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Seasonal Patterns of Asthma Medication Fills among Diverse Populations of the United States

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Abstract

Objective: Nonadherence to controller and overuse of reliever asthma medications are associated with exacerbations. We aimed to determine patterns of seasonal asthma medication use and to identify time period(s) during which interventions to improve medication adherence could reduce asthma morbidity.

Methods: We conducted a retrospective cohort study of asthmatics 4–50 years and enrolled in three diverse health insurance plans. Seasonal patterns of medications were reported by monthly

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Author contributions

KNT participated in study design and results interpretation, drafted and edited the manuscript. TG participated study design, analyzed data, interpreted the results, and edited the manuscript. PW led the study design, was involved in data analysis and results interpretation, edited the manuscript, and obtained funding for the study. TVH oversaw the study design, was involved in data analysis and results interpretation, edited the manuscript, and obtained funding for the study. RLL, AME, CS, NMS, ACW, CI, MGB, EM, JM, and EKL participated in study design and results interpretation, and edited the manuscript.

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prescription fill rates per 1000 individuals with asthma from 1998 to 2013, and stratified by healthcare plan, sex, and age.

Results: There was a distinct and consistent seasonal fill pattern for all asthma medications. The lowest fill rate was observed in the month of July. Fills increased in the autumn and remained high throughout the winter and spring. Compared with the month of May with high medication fills, July represented a relative decrease of fills ranging from 13% (rate ratio, RR: 0.87, 95% confidence interval, 95%CI: 0.72–1.04) for combination of inhaled corticosteroids (ICS) + long acting beta agonists (LABA) to 45% (RR: 0.55, 95%CI: 0.49–0.61) for oral corticosteroids. Such seasonal pattern was observed each year across the 16-year study period, among healthcare plans, sexes, and ages. LABA containing control medications (ICS+LABA and LABA) fills rates were more prevalent in older asthmatics, while leukotriene receptor antagonists were more prevalent in the younger population.

Conclusions: A seasonal pattern of asthma medication fills rate likely represents a reactive response to a loss of disease control and increased symptoms. Adherence to and consistent use of asthma medications among individuals who use medications in reaction to seasonal exacerbations might be a key component in reducing the risk of asthma exacerbations.

Keywords

asthma; medication fills; seasonality; medication adherence; exacerbations

Introduction

Asthma is one of the most common chronic respiratory diseases in the United States and around the world, causing significant morbidity and mortality.^{1,2} In 2010, asthma exacerbations resulted in 14.2 million outpatient visits, 1.8 million emergency room visits, 439,400 hospitalizations, and 4,404 deaths in the United States.³ There is a distinct seasonal pattern in asthma exacerbations, particularly among children, with September being the peak in the Northern Hemisphere.^{4,5}

Asthma controller medications (inhaled corticosteroids [ICS], long acting beta agonists [LABAs], combination of ICS plus LABA [ICS+LABA], and leukotriene receptor antagonists [LTRAs]) are effective in preventing asthma exacerbations; however, adherence to controller medication remains problematic.^{6–10} Underuse of long-term controller medications and overuse of reliever medications (short acting beta agonists [SABAs] and oral corticosteroids [OCS]) for symptoms and/or asthma exacerbations characterize a significant number of asthma exacerbations.¹¹ Further, asthma controller medication use has been shown to be reactive in response to asthma exacerbations, rather than being used to prevent them.^{5,12}

The objective of this study was to examine the seasonal pattern of all classes of asthma medication fills among large, demographically and geographically diverse populations in the United States. Results of the study might shed some light on identifying high risk populations for targeted interventions that aim to reduce the risk of asthma exacerbations.

Methods

Study design and population

We conducted a retrospective cohort study of individuals with asthma ages 4 to 50 years who were continuously enrolled in five distinct healthcare systems. The healthcare systems included: the Department of Defense Military Health System (MHS), 2003–2013; the Tennessee Medicaid program (Medicaid), 1998–2012; and three large Integrated Healthcare Delivery Systems (IHCDs) of the Population-Based Effectiveness in Asthma and Lung Diseases (PEAL) network, 2004–2010, including Harvard Pilgrim Health Care, Kaiser Permanente Georgia, and Kaiser Permanente Northern California. The institutional review board at each site approved the study.

