Remission of persistent childhood asthma: Early predictors of adult outcomes

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Abstract

Background: Few data exist on the predictors of asthma remission by early adulthood in North America.

Objective: The predictors of adult asthma remission were determined in a multiethnic population of patients with mild-to-moderate persistent childhood asthma.

Methods: Asthma remission in early adulthood was measured by using 2 definitions: a clinical and a strict definition. Both included normal lung function and the absence of symptoms, exacerbations, and medication use. The strict definition also included normal airways responsiveness. Predictors were identified from 23 baseline measures by using multivariate logistic regression. The probability of remission was modeled by using decision tree analysis.
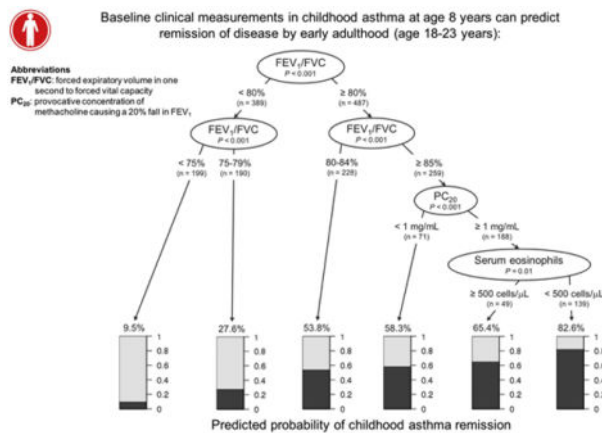
Results: In 879 subjects the mean ± SD baseline age was 8.8 ± 2.1 years, 59.4% were male, and 68.7% were white. By adulthood, 229 (26.0%) of 879 participants were in clinical remission, and 111 (15.0%) of 741 participants were in strict remission. The degree of FEV_1/forced vital capacity (FVC) ratio impairment was the largest predictor of asthma remission. More than half of boys and two thirds of girls with baseline FEV_1/FVC ratios of 90% or greater were in remission at adulthood. Decreased airways responsiveness was also a predictor for both remission definitions (clinical remission odds ratio, 1.23 [95% CI, 1.09–1.39]; strict remission odds ratio, 1.52 [95% CI, 1.26–1.84]). The combination of normal FEV_1/FVC ratio, airways responsiveness, and serum eosinophil count at baseline yielded greater than 80% probability of remission by adulthood.

Conclusion: A considerable minority of patients with persistent childhood asthma will have disease remission by adulthood. Clinical prognostic indicators of asthma remission, including baseline lung function, can be seen from an early age.

Graphical Abstract

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Baseline clinical measurements in childhood asthma at age 8 years can predict remission of disease by early adulthood (age 18-23 years):

Predicted probability of childhood asthma remission

Keywords

Pediatric asthma; asthma remission; prognostication

Predicting the clinical trajectory of childhood asthma has important prognostic implications for patients, parents, clinicians, and researchers. Prior longitudinal studies have estimated between 15% and 64% of patients with childhood asthma go into asthma remission by early adulthood.[1,2] In those studies asthma remission rates have been noted to vary widely by population, and remission has been associated with less allergic sensitization, milder initial asthma severity, and male sex.[2–4] Asthma remission occurs most commonly between the ages of 14 to 21 years.[2] To date, studies characterizing asthma remission have emphasized epidemiologic associations rather than clinical translation and prognostication. Furthermore, limited data exist on asthma remission in multiethnic cohorts representative of the North American population and in cohorts with mild-to-moderate persistent asthma, whose remission rates would be expected to differ from those with either intermittent or severe disease.

In this study we determined which baseline characteristics in early childhood can predict asthma remission by adulthood in a multiethnic cohort of patients with mild-to-moderate persistent asthma. Cross-sectional baseline characteristics representative of a snapshot obtained at a physician's visit were examined that can be used for individualized prognostication.

The Childhood Asthma Management Program (CAMP) was a 4-year, randomized, placebo-controlled trial of inhaled anti-inflammatory treatments for mild-to-moderate persistent asthma in children followed by an additional 13 years of detailed longitudinal follow-up.[5] As such, this cohort is well suited to evaluate the natural history of childhood asthma. After the first 8 years of CAMP, 6% of patients had clinical asthma remission in adolescence.[6] We now study asthma remission at the onset of adulthood in CAMP by using definitions for asthma remission that include both clinical and pulmonary function measurements. Asthma remission was measured at the first CAMP continuation study visit after the age of 18 years, with an average follow-up of 12 years. In addition to determining the prevalence of asthma

remission in early adulthood, we specifically investigated early childhood factors to prognosticate future asthma outcomes.

