ORIGINAL ARTICLE LOWER AIRWAYS

Prescription patterns for asthma medications in children and adolescents with health care insurance in the United States

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To cite this article: Arellano FM, Arana A, Wentworth CE, Vidaurre CF, Chipps BE. Prescription patterns for asthma medications in children and adolescents with health care insurance in the United States. *Pediatr Allergy Immunol* 2011; **22**: 469–476.

Keywords
adolescents; asthma; children; prescription patterns

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Accepted for publication 21 November 2011

DOI:10.1111/j.1399-3038.2010.01121.x

Abstract

Asthma is the most common chronic condition of childhood, and its prevalence has increased over recent decades. However, many children and adolescents with asthma are not being managed in accordance with guideline recommendations. The objective of this study was to analyze prescribing patterns for asthma medications in 6- to 18-yr-olds, with a focus on those aged 6–11 yr. Data from patients enrolled for ≥6 months in PharMetrics were analyzed between June 1, 1995, and September 30, 2008. PharMetrics contains data from 45 million US patients from 85 health care plans, including standard and mail order prescription records. Prescriptions for asthma medication for each patient were recorded. The overall asthma cohort included 659,169 patients; 34,950 (5%) were classified as having severe asthma. The 6- to 11-yr-old subgroup consisted of 374,068 patients (56.7% of the overall asthma cohort). Almost 40% of the population received no medication (severe asthma 1.0%; non-severe asthma 37.6%), with almost identical findings in the 6- to 11-yr-old subgroup. In patients with non-severe and severe asthma, frequency of medication use was as follows: short-acting β_2-agonists (53% and 92%), oral steroids (23% and 64%), leukotriene receptor antagonists (17% and 49%); inhaled corticosteroids alone (15% and 80%) and in combination with long-acting β_2-agonists (10% and 22%), respectively. Results for patients in the 6- to 11-yr subgroup were similar to those of the overall cohort. In conclusion, a considerable proportion of children and adolescents with asthma do not receive any asthma medication. Among those who do receive medication, adherence to current guidelines is questionable.

Asthma is the most common chronic condition of childhood (1). In 2006, the number of children (< 18 yr) with asthma in the United States was estimated to be 6.8 million (2). The prevalence of asthma among 5- to 14-yr-olds has increased over the past few decades (3) and is currently estimated to be 10.9% (4).

The Asthma Insights and Reality in Europe (AIRE) study estimated that 15% of children with asthma (n = 753) had severe persistent asthma symptoms (5). While published definitions of severe asthma vary, they are generally based on poor control of symptoms or near-fatal events. According to the Global Initiative for Asthma (GINA) 2008 report, classification of asthma by severity involves both the severity of the underlying disease and its responsiveness to treatment (6). Severity is not an unvarying feature of an individual patient's asthma, but may change over months or years (6). In observational studies, severity has generally been measured using surrogates based on hospitalizations, heavy use of asthma medication including rescue medication, or oral steroids (7, 8). It is important to note that the signs and symptoms of pediatric asthma often vary from week to week. For example, an analysis of data from five randomized, double-blind, 12-wk studies showed that children with moderate or severe asthma at baseline often move between severity categories, especially if they have inadequately controlled disease (9). Consequently, point estimates may provide an unreliable guide to the overall severity of pediatric asthma.

The National Asthma Education and Prevention Program (NAEPP) guidelines (10) advocate a stepwise approach to the treatment of asthma in children, following assessment of

asthma control. Short-acting β_2-agonist (SABA) relievers, or short courses of oral corticosteroids (OCS) for severe exacerbations, are recommended at Step 1, and low-dose inhaled corticosteroids (ICS) is the preferred Step 2 treatment (alternative [less preferred] treatments include cromolyn, leukotriene receptor antagonists [LTRA], nedocromil, and theophylline). Steps 3–5 involve increasing ICS doses, plus additional adjunctive therapy (long-acting β_2- agonist [LABA], LTRA or theophylline), with high-dose ICS and LABA, and long-term OCS being preferred at Step 6. Step 3 options have not been studied adequately in children aged 5–11 yr, and options in Steps 4–6 are based on evidence extrapolated from adults (10). While previous NAEPP guidelines (11, 12) had four treatment steps, the order of preferred treatments was broadly similar (SABA when required; low-dose ICS; low-to-medium dose ICS with or without a LABA; high-dose ICS plus a LABA and OCS if required).

