

Risk Factors for Asthma Hospitalizations in a Managed Care Organization: Development of a Clinical Prediction Rule

Michael Schatz, MD, MS; E. Francis Cook, ScD; Anita Joshua, MPH;
and Diana Petitti, MD, MPH

Objective: To use a computerized administrative database to develop and validate a clinical prediction rule for the occurrence of asthma hospitalizations.

Study Design: Retrospective cohort.

Methods: Subjects included asthmatic patients ages 3 to 64 who were continuously enrolled in the Southern California Kaiser Permanente managed care organization in both 1998 and 1999. Data were based on linkage of a hospital discharge database, diagnosis and procedures database, membership database, and prescription database. The outcome was any 1999 hospitalization with a primary diagnosis of asthma. The outcome was evaluated and modeled separately for children (ages 3-17) and adults (ages 18-64).

Results: Univariate analyses showed that hospitalized children were younger than nonhospitalized children. Adults and children hospitalized in 1999 had lower mean household incomes, were more likely to have required an emergency department visit or hospitalization in 1998, used more β -agonists and oral corticosteroids in 1998, and had more 1998 prescribers than nonhospitalized patients. In multivariable analysis, independent predictors of 1999 hospitalization in children included age and 1998 hospitalizations, β -agonist dispensings, total anti-inflammatory dispensings, and number of prescribers. Among adults, 1998 hospitalizations and oral steroid dispensings as well as income were independent predictors of hospitalization in 1999. The prediction rules developed in this study identified the 11% to 13% of adults or children with an approximately 6-fold higher likelihood for being hospitalized in the following year.

Conclusion: These models can be used to identify high-risk asthmatic patients in whom targeted intervention might reduce asthma morbidity and cost of care.

(*Am J Manag Care.* 2003;9:538-547)

In the United States, asthma affects 14 to 15 million persons and accounts for more than 100 million days of restricted activity and 470 000 hospitalizations annually.¹ The total estimated cost of asthma in the United States in 1994 was \$5.8 billion,² and it appears that more than 80% of the total cost is generated by the 20% of patients with more severe asthma.² A substantial proportion of these direct costs are due to asthma hospitalizations and emergency department (ED) visits.²

Various interventions have been shown to reduce the risk of hospitalizations or ED visits in asthmatic subjects, including specialty care,³⁻⁷ and organized programs involving personalized education and regular personal or telephone contact.⁸⁻²⁰ Such interventions should both improve quality of life and reduce direct and indirect costs for asthmatic patients. However, cost-effective intervention programs would be best aimed at patients who are at higher risk of adverse outcomes.

A number of studies have tried to identify risk factors for asthma hospitalizations or ED visits.²¹⁻⁸³ Many demographic, clinical, utilization, medication, and social/environmental factors have been associated with an increased risk of asthma hospitalizations or ED visits (Table 1). Among the most consistent or pronounced risk factors were younger age (when children were included in the population studied), African-American or Hispanic race/ethnicity, lower socioeconomic status, more clinically severe asthma, prior utilization, and increased use of rescue medications (inhaled β -agonists and oral corticosteroids). Several studies have suggested that increased use of preventative medications (cromolyn, inhaled corticosteroids) and the use of asthma action plans could decrease the risk of asthma hospitalizations or ED visits. Among patients hospitalized with asthma, there was a strong relationship between age and gender, such that up to twice as many patients under age 20 were males, but up to 3 times as many patients over age 20 were females. However, since many of these studies did not take into

From the Departments of Allergy (MS) and Clinical Services (AJ, DP), Southern California Permanente Medical Group, San Diego and Pasadena, CA; and the Department of Epidemiology, Harvard School of Public Health, Boston, MA (EFC).

This study was funded by the Southern California Permanente Medical Group, San Diego and Pasadena, CA.

Address correspondence to: Michael Schatz, MD, MS, Department of Allergy, Kaiser-Permanente Medical Center, 7060 Claremont Mesa Boulevard, San Diego, CA 92111. E-mail: michael.x.schatz@kp.org.

account the possible age-gender associations among all asthmatics, they cannot adequately assess the role of either factor as a risk factor for hospitalization.

The purposes of the current study were 1) to confirm previously identified risk factors using a computerized administrative database in a large managed care organization; 2) to assess the independent effects of these factors; and 3) to develop a clinically useful prediction rule to identify patients in asthmatic populations at high risk of subsequent asthma hospitalizations.

METHODS

Data Collection

Data for this study were derived from the Southern California Kaiser Permanente Asthma Case Identification Database (ACID), based on linkage of computer data from a hospital discharge database, diagnosis and procedures database, membership database, and prescription database. Patients were identified as having asthma if they met one or more of the following criteria:

- 1) Any discharge diagnosis (principal or other diagnosis) of asthma in the hospitalization database (*ICD-9* code: 493.xx);
- 2) Two or more asthma-related medication dispensings (excluding oral steroids) in a 1-year period in the prescription database, including β -agonists (excluding oral terbutaline), inhaled steroids, other inhaled anti-inflammatory drugs, and oral leukotriene modifiers; and
- 3) ED or regular clinic asthma-related visit in the diagnosis and procedures database.

This algorithm is based on the evidence that identifying "physician-diagnosed asthma" is a valid way to identify asthmatic patients in epidemiological studies.⁸⁴ Physician-diagnosed asthma is captured explicitly with criteria 1 and 3 and implicitly with criterion 2.

