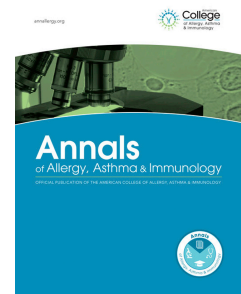


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Use of the Composite Asthma Severity Index in a Pediatric Subspecialty Clinic

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Childhood asthma; control; score; Childhood Asthma Control Test; Asthma Control Test

Abbreviations:

Asthma Control Test (ACT), Composite Asthma Severity Index (CASI), Childhood Asthma Control Test (C-ACT), Cincinnati Children's Hospital Medical Center (CCHMC), electronic health record (EHR), minimally important difference (MID)

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Figures: 1

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Background The Composite Asthma Severity Index (CASI) is a comprehensive tool to assess asthma severity that has been applied in the research setting.

Objective To evaluate, in an outpatient setting, whether a CASI score accurately predicts asthma severity/control as determined via subspecialist assessment. Asthma Control Test (ACT) and childhood ACT (C-ACT) scores were generated to provide additional context for CASI scores in relationship to assessments using another clinical tool. **Methods** Children ages 5-18 years with a physician diagnosis of persistent asthma were recruited from a tertiary care center. A pediatric pulmonologist made determinations about each participant's asthma severity and control during a clinic visit. A CASI and ACT/C-ACT score were generated for each patient. Logistic regression and Spearman correlations were used to determine how well CASI scores predicted physician assessments. Agreement between ACT/C-ACT scores and physician assessment of asthma control was determined in supplemental analyses.

Results CASI scores strongly predicted physician assessment of severity (Spearman correlation 0.61, p-value <0.0001); unadjusted OR 36.67 (95% CI, 8.83 -152.34); and adjusted OR 32.76 (95% CI, 8 5.70-188.44). In supplemental analyses, ACT/C-ACT scores strongly predicted physician assessment of control (Spearman correlation 0.72, p-value <0.0001); unadjusted OR 42.12 (95% CI, 13.34 -133.00); and adjusted OR 55.34 (95% CI, 13.62 - 224.89).

Conclusion Use of the CASI was feasible and accurately predicted physician assessments of asthma severity and control in this sample, which are not distinct entities. The CASI is a robust tool that may be used successfully in ambulatory pediatric asthma care.

INTRODUCTION

Asthma is a complex, heterogeneous and chronic condition that affects 7 million children in the United States.¹ Left unchecked, asthma may be associated with significant morbidity with symptoms that affect daily life, lead to time out of school, limit activity, and when severe exacerbations occur, children may require hospitalization.²⁻⁴ Clinicians that care for children with asthma are tasked with assessing both severity of the condition and how well disease is controlled to inform decision making about next steps in management.⁵ Obtaining information to guide clinical decision making can often be challenging. Historians may be incorrect, not fully aware of true symptom burden, and the data derived from children and from parents may be conflicting.⁶⁻⁸ Social factors at play may also compound complexity (e.g., a child that goes between homes). Assessing asthma severity and control can also be difficult for logistical reasons in the context of relatively short clinic visits and both families and clinicians pressed for time.

Tools to assess asthma severity and control in children have been developed such as the childhood Asthma Control Test (C-ACT) and the Composite Asthma Severity Index (C-ASI).^{9,10} The C-ACT was developed and validated in 2007 for children ages 4-11 years after the ACT had been created for children 12 and older in 2004.^{9,11} The C-ACT facilitates identification of children with asthma that is inadequately controlled. This tool entails a 7-question symptom survey for parents and children and is intended for use in the clinical setting. A score of ≤ 19 on the C-ACT indicates uncontrolled asthma.⁹ An additional designation was added in 2010 indicating scores ≤ 12 reflect very poor asthma control.¹² The ACT has a scoring range of 5-25 and also uses a threshold of ≤ 19 to indicate asthma that is not well controlled. Additionally, a score ≤ 15 indicates asthma is poorly controlled.¹³ The minimal important difference (MID) of the ACT is 3 and 2 for the C-ACT.^{14,15} The CASI was developed by the Inner City Asthma

Consortium and validated in 2012 for children age 6-20 years.¹⁰ Unlike the ACT and C-ACT, this tool assesses both patient reported symptoms (day symptoms and albuterol use, night symptoms and albuterol use) and objective data (current controller treatment, lung function measures, and exacerbations). Information from these areas is incorporated to generate an asthma severity score with a range of 0-20.¹⁰ The MID of the CASI is 1 and risk levels of the CASI have been defined as a score of 3 or less identifying low severity asthma.¹⁶

