Asthma Controller Medication Adherence, Risk of Exacerbation, and Use of Rescue Agents Among Texas Medicaid Patients with Persistent Asthma

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ABSTRACT

BACKGROUND: Adherence to asthma long-term controller medications is one of the key drivers to improve asthma management among patients with persistent asthma. While suboptimal use of controller medications has been found to be associated with more frequent use of oral corticosteroids (OCS), few studies exist regarding the relationship between adherence to controller therapy and the use of short-acting beta2-agonists (SABAs). A better understanding of the association between adherence to asthma controller agents and use of reliever medications will help health care providers and decision makers enhance asthma management.

OBJECTIVE: To determine if there is a relationship between asthma controller adherence, risk of exacerbation requiring OCS, and use of asthma rescue agents.

METHODS: Texas Medicaid claims data from January 1, 2008, to August 31, 2011, were retrospectively analyzed. Continuously enrolled patients aged 5-63 years with a primary diagnosis of asthma (ICD-9-CM code 493) and with 4 or more prescription claims for any asthma medication in 1 year (persistent asthma) were included. The index date was the date of the first asthma controller prescription, and patients were followed for 1 year. The primary outcome variables were SABA (dichotomous: <6 vs. ≥ 6) and OCS (continuous) use. The primary independent variable was adherence (proportion of days covered [PDC]) to asthma long-term controller medications. Covariates included demographics and nonstudy medication utilization. Multivariate logistic and linear regression analyses were employed to address the study objective.

RESULTS: The study sample (n = 32,172) was aged 15.0 ± 14.5 years, and adherence to controller therapy was 32.2% ± 19.7%. The mean number of SABA claims was 3.7 ± 3.1, with most patients having 1-5 claims (73.2%), whereas 19.4% had ≥ 6 SABA claims. The mean number of OCS claims was 1.0 ± 1.4. Adherent (PDC ≥ 50%) patients were 96.7% (OR = 1.967; 95% CI = 1.826-2.120) more likely to have ≥ 6 SABA claims when compared with nonadherent (PDC < 50%) patients ($P < 0.001$). As for OCS use, adherent patients had 0.11 fewer claims compared with nonadherent patients ($P < 0.001$). Importantly, patients with ≥ 6 SABA claims had 0.7 more OCS claims compared with patients with < 6 claims for SABA ($P < 0.001$). The odds of having ≥ 6 SABA claims were higher for concurrent dual therapy users, older age, males, African Americans and higher number of nonstudy medications ($P < 0.001$). Dual therapy users, younger age, Hispanic ethnicity, and higher number of nonstudy medications were associated with an increase in OCS use ($P < 0.005$).

CONCLUSIONS: Adherence to long-term controller medications was suboptimal among patients with asthma. Adherent patients had fewer OCS claims, indicating that adherence to controller therapy is critical in preventing asthma exacerbations requiring OCS use. Although there was a positive relationship between adherence to long-term controller medication and SABA use, increased SABA use served as a predictor of increased OCS use, which indicates poor asthma control. Health care providers should be aware of OCS and SABA use among patients who are both adherent and nonadherent to asthma controller medications.

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What is already known about this subject

- Regular use of asthma long-term controller medications is one of the key drivers to improve persistent asthma management, yet medication adherence among patients with asthma is suboptimal, often ranging from 30%-40% in practice.
- Poor adherence is associated with higher risk for exacerbations requiring oral corticosteroid (OCS) use; however, conflicting results exist regarding the association between adherence to controller therapy and frequency of short-acting beta2-agonists (SABA) use.
- Little is known whether excessive use of SABA may be associated with exacerbations requiring OCS use.

What this study adds

- Real-world information is presented regarding the relationship between adherence to asthma controller medications and the use of asthma rescue agents and how the findings can be applied to asthma management practice.
- Increased SABA use served as a predictor of increased OCS use, which indicates poor asthma control.
- This study demonstrated that even patients who were adherent to controller therapy had evidence of excessive SABA use. Patients should be thoroughly evaluated by health care providers for signs of ineffective asthma management (e.g., improper inhaler technique and suboptimal use of long-term controller therapy), which is associated with higher risk of asthma exacerbation.

