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Development and internal validation of a pediatric acute asthma prediction rule for hospitalization

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Abstract

Background—Clinicians have difficulty predicting need for hospitalization in children with acute asthma exacerbations.

Objective—To develop and internally validate a multivariable Asthma Prediction Rule (APR) to inform hospitalization decision-making in children ages 5-17 years with acute asthma exacerbations.

Methods—Between April, 2008 and February, 2013 we enrolled a prospective cohort of patients ages 5-17 years with asthma who presented to our pediatric emergency department with acute exacerbations. Predictors for APR modeling included 15 demographic characteristics, asthma chronic control measures, and pulmonary examination findings in participants at the time of triage and before treatment. The primary outcome variable for APR modeling was *need for hospitalization* (length-of-stay > 24 hr for those admitted to hospital or relapse for those

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Contributor' Statement:

Donald H. Arnold: Dr. Arnold designed the study, enrolled participants, is the primary author of this work, and is the guarantor of the paper, taking responsibility for the integrity of the work as a whole.

Tebeb Gebretsadik: Ms. Gebretsadik assisted with design of the analytic plan, performed all analyses and assisted with drafting and revising the manuscript.

Karel G.M. Moons: Dr. Moons assisted with design of the study and analytic plan, assisted in drafting and revising the manuscript, and approved the final version of the manuscript.

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discharged). A secondary outcome was the *hospitalization decision* of the clinical team. We used penalized maximum likelihood multiple logistic regression modeling to examine the adjusted association of each predictor variable with the outcome. Backward step-down variable selection techniques were used to yield reduced-form models.

Results—Data from 928 of 933 participants was used for prediction rule modeling, with median [IQR] age 8.8 [6.9, 11.2] years, 61% male, and 59% African-American race. Both full (penalized) and reduced-form models for each outcome calibrated well, with bootstrap-corrected c-indices of 1.74 and 0.73 for *need for hospitalization* and 0.81 in each case for *hospitalization decision*.

Conclusion—The APR predicts the need for hospitalization of children with acute asthma exacerbations using predictor variables available at the time of presentation to an emergency department.

Keywords

pediatric acute asthma exacerbations; clinical prediction rule; hospitalization

INTRODUCTION

Asthma is the most prevalent chronic disease of childhood and the most frequent reason for childhood hospitalization in the United States.[1, 2] A challenging clinical feature of this complex environmental and genetic disease is the heterogeneity of clinical expression.[3] As such, the ability of clinicians to assess severity of acute asthma exacerbations is variable and limited in accuracy.[4]

Approximately thirty-six acute asthma severity scores have been proposed. The purpose of such a score is to assess severity at the bedside in order to assist clinicians in applying appropriate immediate treatment. Systematic reviews of sixteen of these acute severity scores concluded that their predictive validity was inadequate to justify their use for patient hospitalization decisions.[5, 6]

Further, investigators have noted the difficulty that clinicians have in predicting the need for hospitalization or in predicting relapse after evaluation and treatment of exacerbations in emergency departments (EDs).[7] These features of exacerbations fulfill Steill's five criteria that identify the need for a Clinical Prediction Rule (CPR).[8]

A CPR is a decision-making tool that incorporates two or more variables from the history, physical examination, or additional tests.[9, 10] A CPR can be used in individual patients to predict the probability of an event or intervention such as hospital admission. As such, CPRs fulfill a role distinct from that of acute severity scores, assist clinicians in their clinical decision-making, and potentially improve resource utilization. To our knowledge, a CPR has not been developed to predict the need for hospitalization in pediatric patients with acute asthma exacerbations.

We sought to develop and internally validate a multivariable Asthma Prediction Rule (APR) to inform hospitalization decision-making in a population of children ages 5 to 17 years with

acute asthma exacerbations, in accordance with contemporary clinical and biostatistical standards established for CPR development and internal validation.[11-13]

METHODS

Study Participants

Detailed methods for our study have been presented in a previous report.[13] We enrolled a prospective convenience sample aged 5 to 17 years with doctor-diagnosed asthma who presented with acute exacerbations to our academic, tertiary, urban children's hospital emergency department (PED). We excluded patients with chronic lung disease other than asthma or with other causes for pertinent signs and symptoms. We included participants with more than one enrollment for APR modeling as long as the interval between enrollments was greater than 14 days (**Figure 1**). The rationale for this was that patient visits having this chronologic separation were likely to represent distinct exacerbation events.