Subjects in the present cohort were patients included in ACID during 1998 and 1999 who 1) were assigned to the San Diego or Los Angeles medical centers, 2) were continuously enrolled in 1998 and 1999, 3) had prescription drug coverage as a benefit, and 4) were between the ages of 3 and 64. The outcome was any 1999 hospitalization with a primary diagnosis of asthma (*ICD-9* Code: 493.xx) at a Kaiser Foundation Hospital or at an outside

Table 1. Previously Identified Risk Factors for Asthma Hospitalizations or Emergency Department Visits

Age/gender	
Younger age (children) ^{21-32,82}	
Older age (adults) ³³	
Male gender (< age 20) ^{31,34,35-37,82}	
Female gender (> age 20) ^{35,37-42,79}	
Race/ethnicity	
African American ^{26,27,29,30,34,35,43-51,78,79}	
Hispanic ^{25,26,45,46,49}	
Nonwhite/minority ^{21,25,83}	
Socioeconomic	
Lower income ^{21,25,26,34*,43,47,52,78,83}	
Poverty status ^{25,34,37,45,76}	
Problem paying for care ⁵³	
Medicaid/public aid ^{30,50,54,77}	
Deprivation ^{†55}	
Lower educational level ^{25,26, 34*,52,78}	
Unemployment ⁷⁸	
Clinical	
Increased symptom severity or frequency ^{23,52,53,56-59}	
Nocturnal symptoms ^{23,58,60}	
Does not have personal physician ²²	
Missed school ⁵³	
No action plan ^{52,61,62}	
Decreased forced expiratory volume in 1 second ^{60,63}	
Cat/cockroach sensitivity ³⁰	
Low perception of dyspnea ⁸¹	
Utilization	
Prior emergency department visits ^{22,23,52,60,64,65,77,80,83}	
Prior hospitalizations ^{22,54,58,61,63,77,80,83}	
Asthma visit past 6-12 months ^{23,53,77}	
Unscheduled visits for asthma past year ²³	
Medication	
Increased β -agonist use ^{22,52,60,66-68,80}	
Not using cromolyn ^{22,32,66}	
Not using inhaled corticosteroids ^{33,59,66,69-71}	
Low inhaled corticosteroid/ β -agonist ratio ^{25,64,72,73}	
Use of oral corticosteroids ^{22,58,61,63,64,74,77}	
Use of daily medications ²³	
Larger number of prescribers ²²	
Nebulizer at home ⁵²	
Not treated for allergic rhinitis ⁸⁰	
Use of theophylline ⁸⁰	
Social/environmental	
Smoking ⁴⁶	
Damp housing ⁷⁵	
Crowding ²⁶	
Use of oil for heat ²⁶	
Did not wash bedsheets > twice per month ⁵²	
No mattress cover ⁵³	
Low social support ⁵³	
Northeast vs West United States ²⁹	
Maternal depressive symptoms ⁵⁹	

*Socioeconomic index in this study included occupation, educational level, home ownership, income, and access to services.

†Townsend Index, based on unemployment, presence of cars, home ownership, and number of persons per room.

CLINICAL

hospital. The outcome was evaluated and modeled separately for children (ages 3-17) and adults (ages 18-64).

Median household income for each zip code was determined from the 1990 US Census Web site. Potential predictors for the analysis included 1) age, 2) gender, 3) zip code-derived median household income (based on 1998 address), 4) San Diego or Los Angeles location, 5) number of 1998 asthma hospitalizations, 6) number of 1998 asthma ED visits, 7) number of 1998 inhaled β -agonist dispensings, 8) number of 1998 anti-inflammatory medication dispensings, 9) the 1998 ratio of anti-inflammatories to total asthma medications (anti-inflammatories plus inhaled β -agonists) dispensings, 10) number of 1998 oral corticosteroid dispensings, 11) number of 1998 asthma medication prescribers, and 12) interaction terms for 1998 β -agonists with 1998 ED visits, hospitalizations, oral corticosteroid dispensings, and number of prescribers.

Data Analysis

All analyses were conducted using SAS version 6.12 for Windows software. Univariate analyses evaluated the relationships between individual risk factors and asthma hospitalization in children and adults. Hypothesis

testing for continuous predictors was conducted using the Wilcoxon rank sum test. Hypothesis testing for binary predictors was conducted using the Fisher's exact test. A two-sided *P* value of less than .05 was considered statistically significant.

Using all potential predictors, separate logistic regression models using backwards elimination algorithms were constructed for each age group (ie, children and adults). Only variables with final Wald chi-square *P* values of less than .01 were retained for the final models. A *P* value of .01 was chosen so as to limit the potential for over-training and increase the likelihood that the model will generalize to other populations. The intercept and coefficients of the models were used to create prediction rules for asthma hospitalizations in children and adults. These prediction rules were then validated using bootstrap resampling techniques with 500 repetitions each.

From the final validated models, tables of predicted risks for each outcome compared with actual outcomes were constructed using jackknifed estimates.⁸⁵ A jackknifed estimate is one in which many models are fit, each time leaving out one person from the training set. The risk of the "left-out" person is then calculated from

Table 2. Predictor and Outcome Variables in the Study Population

Variable	Children (n = 4197)		Adults (n = 6904)	
	Mean \pm SD	%	Mean \pm SD	%
Demographic				
Age	9.493 \pm 4.105	—	43.672 \pm 12.313	—
Female	—	37.8	—	63.5
Male	—	62.2	—	36.5
Income*	34 687 \pm 10 715	—	35 493 \pm 10 295	—
San Diego	—	65.9	—	71.7
Los Angeles	—	34.1	—	28.3
Utilization				
1999 Hospitalization	.014 \pm .125	1.4	.013 \pm .127	1.2
1998 Hospitalization	.015 \pm .140	1.3	.008 \pm .097	.8
1998 ED visits	.080 \pm .322	6.9	.066 \pm .317	5.4
1998 treatment				
β -agonists	2.643 \pm 3.117	82.8	3.975 \pm 3.884	91.0
Total anti-inflammatories	1.070 \pm 2.810	49.1	1.913 \pm 2.422	67.6
Ratio [†]	.261 \pm .276	—	.324 \pm .286	—
Oral steroid courses	.563 \pm .918	37.4	.560 \pm 1.191	29.8
Number of prescribers	2.371 \pm 1.473	96.0	2.388 \pm 1.458	97.6

ED indicates emergency department.

*Missing = 138 children, 231 adults.

