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Allergology International xxx (xxxx) xxx

Contents lists available at ScienceDirect

Allergology International

journal homepage: http://www.elsevier.com/locate/alit

Original Article

Development and validation of a new asthma questionnaire to help achieve a high level of control in school-age children and adolescents

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ARTICLE INFO

Article history:
Received 26 July 2023
Received in revised form
17 October 2023
Accepted 1 November 2023
Available online xxx

Keywords:
Asthma
Children
Control status
Guidelines
Questionnaire

Abbreviations:
ACT-P, Asthma Control Test for Preschoolers; *ACT-S*, Asthma Control Test for School Children and Adolescents; AIC, Akaike's information criterion; AUC, area under the curve; FEV1, forced expiratory volume in 1 s; JPGL, Japanese Pediatric Asthma Guideline; ROC, receiver operating characteristic

ABSTRACT

Background: Maintaining good asthma control minimizes the risk of exacerbations and lung function decline and is a primary goal of asthma management. The Japanese Pediatric Asthma Guidelines (JPGL) employs different classification criteria for control status from other guidelines, stressing a higher level of control. Based on JPGL, we previously developed a caregiver-completed questionnaire for assessing and achieving best asthma control in preschoolers. In this study, we aimed to develop a questionnaire for school-age children and adolescents.

Methods: A working questionnaire comprising 14 items for patients and 34 items for caregivers was administered to 362 asthma patients aged 6–15 years and their caregivers. Separately, physicians filled out a questionnaire to determine JPGL-defined control. Logistic regression analysis was performed to construct a model to predict control levels using data from a randomly selected set of completed questionnaires from two-thirds of the subjects. Validation was performed using the remaining questionnaires.

Results: A set of 7 questions, encompassing self-assessed control status at the time of the visit and in the past month, and nocturnal/early morning asthma symptoms for patients and frequency of asthma symptoms, dyspnea, rescue beta-agonist use, and asthma hospitalization for caregivers, were selected and the 7-item model showed a good statistical fit with AIC of 110.5. The model has been named the Best Asthma Control Test for School Children and Adolescents (Best ACT-S). Best ACT-S scores differed significantly in the hypothetical direction among the groups of different JPGL-defined control levels, step-up/down treatment decisions, and presence/non-presence of exacerbations in the previous year.

Conclusions: The Best ACT-S is a valid questionnaire for children/adolescents aiming for best asthma control.

Introduction

Asthma control refers to the extent to which the manifestations of asthma have been controlled by treatment.[1] Maintaining good asthma control minimizes the risk of exacerbations and lung function decline,[2–6] and is a primary goal of asthma management.[7–9]

In addition to physician assessment and lung function testing, patient self-assessment is an important method of monitoring asthma.[10] Several questionnaire-based measures of asthma control

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Peer review under responsibility of Japanese Society of Allergology.
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https://doi.org/10.1016/j.alit.2023.11.001

are available, which involve a short set of questions for patients to answer about the status of their asthma.[10,11] For pediatric patients, these tools also require input from the child's caregiver (parent/guardian).[11]

The Japanese Society of Pediatric Allergy and Clinical Immunology[12] recommends that questionnaires suitable for assessing asthma control in children in Japan include the physician-completed Japanese Pediatric Asthma Control Program (JPAC)[13] and the patient/caregiver-completed Childhood Asthma Control Test (C-ACT)[14] for school-age children and adolescents, and the caregiver-completed Best Asthma Control Test for Preschoolers (Best ACT-P) for children of preschool-age.[15]

Amongst the patient-reported measures, the C-ACT, aimed at children aged 4–11 years, was developed in the USA and a verified Japanese translation is available; however, the evaluation of control is based on US guidelines.[14] The Japanese Pediatric Asthma Guidelines (JPGL) employs different classification criteria for control status compared with other guidelines, stressing a higher level of control.[9] Based on the JPGL, we developed the Best ACT-P, a questionnaire for assessing and helping to achieve complete asthma control in preschool children (aged <6 years) in Japan.[15]

Given the young age of the target preschool patient group, the Best ACT-P questionnaire is completed by their caregivers. In contrast, older children are capable of providing some information about their symptoms and asthma control level themselves. This can be helpful because parents may underestimate asthma symptoms and overestimate the level of asthma control in their child.[16,17] Therefore, it was decided to develop a similar questionnaire that was suitable for older children.

The aim of this study was to develop a simple pediatric asthma control questionnaire to assess the control status of school-age and adolescent pediatric asthma patients (aged 6–15 years) based on the high level of control specified by the Japanese guidelines.

Methods

This was a multicenter, cross-sectional observational study, with participants recruited from 11 pediatric clinics/hospitals across Japan. The study complied with the principles of the Declaration of Helsinki (2008) and the Ethical Guidelines for Clinical Research (July 31, 2008). Ethical approval was obtained from the Central Ethical Review Committee for Clinical Research at the National Hospital Organization Mie National Hospital (Approval number: 25–59).

Study population

The study population comprised Japanese children aged 6–15 years old who were diagnosed and being treated for bronchial asthma, and their caregivers (parents/guardians). Patients with concurrent illnesses that required treatment (other than non-severe allergic rhinitis and atopic dermatitis) were excluded, as were patients and caregivers who were unable, or found it difficult, to answer questions about asthma control status due to physical or mental problems. It was planned to enroll 500 children. When possible, spirometry was also performed.