We included individuals with asthma who were enrolled in one of the above healthcare plans for at least half a year. Individuals were included if they had at least one asthma-related exacerbation during the study period and/or had at least two separate dispensing events of asthma specific medications within any six month period. Asthma-related healthcare encounters were defined by 1) a hospitalization or emergency department visit with a primary diagnosis of 493.xx; 2) a hospitalization or emergency department visit with a non-primary diagnosis of asthma along with any other respiratory diagnosis (Data supplement, Table E1); 3) an outpatient visit with a diagnosis of asthma requiring at least a 3 day supply of OCS; and 4) an outpatient visit with an asthma-specific exacerbation code 493.92. Asthma-specific medication use included ICS, LABA, ICS+LABA, LTRAs, and/or at least a 5 day supply of OCS. Individuals with congenital heart disease (ICD9 codes 428.x and 429.x), bronchopulmonary dysplasia (ICD9 code 770.7), chronic obstructive pulmonary disease (ICD9 codes 496, 518.83, 786.05, 786.09, and 799.02), congenital anomaly (ICD9 codes 740.x-759.x), chronic bronchitis and emphysema (ICD9 codes 490, 491, 492, 518.1, and 518.2), bronchiectasis (ICD9 codes 494 and 748.61), cystic fibrosis (ICD9 code 277), pulmonary hypertension (ICD9 codes 416, 415.0, 417.8, and 417.9), immunodeficiency (ICD9 code 279), and neurological disorders (ICD9 codes 343 and 359) were excluded from the study population.

Statistical analysis

Demographic characteristics of individuals with asthma who were enrolled in each healthcare plan were summarized using median and interquartile ranges [IQR, 25th, 75th], or frequency and percent as appropriate. The seasonal fill patterns of asthma-specific medications included controller medications: ICS, LABA, ICS+LABA, and LTRA; and reliever medications: SABA and OCS. Monthly medication fill rates per 1000 person were calculated by dividing the number of fills of asthma medications with the total number of persons eligible per health plan for the calendar year and month. Monthly medication fill rates were estimated for the aggregate cohort and for each health plan (MHS, Medicaid, and IHCDs), by sex and age. Individuals contributed to the monthly rates based on their age at each particular month and were classified into three age groups: 4 to 11 years, 12–17 years, and 18 to 50 years. Analyses were performed with SAS version 9.3 and R version 3.3.0.^{13,14}

Results

A total of 580,020 individuals with asthma were identified in the three populations: 264,987 (45.7%) from the MHS, 84,259 (14.5%) from Medicaid, and 230,774 (39.8%) from IHCDS. Fifty-three percent of the total study population was female. Among the 435,120 (75.0%) individuals for whom race data was available, 64.2% were identified as Caucasians, 22.1% as African Americans, and 13.7% as Other (Table 1).

Overall, SABA was the most commonly filled asthma medication category (Figure 1 and Data supplement, Figure E1). The average fill rate (per 1000 individuals with asthma) of SABA was 66.2 in the MHS, 75.4 in Medicaid, and 100.9 in IHCDS, respectively. Inhaled controller medications containing a corticosteroid (ICS or ICS+LABA) were the most common controllers prescribed for individuals enrolled in MHS (50.0 per 1000) and IHCDS (85.5 per 1000) while LTRA were the most commonly filled controller medication for individuals enrolled in Medicaid (44.1 per 1000). IHCDS inhaled controller prescriptions were heavily weighted towards ICS (70.4 per 1000) while MHS prescriptions were split between ICS and ICS+LABA (28.8 and 21.2 per 1000, respectively). LABA as a single agent was the least filled controller medication in all three healthcare plans (1.0 per 1000 in the MHS, 0.8 per 1000 in Medicaid, and 4.3 per 1000 in IHCDS), and its use decreased over time, with the highest fill rate in the IHCDS. Medicaid had the least use of inhaled corticosteroids, whether ICS alone (22.3 per 1000) or as combination therapy (5.7 per 1000).

There was a consistent seasonal pattern of controller and reliever asthma medication fills. Asthma medication fill rates were lowest in the summer months, increased in the autumn, and remained high throughout the winter months into spring (November through May). July had the lowest fill rate for all asthma medications, while the month with the highest fill rate varied by medication type (Figure 1 and Data supplement Figure E1). All controller medications and SABAs had the highest fill rates during spring (April or May), while OCS consistently had the highest fill rate in February. Overall, compared with the calendar month of May when asthma medications fills were high, July represents a relative decrease of 41% for ICS (rate ratio, RR: 0.59, 95%CI: 0.41–0.85), 13% for ICS+LABA (RR: 0.87, 95%CI: 0.72–1.04), 18% for LABA (RR: 0.82, 95%CI: 0.45–1.49), 19% for LTRA (RR: 0.81, 95%CI: 0.65–1.02), 31% for SABA (RR: 0.69, 95%CI: 0.60–0.81), and 45% for OCS (RR: 0.55, 95%CI: 0.49–0.61). The seasonal pattern of each asthma medication fill was consistent over the entire 16-year study period, across all healthcare plans (Figure 2), and by sex (Data supplement, Figure E2). When we combined all controllers (ICS, ICS+LABA, LABA, and LTRA) and all relievers (SABA and OCS) together, the seasonal pattern of asthma medication fills did not change (Figure 3).