METHODS

A longitudinal study was performed with 879 participants from CAMP who had asthma remission outcomes available at their first follow-up visit on or after age 18 years (range, 18–23 years). The details of CAMP have been described elsewhere.[5,7] Briefly, 1041 children with mild-to-moderate persistent asthma and significant airways responsiveness to methacholine between the ages of 5 and 12 years were enrolled from December 1993 to September 1995. Participants were randomized to receive inhaled budesonide, nedocromil, or placebo for a mean 4.3 years, and observational follow-up continued for an additional 13 years. Parental informed consent with subject assent was obtained, and the study was approved by each CAMP study center institutional review board. More than 80% of subjects participated through the entire duration of observational follow-up.[7]

Asthma remission at early adulthood was defined in 2 ways: a clinical primary definition and a strict secondary definition. Clinical asthma remission was defined as follows: (1) no evidence of airflow obstruction with a ratio of FEV_1 to forced vital capacity (FVC) of 80% or greater, (2) no asthma exacerbations in the prior year, (3) no use of asthma medications in the prior year, and (4) no reported asthma symptoms in the prior year. Strict asthma remission was defined as the above 4 criteria in addition to having negative bronchoprovocation test results by means of methacholine challenge with a provocative concentration of methacholine causing a 20% drop in FEV_1 (PC_{20}) greater than or equal to 25 mg/mL. The absence of bronchial hyperresponsiveness (BHR) in CAMP was defined at a PC_{20} of 25 mg/mL or greater, and thus this cutoff was used for the strict asthma remission definition. FEV_1/FVC ratio was included in the remission definitions to include both objective and subjective criteria from the impairment and risk domains of National Asthma Education and Prevention Program guidelines, and the use of the absolute ratio was chosen according to American Thoracic Society guidelines.[8,9] The clinical remission definition was considered the primary definition because PC_{20} is not typically measured longitudinally in the clinical setting.

Potential baseline predictors of asthma remission were selected based on previously published associations with asthma susceptibility, remission, or both.[10] Twenty-three baseline measures collected at the time of enrollment in CAMP were selected: age at asthma diagnosis, sex, ethnicity, household income, parental education, history of parental asthma, body mass index, history of wheezing (with and without colds), asthma exacerbations after exercise, physician-diagnosed atopic dermatitis or allergies, aeroallergen skin test positivity (as an indicator of allergic sensitization with or without symptoms), exposure to home tobacco smoke, history of maternal smoking during pregnancy, use of a wood stove, any pet ownership, asthma severity classified by a physician, PC_{20}, FEV_1 percent predicted, FEV_1/FVC ratio, serum IgE level, and serum eosinophil count.

Statistical analyses

The characteristics of the 162 subjects missing the primary remission outcome were compared with those of the 879 subjects who had the outcome. We used *t* tests to compare continuous parametric variables, Wilcoxon rank-sum tests for continuous nonparametric variables, and χ^2 and Fisher exact tests for categorical variables. Most variables in the loss to follow-up analysis were not statistically significant (*P*>.05), and significant variables were adjusted for in multivariate models (see Table E1 in this article's Online Repository at www.jacionline.org). R version 3.3.2 was used.

Cross-validated stepwise logistic regression was performed to determine predictors for each asthma remission outcome. Variables that were statistically significant on univariate analyses were placed in a 5-fold cross-validated stepwise logistic regression model with 100 cross-validation repeats by using the caret package.[11] Cross-validation was used to reduce overfitting and improve precision and accuracy. In addition to the statistically significant variables from the loss to follow-up analysis, age, sex, CAMP treatment group, and clinic site were controlled for in all models. Before model building, continuous variables that had a nonlinear relationship with the log odds of remission were log transformed. FEV_1/FVC ratio and PC_{20} were modeled as continuous variables in the main clinical and strict asthma remission models.

Model selection was determined by using the Akaike information criterion, and Wald tests were used to evaluate individual variables. Analyses were restricted to complete cases. Models were then stratified by sex, and the statistically significant variables that differed across sexes were tested as interaction terms.

Sex-stratified analyses for the primary clinical asthma remission definition were planned *a priori* because asthma persistence has been shown to vary by sex.[1,2,4,12] Sex-stratified models were built by using cross-validated stepwise logistic regression. Baseline FEV_1/FVC ratio was divided into 4 categories to reflect spirometric categorizations used in the Global Initiative for Asthma Report (ie, <70%, 70% to 80%, 80% to 90%, and >90%) and baseline PC_{20} was divided into 3 categories (ie, moderate-to-severe BHR, <1 mg/mL; mild BHR, 1–4 mg/mL; and borderline BHR, >4 mg/mL) per American Thoracic Society guidelines to increase clinical interpretability in the sex-stratified models.[13,14] Receiver operating characteristic curves and area under the curve (AUC) were obtained by using the pROC, plotROC, and ggplot2 packages.[15–17] The probability of asthma remission was modeled by using conditional inference trees with case weights from the party package.[18]

A sensitivity analysis of the primary clinical asthma remission definition was performed to examine the effect of the FEV_1/FVC criterion. The FEV_1/FVC ratio was removed from the definition, and a cross-validated stepwise logistic regression model was built, as specified above (see Table E2 in this article's Online Repository at www.jacionline.org). Because airflow obstruction is one of the hallmarks of asthma, the FEV_1/FVC ratio was retained in the primary clinical asthma remission definition.

