Evaluating Asthma Medication Use Before and After an Acute Asthma-related Event

by Jung H. Lee, Sandra D. Cassard, Peter E. Dans, Clare Wheelock, and Joseph D. Ober

Asthma is a chronic inflammatory disease of the airways that affects approximately 4%-5% of the general population. This disorder may cause recurrent wheezing, breathlessness, chest tightness, and coughing. Variable airflow and bronchial hyperresponsiveness to a variety of stimuli are characteristic. The disease, which affects people of all ages, is responsible for approximately 470,000 hospital admissions annually in the United States, with hospitalization rates highest among African-Americans and children.

Over the past 20 years, the prevalence, morbidity, and mortality of asthma has increased in the United States and worldwide. In response to this alarming trend, in 1991 the National Education and Prevention Program (NAEPP) instituted by the National Heart, Lung, and Blood Institute (NHLBI) published guidelines for the diagnosis and management of asthma. Two additional reports have since been prepared by asthma experts in cooperation with the NHLBI: The International Consensus Report on Diagnosis and Treatment of Asthma (NHLBI 1992) and the Global Initiative for Asthma (NHLBI/WHO 1995).

The 1991 Expert Panel Report classified asthma severity as intermittent (step 1), mild persistent (step 2), moderate persistent (step 3), and severe persistent (step 4). Key elements of the recommendations included recognition of the role of inflammation in the pathogenesis of asthma and the use of anti-inflammatory pharmacotherapy early in the treatment of moderate to severe disease; inhaled corticosteroids were considered the standard daily preventive treatment. Several clinical trials have demonstrated their efficacy using parameters such as bronchial responsiveness, peak expiratory flow, and symptom scores. Inhaled corticosteroids have been shown to reduce the frequency of acute episodes of asthma and the need for concurrent medications, lessen the requirements for oral steroids, and lower airway reactivity. They have also been observed to reduce the risk of asthma hospitalization.

New guidelines were published and new therapies approved after the period of our study. In April 1997, NHLBI published Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma. This revised guideline continues to emphasize the importance of daily long-term anti-inflammatory therapy in addition to medications to manage exacerbations in patients with persistent asthma. The latest guidelines incorporate new drugs that add to the armamentarium of long-term control medications. The long-acting inhaled beta-agonist salmeterol is indi-
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cated for long-term prevention of bronchospasm, including nighttime symptoms. The leukotriene modifiers are the newest class of long-term control medications. Zafirlukast and montelukast are leukotriene receptor antagonists, while zileuton is a 5-lipoxygenase inhibitor.

The national guidelines emphasize the importance of patient education, especially on adherence to therapy. It is estimated, however, that adherence to therapy in both the pediatric and the adult asthma populations is only about 50%. Nonadherence to a prescribed therapeutic program is one of the factors suspected of contributing to asthma morbidity and mortality in all populations.

Pharmacy and medical claims data have often been used to study the asthma population in the managed care setting because these large databases can be used to identify specific patient populations (e.g., high risk), monitor appropriateness of care, and evaluate utilization patterns. Prescription usage has been used to infer patient compliance with therapy as well as to observe prescribing patterns of physicians. Although this type of analysis has its limitations, it can provide a broad picture of the utilization patterns of a population and suggest problem areas that may require special attention.

An area that has not yet been extensively explored is clinical management and patient behavior immediately before and after an acute event such as an emergency room visit or hospitalization. An acute event might influence patients to become more aware of their condition as well as more compliant with medication therapy. From the provider’s perspective, the acute event could provide a “teachable moment,” an opportunity to educate patients on an appropriate therapy. This article describes utilization of relevant prescriptions before and after an acute asthma-related event (hospitalization or ER visit) in an effort to determine patterns in patient compliance and physician prescribing.

Study Methodology

This retrospective observational pilot study consists of an analysis of pharmacy claims for short-acting beta-agonists and inhaled anti-inflammatory agents and of medical claims submitted between January 1, 1994, and September 30, 1995, in a 275,000-member preferred provider organization (PPO) in the mid-Atlantic region. Asthmatics were identified from the International Classification of Diseases, Ninth Revision (ICD-9-CM) diagnostic codes on the medical claims. Members between the ages of 1 and 60 years with at least one encounter for a primary or secondary diagnosis code for asthma (ICD-9 codes of 493–493.99) were identified as “asthmatic.” Members with only one acute asthma-related event (ER visit or hospitalization) occurring between July 1, 1994, and March 31, 1995, were included for analysis to ensure that sufficient medical-claim-free periods and pharmacy data were available for analysis before and after the acute event.

