

Accuracy of childhood asthma control test among Thai childhood asthma patients

Sirasuda Sommanus,¹ Chalerat Direkwattanachai,² Saranath Lawpoolsri,³ Raweerat Sitcharungsi⁴

Abstract

Background: The Childhood Asthma Control Test (C-ACT) was developed to assess asthma control in children worldwide. A self-administered questionnaire for children translated into Thai language was used.

Objective: To validate the C-ACT cut-points for evaluating the level of asthma control among Thai children, using the Global Initiative for Asthma (GINA) guideline as a gold standard.

Methods: C-ACT score, FEV1 and assessment of level of asthma control were recorded at baseline, 3-month, 6-month, and 1-year visits among children with asthma. Receiver operating characteristic (ROC) curves was used to determine the area under the curve (AUC) of C-ACT score for determining the level of asthma control. Validity indicators were calculated at different C-ACT cut-points to determine those most appropriate for predicting controlled and uncontrolled asthma.

Results: We enrolled 279 children, 64% males, with mean age 6.87 ± 2.4 years. C-ACT score was significantly correlated with FEV1 at 3-month, 6-month, and 1-year visits (p<0.001). The AUC of C-ACT score compared with GINA score were above 80% at all visits. The suggested C-ACT score cut-point of controlled asthma was \geq 23 (sensitivity 69.5%, specificity 73.3%, positive predictive value (PPV) 81.2%, negative predictive value (NPV) 63.8%); that of uncontrolled asthma was \leq 18 (sensitivity 54.2%, specificity 96.9%, PPV 61.9%, NPV 95.7%).

Conclusions: The Thai version of the C-ACT is an accurate, simple, and useful tool for assessing asthma control among Thai children. The high AUC suggests that the Thai C-ACT is as good as the GINA guideline in predicting asthma control level.

Keywords: Accuracy, Asthma, Childhood asthma control test, Global Initiative for Asthma guidelines, FEV1

From:

- ¹ Department of Pediatrics, Taksin Hospital, Bangkok, Thailand
- ² Department of Pediatrics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand
- ³ Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
- ⁴ Department of Tropical Pediatrics, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Corresponding author:

Raweerat Sitcharungsi Faculty of Tropical Medicine, Mahidol University, Bangkok 10400, Thailand Email: raweeratsitcharungsi@gmail.com

Abbreviations:

C-ACT = Childhood asthma control test FEV1 = Forced expiratory volume in one second GINA = Global Initiative for Asthma DSS = Disease severity score AUC = Area under the curve ROC = Receiver operating characteristic PPV = Positive predictive value NPV = Negative predictive value

Background

Childhood asthma is caused by chronic inflammation, which leads to airway hyper-reactivity, recurrent wheezing, and persistently altered airway function. Asthma is a common disease, affecting approximately 1%–18% of people worldwide.¹ The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three reported that the prevalence of current asthma in children aged 13–14 years was 13.8%, and it was 11.6% in those aged 6–7 years. According to that study, the reported lifetime prevalence of asthma in Thailand was 12.3%.²

Well-controlled asthma requires early diagnosis and proper assessment of asthma control to provide appropriate treatment. A diagnosis of asthma should be given based on patient history, physical examination, and pulmonary function tests, such as forced expiratory volume in 1 second (FEV1), peak flow variability or a bronchial provocation test.³ The goal of asthma therapy is to control symptoms and minimize future risk of exacerbation, decline of lung function and



adverse outcomes. Assessment and monitoring of the level of asthma control are important. According to the Global Initiative for Asthma (GINA) 2017 guideline, the level of asthma control is classified into well-controlled, partly controlled, and uncontrolled asthma groups. The level of asthma control can be determined by daytime and nighttime symptoms, use of rescue medication, limitation of activities, exacerbation, and pulmonary function tests.¹ Pulmonary function testing is usually not available in the primary care setting. Worldwide asthma organizations have developed simplified questionnaires to assess asthma control with no equipment required, to be used in limited resource settings. Validated questionnaires, such as the Childhood Asthma Control Test (C-ACT)⁴ and Disease Severity Score (DSS),⁵ have been adopted and are widely used in primary care units worldwide.