RESULTS

Of the 879 participants, 229 (26.0%) subjects were in asthma remission and 650 (73.9%) were not, as determined by using the primary clinical definition (Table I). The mean baseline age at study entry was 8.8 years (SD ± 2.1 years), 59.4% were male, and 68.7% were white. Within the 879 participants, 741 (84.3%) subjects had PC_{20} measurements, permitting analysis of the secondary strict asthma remission definition. Of these, 111 (15.0%) subjects were in strict asthma remission, and 630 (85.0%) subjects were not (see Table E3 in this article's Online Repository at www.jacionline.org).

Clinical asthma remission predictors

For the entire cohort, sex, baseline history of wheezing with and without colds, exacerbations after exercise, aeroallergen sensitization, physician-classified asthma severity, PC_{20}, FEV_1 percent predicted, FEV_1/FVC ratio, serum IgE level, and serum eosinophil count were significant predictors of asthma remission on univariate analyses (Table I). In the multivariate model only FEV_1/FVC ratio and PC_{20} remained significant. Each 10% increase in baseline FEV_1/FVC ratio was associated with a 4.62 times odds of asthma remission (95% CI, 3.35–6.50; $P < .001$), and each 2-fold increase in PC_{20} was associated with a 23% increase in the odds of asthma remission (odds ratio [OR], 1.23; 95% CI, 1.09–1.39; $P = .001$; Table II). The AUC of the cross-validated model was 0.81 (95% CI, 0.77–0.84; see Fig E1, *A*, in this article's Online Repository at www.jacionline.org).

Predictors of clinical asthma remission by sex

The severity of airflow obstruction was the strongest predictor of clinical asthma remission in both male and female subjects (Fig 1, *A*). Within the subset of subjects with mild baseline airway obstruction, female subjects were more likely to have asthma remission than male subjects (Fig 1, *B*). Female subjects had 8.03 times odds (95% CI, 4.60–14.93; $P < .001$), whereas male subjects had 3.88 times odds (95% CI, 2.62–5.92; $P < .001$) of asthma remission with each 10% increase in FEV_1/FVC ratio (interaction $P = .04$). An FEV_1/FVC ratio of less than 70% was strongly indicative of asthma persistence, particularly in male subjects, in which only 1.4% of subjects had remission (Fig 1, *A*).

In addition, in the sex-specific models of clinical asthma remission, male subjects without peripheral eosinophilia had 1.79 times odds (95% CI, 1.02–3.21; $P = .045$) of asthma remission compared with male subjects with peripheral eosinophilia (Table III). Treatment during the first 4 years of CAMP with inhaled budesonide was also associated with greater odds of remission in male subjects. In female subjects, Hispanic race and airway hyperresponsiveness were additional predictors of asthma remission (Table IV and see Fig E2 in this article's Online Repository at www.jacionline.org). The odds of asthma remission decreased by 63% (OR, 0.37; 95% CI, 0.15–0.89; $P = .03$) in female subjects with moderate airway hyperresponsiveness and 76% (OR, 0.24; 95% CI, 0.09–0.64; $P = .005$) in female subjects with severe airway hyperresponsiveness. The AUC of the cross-validated models were 0.79 (95% CI, 0.75–0.84) for male subjects and 0.85 (95% CI, 0.80–0.89) for female subjects (see Fig E1, *B* and *C*).

Strict asthma remission predictors

Similar to the primary remission analysis, a history of wheezing with and without colds, exacerbations after exercise, aeroallergen sensitization, physician-classified asthma severity, PC_{20}, FEV_1 percent predicted, FEV_1/FVC ratio, serum IgE level, and serum eosinophil count were significant predictors of strict asthma remission status on univariate analyses, along with baseline age at study entry and physician diagnosed allergies (see Table III in this article's Online Repository at www.jacionline. org). In the multivariate model each 10% increase in baseline FEV_1/FVC ratio was associated with 5.71 times odds (95% CI, 3.58–9.45; $P < .001$) of strict asthma remission, and each 2-fold increase in baseline PC_{20} was associated with a 1.52 times odds (95% CI, 1.26–1.84: $P < .001$) of strict asthma remission (see Table E4 in this article's Online Repository at www.jacionline.org). Furthermore, each 2-fold increase in serum IgE level was associated with a 12% decrease in the odds of strict remission (OR, 0.88; 95% CI, 0.78–1.00; $P = .047$), and aeroallergen sensitization was associated with a 52% decrease in the odds of strict remission (OR, 0.48; 95% CI, 0.24–0.97; $P = .04$). The AUC of the cross-validated model was 0.86 (95% CI, 0.83–0.90; see Fig E1, *D*). Predictors of strict asthma remission did not differ between sexes.

