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The Cut-points for Asthma Control Tests are Higher in Mexican Children in Orange County, California

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Keywords

ACT; C-ACT; Hispanic; Spirometry

INTRODUCTION

Asthma is a complex common chronic disease and current guidelines emphasize the importance of achieving and maintaining control of symptoms.^{1, 2} The decision to initiate or step-up therapy to achieve control in children is particularly difficult because it is generally based on a subjective clinical history, which can differ markedly between child and parent,^{3, 4} and can also depend on income, education, ethnic/cultural background and asthma severity.⁵ In addition, standard spirometry, although objective, is usually within the normal range even in children with poorly controlled symptoms.⁶ Consequently, many asthmatic children are undertreated and are at risk for exacerbations.

The Childhood Asthma Control Test (C-ACT) and Asthma Control Test (ACT) are two validated tools developed to assess asthma control and thus assist effective treatment especially for primary care physicians.^{7, 8} The C-ACT is a 7-question survey (score range 0 to 27) for children ages 4–11, in which the questions are completed by both the patient and the parent. The ACT is a patient-completed 5-question survey (score range 5 to 25) designed for adults and adolescents 12 years of age or older. According to published reports, a C-ACT or ACT score of ≤ 19 is defined as having uncontrolled asthma over the previous four weeks.^{7–10} However, these studies did not include an ethnically diverse population,

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particularly inner city children with a higher burden of asthma where there might be the greatest need. Although some studies have shown that this cut-point is accurate and reliable for Caucasian children in France, Germany, UK and Italy, higher optimal cut-points were found in other ethnic populations.^{11–14} However, the C-ACT/ACT cut-points for uncontrolled asthma in Mexican descent children have never been validated before. The purpose of this cross ethnic study was to determine the cut-point for uncontrolled asthma in a Mexican descent population from OC compared to an age and asthma severity matched non-Hispanic cohort.

METHODS

Study participants

Children aged 6 to 17 years who were being actively treated for asthma on a mobile asthma clinic called the Children's Hospital of Orange County (CHOC) Breathmobile™¹⁵ were enrolled in the study. The Breathmobile™ provides comprehensive asthma care to children who have asthma, or are at risk for asthma primarily in low socio-economic status populations as defined by reduced cost or free lunch at school. The majority of the patients (90%) treated on the vans identify themselves as Mexican descent. Children were included in the study if they had a clinical diagnosis of asthma by a physician. Patients were excluded from the study if they were diagnosed with other pulmonary or cardiac disease, had a history of smoking within 12 months of their enrollment, or if they were not able to perform a standard spirometry maneuver. Institutional Review Boards of the University of California, Irvine and the Children's Hospital of Orange County approved the study. Written informed consent and assent were obtained from all participants and their parents or guardians.

Study protocol

All study procedures were performed on the CHOC Breathmobile™. Participants received a nursing assessment to identify their health status, and skin prick testing of 12 common allergens to assess atopic status. Categorization of atopic was based on a single positive wheal (3 millimeters greater than negative control). For children 6–11 years old, the C-ACT was completed by the children (4 questions) and their parents (3 questions). For children 12 years and older, all five questions were completed by the patients. The patients and their family had the choice of using English or Spanish version of C-ACT/ACT. Caregivers were to help the child to read the questionnaire if needed but to allow the child to give the responses themselves. The answers to each question were summed to obtain the total C-ACT or ACT score. In addition, all subjects and families were required to report a complete symptom history during the past 6–8 weeks, including daytime symptoms, nighttime symptoms, exercise symptoms and exacerbations to a pediatrician specialized in BA on the van. It is important to note that although the families gave a complete symptom history of the previous 6–8 weeks to the physician, the C-ACT/ACT questionnaire instructed subjects to only answer questions based on symptoms from the previous 4 weeks. Spirometry maneuvers were performed in accordance with ATS/ERS standards.¹⁶ Albuterol (2 puffs; 180 mcg) was then administered from a metered dose inhaler with a spacer to assess bronchodilator responsiveness. Ten minutes after bronchodilator administration, spirometry measurements were repeated. Asthma severity and control were assessed and a treatment plan developed by the physician using criteria defined in the National Asthma Education and Prevention Program/National Heart, Lung, and Blood Institute guidelines¹. The physician was blinded to the C-ACT/ACT results. For children aged 6–11, controlled asthma was defined as 1/month nighttime symptoms, 2 days/wk daytime symptoms or SABA use, no interference with normal activities and normal spirometry consisting of 80% FEV₁ and FEV₁/FVC 17. For children aged 12 and older, criteria for control are similar except 2/month nighttime symptoms.¹

