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REVIEW

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Validity of the Childhood Asthma Control Test in diverse populations: A systematic review

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Abstract

Purpose: We examined the validity of the Childhood Asthma Control Test (C-ACT) and identified recommended thresholds for uncontrolled asthma in children from varying backgrounds.

Methods: A systematic literature review was performed utilizing PubMed, Ovid Medline, SCOPUS, CINAHL, and conference proceedings. Studies were included if they enrolled children, had a primary outcome of asthma control, examined test validity or psychometrics, and utilized the C-ACT. Along with study design and demographic data, we extracted all outcomes and comparisons used to validate the C-ACT. We evaluated risk of bias using the COSMIN Risk of Bias tool. Our protocol was registered with PROSPERO (CRD42020211119).

Results: Of 4924 records screened, 28 studies were included. Studies were conducted internationally and published between 2007 and 2018. Average number of enrolled participants was 193 (SD = 155, range = 22–671). Ten studies calculated Cronbach's α (mean [SD] = 0.78(0.05), range = 0.677–0.83). Thirteen studies recommended cut-offs for uncontrolled asthma (≤18–≤24). Nine studies found significant agreement or correlation between C-ACT and Global Initiative for Asthma guidelines/physician assessment of asthma control (correlation coefficients range = 0.219–0.65). Correlation coefficients between C-ACT and spirometry were <0.6 in five of six studies that included spirometry. Kappa values for C-ACT and various spirometry measurements ranged 0.00–0.34.

Conclusions: The C-ACT showed good internal consistency and mixed levels of agreement and correlation with various clinical asthma measures. Recommended cut-offs for asthma control varied and had no consistent relationship with nationality, race, ethnicity, or language. Few studies examined cross-cultural validity and multiple populations remain under-studied.

KEYWORDS
asthma, Childhood Asthma Control Test, pediatric, validity

1 | INTRODUCTION

Asthma symptom prevalence varies up to 13-fold between countries[1,2] with a mean of 9.9%.[3] In the United States, Black (15.7%) and Puerto Rican (12.9%) youth disproportionately affected as compared to non-Hispanic white children (7.1%),[4] with such disparities extending to morbidity (e.g., emergency department visits, hospitalizations).[4,5]

To effectively treat asthma and address such disparities, tailored strategies are necessary to minimize symptoms and exacerbations as well as the associated morbidity and costs.[6] Providing appropriate treatment relies on accurate characterization of asthma control.[7,8] In clinical and research settings, asthma control is assessed using various methods, including objective measures of lung function, physician assessment, and self-administered questionnaires.[9,10]

The Childhood Asthma Control Test (C-ACT)[9,11] is among the most used assessments of asthma control for children under 12 years, was specifically designed for children,[12] and is further distinguished from other assessments by its use of pictures.[11] The C-ACT was created in the United States in the 2000s to assess asthma control in children 4–11 years old. The tool consists of seven questions that collect information from both the child and the caregiver. For the child, there are four questions with answers on a Likert scale defined with words and pictures of a child's face. For the caregiver, there are three questions with answers on a Likert scale defined with words alone. When the C-ACT was developed, a score of 19 or less (out of 27) was defined as the cut-off to indicate uncontrolled asthma.[11]

To develop the C-ACT, Liu et al.[11] developed a conceptual framework and designed a 21-item questionnaire based on literature review and child/caregiver interviews. The resulting response option was a four-point Likert scale with pictures of a child's face "to facilitate comprehension by younger children."[11] Faces of different genders were tested; however, there was no mention of testing faces of different nationalities, races, or ethnicities.[11] The face pictured on the C-ACT has characteristics consistent with a prototype of White faces, such as lighter skin and hair.[13] Then, the questionnaire was refined in a cross-sectional study with 343 4–11 year old children from nine clinics to compare questionnaire responses to specialists' ratings of asthma control. Subsequently, seven questions were selected for the C-ACT based on their predictive abilities. A cut-off score for uncontrolled asthma (≤19) was selected to achieve a high sensitivity for identifying patients with uncontrolled asthma while balancing accuracy and clinical validity.[11] The study population had a disproportionately higher percentage of White children than the US (68.13% White, 11.11% Afro-Caribbean/African American, 4.39% Asian/Indian, 5.85% Hispanic/Latino/Spanish American, 0.58% Native American, 9.94% other).[11]

Since it was first developed and validated, the C-ACT has been tested across different populations in numerous studies, with varying conclusions regarding its validity. While these studies have focused on several specific items, including images, language, and cut-off scores to define asthma control, the validity of the C-ACT has not been systematically examined across diverse populations. As such, this review aimed to examine whether C-ACT thresholds to define asthma control differed based on the child's nationality, race, ethnicity, and language. By answering this question, we will determine whether re-interpretation of cut-offs or use of cultural tailoring, including for images, may be needed to improve the validity of the C-ACT in certain populations.

2 | METHODS

This systematic review focused on studies examining the validity of the C-ACT in varying populations. We conducted this work in alignment with PRISMA guidelines.[14] The protocol was registered a priori on PROSPERO (registration number CRD42020211119).

