Asthma is a chronic condition that affects more than 20 million people in the United States and imposes a substantial health and economic burden, eg, 13.6 million physician office visits in 2004, 1.8 million emergency department (ED) visits annually, 504,000 hospitalizations annually from 2001 to 2003,1 and in 2007, more than $14.7 billion in direct medical costs.2 Many of these costs could have been/could be prevented with appropriate asthma management.3 Guidelines for the diagnosis and management of asthma developed by the National Asthma Education and Prevention Program recommend a stepwise approach to pharmacologic therapy.4 For persistent asthma, recommended therapy includes daily use of controller medication to prevent exacerbations and minimize the need for rescue medication. Increasing use of short-acting β₂-adrenergic agonists (SABAs) or use of a SABA more than twice a week to relieve symptoms “generally indicates inadequate asthma control and the need to initiate or intensify anti-inflammatory therapy.”4 Long-term daily use of SABAs is not recommended; however, controller medications remain underprescribed and rescue medications overused.5,6

Previous research suggests that increased SABA use is associated with diminished asthma control and an elevated risk of exacerbations.7-11 Moreover, 3 months of elevated SABA use has been associated with higher asthma-related healthcare costs,12 although annual costs associated with SABA use are unknown. Exacerbation-related hospitalizations and ED visits are an important component of these costs. To determine whether increasing SABA use is associated with greater healthcare utilization and costs, we conducted a retrospective study in a large population of health plan members.

METHODS

Data Source and Patients

Data were obtained from IMS LifeLink, a de-identified, Health Insurance Portability and Accountability Act (HIPAA)–compliant database containing enrollment and claims data for 50 million persons from approximately 70 US health plans. Eligible patients had at least 2 years of continuous enrollment in a health plan during July 1, 2003,
to June 30, 2007, were aged 6 to 56 years, had a diagnosis of asthma, and had at least 1 prescription claim for an asthma medication in each of the preindex and postindex years. Asthma diagnosis criteria consisted of (1) at least 1 asthma-related ED visit, urgent care (UC) visit, or hospitalization with a primary International Classification of Disease, Ninth Revision, Clinical Modification [ICD-9-CM] diagnosis code of 493.xx, or (2) at least 2 asthma-related physician office visits (ICD-9-CM 493.xx), or (3) at least 2 prescription claims for asthma medication (SABA or controller). Primary controllers included inhaled corticosteroids (ICS), ICS/long-acting β₂-agonist combinations (ICS/LABA), and leukotriene modifiers (LMs). Adjunctive controllers included mast cell stabilizers, methylxanthines, and omalizumab. The upper age limit was chosen to exclude patients with a higher likelihood of undiagnosed chronic obstructive pulmonary disease (COPD) and because it is a criterion in the Health Plan Employer Data and Information Set (HEDIS) of the National Committee on Quality Assurance. Exclusion criteria were a diagnosis of COPD, emphysema, chronic bronchitis, bronchiectasis, cystic fibrosis, or respiratory tract cancer, and more than 1 drug claim for ipratropium or tiotropium (surrogate markers for COPD). Patients diagnosed with multiple sclerosis, inflammatory bowel disease, rheumatoid arthritis, systemic lupus erythematosus, polyarthritis, polymyalgia rheumatica, and temporal arteritis were excluded because these conditions often require long-term treatment with oral corticosteroids (OCS).

Measurement

Enrollment and claims data were collected for a 2-year period between July 1, 2003, and June 30, 2007. When more than one 2-year observation period was available for a patient, the most recent period was selected. The index date was defined as the date occurring 1 year after the beginning of the 2-year continuous enrollment period and did not otherwise correspond to the dispensing of any medication or any specific event. The observation period was divided into 12-month preindex and postindex periods, similar to other studies. Baseline characteristics of the population were identified in the preindex period, and the relationships between SABA exposure, exacerbations, and healthcare costs were analyzed in the postindex period.

Data collected included demographics, outpatient prescription drug claims (National Drug Code, dispensing date, quantity dispensed, days of supply, and billed charges), and inpatient and outpatient claims (service date, ICD-9-CM diagnosis codes, Current Procedural Terminology-4 procedure codes, and billed charges). Costs were imputed by IMS LifeLink for claims with missing cost information that were due to capitation arrangements negotiated with participating plans. Pharmacy fills for metered-dose inhaler (MDI) and nebulized SABA and other asthma medications were identified using National Drug Codes.

