
Seasonal patterns in health care use and pharmaceutical claims for asthma prescriptions for preschool- and school-aged children

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Background: In children, hospitalization for asthma is reported to have a distinct seasonal pattern with peaks coincident with the start of school. Although guidelines indicate that asthma controller medications should be used daily, there is limited information on actual seasonal patterns of medication use.

Objective: To describe seasonal patterns of asthma-related health care use and asthma controller and reliever medication claims in children.

Methods: An ecological analysis was conducted of data collected from records for children aged 2 to 12 years from 2002 through 2004 from an automated research database of insurance claims from a large US health care plan. Seasonal patterns for health care use and estimates of prescription asthma controller and reliever use were determined for preschool-aged children (aged 2–5 years) and school-aged children (aged 6–12 years). Rates were constructed by week; deviations from annual mean rates were used to determine peaks in use. Results were confirmed using Poisson regression models, modeling for rates within age group, with factors for week, year, and regions.

Results: Emergency department and outpatient visits and hospitalizations were lowest during summer; rates increased beginning in September, peaking in October or November. Asthma controller and reliever medication claims increased beginning in September, peaking in December. Rates also were elevated in February.

Conclusions: The data suggest that children who reduce their asthma medications during the summer do not resume taking medications until signs or symptoms of asthma worsen. The summer hiatus and other factors may contribute to seasonal increases in health care use and in asthma medication prescriptions, particularly in the fall.

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INTRODUCTION

Asthma is the most common chronic health condition in children. In 2005, nearly 9% of children in the United States younger than 18 years were diagnosed as having asthma.^{1,2} Asthma is associated with substantial health care use, including urgent physician and emergency department (ED) visits, hospitalization, and treatment with additional medications.

Asthma-related health care use has been documented to have seasonal patterns among preschool- and school-aged children, with a sharp peak around the start of the school year and lower rates in the summer months.^{3–8} It is not clear what triggers this seasonal peak.^{4,8–12}

Although asthma treatment guidelines (from the National Institutes of Health and the Global Strategy for Asthma Management and Prevention) recommend daily anti-inflam-

matory treatment for control of mild, persistent asthma, recent literature evaluates whether intermittent or symptom-driven treatment with anti-inflammatory medications may be appropriate for some patients.^{13–15} Although these alternative approaches to dosing patterns for chronic asthma therapies are being evaluated, there are limited data on actual patterns of use of asthma medications in the real-world setting. Thus, although seasonal patterns of asthma-related health care use, especially ED visits and hospitalizations, have been well characterized, there is little information on seasonal patterns for the use of asthma medication.^{4–7,9,11}

Presented herein is a descriptive time series analysis using administrative health care claims for preschool-aged children (aged 2–5 years) and school-aged children (aged 6–12 years) to determine how seasonal patterns of asthma medication prescriptions relate to seasonal patterns of asthma-related health care use.

METHODS

Data Collection

These analyses represent an ecological evaluation of asthma-related health care services and prescribing patterns for asthma medications. Data were derived from Ingenix Research Data Mart, an automated research database of pro-

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vider, facility, and pharmacy insurance claims from a large health care plan in the United States (United Healthcare) that includes individuals from geographically diverse areas of the United States.

Health care claims coded with a primary *International Classification of Diseases, Ninth Revision, Clinical Modification* code indicating asthma (493.xx) for services provided by EDs, outpatient physician visits, and hospitalizations were identified for children aged 2 to 12 years for the years 2002 through 2004.

Claims for asthma prescription medications also were identified based on the National Drug Code, and prescription medications were classified as controller medications (long-acting β_2 -agonists, inhaled corticosteroids, and leukotriene receptor antagonists) or reliever/rescue medications (short-acting β_2 -agonists).

Weekly events were counted, and denominators were constructed to examine the potential for seasonality of health care services and asthma medication prescriptions. Weeks 1 through 52 were defined according to calendar year, beginning with January 1. If an event spanned more than 1 day, the first date of the event was used to map to the date of service. The denominator included all enrollees in the respective age group for the week or the month of interest. Because enrollment is determined by month, each enrollee was eligible to be in the denominator for each week that he or she appeared in the monthly enrollment file. For weeks that spanned 2 months, the number of enrollees (denominator) was prorated according to the number of days in each month to obtain enrollment counts by week.