Statistical analysis

The Mann-Whitney U test was used to compare baseline characteristics, spirometry and C-ACT/ACT scores between different ethnic groups. Internal consistency reliabilities were evaluated for both the C-ACT and ACT using the Cronbach α coefficient and a α value of 0.7 or greater was considered to be an indicator of acceptable internal reliability.¹⁸ Clinical validity of the C-ACT/ACT was evaluated by physicians' assessment of control, change in patient therapy (step up, no change, and step down), and spirometry (FEV₁, FEF₂₅₋₇₅ and FEV₁/FVC ratio). A general linear model was applied to test the correlation between standard spirometry and C-ACT/ACT.

Receiver operating characteristic (ROC) curve was used to assess the performances of C-ACT and ACT scores in screening for physician-assessed uncontrolled asthma. Sensitivity, specificity, positive predictive value, negative predictive value, correctly classified ratio and area under the curve were calculated for various cut-points of C-ACT and ACT. The optimal cut-points were selected by maximizing the total of the sensitivity and specificity.⁸ A *P*-value of less than 0.05 was considered statistically significant.

RESULTS

Study sample and spirometry

One hundred and fifty-one Mexican descent and 48 non-Hispanic children with mild-to-moderate asthma were consented for the study. The non-Hispanic children were comprised of a mixed ethnic population of 38 (80%) Caucasian, 9 (19%) Asian and 1 (1%) Black. Seventy-seven percent of the Mexican descent and 62 percent of the non-Hispanics were treated with inhaled corticosteroids (Step II to IV). About half of the subjects had controlled asthma based on physician's assessment (50% Mexican descent and 54% non-Hispanics). No statistical difference was detected in baseline characteristics, asthma severity, medication step, or spirometry between the two ethnic groups (Table I). Seventy-eight subjects (52%) in the Mexican descent cohort and 25 (48%) in the non-Hispanic cohort have completed ACT/C-ACT questionnaire before, and there was no difference between groups.

Sixty-seven of the Mexican descent population (Group 1) and 21 of the non-Hispanics (Group 2) were younger than 12 years old and completed the C-ACT, while 84 Mexican descent (Group 3) and 27 Non-Hispanics (Group 4) were 12 years and older and completed the ACT. Spirometry results were compared between physician-assessed controlled and uncontrolled asthma in each of the four groups (Table II). The FEV₁/FVC ratio was significantly higher for patients with controlled asthma than uncontrolled asthma in Group 1, 3 and 4. The FEF₂₅₋₇₅ percent predicted was significantly higher in controlled asthma in Group 1 and 3. FEV₁ percent predicted showed no difference between different control statuses. However, there was a larger bronchodilator response of FEV₁ from baseline (BDR) for uncontrolled asthma patients in Group 2 and 3.

C-ACT and ACT

Cronbach α values for the C-ACT and the ACT were 0.76 and 0.80, respectively, indicating that the two tests are reliable in our study population. C-ACT/ACT scores were statistically higher for patients with physician assessed controlled asthma than uncontrolled asthma in all four age and ethnic groups (Table II). In addition, the mean C-ACT/ACT scores were significantly different between subjects who received step up in medication than subjects who had step down or no change in medication (20 and 23, respectively, *P*-value < 0.01).

The overall average C-ACT/ACT scores were higher for the Mexican descent children compared to the non-Hispanic children (22 verses 20, *P*-value < 0.01, Table I). The mean C-

ACT/ACT scores for uncontrolled asthma in Mexican descent were above the standard cut-point of 19 and were significantly higher than the mean scores in the non-Hispanic children (C-ACT: 21 vs. 19, P -value = 0.04 and ACT: 20 vs. 17 P -value < 0.01 respectively). Similarly, for controlled asthma, Mexican descent children also had higher C-ACT/ACT scores than the Non-Hispanic controls (C-ACT: 24 vs. 23, P -value = 0.03 and ACT: 23 vs. 22, P -value = 0.04 respectively). Additionally, the choice of language and its effect in patient and parent responses were also considered during the analysis. A majority of the C-ACT tests were answered in English (90%), and tests showed no significant difference in average C-ACT scores between Spanish and English versions of the questionnaire. Only one patient answered the ACT in Spanish, and so we were unable to perform a similar analysis for ACT questionnaire.