Within clinical practice, asthma severity and control are intertwined, and thus for consistency here, the term asthma “severity/control” will be used when referring to severity and control collectively. These asthma assessment tools highlight this issue as they do overlap to some extent in content. The C-ACT and ACT are frequently used to assess asthma control, and these tools do not account for the risk domain or other proposed facets of asthma severity as defined by asthma guidelines.^{5,17} Although the CASI is a more comprehensive tool that addresses aspects of both asthma severity and control, it has been primarily applied in research settings and has not been readily incorporated into clinical practice.^{10,16} Specifically, it is unclear if a CASI obtained during routine asthma clinic visits would demonstrate similar discriminatory ability in patients outside of a research setting. Our primary objective was to evaluate, in an outpatient setting, whether a CASI score accurately predicts asthma severity/control as determined via subspecialist assessment. We sought to evaluate CASI performance in a clinical setting where standard of care includes the integration of, but is not solely dependent upon, another scoring tool, the ACT/C-ACT.

METHODS

Study design, subjects and procedures

A cross-sectional study was performed in a pulmonary specialty clinic at a tertiary care center. This clinic is dedicated to patients requiring specialty care for asthma and patients require a referral for evaluation in this clinic. All study participants had a physician diagnosis of persistent asthma and no other active chronic disorders apart from allergic disease. The clinic is staffed with three pediatric pulmonologists with expertise in treating childhood asthma.

Patients ages 5 to 18 years old were enrolled between February 2016 and June 2017. Demographic, socioeconomic, and asthma history data were collected on each subject at enrollment via paper questionnaire forms completed by the parents. CASI assessments were also obtained for each patient and scores were calculated using the Asthma TreatSmart Program. This program is a stand-alone, web-based decision support program developed and housed internally.¹⁸ The application utilizes user-friendly interfaces, and with input from the patient or parent, collects symptom information, exacerbation history, and completes medication reconciliation.¹⁸ All patients had lung function assessments with routine spirometry in clinic per American Thoracic Society guidelines¹⁹ and this data was obtained from the electronic health record (EHR) and entered into TreatSmart by research personnel. Per clinic standard of care, parents and patients also completed C-ACT or ACT assessments together and this data was also obtained from the EHR. Each study participant was then seen by one of three pediatric pulmonology specialists (KM, CK, TG) as part of routine clinical care. Each patient's asthma severity/control were determined by the physician at the same visit, based on EPR-3 guidelines,⁵ and these values were obtained from the EHR. Each patient served as his/her own control, with

physician assessment of severity/control considered the gold standard; physician assessment has been used as the standard in previous studies.^{9,10,12} The Institutional Review Board approved the study. Parents provided signed informed consent and children ages 11 years or older were assented.

Outcomes and Measures

The primary outcome was physician assessment of asthma severity/control as determined using two separate variables. Asthma severity was categorized as either mild persistent or moderate to severe persistent based on clinical history and evaluation according to EPR-3 guidelines⁵ (mild persistent used as referent). Asthma control was dichotomized as well controlled or not well controlled based on clinical history (well controlled used as referent); clinicians also had access to the ACT/C-ACT score. We examined the consistency of CASI scores with physician assessment of severity. Since C-ACT and ACT scores are already routinely used in clinical practice, we also examined these scores in relation to physician assessment of asthma control as a supplementary indicator of asthma control, not a primary outcome. This distinction is important as physicians had access to these scores when making assessments, and thus agreement between ACT/C-ACT scores and physician assessments could be biased. Nonetheless, we elected to describe this association to provide additional context for CASI score interpretation and to evaluate for consistency in physician assessments in relation to each tool. CASI scores were categorized using previously established thresholds as CASI score ≤ 3 or > 3 ¹⁶; scores ≥ 4 indicated medium or high asthma severity. C-ACT and ACT scores were categorized as ≤ 19 or > 19 , with scores ≤ 19 indicating uncontrolled asthma.^{9,12} Additional independent variables included demographic characteristics such as age, sex, race (white, African-American, or other),

insurance type, parent education level (any years of college or higher education, yes or no) and patient/family reported history of allergic rhinitis (yes/no), other allergies (yes/no), or eczema (yes or no).

Statistical Analysis.

Descriptive statistics for continuous data were reported as mean with standard deviation or as median with inter-quartile range, and the categorical data as frequency with percentage.

Correlations between the categorical variables were assessed from Spearman correlation.

Unadjusted odds ratio (OR) estimates were calculated from the univariate logistic regression models. Adjusted OR estimates accounted for the following covariates, as each of these could potentially affect asthma phenotype or adherence to controller medications: age in years, sex, race, college or higher education, allergies, and eczema. An alpha of <0.05 was considered statistically significant. Statistical software SAS 9.4 (Cary, NC, USA) was used for all analyses.