Asthma remission decision tree

A decision tree classifying the predicted probability of clinical asthma remission was constructed (Fig 2). The probability of asthma remission was lowest (9.5%) in subjects with baseline FEV_1/FVC ratios of less than 75%. Conversely, subjects with the combination of a baseline FEV_1/FVC ratio greater than or equal to 85%, PC_{20} of at least 1 mg/mL, and absence of peripheral eosinophilia had 82.6% probability of asthma remission.

DISCUSSION

Prognostication of asthma remission at adulthood can be performed from an early age in childhood. We followed 879 children with mild-to-moderate persistent asthma for an average of 12 years until early adulthood and found 26% had asthma remission by focusing on clinical parameters and 15% had asthma remission by using a strict definition that additionally included normal bronchoprovocation testing. Thus a sizeable proportion of patients with childhood asthma have complete remission with no residual evidence of ongoing disease. Decreased airway obstruction and lower airways responsiveness in childhood were strongly associated with both definitions of asthma remission. Although research in other populations has demonstrated associations between greater childhood lung function, less severe airway obstruction, and absence of airway hyperresponsiveness with improved asthma prognosis, prior studies have not yielded prognostic strata related to these measures.[1,4,19,20] The single greatest predictor of asthma remission was the severity of airflow obstruction. Fewer than 10% of children with a baseline FEV_1/FVC ratio of less than 80% "outgrew" their asthma, whereas each 10% increase in baseline FEV_1/FVC ratio was associated with a 4.62 times higher odds of asthma remission (Table II).

For asthmatic patients with well-preserved lung function at baseline (FEV_1/FVC ratio, 90%), more than 54% of boys and 70% of girls were in remission by early adulthood (Fig 1, *A*). Baseline FEV_1/FVC ratio is an excellent predictor of future asthma remission and

lung function, which is consistent with research showing the tracking of lung function growth over time.[1,21] Gains in baseline FEV_1/FVC ratio beyond the threshold of 80% used in current guidelines continued to increase the probability of asthma remission, indicating that higher cutoffs within "normal" FEV_1/FVC ratios continue to stratify patients with pediatric asthma (Fig 1, *B*).[8] In the US general population the reference FEV_1/FVC ratio for healthy preadolescent children approaches 90%.[22] Therefore the cutoff for normal FEV_1/FVC ratio in children regardless of asthma status is likely greater than indicated in current guidelines and has direct implications on future health status. Our findings further emphasize the importance of obtaining baseline spirometry in patients with pediatric asthma, which is recommended in current guidelines but not routinely obtained in all pediatric practices.[8,14]

From a clinical perspective, the probability of asthma remission can be estimated based on baseline FEV_1/FVC ratio, PC_{20}, and serum eosinophil count (Fig 2). Specifically, our decision tree analysis indicated that in children with mild-to-moderate persistent asthma, the predicted probability of adult clinical remission exceeds 80% when FEV_1/FVC ratio is normal, PC_{20} is greater (lower airways responsiveness), and peripheral eosinophilia is absent at baseline. The asthma remission decision tree can be used as a clinical tool for physicians to prognosticate about patients with childhood asthma. Each of the 3 prognostic components is readily available to most pediatric care providers, and several asthma guidelines recommend measuring these components.[8,14,23]

In addition to these overall findings, sex-specific associations with clinical asthma remission were detected. Although sex by itself was not associated with asthma remission in our main multivariable model, we noted differences related to sex in the association of FEV_1/FVC ratio with clinical remission. For each 10% increase in FEV_1/FVC ratio, female subjects were more likely to have clinical asthma remission compared with male subjects (Fig 1, *B*). This contrasts with previous studies that have found either no association between sex and asthma remission or an association between female sex and asthma persistence.[1–4,12,20,24–26]

Female subjects with less severe early-onset asthma are more likely to have remission than male subjects, which suggests that early increases in FEV_1/FVC ratio in female subjects that run counter to the decrements expected from dysanapsis in lung growth might disproportionately affect lung preservation.[27] Within female subjects, Hispanics were more likely to have asthma remission compared with other races, which might reflect ethnic subgroup specific risks within and between races.[28] In male subjects the absence of peripheral eosinophilia and use of inhaled corticosteroid treatment in early childhood (ie, during the clinical trial phase of CAMP) were associated with increased odds of asthma remission (Table III). Inhaled corticosteroid use does not alter the development of asthma in at-risk preschool children, and CAMP treatment group assignment has not been shown to affect lung growth.[29–31] At this juncture, it is not clear whether early inhaled corticosteroids have the potential for a previously undescribed latent effect, and further research is needed to definitively determine the long-term effects of early inhaled corticosteroid use.

