Cost and health care utilization in patients with asthma and high oral corticosteroid use


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**Title:** Cost and Healthcare Utilization in Patients with Asthma and High Oral Corticosteroid-Use

**Running header:** Cost and Utilization in High OCS Asthma Patients

**Authors:** Michael S. Broder, MD, MSHS¹; Karina Raimundo, MS²; Ka Ming Ngai, MD³; Eunice Chang, PhD¹; Noelle M. Griffin, PhD²; Liam G. Heaney, MD⁴

**Affiliations:**
1. Partnership for Health Analytic Research, LLC, Beverly Hills, CA
2. Genentech, Inc., South San Francisco, CA
3. Icahn School of Medicine at Mount Sinai, New York, NY
4. School of Medicine, Dentistry and Biomedical Sciences at Queen’s University Belfast, Belfast, Northern Ireland

**Corresponding author:**
Michael S. Broder, MD, MSHS
Partnership for Health Analytic Research, LLC
280 S. Beverly Dr., Suite 404, Beverly Hills, CA 90212
Phone: 310-858-9555; Fax: 310-858-9552; mbroder@pharllc.com

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**Abbreviations:**
AEs - adverse events; ANCOVA - analysis of covariance; ICS - inhaled corticosteroids; CCI - Charlson Comorbidity Index; COPD - chronic obstructive pulmonary disease; CI - confidence interval; ED - emergency department; EMRs - electronic medical records; EPR-3 - Expert Panel Report 3; HIPAA - Health Insurance Portability and Accountability Act; ICD-9-CM - International Classification of Diseases, Ninth Revision, Clinical Modification; OCS - oral corticosteroids; ORs - odd ratios; SABA - short-acting beta₂-agonist; SD – standard deviation.

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For patients with asthma, oral corticosteroids (OCS) have long been a component of disease management, although known adverse events (AEs) have led to a greater reliance on inhaled corticosteroids (ICS). OCS are also a well-established treatment for patients with chronic obstructive pulmonary disease (COPD). Even with treatment, OCS dependent patients have frequent, severe exacerbations and higher costs. We aimed to compare the clinical and economic outcomes between high-OCS and low-OCS users to identify evidence of the risks and benefits of OCS treatment in patients with asthma and in the subgroup with concomitant COPD.

This retrospective cohort study used a Health Insurance Portability and Accountability Act (HIPAA)-compliant database, containing de-identified data from both electronic medical records (EMRs) and administrative claims. The study was exempt from review by a human subjects protection committee.

We identified patients who had moderate to severe persistent asthma in 2013, based on definitions in The National Heart, Lung and Blood Institute Expert Panel Report 3 (EPR-3), and determined their OCS use. Using a validated method, we identified patients ≥18 years of age who received therapy Steps 4-6. High-OCS users were defined, based on prior research, as those with at least 1 OCS fill with days of supply ≥30 days or at least 6 bursts of OCS. Low-OCS users were those who had no OCS fills with days of supply ≥30 and ≤1 burst of OCS. A subgroup of patients with asthma + COPD patients was defined by the presence of a claim for COPD [491.x, 496.x, 492.x].
The main outcomes of interest were overall and asthma-related healthcare utilization and costs. Additional variables included demographics, smoking and COPD status, use of asthma medications, and evidence of poor asthma control (asthma-related hospitalization/ED visit, ≥2 OCS bursts, or ≥6 short-acting beta2-agonist (SABA) fills in 1 year). To compare the outcomes between high- and low-OCS users, analysis of covariance (ANCOVA) and logistic regression was used for continuous and dichotomous variables respectively. Adjustors were: patient demographics and characteristics, such as age group, gender, race, region, usual physician specialty, Charlson comorbidity index, pneumonia or influenza hospitalization, and EPR-3 step therapy. Adjusted means and odds ratios (ORs) with 95% confidence intervals (CI) were reported. Statistical analyses were performed using SAS® version 9.4 (SAS Institute, Cary, NC). All tests were two-sided with significance level of 0.05.

We identified 17,225 patients with moderate-to-severe persistent asthma. Of these, 3,117 were <18 years old; 8,852 did not receive EPR-3 therapy Steps 4-6; 871 were not continuously enrolled for the 12 months study period; and 1,030 did not meet the definition of either high or low-OCS use. The primary study cohort included 3,355 patients of whom 30.8% (n=1,035) patients had concomitant COPD.