Development of working questionnaire

A preliminary questionnaire involving open-ended questions was administered to patients and their caregivers, asking them to provide free-text responses to the questions “What is a bad asthma condition?”, and “What are the problems of having asthma?”, to elicit information about what they thought was relevant to asthma control.

Based on the answers to the preliminary questionnaire, a group of pediatric allergy specialists developed a working questionnaire for patients comprising 14 questions that were expected to be able to assess asthma control (Supplementary Table 1). Patients' description of their “asthma condition” in the preliminary questionnaire were classified into several concepts of asthma control, and working questions were developed using several slightly different expressions for each concept, while retaining the expressions used by the patients as much as possible.

The working questionnaire for caregivers used 34 questions from the working questionnaire that was developed for the Best ACT-P asthma control study (Supplementary Table 2).[15] Treating physicians completed a 10-item questionnaire (Supplementary Table 3) to determine JPGL-defined control status (Supplementary Table 4). The physician questionnaire, which was also developed for the Best ACT-P study,[15] consists of 6 questions about the frequency of moderate/severe symptoms, mild symptoms and rescue use of short-acting beta2 agonists (for evaluation of asthma control level), and 4 questions about exacerbation episodes in the past year, the need for change in controller medications, JPGL-defined severity, and physician-judged control level (for validation of the control test being developed). In the assessment of asthma control level, scores for moderate/severe symptoms ranged from 0 (none) to 100 (daily); scores for mild symptoms and rescue use of short-acting beta2 agonists ranged from 0 (none) to 50 (daily). Based on sum scores, patients were categorized as well-controlled (score 0), partially controlled (1–9), poorly controlled (10–99) or very poorly controlled (100). The classification ‘very poorly controlled’ is not defined in JPGL but was included to match the Global Initiative for Asthma Strategy (GINA) category of ‘uncontrolled’ asthma.[8]

Patient/caregiver pairs completed the working questionnaires. At the same time, treating physicians completed the physician questionnaire to determine JPGL-defined control status. Where possible, spirometry was performed on the same day.

Development of asthma control model

The completed questionnaires were randomly divided 2:1 into development and validation datasets by using simple random sampling without replacement (SRSWOR). Using the development dataset, a prediction model was constructed using logistic regression analysis, with the objective variable being the control level defined by the physician questionnaire (‘well controlled/partially controlled’ versus ‘poorly/very poorly controlled’) and the explanatory variable being each response to the working questionnaire. Independent analyses were conducted using either the patient response data or the caregiver response data as the explanatory variables. The best combination of questions from the two analyses was selected. Each selected question was scored using a 5-point scale (4, 3, 2, 1, 0), with higher scores indicating better control. The total score (the sum of the individual scores for each question) was then converted to a 0–28 point scale as the final Best ACT-S. The final model was then applied to the validation dataset to evaluate accuracy.

Statistical methods

Baseline variables were described using summary statistics, including mean and standard deviation (SD), median (minimum–maximum) or percentage as appropriate.

Spearman correlation coefficients between explanatory variables were calculated; for any two variables for which the coefficient was >0.9, only one of the variables was selected and the other discarded. Next, logistic regression analysis with backward stepwise elimination was performed to identify factors associated with

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the outcome (control status). Among several candidate regression models, the one with the lowest Akaike's information criterion (AIC) was selected, and a Hosmer–Lemeshow goodness-of-fit test was conducted to determine the area under the curve (AUC) of the receiver operating characteristic (ROC) curve, and the cutoff point at which the sensitivity and specificity were most appropriate. Internal consistency was evaluated using Cronbach's coefficient α. For external validation, the final model was applied to the validation dataset to confirm accuracy, based on sensitivity, specificity and AUC.

Clinical validation was performed using the physicians' ratings of control and severity, change in therapy and presence of exacerbations in the past year, as well as respiratory function results. One-way ANOVA was used for the known-group validation. Testing for a linear trend was performed to examine whether the mean scores in the groups increased (or decreased) systematically in the hypothetical direction. Statistical differences between 3 or more groups were determined by a Tukey–Kramer post hoc test. The effect size, R^2, was calculated as the fraction of the total variance accounted for by the linear trend.

All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and GraphPad Prism 9.1.

Results

Between October 2014 and March 2015, 362 asthma patients aged 6–15 years and their caregivers were enrolled and completed the relevant working questionnaires. Fewer cases than planned were enrolled due to slower than expected recruitment; however, a total of 362 cases was considered acceptable from a statistical perspective. The questionnaires were divided into a development dataset (n = 243 cases [both patient plus caregiver]) and validation dataset (n = 119).

Patient and caregiver characteristics

The demographics of patients and their caregivers, and patients' treatment characteristics, are summarized in Table 1. The mean age of the patients was 9.7 years, the majority were boys, and the most common treatments being used were inhaled corticosteroids and long-acting beta2 agonists. Most caregivers who completed questionnaires were mothers.

Table 1
Demographics of patients and their caregivers.

