Original Article

Utilization and Costs of Severe Uncontrolled Asthma in a Managed-Care Setting

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What is already known about this topic? The high utilization and cost of severe asthma is in disproportion to its frequency among persistent asthmatics, but little is known of the burden of severe uncontrolled asthma (SUA) in a managed-care setting.

What does this article add to our knowledge? The present study identified, characterized, and determined the clinical and economic burden of SUA compared with non-SUA in a cohort of adolescents and adults with persistent asthma in a large managed-care organization. It was found that patients with SUA comprised a minority of persistent asthmatics but had significantly more comorbidities, asthma exacerbations, utilization, and direct total and asthma-related costs in a follow-up year despite being dispensed more controller medications than patients with non-SUA.

How does this study impact current management guidelines? The study highlights that patients with SUA require more intensive interventions, including higher step-level care, better adherence, more specialist care, and specific attention to comorbidities to reduce asthma burden.

BACKGROUND: Clinical and economic burden of patients with severe uncontrolled asthma (SUA) in a real-world managed-care setting required further documentation.
OBJECTIVE: The objective of this study was to determine the characteristics, clinical, and economic burden of SUA in a managed-care setting.
METHODS: This observational study identified patients with persistent asthma aged 12 years or more (N = 25,935) using the International Classification of Diseases, 9th Revision asthma codes and Healthcare Effectiveness Data and Information Set administrative criteria. An SUA subgroup was identified when all of the following 3 criteria were met in 2012: (1) 2 or more asthma exacerbations; (2) 6 or more medium- or high-dose dispensed canisters of inhaled corticosteroid (ICS) as monotherapy or with long-acting β_2-agonist; and (3) 3 or more dispensed non-ICS controllers. Health care utilization and direct costs (all-cause and asthma-related) in 2013 were compared between SUA and non-SUA subgroups using multivariable regression.
RESULTS: Compared with the non-SUA subgroup (N = 25,350, 97.7%), the SUA subgroup (N = 585, 2.3%) at baseline was significantly older and had more comorbidities, asthma specialist care, controller medication dispensed, and asthma exacerbations. During follow-up, patients with SUA exhibited significantly more asthma exacerbations and short-acting β_2-agonist use, and higher all-cause and asthma-related costs than patients with non-SUA. The adjusted asthma-related average direct cost per patient at follow-up was significantly higher for SUA (mean ± SE) ($2325 ± $75) than non-SUA ($1261 ± $9) with an incremental cost of $1056 (95% CI, $907-$1205). Asthma drugs accounted for the major difference (incremental cost of $848/patient; 95% CI, $737-$959).
CONCLUSION: Increases and disparities in health care utilization and direct cost by SUA status suggest that patients with SUA require more intensive therapy, greater attention to adherence and comorbidities, more specialist care, and, possibly, personalized treatment approaches including novel biologic treatments. © **2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;■:■-■)**

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Abbreviations used
CI- Confidence interval
ED- Emergency department
GERD- Gastroesophageal reflux disease
ICD-9- The International Classification of Diseases, 9th Revision
ICS- Inhaled corticosteroids
KPSC- Kaiser Permanente Southern California
LABA- Long-acting β_2-agonist
LM- Leukotriene modifiers
MCO- Managed-care organization
OCS- Oral corticosteroids
PA- Persistent asthma
RR- Risk ratio
SABA- Short-acting β_2-agonists
SARP- Severe Asthma Research Program
SUCAS- Burden of Illness in Severe Uncontrolled Asthma Study

Most patients with asthma have mild to moderate disease that is generally treated with anti-inflammatory controllers such as low- to medium-dose inhaled corticosteroids (ICS) or leukotriene modifiers (LM) and rescue short-acting β_2-agonists (SABA). Patients whose asthma cannot be controlled with ICS alone are treated with the addition of other controllers (eg, long-acting β_2-agonists [LABA] and LM). However, approximately 5%-10% of patients with asthma have severe asthma[1] and only approximately 3.6% have severe refractory asthma.[2] Although severe asthma accounts for only a small portion of the asthmatic population, it causes considerable morbidity and disproportionate burden on health care resources, with a 1.7- to 4-fold higher direct asthma-related cost than for mild persistent asthma (PA).[3]