Screening Accuracy

In the younger age groups, the optimal C-ACT cut-point for uncontrolled asthma was 22 (sensitivity = 74%, specificity = 86%) for Mexican descent children (Group 1). This cut-point was able to correctly classify 79% of the subjects with an estimated area under the curve (AUC) of 0.83. For the Non-Hispanic group (Group 2), 20 was the best cut-point for uncontrolled asthma (sensitivity = 70%, specificity = 91%), and it correctly classified 90% of the population with an AUC of 0.86. (Table III and FIG. 1A)

In the adolescent groups, an optimal ACT cut-point of 22 for the Mexican descent (Group 3) correctly classified 71% of the patients (sensitivity = 78%, specificity = 68%) with an AUC of 0.79. The Non-Hispanics (Group 4) had a cut-point of 20 which correctly classified 79% of the subjects (sensitivity = 83%, specificity = 87%) with an AUC of 0.91 (Table III and FIG. 1B)

Spirometry and C-ACT/ACT

General linear regression indicated that C-ACT/ACT did not correlate with FEV₁, FEF₂₅₋₇₅ (in percent predicted), FEV₁/FVC ratio or the bronchodilator response of FEV₁. Spirometry measurements and C-ACT/ACT scores were not always consistent in assessing asthma control status. For example, among the patients with uncontrolled asthma detected by the C-ACT/ACT cut-points (22 in Mexican descent and 20 in non-Hispanics), 61% and 60% of them had a FEV₁/FVC ratio of 80% or higher (FIG 2A). In contrast, in subjects with C-ACT/ACT defined controlled asthma (> 22 in Mexican descent and > 20 in non-Hispanics), there was still a small proportion of them who had a FEV₁/FVC ratio less than 80% (14% and 18% respectively, FIG 2B). However, there were more subjects with abnormal FEV₁/FVC ratio (< 80%) in patients with uncontrolled asthma (FIG 2A) compared to controlled asthma (FIG 2B) defined by C-ACT/ACT cut-points (P -value < 0.01).

DISCUSSION

Our cross ethnic study demonstrated that the C-ACT and ACT are reliable in a medically underserved Mexican descent population evaluated by pediatricians specializing in asthma and allergy care. The results showed that the overall C-ACT/ACT scores were significantly higher in Mexican descent children compared to non-Hispanics. In addition, the optimal C-ACT/ACT cut-point to detect uncontrolled asthma was 22 in the Mexican descent population, which was 3 points higher compared to published reports, and also 2 points higher than the non-Hispanic cohort in our population. It is important to consider that these results are specific to mild to moderate asthmatics in Mexican descent children in OC, and that these same results may not apply to severe asthmatics or other geographical or socioeconomic settings. Nevertheless, these results suggest that mild to moderate asthmatic

Mexican descent children and their parents in OC seem to under report asthma symptoms, and a higher C-ACT/ACT cut-point is worth consideration for assessing asthma control.

Previous studies developed the asthma control tests in mixed ethnic, primarily Caucasian, populations, in which a cut-point of 19 was selected to identify uncontrolled asthma for both children and adults^{7, 8, 10}. Additional studies validated the cut-point in several different ethnic groups, including Spanish, Chinese and Greek.^{19–21} However, other studies carried out in Spain, Taiwan and Netherlands reported that higher C-ACT or ACT cut-points were more accurate in determining asthma control when compared to Global Initiative for Asthma (GINA) guidelines.^{13, 14, 22} These studies suggested different perceptions of asthma symptoms in different ethnic populations and social settings may give insight into why a higher C-ACT/ACT cut-point is necessary for Mexican descent children in OC. Our results showed that in the Mexican descent children, the standard cut-point of C-ACT/ACT = 19 had high specificities in predicting uncontrolled asthma, with very limited sensitivities (33% for C-ACT and 41% for ACT). By using = 19 as the cut-point in the Mexican descent population, a large proportion of uncontrolled asthmatic children would be missed, thus risking the possibility of exacerbations because of undertreated asthma. On the other hand, a score of C-ACT/ACT = 22 was found to be the optimal cut-point as it achieved the highest sum of sensitivity and specificity, and provided the best correctly classified ratio (79% and 71%, respectively).

