

Association Between Pulmonary Function and Asthma Symptoms



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What is already known about this topic? Asthma guidelines state that pulmonary function may be weakly correlated with asthma symptoms, and evidence in the literature is inconsistent with regard to the magnitude of association reported, ranging from weak to strong correlation.

What does this article add to our knowledge? In a longitudinal study of a managed-care population with persistent asthma, a weak correlation between FEV₁ as a percentage of predicted and 5-item Asthma Control Questionnaire/6-item Asthma Control Questionnaire scores was observed in unadjusted models; however, the correlation became significant after adjusting for covariates.

How does this study impact current management guidelines? Clinical assessments of asthma control should not rely on single measures such as FEV₁ as a percentage of predicted or 5-item Asthma Control Questionnaire/6-item Asthma Control Questionnaire scores, because elements of control may be missed if assessments of both lung function and symptoms are not used.

BACKGROUND: FEV₁ as a percentage of predicted (FEV₁%pred) is commonly measured in asthma clinical studies; however, reports vary on its association with asthma control instruments evaluating symptoms.

OBJECTIVE: Assess the association between FEV₁%pred and Asthma Control Questionnaire (ACQ) scores in a managed-care population with persistent asthma.

METHODS: Retrospective analysis of survey responses and spirometry results of patients (aged ≥12 years) with persistent asthma from the Observational Study of Asthma Control and Outcomes was done. Eligible patients received 4 identical surveys including the 5-item ACQ (ACQ-5)/6-item ACQ (ACQ-6) and completed spirometry in parallel. Longitudinal analyses, comparisons of change over time, and fixed- and random-effects regression analyses were conducted, with/without adjustment for covariates.

RESULTS: There were 1748 survey responses with valid spirometry results. In unadjusted models, coefficients for ACQ-5/ACQ-6 scores were not statistically significant and coefficient of determination (R^2) was low (0.03). When adjusted for covariates, ACQ-5 and ACQ-6 scores were significantly associated with FEV₁%pred ($P < .001$) and R^2 increased to 0.11 and 0.12, respectively. In adjusted models, every 1-point increase in ACQ-5 and ACQ-6 scores was associated with a 1.7% and 1.9% decrease, respectively, in FEV₁%pred. Change in FEV₁%pred and change in ACQ-5/ACQ-6 scores were not significantly associated in regressions with/without covariates.

CONCLUSIONS: The weak and statistically insignificant association between FEV₁%pred and ACQ-5/ACQ-6 scores in unadjusted models suggests a high degree of unexplained variation between these measures. Results support the use of both symptoms and pulmonary function, rather than relying

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Abbreviations used

ACQ- Asthma Control Questionnaire
 ACQ-5- 5-item ACQ
 ACQ-6- 6-item ACQ
 ACQ-7- 7-item ACQ
 ACT- Asthma Control Test
 FEV₁%pred- FEV₁ as a percentage of predicted
 OSACO- Observational Study of Asthma Control and Outcomes

on one measure alone, to assess asthma control in clinical care and outcomes studies. © 2019 The Authors. Published by Elsevier Inc. on behalf of the American Academy of Allergy, Asthma & Immunology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>). (J Allergy Clin Immunol Pract 2019;7:2319-25)

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INTRODUCTION

Asthma is a chronic airway disease affecting more than 26 million people in the United States, approximately 8.3% of the total population.¹ The long-term goals of asthma management are to achieve good disease control; this means that treatment is adjusted in a continuous cycle of assessment, treatment, and review of the patient's current impairment (frequency and intensity of symptoms and functional limitations) and future risk (the likelihood of asthma exacerbations, progressive decline in lung function, or risk of adverse effects from medication).^{2,3} FEV₁ as a percentage of predicted (FEV₁%pred) is an objective measure of airway resistance to expiratory flow and is a common primary end point in clinical trials of asthma. Pulmonary function measures are only one component of the impairment domain of asthma "control"; validated instruments, such as the Asthma Control Questionnaire (ACQ), have been developed to provide a composite measure that includes subjective patient-reported assessments of symptoms such as wheezing, shortness of breath, and activity limitation.⁴ The Global Initiative for Asthma 2018 guidelines and the Expert Panel Report-3 Guidelines for the Diagnosis and Management of Asthma both suggest that pulmonary function measures may be weakly correlated with asthma symptoms,^{2,3} although a review of the literature reveals inconsistent results (ranging from *no significant correlation* to *strong correlation*) and studies have used a range of tools to measure these symptom control and pulmonary function outcomes.⁵⁻¹⁷ The objective of the current study was to assess the association between pulmonary function (FEV₁%pred) and a validated measure of asthma control (ACQ score), in a managed-care population of patients with asthma.

