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The Madison Avenue Effect: How drug presentation style influences adherence and outcome in patients with asthma

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Abstract

Background—Little is known about how drug presentation influences medication adherence.

Objective—Examine the effect of an educational program aimed at increasing expectations of treatment benefit on medication adherence.

Methods—Data are analyzed from 99 participants who underwent electronic drug monitoring during TAPE (Trial of Asthma Patient Education), a randomized placebo-controlled multi-center trial. Participants with suboptimally-controlled asthma were randomized to placebo or montelukast in conjunction with a presentation mode that was either neutral or designed to increase outcome expectancy. Adherence was monitored electronically over 4 weeks, and was defined as $\geq 80\%$ use of prescribed doses. Outcome expectancy, peak expiratory flow, pre-bronchodilator forced expiratory volume, asthma control (ACQ), and asthma-related quality of life were assessed at baseline and at the 4-week follow-up.

Results—Average electronic medication adherence was 69.9%. There was a significant interaction between presentation mode and drug assignment, with participants in the enhanced/montelukast group having a higher change in outcome expectancy ($\Delta 2.1$ points, $p < 0.001$) and better medication adherence (odds ratio 4.0, CI 1.1, 14.3) compared to those in the neutral/placebo group. There was no difference in asthma symptoms, quality of life, or clinical outcomes based on presentation mode. Rather, increased outcome expectancy was associated with modest improvements in asthma symptoms after adjusting for presentation mode, drug assignment, and medication adherence.

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Conclusion—The use of an enhanced presentation aimed at increasing outcome expectancy may lead to improved medication adherence.

Keywords

Asthma; medication adherence; electronic monitoring; outcome expectancy; behavioral intervention

Clinical implications

The way treatment is presented to patients may impact their adherence to therapy. Interventions aimed at increasing patients' expectancy of treatment efficacy may lead to increased medication adherence.

INTRODUCTION

It is well-recognized that adherence to asthma controller therapy is often suboptimal, and that poor adherence can lead to increased asthma-related morbidity and health care expenditures (1–3).

Results from several studies have shown that patient beliefs regarding therapy are predictors of adherence, with negative beliefs and concerns about the safety of therapy associated with decreased medication adherence (4,5). In contrast, positive beliefs about treatment efficacy (i.e., outcomes expectancy) and safety have been shown to be associated with increased adherence (6,7,8). As a result, most intervention studies of asthma adherence have included educational components aimed at addressing patients' beliefs and concerns about therapy (9,10), using methods such as shared decision-making (11) and motivation-enhancing strategies (12). We are unaware of any studies that have examined the effect of specifically promoting the benefits of a therapy (i.e., enhancing outcomes expectancy) on medication adherence.

As part of the Trial of Asthma Patient Education (TAPE) (13), a randomized clinical multicenter trial, we conducted a sub-study electronically monitoring adherence to examine the effect of an educational intervention designed to enhance outcome expectancy on medication adherence. We hypothesized that using an enhanced presentation would lead to more positive outcomes expectancy, which in turn would be associated with higher rates of medication adherence. In addition, the effect of the educational intervention on clinical and patient-reported outcomes was also examined.

METHODS

Study Design and Organization

This study was carried out as a sub-study of the Trial of Asthma Patient Education, TAPE (13). Briefly, this is a multi-center randomized clinical trial conducted by the American Lung Association Asthma Clinical Research Centers (ALA-ACRC) to examine the placebo effect in asthma, and to assess whether it could be augmented using an educational program that targeted patients' expectations of drug efficacy. Participants were enrolled at 19 centers participating in the ALA-ACRC located across the United States. The study was approved by institutional review boards at all participating sites.

The parent study involved four study visits over a 6-week period (Figure 1). After enrollment (Visit 1), there was a 2-week run-in period during which participants were asked

to maintain an asthma diary. Baseline data (outcome expectancy, lung function, asthma questionnaires) were collected during Visit 2, and prior to randomization to one of four intervention groups: enhanced/placebo, enhanced/montelukast, neutral/placebo, and neutral/montelukast. After randomization, participants were shown the first educational session and were dispensed the study drug. The educational session was repeated two weeks later during an interim visit with collection of interim pulmonary function and asthma symptom data. Outcome measures (outcome expectancy, lung function, and asthma symptoms) were reassessed at the end of the study, and unused study drugs were collected.

