Characteristics of Initiators of Asthma Maintenance Medications in 10 Health Care Populations

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CONFLICT OF INTEREST STATEMENT

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ABSTRACT

Background: Level of asthma control can be a source of confounding in observational studies of medication-related asthma mortality. As part of a collaborative feasibility study of medication-related asthma mortality, we enumerated use of asthma medications across a distributed network of health care databases and explored variability in asthma control indicators among treatment groups.

Objective: Describe characteristics of patients initiating different asthma maintenance medications and examine variation across 10 data sources.

Methods: In a cohort (N = 994,627) of persistent asthma patients aged 4-100 years enrolled at 10 United States health plans (2001-2010), use of asthma medications was categorized. New use was first use of any study-defined asthma maintenance treatment medication on or after cohort entry without any prior recorded exposure of interest. We tabulated the frequency of three indicators of asthma control in the 6 months before new exposure in each treatment group, in the pooled cohort and across data sources.

Results: A total of 144,574 persons (15%) had new use: 42% aged ≥ 40 years, 56% female. The three most common treatments were salmeterol+fluticasone propionate (ADVAIR), n = 51,840; inhaled corticosteroid monotherapy (ICS-m), n = 53,798; and ICS+leukotriene receptor agonist (LTRA), n = 26,994. ADVAIR users were older (52% ≥ 40 years vs. 33% ICS-m and 32% ICS+LTRA); this was consistent across the data sources. Overall, 13% had ≥ 1 asthma hospital stay or emergency room visit, ranging across data sources by exposure: ADVAIR, 8%-17%; ICS-m, 7%-16%; ICS+LTRA, 9%-14%. Overall, 33% had ≥ 1 oral corticosteroid dispensing—ADVAIR, 27%-42%; ICS-m, 26%-40%; ICS+LTRA, 27%-52%—and 44% had ≥ 2 short-acting beta-agonist dispensings—ADVAIR, 44%-55%; ICS-m, 49%-66%; ICS+LTRA, 31%-45%.

Conclusions: The observed variation in characteristics of exposure groups across data sources was beyond what would be expected from differences in size and demographics by health plan. Such information will be used in developing adjustment strategies for future pooled analyses of medication-related asthma mortality.

INTRODUCTION

- The goal of pharmacological treatment for asthma is to control asthma by reducing airway inflammation and treating bronchoconstriction. Medications for asthma are classified as *controllers or maintenance medications* (taken daily on a long-term basis and achieve control largely through anti-inflammatory effects) and relievers (used on an as-needed basis for rapid reversal of bronchoconstriction and symptom relief).[1]
- Asthma treatment guidelines are based on treatment steps defined by the number, dose, and strength of controller medications.[1] Indicators of poor clinical control of asthma include frequent need for reliever/rescue treatment, frequent exacerbations, or hospital admissions for asthma.[1] Treatment is stepped up or down based on how well asthma is controlled in a given patient.
- Level of asthma control can be an important source of confounding in observational studies of medication-related asthma mortality. The decision to initiate treatment with long-acting beta-agonist (LABA) therapy combined with an inhaled corticosteroid (ICS) is often related to lack of asthma control while using other therapies; therefore, any study of the risk of asthma mortality related to LABA therapy must adequately control for such confounding. However, clinical indicators of asthma control are difficult to measure directly in administrative claims databases.
- The Asthma Safety Observational Study (ASSESS) is a feasibility study designed to quantify the available sample size and precision to evaluate whether dispensing of LABA combined with an inhaled corticosteroid (LABA+ICS) is associated with an increased risk of asthma mortality.

OBJECTIVE

- To describe characteristics of patients initiating different asthma maintenance medications and examine variation across 10 data sources in the US, in anticipation of proposed future multivariable pooled analyses.