The remission of childhood asthma by adulthood has not been widely studied, and the determination of asthma remission during adolescence might not capture all events. Even

fewer studies have defined asthma remission using both clinical and pulmonary function measurements.[19,20,25] In The Netherlands 22% of 119 asthmatic children followed to ages 32 to 42 years were in complete remission, as defined by having no wheeze or asthma attacks in the previous 3 years, no use of inhaled corticosteroids, normal lung function (FEV$_1$, >90% predicted), and no airway hyperresponsiveness.[19] In a separate cohort from The Netherlands, Panhuysen et al[20] reported 11% of 181 patients with childhood asthma to be in asthma remission at adulthood, as defined by normal lung function (FEV$_1$, >90% predicted), absence of airway hyperresponsiveness (PC$_{20}$, 16 mg/mL), and absence of respiratory symptoms.[20] Our study had a larger multiethnic population and included more frequent follow-up and comprehensive detailing of baseline characteristics compared with prior studies.

The strict remission criteria included normal airways responsiveness and were also associated with decreases in baseline serum IgE levels and absence of aeroallergen sensitization. These results suggest that atopic inflammation can modulate airway smooth muscle physiology, resulting in persistent asthma and airways hyperresponsiveness.[32] A limited number of studies have examined atopic factors as predictors of asthma remission. One study demonstrated an inverse association with allergic sensitization to animals, and a second study did not find an association between atopy and remission.[3,20] Conversely, asthma persistence has been associated with aeroallergen sensitization and history of atopy. [1,2,24,26] The predictors of strict asthma remission did not differ by sex, suggesting that the baseline predictors of airways hyperresponsiveness are not sex specific.

A greater proportion of subjects went into asthma remission by early adulthood in our study compared with a prior study of asthma outcomes at adolescence in this population.[6] Previously, Covar et al[6] found only 6% of subjects had clinical remission of asthma at adolescence based on symptoms, health care use, and medication use after the first 4 years of observational follow-up. The difference in asthma remission rates between the 2 studies is likely due to a combination of different asthma remission definitions and the continued development of asthma remission in subjects followed from late adolescence to early adulthood across the entire 13-year observational follow-up. Covar et al included the absence of local medical provider contact and school absenteeism into their asthma remission definition, whereas we did not include these criteria because their causes are not specific to asthma. Our definitions used criteria specific for asthma remission and thus might have captured subjects who were previously labeled as patients with persistent asthma by Covar et al.

Currently, there is no consensus on the definition of asthma remission. Pulmonary function measurements are used to diagnose asthma and are obtained during follow-up for clinical monitoring per guidelines; hence pulmonary function measurements should bear some relevance in determining remission.[8,14] When FEV$_1$/FVC ratio was removed from the clinical asthma remission definition on sensitivity analysis, sex, baseline asthma severity, and serum IgE level became additional predictors of remission (see Table E2). These additional predictors are likely a proxy for future lung function because sex, disease severity, and allergic sensitization are associated with changes in FEV$_1$/FVC ratios.[33] Spirometric measurements were included in our asthma remission definitions to ensure accurate

classification between persistent and remitted asthma. The primary clinical remission definition reflects current clinical guidelines and practices in which serial methacholine challenge tests are not routinely performed. However, methacholine challenge is the definitive test for airway hyperresponsiveness and was therefore included in the strict definition.

This study had several unique strengths. The CAMP population was ethnically diverse, and more than 84% of the 1041 subjects had longitudinal follow-up. The detailed long-term follow-up from the CAMP study minimized information bias, and we controlled for variables associated with loss to follow-up to reduce selection bias. Severe asthma in childhood is uncommon. This study included only patients with mild-to-moderate persistent childhood asthma, and therefore our results might not be generalizable to patients with mild intermittent or severe childhood asthma. The cutoff for normal airways responsiveness was 25 mg/mL in CAMP, and more participants would have met strict remission criteria had a less conservative cutoff been used. This study examined asthma remission at early adulthood. CAMP subjects were followed until a mean age of 26 years, and the conclusion of CAMP precluded follow-up of asthma outcomes later in life.