There were similar seasonal patterns of asthma medication fill rates observed across the three age groups (4–11 years, 12–17 years, and 18–50 years), with decreased fill rates in summer and increased rates in winter and spring (Data supplement, Figure E3). SABA fill rates indicated a bimodal pattern among 4–11 and 12–17 year age groups. While rates were lowest in these two age groups in July, fill rates peaked in September and spring. We additionally observed a differential fill of asthma controller medications across age groups. LABA containing medications (ICS+LABA and LABA) were more prevalent in older

asthmatics, with lowest fill rates in children 4–11 years. Use of LTRA, on the other hand, was more prevalent in the younger population. Fill rates of LTRA decreased with advancing age. ICS and OCS fill rates were highest in 4–11 and 18–50 year age groups compared with individuals in the 12–17 year age group. Lastly, fills of SABAs were similar across the three age groups.

Despite a consistent seasonal pattern of asthma medications over the study period, medication fill rates changed over time and varied by healthcare system (Figure 2). From 2004 to 2010, we observed a decrease in individual ICS and LABA fill rates, an increase in combined ICS+LABA fill rates, and a relatively stable LTRA fill rates in IHCDS population. MHS data showed ICS fill rates decreased sharply during late 2004/early 2005 and remained low, while both ICS+LABA and LABA fills decreased consistently from 2005 to 2013.. Lastly, we observed consistently low fill rates of ICS, LABA, and ICS+LABA in Medicaid individuals from 1998 to 2012. ICS+LABA fill rates in Medicaid started to increase soon after approval in us market (in 2000),¹⁵ but sharply decreased after 2005. LTRA fill rates in Medicaid, and similar to the MHS populations, had a rapid increase prior to 2005, and remained high. For reliever medications, SABA fill rates showed a downward trend in MHS while it was relatively stable in Medicaid and IHCDS over the periods studied. There was an upward trend in OCS fill rates in the Medicaid population, most notable after 2004. This trend was not noted in the IHCDS and MHS.

Discussion

We observed consistent seasonal patterns of asthma medication fill rates among large, demographically and geographically diverse populations over a 16-year study period. This study is novel in identifying reactive asthma medication fill patterns that closely coincide with known seasonal disease exacerbations for both controller and reliever medications.^{5,16} Medication fills for both controller and reliever asthma medications started to increase beginning in late summer/early autumn in any given year and across all healthcare plans, and peaked during the winter and spring months. The lowest fill rate for all medications was observed in the month of July. These seasonal patterns appear consistently across the study period even when type of controller use changed and when all controllers and reliever medications were combined together, suggesting the pattern is unlikely due to medication switching. We additionally observed a second peak of SABA fills in September in young children and adolescents, which may correspond to the “September asthma epidemic”.⁵ The seasonal pattern of asthma medication fills, both relievers and controllers, coincides with previously described seasonal patterns of asthma exacerbations, suggesting that prescription filling is reactive, following loss of disease control, rather than preventive.^{5,12,16} Our results are also consistent with the previous findings that fill rates for ICS and SABA were low during summer months followed by a rapid increase in prescription fills in the autumn in Canadian children, as well as a reactive filling pattern of ICS and OCS in relationship to asthma exacerbations.^{5,12} ICS fill rates trended with asthma exacerbations and overwhelmingly ICS and OCS fills occurred on the same day.

The reactive fill pattern of reliever medications is a reflection of seasonal patterns of asthma disease exacerbations; however, the reactive fill pattern of controller medications is

problematic if the goal of such medications is the prevention of asthma exacerbations and maintaining disease control. Asthma controller medications (ICS, ICS+LABA, LTRA, and LABA) have all been demonstrated to be effective in reducing disease exacerbations, and adherence to these medications is known to reduce morbidity and mortality from asthma.^{17–20} Concerns regarding increases in severe exacerbations and morbidity have prompted the most recent asthma clinical guidelines to no longer consider LABA an adequate controller medication in the absence of an ICS.²¹ The overall low use and seasonal use of controller medications demonstrated in our study may in part explain the increasing burden of asthma exacerbations.^{22–26} This data provides a means of identifying high-risk individuals in whom promoting proactive regular use of controller medications prior to peaks in use could be an effective way in reducing the risk of disease exacerbation and overall asthma healthcare burden.²⁶

Of additional interest, we observed changes in patterns of medication fills over the 16-year study period, which likely reflected changes in asthma guidelines, new medication approvals, medication safety concerns/black box warnings, and changes in healthcare system formularies and policies. However, despite all these changes in asthma medication use over time, there were consistent seasonal patterns seen over all of these years in all 3 healthcare systems (see Data supplement, Appendix E1 for additional discussions).

