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Validity of the Asthma Control Test Questionnaire among Smoking Asthmatics

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Abstract

Background—Smoking asthmatics respond worse to existing asthma therapies and have more asthma symptoms and exacerbations.

Objective—We evaluated the Asthma Control Test (ACT) for assessing asthma control among smokers.

Methods—Adults with asthma who smoked were enrolled and followed for 6 weeks. The statistical properties, validity and responsiveness of ACT were evaluated. Physician global assessment (GS) of asthma was the “gold standard”.

Results—151 participants were enrolled; female/male: 52/48%. The median [interquartile ranges (IQR)] for age was 35 (27, 43) years, 11 (7, 18) for pack-years and 16 (13, 20) for ACT score. Participants self-identified as African-American: 49%; Non-Hispanic Whites: 38%; and Hispanic Whites 11%. Participants were classified as well controlled (24%), not well-controlled (42%), or very poorly controlled (34%) at enrollment. Cronbach's alpha [95% Confidence Interval

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(CI)] for ACT at enrollment was 0.81 (0.76, 0.85). The intra-class correlation coefficients (95% CI) for agreement of scores at enrollment and 6 weeks was 0.68 (0.57, 0.78) in participant with stable asthma (n=93). ACT scores were associated with GS ($P<0.001$). Area under the receiver operator curve [95% (CI) for an ACT cut-off score of 19 (not well-controlled) was 0.76 (0.67, 0.84). The ACT score with the maximum area under the ROC curve was 18.6.

Conclusion—The ACT questionnaire was reliable and discriminated between levels of asthma control in smoking asthmatics with similar sensitivity and specificity as non-smoking asthmatics, which confirms its' value as a tool for the management of asthma in this prevalent but understudied subgroup of subjects.

Keywords

Asthma; smoking; Asthma Control Test; ACT

Introduction

Current knowledge indicates that smoking asthmatics respond worse to existing asthma therapies and may be more resistant to inhaled corticosteroids.^{1,2} In addition, smoking asthmatics have increased healthcare utilization, lung function decline, and more asthma symptoms and exacerbations.³⁻⁶ Smoking asthmatics may represent a unique asthma endotype that is distinctly different from that of the non-smoking asthmatics as a result of specific biological mechanisms arising from an interaction between smoking, genetics and environmental factors.^{7,8} Furthermore, it is unknown if those who smoke would benefit from asthma therapy that is different from non-smokers.

In fact, smoking asthmatics have consistently been excluded from asthma clinical trials. Asthma guidelines have therefore been developed almost exclusively from studies that exclude smokers and thus, these guidelines can only be extrapolated to smoking asthmatics. If new, more pragmatic, trials are to include this population, then the effect of smoking on patient reported outcomes and other outcomes recommended by expert panels⁹ and GINA clinical guidelines must be understood.^{10,11}

The Asthma Control Test (ACT) has been identified as a core asthma outcome for clinical trials.^{9,12} In this study, we evaluated whether ACT can distinguish clinically significant differences in asthma control among smokers and if ACT is sensitive to changes over time. We evaluated ACT using physician global asthma assessments (GS) as the gold standard in active smokers. We performed additional analyses to refine our understanding of the performance characteristics of the ACT in smokers.¹³

Methods

Study design

The Smoking Cohort Study was a multicenter prospective observational study conducted from April 2013 to May 2015 at 17 clinical centers participating in the American Lung Association Airways Clinical Research Centers (ALA-ACRC). The study was approved and monitored by the institutional review boards (IRB) at all centers. All participants provided

written informed consent. Demographic data, spirometry, ACT and physician assessment scores (GS) were obtained at enrollment and those assessments were repeated after 6 weeks. Participants were instructed to record morning peak flow, symptoms, sleep disturbance, medication and healthcare utilization, and number of cigarettes smoked per day daily on a diary card for the 6 weeks between visits.

