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Albuterol Overuse: A Marker of Psychological Distress?

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Abstract

Background—Albuterol overuse has been associated with more frequent symptoms, worse asthma control, and more frequent exacerbations.

Objective—To describe albuterol use on symptom and symptom free days and identify predictors of albuterol overuse and controller medication underuse.

Methods—Secondary analyses of data from adults with mild asthma from the Trial of Asthma Patient Education (TAPE) were analyzed. Based on expected albuterol use of 80% on symptom days and <20% on symptom free days, participants' were characterized as expected-, over-, or under-users of albuterol. Controller medication adherence was defined as 80% of doses. Data included demographic characteristics, diary data, spirometry, and scores from standardized questionnaires. Bivariate associations were examined between categorization of medication use and measured characteristics.

Results—Of the 416 participants, 212 (51%) were expected-users, 114 (27%) were over-users, and 90 (22%) were under-users of albuterol. No differences were observed among the user groups

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by demographic characteristics or lung function. Expected-users demonstrated the highest asthma-related knowledge, attitudes, and efficacy. Over-users reported the greatest symptom burden, worst asthma control, and highest frequency of symptom days. Over-users also had the highest burden of depression symptoms. Mean controller adherence was high across all groups and there were no differences between the groups.

Conclusion—While over-users experienced more frequent symptom days and used more albuterol on those days, overuse was most attributable to unexpected use on symptom free days. High levels of comorbid depression were observed, particularly among over-users and those non-adherent to controller medication suggesting the potential importance of psychological factors.

Keywords

asthma; albuterol; short-acting beta-agonist; medication adherence; patient compliance; depression

Background

How patients take their prescribed asthma medications is an important predictor of asthma control and exacerbation risk. Underuse of controller medications leads to worse symptom control and more frequent exacerbations.^{1,2} Overuse of quick-relief medication (albuterol) is similarly problematic.³ Albuterol overuse is associated with more frequent symptoms, exacerbations, and health care utilization as well as lower mental and physical functioning.^{4–11} Physiological and psychological dependence to albuterol is possible and can be challenging to distinguish from difficult-to-treat asthma.¹² Older age, male sex, white race, Hispanic ethnicity, coexisting medical conditions, lower educational attainment, current smoking, and physical inactivity have been associated with albuterol overuse.^{6,7,9,11}

Albuterol overuse is an important problem. The 2009 Asthma Insight and Management Survey noted that 25% of patients rely on albuterol monotherapy to manage their persistent asthma, many of whom use albuterol daily.¹³ The 2008–2010 Medical Expenditure Panel Survey noted that 15% of patients with asthma use more than 1 canister of albuterol per month.⁶ Several large claims databases have been used to link albuterol overuse with undesirable health outcomes. About 17% of Medicaid-insured patients and 25% of commercially-insured patients filled 3 canisters of albuterol in a 12 month period.⁵ These patients had twice the risk of an asthma-related emergency department visit or hospitalization as compared to those who filled albuterol less frequently. Each canister filled beyond the first increased exacerbation risk by 8–14% among adults and 14–18% among children. In another commercially-insured population of patients with asthma, 5% were found to have filled more than 3 canisters of albuterol in a single fiscal quarter.⁴ These patients had 3 times the risk of an asthma-related emergency department visit or hospitalization as compared to patients who filled albuterol less frequently.

Patients who overuse albuterol may have fundamentally different perceptions of their asthma.^{14,15} Over-users are more likely to focus on the mechanical effects of bronchoconstriction and the quick relief provided by albuterol rather than on the underlying inflammatory process and the prophylaxis provided by controller medications.¹⁵ In the schema described by Adams *et al.*, patients who overuse albuterol are likely deniers/

distancers who perceive their diagnosis as negatively stigmatizing and therefore threatening to their self-image.¹⁴ These patients appear to have difficulty adapting to their diagnosis as evidenced by their tendency to express anger about asthma's impact on their lives, to underuse controller medication, to overuse albuterol, and to feel panicked when their albuterol inhaler is not available. In contrast, patients who have less difficulty adapting to their diagnosis (acceptors) tend to use their controller medication and albuterol more appropriately, to have more accurate asthma-related knowledge, to rate their health status more favorably, and to have a more positive self-image.^{14,16}

While surveys and claims-based data provide important information on the magnitude of albuterol use, they lack the granularity to describe the pattern of albuterol use in response to symptoms. To address these limitations, we used daily diary data collected from participants enrolled in the American Lung Association-Asthma Clinical Research Centers' Trial of Asthma Patient Education (TAPE).¹⁷ TAPE examined the impact of medication presentation on the response to a leukotriene receptor antagonist (montelukast) among adults with mild persistent asthma. Our goals were to describe the participants' pattern of albuterol use on symptom and symptom free days and to identify characteristics associated with albuterol overuse and montelukast underuse.