The C-ACT was developed to assess childhood asthma control using a self-administered questionnaire with seven items. The questionnaire is divided into two parts. The first four items contain questions to be answered by children aged 4-11 years. The last three items are questions to be answered by parents or caregivers. This questionnaire assesses daytime and nighttime asthma symptoms, use of reliever medication, and limitations of daily activities in the prior 4 weeks. A previous C-ACT study found that scores of more than 19 indicated controlled asthma.4 The C-ACT can be used as an indicator to evaluate change in the clinical status of children with asthma. The C-ACT has been translated into different languages to be used worldwide. The cut-points of the C-ACT score for determining the level of asthma control can vary across countries, owing to variations in patient characteristics.7-15 The Thai version of the C-ACT has been used for decades in Thailand. However, appropriate cut-points of the C-ACT for Thai childhood asthma patients remain uncertain. Therefore, this study was conducted to determine the appropriate C-ACT score cut-points for evaluation of controlled, partly controlled, and uncontrolled asthma among Thai children.

Methods

Study population

Retrospective cohort study was conducted at a pediatric allergy unit at Taksin Hospital in Bangkok, Thailand during April 2012 to April 2016 were reviewed. The inclusion criteria were newly diagnosed asthma patients aged 4–14 years at enrollment. An asthma diagnosis was based on clinical symptoms and the GINA guideline. We excluded those patients who were unable to carry out the pulmonary function test (spirometry) or had underlying diseases including other chronic lung diseases, central nervous system diseases, cardiovascular diseases, and other chronic illnesses.

At diagnosis, each patient was evaluated by a pulmonary function test and asthma severity assessment according to the GINA guideline. C-ACT scores and FEV1 values were recorded at 3-month, 6-month, and 1-year visits, and assessment of the level of asthma control according to the GINA guideline was carried out at each visit. A Thai version of the C-ACT was developed by translating the original one by a linguist. To better understand patients' feelings about their asthma and facilitate good communication between clinicians and patients, the validated version of C-ACT in Thai language was used. Spirometry was performed according to American Thoracic Society standards.⁶

Ethical approval

This study was approved by the Bangkok Metropolitan Administration Ethics Committee for Human Research (BMAEC-S010q/59_EXP). Since this study involved only retrospectively review medical records, informed consent of each participants was not required.

Statistical analysis

Demographic and clinical characteristics of enrolled patients at baseline were described. C-ACT scores and FEV1 values were summarized as mean and standard deviation (SD) at each visit. An ANOVA test was performed to determine the difference in the mean among the three levels of asthma control. Then, the correlation between C-ACT score and FEV1 was determined at each visit, using a Pearson correlation test. The level of asthma control at each visit was assessed according to the GINA guideline (gold standard). Three levels of asthma control were designated: controlled, partly controlled, and uncontrolled. The validity of the C-ACT score to predict controlled and uncontrolled asthma was measured according to the GINA guideline. The receiver operating characteristic (ROC) was used to determine the ability of using C-ACT score to predict asthma control, indicated by the area under the curve (AUC). In addition, validity indicators of the test including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to determine the appropriate C-ACT cut-points. The number of patients with uncontrolled asthma decreased overtime after receiving treatment: therefore, the validity indicators were evaluated only at the 3-month visit.

To determine appropriate cut-points of C-ACT scores, the clinical validity of potential C-ACT cut-points was evaluated by comparison with the percentage of predicted FEV1 value (<60%, 60% to 79%, 80% to 99%, and \geq 100%), the level of control according to the GINA guideline, and the change in medical therapy (step up, no change, and step down) that the patient received.

Results

Subject characteristics

Overall, 279 children were enrolled. Among these, 179 patients (64%) were male and the mean age was 6.87 ± 2.4 years. The mean age at asthma diagnosis was 4.88 ± 2.31 years and age at onset was 3.31 ± 2.05 years. According to severity, most children had moderate persistent (131; 46.6%), mild persistent (70; 25.1%), mild intermittent (30; 10.7%), and severe persistent (48; 17.6%) asthma. During the 1 year of follow-up, 15 children were lost to follow-up at the 6-month visit; a total 230 children (82.4%) completed a 1-year visit. The most common comorbidities were allergic rhinitis (40.5%), snoring (20.1%), and atopic dermatitis (14.7%). More than half of patients had a history of potential risk factors for asthma, including history of hospitalization owing to lower respiratory

tract infection (58.4%), family history of atopy (52.3%), and passive smoking (50.5%), as shown in **Table 1**. According to the GINA guideline, 174 (62.4%), 81 (29%), and 24 (8.6%) patients were categorized as having controlled, partly controlled, and uncontrolled asthma, respectively.

