

# Seasonality of Asthma: A Retrospective Population Study

**AUTHORS:** Herman Avner Cohen, MD,<sup>a,b</sup> Hannah Blau, MBBS,<sup>b,c</sup> Moshe Hoshen, PhD,<sup>d</sup> Erez Batat,<sup>e</sup> Ran D. Balicer, MD<sup>c,f</sup>

<sup>a</sup>*Pediatric Ambulatory Community Clinic, Petach Tikva, Israel;* <sup>b</sup>*Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel;* <sup>c</sup>*Pulmonary Institute, Schneider Children's Medical Center of Israel;* <sup>d</sup>*Chief Physicians Office and* <sup>e</sup>*Information and Research Department, Clalit Research Institute, Clalit Health Services, Tel Aviv, Israel;* and <sup>f</sup>*Department of Epidemiology, Ben-Gurion University of the Negev, Beer-Sheva, Israel*

## KEY WORDS

asthma exacerbations, childhood asthma, primary care diagnoses, return to school-related morbidities

## ABBREVIATIONS

CHS—Clalit Health Services  
CI—confidence interval  
ICS—inhaled corticosteroids  
LTRAs—leukotriene receptor antagonists  
OR—odds ratio  
PC—primary care  
PCP—primary care physician  
URI—upper respiratory infection

Dr Cohen conceptualized and designed the study and drafted the initial manuscript; Dr Blau conceptualized and designed the study and drafted the initial manuscript; Dr Hoshen carried out the initial analyses and reviewed and revised the manuscript; Mr Batat carried out the initial analyses and reviewed and revised the manuscript; Dr Balicer conceptualized and designed the study and drafted the initial manuscript; and all authors approved the final manuscript as submitted.

[www.pediatrics.org/cgi/doi/10.1542/peds.2013-2022](http://www.pediatrics.org/cgi/doi/10.1542/peds.2013-2022)

doi:10.1542/peds.2013-2022

Accepted for publication Jan 21, 2014

Address correspondence to Herman Avner Cohen, MD, PO Box 187, Yehud 56000, Israel. E-mail: [hermanc@post.tau.ac.il](mailto:hermanc@post.tau.ac.il)

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2014 by the American Academy of Pediatrics

**FINANCIAL DISCLOSURE:** The authors have indicated they have no financial relationships relevant to this article to disclose.

**FUNDING:** No external funding.

**POTENTIAL CONFLICT OF INTEREST:** The authors have indicated they have no potential conflicts of interest to disclose.



**WHAT'S KNOWN ON THIS SUBJECT:** Asthma is a clinical condition treated mostly at primary care community clinics. Epidemics of asthma exacerbation occur annually with return to school after summer vacation and have been reported in many countries, including Israel.



**WHAT THIS STUDY ADDS:** In 82 234 asthmatic children, unscheduled primary care physician visits and drug prescriptions for asthma exacerbations peaked in September after a summer trough, with a lesser peak in late autumn and fluctuations through the winter months.

## abstract

**OBJECTIVES:** Seasonal variations in asthma are widely recognized, with the highest incidence during September. This retrospective population study aimed to investigate whether this holds true in a large group of asthmatic children in primary care and to assess the impact of age, gender, urban/rural living, and population sector.

**METHODS:** The key study outcomes were the diagnosis of asthma exacerbations and asthma medication prescriptions, recorded by family physicians during 2005 to 2009. These were analyzed by “week of diagnosis” in Clalit Health Services’ electronic medical record database. Regression models were built to assess relative strength of secular trends, seasonality, and age-group in explaining the incidence of asthma exacerbations.

**RESULTS:** A total of 919 873 children aged 2 to 15 years were identified. Of these, 82 234 (8.9%) were asthmatic, 61.6% boys and 38.4% girls; 49.1% aged 2 to 5 years, 24.1% 6 to 9 years, and 26.8% 10 to 15 years. We observed a 2.01-fold increase in pediatric asthma exacerbations and 2.28-fold increase in prescriptions of asthma bronchodilator medications during September (weeks 37–39 vs weeks 34–36) compared with August. The association between the opening of school and the incidence of asthma-related visits to the primary care physician was greatest in children aged 2 to 5 years (odds ratio, 2.15) and 6 to 11 years (1.90-fold). Adolescents (age 12–15 years) had a lesser peak (1.81-fold). In late fall there was a second rise, lasting with fluctuations throughout winter, with a trough in summer.

**CONCLUSIONS:** Returning to school after summer is strongly associated with an increased risk for asthma exacerbations and unscheduled visits to the primary care physician. *Pediatrics* 2014;133:e923–e932

Epidemics of pediatric asthma exacerbations requiring hospitalization occur annually when children return to school after the summer break, and have been reported in many countries including Israel.<sup>1–9</sup> The underlying mechanisms for this autumnal epidemic of asthma morbidity are thought to include some combination of infectious, allergic, environmental, and climatic stimuli.<sup>2,3</sup> More specifically, environmental allergens, viral respiratory infections, exercise, environmental pollutants, tobacco smoke, and emotional stress may contribute to asthma exacerbations.<sup>2,10,11</sup> Start of school is precisely synchronized with the peak of this epidemiologic phenomenon, and thus the related morbidity may potentially be contained.<sup>4,10,12–15</sup> Although most studies to date were conducted in the hospital or emergency department setting, the seasonality of asthma in the primary care (PC) context remains to be demonstrated. A seasonal increase in asthmatic exacerbations would create a major strain on an overextended PC system, which could potentially be averted by proactive treatment with anti-asthmatic medications.

The primary objective of our study was to investigate the seasonal trends of asthma exacerbations among a large population of Israeli children in the PC clinic setting, and to confirm whether the September epidemic of asthma previously described is also evident within the much wider setting of primary and community medicine. We carried out this study using data from a large managed care electronic medical records database between 2005 and 2009, providing a large study population, comprehensive diagnoses, and rich sociodemographic information.