To improve the care of patients with severe asthma, the American Thoracic Society developed a set of criteria to characterize severe refractory asthma that take into consideration baseline asthma medication requirements, asthma exacerbations, and lung function among other criteria.[4] This definition of severe asthma has subsequently been adopted by the European Respiratory Society and World Health Organization.[5] Severe or difficult-to-treat asthma has been categorized into 5 specific clinical phenotypic clusters based on sex, ethnicity, asthma onset, obesity, biomarkers, lung function reversibility, aspirin sensitivity, controller medication use, and health care utilization by the Severe Asthma Research Program (SARP) in adults[6] and children,[7] the Epidemiology and Natural History of Asthma: Outcomes and Treatment Regimens study,[8] and the British Thoracic Society Severe Refractory Asthma Registry.[9] The relationship of these cluster phenotypes in severe asthma to outcomes has been reported in some studies in adults[8,10]; however, the SARP study found that they did not behave differently with respect to asthma-control—related outcomes.[11]

Among managed-care organizations (MCO), little is known about the characteristics and asthma burden of severe uncontrolled asthma (SUA) phenotypes with multiple asthma exacerbations and intensive asthma controller therapy. In addition, given the advent of new therapies directed at patients with severe or difficult-to-treat asthma, it is important to better understand the prevalence and characteristics of such patients in a general asthma population who may be in need of such novel treatments. To address these needs, we conducted the Burden of Illness in Severe UnControlled Asthma Study (SUCAS) to determine the clinical and economic burden of SUA in adolescents and adults in a real-world setting.

METHODS

Study design

SUCAS was an observational study that characterized and compared the clinical and economic burden of SUA to non-SUA in adolescent and adult patients. Pharmacy and health care utilization data were captured with the use of the Kaiser Permanente Southern California (KPSC) research data warehouse that allowed identification of adolescents and adults with PA. With waiver of written consent, SUCAS was approved by the KPSC Institutional Review Board.

Patients

Patients 12 years or older who had PA in the baseline year 2012 were identified based on an asthma International Classification of Diseases, 9th Revision (ICD-9) code (493.xx excluding 493.2, chronic obstructive asthma) and Healthcare Effectiveness Data and Information Set PA criteria[12] (Figure 1, *A*). Patients had to have continuous health plan enrollment and pharmacy benefit in 2012-2013 (no enrollment gap of >45 days within each calendar year),[13] and no chronic obstructive lung disease or other chronic conditions commonly applied to clinical trials (Figure 1, panel *A* legend). Patients with SUA were identified from the PA cohort if they met all of the following 3 criteria in 2012 (baseline period): (a) 2 or more asthma exacerbations (see below for definition), (b) 6 or more medium- or high-dose ICS canisters dispensed as monotherapy or in combination with LABA, and (c) 3 or more non-ICS controller canisters dispensed. The SUA definition was created to approximate using administrative data the severity inclusion criteria implemented in the pivotal trial of mepolizumab for severe refractory asthma (ClinicalTrials.gov NCT01691521). Patients with PA who did not meet the above criteria for SUA were classified as patients with non-SUA (Figure 1, panel *B* for the consort diagram).

Study measures characterizing clinical burdens

Address information was geocoded to the census block level and linked to census-based block group-level socioeconomic information that included head of household education level and household income. The asthma medication ratio, an administrative-data quality marker predictive of future asthma emergency department (ED) or hospital care, was defined as the number of dispensed asthma controller units (inhaled controller medication canisters or 30-day supplies of oral controller medications) divided by the total number of controller units and SABA canisters dispensed. A ratio of $\geq$0.5 is the minimum quality measure cutpoint for determining controller medication dispensing.[14] ICS products were categorized into low-, medium-, and high-dose, based on the calculated daily dosage and their individual potency using the estimated comparative daily dosages recommended by the Global Initiative for Asthma guideline for the diagnosis and management of adolescent and adult asthma.[15] Prescription of 9 or more units of controllers per year, equivalent to at least 75% adherence, was used as a proxy for adherence to treatment.[16] An asthma exacerbation was defined as an outpatient visit with uncontrolled asthma (ie, acute exacerbation, status asthmaticus, acute asthma attack, uncontrolled asthma, or asthmatic bronchitis indicated by KPSC-specific encounter codes) that required oral corticosteroids dispensed 7 days before or after the visit or an ED visit or hospitalization with a primary asthma diagnosis (ICD-9 493.xx). Asthma exacerbations at least 8 days after discharge