2.1 | Information sources and search strategy

We performed a computerized search of the literature using medical subject headings (MeSH) and keywords with the following search terms: (child OR pediatric OR childhood OR adolescent) AND Asthma AND ("Control Disease" OR "Asthma Control" OR "disease control"). The following electronic databases were searched on October 15, 2020: PubMed, Ovid Medline, SCOPUS, and CINAHL. We also conducted a search in October 2020 of the gray literature with conference proceedings from the following organizations: American Academy of Allergy, Asthma & Immunology, American Thoracic Society, CHEST, and Pediatric Academic Societies. No study design, date, or language requirements were imposed on the search. These search strategies were developed in consultation with a medical librarian.

2.2 | Screening

Titles and abstracts of the identified articles were reviewed independently by one of three authors (A. V., F. C., N. K.). Articles were excluded if they included only adult participants, did not pertain to asthma, were not related to disease control, did not focus on test validity or psychometrics, and/or focused on basic science only. Of the excluded articles, 10% were reviewed by an additional reviewer (kappa = 0.99). When a reviewer was unsure about eligibility, the three reviewers discussed until agreement was reached.

Next, articles were reviewed in full to determine whether the C-ACT was utilized in the study. Along with the above reasons for exclusion, articles were excluded if the full-text was not available (only abstract available), if the article was not available in English, and/or if the study did not utilize the C-ACT.

2.3 | Data extraction

Two authors (F. C., N. K.) used a standardized tool to extract data for all articles. Specific data elements included title, authors, publication year, funding sources, and regulatory approval (e.g., IRB). Regarding study design, data was extracted about site information (location, type, number of sites), language of C-ACT, enrollment dates, inclusion criteria, sample size, validity types assessed, and comparison groups. Characteristics of study participants, such as age, race, ethnicity, and sex, were recorded. C-ACT comparisons were extracted in the following areas when available: spirometry (FEV), nitric oxide, Global Initiative for Asthma (GINA), and change in therapy. All relevant statistics (e.g., kappa, correlation coefficients, area under curve) were extracted for these comparisons when available. Finally, we extracted Cronbach's α and any recommended cut-offs for the C-ACT. For studies that included additional age groups (i.e., group of older children who completed ACT), we extracted and reported only data pertaining to the group that received the C-ACT.

2.4 | Analysis

The extracted information was collected in a spreadsheet, which was then cleaned and organized. We identified commonly used comparisons to the C-ACT. Descriptive analysis was performed to summarize available variables and outcomes in the studies with proportions, means, standard deviations, medians, and ranges as appropriate.

2.5 | Risk of bias assessment

Risk of bias was assessed for each article using the COSMIN Risk of Bias tool.[15] Two authors (F. C., N. K.) initially completed the entire tool (boxes 1–10) for three included studies and reviewed findings with the team. Based on these findings and the goals of this review, we identified six items from the tool as most relevant to our research objective: internal consistency (box 4), cross-cultural validity/measurement invariance (box 5), reliability (box 6), measurement error (box 7), criterion validity (box 8), and hypotheses testing for construct validity (box 9). Box 1 (patient-reported outcome measure development) was assessed previously[16] and therefore did not need to be re-assessed.[17] Box 2 (content validity) focuses on patient and physician perspectives of the relevance, comprehensiveness, or comprehensibility of the patient-reported outcome measure,[17] which were not part of studies in this review and thus this Box was not assessed. One reviewer (F. C.) assessed each article for risk of bias using these six items, and another reviewer (N. K.) completed these items in duplicate for three studies, with good agreement (kappa = 0.87). GINA guidelines and physician assessment were considered the “gold standard” for criterion validity (box 8). Scores for each item were reported using the “worst score counts” principle, consistent with the COSMIN Risk of Bias user manual.[15]

3 | RESULTS

3.1 | Study selection

Our initial search of the databases and conference proceedings identified a total of 11,709 records. After removing duplicates, 4924 records remained and were screened in the title and abstract review. Of these, 152 were selected for full-text review and 28 were included in our study (Figure 1). Among the records excluded, three studies (two in Japanese, one in Spanish) were removed because they lacked English translation.

3.2 | Study characteristics

The included studies (Table 1) were published between 2007 and 2018. Of the 28 studies included, five were conducted in the United States,[11,18–21] eight in Asia (East, South, or Southeast Asia),[23–29] eight in Europe,[30–37,44] four in the Middle East,[38–41] two in South America,[12,42] and one in Africa.[43] Twenty-two studies reported the language used to administer the C-ACT, and the languages varied.[11,12,18,19,22–26,29,31,32,34–43] Only nine studies reported the race or ethnicity of participants.[11,12,18–21,39,42,43] Overall, 5400 subjects were included across all of these studies. The average number of enrolled participants was 193 (SD = 155, range = 22–671). Gender of the study participants ranged from 47% to 72% male, and participants ranged from 4 to 14.2 years old. Three studies included children outside of the C-ACT's intended age range of 4–11, instead including ages 5–14,[27] 4–12,[28] and 4–14.2.[29]

The most commonly reported types of validity studied were clinical validity (six studies),[11,18,19,29,36,37] construct validity (four studies),[11,21,36,42] and criterion validity (three studies)[22,38,42] (Table 2). Seventeen studies did not mention any type of validity.

3.3 | Risk of bias

All studies were rated in at least one category in the risk of bias tool. Ten of 28 studies were rated for internal consistency; three for cross-cultural validity; seven for reliability; 20 for criterion validity; and 21 for hypothesis testing for construct validity. Studies were not rated in a given category if they did not assess the relevant type of validity. Six studies were rated as “doubtful” or “inadequate” in at least one category under the COSMIN Risk of Bias tool (Table 3) primarily because of small sample sizes or failure to describe subgroups.[18,19,24,30,38,43] Internal consistency and criterion validity were rated as “very good” for all included studies looking at relevant outcome measures. All studies examining reliability received an “adequate” rating for reliability, primarily because they calculated intraclass correlation coefficient but did not report the model or formula of the intraclass correlation coefficient. Ratings for cross-cultural validity/measurement invariance and hypothesis testing for construct validity were more variable.