		Development dataset (n = 243)	Validation dataset (n = 119)
Patients who completed the 14-item questionnaire			
Age (year)	mean (SD)	9.7 (2.5)	9.7 (2.7)
Gender	boy/girl/not stated, n	155/87/1	77/40/2
Caregivers who completed the 34-item questionnaire			
Relationship to patient	mother/father/grand parent, n	228/8/7	104/9/6
Primary caregiver?	yes, n (%)	239 (98%)	114 (97%)
Treatment			
ICS	n (%)	228 (94%)	107 (90%)
ICS dose	median (min–max), μg	200 (50–400)	200 (50–400)
LABA	n (%)	55 (23%)	21 (18%)
LTRA	n (%)	177 (73%)	83 (70%)
Omalizumab	n (%)	6 (2%)	1 (0.8%)

ICS, inhaled corticosteroids; LABA, long-acting beta2 agonists; LTRA, leukotriene receptor antagonists; SD, standard deviation.

Table 2
Asthma control defined by physicians' questionnaire and lung function testing.

		Development dataset	Validation dataset
Control levels based on JPGL criteria		(n = 243)	(n = 119)
Well controlled	n (%)	101 (42%)	48 (40%)
Partially controlled	n (%)	69 (28%)	33 (28%)
Poorly controlled	n (%)	63 (26%)	31 (26%)
Very poorly controlled	n (%)	10 (4%)	7 (6%)
FEV1 % predicted by control level		(n = 64)	(n = 25)
Well controlled	mean (SD), n	94.8 (9.5), 26	89.4 (6.2), 10
Partially controlled	mean (SD), n	93.8 (14.7), 20	98.9 (11.4), 9
Poorly controlled	mean (SD), n	82.7 (10.0), 14	97.8 (16.3), 6
Very poorly controlled	mean (SD), n	87.2 (20.9), 4	No data

FEV1, forced expiratory volume in 1 s; JPGL, Japanese Pediatric Asthma Guideline; SD, standard deviation.

Asthma control

Table 2 summarizes asthma control as assessed by the physicians (10-item questionnaire) and based on spirometry-assessed lung function.

Model development

Logistic regression analysis of the development dataset identified 7 questions as meeting the criteria for assessment of good asthma control (Table 3). The selected items included 3 from the patient questionnaire (self-assessed control status at the time of the visit and in the past month, nocturnal/early morning asthma

Table 3
Questions selected in a logistic regression model for Best ACT-S.

Questions and response options	Adjusted OR	95% CI	P value
Patient Q1: How is your asthma condition today? A1: very good, good, a little bad, bad, very bad	1.772	1.052 –2.985	0.0315
Patient Q8: How was your asthma condition in the past month? A1: very good, good, a little bad, bad, very bad	2.657	1.692 –4.174	<0.0001
Patient Q13: Do you have cough, wheeze, or hiss when you go to bed at night or wake up in the morning because of your asthma? A13: never, no, sometimes, yes, all the time	1.510	1.055 –2.160	0.0242
Caregiver Q5: How often did your child have coughing, wheezing and/or whistling in the last 4 weeks? A5: none, once in 4 weeks, 2–3 times in 4 weeks, every week, daily	2.720	1.643 –4.503	0.0001
Caregiver Q7: How often did your child have difficulty breathing due to coughing, wheezing and/or whistling in the last 4 weeks? A7: none, once in 4 weeks, 2–3 times in 4 weeks, every week, daily	13.16	2.220 –78.001	0.0045
Caregiver Q20: How often did your child require medication -oral medication, inhalation, patch, etc. – for asthma attacks due to coughing, wheezing, and/or whistling in the last 4 weeks? A20: none, once in 4 weeks, 2–3 times in 4 weeks, every week, daily	2.130	1.303 –3.483	0.0026
Caregiver Q29: How often was your child hospitalized for wheezing and/or whistling in the last 1 year? A29: none, once, 2 times, 3 times, 4 times, or more	7.123	1.373 –36.948	0.0194

A, answer; CI, confidence interval; OR, odds ratio; Q, question.

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symptoms) and 4 from the caregiver questionnaire (frequency of asthma symptoms, dyspnea, rescue beta-agonist use, and asthma hospitalization). The 7-item model, which showed good statistical fit with an AIC of 110.5 and AUC of 0.934, was named the Best Asthma Control Test for School Children and Adolescents (Best ACT-S). With respect to internal consistency, Cronbach's coefficient α was 0.952 and 0.837 in the development and validation datasets, respectively.

Accuracy and validity

ROC curves of Best ACT-S scores for the discrimination of 'well controlled/partially controlled' versus 'poorly controlled/very poorly controlled' asthma based on JPGL classification are shown for the development and validation datasets in Figure 1. The AUC was 0.9126 (95% CI 0.8689–0.9563) in the development dataset and 0.8615 (95% CI 0.7795–0.9435) in the validation dataset.

The performance of Best ACT-S for screening control levels specified in the JPGL guideline was evaluated, and a cut-off score of 25 provided the best balance between sensitivity and specificity and best discrimination between patients with 'well controlled/partially controlled' versus 'poorly controlled/very poorly controlled' symptoms, in both the development and validation datasets (Table 4).

The ability of Best ACT-S to discriminate 'well controlled' asthma from other levels of control ('partially/poorly/very poorly controlled'), and to discriminate 'very poorly controlled' asthma from other levels of control (well/partially/poorly controlled) were also evaluated, and a cut-off score of 27 and 18 appeared the best balance between sensitivity and specificity to discriminate 'well controlled' and 'very poorly controlled' from other levels of control, respectively (Supplementary Table 5, 6). Due to the small number of patients with control levels in the categories at both ends, the cutoff values for the maximum Youden index in the development and validation datasets did not match; however, we chose these cutoff values for future clinical applications and higher specificity.

