

Predicting the long-term outcome of preschool wheeze: Are we there yet?

Graham Roberts, DM, MSc, MRCPCH *Southampton and Newport, United Kingdom*

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Asthma is one of the more difficult diagnoses for doctors to make in the preschool age group. Wheeze as a symptom is often inaccurately reported by parents,¹ and many children with wheeze have diagnoses other than asthma. In this month's issue of the *Journal*, Caudri et al² present a clinical risk score to improve the diagnosis of asthma in preschool children. They have used data from the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort, in which participants were assessed on a yearly basis to the age of 8 years. The cohort study enrolled 3963 children and has achieved excellent follow-up rates, with 80% of the eligible study population providing data at 8 years of age. In the subgroup of children who reported wheeze or coughing at night without a cold until age 4 years, they assessed possible predictors for asthma at 7 to 8 years of age. They found that male sex, postterm delivery, parental education, inhaled medication, wheezing frequency, wheeze/dyspnea apart from colds, respiratory infections, and eczema all independently predicted later asthma.

One of the challenges of asthma research is the absence of a gold standard diagnostic test. The authors have defined asthma on the basis of wheeze, the prescription of inhaled corticosteroids, or a doctor's diagnosis of asthma during each of the seventh and eighth years of life. This definition does lead to the potential for misclassification bias, resulting in overdiagnosis of asthma, because parents are very poor at accurately reporting wheeze.¹ Given that only 10% of children with asthma were diagnosed just on the basis of reported wheeze, any bias should be minimal.

Over the last decade, a number of asthma predictive scores have been put forward. The authors compare and contrast their score with the predictive index of Castro-Rodriguez et al.³ This was developed in a much smaller birth cohort with a very different ethnic mix. Castro-Rodriguez et al included eosinophilia as a minor criterion, although a complete blood count is not generally part of the work up of a preschool child presenting wheeze. By using more predictive factors, Caudri et al² seem to have generated a more accurate predictive score with their chosen cut-off levels. A

number of other groups have put forward their own asthma risk scores. For example, using the Isle of Wight 1989 birth cohort, Kurukulaaratchy et al⁴ proposed a simple scoring system based on recurrent chest infections, family history of asthma, atopy on skin prick testing, and nasal symptoms to predict the persistence of wheeze at 10 years of age. The differences in the variables included in these 3 asthma prediction scores call into question whether they can be successfully used in other populations. All 3 include some reference to a family history of asthma, but only 2 have any mention of eczema, rhinitis, or wheezing apart from colds. However, it is possible that the recurrent chest infections identified in the Isle of Wight cohort are actually misreported episodes of recurrent wheeze. All this emphasizes the need to test the different predictive scoring systems in different populations to give clinicians the confidence that these predictive systems are applicable to other populations.

The methodology for constructing predictive indexes and their presentation has developed considerably in the last decade. Castro-Rodriguez et al³ use a major and minor criteria system based on a univariate analysis of their cohort data. Kurukulaaratchy et al⁴ combine the 4 independent predictors from the multivariate analysis of their cohort data to generate a simple scoring system whereby each predictor contributes 1 unit to the 0 to 4 score. Both studies then present sensitivity, specificity, and positive and negative predictive values for the scoring systems at different cut-offs. Sensitivity and specificity provide a population perspective that often exaggerates the apparent diagnostic certainty of the test at the level of individual patients.⁵ This is overcome by the use of positive and negative predictive values, but these are influenced by the prevalence of asthma in the population being assessed.⁶ Caudri et al² have taken a more complicated approach, making use of the odds ratios for individual predictors from their multivariate analysis. Although this seems to have generated a more accurate predictive model, the application of the scoring system becomes somewhat laborious, with different factors having different weightings. However, they do neatly overcome the drawback of having 1 cut-off point by presenting a probability curve relating the asthma prediction score to the predictive risk of asthma in their population. By using this approach, they have maximized the information available from their asthma prediction score.⁷ Two words of caution are required. First, this predictive risk of asthma is still dependent on the prevalence of asthma in the population, so it may not be completely generalizable. Second, the authors provide no indication of the precision of the predictive risk as would have been given by additional lines highlighting the 95% CI.

In general, clinicians very rarely use prognostic models. One of the major reasons for this is that they are too time-consuming to use in everyday clinical settings.⁸ Clinicians seem to be weary of

From the School of Medicine, University of Southampton; and the David Hide Asthma and Allergy Research Center, St Mary's Hospital, Newport.

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Reprint requests: Graham Roberts, DM, MSc, MRCPCH, Paediatric Allergy and Respiratory Medicine, University Child Health (MP803), Southampton University Hospital NHS Trust, Tremona Road, Southampton SO16 6YD, United Kingdom. E-mail: g.c.roberts@southampton.ac.uk.

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these models with their lack of validation in different settings, particularly their own. There may also be an anxiety among some clinicians that prediction models are a means of doing away with the need for a doctor.

If clinicians are to use predictive scores more widely, we need to improve the way predictive scores are presented, validated, and assessed in terms of their clinical impact. Scores will be used by busy clinicians only if they are easy to remember and use or if they come packaged within a clinical information system. Perhaps the biggest hurdle, though, is the failure to validate the current asthma predictive scoring systems adequately by testing them in other populations. There are many reasons why a predictive score may not be generalizable. Examples are the failure to include a factor that is an important predictor in other populations, important differences in patient characteristics between populations, or differing health beliefs or reporting behavior. An example of a successfully validated system is the predictive values for skin prick testing and specific IgE. These have been extensively validated in different populations for food allergy and are now being used in clinical practice.^{7,9} The last hurdle is to demonstrate clinical impact. This is rarely assessed,¹⁰ meaning that clinicians do not know whether predictive scores are going to improve the care of patients. Doctors instinctively use multiple parameters to make management decisions based on their own training and their own personal experience. They therefore need to be convinced that a predictive scoring system developed in another locality can improve the clinical care that they deliver.

Although Caudri et al² have further developed the concept of a predictive index for asthma, we still do not have a system that clinicians are likely to use routinely. With the multitude of causes of preschool wheeze and the heterogeneity of childhood asthma, it may actually prove impossible to develop a more accurate model

without increasing the number of variables to cover specific genetic polymorphisms, environmental factors, socioeconomic factors, pre-existing illness such as eczema, sex, ethnicity, and health beliefs. Even then, to be taken up by busy clinicians, a model needs to be easy to apply, validated in different populations, and shown to improve patient outcome.

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