



Published in final edited form as:

*Ann Allergy Asthma Immunol.* 2022 June ; 128(6): 729–730. doi:10.1016/j.anaai.2022.03.026.

## The Pediatric Asthma Risk Score (PARS): more does not mean better

Missy MacDonald, BS<sup>1,\*</sup>, Wan-Chi Chang, MS<sup>1,\*</sup>, Lisa J Martin, PhD<sup>2,3</sup>, Gurjit K Khurana Hershey, MD, PhD<sup>1,3</sup>, Jocelyn M Biagini, PhD<sup>1,3</sup>

<sup>1</sup>Division of Asthma Research, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

<sup>2</sup>Division of Human Genetics, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

<sup>3</sup>Department of Pediatrics, College of Medicine, University of Cincinnati, Cincinnati, OH

### Keywords

PARS; asthma; children; prediction

Asthma is a chronic inflammatory lung disease that affects 6.2 million children worldwide<sup>1</sup>. The vast heterogeneity in endotypes makes it difficult to predict which children will develop asthma. The Pediatric Asthma Risk Score (PARS) is a quantitative risk score for asthma developed using clinical and demographic data that can be used by healthcare providers, parents and researchers<sup>2</sup>. PARS was developed using data from the Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) birth cohort<sup>3</sup> to identify risk factors predicting asthma development at age 7. Using just six factors, PARS outperforms and/or is less invasive than 30 published models for asthma development in children included in a 2015 systematic review<sup>2,4</sup>. The factors include eczema, early wheezing, wheezing apart from colds, and polysensitization to aero or food allergens before age 3 years, parental asthma and African-American race. PARS has increased sensitivity compared to the Asthma Predictive Index (API) and is significantly more robust in identifying children with mild-to-moderate asthma risk<sup>2</sup>.

As asthma is a complex disease with a myriad of environmental risk factors not originally included in the PARS model, we sought to determine if adding these and other additional demographic and clinical factors would further increase the performance of PARS in CCAAPS. Children participating in CCAAPS completed exams at ages 1–4 and 7 where questionnaires collected allergy and asthma symptoms, demographics and exposure information and children underwent skin prick testing (SPT) to aeroallergens and foods<sup>3</sup>. All

Corresponding Author: Jocelyn M Biagini, PhD, Associate Professor of Pediatrics, Cincinnati Children's Hospital Medical Center, Phone 513-803-1110, Fax 513-636-1657, biam8v@cchmc.org.

\*These authors contributed equally.

**Conflict of interest:** none declared.

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

predictors for PARS were collected from the visits at ages 1–3. Asthma was defined at age 7 years in CCAAPS based on reported symptoms and objective measures of lung function<sup>2</sup>.

In the present analysis, new factors considered in addition to the 6 original PARS factors were: environmental exposures including traffic pollution (defined as elemental carbon attributable to traffic (ECAT))<sup>5</sup>, secondhand smoke (defined as a positive response to a smoker living in the child's home, smoking in the car when the child is present or >0 hours per day in the same area as someone smoking<sup>6</sup>), cat and dog ownership, demographic factors including family income, insurance type and parental education level, breastfeeding and daycare attendance.

These factors were chosen because they have previously been shown to be associated with asthma in the CCAAPS cohort<sup>7, 8</sup> or in the literature<sup>9, 10</sup>. We also included early frequent wheezing (defined as 10 or more episodes of wheezing in the past 12 months (top 15th percentile) at age 1, 2, or 3 years) and allergic rhinitis (AR, defined as clinician report of “probable” or “definitive” AR at age 1, 2, or 3 years based on SPT results and symptoms) which were considered but not retained in the original PARS model<sup>2</sup>.

The association of each potential predictor with asthma was assessed using univariate logistic regression, followed by log-likelihood ratio tests. All significant predictors were included in a multivariable logistic model, and backward selection was used to remove factors that were least significant. For each predictor, the odds ratio (OR) was calculated, and a weight was assigned by rounding the OR to the nearest whole number. These weights were then used to calculate the updated PARS score for each subject in the CCAAPS cohort. To evaluate the predictability of the updated PARS model on asthma, a logistic regression model was generated using PARS score as the primary predictor of asthma risk. This logistic regression model was used to calculate the area under the curve (AUC) for continuous PARS measure, and the sensitivity, specificity, positive (PPV) and negative predictive values (NPV) were estimated by using a threshold of 6 and 5 for the original model and updated model, respectively, to maximize both sensitivity and specificity. Model discriminatory power was assessed by constructing receiver operating characteristic (ROC) curves and comparing the AUCs using DeLong's test. To minimize the potential effect of sample size in model comparison, we fitted the original model restricted to the n=550 subjects included in the updated model. Statistical significance was defined as  $P < 0.05$ . Statistical analyses were performed in R version 4.1.0 (R core team, 2021).