METHODS

Study design and patients

The Observational Study of Asthma Control and Outcomes (OSACO) was a prospective survey and retrospective claims-based analysis of patients in a large health maintenance organization in

Colorado. Details of OSACO have been published previously; no additional inclusion criteria were imposed because the current study was a retrospective analysis of existing data.¹⁸ In the original study, patients enrolled in a managed-care population were invited to participate if they met the following criteria: age 12 years or more; diagnosed with persistent asthma within the previous 12 months by an internal diagnostic algorithm (consistent with Expert Panel Report-3 Guidelines for the Diagnosis and Management of Asthma definitions of persistent asthma³) or prescription drug utilization (evidenced by 2 prescriptions of inhaled corticosteroid or >2 canisters of albuterol or equivalent within the previous 3 months); and continuously enrolled for 1 year or more with prescription drug benefits before the first survey date.

In the original OSACO, eligible patients received 3 identical surveys (waves 1-3) over the course of 15 months from April 2011 to June 2012. Surveys included the 5-item ACQ (ACQ-5)/6-item ACQ (ACQ-6). Subsequent surveys were sent to only those patients who completed the previous round. For each round, patients who did not respond after 2 attempted mailings were contacted and offered the survey by telephone. A subsequent survey, identical to the previous 3 (wave 4), starting in August 2012, was sent to only the completers of the previous waves (≥2 of 3 completed surveys) with poorly controlled asthma (ACQ score ≥1.5). A subset of survey respondents in all 4 waves chose to undergo spirometry when invited to do so. These patients completed the ACQ-5/ACQ-6 at the same time as FEV₁%pred was measured. Wave 4 included pulmonary function testing for all patients. Only patients with both completed spirometry and surveys (ACQ) were included in this study.

Asthma Control Questionnaire

The ACQ is a multidimensional instrument for assessing asthma control. The 7-item ACQ (ACQ-7) includes symptoms, extent of activity limitation, use of short-acting β₂-agonists, and FEV₁%pred.⁴ The ACQ-5 and ACQ-6 are subsets of the ACQ-7 and have been independently validated, showing good measurement properties.¹⁹ The ACQ-5 includes 5 patient-reported questions with a 7-day recall of (1) frequency of nighttime awakening, (2) severity of asthma symptoms upon awakening, (3) extent of activity limitations, (4) frequency of shortness of breath, and (5) frequency of wheezing. Results are in the form of a continuous score from 0 to 6, with a lower score representing better asthma control. The ACQ-6 includes the 5 items of the ACQ-5 in addition to a sixth question about the use of short-acting β₂-agonists.⁴

Statistical analyses

Descriptive statistics of sociodemographic variables, clinical variables, and clinical outcomes were assessed. Unadjusted means and SDs for FEV₁%pred were calculated across ACQ-score categories. Fixed- and random-effects regression analyses (both unadjusted and adjusted) were conducted as appropriate following a Hausman test. FEV₁%pred was regressed on ACQ score, adjusting for the following covariates: survey wave and month, age, sex, family income level, race, educational attainment, ethnicity, and smoking status. A regression restricted to ACQ scores (no adjustment for covariates) was also conducted. As with all regression analyses, the coefficient of determination (*R*²) signified the amount of variance in the dependent variable (FEV₁%pred) explained by the independent variable(s) (ACQ scores with or without covariates). Individuals with at least 1 set of completed survey responses and spirometry results were included. Individuals without any observations were not included, and no data imputation was conducted for missing values.