Statistical Analysis

Weekly rates were modeled using Poisson regression, which assumes that rates can be expressed as a function of the predictors in the model. These were modeled by expressing the number of events per week as the dependent variable, with factors for year and region; the log of the total number of patients enrolled was included in the model as an offset parameter. In addition, rates for each event were estimated for each week relative to the lowest mean weekly value for all years combined (week 27 [July]), adjusted for region and year. Hospitalizations were not adjusted for region because of the few events for that variable. Poisson regression is particularly appropriate for rare events but assumes that the variance is equal to the mean. Count data often exhibit variability that exceeds the mean, as was the case herein, and are referred to as overdispersion. PROC GENMOD, SAS version 9.1 (SAS Institute Inc, Cary, NC), was used with a scaling factor to correct for overdispersion.

Data were examined for age groups separately and all ages combined (2–12 years). To generate the weekly graphs, data for each event were aggregated over the 3 years to obtain more robust weekly estimates. The percentage difference from the overall average rate was calculated for visits to the ED and prescribing rates for asthma medications.

RESULTS

Overall Rates of Health Care Use and Prescriptions by Age

Rates of health care use and prescriptions dispensed for each age group from the Poisson model, adjusted for region, year, and week, are given in Table 1. Rates of health care use and asthma medication subscriptions varied substantially by age group. Overall, the yearly rate of ED visits per 100,000 children was 28.3 (95% confidence interval [CI], 26.5–30.3) visits in preschool-aged children and 17.6 (95% CI, 16.6–18.6) visits in school-aged children. Yearly rates of outpatient visits per 10,000 children were relatively similar between the 2 age groups: 27.1 (95% CI, 26.7–27.5) for preschool-aged children and 23.9 (95% CI, 23.7–24.2) for school-aged children. Prescription rates for asthma controller medications per 10,000 children were 69.5 (95% CI, 68.7–70.3) for preschool-aged children and 69.2 (95% CI, 68.5–69.9) for school-aged children. Prescription rates per 10,000 children for asthma reliever medications were higher for preschool-aged children (65.3; 95% CI, 64.4–66.1) than for the older children (48.7; 95% CI, 48.1–49.3).

Seasonal Patterns

Seasonal patterns for ED visits and asthma medication prescriptions are illustrated in Figure 1, Figure 2, and Figure 3, grouped by weeks within months and season: January to March (winter), April to June (spring), July to September (summer), and October to December (autumn). Rates and confidence intervals for health care services and asthma medications for selected weeks relative to the annual lowest mean weekly value (week 27) are given in Table 2.

ED Visits

Temporal trends for ED use are shown by age group and overall in Figure 1A–C. There is some variability in the trends for preschool-aged children relative to the annual average rate in the weeks from January until April, when ED use deviated in a negative direction (Fig 1A). However, there was a strong inflection point at week 36 (early September) in each of the

Table 1. Rates of Health Care Use and Prescription Claims Within Age Group From the Poisson Model, Adjusted for Region, Year, and Week

Type of health care use	Age group, y	Rate, mean (95% CI)
Emergency department	2–5	28.3 (26.5–30.3) ^a
	6–12	17.6 (16.6–18.6) ^a
Outpatient visits	2–5	27.1 (26.7–27.5) ^b
	6–12	23.9 (23.7–24.2) ^b
Controller medication	2–5	69.5 (68.7–70.3) ^b
	6–12	69.2 (68.5–69.9) ^b
Reliever medication	2–5	65.3 (64.4–66.1) ^b
	6–12	48.7 (48.1–49.3) ^b

Abbreviation: CI, confidence interval.

^a Data are expressed as rate per 100,000.

^b Data are expressed as rate per 10,000.