Inclusion & Exclusion Criteria

Eligible participants were patients with suboptimally-controlled asthma age 15 years or older who could potentially benefit from use of an additional asthma controller medication. Inclusion criteria were a history of physician diagnosed asthma with regular use of asthma medication in the preceding year; and one or more indicators of poor asthma control. Suboptimal asthma control was defined as an asthma control questionnaire (ACQ) score ≥ 1.5 (14), use of beta-agonists for asthma symptoms two or more times per week, or nocturnal awakening for asthma one or more times per week. Participants were excluded if they had other serious health problems, were currently using, or had prior intolerance to montelukast.

Drug Assignment

Study tablets were over-encapsulated with gelatin capsules and back-filled with methylcellulose. The active medication treatment was montelukast taken 10 mg orally at bedtime (Singulair, Merck & Co. Whitehouse Station, N.J.). Encapsulation had no effect on the absorption or elimination characteristics of montelukast. The placebos consisted of identical capsules filled with methylcellulose.

Presentation Mode

The educational intervention consisted of an interactive computer-based multimedia presentation about asthma self-care and treatment. The program was given post-randomization after collection of baseline data, and repeated two weeks later at an interim visit. A copy of the presentations can be viewed at the following website: http://www.cctrials.org/Public/TAPE_Patient_Education_Presentation.htm.

The enhanced presentation was designed to increase expectancy regarding the ability of montelukast to adequately control asthma symptoms. Specifically, it included a scripted introduction by a study coordinator, followed by a multimedia presentation embedded with both direct and indirect messages aimed at increasing expectancy of optimal asthma control with use of the medication. As part of the presentation, participants were also shown a consumer-directed television commercial for montelukast to further reinforce the positive message regarding drug efficacy. In contrast, the neutral presentation consisted of a scripted introduction followed by a multi-media presentation with information on asthma care and self-management but without discussion of the benefits of montelukast. An asthma action plan was provided to all participants as part of the study.

Sub-study description

Participants at the five participating centers with electronic adherence monitoring capabilities were enrolled in the sub-study. Electronic monitoring was carried out using Medication Events Monitoring Systems (MEMS) caps (AARDEX Ltd., Zug, Switzerland), which are devices fitted on the study drug bottles to record the date and time of each bottle opening. Adherence was monitored electronically post-randomization over four weeks. In

addition, medication adherence was assessed using 2-week recall, daily asthma diaries, and pill count.

Outcome Measures

The primary outcome of interest was adherence based on electronic monitoring. Adherence data were collected post-randomization for four weeks, and truncated at 100% per day, with credit given for one opening per 24-hour period to account for inappropriate use or medication dumping (15). Mean adherence was calculated as the percent of medication taken as prescribed (actual use/prescribed use *100) over the monitoring period. Good adherence was defined as appropriate use on $\geq 80\%$ of the monitored days based on the MEMS recorded events.

Outcome expectancy was evaluated using two Likert scale questions completed at randomization prior to viewing the multimedia presentation and at completion of the study. Participants were asked to rate their agreement or disagreement with the following items embedded in an asthma perception questionnaire, using a scale of 1 to 9: 1) "If I were to take Singulair (montelukast), it would help my asthma" and 2) "Singulair (montelukast) is likely to help people with asthma". Outcomes expectancy was analyzed as the sum of the ratings given to the two questions.

Asthma outcomes, including peak expiratory flow (PEF), forced expiratory volume (FEV₁), Asthma Control Questionnaire, ACQ (16), and the Asthma Quality of Life Questionnaire (17), were obtained at baseline prior to randomization, during the interim visit, and at the end of the study. The ACQ scores range from 0 to 6, with higher scores reflecting poorer asthma control. The Asthma Quality of Life Questionnaire consists of 15 questions with scores ranging from 1 (severely impaired) to 7 (not at all impaired). The change in FEV₁, PEF, ACQ and quality of life over the 4-weeks monitoring period was calculated as the difference between Visit 4 and baseline.