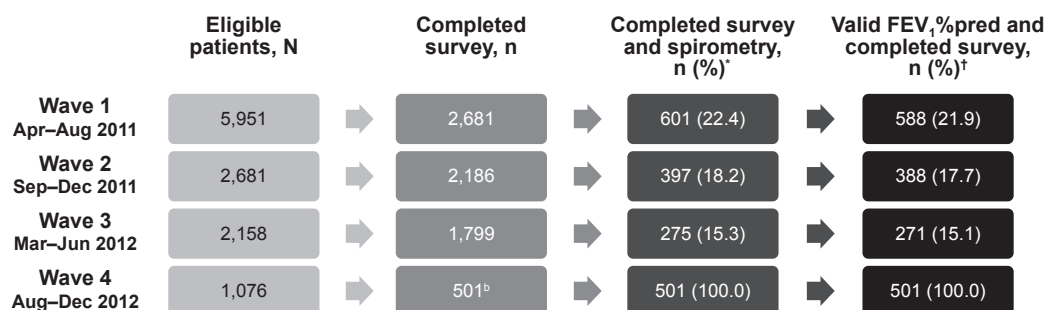


FIGURE 1. Patient distribution for each survey wave (1–4) in OSACO. ^{*}Percentage of all patients who completed the survey in that wave. [†]Completers of 2 or more of the 3 surveys administered in waves 1 to 3.

In addition, analyses of the association between the change in FEV₁%pred and the change in ACQ score were conducted. For each individual and each pair of chronological surveys, a change in FEV₁%pred and change in ACQ-5/ACQ-6 score was calculated: (1) from wave 1 to wave 2; (2) from wave 2 to wave 3; and (3) from wave 3 to wave 4. Based on the results of the Hausman test, fixed- or random-effects regression analyses were used to regress the dependent variable (change in FEV₁%pred) on the independent variable(s) (change in ACQ score with and without covariates). Both the fixed- and random-effects regression analyses and the comparisons of change over time within an individual (both conducted with and without covariates) addressed the possible correlation of errors from multiple time-period responses of the same patient in this longitudinal analysis.

The imputation of missing data for the ACQ followed the guidelines suggested by the creators of the instrument. Responses where a total score could not be computed with the recommended imputation guidance were not included in the analysis. Likewise, individuals with missing FEV₁%pred scores were not included in the analysis. Missing values for categorical variables listed above were coded as “NA” and the individuals were included in the analysis. For each group (including NA) of the categorical variable, an indicator (dummy) variable was created for the regression analysis.

RESULTS

Study population

In the original OSACO, a total of 5951 patients met the inclusion criteria and were invited to participate via a mailed survey. Of these, 2657 subjects had valid claims data and ACQ-5/ACQ-6 scores at baseline. The subset of survey respondents with ACQ-5/ACQ-6 scores and FEV₁%pred results was 588, 388, 271, and 501 patients in waves 1, 2, 3, and 4, respectively. Patient distribution for each survey wave is shown in [Figure 1](#). As wave 4 was sent to completers of 2 or more of 3 surveys from across the previous 3 waves (as opposed to only those patients who completed the previous round, ie, wave 3), a greater number of survey respondents with ACQ-5/ACQ-6 scores and FEV₁%pred results completed wave 4 compared with waves 2 and 3. In addition, all individuals in wave 4 were invited to complete spirometry (compared with only a subset of patients in waves 1–3).

This resulted in a total of 1748 survey results that could be paired with valid spirometry for the current analysis. Of the 1748 survey responses with valid spirometry results, individuals may have had between 1 and 4 repeated observations (FEV₁%pred and ACQ-5/ACQ-6 score combinations) over time. Individuals with at least 1 observation were included in the final sample

([Table I](#)). Most patients in the final sample were aged 35 to 74 years (80.4%), were female (67.6%), and white (87.1%). In addition, 82.3% of the patients with a complete survey and valid spirometry had family incomes greater than \$30,000 per year, and 80.2% had at least some college education. Approximately one-third of patients had smoking history, with 3.3% being current smokers.

