



Letters

Use of the Pediatric Asthma Risk Score to predict allergic and nonallergic asthma

Asthma is a heterogeneous disease that includes allergic, nonallergic, and other endotypes that complicate the development of tools to identify at-risk children. The Asthma Predictive Index (API) was developed in 2000¹ and has remained a useful clinical and research tool to identify children at risk for developing asthma. The API, however, is more specific than sensitive and is dichotomous, limiting its utility in identifying children at moderate risk. Subsequent iterations, such as the Modified API (mAPI),² have made only incremental improvements in accuracy.

The Pediatric Asthma Risk Score (PARS) is a quantitative scoring system developed using clinical and demographic data that can be collected during a typical outpatient visit with any health care practitioner (eFig 1).³ The PARS risk factors are parental asthma, eczema at ages 1 to 3 years, early wheezing at ages 1 to 3 years, wheezing apart from colds, polysensitization (aeroallergens or food allergens), and African ancestry.

The PARS has a higher sensitivity and similar specificity compared with the API and mAPI.³ We sought to determine the accuracy of PARS in predicting allergic and nonallergic asthma subtypes in 2 cohorts of children and compare these results with those of the API and mAPI.

The primary population was the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS), an at-risk cohort of 762 infants born to atopic parents. Children were identified by birth records from Greater Cincinnati, Ohio, from 2001 to 2003.⁴ Children underwent examinations at 1, 2, 3, 4, and 7 years of age, with allergy symptoms, wheezing frequency, wheezing apart from colds, and skin symptoms recorded. At 7 years of age, 589 children were assessed, and 95 had asthma based on reported symptoms and measures of lung function.⁵ Allergic asthma ($n = 71$) and nonallergic asthma ($n = 24$) were defined as asthma with or without a positive skin prick test result at any time point, respectively.

The UK population-based, Isle of Wight (IOW) 1989–1990 birth cohort of 1456 children of European descent served as the replication population.⁶ Asthma and allergy data were collected at birth and at 1, 2, 4, and 10 years of age. Allergy was defined as a positive skin prick test result at any time point. Asthma ($n = 156$, 90 allergic and 66 nonallergic children) was defined at 10 years of age based on physician diagnosis plus at least 1 episode of wheezing in the prior 12 months. For CCAAPS and IOW, the PARS was calculated according to the scoring sheet (eTable 1).

The receiver operator characteristic (ROC) curves for the API (both stringent [early frequent wheezing and 1 major or 2 minor

criteria] and loose [early wheezing and 1 major or 2 minor criteria]) and mAPI for the CCAAPS and IOW cohorts were calculated on the basis of published criteria. The ROC curve for PARS for all possible scores was determined for both cohorts. The area under the curve (AUC) was compared using the DeLong test ($P < .05$ considered significant). Sensitivity, specificity, predictive values, and likelihood ratios were determined for all possible scores, with the optimal sensitivity and specificity reported. Analyses were performed using R software.⁷

The AUC analysis (Fig 1 and eTable 1) demonstrates that the PARS (Fig 1) predicted allergic asthma significantly better than the API (loose criteria, Fig 1) in the CCAAPS (AUC, 0.82 [95% CI, 0.77–0.87] vs 0.71 [95% CI, 0.65–0.77], $P = .004$) and the IOW cohorts (AUC, 0.87 [0.84–0.91] vs 0.74 [0.69–0.79], $P = 7 \times 10^{-5}$). The PARS (Fig 1) also predicted nonallergic asthma better than the API (green line) in both cohorts, although it was only significant in IOW (CCAAPS: 0.71 vs 0.63, $P = .32$; IOW: 0.74 vs 0.64, $P = .04$). Results for the mAPI (Fig 1) were similar to those of the API in both populations for allergic and nonallergic asthma.

For allergic asthma, the PARS (at the cut point of optimal sensitivity and specificity) had an increased sensitivity when compared with the API (loose) in the CCAAPS (0.72 vs 0.61) and the IOW (0.83 vs 0.62) cohorts (eTable 1). Similarly, in nonallergic asthma, the PARS had an increased sensitivity in both CCAAPS (0.58 vs 0.46) and IOW (0.62 vs 0.42) cohorts. The specificity of the PARS was lower than the other indexes in both allergic (CCAAPS: 0.77 vs 0.81; IOW: 0.78 vs 0.86) and nonallergic asthma (CCAAPS: 0.77 vs 0.81; IOW: 0.84 vs 0.86). The negative predictive values for all indexes in both allergic and nonallergic asthma were similar and greater than 0.90. The positive predictive values for all indexes were low in both allergic and nonallergic asthma for the 2 cohorts.

The PARS outperformed both the API and mAPI in predicting allergic and nonallergic asthma development in 2 different cohorts of children, with a substantial increase in the AUC and an improved sensitivity with only a marginal decrease in specificity. When compared with the API, there was little effect on the negative predictive value or positive predictive value and, compared with the mAPI, a small decrease in the positive predictive value for allergic asthma. In nonallergic asthma, the AUC was significant in the IOW cohort but not in the CCAAPS cohort (possibly related to statistical power). The sensitivity for nonallergic asthma was improved with only a marginal decrease in specificity. The positive predictive value was similar in all indexes for nonallergic asthma.