Statistical Analysis

Descriptive statistics were calculated using means and standard deviations (SD) for continuous variables, and proportions for categorical variables. Continuous outcome measures were analyzed as changes from baseline values. Statistical analysis of outcomes was performed using one-way ANOVA with Bonferroni adjustment and logistic regression. Models were adjusted for age, gender, ethnicity, education level, drug assignment, the interaction of presentation mode and treatment assignment, and mean adherence as indicated. Based on the sample size of 50 participants per group (enhanced presentation, regular presentation), we had $\geq 80\%$ power to detect a 30% between-group difference in adherence. All analyses were performed based on treatment assignment (intention to treat) using STATA Version 10.0 (StataCorp; College Station, TX).

RESULTS

Participant characteristics

Table 1 shows the baseline characteristics of the four study groups: enhanced/placebo, enhanced/montelukast, neutral/placebo and neutral/montelukast. The majority were white (60.6%) and female (71.7%), with mean ($\pm$ SD) age of 34.7 ± 14.5 years. Despite imbalances in some baseline characteristics, including the number of females, percentage of participants with higher education and prior asthma-related hospitalization in the enhanced/placebo group compared to the other groups, these were not statistically significant. The groups had other similar baseline characteristics, except for significantly higher baseline peak expiratory flow (PEF) in the enhanced/placebo group.

Effect of presentation mode on outcome expectancy

At baseline, the majority of participants (95%) agreed that montelukast was an effective drug for asthma, with a mean expectancy score (OE) of 12 out of 18 among the groups. At completion of the study, outcome expectancy tended to increase in those participants exposed to active drug, enhanced presentation, or both (Figure 2). The effects of exposure to active drug on OE was additive to that of the enhanced presentation, with the enhanced/montelukast group having the greatest change in OE ($\Delta 2.7 \pm 3.0$ points), compared to the neutral/placebo group ($\Delta 0.1 \pm 2.8$ points).

Effect of presentation mode on medication adherence

Of the four adherence measures, electronic monitoring had the lowest overall mean adherence with 69.9% of doses taken as prescribed compared to pill count (88.1%), 2-week patient recall (95.2%), and asthma diary (89.7%). Medication adherence was not associated with baseline demographics, except for lower adherence rates in those with a history of acute care utilization in the previous 12 months.

As there was a significant interaction between treatment assignment and presentation mode in predicting adherence, subsequent analyses were stratified by treatment assignment. There was a differential effect of presentation mode on medication adherence depending on whether it was combined with active drug or placebo (Figure 3), with increased adherence (76.0%) when combined with active drug and decreased adherence (26%) when combined with placebo ($p < 0.001$). There was no difference in adherence to active drug or placebo using the neutral presentation mode (52.0% vs. 47.8% respectively, $p = 0.78$). Compared to those in the neutral/placebo group, participants in the enhanced/montelukast group had significantly higher adherence rates (OR 4.0, CI 1.1, 14.3), which persisted after adjusting for age, race and gender (Table 2). Although those in the enhanced/placebo group had the lowest adherence rate (26.9%), this was not statistically significant compared to the neutral/placebo group.

Effect of presentation mode on asthma outcomes

Presentation mode was not associated with any significant change in any of the asthma outcome measures assessed, including asthma control ($p = 0.50$), asthma quality of life ($p = 0.16$), FEV₁ ($p = 0.12$), and peak flow ($p = 0.39$). There was an overall trend for improvements in patient reported outcomes over the 4-week treatment period (Table 3), especially in the enhanced/montelukast group. Compared to the neutral/placebo group, the enhanced/montelukast group showed a trend for higher improvements in quality of life ($\Delta 0.62$, CI 0.28, 0.97), along with statistically greater improvements in FEV₁ ($\Delta 0.15$, CI 0.03, 0.26) (Table 4).