Pulmonary function according to patient characteristic

Unadjusted mean values for FEV₁%pred by characteristic for the final sample (n = 1748) are presented in [Table I](#). The mean FEV₁%pred was 86.8 ± 16.4 across survey waves and was the same across all broad sociodemographic categories: 86.8 ± 16.4 for age, sex, race, education attainment, and smoking history categories; 86.7 ± 16.4 for income status. Within categories, the trend was for lower mean FEV₁%pred in older versus younger patients; an exception to this trend was patients aged 85 years or older, although there were only 14 patients in this age category. Current smokers had lower FEV₁%pred compared with patients who had previously smoked or never smoked.

Association between pulmonary function and asthma symptom control

Unadjusted mean FEV₁%pred values for each category of ACQ score for all patients with a valid spirometry measurement and a completed survey are presented in [Table I](#). Mean FEV₁%pred for all patients completing ACQ-5 or ACQ-6 surveys was 86.7 ± 16.3. As ACQ-5 or ACQ-6 score category increased, mean FEV₁%pred decreased. For patients with poorly controlled asthma (ACQ-5/ACQ-6 score ≥ 1.5), mean FEV₁%pred was 83.0 ± 16.3. For those with well-controlled asthma (ACQ-5/ACQ-6 score < 0.75), mean FEV₁%pred was 89.6 ± 15.5.

In a fixed-effects regression model, with FEV₁%pred as the dependent variable, unadjusted for covariates, coefficients for ACQ-5 and ACQ-6 scores were not statistically significant ($P = .08$ and $P = .07$, respectively; [Table II](#)). This suggests no significant association between FEV₁%pred and ACQ-5/ACQ-6 scores in the unadjusted models. The overall R^2 (0.03) is equivalent to a correlation coefficient of -0.17 , indicating a weak negative correlation when covariates were not included.

In a random-effects regression model adjusted for covariates, it was observed that for every 1-point increase in ACQ-5 or ACQ-6 score, FEV₁%pred decreased by 1.7% and 1.9%, respectively ([Table II](#)). ACQ-5 and ACQ-6 scores were statistically significantly associated with FEV₁%pred ($P < .001$; [Table II](#)). In

TABLE I. Unadjusted FEV₁%pred by patient characteristic and ACQ-5/ACQ-6 score

Characteristic	Sample size, n (%) [*]	FEV ₁ %pred, mean ± SD
Survey wave	1748	86.8 ± 16.4
1	588 (33.6)	89.0 ± 16.8
2	388 (22.2)	88.9 ± 16.0
3	271 (15.5)	89.0 ± 15.4
4	501 (28.7)	81.3 ± 15.5
Age category (y)	1748	86.8 ± 16.4
12-24	135 (7.7)	97.2 ± 13.0
25-34	104 (5.9)	92.3 ± 15.6
35-44	216 (12.4)	88.5 ± 14.0
45-54	347 (19.9)	87.2 ± 16.1
55-64	572 (32.7)	84.0 ± 16.6
65-74	269 (15.4)	83.8 ± 16.4
75-84	91 (5.2)	84.3 ± 16.8
≥85	14 (0.8)	94.6 ± 26.5
Sex	1748	86.8 ± 16.4
Female	1182 (67.6)	86.7 ± 16.1
Male	566 (32.4)	87.0 ± 17.0
Race	1748	86.8 ± 16.4
White	1522 (87.1)	86.9 ± 16.2
Asian	29 (1.7)	76.9 ± 15.3
Black	71 (4.1)	88.5 ± 18.2
Native American	67 (3.8)	83.9 ± 19.8
Native Hawaiian	18 (1.0)	83.2 ± 12.9
Mixed Race	0 (0.0)	0 ± 0.0
NA	41 (2.3)	91.1 ± 12.7
Income (\$ per year)	1746 [†]	86.7 ± 16.4
<10,000	25 (1.4)	89.2 ± 12.7
10,000-30,000	129 (7.4)	86.4 ± 15.7
30,000-50,000	282 (16.2)	86.0 ± 17.3
50,000-70,000	297 (17.0)	85.5 ± 17.0
70,000-90,000	294 (16.8)	85.2 ± 15.0
>90,000	564 (32.3)	88.2 ± 16.2
NA	47 (2.7)	99.1 ± 13.8
"Prefer not to answer"	108 (6.2)	83.2 ± 16.9
Education attainment	1748	86.8 ± 16.4
<Eighth grade	30 (1.7)	96.4 ± 15.5
High school but did not graduate	88 (5.0)	95.8 ± 15.4
High school graduate or GED	226 (12.9)	84.7 ± 16.0
Some college	461 (26.4)	84.3 ± 16.2
College graduate	443 (25.3)	87.3 ± 16.0
Postgraduate	499 (28.5)	87.4 ± 16.6
NA	1 (0.1)	86.0 ± 0.0
Smoking history, n (%)	1748	86.8 ± 16.4
Never smoked	1118 (64.0)	87.1 ± 16.0
Current smoker	58 (3.3)	83.9 ± 16.8
Previous smoker	548 (31.4)	86.5 ± 16.9
NA	24 (1.4)	83.7 ± 21.5
ACQ-5 completers	1733 [‡]	86.7 ± 16.3
ACQ-5 score category		
0-1	551	90.2 ± 15.4
1-2	740	86.3 ± 16.3
2-3	348	83.7 ± 16.8