[†]ratio = total anti-inflammatories/total anti-inflammatories + β -agonists; data missing for 592 children, 258 adults.

the model for which that person was not part of the training set. The summary risk calculated using this approach gives a more valid estimate of risk.⁸⁵ From these risk tables, sensitivities, specificities, positive predicted values (PPV), and negative predictive values (NPV) for various probability cut-offs were calculated. For each model, the probability cut-off that maximized the sensitivity and PPV was determined.

RESULTS

The final case identification cohort included 4197 children aged 3 to 17 and 6904 adults younger than age 65. Characteristics of the population are shown in Table 2. Sixty-two percent of asthmatic children were male, while 63% of asthmatic adults were female. Approximately 70% of the persons in the database were from the San Diego medical center. The overall 1999 hospitalization rate was 1.4% in children and 1.2% in adults. The medication treatment of this cohort in 1998 is also described in Table 2.

Univariate analyses between asthma hospitalizations and potential predictors for children and adults are

shown in Table 3. Hospitalized children were younger than nonhospitalized children. There was no significant relationship between gender and hospitalization in children or adults. Both hospitalized children and adults lived in zip codes with lower mean household incomes than patients who were not hospitalized. Hospitalized children were less likely to have been from the San Diego medical center than nonhospitalized children. Adults and children hospitalized in 1999 were much more likely than nonhospitalized patients to have had a hospitalization or ED visit in 1998. Hospitalized patients used more β -agonists and oral steroids and had more prescribers than nonhospitalized patients. Although hospitalized patients used more anti-inflammatory medication and had a lower anti-inflammatory to total asthma medication ratio than nonhospitalized patients, these differences were not statistically significant.

The final regression models are shown in Table 4. Independent predictors for 1999 asthma hospitalizations in children were younger age and increased number of 1998 hospitalizations, β -agonist dispensings, and prescribers. Increased total anti-inflammatory treatment also was associated with a reduced likelihood of hospital-

Table 3. Univariate Analyses of the Relationships Between 1999 Hospitalizations and Predictor Variables

Parameter	Children Hospitalized	Children Not Hospitalized	Adult Hospitalized	Adult Not Hospitalized
n	57	4140	83	6821
Age	7.53 \pm 3.67 [†]	9.52 \pm 4.10	41.48 \pm 11.94	43.70 \pm 12.32
Female	38.6%	37.8%	69.9%	63.4%
Income	31 438 \pm 10 205*	34 733 \pm 10 716	32 147 \pm 9244 [†]	35 532 \pm 10 300
San Diego location	50.9%*	66.1%	72.3%	71.7%
Any 1998 hospitalizations	10.5% [†]	1.2%	8.4% [†]	.7%
Mean 1998 hospitalizations	.193 \pm .639 [†]	.013 \pm .118	.108 \pm 0.383 [†]	.007 \pm .088
Any 1998 ED visits	17.5% [†]	6.7%	16.9% [†]	5.2%
Mean 1998 ED visits	.316 \pm 0.805 [†]	.076 \pm .309	.253 \pm .730 [†]	.064 \pm .308
β -agonists	5.02 \pm 4.58 [†]	2.61 \pm 3.08	5.67 \pm 4.69 [†]	3.95 \pm 3.87
Total anti-inflammatories	1.37 \pm 2.06	1.07 \pm 1.67	2.27 \pm 3.15	1.91 \pm 2.41
Ratio [§]	.21 \pm .24	.26 \pm .28	.28 \pm .27	.32 \pm .29
Oral steroid courses	1.37 \pm 1.68 [†]	.55 \pm .90	1.54 \pm 1.91 [†]	.55 \pm 1.17
Number of prescribers	3.61 \pm 2.19 [†]	2.35 \pm 1.45	3.19 \pm 1.89 [†]	1.45

ED indicates emergency department.

*P < .05.

[†]P < .01.

[‡]P < .001.

[§]Ratio = total anti-inflammatories/total anti-inflammatories + β -agonists

CLINICAL

ization among children in the final model. Independent predictors for 1999 hospitalizations in adults included lower income and the number of 1998 hospitalizations and oral steroid dispensings. The discrimination of the pediatric model was higher than that of the adult model, based on the *C* statistic for the area under the ROC curve (Table 4).

The performance of the final prediction rules was evaluated in a jackknifed sample of children and adults. For cut-off high-risk probabilities ranging from 1.0% to 3.0% in children, sensitivities ranged from 35.1% to 82.5%, specificities from 58.3% to 92.9%, PPVs from 2.7% to 6.4%, and NPVs from 99.0% to 99.6%. Using a cut-off predicted probability of hospitalization of 2.5 % in children, approximately 11% were identified as high risk (Table 5). This high-risk group included 44% of the children actually hospitalized. Of these high-risk children, 5.6% were hospitalized compared with .9% of children identified as low risk (relative risk = 6.2). For cut-off high-risk probabilities ranging from 1.0% to 3.0% in adults, sensitivities ranged from 20.5% to 66.7%, specificities from 62.7% to 97.3%, PPVs from 3.1% to 8.2%, and NPVs from 99.0% to 99.4%. Using a cut-off predicted probability of hospitalization of 1.5% in adults, approximately 13% were identified as high risk (Table 5). This high-risk group included 45% of the adults actually hospitalized. Of these high-risk adults, 3.9% were hospitalized compared with .7% of adults identified as low risk (relative risk = 5.6).

The importance of prior hospitalizations as a risk factor in both adults and children and the relatively low PPVs achieved by the models derived in this study suggested 2 additional analyses. First, the models were fitted only in patients with prior utilization (1998 hospitalization or ED visits for asthma). This process identified 8% to 12% of the prior utilizers with a substantially higher PPV—14% to 19% of the high-risk group from this population would be hospitalized in the subsequent year (Table 5).

Second, a model only using 1998 hospitalizations as a predictor was fit in children and adults. This model had substantially less discrimination than the complete models in both children (*C* statistic = .547 versus .781) and adults (*C* statistic = .539 versus .712). Moreover, the maximum sensitivity achievable with this model (with greater than 0% specificity) was only 10.5% in children and 8.4% in adults.