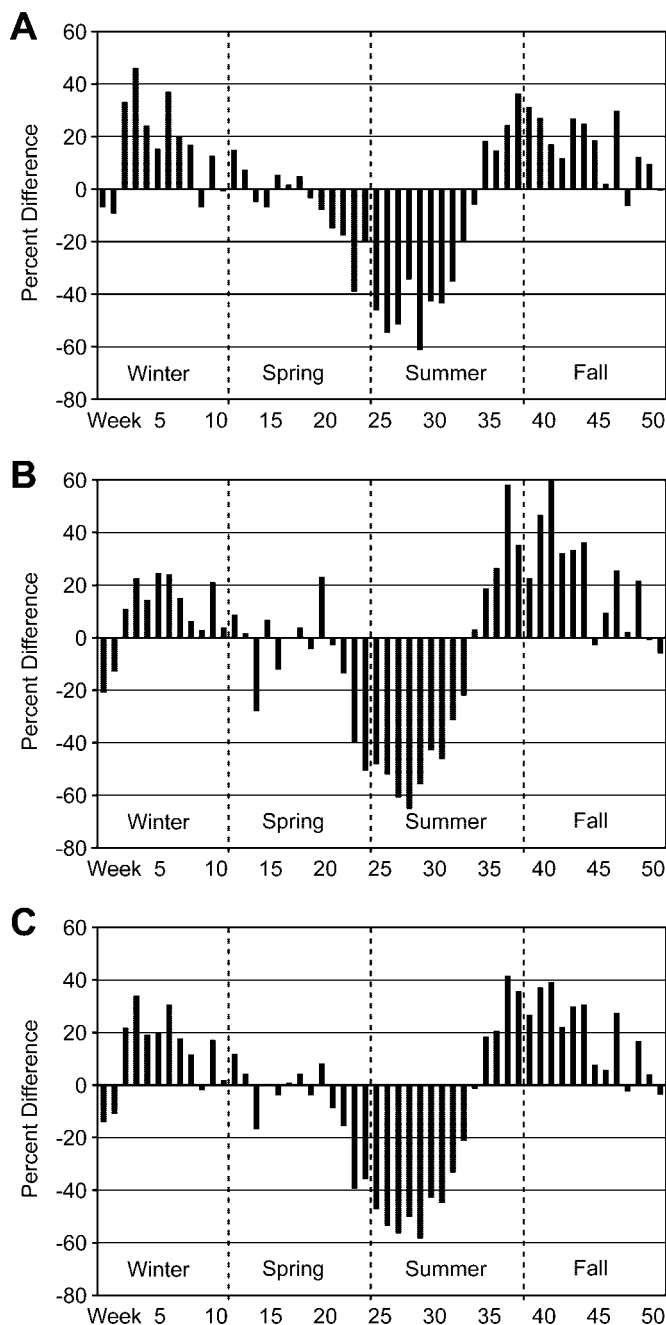


Figure 1. Annual trends for asthma-related emergency department visits relative to annual average rate for preschool-aged children (A), school-aged children (B), and both age groups combined (C).

3 years (data not shown), which may coincide with many school openings.

Patterns for ED visits for school-aged children were similar to those for preschool-aged children, although they demonstrated slightly more variability in the spring, then showed a similar decrease in early and mid summer (Fig 1B). There

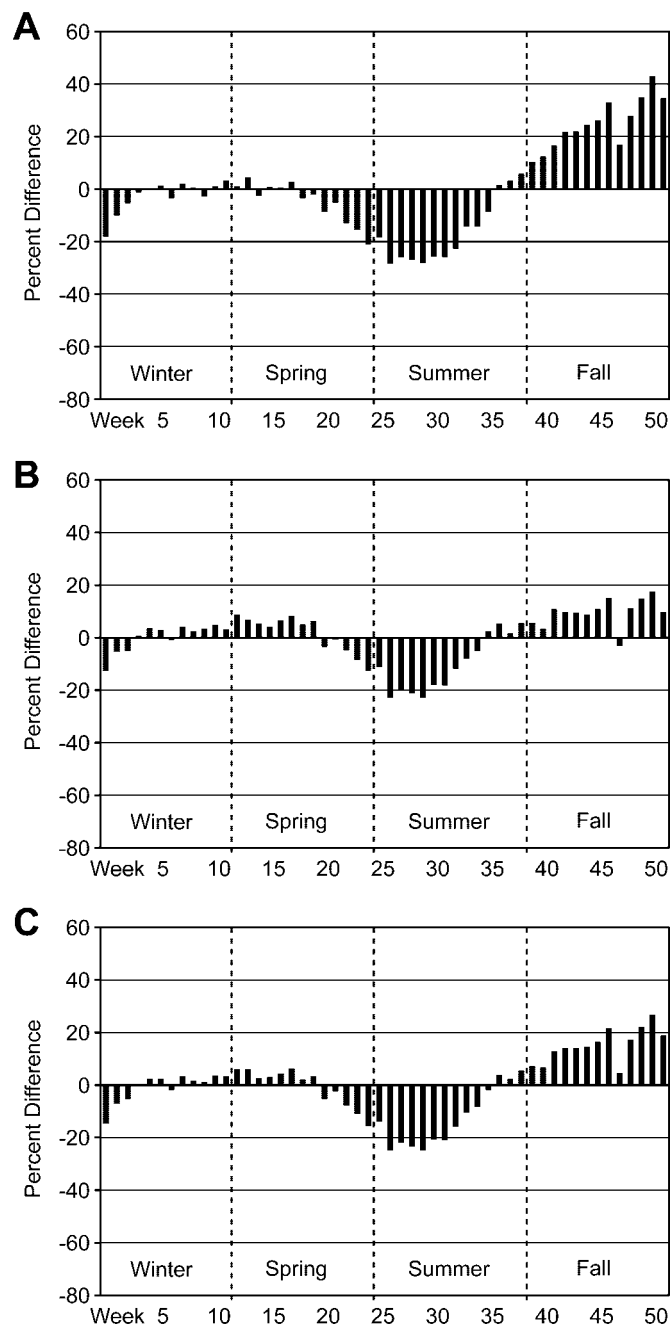


Figure 2. Annual trends for asthma controller medication prescriptions relative to annual average rate for preschool-aged children (A), school-aged children (B), and both age groups combined (C).

was a small peak at week 35 (end of August to early September) but a more remarkable peak at week 36, which represented an 18.6% increase over the aggregate average yearly rate.