Effect of outcome expectancy on asthma outcomes

Outcome expectancy (OE) was associated with significant improvements in asthma control scores (regression coefficient -0.08 , $p = 0.004$) regardless of age, gender, race, drug assignment or adherence. This effect was clinically modest, however, requiring large changes in outcome expectancy (approximately 7 points) for a meaningful change in asthma control to occur. OE was associated with a trend for modest improvements in asthma quality of life (regression coefficient 0.06 , $p = 0.08$), with no statistically significant effect on FEV₁ ($p = 0.12$) or peak expiratory flow ($p = 0.23$).

Discussion

In this prospective multi-center intervention trial, an enhanced presentation mode designed to influence patients' outcome expectancy regarding treatment efficacy was associated with

improved adherence to taking active drug and FEV₁, with potentially detrimental effects on adherence to placebo. In addition, increased outcome expectancy was found to be independently associated with improved an asthma control score (ACQ) with a trend for improvements in asthma-specific quality of life. These results suggest that the manner in which medications are introduced to patients may not only affect their expectations about the potential benefits of a therapy, but may also impact their level of adherence.

According to social cognitive theory, an individual's expectations of a given outcome can act as an incentive (either positive or negative) to influence subsequent behavior (18). Thus beliefs regarding the outcome of an action/behavior may influence both a person's motivation and behavior. This theory is well-recognized by advertisers. Marketing messages are effective in promoting sales when the message convinces consumers that they will benefit from buying the product. Similarly, in the present study, we were able to successfully increase outcome expectancy using a multi-media presentation by increasing a patient's expectations of treatment benefit, with an additive effect of presentation mode and drug assignment on medication adherence.

Few studies have focused on assessing the role of increasing outcome expectancy on medication adherence. A study by Olsen et al. examined the effect of expectancy on adherence to continuous positive airway pressure (CPAP) and found that positive expectancies explained most of the variance in CPAP adherence. (19). Le et al. found negative beliefs regarding asthma treatment were a significant mediator of the association between minority status and poor adherence (20). Taken together, these findings suggest that the improved adherence to active drug in response to enhanced presentation may in part be mediated via increased outcome expectancy.

The interaction between outcome expectancy and medication adherence is, however, rather complex. Our study also found that although enhanced presentation was associated with increased adherence and FEV₁, enhanced expectancy had a negative effect on medication adherence when paired with an ineffective treatment (placebo). This highlights the importance of aligning patients' expectations with the potential benefits of the treatment. While the reason for the decreased adherence to placebo in the enhanced group is uncertain, we speculate that this finding may be due to a discrepancy between outcome expectancy and drug efficacy, such that failure to notice the expected benefit may have negatively affected adherence. The effect of the enhanced presentation on adherence to placebo was seen within the first week of follow-up, with mean adherence rates of 52% vs. 85% in the enhanced/montelukast group. This difference persisted over the 4-week follow-up, despite a progressive decline in mean adherence over time in all four groups.

We also found outcome expectancy to be associated with improvements in patient reported outcomes (PROs), mainly with regard to asthma control. This effect was independent of drug assignment or medication adherence, suggesting that patient expectations may play a role in perceived benefit, especially as measured by PROs. Patients who believed that their therapies were effective reported health benefits, even when objective measures such as spirometry failed to capture those benefits. This may account for the observed improvements in patient-reported outcome in the enhanced/placebo group. Such observation is consistent with findings from the parent TAPE study, which showed a placebo effect that was augmented using the enhanced presentation mode (13).

One of the strengths of the present study is the use of electronic monitoring to measure medication adherence objectively. Studies comparing electronic monitoring, pill count, and self report to biological measures of adherence have shown electronic monitoring to be the most valid measure of adherence (21,22). As with other studies, we found that pill counts

and self-reports significantly overestimated actual medication use. The current study design is further strengthened by the use of a formalized protocol to increase outcome expectancy which standardized the intervention. The generalizability of our findings is, however, uncertain. Since participants were aware that they would be randomized to placebo or active drug as part of the consent process, the possibility of taking a placebo drug may have influenced their adherence to the therapy. Furthermore, although patients were randomized to the four study groups by center, there were imbalances in baseline demographics which were adjusted for using multiple regression analyses. In addition, the 2-week run-in period may have led to the selection of a very motivated group with higher adherence compared to the general population. However, one would expect such selection bias, if present, to underestimate the effect of the intervention on adherence. It is also unclear whether the observed effect of enhanced presentation on adherence to montelukast would apply to other therapies prescribed to control asthma, such as inhaled corticosteroids, or whether these effects would persist longer than four weeks.