Asthma exacerbations were identified using primary diagnosis codes in healthcare claims, with an exacerbation defined as an asthma-related (ICD-9-CM 493.xx) ED or UC visit; an asthma-related hospitalization; or a pharmaceutical claim for an OCS. Each OCS claim, regardless of days of supply, was counted as 1 dispensing (90% of OCS fills had a supply of 21 days or fewer). Proxy variables for asthma severity were created based on the presence of 1 or more claims in the preindex period for OCS and asthma-related ED/UC visits and hospitalizations. Healthcare costs were derived from billed charges in inpatient, outpatient, and pharmaceutical claims in the postindex period.

SABA exposure was calculated using methods similar to those previously published. Canister equivalents (CEs) were assigned to each dispensed SABA product to account for MDI and nebulized SABA use. A standard MDI canister size, or 1 CE, was defined as 200 metered actuations of albuterol; levalbuterol was considered to be equivalent in potency to albuterol. For pirbuterol, in which a standard dispensing contains 400 actuations, 1 canister was considered to be 2 CEs. For claims in which canister size was unclear, CEs were imputed based on days of supply. We considered a 3-mL ampule of nebulized albuterol to be equivalent to 4 actuations of albuterol from an MDI, so 50 3-mL ampules of nebulized SABA was considered 1 CE. For analysis, CEs were rounded to the nearest one-half CE. A categorical variable adapted from a previously validated risk stratification scheme was created to characterize SABA exposure as 0 CE (no use), ½ to 2 CEs (low use), 2½ to 6 CEs (moderate use), 6½ to 12 CEs (high use), or >12 CEs (excessive use).
Relationship Between SABA Use and Healthcare Costs

Table 1. Preindex SABA Use by Level of SABA Use in the Postindex Period

<table>
<thead>
<tr>
<th>Preindex SABA Use Category</th>
<th>All Levels (N = 93,604)</th>
<th>0 CE (n = 24,857)</th>
<th>½ to 2 CEs (n = 38,241)</th>
<th>2½ to 6 CEs (n = 20,071)</th>
<th>6½ to 12 CEs (n = 7264)</th>
<th>&gt;12 CEs (n = 3171)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 CE</td>
<td>22,653 (24.2)</td>
<td>12,539 (50.4)</td>
<td>7676 (20.1)</td>
<td>2145 (10.7)</td>
<td>256 (3.5)</td>
<td>37 (1.2)</td>
</tr>
<tr>
<td>½ to 2 CEs</td>
<td>40,142 (42.9)</td>
<td>9101 (36.6)</td>
<td>22,985 (60.1)</td>
<td>7152 (35.6)</td>
<td>818 (11.3)</td>
<td>86 (2.7)</td>
</tr>
<tr>
<td>2½ to 6 CEs</td>
<td>20,348 (21.7)</td>
<td>2759 (11.1)</td>
<td>6838 (17.9)</td>
<td>8104 (40.4)</td>
<td>2344 (32.3)</td>
<td>303 (9.6)</td>
</tr>
<tr>
<td>6½ to 12 CEs</td>
<td>7322 (7.8)</td>
<td>389 (1.6)</td>
<td>668 (1.8)</td>
<td>2367 (11.8)</td>
<td>2973 (40.9)</td>
<td>925 (29.2)</td>
</tr>
<tr>
<td>&gt;12 CEs</td>
<td>3139 (3.4)</td>
<td>69 (0.3)</td>
<td>74 (0.2)</td>
<td>303 (1.5)</td>
<td>873 (12.0)</td>
<td>1820 (57.4)</td>
</tr>
</tbody>
</table>

CE indicates canister equivalent; SABA, short-acting β2-adrenergic agonist.