RESULTS

Sample characteristics

The study cohort's demographic features were reflective of the typical asthma population seen in our center with a higher proportion of males in the younger age group, a sizeable African American population, >50% of the patients covered by public insurance, and an overwhelming majority of patients with reported allergic rhinitis (Table 1).

Of the 108 study participants, physician assessment of asthma severity was as follows: 14 (13%) had mild persistent asthma, 41 (38%) had moderate persistent asthma, and 53 (49%) had severe persistent disease (Fig 1). Physician assessment of asthma control included: 59 (55%) well controlled, 42 (39%) not well controlled, and 7 (6%) very poorly controlled patients.

Primary outcome

The mean CASI score and standard deviation (SD) for each severity category was 3.1 (1.6) for mild persistent, 6.2 (2.5) for moderate, and 7.7 (2.4) for severe persistent (Fig 1). The CASI score strongly predicted physician assessment of severity, in the unadjusted analysis (OR 36.67, 95% CI, 8.83 -152.34), and the adjusted analysis (OR 32.76, 95% CI, 5.70-188.44). The c-statistic for multivariable logistic model was 0.87 (Table 2). There was a statistically significant correlation between CASI scores and physician assessment of severity, with Spearman correlation of 0.61 (p-value <0.0001).

Supplementary indicator of asthma control: ACT/C-ACT

The mean ACT/C-ACT score and standard deviation (SD) for each controlled category was 22.7 (2.6) for well controlled, 17.1 (3.4) for not well controlled, and 15.1 (3.2) for very poorly controlled. ACT/C-ACT scores strongly predicted physician assessment of control with an unadjusted OR 42.12 (95% CI, 13.34 -133.00), and an adjusted OR 55.34 (95% CI, 13.62 -

224.89). The c-statistic for the multivariable logistic model was 0.91 (Table 2). ACT/C-ACT scores also strongly correlated with the physician assessment of control with Spearman Correlation of 0.72 (p-value <0.0001).

DISCUSSION

The CASI, a tool that incorporates all the domains of asthma severity/control as identified by the National Asthma Education and Prevention Program Expert Panel Report 3,⁵ generated scores that consistently reflected physician assessments of asthma severity in a clinical population. Use of the CASI was feasible and provided useful and accurate assessments in a busy, outpatient clinical setting with a study sample reflective of our typical asthma population. To our knowledge, this is the first attempt to study CASI in a clinical setting.

Limited prior work has examined thresholds at which asthma severity/control can be appropriately categorized using CASI. The value we identified with CASI scores indicating mild persistent versus moderate and severe persistent asthma was similar to that identified by Krouse et al in 2017.¹⁶ Their analysis indicated that a CASI score of 3 or less was optimal to discriminate between low asthma severity from medium or high severity,¹⁶ while the mean CASI score for children with mild persistent asthma in our sample was 3.1. Krouse et al also identified the minimally important difference (MID) for CASI was 1, indicating that incremental changes of just one point reflect meaningful clinical changes. More specifically, a 1-point change in score may reflect improving or worsening symptom control, adjustments to medication use, or even the need for oral steroids during an exacerbation.¹⁶ This is in comparison to ACT for which the MID is 3.¹⁴ CASI has also been shown to demonstrate better within-subject stability as compared to other measures such as symptom days.¹⁰ To date, CASI thresholds for discriminating between

moderate and severe persistent asthma have not been conclusively identified and will still need to be determined. The mean scores for moderate persistent and severe persistent asthma in our study (mean of 6.2 and 7.7, respectively) may inform future work in this area.

Although the CASI is intended to capture asthma severity, and C-ACT/ACT intended to reflect asthma control, it is important to highlight that asthma severity and control are not distinct entities. In fact, these tools incorporate some of the same pieces of information into the assessments. The CASI is a more robust tool in that it integrates medication regimen and lung function.¹⁰ However, both tools address patient reported symptomatology and the degree to which symptoms interfere with function. The broader scope of the CASI is likely to be beneficial in the clinical setting to physicians who need to assess both severity and control while considering current medication regimen and lung function. Guidelines suggest that asthma management should incorporate elements of impairment and risk, and the multidimensional nature of CASI is well suited to assist in this task.^{5,17}

The discriminatory ability of CASI, as documented previously¹⁶ and in this clinical study, is likely to be of benefit not only in clinical care but also in quality improvement efforts for children with asthma. Multiple phenotypes exist in childhood asthma and thus this population is quite heterogenous and ripe for a variety of potential approaches to improve care.²⁰⁻²² The variability within this population also poses challenges to improvement efforts, however, as objective changes must be detected over time to inform next steps and establish best practices. A tool such as CASI that integrates many aspects of asthma severity/control, and is able to detect relatively small changes, could therefore be useful in future asthma-related improvement work. CASI is widely available (www.asthmaseverity.org),²³ and given its strong discriminatory ability, would likely be a more sensitive outcome for quality improvement work than the ACT.