(continued)

TABLE I. (Continued)

Characteristic	Sample size, n (%) [*]	FEV ₁ %pred, mean ± SD
3-4	84	82.6 ± 16.0
4-5	7	77.3 ± 15.6
5-6	3	58.7 ± 9.0
6-7	0	0 ± 0.0
ACQ-5 score cutoff		
<0.75	754	89.7 ± 15.5
≥0.75	979	84.4 ± 16.6
<1.5	1291	88.0 ± 6.0
≥1.5	442	83.2 ± 6.7
ACQ-6 completers	1721 [§]	86.7 (16.3)
ACQ-6 score category		
0-1	476	90.5 ± 15.5
1-2	796	86.5 ± 16.3
2-3	357	83.7 ± 16.3
3-4	83	81.5 ± 15.7
4-5	6	76.5 ± 16.2
5-6	3	58.7 ± 9.0
6-7	0	0 ± 0.0
ACQ-6 score cutoff		
<0.75	796	89.6 ± 15.5
≥0.75	925	84.2 ± 16.6
<1.5	1272	88.0 ± 16.1
≥1.5	449	83.0 ± 16.3

GED, General Education Diploma; NA, patient did not select an answer for the question.

Percentages may not add up to 100 because of rounding.

^{*}Completed surveys with valid spirometry for the current analysis.

[†]Patients for whom there was an incomplete response: n = 2.

[‡]Patients for whom there was an incomplete ACQ-5: n = 15.

[§]Patients for whom there was an incomplete ACQ-6: n = 27.

addition, after adjusting for covariates, the overall R^2 increased to 0.11 and 0.12, respectively, for ACQ-5 and ACQ-6 ($P < .001$); these are comparable to correlation coefficients of an absolute magnitude of 0.33 and 0.35, respectively, indicating a moderate correlation between the dependent variable (ACQ score) and the independent variables (FEV₁%pred and covariates).

Association between change in pulmonary function and change in ACQ score over time

A fixed-effects regression model unadjusted for covariates showed that the coefficients for change in FEV₁%pred were not statistically significantly associated with change in ACQ-5 or ACQ-6 scores ($P = .20$ and $P = .15$, respectively; Table III). This suggests no significant association between change in FEV₁%pred and change in ACQ-5/ACQ-6 score in the unadjusted models. The overall R^2 values (ACQ-5, 0.005; ACQ-6, 0.006) suggest a very weak correlation. After including covariates in a random-effects regression model, the coefficient for change in FEV₁%pred was not statistically significant for change in either ACQ-5 score or ACQ-6 score ($P = .10$ and $P = .06$, respectively; Table III). After adjusting for covariates, the overall R^2 values increased to 0.03 (ACQ-5) and 0.04 (ACQ-6), equivalent to a correlation coefficient of absolute magnitude of 0.2 or less. This indicates a weak to moderate correlation after including covariates.