Best ACT-S scores differed in the hypothetical direction among the individual control levels (well controlled, partially controlled, poorly controlled, very poorly controlled) in both the development and validation datasets (Fig. 2), with the highest scores seen for 'well-controlled' asthma and the lowest scores seen for 'very poorly controlled' asthma. Based on ANOVA and a Tukey–Kramer post hoc test, significant differences were found between individual control levels, except between 'well controlled' and 'partially controlled' in the development dataset. Stratified analysis by age group (6–9, 10–12, and 13–15 years) yielded similar results (Supplementary Table 7).

Table 4
Cutoff scores of Best ACT-S for differentiation of patients with 'well controlled/partially controlled' versus 'poorly controlled/very poorly controlled' asthma symptoms.

Cutoff point	Sensitivity	Specificity	PPV	NPV	Correctly assessed	Youden
Development dataset (n = 243)						
<22	0.971	0.550	0.830	0.892	0.842	0.521
<23	0.927	0.667	0.863	0.800	0.847	0.593
<24	0.890	0.767	0.896	0.754	0.852	0.656
<25	**0.816**	**0.850**	**0.925**	**0.671**	**0.827**	**0.666**[†]
<26	0.699	0.933	0.960	0.577	0.770	0.632
<27	0.552	0.967	0.974	0.487	0.679	0.518
<28	0.353	0.983	0.980	0.401	0.546	0.336
Validation dataset (n = 119)						
<22	0.971	0.550	0.830	0.892	0.842	0.521
<23	0.927	0.667	0.863	0.800	0.847	0.593
<24	0.890	0.767	0.896	0.754	0.852	0.656
<25	**0.816**	**0.850**	**0.925**	**0.671**	**0.827**	**0.666**[†]
<26	0.699	0.933	0.960	0.577	0.770	0.632
<27	0.552	0.967	0.974	0.487	0.679	0.518
<28	0.353	0.983	0.980	0.401	0.546	0.336

NPV, negative predictive value; PPV, positive predictive value.
[†] Largest Youden index value and corresponding figures are shown in bold.

Best ACT-S scores also differed in the hypothetical direction based on physicians' step-up/step-down treatment decisions and physicians' rating of asthma control (Fig. 3), with significant differences observed between categories based on ANOVA, except between treatment 'step down' and 'no change' in the development dataset and between 'step up' and 'no change' in the validation dataset. Best ACT-S scores also differed in the hypothetical direction based on JPGL-defined severity (Supplementary Table 8), and were significantly higher in the patients who had asthma exacerbations in the previous year than those who did not (Supplementary Table 9). Lung function differed significantly between high and low Best ACT-S scores (cut-off score 25) in the development dataset but not the validation dataset (Fig. 4).

Discussion

The Best ACT-S questionnaire was developed to assess asthma control level, in order to help achieve best asthma control, in children aged 5–16 years.

Evaluation of asthma control is an important part of the management of patients with the disease. Current poor control is

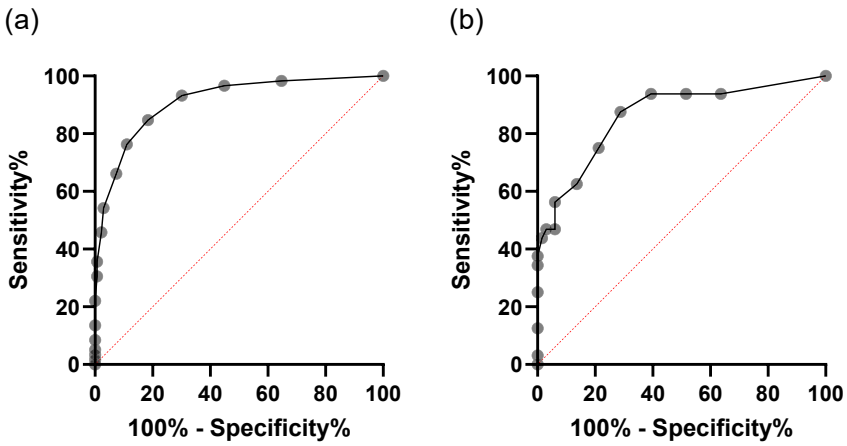

Fig. 1. Receiver operating characteristic (ROC) curves of Best ACT-S scores to discriminate 'well controlled/partially controlled' versus 'poorly controlled/very poorly controlled' based on JPGL classification in **(a)** the development dataset, and **(b)** the validation dataset.