Although our study included the use of the TreatSmart Program,¹⁸ a web-based program developed internally to calculate CASI, integrating CASI into routine clinical care is possible without this tool. Through the web application, printable CASI forms are available as well as an online calculator.²³ Although the TreatSmart Program maximized efficiency in our work, linking CASI with our EHR and integrated systems is not necessary. Likewise, the ACT and C-ACT are readily available online for clinicians to use and conduct comparisons in other clinical settings.^{24,25}

Limitations of this study included the small sample size which likely contributed to the wide confidence interval estimates from our models. It is also possible that drawing information from the EHR may have led to some inaccuracies in data collection in our study. For example, it is possible that race, insurance information, or other variables may have been entered incorrectly in the EHR. Additionally, comorbidities such as allergic rhinitis or eczema may have been present but not documented by the clinician. These types of errors may have led to misclassification. However, those errors were likely minimal and other centers could use the CASI without integrating data from the EHR if so desired. This was also a single center study with a limited number of physicians who had access to the patient's C-ACT and ACT scores as part of clinical practice; knowledge of these scores could have biased their clinical evaluations and affected results in favor of the C-ACT/ACT. Thus, our results must be considered in this context and the validity of the statistical association is likely diminished. However, many factors other than the C-ACT/ACT are considered in determining a patient's asthma control including frequency of exacerbations, lung function, daily activity impairment, chronic symptoms, and other factors. Finally, while CASI has shown promise in two research studies conducted over 12 month periods,^{26,27} its longitudinal performance has yet to be examined in a clinical setting.

202 Our work demonstrates that CASI is relevant to the care of children with asthma in an
203 outpatient setting and accurately reflects physician assessments of asthma severity/control.
204 Further studies should confirm the adaptability of CASI to clinical care among larger populations
205 and in additional clinical settings.

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268 **TABLE 1. Demographic and clinical characteristics of study population**

	All n=108
Mean Age in yrs (SD)	10.6 (4.0)
Sex (%male)	64(59.3%)
Race	
Responses	106
White	50.00%
African American	31.10%
Other	18.90%
Annual Household Income ^a	
Responses	79
Below National Poverty Line	26.60%
Insurance	
%Public	58.30%
Highest Educational Household Level	
Responses	104
%HS/GED or Less	30(28.9%)
%Some College or Higher	74(71.1%)
Mean Age of Onset of Asthma Symptoms in yrs (SD) ^b	3.8(3.6)
Allergic Rhinitis (%) ^b	98(90.8%)
Eczema (%) ^b	71(65.7%)
C-ACT/ACT Score Median (Range)	21 (9-27)
Total CASI Score Median (Range)	7 (2-15)
Average FEV1 % Predicted (SD)	96.4(16.4)
Average FEV1/FVC Ratio (SD)	80.5(10.3)
Medication Step Median (Range) ^c	5(2-5)
Exacerbations in past 2 months Median (Range) ^d	0(0-4)

a. National Poverty Level Guidelines for a family of 4: 24,600 (<https://aspe.hhs.gov/poverty-guidelines>)

b. Per parental report or medical chart documentation

c. Per NAEPP guidelines

d. Defined as number of hospitalizations and steroid bursts

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Table 2: Odds ratio (OR) estimates with 95% CI, p-values and model c-statistics from each logistic regression model. Adjusted model includes the covariates: age in years, sex, race, college or higher education, allergies, and eczema.

