Evidence Table 1. Assessment and Monitoring: Predictors of Exacerbation

Abbreviations used in table:

AAI	**acute asthma index**
AQLQ	**Asthma-Related Quality of Life Questionnaire**
AR	**allergic rhinitis**
AHR	**airway hyperresponsiveness**
BTS	**British Thoracic Society**
CAS	**Clinical Asthma Score**
CI	**confidence interval**
COPD	**chronic obstructive pulmonary disease**
ED	**emergency department**
FEV_1	**forced expiratory volume in 1 sec**
FVC	**forced vital capacity**
IBA	**inhaled beta-agonist**
ICS	**inhaled corticosteroid**
ICU	**intensive care unit**
IDR	**incidence density ratio**
LA	**long acting**
OCS	**oral corticosteroid**
OR	**odds ratio**
NAG	**National Asthma Guidelines**
PEF	**peak expiratory flow**
PASS	**Asthma Severity Score**
PEFR	**PEF rate**
PL	**placebo**
ROC	**receiver operating characteristics**
RR	**relative risk**
SA	**short acting**
TRUST	**The Regular Use of Salbutamol Trial**

Evidence Table 1. Assessment and Monitoring: Predictors of Exacerbation

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Connolly et al. The Darlington and Northallerton Prospective Asthma Study: best function predicts mortality during the first 10 years. Respir Med 1998;92(11): 1274–1280. (National Asthma Campaign, United Kingdom; Breathe North, GlaxoWellcome)	Prospective 10-year followup study (hospital and private clinics)	To follow mortality, change in best function, and treatment necessary to maintain optimal control, in the light of the socio-demographic variables and pulmonary function	628	**Age** >18 yr, mean = 51.7 yr **Gender** 49.4% male, 50.6% female **Smoking** 15.6% current smokers, 38.2% exsmokers, 46.2% nonsmokers	Persons with asthma referred to secondary care Mean duration = 19.5 yr FEV_1 mean = 2.07 L PEF ≥15% reversibility to ≥200 L/min PEF mean = 318 L/min Median best function approximately 80% predicted for vital capacity and peak flow Treatment: 22.8% on bronchodilators alone, 7.7% on cromoglycate, 48.8% on ICS, and 20.5% on oral corticosteroids (OCS)	Study began in 1983 with review and new entry at 5-year intervals.		Standardized Mortality Ratio 1.47 (95% CI 1.20 to 1.71). Observed proportion of respiratory deaths was 56% (expected 10%). Adjusting for age and gender, OR for dying was 1.51 (95% CI 1.33–1.72) for each 10% deficit in FVC. There was no difference between smokers and nonsmokers. Those in worst quartile of FVC were 5.5 times more likely to die than those in the best quartile, but pattern varied with age. Adjusting for age and gender, first quartile FVC OR=1.80, second quartile OR 1.98, fourth quartile OR 1.18. Best FVC was a strong predictor of mortality in subjects <65 yr at entry.	

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Lieu et al. Computer-based models to identify high-risk children with asthma. Am J Respir Crit Care Med 1998;157(4 Pt 1): 1173–1180. (Kaiser Permanente Innovation Program)	Retrospective cohort design (computerized database from a regional health maintenance organization)	(1) To develop and validate prediction models that use computerized data to identify children at high risk for asthma-related hospitalization or ED visits and (2) to evaluate the projected cost-effectiveness of a hypothetical asthma-management program with these models	16,520 (14,963 person-years of followup)	**Age** 0–14 yr, median 7 yr **Gender** 61% male, 39% female 88% with outpatient copayment $0–5; 81% with medication copayment $0–5	All with asthma-related health services utilization 3% had been hospitalized and 10% had ED visits in 12 months before start of followup period 22% had ≥3 prescriptions filled for beta-agonists, 20% received cromolyn, 9% received ICS, and 26% received OCS	Used split-sample validation with receiver operating characteristics (ROC) curves to validate the proportional hazards models.	Age (RR=0.90), having a personal physician listed (RR=0.64), number of prior hospitalizations (RR=1.74), number of prior ED visits (RR=1.50), number of different physicians prescribing asthma medications (RR=1.19), obtaining oral steroids (RR=1.88), and obtaining ≥3 units of beta-agonists (RR=1.53) were predictive of subsequent hospitalization. Classification tree identified hospitalization during prior 6 months and obtaining >6 units of beta-agonists (sensitivity of model = 32±8%; specificity 94±0.5%). Number of ED visits (RR=2.14), number of different physicians prescribing asthma medications (RR=1.31), ≥3 units of beta-agonists (RR=1.46), receiving oral steroids (RR=1.28), number of cromolyn units (RR=0.86), outpatient visit copayment (RR=0.96), and medication copayment (RR=1.01) were associated with subsequent ED visits. Classification tree identified ED visit during prior 6 months and ≥3 physicians prescribing asthma medications during prior 6 months as predictive of subsequent ED visits (sensitivity 48±5%, specificity 82±0.9%).		In 1995, the average cost of a hospital day was approximately $1,200; the average cost of an ED visit was $230. Using the most inclusive prediction criteria to select hypothetical patients for intervention, 3 hospital days and 27 ED visits could be prevented at a net cost to the health plan of $46,000 and net cost to society of $21,000.