## METHODS

### Setting

Clalit Health Services (CHS) is Israel's largest health fund and serves as both

insurer and health care provider, insuring 54% of Israel's population and supplying most of the health care services within its system. These services include primary, secondary, and tertiary care (including a third of the acute care beds in Israel), as well as pharmacies and paramedical services. In CHS, children are predominantly treated at community PC clinics by board-certified pediatricians, non-board-certified pediatricians, and general practitioners. Membership in 1 of the 4 Israeli health funds is mandatory and, although transferring is simple, members rarely move between funds (~1% per year), thus enabling long-term case histories. All of CHS's primary and secondary care physicians use an advanced electronic medical records system, which feeds into the central database of the organization. This database contains over a decade of patient-level data, including sociodemographic, clinical, health care use, and drug purchasing data. In addition, the system includes registries of chronic diagnoses.

### Study Population

We conducted a historical population study between 2005 and 2009 including children 2 to 15 years of age. The CHS PC database includes both classification of underlying disease diagnosis and recording of acute episodes. Children were included if classified by their physician as having an underlying diagnosis of asthma. Among these children we analyzed acute episodes of asthma or wheezing between 2005 and 2009.

### Variables

Asthma event: A diagnosis of acute asthma during a primary care physician (PCP) visit in the primary clinic setting was regarded as an exacerbation event. Often the asthma event was treated over a series of doctor's visits,

so an algorithm was developed to identify the date that the child first visited the doctor and received the diagnosis.

The week (Sunday–Saturday) within a calendar year was taken as an ordinal variable calculating from January 1 each year. School return occurs in general Jewish schools on the weekday closest to September 1 each year, usually the end of week 35 of the year beginning January 1. In ultra-orthodox boys' schools, return is based on the lunar Jewish calendar and therefore varies by several weeks according to the Gregorian calendar referred to above, each year.

Asthma medications included filled prescriptions of any of the following: bronchodilators, inhaled corticosteroids (ICS), leukotriene receptor antagonists (LTRAs), or combination therapies.

We collected data of all physician-diagnosed "upper respiratory infection" (URI) visits in the CHS PCP database for the period, and compared with asthma-related visits. We studied the ratio of these visit counts per week over 2 annual periods, the summer weeks 15 to 36 and the winter weeks 1 to 14 and 37 to 52.

Other covariates included age (categorized into 3 groups: 2–5 years, 6–9 years, and 10–15 years), gender, date of visit, type of locality (large town >100 000 inhabitants, small town 2000–100 000, or rural settlements <2000), and population sector (at the CHS clinic level, as to whether it served predominantly General-Jewish, Ultraorthodox-Jewish, or Arab populations).

### Statistical Analysis

Incidence of asthma exacerbations was calculated on a weekly basis. The analysis was performed by several methods. The first stage was examining autocorrelation of weekly asthma exacerbations in the community. As

52 weeks was indeed the leading lag time for repetition of peaks, we used annual recurrence as the basic model. To begin with the annual modeling, we separated the weekly pattern into annual recurrent patterns, inter-annual trends, and residual variation (using the R function *acf*). We searched for the first peak in the seasonal pattern. In addition, we calculated the time derivative of the weekly pattern (subtracting from the weekly rate the rate the week before) and again decomposed the seasonality pattern. We looked here for the highest seasonal peaks in the first derivative raw values, and for the highest peak in the seasonal pattern of the first derivative.

In addition, we looked at the raw counts by week of calendar year using regression, focusing on comparing calendar weeks 37 to 39 (mid-September) versus weeks 34 to 36 (August to early September), year (as a categorical value, to correct for random inter-annual variation), and accumulated for the entire study group and for various subgroup strata. The relative frequency of asthma-related visits as a fraction of all PCP visits per week was calculated to attain seasonal patterns for the entire study group and different subgroups. The frequency of medication purchasing as a function of season was modeled similarly. ANOVA compared the relative incidence between gender groups, population sectors, and urban/rural dwelling to test the relative strength of the September effect within each sub-segment. Interaction terms between calendar year and age group were tested to determine evidence of secular trends in asthma exacerbations over the study period. We further looked at weeks 31 to 41 and tested whether a step function (attributing a value 1 for weeks 37–41 and 0 for weeks 31–36) was predictive of a rise in asthma exacerbation incidence. This step function was entered into linear

regression models to test for the significance of the association between asthma exacerbations and being within the school year beyond calendar year and ethnicity.

The study was approved by the institutional review board at Meir Medical Center in Israel.

## RESULTS

A total of 919 873 members aged 2 to 15 years were identified in the CHS database during the study period. Described in Table 1, 82 234 (8.9%) children were diagnosed as suffering from asthma or wheezing: 60.9% were boys and 39.1% girls; 28.8% aged 2 to 5 years, 31.1% aged 6 to 9 years, and 40.1% aged 10 to 15 years. Among the 30 967 children who had at least 1 visit associated with asthma exacerbation, 61% were boys and 39% girls; 49.1% were aged 2 to 5 years, 24.1% were aged 6 to 9 years, and 26.8% were aged 10 to 15 years.

The autocorrelation for both the incidence and the derivative of the incidence at lag 52 weeks was indeed the highest, with an autocorrelation factor of 0.25, which was significant at the  $P < .001$  level. In Fig 1 we present the seasonal pattern of the incident cases for