Methods

TAPE was a multi-center clinical trial that used a 2×2 factorial design to determine whether response to placebo or montelukast was augmented by messages that increased the expectation of benefit. A fifth group (usual care) was also followed to estimate the impact of clinical trial enrollment on the primary outcome of peak expiratory flow after 4 weeks of treatment. Participants were 15 years of age, had physician diagnosed asthma, previously used controller medication, had a forced expiratory volume in 1 second (FEV₁) >75% of predicted, and had 1 indicator of poor asthma control. The study was approved by the Institutional Review Boards at each center; patients provided written consent.

The analytic sample comprised 416 of 601 original TAPE participants who reported both symptom and symptom-free days, who had complete diary data, and who were categorized as either expected-, over-, or under-users of albuterol. Most (174) participants were excluded because they reported only symptom days or only symptom free days. Data included demographic characteristics, daily diary data, spirometry, and scores from the Mini Asthma Quality of Life Questionnaire (MiniAQLQ),¹⁸ the Asthma Symptom Utility Index (ASUI),¹⁹ the Asthma Control Questionnaire (ACQ),²⁰ the Knowledge, Attitude, and Self-Efficacy Asthma Questionnaire (KASE-AQ),²¹ the Short-form Health Survey (SF-36),²² the Shortness-of-Breath Questionnaire (SOBQ),²³ and the Center for Epidemiological Studies-Depression (CES-D) questionnaire.²⁴ All data were obtained from the baseline visit except for diary data which was recorded during the 4 week treatment period.

Participants recorded their albuterol use, montelukast or placebo use, and asthma symptoms on daily diary cards. While pill counts were recorded, adherence assessment was restricted to diary reporting of number of albuterol actuations and use/no use of controller medication on each day. Participants were instructed to only record rescue albuterol use and not pre-

exercise use. Symptom days included any with symptoms including nighttime awakenings. *A priori*, we expected albuterol to be used on 80% of symptom days and on <20% of symptom free days. Based on symptom and symptom free day albuterol use, participants' were characterized as expected-, over-, or under-users. (Table 1) A fourth category of participants who used albuterol on <80% of symptom days and 20% of symptom free days was excluded because few participants (n=11, 3%) met these criteria. Adherence to montelukast or placebo was characterized as adherent if 80% of doses were taken. Adherence was not recorded among usual care participants.

Based on the characterization of albuterol use (expected-, over-, or under-user) and controller use (adherent or non-adherent), bivariate associations were examined between category of medication use and measured demographic and clinical characteristics. To estimate the drivers of overuse, we calculated the incremental contribution of more frequent symptom days, greater symptom day use, and greater symptom free day use of the average over-user as compared to the average expected-user. Descriptive statistics (mean, standard deviation, count, and proportion) were used to summarize baseline demographics. We compared continuous measurements (e.g., FEV₁, ACQ scores, etc.) among participants based on their albuterol usage using the Kruskal-Wallis rank tests since not all of the measurements were normally distributed. Chi-square (χ^2) tests were used for categorical variables to test for statistically significant differences. We also compared controller adherence among montelukast and placebo participants using similar methods. For categorical variables that had cells with less than 5 entries, Fisher's tests were performed. Results were not adjusted for baseline covariates because there was no evidence of an imbalance across the groups at baseline. Two-sided P-values <0.05 were considered to indicate statistical significance. No corrections were made for multiple comparisons in this exploratory analysis; therefore, results should be interpreted with appropriate caution. SAS 9.3 (SAS Institute Inc., Cary, NC) was used to perform all analyses.