Despite intensive treatment, many children with asthma are not achieving good symptom control. This lack of control was evident in the results from an observational study of children and adolescents (6–17 yr) with severe or difficult-to-treat asthma (the TENOR study), which revealed high rates of health care use and loss of lung function despite use of multiple maintenance therapies (13). There is also evidence of underuse of ICS even in children with moderate or severe persistent asthma, and over-reliance on SABA rescue medication (14).

The objective of this study was to analyze the prescribing patterns for asthma medications in 6- to 18-yr-old patients, with a focus on those aged 6–11 yr.

Methods

Data source

PharMetrics contains data from 45 million US patients from 85 health care plans, including demographics, medical services, specialist and hospital diagnoses, inpatient and outpatient diagnoses, standard and mail order prescription records. Only health plans submitting data for all members are included. Quality checks were performed to ensure a standardized format and low error rates.

Cohort definition and follow-up

Data on patients aged 6–18 yr with asthma (ICD 9 code 493.xx), enrolled for ≥6 months in PharMetrics, were analyzed between June 1, 1995, and September 30, 2008. Patients included in the severe asthma subgroup fulfilled one of the following criteria: ≥2 hospital admissions for asthma during the year after study entry; high-risk pharmacological profile (≥3 OCS prescriptions, ≥1.5 SABA metered-dose inhalers per month for ≥3 months, or high-level dispensing [highest quartile of dispensing] of ICS during the year after study entry).

A subgroup of patients aged 6–11 yr was also examined. To account for patients carrying over treatments from when they were <6 yr old (thereby appearing to start therapy on multiple medications or higher treatment steps), a subcohort of naïve patients was created who were diagnosed with asthma only after their sixth birthday; a subgroup of patients with severe asthma within the naïve subcohort was also examined.

Patients were followed from study entry to the date of the latest available PharMetrics update or death. The only exclusion criterion was patients with cancer.

Study assessments

Prescriptions for asthma medication for each patient were monitored for medication used, including doses and number of prescriptions per year. Asthma medications included SABAs, LABAs, ICS, OCS, LTRAs, anti-IgE, cromolyn sodium/nedocromil, xanthines and derivatives, and isoproterenol.

The duration of therapy was calculated using the prescription date and 'days supplied' field. If another prescription was dispensed before or soon after the expected refill date, therapy was considered to be continuous. An OCS burst was defined as continuous use for 3–15 days. Chronic OCS use was defined as continuous use >15 days.

The number and duration of hospitalizations for asthma, and the number of physician's visits and emergency room (ER) visits for asthma were also calculated.

Statistical analysis

Descriptive analyses were performed on data using SAS version 9.1 (SAS Institute Inc., Cary, NC, USA) and STATA version 7.0 (StataCorp LP, College Station, TX, USA).

Results

Patient characteristics

The overall asthma cohort included 659,169 patients; 297,012 (45%) were female; 34,950 (5%) were classified as having severe asthma. The 6- to 11-yr-old subgroup consisted of 374,068 patients (56.7% of the overall asthma cohort); of these, 152,238 (41%) were female, and 25,077 (7%) had severe asthma. The overall naïve asthma subcohort (6–18 yr) consisted of 595,619 patients, 27,387 of whom had severe asthma.

Medication use (overall cohort)

Fig. 1 summarizes the number of classes of medication used per patient in the 6- to 18-yr cohort. Subgroup analysis showed that the number of classes of medication used in patients aged 6–11 yr was almost identical to the 6- to 18-yr cohort; 38% and 0.7% of non-severe and severe patients, respectively, were not prescribed asthma medication; 24% of non-severe patients were prescribed one drug, and 73% of severe patients were prescribed at least three (data not shown).

