

Correspondence

Applying the CAMP trial asthma remission prediction model to the Dutch asthma remission studies

To the Editor:

A small subset of patients with asthma can go into spontaneous remission later in life.^{1,2} Predicting this clinical trajectory would be of great interest, because these asthma remission subjects are not burdened by symptoms anymore and no longer require any medication. Wang et al³ created a prediction model that could predict asthma remission outcome. They showed that the combination of normal FEV₁/forced vital capacity (FVC) ratio, less severe bronchial hyperresponsiveness, and blood eosinophil counts of less than 500 cells/ μ L at age 8 years yields more than 80% probability to achieve asthma remission by adulthood.

We were interested in the generalizability of predicting remission in childhood and applied this prediction model on our Dutch asthma remission cohorts. Children included in these cohorts described by Vonk et al (cohort 1, n = 94) and Carpaij et al (cohort 2, n = 157) had doctor-diagnosed asthma and were bronchial hyperresponsive (ie, substance provocative concentration causing a 20% drop in FEV₁ [PC₂₀] $\leq$ 16 mg/mL histamine).^{1,2} Similar to the definition used by the Childhood Asthma Management Program (CAMP), we defined asthma remission at follow-up as no wheeze or asthma attacks in the

last year, having an FEV₁/inspiratory vital capacity (IVC) ratio of greater than or equal to 80%, and no use of asthma-related medication. We used a different measure for airway obstruction, that is, FEV₁/IVC, because no data on FVC were available. Subjects with missing data were excluded. Normally and nonnormally distributed variables were compared with *t* test and Mann-Whitney *U* test, respectively. We constructed 6 groups on the basis of baseline criteria provided in Wang et al and calculated the prevalence of subjects in remission for each group.

After combining cohorts 1 and 2, the clinical and complete remission rate was 10.0% compared with 26.1% in CAMP (Table I). Like Wang et al, we observe an increase if the prevalence of remission as baseline FEV₁/IVC% is higher. In subjects with an FEV₁/IVC ratio of greater than or equal to 85%, PC₂₀ value of greater than or equal to 1 mg/mL, and an eosinophil level of less than 500 cells/ μ L has additional value to predict asthma remission. In this group, the prevalence of remission was 40%, whereas those with greater than or equal to 500 eosinophils/ μ L had a 10% prevalence of remission. In accordance to the CAMP study, children in cohorts 1 + 2 had a significantly higher FEV₁, FEV₁/IVC%, and PC₂₀ threshold and significantly lower serum eosinophils in the asthma remission group compared with the persistent asthma group. These are known clinical features associated with asthma remission.⁴⁻⁶ The FEV₁/FVC% measured in CAMP was higher than in cohorts 1 + 2, resulting

TABLE I. Baseline clinical characteristics of 3 prospective childhood cohorts and application of the prediction model