The graph showing ED use for the 2 age groups combined (Fig 1C) smoothes out some of the variability seen for school-

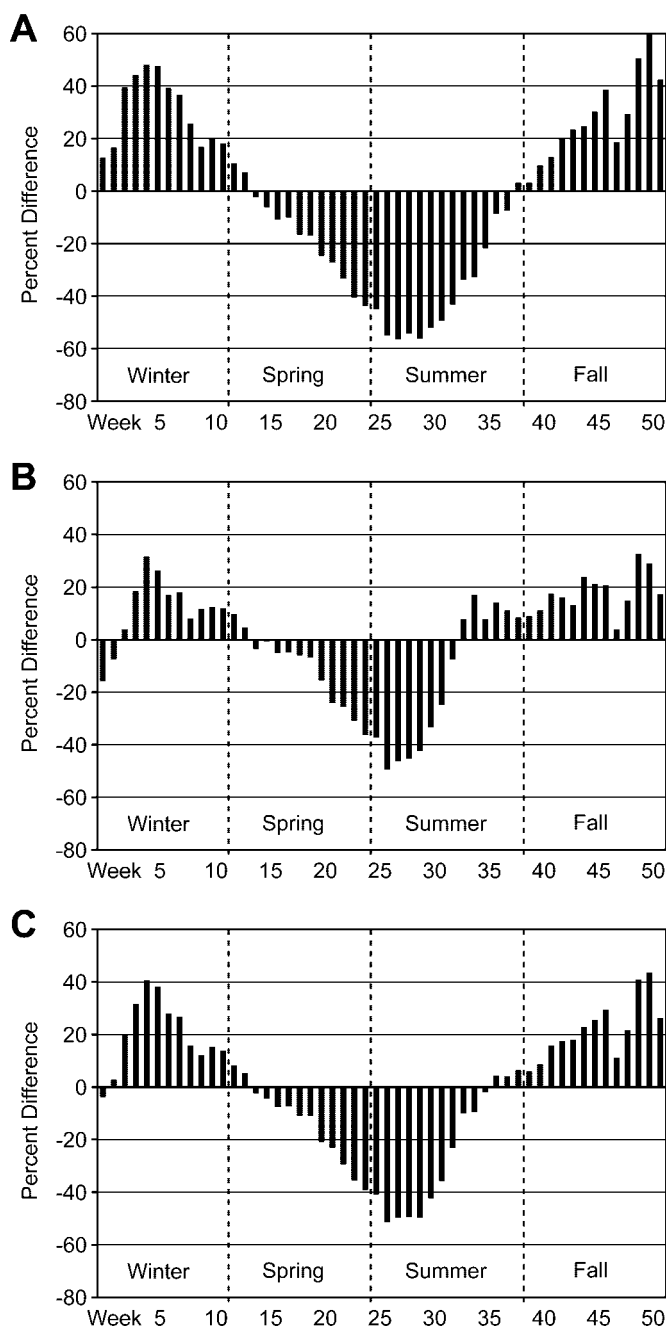


Figure 3. Annual trends for asthma reliever medication prescriptions relative to annual average rate for preschool-aged children (A), school-aged children (B), and both age groups combined (C).

aged children and presents a weighted average of the same data described previously for the individual age groups (Fig 1A and B). There is a strong seasonal increase at the end of summer (week 36), continuing through approximately week 44. Another increase in ED visits, slightly less in magnitude, occurred at week 3 and remained elevated through week 9.

Rates for ED visits relative to the lowest annual rate frequently were marginally higher for preschool-aged children than for school-aged children (Table 2). The highest relative rates for both age groups occurred in February (3.06 [95% CI, 2.16–4.32] for preschool-aged children and 2.36 [95% CI, 1.69–3.31] for school-aged children) and in October (2.94 [95% CI, 2.08–4.18] for preschool-aged children and 2.41 [95% CI, 1.72–3.37] for school-aged children).