Table 1a shows the number of patients using each class of medication in the overall patient cohort (6–18 yr of age). In patients with non-severe asthma, SABAs were the most frequently used medication (53%), followed by OCS (23%)

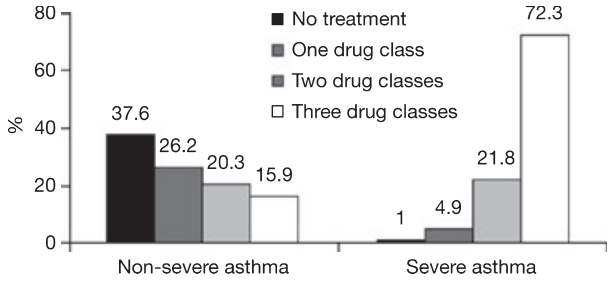

Figure 1 Number of asthma medications per patient in the overall asthma cohort (6–18 yr).

and LTRAs (17%). ICS and ICS/LABA combination therapy were used by 15% and 10% of patients, respectively. Among patients with severe asthma, SABAs were the most frequently used medication (92%), followed by ICS (80%), OCS (64%), LTRAs (49%), and ICS/LABA combination (22%). Results for patients in the 6- to 11-yr subgroup were similar to those of the overall cohort, for both non-severe and severe asthma (Table 1b).

Examining both age subcohorts of the overall asthma cohort (6–18 yr and 6–11 yr), most non-severe patients appeared to start their treatment with a SABA (44% and 42%, respectively). Other apparent common starting medications were OCS (14% and 16%), LTRAs (9% and 11%), and ICS (8% and 9%); 4% of 6- to 18-yr-olds and 5% of 6- to 11-yr-olds appeared to start on ICS/LABA combination. In severe patients (6–18 yr and 6–11 yr), the most common starting medications were SABA (55% and 53%), ICS (43% and 45%), OCS (32% for both groups), and LTRAs (17% and 19%); 3% of 6- to 18-yr-olds and 2% of 6- to 11-yr-olds appeared to start on ICS/LABA combination. Subgroup analysis showed that the number of classes of medication used in patients aged 6–11 yr was almost identical to the 6- to 18-yr cohort (data not shown).

Medication use in treatment-naïve asthma patients

Examining starting medications in patients who were diagnosed with asthma only after their sixth birthday, the patterns in the overall naïve asthma cohort and the naïve severe asthma subgroup were similar, although fewer severe patients received no medication at diagnosis, and more started their treatment with ICS (12% and 2.8%; Table 2). As expected, a smaller proportion of patients in the naïve cohort started on higher step treatments or combination therapy than as detected in the overall cohort (Table 2).

Additions and changes to medication in those patients starting on SABAs, ICS, and ICS/LABA combination are described in Table 3. Within the overall naïve cohort, of the patients who started treatment on a SABA, 39% remained on SABAs only (3% in severe patients). The drugs most frequently added to SABAs were ICS (13%), chronic OCS (12%), LTRA (6%), and ICS/LABA combination (4%); 7% received OCS bursts. In severe naïve patients, the medications most frequently added were ICS (34%), chronic OCS (18%), and LTRAs (7%); 17% received OCS bursts. In the naïve cohort, 23% of patients starting with SABAs switched to other therapies, the most common being chronic OCS (8%), ICS (6%), LTRA (5%), and ICS-LABA (3%). In the severe patients, 30% switched from SABAs to other therapies, the most common being ICS (14%), chronic OCS (9%), and LTRAs (4%).

