Comparative safety and costs of stepping down asthma medications in patients with controlled asthma

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Background: Limited data exist regarding outcomes after stepping down asthma medication.
Objective: We sought to compare the safety and costs of stepping down asthma controller medications with maintaining current treatment levels in patients with controlled asthma.
Methods: Patients with persistent asthma were identified from the US Medical Expenditure Panel Survey years 2000-2010. Each patient had Medical Expenditure Panel Survey data for 2 years, and measurement was divided into 5 periods of 4 to 5 months each. Eligibility for stepping down asthma controller medications included no hospitalizations or emergency department visits for asthma in periods 1 to 3 and no systemic corticosteroid and 3 or less rescue inhalers dispensed in periods 2 and 3. Steps were defined by type and dose of chronic asthma medication based on current guidelines when comparing period 4 with period 3. The primary outcome of complete asthma control in period 5 was defined as no asthma hospitalizations, emergency department visits, and dispensed systemic corticosteroids and 2 or fewer dispensed rescue inhalers. Multivariable analyses were conducted to assess safety and costs after step down compared with those who maintained the treatment level.
Results: Overall, 29.9% of patients meeting the inclusion criteria (n = 4235) were eligible for step down; 89.4% (95% CI, 86.4% to 92.4%) of those who stepped down had preserved asthma control compared with 83.5% (95% CI, 79.9% to 87.0%) of those who were similarly eligible for step down but maintained their treatment level. The average monthly asthma-related cost savings was $34.02/mo (95% CI, $5.42/mo to $61.24/mo) with step down compared with maintenance of the treatment level.
Conclusion: Stepping down asthma medications in those whose symptoms were controlled led to similar clinical outcomes at reduced cost compared with those who maintained their current treatment level. (J Allergy Clin Immunol 2016;137:1373-9.)

Key words: *Asthma, antiasthma agents, anti-inflammatory agents, step down, de-escalate, reduce, taper, withdraw, health services*

The goal of asthma management is to control symptoms and prevent exacerbations by using the least amount of medication. Accomplishing this goal requires patients and their providers to step down their medication and to evaluate whether taking a lower dose (or fewer overall controller medications) can produce similar outcomes as with more medication. Decisions about stepping down asthma medications depend in part on the patient's or provider's perceived safety risks of worsening asthma symptoms or exacerbations, and these estimates can be imprecise. The reasons why more patients do not step down their asthma medications when they appear eligible to do so are unclear but might be related to lack of precise risk estimates.

Although asthma guidelines suggest that stepping down medication should be considered if asthma is stable for 3 months or longer, the evidence ratings to support these recommendations range from grades A to D, depending on the specific step-down choice being considered.[1,2] Systematic reviews and meta-analyses of randomized controlled trials show that the risks of an asthma exacerbation is doubled over the subsequent 6 months when stopping low-dose inhaled corticosteroids (ICSs)[3]; however, this risk appears to be significantly lower if the ICS dose is decreased by 50% rather than stopped altogether.[4] Risks associated with stepping down to ICSs alone from a combination of ICSs and long acting β-agonists (LABAs) appear to be small, although the numbers of asthma exacerbation events captured in these trials were limited.[5] Outcomes from small noncontrolled studies in real-world settings have been favorable for stepping down asthma medications.[6] Data from real-world observational studies are needed to improve risk estimates for outcomes after stepping down asthma medications because real-world asthma samples differ substantially from those recruited into clinical trials.[7]

To further explore the indications and consequences of stepping down asthma medications in a real-world setting, we

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Abbreviations used
COPD: Chronic obstructive pulmonary disease
ED: Emergency department
EPR-3: National Asthma Education and Prevention Program Expert Panel Report 3
FPL: Federal poverty level
GERD: Gastroesophageal reflux disease
ICS: Inhaled corticosteroid
LABA: Long-acting β-agonist
MEPS: Medical Expenditure Panel Survey

performed an analysis of asthma outcomes after step down of asthma medications in a sample representative of the US population. Our hypothesis was that patients who were eligible for stepping down asthma medications and did step down would have similar clinical outcomes at a reduced cost compared with those eligible for stepping down asthma medications but who maintained their current level of asthma treatment while controlling for multiple key variables. The objective of this study was to compare the safety and costs of stepping down asthma controller medications with maintaining current treatment level in patients with controlled asthma.

METHODS

Sample

Patients were identified from the Medical Expenditure Panel Survey (MEPS), a 2-year panel survey administered through the Agency for Healthcare Research and Quality.[8] MEPS is representative of noninstitutionalized patients in the United States and administered to each patient for 2 consecutive years, with surveys administered 5 times 4 to 5 months apart. The MEPS is organized into the Household Component and the Insurance Component. We accessed the Household Component for this study, which is administered to both a single patient within each sampled household, as well as their medical providers. The MEPS Household Component is designed to be nationally representative of the US civilian noninstitutionalized population. The Household Component is organized into several data files. Our study used the following data files: Full-Year Consolidated Data, Medical Conditions, Prescribed Medications, Hospital Inpatient Visits, Emergency Room Visits, Outpatient Visits, and Office-Based Medical Provider Visits. Pertinent to our study, MEPS collects key health care use measures for asthma, including emergency department (ED) visits, hospitalizations, outpatient visits, and asthma medications use based on pharmacy dispensing. Data are deidentified and freely available, and institutional review board waivers were obtained from the authors' primary institutions. For this study, the most recent decade of the sample were used (2000-2010).