Strengths of our study include the use of large healthcare plans representing demographically and geographically diverse US populations. Our study population is representative of public, private, and military healthcare plans. Our data also spans a 16-year study period to discern the seasonal medication fill patterns over time. The multi-year aggregate estimations minimize year-to-year random variations. Further, the 16-year study period allows us to detect temporal changes in response to guideline recommendations, addition of new medications, adherence to controller medications, and/or preferences for certain medication by specific populations. Our study has limitations that also need to be considered. This study is ecological, and although we observed a seasonal pattern of asthma medication fills coinciding with the seasonal pattern of asthma exacerbations, a causal relationship between medication fills and exacerbations cannot be determined. Second, this study is based on the medication fill data and we do not know whether those who filled prescriptions took the medication and whether those who took medication inhaled it correctly, however, filling a prescription is the first step of pharmacotherapy in disease management^{27,28}. Although free samples from physicians are possible, it likely constitutes a very small proportion of medications as our study population has the full prescription coverage. It is unlikely that the seasonal variations observed in this study are due to free samples. Additional limitation includes potential impact of differential prescribing preference by brand and by specialty of the prescribing physician.

Conclusions

Asthma controller and reliever medication fills follow a seasonal pattern that is consistent across diverse study populations, geographic regions, and over more than a decade study period. A reactive fill pattern of controller medications tracking with asthma exacerbations likely represents missed opportunities for targeted seasonal asthma exacerbation prevention.

Increasing rates of asthma controller fills prior to the peaks, and appropriate use of and adherence to asthma controller medications could reduce the risk of asthma exacerbations. Asthma medication fill patterns may help to identify at-risk populations and critical time periods for targeted intervention to prevent and/or reduce the risk of seasonal asthma exacerbations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Seasonal patterns of asthma medication fill rates by medication type and healthcare plan, aggregated across the study periods (MHS: 2003–2013; Medicaid 1998–2012; and IHCDS: 2004–2010).

Figure 2.

Trend of asthma medication seasonal patterns and fill rates by healthcare plan, across the study periods (MHS: 2003–2013; Medicaid: 1998–2012; and IHCDs: 2004–2010).

Figure 3. Seasonal patterns of combined asthma controller and reliever medications by healthcare plan, aggregated across the study periods (MHS: 2003–2013; Medicaid: 1998–2012; and IHCDS: 2004–2010).

Table 1.

Demographics of the study population.

Characteristics	MHS, 2003–2013 (n=264,987)	Medicaid, 1998–2012 (n=84,259)	IHCDS, 2004–2010 (n=230,774)
Birth Year [*]			
1948–1970	29,978 (11.3%)	4,939 (5.9%)	60,972 (26.4%)
1971–1990	97,355 (36.7%)	18,842 (22.4%)	75,351 (32.6%)
1991–2009	137,654 (51.9%)	60,478 (71.8%)	94,451 (40.9%)
Race (n=435, 120) [‡]			
African American	47,873 (21.8%)	28,696 (34.8%)	19,489 (14.6%)
Caucasian	137,253 (62.6%)	48,318 (58.5%)	93,828 (70.5%)
Other	32,471 (15.6%)	5,573 (6.8%)	19,819 (14.9%)
Sex			
Female	143,172 (54%)	41,973 (50%)	121,725 (53%)
Male	121,815 (46%)	42,881 (50%)	109,041 (47%)
Individuals' asthma study entry criteria (in addition to ICD-9 Dx code 493.xx):			
Healthcare visit for asthma exacerbation only	45,769 (17%)	11,455 (14%)	32,617 (14%)
Asthma medication fill only	125,425 (47%)	29,835 (35%)	120,182 (52%)
Both healthcare visit for asthma exacerbation and medication fill	93,793 (35%)	42,969 (51%)	77,975 (34%)

^{*} Because the study periods varied for each healthcare system, individuals born between 1953 to 2009 and enrolled in the Department of Defense Military Health System (MHS), those born between 1948 to 2008 and enrolled in the Tennessee Medicaid program (Medicaid), and those born between 1954 to 2006 and enrolled in three large Integrated Healthcare Delivery Systems (IHCDS) of the Population-Based Effectiveness in Asthma and Lung Diseases (PEAL) network were eligible to be included in the cohort.

[‡] Race information was not available for 45,590 (17.2%) of MHS, 1,672 (2.0%) of Medicaid, and 97,638 (42.3%) of IHCDS subjects, respectively.