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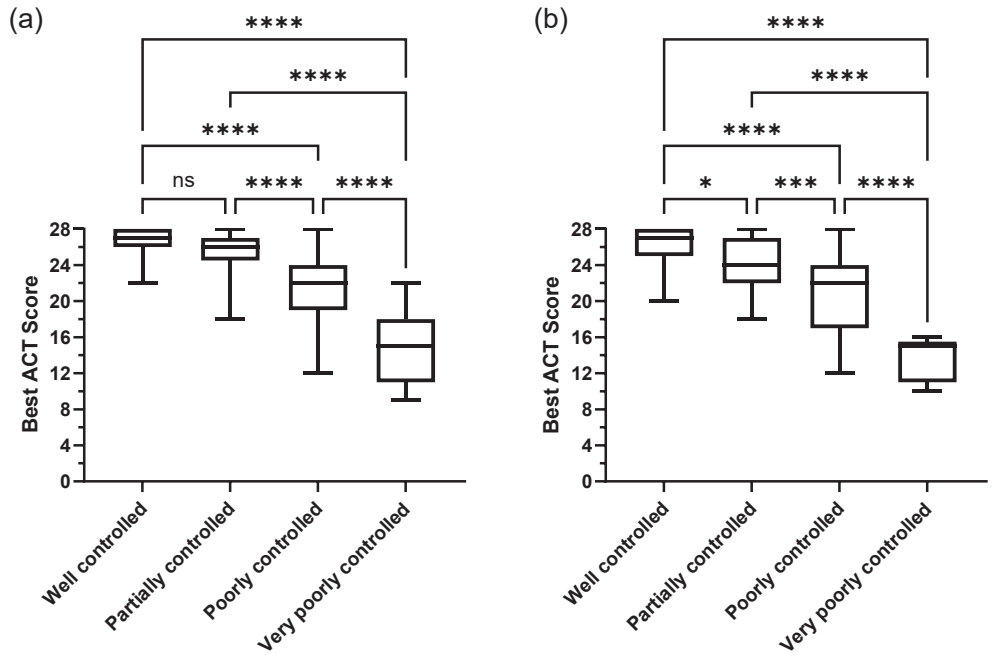

Fig. 2. Best ACT-S scores with modified JPGL classifications of control in **(a)** the development dataset, and **(b)** the validation dataset. Box and whisker plots: bottom of box = 25th percentile, middle = median, top = 75th percentile; lower end of whisker = 2.5th percentile, top end of whisker = 97.5th percentile. ANOVA followed by Tukey–Kramer post-hoc test, *p < 0.05, ***p < 0.001, ****p < 0.0001.

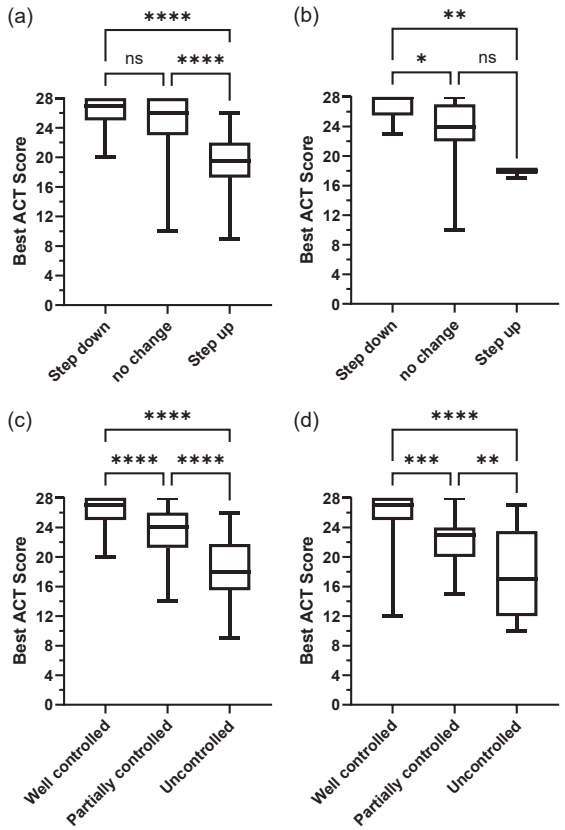

Fig. 3. Evaluation of criterion-based validity of Best ACT-S. Top: Physician's recommendation for change in therapy in **(a)** the development dataset, and **(b)** the validation dataset. Bottom: Physician's rating of asthma control in **(c)** the development dataset, and **(d)** the validation dataset. Box and whisker plots: bottom of box = 25th percentile, middle = median, top = 75th percentile; lower end of whisker = 2.5th percentile, top end of whisker = 97.5th percentile. ANOVA followed by Tukey's multiple comparisons test, *p < 0.05, **p < 0.01, ***p < 0.001, ****p < 0.0001.

predictive of poor control in the future,[2] and poor control is associated with an increased risk of exacerbations and other severe asthma-related healthcare events, and with worse lung function.[2,3,5,6,18] It has been shown that it is possible to achieve guideline-derived asthma control in most patients.[19]

Various patient-reported measures are available to evaluate asthma control in children.[10,11] They allow standardized assessment and provide a quick overview of a patient's asthma control level during treatment.[11] The 7-item C-ACT is a widely used validated instrument for children aged 4–11 years, which includes a visual scale to assist the child in responding to questions about perception of asthma control, limitations of activities, coughing and nocturnal awakening, as well as questions for their caregiver about daytime symptoms, daytime wheezing and nocturnal awakenings.[14] However, it was developed in a predominantly White US population and there is evidence that it may need some level of cultural tailoring to improve validity in diverse populations.[20] In addition, the evaluation of control in C-ACT is based on US guidelines and does not necessarily meet the medical needs in Japan, where a higher level of asthma control may be aimed for.[9] For example, patients can have symptoms for up to 2 days per week and be classified as well controlled according to the US guidelines,[21] whereas they would be classified as poorly controlled according to the JPGL.[9]