3.4 | Internal consistency

Ten studies reported Cronbach's α as a measure of internal consistency of the C-ACT.[11,12,19,21,22,36–38,41,42] Cronbach's α values ranged from 0.677 to 0.83 (mean = 0.78, SD = 0.05).

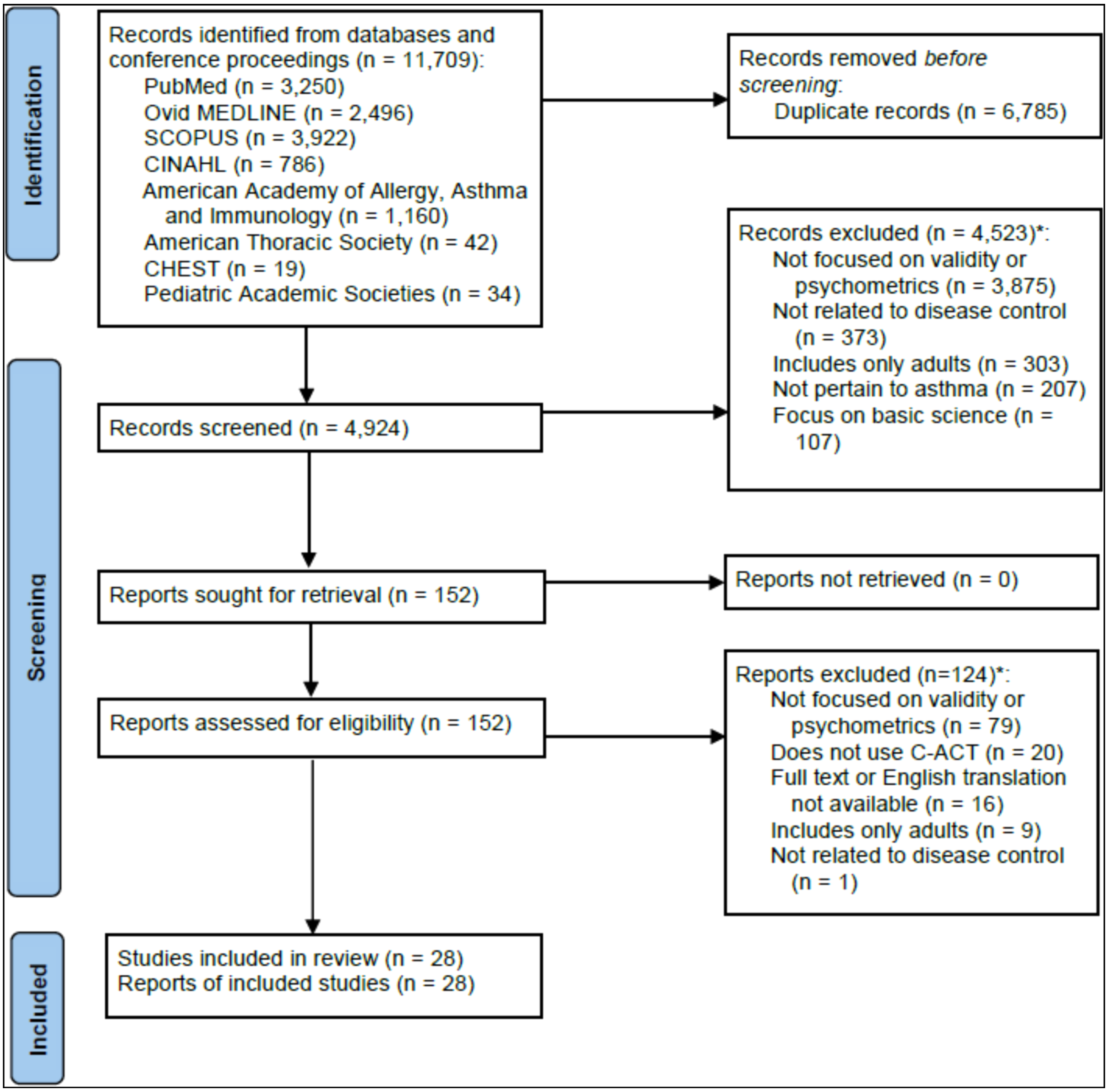

FIGURE 1 PRISMA flow diagram of study identification and inclusion. [Color figure can be viewed at wileyonlinelibrary.com]

3.5 | Cut-offs

In addition to the original study by Liu et al.[11] 13 other studies identified a recommended cut-off for uncontrolled asthma, ranging from ≤18 to ≤24.[19,20,23,25–29,35,36,38,39,41] Of these 13 studies, three recommended the original cut-off of ≤19,[26,27,38] eight recommended a cut-off higher than the original,[19,23,25,28,35,36,39,41] and two recommended a lower cut-off of ≤18.[20,29] When examining the studies by region, three of eight studies done in Asia,[23,25,28] two of four in the Middle East,[39,41] and two of eight in Europe[35,36] recommended a cut-off higher than ≤19. The remaining study that recommended a higher cut-off enrolled a population composed of 76.1% participants of Mexican descent in the United States.[19] Additionally, one of eight studies from Asia[29] and one of five from the United States[20] recommended a lower cut-off of ≤18.