The clinical team maintained exclusive decision-making capacity regarding all management and hospitalization decisions. Study data were not made available to the clinical team, and the study protocol did not include informing clinical management. The study protocol was reviewed and approved by the Vanderbilt University IRB (protocol #080058); parents and participants provided informed written consent and assent.

Participant Measurements and Data Acquisition

Baseline data included medical history, family asthma history, demographic and social information, medications in use, coexisting illness, asthma symptom history, and asthma characteristics that encompassed chronic disease control, environmental exposures and prior adverse events.[13] Additional clinical variables were measured and recorded before initiating treatment. These included oxygen saturation (SpO_2) on room air, assessment for accessory muscle use (scalene, sternocleidomastoid-suprasternal, intercostal, subcostal), lung auscultation (inspiratory to expiratory ratio, wheezing, air entry) exhaled nitric oxide (eNO), and spirometry for %-predicted forced expiratory volume in 1-second ($\%FEV_1$).[14, 15] Using bedside physical findings and SpO_2 we calculated the Acute Asthma Intensity Research Score (AAIRS), a validated bedside acute severity score (though not a clinical prediction rule).[16]

Candidate Predictor Variables

Candidate predictor variables for a CPR should be clinically and biologically plausible, ideally with some established evidence of predictive value. For example, we have previously reported that accessory muscle group use is a physical sign readily assessed at the bedside and has a dose-response association with $\%FEV_1$.[15, 16] Additionally, an APR will be more practical and widely used by clinicians if the predictor variables are available at the bedside.

We considered candidate predictor variables for APR development in accordance with these principles (**Table 1**). These included participant demographic and asthma characteristics, pulmonary exam findings, and measures of lung function and inflammation.

A variable was excluded after data acquisition but before APR modeling if its value was subject to our hospital's local practice and not generalizable (e.g., PCCU admission criteria), had high measurement variability or did not calibrate well to severity (e.g., respiratory rate), was rarely abnormal (e.g., scalene retractions), displayed multiple colinearity with another variable (e.g., air entry), had a high proportion of missing data (e.g., FEV_1), or was difficult to measure or not available in clinical settings where acute asthma may be managed (e.g., exhaled nitric oxide, plethysmograph estimate of pulsus paradoxus). As a result, seven candidate variables were excluded (**Table E1**), and the final model included the fifteen predictor variables in Table 1.

Outcome Variables

A CPR must predict an outcome that is both clearly defined and clinically important.[9, 17] The primary outcome variable was *need for hospitalization*, defined as length of stay >24 h (for admitted participants) or unscheduled return for asthma care to a physician or hospital within 48 h (for discharged participants).[13] Prior to prediction rule modeling an expert studio panel recommended that a second pragmatic and relevant primary outcome variable would be the *hospitalization decision* of the clinical team. This outcome encompasses the multiplicity of factors that the clinical team considers in disposition decision-making, as well as individual variability within a culture of approximately 25 attending physicians for assessment of exacerbation severity, risk-tolerance, cost-efficiency and other characteristics that may influence this decision.[18] This outcome has also been used for evaluation of acute asthma severity scores.[19, 20]

Statistical Analysis

Sample size calculation—Sample size for CPR modeling must be sufficiently large or the number of predictor variables must be sufficiently conservative for the model to be reliable and accurate on a future stream of similar patients.[11] Specifically, there must be at least 10 participants having the primary outcome (i.e., hospitalization) per degrees of freedom (*df*) of all candidate predictor variables.[21] Our model had 15 predictors and19 *df* (Table 1). There were 158 participants who met *need for hospitalization* criteria, thus allowing approximately 15 *df* for this model to avoid overfitting. In addition, there were 214 hospitalizations amongst 928 participants that would allow up to 21 *df* for the *hospitalization decision* model.

Statistical Modeling of the full-model APR—We used penalized maximum likelihood estimation logistic regression models to examine the independent association of each pre-specified predictor variable with the two outcomes *need for hospitalization* and *hospitalization decision* of the clinical team. We retained all pre-specified predictor variables in the full models and did not remove any of these variables based on statistical significance because doing so could introduce bias of the estimated regression coefficients for the remaining predictor variables as well as corresponding standard errors that are too low and confidence intervals that are falsely narrow.[11, 22-24] Prediction models that retain all pre-specified predictor variables and that apply shrinkage of estimated regression coefficients might have greater predictive performance when used for future patients with similar characteristics.[11, 25] Age and BMI were included as flexible smooth parameters

using restricted cubic splines. We estimated the variance using the Huber-White robust sandwich estimator to account for correlated data due to repeated enrollment measurements from the same patient.[26, 27] For odds ratios (OR), 95% confidence intervals (CI) were calculated.

