Health Care Use and Costs Among Medicare Patients With Chronic Obstructive Pulmonary Disease Treated With Short-Acting Beta Agonists or Long-Acting Beta Agonists

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ABSTRACT: Chronic obstructive pulmonary disease (COPD) has a high prevalence among older adults and is the third leading cause of mortality in the United States. COPD exacerbations can require hospitalizations, resulting in high morbidity and economic burden. In this retrospective cohort study, Medicare administrative claims data were used to compare inpatient resource use and direct health care costs among patients with COPD treated with short-acting beta agonists (SABAs) or long-acting beta agonists (LABAs). Prior to adjusting for background characteristics, LABA patients (n = 833) were less likely than SABA patients (n = 2134) to be hospitalized (16.0% vs 23.0%; P < .001), had fewer inpatient days (3.2 days vs 6.4 days; P < .001), and had lower total health care costs ($6928 vs $8806; P < .001). After adjusting for covariates, LABA-treated patients had an average of 1.53 fewer inpatient days (P = .043) and 16% lower total health care costs when compared with SABA-treated patients (P < .001). Treatment with LABAs for patients with COPD may reduce hospitalization days and lower health care costs.

KEY WORDS: chronic obstructive pulmonary disease, beta agonists, Medicare, health care costs, health care utilization

COPD is the third leading cause of mortality in the United States. Overall, an estimated 14.8 million US adults have been diagnosed with COPD. National expenditures related to COPD are approximately $49.9 billion annually, including $29.5 billion in direct costs and $20.9 billion in indirect costs. Depending on disease severity, the estimated costs of managing COPD range from $5600 to more than $21,400 per patient per year. Thus, COPD represents a substantial cost burden. In a survey of patients with COPD between 2006 and 2010, 34% of COPD patients were Medicare beneficiaries, with the remaining patients having Medicaid or private insurance. Overall, 51% of total medical costs for COPD were paid by Medicare, 25% by Medicaid, and 18% by private insurance in 2010. In general, exacerbations account for 70–90% of the direct health care costs associated with COPD, stemming primarily from higher rates of emergency department use and hospitalizations.
The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommend maintenance therapy with long-acting bronchodilators, including beta agonists and anticholinergics, for patients with moderate to severe COPD and short-acting bronchodilators for use as rescue medications or to treat intermittent symptoms for patients with mild COPD. The guidelines also suggest considering prescribing pharmacotherapy, such as long-acting bronchodilator therapy, before a patient is discharged for a COPD-related hospitalization in order to reduce exacerbations and delay re-hospitalization. Long-acting bronchodilator therapy has been shown to lower the risks of both initial and repeat hospitalizations in managed Medicare beneficiaries, primarily due to reducing the incidence of COPD exacerbations. In a comparison between treatment with the long-acting beta agonist (LABA) and inhaled corticosteroid therapy (fluticasone/salmeterol combination) and treatment with anticholinergic therapy (tiotropium, ipratropium, ipratropium/albuterol combination), COPD patients in a managed Medicare population treated with fluticasone/salmeterol therapy had fewer hospitalizations and ED visits than patients receiving anticholinergics. Despite these established disease management guidelines, however, short-acting beta agonists (SABAs) appear to be widely used as maintenance treatment in usual clinical care for patients with COPD of all severities. Among managed Medicare beneficiaries with COPD, nearly 71% are not prescribed any maintenance therapy.

Although the current COPD literature focuses heavily on various health outcomes, including health service utilization patterns and costs, existing studies are almost exclusively limited to commercial health plans or managed Medicare populations. A recent analysis conducted in a fee-for-service Medicare population in patients newly initiating COPD therapy revealed that patients receiving LABA therapy had longer time to all-cause hospitalization and lower risk for hospitalization than patients on SABA therapy, demonstrating that LABA therapy may provide increased benefit compared with SABA therapy. The authors are unaware of any studies that have directly compared the potential benefits of LABA treatment versus SABA treatment in relation to number of inpatient days and total health care costs. The purpose of this study was to compare differences in inpatient resource use and total health care costs using a national sample of Medicare beneficiaries with COPD who initiated treatment with LABA or SABA medications.

