

Correspondence

The Asthma Predictive Index: Not a useful tool in clinical practice

To the Editor:

Dr Castro-Rodriguez¹ provides an interesting overview of indices developed to predict whether wheeze in preschool children will persist beyond the age of 6 years or will disappear. The Asthma Predictive Index (API) is presented as a “very useful tool” to predict the long-term outcome of preschool wheeze “in every health care setting worldwide.” There are 3 reasons, however, why I disagree with this conclusion.

First, the API predicts the outcome of wheeze ever and not the outcome of recurrent wheeze. In the Tucson birth cohort study children have been characterized at the age of 3 years as “wheezing” when they had experienced at least 1 episode of wheeze ever before their third birthday.² It was noted that most of these early wheezers ceased to wheeze between the ages of 3 and 6 years (transient early wheeze), whereas a minority continued to wheeze until the age of 6 years (persistent wheeze).² Therefore the API was developed to predict which of these preschool ever wheezers would have persistent wheeze by the age of 6 years.³ In clinical practice, although children with an isolated episode of wheeze ever might visit a health care professional for the management of the acute wheezing episode, the question of whether wheezing will persist beyond the sixth birthday is much more pertinent in preschool children with recurrent wheeze. Unfortunately, the API was neither developed for use nor ever tested in a population of preschool children with recurrent wheeze presenting to a physician for diagnosis and management. Before such studies have been carried out, it cannot be concluded that the API is useful to predict the outcome of recurrent wheeze in preschool children. This is an important issue because half of the young children with wheeze ever will in fact wheeze only once.⁴

Second, it is a basic rule in clinical epidemiology that a prediction rule developed in any given population can only be applied in clinical practice when it has been validated prospectively and independently in a different cohort.⁵ To my knowledge, this has never been done with the API. Although it has been used in clinical trials, its predictive value has not been formally tested in an independent different cohort of children with preschool wheezing. As Dr Castro-Rodriguez¹ points out in his excellent review, other population-based cohort studies have yielded different predictive indices for the outcome of preschool wheezing. Although this might be partly due to the use of different prognostic variables and statistical techniques, it is highly likely that the API will perform differently in predicting the outcome of preschool wheeze in other populations than the original one in which it was developed. Before concluding that the API can be used in different populations, formal validation studies must be performed.

Third, and perhaps most important, the predictive value of any diagnostic test, including the API, is highly dependent on the prior probability (prevalence) of asthma in the cohort in which it is being used. Although this is acknowledged by Dr Castro-Rodriguez¹ in his article, this critical issue is apparently overlooked in formulating the conclusion of the article. The effect of prevalence on the diagnostic value of the API can best be illustrated by a numeric example.

TABLE I. Performance of the API in predicting the outcome of preschool wheeze ever in a population of 1000 children using the values found in the Tucson study

	Asthma at age 6 y	No asthma at age 6 y	Total
API positive	204	720	924
API negative	2	74	76
Total	206	794	1000

TABLE II. Performance of the API in predicting the outcome of preschool wheeze ever in a population of 1000 children when the prior probability (prevalence) of asthma is greater (40%) than in the population-based Tucson study, as can be expected in a cohort of children visiting a physician for the management of recurrent wheeze

	Asthma at age 6 y	No asthma at age 6 y	Total
API positive	88	18	106
API negative	312	582	894
Total	400	600	1000

In such a more high-risk cohort, the negative predictive value decreases to 59%.

If the values for sensitivity, specificity, and positive and negative predictive value of the API¹ are being applied to a population of 1000 children, the numbers in [Table I](#) appear. Based on these numbers, Dr Castro-Rodriguez¹ concludes that the API shows “impressive ... ability to rule out the likelihood of asthma by school age in young children with wheezing.” The high negative predictive value on which this statement is based is primarily caused by the very low number of children who do have asthma, although they had a negative API result ([Table I](#)). Unfortunately, this number increases dramatically when the prior probability of asthma increases. [Table II](#) shows the performance of the API when the prevalence of asthma is 40% instead of the 20% value in the Tucson study. Sensitivity and specificity of a diagnostic test are independent of prior probability⁵; by using the values of these parameters as reported by Castro-Rodriguez,¹ the negative predictive value of the API deteriorates considerably to 59% ([Table II](#)). Although this is offset by a slight improvement of the positive predictive value from 77% to 83%, in this scenario the ability of the API to rule out asthma by school age is clearly insufficient. Further increasing the prevalence of asthma to 70% reduces the negative predictive value to 35%. It should be stressed that such a higher prior probability of asthma will be present in wheezy preschool children with a higher risk profile, such as children with recurrent wheezing instead of wheeze ever¹ or children who have been admitted to the hospital for severe wheeze.^{6,7} Basic clinical epidemiology therefore dictates that the performance of the API to predict the outcome of preschool wheeze will be poorer in more high-risk populations.

Although the API might be useful to predict the outcome of wheeze ever in a population-based sample of children in whom the prior probability of having asthma at school age is as low as 20%, the index is not useful in predicting the long-term prognosis of preschool children with more severe or recurrent wheeze in clinical practice. Clinicians should counsel parents who visit their practice with their preschool child for troublesome recurrent

wheeze that it is impossible to reliably predict whether their child's respiratory symptoms will disappear or persist beyond the sixth birthday.

Paul L. P. Brand, MD, PhD

From the Princess Amalia Children's Clinic, Isala Klinieken, Zwolle, The Netherlands, and the UMCG Postgraduate School of Medicine, University Medical Centre, Groningen, The Netherlands. E-mail: p.l.p.brand@isala.nl.

Disclosure of potential conflict of interest: The author has declared that he has no conflict of interest.

REFERENCES

1. Castro-Rodriguez JA. The Asthma Predictive Index: a very useful tool for predicting asthma in young children. *J Allergy Clin Immunol* 2010;126:212-6.
2. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ, et al. Asthma and wheezing in the first six years of life. *N Engl J Med* 1995;332:133-8.
3. Castro-Rodriguez JA, Holberg CJ, Wright AL, Martinez FD. A clinical index to define risk of asthma in young children with recurrent wheezing. *Am J Respir Crit Care Med* 2000;162:1403-6.
4. Visser CA, Garcia-Marcos L, Eggink J, Brand PL. Prevalence and risk factors of wheeze in Dutch infants in their first year of life. *Pediatr Pulmonol* 2010;45:149-56.
5. Haynes RB, Sackett DL, Guyatt G, Tugwell P. *Clinical epidemiology: how to do clinical practice research*, 3rd ed. New York, Lippincott: Williams and Wilkins; 2006.
6. Goksör E, Amark M, Alm B, Gustafsson PM, Wennergren G. Asthma symptoms in early childhood—what happens then? *Acta Paediatr* 2006;95:471-8.
7. Bacharier LB, Phillips BR, Bloomberg GR, Zeiger RS, Paul IM, Krawiec M, et al. Severe intermittent wheezing in preschool children: a distinct phenotype. *J Allergy Clin Immunol* 2007;119:604-10.

doi:10.1016/j.jaci.2010.10.012