

Subacute Lack of Asthma Control as a Predictor of Subsequent Acute Asthma Exacerbation in a Managed Care Population

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Objective: To evaluate whether an assessment of subacute lack of asthma control (SALAC) predicts subsequent acute asthma exacerbation (AAE).

Study Design: This retrospective administrative claims study used medical and pharmacy claims from the HealthCore Integrated Research Database to identify patients aged 6 to 64 years with asthma and having 3 years' continuous enrollment from January 1, 2003, through December 31, 2005.

Methods: Study inclusion criteria were at least 2 outpatient visits or at least 1 hospitalization or emergency department (ED) visit with an asthma diagnosis (*International Classification of Diseases, Ninth Revision, Clinical Modification* code 493.xx) in at least 1 of 3 years (2003-2005). SALAC was defined as more than 4 asthma outpatient visits or more than 5 short-acting β_2 -agonist (SABA) prescriptions per year, and AAE was defined as at least 1 hospitalization or ED visit with a primary asthma diagnosis or an oral corticosteroid burst prescription. Generalized estimating equations modeled the risk of subsequent-year AAE as a function of 2 sets of variables to determine the independent effect of prior-year SALAC and its components on subsequent-year AAE. The first set included age, sex, geographic region, prior-year AAE, and prior-year SALAC. The second set included age, sex, geographic region, prior-year AAE, high prior-year SABA use, and frequent prior-year asthma outpatient visits.

Results: Of 35,806 patients with asthma, 46.6% were male, and 35.8% were younger than 18 years. The mean annual prevalence of SALAC was 12.1%. Controlling for all other variables, the generalized estimating equation results indicate that prior-year SALAC is associated with a 60% increased risk of subsequent-year AAE ($P < .001$). Increased prior-year asthma outpatient visits and SABA use are associated with 34% and 85%, respectively, greater risks of subsequent-year AAE ($P < .001$ for both).

Conclusion: SALAC and its components can aid in predicting patients at risk for AAE.

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For author information and disclosures, see end of text.

Asthma, one of the most common chronic conditions in the United States, affected more than 22 million Americans (16 million adults) in 2005.¹ Approximately 77% of these patients have moderate-to-severe persistent disease.² Disease control is the primary goal of current management strategies and evidence-based consensus guidelines^{1,3} and has been differentiated from disease severity.⁴ Despite improved understanding of asthma pathogenesis, better disease management, and more widespread use of recommended therapies, asthma remains a frustrating disease for patients and healthcare providers because of the dynamic nature of the disease. For example, patients with asthma may experience variability in asthma control^{5,6} over time such that patients with asthma that is mild in severity⁷ or well controlled with therapy² may experience acute asthma exacerbation (AAE) requiring urgent medical care. Control is an issue that is relevant for all levels of asthma severity, but its measurement remains problematic. The wide range of estimates of the proportion of patients who are inadequately controlled (17%⁸ to 83%⁹) is primarily because of differing definitions of control.

The implications of poor asthma disease control are considerable. Approximately 4000 individuals die each year from asthma exacerbation.¹⁰ Uncontrolled disease results in a disproportionate use of emergency department (ED) and hospitalization resources^{8,9,11-13} and is a major component of the \$14.7 billion attributed to asthma costs in the United States in 2002.¹⁴ A recent study⁹ estimated that costs for uncontrolled patients were more than twice those for controlled patients and were significantly higher even among patients who were receiving maximum guideline-recommended pharmacotherapy.

As a result of the substantial clinical,¹⁵ economic,^{8,9} and humanistic^{9,16} consequences associated with poor asthma control, there is a need to discern valid predictive markers that may allow for early identification of the at-risk patient. However, predicting asthma symptom occurrence on a short-term basis is a well-recognized clinical challenge. Factors that have been found to be predictive of future severe acute asthma episodes, including hospitalization and death, are repeated hospitalizations or ED visits, frequent use of short-acting β_2 -agonist (SABA) medications, current use of or recent withdrawal from oral corticosteroid use, and prior recent severe asthma exacerbation.¹⁷⁻²⁸

While the existing literature about the prediction of patients prone to AAE provides essential insight into disease management,

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there are limitations to its usefulness within typical clinical practice. Health plans and clinicians are in need of disease control markers that are valid, simple, free from the potential biases associated with patient and physician assessments, and easily attainable in a usual care setting and within most typical administrative claims databases.