Acute events were defined as (1) a hospitalization caused by asthma (primary ICD-9 code of 493–493.99) or (2) an asthma-related ER visit (primary ICD-9 code of 493–493.99 and Current Procedural Terminology (CPT) codes of 99281, 99282, 99283, 99284, 99285, or 99288). The study population was also limited by including only those who had a continuous pharmacy benefit. It was assumed that patients were continuously enrolled with a pharmacy benefit throughout the study period if they had pharmacy claims submitted in the first (January–March 1994) and last (July–September 1995) quarters of the study. Patients were excluded if they had a diagnosis of cystic fibrosis (ICD-9 codes of 277–277.99) or chronic obstructive pulmonary disease (ICD-9 codes of 491–492.99).

Once the study cohort was identified, the medical and pharmacy claims were integrated to create a profile for each patient. The acute event was considered to be “time zero” and the pharmacy data surrounding the acute event was incorporated into a time line. The period before “time zero” was divided into 90-day pre-acute event periods and the time period after “time zero” was divided into 90-day post-acute event periods. The profiles were then evaluated for trends in utilization of short-acting beta-agonists and inhaled anti-inflammatory medications before and after “time zero.”

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Pre-event Short-Acting Beta-Agonist Use by Post-event Short-Acting Beta-Agonist Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency/Percent</td>
<td>No</td>
</tr>
<tr>
<td>Pre-event “yes” — Patient had prescription filled for short-acting beta-agonist in the pre-event period</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>3/3.61%</td>
</tr>
<tr>
<td>Yes</td>
<td>9/10.84%</td>
</tr>
<tr>
<td>Total</td>
<td>12/14.46%</td>
</tr>
</tbody>
</table>

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Pre-event “no” — Patient did not have prescription filled for short-acting beta-agonist in the pre-event period

Post-event “yes” — Patient had prescription filled for short-acting beta-agonist in the post-event period

Post-event “no” — Patient did not have prescription filled for short-acting beta-agonist in the post-event period.

McNemar test of significant changes reveals a statistically significant change (p<0.05) in that a greater number of patients changed from not using short-acting beta-agonists in the pre-event period to using them in the post-event period (n=21) than the number of patients who changed from using the short-acting beta-agonists in the pre-event period to not using them in the post-event period (n=9).
The asthma medications analyzed in this study were the short-acting beta-agonists (albuterol, pirbuterol, bitolterol, metaproterenol, and terbutaline), inhaled corticosteroids (beclomethasone, flunisolide, fluticasone, and triamcinolone), inhaled cromolyn, and inhaled nedocromil. Statistical differences were determined using the McNemar test for significant changes. The McNemar test can be used when there are two nominal scale responses that are recorded before and after some event. The test was appropriate for this study because we had paired dichotomous data. The McNemar test compared the off-diagonal frequencies in a 2 x 2 table (see Tables 1, page 304, and 2, above). The a priori level of significance was defined as p<0.05.

**Results**

Of the approximately 8,000 members with a primary or secondary diagnosis code of asthma, 83 met the inclusion and exclusion criteria. Acute exacerbations of asthma led to ER visits for 56% of these patients and hospitalizations for 42%. Hospitalizations include patients who were initially admitted to the ER.

A greater number of patients (86%) received a prescription for short-acting beta-agonists after an acute event than before (71%).

The McNemar test for significant changes found a statistically significant greater number of patients using short-acting beta-agonists in the post-acute event period compared to patients who did the reverse (i.e., patients who used short-acting beta-agonists pre-acute event but not post-acute event) (p<0.05). In the calculation, the number of patients who have a "no" response pre-acute event and a "yes" response post-acute event are compared to the number of patients who have a "yes" response pre-event and a "no" post-event. Table 1 represents the patients who changed their usage of short-acting beta-agonists. A statistically significant result was obtained (p<0.05) comparing the 21 patients in the upper right cell to the 9 patients in the lower left cell of the 2 x 2 table.

The number of patients using inhaled anti-inflammatory agents, however, did not change significantly between the pre-acute event period and the post-acute event period (p=n.s.) (Table 2). A closer look at the cross-tab analysis of the inhaled anti-inflammatory medications (Table 2) reveals that 47 of the 83 patients were not on any inhaled anti-inflammatory medication before or after the acute event; 7 were on an inhaled anti-inflammatory medication before but not after; 14 were on an inhaled anti-inflammatory medication after but not before; and only 15 were on an inhaled anti-inflammatory medication before and after the acute event.

In total, only 29 out of 83 patients (35%) were on an inhaled anti-inflammatory medication after an acute asthma-related ER visit or hospitalization.

In a separate analysis, the proportion of patients using short-acting beta-agonists or inhaled anti-inflammatory medications was determined for each time period (see Figure 1, page 306). The proportion of patients using a short-acting beta-agonist or an inhaled anti-inflammatory medication was highest during post-acute event period one (70% of patients [58] received short-acting beta-agonists and 28% [23] received inhaled anti-inflammatory medications). Figure 1 depicts the overall use of asthma medications in the periods surrounding an acute event. As expected, more patients used asthma-related medications in the 90 days after the acute event, but that number declined with time.