Statistical modeling of the reduced-form APR—To decrease the complexity of the full model and to yield reduced-form models that would be more practical for bedside use, we performed step-down backward variable selection with an alpha criterion of 0.25 (type I error) within bootstrap validation.. We assessed model performance using the metrics described below and compared these with the respective full model performance metrics.

Assessment for Age-Gender Interaction—Males ages 5 – 17 years have been noted to have a higher rate of hospitalization for asthma, particularly amongst those males ages 5 – 10 years.[2] With this in mind, interaction between age and sex was assessed to study whether effects of age were different for males and females.

Model Performance and Internal Validation—We assessed model performance using two metrics, calibration and discrimination.[24, 28] Calibration is the accuracy of agreement of the predicted probability of the outcome provided by the model with the observed frequency of the outcome. A graphical assessment of calibration is possible with predictions on the x-axis and the actual outcomes on the y-axis. A 45° line represents perfect model calibration; deviation from this line represents bias in predicted values. For dichotomous outcomes, the plot contains only 0 and 1 values for the y-axis. Smoothing techniques (Loess algorithm) were used to estimate the observed probabilities of the outcome in relation to the predicted probabilities.

We assessed predictive discrimination for the ability of the model to distinguish between patients with different outcomes using the c-index and a histogram of predicted probabilities. The c-index is a rank order statistic that estimates the probability of concordance between predicted and observed outcomes and measures how well the model discriminates between different outcomes. For example a model with a high discriminative c-index (0.9) will be able to define high-risk groups better than one with low discriminative c-index (0.6).

Bootstrap internal Validation—Internal validation of the prediction model was assessed using 300 bootstrap replications with replacement.[12, 24, 28-30] Bootstrap validation involves estimation of the likely future performance of the model on new patients of the same types, which involves estimation of the drop-off in performance when the model is applied to a new sample. Bootstrapping is also an efficient technique that involves random samples that are drawn with replacement from the original data set and that are the same size as the original cohort. Thus a patient in a bootstrap sample could be represented multiple times and another could appear 0 times.

The bootstrapping validation algorithm was applied as follows: 1) We first estimated the apparent predictive ability with the original sample dataset used to fit the model; 2) 300 bootstrap samples were drawn from the original sample, and for each bootstrap sample we

fit the model and measured the apparent predictive ability; 3) We tested the accuracy measure by applying the bootstrap model to the original sample; 4) The optimism in predictive ability for this bootstrap model was calculated as the difference in performance between the bootstrap model and the original dataset; and 5) We used the average of the optimism over all 300 bootstrap samples as a correction factor to estimate a validated performance measure by subtracting the estimated optimism from the apparent predictive ability. The algorithm described above can be used to internally validate any measure of model calibration or discrimination.

Shrinkage using Penalized Maximum Likelihood Estimation—To correct for overfitting we applied penalized maximum likelihood estimation (PMLE).[31] PMLE maximizes the *penalized* log likelihood rather than maximizing the log likelihood as in conventional logistic regression. Thus, the maximum log likelihood of the full model is adjusted (shrunk) by a penalty factor. The estimated regression coefficients are individually adjusted for overfitting in contrast to a uniform shrinkage method. PMLE provides smaller prediction errors and preserves the discriminative ability of the model while shrinking each predictor for overoptimism. The full penalized model and its internal validation are presented. Analyses were performed using R-software v. 3.1 (R statistical software, Institute for Statistics and Mathematics, Vienna, Austria).[29, 30]

RESULTS

Participant Characteristics

During the period of enrollment, April 8, 2008 to February 12, 2013 we invited 974 patients to participate in the study, 41 declined and 933 participated, 928 of whom were unique participants or previously enrolled participants with intervals between enrollments of at least 14 days (**Figure 1**). Thus 928 participants were included in APR modeling. Demographic and asthma characteristics of these participants are displayed in **Table 2** along with the overall group of patients ages 5 – 17 years who presented to our PED with exacerbations during the study period.