METHODS

- ASSESS is a retrospective cohort study using medical claims data or electronic medical records from 10 large insurers/data partners. Data were extracted and transformed into a common data model by each data partner based on the Food and Drug Administration Mini-Sentinel data model.[2] Data are analyzed under a distributed data approach, with programming code supplied by a central coordinating center.
- From an initial extract of individuals with claims evidence of asthma (general asthma cohort), a persistent asthma cohort (PAC) was constructed.
- Criteria for the PAC were as follows:
  - Had four or more dispensings for any asthma medication during any 12-month interval in the study period during which the individual had continuous enrollment in a health plan (both medical and pharmacy/prescription drug coverage).
  - Had at least one outpatient, inpatient, or emergency department record with a diagnosis of asthma (ICD-9-CM code 493.x) and with a date of service, visit date, or admission date between January 1, 2000, and the date of the fourth qualifying dispensing of an asthma medication (inclusive). The date of the fourth qualifying asthma medication was the asthma index date (date of cohort entry).
  - Aged 4 years or older
  - Had at least 12 months of continuous enrollment in a health plan (both medical and pharmacy coverage) as of the asthma index date.
- Patients in the PAC were followed until the earliest of (1) start of an enrollment gap greater than 35 days, (2) end of enrollment, (3) date of death, (4) date of dispensing of a prescription for omalizumab, or (5) end of study period (December 31, 2010).
- New use of a category of asthma medication was defined as the first new dispensing of a medication in any of eight exposure categories on or after the asthma index date without any prior recorded dispensing for the exposure of interest. Exposures of interest were salmeterol+fluticasone propionate in a single inhaler (ADVAIR), formoterol+budesonide in a single inhaler (Symbicort), salmeterol+ICS in separate inhalers, formoterol+ICS in separate inhalers, ICS-m, ICS+LTRA, ICS+theophylline, and ICS+other non-LABA controller).
- Three indicators of asthma control were examined in the 6 months before initiation of new use of asthma medication:
  - At least two short-acting beta-agonist (SABA) dispensings (indicator of frequent use of reliever medication)
  - At least one oral corticosteroid dispensing (indicator of asthma exacerbation)
  - At least one asthma hospital stay or emergency room visit (indicator of serious asthma exacerbation)
- The three most common categories of asthma controller medications were included in the current analysis:
  - ICS-m
  - ADVAIR
  - ICS+LTRA
- Analyses were descriptive. The frequency of each indicator was tabulated in the 6 months before new exposure to each of the three exposure categories. Frequencies were tabulated in the pooled cohort overall and across the 10 data sources.

RESULTS

- A total of 994,627 patients entered the PAC between January 1, 2001, and December 31, 2010. Of these, 56% were female, and 42% were aged 40 years or older. A total of 144,574 patients (15%) had new use of any of the asthma medications of interest after cohort entry. Variation was noted across the 10 data partners in the age distribution and the proportion with new use (Table 1). Overall, more than half of the PAC were female (56%), and this varied somewhat across data partners, from 52% to 59% (Table 1).
- Of the 144,574 patients with new use, the three most common treatments were ICS-m (n = 53,798), ADVAIR (n = 51,840), and ICS+LTRA (n = 26,994).
- ADVAIR new users were older, and a higher proportion were female than the other two exposure categories; this was consistent across the data partners (Table 2).

Table 1. Number of Patients in the PAC, Age and Sex at Cohort Entry, and New Use of Any Asthma Exposure of Interest Overall and by Data Partner

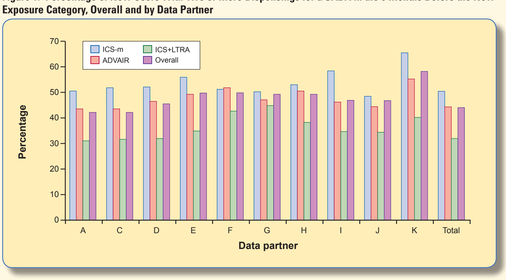
Data Partner	Patients in PAC	Characteristics (%)		New Use of Any Asthma Exposure of Interest (%)
		Age ≥ 40 years	Female	
A	348,367	45	57	14
C	311,063	42	56	14
D	42,985	36	54	12
E	46,131	38	56	15
F	8,976	34	56	19
G	13,155	28	52	20
H	15,666	38	59	16
I	5,162	33	54	20
J	191,599	40	54	15
K	11,523	54	57	19
Total	994,627	42	56	15