Table 1. Patient baseline clinical characteristics at the first visit.

Characteristics	Number	Percentage	
Total number	N = 279	100%	
Male	179	64.2%	
Female	100	35.8%	
Characteristics N=279	Years	Range	
Age (year), mean ± SD	6.87±2.49	(4-14.2)	
Age of diagnosis (year), mean ± SD	4.88±2.31	(1-12)	
Age of onset (year), mean ± SD	3.31±2.05	(0.5-10)	
Duration of disease before diagnosis (year), mean ± SD	1.57±1.35	(0-8)	
Severity of asthma N=279	Number	Percentage	
Mild intermittent (>80% predicted FEV1)	30	10.7%	
Mild persistent (>80% predicted FEV1)	70	25.1%	
Moderate persistent (60-80% predicted FEV1)	131	46.6%	
Severe persistent (<60% predicted FEV1)	48	17.6%	
Co-morbid diseases N=279	Number	Percentage	
Allergic rhinitis	113	40.5%	
Atopic dermatitis	41	14.7%	
Food allergy	19	6.8%	
History of sinusitis	37	13.3%	
History of urticarial rash	14	5%	
Snoring	56	20.1%	
History of admission due to lower respiratory tract infection	163	58.4%	

Abbreviations: SD, standard deviation; FEV1, Forced expiratory volume in 1 second.

Correlation between C-ACT score and FEV1

Table 2 shows the mean (SD) C-ACT score and FEV1 at 3-month, 6-month, and 1-year visits for the controlled, partly controlled, and uncontrolled asthma groups. The means of C-ACT score and FEV1 were significantly different among the three asthma control levels. A significantly positive correlation between C-ACT score and FEV1 was found at the 3-month (r = 0.48 and p < 0.001), 6-month (r = 0.558 and p < 0.001), and 1-year visits (r = 0.421 and p < 0.001).

Validity of C-ACT score

According to the ROC, C-ACT scores showed good performance in predicting controlled and uncontrolled asthma, using GINA guideline classification as the gold standard. The AUC of C-ACT score was above 80% and 90% for detection of controlled and uncontrolled asthma, respectively, at all follow-up visits. The AUC of C-ACT score for controlled asthma was 0.81 (0.76–0.87), 0.84 (0.78–0.90), and 0.82 (0.75– 0.90) for 3-month, 6-month, and 1-year visits, respectively. The AUC of C-ACT score for uncontrolled asthma was 0.93 (0.89–0.97), 0.91 (0.85–0.97), and 0.92 (0.87–0.97) for 3-month, 6-month, and 1-year visits, respectively.

A C-ACT score of 20–24 indicated controlled asthma at the 3-month visit, with sensitivity ranging from 47.7% to 95.4% and specificity ranging from 44.8% to 87.6% (**Figure 1**),(**Table 3**). A cut-point value of \geq 23 demonstrated 69.5% sensitivity, 73.3% specificity, 81.2% PPV, and 63.8% NPV. A C-ACT score of 17–21 indicated uncontrolled asthma, with sensitivity ranging from 45.8% to 91.7% and specificity ranging from 78.8% to 99.2% (**Figure 1**). A cut-point value of

Table 3. Sensitivity, specificity, positive predictive value, and negative predictive value of C-ACT scores to detect controlled asthma.

C-ACT (≥)	Sensitivity	Specificity	PPV (%)	NPV (%)
20	0.954	0.448	74.11	85.45
21	0.902	0.562	77.34	77.63
22	0.828	0.638	79.12	69.07
23	0.695	0.733	81.21	63.81
24	0.477	0.876	82.76	59.42

Abbreviations: C-ACT, Childhood Asthma Control Test; PPV, positive predictive value; NPV, negative predictive value.

Table 2. Mean(SD) of C-ACT scores and FEV1 values at all visits.

	At 3 months			At 6 months			At 1 years		
	N (279)	FEV1	C-ACT	N (264)	FEV1	C-ACT	N (230)	FEV1	C-ACT
Controlled	174	94.39 (12.97)	24.15 (1.84)	185	93.61 (12.20)	24.32 (1.60)	176	93.77 (12.82)	24.68 (1.71)
Partly controlled	81	72.66 (7.94)	21.89 (2.47)	62	71.66 (8.22)	21.29 (17.53)	46	73.50 (6.29)	21.89 (2.69)
Uncontrolled	24	57.23 (8.49)	18.08 (2.50)	17	58.20 (7.78)	17.53 (3.84)	8	55.48 (8.32)	19.25 (2.61)
p-value*		<0.001	<0.001		<0.001	<0.001		<0.001	<0.001

*ANOVA p-value comparing the different levels of asthma control.