TABLE II. Regression analyses to assess the association between ACQ-5/ACQ-6 score and FEV₁%pred

Score	Unadjusted fixed-effects regression analysis					Adjusted random-effects regression analysis*				
	Coefficient	SE	P value	95% CI	Overall R ²	Coefficient	SE	P value	95% CI	Overall R ²
ACQ-5 score	−0.76	0.43	.08	−1.61 to 0.10	0.03	−1.72	0.38	<.001	−2.45 to −0.98	0.11
ACQ-6 score	−0.83	0.46	.07	−1.73 to 0.07	0.03	−1.85	0.40	<.001	−2.64 to −1.07	0.12

*Adjusted for covariates: survey wave and month, age, sex, family income level, race, educational attainment, ethnicity, and smoking status.

TABLE III. Regression analyses to assess the association between change in ACQ-5/ACQ-6 score and change in FEV₁%pred

Change in score	Unadjusted fixed-effects regression analysis					Adjusted random-effects regression analysis*				
	Coefficient	SE	P value	95% CI	Overall R ²	Coefficient	SE	P value	95% CI	Overall R ²
Change in ACQ-5 score	−0.73	0.57	.20	−1.86 to 0.39	0.005	−1.08	0.65	.10	−2.36 to 0.20	0.03
Change in ACQ-6 score	−0.87	0.61	.15	−2.07 to 0.33	0.006	−1.30	0.70	.06	−2.67 to 0.07	0.04

Dependent variable is change in FEV₁%pred.

*Adjusted for covariates: survey wave and month, age, sex, family income level, race, educational attainment, ethnicity, and smoking status.

Figure 2 highlights the findings of the multiple regression analyses that there is a high degree of variability in FEV₁%pred that does not appear to be well correlated with ACQ-5 scores (results were similar for ACQ-6 scores; data not shown).

DISCUSSION

This study demonstrates a weak and statistically insignificant correlation between FEV₁%pred and ACQ-5/ACQ-6 scores when covariates are not included in the model. This indicates that there is a substantial amount of unexplained variation in the direct relationship between pulmonary function and ACQ scores. However, when important covariates were added to the model, the coefficients for ACQ-5/ACQ-6 scores became statistically significant and the combination of covariates and ACQ-5/ACQ-6 scores explained a much greater amount of the variance in FEV₁%pred (as evidenced by a higher R² value). Thus, the combination of covariates and ACQ-5/ACQ-6 scores resulted in a greater degree of association (equivalent to a moderate correlation coefficient of ~0.33), compared with the weak and statistically insignificant association between ACQ-5/ACQ-6 scores and FEV₁%pred alone (correlation coefficient, 0.17). The addition of covariates such as age, sex, income, race, educational attainment, ethnicity, and smoking status appears to be more strongly correlated with FEV₁%pred than with ACQ-5/ACQ-6 scores alone. The comparison of the 2 models (ACQ-5/ACQ-6 without covariates and ACQ-5/ACQ-6 with covariates) highlighted the explanatory power of the covariates and, conversely, the lack of explanatory power of the ACQ-5/ACQ-6 alone. This suggests that the included covariates explain a substantially greater proportion of the variation in FEV₁%pred than in ACQ-5/ACQ-6 scores. However, the change in FEV₁%pred was not statistically significantly associated with the change in ACQ-5/ACQ-6 scores over time with or without covariates, suggesting a very weak association between the responsiveness of each measure over time in this sample.

Our surveys assessed both ACQ-5 and ACQ-6 scores; it has been suggested previously that both versions of the ACQ produce clinically equivalent data,¹⁹ and in the current analyses no notable differences between the 2 measures were identified. Controlling for covariates, including sociodemographic characteristics, led to a more robust statistical association with FEV₁%pred than with ACQ-5/ACQ-6 score alone. These findings

provide relevant data on the nature of this association, taken across 4 study waves, in a managed-care population. It is known that an individual's asthma symptoms can fluctuate over time and season. The longitudinal nature of the 4 waves allowed for data capture across different seasons and incorporated the variability in symptoms and pulmonary function within an individual over time.

