prevalence,<sup>2</sup> lung function at birth versus asthma at 10 years of age<sup>3</sup> and asthma genetics.<sup>4</sup> Our definitions of asthma and current asthma are stricter than in many other studies including, but not limited to, "wheeze" alone, requiring at least two out of three criteria (symptoms/medication or the presence of EIB in the last year or during the investigation) to acquire a definition of asthma.<sup>2</sup> While "wheeze" as the outcome may be appropriate in English speaking countries, it is not a term used in most other languages. Consequently, it appears less stringent, more prone to subjective reporting but nonetheless seems to be more frequent in our<sup>2</sup> and other studies than a history of asthma and current asthma. Furthermore, the authors themselves have also used the term "asthma" when reporting from their own birth cohort study.<sup>5</sup>

Raza *et al* further criticise the fact that we did not cite their paper,<sup>6</sup> describing their risk score for persistent wheeze at the age of 10 years. Although this may be an omission, our aim was not a retrospective risk assessment of persistent wheeze but prospectively to assess the risk for current asthma at 10 years in children with recurrent bronchial obstruction at 2 years. Furthermore, as the authors themselves demonstrated in their cohort, the positive predictive value (PPV) for wheeze at 10 years from the score applied at 4 years was much higher than when applied at 2 years (PPV = 0.475),<sup>6</sup> which is considerably less than our 2 year score. The severity score applied is probably age specific, highlighted by our own score which was not found to be useful at 1 year of age.<sup>1</sup>

In our view, the comments of Raza *et al* do not diminish the validity of our severity score, but we stress that the present as well as any other scores must be confirmed in other studies in different populations before any general acceptance can be reached.

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