We developed a simple questionnaire to be completed by the patient and their caregiver, based on the JPGL classification of control. In the latest JPGL update, the categories are termed 'good', 'relatively good' and 'poor'.[9] However, at the time the model was developed, JPGL used the terms 'well controlled', 'partially controlled' and 'poorly controlled',[12] and we have retained this terminology for our model. The final model comprised 7 questions, 3 of which were answered by the child and 4 by their caregivers. It showed good discrimination between 'well controlled/partially controlled' and 'poorly controlled/very poorly controlled' (based on JPGL classification), with an AUC of 0.913 in the development dataset and 0.862 in the validation dataset. It also showed good discrimination between 'well controlled' asthma and lower levels

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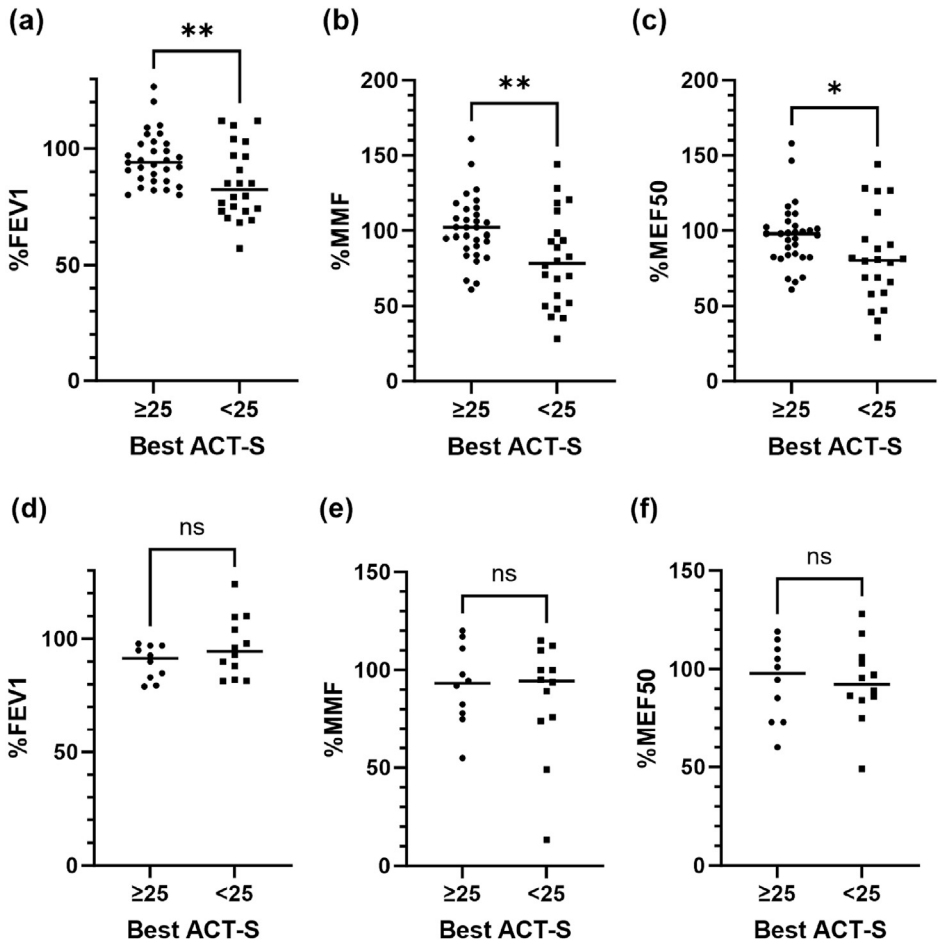

Fig. 4. Comparison of lung function between high and low Best ACT-scores for the development dataset **(a,b,c)** and the validation dataset **(d,e,f)**. Student t test, *p < 0.05, **p < 0.01, ns = not significant. %FEV1 = forced expiratory volume in 1 s % predicted, %MEF50 = maximal expiratory flow at 50% of the forced vital capacity % predicted, %MMF = mean maximal flow % predicted.

of asthma control. Best ACT-S scores differed in the expected direction across the individual control levels, and based on step-up/step-down treatment decisions, physician's rating of asthma control, and lung function.

Lung function reflects the physiological properties of the lungs and is an important biomarker for asthma severity, control, and future outcomes.[22,23] However, lung function measurements in children are more variable than in adults due to both the physiology of the chest wall muscles as well as cognitive development, which may influence test quality and biological variability.[24] As a result, a lack of correlation between lung function and clinical phenotypes of asthma has been reported[25,26] and evaluation of asthma should be comprehensive, including control levels. Nonetheless, in this study, lung function parameters in subjects with low Best ACT-S scores were significantly lower than those with high scores in the development cohort. Due to the highly variable nature of lung function measurement in children, the lack of the trend in the validation cohort with fewer subjects may have been inevitable. In addition, there was no subject who experienced hospitalization due to asthma exacerbation (which could affect lung function) within the past 4 weeks and only 1 subject within the past 12 months in the validation dataset, whereas there were 3 subjects with hospitalization within the past 4 weeks and 12 months in the development dataset (data not shown). Further studies are needed to confirm that Best ACT-S may represent lung function in children and adolescents.