Data Analyses and Statistical Methods

Cross-sectional bivariate analyses and multivariate regression models were used to determine the relationships between SABA use, asthma exacerbations, and asthma-related and total (all-cause) healthcare costs in the postindex period. In the bivariate analyses, differences between groups were assessed using the 2-tailed t test or analysis of variance test for continuous variables and the β2 test for categorical variables. These methods also were used to evaluate the association between SABA exposure, outcomes, and covariates. Potential comorbidities for multivariate models were tested using the β2 test; comorbidities demonstrated to be significant in previous research and/or significant at the 5% level in our bivariate analyses were included. The comorbid conditions included in the multivariate regression models were allergies/rhinitis, chronic sinusitis, diabetes mellitus, gastroesophageal reflux disease, obstructive sleep apnea syndrome, tonsil and adenoid disease, acute pharyngitis, acute sinusitis, and upper respiratory infection.5-8,26-30 Logistic regression models were used to determine adjusted associations between SABA use and exacerbations, and generalized linear models with a gamma family distribution and log-link were used to estimate asthma-related and all-cause healthcare costs by SABA strata. Cost differences were calculated between the means of the predicted costs, and 95% confidence intervals (CIs) were calculated using the percentile method with 1000 bootstrapped simulations. All analyses were conducted with SAS version 9.1.3 for Windows (SAS Institute, Cary, NC) or Stata version 10 for Windows (StataCorp LP, College Station, TX).

RESULTS

Patient Characteristics

In the postindex period, 26.6% of patients had no drug claims for SABAs, 40.9% were dispensed between ½ and 2 CEs, 21.4% were dispensed between 2½ and 6 CEs, 7.8% were dispensed between 6½ and 12 CEs, and 3.4% were dispensed more than 12 CEs. Nebulized SABAs were prescribed to 12.9% of patients and were used 3 times as often in excessive SABA users (31.6%) and 2.4 times as often in high SABA users (25.9%) compared with low SABA users (10.6%) (data not shown). In general, SABA use by patients did not vary greatly from preindex year to postindex year (Table 1).

Out of an initial pool of 946,859 patients with asthma, 93,604 met study eligibility criteria (Appendix available at www.ajmc.com). Demographic and baseline clinical characteristics of the cohort are shown in Table 2. The study population was 45.2% male, and the largest proportion of patients (48.9%) resided in the midwestern United States. More than one-third of the population was pediatric, but only 22% of subjects in the high and excessive SABA use groups were children. The most frequent chronic comorbidities in the preindex or postindex periods were allergies/rhinitis and chronic sinusitis. The prevalence of comorbid conditions generally decreased with increasing SABA exposure. This relationship was especially apparent for allergies/rhinitis; non-SABA users had this diagnosis 70% more often than excessive users. Specialist consultations were obtained by 30.9% of subjects, with a 33% higher occurrence in non-SABA users than excessive users. In the preindex period, 2046 members (2.2%) had an asthma-related ED/UC visit, 876 (0.9%) had an asthma-related hospitalization, and 28,892 (30.9%) had OCS treatment. The frequency of these exacerbation events increased with greater postindex SABA exposure.

Controller Medication Use

Controller medication dispensed in the postindex period varied substantially by SABA exposure (Table 3, Figure 1). In general, controller use (primary or any) was highest in excessive SABA users, followed closely by nonusers and high users. Excessive SABA users had nearly twice as many mean
days of supply of any controller medication as low SABA users (209 days versus 111 days). Despite elevated levels of controller use as a group, almost half of high and excessive SABA users had either low (1 to 120 days of supply) or no use of any controller medication.

The most frequently prescribed controller medications at all levels of SABA use were ICS/LABAs and LMs (Table 3). In the high and excessive SABA use groups, many of the patients on an ICS (without a LABA) and LM were on monotherapy (46% of ICS users and 18% of LM users). The percentage of patients on monotherapy was 56% overall, and it was higher in the non-SABA group (78%) compared with the low (48%), moderate (51%), high (50%), and excessive (44%) SABA groups. Adjunctive controllers were used sparsely overall but most frequently in excessive SABA users, who were dispensed theophylline 7 times more often and omalizumab 8 times more often than low SABA users.

**Exacerbations**

The adjusted associations between postindex SABA use and exacerbations, as measured by asthma-related ED/UC visits, hospitalizations, and OCS claims, are shown in Figure 2. 

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**Table 2. Demographic and Baseline Clinical Characteristics by Level of SABA Use in the Postindex Period**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Levels (N = 93,604)</th>
<th>0 CE (n = 24,857)</th>
<th>½ to 2 CEs (n = 38,341)</th>
<th>2½ to 6 CEs (n = 20,071)</th>
<th>6½ to 12 CEs (n = 7,264)</th>
<th>&gt;12 CEs (n = 3,171)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, 6-17 y</td>
<td>33,951 (36.3)</td>
<td>8138 (32.7)</td>
<td>15,717 (41.1)</td>
<td>7,769 (38.7)</td>
<td>1,793 (24.7)</td>
<td>534 (16.8)</td>
</tr>
<tr>
<td>Age, 18-56 y</td>
<td>59,653 (63.7)</td>
<td>16,719 (67.3)</td>
<td>22,524 (58.9)</td>
<td>12,302 (61.3)</td>
<td>5,471 (75.3)</td>
<td>2,637 (83.2)</td>
</tr>
<tr>
<td>Male</td>
<td>42,266 (45.2)</td>
<td>10,795 (43.4)</td>
<td>16,871 (44.1)</td>
<td>9,512 (47.4)</td>
<td>3,483 (48.0)</td>
<td>1,605 (50.6)</td>
</tr>
</tbody>
</table>