In conclusion, we observed that the manner in which information about an asthma drug was presented to patients significantly influenced their expectations about treatment efficacy and resulted in increased medication adherence to active drug, along with improvements in FEV₁. Borrowing a lesson from Madison Avenue, we found that marketing the benefits of therapy increased “sales.” In addition, increased outcome expectancy was associated with improvements in patient-reported outcomes, although not objectively measured indices of asthma control. These results suggest that the methods by which treatment options are introduced to patients not only affect adherence to therapy and clinical outcomes, but also impact self-reported outcomes.

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Abbreviations used

PEF	Peak Expiratory Flow
ACQ	Juniper asthma control questionnaire
FEV₁	Forced expiratory volume in 1 second

References

1. Bender BG, Rand C. Medication non-adherence and asthma treatment cost. *Curr Opin Allergy Clin Immunol* 2004 Jun;4(3):191–195. [PubMed: 15126940]
2. Delea TE, Stanford RH, Hagiwara M, Stempel DA. Association between adherence with fixed dose combination fluticasone propionate/salmeterol on asthma outcomes and costs*. *Curr Med Res Opin* 2008 Dec;24(12):3435–3442. [PubMed: 19032125]
3. Williams LK, Pladevall M, Xi H, Peterson EL, Joseph C, Lafata JE, et al. Relationship between adherence to inhaled corticosteroids and poor outcomes among adults with asthma. *J Allergy Clin Immunol* 2004 Dec;114(6):1288–1293. [PubMed: 15577825]
4. Conn KM, Halterman JS, Lynch K, Cabana MD. The impact of parents' medication beliefs on asthma management. *Pediatrics* 2007 Sep;120(3):e521–6. [PubMed: 17766496]
5. Horne R, Weinman J. Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *J Psychosom Res* 1999 Dec;47(6):555–567. [PubMed: 10661603]