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Rodrigo & Rodrigo. Early prediction of poor response in acute asthma patients in the emergency department. Chest 1998;114(4): 1016–1021.	Prospective predictive study plus validation sample (tertiary care hospital)	To develop an acute asthma index (AAI) for early differentiation between patients with poor and good therapeutic response in the ED setting Poor response defined as FEV_1 ≤45% of predicted after 3 hours of treatment Items on AAI: PEF at 30 minutes (0 if ≥50, 1 if 40–49, 2 if <40) and change in PEF from baseline at 30 minutes (0 if ≥90, 1 if 60–89, 2 if <60)	145 + validation sample of 77	(original sample) **Age** ≥18 yr, mean = 33.7 yr **Gender** 33.7% male, 66.3% female **Ethnicity** Not reported	(original sample) Severely asthmatic FEV_1 mean = 0.73 L FEV_1 % pred. mean = 23.6 PEF mean 128.2 L/min PEF % pred. mean = 27.7 Heart rate, mean 105.4 beats/min Respiratory rate, mean = 21.4 breaths/min Duration of attack, mean = 24.3 h	After initial assessment, patients were treated with salbutamol, 4 puffs at 10-minute intervals for 3 hours. Then, all with poor response received 500 mg IV hydrocortisone. Each received O_2 through nasal prongs at a rate of 4 L/min.	Thirteen (26.5%) with a score of 4 were admitted vs. 6.2% with a score of <4 (p=.012).		A score of 4 on the AAI has sensitivity 0.79, specificity 0.96, area under the ROC curve 0.87, positive predictive value 0.94, negative predictive value 0.86, OR 99.6 (95% CI 25.1–541.0). In the validation sample, sensitivity was 0.80, specificity 0.88, positive predictive value 0.85, negative predictive value 0.84, and area under ROC curve 0.89. Of the original sample, 64.8% had a score of <4 and 35.2% had a score of 4.
Adams et al. Factors associated with hospital admissions and repeat emergency department visits for adults with asthma. Thorax 2000;55(7):566–573. (University of Adelaide, The Queen Elizabeth Hospital Research Foundation)	Longitudinal observational design	To investigate what factors measured at baseline were associated with future hospital admissions and ED visits for asthma over a 12-month period	293 (212)	**Age** 41% 15–34 yr, 14% 35–44 yr, 15% 45–54 yr, 17% 55–64 yr, 13% 65 yr or older; mean age = 42 yr **Gender** 33% male, 67% female **Education** 46% ≤10 yr, 26% >10 yr, 28% some postschool **Smoking** 18% current smokers	42% moderate, 58% severe (NAEPP criteria) FEV_1 % pred. 30% <60%, 40% 60%–80%, 30% ≥80% ICS use, 80%; regular OCS use, 40%; long-acting beta-agonist use, 18%; other asthma medications, 44% Written asthma action plan, 55% yes		39% admitted to hospital; 58% had ED visits. Adjusting for age, gender, education, income, and employment, OR (95% CI) for admission over next 12 months were moderate severity, OR=0.6 (0.2–0.9); no admission in past 12 months, OR=0.1 (0.01–0.2); no written asthma action plan, OR=4.0 (1.5–10.7); less use of avoidance coping, OR=0.4 (0.3–0.7); lower preference for autonomy in management decisions, OR=1.4 (0.96–2.0). Adjusted OR (95% CI) for repeated ED visits were admission in past year, OR=2.9 (1.8–4.8); moderate severity, OR=0.3 (0.1–0.8); regular use of OCS, OR=10.0 (3.1–32.4); no written asthma action plan, OR=2.2 (1.1–5.6); and less dislike of asthma medication, OR=0.7 (0.5–0.9).		

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Black et al. Sensitivity to fungal allergens is a risk factor for life-threatening asthma. Allergy 2000;55(5):501–504.	Retrospective case control	To study the relationship between skin tests for fungal spores and admission to an intensive care unit (ICU) for asthma	137	**Age** 18–50 yr, mean = 34.7 yr **Gender** 31.4% male, 68.6% female	Community group: Never admitted to hospital because of asthma and never required nebulized bronchodilators Hospital group: admitted with acute exacerbation or treated with nebulized bronchodilators Intensive care: admitted to ICU with acute, severe attack of asthma	Community sample (n=50) from disease registers of 4 general practitioners Hospital sample (n=50) and ICU sample (n=37) from 1 hospital			54% of ICU subjects vs. 30% of community and hospital groups were skin-test-positive for 1 or more of the fungal allergens (p=0.005). 59.5% of ICU patients were skin-test-positive for grass mix vs. 76% in hospital and 72% in community group (p>0.05). 51.4% of ICU patients responded to cat dander vs. 58% of community and 62% of hospital subjects (p>0.05). No difference in mean wheal diameter for any of the allergens.
Hoskins et al. Risk factors and costs associated with an asthma attack. Thorax 2000;55(1):19–24. (AstraZeneca Pharmaceutical)	Retrospective cohort design (393 practices in the United Kingdom)	To identify the health service utilization patterns of a representative sample of U.K. patients with asthma observed over a 12-month period	12,203	**Age** 5% <5 yr, 28% 5–15 yr, 35% 16–44 yr, 28% 45–74 yr, 4% ≥75 yr **Gender** 50% male, 50% female	74% on step 2 or above of the British Thoracic Society (BTS) asthma guidelines 22% had at least 1 asthma attack during the year of data collection 16% had poor compliance with medication 9% had poor inhaler technique			For those patients who were younger than 5 years of age and those 75 years of age and older, there were no factors associated with incidence of attack, but group sizes were small. For other age groups, there was a strong association between attack incidence and each of BTS treatment steps and nighttime symptoms. Significant risk factors were exercise-induced symptoms in the 5–15 age group and poor inhaler technique for those 16–44 years old. 22% of patients in the attack group accounted for about 50% of total resource use costs. Average total costs per patient were 3.5 times higher (95% CI 3.2–3.87) in the attack group than in the nonattack group.	

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Cowie et al. Predicting emergency department utilization in adults with asthma; a cohort study. Journal of Asthma 2001;38(2):179–184. (Alberta, Canada, Lung Association)	Prospective cohort study	To determine whether any initial characteristics might predict subsequent visits for treatment of asthma in an ED	378 (378)	**Age** 16–85 yr, mean = 40 yr **Gender** 38% male, 62% female **Smoking** 11% current smokers 22% smoker in household **Animals** 48% animal in home	Duration of asthma, range 1–69 yr, mean = 16 yr FEV_1 % pred., mean = 79% Beta-agonist use, 79%; mean = 4.8 doses/day Waking at night with asthma, 38%	Consecutive sample of individual attending an asthma clinic and education program. Cohorts were formed on the basis of emergency treatment in following 1 year (19.3% yes, 80.7% no).	Factors associated with ED treatment were previous ED visits (OR=2.6, 95% CI 1.61–4.07), previous hospital admission for asthma (OR=2.4, 95% CI 1.61–3.58), initial lifestyle restriction index >3 out of 10 (OR=3.5, 95% CI 1.86–6.59), waking at night (OR=2.0, 95% CI 1.31–3.19), and using $\geq$1 dose $beta_2$-agonist per day (OR=2.2, 95% CI 1.11–4.43). In multivariate logistic regression, lifestyle restriction score of $\geq$4 (p=0.0001) and previous admission to hospital for asthma (p=0.001) were significant factors.		
Eisner et al. Beta agonists, inhaled steroids, and the risk of intensive care unit admission for asthma. Eur Respir J 2001;17(2): 233–240. (National Research Service Award and NHLBI, NIH)	Retrospective cohort design (Northern California Kaiser Permanente)	To examine the impact of ICS and inhaled beta-agonist (IBA) on the risk of ICU admission, a surrogate for life-threatening asthma exacerbation	2,344	**Age** >18 yr, mean = 55.5 yr **Gender** 31% male, 69% female **Ethnicity** 67% White	All hospitalized for asthma	Examined medications dispensed during the 3 months prior to index hospitalization.	12.2% (11.8–14.6%) were admitted to the ICU. (OR adjusted for systemic corticosteroid use, other asthma medications, and demographic characteristics) Compared to no IBA dispensing, high-level ($\geq$4 units) IBA therapy was associated with increased risk of ICU admission, OR=1.4 (95% CI 1.0–2.0). Both medium- (2–3 units) and high-level IBA were associated with risk of intubation, OR=1.6 (95% CI 1.0–2.7) and 1.9 (95% CI 1.2–3.1), respectively. Compared to no ICS dispensing, high-level ICS dispensing ($\geq$4 units) was associated with a decreased risk of ICU admission, OR=0.7 (95% CI 0.4–0.96). Among ICS nonusers, high-level IBA use increased risk of ICU admission, OR=1.6 (95% CI 1.02–2.4). No association between IBA use and ICU admission among ICS users.		