In a prior study,²⁹ the construct of subacute lack of asthma control (SALAC) was introduced as a means of easily identifying patients with uncontrolled asthma within a managed care database. In that study, SALAC was defined as more than 4 asthma outpatient visits per year, at least 2 asthma outpatient visits per quarter, or more than 5 SABA prescriptions per year. More than two-thirds of patients experienced SALAC at some point during the 4-year analysis, and SALAC occurred almost every year in about 20% of patients. Moreover, patients with SALAC had a higher rate of subsequent asthma exacerbation (63% excess clinic visits per year). The present study was designed to assess how well an administrative claims–derived measure of SALAC consisting of high prior-year SABA use and frequent prior-year asthma outpatient visits predicts subsequent-year AAE in a managed care population. The results may assist US health plans in gauging the burden of uncontrolled asthma among their patients with asthma and in identifying markers of uncontrolled asthma that predict AAE.

METHODS

Data Source

This retrospective, longitudinal, cohort study used medical and pharmacy claims from 3 managed care health plans contained in the HealthCore Integrated Research Database for healthcare services incurred during the 3-year period from January 1, 2003, through December 31, 2005. All study materials were handled in compliance with the Health Insurance Portability and Accountability Act of 1996, and a limited data set was used for the analyses.

Sample Selection Criteria

Patients aged 6 to 64 years with medical claims for at least 2 outpatient visits or at least 1 hospitalization or ED visit with a primary or secondary diagnosis code for asthma in at least 1 of 3 years (2003-2005) and with 3 years' continuous enrollment from January 1, 2003, through December 31, 2005, were identified. An asthma diagnosis was defined as *International Classification of Diseases, Ninth Revision, Clinical Modification*

Take-Away Points

Despite improved understanding of asthma pathogenesis, disease management, and use of recommended therapies, many patients have inadequately controlled asthma, resulting in increased health plan resource utilization and costs.

- This study uses administrative claims data to identify patients who have subacute lack of asthma control (SALAC), defined as more than 4 asthma outpatient visits or more than 5 short-acting β_2 -agonist prescriptions per year.
- Patients with SALAC have a 60% higher risk of subsequent-year acute asthma exacerbation than patients without SALAC.
- The use of SALAC may provide health plans with opportunities to improve members' asthma control and to reduce healthcare utilization associated with asthma exacerbation.

(ICD-9-CM) code 493.xx, and the initial year of observation (calendar year 2003) was defined as the baseline year for the purpose of describing patient demographic characteristics. Patients were excluded if they had at least 1 medical claim with a primary or secondary diagnosis code for cystic fibrosis (ICD-9-CM code 277.xx) or chronic obstructive pulmonary disease (ICD-9-CM codes 490.xx-492.xx or 496.xx) at any time during the study period.

Asthma Control Definitions

For the purpose of this study, asthma control was determined through the use of healthcare services identifying SALAC. SALAC was defined as more than 4 asthma outpatient visits or more than 5 SABA prescriptions per year.

Outcomes Assessment

Acute asthma exacerbation was defined as at least 1 hospitalization or ED visit with a primary asthma diagnosis or at least 1 oral corticosteroid burst prescription (<21 days' supply) per year. This definition is based on the National Asthma Education and Prevention Program Expert Panel Report 3 guidelines,¹ which classify severe exacerbation as that requiring hospitalization or ED visit or oral systemic corticosteroids. The proportion of patients with 1 or more asthma-related healthcare event was assessed for each year from 2003 through 2005. These events included AAE, SALAC, and its SALAC (ie, >4 asthma outpatient visits or >5 SABA prescriptions per year). The adjusted association between SALAC in the prior year with AAE in the subsequent year was assessed (ie, the association between the occurrence of SALAC in 2003 and the occurrence of AAE in 2004 and the occurrence of SALAC in 2004 and the occurrence of AAE in 2005 was determined). The adjusted association between increased prior-year asthma outpatient visits and SABA use and the occurrence of subsequent-year AAE was similarly determined.