We previously developed the Best ACT-P questionnaire for preschool children, a validated instrument that is completed by parents/guardians.[15] As a starting point for the development of the Best ACT-S questionnaire in the current study, we were able to use the working questionnaire for caregivers and the physician questionnaire that had both been developed as preparation for constructing the Best ACT-P instrument. The two questionnaires can serve as companion instruments for use in relevant pediatric age groups when aiming for best possible asthma control.

The main limitation of the current study is that fewer patients were enrolled than were planned, which could potentially have affected some results. For example, although clear trends were evident, statistical significance was not achieved in all ANOVA analyses, possibly because of the smaller sample size. In addition, the instrument was developed in a Japanese population, and further studies will be needed to confirm it is appropriate for use in other populations. Another limitation may be the wide age range covered by the Best ACT-S, from 6 to 15 years old. There may be differences in understanding between younger children and adolescents for the same questions. Parents may not be fully aware of the health status of their adolescents. To address this issue, we conducted a post-hoc analysis by age group and found an identical trend in each age group. Therefore, the questionnaire we developed can be applied for all ages from 6 to 15 years.

In conclusion, the patient/caregiver-completed Best ACT-S questionnaire has been developed to assess asthma control level,

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and to help achieve best asthma control, in children aged 6–15 years. It was developed and validated in a Japanese population and additional studies are needed to validate its use in ethnically and culturally diverse populations around the world.

Acknowledgments

Funding for the study was received from the Waksman Foundation of Japan INC. Medical writing and editing assistance were provided by Content Ed Net (Auckland, New Zealand).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.alit.2023.11.001.

Conflict of interest

The authors have no conflict of interest to declare.

Authors' contributions

All authors contributed to this manuscript. TF was responsible for the study concept, planning and design. MN, MI, CM, MK, YY, and AT were involved in data collection. TF, MM, and YS performed the data analysis, and TF, MN and MM interpreted the results. MM and TF contributed to the writing of the manuscript, and IM provided critical revision of the manuscript. All authors approved the final version for submission.

References

1. Taylor DR, Bateman ED, Boulet LP, Boushey HA, Busse WW, Casale TB, et al. A new perspective on concepts of asthma severity and control. *Eur Respir J* 2008;**32**:545–54.
2. Sullivan SD, Wenzel SE, Bresnahan BW, Zheng B, Lee JH, Pritchard M, et al. Association of control and risk of severe asthma-related events in severe or difficult-to-treat asthma patients. *Allergy* 2007;**62**:655–60.
3. Racine G, Forget A, Moullec G, Jiao T, Blais L, Lemiere C. Predictors of asthma control and exacerbations: a real-world study. *J Allergy Clin Immunol Pract* 2021;**9**:2802–11. e2.
4. Castillo JR, Peters SP, Busse WW. Asthma exacerbations: pathogenesis, prevention, and treatment. *J Allergy Clin Immunol Pract* 2017;**5**:918–27.
5. Kaminsky DA, Irvin CG. What long-term changes in lung function can tell us about asthma control. *Curr Allergy Asthma Rep* 2015;**15**:505.
6. Heijkenskjöld Rentzhog C, Janson C, Berglund L, Borres MP, Nordvall L, Alving K, et al. Overall and peripheral lung function assessment by spirometry and forced oscillation technique in relation to asthma diagnosis and control. *Clin Exp Allergy* 2017;**47**:1546–54.
7. Papadopoulos NG, Arakawa H, Carlsen KH, Custovic A, Gern J, Lemanske R, et al. International consensus on (ICON) pediatric asthma. *Allergy* 2012;**67**:976–97.
8. Reddel HK, Bacharier LB, Bateman ED, Brightling CE, Brusselle GG, Buhl R, et al. Global Initiative for Asthma Strategy 2021: executive summary and rationale for key changes. *Eur Respir J* 2021;**59**:2102730.
9. Adachi Y, Takizawa T, Futamura M, Fujisawa T, Yoshihara S, Committee for Japanese Pediatric Guideline for the Treatment and Management of Asthma Japanese Society of Pediatric Allergy and Clinical Immunology, et al.. Executive summary: Japanese pediatric guideline for the treatment and management of asthma (JPGL) 2020. *Allergol Int* 2022;**71**:472–80.
10. Alzahrani YA, Becker EA. Asthma control assessment tools. *Respir Care* 2016;**61**:106–16.
11. Voorend-van Bergen S, Vaessen-Verberne AA, Landstra AM, Brackel HJ, van den Berg NJ, Caudri D, et al. Monitoring childhood asthma: web-based diaries and the asthma control test. *J Allergy Clin Immunol* 2014;**133**:1599–605. e2.
12. Hamasaki Y, Kohno Y, Ebisawa M, Kondo N, Nishima S, Nishimuta T, et al. Japanese guideline for childhood asthma 2014. *Allergol Int* 2014;**63**:335–56.
13. Nishimuta T, Satou K, Ebisawa M, Fujisawa T, Mizuuchi H, Ikeda M, et al. Investigation of the correlation between and interchangeability of the Japanese pediatric asthma control program (JPAC) and the childhood asthma control test (C-ACT). *Nihon Shoni Arerugi Gakkaishi [Jpn J Pediatr Allergy Clin Immunol* 2009;**23**:129–38.
14. Liu AH, Zeiger R, Sorkness C, Mahr T, Ostrom N, Burgess S, et al. Development and cross-sectional validation of the childhood asthma control test. *J Allergy Clin Immunol* 2007;**119**:817–25.
15. Sato K, Sato Y, Nagao M, Shimojo N, Yoshihara S, Adachi Y, et al. Development and validation of asthma questionnaire for assessing and achieving best control in preschool-age children. *Pediatr Allergy Immunol* 2016;**27**:307–12.
16. Carroll WD, Wildhaber J, Brand PL. Parent misperception of control in childhood/adolescent asthma: the Room to Breathe survey. *Eur Respir J* 2012;**39**:90–6.
17. Voorend-van Bergen S, Brackel H, Caudri D, de Jongste J, Pijnenburg M. Assessment of asthma control by children and parents. *Eur Respir J* 2013;**41**:233–4.
18. Papakosta D, Latsios D, Manika K, Porpodis K, Kontakioti E, Gioulekas D. Asthma control test is correlated to FEV1 and nitric oxide in Greek asthmatic patients: influence of treatment. *J Asthma* 2011;**48**:901–6.
19. Bateman ED, Boushey HA, Bousquet J, Busse WW, Clark TJ, Pauwels RA, et al. GOAL Investigators Group. Can guideline-defined asthma control be achieved? The Gaining Optimal Asthma ControL study. *Am J Respir Crit Care Med* 2004;**170**:836–44.
20. Chu F, Kappel N, Akel M, Press VG, Alexander JT, Volerman A. Validity of the childhood asthma control test in diverse populations: a systematic review. *Pediatr Pulmonol* 2023;**58**:1322–36.
21. National Asthma Education and Prevention Program. Expert Panel Report 3 (EPR-3): guidelines for the diagnosis and management of asthma-summary report 2007. *J Allergy Clin Immunol* 2007;**120**(5 Suppl):S94–138.
22. Moeller A, Carlsen KH, Sly PD, Baraldi E, Piacentini G, Pavord I, et al. Monitoring asthma in childhood: lung function, bronchial responsiveness and inflammation. *Eur Respir Rev* 2015;**24**:204–15.
23. Gaffin JM, Petty CR, Sorkness RL, Denlinger LC, Phillips BR, Ly NP, et al. Determinants of lung function across childhood in the severe asthma Research program (SARP) 3. *J Allergy Clin Immunol* 2023;**151**:138–46. e9.
24. Stanojevic S, Kaminsky DA, Miller MR, Thompson B, Aliverti A, Barjaktarevic I, et al. ERS/ATS technical standard on interpretive strategies for routine lung function tests. *Eur Respir J* 2022;**60**:2101499.
25. Verini M, Rossi N, Dalfino T, Verrotti A, Di Gioacchino M, Chiarelli F. Lack of correlation between clinical patterns of asthma and airway obstruction. *Allergy Asthma Proc* 2001;**22**:297–302.
26. Mogensen I, Hallberg J, Ekstrom S, Bergstrom A, Melen E, Kull I. Uncontrolled asthma from childhood to young adulthood associates with airflow obstruction. *ERJ Open Res* 2021;**7**:00179-2021.