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Eisner et al. Risk factors for hospitalization among adults with asthma: the influence of sociodemographic factors and asthma severity. Respir Res 2001;2(1):53–60. (NHLBI; National Institute for Occupational Safety and Health, Centers for Disease Control; and National Research Service Award)	Prospective longitudinal cohort study (allergy and pulmonary physician practices in Northern California)	To evaluate the effects of gender, race, income, and asthma severity on hospitalization, independent of health care access	242	**Age** 18–50 yr, mean = 40.5 yr **Gender** 27% male, 73% female **Ethnicity** 71% White, 29% non-White **Smoking** 7% current smokers, 36% exsmokers, 57% nonsmokers	48% childhood onset 82% atopic history 25% hospitalization during 12 months prior to baseline or 18 months prior to 18-month followup interview SF-36 Physical component score, mean = 43.1; Mental component score mean = 44.3		16% had at least 1 hospitalization for asthma during the prospective 18-month followup period. Factors associated with hospitalization controlling for asthma severity were non-White race (OR 3.1, 95% CI 1.1–8.8), current smoking (OR 1.4, 95% CI 0.2–7.9), past smoking (OR 0.7, 95% CI 0.2–2.0), severity of asthma score (OR 3.4 per 5 points, 95% CI 1.7–6.8), recent asthma hospitalization (OR 8.3, 95% CI 2.1–33.4), and reliance on ED for urgent care (OR 3.2, 95% CI 1.0–9.8) based on multivariate analysis.		
Ford et al. Patterns and predictors of asthma-related emergency department use in Harlem. Chest 2001;120(4): 1129–1135. (NHLBI, NIH)	Cross-sectional survey (Harlem Hospital Center)	To assess criteria used to classify asthma severity and to test hypotheses that frequent ED use is associated with poor access to care, psychological risk factors, and asthma severity	375	**Age** Mean = 40 yr **Gender** 36% male, 64% female **Ethnicity** 93% Black or African American **Smoking** 46% current smokers, 15% exsmokers, 39% never smoked **Education** 59% ≥12 yr	Visited the emergency department (ED) for asthma 28% with comorbid bronchitis		In 12 months prior to interview, there were no differences between one-time and frequent ED users in age, gender, ethnicity, education, employment status, or annual household income. Persons with moderate or severe persistent asthma were more likely to be frequent ED users compared to those with mild asthma, OR=3.8 (95% CI 2.2–6.6). History of hospitalization for asthma, OR=2.5 (95% CI 1.2–5.5); ICU use, OR=10.0 (95% CI 1.3–72.7); and intubation, OR=4.4 (95% CI 1.3–14.6) were associated with frequent ED use. Controlling for asthma severity, having visited a doctor's office for asthma was associated with frequent ED use, OR=1.8 (95% CI 1.1–3.4).		Based on self-report, classification by the 3 NAEPP severity criteria for mild asthma converged for only 25% of the patients and classification by 2 criteria converged for 36% of patients. For moderate and severe persistent asthma, all 3 criteria converged for 38% of patients, and 2 criteria converged for 32% of patients.

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Fuhlbrigge et al. FEV(1) is associated with risk of asthma attacks in a pediatric population. J Allergy Clin Immunol 2001;107(1):61–67. (AstraZeneca Pharmaceutical and NHLBI, NIH)	Retrospective cohort design (6 U.S. cities)	To explore whether a relationship could be observed between FEV_1 and subsequent asthma attacks within a pediatric population	3,542 children; 31,075 observations	**Age** Mean = 13.0 yr (observations) **Gender** 51% male, 49% female (observations) **Ethnicity** 90.4% White (observations)	FEV_1 % pred (observations): 0.3% ≤60% 5.5% >60%–80% 50.9% >80%–100% 43.3% >100%	All first- and second-graders within 6 communities enrolled with other first-graders added until 1,500–2,000 children in each community. Children were followed for a maximum of 15 years. The sample in this study consisted of those observations for which a questionnaire could be paired with FEV_1 value. The questionnaire was completed by a parent/guardian for children up to grade 9 and in most cases by the child thereafter.		FEV_1 % was associated with risk of asthma attack during the year after its measurement with a progressive decrease, in the proportion reporting an attack in association with increasing FEV_1 %. Within parental report group (children up to grade 9), 60.4% of observations with FEV_1 % <60 reported attack compared with only 25.4% of observations with FEV_1 % >80. A similar pattern found for self-report group (73.9% vs. 29.4%). Adjusting for age, gender, previous attack, and smoking, FEV_1 % OR=2.1 (95% CI 1.3–3.4) and OR=1.4 (95% CI 1.2–1.7) for FEV_1 % <60% and 60%–80%, respectively, compared to >80% for younger group; for older group, OR were 5.3 (95% CI 2.2–12.9) and 1.4 (95% CI 1.2–1.7), respectively.	
Keogh et al. Predictors of hospitalization in children with acute asthma. J Pediatr 2001;139(2): 273–277.	Prospective cohort study (tertiary care university hospital)	To prospectively identify clinical predictors of the need for long duration of frequent bronchodilator therapy (i.e., hospitalization) in children ≥12 months of age presenting to the ED with an acute asthma exacerbation	278 (172)	**Age** ≥1 yr, mean = 4.9 yr **Gender** 66% male, 34% female **Ethnicity** Not reported	Diagnosis of asthma or bronchodilator use or first-time wheezing if >24 months of age 10% previous ICU admission 7.3% ≥3 admissions in year SaO_2 mean = 94.1% Clinical Asthma Score (CAS) median 6/9	Usual initial asthma therapy in ED is 3 doses of nebulized albuterol, 0.15 mg/kg, and ipratropium bromide, 250 mcg/dose. All also received oral prednisone, 2 mg/kg; oral dexamethasone, 0.3 mg/kg; or intravenous hydrocortisone, 5 mg/kg.	Five predictors of need for long duration of therapy: previous ICU admission (OR 7.2, 95% CI 1.85–27.7), baseline SaO_2 ≤92% (OR 2.57, 95% CI 0. 89–7.4), 4-hour SaO_2 ≤92% (OR 6.55, 95% CI 1.34–32.0), 4-hour CAS score ≥6/9 (OR 2.9, 95% CI 1.9–4.37), and 4-hour albuterol > every hour (OR 4.82, 95% 0.82–22.12) based on multivariate analysis. Presence of only 1 predictor associated with 40%–60% probability of long-term therapy and presence of ≥3 associated with ≥92% probability of long-term therapy. Of those with 4-hour SaO_2 ≤92%, 4-hour CAS score ≥6/9 and 4-hour albuterol > every hour, 97% required long-term therapy.		