Statistical Analysis

Descriptive statistics were used to describe the study population and the prevalence of asthma control indicators. A

■ **Table 1.** Baseline Characteristics of 35,806 Patients With Asthma

Characteristic	Value
Male sex, No. (%)	16,698 (46.6)
Age group in 2003, y, No. (%)	
6-11	6742 (18.8)
12-17	6100 (17.0)
18-24	1862 (5.2)
25-34	3641 (10.2)
35-44	6277 (17.5)
45-54	6968 (19.5)
55-64	4216 (11.8)
Age, mean (SD), y	31.6 (17.9)
Geographic region, No. (%)	
Midwest	2321 (6.5)
South	5678 (15.9)
West	27,807 (77.7)
Health plan type, No. (%)	
Health maintenance organization or point of service	7883 (22.0)
Preferred provider organization	26,136 (73.0)
Other, unknown, or missing	1787 (5.0)

generalized estimating equation (GEE) was used to model the risk of subsequent-year AAE as a function of prior-year SALAC, controlling for age, sex, geographic region, and prior-year AAE. A separate GEE model was developed to assess the risk of subsequent-year AAE as a function of high prior-year SABA use (>5 prescriptions per year) and frequent prior-year asthma outpatient visits (>4 visits per year). The binary dependent variable in each of the GEE models was the occurrence of AAE in 2004 and 2005. All statistical analyses were performed using SAS (version 9.1 for Windows; SAS Institute Inc, Cary, NC).

RESULTS

A total of 35,806 patients met the study criteria. As summarized in **Table 1**, 46.6% were male, the mean (SD) age was 31.6 (17.9) years, and 35.8% were younger than 18 years. Approximately three-fourths of the population were from the western United States. Preferred provider organizations were the dominant health plan type (73.0%).

Table 2 gives data on the number of patients with AAE and SALAC. From 2003 through 2005, the mean percentage of patients per year with at least 1 AAE was 21.2%; 18.8% had at least 1 oral corticosteroid burst prescription, 4.3% had at least 1 ED visit, and 1.2% had at least 1 hospitalization. For the same period, the mean percentage of patients with

SALAC having high SABA use was 5.7%, and 7.1% had frequent asthma outpatient visits. On average, 0.7% of patients had both increased SABA use and asthma outpatient visits, indicating that the 2 measures were virtually independent, and interaction between the 2 variables was not assessed. More than 12% of patients had SALAC during the 3-year study period. **Figure 1** shows the mean annual prevalence of SALAC and its components (high SABA use and frequent asthma outpatient visits) from 2003 through 2005.

Figure 2 shows the percentage of patients with at least 1 AAE in the year following assessment of SALAC, stratified by SALAC status. Compared with patients without SALAC or its components, significantly more patients with SALAC or its components experience at least 1 subsequent-year AAE.

A GEE model was used to assess the association between prior-year SALAC as measured by asthma-associated resource

use (ie, >4 asthma outpatient visits or >5 SABA prescriptions per year) and subsequent-year AAE (ie, 2003 compared with 2004 and 2004 compared with 2005). After controlling for covariates, patients with prior-year SALAC had a 60% higher risk of subsequent-year AAE (odds ratio [OR], 1.601; 95% confidence interval [CI], 1.514-1.692; $P < .001$) compared with patients without SALAC (**Table 3**). After controlling for covariates, patients having more than 4 asthma outpatient visits per year versus 4 or fewer had a 34% greater risk of subsequent-year AAE (OR, 1.340; 95% CI, 1.249-1.438; $P < .001$). Similarly, patients having more than 5 SABA prescriptions per year versus 5 or fewer had an 85% increased risk of subsequent-year AAE (OR, 1.854; 95% CI, 1.719-2.000; $P < .001$).