**METHODS**

**Data Source and Sample Selection**

The study proposal was submitted to the institutional review board at the University of Southern California and was granted a waiver prior to initiation. A retrospective cohort analysis was conducted using data from a 5% national sample of Medicare beneficiaries between 1/1/2006 and 12/31/2008. Patients with at least two claims for COPD (ICD-9-CM codes: 491.xx, 492.xx, 494.xx, or 496.xx), N = 219,700. Patients enrolled in Medicare Parts A and B, n = 187,651. Fee-for-service patients, n = 165,893. Patients with at least one claim under Medicare Part D, n = 100,177. Patients with at least one claim for oxygen treatment or COPD medication under Medicare Parts B or D, n = 84,388. Patients aged ≥ 65 years, n = 69,076. Patients without asthma, n = 44,937. Medicare beneficiaries continuously enrolled for ≥ 18 months who had no COPD therapy during 6 months and LABA and/or SABA users during the treatment period, n = 3017.

**Figure 1. Sample Selection Flow Chart**

At least one claim for SABA or LABA. Abbreviations: COPD, chronic obstructive pulmonary disease; LABA, long-acting beta agonist; SABA, short-acting beta agonist.
sample of Medicare beneficiaries between January 1, 2006, and December 31, 2008. The database contained information on inpatient and outpatient diagnoses based on the International Classification of Diseases 9th Revision–Clinical Modification (ICD-9-CM), along with all procedure codes and medications dispensed to the patient. The database included inpatient facility claims (Part A), outpatient medical service claims (Part B), and prescription drug claims (Part D). The analysis was restricted to patients who had a fee-for-service Medicare plan and did not include beneficiaries enrolled in the Medicare Advantage supplemental insurance (Part C). Additionally, patients were included if they had two claims for a primary COPD diagnosis (ICD codes 491.xx, 492.xx, 494.xx, 496.xx), enrolled in Medicare Parts A and B, and had at least one claim under Medicare Part D. The final sample selection followed the application of sequential inclusion criteria as delineated in Figure 1.

**Study Design**

Three time periods (baseline, treatment, and follow-up) were determined for each patient in the database (Figure 2). First, an index date was determined based on the first prescription fill date for a SABA (metered-dose inhaler or nebulizer) or a LABA (metered-dose inhaler, dry powder inhaler, or nebulizer) treatment using Medicare Parts B and D claims. The baseline period was determined to be a minimum period of 6 months before the index date. New users of COPD medications were identified as patients who did not receive any SABA or LABA treatment during the baseline period. Patients were categorized as SABA-treated patients or LABA-treated patients based on the COPD treatments received during the 6-month treatment period following the index date. Patients who received a LABA maintenance therapy on the index date were categorized as LABA-treated patients. Patients who received a SABA on the index date and did not have any LABA prescription during the follow-up period were categorized as SABA-treated. Patients classified as LABA-treated could have been treated with SABA therapy during the follow-up period.

In the absence of information on COPD disease severity among patients who were newly prescribed COPD pharmacotherapies, a 6-month treatment period was selected to permit sufficient lapsed time from which clinically meaningful results could be attributed to LABA or SABA therapy, while controlling for potential underlying differences between the groups. Patients were then followed for an additional 6 months, during which inpatient admissions and total health care costs were evaluated.

**Independent and Dependent Variables**

Multiple background variables were analyzed. Demographic characteristics included age, sex, and race/ethnicity. Clinical indicators included primary diagnosis (ie, COPD); number and type of comorbid conditions (such as depression,
vascular disease, congestive heart failure, hypertension, and hyperlipidemia); number of spirometry tests; and prescription (ie, SABA, LABA, and oral corticosteroid [OCS]). Health service utilization variables included physician office visits, outpatient visits, ED visits, and hospitalizations.

Dependent variables related to health care resource use and costs were examined, including the following: (1) percentage of patients with one or more hospitalizations; (2) number of inpatient days, defined as the sum of all hospital stay days during the entire follow-up period for any reason; (3) all-cause health care resource use; and (4) all-cause total health care costs. The cost estimates were derived from claims paid by Medicare Parts A, B, and D during the 6-month follow-up period for pharmacy services and medical care specific to physician and outpatient visits, ED visits, and hospitalizations.