Participants were primarily in middle childhood, and the majority were male, African-American and publicly insured. Approximately 7% were of Hispanic or Latino ethnicity, and parents identified a primary race category independent of ethnicity designation (Table 2).[32] Using the GINA chronic asthma control criteria for the preceding 3-month period, 16% of participants were controlled, 15% partly controlled, and 69% uncontrolled.[33] In addition, a majority of participants had nocturnal awakenings due to asthma during this 3-month period, and 62% had an exacerbation in the preceding year that necessitated CCS treatment. Thirty-seven percent of our participants were exposed to second-hand smoke, and 22% had prior PCCU admissions for asthma. The majority of exacerbations necessitating the PED visit were of moderate severity measured using the AAIRS, and 24% were hospitalized. Of note, female participants greater than 6 years of age were more likely to be hospitalized than were males, in contrast to previous reports.[2] The distributions of predicted probabilities of the outcomes for the full models are presented in **Figure E1** with vertical bars representing probability by 5% increments.

Asthma Prediction Rule Modeling

Full models—We modeled the APR using penalized multiple logistic regression with the 15 predictor variables (Table 1). No statistically significant interaction between age and gender was detected ($p > 0.3$) thus we proceeded with the APR regression modeling without interaction terms. The final penalized full-model results are presented in **Figure E2**. These models compute the predicted probability of the outcomes for an individual patient, and the corresponding nomograms for these calculations are displayed in **Figures E3 and E4**. Of note, the *Total Points* and *Predicted Probability* scales do not align due to non-linearity of some associations.

Odds ratios and 95% confidence intervals (CIs) for the association of these predictor variables on the outcomes of interest are presented in **Table 3**. Two predictor variables were most strongly associated with *need for hospitalization*. These included SpO_2 on room air (for 94% vs. 98%, OR 2.4, 95% confidence interval [CI] 1.9, 3.1) and inspiratory to expiratory ratio (≤ 1:3 vs. 1:1, OR 1.9, 95% CI 1.1, 3.1). Four predictor variables were most strongly associated with the *hospitalization decision* of the clinical team. These included SpO_2 on room air (for a 4% decrease, OR 3.9, 95% CI 3.0, 5.0), intercostal retractions (OR 1.6, 95% CI 1.0, 2.4), inspiratory to expiratory ratio (≤ 1:3 vs. 1:1, OR 2.0, 95% CI 1.1, 3.7) and wheezing (inspiratory and expiratory vs. none, OR 2.1, 95% CI 1.2, 3.7). The penalized models yielded bootstrapping-corrected estimates of the c-indexes for discrimination of 0.74 (*need for hospitalization)* and 0.81 (*hospitalization decision*) with the calibration curves presented in **Figure E5**.[11, 12] The models' calibration estimates have minimal deviations from the apparent probabilities.

Reduced-form models—Backward step-down variable selection yielded the reduced-form models displayed in **Table 4**. The *need for hospitalization* model included age, gender, SpO_2 on room air, need for albuterol > 2/wk, and expiratory phase prolongation, whereas the *hospitalization decision* model included age, BMI, SpO_2 on room air, intercostal muscle retractions, expiratory phase prolongation, and wheezing. The reduced-form models yielded bootstrapping-corrected estimates of the c-indices for discrimination of 0.73 (*need for hospitalization)* and 0.81 (*hospitalization decision*) with the calibration curves presented in **Figure E6**.[11, 12]

Nomograms—The APR nomograms (after shrinkage) for the full models are presented in **Figures E3 and E4** and for the reduced-form models in **Figures 2 and 3.** To use the nomograms for an individual patient, the *Points* grid-line at the top of the nomogram is used to assign point values for each variable by aligning a vertical line from the grid-line to the line adjacent to the variable. The individual variable points are summed and a vertical line from the summed points on the *Total Points* grid-line to the *Predicted Probability of Need of Hospitalization* (Figure 2) provides an estimated probability of need for hospitalization. For example, for a female aged 14 years who does not use albuterol more than twice weekly and who has an inspiratory to expiratory ratio of 1:3 and a room-air oxygen saturation of 92%,the total point score is about 105 with a corresponding probability of need for hospitalization of approximately 74%. This calculation is further illustrated in **Figure E7.** As with all clinical prediction rules, this predicted probability might reduce uncertainty and

assist the clinician in accurate decision-making for hospitalization but is not intended to prescribe a specific disposition or management plan.[9, 10, 34]

DISCUSSION

We have modeled and internally validated the Asthma Prediction Rule for children ages 5 – 17 years with acute asthma exacerbations in accordance with clinical and biostatistical standards established for CPR development.[11-13, 22, 30, 35] To our knowledge, this is the first CPR for acute asthma exacerbations.