Fritz, et al.²³ reported that Latino children with asthma were less accurate at subjectively assessing their lung function compared to non-Latino white children.. In this Latino population, which was Puerto Rican, heterogeneity was also seen and the island Puerto Ricans had less accuracy than Rhode Island Latinos thought to be due to such factors as poverty and lower intelligence.²⁴ Therefore, other factors than ethnicity may be playing a role in the perception of clinical asthma. However, asthma severity, access to care, trust in the medical system, insurance (Medicaid), and poverty level in the children of Mexican descent and the non-Hispanic comparators in OC were the same. Other factors such as level of education and stressors were not assessed and could be confounding factors. Furthermore, it is known that Puerto Ricans have much more severe asthma than those of Mexican descent.²⁴ This is consistent with our observation that the majority of the Mexican American children in our study had mild-to-moderate asthma (98%). Therefore, the overestimation of asthma control among our Mexican descent population in OC might also be explained by a lower sensitivity towards asthma symptoms..

Numerous studies have previously shown poor correlations between asthma control tests and lung function measured by traditional spirometry^{13, 20, 22, 25}. In the present study, spirometry measurements did not correlate well with C-ACT/ACT scores. Previous reports have shown that although standard spirometry can provide objective information, it is not extremely useful in detecting uncontrolled asthma in children because the values are usually normal in children with mild to moderate asthma.^{6, 26} In our study, a large proportion of the subjects, including the Mexican Americans as well as the non-Hispanics, who by the C-ACT/ACT were determined to have uncontrolled asthma showed normal spirometry results. On the other hand, several subjects who had controlled asthma based on their C-ACT/ACT had abnormal spirometry. These results suggest that the two measurements do not reflect the same aspect of asthma. For example, spirometry captures the pulmonary function status at a single time point, and thus may not adequately reflect symptoms occurring over several weeks as determined by the C-ACT/ACT. Thus, C-ACT and ACT cannot simply replace traditional spirometry, but provide additional information to spirometry, which is necessary to improve the assessment of asthma control in children.

In our study, the C-ACT/ACT scores were compared to the “gold standard” of asthma control, which was the assessment made by four physicians who were a mixture of asthma specialists and pediatricians trained in allergy and asthma. The elevated C-ACT/ACT cut-point in Mexican descent could be caused by the underestimation of those patients who were controlled by the small number of physicians. However, our age matched non-Hispanic control groups argue against this possibility. The mean C-ACT/ACT scores were consistently lower in the non-Hispanics than those of Mexican descent. In addition, the optimal C-ACT/ACT cut-point for uncontrolled asthma in the non-Hispanic groups was 20 and was very close to 19 as suggested by published reports. Our non-Hispanic control groups had a majority of children who were Caucasian, which was very similar to the ethnicities of the early C-ACT/ACT validation studies^{7, 8}. These results validated our physician-assessed asthma control and suggested that the Mexican descent children from OC were under reporting their symptoms in the surveys.

Another potential limitation of the study was the small sample size, especially for the non-Hispanic controls. We recognized that the sample size in this pilot study was small compared to previous works,^{7, 8} and the accuracy of C-ACT/ACT cut-points could be improved by increasing the sample size. However our study population number was adequate to show statistical differences in C-ACT/ACT between Mexican descent and other ethnicities. Finally, our study investigated the cut-point of C-ACT/ACT in the Mexican descent children cross-sectionally, and there was no longitudinal data to repeatedly validate the reliability of this cut-point in discriminating controlled and uncontrolled asthma.

In conclusion, our preliminary study, which evaluated ACT/C-ACT across different ethnic and cultural populations, demonstrated that the underserved inner city asthmatic children and family generally underestimate poor control. However, children of Mexican descent living in OC were less sensitive in perceiving their asthma symptoms compared to non-Hispanic children and thus have an even greater underestimation of the true level of uncontrolled asthma. Providers, particularly primary care physicians, need to recognize that the C-ACT/ACT cut-points for uncontrolled asthma may vary in different populations. Our study shows that in Mexican descent children a cut-point of 22 should be considered for uncontrolled asthma, rather than the traditional cut-point of 19. Finally, these data suggest the need for a better controlled, more comprehensive perspective study in a variety of geographical and socioeconomic settings.