Table 1. Demographic Characteristics, Comorbidities, Health Service Utilization Patterns, and Health Care Costs of the Study Population During the 6-Month Treatment Period

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>SABA-Treated (n = 2134)</th>
<th>LABA-Treated (n = 883)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>1429 (67.0)</td>
<td>570 (64.5)</td>
<td>.205</td>
</tr>
<tr>
<td>White, non-Hispanic, n (%)</td>
<td>1888 (88.5)</td>
<td>791 (89.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>78.5 (8.2)</td>
<td>77.0 (7.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Top five comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression, n (%)</td>
<td>1764 (83.0)</td>
<td>710 (80.4)</td>
<td>.145</td>
</tr>
<tr>
<td>Vascular disease,a n (%)</td>
<td>1220 (57.2)</td>
<td>560 (63.0)</td>
<td>.002</td>
</tr>
<tr>
<td>Congestive heart failure, n (%)</td>
<td>794 (37.2)</td>
<td>264 (29.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hypertension uncomplicated, n (%)</td>
<td>786 (36.8)</td>
<td>234 (26.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hyperlipidemia, n (%)</td>
<td>708 (33.2)</td>
<td>225 (25.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Health service use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spirometry, n (%)</td>
<td>83 (4.0)</td>
<td>52 (6.0)</td>
<td>.028</td>
</tr>
<tr>
<td>Oral corticosteroid use, n (%)</td>
<td>401 (19.0)</td>
<td>171 (19.0)</td>
<td>.280</td>
</tr>
<tr>
<td>Specialist visit, n (%)</td>
<td>102 (5.0)</td>
<td>93 (10.5)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Physician visit, n (%)</td>
<td>1591 (74.0)</td>
<td>820 (93.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Emergency department visit, n (%)</td>
<td>497 (23.0)</td>
<td>158 (18.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hospitalization, n (%)</td>
<td>809 (38.0)</td>
<td>266 (30.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Inpatient days, mean (SD)</td>
<td>11.0 (28.0)</td>
<td>5.4 (15.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Health care costs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pharmacy, mean (SD)</td>
<td>9204 (1221)</td>
<td>1005 (1182)</td>
<td>.078</td>
</tr>
<tr>
<td>Medical,b mean (SD)</td>
<td>9333 (15044)</td>
<td>6637 (11836)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total, mean (SD)</td>
<td>10253 (15225)</td>
<td>7642 (11957)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

aDefined as peripheral vascular disease, unspecified (ICD-9-CM 443.9)
bIncludes all physician visits, outpatient visits, and hospitalizations.

Abbreviations: LABA, long-acting beta agonist; SABA, short-acting beta agonist; SD, standard deviation.

Statistical Analysis

Descriptive statistics, bivariate comparisons, and multivariate regression analyses using ordinary least-squares (OLS) modeling techniques were performed using SAS version 9.2 (SAS Institute, Cary, NC). Differences in mean number of inpatient days and health care costs were assessed using Student t tests.

The following variables from both the baseline and treatment periods were included in the regression models: number of spirometry tests, number of physician visits, log of total health care costs, number of days on OCS, and total number of inpatient days. Two OLS regression models were fitted for the follow-up period: one with the log of total health care costs without regard to diagnosis (ie, as “all cause”) as the outcome variable, and one with number of inpatient days as the outcome variable. For the cost model, the log of total health costs.
care costs was examined as a function of LABA or SABA treatment while adjusting for the aforementioned confounding variables (number of inpatient days not included). Log of total costs was used due to the skewness to the right in the distribution of cost data. For the inpatient days model, the number of inpatient days was examined as a function of LABA or SABA treatment while adjusting for potential confounders (costs not included). In addition, both models adjusted for age, sex, race/ethnicity, and Charlson Comorbidity Index score. Statistical significance was set at \( P < .05 \).

RESULTS

Descriptive Findings

The final sample included 3017 patients with COPD newly initiating treatment: 2134 categorized as SABA-treated patients, and 883 categorized as LABA-treated patients. SABA-treated patients were slightly older than the LABA-treated patients (\( P < .001 \)) and were more likely to have comorbid congestive heart failure (\( P < .001 \)), uncomplicated hypertension (\( P < .001 \)), and hyperlipidemia (\( P < .001 \); Table 1). However, a significantly higher percentage of LABA-treated patients had comorbid vascular disease compared with SABA-treated patients (\( P = .002 \)).