Results

Data were analyzed in a single analytic sample as there were no observed differences in the distribution of albuterol user types by enhanced versus neutral medication presentation, montelukast versus placebo assignment, or usual care versus any combination of medication presentation or assignment (data not shown).

Of the 416 participants, 212 (51%) were expected-users, 114 (27%) were over-users, and 90 (22%) were under-users. (Table 1) Of the 212 expected-users, 108 (51%) used albuterol on every symptom day and never on symptom free days. Of the 114 over-users, 51 (45%) used albuterol every day. Seventy-five percent of albuterol use occurred on symptom days and 25% on symptom free days. Albuterol was used on 20% of all symptom free days and 88% of this use was attributable to over-users. Over-users had higher mean (SD) albuterol use, equivalent to 4 canisters per year, than expected-users or under-users ($p<0.001$). (Table 2)

No differences were observed among user groups by age, gender, race/ethnicity, smoking status, or lung function. (Table 3) Expected-users demonstrated more favorable asthma-related knowledge ($p=0.06$), attitudes ($p<0.01$), and efficacy ($p=0.04$) than over- or under-

users. Over-users reported the greatest symptom burden as evidenced by more frequent symptom days ($p<0.01$) and worse scores on the ACQ ($p<0.001$), ASUI ($p<0.001$), and SOBQ ($p<0.001$) questionnaires. At an ACQ cut-point of 1.5, 67% of over-users had poorly controlled asthma as compared to 52% of under-users or 45% of expected users ($p<0.001$). Over-users reported lower asthma-related quality-of-life ($p<0.001$), worse physical functioning ($p<0.01$), and worse mental functioning ($p=0.04$) than expected- or under-users. Over-users had the highest mean CES-D scores ($p<0.001$). Using a CES-D threshold of 16; 32% of over-users were at risk of clinical depression as compared to 19% of under-users or 17% of expected-users ($p<0.01$). Despite greater asthma burden, over-users did not report more frequent oral corticosteroid-requiring exacerbations ($p=0.17$) or unscheduled clinic visits ($p=0.16$) in the year prior to enrollment.

When the symptom days and albuterol use among over-users and expected users was compared, over-users experienced 3.5 additional symptom days per month, reported 1.14 additional albuterol actuations on symptom days, and reported 1.78 additional actuations on symptom free days. (Table 4) In a given month, over-users had approximately 53 more albuterol actuations than expected users meaning that more frequent symptom days accounted for 15% of overuse, greater use on symptom days accounted for 31%, and use on symptom free days accounted for 54% of overuse.

Mean controller adherence was 90% across all 3 albuterol use categories during the 4 week treatment period. (Table 5) There was no difference in mean adherence to montelukast or placebo between the 3 groups ($p=0.76$). When the montelukast and placebo groups were combined, only 29 of 325 (9%) participants had $<80\%$ adherence. (Table 6) Non-adherent participants were more likely to be Hispanic ($p<0.01$), otherwise there were no differences by age, gender, race, smoking status, or lung function. Non-adherent participants did not report differences in symptom burden as evidenced by symptom days or scores on the ACQ, ASUI, or SOBQ questionnaires. Non-adherent participants reported worse mental functioning ($p=0.04$) and greater depressive symptoms ($p=0.04$) than adherent participants, but not worse asthma-specific quality-of-life ($p=0.06$) or physical functioning ($p=0.58$). Forty-one percent of non-adherent participants were at risk of clinical depression as compared to 20% of adherent participants ($p<0.01$). Non-adherent participants did not report more frequent oral corticosteroid-requiring exacerbations ($p=0.35$) or unscheduled clinic visits ($p=0.50$) in the year prior to enrollment.

Conclusion

In this clinical trial of adolescents and adults with mild persistent asthma, 27% of participants were classified as albuterol over-users including 12% who used albuterol daily. Over-users consumed more than twice the amount of albuterol as expected users, approximately 4 canisters per year. This amount of albuterol use has been previously associated with higher exacerbation risk among adults and children.⁵ By our calculation, more frequent symptom days accounted for 15% of overuse whereas greater use on symptom days accounted for 31% and greater use on symptom free days accounted for 54%. While overusers experienced more frequent symptom days and used more albuterol on those days, overuse was most attributable to frequent use on symptom free days. Practically

speaking, many over-users use albuterol as if it were a daily controller medication. Scheduled use of albuterol has not been shown to be beneficial,²⁵ and if used frequently, may induce the “ β -agonist paradox” whereby continuous exposure enhances, rather than attenuates, airway hyper-responsiveness.³ For these reasons, reducing albuterol use on symptom free days is a logical target for intervention among over-users.