Although a number of CPRs have been derived for other conditions in pediatric patients, few have been validated, and other quality indicators have demonstrated various weaknesses of these models.[9, 10] The APR includes predictor variables that are clinically intuitive and available at the bedside at the time of triage (before treatment). In addition, the rule internally validates well and might improve outcome prediction at the time of patient presentation, without the need to wait hours for assessment of response to therapy. As informatics-based clinical support becomes better integrated into patient care, the full-model APR can become electronically-automated and might enhance decision-support for clinicians. This might improve triage, patient management and resource utilization.

In addition, the reduced-form APR appears to be competitive with the full model for each outcome of interest. Clinicians might find the reduced-form and the accompanying nomogram to be more useful at the bedside because the limited number of predictor variables is less cumbersome.

Because the decision whether or not to hospitalize may be most clear for patients with mild or severe exacerbations, the APR may be of greatest use for those with moderate severity exacerbations. Indeed, study participants had a median AAIRS value of 5 [IQR 2, 8], indicating moderate severity episodes.[16] It should also be noted that our cohort had a number of high-risk features, including the prevalence of uncontrolled chronic asthma measured using the GINA criteria, second-hand smoke exposure, and prior PCCU admission for asthma, yet a substantial proportion (46%) reported use of inhaled CCS. These participant characteristics are similar to other cohorts of pediatric patients with acute asthma exacerbations seeking care in PEDs.[36]

Although clinicians may determine that one of these outcomes, *need for hospitalization* or *hospitalization decision*, is most appropriate for their practice, oxygen saturation and expiratory phase prolongation contributed notably to each model. We believe that this is because these physical signs represent the most prominent physiologic derangements during acute asthma exacerbations, ventilation-perfusion mismatch and dynamic airway compression..

There are several limitations to our study. First, we enrolled a convenience sample of pediatric patients in an urban, tertiary, academic children's hospital. Although the APR demonstrates strong internal validation, it may not be robust to change in measurement methods or clinical practice in other settings; as with all CPRs, external validation is needed.[17, 34] We believe there is reason for optimism that this instrument will externally

validate sufficiently to improve patient care and resource utilization. In this regard, a secondary outcome variable used for APR modeling was the decision of the clinical team for hospitalization. This included the decision-making of a large number of emergency medicine and pediatric emergency medicine attending physicians. This feature may reflect widely-applicable clinical practice and enhance external validity. Second, although the APR includes variables available at the bedside, calculating the probability of hospitalization using either the full-model nomograms or the underlying algebraic formulae may be cumbersome. We acknowledge that the full-model APR will be of greatest utility as a component of electronic decision-support. Finally, we have not demonstrated whether the APR will improve clinical outcomes or resource utilization, and the next step is an impact analysis to examine the effect of the APR on these important outcomes.[34, 37]

In summary, we developed an APR using predictor variables that are clinically intuitive and available at the bedside at the time of triage. The APR has the potential to facilitate expeditious triage, hospitalization and disposition decisions for pediatric patients with acute asthma exacerbations and may thus improve acute management and resource utilization. External validation and an impact analysis of the APR are the next steps before incorporation of this instrument into electronic decision-support.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AAIRS	acute asthma intensity research score
APR	asthma prediction rule
BMI	body mass index
CCS	corticosteroid
CPR	clinical prediction rule
df:	degrees of freedom
ED	emergency department
eNO	exhaled nitric oxide
%FEV$_1$	%-predicted forced expiratory volume in 1 second

GINA	global initiative for asthma
IQR	inter-quartile range
PCCU	pediatric critical care unit
PED	pediatric emergency department
PMLE	penalized maximum likelihood estimation
SpO_2	oxygen saturation by pulse oximetry

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HIGHLIGHTS BOX

What is already known about this topic?

- Clinicians have limited tools to inform asthma hospitalization decisions.
- The predictive validity of available acute asthma severity scores is inadequate to justify use for hospitalization decisions.
- An effective clinical prediction rule might facilitate hospitalization decision-making.

What does this article add to our knowledge?