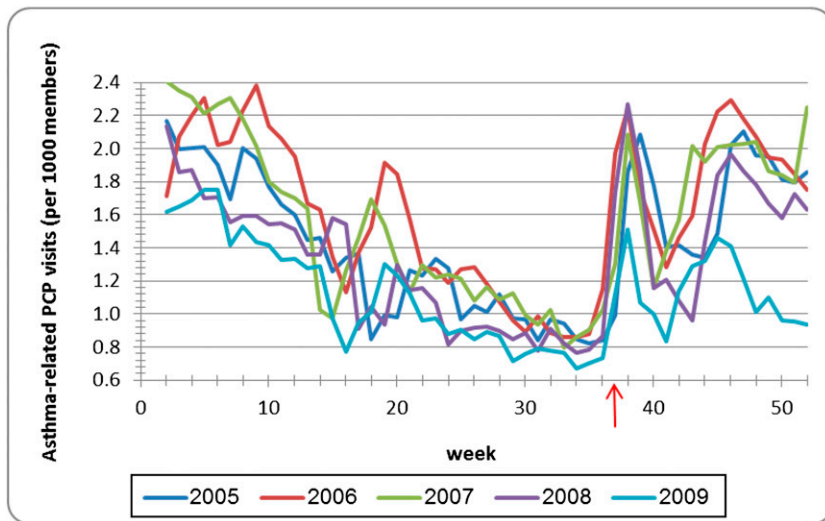
the general population. The vertical arrow represents the 37th week of each year (2 weeks after return to school). Inspecting the derivative function we observe that the largest changes each year coincide with week 37. In addition, we tested the correlation between a step function for a step with value 0 between weeks 19 and W-1 (variable) and 1 elsewhere, with W between 20 and 50. The function peaked at 0.609 for  $W = 37$ .

From 2005 to 2009 there was an annual peak in incidence of asthma-related clinic visits beginning the 37th to 38th week of the calendar year (corresponding to the 1–2 weeks after the start of school in September at week 35–36) and lasting until week 40. However, the size and shape of the peak was not consistent over the years, with clear inter-annual variation. After this initial peak, higher rates of asthma-related PCP visits continue, although with much fluctuation, until the spring (approximately week 12 of the next year). A complex age- and season-dependent peak pattern was evident in Fig 2, with a 2.15-fold increase in incidence in the fraction of asthma-related PCP visits from weeks 34 to 36 (August 20 to September 9, including return to school at the end of

**TABLE 1** Demographic Characteristics, Asthma Diagnoses, and Number of Asthma-Related PCP Visits Among Pediatric Clalit Members Aged 2 to 15 Years

	Clalit Pediatric Members		Asthmatic Children	
	N (%)	N (%)	N (%)	Asthma Visits N (%)
Total	919 873	82 234	30 967	
Gender				
Male	471 177 (51.2)	50 058 (60.9)	19 069 (61.6)	
Female	448 696 (48.8)	32 176 (39.1)	11 899 (38.4)	
Age (years)				
2 to 5	281 259 (30.6)	23 706 (28.8)	15 197 (49.1)	
6 to 9	260 921 (28.4)	25 612 (31.1)	7 458 (24.1)	
10 to 15	377 693 (41.1)	32 916 (40.1)	8 313 (26.8)	
Cultural group				
General	525 270 (57.1)	56 966 (69.3)	21 155 (68.3)	
Ultra-orthodox	44 837 (4.9)	2584 (3.1)	1138 (3.7)	
Arab	349 765 (38.0)	22 684 (27.6)	8675 (28.0)	

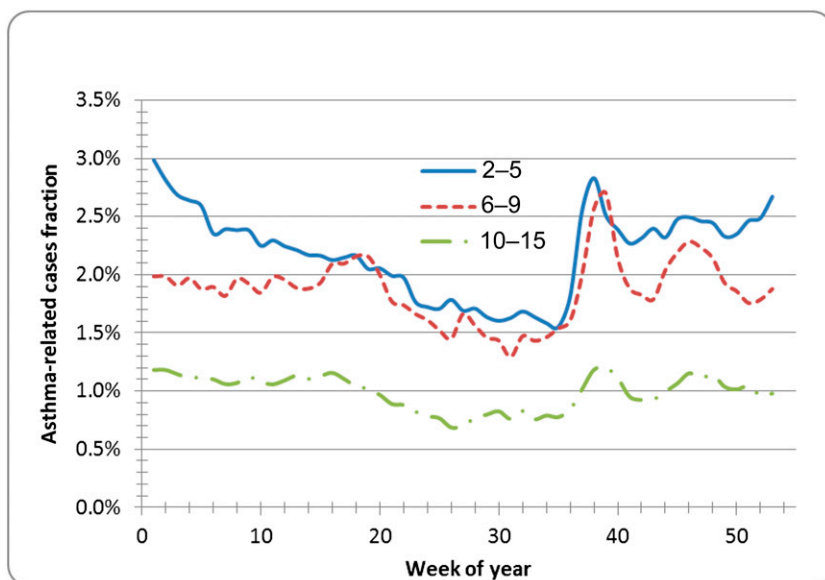
PCP are board-certified pediatricians, non-board-certified pediatricians, board-certified family physicians, and general practitioners.



**FIGURE 1** Incidence rates of asthma-related PCP visits by week among 2- to 15-year-old members (per 1000 members), 2005 to 2009. PCP are board-certified pediatricians, non-board-certified pediatricians, board-certified family physicians, and general practitioners. The red arrow marks the 37th week.

week 35) until weeks 37 to 39 (September 10–30) among preschool children, a 1.91-fold increase among children aged 6 to 9 years, and a 1.82-fold increase for older children aged 10 to 15 years. The highest number of asthma-related clinic visits among

those aged 10 to 15 years occurred in the last 4 weeks of the year. This gradually receded until the end of the summer vacation. In children aged 6 to 9 years, peaks in asthma exacerbations corresponded to the weeks following the return to school after

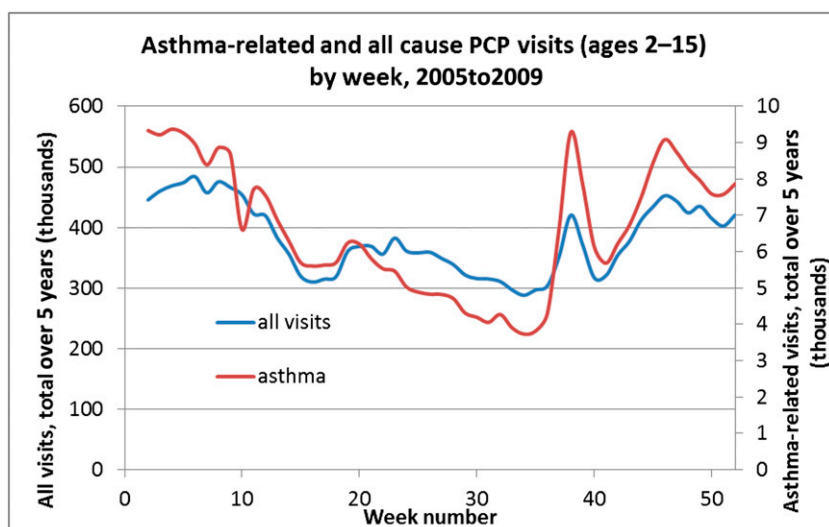


**FIGURE 2** Weekly proportion of PCP visits attributable to asthma (2005–2009) by age in years. PCP are board-certified pediatricians, non-board-certified pediatricians, board-certified family physicians, and general practitioners.

school vacations in September, with additional, smaller peaks in late October (after the Jewish New Year and Succot vacation) and May (perhaps relating to the Passover vacation).