Controller Medications

Controller medication prescription claims are illustrated in Figure 2A-C. There was a slight negative deviation from the annual weekly average rate in the first few weeks of the year for preschool-aged children, and claims hovered near the annual average until around week 20 (May) (Fig 2A). After week 21, there was a gradual decline until week 37 (mid September), which marked a turning point toward increased use. The rate for asthma controller medication claims in preschool-aged children peaked at week 51 in December (relative rate, 1.94; 95% CI, 1.80–2.09) (Table 2).

The pattern for controller medication prescriptions by school-aged children was similar to that for the preschool-aged children; however, changes through the year were not as significant as those for the younger children (Fig 2B). For the first few weeks of the year, prescription rates for controller medication for school-aged children were slightly below the annual average, similar to the younger children. Instead of remaining at a relatively stable rate in the early months of the year, however, the older children had a slight increase in the controller medication prescription rate at week 4 that remained essentially stable until approximately week 20. The timing of the inflection for the older children was similar to that for the preschool-aged children, but the degree of inflection was somewhat less. The peak rate of controller medication prescriptions for school-aged children occurred at week 51 (1.50; 95% CI, 1.40–1.59), similar to the timing for the preschool-aged children (Table 2).

Reliever Medications

The pattern of seasonality was more pronounced for reliever medication claims than for controller medications in both age groups, despite more claims for controller medications (Fig 3A-C).

For preschool-aged children, there was a very distinct seasonal pattern for reliever medication claims. From January 1 until April 8 (week 14), prescription rates remained higher than the average annual weekly rate (Fig 3A). During this period, the prescription rate resembled a bell-shaped curve, with a winter peak at the end of January to early February. From week 15 to week 38 (April to September), prescription rates for reliever medications were well below the average weekly rate. From week 39 on, prescription rates trended higher than the average weekly rate, peaking at week 51 (relative rate, 3.43; 95% CI, 3.11–3.78) (Table 2).

The pattern of reliever medication prescription dispensing for school-aged children appeared to follow a similar pattern

Table 2. Rates for Use of Health Care Services and Asthma Medications Relative to the Annual Mean Low Weekly Value (Week 27), Adjusted for Region

Week	Month	Relative rate (95% CI)				
		Controller medication	Reliever medication	ED visits	Outpatient visits	Hospitalizations ^a
Children aged 2–5 y						
1	Jan	1.15 (1.06–1.25)	2.50 (2.26–2.77)	2.10 (1.46–3.03)	1.86 (1.64–2.11)	2.69 (1.48–4.86)
7	Feb	1.36 (1.26–1.47)	3.09 (2.80–3.41)	3.06 (2.16–4.32)	2.27 (2.01–2.56)	3.54 (2.00–6.29)
14	Apr	1.46 (1.35–1.58)	2.37 (2.14–2.63)	2.33 (1.63–3.34)	2.17 (1.92–2.45)	3.08 (1.72–5.53)
20	May	1.38 (1.27–1.49)	1.85 (1.67–2.06)	2.30 (1.60–3.30)	1.90 (1.68–2.16)	3.25 (1.82–5.80)
27	Jul	1.00	1.00	1.00	1.00	1.00
33	Aug	1.08 (0.99–1.17)	1.26 (1.13–1.42)	1.52 (1.03–2.24)	1.25 (1.09–1.43)	2.25 (1.22–4.15)
40	Oct	1.52 (1.41–1.64)	2.26 (2.04–2.51)	2.94 (2.08–4.18)	2.71 (2.41–3.05)	3.59 (2.02–6.39)
46	Nov	1.73 (1.61–1.87)	2.86 (2.59–3.16)	2.81 (1.97–4.00)	3.30 (2.94–3.70)	3.65 (2.06–6.49)
51	Dec	1.94 (1.80–2.09)	3.43 (3.11–3.78)	2.38 (1.66–3.41)	3.01 (2.68–3.38)	3.40 (1.90–6.07)
52	Dec	1.86 (1.73–2.01)	3.14 (2.84–3.46)	2.19 (1.52–3.15)	2.25 (2.00–2.55)	2.29 (1.24–4.23)
Children aged 6–12 y						
1	Jan	1.14 (1.07–1.22)	1.64 (1.48–1.81)	1.62 (1.13–2.32)	1.57 (1.40–1.75)	1.35 (0.67–2.72)
7	Feb	1.29 (1.21–1.38)	2.30 (2.09–2.53)	2.36 (1.69–3.31)	2.25 (2.02–2.50)	4.01 (2.22–7.26)
14	Apr	1.39 (1.30–1.48)	2.03 (1.84–2.24)	2.01 (1.42–2.84)	2.23 (2.01–2.48)	3.97 (2.19–7.20)
20	May	1.38 (1.29–1.47)	1.83 (1.66–2.02)	1.88 (1.32–2.66)	2.18 (1.96–2.42)	3.44 (1.88–6.30)
27	Jul	1.00	1.00	1.00	1.00	1.00
33	Aug	1.14 (1.06–1.22)	1.80 (1.63–1.99)	1.32 (0.91–1.92)	1.56 (1.39–1.75)	2.21 (1.16–4.20)
40	Oct	1.36 (1.27–1.45)	2.10 (1.91–2.32)	2.41 (1.72–3.37)	2.69 (2.42–2.98)	5.24 (2.93–9.37)
46	Nov	1.42 (1.34–1.52)	2.36 (2.15–2.60)	1.86 (1.31–2.65)	3.08 (2.78–3.41)	5.60 (3.14–9.99)
51	Dec	1.50 (1.40–1.59)	2.51 (2.28–2.76)	1.91 (1.34–2.71)	2.52 (2.27–2.80)	4.49 (2.49–8.11)
52	Dec	1.43 (1.34–1.52)	2.23 (2.03–2.46)	1.97 (1.39–2.79)	1.81 (1.62–2.02)	1.97 (1.02–3.80)