In summary, in a multiethnic clinical trial population from North America, a considerable minority (15% to 26%) of children with mild-to-moderate persistent asthma outgrew their disease by early adulthood. Our asthma remission definitions used clinical measurements readily available in most patients and can be applied to future studies and clinical settings. The clinical trajectory of patients with childhood asthma can be predicted by using baseline FEV_1/FVC ratio, PC_{20}, and serum eosinophil measurements. Moderate-to-severe decreases in FEV_1/FVC ratio during early childhood asthma, whether because of increased disease severity or abnormal lung development, imply lifelong persistence of disease. In contrast, the majority of patients with childhood asthma with well-preserved lung function will have remission by adulthood. Our results also suggest that the increases in FEV_1/FVC ratio above the current normal threshold of 80% are informative in patients with childhood asthma, and further characterization of FEV_1/FVC ratio above this threshold is meaningful for clinical prognostication. Together, these findings strongly support the use of baseline spirometry in childhood asthma as an easily measurable and important prognostic component.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Abbreviations used

AUC	Area under the curve
BHR	Bronchial hyperresponsiveness
CAMP	Childhood Asthma Management Program
FVC	Forced vital capacity
OR	Odds ratio

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Clinical implications:

Lung function measurements and serum eosinophil counts obtained in early childhood predict asthma remission in early adulthood. Spirometry should be performed in all patients with childhood asthma for clinical prognostication.
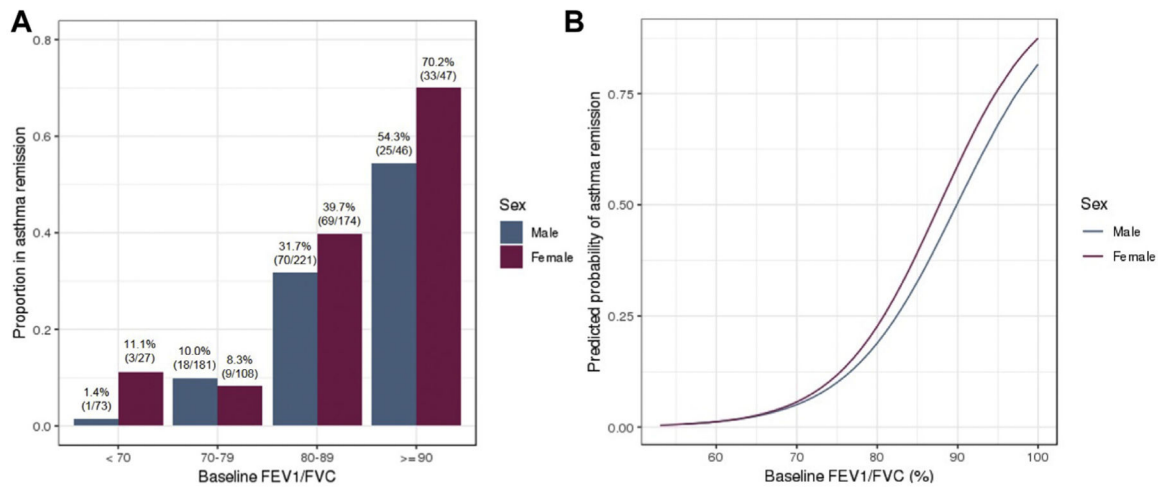
FIG 1.
A, The proportion of patients with childhood asthma who had asthma remission in early adulthood increased as baseline FEV_1/FVC ratios increased. **B**, Female subjects with greater baseline FEV_1/FVC ratios were more likely to have remission than their male counterparts. For each 10% increase in FEV_1/FVC ratio, female subjects had 8.03 times odds (95% CI, 4.60–14.93) of asthma remission, whereas male subjects had 3.88 times odds (95% CI, 2.62–5.92) of asthma remission (interaction $P = .04$).
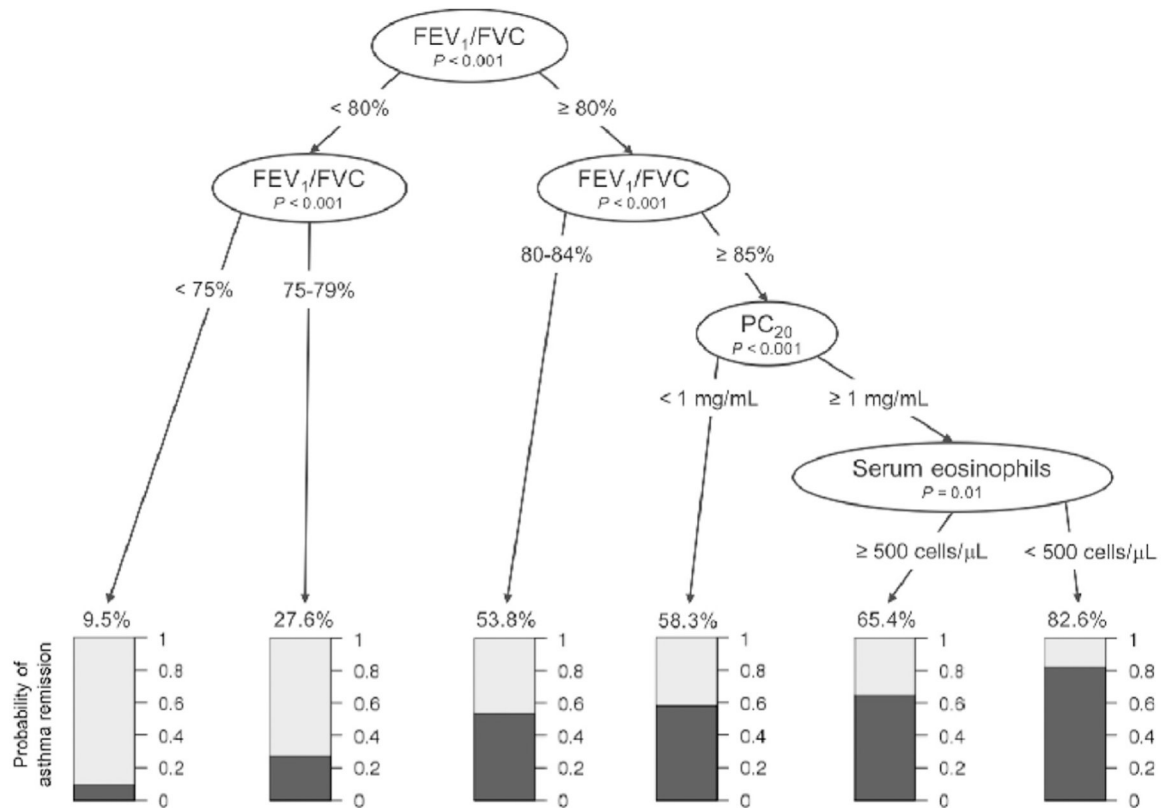
FIG 2.
The probability of asthma remission by adulthood increases as baseline FEV_1/FVC ratio increases. When the baseline FEV_1/FVC ratio was at least 85%, the probability of asthma remission is dependent on baseline PC_{20} and serum eosinophil counts. In this subgroup the probability of asthma remission was 58.3% when the baseline PC_{20} was less than 1 mg/mL. When the baseline PC_{20} was greater than or equal to 1 mg/mL, the probability of asthma remission was 65.4% in those with peripheral eosinophilia and 82.6% in those without peripheral eosinophilia.