**Discussion**

Nonadherence with recommended therapy has been documented as a contributing factor in asthma morbidity and mortality. A study that evaluated five urban teaching hospital emergency departments evaluated the correlates of compliance with follow-up appointments and prescription filling after an emergency department visit. Of the 1,386 patients interviewed, only 45% (408 patients) recalled being advised to take a medication and 12% (50) reported that they did not obtain the medications. In a 1997 study by Ordonez et al., children aged 3 to 15 years admitted to an Australian hospital with an acute asthma attack were evaluated to identify factors that might prevent future hospitalizations.
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This study found evidence of inadequate preventive treatment as well as poor compliance within the 12 months prior to an acute asthma attack. There is also evidence that many physicians do not adhere to existing guidelines for the emergency management of asthma. For example, in a 1997 Canadian study, a cross-sectional survey determined that many Canadian emergency physicians did not follow published recommendations for the care of patients with acute asthma. This was especially true with regard to the aggressive use of beta-2-agonists and the use of corticosteroids.

Testing our assumption that an acute event would lead to more optimal therapy and better patient compliance, our results showed that this was only partially true, in that the only asthma medications whose use significantly increased after the acute event were short-acting beta-2-agonists. Although more patients did receive inhaled anti-inflammatory medications after the acute event, the number was not statistically significant. This result may indicate either poor patient compliance or physician failure to prescribe these important long-term therapies.

Our results show that the number of patients receiving short-acting beta-agonists steadily increases as time nears the acute event, with 42 of 83 patients receiving inhaled short-acting beta-agonists during the 90 days beforehand (Figure 1). This may be an indication that patients were relying on the short-acting beta-agonists to obtain quick relief of their worsening symptoms.

The proportion of patients using both the short-acting beta-agonists and the inhaled anti-inflammatory medications was highest during the 90 days after the event. This suggests some support for the hypothesis that an acute event leads to more optimal treatment. However, as time passed, the use of anti-inflammatory agents decreased.

Finally, the low proportion of patients receiving inhaled anti-inflammatory medications throughout the periods before and after the acute event suggests either low patient compliance or physician failure to prescribe these long-term controller medications.

**Limitations**

This study used medical and pharmacy claims data for the purpose of observing utilization trends in a broad population. Although informative, administrative claims data have several limitations:

- The accuracy can be disputed. Accuracy of both medical and pharmacy claims relies on how well the data are entered (e.g., the ICD-9-CM and CPT diagnostic coding).
• Use of prescription claims only assures that the medication was dispensed, not that the patient is actually taking the medications or using them correctly.
• Likewise, we cannot distinguish between patient noncompliance and physician failure to prescribe when a medication is not dispensed.
• Claims data does not take into account the use of samples.
• Additionally, claims data does not provide the clinical information required to assess the severity of an illness.
• Also, because of the exclusion criteria, we studied only those patients with one acute event during the study period. It is possible that these patients were not moderate-severe asthmatics who required anti-inflammatory medications but mild-intermittent asthmatics who only required the “as needed” use of short-acting beta-agonists.

This pilot study specifically evaluated the short-acting beta-agonists, inhaled corticosteroids, inhaled cromolyn, and inhaled nedocromil. The use of other asthma medications, including theophylline, ipratropium, oral corticosteroids, salmeterol, and leukotriene modifiers (which were not Food and Drug Administration–approved or available during the study period), was likely to have affected utilization of the short-acting beta-agonists and inhaled anti-inflammatory medications. Extending this study’s methodology to all the available asthma therapies could provide a better picture of actual drug utilization in the asthmatic population.

Finally, the generalizability of this study’s conclusions is limited by the small sample size resulting from the strict inclusion criteria. A larger study population and evaluation of data for a longer period of time might provide a better picture of the trends in utilization.

†† Conclusion
Nevertheless, the study provides some valuable lessons. First, although evaluations of claims data may lack clinical detail to render definitive judgments, they can raise important issues about the quality of care.20 Claims data can be used to improve appropriate utilization, target continuing medical education, help manage complex patients, identify underserved patients, and detect misprescribing as well as fraud and abuse.21–23 This study examined the pharmacy claims of a population with a condition that is highly prevalent yet difficult to control in many cases. The results suggest a lack of compliance with recommended therapies and missed opportunities of education and intervention during an acute event. Finally, this evaluation can provide a framework for future initiatives that focus on patient compliance and utilization around a sentinel event, a fruitful area of research that has not been sufficiently exploited.

References
7. Donahue JG et al., Inhaled steroids and the risk of hospitalization for asthma. JAMA 1997; 277: 887–91.