Our definition of overuse, based on symptom and symptom free day use, yielded a prevalence estimate of 27% which is consistent with those based on the rate of albuterol refills in claims data. Stanford *et al.* noted that 17% of Medicaid-insured and 24% of commercially-insured adults with asthma filled 3 canisters of albuterol in a 12 month period.⁵ Using multiple canister (1, 2, 3, 4, 5, or 6 canisters) and time (3, 6, or 12 months) thresholds, the most accurate predictor of future exacerbation risk was 2 refills in 12 months for adults and 3 refills in 12 months for children. For patients exceeding these thresholds, the odds of an asthma-related emergency department visit or hospitalization was increased approximately two-fold. This relationship was consistent for children and adults whether they were Medicaid-insured or commercially-insured. These associations substantiate that our overuse definition likely identified patients who were at increased risk of poor health outcomes.

While others have found older age, male sex, white race, Hispanic ethnicity, and current smoking to predict overuse,^{6,7,9,11} we did not find any demographic characteristics to be associated with overuse. Jobin *et al.* examined predictors of appropriate use and identified 4 potential predictors: accurate knowledge of asthma medications, higher self-reported health status, prior consultation with a specialist, and difficulty affording medications.¹⁶ We examined asthma-related knowledge, attitudes, and efficacy using the KASE-AQ questionnaire and found expected users to have somewhat higher (or better) scores than either over-users or under-users suggesting that asthma-specific knowledge is an important mediator and that educational interventions could be of value in reducing overuse.

Diette *et al.* observed over-users to report substantially higher symptom burden including cough, chest tightness, wheezing, and nighttime awakenings than appropriate users.¹¹ Furthermore, 26% of over-users reported having symptoms most of the time between attacks compared to only 7% of appropriate users. We also found over-users to have greater symptom burden on multiple standardized measures and observed over-users to report more symptom days than expected-users, 48% versus 37%, respectively. Interestingly, greater symptom burden was not associated with worse pulmonary function as measured by FEV₁ or worse health outcomes as measured by oral corticosteroid-requiring exacerbations or unscheduled clinic visits in the year prior to enrollment.

Psychological factors and/or the patient's perception of asthma symptoms may partially explain why higher symptom burden among over-users was not associated with worse pulmonary function. Emotional affect, particularly depression, can influence disease perception and medication behaviors among those with chronic illness.²⁶ Among patients with asthma, depression has been associated with greater symptom reporting, lower quality-of-life, and lower adherence to controller medication.²⁷ Recently, the Asthma Outcomes workshop recognized the importance of depression as a disease mediator by recommending

that it be measured in clinical trials of asthma.²⁸ Using a CES-D threshold of 16 to identify participants at risk of clinical depression, more over-users were at risk (32%) than either under-users (19%) or expected-users (17%). However, the directionality of association is unclear; over-users could have greater disease burden leading to depressive symptoms or could more acutely experience asthma because they are depressed. Given that over-users did not have worse lung function, differential perception of symptoms and disease burden among those with depression may be an important mechanism driving overuse.

Steele *et al.* recently examined the relationship between anxiety, depression, and patients' perceptions of asthma control.²⁹ Patients were classified as over- (40%), under- (16%), or normal (32%) symptom perceivers based on a comparison of self-reported asthma control with FEV₁ percent predicted. The Hospital Anxiety and Depression Scale (HADS) was used to identify patients at risk of clinically meaningful anxiety (35%) and depression (29%). Neither anxiety, nor depression predicted symptom perception classification. However, asthma-specific anxiety as measured by the panic/fear subscale of the Asthma Symptom Checklist was associated with symptom perception. Low asthma-specific anxiety was associated with being an under-perceiver, but high asthma-specific anxiety was not associated with being an over-perceiver. These data attest to the high levels of comorbid anxiety and depression among patients with asthma and allude to the potential importance of asthma-specific anxiety as a mediator of symptom perception.