**Chronic comorbid conditions**

- Allergies/rhinitis: 28,760 (30.8), 8,914 (36.0), 11,562 (30.3), 5,889 (29.4), 1,724 (23.8), 671 (21.2)
- Chronic sinusitis: 9,785 (10.5), 2,929 (11.8), 3,860 (10.1), 2,011 (10.0), 665 (9.2), 320 (10.5)
- Diabetes mellitus: 4,006 (4.3), 1,251 (5.1), 1,445 (3.8), 812 (4.1), 319 (4.4), 179 (5.7)
- GERD: 5,896 (6.3), 1,842 (7.4), 2,253 (5.9), 1,168 (8.8), 453 (6.3), 179 (5.7)
- OSAS: 4,922 (5.3), 1,515 (6.1), 1,929 (5.1), 921 (4.6), 369 (5.1), 188 (5.9)
- Tonsil and adenoid disease: 4,282 (4.6), 1,144 (4.6), 1,888 (4.9), 867 (4.3), 276 (3.8), 107 (3.4)

**Acute comorbid conditions**

- Acute pharyngitis: 13,410 (14.4), 3,101 (12.5), 6,059 (15.9), 3,091 (15.4), 840 (11.6), 319 (10.1)
- Acute sinusitis: 13,590 (14.5), 3,703 (14.9), 5,699 (14.9), 2,862 (14.3), 935 (12.9), 391 (12.4)
- URI: 18,795 (20.1), 4,425 (17.9), 8,316 (21.8), 4,038 (20.2), 1,409 (19.4), 607 (19.2)

**Specialist consultation**

- 28,889 (30.9), 8,754 (35.3), 11,009 (28.8), 6,251 (31.2), 2,032 (28.0), 843 (26.6)

**PFT performed**

- 33,357 (31.3), 9,130 (38.8), 13,439 (35.2), 7,396 (36.9), 2,402 (33.1), 990 (33.3)

**Exacerbations (preindex period)**

- ED/UC visit: 2046 (2.2), 257 (1.0), 753 (2.0), 578 (2.9), 267 (3.7), 191 (6.0)
- Hospitalization: 876 (0.9), 182 (0.7), 265 (0.7), 220 (1.1), 128 (1.8), 81 (2.6)
- OCS treatment: 28,892 (30.9), 6,950 (28.0), 11,349 (29.7), 6,651 (33.1), 2,604 (35.9), 1,338 (42.2)

**Exacerbations (postindex period)**

- ED/UC visit: 1692 (1.8), 142 (0.6), 574 (1.5), 527 (2.6), 285 (3.9), 164 (5.2)
- Hospitalization: 608 (0.7), 71 (0.3), 159 (0.4), 190 (1.0), 115 (1.6), 73 (2.3)
- OCS treatment: 26,463 (28.3), 4,970 (20.0), 10,473 (27.4), 6,836 (34.1), 2,766 (38.1), 1,418 (44.7)

CE indicates canister equivalent; ED/UC, emergency department/urgent care; GERD, gastroesophageal reflux disease; OCS, oral corticosteroid; OSAS, obstructive sleep apnea syndrome; PFT, pulmonary function test; SABA, short-acting β₂-adrenergic agonist; URI, upper respiratory infection.

*Statistical analysis was done using β² tests. Differences among SABA subgroups were significant in the comparisons shown in all rows. All P values <.001.

*Pulmonologist or allergist visit in either the preindex or the postindex period.

*Exacerbations occurring in either the preindex or the postindex period.