Abbreviations: C-ACT, Childhood Asthma Control Test; SD, standard deviation; FEV1, Forced expiratory volume in 1 second.

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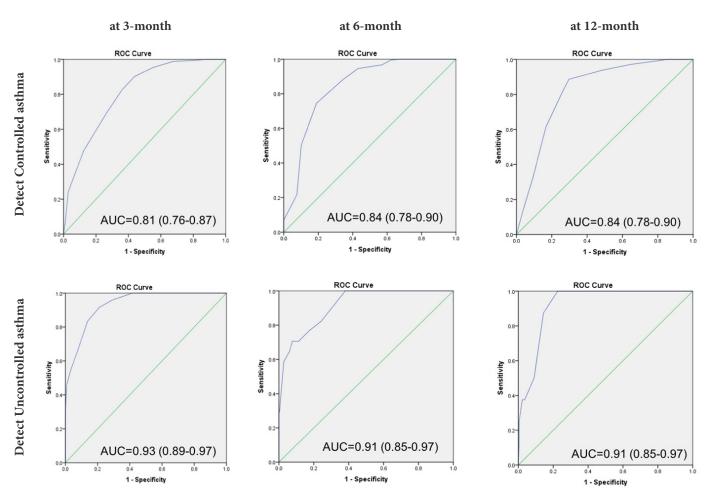


Figure 1. The receiver operating characteristic curves (ROC) of C-ACT score to detect controlled and uncontrolled asthma at 3-month, 6-month, and 12-month after initial treatment

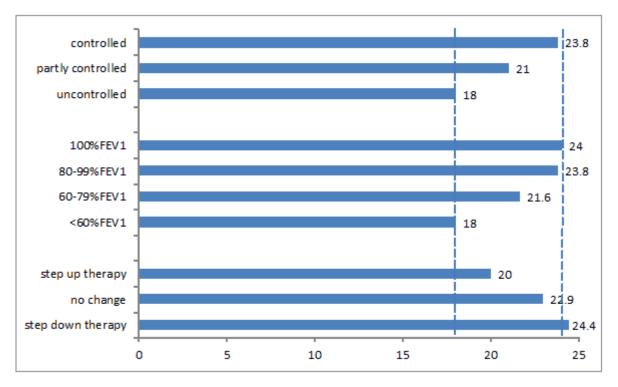


Figure 2. C-ACT cut-point score compared with clinical measures at 3-month visits. The cut-point scores for uncontrolled and controlled asthma levels were 18 and 23, respectively.



	GINA guideline	C-ACT cut-point 23&18	C-ACT cut-point 24&18	C-ACT cut-point 24&19
		Step up	therapy (N=73)	
Controlled	4	18	13	13
Partly controlled	46	35	40	30
Uncontrolled	23	20	20	30
		No cl	hange (N=82)	
Controlled	48	56	46	46
Partly controlled	33	13	23	30
Uncontrolled	1	13	13	6
		Step down	n therapy (N=124)	
Controlled	122	108	90	90
Partly controlled	2	16	34	34
Uncontrolled	0	0	0	0

Table 4. C-ACT cut-point score compared with the level of asthma control according to the GINA guideline.

Abbreviations: C-ACT, Childhood Asthma Control Test; GINA, Global Initiative for Asthma.

 \leq 18 demonstrated a sensitivity of 54.2%, specificity of 96.9%, PPV of 61.9%, and NPV of 95.7%.

Clinical correlation with C-ACT score was estimated by the level of asthma control according to the GINA guideline, the change in medical treatment, and percentage of predicted FEV1 value, as given in **Figure 2**. A C-ACT score of 23.8 represented controlled asthma whereas a score of 18 demonstrated uncontrolled asthma. Among patients with FEV1 less than 60% of the predicted value, the average mean C-ACT score was 18. For those with FEV1 more than 80% of the predicted value, which demonstrated controlled asthma, the average C-ACT score was 23.8 (**Figure 2**).