Asthmatics were more likely to have been formula fed ( $p=0.001$ ), have a family annual income less than \$30,000 ( $p<0.001$ ), attend daycare ( $p=0.027$ ), have no commercial insurance ( $p<0.001$ ), have at least one parent with a college degree ( $p<0.001$ ), been exposed to secondhand smoke ( $p<0.001$ ), have an average ECAT 0.41  $\mu\text{g}/\text{m}^3$  ( $p=0.042$ ) and be less likely to own a dog ( $p=0.030$ ) in their first 3 years of life (Table 1).

Backward selection of all factors yielded a new model which included 5 of the 6 original PARS factors (parental asthma, eczema, wheezing apart from colds, early wheezing, polysensitization to two or more allergens) and 3 new factors (formula feeding, family annual income at age 1  $< \$30,000$ , and daycare attendance before age 3) as significant risk

factors (Table 1). To examine the predictive accuracy of the original and updated PARS model on asthma, we compared the sensitivity, specificity, PPV and NPV (Table 1). The updated model had a slight increase in sensitivity (0.64 vs. 0.69) and a slight decrease in specificity (0.81 vs. 0.77, Table 1). The NPV and PPV between the two models were similar and the accuracy was unchanged (both AUCs 0.80 [0.75–0.85];  $p=0.89$ , Table 1).

Although these additional factors are associated with asthma in CCAAPS, including them in the PARS model does not increase model performance. The updated model contained 8 factors, including 5 of the 6 original factors. The 5 original factors were all more strongly associated with asthma than the 3 new factors, further supporting the robustness of the original PARS model. The original PARS model contained African-American race, while household income age 1 <\$30,000 was retained in the updated model. It is important to recognize that race is a proxy for sociodemographic factors<sup>11</sup>, so it is not unexpected as race and income are highly correlated in CCAAPS (spearman correlation coefficient 0.50,  $p<0.001$ ). Collectively, these results suggest that the 6 factors identified in the original PARS model are the minimum set of questions required to predict asthma in CCAAPS.

In conclusion, the performance of the PARS model was not enhanced by the addition of environmental exposures, demographics, or clinical diagnoses. Future studies should continue to evaluate the performance of the PARS model in diverse populations.

### Funding:

This work was funded by NIH grant R01ES011170

### Abbreviations:

<b>AR</b>	allergic rhinitis
<b>AUC</b>	area under the curve
<b>CCAAPS</b>	Cincinnati Childhood Allergy and Air Pollution Study
<b>ECAT</b>	elemental carbon attributable to traffic
<b>NPV</b>	negative predictive value
<b>OR</b>	odds ratio
<b>PARS</b>	Pediatric Asthma Risk Score
<b>PPV</b>	positive predictive value
<b>ROC</b>	receiver operating characteristic
<b>SPT</b>	skin prick test