It is not unexpected that PARS, mAPI, and API performed better in allergic asthma than nonallergic asthma given that the factors in these indexes include sensitization, eczema, eosinophilia, and allergic rhinitis. However, the PARS, a continuous scoring system,

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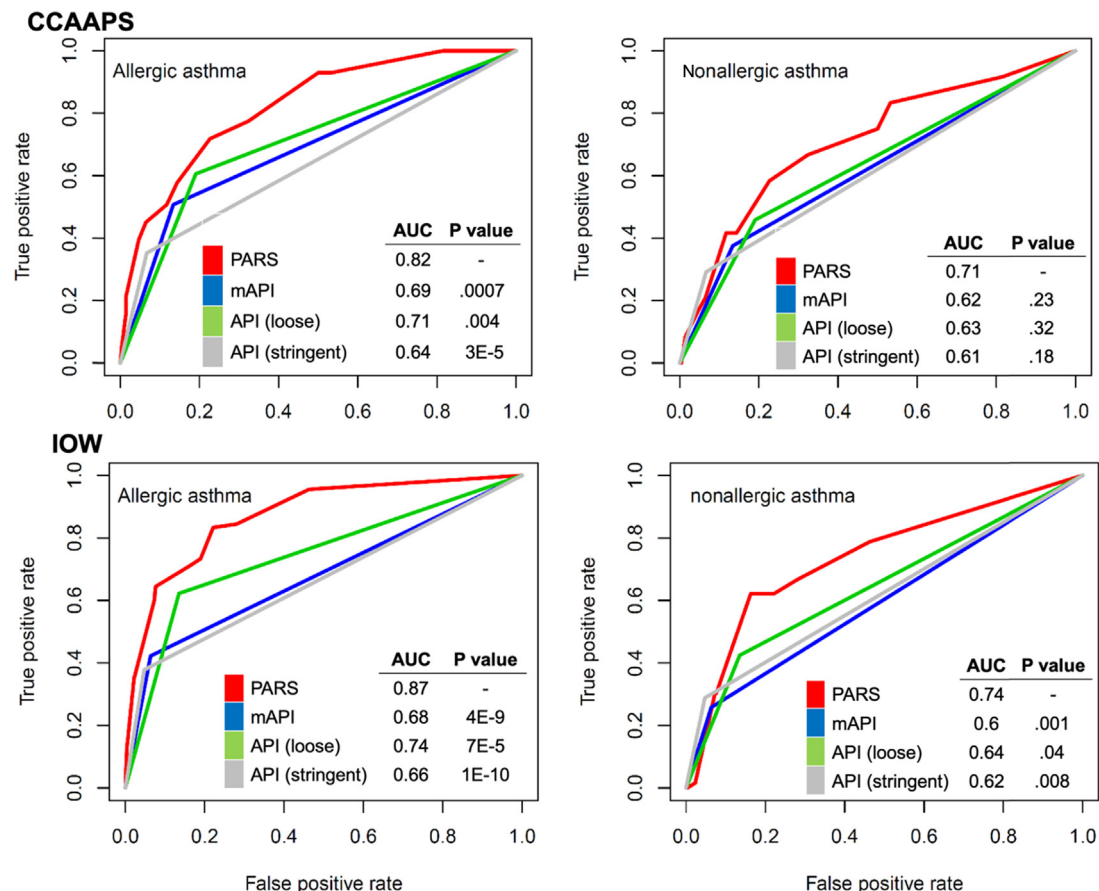


Figure 1. Receiver operating characteristic curves for asthma prediction models applied to allergic and nonallergic asthma in the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) and Isle of Wight (IOW) cohorts. API, Asthma Predictive Index; AUC, area under the curve; mAPI, Modified Asthma Predictive Index; PARS, Pediatric Asthma Risk Score.

was more accurate at predicting both allergic and nonallergic asthma than the mAPI and API (both dichotomous), reinforcing that a quantitative measure is more informative. Comparing the statistics of the indexes beyond the AUC of the ROC curve is somewhat difficult. The PARS has variable sensitivity, specificity, and predictive values for each possible score, whereas the API and mAPI, being dichotomous, have fixed values. The increased accuracy of these predictive tests for allergic asthma is clinically meaningful because this endotype is most prevalent and the rate is increasing.⁸

In conclusion, the PARS had a significant performance improvement in the ability to accurately forecast the development of allergic and nonallergic asthma over the API and mAPI. Future studies need to be directed at replicating and building on these findings in larger and diverse cohorts with ethnicity not represented here and applying the PARS to identify at-risk children for asthma intervention trials.

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Supplementary Data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.anai.2020.03.010>.

References

1. Castro-Rodríguez 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(4 Pt 1):1403–1406.
2. Guilbert TW, Morgan WJ, Krawiec M, et al. The Prevention of Early Asthma in Kids study: design, rationale and methods for the Childhood Asthma Research and Education network. *Control Clin Trials*. 2004;25(3):286–310.
3. Biagini Myers JM, Schauburger E, He H, et al. A Pediatric Asthma Risk Score to better predict asthma development in young children. *J Allergy Clin Immunol*. 2019;143(5):1803–1810.e2.
4. LeMasters GK, Wilson K, Levin L, et al. High prevalence of aeroallergen sensitization among infants of atopic parents. *J Pediatr*. 2006;149(4):505–511.