Participant selection

Males and females between the ages of 18 and 50 years old who smoked 5 or more cigarettes per day and had a positive urinary cotinine level [value ≥ 3 , equivalent to 100 ng/mL , (NicAlert, Nymox Pharmaceutical Corporation, Bahamas)] were eligible. Asthma was determined by a prior diagnosis of asthma by a physician and either bronchodilator responsiveness ($\geq 12\%$ increase in FEV_1 after inhaling 2-4 puffs of albuterol) or a positive methacholine challenge ($\geq 20\%$ fall in FEV_1 at less than 16 mg/mL) in the past 2 years. Participants were required to have a pre-bronchodilator $\text{FEV}_1 \geq 40\%$ predicted and agree to be in the study as indicated by a signed consent statement. Individuals with a prior physician diagnosis of Chronic Obstructive Pulmonary Disease (COPD) or emphysema, pregnancy, or other major chronic illnesses that in the opinion of the investigator might interfere with the study (e.g. including but not limited to hyperthyroidism, seizure disorders, unstable psychiatric illness), lung disease other than asthma (e.g. bronchiectasis, sarcoidosis), near fatal asthma (intubation or Intensive Care Unit admission for asthma) within 2 years of enrollment, unstable cardiac disease, or substance abuse in the prior 6 months were not eligible. Individuals older than 50 years were not enrolled to exclude patients with concurrent COPD. All participants enrolled in this study continued their routine asthma care with their asthma care provider including pharmacotherapy and environmental interventions. Furthermore, all participants received smoking cessation materials and a personalized Asthma Action Plan.¹⁴

Measures

Asthma Control Test (ACT)—The ACT is a tool developed by Nathan and collaborators a decade ago for evaluating asthma control.¹⁵ It consists of five questions with five possible answers each. A maximum score of 25 points indicates complete asthma control. A score between 20 and 25 represents well controlled asthma, while a score of 19 or below represents not well controlled asthma, and a score less than 16 indicates very poorly controlled asthma. The minimally important clinical difference has been determined to be 3 points.¹⁶

Physician Global Assessment Score (GS)—Physicians assessed asthma control at enrollment and 6 weeks in one of five categories: 1- not controlled; 2- poorly controlled; 3- somewhat controlled; 4- well controlled; and, 5- completely controlled. For diagnostic analyses, those 5 categories were collapsed into 3: “poorly controlled” for scores of 1 to 2, “somewhat controlled” for a score of 3, and “good control” for scores of 4 or 5. The GS assessment score was based on a physical exam, patient history and lung function tests without knowledge of the participant's responses on the ACT questionnaire. The assessment was performed by physicians skilled in assessing asthma severity and familiar with National Asthma Education and Prevention (NAEPP) Expert Panel Report-3 (EPR-3) guidelines.¹⁴

The assessments included a participant interview by the individual determining the GS classification and a review of lung function tests from the clinic visit.¹⁴ Questions about frequency daytime or night time symptoms, frequency of rescue therapy (short-acting bronchodilator, β_2 or anticholinergic) use, interference with daily activities, spirometry results, and exacerbation history were included in the evaluation. The same physician was to do the assessment at both visits.

Spirometry—A baseline spirometry was obtained according to American Thoracic Society and European Respiratory Society (ATS/ERS task force)¹⁷ standards using the Koko portable spirometer (Nspire Health, Longmont, CO, USA) at the enrollment and follow-up visits.

Patient reported outcomes—Participants were instructed to complete diary cards daily throughout the 6-week study to record asthma symptoms, rescue and controller medication use, peak flow and daily cigarette consumption. Diary card entries were used to calculate percent of symptom-free days, which were days without rescue medication use, urgent care, night awakenings or initiation of new controller medications, and an asthma symptom score of 0 on a scale of 0-3. The daily symptom score scale was: (0) = no asthma episodes; (1) = 1 to 3 mild asthma episodes, each lasting 2 hours or less; (2) = 4 or more mild asthma episodes, or 1 or more asthma episodes that interfered with activity, play, school, or sleep for less than 2 hours; and, (3) = 1 or more asthma attack episodes which last longer than 2 hours, or result in shortening normal activity, seeing a doctor, or going to the hospital.

Statistical analysis

We performed comparisons of characteristics of participants who completed both visits to those who did not return for follow-up with Kruskal-Wallis tests for continuous variables and chi-squared statistics for categorical variables. The ACT cutoffs of primary interest were the established ones of 19 or less and less than 16.¹⁵ For analyses that included multiple categories (e.g. physician global assessment of asthma control), ANOVA was used. Odds ratios, sensitivity, specificity, and area under the receiver operating characteristic curve (ROC) were calculated using established definitions.^{18,19} Other diagnostic criteria that were calculated were those commonly used to evaluate the questionnaire properties:

Internal consistency—Cronbach's alpha based on ACT responses at the enrollment and follow-up visits, separately.²⁰

Reliability—Test-retest variability of the ACT was assessed with the intraclass correlation coefficient (ICC) with data from all participants who completed the study and from the subgroup with stable asthma control between the two visits, i.e., category of asthma control (3 groups) as assessed by the physician's GS was the same at enrollment and follow-up visits.²¹

Construct validity—The ability of the ACT to measure asthma control was assessed by comparing mean ACT scores among groups defined by the gold standard, i.e., the

physician's global assessment at enrollment and by the association of the percent of symptom-free days during follow-up with ACT score at the 6-week visit using ANOVA.