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Leuppi et al. Predictive markers of asthma exacerbation during stepwise dose reduction of inhaled corticosteroids. Am J Respir Crit Care Med 2001;163(2): 406–412. (National Health and Medical Research Council, the Australian ARDS Association, and Rhone-Poulenc Rorer, Australia)	Prospective design	To identify predictors for failure of ICS dose reduction with loss of control	50	**Age** 18–69 yr, mean = 43.7 yr **Gender** 48% male, 52% female **Smoking** 28% exsmokers	8% severe, 22% moderate, 70% mild Duration of asthma 2.5–60 yr, mean = 24.2 yr Mean duration of ICS use = 6.2 yr ICS drug: 31% fluticasone, 51% budesonide, 18% beclomethasone Mean ICS dose = 1,344 mcg beclomethasone equivalent 30% had airway hyperresponsiveness (AHR) to histamine, 48% to mannitol, and 26% to both in run-in period.	4-week run-in phase (baseline) and a dose-reduction phase in which current ICS dose was halved every 8 weeks until the patient suffered an asthma exacerbation or was weaned off ICS for 8 weeks. ICS treatment was stopped after a dose of 200 mcg of budesonide or beclomethasone or 125 mcg of fluticasone was achieved.		78% suffered exacerbation of asthma—26% after first ICS dose reduction, 38% after second ICS reduction, 10% after third reduction, and 4% after fourth reduction.	Being hyperresponsive to both direct (histamine) and indirect (mannitol) challenge test at baseline was a significant predictor for failure at or before the second ICS reduction, OR=4.38 (95% CI 1.03–18.56). Age older than 40 years was borderline (p=0.059). Sputum eosinophils, eNO and PEF lowest percentage best were not significant. Survival analysis indicated hyperresponsiveness to mannitol was a predictor for failure of ICS reduction. Failure was not predicted by FEV_1 % predicted, PEF % predicted, or eNO.
Lovis et al. Elevation of creatine kinase in acute severe asthma is not of cardiac origin. Intensive Care Med 2001;27(3): 528–533.	Prospective design	To evaluate whether the cause of the increase of plasma creatine kinase and creatine kinase MB isoenzyme in acute severe bronchial asthma is of cardiac origin, and to determine the utility of troponin measurement in those patients	15	**Age** 17–61 yr, mean = 36 yr **Gender** 60% male, 40% female **Smoking** 27% smokers	Acute severe bronchial asthma Admitted to ICU 53% had grade III asthma and 47% had grade IV FVC mean = 91% FEV_1 % pred, mean = 77%				Five of 15 patients had elevated plasma creatine kinase, 4 with an increase in creatine kinase MB isoenzyme fraction (mean = 22±6%). At admission to ICU, myoglobin and creatine kinase were correlated (r=0.76, p<0.001). No difference in clinical signs or symptoms, medical history, laboratory values or ECG in patients with or without creatine kinase elevation. Only arterial pH (7.41 vs. 7.31, p<0.001) and arterial PCO_2 (kPa) (5.29 vs. 6.41, p<0.006) differed significantly.
Crystal-Peters et al. Treating allergic rhinitis in patients with comorbid asthma: the risk of asthma-related hospitalizations and emergency department visits. J Allergy Clin Immunol 2002;109(1):57–62. (Integrated Therapeutics Groups, Inc., subsidiary of Schering Plough)	Retrospective cohort analysis using 1994–95 MarketScan claims data	To assess the relationship between prescription medication use for the treatment of allergic rhinitis (AR) and subsequent asthma-related ED visits and hospitalizations for patients with AR and comorbid asthma	4,944	**Age** 12–60 yr; 22.1% ages 12–20, 8.4% ages 21–30, 19.4% ages 31–40, 50.1% ages 41–60 **Gender** 36.1% male, 63.9% female	Diagnosed with both asthma and allergic rhinitis (AR) In prior year: ICS use, 46.6%; oral steroid use, 34.4%; theophylline use, 22.7% In prior year, 3.8% had asthma ED visit and 1.25% were hospitalized for asthma	Analysis variables constructed using the 1995 claims experience of patients included in the 1994 analytical sample. The study period was defined as time between January 1, 1995, and first asthma-related ED visit or hospitalization or December 31, 1995.	The incidence density ratio (IDR) for risk of asthma-related event for those treated with AR was 0.49 (p=0.001). Predictors of asthma hospitalization or ED visit were treatment for AR (IDR 0.53, p=0.0001), ≥7 beta-agonists (IDR 2.2, p=0.0001), ≥7 inhaled steroids (IRD 0.52, p=0.05), use of theophylline (IDR 1.88, p=0.0007), use of cromolyn (IDR 1.48, p=0.043), 1 ED visit (IDR 5.82, p=0.0001), ≥2 ED visits (IDR 7.76, p=0.0001), and ≥1 inpatient stay (IDR 4.14, p=0.0001) based on multivariate Poisson regression.		