Additional qualitative evidence suggests a link between asthma-specific anxiety and albuterol overuse.¹⁵ When describing the behaviors of young adults who were identified as albuterol over-users, Cole *et al.* note, "Although respondents from both groups described always having a bronchodilator with them, high users reported 'having them everywhere' and being 'panicky' without one, with elaborate arrangements for having access to bronchodilators."¹⁵ Additional study is needed to disentangle the complex interactions between symptom perception, affect, and medication related behaviors among albuterol over-users. Unfortunately, neither general anxiety, nor asthma-specific anxiety was measured in TAPE; therefore, this analysis cannot draw any conclusions regarding the role or impact of anxiety on adherence behaviors.

It is important to consider albuterol use in the context of coexisting controller medication use. The literature suggests that exacerbation risk is higher when the ratio of controller medication use to total asthma medication use is <0.5 among commercially-insured patients or <0.7 in Medicaid-insured patients.³⁰ A low ratio can be explained by underuse of controller medication, overuse of albuterol, or both simultaneously. In our study, adherence to daily controller medication was uniformly high, >90%. Because controller adherence was uniformly high across all albuterol user-types, nonadherence to controller medication did not appear to be a major driver of albuterol overuse in our study. Among the small number (n=29) of participants who were non-adherent to montelukast, depression was a statistically significant predictor of adherence; non-adherent participants were twice as likely to be at risk of depression as adherent participants, 41% versus 20%, respectively. These data suggest that albuterol overuse is more complex than simply nonadherence to controller medication.

Our study has a number of limitations of which generalizability is one of the most important. Because TAPE enrolled only participants with mild asthma, the findings may not be generalizable to those who have more severe disease. Furthermore, our participants tended to be relatively young, almost exclusively never smokers, mostly female, and highly adherent to controller medication. Because the prevalence of depression is higher among women than men and is higher among working age adults, TAPE unintentionally enrolled participants at higher than average risk of depression.³¹ Our participants also demonstrated high adherence to controller medication consistent with participation in a clinical trial and short treatment duration. In the real world, controller adherence is markedly lower and albuterol use tends to be higher.

The limited treatment duration and the reliance on patient reported outcomes constrains the conclusions that can be drawn regarding more objective outcomes such as pulmonary function and health care utilization, particularly as manifested over longer periods of time. While other studies have shown a correlation between albuterol overuse and health care utilization, we are unable to independently verify this association. Nevertheless, when investigating the patient's asthma burden, comorbid affective disorders, and behavioral practices, patient-reported outcomes have high validity. Lastly, anxiety as a separate affective condition was not measured; therefore, the association between albuterol overuse and controller underuse and depression could be subject to unmeasured confounding by anxiety disorders.

Summary

Overuse of albuterol is a relatively common among patients with asthma and is a risk factor for poor outcomes. While overuse may coincide with nonadherence to daily controller medication, an important driver of overuse is unexpected use of albuterol on symptom free days. In fact, many over-users use albuterol as if it was a controller medication. While the cause of overuse is likely multi-factorial, patients' affective experience including depression and asthma-specific anxiety is important. Without a better understanding of overuse, clinicians may find it difficult to intervene when the problem is recognized. Future study is needed to better understand the psychological origins of albuterol overuse and the extent to which patients might be responsive to interventions promoting more appropriate use.

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Abbreviations

ACQ	Asthma Control Questionnaire
ASUI	Asthma Symptom Utility Index questionnaire
CES-D	Center for Epidemiological Studies-Depression questionnaire
FEV₁	forced expiratory volume in 1 second

KASE-AQ	Knowledge, Attitude, and Self-Efficacy Asthma Questionnaire
MiniAQLQ	Mini Asthma Quality of Life Questionnaire
SD	standard deviation
SF-36	Short-form Health Survey
SOBQ	Shortness-of-Breath Questionnaire
TAPE	Trial of Asthma Patient Education

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What is already known about this topic?

One-quarter of patients with asthma overuse albuterol. Overuse is associated with worse asthma control and more frequent exacerbations. Depression is associated with greater symptom reporting, lower quality-of-life, and lower controller adherence among patients with asthma.

What does this article add to our knowledge?