The aims of asthma treatment are to achieve asthma symptom control, maintain good quality of life, and minimize the medication needed for maintaining well-controlled asthma. After good asthma control had been achieved and maintained for about 3 months, a step down to a lower medication dose can be made as long as control of both symptoms and acute exacerbation is maintained.⁸⁻¹⁰ Figure 2 illustrates that step-up therapy is generally prescribed when C-ACT = 19.97, no change when C-ACT = 22.92, and step-down therapy when C-ACT = 24.39. In the step-up therapy group, an uncontrolled asthma group including 23 children was obtained, based on the level of asthma control according to the GINA guideline by specialist assessment; a group including 20 children was obtained by using a C-ACT score of 18 (Table 4). However, if a C-ACT score of 19 was considered, an uncontrolled group including 30 children requiring step-up therapy was obtained, which represents an overtreatment compared with a C-ACT score of 18.

For the controlled asthma group, using the ROC curve a C-ACT score cut-point of ≥ 23 was chosen, consistent with step-down therapy. Specifically, no change and step-down therapy at the 3-month visit can be referred to with C-ACT scores of 22.9 and 24.4, respectively, as depicted in **Figure 2**.

Based on the level of asthma control by the GINA guideline, a group of 122 children with controlled asthma was obtained by specialist assessment whereas a group of 108 children was obtained using a C-ACT score of 23 in a step -down therapy group (**Table 4**). In contrast, a controlled group of 90 children in step-down therapy was found using a C-ACT score of 24. However, a C-ACT score of more than 24 represented an overtreatment.

Moreover, we found that the C-ACT score cut-point for controlled and uncontrolled asthma groups at the 6-month visit had results similar to those at the 3-month visit (**Figure 1**). Specifically, at C-ACT score ≥ 23 , we found 74.6% sensitivity and 81%specificity, representing controlled asthma. At C-ACT score ≤ 18 , we found 64.7% sensitivity and 93.9% specificity, demonstrating uncontrolled asthma. This result coincided with the correlation between C-ACT score and FEV1 at the 6-month visit, as given in **Table 2**. However, C-ACT score cut-points at the 1-year visit were not determined owing to a small number of patients with uncontrolled asthma at a follow-up visit 1year after treatment.

Discussion

The C-ACT has been translated into regional languages and used for assessing the level of control of asthma. Several studies have showed good clinical correlation with translated versions of the C-ACT.⁷⁻¹⁶ The GINA guideline is the gold standard for validating a translated version of the C-ACT. Pulmonary function tests have been used as a predictor of asthma control. FEV1 is one of the main methods of assessing pulmonary function as well as the level of asthma control, according to the GINA guideline.1,6 The C-ACT was developed to provide a simple self-administered questionnaire that is easy to use in primary care settings. A validated, translated version of the C-ACT is a useful tool for assessing asthma control.



Statistical significance correlations between C-ACT score and FEV1 indicated that the C-ACT is a good predictor of asthma control. This study showed significantly positive correlations between C-ACT score and FEV1 at all visits. The results of our study were similar to those of other studies.7-8 Alvarez-Gutiérrez et al. found a correlation between the baseline FEV1 and C-ACT score (r=0.19 and p<0.01).7 Chalise et al. found a significantly positive correlation between C-ACT score and FEV1 at enrollment (r=0.772 and p<0.001), the 3-month visit (r=0.815 and p <0.001), and 6-month visit (r=0.908 and p<0.001).8 Finally, Lee et al. found that patients with a C-ACT score > 19 had better pulmonary function test results, but there was weak correlation between pulmonary function test results and C-ACT score, with a correlation coefficient for FEV1 of 0.061 (95% confidence interval: -0.022 to 0.049).9

A study of the Tunisian Arabic version of the C-ACT administered to 51 patients found that a C-ACT score of 19 identified uncontrolled asthma (sensitivity 73.7% and NPV 86.5%), and good correlation was found between C-ACT and clinical evaluation.¹⁰ A study of the Nepali version of the C-ACT among 65 patients found that a C-ACT score \geq 19 indicated controlled asthma (sensitivity 98.5%, specificity 89.1%, PPV 94.9%, and NPV 96.6%).⁸