DISCUSSION

This study confirms previous findings of a positive link between the risk of asthma hospitalization and the following factors: younger age (in children), lower median household income, prior hospitalization or ED visits, increased use of β -agonists, use of oral corticosteroids, and greater number of prescribers (Table 1). This study also developed predictive models that were able to identify 11% to 13% of adults or children who were approximately 6 times more

Table 4. Final Models for the Prediction of Asthma Hospitalizations in Adults and Children

Variable	Children		Adults	
	Parameter Estimate (<i>P</i> value)	Odds Ratio (95% Confidence Interval)	Parameter Estimate (<i>P</i> value)	Odds Ratio (95% Confidence Interval)
Intercept	-3.9671 (.0001)	—	-3.5539 (.0001)	—
Hospitalizations*	1.2142 (.0013)	3.37 (1.61-7.04)	1.6817 (.0001)	5.38 (2.53-11.42)
β -agonists*	.1556 (.0001)	1.17 (1.10-1.25)	—	—
Total anti-inflammatories*	-.3164 (.0024)	0.73 (0.59-0.89)	—	—
Number of prescribers*	.3265 (.0021)	1.39 (1.13-1.71)	—	—
Age	-.1803 (.0001)	0.84 (0.77-0.91)	—	—
Oral steroids*	—	—	.2850 (.0001)	1.33 (1.21-1.47)
Income	—	—	-.00004 (.0043)	1.00 (1.00-1.00)
<i>C</i> statistic [†]	.781	—	.712	—

*1998 values.

[†]Area under the receiver–operating characteristic curve.

likely to be hospitalized in the following year, accounting for approximately 45% of the patients actually hospitalized.

Several previously identified factors were not found to be significant in this study. For example, males under age 20 have been reported to be more likely to be hospitalized than are their female counterparts, while females over age 20 are more likely to be hospitalized than are their male counterparts. However, many studies did not take into account the age–gender associations among all asthmatics. The present study confirms that more than 60% of children with asthma are male and more than 60% of adults with asthma are female, but did not show an effect of gender of the risk of asthma hospitalizations.

Older age has been identified as a risk factor in adults in a prior study,³³ but was not linked to hospitalizations in the present study. This may be because the upper age limit in the present study was 64—a wider age range may be necessary to demonstrate a relationship between older age and asthma hospitalizations in adults. Prior studies also have suggested that appropriate prophylactic anti-inflammatory therapy may mitigate the risk of asthma hospitalization (Table 1). The current study only partially confirmed these findings. Total use of anti-inflammatory medications was increased among hospitalized vs nonhospitalized patients, although this difference was not statistically significant. This may reflect an effect of inherent severity. However, when other risk factors were simultaneously considered, increased use of anti-inflammatory prophylactic medications (cromolyn, nedocromil, inhaled corticosteroids, or leukotriene modifiers) significantly reduced the risk of hospitalization in children but not in adults (Table 4).

Another means of attempting to define appropriate prophylactic therapy is the ratio of anti-inflammatory to β -agonist or total medication use, which has been previously reported to be significantly lower in patients who are subsequently hospitalized for asthma (Table 1). In the current study, these ratios were somewhat lower among hospitalized versus nonhospitalized children and adults, but the difference was not statistically significant. In addition, when considered in the context of the other predictors in the multivariate models, the prophylactic anti-inflammatory to total medication ratio

Table 5. Jackknifed Estimates of the Performance of the Final Model in Children and Adults*

Subjects	P Level Cut-off	% Predicted High Risk	Sensitivity (%)	Specificity (%)	PPV(%)	NPV (%)
All						
Children	.025	10.9	43.9	89.8	5.6	99.1
Adults	.015	13.3	44.9	87.0	3.9	99.3
Prior Utilization [†]						
Children	.090	9.8	46.2	91.8	19.4	97.6
Adults	.065	12.5	46.7	88.8	14.0	97.7

PPV indicates positive predictive value; NPV, negative predictive value.

*Cut-offs deemed most clinically useful (based on sensitivity >40% and maximum PPV).

[†]1998 asthma emergency department visit or hospitalization.

did not emerge as a significant independent predictor. One reason for this may be that the ratios in these calculations were based on dispensings, rather than number of canisters, which was not available in this data set. One would predict that number of canisters, especially if adjusted for doses per canister and drug potency, would provide a more sensitive measure of actual prophylactic versus rescue therapy dispensed and be a better predictor.

Two differences between children and adults were identified in the univariate analyses. The first is that younger age increased the risk of hospitalization among children but not among adults, which is consistent with prior findings. The other difference is that hospitalized children (but not adults) were less likely to be from the San Diego service area than nonhospitalized children. One could speculate that environmental differences between San Diego and Los Angeles, such as air pollution, could account for these findings, assuming that these factors have a greater effect on children than adults younger than age 65.

Multivariate models also revealed differences among children and adults (Table 4). In fact, the only factor common to final models in both children and adults was prior hospitalizations, which had the highest parameter estimate in both models. As in the univariate analysis, younger age was a risk factor in children but not adults. While β -agonists, total anti-inflammatories (inverse relation), and number of prescribers were independent predictors in children, oral steroids and lower income were independent predictors in adults. Furthermore, the model for hospitalization in children appeared to be more discriminating, based on the area under the receiver–operating characteristic curve (*C* statistic). The reasons for these differences are unclear, but they do suggest that predictive models for asthma hospital-

izations may be more discriminating if they evaluate children and adults separately.