Asthma is reported as a "common, deadly, disruptive, and expensive" condition, so the question of what can be done to improve its management is of interest.[1] Several factors contribute to poor asthma management, one of which is low adherence to long-term controller medications (i.e., inhaled corticosteroids [ICS], long-acting beta-agonists

[LABA], and leukotriene receptor agonists [LTRA]) among patients with persistent asthma.[2] Nonadherence contributes to poor asthma control in conjunction with increased mortality; increased health care utilization (hospitalizations and emergency department [ED] visits); reduced lung function; and decreased quality of life.[3-9] Medication adherence to controller therapy is consistently low, ranging between 30% and 70% overall and from 30% to 40% in clinical practice settings.[10-16] Therefore, addressing adherence to controller medications is critical in asthma management.

Several studies have demonstrated that low adherence to controller medications is associated with an increase in the number of hospitalizations and ED visits.[3,8-10,17-21] Other indicators of poor asthma control are use of oral corticosteroids (OCS) and excessive use of short-acting beta2-agonists (SABA; usually 6 and more claims per year).[22-26] Asthma symptoms that require OCS or frequent SABA use (more than 2 days per week) signal ineffective asthma management and may serve as a preliminary indicator of poor asthma control.[2] Recent Global Initiative for Asthma guidelines stressed the importance of assessing patients with excessive SABA use and ICS nonadherence, which are among risk factors for poor outcomes.[27]

Studies have found inconsistent results regarding the relationship between controller therapy adherence and OCS/SABA use. Several studies have reported that patients with higher controller therapy adherence were less likely to use OCS and SABA inhalers.[3,10,18,28,29] However, other studies have found no association between adherence to controller therapy and OCS/SABA use, and 1 study found a positive association between the level of adherence and SABA use.[10,17,30,31]

Williams et al. (2004) found that a 25% increase in ICS nonadherence was significantly associated with an increase in the number of OCS fills (relative risk [RR] = 1.49, 95% confidence interval [CI] = 1.10-2.02, $P < 0.05$) in a prospective cohort study.[3] Similarly, Delea et al. (2008) found in a large retrospective database study that every 25% of improvement in ICS adherence was associated with a reduction in OCS use by 3% (odds ratio [OR] = 0.97, 95% CI = 0.94-0.996, $P = 0.027$).[18] Regarding SABA use, patients with low ICS adherence (medication possession ratio [MPR] < 25%) filled more SABA inhalers compared with patients with high ICS adherence (MPR ≥ 75%; OR = 0.83, 95% CI = 0.77-0.89, $P < 0.001$). Every 25% increase in ICS adherence was associated with a reduction in SABA use by 10% (OR = 0.90, 95% CI = 0.89-0.92, $P < 0.001$).[18] Although the relationship between controller therapy adherence and SABA use was negative, a study conducted by Smith et al. (2009) showed that patients who were highly adherent (measured by > 80% of subjects who filled their prescriptions within 60 days of the prior refill) to controller medications filled more SABA inhalers compared with those with lower adherence (measured by < 50% of subjects who filled their prescriptions within 60 days of the prior refill; incident rate ratio = 1.62, 95% CI = 1.26-1.97, $P < 0.001$).[31] A better understanding of this association is needed.

The objective of this study was to evaluate the relationship between asthma controller adherence and SABA and OCS use utilizing a large retrospective database.