3.6 | Comparisons to C-ACT

GINA guidelines, physician assessment of asthma control, spirometry, fractional exhaled nitric oxide (FeNO), and change in therapy were identified as the commonly used comparisons to the C-ACT. GINA guidelines/physician assessment of asthma control and spirometry were the most commonly used measures compared to the C-ACT. Because of the limited number of studies, the variation of comparisons to the C-ACT across studies, and the heterogeneity of the data, it was not possible to perform a meta-analysis.

3.6.1 | GINA guidelines and physician assessment

Thirteen studies compared C-ACT score to the level of asthma control defined by GINA guidelines and/or physician assessment

TABLE 1 Participants' characteristics of the 28 included studies.

Citation	Country	Language used on C-ACT	Sample size[a]	Race, *N* (%)	Ethnicity, *N* (%)	Age, mean (SD, range)	Gender, male *N* (%)
North America							
Liu et al.[11]	United States	English	343	38 (11.11%) Afro-Caribbean/African American, 15 (4.39%) Asian/Indian, 233 (68.13%) North American/European/White, 2 (0.58%) Native American, 34 (9.94%) other	20 (5.85%) Hispanic/Latino/Spanish American	8.1 (2.39, 4–11)	211 (61.5%)
Liu et al.[18]	United States	English	671	92 (13.7%) Afro-Caribbean/African American, 29 (4.3%) Asian/Indian, 1 (0.1%) North African/Middle Eastern, 428 (63.8%) North American/European/white, 5 (0.7%) Native American, 56 (8.3%) other, two missing	58 (8.6%) Hispanic/Latino/Spanish American	7.8 (2.3, 4–11)	406 (60.5%)
Shi et al.[19]	United States	English or Spanish (family's choice)	88		67 (76.1%) Mexican descent, 21 (23.9%) non-Hispanic	(6–11)	-
Todoric et al.[20]	United States		22	22 (100%) African American		(5–11)	-
Bime et al.[21]	United States	-	161	45 (28%) White, 80 (50%) Black, 7 (4%) Other	29 (18%) Hispanic	9 (1.6, 6–11)	102 (63%)
Asia (East, South, and Southeast)							
Chen et al.[22]	Taiwan	Chinese	247			7.88 (2.33, 4–11)	163 (66%)
Leung et al.[23]	China	Chinese	113			9.1 (2, 4–11)	70 (61.9%)
Leung et al.[24]	China	Chinese	97			9.2 (2, 4–11)	56 (57.7%)
Ito et al.[25]	Japan	Japanese	258			9 (5–11)	176 (68.2%)
Wong et al.[26]	China, India, Indonesia, Malaysia, Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand, and Vietnam	English or Chinese	162			(4–11)	-
Chalise et al.[27]	Nepal	-	65			(5–14)	35 (53.8%)
Somashekar et al.[28]	India	-	97			(4–12)	64 (66%)
Sommanus et al.[29]	Thailand	Thai	279			6.87 (2.4, 4–14.2)	179 (64%)
Europe							
Koolen et al.[30]	Netherlands	-	97			8.5 (2.3, 4–11)	57 (65%)

(Continues)

TABLE 1 (Continued)

Citation	Country	Language used on C-ACT	Sample size[a]	Race, *N* (%)	Ethnicity, *N* (%)	Age, mean (SD, range)	Gender, male *N* (%)
Koolen et al.[31]	Netherlands	Dutch	173			8.5 (2.3, 4–11)	54 (64%)
Waibel et al.[32]	Austria	German	107			12 (2.9)	77 (72%)
Rapino et al.[33]	Italy	-	80			9.6 (3.3)	53 (66%)
Deschildre et al.[34]	France	French	525			7.7 (2.2)	348 (66%)
Voorend-Van Bergen et al.[35]	Netherlands	Dutch	151			8.7 (1.8, 4–11)	106 (70%)
Perez-Yarza et al.[36]	Spain	Spanish	382			7.9 (2.4, 4–11)	219 (57.3%)
Felix et al.[37]	Portugal	Portuguese	60			9 (1.75, 6–11)	28 (47%)
Middle East							
Sekerel et al.[38]	Turkey	Turkish	368			8.3 (2.3, 4–11)	210 (57%)
Yavuz et al.[39]	Turkey	Turkish	76	76 (100%) White		8.7 (1.4, 6–11)	47 (61.8%)
Shefer et al.[40]	Israel	Hebrew	354			7.81 (2.73, 4–11)	231 (65.3%)
AlTeneiji et al.[41]	United Arab Emirates	Arabic	105			7.9 (2.4, 4–11.8)	64 (61%)
South America							
Rodriguez-Martinez et al.[42]	Colombia	Spanish	143		143 (100%) Hispanic	7.1 (1.9, 4–11)	70 (49.0%)
Oliveira et al.[12]	Brazil	Brazilian Portuguese	105	67 (63.8%) Caucasian		7.8 (2.13, 4–11)	65 (61.9)
Africa							
Green et al.[43]	South Africa	English	71	43 (61%) Black African		8.4 (4–11)	46 (64.8%)

Note: Studies present by region, and chronologically within each region. Terminology used for race reflects the original paper.

[a]Portion of study population that completed Childhood Asthma Control Test.