*Based on ED/UC and hospitalization claims with a primary diagnosis of asthma, or a pharmacy claim for OCS.
Relationship Between SABA Use and Healthcare Costs

Table 3. Asthma Medication Use by Level of SABA Use in the Postindex Period

<table>
<thead>
<tr>
<th>Variable</th>
<th>All Levels (N = 93,604)</th>
<th>0 CE (n = 24,857)</th>
<th>½ to 2 CEs (n = 38,241)</th>
<th>2½ to 6 CEs (n = 20,071)</th>
<th>6½ to 12 CEs (n = 7264)</th>
<th>&gt;12 CEs (n = 3171)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any primary controller</td>
<td>72,278 (77.2)</td>
<td>24,412 (98.2)</td>
<td>24,518 (64.1)</td>
<td>15,233 (75.9)</td>
<td>5713 (78.7)</td>
<td>2402 (75.8)</td>
</tr>
<tr>
<td>Two or more controllers</td>
<td>19,482 (20.8)</td>
<td>5046 (20.3)</td>
<td>6339 (16.6)</td>
<td>5025 (25.0)</td>
<td>2066 (28.4)</td>
<td>1006 (31.7)</td>
</tr>
<tr>
<td>Primary controller type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICS</td>
<td>22,044 (23.6)</td>
<td>5202 (20.9)</td>
<td>8408 (22.0)</td>
<td>5675 (28.3)</td>
<td>1975 (27.2)</td>
<td>784 (24.7)</td>
</tr>
<tr>
<td>ICS/LABA</td>
<td>34,799 (37.2)</td>
<td>10,949 (44.1)</td>
<td>11,271 (29.5)</td>
<td>7863 (39.2)</td>
<td>3313 (45.6)</td>
<td>1403 (44.2)</td>
</tr>
<tr>
<td>Leukotriene modifier</td>
<td>37,834 (40.4)</td>
<td>13,846 (55.7)</td>
<td>12,236 (32.0)</td>
<td>7621 (38.0)</td>
<td>2803 (38.6)</td>
<td>1328 (41.9)</td>
</tr>
<tr>
<td>Adjunct controller type</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mast cell stabilizers</td>
<td>546 (0.6)</td>
<td>134 (0.5)</td>
<td>193 (0.5)</td>
<td>138 (0.7)</td>
<td>55 (0.8)</td>
<td>26 (0.8)</td>
</tr>
<tr>
<td>Methylxanthines</td>
<td>1116 (1.2)</td>
<td>360 (1.5)</td>
<td>236 (0.6)</td>
<td>213 (1.1)</td>
<td>169 (2.3)</td>
<td>138 (4.4)</td>
</tr>
<tr>
<td>Omalizumab</td>
<td>261 (0.3)</td>
<td>81 (0.3)</td>
<td>50 (0.1)</td>
<td>62 (0.3)</td>
<td>35 (0.5)</td>
<td>33 (1.0)</td>
</tr>
</tbody>
</table>

CE indicates canister equivalent; ICS, inhaled corticosteroid; LABA, long-acting β2-adrenergic agonist; SABA, short-acting β2-adrenergic agonist. Variables are for postindex period unless otherwise noted. Claims for >2 different primary or adjunct controllers (ICS/LABA combination therapies were considered 1 controller in this analysis).

Figure 1. Primary and Any Controller Medication Use by Level of SABA Use in the Postindex Period

CE indicates canister equivalent; ICS, inhaled corticosteroid; LABA, long-acting β2-adrenergic agonist; LM, leukotriene modifier; SABA, short-acting β2-adrenergic agonist. Primary controllers included ICS, ICS/LABA combination, and LM (not adjusted for differences in efficacy). Included primary (ICS, ICS/LABA combination, and LM) and adjunct (mast cell stabilizers, methylxanthines, LABA alone, and omalizumab) controller medications (not adjusted for differences in efficacy).

Days of supply of controller (primary or any) medication in postindex period.
all, after adjustment for demographic characteristics, selected individual comorbidities, primary asthma controller medication use, and asthma severity, high and excessive SABA users had statistically significant higher odds (odds ratio [95% CI]) for an asthma-related ED/UC visit (6.47 [5.25, 7.98] and 7.68 [6.04, 9.76], respectively), hospitalizations (5.37 [3.96, 7.29] and 6.90 [4.90, 9.73], respectively), and OCS claims (2.89 [2.72, 3.08] and 3.71 [3.41, 4.03]) compared with SABA nonusers. Similar patterns of associations emerged for the pediatric and adult age strata (data not shown).

Healthcare Costs
Unadjusted total asthma-related healthcare costs in the 12-month postindex period were lowest in the low SABA use group (½ to 2 CEs per year): 33% lower than the costs for the group not using a SABA (P < .05) (Table 4). This difference was almost entirely due to asthma prescription drug costs, which were $316 lower in the low SABA use group.