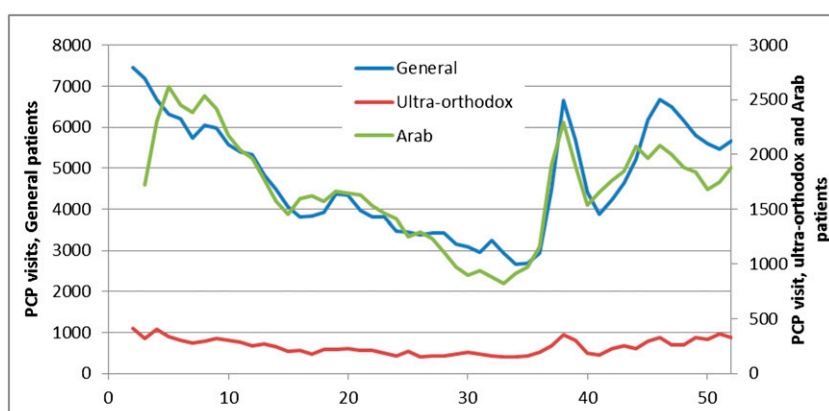
In the general pediatric population, there was a seasonal pattern for PCP visits as well, with a drop in visits during the summer vacation and a rise (1.26-fold; confidence interval [CI], 1.03–1.48) comparing weeks 37 to 39 to weeks 34 to 36. However, we found that the relative proportion of asthma-related visits compared with all PCP visits among the asthmatic population increased in September 1.55-fold (weeks 37–39 vs weeks 34–36) (Fig 3). This pattern varied between age groups, with the highest effect for asthma-related visits found among younger age groups (1.59 and 1.60-fold for ages 2–5 years and 6–9 years, respectively, compared with 1.4 for ages 10–15 years). Although total PCP visits increased in September compared with August for the general population by 1.321-fold (CI, 1.105–1.536, using inter-annual variation), the rate in the ultra-orthodox population increased 1.196 (CI, 0.912–1.479) times and among Arabs 1.239 (CI, 1.148–1.329) times (Fig 4). The rate of asthma-related cases increased in September compared with August, by 1.784, 1.993, and 2.009-fold for the general population, the ultra-orthodox, and the Arab populations, respectively. Overall, the relative increase in asthma-related PCP visits compared with all PCP visits during this time period was 67% and 62% for ultra-orthodox and Arab children, respectively, while for the general population the fraction of asthma-related PCP visits increased by only 35%.

To test the association between URI and asthma exacerbations we analyzed the ratio between the number of visits with diagnosis of URI to that of asthma, splitting by age group (Figs 5 and 6). We saw that the September peak among



**FIGURE 3**

Weekly count (in thousands) of asthma-related and all-cause pediatrician visits at CHS clinics (aged 2–15 years) accumulated over years 2005 to 2009. PCP are board-certified pediatricians, non-board-certified pediatricians, board-certified family physicians, and general practitioners.



**FIGURE 4**

Weekly PCP visits attributable to asthma (2005–2009) by population sector. PCP are board-certified pediatricians, non-board-certified pediatricians, board-certified family physicians, and general practitioners.

the older children<sup>10–15</sup> was far more pronounced for URI than asthma exacerbations, whereas for the younger children the ratio was almost constant, and that URI- and asthma-related visits had similar frequencies, including comparable rises in September.

An ANOVA model examining the ratios by week and age group explained 95% of the variance, while a model evaluating the ratios by week and population sector explained 93% of the variance. Both models were highly predictive

( $P < 10^{-16}$  for the weeks in each model). There were no major differences in asthma incidence between children living in large/small cities or rural settlements. There was a slightly lower incidence in Arab clinics.

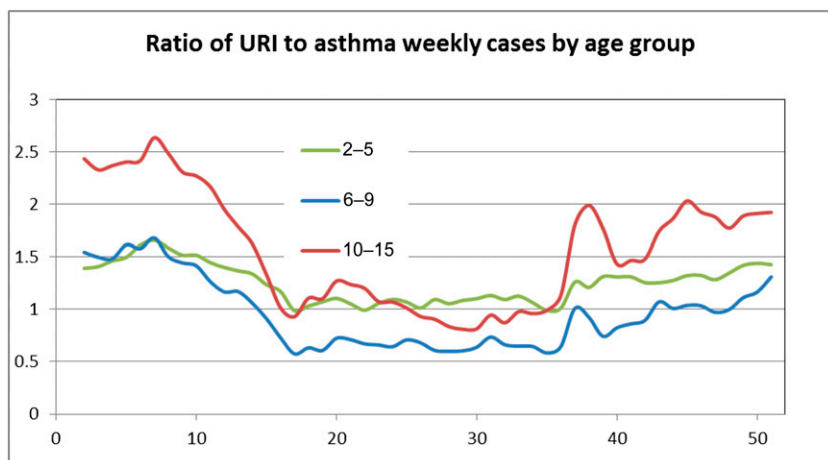
A similar seasonal pattern was observed for the supply of asthma medications (Fig 7). There was a 2.28 (CI, 1.584–2.969) -fold increase in prescriptions filled for bronchodilators, the most frequently dispensed asthma medication, during weeks 37 to 39

compared with weeks 34 to 36. There was also a rise in other asthmatic treatments, but to a lesser extent: 2.044-fold (CI, 1.425–2.664) for ICS, 1.463 (CI, 1.167–1.758) for LTRAs, and 1.533-fold (CI, 1.263–1.803) for combination therapies (Fig 8).