- We have developed and internally validated an Asthma Prediction Rule (APR) for *need for hospitalization* using predictor variables readily available before treatment.
- SpO_2 and expiratory prolongation were most strongly associated with *need for hospitalization.*

How does this study impact current management guidelines?

- The APR might facilitate hospitalization decisions for children with acute asthma exacerbations and improve resource utilization.
- External validation and an impact analysis are next steps before incorporation of the APR into routine decision-support.

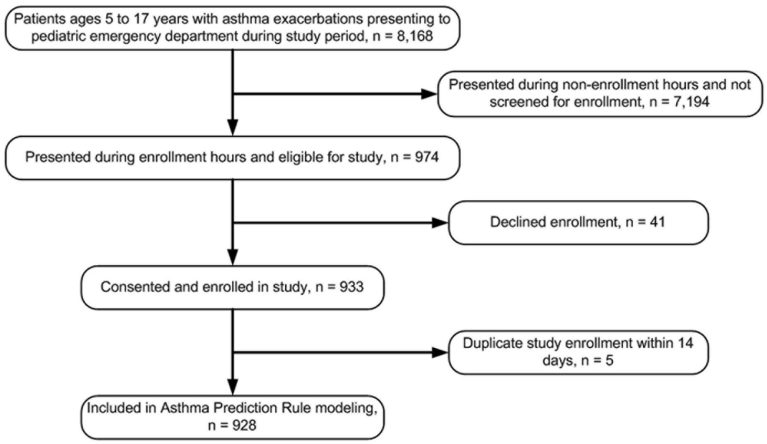

Figure 1. Participant recruitment and study implementation
Does not require a legend.

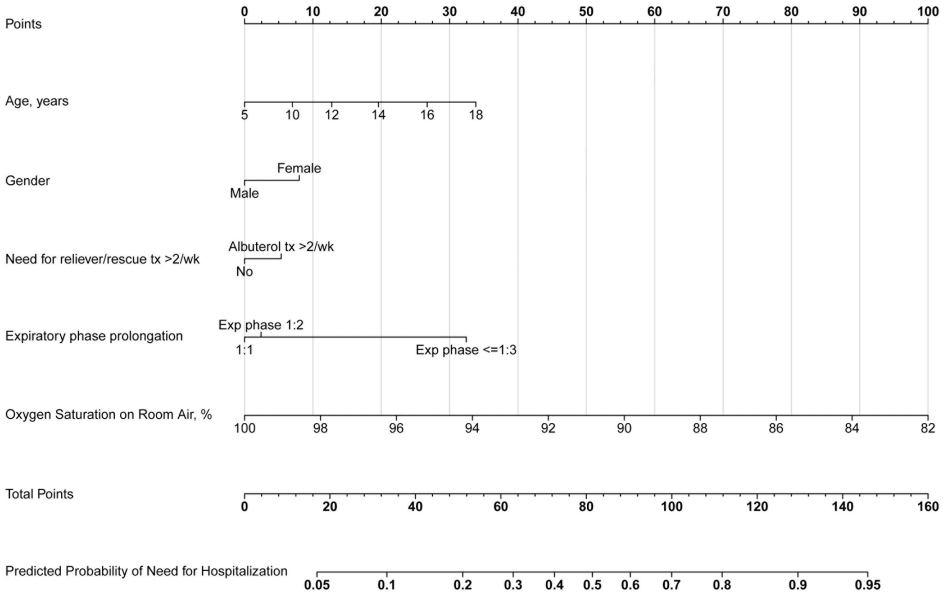

Figure 2.

Asthma Prediction Rule reduced-form nomogram for *need for hospitalization*: To use the nomogram for an individual patient, the points (top grid-line) for each predictor variable are first assigned and the total points calculated. A vertical line from this value on the Total Points grid-line provides a Probability of Need of Hospitalization grid-line. Exp = Expiratory; Ins = Inspiratory.