In the naïve cohort, among patients who were started on ICS, 21% remained on ICS only (7% in severe patients). The medications most frequently added to ICS were SABAs (15%), LTRAs (9%), and chronic OCS (5%; Table 3); 8% received OCS bursts. In severe naïve patients, the medications most frequently added to ICS were also SABAs (28%), LTRAs (12%), and chronic OCS (5%); 14% received OCS bursts. Forty-seven percent of patients in the naïve cohort and 43% of severe naïve patients switched from ICS to other therapies. Similar proportions of patients in each group were switched from ICS to SABAs (34.6% and 31.5%), LTRAs (5% and 5%), and chronic OCS (5% and 5%).

Among patients who were started on ICS/LABA combination, 30% received only ICS/LABA; no patients in the severe naïve group remained on this combination alone (Table 3). The medications most frequently added to ICS/LABA in severe naïve patients were SABAs (26%), chronic OCS (8%), and LTRAs (6%); 24% received OCS bursts. Fifty-nine percent of severe naïve patients switched to other therapies, the most common being SABAs (38%), chronic OCS (9%), ICS (6%), and LTRAs (5%).

Table 4a shows the pattern of medication use during the first year after study entry in the naïve cohort. The pattern of use in yr 2 and 3 was similar to YR 1, although the number of patients starting each year on SABAs alone decreased with each successive year. ICS (20–22% of patients), chronic OCS (17–23%), and LTRAs (15–20) were the most frequent additions to SABAs.

Among ICS starters, 19%, 41%, and 47% of patients were classified as severe over the first, second, and third years, respectively, suggesting that severe patients tended to retain ICS as part of their therapy. Aside from adding SABAs (52–69% of patients), the most frequently added medications were LTRAs (21–27%) and chronic OCS (18–19%; Table 4 b).

The proportion of naïve patients classified as severe in the ICS/LABA starter group over the first, second, and third years were 3%, 4%, and 5%, respectively. Aside from adding SABAs (44–60% of patients), the most frequently added medications were LTRAs (16–26%) and chronic OCS (15–17%; Table 4c).

The majority of naïve patients (94%) did not receive steroid bursts (defined as continuous use of prednisone, prednisolone or methyl-prednisolone for 3–15 days) during the first year of the study. Five percent of naïve patients received one OCS burst and almost 1% received two or more bursts. A higher proportion of patients starting on xanthines received one or more OCS bursts compared with those starting on other medications, in whom the number of OCS bursts was similar by starting medication.

Table 1 Asthma medication use in children with asthma aged 6–18 (a) and 6–11 (b)

	Non-severe asthma			Severe asthma		
	Number of patients (%)*	Number of prescriptions	Mean prescriptions per patient per year	Number of patients (%)*	Number of prescriptions	Mean prescriptions per patient per year
	Total patients (n = 624,219)	Total patient-years (1, 028,310)		Total patients (n = 34,950)	Total patient-years (71,493)	
a						
SABA	328,695 (52.7)	821,511	0.80	32,132 (91.9)	217,097	3.04
OCS	143,558 (23.0)	208,133	0.20	22,225 (63.6)	70,053	0.98
LTRA	103,547 (16.6)	535,724	0.52	17,016 (48.7)	149,752	2.09
ICS	95,318 (15.3)	170,950	0.17	27,887 (79.8)	169,712	2.37
ICS/LABA	63,087 (10.1)	236,903	0.23	7625 (21.8)	45,782	0.64
Cromoglycates	8722 (1.4)	20,123	0.02	1675 (4.8)	6738	0.09
LABA	7572 (1.2)	17,300	0.02	2475 (7.1)	13,551	0.19
ACH	2743 (0.4)	4276	0	1093 (3.1)	2798	0.04
SABA/ACH	2723 (0.4)	4721	0	606 (1.7)	1720	0.02
Xanthines	639 (0.1)	1641	0	225 (0.6)	1071	0.01
Anti-IgE	31 (0)	212	0	22 (0.1)	277	0
b	Total patients (n = 348,991)	Total patient-years (484,701)		Total patients (n = 25,077)	Total patient-years (45,176)	
SABA	178,668 (51.2)	408,982	0.84	22,959 (91.6)	128,917	2.85
OCS	87,066 (24.9)	125,399	0.26	16,226 (64.7)	49,189	1.09
LTRA	66,008 (18.9)	342,293	0.71	12,805 (51.1)	112,344	2.49
ICS	61,104 (17.5)	108,825	0.22	20,803 (83.0)	124,682	2.76
ICS/LABA	28,657 (8.2)	107,768	0.22	4555 (18.2)	26,338	0.58
Cromoglycates	5211 (1.5)	12,392	0.03	1168 (4.7)	4553	0.10
LABA	2853 (0.8)	6577	0.01	1340 (5.3)	6752	0.15
ACH	1566 (0.4)	2295	0	762 (3)	1895	0.04
SABA/ACH	1015 (0.3)	1597	0	378 (1.5)	1041	0.02
Xanthines	251 (0.1)	595	0	112 (0.4)	380	0.01
Anti-IgE	10 (0)	50	0	8 (0)	112	0