In addition to identifying independent predictors from administrative data, a major goal of this study was to develop a valid and clinically useful prediction model for asthma hospitalizations. The ideal validation of a model derived from one population is testing it in a totally independent population.⁸⁶ However, the bootstrapping validation technique used to validate the current models is considered an appropriate form of internal validation.⁸⁶ In addition, this study's use of jackknifed estimates of the performance of the predictive models is more conservative and better approximates its expected performance in an independent data set.⁸⁵

There are several strengths of the predictive performance of the current models. They identify less than 13% of the total population who will account for nearly 45% of the patients subsequently hospitalized. Compared with patients deemed to be at low risk, patients identified as being at high risk were approximately 6 times more likely to be hospitalized. However, the weakness of the models is their low positive predictive value—only 4% to 6% of patients identified as high risk are actually hospitalized in the subsequent year. This means that for every patient correctly identified, approximately 19 patients are incorrectly identified. This may still be clinically acceptable. For example, a relatively low cost intervention may be cost effective if it can prevent some hospitalizations in these high-risk patients. Moreover, the PPV of the current model could be substantially increased (to 14% to 19%) by restricting the population to those with prior hospital or ED utilization (Table 5). Furthermore, patients identified as high risk may be at risk of other morbidity not specifically assessed in this study, such as hospitalization beyond a year later, ED visits, missed work, or missed school. Indeed, analysis of the current data (not presented) shows that 13.6% of children assessed as being high risk visited the emergency department in 1999 (versus 5.3% of children not identified as high risk), and 15.6% of adults assessed as being high risk visited the emergency department in 1999 (versus 5.0% of adults not identified as high risk). Thus, intervention in a group of patients deemed to be at high risk by the current models may very well prove to be cost effective to prevent a wider variety of asthma morbidity.

One potential limitation in the current study is the possibility of missed hospitalizations of Kaiser Permanente members at non-Kaiser Permanente affiliated hospitals. However, this number should be very small and would probably have only a minor impact on the results. Secondly, although the models developed in this study may be more sensitive for use in a large managed

care organization population than any models developed to date, it would be expected that their performance could be improved by a number of modifications. As discussed previously, expressing medication use as number of canisters (or anti-leukotriene medication dispensings), weighted on the basis of number of doses per canister/dispensing and on the relative potency of each dose, would be expected to improve predictions based on use of inhaled β -agonists, prophylactic anti-inflammatory medications, or their ratio.

A third limitation is that assessment of race/ethnicity should improve the ability to predict asthma hospitalizations. In fact, many studies have suggested that African-American or Hispanic race/ethnicity substantially increase the risk of asthma hospital or ED utilization (Table 1). Moreover, some of these studies have found that this effect is independent of socioeconomic factors or access to care.^{34,43-45,51} Similarly, since many studies have suggested that lower socioeconomic status is correlated with increased asthma hospitalizations (Table 1), a more individual and robust measure of socioeconomic status than was used in this study would be expected to improve the performance of a predictive model. However, this information is not likely to be available in an administrative database or even from clinical data.

Finally, this study was not able to utilize clinical information, such as symptom intensity or pulmonary function, or environmental/social risk factors (Table 1) as potential predictors. Whether or not these characteristics would prove to be independent risk factors when the information taken into account in this study—especially if improved as above—is also considered requires further study. In addition, the value of obtaining this information would have to be balanced against the cost and difficulty of obtaining such data on a large scale.

Several other authors have attempted to develop prediction models for asthma hospitalizations using administrative data, and their results can be compared to the results of the current study (Table 6). Not included in this Table is the study of Li et al⁶³ that used clinical rather than administrative data and that of Lieu et al⁶⁴ that modeled either an asthma hospitalization or ED visit, which is both a more prevalent and more heterogeneous outcome than the asthma hospitalization outcome modeled in this study. In a large cross validation study, Grana et al⁷⁷ identified a high-risk population of 3.7% of the total population of 75 124 asthmatic patients who accounted for 30% of asthma hospitalizations the year following the prediction calculation. However, other parameters of the performance of their final risk stratification scheme (eg, sensitivity, positive predictive value) are not clearly defined in their report. Lieu et al²² developed 2 models for the prediction of

Table 6. Comparison of the Predictive Models Derived From Administrative Data

Authors	Population	% Hospitalized	% High Risk	% Sensitivity/ % Specificity	% PPV/% NPV
Grana et al ⁷⁷	75 124 adults and children	1.9%	4	30/—	—
Lieu et al ²² Model A	16 520 children	1.6%	1	10/99	19/99
Lieu et al ²² Model B	16 520 children	1.6%	7	32/94	7/99
Current study: children	4197 children	1.4%	11	44/90	5.6/99.1
Current study: adults	6904 adults	1.2%	13	45/87	3.9/99.3

NPV indicates negative predictive value; PPV, positive predictive value.

asthma hospitalizations in children using administrative data and a population similar to the current one. By means of recursive partitioning, she and her colleagues could develop a model with a higher positive predictive value but a much lower sensitivity than those of the models developed herein. Overall the sensitivities of the current models were substantially higher (44-45%) than those of the previously published models ($\leq 32\%$) or that which could be accomplished based on a prior asthma hospitalization alone ($< 10.5\%$).

The prediction rules developed in this study and the processes used for their development could be utilized in 2 specific ways for risk stratification in asthma population management. First, managed care organizations with similar populations and similar administrative data could directly use the regression equations and probability cut-offs developed herein to define high-risk asthmatic groups for targeted intervention. Second, the processes used in this study could be applied to other large asthmatic patient populations in which potential risk factors can be prospectively identified and outcomes tracked. By means of the logistic regression modeling technique, independent predictors in that population could be identified. Utilizing the regression equations in jackknifed samples, the most useful high-risk cut-offs could then be determined. Finally, the predictive performance of the derived prediction rules could then be externally or internally validated in that or a similar asthmatic population.

CONCLUSIONS

In summary, this study makes a number of important contributions to the literature. First, it shows that administrative data can be successfully used as measures of previously defined demographic and utilization risk factors. Second, it shows that some previously defined risk factors for asthma hospital utilization may be related to each other, while others are independent

of each other, which may have both pathophysiologic and measurement implications. Third, it shows that a previous hospitalization is the strongest independent predictor of a subsequent hospitalization in both children and adults with asthma. Finally, it demonstrates that the independent risk factor profile for children is different from that of adults.