Abbreviations: CI, confidence interval; ED, emergency department.

^a Not adjusted for region.

as that for the younger counterparts (Fig 3B). For the older children, a slight decrease in prescriptions for reliever medication in the beginning of the year was coincident with the dispensing of prescription controller medications. There was, however, a more marked decrease in the middle of the year than was seen with controller medications. As with the preschool-aged children, the seasonal peak occurred at week 51 (relative rate, 2.51; 95% CI, 2.28–2.76) (Table 2).

Outpatient Visits

Asthma-related physician visits increased for both age groups from February through April, then declined through late spring and summer, with significant increases in the relative rate beginning in October, peaking around week 46 (November) (preschool-aged children, 3.30 [95% CI, 2.94–3.70]; school-aged children, 3.08 [95% CI, 2.78–3.41]) (Table 2).

Hospitalizations

Patterns for hospitalizations were similar to those for ED visits and outpatient visits; however, there was more variability within both age groups because of the lower number of events (Table 2). Relative rates were higher for school-aged children than for preschool-aged children, but rates for both age groups peaked in November relative to the annual low average weekly rate (school-aged children, 5.60 [95% CI, 3.14–9.99]; preschool-aged children, 3.65 [95% CI, 2.06–

6.49]). Elevated rates also were observed in February (Table 2).

DISCUSSION

The present study used a large database that is representative of the insured population in the United States during the 3 years studied. This study is the first, to our knowledge, to examine patterns of medication prescription rates for asthma as they relate to ED and other health care use on a weekly and a seasonal basis. Previous studies have described seasonal patterns for asthma-related ED visits in major metropolitan areas.⁴

There is evidence that many prescriptions for asthma controller medications are not filled, and some patients have poor adherence to the prescribed treatment regimen.¹⁶ In the present study, it was anticipated that children would begin using their asthma medications as symptoms increased, which would be around the same time an exacerbation occurred, and that health care use would soon follow. Therefore, we expected the patterns for asthma medication prescriptions and asthma-related health care to be similar.

The present study demonstrated a clear reduction in the filling of asthma controller and reliever medication prescriptions during the summer months of July and August. A similar finding was reported by Johnston and Sears,¹⁰ which

leads to the hypothesis that many asthmatic children take a “drug holiday” from their controller medications during the summer months. Coincidentally, the summer months had the lowest rates of health care use. As reported in several other studies, rates of hospitalization and other health care for asthma-related problems begin to increase around the end of summer, with peaks generally occurring during September, approximately 17 to 19 days after their return to school.^{3,7,9,17,18} Average peak epidemics for preschool-aged children and adults, although of lesser magnitude, tend to follow behind those of schoolchildren by approximately 2 and 6 days, respectively.^{3,17}

Patterns for physician visits were very similar to those for ED visits.