Responsiveness—Responsiveness of the ACT was assessed by comparing the mean changes in scores from the enrollment to 6-week follow-up visits by levels of asthma control based on GS scores (3 groups) using ANOVA. Participants were categorized as “worsened” if the GS category went from well controlled to somewhat controlled or poorly controlled, or from somewhat controlled to poorly controlled; as “stable” if the GS category was the same at both visits; and “improved” if category went from poorly controlled to somewhat or well controlled, or from somewhat controlled to well controlled.

Diagnostic assessment—The gold standard was the physician's GS of asthma control. The diagnostic accuracy for differentiating well controlled asthma (GS scores 4 or 5) from somewhat controlled and poorly controlled asthma (GS scores 1 to 3) was assessed. An alternative definition of asthma control was also assessed, i.e., poorly controlled vs somewhat or well controlled. Area under the curve (AUC) for receiver operator curves (ROC), sensitivity, specificity and other diagnostic measures were calculated for a range of ACT scores including the established cut-offs of <16 for very poorly controlled asthma and 19 for not well controlled asthma.

Analyses were performed using SAS (v.9.4 SAS Institute Inc. Cary, NC, USA), and R (R Core, Vienna, Austria, <https://r-project.org>).

Results

Study population

One hundred and fifty-one participants were enrolled between April 2013 and May 2015. About half were women and half were African-American. The median pack-years was 11, and 24% had well-controlled asthma as assessed by the study physician (Table 1). Of the initial sample, 124 (82%) completed the follow-up visit (Table 1). The group that completed the follow-up visit (completers) was significantly older ($p<0.01$), more likely to be female ($p=0.03$), more educated ($p=0.01$) and had more pack-years of exposure ($p<0.01$). There were no differences in median ACT scores, asthma symptoms, asthma characteristics and treatments, or co-morbidities (e.g. presence of eczema or food allergies) between completers and dropouts. The most common reasons for dropping out was because the participant could not be contacted or refused (90%).

Internal consistency

Cronbach's alpha (95% confidence intervals (CI)) for the ACT 0.81 (0.76, 0.85, $n=151$) at the baseline visit and 0.85 (0.80, 0.89, $n=124$) at the follow-up visit.

Reliability

The median (IQR) for the ACT scores at baseline and follow-up visit were 16 (12, 20) and 16 (13, 20), respectively; the mean difference in an individual's scores was 0.5 (3.6). The intra-class correlation coefficient (ICC) and 95% CIs for repeat measurements of ACT

scores were 0.66 (0.55, 0.75, n=124) in all participants and 0.68 (0.57, 0.78, n=93) for participants with the same level of asthma control as judged by the study physicians at both visits, e.g., “well controlled” at both visits.

Construct validity

Median (IQR) ACT score for participants with poorly controlled asthma as assessed by study physician was 14 (11, 17); 16 (13, 19) for somewhat controlled asthma; and 21 (18, 22) for well controlled asthma, $p<0.0001$ (Figure 1). The ACT was correlated with the physician GS at baseline (correlation coefficient =0.50, $p<0.0001$). At 6 weeks, the physician assessments (GS category) was associated with the percent of symptom-free days during the prior 6 weeks (Figure 2a, $p<0.0001$). ACT scores at 6 weeks were also associated with percent symptom-free days in the prior period (Figure 2b, $p=0.0042$). There was a modest, non-significant correlation of ACT score with percent predicted FEV₁ at baseline, the Pearson correlation coefficient (95% CI) was 0.16 (-0.005, 0.309).

Responsiveness

Change in physician assessed GS was associated with a change with ACT score (Figure 3, $p=0.022$) indicating the ACT was responsive to changes in clinical status. Mean change (standard deviation (SD)) in ACT for subjects who continued to have the same level of asthma control was 0.27 (3.47). In contrast, mean changes (SD) in scores for participants with either improved or deteriorating control during the period were +2.33 (3.84) or -1.25 (4.06), respectively.