TABLE I.

Baseline characteristics for all participants in the study stratified by clinical asthma remission status (n = 879)

	No asthma remission (n = 650)	Asthma remission (n = 229)	P value
Baseline age (y), mean ± SD	8.8 ± 2.1	8.6 ± 1.9	.07
Age at asthma diagnosis (y), mean ± SD	3.8 ± 2.5	4.1 ± 2.5	.07
Sex			.001
Male	407 (62.6%)	115 (50.2%)	
Female	243 (37.4%)	114 (49.8%)	
Ethnicity			.90
White	450 (69.2%)	154 (67.2%)	
Black	89 (13.7%)	35 (15.3%)	
Hispanic	57 (8.8%)	22 (9.6%)	
Other	54 (8.3%)	18 (7.9%)	
Baseline household income (USD)			.95
<$29,999	140 (22.3%)	48 (22.3%)	
$30,000–$49,999	215 (34.2%)	71 (33.0%)	
$50,000	274 (43.6%)	96 (44.7%)	
Parental highest education			.38
High school or less	116 (17.8%)	35 (15.3%)	
Some college or higher	534 (82.2%)	194 (84.7%)	
CAMP treatment group			.15
Budesonide	178 (27.4%)	78 (34.1%)	
Nedocromil	204 (31.4%)	63 (27.5%)	
Placebo	268 (41.2%)	88 (38.4%)	
Parental history of asthma	270 (44.3%)	94 (45.2%)	.82
Body mass index (kg/m²), mean ± SD	18.2 ± 3.6	17.9 ± 3.1	.33
Wheezes with colds	601 (92.6%)	199 (86.9%)	.009
Wheezes apart from colds	524 (80.7%)	168 (73.4%)	.02
Exacerbations after exercise	527 (81.1%)	164 (71.9%)	.004
Aeroallergen sensitization on skin testing	584 (89.8%)	190 (83.0%)	.006
History of physician-diagnosed allergies	445 (68.5%)	152 (66.4%)	.56

