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Predicting the outcome of early childhood wheeze: mission impossible

See linked article by Cano-Garcinuño *et al.* on pg 60

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Every general practitioner (GP) knows that many young children wheeze during upper respiratory tract infections, and that most of these children do not become asthmatic later during childhood. Data from population-based studies show that one in three children will have at least one episode of wheezing during

the first three years of life.¹ Two-thirds of these preschool wheezers outgrow their symptoms by the age of six, and the remaining third develop asthma.^{1,2} Wouldn't it be great if we could predict which preschool wheezer will become asthmatic and which will not? Such knowledge would not only be useful for counselling parents, but could also be used to target therapy. Given our ongoing concerns over the safety of inhaled corticosteroids, particularly in young children,³ we prefer to avoid treating transient preschool wheezers unnecessarily with daily controller treatment for asthma.

Until recently, the knowledge about which factors were associated with the persistence or remittance of preschool wheeze came from general population birth cohort studies.¹ The asthma predictive scores based on these studies show a statistically significant association with asthma and wheeze at age six years, but their value for predicting the outcome of preschool wheeze in individual cases is poor.⁴ Since not all young children with wheeze are brought to their GP, the applicability of these asthma predictive scores in primary care is unclear. In addition, because parents use the word "wheeze" to describe a range

of respiratory sounds and phenomena in their children,⁵ and only doctor-confirmed wheeze is associated with airway obstruction in preschool children,⁶ asthma prediction scores from population studies should be validated against doctor-confirmed wheeze in primary care.

In this issue of the *PCRJ*, Cano-Garcinuño and colleagues present results from a review of medical records of preschool children from 29 primary care health centres in northern Spain.⁷ If the primary care physician recorded wheeze on auscultation in the chart of a child presenting with respiratory symptoms, this was defined as a wheezing episode. Children were followed up to the age of six years. Data were analysed with innovative statistical techniques, comprising both latent class analysis and linear joinpoint regression, allowing, in the words of the authors, “a high-resolution analysis of incidence”. The authors conclude that such incidence analysis helps to clarify the natural history of early childhood wheezing.

Let us examine their results in a little more detail. Almost half of the children (45.6%) had at least one episode of wheeze during the first three years of life, and 25% of these were diagnosed with active asthma (a doctor's diagnosis plus prescription of at least one anti-asthma drug) by the age of six years. Interestingly, the prevalence of wheeze was considerably higher in this Spanish primary care study than in two earlier population-based birth cohort studies from the UK and the Netherlands.⁸ This is unlikely to be caused by a smaller denominator (i.e., not all children visiting their primary care practitioner), since the primary care physician for children in Spain is the community paediatrician who sees all children both for prevention purposes (well baby visits and immunisations) and for symptoms or illness. It is also unlikely that the true population prevalence of wheeze in young children is higher in Spain than in other western European countries; previous work using parent-reported prevalence of wheeze in young children showed slightly lower wheeze prevalence in Spain than in the Netherlands.⁹ Spanish primary care paediatricians may thus be more likely to record chest auscultation findings in young children as “wheeze” than their English and Dutch colleagues. These results call for further studies examining the differences between physicians from different countries in their interpretation of chest auscultation findings in young children.

Did the primary care setting of the study⁷ – with doctor-confirmed instead of parent-reported wheeze – improve the value of clinical signs and symptoms in predicting asthma at age six? No. Almost half of the children with active asthma at age six (46.6%) belonged to the never/infrequent wheeze group in the first three years of life (children who had never (74%) or very infrequently wheezed (never more than three wheezing episodes, 26%). The sensitivity of wheeze pattern in early life for predicting asthma was therefore poor. Likelihood ratios were also too small to be clinically useful. The incidence patterns of wheeze identified in this Spanish study are insufficiently distinctive to allow reliable prediction of the outcome of early childhood wheeze. Very recently, data from the Leicester birth cohort study have shown similar results.¹⁰ Simple clinical characteristics – such as wheeze not

associated with a cold, wheeze frequency, disturbance of activities, personal history of eczema, and family history of atopy – helped a little bit, but not much, in predicting the outcome of early childhood wheeze presenting to a GP.¹⁰

Experienced GPs know this already. They also know that you can never tell in an individual case. This is likely due to the multifactorial nature of both early childhood wheeze and childhood asthma, which are both only partly understood. I think it extremely unlikely that any other prospective cohort study using only clinical characteristics and perhaps some lung function and allergic sensitisation data is going to change this. Unless we find a better way to understand the genetic, immunologic, functional and pathological mechanisms of preschool wheeze and childhood asthma, predicting the outcome of wheeze in preschool children is, and is likely to remain, a mission impossible.

Conflicts of interest The author declares that he has no conflicts of interest in relation to this article.

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