Methods

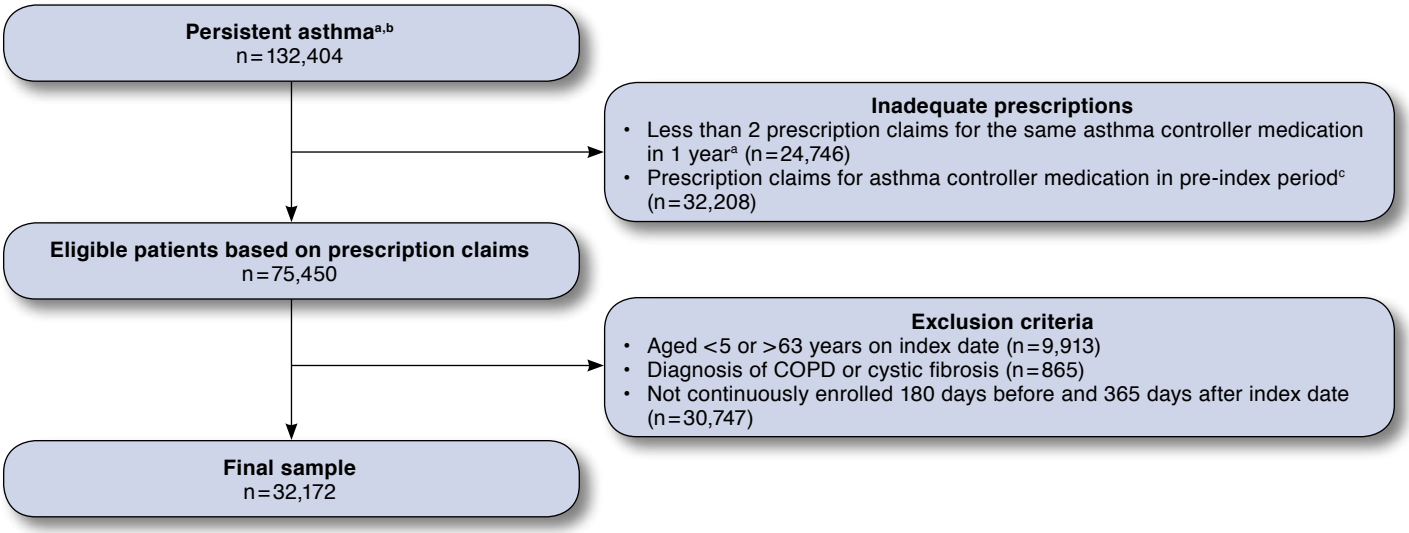
Data Source and Sample Inclusion Criteria

Texas Medicaid enrollment, medical services, and prescription claims data from January 1, 2008, to August 31, 2011, were used. The study inclusion criteria were patients aged 5 to 63 years at index who were continuously enrolled for at least 18 months (i.e., 6 months pre-index and 12 months post-index date), diagnosed with asthma (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] code 493.xx), and had 4 or more prescription claims for any asthma medication in 1 year. Patients younger than 5 years were excluded because of possible wheezing symptoms that can be incorrectly labeled as asthma, and patients aged 63 years and older were excluded because of potential dual eligibility with Medicare. Persistent asthma was defined based on the criterion of 4 or more prescription claims for any asthma medication in 1 year, which was established by the National Committee for Quality Assurance (NCQA).[32] The index date was defined as the first prescription in a series of 4 or more prescription claims for any asthma medication over a 1-year period of observation between July 1, 2008, and August 31, 2010. Patients were included if they had at least 2 claims for the same study asthma controller medication (ICS, LTRA, and ICS plus LABA) in the 12-month post-index period and did not have claims for any asthma controller medication within the 6-month pre-index period. Patients with diagnoses of chronic obstructive pulmonary disease (ICD-9-CM codes 496.00, 496.01, 493.20, or 493.21) or cystic fibrosis (ICD-9-CM codes 277.00 or 277.01) were excluded.

Study Design and Variables

A retrospective cohort design was used. First, the groups were identified based on the index medication prescribed: monotherapy controller medications (ICS, LTRA) and dual therapy (fixed dose dual therapy, concurrent dual therapy). Asthma controller medications included ICS (beclomethasone, budesonide, ciclesonide, flunisolide, fluticasone, mometasone, and triamcinolone); LTRA (montelukast, zafirlukast, and zileuton); ICS plus LABA (concurrent use: an ICS plus formoterol or salmeterol; fixed dose: fluticasone/salmeterol, budesonide/formoterol, or mometasone/formoterol); ICS plus LTRA (an ICS plus an LTRA); and ICS/LABA fixed dose plus LTRA. Dual therapy of fixed dose medications did not require additional data manipulation, since a single canister contains 2 medications. However, for concurrently used dual therapy, the following strategies were employed: (a) the 2 asthma controller medications must have been filled during at least 2 overlapping periods of 15 days and (b) if there was a period of time between

FIGURE 1 Patient Attrition Among Texas Medicaid Recipients Diagnosed with Asthma



[a]*July 1, 2008, to August 31, 2010.*
[b]*Persistent asthma based on a criterion of having 4 or more prescription claims for any asthma medication in 1 year (National Committee for Quality Assurance).*[32]
[c]*January 1, 2008, to March 1, 2011.*
COPD = chronic obstructive pulmonary disease.

the concurrent dual therapy overlap (e.g., patient on monotherapy), then that period had to be 30 days or less.