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Diette et al. Asthma in older patients: factors associated with hospitalization. Arch Intern Med 2002;162(10): 1123–1132. (Managed Health Care Association, Washington, DC)	Prospective cohort design (15 managed care organizations)	To determine whether quality of care was less favorable for older adults and whether patient characteristics such as symptom severity and comorbid illness explain the different age-related rates of hospitalization in patients enrolled in managed care	6,590 at baseline; 4,870 at 1 year	**Age** 27% 18–34 yr, 65% 35–64 yr, 8% 65 yr or older **Gender** 48% male, 52% female **Ethnicity** 82% White, 11% Black, 7% other **Smoking** 45% ever smoked	46% sinusitis; 26% chronic bronchitis; 5% emphysema; 79% allergy or hay fever	Multiple conditional imputations used for missing data	Older patients were more likely to be hospitalized during followup year than were younger patients (14% vs. 7%, p<0.001). Being female OR=1.8 (95% CI 1.3–2.4); Black OR=1.8 (95% CI 1.3–2.4) or other nonwhite OR=2.0 (95% CI 1.2–3.3); less educated, less physically healthy OR=0.99 (95% CI 0.98–0.99); and with more severe asthma symptoms OR=1.5 (95% CI 1.4–1.7) were associated with future hospitalization in multivariate analysis.		Older adults had higher asthma symptom score (2.9 vs. 2.7, p<0.001) and reported more concomitant lung conditions (p<0.001). Older patients were less likely to report difficulty reaching a physician by telephone (p<0.001), difficulty getting an appointment (p<0.001), or getting medications (p<0.001). Older patients were more likely to use medications including theophylline (51% vs. 32%), inhaled ipratropium bromide (22% vs. 6%), oral beta-agonists (37% vs. 23%), and OCS (37% vs. 15%) (all p<0.001). Older patients were more likely to report receiving information about severe flareup (61% vs. 49%, p<0.001), use peak flow meter daily (28% vs. 12%, p<0.001), and less likely to use asthma medications for worsening of symptoms.
Golan et al. Asthma in adventure travelers: a prospective study evaluating the occurrence and risk factors for acute exacerbations. Arch Intern Med 2002;162(21): 2421–2426.	Prospective study of travelers	To define the patterns of asthma during travel and to identify pretravel and intratravel risk factors for exacerbation	203	**Age** ≥18 yr, mean = 23.9 yr **Gender** 50% male, 50% female **Ethnicity** Not reported **Smoking** 32% current smokers	76% seasonal asthma 59% diagnosed before 10 years of age 83% used bronchodilators during previous year 9% had ED visits for asthma during previous year	Subjects visited a single travel clinic in Tel Aviv, Israel, for pretravel consultation.			43% had asthma attacks during travel with 5.4% reporting life-threatening attacks. Controlling for length of travel, inhaled bronchodilator use ≥3 times/week (RR 3.35, 95% CI 1.75–6.39) and participation in intensive physical exertion during treks (RR 2.04, 95% CI 1.04–3.98) were associated with asthma attacks during travel based on multivariate analysis. With both risk factors present, RR increased to 5.52 (95% CI 2.81–10.84).

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Goldman et al. Within- and between-day variability of respiratory impedance, using impulse oscillometry in adolescent asthmatics. Pediatr Pulmonol 2002;34(4):312–319. (NIH/NCRR/RCMI Clinical Research Infrastructure and Clinical Center of Research Excellence)	Clinical trial; testing of single group on 3 consecutive days	To assess the reproducibility of replicate spirometric indices and respiratory impedance with forced oscillation, using impulse oscillometry measures at a single sitting and serial data over 3 consecutive days, comparing inspiratory with expiratory R and X and to assess the effects of hand support of cheeks	24	**Age** 10–17 yr, mean = 12.7 yr **Gender** 50% male, 50% female	Varied from mild intermittent to severe persistent Stable drug regimen and well-controlled at time of testing FEV_1 1.3–5.4 L, mean = 2.89 L FEV_1 % pred 49–106, = mean 88.3 FVC 1.9–6.9 L, mean = 3.45 L FEV_1/FVC 55%–95%, mean = 83.1%	Testing occurred on 3 consecutive days 1–3 hours after morning medications; all subjects were bronchodilated at time of testing.			There was no difference in spirometric data from day to day (p>0.05). Significant differences from day-to-day in mean IOS R5 (p<0.03), R5–R15 (p<0.004), and AX (p<0.0001), but not in X5. Day-to-day differences in inspiratory R5 were significant (p<0.002), but those for expiratory R5 (p>0.07) were not. For those with asthmatic airflow obstruction, significant difference between inspiratory and expiratory R5 (0.46 and 0.53 kPa/Lps, respectively) averaging 3 consecutive days (p<0.0001).
Hartert et al. Risk factors for recurrent asthma: hospital visits and death among a population of indigent older adults with asthma. Ann Allergy Asthma Immunol 2002;89(5):467–473. (American Federation of Aging Research, Foundation for Fellows in Asthma Research, American Lung Association, Agency for Healthcare Research and Quality, and Geriatric Research Education and Clinical Center Department of Veterans Affairs)	Retrospective cohort analysis	To determine whether an initial hospital visit for asthma was associated with an increase in use of inhaled corticosteroids (ICS) at discharge and to identify risk factors for recurrent asthma hospital visits and death	510	**Age** 51% ages 65–74, 36% ages 75–84, 13% age ≥85 **Gender** 21% male, 79% female **Ethnicity** 73% White, 20% Black, 7% other/ unknown **Smoking** 17% current smoker, 60% noncurrent smoker, 24% unknown **Comorbidities** 56% chronic heart disease, 10% depression, 14% diabetes, 9% cancer, 50% hypertension	All required hospital care for asthma. 19% intermittent, 67% moderate-to-severe persistent, 14% near-fatal asthma None required asthma hospital visits during previous year. 62% with definite and 38% with probable asthma 53% of those with confirmed asthma also had recorded diagnosis of chronic obstructive pulmonary disease (COPD).	Cohort assembled from persons enrolled in Tennessee Medicaid program with discharge diagnosis of asthma in 1992 and no hospitalization or ED visit for asthma in the previous year. Subjects were followed to death, recurrent hospital visit for asthma, or 1 year.	23% had recurrent hospital visits for asthma during followup period (32% ED and 68% hospitalization). Mean time to recurrent visit = 115 days. Risk factors were disease severity (RR for moderate- to-severe 1.92, 95% CI 1.01–3.66; RR for near-fatal 2.28, 95% CI 1.01–5.13) and ICS use at time of discharge (RR 1.69, 95% CI 1.02–2.77).	12% died during followup; mean time to death = 161 days. Risk factors were disease severity (RR for moderate-to-severe 2.99, 95% CI 1.07–8.32; RR for near-fatal 4.44, 95% CI 1.34–14.69), male (RR 2.03, 95% CI 1.15–3.57), and cancer (RR 2.29, 95% CI 1.08–4.85).	

