# Disease Burden And Treatment Adherence Among Children And Adolescent Patients With Asthma

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Carlyne M. Averell[1], François Laliberté[2], Guillaume Germain[2], David J. Slade[1], Mei S. Duh[3], Robson Lima[1], Joseph Spahn[1]

[1]GlaxoSmithKline, Research Triangle Park, NC; [2]Groupe d'analyse, Ltée, Montréal, QC, Canada; [3]Analysis Group, Inc., Boston, MA

## Introduction

Less frequent dosing regimens have been suggested as a way to increase adherence to respiratory therapy.[1-4] However, there is limited real-world information in the US regarding clinical characteristics, treatment patterns including adherence, and associated burden among children and adolescents using twice-daily ICS-containing controller medications. This study assessed disease burden among asthma patients 5-17 years of age, and medication adherence of twice-daily ICS and ICS/LABA users in a large US claims database.

## Methods

**Study Design:** Retrospective observational study, using IQVIA™ Real-World Data Adjudicated Claims US Database, of patients aged 5-17 years diagnosed with asthma (asthma cohort) and those initiating twice-daily ICS or ICS/LABA (treatment cohorts) between January 1, 2012 and September 30, 2017.

**Inclusion criteria**

**Asthma Cohort**:
- ≥1 asthma diagnosis with ≥12 months prior enrollment (index date=first asthma diagnosis after 12-month enrollment) plus ≥1 asthma diagnosis in 12-month baseline prior to index date
- Age 5-17 years at index
- ≥12 months enrollment after index date

**Treatment Cohort**:
- Initiation of twice-daily ICS or ICS/LABA (index date=date of first dispensing)
- ≥12 months enrollment before (baseline) and ≥3 months enrollment after the index date (follow-up period)
- ≥2 asthma diagnoses with ≥1 asthma diagnosis during baseline or on index date, and ≥1 diagnosis during follow-up

**Exclusion criteria**

**Asthma Cohort**:
- ≥1 diagnosis of chronic bronchitis any time during the study period
- ≥1 diagnosis of cystic fibrosis any time during the study period

**Treatment Cohort**:
- ≥1 diagnosis of chronic bronchitis any time during the study period
- ≥1 diagnosis of cystic fibrosis any time during the study period
- ≥1 prescription fill for an ICS or ICS/LABA medication during the baseline period for patients who were initiated on twice-daily ICS and twice-daily ICS/LABA, respectively

**Outcomes**

Treatment Patterns and Exacerbations

Adherence and Persistence to Twice-daily ICS and ICS/LABA

**Treatment Cohorts:** outcomes assessed in 12-month post-index (follow up) period

- **Adherence** was measured as mean proportion of days covered (PDC), and proportion of patients adherent was measured as PDC≥80% and ≥50%, respectively.

$$\text{PDC} = \frac{\text{Total days covered by index medication in follow-up period}}{\text{Total days in follow-up}}$$

- **Persistence** rates: no treatment discontinuation gap >60 days between dispensings

## Results

### Baseline Characteristics

The asthma cohort included 186,868 patients, comprised of 112,689 children and 74,179 adolescents. The mean age overall was 10.5 years (children: 7.9; adolescents: 14.3). During the baseline, 25.7% of overall asthma patients used ICS, 8.8% used ICS/LABA, 24% used OCS, 20% had ≥1 asthma exacerbation, 2.2% had ≥1 severe asthma exacerbation, 11.1% had ≥1 asthma-related ER visit, and 2.2% had ≥1 asthma-related hospitalization **(Table 1)**.

**Table 1. Baseline Demographic and Clinical Characteristics**

| Characteristic (Asthma Cohort) | Overall, Age 5-17 years (N=186,868) | Children, Age 5-11 years (N=112,689) | Adolescents, Age 12-17 years (N=74,179) |
|---|---|---|---|
| **Age,** mean (SD) | 10.5 (3.6) | 7.9 (2.0) | 14.3 (1.7) |
| **Female,** n (%) | 75,406 (40.4) | 42,549 (37.8) | 32,857 (44.3) |
| **≥ 1 ICS,** n (%) | 47,982 (25.7) | 33,380 (29.6) | 14,602 (19.7) |
| **≥ 1 ICS/LABA,** n (%) | 16,367 (8.8) | 7,171 (6.4) | 9,196 (12.4) |
| **≥ 1 LTRA,** n (%) | 36,619 (19.6) | 22,531 (20.0) | 14,088 (19.0) |
| **≥ 1 SABA,** n (%) | 82,689 (44.2) | 49,718 (44.1) | 32,971 (44.4) |
| **≥ 1 OCS,** n (%) | 44,764 (24.0) | 29,979 (26.6) | 14,785 (19.9) |
| **≥ 1 Asthma exacerbation**, n (%) | 37,405 (20.0) | 25,704 (22.8) | 11,701 (15.8) |
| **≥ 1 Severe asthma exacerbation**, n (%) | 4,182 (2.2) | 3,110 (2.8) | 1,072 (1.4) |
| **≥ 1 Asthma-related ER visit**, n (%) | 20,669 (11.1) | 14,204 (12.6) | 6,465 (8.7) |
| **≥ 1 Asthma-related hospitalization**, n (%) | 4,157 (2.2) | 3,091 (2.7) | 1,066 (1.4) |
| **Characteristic (Treatment Cohorts)** | **Twice-Daily ICS (N=47,276)** | **Twice-Daily ICS/LABA (N=10,247)** | |
| **Age,** mean (SD) | 9.9 (3.7) | 12.5 (3.3) | |
| **Female,** n (%) | 20,748 (43.9) | 4,938 (48.2) | |
| **Primary Care Prescribing Provider[2],** n (%) | 30,514 (64.5) | 4,984 (48.6) | |
| **Respiratory Specialist Prescriber[2],** n (%) | 6,054 (12.8) | 2,568 (25.1) | |
| **≥ 1 ICS,** n (%) | 0 (0.0) | 614 (6.0) | |
| **≥ 1 LTRA,** n (%) | 10,929 (23.1) | 3,163 (30.9) | |
| **≥ 1 SABA,** n (%) | 30,940 (65.4) | 6,785 (66.2) | |
| **≥ 1 OCS,** n (%) | 18,399 (38.9) | 4,164 (40.6) | |
| **≥ 1 Asthma exacerbation**, n (%) | 10,368 (21.9) | 2,298 (22.4) | |
| **≥ 1 Severe asthma exacerbation**, n (%) | 1,315 (2.8) | 196 (1.9) | |
| **≥ 1 Asthma-related ER visit**, n(%) | 3,732 (7.9) | 775 (7.6) | |
| **≥ 1 Asthma-related hospitalization**, n(%) | 1,368 (2.9) | 198 (1.9) | |