	No asthma remission (n = 650)	Asthma remission (n = 229)	P value
Exposure to home tobacco smoke	256 (39.6%)	97 (42.7%)	.45
Baseline asthma severity			.01
Mild	296 (45.5%)	117 (55.5%)	
Moderate	354 (54.5%)	102 (44.5%)	
Baseline PC_{20} (mg/mL), median ± IQR	0.9 ± 1.6	1.7 ± 3.6	<.001
Baseline FEV_1 (% predicted), mean ± SD	92.2 ± 14.1	99.0 ± 12.7	<.001
Baseline FEV_1/FVC ratio (%), mean ± SD	77.9 ± 7.9	85.6 ± 6.3	<.001
Baseline serum IgE level (ng/mL), median ± IQR	516.0 ± 1166.0	343.0 ± 924.5	<.001
Baseline eosinophil count (cells/mL), median ± IQR	422.0 ± 493.5	320.5 ± 327.3	<.001
Atopic dermatitis	145 (76.7%)	44 (74.6%)	.74
Mother smoked while pregnant	90 (13.9%)	31 (13.5%)	.88
Used wood stove for heating or cooking	67 (10.3%)	16 (7.0%)	.14
Pet ownership	51 (7.8%)	12 (5.2%)	.19
Clinic site			.06
Albuquerque	77 (11.8%)	23 (10.0%)	
Baltimore	75 (11.5%)	33 (14.4%)	
Boston	73 (11.2%)	39 (17.0%)	
Denver	90 (13.8%)	19 (8.3%)	
San Diego	70 (10.8%)	27 (11.8%)	
Seattle	91 (14.0%)	32 (14.0%)	
St Louis	101 (15.5%)	25 (10.9%)	
Toronto	73 (11.2%)	31 (13.5%)	

IQR, Interquartile range.

TABLE II.

Baseline predictors of clinical asthma remission[*][†]

Variable	OR	95% CI	*P* value
10% Increase in FEV_1/FVC ratio	4.62	3.35–6.50	<.001
Two-fold increase in PC_{20}	1.23	1.09–1.39	.001

[*]Covariates included in the cross-validated model: age, sex, race, CAMP treatment group, clinic site, household income level, history of wheezing with colds, history of exacerbations after exercise, and history of exposure to home tobacco smoke.

[†]Quantitative variables were modeled continuously.

TABLE III.

Baseline predictors of clinical asthma remission in male subjects [*†]

Clinical phenotype	OR	95% CI	*P* value
Serum eosinophil count <500 cells/μL	1.79	1.02–3.21	.045
Inhaled budesonide treatment[‡]	2.05	1.11–3.83	.02
Inhaled nedocromil treatment[‡]	1.30	0.70–2.42	.41
FEV$_1$/FVC ratio 90%[§]	73.81	13.07–1404.13	<.001
FEV$_1$/FVC ratio 80% to 89%[§]	25.10	5.16–453.35	.002
FEV$_1$/FVC ratio 70% to 79%[§]	6.59	1.28–120.93	.07

[*] Covariates included in the cross-validated model: age, race, CAMP treatment group, clinic site, household income level, history of wheezing with colds, history of exacerbations after exercise, history of exposure to home tobacco smoke, baseline asthma severity, and serum IgE level.

[†] Quantitative variables were modeled categorically.

[‡] Reference group is placebo treatment.

[§] Reference level is an FEV$_1$/FVC ratio of less than 70%.

TABLE IV.

Baseline predictors of clinical asthma remission in female subjects[*†]

Clinical phenotype	OR	95% CI	*P* value
Hispanic race	9.84	2.60–39.39	<.001
Moderate airway hyperresponsiveness (PC$_{20}$ 1–4 mg/mL)[‡]	0.37	0.15–0.89	.03
Severe airway hyperresponsiveness (PC$_{20}$ <1 mg/mL)[‡]	0.24	0.09–0.64	.005
FEV$_1$/FVC 90%[§]	54.76	7.56–1166.80	<.001
FEV$_1$/FVC 80% to 89%[§]	12.13	2.00–239.14	.02
FEV$_1$/FVC 70% to 79%[§]	1.44	0.20–29.90	.75

[*] Covariates included in the cross-validated model: age, CAMP treatment group, clinic site, household income level, history of wheezing with colds, history of exacerbations after exercise, history of exposure to home tobacco smoke, and serum IgE level.

[†] Quantitative variables were modeled categorically.

[‡] Reference level is a PC$_{20}$ of greater than 4 mg/mL.

[§] Reference level is an FEV$_1$/FVC ratio of less than 70%.