Diagnostic assessment for detecting poorly controlled asthma among groups

The diagnostic accuracy for differentiating well controlled asthma (GS scores 4 or 5) from somewhat controlled or poorly controlled asthma (GS scores 1 to 3) for ACT ranging from 14 to 20 are provided in Table 2. The AUC (95% CI) for the established ACT cut-points of less than 16 (15) for very poorly controlled asthma and 19 for not well controlled were 0.69 (0.61, 0.76) and 0.76 (0.67, 0.84), respectively. Figure 4 depicts the sensitivity and specificity curves across a range of ACT scores. The intersection of those curves was an ACT of 18.6, which maximises AUC. If an alternative definition of asthma control was used, i.e., poorly controlled vs somewhat or well controlled, the ACT was less able to discriminate between poor and good control; the maximum AUC (95% CI) was 0.65 (0.57, 0.74) at an ACT score of 14.

Discussion

We found that the ACT questionnaire is a reliable and responsive tool to assess asthma control in adult asthmatics that smoke. This is an important finding because up to a third of subjects with asthma currently smoke.^{22,23} Hence, we have demonstrated that ACT can be used to assess asthma control in this large group of subjects who have traditionally been excluded from clinical trials. Sensitivity and specificity for the established thresholds were similar to results among non-smoking asthmatics.^{14,20} We determined that the threshold value for maximizing sensitivity and specificity was 18.6, which is consistent with the established cut-off values of 19 and <16 established in seminal studies.^{15,24}

The ACT demonstrated good internal consistency among smokers based on Cronbach's Alpha value of 0.81. A value of greater than 0.70 is considered internally consistent to compare different study groups, whereas an alpha value greater than 0.90²⁵ suggests the presence of redundant questions. Construct validity was established by the cross-sectional association of ACT scores with the physician global assessment at enrolment and the association of symptom-free days with the ACT score at the end of follow-up. Test-retest reliability measured by the intra-class correlations of the ACT scores at the two visits in participants with stable control was moderately strong, ICC=0.68.

Continuous assessment of asthma control with treatment interventions dictated by control is a cornerstone of the NAEPP guidelines.¹⁴ However, historically asthma studies excluded participants who smoke to avoid potential confusion with COPD or a potential inflammatory effect of smoking. However, most asthma drugs have not been evaluated among smokers with asthma. Treatment strategies for these patients have been adopted based on evidence from non-smokers, despite known differences between these subgroups of asthmatics.^{23,26} Disease progression, response to treatment, severity of exacerbations, emergency department visits, and prognosis have all been shown to differ between smoking asthmatics and non-smokers.⁶ As expected, smokers have more difficult-to-control disease, and are less responsive to inhaled or oral corticosteroids than non-smokers.²³

Technologies have significantly evolved over the past decade (e.g. genetic phenotyping or inflammatory cytokines assays) and new hypotheses affecting therapeutic approaches have been generated. Furthermore, a comprehensive and personalized evaluation of each patient with asthma may be necessary to accomplish true precision medicine and a patient-centred approach in asthma, as it is emerging in other respiratory conditions such COPD or lung cancer.^{27,28} Therefore, specific guidelines to treat and monitor smoking asthmatics are necessary. Hence, it is important to ensure that the instruments we would use to assess asthma control are valid for a smoking population.

This study has several strengths. First, it involved a relatively large number of subjects from multiple sites with a substantial representation of minorities. The study used validated measures of asthma control, including symptoms and objective assessment tools such spirometry to construct the Physician Global Assessment score, which were collected at both visits. The study physicians had extensive experience with asthma evaluation and management from previous asthma trials and could review all clinical data, including spirometry and personal history of the participant, to evaluate GS but were masked to ACT scores.

We also acknowledge some study limitations. First, we selected a group of relatively young participants with asthma to avoid, as much as possible, the presence incipient COPD, which sometimes presents with clinically profiles as asthma including the asthma-COPD overlap syndrome (ACOS).^{8,29,30} We recognize that ACOS is an important subset of subjects but our study was not intended to characterize or evaluate this syndrome. Furthermore, it is plausible that age influences disease progression, and therefore, we may need to validate ACT in an older cohort of smoking asthmatics. Second, follow-up was short at only six weeks. Third and finally, although we used a common tool to evaluate asthma control, there are in clinical

practice other validated questionnaires that may perform as good or better than ACT on this subgroup of subjects and our study did not include those.

Conclusion

In summary, we demonstrated that the ACT is an instrument with acceptable psychometric properties when applied to a cohort of smoking asthmatics with different levels of asthma control. We found also a positive association of ACT scores with symptom-free days, and scores were associated with the independent physician assessment of asthma control in smoking asthmatics. Moreover, differences in ACT scores between visits were associated with the stability of asthma control between visits. Therefore, ACT can be used in both clinical research and clinical practice to evaluate intervention response among this important group of patients and is a step forward for studying and promoting personalized therapeutic strategies among this understudied, but prevalent group of patients with asthma.