*Patients receiving multiple medications are included within the totals for each medication received (column totals are thus greater than the total number of patients).

SABA, short-acting β_2-agonist; LABA, long-acting β_2-agonist; ICS, inhaled corticosteroids; ACH, anticholinergics; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroids.

Medical service use

During the first year of the study, the mean (s.d.) number of outpatient visits was 2 (2.0) in the overall cohort and 4 (3.5) in severe patients (Fig. 2). In the second and third years, patterns were similar, although there was a tendency for patients to see their physician more; ≥3 visits were reported for 16%, 19%, and 20% of non-severe patients and 57%, 59%, and 59% of severe patients in YR 1, 2, and 3, respectively (data not shown).

Fig. 3 shows the number of ER visits during the first year of the study in the overall cohort. The mean (s.d.) number of visits in the first year was 0.13 (0.40) in the overall cohort and 0.29 (0.73) in severe patients. The number of ER visits remained similar in the second and third years (data not shown). The majority of patients (98.7%) were not hospitalized at all in the first year of the study, 1.2% were admitted only once, and 0.1% were admitted twice (mean [s.d.] duration: 4.18 [6.47] days). Medication at the start of therapy was not associated with hospitalization rates.

Discussion

Records in the PharMetrics database are representative of the national managed care population, based on a variety of patient and health plan demographic measures that include geographic region, age, gender, and plan type with the exception of persons ≥65 (8% in PharMetrics vs. 13% in the US census). To study a representative commercially insured population of the United States, we avoided as many exclusion criteria as possible.

The symptoms of pediatric asthma are highly variable, and the severity of the condition often fluctuates over time, especially in children whose asthma is inadequately controlled (9). Consequently, it can be difficult to estimate the prevalence of severe asthma. In the International Study of Asthma

Table 2 Initial asthma medication use in children with asthma aged 6–18, 'naïve' to therapy

	Overall naïve cohort (n = 595,619) n (%)	Severe naïve (n = 27,387) n (%)
SABA	309,947 (52.0)	17,836 (65.1)
OCS	41,445 (7.0)	2742 (10.0)
LTRA	36,857 (6.2)	2248 (8.2)
ICS	16,783 (2.8)	3198 (11.7)
ICS/LABA	13,980 (2.3)	444 (1.6)
LABA	3211 (0.5)	361 (1.3)
Cromoglycates	2363 (0.4)	208 (0.8)
SABA/ACH	902 (0.2)	28 (0.1)
Xanthines	337 (0.1)	39 (0.1)
ACH	314 (0.1)	25 (0.1)
Anti-IgE	7 (0)	0 (0)
No asthma medication use	169,473 (28.5)	258 (0.9)
TOTAL 'naïve' patients (aged 6–18)	595,619 (100)	27,387 (100)

SABA, short-acting β_2-agonist; LABA, long-acting β_2-agonist; ICS, inhaled corticosteroids; ACH, anticholinergics; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroids.