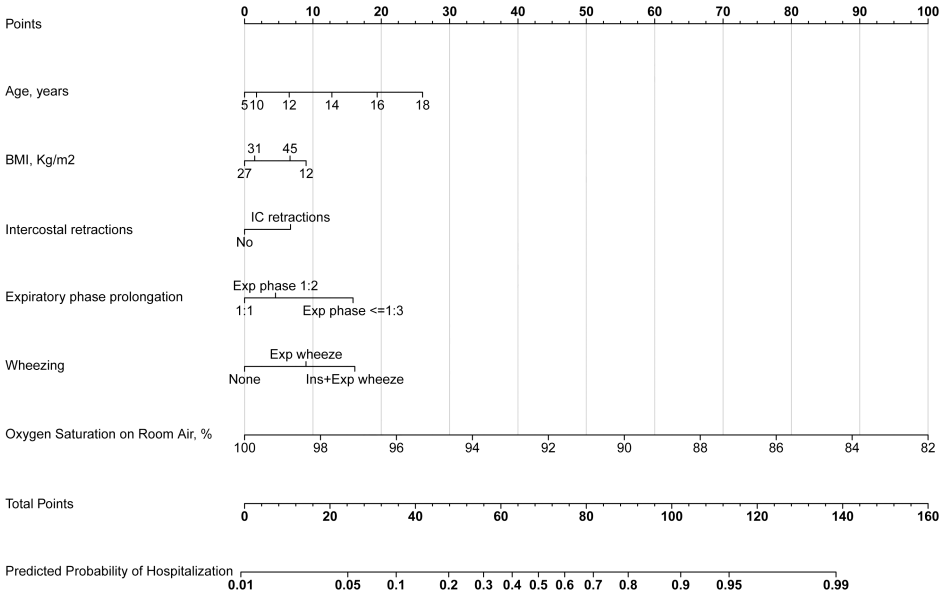

Figure 3.

Asthma Prediction Rule reduced-form nomogram for *hospitalization decision* of the clinical team: To use the nomogram for an individual patient, the points (top grid-line) for each predictor variable are first assigned and the total points calculated. A vertical line from this value on the Total Points grid-line provides a probability value on the Predicted Probability of Hospitalization grid-line. Exp = Expiratory; Ins = Inspiratory.

Table 1

Pre-specified predictor variables for modeling the Asthma Prediction Rule

Variable	Type	*d.f.*
Age	Continuous	2
BMI		2
Race	Dichotomous	1
Gender		1
Gina chronic control		
Daytime sx > 2/wk		1
Nocturnal sx > 1/wk		1
Activity limitation	Dichotomous	1
Need for albuterol > 2/wk		1
Asthma exacerbation tx with CCS (prior yr)		1
SpO_2	Continuous	1
Accessory muscle use		
SCM		1
Intercostal	Dichotomous	1
Subcostal		1
Inspiratory to expiratory ratio	Ordinal	2
Wheezing		2
	Total d.f.	**19**

d.f. = Degrees of freedom; BMI = Body mass index; sx = symptoms; tx = treatment; SpO_2 = oxygen saturation on room air; SCM = sternocleidomastoid

Table II

Characteristics of participants and of patients aged 5 - 17 years with acute asthma admitted to pediatric emergency department during study period

	Study Participants (n = 928)	PED Asthma Patients[a] (n = 8,168)
Age	8.8 [6.9,11.2]	7.1 [4.7, 10.3]
Male	566 (61)	5,135 (63)
BMI (Kg/M^2)	18.0 [15.6, 21.9]	NA
BMI percentile	72.5 [41.5, 93.7]	
Race		
African-American	547 (59)	4,623 (57)
White	374 (40)	2,792 (34)
Asian	6 (1)	86 (1)
Other	2 (<1)	667 (8)
Ethnicity[b]		
Hispanic or Latino	68 (7)	
Not Hispanic or Latin0	860 (93)	NA[d]
Not reported/unknown	0 (0)	
Medicaid	581 (63)	5,198 (64)
Asthma characteristics		
Asthma control and future risk[c]		
Daytime sx > 2/wk	457 (49)	
Nocturnal sx/awakening	519 (56)	
Activity limitation	471 (49)	
Need for rescue tx > 2/wk	451 (49)	
Exacerbation in past year	572 (62)	
Using inhaled corticosteroid	430 (46)	
Second-hand smoke exposure	341 (37)	NA[d]
Prior PCCU admission	200 (22)	
Prior ETI	42 (5)	
AAIRS	5 [2, 8]	
Hospitalization decision of clinical team		
Discharge to home	712 (77)	
Admit to floor bed	163 (18)	
Admit to PCCU	51 (6)	

n (%) except Age and AAIRS, which are median [IQR] AAIRS = acute asthma intensity research score;[15] PCCU = pediatric critical care unit; ETI = endotracheal intubation for asthma