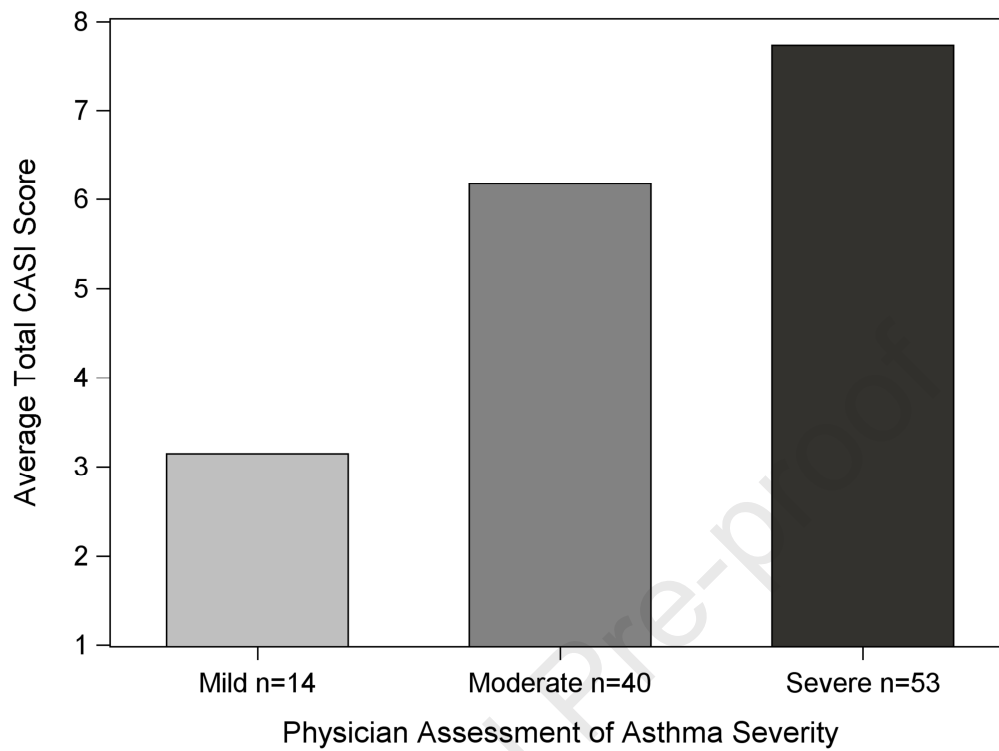
Response variable		Unadjusted estimate			Adjusted estimate		
		OR (95% CI)	p-value	Model c-statistics	OR (95% CI)	p-value	Model c-statistics
Physician severity/control (reference category: mild persistent)	CASI (reference category: ≤ 3)	36.67 (8.83, 152.34)	<.0001	0.825	32.76 (5.70, 188.44)	<.0001	0.869
Physician not-well-control/control (reference category: well controlled)	ACT/C-ACT (reference category: > 19)	42.12 (13.34, 133.00)	<.0001	0.856	55.34 (13.62, 224.89)	<.0001	0.913

280 Figure Legend:

281 Figure 1: Mean CASI score for each asthma severity category

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283 Figure 1.



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INTRODUCTION

Asthma is a complex, heterogeneous and chronic condition that affects 7 million children in the United States.¹ Left unchecked, asthma may be associated with significant morbidity with symptoms that affect daily life, lead to time out of school, limit activity, and when severe exacerbations occur, children may require hospitalization.²⁻⁴ Clinicians that care for children with asthma are tasked with assessing both severity of the condition and how well disease is controlled to inform decision making about next steps in management.⁵ Obtaining information to guide clinical decision making can often be challenging. Historians may be incorrect, not fully aware of true symptom burden, and the data derived from children and from parents may be conflicting.⁶⁻⁸ Social factors at play may also compound complexity (e.g., a child that goes between homes). Assessing asthma severity and control can also be difficult for logistical reasons in the context of relatively short clinic visits and both families and clinicians pressed for time.

Tools to assess asthma severity and control in children have been developed such as the childhood Asthma Control Test (C-ACT) and the Composite Asthma Severity Index (C-ASI).^{9,10} The C-ACT was developed and validated in 2007 for children ages 4-11 years after the ACT had been created for children 12 and older in 2004.^{9,11} The C-ACT facilitates identification of children with asthma that is inadequately controlled. This tool entails a 7-question symptom survey for parents and children and is intended for use in the clinical setting. A score of ≤ 19 on the C-ACT indicates uncontrolled asthma.⁹ An additional designation was added in 2010 indicating scores ≤ 12 reflect very poor asthma control.¹² The ACT has a scoring range of 5-25 and also uses a threshold of ≤ 19 to indicate asthma that is not well controlled. Additionally, a score ≤ 15 indicates asthma is poorly controlled.¹³ The minimal important difference (MID) of the ACT is 3 and 2 for the C-ACT.^{14,15} The CASI was developed by the Inner City Asthma

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49 **METHODS**50 *Study design, subjects and procedures*

51 A cross-sectional study was performed in a pulmonary specialty clinic at a tertiary care
52 center. This clinic is dedicated to patients requiring specialty care for asthma and patients require
53 a referral for evaluation in this clinic. All study participants had a physician diagnosis of
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59 obtained for each patient and scores were calculated using the Asthma TreatSmart Program. This
60 program is a stand-alone, web-based decision support program developed and housed
61 internally.¹⁸ The application utilizes user-friendly interfaces, and with input from the patient or
62 parent, collects symptom information, exacerbation history, and completes medication
63 reconciliation.¹⁸ All patients had lung function assessments with routine spirometry in clinic per
64 American Thoracic Society guidelines¹⁹ and this data was obtained from the electronic health
65 record (EHR) and entered into TreatSmart by research personnel. Per clinic standard of care,
66 parents and patients also completed C-ACT or ACT assessments together and this data was also
67 obtained from the EHR. Each study participant was then seen by one of three pediatric
68 pulmonology specialists (KM, CK, TG) as part of routine clinical care. Each patient's asthma
69 severity/control were determined by the physician at the same visit, based on EPR-3 guidelines,⁵
70 and these values were obtained from the EHR. Each patient served as his/her own control, with

physician assessment of severity/control considered the gold standard; physician assessment has been used as the standard in previous studies.^{9,10,12} The Institutional Review Board approved the study. Parents provided signed informed consent and children ages 11 years or older were assented.