Mean total asthma-related costs increased almost linearly with increasing SABA exposure; compared with low SABA users, moderate users (2½ to 6 CEs per year) had 1.7 times higher costs ($988, 95% CI = $961, $1014), high users had 2.2 times higher costs ($1326, 95% CI = $1256, $1395), and excessive users had 3.0 times higher costs ($1791, 95% CI = $1670, $1913).

A comparison of mean all-cause healthcare costs between the SABA exposure groups followed the same pattern, with the low SABA use group having the lowest total all-cause costs ($4281; 95% CI = $4069, $4493) and the excessive SABA use group the highest ($5962; 95% CI = $5461, $6463) (Table 4). However, the relative cost differences between SABA use groups were much less pronounced for all-cause costs than for asthma-related costs. Differences in all-cause costs were mostly accounted for by the differences in asthma-related costs.

After adjustment for demographic characteristics, specialist consultation, asthma severity, and significant selected comorbidities, total asthma-related cost differences were much lower for those with no SABA fills compared with high and excessive users, primarily because of differences in pharmaceutical costs (Table 4). Conversely, medical costs were relatively unaffected by the adjustment. Adjustment of all-cause
medical costs amplified the difference between the low and excessive SABA groups, but similar to asthma-related costs, pharmaceutical cost differences between these groups were attenuated.

Additional analyses showed that with increasing asthma controller medications dispensed, asthma-related pharmaceutical costs (data not shown) increased as expected, but medical expenses remained remarkably similar across all groups, most notably in the low ($174; 95% CI = $163, $184), moderate ($221; 95% CI = $192, $250) and high ($221; 95% CI = $205, $237) controller use groups.

### DISCUSSION

This retrospective study of 93,604 asthma patients found a strong relationship between the amount of SABA dispensed annually and asthma-related and all-cause healthcare costs. Excessive SABA users had 3 times higher asthma-related healthcare costs than low SABA users. This finding was similar to that of Stempel et al, who reported that total asthma-related costs were 3 times higher in patients with an average SABA use of more than 1 canister per month for at least 3 months compared with the “average asthmatic.”

Although much of the increased cost in the high and excessive SABA use groups was due to a higher rate of asthma exacerbations and increased asthma severity in the present study, higher costs remained after adjustment for asthma severity, albeit to a much lesser degree for pharmaceutical costs.

Schatz et al reported that use of 7 to 12 canisters and more than 12 canisters of SABA annually was associated with worsening asthma control. When considering the significantly higher odds for exacerbation-related events in patients with greater SABA use even after adjustment for asthma severity, it is likely that the high and excessive SABA use groups in our study had diminished asthma control. This diminished control may have been the result of several factors, including deficient specialty care and comorbidity management, increased asthma severity, and inappropriate or inadequate controller therapy. Allergy was diagnosed substantially less in these groups, consistent with a lack of allergy management because a lower rate of allergy control. This diminished control may have been the result of several factors, including deficient specialty care and comorbidity management, increased asthma severity, and inappropriate or inadequate controller therapy. Allergy was diagnosed substantially less in these groups, consistent with a lack of allergy management because a lower rate of allergy control. More severe asthma is indicated by higher rates of preindex exacerbation events and greater postindex adjunctive controller, multiple controller, and nebulized SABA use. Nonetheless, nearly half of patients in the high and ex-
cessive SABA use groups had either suboptimal or no use of controller medication.

Increasing costs with greater SABA use likely were driven by multiple factors. Medical costs were very similar when stratifying patients by level of controller use, but not when stratifying patients by increasing SABA use, indicating that those with more severe asthma may have required more medication to prevent increased exacerbations and costs. Obviously, patients with more severe asthma tend to incur higher pharmacy costs to adequately treat their disease. Accordingly, after adjustment for asthma severity, differences among the SABA use groups substantially decreased for pharmaceutical costs but not for medical costs. Thus, increased total asthma-related costs with increasing SABA use likely were associated with exacerbation management in addition to increased asthma severity.