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Abbreviations

ACT	Asthma control test
GS	Physician global assessment score
COPD	Chronic obstructive pulmonary disease
NAEPP	National asthma education and prevention
EPR-3	Expert panel report-3 guidelines
ROC	Operating characteristic curve
ICC	Intraclass correlation coefficient

AUC	Area under the curve
IQR	Interquartile range
CI	Confident interval
SD	Standard deviation
OR	Odds ratio
PPV	Positive Predictive Value
NPV	Negative Predictive Value
ALA-ACRC	American Lung Association Airways Clinical Research Centers
IRB	Institutional Review Board
ATS	American Thoracic Society
ERS	European Respiratory Society
FEV₁	Forced Expiratory Volume in 1 second
FVC	Forced Vital Capacity
GERD	Gastroesophageal reflux disease

Highlights Box text**What is already known about this topic?**

The ACT questionnaire is a validated measure of asthma control in people with asthma who do not smoke.

What does this article add to our knowledge?

This is the first study to validate ACT as a measure of asthma control in people with asthma who are current cigarette smokers.

How does this study impact current management guidelines?

Availability of a validated questionnaire for measuring asthma control in people with asthma who smoke will provide a tool for generation of treatment guidelines in this under-studied population.

Figure 1.

ACT Score by Gold Standard Physician Global Assessment at Baseline. Footer: Symbols: diamond= mean; mid-line in box= median; height of box= interquartile range; whiskers are minimum and maximum values or $1.5 \times (IQR)$, if values are more extreme than that; open circle = outliers exceeding $1.5 \times (IQR)$.

Figure 2.

Percent of symptom-free days during follow-up by (a) Physician Global Assessment and (b) ACT at 6 weeks (Visit 2). 2a. Physician Global Assessment. 2.b ACT score at 6 weeks (Visit 2). Footer: Symbols: diamond= mean; mid-line in box= median; height of box= interquartile range; whiskers are minimum and maximum values or $1.5 \times (\text{IQR})$.

Figure 3.

Change in ACT by Change in Global Physician Assessment. Footer: Worsened=declined 1 or more categories; Stable=stayed in same category and improved=improved by 1 or more categories based on GS categories of poorly, somewhat and good control. Symbols: diamond= mean; mid-line in box= median; height of box= interquartile range; and whiskers are minimum and maximum values or 1.5*(IQR), if values are more extreme than that; open circle = outliers exceeding 1.5*(IQR).

Figure 4.
Sensitivity and Specificity performance by Asthma Control Test (ACT) score.

Table 1

Characteristics of all enrollees, completers and those lost to follow up.

Characteristic	Total (n=151)	Lost (n=27)	Completers (n=124)	P Value [*]
Individual Characteristics				
Age (years), Median (IQR)	35(27,43)	25(23,35)	38(28,44)	<.001
Male, N (%)	72(48%)	18(67%)	54(44%)	0.03
Race/Ethnicity, N (%)				
White	57(38%)	9(33%)	48(39%)	0.39
Black	74(49%)	13(48%)	61 (49%)	
Hispanic	16(11%)	3(11%)	13(10%)	
Other	4(3%)	2(7%)	2(2%)	
Education, N (%)				
Less than high school diploma	14(9%)	3(11%)	11(9%)	0.01
High school graduate/equivalent	45(30%)	15(56%)	30(24%)	
Some college	50(33%)	5(19%)	45(36%)	
2 year college degree or technical school	22(15%)	1 (4%)	21 (17%)	
>4 year college degree	18(12%)	2(7%)	16(13%)	
Refused to answer	2(1%)	1 (4%)	1(1%)	
Smoking Characteristics, Median (IQR)				
Packs per day	1 (0.5, 1)	1 (0.5, 1)	1 (0.5, 1)	0.47
Pack years	11(7,18)	8(6,12)	11(7,19)	0.02
Cotinine	6(5,6)	6(5,6)	6(4,6)	0.67
Daily asthma symptoms, N (%)				
Cough	29(19%)	6(22%)	23(19%)	0.66
Sputum	33(22%)	7(26%)	26(21%)	0.57
Chest tightness	23(15%)	4(15%)	19(15%)	0.95
Wheezing	35(23%)	9(33%)	26(21%)	0.17
Shortness of breath	34 (23%)	9 (33%)	25 (20%)	0.14
Night time symptoms	12(8%)	3(11%)	9 (7%)	0.50
Asthma Characteristics				
Age of onset, Median (IQR)	7(2, 18)	7(2, 18)	7(2, 17)	0.81
Urgent care, past year, N (%)	66 (44%)	11 (41%)	55 (44%)	0.73
Daily asthma treatments, N (%)				
Inhaled corticosteroids	17(11%)	2 (7%)	15(12%)	0.49
Inhaled corticosteroids combination ^{\$}	32(21%)	3(11%)	29 (23%)	0.16
Oral anti-leukotriene	10(7%)	0 (0%)	10(8%)	0.13
Any daily controller	54 (36%)	5(19%)	49 (40%)	0.04
Inhaled short-acting beta-agonist	52 (34%)	9 (33%)	43 (35%)	0.89
Asthma questionnaire scores, Median (IQR) [‡]				
ACT	16(13,20)	16(12,20)	16(13,20)	0.88
ACT control category, N (%)				
15 (very poorly)	66 (44%)	12 (44%)	54 (44%)	0.95