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Kelly et al. Patients with a longer duration of symptoms of acute asthma are more likely to require admission to hospital. Emerg Med (Fremantle) 2002;14(2):142–145. [Asthma Snapshot 2000 group)	Prospective observational design (20 EDs throughout Australia)	To determine whether, for patients with moderate or severe asthma presenting to EDs, there is a difference in need for hospitalization between those with duration of symptoms less than 6 hours and those with a longer duration of symptoms	381 (348)	**Age** 1–60 yr **Gender** Not reported	Moderate or severe (NAG)		Patients with duration of symptoms more than 6 hours were more likely to require hospital admission or transfer (57% vs. 26%, p<0.0001). Relative risk of hospital admission or transfer for patients with duration of symptoms of more than 6 hours compared with those less than 6 hours was 2.2 (95% CI 1.5–3.2).		
Weber et al. A prospective multicenter study of factors associated with hospital admission among adults with acute asthma. Am J Med 2002;113(5): 371–378. (MARC supported by National Institutes of Health, GlaxoWellcome Inc., and Monaghan Medical Corp, Syracuse, NY)	Secondary data analysis from 4 prospective cohort studies (64 EDs in 21 U.S. States and 4 Canadian provinces)	To determine which patient factors were associated with hospital admission among adults with asthma exacerbations who presented to the ED, and whether disposition followed consensus recommendations	1,805	**Age** ≥18 yr, mean = 35 yr **Gender** 35% male, 65% female **Ethnicity** 7.6% White, 62.5% Black, 26.9% Hispanic, 3.0% other **Smoking** 35% current smokers	Acute asthma 61% ever hospitalized for asthma 29% admitted for asthma in past year Systemic corticosteroids during past 4 weeks: 85% not on oral steroids, 6% on chronic steroids, 6% on short-course oral steroids Inhaled beta-agonists during past 4 weeks: 86% ICS during past 4 weeks: 44% Use of home nebulizer during past 4 week:, 29% Other asthma medications during past 4 weeks: 37%	Admissions included 307 admitted to inpatient units and 56 to observation units. Public hospitals accounted for 36% of the sites with the remaining private not-for-profit hospitals.	Overall admission rate was 20% with 49% for those with severe exacerbations, 23% for those with moderate exacerbations, and 8% for those with mild exacerbations. Female gender (OR 2.1), Black race (OR 2.0), use of home nebulizer (OR 2.7), recent chronic steroids (OR 2.2), recent short-course steroids (OR 2.5), initial respiratory rate (OR 1.3 per 5 breaths/min), initial PEF (OR 1.4 per 10% predicted increase), final PEF (OR 2.5 per 10% predicted decrease), and beta-agonist use in ED (OR 1.4) increased likelihood of admission. Area under the ROC curve was 0.91. Results were consistent among types and locations of hospitals.		Among patients discharged from the ED, 5% relapsed within 72 hours. Mean PEF was 79% predicted in those who relapsed vs. 76% in those who did not relapse (p=0.39).

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Wilson et al. A prospective evaluation of the 1-hour decision point for admission versus discharge in acute asthma. J Intensive Care Med 2003;18(5):275–285. (Program for Healthcare Innovation, U. of Massachusetts Medical Center)	Prospective preintervention and postintervention comparison	(1) To evaluate the 1-hour decision point for discharge or admission for acute asthma, (2) to compare this decision point to the admission recommendations of the Expert Panel Report–2 guidelines, and (3) to develop a model for predicting need for admission in acute asthma	50	**Age** 6–48 yr, mean = 24 yr **Gender** 38% male, 62% female **Smoking** 32% current smokers	Acute asthma Mean duration of asthma = 12 yr Regular outpatient monitoring of PEFR by 40% 4% with prior history of intubation for acute asthma	Patients were randomly assigned to receive albuterol either by metered-dose inhaler or by updraft nebulizer in a double-blind, placebo-controlled manner. Treatments were repeated every 20 minutes with a minimum of 3 and a maximum of 6 treatments.	22% were admitted to the hospital, 68% were discharged successfully to home from the ED, and 32% were discharged and relapsed. Patients successfully discharged differed only in FEV_1, accessory muscle use, and the ability to lie flat without dyspnea ($p<0.01$). Maximal accuracy of the admit versus discharge decision occurred at 1 hour of therapy based on FEV_1 plus ability to lie flat without dyspnea (sensitivity 97.1%, specificity 62.5%). Predictive index is based on points assigned to degree of airway obstruction and ability to lie flat without dyspnea. Mean area under the curve for 1,500 bootstrap samples was 0.86 (95% CI 0.804–0.916). The model developed performed better than EPR–2 guidelines ($p=0.0054$).		

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Belessis et al. Risk factors for an intensive care unit admission in children with asthma. Pediatr Pulmonol 2004;37(3):201–209. (Sydney, Australia, Children's Hospital Foundation Fellowship)	Case-control design	To investigate risk factors for acute severe asthma needing an ICU admission	141 (141)	**Age** Mean = 5.3 yr; 62% 1–4 yr, 24% 59 yr, 14% 10–15 yr **Gender** 80% male, 20% female **Ethnicity** 74% White 26% other **Other** 47% with bronchiolitis 12% born prematurely 55% breast-fed 6 months 19% mother smoked during pregnancy; 22% mother smoked after pregnancy 86% first-degree relatives with asthma, eczema, or hay fever	Oxygen saturation on presentation, mean = 92; 38% were ≤91% Median time from onset of asthma to receiving bronchodilator, 2 hours Median time from onset to visiting doctor, 10 hours Median time from onset to receiving oral steroid, 12 hours	Cases (n=70) were admitted to the ICU with acute severe asthma; controls (n=71) were admitted to a general medical ward with an acute asthma exacerbation. Cases and controls matched on ethnicity, medical insurance status, premorbid conditions, and prevalence of asthma, eczema, or hay fever in first-degree relatives.	Univariate predictors of ICU admission were lower oxygen saturation on presentation (90 vs. 94, p=0.001), frequent episodic/persistent asthma (p=0.01), multiple prior hospital admissions (p=0.01), admission to the general ward in the last year (p=0.003), ≥3 ED presentations in previous year (p=0.01), longer duration of asthma (p=0.010), maternal education (p=0.004), and IgE score (p=0.05). In multivariate analysis, predictors of admission were IgE level (OR 1.001, 95% CI 1.000–1.002), duration of asthma (OR 1.019, 95% CI 1.003–1.036), ≥3 ED presentations in previous year (OR 4.649, 95% CI 1.671–12.931), and oxygen saturation on presentation ≤91% (OR 9.005, 95% CI 2.077–39.042).		
Gorelick et al. Difficulty in obtaining peak expiratory flow measurements in children with acute asthma. Pediatr Emerg Care 2004;20(1):22–26. (Maternal and Child Health Bureau, Health Resources and Services Administration, U.S. Department of Health and Human Services)	Observational, prospective cohort study (2 EDs)	To evaluate the reliability, validity, and responsiveness of a new clinical asthma score, the Pediatric Asthma Severity Score (PASS) Three item PASS: wheezing, prolonged expiration, and work of breathing Two additional items: air entry and mental status	1,221 ED1, n=852 ED2, n=369	**Age** 1–18 yr, mean = 7.0 (ED1) and 5.9 (ED2) **Gender** 61% male, 39% female **Ethnicity** (ED1) 7.8% White, 89.9% African American, 0.8% Hispanic, 1.5% other (ED2) 23.3% White, 15.7% African American, 60.2% Hispanic, 0.8% other	(ED1) 66.5% mild intermittent, 17.5% mild persistent, 9.1% moderate persistent, 3.9% severe persistent (ED2) 49% mild intermittent, 26% mild persistent, 21% moderate persistent, 4% severe persistent Use of bronchodilators: 17% regular use and 83% use as needed	Children were treated for acute asthma in 2 urban, academic pediatric EDs. All received inhaled albuterol in the ED with a mean of 3.3 treatments/patient; 36% received at least 1 dose of inhaled ipratropium bromide, and 78% were given systemic corticosteroids.	32% at ED1 were admitted and 62% at ED2 were admitted.		Interobserver reliability was good to excellent (weighted kappa 0.79, 0.81, and 0.83 for three-, four-, and five-item score). Validity: Correlation of PASS with PEF from 0.22 to 0.42 and with pulse oximetry from 0.28 to 0.47. Discrimination between patients admitted and discharged and between those requiring and not requiring admission had c-statistics >0.8. Responsiveness: Ability of change in score to categorize patients by disposition had c-statistic of 0.79 for5items and 0.81 for 3 and 4 items.