Inpatient rates were highly variable because of small numbers; however, trends were similar to other health care end points. Seasonal patterns for visits to the ED for treatment of asthma exacerbations in countries in the northern and southern hemispheres are consistent with those for hospitalizations previously reported.^{4,18–20}

Recent clinical trials have compared alternative dosing approaches with long-term daily use on asthma outcomes in adult patients with mild persistent asthma.¹⁴ Boushey et al¹⁴ found that adults with mild, persistent asthma treated with short, intermittent courses of inhaled or oral corticosteroids during periods of worsening symptoms during a 1-year period had improved morning peak expiratory flow and had similar rates for asthma exacerbations as did those who were treated daily with either inhaled budesonide or oral zafirlukast. The impact of this symptom-driven, intermittent treatment pattern on the development of more serious asthma or progressive loss of lung function during an extended period is not clear.²¹

Inherent in any claims analysis are limitations that cannot directly be addressed. Specifically, we chose to look only at claims as the unit of analysis; therefore, we do not have longitudinal data on services that may be indicative of use by any particular child. Although racial or ethnic disparities may exist in asthma-related health care use,²² which may affect seasonal patterns of use, these possible disparities could not be evaluated from these data, because race is not recorded. In addition, the analysis yields aggregate health care data from all areas of the country; therefore, it will not account for any regional differences due to different climates and school opening dates. Finally, the Ingenix Research Data Mart database is representative of an insured population; thus, seasonal patterns of medication and health care use in underinsured or uninsured children may differ. Therefore, the analysis conducted herein is limited in external validity only for children covered on health plans maintained by a health insurance-enrolled parent or guardian.

We also considered evaluating rates of prescriptions of oral corticosteroids associated with ED and physician office visits, which could potentially provide greater confirmation of the urgency of the asthma visit. However, oral corticosteroids are prescribed for a variety of conditions unrelated to asthma and may also be prescribed as part of action plans for wors-

ening asthma. As such, prescriptions for oral corticosteroids may lack specificity to identify a specific urgent asthma event.

It may also be possible that some of the increase in short-acting β_2 -agonist prescriptions in September could be related to the need for extra inhalers to keep at school for urgent use. However, because the same peak is identified in the preschool-aged children, the impact of prescription fills for this reason is not likely to be the sole explanation for the observed peak.

Although it is not possible to determine actual use (or adherence to the prescribed regimen) of prescription medications from these data, examination of the relationship of asthma prescription fill patterns to seasonal patterns of asthma-related health care use could facilitate development of efficient patterns of asthma care for these age groups that anticipate actual seasonal use. Actual asthmatic drug use may be underrepresented because of a lack of claim submission (patient paid directly out of pocket or cost of drug was less than the deductible).

Several theories have been investigated to isolate triggers responsible for temporal trends in peaks that occur in asthma exacerbations in the autumn. These triggers may include indoor irritants (eg, tobacco smoke), outdoor/environmental pollutants, allergens (eg, dust mites, cockroaches, cats, and mice), climatic variables, and stress.^{4,7–12} However, the investigators reporting those theories did not sense that trends observed in their study provided strong evidence to associate trends for these variables with asthma rates. Some factors that have been identified as asthma triggers for children, such as exposure to rhinovirus and allergens, are unavoidable. High rates of viral infections, predominantly rhinovirus, have been associated with asthma exacerbations that occur in school-aged children shortly after Labor Day.^{17,23} Many children are susceptible to these viruses when the school year begins, after several weeks of having minimal exposure to new viruses.^{7,9,10,17,24} The stress of returning to school is also reported to be a contributor to the increases in asthma-related hospitalizations and ED visits; however, preschool-aged children experience similar peaks in asthma-related health care use without exposure to the same stress factors as for the older children and there is some variability from year to year in the timing of the first autumn peak, suggesting that the start of the new school year is not the only factor influencing increases in asthma-related health care use.⁷

The present study shows that asthma medication prescriptions generally peaked around the same time or just a few days later than the use of asthma-related health care services, which is logical because a health care visit is generally needed to obtain the prescription. The data suggest that children reduce their asthma medications because of the absence of worsening signs or symptoms of asthma during the summer months and do not resume taking medications until signs or symptoms of asthma worsen. It is believed that the summer hiatus, coupled with other identified and unidentified factors, contributes to seasonal increases in health care

use and asthma medication prescriptions in the early spring and even more in the fall, generally coinciding with the start of the school year.

It may be possible to reduce the incidence of seasonal asthma outbreaks (particularly in the fall when children return to school) by anticipating seasonal increases in asthma symptoms and initiating asthma controller medications shortly before returning to school, rather than waiting until symptoms appear.