Outcomes and Measures

The primary outcome was physician assessment of asthma severity/control as determined using two separate variables. Asthma severity was categorized as either mild persistent or moderate to severe persistent based on clinical history and evaluation according to EPR-3 guidelines⁵ (mild persistent used as referent). Asthma control was dichotomized as well controlled or not well controlled based on clinical history (well controlled used as referent); clinicians also had access to the ACT/C-ACT score. We examined the consistency of CASI scores with physician assessment of severity. Since C-ACT and ACT scores are already routinely used in clinical practice, we also examined these scores in relation to physician assessment of asthma control as a supplementary indicator of asthma control, not a primary outcome. This distinction is important as physicians had access to these scores when making assessments, and thus agreement between ACT/C-ACT scores and physician assessments could be biased. Nonetheless, we elected to describe this association to provide additional context for CASI score interpretation and to evaluate for consistency in physician assessments in relation to each tool. CASI scores were categorized using previously established thresholds as CASI score ≤ 3 or > 3 ¹⁶; scores ≥ 4 indicated medium or high asthma severity. C-ACT and ACT scores were categorized as ≤ 19 or > 19 , with scores ≤ 19 indicating uncontrolled asthma.^{9,12} Additional independent variables included demographic characteristics such as age, sex, race (white, African-American, or other),

insurance type, parent education level (any years of college or higher education, yes or no) and patient/family reported history of allergic rhinitis (yes/no), other allergies (yes/no), or eczema (yes or no).

Statistical Analysis.

Descriptive statistics for continuous data were reported as mean with standard deviation or as median with inter-quartile range, and the categorical data as frequency with percentage.

Correlations between the categorical variables were assessed from Spearman correlation.

Unadjusted odds ratio (OR) estimates were calculated from the univariate logistic regression models. Adjusted OR estimates accounted for the following covariates, as each of these could potentially affect asthma phenotype or adherence to controller medications: age in years, sex, race, college or higher education, allergies, and eczema. An alpha of <0.05 was considered statistically significant. Statistical software SAS 9.4 (Cary, NC, USA) was used for all analyses.

RESULTS

Sample characteristics

The study cohort's demographic features were reflective of the typical asthma population seen in our center with a higher proportion of males in the younger age group, a sizeable African American population, >50% of the patients covered by public insurance, and an overwhelming majority of patients with reported allergic rhinitis (Table 1).

Of the 108 study participants, physician assessment of asthma severity was as follows: 14 (13%) had mild persistent asthma, 41 (38%) had moderate persistent asthma, and 53 (49%) had severe persistent disease (Fig 1). Physician assessment of asthma control included: 59 (55%) well controlled, 42 (39%) not well controlled, and 7 (6%) very poorly controlled patients.

Primary outcome

The mean CASI score and standard deviation (SD) for each severity category was 3.1 (1.6) for mild persistent, 6.2 (2.5) for moderate, and 7.7 (2.4) for severe persistent (Fig 1). The CASI score strongly predicted physician assessment of severity, in the unadjusted analysis (OR 36.67, 95% CI, 8.83 -152.34), and the adjusted analysis (OR 32.76, 95% CI, 5.70-188.44). The c-statistic for multivariable logistic model was 0.87 (Table 2). There was a statistically significant correlation between CASI scores and physician assessment of severity, with Spearman correlation of 0.61 (p-value <0.0001).

Supplementary indicator of asthma control: ACT/C-ACT

The mean ACT/C-ACT score and standard deviation (SD) for each controlled category was 22.7 (2.6) for well controlled, 17.1 (3.4) for not well controlled, and 15.1 (3.2) for very poorly controlled. ACT/C-ACT scores strongly predicted physician assessment of control with an unadjusted OR 42.12 (95% CI, 13.34 -133.00), and an adjusted OR 55.34 (95% CI, 13.62 -

224.89). The c-statistic for the multivariable logistic model was 0.91 (Table 2). ACT/C-ACT scores also strongly correlated with the physician assessment of control with Spearman Correlation of 0.72 (p-value <0.0001).