Characteristic	Persistent asthma			Asthma remission		
	Cohort 1: Vonc et al ² (n = 79)	Cohort 2: Carpaij et al ¹ (n = 147)	CAMP: Wang et al ³ (n = 650)	Cohort 1: Vonc et al ² (n = 15) (15%)	Cohort 2: Carpaij et al ¹ (n = 10) (6.4%)	CAMP: Wang et al ³ (n = 229) (26.1%)
Enrollment year range	1966-1969	1972-1976	1993-1995	1966-1969	1972-1976	1993-1995
Age at baseline (y), mean $\pm$ SD	9.9 $\pm$ 2.0	9.7 $\pm$ 1.4	8.8 $\pm$ 2.1	9.6 $\pm$ 2.0	10.2 $\pm$ 1.2	8.6 $\pm$ 1.9
Mean follow-up (y)	16	15	12	16	15	12
Male sex, n (%)	58 (73.4)	105 (71.4)	407 (62.6)	9 (60.0)	7 (70.0)	115 (50.2)
FEV ₁ % predicted, mean $\pm$ SD	82.1% $\pm$ 16.5%*	75.4% $\pm$ 14.3%*	92.2% $\pm$ 14.1%*	85.7% $\pm$ 17.2%*	82.0% $\pm$ 10.6%*	99.0% $\pm$ 12.7%*
FEV ₁ /VC ratio, mean $\pm$ SD†	75.0% $\pm$ 12.2%*	72.3% $\pm$ 7.9%*	77.9% $\pm$ 7.9%*	78.1% $\pm$ 12.0%*	79.7% $\pm$ 7.1%*	85.6% $\pm$ 6.3%*
PC ₂₀ threshold (mg/mL), median (IQR)†	2.0 (7.0)*	4.0 (6.0)*	0.9 (1.6)*	8.0 (30.0)*	8.0 (4.0)*	1.7 (3.6)*
Serum eosinophil count (cells/ μ L), median (IQR)	462.0 (495.0)*	385.0 (396.0)*	422.0 (493.5)*	220.0 (297.0)*	286.0 (236.5)*	320.5 (327.3)*
Prediction model						
	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
	FEV ₁ /FVC% $\leq$ 75%	FEV ₁ /FVC% 75%-79%	FEV ₁ /FVC% 80%-84%	FEV ₁ /FVC% $\geq$ 85%; PC ₂₀ < 1 mg/mL	FEV ₁ /FVC% $\geq$ 85%; PC ₂₀ $\geq$ 1 mg/mL; blood eosinophils $\geq$ 500 cell/ μ L	FEV ₁ /FVC% $\geq$ 85%; PC ₂₀ $\geq$ 1 mg/mL; blood eosinophils < 500 cell/ μ L
CAMP (n = 876) Predicted probability	9.5% (n = 199)	27.6% (n = 190)	53.8% (n = 228)	58.3% (n = 71)	65.4% (n = 49)	82.6% (n = 139)
Cohorts 1 + 2 (n = 251)	5.5% (n = 3 of 55)	5.6% (n = 7 of 126)	15.4% (n = 6 of 39)	0.0% (n = 0 of 1)	10.0% (n = 1 of 10)	40.0% (n = 8 of 20)

NA, Not applicable; VC, vital capacity.

*Either significant difference (*P* < .05) between asthma remission and persistent asthma within cohorts 1 + 2 or CAMP.

†FEV₁/IVC and PC₂₀ histamine threshold on cohorts 1 and 2; FEV₁/FVC and PC₂₀ methacholine threshold in CAMP.

in a higher proportion of subjects subdivided in group 2. The definition for airway obstruction is not expected to be the cause, because the difference between FEV₁/FVC% and FEV₁/IVC% is marginal in children and young adults with mild to moderate asthma.⁷

Taking this into account, we show that the model proposed by Wang et al can correctly predict future development of asthma remission in up to 40% of cases. Although usable, more research is needed to disentangle the pathophysiology of asthma remission, which is a highly relevant yet poorly understood outcome of childhood asthma.

Orestes A. Carpaij, MD^{a,b}

Judith M. Vonk, PhD^{a,c}

Martijn C. Nawijn, PhD^{a,d}

Huib A. M. Kerstjens, MD, PhD^{a,b}

Gerard H. Koppelman, MD, PhD^{a,e}

Maarten van den Berge, MD, PhD^{a,b}

From ^athe Groningen Research Institute for Asthma and COPD (GRIAC), Departments of ^bPulmonology, ^cEpidemiology, ^dPathology and Medical Biology, University of Groningen, University Medical Center Groningen, and ^ethe Department of Pediatric Pulmonology and Pediatric Allergology, Beatrix Children's Hospital, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands. E-mail: o.a.carpaij@umcg.nl.

Disclosure of potential conflict of interest: M. C. Nawijn reports grant support from GlaxoSmithKline and Health Holland; unrestricted research grant on this topic; and unrestricted research grants sponsored by GlaxoSmithKline, TETRI Foundation, and Lung Foundation, SAB. H. A. M. Kerstjens received fees per patient for recruitment in trials from GlaxoSmithKline, NOVARTIS, and FLUIDDA and grants for investigator-initiated studies from GlaxoSmithKline, NOVARTIS, and Boehringer.

In addition, his institution has through his work received consultancy fees from Novartis, AstraZeneca, Boehringer Ingelheim, and GlaxoSmithKline. G. H. Koppelman received grant support from the Lung Foundation of the Netherlands, TETRI Foundation, TEVA the Netherlands, UBBO EMMIUS Foundation, Vertex, and GlaxoSmithKline (money to institution). M. van den Berge had grants paid to university from GlaxoSmithKline, Chiesi, Teva, AstraZeneca, and Genentech. The rest of the authors declare that they have no relevant conflicts of interest.

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<https://doi.org/10.1016/j.jaci.2019.01.040>