The Spanish version of the C-ACT has been demonstrated to be are liable and valid questionnaire for evaluating asthma control, with a cut-point score ≥ 21 indicating good asthma control (sensitivity ranging from 73% to 57.3%, specificity ranging from 47.1% to 60.9%, and correlation coefficient ≥0.85).¹¹ The previous study of Thai version of the C-ACT for 83 patients showed that the C-ACT score < 22 determined uncontrolled asthma (sensitivity 73.9%, specificity 96.7%, PPV 93.2%, NPV 93.2% and AUC 0.91). However, the controlled or partly controlled asthma group was not mentioned.12 The Brazilian Portuguese version of the C-ACT showed statistically significance among GINA categories ($r \ge 0.3$ and p < 0.01). Specifically, this indicated C-ACT scores for controlled (22 ± 2.9) , partly controlled (20 ± 4) , and uncontrolled (16.3 ± 5.3) asthma groups, which was similar to our study where the C-ACT scores were \geq 23, 19–22, and \leq 18 for these groups, respectively. Furthermore, there was no significant correlation between C-ACT score and spirometry or exhaled nitric oxide (r=0.02 and p=0.866, r =0.035 and p=0.753, respectively).¹³

Most studies on a translated version of the C-ACT have found clinical correlations showing that the test can be used as a tool for assessing asthma control.7-16 A Turkish version of the C-ACT was found to be an accurate and reliable tool for evaluating asthma control, with significant correlation between C-ACT and a physician's assessment of asthma control (r=0.65 and p < 0.001).¹⁴ The reliability and validity of the C-ACT in a population of Chinese children with asthma was demonstrated, with internal consistency reliability 0.741 at baseline and 0.759 at a follow-up visit. Reliability between the C-ACT and a specialist's rating of asthma control at baseline and follow-up was r=0.546 (p<0.001).15 The original C-ACT study found a correlation between specialist-assessed change in therapy (step-up or step-down therapy) and C-ACT score (p<0.0001).⁴ Relevant to our study, a change in medication (step-up or step-down therapy) was related to the C-ACT score cut-point obtained from the ROC curve (Table 4).

On longitudinal analysis, we found that C-ACT was useful for predicting controlled asthma at 3-month and 6-month visits but not at 1-year visits. This result is similar to a study by Leung et al., which found that the C-ACT can be useful to predict asthma exacerbation. Changes in C-ACT score are correlated with changes in asthma control status, DSS, and FEV1 (p = 0.019, 0.034, and 0.020, respectively).¹⁶ Conversely, the Nepali C-ACT was found not to be useful for 6-month visits.8 At 1-year visits in our study, we found a discrepancy between C-ACT correlated with FEV1 (Table 2) and C-ACT chosen by the ROC curve. This might be because at the 1-year visit, a group of uncontrolled asthma at 1-year visit decreased from 24 to 8 persons. Because this study is a follow-up study, we found some patients had lost to follow-up or some patients had better clinical outcome than the previous visit, which caused them to be discarded from an uncontrolled asthma group. Therefore, these reasons results in decreasing a sample size of the uncontrolled asthma group to 8 persons, which in turn can affect the accuracy of C-ACT chosen by the ROC curve and also leads to the discrepancy between the C-ACT correlated with FEV1 (Table 2) and the C-ACT chosen by the ROC curve at a 1-year visit.

In particular, the C-ACT score cut-point for predicting uncontrolled asthma from the original C-ACT study was \leq 19,4 but that cut-point cannot predict partly controlled or uncontrolled asthma, according to the GINA guideline. For the C-ACT, scored >19 were also associated with "well controlled" or "totally controlled" asthma, scored of <16 were considered "poorly controlled" or "not controlled at all," and scored of 16-19 corresponded to "somewhat controlled" asthma. The discrepancy between our study and previous study may be because the patients and/or parent behavior in answering questionnaire is differences for each country, for example, in Thailand, people usually answer questionnaire positivity. Our study demonstrated the C-ACT score cutpoint for predicting the levels of asthma control in the GINA guideline and showed the correlation with FEV1. Therefore, the patient who had C-ACT score less than 23 had acute asthmatic attack once in one year and if the patient who had C-ACT score less than18 had limited activity and exacerbation. The Thai version of the C-ACT can predict the level of asthma control without pulmonary function testing, which makes it easy to use in primary care settings.

Conclusion

The Thai version of the C-ACT is an accurate, simple, and useful tool for assessing asthma control among Thai children. A short, self-administered questionnaire for patients and caregivers is suitable for clinical practice settings. The correlation between C-ACT and FEV1 shows that it coincides with the GINA guideline. Although the C-ACT score cannot compare with GINA guideline which is the gold standard for asthma diagnosis, it can help clinicians in a primary care setting to decide an appropriate medical treatment for asthma patients.

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Thai version of C-ACT



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The authors declare that they have no conflicts of interest regarding the publication of this paper.

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