Furthermore, the predictive models developed in this study have sufficient validity and predictive power to be potentially clinically useful. It is hoped that these models, or improvements on them, will be used in the future to identify high-risk patients for targeted intervention and that such intervention will lead to substantially reduced asthma morbidity.

Acknowledgments

This research was supported by the Southern California Permanente Medical Group. We would like to thank Aili Gong, MS, for providing the Excel data files from the mainframe databases; Janis Yao, MS, for converting the Excel files to SAS data files; Shimon Shaykevich, MS, for his help with the bootstrap validation; Gladys Tom, MS, and Michael Johnson, MS, for their helpful discussions regarding this project; John Williams, BA, Diana McRae, BA, and the staff of the San Diego Kaiser Computing and Telecommunication Services department for their information technology support; and Sheila Latus, MALS, Laurel Windrem, MLS, and the staff of the San Diego Kaiser Foundation Hospital Medical Library for their help with the references.

REFERENCES

1. National Asthma Education and Prevention Program Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma. National Heart, Lung and Blood Institute, NIH Publication Number 97-4051A, May 1997.
2. Smith DH, Malone DC, Lawson KA, et al. A national estimate of the economic costs of asthma. *Am J Resp Crit Care Med.* 1997;156:787-793.
3. Zeiger RS, Heller S, Mellon MH, et al. Facilitated referral to asthma specialist reduces relapses in asthma emergency room visits. *J Allergy Clin Immunol.* 1991;87:1160-1168.

4. Mahr TA, Evans R 3rd. Allergist influence on asthma care. *Ann Allergy*. 1993;71:115-120.
5. Storms B, Olden L, Nathan R, Bodman S. Effect of allergy specialist care on the quality of life in patients with asthma. *Ann Allergy Asthma Immunol*. 1995;75:491-494.
6. Westley CR, Spiecher B, Starr L, et al. Cost effectiveness of an allergy consultation in the management of asthma. *Allergy Asthma Proc*. 1997;18:15-18.
7. Vollmer WM, O'Hollaren M, Ettinger KM, et al. Specialty differences in the management of asthma. A cross-sectional assessment of allergists' patients and generalists' patients in a large HMO. *Arch Int Med*. 1997;157:1201-1208.
8. Taitel MS, Kotses H, Bernstein IL, Bernstein DI, Creer TL. A self-management program for adult asthma. Part II: cost benefit analysis. *J Allergy Clin Immunol*. 1995;95:672-676.
9. Lahdensuo A, Haahtela T, Herrala J, et al. Randomized comparison of cost effectiveness of guided self management and traditional treatment of asthma in Finland. *BMJ*. 1998;316:1138-1139.
10. Hughes DM, McLeod M, Garner B, Goldbloom RB. Controlled trial of a home and ambulatory program for asthmatic children. *Pediatrics*. 1991;87:54-61.
11. Mayo PH, Richman J, Harris HW. Results of a program to reduce admissions for adult asthma. *Ann Intern Med*. 1990;112:864-871.
12. Greineder DK, Loane KC, Parks P. A randomized controlled trial of a pediatric asthma outreach program. *J Allergy Clin Immunol*. 1999;103:436-440.
13. Wilson SR, Scamagas P, German DF, et al. A controlled trial of two forms of self-management education for adults with asthma. *Am J Med*. 1993;94:564-576.
14. Pauley TR, Magee MJ, Cury JD. Pharmacist-managed, physician-directed asthma management program reduces emergency department visits. *Ann Pharmacother*. 1995;29:5-9.
15. Greineder DK, Loane KC, Parls P. Reduction in resource utilization by an asthma outreach program. *Arch Pediatr Adolesc Med*. 1995;149:415-420.
16. Clark NM, Feldman CH, Evans D, et al. The impact of health education on frequency and cost of health care use by low-income children with asthma. *J Allergy Clin Immunol*. 1986;78:108-115.
17. Buchner DA, Butt LT, De Stefano A, et al. Effects of an asthma management program on the asthmatic member: Patient-centered results of a 2-year study in a managed care organization. *Am J Manag Care*. 1998;4:1288-1297.
18. Cote J, Bowie DM, Robichaud P, et al. Evaluation of two different educational interventions for adult patients consulting with an acute asthma exacerbation. *Am J Respir Crit Care Med*. 2001;163:1415-1419.
19. Harish Z, Bregante AC, Morgan C, et al. A comprehensive inner-city asthma program reduces hospital and emergency room utilization. *Ann Allergy Asthma Immunol*. 2001;86:185-189.
20. Kelly CS, Morrow AL, Shults J, et al. Outcomes evaluation of a comprehensive intervention program for asthmatic children enrolled in Medicaid. *Pediatrics*. 2000;105:1029-1035.