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Kelly et al. Is severity assessment after one hour of treatment better for predicting the need for admission in acute asthma? Respir Med 2004;98(8):777–781. (Commonwealth Department of Health and Aged Care, Australia)	Prospective, observational study (36 EDs in Australia)	To determine if severity assessment after 1 hour of treatment is better than assessment at presentation for predicting the requirement for hospital admission for ED patients presenting with acute asthma	720	**Age** 1–55 yr, 62% under 16 yr **Gender** 56% male, 44% female **Ethnicity** Not reported	Acute asthma 60% mild, 36% moderate, 4% severe (NAG classification)		Less than 20% mild at either time were admitted. Initial assessment as moderate was poor predictor of need for admission (57% admitted, 43% discharged); 84% assessed as moderate at 1 hour required admission. More than 85% assessed as severe at either time required admission. Only 25% initially severe but 42% severe at 1 hour required ICU admission.		
Tierney et al. Assessing symptoms and peak expiratory flow rate as predictors of asthma exacerbations. J Gen Intern Med 2004;19(3):237–242. (Agency for Healthcare Research and Quality)	Analysis of data gathered as part of a randomized controlled trial of a pharmaceutical care intervention (36 commercial drug stores randomly assigned)	To investigate ability of peak expiratory flow rate (PEFR) and asthma-related quality of life questionnaire (AQLQ) scores to predict asthma-related ED visits and hospitalizations	660	**Age** >17 yr, mean = 45 yr **Gender** 18% male, 82% female **Ethnicity** 81% White, 17% Black, 2% other	Had prescription filled for a breathing medication in previous 3 months 3% had asthma-related ED or hospitalization in month prior to enrollment PEFR mean = 351 L/min % pred. PEFR 71 Overall mean Asthma Quality of Life Questionnaire mean item score = 4.4 out of 7.0			Neither PEFR nor predicted maximum PEFR were significant univariate predictors of exacerbations within either 4 months or 12 months of baseline. PEFR <50% was a significant predictor of exacerbations within 12 months of enrollment (p=0.027) in univariate, but not multivariate analysis. In multivariate analysis, lower overall score on AQLQ predicted exacerbation within 4 months (p=0.005) and 12 months (p<0.001). Exacerbation in months prior to enrollment was predictor of subsequent exacerbation within 4 months (p<0.001) and 12 months (p<0.001). Patient with overall AQLQ >5.0 was almost 3 times more likely to have exacerbation during the 12 months than a patient with a score of <4.0 (p<0.001).	

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Yurk et al. Predicting patient-reported asthma outcomes for adults in managed care. Am J Manag Care 2004;10(5):321–328. (Managed Health Care Association Outcomes Management System Asthma Project)	Prospective cohort design (16 managed care organizations in the United States)	To develop a brief set of patient-reported questions that could be used to predict a broad array of outcomes, including severe symptoms, reduced activities, ED use, and hospitalization	4,888 (10,539 in original study; study sample of 4,888 completed both baseline and 1-year questionnaires)	**Age** >17 yr, mean = 45 yr **Gender** 31% male, 69% female **Ethnicity** 83% White, 13% Black, 4% other **Smoking** 46% current or former smokers	Moderate-to-severe asthma 39% had hospitalization or ED visit in previous 2 years	Potential predictors were identified from the literature and clinical judgment: demographic characteristics, generic health status, asthma-specific health status, asthma treatment, asthma service use, and access to care. Outcome indicators were (1) hospitalization, (2) ED treatment, (3) reduced activities for ≥7 days due to asthma or missed work ≥5 days in past month and (4) ≥ five asthma attacks/week in past month or symptoms most of time between attacks.			Twenty-one items were retained in the final 5 risk models with between 4 and 11 predictors significant in various 1-year outcomes. Strongest predictors were comorbidity and prior ED use. Areas under the ROC curve ranged from 0.67 to 0.78 with no significant variation for sex, race, and education for those younger than 65 years of age. A scoring system to capture patient risk includes: non-White race, < college education, younger than 34 years of age or older than 65 years of age, female gender, history of myocardial infarction or emphysema or chronic bronchitis, history of ulcer or gastrointestinal bleeding, ED visit for asthma in past 12 months, physician visit within past 6 months, asthma affected activities in past 4 weeks, asthma attacks >1/week in past 4 weeks, symptoms some days between asthma attacks, self-rated general heath as poor or fair, and methylxanthine treatment in past 4 weeks.