Adherence to asthma long-term controller medications was measured using proportion of days covered (PDC). PDC is determined by dividing the number of days that the medication was available by the number of days in the specific interval or study period (i.e., 365 days for this study). PDC is a more conservative method of adherence estimation than MPR, another common adherence measure, for multiple medication use, drug switches, or therapeutic duplication.[33] Continuous and categorical (i.e., adherent: PDC ≥ 50% and nonadherent: PDC < 50%) measures of adherence were used. Fifty percent adherence as a cutoff value was chosen based on the published literature where, on average, adherence to long-term controller medications was less than 20%.[8,9] Because of the lower cutoff value, sensitivity analyses were not conducted.

As mentioned previously, patients with adequately controlled persistent asthma should have a minimal number of SABA claims (acceptable use is no more than 2 days per week, which would equate to 2-6 fills). Although the clinically relevant cutoff value for the number of SABA claims related to adverse events is unknown, the most frequently used and relatively conservative cutoff value is 6 claims per year.[22-26,34-36] Thus, SABA claims were summed, and patients were dichotomized into 2 groups: those who had 6 or more claims in the post-index period and those who had less than 6 claims. Any claim for OCS typically indicates asthma exacerbation, and OCS use in the post-index period was summed and operationalized as a continuous variable.

Statistical Analyses

Descriptive statistics (mean, standard deviation [SD], median, and frequency) of demographic characteristics and medication utilization patterns were employed to provide a general overview of Texas Medicaid beneficiaries with persistent asthma. A multivariate logistic regression model was used to identify the relationship between adherence (dichotomized) to controller therapies and rescue medications use while controlling for confounding variables. Multivariate linear regression was used for continuous adherence. All statistical tests were performed with SAS version 9.3 (SAS Institute, Cary, NC). Statistical tests were two-sided with an a priori significance level of $P < 0.05$.

Results

During the study period, 366,012 patients had an asthma diagnosis. After employment of inclusion and exclusion criteria, the final sample size was 32,172 (see Figure 1). The majority of the total sample was aged between 5 and 11 years (63.1%), Hispanic (54.7%), and male (51.8%). Overall mean ± SD age was 15.0 ± 14.5. Most of the subjects were on asthma monotherapy (58.9%). Among the 5 study asthma controller treatments, 38.6% of subjects were prescribed LTRA at index, followed by ICS/LABA fixed dose combination therapy (21.3%) and ICS (20.3%). Mean adherence to controller

TABLE 1 Baseline Summary Statistics of Study Sample

	N	%
Demographic Characteristics		
Age groups		
5-11	20,283	63.1
12-18	6,508	20.2
Mean (SD) for children	9.1 (3.4)	
19-40	1,763	5.5
41-63	3,618	11.3
Mean (SD) for adults	44.6 (12.1)	
Mean (SD) overall	15.0 (14.5)	
Race/ethnicity		
Caucasian	6,034	18.8
African American	6,746	21.0
Hispanic	17,603	54.7
Other[a]	1,789	5.6
Gender		
Female	15,503	48.2
Male	16,669	51.8
Clinical Characteristics		
Therapy		
Monotherapy	18,948	58.9
Fixed dose dual therapy	6,868	21.3
Concurrent dual therapy[b]	6,356	19.8
Index asthma controller therapy		
ICS	6,522	20.3
LTRA	12,426	38.6
ICS/LABA fixed dose dual therapy	6,868	21.3
ICS+LTRA concurrent dual therapy	2,828	8.8
ICS/LABA fixed dose+LTRA	3,528	11.0
Controller therapy adherence		
PDC ≥ 80%	1,332	4.1
PDC ≥ 70%	2,200	6.8
PDC ≥ 60%	3,338	10.4
PDC ≥ 50%	4,792	14.9
Mean (SD)	32.2 (19.7)	
Asthma reliever utilization		
SABA		
None	2,381	7.4
1-5	23,563	73.2
6 or more	6,228	19.4
Mean (SD)	3.7 (3.1)	
OCS		
None	15,725	48.9
1	8,583	26.7
2	4,199	13.0
3	1,952	6.1
4 or more	1,713	5.3
Mean (SD)	1.0 (1.4)	
Total number of unique nonstudy medications at index date		
0	6,005	18.7
1	6,836	21.2
2	5,979	18.6
3	4,059	12.6
4 or more	9,293	28.9
Mean (SD)	2.9 (3.3)	