Regional differences were included in the model to adjust for the disproportionate representation of our patient sample from the western United States and was not meant to provide insight about the association between geographic region and AAE, as we had no prior hypothesis about this potential relationship. Therefore, the main independent covariates of interest (SALAC and its components) are not confounded (ie, remain statistically significant) by the disproportionate distribution of the patients in each of our geographic regions.

DISCUSSION

This analysis of a large demographically and geographi-

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Table 2. Findings Among 35,806 Patients With Acute Asthma Exacerbation (AAE) or Subacute Lack of Asthma Control (SALAC)

Patients With AAE, No. (%)				
Year	≥1 Hospitalization Per Year	≥1 Emergency Department Visit Per Year	≥1 Oral Corticosteroid Burst Prescription Per Year	≥1 AAE Per Year
2003	776 (2.2)	2894 (8.1)	8429 (23.5)	10,100 (28.2)
2004	299 (0.8)	835 (2.3)	5788 (16.2)	6261 (17.5)
2005	237 (0.7)	899 (2.5)	5997 (16.7)	6429 (18.0)
Mean	437 (1.2)	1543 (4.3)	6738 (18.8)	7597 (21.2)
Patients With SALAC, No. (%)				
Year	>5 SABA Prescriptions Per Year	>4 Asthma Outpatient Visits Per Year	>5 SABA Prescriptions and >4 Asthma Outpatient Visits Per Year	Prevalence of SALAC Per Year
2003	2240 (6.3)	3455 (9.6)	312 (0.9)	5383 (15.0)
2004	1983 (5.5)	2229 (6.2)	205 (0.6)	4007 (11.2)
2005	1940 (5.4)	1914 (5.3)	203 (0.6)	3651 (10.2)
Mean	2054 (5.7)	2533 (7.1)	240 (0.7)	4347 (12.1)

SABA indicates short-acting β_2 -agonist.

cally dispersed managed care population shows a mean annual prevalence from 2003 through 2005 of more than 12% of patients with SALAC. Based on GEE results and after controlling for covariates, patients with SALAC were 60% more likely to have subsequent-year AAE than patients without SALAC. Moreover, patients with versus without components of SALAC were 34% (for those with >4 asthma outpatient visits) and 85% (for those with >5 SABA prescriptions) more likely to have subsequent-year AAE. Although high SABA use was a significant predictor of AAE, the addition of asthma outpatient visits to the model demonstrated it to be an independently significant predictor of subsequent AAE. This suggests that SALAC may be a useful predictive measure for improving asthma control and for reducing healthcare utilization associated with asthma exacerbation.

Several studies report the disadvantages associated with patient-reported assessment of asthma control, including exacerbation^{26,30} and healthcare resource utilization,^{31,32} as well as physician and patient assessments of asthma severity.³³⁻³⁵ Our study used administrative claims data and, as such, was not subject to the potential biases associated with recall or subjective assessments of disease. Because SALAC consists of easy-to-monitor components (medical claims-coded asthma outpatient visits or SABA prescription claims) that are not biased by recall, clinicians and health plans can effectively identify these potentially at-risk patients for targeting with additional monitoring and resources. SALAC is a measure based on administrative health plan data that fulfills an un-

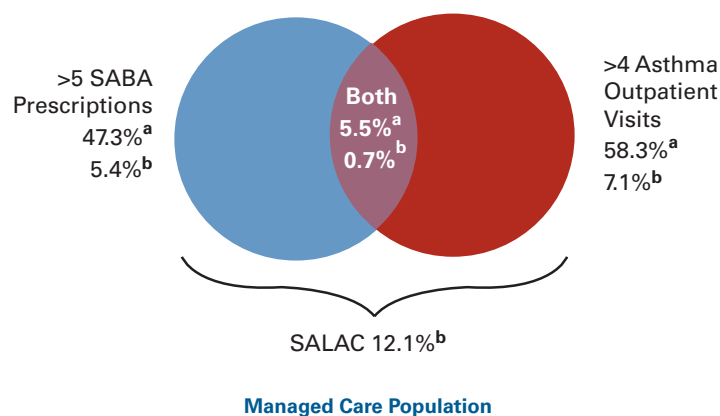
met need, as clinicians frequently fail to assess asthma control because of lack of patient inquiry or status documentation.^{36,37} Moreover, because SALAC predicts subsequent-year exacerbation, the near-term temporal prediction further simplifies its usefulness within a patient surveillance program.