TABLE 2 Main conclusions of the 28 included studies.

Citation	Types of validity assessed[a]	Comparisons	Cronbach's α	Recommended cut-off for uncontrolled asthma for C-ACT[b]
North America				
Liu et al.[11]	Construct, clinical, concurrent	Spirometry, change in therapy, physician assessment of control, PAQLQ/PACQLQ	0.79	≤19
Liu et al.[18]	Clinical	Spirometry, change in therapy, physician assessment of control		≤12 (very poorly controlled asthma)
Shi et al.[19]	Clinical	Spirometry, physician assessment of control	0.76	≤22
Todoric et al.[20]		Spirometry, physician assessment of control		≤18
Bime et al.[21]	Construct	Spirometry, episodes of poor asthma control, ACQ-6, ASUI, PAQLQ	0.76	
Asia (East, South, and Southeast)				
Chen et al.[22]	Criterion, discriminant	Change in therapy, physician assessment of control, pre-bronchodilator peak expiratory flow rate	0.741 (baseline), 0.759 (follow-up)	
Leung et al.[23]		GINA		≤24
Leung et al.[24]		Spirometry, FeNO, disease severity score, exacerbations		≤24 (asthma exacerbations)
Wong et al.[26]		GINA-derived symptom control index		≤19
Ito et al.[25]		Spirometry		≤22
Chalise et al.[27]		Spirometry, GINA		≤19
Somashekar et al.[28]		Spirometry, GINA, ATAQ		≤20
Sommanus et al.[29]	Clinical	Spirometry, GINA, change in therapy		≤18
Europe				
Koolen et al.[30]				
Koolen et al.[31]		GINA		
Waibel et al.[32]		Spirometry, FeNO, GINA		
Rapino et al.[33]		GINA, exercise airways hyperresponsiveness, ATAQ, use of short acting beta 2 agonist agents		
Deschildre et al.[34]		GINA		
Voorend-Van Bergen et al.[35]		Spirometry, FeNO, PAQLQ		≤21
Perez-Yarza et al.[36]	Construct, clinical, concurrent, longitudinal	Spirometry, change in therapy, perception of asthma control, PAQLQ, asthma classification, exacerbations	0.81	≤21
Felix et al.[37]	Clinical		0.716	
Middle East				
Sekerel et al.[38]	Criterion, discriminant	Spirometry, physician assessment of control	0.82, 0.83, 0.82, 0.82, 0.80 (5 timepoints)	≤19
Yavuz et al.[39]		FeNO, GINA		≤22
Shefer et al.[40]		Spirometry, GINA		

(Continues)

TABLE 2 (Continued)

Citation	Types of validity assessed[a]	Comparisons	Cronbach's *α*	Recommended cut-off for uncontrolled asthma for C-ACT[b]
AlTeneiji et al.[41]		GINA, change in therapy	0.81	≤20
South America				
Rodriguez-Martinez et al.[42]	Construct, criterion	GINA, change in therapy, PACQLQ, improvement in clinical status	0.8276	
Oliveira et al.[12]	Concordant	Spirometry, FeNO, GINA	0.677	
Africa				
Green et al.[43]		Spirometry, FeNO, physician assessment of control		

Abbreviations: ACQ-6, Asthma Control Questionnaire; ATAQ, Asthma Therapy Assessment Questionnaire; C-ACT, Childhood Asthma Control Test; FeNO, fractional exhaled nitric oxide; GINA, Global Initiative for Asthma; PACQLQ, Pediatric Asthma Caregiver's Quality of Life Questionnaire; PAQLQ, Pediatric Asthma Quality of Life Questionnaire.

[a]Stated in the text.

[b]If unspecified, assumed cut-off for uncontrolled/controlled asthma were the same.

(Table 4).[11,12,18,20,22,23,28,31,32,38,40,41,43] Of these, 11 studies examined agreement or correlation between C-ACT and GINA/physician assessment and nine reported a *p*-value < 0.05 (Green et al. did not report *p* value[43]; Todoric et al. reported *p*-value = 0.10[20]). Four papers performed receiver-operating characteristic (ROC) analysis of this comparison, and the resulting areas under the curve ranged from 0.647 to 0.898.[18,28,31,41]

3.6.2 | Spirometry

Eleven studies compared C-ACT score to spirometry scores, usually FEV1 or FEV1% (Table 5).[12,19,20,25,27,29,32,35,38,43] Five studies examined correlation between C-ACT and spirometry (some at multiple time points), reporting correlation coefficients between 0.007 and 0.908.[12,27,29,32,38] For two studies examining agreement between C-ACT and spirometry, kappa values ranged from 0.00 to 0.34.[20,43]

3.6.3 | FeNO

Four studies compared C-ACT to FeNO (Table 6)[12,24,35,43]: one found a B value of 0.015 (*p* = 0.051),[24] one found a kappa of 0.00,[43] one found a correlation coefficient of 0.035 (*p* = 0.753),[12] and one reported only a *p* value of 0.78.[35]

3.6.4 | Change in therapy

Four studies compared C-ACT scores to change in therapy, specifically whether the patient had step-up or step-down in therapy during the study (Table 7).[22,36,41,42] All four studies found good correlation between C-ACT and change in therapy or good ability of the C-ACT to discriminate between different categories of change in therapy (e.g., step up, no change, step down).