Among adults with mild asthma, albuterol use on symptom free days is the most important driver of overuse. Up to 30% of over-users are at risk for clinical depression, about twice that of expected users.

How does this study impact current management guidelines?

When clinicians suspect albuterol overuse to be a problem, depression should be considered as a potential comorbidity.

Table 1

Classification of Participants by Albuterol Use on Symptom and Symptom-Free Days (N=416)

Use on Symptom Free Days	Use on Symptom Days	
	80%	<80%
20%	212 (51%) Expected-Users	90 (22%) Under-Users
>20%	114 (27%) Over-Users	*

*
11 participants in this category were excluded.

Table 2

Mean Albuterol Actuations per Day, Symptom Day, and Symptom Free Day

Actuations	Mean (SD) Albuterol Puffs per Day			p
	Under-User	Expected	Over-User	
Overall	0.435 (0.524)	0.877 (0.846)	2.434 (1.401)	<.0001
Symptom Days	0.875 (0.848)	2.168 (1.029)	3.307 (2.001)	<.0001
Symptom Free Days	0.044 (0.099)	0.054 (0.107)	1.831 (1.315)	<.0001

Table 3

Selected Demographic and Clinical Characteristics by Albuterol Use Classification

	Under-User n=90	Expected User n=212	Over-User n=114	p
Age , mean (SD)	38.2 (13.9)	36.5 (13.9)	37.9 (14.0)	0.44
Gender (male) , n (%)	18 (20.0)	66 (31.1)	28 (24.6)	0.11
Ethnicity (non-Hispanic) , n (%)	86 (95.6)	197 (92.9)	107 (93.9)	0.69
Race (white) , n (%)	57 (63.3)	130 (61.3)	56 (49.1)	0.13
Smoking status (never) , n (%)	80 (88.9)	186 (87.8)	95 (83.3)	0.43
Spirometry (% predicted)				
(pre) FEV ₁ , mean (SD)	87.6 (12.9)	86.0 (13.7)	86.4 (14.1)	0.54
PEFR, mean (SD)	91.1 (18.8)	87.6 (15.4)	86.7 (16.7)	0.25
KASE-AQ				
Knowledge, mean (SD)	11.6 (3.2)	11.9 (2.9)	11.1 (2.8)	0.06
Attitude, mean (SD)	84.4 (7.0)	86.7 (6.7)	84.8 (6.7)	<0.01
Efficacy, mean (SD)	80.5 (8.8)	82.8 (8.8)	80.1 (9.9)	0.04
Patient Reported Outcomes				
% Symptom Days, mean (SD)	42.1 (26.6)	36.7 (25.6)	48.4 (28.4)	<0.01
ACQ, mean (SD)	1.5 (0.7)	1.4 (0.7)	1.8 (0.8)	<0.001
ASUI, mean (SD)	0.8 (0.1)	0.8 (0.1)	0.7 (0.2)	<0.001
SOBQ, mean (SD)	23.8 (18.9)	19.3 (17.9)	26.6 (17.6)	<0.001
Mini-AQLQ, mean (SD)	5.0 (0.8)	5.2 (1.0)	4.6 (1.1)	<0.001
SF-36 (physical), mean (SD)	46.5 (9.2)	49.1 (8.6)	46.1 (9.2)	<0.01
SF-36 (mental), mean (SD)	50.4 (8.0)	50.4 (9.7)	47.9 (10.5)	0.04
CES-D, mean (SD)	10.2 (6.7)	9.5 (8.5)	13.0 (9.9)	<0.001
Healthcare Utilization				
OCS past year, n (%)	50 (47.6)	50 (47.6)	19 (18.1)	0.17
Unscheduled visit, n (%)	53 (44.5)	53 (44.5)	26 (21.9)	0.16

ACQ, Asthma Control Questionnaire; ASUI, Asthma Symptom Utility Index questionnaire; CES-D, Center for Epidemiological Studies-Depression questionnaire; FEV₁, forced expiratory volume in 1 second; KASE-AQ, Knowledge, Attitude, and Self-Efficacy Asthma Questionnaire; MiniAQLQ, Mini Asthma Quality of Life Questionnaire; SD, standard deviation; SF-36, Short-form Health Survey; SOBQ, Shortness-of-Breath Questionnaire.