Failure to adequately assess asthma control has led to treatment inconsistency, suboptimal clinical management, and high costs of disease. Our results and those of others³⁸⁻⁴² indicate that many patients with asthma are not meeting therapeutic goals because of poor disease management and variations in practice patterns, despite the availability of evidence-driven guidelines,^{1,3} numerous quality improvement initiatives,^{41,43} and effective asthma controller medications.¹ In the present study, more than 50% of patients did not fill a prescription for an asthma controller medication.

Uncontrolled asthma has significant economic consequences, especially when hospitalization is required.⁸ Our research suggests that patients with SALAC have significantly higher resource utilization associated with AAE.

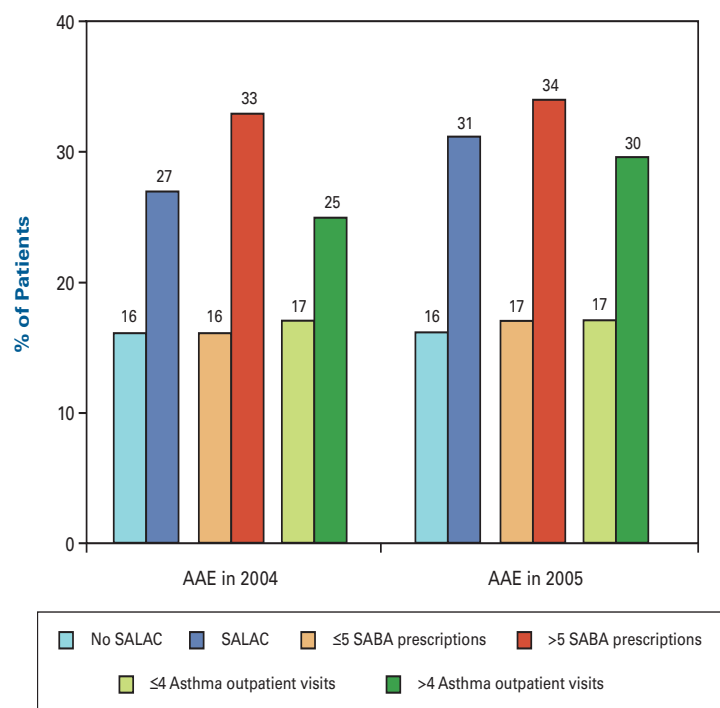
Studies^{11,12,44,45} show that disproportionately few patients are responsible for a large component of total asthma direct medical costs. Targeting these patients in the SALAC phase and returning them to disease stability may lead to reduced costs and resource utilization. The proportion of patients in the present study who in 2005 had at least 1 ED visit was 2.5%, and 0.7% had at least 1 hospitalization. Therefore, the implications of using SALAC for early identification of patients with uncontrolled asthma and potentially reducing

■ **Figure 1.** Mean Annual Prevalence of Subacute Lack of Asthma Control (SALAC) and Its Components Among 35,806 Patients From 2003 Through 2005



SABA indicates short-acting β_2 -agonist.
^aPercentage of patients with SALAC.
^bPercentage of total sample.

■ **Figure 2.** Percentage of Patients With at Least 1 Acute Asthma Exacerbation (AAE) by Subacute Lack of Asthma Control (SALAC) Status and Its Components



SABA indicates short-acting β_2 -agonist.

their healthcare costs are compelling but were not examined directly in this study. Future studies should go beyond the outcomes measures of this study and capture all asthma-related healthcare costs, including outpatient care and pharmacy costs.

The practical usefulness of SALAC may be contrasted with another predictive measure of asthma control, recent severe exacerbation, which has also been demonstrated to be a strong independent predictor of future severe exacerbation (OR, 6.33; 95% CI, 4.57-8.57).²⁶ In a study by Miller et al, recent severe asthma exacerbation was defined as an “asthma-related emergency department visit or night of hospitalization in the 3 months prior to study visit [during 18 months of follow-up].”^{26(p481)} SALAC provides the benefit of potential intervention before the patient experiences significant lack of disease control, has loss of health-related quality of life, or incurs substantial costs to the healthcare system.