[a]Baseline Population: all patients aged 5 to 17 years presenting to pediatric emergency department during study period with final primary diagnosis of asthma exacerbation by ICD code 493, including study sample

[b]Hispanic ethnicity is not mutually exclusive of race.[32]

[c] Global Initiative for Asthma (GINA) chronic control characteristics for preceding 3-month period.[33]

[d] Not available in database used to identify PED asthma population

Table III

Full Asthma Prediction Rule models, penalized odds ratios for associations of predictor variables with primary outcome of *need for hospitalization* and secondary outcome of *decision of the clinical team for hospitalization* in 928 participants aged 5 - 17 years with asthma exacerbations

	Need for hospitalization	Hospitalization decision of the clinical team
Age (Years, change from 6.9 to 11 years)	1.4 (1.1 – 1.9)	1.3 (1.0 - 1.8)
BMI (Kg/M^2) change from 15.6 to 22)	1.0 (0.8 – 1.3)	0.9 (0.7- 1.2)
SpO_2 (%, change from 98 to 94%)	2.4 (1.9 – 3.0)	3.9 (3.0 - 5.0)
Gender (Female:Male)	1.3 (0.9 – 1.8)	1.1 (0.8 - 1.6)
Race (white:other)	1.1 (0.8 – 1.6)	0.9 (0.7 - 1.3)
Daytime asthma sx > 2/wk	1.1 (0.7 -1.6)	1.1 (0.7 - 1.7)
Nocturnal asthma sx or awakening	1.0 (0.7 – 1.4)	0.9 (0.6 - 1.4)
Limitation of activity due to asthma	1.1 (0.8 – 1.6)	1.1 (0.8 - 1.6)
Need for albuterol > 2/wk	1.1 (0.8 – 1.7)	1.0 (0.7 - 1.6)
Asthma exacerbation in past year	1.1 (0.8 – 1.6)	1.1 (0.8 - 1.6)
Sternomastoid-suprasternal retractions	1.0 (0.7 – 1.5)	1.1 (0.7 - 1.7)
Intercostal retractions	1.4 (0.9 – 2.0)	1.6 (1.0 - 2.4)
Subcostal retractions	1.0 (0.7 – 1.4)	1.0 (0.7 - 1.5)
Inspiratory:Expiratory ratio (1:2 vs. 1:1)	1.0 (0.7 – 1.5)	1.3 (0.8 – 2.0)
Inspiratory:Expiratory ratio (≤ 1:3 vs. 1:1)	1.9 (1.1 – 3.1)	2.0 (1.1 - 3.7)
Wheezing (expiratory:none)	1.2 (0.8 – 1.90)	1.4 (0.8 - 2.5)
Wheezing (inspiratory + expiratory vs. none)	1.23 (0.8 – 2.0)	2.1 (1.2 - 3.7)

Age and BMI included as flexible smooth variables using restricted cubic splines.

BMI = body mass index; SpO_2 = oxygen saturation on room air Values are odd ratios (95% CI) estimated using penalized maximum likelihood logistic regression.

Table IV

Reduced-form Asthma Prediction Rule models, odds ratios for associations of predictor variables with primary outcome of *need for hospitalization* and secondary outcome of *hospitalization decision* of the clinical team in 928 participants aged 5 - 17 years with asthma exacerbations

	Need for hospitalization	**Hospitalization decision of the clinical team**
Age (change from 6.9 to 11 years)	1.5 (1.0 – 2.1)	1.6 (1.2 – 2.2)
BMI (Kg/M^2,change from 16 to 22)	NA	0.7 (0.5 – 1.1)
Female gender	1.44 (1.0 – 2.1)	NA
SpO_2 (%, change from 98 to 94%)	2.8 (2.1 – 3.6)	4.4 (3.3 - 5.7)
Need for albuterol > 2/wk	1.3 (0.9 – 1.9)	NA
Intercostal muscle retractions	NA	1.6 (1.0 – 2.6)
Inspiratory:Expiratory ratio (≤ 1:3 vs. 1:1)	4.4 (2.3 – 8.61)	2.9 (1.3 – 6.5)
Wheezing (inspiratory + expiratory vs. none)	NA	2.9 (1.4 – 5.6)

Age and BMI included as flexible smooth variables using restricted cubic splines.

BMI = Body mass index; SpO_2 = oxygen saturation on room air; NA = not included in this model (P > 0.25)

Values are odd ratios (95% CI) estimated using logistic regression.