Table 4

Contributions of Symptom Day Frequency and Albuterol Use on Symptom and Symptom Free Days to Overall Albuterol Overuse

	Over-User	Expected-User	Difference
Symptom Days (per 30)	14.5	11.0	3.5
Symptom Free Days (per 30)	15.5	19.0	3.5
Symptom Day Actuations	3.31	2.17	1.14
Symptom Free Day Actuations	1.83	0.05	1.78
(14.5 – 11.0) * 2.17 = 7.59 of 52.49 (14%) additional symptom days			
14.5 * (3.31 – 2.17) = 16.52 of 52.49 (31%) additional symptom day albuterol use			
15.5 * 1.83 = 28.38 of 52.49 (54%) additional symptom free day albuterol use			

Table 5

Percent of Albuterol Expected-Users, Over-Users, and Under-Users Who Were Adherent to Controller Medication by Treatment Assignment

Controller	Controller Adherence 80%			p
	Under-User	Expected-User	Over-User	
Montelukast (n=168)	28/31 (90%)	80/89 (90%)	42/48 (88%)	0.89
Placebo* (n=157)	44/45 (98%)	69/73 (95%)	33/39 (85%)	0.05
	Mean (SD) Percent Controller Adherence			p
	Under-User	Expected-User	Over-User	
Montelukast (n=168)	90.5 (14.4)	92.2 (12.0)	89.9 (20.5)	0.70
Placebo* (n=157)	95.3 (5.5)	94.4 (6.9)	91.4 (14.1)	0.76

* Placebo was considered a daily controller medication.

Table 6

Characteristics Associated with Controller Adherence among Montelukast and Placebo Participants (N=325)

	Adherent* n=296	Not Adherent n=29	p
Age , mean (SD)	37.1 (13.4)	38.8 (14.5)	0.59
Gender (male) , n (%)	84 (28.4)	4 (13.8)	0.07 ^F
Ethnicity (non-Hispanic) , n (%)	281 (94.9)	24 (82.8)	<0.01
Race (white) , n (%)	180 (60.8)	14 (48.3)	0.28 ^F
Smoking status (never) , n (%)	254 (85.8)	25 (86.2)	0.61 ^F
Spirometry (% predicted)			
(pre) FEV ₁ , mean (SD)	86.4 (13.8)	87.7 (14.4)	0.76
PEFR, mean (SD)	88.0 (16.5)	92.4 (15.7)	0.13
KASE-AQ			
Knowledge, mean (SD)	11.8 (2.9)	10.7 (2.6)	0.06
Attitude, mean (SD)	86.1 (6.8)	84.2 (6.8)	0.12
Efficacy, mean (SD)	81.7 (9.0)	81.4 (8.3)	0.62
Patient Reported Outcomes			
% Symptom Days, mean (SD)	39.1 (26.5)	36.6 (28.4)	0.56
ACQ, mean (SD)	1.5 (0.8)	1.5 (0.8)	0.83
ASUI, mean (SD)	0.8 (0.1)	0.8 (0.2)	0.94
SOBQ, mean (SD)	21.2 (18.6)	23.8 (17.6)	0.24
Mini-AQLQ, mean (SD)	5.1 (1.0)	4.7 (1.0)	0.06
SF-36 (physical), mean (SD)	48.3 (9.0)	47.3 (9.6)	0.58
SF-36 (mental), mean (SD)	49.9 (9.9)	46.0 (11.3)	0.04
CES-D, mean (SD)	10.1 (8.2)	15.9 (12.8)	0.04
Healthcare Utilization			
OCS past year, %	69 (23.3)	9 (31.0)	0.35
Unscheduled visit, %	75 (25.3)	9 (31.0)	0.50

^F Fisher's test;

* Adherence defined as ≥80%, non-adherence <80%. ACQ, Asthma Control Questionnaire; ASUI, Asthma Symptom Utility Index questionnaire; CES-D, Center for Epidemiological Studies-Depression questionnaire; FEV₁, forced expiratory volume in 1 second; KASE-AQ, Knowledge, Attitude, and Self-Efficacy Asthma Questionnaire; MiniAQLQ, Mini Asthma Quality of Life Questionnaire; SD, standard deviation; SF-36, Short-form Health Survey; SOBQ, Shortness-of-Breath Questionnaire.