21. Claudio L, Tulton L, Doucette J, Landrigan PJ. Socioeconomic factors and asthma hospitalization rates in New York City. *J Asthma*. 1999;36:343-350.
22. Lieu TA, Quesenberry CP, Sorel, Mendoza GR, Leong AB. Computer-based models to identify high-risk children with asthma. *Am J Respir Crit Care Med*. 1998;157:1173-1180.
23. Tough SC, Hessel PA, Green FH, et al. Factors that influence emergency department visits for asthma. *Can Respir J*. 1999;6:429-435.
24. Gergen PJ, Weiss KB. Changing patterns of asthma hospitalization among children: 1979-1987. *JAMA*. 1990;264:1688-1692.
25. Gottlieb DJ, Beiser AS, O'Connor GT. Poverty, race, and medication use are correlates of asthma hospitalization rates: a small area analysis in Boston. *Chest*. 1995;108:28-35.
26. Lin S, Fitzgerald E, Hwang SA, Munsie JP, Stark A. Asthma hospitalization rates and socioeconomic status in New York State (1987-1993). *J Asthma*. 1999;36:239-251.
27. Asthma hospitalizations and readmissions among children and young adults—Wisconsin 1991-1995. *MMWR*. 1997;46:726-729.
28. Asthma mortality and hospitalization among children and young adults—United States 1980-1993. *MMWR*. 1996;45:350-353.
29. Mannino DM, Homa DM, Pertowski CA, et al. Surveillance for asthma—United States, 1960-1995. *MMWR*. 1998;47:1-27.
30. Sarpong SB, Karrison T. Sensitization to indoor allergens and the risk of asthma hospitalization in children. *Ann Allergy Asthma Immunol*. 1997;79:455-459.
31. To T, Dick P, Feldman W, Hernandez R. A cohort study on childhood asthma admissions and readmissions. *Pediatrics*. 1996;98:191-195.
32. Adams RJ, Fuhlbrigge A, Finkelstein JA, et al. Impact of inhaled anti-inflammatory therapy on hospitalization and emergency department visits for children with asthma. *Pediatrics*. 2001;107:706-711.
33. Laumann JM, Bjornson DC. Treatment of Medicaid patients with asthma: Comparison of treatment guidelines using disease-based drug utilization review methodology. *Ann Pharmacother*. 1998;32:1290-1294.
34. Joseph CL, Havstad SL, Ownby DR, Johnson CC, Tilley BC. Racial differences in emergency department use persist despite allergist visits and prescriptions filled for anti-inflammatory medications. *J Allergy Clin Immunol*. 1998;101:484-490.
35. Von Behren J, Kreutzer R, Smith D. Asthma hospitalization trends in California, 1983-1996. *J Asthma*. 1999;36:575-582.
36. Schaubel D, Johansen H, Mao Y, Dutta M, Manfreda J. Risk of preschool asthma: incidence, hospitalization, recurrence, and readmission probability. *J Asthma*. 1996;33:97-103.
37. Skobelloff EM, Spivey WH, St. Clair SS, Schoffstall JM. The influence of age and sex on asthma admissions. *JAMA*. 1992;268:3437-3440.
38. Awadh N, Chu S, Grunfeld A, Simpson K, FitzGerald JM. Comparison of males and females presenting with acute asthma to the emergency department. *Respir Med*. 1996;90:485-489.
39. Osborne ML, Vollmer WM, Linton KL, Buist AS. Characteristics of patients with asthma within a large HMO: A comparison by age and gender. *Am J Respir Crit Care Med*. 1998;157:123-128.
40. Prescott E, Lange P, Vestbo J. Effect of gender on hospital admissions for asthma and prevalence of self-reported asthma: a prospective study based on a sample of the general population. *Thorax*. 1997;52:287-289.
41. Singh AK, Cydulka RK, Stahmer SA, Woodruff PG, Camargo CA. Sex differences among adults presenting to the emergency department with acute asthma. *Arch Intern Med*. 1999;159:1237-1243.
42. Wilkins K, Mao Y. Trends in rates of admission to hospital and death from asthma among children and young adults in Canada during the 1980s. *CMAJ*. 1993;148:185-190.
43. Ray NF, Thamer M, Fadillioğlu B, Gergen PJ. Race, income, urbanicity, and asthma hospitalizations in California: a small area analysis. *Chest*. 1998;113:1277-1284.
44. Zoratti EM, Havstad S, Rodriguez J, Robens-Paradise Y, Lafata JE, McCarthy B. Health service use by African Americans and Caucasians with asthma in a managed care setting. *Am J Respir Crit Care Med*. 1998;158:371-377.
45. Carr W, Zeitel L, Weiss K. Variations in asthma hospitalizations and deaths in New York City. *Am J Public Health*. 1992;82:59-65.
46. Cassino C, Ito K, Bader I, Ciotoli C, Thurston G, Reibman J. Cigarette smoking and ozone-associated emergency department use for asthma by adults in New York City. *Am J Respir Crit Care Med*. 1999;159:1773-1779.