We further studied the multivariable interaction between week and year in examining the effect of the week 31 to 41 period on asthma exacerbations. We first split the population by population sector and then assessed the interaction terms. We found that the week 37 indicator (as a step function, whether the week number was 31–36 or later) was a significant predictor ( $P < 10^{-15}$ ). The interaction between population sector and week revealed a difference in the association between sectors. Among the ultra-orthodox the model of a 37-week step function and year was far less powerful, explaining 36% of variance, as opposed to explaining 69% and 58% variance for Arab and general Jewish sectors respectively, reflecting a smoother onset of the peak (Fig 4). No interaction was found between urban and rural areas; within both settings there was a strong seasonal pattern with a highly significant spike at week 37.

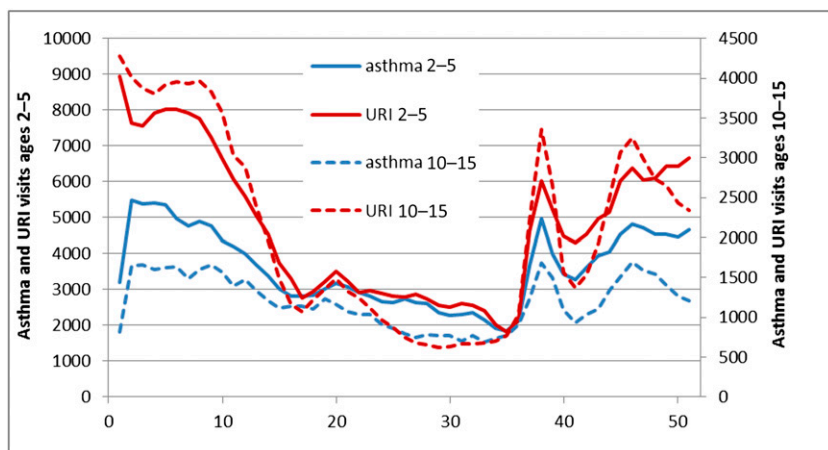
## DISCUSSION

In this paper, we describe the largest epidemiologic study to date on seasonality of asthma exacerbations within a community setting. The US National Health Statistics Report has documented the prevalence of asthma as 9.6%, and has reported on health care use and mortality for 2005 to 2009 among 7.1 million asthmatic children aged 0 to 16 years.<sup>16</sup> Our results show similar prevalence rates, with 8.9% of children diagnosed with asthma or wheezing. Our findings were also consistent with the US national report with no difference in prevalence rates between residents of urban and non-urban areas. The report, however, did



**FIGURE 5**

Weekly ratio of URI-related to asthma-related PCP visits (2005–2009) by age group. PCP are board-certified pediatricians, non-board-certified pediatricians, board-certified family physicians, and general practitioners.



**FIGURE 6**

Asthma- and URI-related PCP visits, 2005 to 2009 by age group. PCP are board-certified pediatricians, non-board-certified pediatricians, board-certified family physicians, and general practitioners.

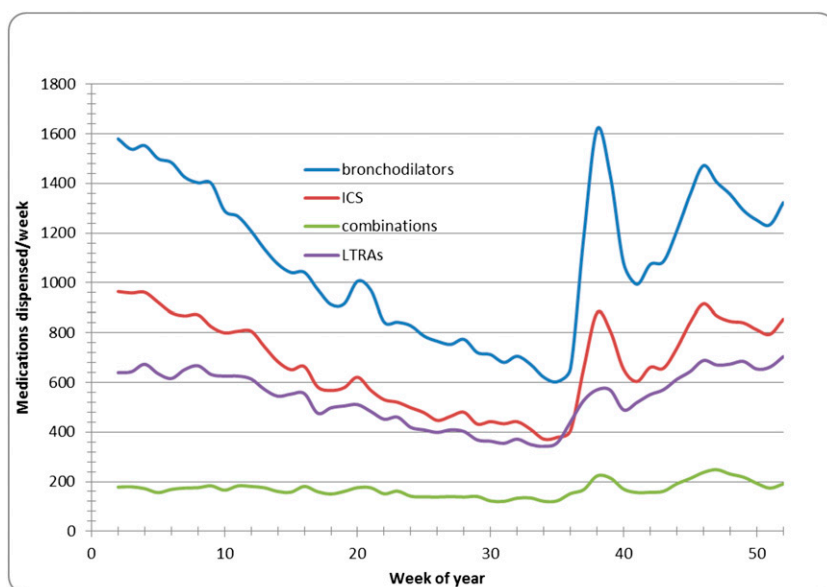
not describe the seasonality of asthma exacerbations within their population. Although there have been numerous reports on the September asthma epidemic in the hospital setting, these epidemiologic data extracted from hospital records should be interpreted cautiously, particularly when temporal trends are being evaluated, because patterns of health service use for asthma have changed significantly over the last 2 decades. PC service consumption has increased while inpatient hospital admission rates have declined.<sup>5</sup> Fleming et al<sup>17</sup> found 3 stud-

ies<sup>18–20</sup> showing decreased numbers of hospital admissions for asthma, and these results aroused speculation that more asthma attacks were treated in PC settings. Asthma is therefore perceived as a condition treated primarily in the community, by PCPs who manage both the chronic disease and acute episodes. Only those children who have severe asthma are referred to specialized hospital asthma clinics and these cases are relatively few. Therefore, the true incidence in the PC setting is more relevant for the physicians involved in treating this condition.

Previous studies that were community-based have generally been limited to small cohorts.<sup>10</sup> The current study, accessing a database of almost a million children including over 80 000 asthmatic children in the community setting, substantiates the magnitude of this seasonal variation as well as identifying other seasonal trends not previously emphasized. This is supported by robust and statistically significant data.