Cohort definitions

Our cohort was comprised of patients 4 years and older who had MEPS data available for both years of any of the 2-year panel surveys from 2000-2010 and who met the Healthcare Effectiveness Data and Information Set criteria for persistent asthma.[9] Patients with cystic fibrosis, bronchiectasis, and sarcoidosis were excluded.

Asthma medication categorization

Pharmacy claims data from MEPS serve as the basis for determining medication categorization. Asthma medications were categorized by determining an average "step level" (range, 0-6) based on the National Asthma Education and Prevention Program Expert Panel Report 3 (EPR-3)[2] description of discrete medication treatment steps. To distinguish patients who had controller medications dispensed but not enough to cover more than half of the days in the round to meet criteria for EPR-3 level 2, we created a step 1 level for the purposes of the study. We then created a step 0 level for the study that included patients who had no asthma controller medications dispensed during the entire panel round. The step 1 and step 0 categories created for this study diverge from the EPR-3 levels and were created solely for the purpose of differentiating those 2 categories of patients.

We first categorized each asthma medication into 3 groups: rescue medications, controller medications, or systemic corticosteroids (used both to classify into EPR-3 step 6 and as a surrogate for an asthma exacerbation). We created additional controller medication categories: leukotriene modifiers, including 5-lipoxygenase inhibitors; ICSs classified as low-dose ICSs, medium-dose ICSs, or high-dose ICSs based on EPR-3 tables for ICS potency[2]; combination ICSs and long-acting β-agonists (LABA) classified as low-dose ICS/LABA, medium-dose ICS/LABA, and high-dose ICS/LABA; omalizumab; theophylline; and mast cell stabilizers served as separate categories. For the purposes of this study, we defined EPR-3 step level 6 as 4 or more systemic corticosteroid treatments over the course of 1 panel period (periods were an average of 5 months) because there has not previously been an agreed upon definition of step 6 for administrative studies. We were unable to capture allergen immunotherapy in this database specifically as treatment for asthma. The average step level was calculated by defining each medication combination as a certain step level (eg, medium-dose ICS + LABA = step 4, low-dose ICS and leukotriene modifier = step 3), multiplying this by months at each step level, and then averaging over the panel round (approximately 5 months).

Step-down eligibility determination

The eligibility, step-change, and outcome determination in relation to the 5 periods comprising the 2-year survey are summarized in Fig 1. Determination of eligibility for stepwise adjustment of asthma medication (step down, step up, or neither) was based on periods 1 to 3 of the panel survey (approximately 14 months). Patients were considered eligible for stepping down asthma medications if all of the following were true: (1) they had no hospitalizations with asthma listed as a primary diagnosis during periods 1 to 3; (2) they had no ED visits with asthma listed in the first diagnostic position or systemic corticosteroid dispensing linked to an outpatient visit with asthma in the first or second diagnostic position in periods 2 to 3; (3) they had 3 or fewer rescue inhalers dispensed in periods 2 and 3; and (4) they were not at step level 0 in period 3. Patients at step level 0 in period 3 who otherwise met the first 3 stability criteria were assigned a separate category labeled "stable, but not eligible to step down because already at the lowest level." Patients at step level 6 in period 3 who met the eligibility criteria for stepping up asthma medications were assigned a separate category labeled "unstable, but not eligible for step up."

These eligibility criteria were developed based on EPR-3 guidelines of asthma stability in risk and impairment domains; a previous definition of being "eligible for step down of asthma medicines" has not been previously reported by using administrative data. Asthma exacerbations represent the risk domain, whereas the number of rescue inhalers dispensed has been validated by using administrative data as a measure for the impairment domain.[10] Patients were considered eligible for stepping up asthma medications if during periods 1 to 3 they had (1) 2 or more asthma exacerbations or (2) 7 or more rescue inhalers dispensed. Patients who were neither eligible for stepping up nor stepping down asthma medications were categorized into a "not eligible for change" category.

Step-change determination

Stepping down asthma medications was defined by comparing periods 4 and 3 of the panel survey and finding a decrease in 1 or more EPR-3 steps, stepping up asthma medications was defined as an increase in 1 or more EPR-3 steps, and no stepwise adjustment ("no change") was defined as not meeting the criteria for stepping down or stepping up asthma medications.

Comparison groups

In this analysis the primary comparison is between patients who were eligible to step down asthma medications and did so and those who were