and Allergies in Childhood (ISAAC) surveys, the prevalence of severe asthma (≥4 attacks of wheezing in the past 12 months) in 13- to 14-yr-old children was 2.0–8.3% in Western Europe and 6.1% in the USA (15). Given the burden of the illness (16), it is surprising that a high proportion of patients in this study did not receive treatment for their asthma. The proportion of untreated patients in the severe subgroup was negligible (< 1%), and a similar proportion of untreated patients has been reported previously (17). This may represent a shortfall in the treatment of asthma in children and adolescents; however, it may also indicate that some physicians are hesitant to treat cases of wheezing that may be miscoded as asthma, particularly where a database does not have a specific code for wheezing (18). PharMetrics has a code for wheezing, which is based on the ninth International Classification of Disease (ICD-9) code 786.07 (wheezing, excludes asthma), making the misclassification of wheezing as asthma less likely.

While our study indicates that asthma medications are underprescribed in insured patients in the US, asthma medications may be overprescribed in some countries. For example, an Italian study showed that the percentage of children who had been prescribed an asthma medication was substantially higher than the percentage that had asthma (19), indicating that many prescriptions were given to non-asthmatic children. Other studies have indicated that there are wide variations in the prevalence of prescriptions for pediatric asthma between countries, with 19% of all children in Italy receiving asthma medication, compared with 18% in Canada, 14.6% in the US, 13.9% in Denmark, 9.1% in Norway, and 6.2% in the Netherlands (20). Consequently, although our findings are representative of the insured population in the USA, they are not necessarily applicable to other countries.

Our study showed that, in line with guideline recommendations (6, 10–12), the majority of patients received SABAs

Table 3 Additional or alternative asthma therapy in children (≥1%) with asthma aged 6–18, 'naïve' to therapy, who initiated treatment on SABA, ICS, or ICS/LABA combination therapy

	SABA starters		ICS starters		ICS/LABA starters	
	Naïve cohort (n = 309,947), %	Severe naïve (n = 17,836), %	Naïve cohort (n = 16,783), %	Severe naïve (n = 3198), %	Naïve cohort (n = 13,980), %	Severe naïve (n = 444), %
SABA only	39.2	2.9	–	–	–	–
ICS only	–	–	21.0	7.2	–	–
ICS/LABA only	–	–	–	–	30.1	0
Add SABA	–	–	14.9	28.4	16.7	26.4
Switch to SABA	–	–	34.6	31.5	30.8	37.8
Add ICS	13.2	33.8	–	–	0.1	0
Switch to ICS	5.7	14.3	–	–	1.4	6.1
Add LABA	0.7	1.9	0.4	1.0	–	0
Add LTRA	6.0	6.8	9.3	12.5	3.9	5.6
Switch to LTRA	5.0	3.9	5.1	4.8	6.4	5.6
Add cromoglycates	1.5	2.8	0.7	1.3	0.1	0
Add ICS/LABA	4.0	2.9	0.3	0.3	–	–
Switch to ICS/LABA	3.0	1.5	1.6	0.4	–	–
Add chronic OCS	12.5	18.4	5.0	5.5	4.2	7.7
Switch to chronic OCS	7.7	8.8	5.0	4.8	5.2	9.2
OCS burst	7.0	17.0	8.4	14.4	8.0	24.3

SABA, short-acting β_2-agonist; LABA, long-acting β_2-agonist; ICS, inhaled corticosteroids; ACH, anticholinergics; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroids.

Table 4 Sequence of drug use for 'naïve' asthma patients, initiating with (a) SABA, (b) ICS, or (c) ICS/LABA