4 | DISCUSSION

This is the first systematic review examining the validity of the C-ACT in children with varied nationality, race, ethnicity, and language. Among 28 articles pertaining to validity of the C-ACT, we found that while the C-ACT showed good internal consistency, it also showed poor correlation or agreement with spirometry and had mixed levels of correlation with GINA guidelines, physician assessment of asthma control, FeNO, and change in therapy. These findings, therefore, suggest the C-ACT may require some level of re-interpretation or cultural tailoring to improve validity in diverse populations.

Recommended C-ACT cut-offs for uncontrolled asthma ranged from ≤18 to ≤24, making it unclear which cut-off to use in clinical practice. Most studies recommended a cut-off higher than the ≤19 in the original study of C-ACT, speculating that higher cut-offs were needed to account for cultural differences between their target population and the primarily White participants in the original study.[19,23] Notably, parent and child perception is an important part of assessing asthma control using the C-ACT. As such, it is possible these differences in the recommended C-ACT cutoffs arise because individuals from various demographic backgrounds and social environments may perceive asthma symptoms differently. Shi et al. notes this varied perception of symptoms is true for children of Mexican descent and could be true for patients of other racial and ethnic groups.[19] However, the effect of race/ethnicity itself is unclear as studies conducted in Turkey (all white participants), the

TABLE 3 COSMIN risk of bias ratings.[a]

Citation	Country	Language used on C-ACT	Sample Size[a]	Internal consistency	Cross-cultural validity/ measurement invariance	Reliability	Criterion validity	Hypothesis testing for construct validity
North America								
Liu et al.[11]	United States	English	343	Very good			Very good	Adequate
Liu et al.[18]	United States	English	671				Very good	Doubtful
Shi et al.[19]	United States	English or Spanish (family's choice)	88	Very good	Inadequate		Very good	Adequate
Todoric et al.[20]	United States	-	22				Very good	Adequate
Bime et al.[21]	United States	-	161	Very good		Adequate		Very good
Asia (East, South, and Southeast)								
Chen et al.[22]	Taiwan	Chinese	247	Very good		Adequate	Very good	Very good
Leung et al.[23]	China	Chinese	113				Very good	
Leung et al.[24]	China	Chinese	97					Doubtful
Ito et al.[25]	Japan	Japanese	258					Very good
Wong et al.[26]	China, India, Indonesia, Malaysia, Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand, and Vietnam	English or Chinese	162				Very good	
Chalise et al.[27]	Nepal	-	65					Very good
Somashekar et al.[28]	India	-	97				Very good	
Sommanus et al.[29]	Thailand	Thai	279				Very good	Adequate
Europe								
Koolen et al.[30]	Netherlands	-	97		Doubtful	Adequate		
Koolen et al.[31]	Netherlands	Dutch	173				Very good	
Waibel et al.[32]	Austria	German	107				Very good	Adequate
Rapino et al.[33]	Italy	-	80					Adequate
Deschildre et al.[34]	France	French	525				Very good	Adequate
Voorend-Van Bergen et al.[35]	Netherlands	Dutch	151				Very good	Very good
Perez-Yarza et al.[36]	Spain	Spanish	382	Very good		Adequate	Very good	Adequate
Felix et al.[37]	Portugal	Portuguese	60	Very good				

(Continues)

TABLE 3 (Continued)

Citation	Country	Language used on C-ACT	Sample Size[a]	Internal consistency	Cross-cultural validity/ measurement invariance	Reliability	Criterion validity	Hypothesis testing for construct validity
Middle East								
Sekerel et al.[38]	Turkey	Turkish	368	Very good		Adequate	Very good	Doubtful
Yavuz et al.[39]	Turkey	Turkish	76					Very good
Shefer et al.[40]	Israel	Hebrew	354		Very good		Very good	
AlTeneiji et al.[41]	United Arab Emirates	Arabic	105	Very good			Very good	Adequate
South America								
Rodriguez-Martinez et al.[42]	Colombia	Spanish	143	Very good		Adequate	Very good	Very good
Oliveira et al.[12]	Brazil	Brazilian Portuguese	105	Very good		Adequate	Very good	Very good
Africa								
Green et al.[43]	South Africa	English	71				Very good	Doubtful

[a]Ratings reported using the "worst score counts" principle. Empty boxes indicate that an article did not examine a particular construct, and these areas were left blank in the risk of bias tool.

Netherlands (participants' race/ethnicity undefined), and Spain (participants' race/ethnicity undefined) also recommended cut-offs higher than 19.[35,45] It is possible other factors, such as educational background, health literacy, language, and translation of C-ACT, could also contribute to these differences. Additionally, further research is needed with under-studied populations, as only two studies took place in South America and one in Africa, to fill the gap in knowledge about the current C-ACT's validity and optimal cut-off threshold. Rigorous work examining cross-cultural validity is also needed as only three included studies examined cross-cultural validity,[19,30,40] two of which were poorly rated ("inadequate" or "doubtful") using the Risk of Bias tool.