Table 2. Age and Sex by New Medication Exposure Category

Exposure Category	Age ≥ 40 Years		Female	
	N	%	n	%
ICS-m	17,857	33	28,349	53
ADVAIR	27,035	52	30,370	59
ICS+LTRA	8,563	32	14,619	54
Overall	60,782	42	80,590	56

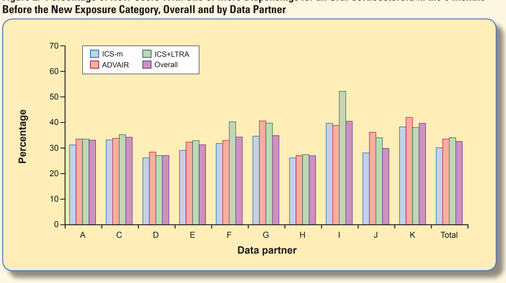
Figures 1 through 3 display the percentage of initiators of each of the three asthma medications of interest with each of the indicators of asthma control in the 6 months before new use, in the PAC overall and by medication category within each data partner.

Figure 1. Percentage of New Users With Two or More Dispensings for a SABA in the 6 Months Before the New Exposure Category, Overall and by Data Partner



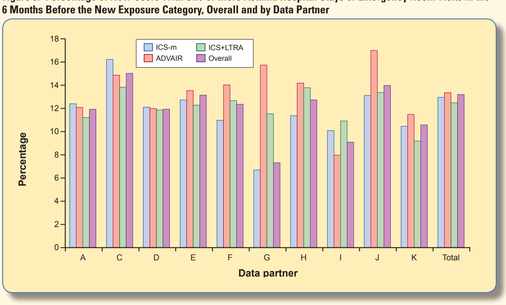
- Overall, 44% of new users had at least two SABA dispensings in the 6 months before initiation of new exposure. This percentage varied by type of exposure: ICS-m, 51%; ADVAIR, 44%; ICS+LTRA, 32%. Variation also was observed within exposure across data sources: ICS-m, 49%-66%; ADVAIR, 44%-55%; ICS+LTRA, 31%-45%.

Figure 2. Percentage of New Users With One or More Dispensings for an Oral Corticosteroid in the 6 Months Before the New Exposure Category, Overall and by Data Partner



- Overall, 33% of new users had at least one oral corticosteroid dispensing in the 6 months before initiation of new exposure. This percentage did not vary greatly by exposure category but varied within exposure across data sources: ICS-m, 26%-40%; ADVAIR, 27%-42%; ICS+LTRA, 27%-52%.

Figure 3. Percentage of New Users With One or More Asthma Hospital Stays or Emergency Room Visits in the 6 Months Before the New Exposure Category, Overall and by Data Partner



- Overall, 13% of new users had at least one hospital stay or emergency room visit for asthma in the 6 months before initiation of the new exposure. This percentage did not vary greatly by type of exposure, but variation was noted within exposure across data sources: ICS-m, 7%-16%; ADVAIR, 8%-17%; ICS+LTRA, 9%-14%.

CONCLUSIONS

- In the PAC, new users of ADVAIR were older than new users of the other medication groups; thus, age could be an important confounder of the relation between ADVAIR and asthma mortality in pooled multivariable analyses.
- The only indicator of asthma control that varied substantially by exposure category was use of SABAs, which was less frequent in the 6 months before new use of ICS+LTRA than ADVAIR or ICS-m.
- Variation in frequency of all three indicators was observed across the 10 data partners within exposure group.
- The current analyses are a first step in improved understanding of potential confounding when evaluating adverse asthma outcomes. Such information will be useful in developing adjustment strategies for proposed future pooled multivariable analyses of the relation between LABA+ICS therapy and asthma mortality in ASSESS.

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