[a]*American Indian, Asian, unknown.*

[b]*Concurrent dual therapy includes an inhaler and oral medication: ICS+LTRA and ICS/LABA fixed dose therapy+LTRA. Any other concurrent therapy was not included, since they accounted for less than 2% of the concurrent dual therapy cohort.*

ICS = inhaled corticosteroids; LABA = long-acting beta-agonist; LTRA = leukotriene receptor antagonists; OCS = oral corticosteroids; PDC = proportion of days covered; SABA = short-acting beta2-agonists; SD = standard deviation.

therapies was 32.2% ± 19.7%. When adherence was dichotomized at the cutoff points of 80%, 70%, 60%, and 50%, the following percentage of adherent patients were 4.1%, 6.8%, 10.4%, and 14.9%, respectively (Table 1). Regarding asthma rescue medications, the majority of the sample was prescribed SABA inhalers (92.6%), with 73.2% receiving between 1 to 5 SABA inhalers, and the overall mean number of SABA inhaler claims was 3.7 ± 3.1. Slightly more than one half of the sample (51.1%) had a prescription for an OCS. About one quarter of the sample (26.7%) received 1 prescription for OCS, and the mean number of OCS prescriptions was 1.0 ± 1.4. At index date, 28.9% of the sample had claims for 4 or more nonstudy medications with a mean of 2.9 ± 3.3.

Among LTRA monotherapy users, 19.9% were adherent (PDC ≥ 50%), compared with 8.9% of ICS users. Similarly, mean adherence for LTRA was higher than for ICS: 36.1% ± 21.4% versus 28.0% ± 16.4%. Among dual therapy users, a higher percentage of patients on fixed dose dual therapy (18%) were adherent (PDC ≥ 50%), compared with only 6% using ICS and LTRA (concurrent dual therapy) and 9% using ICS/LABA fixed dose inhaler in combination with LTRA.

Adherent patients were 96.7% more likely to have 6 or more prescription claims for SABA when compared with nonadherent patients (OR = 1.967, 95% CI = 1.826-2.120, $P < 0.001$; Table 2). Similarly, as continuous adherence increased, the likelihood of having 6 or more claims for SABA increased as well ($P < 0.001$). For every 1-unit increase in adherence, subjects were 5.8 times more likely to have 6 or more prescription claims for SABA in the post-index period (OR = 5.805, 95% CI = 5.037-6.690). Additionally, patients with 6 or more SABA claims had 0.7 more OCS claims compared with patients with less than 6 claims for SABA ($P < 0.001$; Table 3).

Adherent patients had 0.11 fewer OCS claims compared with nonadherent patients ($P < 0.001$; Table 4). Compared with patients on ICS monotherapy, patients on dual therapies (ICS/LABA fixed dose dual therapy, ICS plus LTRA concurrent dual therapy, and ICS/LABA fixed dose plus LTRA therapy) had significantly more claims for OCS, respectively ($P < 0.05$). Children (aged 5-11 years) and adults (aged 41-63 years), Hispanic patients, and those who had a higher number of nonstudy medications at index date were more likely to experience exacerbations requiring an OCS claim ($P < 0.005$).

Discussion

The present study examined the association between adherence to controller therapy among Texas Medicaid patients with persistent asthma and risk of exacerbation requiring OCS use and the use of quick-relief agents (SABA), both of which served as indicators of asthma control. Higher adherence to controller therapy was associated with a significant reduction in OCS use, whereas adherent patients were more likely to have a higher number of SABA claims.