Numerous studies have demonstrated that adherence to clinical guidelines reduces resource utilization and healthcare costs. Patients with high or excessive SABA use and inadequate or inappropriate controller prescribed likely were not being treated in accordance with the stepwise treatment approach recommended by current guidelines. The high ICS/LABA combination use in the SABA nonusers could represent patients with either moderate to severe asthma that was well controlled or mild asthma that was overtreated, the latter situation being inconsistent with treatment guidelines, which may account for the higher cost of medication but little reduction in medical costs in SABA nonusers. Guidelines also were likely not adhered to in the large number of patients who had high or excessive SABA use and were on monotherapy with an ICS or LM.

A particular strength of this study was the incorporation of methods to standardize the measurement of SABA use, including nebulized SABA, by converting dispensed amounts to CEs. Additional strengths are the large sample and data capture across the complete spectrum of healthcare.

This observational study used administrative data and lacked a randomized design; controlling for some confounding variables was impossible. Most important of these variables were pulmonary function test results, race/ethnicity, and smoking. It is possible that this study’s eligibility criteria might make the results less generalizable because uninsured patients or those with zero pharmacy claims for SABA and controller medication were not captured. These patients, possibly without medical care or medication, might be expected to have worse outcomes than patients in the non-SABA group in the present study who had some asthma medication use. In addition, interpretation of the results for primary controller medication use, broken out by SABA use category, may be limited, as ICS data were not stratified by dose and adjustments were not made based on differences in efficacy for ICS, ICS/LABA combination, and LMs. Finally, the amount of SABA or controller medication that was actually used could not be determined because exposure data were derived from prescription drug claims.

Although other studies9,19,31-33 have examined the association between SABA use and either asthma severity, exacerbations, or costs, to our knowledge this is the first study to show the relationship between increased SABA use, exacerbations, and direct asthma-related and total healthcare costs.

CONCLUSIONS

High and excessive SABA users likely represent patients at a higher risk for asthma exacerbations because they frequently have more severe asthma, poor control due to inadequate or inappropriate treatment, or both. These groups also could represent patients with severe asthma that is difficult to manage despite appropriate therapy, or patients without exacerbations as defined who are overreliant on SABA to manage asthma. Moreover, these patients incur much higher asthma-related and all-cause healthcare costs, even after controlling for asthma severity. Patients’ SABA claims in the preindex year and in the postindex year were strongly correlated, suggesting that the previous year’s SABA claims may be a useful marker for increased healthcare costs. These findings suggest that substantial opportunity exists to improve asthma management, reduce morbidity, and lower exacerbation-related healthcare costs in patients with elevated SABA claims.

Acknowledgments

We thank Judith Hurley, MS, who received payment from the Lovelace Respiratory Research Institute for medical writing services, and Susan Berry, MSW, of Lovelace Respiratory Research Institute, for editing assistance.

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Funding Source: Support for this study was provided by AstraZeneca LP.

Author Disclosures: Dr Silver and Blanchette report receiving grants from AstraZeneca LP. Dr Meddis is an employee of AstraZeneca LP and reports owning stock in the company. The other authors (SK, HP, MAL, BG) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (HSS, CMB, SK, DM, BG); acquisition of data (HP, MAL, BG); analysis and interpretation of data (HSS, CMB, SK, HP, DM, BG); drafting of the manuscript (HSS, CMB, DM); critical revision of the manuscript for important intellectual content (HSS, CMB, SK, HP, DM, BG); statistical analysis (HSS, CMB, MAL); obtaining funding (CMB); administrative, technical, or logistic support (HSS, CMB, MAL); and supervision (CMB).
REFERENCES


**eAppendix. Patient Selection**

All patients in the PharMetrics database 7/1/03 to 6/30/07: ~40,000,000

Patients with a primary or secondary asthma diagnosis during a hospitalization, ED/UC visit, or any outpatient visit: 946,859

Patients with 2 years of continuous enrollment: 587,786

Age 6-56 years: 467,017

Patients with 1 hospitalization, 1 ED/UC visit, 2 outpatient visits for asthma, or any 2 prescription claims for asthma medication: 322,828

Patients with ≥1 asthma medication claim during each of the preindex and postindex years: 122,479

Patients without a diagnosis of COPD, chronic bronchitis, emphysema, bronchiectasis, or cystic fibrosis: 115,467

Patients without a diagnosis of multiple sclerosis, inflammatory bowel disease, rheumatoid arthritis, systemic lupus erythematosus, psoriasis, polymyalgia rheumatica, temporal arteritis, or respiratory tract cancer: 95,275

Patients with <2 prescription claims for anticholinergics: 93,604

COPD indicates chronic obstructive pulmonary disease; ED/UC, emergency department/urgent care.