The goal of asthma management is to achieve and maintain control of the disease without adverse effects from therapies,^{1,46} and the degree of asthma control has been recommended as a clinical outcomes measure for titrating anti-inflammatory pharmacotherapy.¹⁵ Health plans and clinicians should be made more aware of SALAC, as assessed by increased asthma outpatient visits and SABA use. Disease management programs should consider the inclusion of these outcomes assessments on a rolling quarterly and annual basis, and clinical responses should be developed that minimize the risk of AAE. Moreover, asthma treatment guidelines should consider these outcomes in the assessment of patients with asthma. Future research may include SALAC evaluation with asthma severity classification.

Although this study provides valuable insight into a new predictive measure of asthma control, there are limitations that warrant mention. The study design was nonrandomized; therefore, causality cannot be ascribed. Because the study design used administrative claims, the database did not contain data on many sociodemographic characteristics (eg, race/ethnicity, education, income) or other potentially relevant clinical variables (eg, smoking status). Because smoking status was indiscernible, the identification of patients having chronic obstructive pulmonary disease via the presence of diagnosis alone may lack sensitivity sufficient to fully exclude all patients with the disorder from this study. As with all retrospective analyses, coding accuracy is a potential limitation. The asthma-attributable resource use and the definition of SALAC are based on accurate diagnostic coding of asthma, and coding or other administrative

claims errors may affect the validity of our results.

The multivariate GEE model controlled for specific clinical and demographic covariates, and the results remained consistent; however, other patient, physician, and clinical characteristics such as asthma severity or absenteeism from work or school that were unavailable for analysis could have influenced the specific ORs. Further research exploring the use of SALAC to identify patients at high risk of exacerbation is warranted. The study sample was restricted to patients enrolled in managed care plans predominantly from the western and southeastern United States, which may limit the generalizability of our results. This population demographically matches populations evaluated in other large epidemiologic trials,^{17,29} which provides robustness to the conclusions and supports the generalizability of our results.

Although there is a lack of agreement about asthma severity criteria,^{3,33,47} the severity of the condition may have been an influential factor in predicting AAE, and this was not explicitly assessed within the construct of SALAC. However, other evidence suggests that asthma control (as measured by recent severe asthma exacerbation) is a better predictor of future asthma exacerbation than a composite measure of severity based on symptoms, lung function, and inhaler use.²⁶

In conclusion, this study demonstrates that prior-year SALAC and its components (high SABA use and frequent asthma outpatient visits) were associated with subsequent-year AAE. The use of SALAC may assist health plans in identifying opportunities to simultaneously improve members' asthma control and reduce healthcare utilization associated with asthma exacerbation.

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Table 3. Generalized Estimating Equation Models

Covariate	Odds Ratio (95% Confidence Interval) for Subsequent-Year AAE
Prior-Year SALAC Model	
Prior-year SALAC	1.601 (1.514-1.692)
Age	1.003 (1.002-1.004)
Male sex	0.910 (0.872-0.949)
Prior-year AAE	1.818 (1.773-1.864)
Geographic region	
South	1.752 (1.665-1.842)
Midwest	1.373 (1.269-1.484)
West	1 [Reference]
Prior-Year SABA Prescription and Asthma Outpatient Visit Model	
>5 SABA prescriptions	1.854 (1.719-2.000)
>4 Asthma outpatient visits	1.340 (1.249-1.438)
Age	1.003 (1.002-1.005)
Male sex	0.906 (0.869-0.945)
Prior-year AAE	1.814 (1.769-1.859)
Geographic region	
South	1.749 (1.662-1.841)
Midwest	1.378 (1.271-1.494)
West	1 [Reference]
AAE indicates acute asthma exacerbation; SABA, short-acting β_2 -agonist; SALAC, subacute lack of asthma control.	

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