TABLE 2 Logistic Regression Analysis Comparing Likelihood of Having 6 or More Prescription Claims for SABA Among Adherent Versus Nonadherent Patients (N = 32,172)[a]

	Odds Ratio	95% CI		Wald X^2	*P* Value[b]
Adherence to Controller Therapy[c]					
Controller adherence (PDC ≥ 50%)	1.967	1.826	2.120	313.9342	<0.0001
Covariates					
Treatment[c]					
LTRA	0.697	0.641	0.757	72.0152	<0.0001
ICS/LABA fixed dose dual therapy	1.070	0.975	1.174	2.0141	0.1558
ICS+LTRA concurrent dual therapy	1.662	1.492	1.851	85.0794	<0.0001
ICS/LABA fixed dose + LTRA	1.962	1.779	2.165	181.2997	<0.0001
Age group[c]					
5-11	0.832	0.748	0.925	11.5388	0.0007
12-18	0.881	0.788	0.985	4.9318	0.0264
19-40	1.114	0.975	1.273	2.5148	0.1128
Female	0.844	0.795	0.896	30.9044	<0.0001
Race/ethnicity[c]					
African American	1.322	1.214	1.440	41.1367	<0.0001
Hispanic	0.881	0.788	0.985	15.6113	<0.0001
Other[d]	1.114	0.975	1.273	0.0176	0.8943
Total number of nonstudy medications	1.052	1.043	1.061	132.3529	<0.0001

[a]*Model chi-square = 1427.56, df = 10, P < 0.0001.*
[b]*Significant at P < 0.05.*
[c]*Reference categories: nonadherence (PDC < 50%), ICS, 41-63 years, Caucasian.*
[d]*American Indian, Asian, unknown.*
CI = confidence interval; ICS = inhaled corticosteroids; LTRA = leukotriene receptor agonists; PDC = proportion of days covered; SABA = short-acting beta2-agonists.

Overall, mean adherence to controller therapy in the study sample was low (32.2% ± 19.7%), which is within the reported ranges of previously conducted studies using retrospective databases.[8,9,19,24,37] One of the main explanations for low adherence to controller medications may be related to characteristics of Medicaid recipients (e.g., lower socioeconomic status and predominantly Hispanics and African Americans) who have been shown to be less adherent to controller medications, compared with those enrolled in private insurance plans.[38] The finding that less than 10% of patients who met the NCQA criteria for persistent asthma in the present study were adherent (PDC ≥ 50%) to ICS therapy suggests an opportunity to educate/reeducate patients with persistent asthma and their providers regarding the need for regular ICS use. In addition, health care providers should consider a more vigilant focus on at-risk populations such as younger patients (and their parents) and ethnic minorities (i.e., African-American and Hispanic patients). In this study, these patients were more likely to be nonadherent, which is congruent with earlier reported findings.[5,39-41] The Hispanic population is less likely to use preventive asthma medications because of several contributing factors, including language barriers, inadequate health literacy, and cultural beliefs.[42-45] Addressing these barriers in practice has shown positive results on childhood asthma among low-income minority children.[46,47] However, low levels of adherence to controller medications found in the present study in combination with recent findings from another study that reported suboptimal knowledge of metered dose inhaler spacer use among caregivers of urban minority children reflects a need for education among young patients with asthma.[48]

Another potential explanation for low adherence to ICS can be the concept of "as needed" treatment. Although the Expert Panel Report 3 guidelines recommend daily use of ICS for all patients with persistent asthma, several clinical trials have acknowledged that ICS can be used "as needed" (when asthma symptoms worsen) for mild asthma.[49-52] One of these studies (the BASALT trial) reported that "as needed" symptom-based use of ICS and traditional daily use of ICS did not differ in the time to clinical worsening of asthma.[49] Nonetheless, there is not enough evidence currently to promote intermittent use of ICS for patients with mild-to-moderate asthma, even though it may occur in clinical practice.[52] A higher number of nonstudy medications at the index date was associated with higher controller therapy adherence, which has been shown in other Texas Medicaid adherence studies.[53,54]

SABAs are used for quick relief of symptoms and are not recommended for regular use. Patients with adequately controlled persistent asthma should have a minimal number of SABA claims (acceptable use is no more than 2 days per week). Excessive SABA use indicates poor asthma control and is associated with increased asthma exacerbations and adverse asthma events.[34,36,55] Patients on ICS monotherapy had a

TABLE 3 Multiple Regression Analysis Comparing OCS Use for Patients with 6 or More Prescription Claims for SABA Versus Patients with Less Than 6 Claims for SABA (N = 32,172)[a]