*Abbreviations:* AMR: asthma medication ratio, ICS: inhaled corticosteroid, LABA: long-acting bronchodilator, OCS: oral corticosteroid, LTRA: leukotriene receptor antagonists. SABA: short-acting bronchodilator, ER: emergency room. 1. All costs in US$ 2018. 2. Patients were classified as having either a respiratory specialist (pulmonologist, allergist) or primary care provider (pediatrician, internal medicine, family medicine practitioner, nurse practitioner) as a prescribing provider specialty 3. Overall asthma exacerbations defined as an asthma-related outpatient visit or ER visit with a systemic corticosteroid dispensing within ± 5 days, or asthma-related ER visit leading to an asthma-related hospitalization within +1 day, or an asthma-related hospitalization. Severe exacerbations defined as an asthma-related hospitalization or an asthma-related ER visit that results in a hospitalization within the next day.

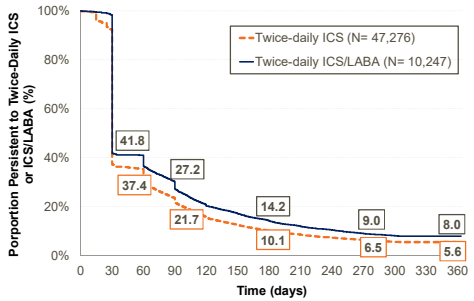
Among treatment cohorts, 47,276 and 10,247 of patients initiated twice-daily ICS and ICS/LABA, respectively. Mean age of the cohorts was 9.9 and 12.5 years, respectively **(Table 1)**.

### Adherence and Persistence

Mean PDC adherence to twice-daily ICS and ICS/LABA was 30% and 34% at 6-months, and 21% and 24% at 12-months, respectively. The proportion of patients with PDC≥80% among the twice-daily ICS and ICS/LABA cohorts was 4.3% and 6.1% at 6-months, and 1.8% and 2.8% at 12-months, respectively **(Table 2)**.

Persistence to twice-daily ICS was 37.4%, 21.7%, 10.1%, 6.5%, and 5.6% at 30, 90, 180, 270, and 365 days post-treatment initiation. Persistence to twice-daily ICS/LABA was similarly low, specifically 41.8%, 27.2%, 14.2%, 9.0%, and 8.0% at 30, 90, 180, 270, and 365 days post-treatment initiation, respectively **(Figure 1)**.

**Figure 1. Treatment Cohorts: Persistence to Twice-Daily ICS and ICS/LABA in Follow-up Period**




| No. At Risk | | | | | |
|---|---|---|---|---|---|
| Twice-daily ICS | 17,666 | 10,248 | 4,246 | 2,347 | 1,759 |
| Twice-daily ICS/LABA | 4,287 | 2,787 | 1,309 | 747 | 596 |

**Table 2. Treatment Cohorts: Adherence to Twice-Daily ICS and ICS/LABA in Follow-up Period**

| | Twice-daily ICS (N=47,276) | Twice-daily ICS/LABA (N=10,247) |
|---|---|---|
| Observation period, days, mean ± SD [median][1] | 341 ± 60 [366] | 342 ± 59 [366] |
| At 180 days | | |
| Number of patients | 44,814 | 9,716 |
| PDC, mean ± SD [median] | 0.30 ± 0.20 [0.17] | 0.34 ± 0.22 [0.32] |
| Proportion with PDC ≥50%, n (%) | 8,706 (19.4) | 2,592 (26.7) |
| Proportion with PDC ≥80%, n (%) | 1,915 (4.3) | 595 (6.1) |
| At 365 days | | |
| Number of patients | 37,943 | 8,341 |
| PDC, mean ± SD [median] | 0.21 ± 0.18 [0.16] | 0.24 ± 0.20 [0.16] |
| Proportion with PDC ≥50%, n (%) | 2,721 (7.2) | 887 (10.6) |
| Proportion with PDC ≥80%, n (%) | 694 (1.8) | 230 (2.8) |

## Limitations

- This study used pharmacy claims data which is an indirect measure of adherence, and as such it is unknown if patients actually consumed the medication.
- Dosing frequency was assumed to be in accordance with the Prescribing Information for each product.

## Conclusions

A large disease burden and unmet need exists among children and adolescents with asthma in the US as evidenced by:

- Underutilization, and low adherence and persistence to ICS-containing medication
- Substantial proportion of OCS users, and
- Notable asthma-related ER and hospitalization rates.

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