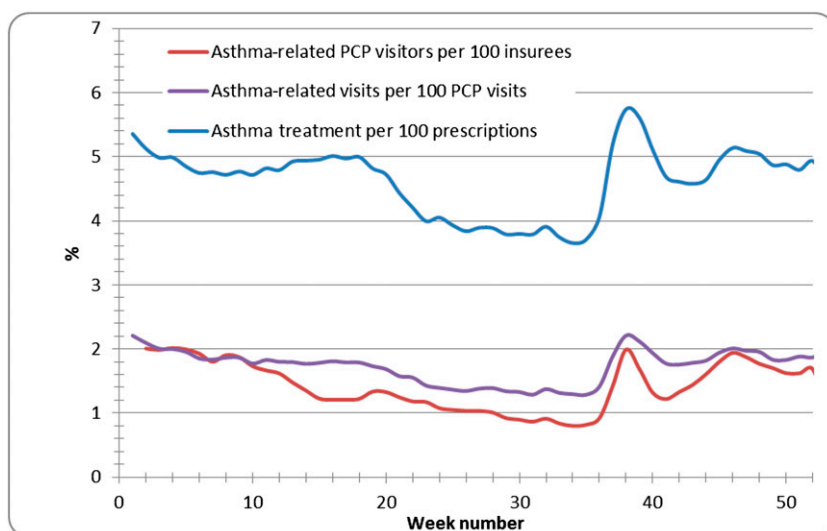
We chose to examine the data in 2 ways, studying the increase in asthma exacerbations as a count per 1000 CHS members, and also as the fraction of all visits to the PCP. We believe this provided a further perspective on seasonal variations in asthma visits. Thus, although the change in fraction of asthma/all encounters could be attributable to changes in either the denominator or numerator, looking at the total counts showed clearly that asthma visits dropped lower in summer and rose higher after the return to school, compared with all PCP visits.

In our population, 2 processes seem to be taking place. There is a sudden increase in asthma episodes related to the beginning of the school year and a first peak in URI, and an additional peak 2 months later that is related, especially among the younger children, to a second peak in URI. This may well be season-associated. During the summer months the incidence of URI and asthma decrease dramatically. The considerable peak in asthma exacerbations observed immediately after the summer vacation when children return to school was inversely associated with child age, and thus less evident in adolescents. Although there was an overall increase in pediatric visits during this period after the long vacation when families commonly travel, the asthma-related visits increased disproportionately, indicating a true rise in incidence rather than a surge in access



**FIGURE 7**

Average number of medications dispensed weekly for treatment of asthma to CHS insurees aged 2 to 15 years during the period 2005 and 2009 by week of year and by drug family,  $\beta_2$ -agonist inhalant treatments (bronchodilators), ICS, LTRAs, or ICS+  $\beta_2$ -agonist (combinations).



**FIGURE 8**

Asthma-related PCP visits per 100 PCP visitors and PCP members and asthma treatment as fraction of all prescriptions, weekly proportions averaged years 2005 to 2009. PCP are board-certified pediatricians, non-board-certified pediatricians, board-certified family physicians, and general practitioners.

to medical services. Asthma-related visits during the period amount to some 2% to 3% of all pediatric clinic visits during the first weeks of September, thereby adding a greater burden on resources that are already overstretched. This seasonal asthma-related morbidity has been observed

in all countries studied. Despite generally declining admittance rates for asthma-related conditions, this leads to a substantial seasonal rise in hospitalizations and emergency department visits and disrupts the quality of life for families who have children with asthma, as reported in Canada, Australia,

and Israel.<sup>1,3,4,12</sup> The peaks in emergency department visits, which are identical to those of inpatient hospital admissions in late September (around week 38), are of greatest magnitude in children and decline considerably with age.

When examining sub-segments of the study population, results of our study showed no difference in the asthma exacerbation trends between rural and urban settings, but yielded some differences among various cultural groups. A previous epidemiologic study in Israel suggested that asthma is significantly more prevalent in densely populated and urban areas than in rural regions.<sup>21</sup> However, our findings did not support these results. Although that study looked at differences in locality, it did not look at variations among different cultural sub-segments. We observed differences in the extent of the September incidence rise based on cultural group, with distinctions potentially attributable to variations in school schedules among the 3 groups studied. In general, schools in Israel open the first of September, week 35 of the year, after 2 months' summer vacation. The onset of the rise in incidence during September was not as pronounced in the ultra-orthodox sector, which may be explained by the fact that ultra-orthodox boys' (but not girls') schools open according to the lunar calendar, which causes the start-date to be earlier than the schedule of the general schools and to vary considerably each year, smoothing slightly the uniform peak over several years. In contrast, the rate of increase at week 37 among Arab children was more pronounced. Notably, Arab schools commence studies on September 1 every year, just as do the general Jewish schools.

Several explanations of the underlying causes of the seasonality of asthma exacerbations have been explored in previous research. It has been suggested

that stress, possibly associated with school return, can worsen asthma symptoms in school children<sup>22</sup> and high levels of environmental allergens occur in the late summer.<sup>23</sup> Children returning to school after the summer vacation are re-exposed to respiratory viral infections,<sup>10,12,13</sup> most commonly rhinovirus at that time,<sup>24</sup> and sensitizing allergens in the school environment.<sup>11,25</sup> Students in classrooms are at increasing risk for infection. Younger children may attend preschool, potentially exposing them to similar triggers as the older children. Furthermore, a child can expose siblings to viruses, with secondary cases of rhinoviruses in families typically occurring 1 to 5 days after initial exposure.

Children in the younger age group were more susceptible to asthma exacerbations at the start of preschool, whereas peaks in the older age groups occurred later. This suggests either that children aged 2 to 5 years may be the primary vectors of agents causing asthma, or are the most likely to present with symptoms of asthma at this time, while the triggers are carried by all siblings, including asymptomatic older children. The seasonality we have demonstrated for URI and its ratio to asthma episodes in the different age groups supports the latter possibility.