During the treatment period, there were significant differences between the study groups in health service utilization and associated costs (Table 1). SABA-treated patients had significantly more COPD-related ED visits (23% vs 18%; \( P < .001 \)), hospitalizations (38% vs 30%; \( P < .001 \)), and inpatient days (28% vs 15%; \( P < .001 \)) than LABA-treated patients, whereas LABA-treated patients had significantly more COPD-related outpatient visits to physicians (93% vs 74%; \( P < .001 \)) and specialists (10.5% vs 5%; \( P < .001 \)) than SABA-treated patients. Along with the greater inpatient service use, SABA-treated patients also had significantly higher medical costs ($9333 vs $6637; \( P < .001 \)) and total health care costs ($10,253 vs $7642; \( P < .001 \)) during the treatment period than LABA-treated patients.

Health Service Utilization and Costs During the Follow-up Period

Unadjusted comparisons during the 6-month follow-up period revealed that SABA-treated patients were significantly more likely to have used OCS (15% vs 14%; \( P = .02 \)) and were significantly more likely to have a greater number of hospitalizations compared with LABA-treated patients (23% vs 16%; \( P < .001 \); Figure 3). However, LABA-treated patients...
patients were more likely to have had a greater number of physician visits (85% vs 65%; \( P < .001 \)), including specialist visits (6% vs 3%; \( P < .002 \)), than SABA-treated patients. Additionally, LABA-treated patients had significantly lower average medical costs ($6094 vs $8020; \( P = .012 \)) as well as lower average total health care costs from all causes compared with SABA-treated patients ($6928 vs $8806; \( P = .001 \); Figure 4).

After adjusting for potential confounders, the regression models revealed that LABA-treated patients had fewer inpatient days and lower overall total health care costs than SABA-treated patients. LABA-treated patients had 1.53 fewer inpatient days than SABA-treated patients (\( P = .043 \)) during the 6-month follow-up period. In addition, LABA-treated patients had 16% lower relative total health care costs than SABA-treated patients (\( P < .001 \)).

**DISCUSSION**

COPD is a chronic, progressive disease in which many patients experience episodic worsening of symptoms or exacerbations.\(^9,10\) On average, a patient with COPD experiences between fewer than one and three exacerbations per year.\(^{16-22}\) Exacerbations may increase patients’ risk of hospitalization up to 70% and result in a substantial economic burden.\(^8,23\) To mitigate the risk of preventable hospitalizations secondary to COPD exacerbations, global treatment guidelines for best practices recommend the use of long-acting bronchodilators, such as LABA, for maintenance treatment, and recommend its initiation prior to hospital discharge.\(^9,10\)

The findings from this real-world analysis lend support to these guidelines by showing that, among Medicare beneficiaries with COPD, treatment with a LABA resulted in fewer inpatient days and 16% lower total health care costs than treatment with a SABA.

The findings from this analysis are consistent with research in other smaller subpopulations of Medicare beneficiaries demonstrating the benefits of LABA maintenance therapy. Simoni-Wastila et al\(^{12}\) reported that managed Medicare patients with COPD who were treated with inhaled corticosteroids and LABA combination therapy had an 18% lower relative risk of COPD-related hospitalization and ED visit compared with patients treated with alternative therapies. Lower costs are associated with lower health care utilization subsequent to fewer incidents of COPD-related exacerbations.\(^{14}\) Similarly, Stuart et al\(^{11}\) found that patients receiving maintenance therapy that included
LABA use had average annual Medicare expenditures of approximately $3916 less than those for patients receiving no maintenance therapy. Those authors concluded that Medicare beneficiaries with COPD who failed to take the recommended maintenance medications for COPD were at increased risk for hospitalizations and corresponding increases in Medicare expenditures.

While there are numerous studies evaluating outcomes with LABA therapy, the majority have assessed readmission risk or patient outcomes after hospital discharge. To the best of our knowledge, our study is currently the only analysis that evaluates the impact of LABA and SABA therapy on hospital days and costs and in a fee-for-service Medicare population. Overall, the results of our study demonstrate that the use of LABA therapy provides value to Medicare in terms of health care cost savings compared with SABA therapy.