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Dennis et al. Increase in daytime symptoms is a sensitive and specific criterion for predicting corticosteroid-treated exacerbations in a clinical asthma trial. Clin Exp Allergy 2005;35(3):308–312.	Secondary data analysis of diary card observations from a randomized controlled trial	To determine which diary card variables are the most predictive for administration of additional courses of corticosteroids using The Regular Use of Salbutamol Trial (TRUST) data set	983 patients and more than 200,000 days of diary card observations	**Age** Not reported **Gender** Not reported	Mild-to-moderate asthma	Patients were randomized to receive salbutamol or placebo and were followed for 12 months with an average followup of 8.5 months. Patients recorded morning and evening PEF, daytime and night-time symptoms, use of rescue inhaled beta$_2$-agonists, additional corticosteroid usage, visits to the doctor or hospital for asthma and days off work/school for asthma.		(OR adjusted for age, sex, inhaled steroid level, baseline values and accounted for clustering within patient.) Increase in daytime symptoms of 2 to 5 units over baseline associated with increase in odds of starting course of oral corticosteroids (OR 4.34 to 60.62) and increase of 1 to 5 units for inhaled corticosteroids (OR 2.52 to 26.1). Increase in night-time symptoms and increase in rescue beta$_2$-agonist use not associated with oral corticosteroid use. Increase in staring oral corticosteroids with fall in evening PEF of more than 20% vs. no change in PEF (OR 4.85, 95% CI 1.56–20.3, p<0.05) but no relationship to starting inhaled corticosteroids. No relationship to starting either oral or inhaled corticosteroids in response to fall of 20% or more in morning PEF.	

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Frey et al. Risk of severe asthma episodes predicted from fluctuation analysis of airway function. Nature 2005;438(7068): 667–670. (Swiss National Science Foundation and U.S. National Science Foundation)	Secondary time series analysis of peak expiratory flow data from a randomized, placebo-controlled, double-blind, crossover study	To examine whether the statistical and correlation properties of the time series of PEF recordings can be used to predict the risk of subsequent exaggeration of airway instability	165 (80)	**Age** 19–64 yr, mean = 42.4 yr **Other** Nonsmokers	Persistent asthma	Twice daily, PEFs were obtained in 3 t-month treatment periods comparing regular short-acting beta$_2$-agonist (albuterol 400 mcg 4 times daily; SA) and regular long-acting beta$_2$-agonist (salmeterol, 50 mcg twice daily; LA) with those of matching placebo (PL) period.			Time series of PEF show substantial fluctuations, especially in SA period. Compared with PL, the distribution of PEF in LA period shifts to higher values consistent with improved airway function. Means of individual PEF series averages are higher ($p<0.001$) in LA than either SA or PL period, and those in SA are higher than in PL period. Variability of PEF series is higher in SA than either LA or PL period ($p<0.005$) and lower in LA than in PL period ($p=0.001$). Detrended fluctuation function indicates SA fails to increase the mean PEF, increases variability of PEF, and alters correlations of PEF to become more random. Probability that moderate airflow obstruction occurs within 30 days decreases from almost 100% at initial PEF values <200 L/min to 10–30% for initial PEF values >550 L/min depending on treatment period. For any PEF, LA decreases the risk as compared with PL ($p<0.004$) and SA ($p<0.02$). Albuterol increases risk of future moderate or severe airflow obstruction beyond that with PL especially for near normal values of PEF.

Citation (Sponsor)	Study Design	Purpose/Objective	Study N (Number Evaluable)	Population Characteristics	Asthma Severity at Baseline (if reported)	Other	Admission/Emergency Department Visits	Exacerbation/Mortality	Other
Sturdy et al. Deaths certified as asthma and use of medical services: a national case-control study. Thorax 2005; 60(11):909–915. (National Research and Development Asthma Management Programme, United Kingdom; National Asthma Campaign, United Kingdom, through grant from GloxoSmithKline)	Case-control design	To examine the use of health services in previous 5 years of cases (asthma deaths) and controls	1,064 (1,064)	**Age** Median 53 yr **Gender** 38% male, 62% female **Other** 24% family history of asthma, 58% history of smoking, 44% major nonrespiratory illness	Cases identified as asthma deaths; controls had primary hospital discharge diagnosis of asthma	Cases identified as asthma death from death certificate; live hospital controls discharged with primary diagnosis of asthma matched on admission date (index date) and age selected from hospitals where asthma deaths occurred.			Length of time between last general practice contact and index data was 86.5 days for cases and 48.3 days for controls (p<0.001). Cases had significantly fewer general practice contacts (OR 0.90, 95% CI 0.84 to 0.98, p=0.009 per 5 contacts) and respiratory consultations (OR 0.85, 95% CI 0.75 to 0.96, p=0.006 per 5 consultations) in past year. Cases had more home visits in past year for respiratory illness (OR 1.12, 95% CI 1.04 to 1.20, p<0.001 per visit) and for nonrespiratory illness (OR 1.19, 95% CI 1.09 to 1.32, p<0.001 per visit). (Adjusted for gender and mutual adjustment) In the year before index data, 5 additional general practice contacts were associated with 18% lower risk of asthma death, an additional home visit with a 14% higher risk, and an additional PEF taken in last 3 months associated with 17% lower risk.
Boychuk et al. Correlation of initial emergency department pulse oximetry values in asthma severity classes (steps) with the risk of hospitalization. Am J Emerg Med 2006;24(1): 48–52. (The Robert Wood Johnson Foundation)	Multicenter prospective cohort study (6 emergency care centers, including tertiary care medical center, 2 general community hospitals, urgent care center, rural general hospital, rural clinic)	To determine whether the predictive value of pulse oximetry is enhanced by the stratification of the NIH severity class groups (steps)	706 encounters in Phase I; 513 encounters in Phase 2; total of 1,008 unique patients	**By encounters** **Age** 54% 1–3 yr, 37% 4–11 yr, 9% 12–17 yr; mean = 4.3 yr **Gender** 62% male, 38% female	(By encounters) Diagnosed with wheezing or bronchospasm Severity classification: 45% mild intermitted (step 1), 14% mild persistent (step 2), 18% moderate persistent (step 3), 23% severe-persistent (step 4) Disposition: 85% discharged home, 15% hospitalized In previous 4 months: 0.84 ED visits, 1.66 office visits In previous 12 months: 1.74 ED visits, 3.75 office visits Medication use before ED encounter: 64% beta agent, 11% as-needed controller medication, 13% daily controller medication	Phase I (12-month period) formed baseline study group; during phase 2 (10-month period) an active intervention consisted of an educational video to most participants while in ED and provided written asthma action plan specific for the severity classification (step) to “nearly all” patients discharged from ED.	From 95% to 100% oxygen saturation, hospitalization rates are similar between severity groups. In 93% to 94% oxygen saturation group, hospitalization rate is 43% in step 4 compared with 27%, 24%, and 13% for steps 1, 2, and 3, respectively, but differences are not significant. At values of 90% and below, hospitalization rates are higher, number of patients in each step category is smaller, and there is no significant difference between categories.		