The real peak of asthma exacerbation may be even higher than reported. The increasing availability of asthma medications, as well as improved counseling on how these should be used, may have limited the need for parents to consult during their child's acute asthma exacerbations.<sup>19</sup> These medications include  $\beta$ -agonist bronchodilators as relievers and ICS and/or oral LTRAs as controllers. Because families have supplies of all these asthma medications at home, they may start the treatment of a mild to moderate asthma exacerbation themselves. They may either visit the PCP later or manage

the exacerbation entirely on their own. Indeed, there has been a recent decreasing trend in the use of long-term prophylactic controller medication, suggesting that giving controller medication as needed may provide similar benefit.<sup>26</sup>

Nevertheless, in most families, when children who have asthma return to school and are re-exposed to risk factors, whether viral, allergic, stress-related, or other, the lack of adequate controller medication may contribute to their risk for worsening asthma at this time.

Our data show fewer filling of prescriptions for asthma medication during the summer months. Hence, use of asthma controller therapy may be at its lowest level of the year immediately before school return. Indeed, adherence to ICS daily therapy in children has generally been shown to be poor, inconsistent, and highly seasonal,<sup>27</sup> and lowest in summer months when children are on vacation and not following their routine schedules.<sup>1,13</sup>

Prescription of asthma medications in children increases substantially during September. Scheuerman et al<sup>1</sup> reported an increased prescription rate of 63% and 60% in children aged 1 to 4 years and 5 to 14 years, respectively. This increment of prescriptions for asthma in September underscores the seasonality of asthma morbidity.

The trends in asthma incidence that we have observed could help in designing more effective preventive and treatment interventions. LTRAs have been shown by some to reduce the likelihood of exacerbations in children who have asthma during the September asthma epidemic.<sup>28</sup> Johnston and colleagues reported that, during the study period from September 1 to October 15, there was a 53% reduction in days with worse asthma symptoms (cough, wheeze, or trouble breathing) and a 78% reduction

in unscheduled physician visits for asthma with montelukast therapy compared with placebo use.<sup>28</sup> That study demonstrated the effect to be greater in younger boys (aged 2–5 years) and older girls (aged 10–14 years), which is generally consistent with the present findings of increased efficacy in boys and older girls. In contrast, Weiss et al reported that montelukast use was not significantly more effective than was placebo use in reducing the percentage of days with worsening asthma when initiated at the start of the school year.<sup>29</sup> They also suggest that the period of risk on return may not extend beyond 4 weeks, after which treatment would not be expected to have an effect. Our data do not support this suggestion, as it shows that in our population a second peak occurs later in the fall and persists throughout winter, suggesting that controller therapy may be required for longer.

Previous studies in children have shown limited efficacy of ICS,<sup>30</sup> anticholinergic drugs,<sup>31</sup> and parent-initiated oral corticosteroids<sup>32</sup> in episodic childhood wheezing, which is thought to be primarily viral in nature. Similarly, montelukast was not efficacious in post-respiratory syncytial virus bronchiolitis despite its well-established efficacy in atopic asthma. Trials of montelukast for episodic wheezing in children have yielded primarily positive but inconsistent results.

It is possible that the September epidemic, which has a strong association with viral infections, is similarly less amenable to intervention with traditionally efficacious medications. However, others have shown that adherence to ICS in preschool asthmatic children, when accompanied by effective training in self-management, was associated with significantly better asthma control. This study took into account the seasonality of asthma.<sup>30</sup> Increasing adherence to prescribed inhaled asthma



controller medication before and during the September school return period could be of benefit during this high-risk period, at least in the subgroup of children who have multifactorial asthma, and thus it may be effective in reducing morbidity.

## CONCLUSIONS

Our study shows that returning to school after the summer vacation is strongly associated with an increased risk for a child experiencing an asthma exacerbation requiring medical attention. We propose that prophylactic

treatment of asthma starting at the end of August should be considered in certain asthmatic children.

## ACKNOWLEDGMENT

We thank Dorit Krash of Clalit Health Services for the statistical analysis.