Characteristic	Total (n=151)	Lost (n=27)	Completers (n=124)	P Value *
16-19 (not controlled)	41 (28%)	8 (30%)	33 (27%)	
20 (well controlled)	42 (28%)	7 (26%)	35 (29%)	
Physician Global Assessment				
Poorly controlled	51 (34%)	10(37%)	41 (33%)	0.77
Somewhat controlled	64 (42%)	12 (44%)	52 (42%)	
Well controlled	36 (24%)	5(19%)	31 (25%)	
Pulmonary Function, %predicated, Median (IQR)				
Pre-bronchodilator FEV ₁ ‡	77 (65, 88)	83(71,91)	76 (64, 86)	0.18
Pre-bronchodilator FVC ‡	92(80, 104)	102(87, 111)	91 (78, 102)	<0.01
Peak flow (% predicted) ‡	78(61,91)	70 (60, 88)	79(61,91)	0.35
Daily asthma symptoms, N (%)				
Cough	29(19%)	6 (22%)	23(19%)	0.66
Sputum	33 (22%)	7 (26%)	26(21%)	0.57
Chest tightness	23(15%)	4(15%)	19(15%)	0.95
Wheezing	35 (23%)	9 (33%)	26(21%)	0.17
Shortness of breath	34 (23%)	9 (33%)	25 (20%)	0.14
Conditions other than asthma, N (%)				
GERD	38 (25%)	4(15%)	34 (27%)	0.17
Eczema	26(17%)	4(15%)	22(18%)	0.72
Rhinitis	72 (48%)	9 (33%)	63 (51 %)	0.10
Food Allergies	32(21%)	5(19%)	27 (22%)	0.70
Allergies worsen asthma	100(66%)	15(56%)	85 (69%)	0.20

* P-values are based upon Chi-squared and Kruskal-Wallis tests for categorical and continuous characteristics, respectively.

§ Combination of inhaled corticosteroids and long-acting beta-agonist.

‡ Missing: 2 Asthma questionnaires (ACT score), 2 FEV₁ 2 FVC, and 3 peak flow.

Table 2

Diagnostic metrics for ACT score cut-offs at baseline.

ACT Cut-point	OR (95% CI)	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%)	NPV (%)	ROC area (95% CI)
14	3.71 (1.43,9.61)	43 (34, 52)	83 (71,96)	89	31	0.63 (0.55,0.71)
15	5.85 (2.26,15.13)	54 (45, 63)	83 (71,96)	91	36	0.69 (0.61,0.76)
16	8.37 (3.22,21.74)	63 (54,71)	83 (71,96)	92	41	0.73 (0.65,0.81)
17	9.87 (3.94, 24.70)	70 (62, 79)	81 (68, 93)	92	46	0.75 (0.68, 0.83)
18	9.86 (4.18,23.22)	79 (72, 87)	72 (58, 87)	90	52	0.76 (0.67, 0.84)
19	10.78 (4.58,25.37)	84 (78,91)	67 (51,82)	89	57	0.76 (0.67, 0.84)
20	12.02 (4.92, 29.33)	90 (84, 95)	58 (42, 74)	87	64	0.74 (0.65, 0.83)

Abbreviations: OR: Odds Ratio for poor control; PPV: Positive Predictive Value; NPV: Negative Predictive Value; ROC: Receiver Operating Characteristic area; 95% CI: 95% confidence interval.