Mean age was 58.8 years (SD 15.9), 66.6% were female, and 8.9% (n=300) were current smokers, while 29.2% (n=979) previously smoked. There were 517 (15.4%) patients classified as high-OCS users. Patients with asthma alone had mean age 56.8 years among high-OCS users and 54.6 years among low-OCS users. In asthma+COPD patients, mean ages were 67.1 and 67.9
years, respectively. High-OCS users had more all-cause office visits than low-OCS users overall (22.4 vs 14.9, p<.001) and in both the asthma-only and asthma+COPD subgroups. High-OCS users also had more hospitalizations and ED visits compared to low-OCS users (with the same pattern in subgroups). Mean total annual healthcare cost was $63,939 in high-OCS users and $27,494 (p<0.001) in low-OCS users. In patients with asthma alone, high-OCS users had a mean total annual healthcare cost of $40,933 compared to $19,365 for low-OCS (p<0.001). In asthma+COPD patients, high-OCS users had a mean total annual healthcare cost of $80,580 compared to $50,752 (p<0.001) for low-OCS.

In adjusted analyses, among patients with asthma alone, high-OCS users had higher odds of hospitalization than low-OCS users (all-cause OR 1.81, 95% CI 1.25-2.62; asthma-related OR 4.95, 95% CI 1.98-12.40) (Figure). They had an excess of $17,122 (SE $2,395, p<0.001) in total annual healthcare costs compared to low-OCS users. High-OCS users also had an excess of 7.2 (SE 0.9, p<0.001) annual office visits, and 2.0 (SE 0.2, p<0.001) annual asthma-related office visits. In asthma+COPD patients, OR for all-cause hospitalization in high- vs. low-OCS users was 2.03 (95% CI 1.52 - 2.71) and for asthma-related hospitalization was 3.94 (95% CI 2.32 - 6.68). High-OCS users had an excess of $23,180 (SE $5,422, p<0.001) in total annual healthcare costs compared to low-OCS users. They also had an excess of 3.9 (SE 0.9, p<0.001) annual office visits, and 0.8 (SE 0.2, p<0.001) annual asthma-related office visits.

OCS are associated with significant adverse effects.2-6 Efforts to reduce OCS use have focused on alternative therapies such as inhaled steroids. Despite the availability of these treatments, our study demonstrates that patients heavily treated with steroids, whether use is chronic (OCS fills ≥
30 days in a year) or sporadic (≥ 6 bursts in a year), have more than double the odds of all-cause hospitalizations and 4 times the odds of asthma-related hospitalizations compared to their low-OCS using counterparts, even after adjusting for multiple patient- and disease-related factors. Results were consistent whether examining patients with asthma alone or those with asthma+COPD. Costs are also dramatically higher in high-OCS users than low-OCS users—nearly double in patients with asthma alone and more than 40% higher in patients with asthma+COPD.

Limitations include the lack of a direct measure of disease severity, possible miscoding of both asthma and COPD, and missing data. Not all differences between groups could be adjusted for in models. High-OCS patients are likely to have worse underlying disease. They also may be insensitive to steroids or non-adherent to other therapy. Thus, our findings do not necessarily suggest that the use of OCS increases cost or utilization. Rather, in asthma patients with and without COPD, high-OCS exposure may be a marker for disease severity and lack of control with a resultant increase in resource use and costs. It may be that care for these patients by clinicians with significant expertise would decrease utilization.
123 References


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Tables and Figures

Figure: Adjusted Odds Ratio for Utilization – High vs Low OCS

Asthma Alone

- Rate of inpatient hospitalization: 1.81 (1.25 – 2.62)
- Rate of emergency department visits: 1.76 (1.20 – 2.40)
- Rate of asthma-related inpatient hospitalizations: 4.95 (1.98 – 12.40)
- Rate of asthma-related emergency department visits: 1.98 (0.84 – 4.64)
- Rate of 6 or more SABA fills: 2.36 (1.66 – 3.35)

Asthma+COPD

- Rate of inpatient hospitalization: 2.03 (1.52 – 2.71)
- Rate of emergency department visits: 1.31 (0.98 – 1.75)
- Rate of asthma-related inpatient hospitalizations: 3.94 (2.32 – 6.68)
- Rate of asthma-related emergency department visits: 4.15 (2.03 – 8.52)
- Rate of 6 or more SABA fills: 3.38 (2.51 – 4.56)

*Claims with primary diagnosis of asthma