DISCUSSION

The CASI, a tool that incorporates all the domains of asthma severity/control as identified by the National Asthma Education and Prevention Program Expert Panel Report 3,⁵ generated scores that consistently reflected physician assessments of asthma severity in a clinical population. Use of the CASI was feasible and provided useful and accurate assessments in a busy, outpatient clinical setting with a study sample reflective of our typical asthma population. To our knowledge, this is the first attempt to study CASI in a clinical setting.

Limited prior work has examined thresholds at which asthma severity/control can be appropriately categorized using CASI. The value we identified with CASI scores indicating mild persistent versus moderate and severe persistent asthma was similar to that identified by Krouse et al in 2017.¹⁶ Their analysis indicated that a CASI score of 3 or less was optimal to discriminate between low asthma severity from medium or high severity,¹⁶ while the mean CASI score for children with mild persistent asthma in our sample was 3.1. Krouse et al also identified the minimally important difference (MID) for CASI was 1, indicating that incremental changes of just one point reflect meaningful clinical changes. More specifically, a 1-point change in score may reflect improving or worsening symptom control, adjustments to medication use, or even the need for oral steroids during an exacerbation.¹⁶ This is in comparison to ACT for which the MID is 3.¹⁴ CASI has also been shown to demonstrate better within-subject stability as compared to other measures such as symptom days.¹⁰ To date, CASI thresholds for discriminating between

moderate and severe persistent asthma have not been conclusively identified and will still need to be determined. The mean scores for moderate persistent and severe persistent asthma in our study (mean of 6.2 and 7.7, respectively) may inform future work in this area.

Although the CASI is intended to capture asthma severity, and C-ACT/ACT intended to reflect asthma control, it is important to highlight that asthma severity and control are not distinct entities. In fact, these tools incorporate some of the same pieces of information into the assessments. The CASI is a more robust tool in that it integrates medication regimen and lung function.¹⁰ However, both tools address patient reported symptomatology and the degree to which symptoms interfere with function. The broader scope of the CASI is likely to be beneficial in the clinical setting to physicians who need to assess both severity and control while considering current medication regimen and lung function. Guidelines suggest that asthma management should incorporate elements of impairment and risk, and the multidimensional nature of CASI is well suited to assist in this task.^{5,17}

The discriminatory ability of CASI, as documented previously¹⁶ and in this clinical study, is likely to be of benefit not only in clinical care but also in quality improvement efforts for children with asthma. Multiple phenotypes exist in childhood asthma and thus this population is quite heterogenous and ripe for a variety of potential approaches to improve care.²⁰⁻²² The variability within this population also poses challenges to improvement efforts, however, as objective changes must be detected over time to inform next steps and establish best practices. A tool such as CASI that integrates many aspects of asthma severity/control, and is able to detect relatively small changes, could therefore be useful in future asthma-related improvement work. CASI is widely available (www.asthmaseverity.org),²³ and given its strong discriminatory ability, would likely be a more sensitive outcome for quality improvement work than the ACT.

Although our study included the use of the TreatSmart Program,¹⁸ a web-based program developed internally to calculate CASI, integrating CASI into routine clinical care is possible without this tool. Through the web application, printable CASI forms are available as well as an online calculator.²³ Although the TreatSmart Program maximized efficiency in our work, linking CASI with our EHR and integrated systems is not necessary. Likewise, the ACT and C-ACT are readily available online for clinicians to use and conduct comparisons in other clinical settings.^{24,25}

Limitations of this study included the small sample size which likely contributed to the wide confidence interval estimates from our models. It is also possible that drawing information from the EHR may have led to some inaccuracies in data collection in our study. For example, it is possible that race, insurance information, or other variables may have been entered incorrectly in the EHR. Additionally, comorbidities such as allergic rhinitis or eczema may have been present but not documented by the clinician. These types of errors may have led to misclassification. However, those errors were likely minimal and other centers could use the CASI without integrating data from the EHR if so desired. This was also a single center study with a limited number of physicians who had access to the patient's C-ACT and ACT scores as part of clinical practice; knowledge of these scores could have biased their clinical evaluations and affected results in favor of the C-ACT/ACT. Thus, our results must be considered in this context and the validity of the statistical association is likely diminished. However, many factors other than the C-ACT/ACT are considered in determining a patient's asthma control including frequency of exacerbations, lung function, daily activity impairment, chronic symptoms, and other factors. Finally, while CASI has shown promise in two research studies conducted over 12 month periods,^{26,27} its longitudinal performance has yet to be examined in a clinical setting.

202 Our work demonstrates that CASI is relevant to the care of children with asthma in an
203 outpatient setting and accurately reflects physician assessments of asthma severity/control.
204 Further studies should confirm the adaptability of CASI to clinical care among larger populations
205 and in additional clinical settings.