Published evidence to date on the association between asthma control measures and pulmonary function in cross-sectional analyses is inconclusive. Although some studies have reported a lack of a significant correlation between the validated Asthma Control Test (ACT) scores and FEV₁,^{6,11} others report weak to moderate correlations between ACT scores and either FEV₁ or FEV₁%pred.^{7,8,12,15,16} Significantly moderate-to-strong negative correlations have been reported between ACQ-7 scores (item 7 relates to spirometry testing) and FEV₁ in adults with a range of asthma severity ($r = -0.59$; $P < .001$),¹⁷ and between ACQ-7 scores (including spirometry) and FEV₁% in a cross-sectional study of nonsmoking adults with asthma (Pearson correlation coefficient = -0.586 ; $P < .001$).¹⁰ Because FEV₁%pred is one of the components of the ACQ-7 score, it is unsurprising to find a significant correlation between them.

Previous longitudinal studies also reported weak to moderate correlation between changes in ACT or ACQ scores and changes in pulmonary function.¹²⁻¹⁴ In a longitudinal validation study of the ACT in patients with asthma new to the care of an asthma specialist (N = 313), changes in ACT scores from baseline to the follow-up visit (4-12 weeks apart) were correlated with changes in FEV₁%pred values ($r = 0.29$; $P < .001$).¹⁴ The authors concluded that the ACT was suitable for periodic monitoring of patients with asthma, as demonstrated by the responsiveness of ACT scores to changes in asthma control over time (specifically specialist control ratings, FEV₁%pred, and ACQ).¹⁴ Picado et al¹³ also evaluated the longitudinal validity of the ACQ (Spanish version) in consecutive adult patients with persistent asthma (N = 607) at 3 study visits over 6 weeks.¹³ The authors reported that changes in ACQ scores were significantly associated with changes in FEV₁ ($P < .001$; small-to-moderate global effect size [0.46]).¹³ In a third longitudinal study to evaluate the relationship of asthma control with pulmonary function in newly diagnosed patients with asthma before and after initiation of treatment (N = 160), change in ACT scores between baseline

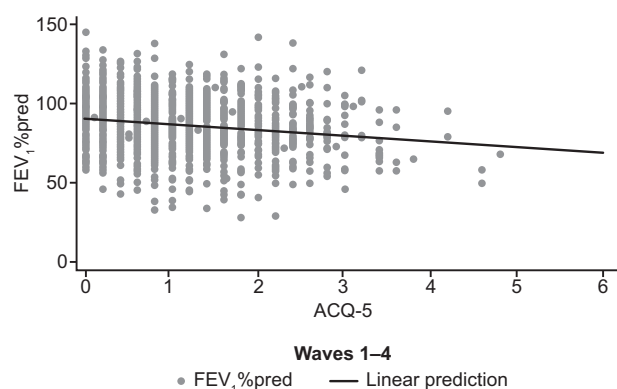


FIGURE 2. Scatter plot and linear prediction showing the relationship between FEV₁%pred values and ACQ-5 scores in waves 1 to 4.

and follow-up (4-12 weeks later) was significantly associated with change in FEV₁ ($r = 0.538$; $P < .001$).¹² In this study, although the ACT score was statistically significantly and weakly positively correlated with %FEV₁ at baseline ($r = 0.177$; $P = .03$), at follow-up, no correlation was observed ($P = .09$), leading the authors to conclude that asthma follow-up evaluation cannot be inferred from single measures of ACT score.¹² In the current study, we found no statistically significant association between change in FEV₁%pred and change in ACQ-5/ACQ-6 score in models unadjusted or adjusted for covariates. It is unclear why our results are different from those of previous studies comparing the change in ACQ or ACT score to the change in FEV₁%pred; however, there are some potential explanations. Our study design was different in many respects. The aforementioned studies typically compared patients before and after an intervention or treatment where change or improvement was expected (thus leading to an a priori expectation of positive change, and thus correlation, for both measures). Ours was a noninterventive study of up to 4 different time points without any clear expectation of change. The study duration was up to 15 months, whereas other clinical studies were of much shorter duration. Finally, as discussed below, our study was conducted in a general persistent asthma population rather than specialty care or clinical trial populations typical of the previous studies. Measuring the responsiveness (change over time) in pulmonary function and asthma control offers a unique insight into longitudinal disease processes that is not afforded by one-off measurements.