a	1st year Number of patients (n = 309,947), %	2nd year Number of patients (n = 106,987), %	3rd year Number of patients (n = 61,337), %
SABA	100	100	100
Add ICS	20.6	22.5	20.3
Add LABA	1.6	1.9	1.8
Add ICS/LABA	9.4	13.4	13.1
Add LTRA	14.7	20.1	19.4
Add ICS + LTRA	4.7	6.6	6.4
Add chronic OCS	22.8	19.1	17.5
OCS bursts (3–15 days)	5.6	5.2	5.2
b	1st year Number of patients (n = 16, 783), %	2nd year Number of patients (n = 5696), %	3rd year Number of patients (n = 2911), %
ICS	100	100	100
Add SABA	52.5	68.6	68.4
Add LABA	2.4	3.8	3.7
Add ICS/LABA	5.8	6.5	3.8
Add LTRA	20.8	27.1	26
Add LABA + LTRA	0.7	1.6	1.8
Add LABA/ICS + LTRA	2.4	3.2	3.3
Add LABA/ICS + LTRA + LABA	0.1	0.3	0.3
Add chronic OCS	18.5	19.3	18.9
OCS bursts (3–15 days)	5.8	6.3	6.5
c	1st year Number of patients (n = 13,980), %	2nd year Number of patients (n = 4902), %	3rd year Number of patients (n = 2690), %
ICS/LABA	100	100	100
ICS (high dose)/LABA	3.2	4.5	5.2
Add SABA	44	57.4	60.4
Add LABA	0.6	0.6	0.3
Add ICS	5.6	5.5	4.8
Add LTRA	16.2	24.8	26.5
Add LABA + LTRA	0.3	0.3	0.1
Add ICS + LTRA	1.8	2.5	3
Add ICS/LABA + LTRA	0.2	0.1	0
Add chronic OCS	15.1	16.0	16.9
OCS bursts (3–15 days)	5.4	5.4	5.7

SABA, short-acting β_2-agonist; LABA, long-acting β_2-agonist; ICS, inhaled corticosteroids; ACH, anticholinergics; LTRA, leukotriene receptor antagonist; OCS, oral corticosteroids.

as their first treatment, but a considerable proportion appeared to start treatment on ICS, LTRAs or chronic OCS, rather than SABAs, which taken at face value is surprising; however, this may be attributable to some distortion owing to study methodology: as SABAs are recommended for use as needed rather than as regular maintenance therapy, repeat prescriptions for SABAs may have been presented after the 'expected refill date' used to compute continuing therapy, thereby underestimating continuing use of SABAs as relievers. Guidelines recommend ICS as the next treatment step after SABAs, and ICS was added or switched to in 19% of the naïve cohort and 48% of the severe naïve cohort. Chronic OCS and LTRAs were added to SABAs in a considerable proportion of patients. Only a small number of patients, even within the severe subgroup, were started on, switched to or had added a LABA or a LABA/ICS combination, perhaps reflecting reluctance among prescribers to use LABA therapy within this age group. Almost a quarter of patients appeared to switch from (i.e. discontinue) SABAs to other therapies, but this may again be attributable to inadequate detection of continuing use of SABAs as relievers. Among patients starting on ICS and ICS/LABA combination, the SABAs were most frequently added, presumably as reliever medication, but almost a third of patients were

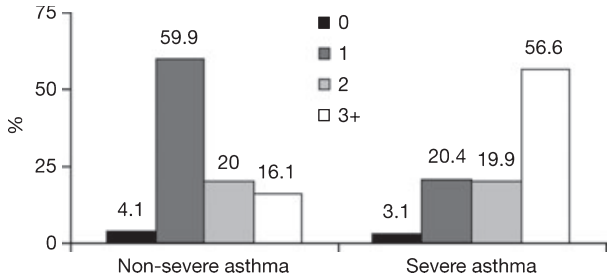

Figure 2 Asthma-related outpatient physician visits in the first year (patients with severe and non-severe asthma).