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268 **TABLE 1. Demographic and clinical characteristics of study population**

	All n=108
Mean Age in yrs (SD)	10.6 (4.0)
Sex (%male)	64(59.3%)
Race	
Responses	106
White	50.00%
African American	31.10%
Other	18.90%
Annual Household Income ^a	
Responses	79
Below National Poverty Line	26.60%
Insurance	
%Public	58.30%
Highest Educational Household Level	
Responses	104
%HS/GED or Less	30(28.9%)
%Some College or Higher	74(71.1%)
Mean Age of Onset of Asthma Symptoms in yrs (SD) ^b	3.8(3.6)
Allergic Rhinitis (%) ^b	98(90.8%)
Eczema (%) ^b	71(65.7%)
C-ACT/ACT Score Median (Range)	21 (9-27)
Total CASI Score Median (Range)	7 (2-15)
Average FEV1 % Predicted (SD)	96.4(16.4)
Average FEV1/FVC Ratio (SD)	80.5(10.3)
Medication Step Median (Range) ^c	5(2-5)
Exacerbations in past 2 months Median (Range) ^d	0(0-4)

a. National Poverty Level Guidelines for a family of 4: 24,600 (<https://aspe.hhs.gov/poverty-guidelines>)

b. Per parental report or medical chart documentation

c. Per NAEPP guidelines

d. Defined as number of hospitalizations and steroid bursts

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Table 2: Odds ratio (OR) estimates with 95% CI, p-values and model c-statistics from each logistic regression model. Adjusted model includes the covariates: age in years, sex, race, college or higher education, allergies, and eczema.

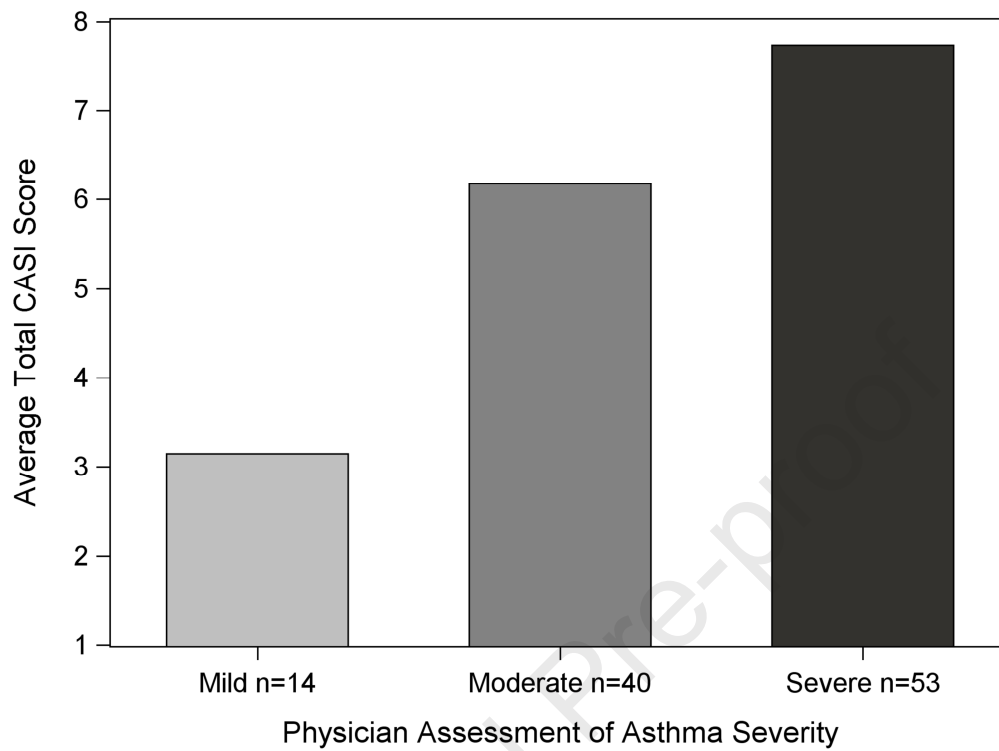
Response variable		Unadjusted estimate			Adjusted estimate		
		OR (95% CI)	p-value	Model c-statistics	OR (95% CI)	p-value	Model c-statistics
Physician severity/control (reference category: mild persistent)	CASI (reference category: ≤ 3)	36.67 (8.83, 152.34)	<.0001	0.825	32.76 (5.70, 188.44)	<.0001	0.869
Physician not-well-control/control (reference category: well controlled)	ACT/C-ACT (reference category: > 19)	42.12 (13.34, 133.00)	<.0001	0.856	55.34 (13.62, 224.89)	<.0001	0.913

280 Figure Legend:

281 Figure 1: Mean CASI score for each asthma severity category

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283 Figure 1.



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