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ABBREVIATIONS

ACT	Asthma Control Test
C-ACT	Childhood Asthma Control Test
BDR	Bronchodilator response of FEV ₁
ROC	Receiver operating characteristic
PPV	Positive predictive value
NPV	Negative predictive value

AUC Area under the curve

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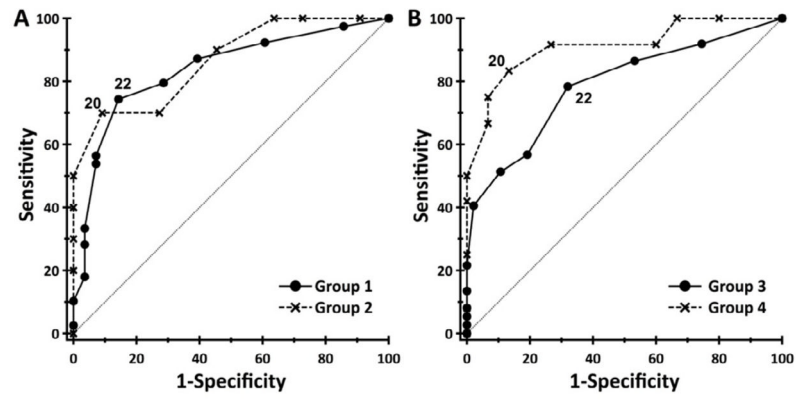


Figure 1.

ROC curves of C-ACT/ACT in predicting physicians' assessed uncontrolled asthma. Optimal C-ACT cut-points (A) for Mexican descent and non-Hispanic children were 22 (Group 1, AUC (Area under the curve) = 0.83) and 20 (Group 2, AUC = 0.86) respectively. Optimal ACT cut-points (B) for Mexican descent and non-Hispanic children were 22 (Group 3, AUC = 0.79) and 20 (Group 4, AUC = 0.91) respectively.

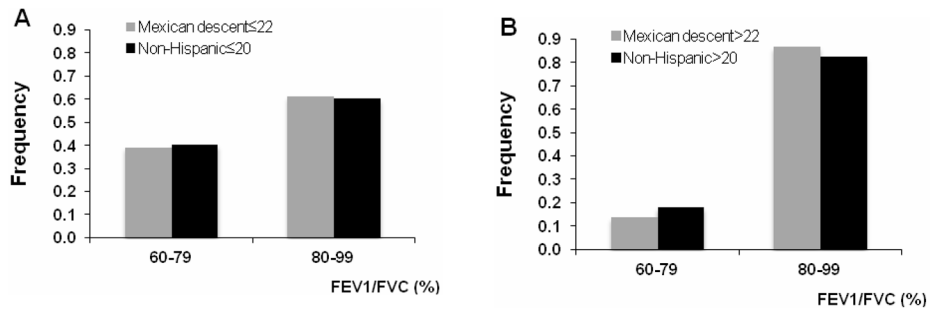


Figure 2.

A) Percentage of patients (frequency) with uncontrolled asthma (C-ACT/ACT ≤ 22 for Mexican descent and C-ACT/ACT ≤ 20 for non-Hispanics) stratified by FEV1/FVC ratio. B) Percentage of patients with controlled asthma (C-ACT/ACT > 22 for Mexican descent and C-ACT/ACT > 20 for non-Hispanics) stratified by FEV1/FVC ratio.

TABLE I

Summary of characteristics of Mexican descent and non-Hispanic subjects.

	Mexican <u>descent</u>	Non-Hispanic	P-value
n	151	48	
Age, yrs	12 [6–17]	12 [6–17]	.9390
Gender Male, n (%)	81(54)	25 (52)	.9583
Height, cm	150 [114–180]	150 [120–175]	.9888
BMI	23 [15–41]	16.7[14.7–28.7]	.2947
Atopic, %	74	83	.1948
Severity			
Intermittent/Mild/Moderate Persistent, %	60/38/2	65/23/12	.6421
Medication step 1/2/3/4/5, %	23/44/26/5/2	38/35/21/4/2	.1090
Spirometry			
FVC% predicted	105 [66–148]	104 [81–129]	.6400
FEV ₁ % predicted	96 [60–126]	98 [80–135]	.4666
FEF _{25–75} % predicted	81 [36–126]	87 [45–168]	.0957
FEV ₁ /FVC, %	82 [63–98]	83 [66–99]	.4590
BDR, %	6 [0–24]	6 [0–25]	.9309
Physician assessed controlled asthma, n (%)	75 (50)	26 (54)	.5892
C-ACT/ACT	22 [10–27]	20 [6–27]	.0083**

Numbers are shown as mean [range]. U-Test was used to test the difference between Mexican descent and non-Hispanics.