## References

1. Zahran HS, Bailey CM, Damon SA, Garbe PL, Breyse PN. Vital Signs: Asthma in Children - United States, 2001–2016. *MMWR Morb Mortal Wkly Rep.* 2018;67:149–155. [PubMed: 29420459]
2. 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;143:1803–1810 e1802. [PubMed: 30554722]
3. LeMasters GK, Wilson K, Levin L, et al. High prevalence of aeroallergen sensitization among infants of atopic parents. *J Pediatr.* 2006;149:505–511. [PubMed: 17011322]
4. Luo G, Nkoy FL, Stone BL, Schmick D, Johnson MD. A systematic review of predictive models for asthma development in children. *BMC Med Inform Decis Mak.* 2015;15:99. [PubMed: 26615519]
5. Ryan PH, Lemasters GK, Levin L, et al. A land-use regression model for estimating microenvironmental diesel exposure given multiple addresses from birth through childhood. *Sci Total Environ.* 2008;404:139–147. [PubMed: 18625514]
6. Biagini Myers JM, Khurana Hershey GK, Deka R, et al. Asking the right questions to ascertain early childhood secondhand smoke exposures. *J Pediatr.* 2012;160:1050–1051. [PubMed: 22494871]
7. LeMasters G, Levin L, Bernstein DI, et al. Secondhand smoke and traffic exhaust confer opposing risks for asthma in normal and overweight children. *Obesity (Silver Spring).* 2015;23:32–36. [PubMed: 25407437]
8. Brunst KJ, Ryan PH, Brokamp C, et al. Timing and Duration of Traffic-Related Air Pollution Exposure and the Risk for Childhood Wheeze and Asthma. *Am J Respir Crit Care Med.* 2015.
9. Hesselmar B, Aberg N, Aberg B, Eriksson B, Bjorksten B. Does early exposure to cat or dog protect against later allergy development? *Clin Exp Allergy.* 1999;29:611–617. [PubMed: 10231320]
10. Beck AF, Huang B, Auger KA, Ryan PH, Chen C, Kahn RS. Explaining Racial Disparities in Child Asthma Readmission Using a Causal Inference Approach. *JAMA Pediatr.* 2016;170:695–703. [PubMed: 27182793]
11. Borrell LN, Elhawary JR, Fuentes-Afflick E, et al. Race and Genetic Ancestry in Medicine - A Time for Reckoning with Racism. *N Engl J Med.* 2021;384:474–480. [PubMed: 33406325]

**Table 1.**

Association of original and additional PARS risk factors with asthma, updated multivariable PARS model and comparison to original PARS model.

	Unadjusted Associations			Factors Retained in Multivariable Model			
	Asthmatics	Non-asthmatics	<i>P</i> -value	OR	95% CI	<i>P</i> -value	Weight
	n = 89	n = 461					
<b>Original PARS Risk Factors</b>	N (%)	N (%)					
Parental asthma	50 (56.2)	171 (37.1)	<0.001	1.0 9	1.03–1.15	0.00 5	1
Eczema before age 3	40 (44.9)	112 (24.3)	<0.001	1.0 8	1.02–1.15	0.01 4	1
Wheezing apart from colds age before age 3	39 (43.8)	58 (12.6)	<0.001	1.1 7	1.07–1.29	0.00 1	1
Early wheezing before age 3	61 (68.5)	138 (29.9)	<0.001	1.1 4	1.05–1.22	0.00 1	1
2 positive SPT response to aero/ food allergens age 1–3	56 (62.9)	176 (38.2)	<0.001	1.1 3	1.07–1.20	<0.0 01	1
African-American race	34 (38.2)	88 (19.1)	<0.001				
<b>Additional Risk Factors Considered</b>							
<b>Clinical Factors</b>							
Early frequent wheezing age before age 3	32 (36.0)	49 (10.6)	<0.001				
Allergic rhinitis before age 3	49 (55.1)	158 (34.3)	<0.001				
<b>Demographic and socioeconomic risk factors</b>							
Exclusively formula fed	37 (41.6)	112 (24.3)	0.001	1.0 7	1.00–1.14	0.04 6	1
Age 1 household income <\$30k	37 (41.6)	99 (21.5)	<0.001	1.0 8	1.01–1.16	0.02 2	1
Daycare attendance before age 3	54 (60.7)	221 (47.9)	0.027	1.0 6	1.01–1.13	0.03 1	1
No commercial insurance age 1	36 (40.4)	91 (19.7)	<0.001				
1 parent with college degree age 1	279 (60.5)	36 (40.4)	<0.001				
<b>Environmental risk factors</b>							
Secondhand smoke exposure before age 3	47 (52.8)	146 (31.7)	<0.001				
ECAT mean age 1–3 0.41 ug/m <sup>3</sup>	37 (41.6)	140 (30.4)	0.042				
Cat ownership before age 3	20 (22.5)	139 (30.2)	0.13				
Dog ownership before age 3	29 (32.6)	207 (44.9)	0.03				
<b>Comparison of Performance of the original and updated PARS models.</b>							
	<b>Thresh old</b>	<b>Sensitivity</b>	<b>Specificity</b>	<b>PPV</b>	<b>NPV</b>	<b>AUC (95%CI)</b>	
Original PARS Model	6	0.69	0.77	0.37	0.93	0.80 (0.75–0.85)	
Updated PARS Model	5	0.64	0.81	0.39	0.92	0.80 (0.75–0.85)	

AUC: area under the curve, CI: confidence interval, NPV: negative predictive value. OR: odds ratio PARS: Pediatric Asthma Risk Score. PPV: positive predictive value.