Applying the appropriate cut-off for uncontrolled asthma has implications for clinical practice. First, using the original cut-off of ≤19 across all populations could result in under-identification of children with uncontrolled asthma. On the other hand, increasing the threshold too much could result in over-treatment of asthma, with resultant medication side effects and economic burden. Second, it is critical that the C-ACT provide an accurate measure of disease control to inform eligibility for therapy and decisions about management. If perceptions of asthma control vary across cultures or populations, this may be an important confounder that may give rise to treatment inequities among patients with asthma. Recent studies in medicine suggest it is critical to examine the use of race in clinical tools, given that race/ethnicity are socially constructed categories whose use in clinical tests may not be relevant and could reinforce existing disparities. Discussions are currently ongoing about the use of race/ethnicity in pulmonary function tests, given that race adjustments may result in underdiagnosis of respiratory disease in non-White groups and worse inequities in outcomes.[46] Similarly, research has focused on the benefits and problems of using race to estimate glomerular filtration rate (eGFR) with direct impact on diagnosis, monitoring, and management of chronic kidney disease.[47–49] Further, data has emerged showing that Black patients have greater frequency of hypoxemia than detected by pulse oximetry as compared to White patients, suggesting potential racial biases in oxygen saturation.[50] Both of these tools, like the C-ACT, are important for assessing disease status and determining management plans and also highlight potential risks of "racializing" medicine. Notably, C-ACT differs from these examples, which are a blood test and biophysical result, in that it is a patient questionnaire with psychometric properties. Regardless of the type of tool, when considering the use of race/ethnicity in tests, it is essential to consider (1) if the need for race correction is based on robust evidence, (2) if the race correction is justified by a plausible causal mechanism, and (3) if implementing the race correction would mitigate existing disparities.[51]

In addition to the clinical setting, the C-ACT is commonly used in research with a cut-off of ≤19 to recruit participants for studies and/or evaluate programs and interventions to assess impact.[52–54] Recruitment using the ≤19 cutoff to determine asthma control may lead to misclassification of participants as controlled or uncontrolled. Also, the routine use of this cutoff could affect whether programs are

TABLE 4 Comparisons of Childhood Asthma Control Test (C-ACT) to Global Initiative for Asthma (GINA) guidelines and physician assessment of asthma control.

	Correlation/agreement/discrimination between C-ACT and GINA or physician assessment				Receiver-operating characteristic (ROC) analysis	
Citation	Description	*r* Value	*p* Value	kappa	Description	Area under ROC curve
North America						
Liu et al.[11]	C-ACT and physician assessment		<0.0001			
Liu et al.[18]	C-ACT and physician assessment ("very poorly controlled" vs. "not well controlled")		<0.05		C-ACT and physician assessment	0.688
	C-ACT and physician assessment ("not well controlled" vs. "well controlled")		<0.001			
Todoric et al.[20]	C-ACT and physician assessment		0.10			
Asia (East, South, Southeast)						
Chen et al.[22]	C-ACT and physician assessment	0.219	<0.001			
Leung et al.[23]	C-ACT and GINA		<0.001			
Somashekar et al.[28]					C-ACT and GINA	0.647
Europe						
Koolen et al.[31]					C-ACT and GINA	0.89 (95% CI 0.82–0.96)
Waibel et al.[32]	C-ACT and GINA		0.000			
Middle East						
Sekerel et al.[38]	C-ACT and physician assessment (visit 1)	0.65	<0.001			
	C-ACT and physician assessment (visit 2)	0.38	<0.001			
	C-ACT and physician assessment (visit 3)	0.41	<0.001			
Shefer et al.[40]	C-ACT and physician assessment		<0.001	0.529		
AlTeneiji et al.[41]	C-ACT and GINA		<0.001		C-ACT and GINA	0.898 (95% CI 0.83–0.96)
South America						
Oliveira et al.[12]	C-ACT and GINA		<0.01			
Africa						
Green et al.[43]	C-ACT and physician assessment			0.37		

Note: Definitions: Kappa, measure of agreement; *r* value, correlation coefficient.

perceived to be successful or adopted in practice and potentially as part of evidence-based guidelines. As we found, C-ACT correlates poorly with spirometry findings, and a significant degree of caution should be incorporated when interpreting these findings in both the clinical and research contexts.

The results of our systematic review suggest a need for further studies exploring how individual or cultural tailoring could be applied effectively to the C-ACT in clinical and research settings. It is unclear what form of tailoring would be most effective. One possibility is that the phrasing of the C-ACT could be altered to be more culturally appropriate or the pictures of the child's face on the C-ACT could be adapted to better reflect the population of patients being assessed, as the current features and facial expressions of the face on the C-ACT may not be universal.[55,56] Another option is that cut-offs of the C-ACT could be altered for different populations, but it is uncertain whether this adjustment could be effectively implemented and whether it would be most effective at the level of the individual, community, or racial/ethnic/national group. There is some evidence that cultural tailoring can result in positive outcomes for children and adolescents with asthma, for example in asthma education programs, but this research has been limited.[57,58] More studies are needed to assess the impact of the changes to the questionnaire, determine their effect on the validity of the C-ACT, as well as separate effects of nationality, race, ethnicity, and language on the C-ACT's validity and optimal cut-point. In doing these studies, it would be important to revalidate the C-ACT in a large, diverse population that is more representative of its widespread use. Inclusion of diverse groups may pose challenges given

TABLE 5 Comparisons of Childhood Asthma Control Test (C-ACT) to spirometry.