Factors	Unstandardized Coefficient, B	Statistic, T	*P* Value[b]
SABA claims (≥6)[c]	0.70391	34.86	<0.0001
PDC (continuous)	-0.43870	-10.37	<0.0001
Treatment[c]			
LTRA	0.01644	0.76	0.4471
ICS/LABA fixed dose dual therapy	0.10372	4.04	<0.0001
ICS+LTRA concurrent dual therapy	0.02557	0.81	0.4163
ICS/LABA fixed dose + LTRA	0.18076	6.14	<0.0001
Age group[c]			
5-11	0.17796	5.70	<0.0001
12-18	-0.20675	-6.31	<0.0001
19-40	-0.06780	-1.65	0.0981
Female	-0.01007	-0.62	0.5334
Race/ethnicity[c]			
African American	-0.07096	-2.86	0.0043
Hispanic	0.10973	5.10	<0.0001
Other[d]	-0.13495	-3.59	0.0003
Total number of nonstudy medications	0.04674	17.79	<0.0001

[a] *$F = 167.43$, adjusted $R^2 = 0.0637$, $P < 0.0001$.*

[b] *Significant at $P < 0.05$.*

[c] *Reference categories: SABA claims (<6), ICS, 41-63 years, Caucasian.*

[d] *American Indian, Asian, unknown.*

ICS = inhaled corticosteroids; LABA = long-acting beta2-agonists; LTRA = leukotriene receptor agonists; OCS = oral corticosteroids; PDC = proportion of days covered; SABA = short-acting beta2-agonists.

significantly greater likelihood (40.8% higher) of having 6 or more SABA claims than those on LTRA. The present study's findings were consistent with several published studies.[22,24,56] A possible explanation for this finding could be related to asthma severity, since patients with more severe disease may be treated with ICS and require more SABA inhalers.

Interestingly, patients who were adherent to their monotherapy controller medications were more likely to have 6 or more claims for SABAs, when compared with nonadherent patients. Other studies have found similar results.[5,14,23] The first explanation for this finding relates to the severity of asthma: it is likely that those who have less severe asthma are not highly adherent to therapy and, at the same time, have no need for excessive SABA use. However, in this study, only patients with persistent asthma were included, and total number of nonstudy medications at the index date was used as a proxy for a patient's general health status. However, factors such as allergens and other triggers, presence of comorbid conditions, or psychosocial issues may contribute to poor asthma control, even among adherent patients.[57] Increasing SABA use along with increasing controller adherence may also signal to the provider that the patient may need to be evaluated for more intensive controller therapy, such as an additional agent if on monotherapy, or an increase in dose. Next, it may be that some patients filled a prescription for a SABA, but may not have used it or only used it rarely. Additionally, some patients, specifically children, may have an inhaler for home use and another inhaler for school use.

Patients on fixed dose dual therapy were 43.8% less likely to have 6 or more prescription claims for SABA than concurrent dual therapy users, which was consistent with the study by Tan et al. (2009).[22] When patients on dual therapy were adherent to controller therapy, they were less likely to have 6 or more claims for SABA (by 58.8%), compared with nonadherent patients on dual therapy. Earlier studies report conflicting results regarding the association between adherence and excessive SABA use.[23,31,57] Ambiguous results may be due to factors that are not identifiable through the prescription claims database, such as inadequate dosing or inappropriate inhalation technique. These factors can be associated with poor asthma control and, as a result, with excessive SABA use.[57-59] Even though frequent use of SABA signals poor asthma control and serves as a predictor of asthma-related outcomes/subsequent exacerbations, the association between adherence to controller therapy and excessive SABA use is still unclear.[2,5,14,18,26,31,36,55,58,60] Nevertheless, this study demonstrated that increased SABA use served as a predictor of increased OCS use, which indicates poor asthma control. Health care providers should be aware of SABA use among patients who are adherent and nonadherent to asthma controller medications. Patients with excessive SABA use should be examined for their inhaler technique and whether the dose of the controller medication is optimal. Zeiger et al. (2014) used this criterion by examining electronic medical records for excessive SABA use and intervening with an outreach program. The researchers reported a reduction in the number of subsequent SABA claims.[61]

OCS are used for asthma exacerbation management, which signals uncontrolled asthma. In contrast to SABA quick-relief use, this study found that better adherence to controller therapy was associated with a lower number of OCS claims, which was in line with previous research.[3,18] Better adherence to controller therapy, especially among patients on dual therapy, can prevent future exacerbations and the need for OCS.