** Significance level of $P < 0.01$.

TABLE II

Spirometry and C-ACT/ACT comparison for each age and ethnic group.

4-11 years	Group 1: Mexican descent			Group 2: Non-Hispanic		
	Controlled	Uncontrolled	P-value	Controlled	Uncontrolled	P-value
Physician's assessment						
n	28	39		11	10	
FVC% predicted	109 [77-145]	111 [66-148]	.2549	104 [85-126]	103 [81-116]	.9438
FEV ₁ % predicted	98 [80-118]	96 [61-114]	.5267	101 [80-135]	91 [81-110]	.1205
FEF ₂₅₋₇₅ % predicted	87 [65-126]	75 [48-124]	.0020**	93 [53-154]	75 [45-106]	.1852
FEV ₁ /FVC, %	85 [80-95]	79 [63-90]	.0002**	85 [81-91]	79 [66-93]	.0699
BDR, %	4 [0-9]	7 [0-24]	.0787	4 [0-13]	14 [3-25]	.0015**
C-ACT	24 [17-27]	21 [10-27]	<.0001**	23 [20-27]	19 [15-23]	.0051**
12 years						
	Group 3: Mexican descent			Group 4: Non-Hispanic		
Physician's assessment						
n	47	37		15	12	
FVC% predicted	100 [80-126]	103 [70-128]	.2137	104 [88-129]	106 [88-118]	.4341
FEV ₁ % predicted	98 [81-126]	92 [60-114]	.0547	101 [85-126]	99 [84-114]	.6960
FEF ₂₅₋₇₅ % predicted	90 [63-124]	72 [36-101]	<.0001**	95 [68-168]	83 [54-104]	.1944
FEV ₁ /FVC (%)	86 [80-98]	79 [65-91]	<.0001**	86 [80-99]	80 [69-90]	.0135*
BDR (%)	4 [0-14]	8 [0-21]	.0025**	3 [0-9]	6 [0-18]	.1808
ACT	23 [19-25]	20 [10-25]	<.0001**	22 [18-25]	17 [6-23]	.0003**

Numbers are shown as mean [range]. U-Test was used to test the difference between physician's assessed controlled and uncontrolled asthma in each group.

* Significance level of $P < 0.05$.

** Significance level of $P < 0.01$

TABLE III
Screening accuracy of the C-ACT/ACT cut-points predicting physicians' assessed uncontrolled asthma.

Group 1: Mexican descent (n = 67)						Group 2: Non-Hispanic (n = 21)					
C-ACT	Sensitivity	Specificity	PPV	NPV	Accuracy	C-ACT	Sensitivity	Specificity	PPV	NPV	Accuracy
17	18	96	88	46	51	17	30	100	100	61	74
18	28	96	92	49	57	18	40	100	100	65	79
19	33	96	93	51	60	19	50	100	100	69	84
20	54	93	91	59	70	20	70	91	88	77	90
21	56	93	92	60	72	21	70	73	70	73	79
22	74	86	88	71	79	22	90	55	65	86	79
23	79	71	79	71	76	23	100	36	59	100	73
24	87	61	76	77	76	24	100	27	55	100	68
Group 3: Mexican descent (n = 84)						Group 4: Non-Hispanic (n = 27)					
ACT	Sensitivity	Specificity	PPV	NPV	Accuracy	ACT	Sensitivity	Specificity	PPV	NPV	Accuracy
17	14	100	100	60	61	17	50	100	100	71	72
18	22	100	100	62	64	18	67	93	88	78	76
19	41	98	94	68	71	19	75	93	90	82	79
20	51	89	78	70	71	20	83	87	84	86	79
21	57	81	70	71	69	21	92	73	73	92	76
22	78	68	66	80	71	22	92	40	55	86	59
23	86	47	56	81	63	23	100	33	54	100	58
24	91	26	49	79	53	24	100	20	50	100	52