	Correlation/agreement between C-ACT and spirometry				Receiver-operating characteristic (ROC) analysis	
Citation	**Description**	***r* Value**	***p* Value**	**kappa**	**Description**	**Area under ROC curve**
North America						
Shi et al.[19]	C-ACT did not correlate with FEV1, FEF25-75 (percent predicted), FEV1/FVC ratio, or bronchodilator response of FEV1					
Todoric et al.[20]	C-ACT and FEV1>80%		0.0095	0.34		
Asia (East, South, and Southeast)						
Leung et al.[24]	Changes in C-ACT ascore and changes in FEV1		0.020			
Ito et al.[25]					Accuracy of C-ACT for screening asthmatic children with FEV1 > 80%	71.5% (95% CI = 62.8%–80.2%, $p < 0.001$)
Chalise et al.[27]	C-ACT and FEV1 (baseline)	0.772	<0.001			
	C-ACT and FEV1 (3 months)	0.815	<0.001			
	C-ACT and FEV1 (6 months)	0.908	<0.001			
Europe						
Waibel et al.[32]	C-ACT and FEV1	0.36	<0.000			
Voorend-Van Bergen et al.[35]	C-ACT and FEV1		0.72			
Middle East						
Sekerel et al.[38]	C-ACT and FEV1% (first visit)	0.11				
	C-ACT and FEV1% (second visit)	0.024	0.72			
	C-ACT and FEV1% (third visit)	0.007	0.92			
AlTeneiji et al.[41]	C-ACT and FEV1 (3 months)	0.48	<0.001			
	C-ACT and FEV1 (6 months)	0.558	<0.001			
	C-ACT and FEV1 (1 year)	0.421	<0.001			
South America						
Oliveira et al.[12]	C-ACT and spirometry	0.02	0.866			
Africa						
Green et al.[43]	C-ACT and FEV1			0.24		
	FEF25-75			0.18		
	PEFR			0.03		
	FEV1/FVC			0.00		

Note: Definitions: Kappa, measure of agreement; *r* value, correlation coefficient.

Abbreviations: FEF25-75, forced mid-expiratory flow; FEV1, forced expiratory volume in 1 s; FEVC, forced expiratory vital capacity; PEFR, peak expiratory flow rate.

historical underrepresentation in studies due to distrust in medical systems, requirement to travel, and inflexibility with work or childcare. Efforts that overcome some of these barriers, including leveraging the rise of telehealth, could help enhance participation of under-represented groups.

5 | LIMITATIONS

Studies were only included in our review if full-text English versions were available. Therefore, some articles, particularly those which may have been more likely to describe the use of the C-ACT in diversified or non-White populations, may have been excluded from our analysis. It is likely this methodology did not significantly affect our findings as the use of language restrictions in systematic review has been shown to have no systematic bias.[59] Although we sought to determine the validity of the C-ACT among children of varying cultural backgrounds, only nine of the 28 articles included reported participants' race or ethnicity.[12,18–21,39,42,43] Finally, it was difficult to compare the C-ACT to some measures, such as FeNO, because of the small number of papers that performed certain comparisons.

TABLE 6 Comparisons of Childhood Asthma Control Test (C-ACT) to fractional exhaled nitric oxide (FeNO).

Citation	Correlation/agreement between C-ACT and FeNO			
	r Value	*p* Value	*B* Value	kappa
Asia				
Leung et al.[24]		0.051	0.015	
Europe				
Voorend-Van Bergen et al.[35]		0.78		
South America				
Oliveira et al.[12]	0.035	0.753		
Africa				
Green et al.[43]				0.00

Note: Definitions: B value, logistic regression; Kappa, measure of agreement; *r* value, correlation coefficient.

6 | CONCLUSION

While studies have shown mixed levels of agreement or correlation between C-ACT and GINA guidelines or physician assessment of asthma control, agreement and correlation between C-ACT and spirometry are poor. Information is lacking on comparisons between C-ACT and FeNO and change in therapy, and findings on optimal cut-offs vary. More work is needed to identify ideal scoring cut-offs and examine different methods of cultural tailoring for the C-ACT. Given the high utilization of the C-ACT in clinical practice and research globally, proper validation across diverse populations is critical to maximize clinical confidence and minimize inequities in childhood asthma management.

AUTHOR CONTRIBUTIONS

Anna Volerman and Valerie G. Press conceptualized this study. Anna Volerman, Valerie G. Press, Jason T. Alexander, Mary Akel, Francesca Chu, and Nicole Kappel helped with design of the study. Francesca Chu, Nicole Kappel, and Anna Volerman assisted with data collection and analyses. Francesca Chu, Nicole Kappel, Mary Akel, and Anna Volerman interpreted the data. Francesca Chu initially drafted the manuscript. All authors critically revised the manuscript and approved the final work. All authors agree to be accountable for all aspects of the work.

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TABLE 7 Comparisons of Childhood Asthma Control Test (C-ACT) to change in therapy.

Citation	Correlation/agreement/discrimination between C-ACT and change in therapy			Receiver-operating characteristic (ROC) analysis	
	Description	*p* Value	*F* statistic	Description	Area under ROC curve
Asia					
Chen et al.[22]	Differences in C-ACT score by change in therapy status (step up vs. no change vs. step down)	<0.001	39.61		
Europe					
Perez-Yarza et al.[36]	Differences in C-ACT score by change in therapy status	<0.001			
Middle East					
AlTeneiji et al.[41]	C-ACT and change in therapy (step up vs. no change vs. step down)	<0.001		C-ACT classification of treatment change category	0.749 (95% CI 0.66–0.85)
South America					
Rodriguez-Martinez et al.[42]	Differences in C-ACT score by change in therapy status (step up vs. no change vs. step down)	<0.001			

Note: Definitions: *F* statistic, ANOVA test.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable as no new data were created or analyzed in this study.

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