## REFERENCES

- Scheurman O, Meyerovitch J, Marcus N, Hoffer V, Batt E, Garty BZ. The September epidemic of asthma in Israel. *J Asthma*. 2009;46(7):652–655
- Garty BZ, Kosman E, Ganor E, et al. Emergency room visits of asthmatic children, relation to air pollution, weather, and airborne allergens. *Ann Allergy Asthma Immunol*. 1998;81(6):563–570
- Johnston NW, Sears MR. The epidemiology of asthma exacerbations. *Thorax*. 2006;61:722–728
- 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(9):854–862
- Weiss KB. Seasonal trends in US asthma hospitalizations and mortality. *JAMA*. 1990;263(17):2323–2328
- Newson R, Strachan D, Archibald E, Emberlin J, Hardaker P, Collier C. Acute asthma epidemics, weather and pollen in England, 1987–1994. *Eur Respir J*. 1998;11(3):694–701
- Rosas I, McCartney HA, Payne RW, et al. Analysis of the relationships between environmental factors (aeroallergens, air pollution, and weather) and asthma emergency admissions to a hospital in Mexico City. *Allergy*. 1998;53(4):394–401
- Harju T, Keistinen T, Tuuponen T, Kivelä S-L. Seasonal variation in childhood asthma hospitalisations in Finland, 1972–1992. *Eur J Pediatr*. 1997;156(6):436–439
- Monteil MA, Juman S, Hassanally R, et al. Descriptive epidemiology of asthma in Trinidad, West Indies. *J Asthma*. 2000;37(8):677–684
- Johnston SL, Pattermore PK, Sanderson G, et al. Community study of role of viral infections in exacerbations of asthma in 9–11 year old children. *BMJ*. 1995;310(6989):1225–1229
- Ad Hoc Working group on environmental allergens and asthma. Environmental allergen avoidance in allergic asthma. *J Allergy Clin Immunol*. 1999;103:203–205
- Johnston NW, Johnston SL, Norman GR, Dai J, Sears MR. The September epidemic of asthma hospitalization: school children as disease vectors. *J Allergy Clin Immunol*. 2006;117(3):557–562
- 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(1):132–138
- Silverman RA, Ito K, Stevenson L, Hastings HM. The relationship of fall school opening and emergency department asthma visits in a large metropolitan area. *Arch Pediatr Adolesc Med*. 2005;159(9):818–823
- Guilbert T, Morgan W. Increased asthma symptoms and healthcare utilization during the fall and winter seasons in children with asthma living in the inner city: opportunity for school-based intervention. *J Pediatr*. 2002;141(5):604–605
- Akinbami LJ, Moorman JE, Liu X. Asthma prevalence, health care use and mortality: United States, 2005–2009. *Natl Health Stat Rep*. 2011;32
- Fleming DM, Sunderland R, Cross KW, Ross AM. Declining incidence of episodes of asthma: a study of trends in new episodes presenting to general practitioners in the period 1989–98. *Thorax*. 2000;55(8):657–661
- Garrett J, Kolbe J, Richards G, Whitlock T, Rea H. Major reduction in asthma morbidity and continued reduction in asthma mortality in New Zealand: what lessons have been learned? *Thorax*. 1995;50(3):303–311
- Wennergren G, Kristjánsson S, Strannegård IL. Decrease in hospitalization for treatment of childhood asthma with increased use of antiinflammatory treatment, despite an increase in prevalence of asthma. *J Allergy Clin Immunol*. 1996;97(3):742–748
- Strömberg L. Decreasing admissions for childhood asthma to a Swedish county hospital. *Acta Paediatr*. 1996;85(2):173–176
- Laor A, Cohen L, Danon YL. Effects of time, sex, ethnic origin, and area of residence on prevalence of asthma in Israeli adolescents. *BMJ*. 1993;307(6908):841–844
- Sandberg S, Paton JY, Ahola S, et al. The role of acute and chronic stress in asthma attacks in children. *Lancet*. 2000;356(9234):982–987
- Dales RE, Cakmak S, Judek S, et al. Influence of outdoor aeroallergens on hospitalization for asthma in Canada. *J Allergy Clin Immunol*. 2004;113(2):303–306
- Monto AS. Epidemiology of viral respiratory infections. *Am J Med*. 2002;112(suppl 6A):4S–12S
- Tortolero SR, Bartholomew LK, Tyrrell S, et al. Environmental allergens and irritants in schools: a focus on asthma. *J Sch Health*. 2002;72(1):33–38
- Zeiger RS, Mauger D, Bacharier LB, et al. CARE Network of the National heart, lung and Blood Institute. Daily or intermittent budesonide in preschool children with recurrent wheezing. *N Engl J Med*. 2011;365(21):1990–2001
- Sloan CD, Gebretsadik T, Wu P, Mitchel EF, Hartert TV. Reactive versus proactive patterns of inhaled corticosteroid use. *Ann Am Thorac Soc*. 2013;10(2):131–134
- 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(3). Available at: [www.pediatrics.org/cgi/content/full/120/3/e702](http://www.pediatrics.org/cgi/content/full/120/3/e702)
- Weiss KB, Gern JE, Johnston NW, et al. The Back to School asthma study: the effect of montelukast on asthma burden when initiated prophylactically at the start of the school year. *Ann Allergy Asthma Immunol*. 2010;105(2):174–181
- Bisgaard H, Hermansen MN, Loland L, Halkjaer LB, Buchvald F. Intermittent inhaled corticosteroids in infants with

episodic wheezing. *N Engl J Med.* 2006;354 (19):1998–2005

31. Everard ML, Bara A, Kurian M, Elliott TM, Ducharme F, Mayowe V. Anticholinergic drugs for wheeze in children under the age

of two years. *Cochrane Database Syst Rev.* 2005;3(3):CD001279

32. Vuillermin P, South M, Robertson C. Parent-initiated oral corticosteroid therapy for intermittent wheezing illnesses in children.

*Cochrane Database Syst Rev.* 2006;3(3): CD005311 [Children in the inner city have a high risk-environment with exposure to cigarette smoke, crowding, and indoor allergens.]

## Seasonality of Asthma: A Retrospective Population Study

Herman Avner Cohen, Hannah Blau, Moshe Hoshen, Erez Batat and Ran D. Balicer  
*Pediatrics* 2014;133:e923; originally published online March 10, 2014;  
DOI: 10.1542/peds.2013-2022

<b>Updated Information &amp; Services</b>	including high resolution figures, can be found at: <a href="/content/133/4/e923.full.html">/content/133/4/e923.full.html</a>
<b>References</b>	This article cites 31 articles, 7 of which can be accessed free at: <a href="/content/133/4/e923.full.html#ref-list-1">/content/133/4/e923.full.html#ref-list-1</a>
<b>Citations</b>	This article has been cited by 3 HighWire-hosted articles: <a href="/content/133/4/e923.full.html#related-urls">/content/133/4/e923.full.html#related-urls</a>
<b>Subspecialty Collections</b>	This article, along with others on similar topics, appears in the following collection(s): <b>Public Health</b> <a href="/cgi/collection/public_health_sub">/cgi/collection/public_health_sub</a> <b>Allergy/Immunology</b> <a href="/cgi/collection/allergy:immunology_sub">/cgi/collection/allergy:immunology_sub</a> <b>Asthma</b> <a href="/cgi/collection/asthma_sub">/cgi/collection/asthma_sub</a>
<b>Permissions &amp; Licensing</b>	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: <a href="/site/misc/Permissions.xhtml">/site/misc/Permissions.xhtml</a>
<b>Reprints</b>	Information about ordering reprints can be found online: <a href="/site/misc/reprints.xhtml">/site/misc/reprints.xhtml</a>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2014 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



# PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

## **Seasonality of Asthma: A Retrospective Population Study**

Herman Avner Cohen, Hannah Blau, Moshe Hoshen, Erez Batat and Ran D. Balicer

*Pediatrics* 2014;133:e923; originally published online March 10, 2014;

DOI: 10.1542/peds.2013-2022

The online version of this article, along with updated information and services, is located on the World Wide Web at:

</content/133/4/e923.full.html>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2014 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