47. Miller JE. The effects of race/ethnicity and income on early childhood asthma prevalence and health care use. *Am J Public Health*. 2000;90:428-430.
48. Blixen CE, Havstad S, Tilley BC, Zoratti E. A comparison of asthma-related healthcare use between African-Americans and Caucasians belonging to a health maintenance organization (HMO). *J Asthma*. 1999;36:195-204.
49. De Palo VA, Mayo PH, Friedman P, Rosen MJ. Demographic influences on asthma hospital admission rates in New York City. *Chest*. 1994;106:447-451.
50. Wissow LS, Gittelsohn AM, Szklo M, Starfield B, Mussman M. Poverty, race, and hospitalization for childhood asthma. *Am J Public Health*. 1988;78:777-782.
51. Lozano P, Connell FA, Koepsell TD. Use of health services by African-American children with asthma on Medicaid. *JAMA*. 1995;274:469-473.
52. Lieu TA, Quesenberry CP, Capra AM, Sorel ME, Martin KE, Mendoza GR. Outpatient management practices associated with reduced risk of pediatric asthma hospitalization and emergency department visits. *Pediatrics*. 1997;100:334-341.
53. Rand CS, Butz AM, Kolodner K, Huss K, Eggleston P, Malveaux F. Emergency department visits by urban African American children with asthma. *J Allergy Clin Immunol*. 2000;105:83-90.
54. Finkelstein JA, Barton MB, Donahue JG, Algatt-Bergstrom P, Markson LE, Platt R. Comparing asthma care for Medicaid and non-Medicaid children in a health maintenance organization. *Arch Pediatr Adolesc Med*. 2000;154:563-568.
55. Watson JP, Cowen P, Lewis RA. The relationship between asthma admission rates, route of admission, and socioeconomic deprivation. *Eur Respir J*. 1996;9:2087-2093.
56. Bailey WC, Richards JM, Manzella BA, Brooks CM, Windsor RA, Soong SJ. Characteristics and correlates of asthma in a university clinic population. *Chest*. 1990;98:821-828.
57. Janson-Bjerkie S, Ferketich S, Benner P, Becker G. Clinical markers of asthma severity and risk: Importance of subjective as well as objective factors. *Heart Lung*. 1992;21:265-272.
58. Wakefield M, Ruffin R, Campbell D, Staugas R, Beilby J, McCaul K. A risk screening questionnaire for adult asthmatics to predict attendance at hospital emergency departments. *Chest*. 1997;112:1527-1533.
59. Bartlett SJ, Kolodner K, Butz AM, Eggleston P, Malveaux FJ, Rand CS. Maternal depressive symptoms and emergency department use among inner-city children with asthma. *Arch Pediatr Adolesc Med*. 2001;155:347-353.
60. Cowie RL, Underwood MF, Revitt SG, Field SK. Predicting emergency department utilization in adults with asthma: A cohort study. *J Asthma*. 2001;38:179-184.
61. Adams RJ, Smith BJ, Ruffin RE. Factors associated with hospital admissions and repeat emergency department visits for adults with asthma. *Thorax*. 2000;55:566-573.
62. Cowie RL, Revitt S, Underwood MF, Field SK. The effect of a peak flow-based action plan in the prevention of exacerbations of asthma. *Chest*. 1997;112:1534-1538.
63. Li D, German D, Lulla S, Thomas RG, Wilson SR. Prospective study of hospitalization for asthma: A preliminary risk factor model. *Am J Respir Crit Care Med*. 1995;151:647-655.
64. Lieu TA, Capra AM, Quesenberry CP, Mendoza GR, Mazar M. Computer-based models to identify high-risk adults with asthma: is the glass half empty or half full? *J Asthma*. 1999;36:359-370.
65. Taylor BW. The identification of high-risk asthmatic children using the emergency department asthma visit count. *J Emerg Med*. 1999;17:953-956.
66. Donahue JG, Weiss ST, Livingston JM, Goetsch MA, Greineder DK, Platt R. Inhaled steroids and the risk of hospitalization for asthma. *JAMA*. 1997;277:887-891.
67. Nestor A, Calhoun AC, Dickson M, Kalik CA. Cross-sectional analysis of the relationship between national guideline recommended asthma drug therapy and emergency/hospital use within a managed care population. *Ann Allergy Asthma Immunol*. 1998;81:327-330.
68. Anis AH, Lynd LD, Wang X-H, et al. Double trouble: impact of inappropriate use of asthma medication on the use of health care resources. *CMAJ*. 2001;164:625-631.
69. Balkrishnan R, Norwood GJ, Anderson A. Outcomes and cost benefits associated with the introduction of inhaled corticosteroids in a Medicaid population of asthmatic patients. *Clin Ther*. 1998;20:567-580.
70. Blais L, Ernst P, Boivin JF, Suissa S. Inhaled corticosteroids and the prevention of readmission to hospital for asthma. *Am J Respir Crit Care Med*. 1998;158:126-132.
71. Balkrishnan R, Christensen DB. Inhaled corticosteroid nonadherence and immediate avoidable medical events in older adults with chronic pulmonary ailments. *J Asthma*. 2000;37:511-517.
72. Frischer M, Heatlie H, Chapman S, Norwood J, Bashford J, Millson D. Should the corticosteroid to bronchodilator ratio be promoted as a quality prescribing marker? *Public Health*. 1999;113:247-250.
73. Osman LM, Friend JAR, Legge JS, Douglas JG. Requests for repeat medication prescriptions and frequency of acute episodes in asthma patients. *J Asthma*. 1999;36:449-457.
74. Leone FT, Grana JR, McDermott P, MacPherson S, Hanchak NA, Fish JE. Pharmaceutically-based severity stratification of an asthmatic population. *Respir Med*. 1999;93:788-793.
75. Wever-Hess J, Kouwenberg JM, Duiverman EJ, Hermans J, Wever AMJ. Risk factors for exacerbations and hospital admissions in asthma of early childhood. *Pediatr Pulmonol*. 2000;29:250-256.
76. Halfon N, Newacheck PW. Childhood asthma and poverty: Differential impacts and utilization of health services. *Pediatrics*. 1993;91:56-61.
77. Grana J, Preston S, McDermott PD, Hanchak NA. The use of administrative data to risk-stratify asthmatic patients. *Am J Med Qual*. 1997;12:113-119.
78. Castro M, Schechtman KB, Halstead J, Bloomberg G. Risk factors for asthma morbidity and mortality in a large metropolitan city. *J Asthma*. 2001;38:625-635.
79. Krishnan JA, Diette GB, Skinner EA, Clark BD, Steinwachs D, Wu AW. Race and sex differences in consistency of care with national asthma guidelines in managed care organizations. *Arch Intern Med*. 2001;161:1660-1668.
80. Crystal-Peters J, Neslusan C, Crown WH, Torres A. Treating allergic rhinitis in patients with comorbid asthma: the risk of asthma-related hospitalizations and emergency department visits. *J Allergy Clin Immunol*. 2002;109:57-62.
81. Magadle R, Berar-Yanay N, Weiner P. The risk of hospitalization and near-fatal and fatal asthma in relation to the perception of dyspnea. *Chest*. 2002;121:329-333.
82. Kao C-C, See L-C, Yan D-C, Ou L-S, Huang J-L. Time trends and seasonal variation in hospital admissions for childhood asthma in Taiwan from 1990 to 1998. *Asian Pac J Allergy Immunol*. 2001;19:63-68.
83. Eisner MD, Katz PP, Yelin EH, Shiboski SC, Blanc PD. Risk factors for hospitalization among adults with asthma: the influence of sociodemographic factors and asthma severity. *Respir Res*. 2001;2:53-60.
84. Toren K, Brisman J, Jarvholm B. Asthma and asthma-like symptoms in adults assessed by questionnaires: A literature review. *Chest*. 1993;104:600-608.
85. SAS Institute, Inc: Logistic regression examples using the SAS system, Version 6, First edition, Cary NC, 1995.
86. Altman DG, Royston P. What do we mean by validating a prognostic model? *Statist Med*. 2000;19:453-473.