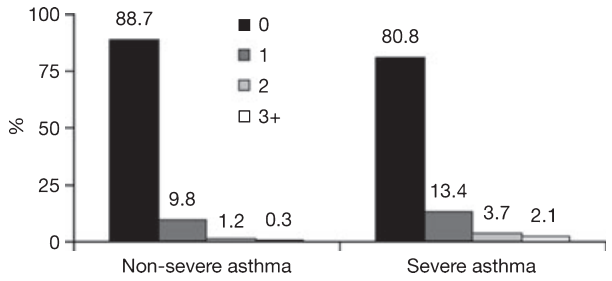

Figure 3 Asthma-related emergency room visits in the first year (patients with severe and non-severe asthma).

switched to SABAs. Nine percent of the naïve cohort and 17% of the severe naïve cohort had chronic OCS added to ICS/LABA combination. These results indicate that adherence to prescribing guidelines among physicians is suboptimal, perhaps based on individual preconceptions on efficacy or side effects associated with asthma therapies, or a paucity of high-quality evidence on their use in children, and guidelines noting that their recommendations are by necessity extrapolated from studies in adults (12).

There were considerable differences in the continuous duration of therapy between use of OCS in bursts and 'chronic' use of OCS. The former had a median duration of 9 days (range 7–15 days), while chronic users had a median duration of 30 days (range 16–120 days). Approximately 10% of severe patients started treatment on chronic OCS. The majority of OCS use was chronic rather than in bursts. While most (94.5%) patients did not receive an OCS burst during the first year following asthma diagnosis, 24% received OCS in the first year, and only two-thirds were steroid-free during that period. The proportion of patients that required ≥2 OCS bursts per year was low. There did not appear to be an association between starting medication and OCS bursts. The relatively high levels of OCS use is surprising considering that regular OCS use is associated with significant systemic side effects including cataracts, high blood sugar among non-diabetics, osteoporosis, acne, weight gain, sleep, and mood disturbances (21, 22).

The majority of non-severe patients visited the outpatient physician once per year, while the majority of severe patients had ≥3 visits. ER visits were relatively infrequent, but the frequency of visits in severe patients was double that in non-severe patients. Severe patients had a higher frequency of multiple visits. Only 1.2% of patients were hospitalized in the first year.

The limitations of this study are that inclusion criteria for severity are also used to define some of the outcomes. Also, as PharMetrics data are derived from private insurers, results may not represent the uninsured US population (asthma tends to be more severe in poor, uninsured, minority communities). Asthma may also be more prevalent and less adequately treated among children without private insurance, who have been shown to have a greater than twofold higher risk of hospitalization for asthma (227.2 cases per 100,000 individuals) compared with privately insured children (96.0 cases per 100,000 individuals) (23). PharMetrics data do not include over-the-counter medication; however, as asthma medications are not generally available over the counter, this is unlikely to result in significant bias. Reliable information on ICS dosing could not be obtained to calculate dose increases or decreases.

In conclusion, a significant proportion of children and adolescents with asthma do not receive any asthma medication. Among those who do receive medication, adherence to the guidelines is questionable, perhaps because of physicians' beliefs regarding existing therapy options, or a lack of evidence from well-designed trials in children with asthma. Furthermore, the use of chronic OCS, even at early stages of treatment, is surprisingly high.

Acknowledgments

The authors were assisted in the preparation of the manuscript by professional medical writer Tom McMurray (ACUMED). This writing support was funded by Novartis Pharma AG.

Conflict of interest

The study was funded by an unrestricted grant from Novartis Pharma AG. Risk Management Resources had the contractual right and the determination to publish the results as well as the final decision on the content of the manuscript. Risk Management Resources (which involved Alejandro Arana, Felix M Arellano and Charles Wentworth) had consultancy relationships with Schering Plough and is currently receiving a grant from Novartis. Alejandro Arana has been previously employed by Novartis and Pfizer.

Bradley Chipps has consulting arrangements with Aventis, Genentech, AstraZeneca, GlaxoSmithKline, MedPoint, Novartis, Schering, Sepracor, and Merck; has received grant support from Aventis, Genentech, AstraZeneca, GlaxoSmithKline, Novartis, Schering, Sepracor, and Merck; is on the speakers' bureau for Aventis, Genentech, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, MedPoint, Novartis, Pfizer, Schering, Sepracor, and Merck; and has served as an expert witness in mold litigation. Carlos Fernandez-Viadaurre is an employee of Novartis.

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