REFERENCES

1. Akinbami L. Asthma prevalence, health care use and mortality: United States, 2003–05. Available at: [http://www.cdc.gov/nchs/products/pubs/pubd/hestats/ashtma\[sic\]03-05.htm](http://www.cdc.gov/nchs/products/pubs/pubd/hestats/ashtma[sic]03-05.htm). Accessed April 24, 2008.
2. Popovic JR. 1999 National Hospital Discharge Survey: annual summary with detailed diagnosis and procedure data. *Vital Health Stat* 13. 2001; (151):i–v, 1–206.
3. Lincoln D, Morgan G, Sheppard V, Jalaludin B, Corbett S, Beard J. Childhood asthma and return to school in Sydney, Australia. *Public Health*. 2006;120:854–862.
4. Silverman RA, Stevenson L, Hastings HM. Age-related seasonal patterns of emergency department visits for acute asthma in an urban environment. *Ann Emerg Med*. 2003;42:577–586.
5. Fleming DM, Cross KW, Sunderland R, Ross AM. Comparison of the seasonal patterns of asthma identified in general practitioner episodes, hospital admissions, and deaths. *Thorax*. 2000;55:662–665.
6. Bundy DG. Hospitalizations with primary versus secondary discharge diagnoses of asthma: implications for pediatric asthma surveillance. *J Pediatr*. 2007;150:446–449.
7. Kimes D, Levine E, Timmins S, Weiss SR, Bollinger ME, Blaisdell C. Temporal dynamics of emergency department and hospital admissions of pediatric asthmatics. *Environ Res*. 2004;94:7–17.
8. Johnston NW, Mandhane PJ, Dai J, et al. Attenuation of the September epidemic of asthma exacerbations in children: a randomized, controlled trial of montelukast added to usual therapy. *Pediatrics*. 2007;120:e702–e712. Available at: <http://pediatrics.aappublications.org/cgi/content/abstract/120/3/e702>. Accessed March 18, 2008.
9. Murray CS, Poletti G, Kebabdz T, et al. Study of modifiable risk factors for asthma exacerbations: virus infections and allergen exposure increase the risk of hospital admissions in children. *Thorax*. 2006;61:376–382.
10. Johnston NW, Sears MR. Asthma exacerbations, 1: epidemiology. *Thorax*. 2006;61:722–728.
11. Ivey MA, Simeon DT, Monteil MA. Climatic variables are associated with seasonal acute asthma admissions to accident and emergency room facilities in Trinidad, West Indies. *Clin Exp Allergy*. 2003;33:1526–1530.
12. Gergen PJ, Mitchell H, Lynn H. Understanding the seasonal pattern of childhood asthma: results from the National Cooperative Inner-City Asthma Study (NCICAS). *J Pediatr*. 2002;141:631–636.
13. O’Byrne PM, Barnes PJ, Rodriguez-Roisin R, et al. Low dose inhaled budesonide and formoterol in mild persistent asthma: the OPTIMA randomized trial. *Am J Respir Crit Care Med*. 2001;164:1392–1397.
14. Boushey HA, Sorkness CA, King TS, et al; for the National Heart, Lung, and Blood Institute’s Asthma Clinical Research Network. Daily versus as-needed corticosteroids for mild persistent asthma. *N Engl J Med*. 2005;352:1519–1528.
15. Jones A, Pill R, Adams S. Qualitative study of views of health professionals and patients on guided self management plans for asthma. *BMJ*. 2000;321:1507–1510.
16. Jones C, Santanello N, Bocuzzi S, Wogen J, Strub P, Nelsen LM. Adherence to prescribed treatment for asthma: evidence from pharmacy benefits data. *J Asthma*. 2003;40:93–101.
17. Johnston NW, Johnston SL, Norman GR, Dai J, Sears MR. The September epidemic of asthma hospitalizations: school children as disease vectors. *J Allergy Clin Immunol*. 2006;117:557–562.
18. Sears MR, Johnston NW. Understanding the September asthma epidemic. *J Allergy Clin Immunol*. 2007;120:526–529.
19. Blaisdell CJ, Weiss SR, Kimes DS, et al. Using seasonal variations in asthma hospitalizations in children to predict hospitalization frequency. *J Asthma*. 2002;39:567–575.
20. Harju T, Keistinen T, Tuuponen T, Kivelä SL. Seasonal variation in childhood asthma hospitalisations in Finland, 1972–1992. *Eur J Pediatr*. 1997;156:436–439.
21. Fabbri LM. Does mild persistent asthma require regular treatment [editorial]? *N Engl J Med*. 2005;352:1589–1591.
22. Akinbami LJ, Schoendorf KC. Trends in childhood asthma: prevalence, healthcare utilization, and mortality. *Pediatrics*. 2002;110:315–322.
23. Message SD, Johnston SL. Viruses in asthma. *Br Med Bull*. 2002;61:29–43.
24. Johnston NW, Johnston SL, Duncan JM, et al. The September epidemic of asthma exacerbations in children: a search for etiology. *J Allergy Clin Immunol*. 2005;115:132–138.

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