5. Reponen T, Vesper S, Levin L, et al. High environmental relative moldiness index during infancy as a predictor of asthma at 7 years of age. *Ann Allergy Asthma Immunol*. 2011;107(2):120–126.
6. Kurukulaaratchy RJ, Fenn MH, Waterhouse LM, Matthews SM, Holgate ST, Arshad SH. Characterization of wheezing phenotypes in the first 10 years of life. *Clin Exp Allergy*. 2003;33(5):573–578.
7. R Development Core Team. *R: A Language and Environment for Statistical Computing*. Vienna, Austria: R Foundation for Statistical Computing; 2007.
8. Backman H, Räisänen P, Hedman L, et al. Increased prevalence of allergic asthma from 1996 to 2006 and further to 2016-results from three population surveys. *Clin Exp Allergy*. 2017;47(11):1426–1435.

Supplementary Data

eTable 1

Application of PARS, Published API, and mAPI Criteria to CCAAPS and IOW Cohorts for Allergic Asthma and Nonallergic Asthma

	Sensitivity	Specificity	PPV	NPV	LR+	LR–	AUC (95% CI)
Allergic asthma							
CCAAPS							
PARS ^a	0.72	0.77	0.31	0.95	3.17	0.36	0.82 (0.77–0.87)
mAPI	0.51	0.87	0.35	0.92	3.79	0.57	0.69 (0.63–0.75)
Loose API	0.61	0.81	0.31	0.93	3.18	0.49	0.71 (0.65–0.77)
Stringent API	0.35	0.93	0.43	0.91	5.26	0.69	0.64 (0.59–0.70)
IOW							
PARS ^b	0.83	0.78	0.23	0.98	3.77	0.21	0.87 (0.84–0.91)
mAPI	0.42	0.94	0.35	0.95	6.65	0.62	0.68 (0.63–0.73)
Loose API	0.62	0.86	0.27	0.97	4.61	0.44	0.74 (0.69–0.79)
Stringent API	0.38	0.95	0.39	0.95	7.97	0.65	0.66 (0.61–0.72)
Nonallergic asthma							
CCAAPS							
PARS ^a	0.58	0.77	0.11	0.97	2.57	0.54	0.71 (0.60–0.83)
mAPI	0.38	0.87	0.12	0.97	2.80	0.72	0.62 (0.52–0.72)
Loose API	0.46	0.81	0.10	0.97	2.40	0.67	0.63 (0.53–0.74)
Stringent API	0.29	0.93	0.18	0.96	4.36	0.76	0.61 (0.52–0.71)
IOW							
PARS ^a	0.62	0.84	0.18	0.98	3.81	0.45	0.74 (0.67–0.80)
mAPI	0.26	0.94	0.19	0.96	4.06	0.79	0.60 (0.54–0.65)
Loose API	0.42	0.86	0.16	0.96	3.14	0.67	0.64 (0.58–0.71)
Stringent API	0.29	0.95	0.26	0.96	6.07	0.75	0.62 (0.56–0.68)

Abbreviations: API, Asthma Predictive Index; AUC, area under the curve; CCAAPS, Cincinnati Childhood Allergy and Air Pollution Study; IOW, Isle of Wight; LR+, positive likelihood ratio; LR–, negative likelihood ratio; mAPI, Modified Asthma Predictive Index; NPV, negative predictive value; PARS, Pediatric Asthma Risk Score; PPV, positive predictive value.

^aCut point of 6 (chosen at maximal sensitivity and specificity).

^bCut point of 4 (chosen at maximal sensitivity and specificity).

PARS Scoring Sheet			
	Possible scores		Child's score
	No	Yes	
1. Parental asthma	0	2	
2. Eczema before age 3 years	0	2	
3. Wheezing apart from colds	0	3	
4. Wheezing before age 3 years	0	3	
5. African American race	0	2	
6. Skin prick test (SPT) positive to ≥ 2 aero and/or food allergens	0	2	
Child's PARS (add lines 1-6 above):			

PARS Interpretation			
Score	Risk of asthma by age 7 years	Interpretation	
0	3%	LOW RISK	Children with these scores have a 1 in 33 [score of 0] to a 1 in 9 [score of 4] risk of developing asthma by age 7 years
2	6%		
3	8%		
4	11%		
5	15%	MODERATE RISK	Children with these scores have a 1 in 7 risk [score of 5] to a 1 in 3 [score of 8] risk of developing asthma by age 7 years
6	19%		
7	25%		
8	32%		
9	40%	HIGH RISK	Children with these scores have a 2 in 5 [score of 9] to a 4 in 5 [score of 14] risk of developing asthma by age 7 years
10	49%		
11	58%		
12	66%		
14	79%		

Figure 1. Pediatric Asthma Risk Score (PARS) scoring sheet and interpretation.