6. Menckeborg TT, Bouvy ML, Bracke M, Kaptein AA, Leufkens HG, Raaijmakers JA, et al. Beliefs about medicines predict refill adherence to inhaled corticosteroids. *J Psychosom Res* 2008 Jan; 64(1):47–54. [PubMed: 18157999]
7. Conn KM, Halterman JS, Lynch K, Cabana MD. The impact of parents' medication beliefs on asthma management. *Pediatrics* 2007 Sep;120(3):e521–6. [PubMed: 17766496]
8. Ponienman D, Wisnivesky JP, Leventhal H, Musumeci-Szabo TJ, Halm EA. Impact of positive and negative beliefs about inhaled corticosteroids on adherence in inner-city asthmatic patients. *Ann Allergy Asthma Immunol* 2009 Jul;103(1):38–42. [PubMed: 19663125]
9. Otsuki M, Eakin MN, Rand CS, Butz AM, Hsu VD, Zuckerman IH, et al. Adherence feedback to improve asthma outcomes among inner-city children: a randomized trial. *Pediatrics* 2009 Dec; 124(6):1513–1521. [PubMed: 19948623]
10. Bender BG, Apter A, Bogen DK, Dickinson P, Fisher L, Wamboldt FS, et al. Test of an interactive voice response intervention to improve adherence to controller medications in adults with asthma. *J Am Board Fam Med* 2010 Mar–Apr;23(2):159–165. [PubMed: 20207925]
11. Wilson SR, Strub P, Buist AS, Knowles SB, Lavori PW, Lapidus J, et al. Shared treatment decision making improves adherence and outcomes in poorly controlled asthma. *Am J Respir Crit Care Med* 2010 Mar 15;181(6):566–577. [PubMed: 20019345]
12. Borrelli B, Riekert KA, Weinstein A, Rathier L. Brief motivational interviewing as a clinical strategy to promote asthma medication adherence. *J Allergy Clin Immunol* 2007 Nov;120(5): 1023–1030. [PubMed: 17904625]
13. Wise RA, Bartlett SJ, Brown ED, Castro M, Cohen R, Holbrook JT, et al. Randomized trial of the effect of drug presentation on asthma outcomes: the American Lung Association Asthma Clinical Research Centers. *J Allergy Clin Immunol* 2009 Sep;124(3):436–44. 444e1–8. [PubMed: 19632710]
14. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999;10;14(0903–1936; 4):902–907.
15. Apter AJ, Boston RC, George M, Norfleet AL, Tenhave T, Coyne JC, et al. Modifiable barriers to adherence to inhaled steroids among adults with asthma: it's not just black and white. *J Allergy Clin Immunol* 2003 Jun;111(6):1219–1226. [PubMed: 12789220]
16. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J* 1999 Oct;14(4):902–907. [PubMed: 10573240]
17. Juniper EF. Health-related quality of life in asthma. *Curr Opin Pulm Med* 1999 Mar;5(2):105–110. [PubMed: 10813260]
18. Bandura A, Wood R. Effect of perceived controllability and performance standards on self-regulation of complex decision making. *J Pers Soc Psychol* 1989 May;56(5):805–814. [PubMed: 2724068]
19. Olsen S, Smith S, Oei TP. Adherence to continuous positive airway pressure therapy in obstructive sleep apnoea sufferers: a theoretical approach to treatment adherence and intervention. *Clin Psychol Rev* 2008 Dec;28(8):1355–1371. [PubMed: 18752879]
20. Le TT, Bilderback A, Bender B, Wamboldt FS, Turner CF, Rand CS, et al. Do asthma medication beliefs mediate the relationship between minority status and adherence to therapy? *J Asthma* 2008 Jan–Feb;45(1):33–37. [PubMed: 18259993]
21. Remington G, Kwon J, Collins A, Laporte D, Mann S, Christensen B. The use of electronic monitoring (MEMS) to evaluate antipsychotic compliance in outpatients with schizophrenia. *Schizophr Res* 2007 Feb;90(1–3):229–237. [PubMed: 17208414]
22. Lee JY, Kusek JW, Greene PG, Bernhard S, Norris K, Smith D, et al. Assessing medication adherence by pill count and electronic monitoring in the African American Study of Kidney Disease and Hypertension (AASK) Pilot Study. *Am J Hypertens* 1996 Aug;9(8):719–725. [PubMed: 8862216]

Figure 1.
Study design

Figure 2.
Change in outcome expectancy score over 4-week treatment period.

Figure 3.
Mean adherence rate over four weeks by study condition in participants with asthma.

Table 1

Baseline characteristics

	Enhanced		Neutral		p-value
	Placebo N=26	Montelukast N=25	Placebo N=23	Montelukast N=25	
Demographic Characteristics					
Age	33.3 ± 2.9	33.2 ± 2.8	39.6 ± 3.2	33.1 ± 2.8	0.92
Female sex (%)	53	84	74	76	0.10
Race or Ethnicity (%)					
White	50	52	70	80	0.12
Black	46	44	22	12	
Hispanic	4	4	4	4	
Other	0	0	4	4	
Education level - (%)					
Completed high school only	15	16	22	4	0.35
Higher education	65	80	74	88	0.27
Former smoker (%)	12	12	22	24	0.53
Asthma History					
Hospitalized or seen in acute care over past year- (%)	23	16	17	8	0.54
Current asthma medication/treatment - no. (%)					
Long Acting Beta Agonist	14(54)	11(44)	9 (39)	9(36)	0.60
Inhaled Corticosteroids	16 (62)	15(60)	14(61)	14(56)	0.98
Oral antileukotriente	0	0	1(4)	0	0.45
Lung Function*					
FEV1 % predicted	82.8 (2.1)	81.0 (2.5)	82.2 (2.5)	83.3 (3.0)	0.44
FVC % predicted	88.5 (2.3)	88.5 (2.7)	88.5 (2.4)	92.6 (3.1)	0.46
PEF (L/min)	433.3 (21.5)	366.8 (13.4)	379.1 (19.4)	384.0 (13.8)	0.04
Juniper Asthma Control (ACQ)	1.1(0.6)	0.9 (0.6)	1.4(0.8)	1.1 (0.7)	0.09
Asthma Quality of Life	5.1(1.2)	5.0 (1.1)	5.2(1.0)	5.1(1.0)	0.97
Outcome expectancy score	12 (3)	11 (2)	12 (3)	12 (3)	0.26