Previous analyses have evaluated the economic impact of COPD, including hospitalizations, on the Medicare system; however, the cost estimates vary. The average annual per-patient treatment costs for a Medicare COPD beneficiary have been estimated at $21,409 (excluding pharmacy costs).6 A prior report examining only the costs attributable to COPD estimated the average annual costs among Medicare enrollees at $6300.24 Dalal et al16 reported COPD-related costs of $7544 for hospitalization of Medicare patients with simple admissions; however, when exacerbations require intensive care unit admission and intubation, costs increased to $45,607 per hospitalization. Estimates of cost burden to the Medicare system vary across studies due to methodological differences, such as the year in which expenditures were incurred; COPD disease severity; Medicare sampling strategy (managed care, fee-for-service, or both); services included in cost computations; the duration of follow-up to capture costs; and factors used in adjusting costs to achieve comparability among study populations. Notwithstanding the variations in estimates of cost burden, the consistent message from the evidence-based literature is that reducing COPD exacerbation frequency and severity reduces the incidence of first-time and repeated COPD-related hospitalizations, resulting in considerable cost savings. Given that Medicare spending is projected to grow from $512 billion in 2014 to $858 billion in 2024, the implications of improved chronic disease management for conditions such as COPD, which ranks among the most costly to the Medicare system, are substantial.25,26

As is the case with all research, the results of the present study must be interpreted in light of certain limitations. First, findings from these retrospective claims of Medicare beneficiaries may not be generalizable to other patient populations with COPD. Second, retrospective database reviews are dependent on information recorded in medical records and may be subject to coding errors or data omissions. Third, the analysis did not control for use of inhaled steroids, a class of medication that has been shown to positively impact the parameters evaluated in this study (including COPD exacerbations and hospitalizations). Fourth, potential residual confounding could have arisen from factors such as COPD disease severity, current or past smoking status, and relevant clinical lab values (eg, spirometry test results, peak inspiratory flow rate), which were not available for examination.27 To mitigate the potential effects of such unmeasured confounders, multivariate analyses included several proxies of disease severity such as OCS use and number of physician visits. Fifth, the specific details of patients’ treatment persistence or adherence were not available, and poor patient treatment adherence has been associated with increased COPD exacerbations, excessive health service use, and increased COPD-related treatment costs.9,10,28,29 Sixth, the sample size was insufficient to restrict the analysis to a specific mode of treatment delivery and formulation (eg, comparison of nebulized LABA with nebulized SABA). Seventh, the study’s findings are based on a relatively short follow-up period of 6 months; therefore, the true long-term impact of treatment with a LABA, either alone or in combination therapy, remains unclear. Finally, the analysis examined the costs reimbursed by Medicare for services, which did not include out-of-pocket expenses or cost sharing by patients for services not covered by Medicare; therefore, it may underestimate the per-patient burden of COPD.

Despite these limitations, the results of this study examining the effects of recommended maintenance therapy with LABA on inpatient days and health care costs in the broader Medicare population ultimately provide two important additions to the literature. First, past studies have limited generalizability because they have primarily focused on Medicare managed care populations that constitute a specific population of only 30% of all Medicare enrollees.30 By contrast, the results presented in the current study are more generalizable to Medicare beneficiaries; approximately 70% of Medicare patients receive traditional fee-for-service benefits.30 Second, these results may guide improved clinical decision-making to the betterment of care for patients with COPD and with important implications for potential cost savings.

CONCLUSION

Findings from the present study suggest that initiating maintenance treatment for COPD with a LABA instead of a SABA is associated with a reduction in inpatient days and a reduction in total health care costs. These findings may have significant implications for health care cost savings with LABA treatment. The findings highlight the potential need for a major educational effort to disseminate evidence-based guidelines to health care providers and their patients on the long-term benefits of maintenance therapy for COPD management. In order to advance COPD
research that can enhance clinical decision-making specific to pharmacologic approaches to disease management, future studies on longer-term outcomes and differences in the modes of treatment delivery (eg, nebulizer vs dry-powder inhaler) for a LABA versus a SABA would be valuable. Additionally, studies comparing numerous timeframes and longer follow-up might also be valuable.

REFERENCES