Studies investigating associations between pulmonary function and other less frequently used measures such as visual analog scales and symptom-based measures have also reported weak to moderate correlations.²⁰⁻²⁴ It should be noted that the studies discussed have frequently differed with respect to design, measurement tool used, sample size, and statistical methodology; thus, any direct comparisons may not be valid. Of note, the baseline level of control experienced by participants in these studies may be an important component that influences the correlation between the 2 measures. Many previous studies on this issue have been conducted in short-term controlled clinical studies. The population studied in this research was considerably different and included a longitudinal general asthma population. Consequently, the results of this study may not be comparable to the results in clinical trials or in other dissimilar populations.

Asthma control, as measured by ACQ score, is a composite measure of asthma health status and includes assessment of symptoms (ACQ-5), rescue β -agonist use (ACQ-6), and lung function (ACQ-7).²⁵ The shortened versions (ACQ-5/ACQ-6) are validated, and commonly used in clinical practice and research, yet the ACQ (ACQ-7) was originally designed to include both subjective and objective measures. Although there is some correlation between each of the components, factor analysis performed by Juniper et al¹⁹ and others^{14,26,27} has demonstrated the independent information that symptoms, rescue β -agonist use, and lung function contribute to the assessment of asthma health status. The importance of composite measures is increasingly recognized in the literature.^{28,29} The principal advantage of composite measures is that they capture multiple aspects of asthma disease severity, control, or both, thereby collectively strengthening the content validity of the outcome measure. Our results, which demonstrate weak correlation between these 2 separate constructs of symptoms/rescue β -agonist use (ACQ-5/ACQ-6 score) and lung function (FEV₁%pred) after adjusting for covariates, support the importance of assessing composite measures to accurately assess asthma health status, independently in clinical practice.^{28,29} The Expert Panel Report-3 Guidelines for the Diagnosis and Management of Asthma endorse the separate elements of impairment and risk in the assessment of asthma control,³ and state that assessment of both symptoms and lung function (via spirometry) is required.³

A strength of the current study is its generalizability to a population of patients with persistent asthma. As expected for a general sample, very few subjects had an ACQ-5/ACQ-6 score of greater than 4.0; thus, conclusions regarding these very poorly controlled patients must be made with caution. Potential limitations of the study include selection bias (subjects who were willing to participate in this study, and those willing to participate in spirometry, might differ from other subjects with asthma); geographic location of the survey (the study population in Colorado may not be generalizable to other regions); an assumed linear relationship between measures (FEV₁%pred values and ACQ-5/ACQ-6 scores) in the multiple regression analyses (although the scatter plot of the results suggested a linear relationship, this may be a limitation of our approach). In addition, wave 4 of the survey was only sent to patients with poorly controlled asthma (ACQ score ≥ 1.5). Because the first 3 survey waves included all individuals with persistent asthma, this poorly controlled subset was selected to ensure adequate representation of individuals with poor control. This may have resulted in a higher representation of poorly controlled patients in the final sample. It should be noted, however, that the survey wave was included as a control variable in all analyses. Another potential limitation is missing data; it is possible that the individuals with missing data are different compared with those who completed the survey questions. Results should be interpreted with caution within this context.

This study adds relevant, longitudinal data collected over 15 months to the evidence published to date, which often comprises cross-sectional or short-term longitudinal analyses in clinical trial or specialty clinic populations. Our results may provide insight for the development of future studies to determine the psychometric properties of asthma symptoms captured by instruments such as the ACQ-5/ACQ-6, and how they are influenced by pulmonary function measures such as FEV₁%pred. In addition,

our results may help inform studies that differentially assess the predictive ability of FEV₁%pred with and without asthma symptoms (such as those measured by the ACQ-5/ACQ-6) on asthma-related clinical outcomes. Another area of consideration for future research is the examination of the correlation between specific sociodemographic variables and pulmonary function or asthma symptoms, to determine how much of the variation in these measures may be explained by age, sex, ethnicity, smoking status, or education level, for instance.

Data from our study, together with other published work, indicate the importance of not relying on a single measure such as FEV₁%pred or symptoms to assess asthma control in clinical care and outcomes studies. Despite evidence of some correlation between asthma control, measured by shortened versions of the ACQ or ACT, and pulmonary function, in routine clinical practice, assessments of asthma control should include both evaluation of symptoms/rescue β -agonist use and spirometry.

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