Limitations

The present study provides comprehensive analyses of adherence to various controller therapies, risk of exacerbation, and the association with rescue medication use. However, several limitations may impact the findings. First, adherence was operationalized as PDC, which may not reflect actual adherence. Just because a patient filled a prescription does not guarantee that it was used, used as prescribed, and, in the case of

TABLE 4 Multiple Regression Analysis Comparing OCS Use Among Adherent Versus Nonadherent to Controller Therapy (N = 32,172)[a,b]

	Unstandardized Coefficient, B	Statistic, T	*P* Value[c]
Adherence to Controller Therapy[d]			
Adherence (PDC ≥ 50%)	-0.11125	-4.83	< 0.0001
Covariates			
Treatment[d]			
LTRA	-0.03236	-1.48	0.1391
ICS/LABA fixed dose dual therapy	0.10715	4.10	< 0.0001
ICS + LTRA concurrent dual therapy	0.09109	2.85	0.0044
ICS/LABA fixed dose + LTRA	0.26946	9.02	< 0.0001
Age group[d]			
5-11	0.17173	5.42	< 0.0001
12-18	-0.20480	-6.16	< 0.0001
19-40	-0.04747	-1.14	0.2553
Female	-0.02771	-1.68	0.0923
Race/ethnicity[d]			
African American	-0.03255	-1.29	0.1976
Hispanic	0.10294	4.71	< 0.0001
Other[e]	-0.13610	-3.56	0.0004
Total number of nonstudy medications	0.05288	19.80	< 0.0001

[a] *F = 72.72, adjusted R2 = 0.0282, P < 0.0001.*
[b] *Adherent = PDC ≥ 50%; nonadherent = PDC < 50%.*
[c] *Significant at P < 0.05.*
[d] *Reference categories: nonadherence (PDC < 50%), ICS, 41-63 years, Caucasian.*
[e] *American Indian, Asian, unknown.*
ICS = inhaled corticosteroids; LABA = long-acting beta2-agonists; LTRA = leukotriene receptor agonists; OCS = oral corticosteroids; PDC = proportion of days covered.

inhalers, used with the correct technique. Second, some dual therapy patients could be primarily monotherapy users who added another agent only for specific time periods. However, this study defined dual therapy as two 15-day overlapping periods, which lends validity to dual therapy use. Third, the use of a retrospective database allows only the use of the covariates that are available and gives no access to other important factors, such as clinical parameters; symptoms; and designation of mild, moderate, or severe asthma. To overcome this barrier, we used NCQA criteria for persistent asthma. Fourth, this study was cross-sectional, and causality cannot be established. Fifth, adherence to ICS can be underestimated, since a prescription reading "1-2 puffs 1-2 times daily" could result in wide variations for days supply. However, pharmacists typically assume maximum use, which translates into shorter days supply. Sixth, the severity of asthma can significantly influence adherence and outcomes; however, in this study, there was no opportunity to assess this factor directly (it was not ascertainable through claims data). However, our inclusion criteria targeted patients with persistent asthma only. Finally, this study's findings are unique to the Texas Medicaid population, so they may not be generalizable to populations from other health care systems or to other state Medicaid programs.

Conclusions

Adherence to long-term controller medications was low among patients with asthma. Adherent patients had fewer OCS claims, indicating that adherence to controller therapy is critical in prevention of asthma exacerbations requiring OCS use. Although there was a positive relationship between adherence to long-term controller medication and SABA use, increased SABA use served as a positive predictor of increased OCS use, which indicates poor asthma control. Health care providers should be aware of OCS and SABA use among patients who are adherent and nonadherent to asthma controller medications.

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DISCLOSURES

The authors report no potential conflicts of interest.

Makhinova and Barner collaborated on the conception of the project, study design, data analysis, and writing the manuscript. Richards and Rascati critically reviewed the study design, data analysis, and results interpretation and contributed to the development and editing of the manuscript.

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