Values represent Mean (± SD) unless otherwise indicated. PEF= peak expiratory flow; FEV1=forced expiratory volume in 1 second; FVC= forced vital capacity

Table 2

Odds of adherence to study drug based on study condition.

	Adherence		
	Rate	OR* (95% CI)	p-value
Neutral/Placebo (N=23)	47.8	Referent	--
Neutral/Montelukast (N=25)	52.0	1.2 (0.4,3.8)	0.77
Enhanced/Placebo (N=26)	26.9	0.5 (0.1,1.6)	0.13
Enhanced/Montelukast (N=25)	76.0	4.0 (1.1,14.3)	0.04

* Odds ratio from multiple regression analysis adjusted for age, race, and gender.

Table 3

Mean change in asthma symptoms and asthma quality of life over four weeks by study condition.

		Multiple Linear Regression (MLR)*	
	Crude Mean Change (95% CI)	Regression coefficient (95% CI)	p-value
Juniper Asthma Control (ACQ) [#]			
Neutral/Placebo (N=23)	−0.24 (−0.47, −0.00)	0.00	--
Neutral/Montelukast (N=25)	−0.41 (−0.68, −0.13)	−0.20 (−0.62,0.22)	0.34
Enhanced/Placebo (N=26)	−0.26 (−0.62, 0.02)	−0.11 (−0.52,0.31)	0.61
Enhanced/Montelukast (N=25)	−0.56 (−0.89, −0.22)	−0.32 (−0.74,0.10)	0.14
Asthma Quality of Life			
Neutral/Placebo (N=23)	0.13 (−0.1, 0.44)	0.00	--
Neutral/Montelukast (N=25)	0.58 (0.29, 0.88)	0.47 (−0.31,0.76)	0.08
Enhanced/Placebo (N=26)	0.62 (0.13, 1.10)	0.50 (−0.28,0.77)	0.06
Enhanced/Montelukast (N=25)	0.62 (0.28, 0.97)	0.47 (−0.30,0.76)	0.08

* MLR of the change in patient-reported outcomes (i.e ACQ and asthma quality of life) for each group compared to the neutral/placebo group adjusted for age, race, and gender

[#] Lower scores represent better asthma control.

Table 4

Mean change in selected tests of pulmonary function after four weeks by study condition.

	Crude Mean Change (95% CI)	Multiple Linear Regression (MLR)*	
		Regression coefficient (95% CI)	p-value
FEV ₁ (L)			
Neutral/Placebo (N=23)	-0.01 (-0.07, 0.06)	0.00	--
Neutral/Montelukast (N=25)	0.04(-0.02,0.09)	0.06 (-0.06, 0.17)	0.34
Enhanced/Placebo (N=26)	0.03 (-0.06, 0.12)	0.04 (-0.08,0.15)	0.53
Enhanced/Montelukast (N=25)	0.13 (0.02, 0.24)	0.15 (0.03,0.26)	0.02
Peak expiratory flow (L/min)			
Neutral/Placebo (N=23)	2.56 (-2.36, 7.48)	0.00	
Neutral/Montelukast (N=25)	0.26 (-5.23, 5.75)	-2.71 (-11.15,5.74)	0.53
Enhanced/Placebo (N=26)	-1.17 (-5.78, 3.44)	-4.13 (-12.53,4.24)	0.33
Enhanced/Montelukast (N=25)	9.19 (1.15,17.24)	6.84 (-1.61,15.28)	0.11

* MLR of the change in physiologic outcomes (i.e. FEV₁ and Peak expiratory flow) for each group compared to the neutral/placebo group adjusted for age, race, and gender