List of Supplementary Tables

Supplementary Table 1　14-Item working questionnaire for patients aged 6–15 years

Please circle the answer which applies to you.

1）How is your asthma condition today?

Very Good　Good　A Little Bad　Bad　Very Bad

2）Do you cough because of your asthma?

Never　No　Sometimes　Yes　All The Time

3）Have you felt out of breath because of your asthma?

Never　No　Sometimes　Yes　All The Time

4）Have you ever experienced any chest pain or tightness because of your asthma?

Never　No　Sometimes　Yes　All The Time

5）Have you ever experienced any puffing and panting because of your asthma?

Never　No　Sometimes　Yes　All The Time

6）Have you ever woken up in the middle of the night coughing or being out of breath?

Never　No　Sometimes　Yes　All The Time

7）Do you feel troubled in your daily life because of asthma?

Not at all　No　A Little　Yes　All The Time

8） How is your asthma condition in the past month?

Very Good　Good　A Little Bad　Bad　Very Bad

9） Have you ever experienced any puffing and panting during PE class or club activities?

Never　No　Sometimes　Yes　All The Time

10） Do you have any problems during PE class or club activities because of your asthma?

Not at all　No　A Little　Yes　All The Time

11） Have you ever experienced any puffing and panting when inhaling smoke or cold air?

Never　No　Sometimes　Yes　All The Time

12） Do you wake up in the middle of the night because of your asthma?

Never　No　Sometimes　Yes　All The Time

13） Have you ever experienced any puffing and panting when sleeping at night because of your asthma?

Never　No　Sometimes　Yes　All The Time

14） Do you have any problems at school because of your asthma?

Never　No　Sometimes　Yes　All The Time

Thank you for your participation!

Supplementary Table 2 The 34-item working questionnaire for caregivers.

The following questions are about how often your child has had asthma-related symptoms in the last 4 weeks. Even though questions may appear to be similar or repeated, answer all questions.

		None	Once in 4 weeks	2-3 times in 4 weeks	Every week	Daily
Q. 01	How often did your child have wheezing and/or whistling when exhaling (breathing out) in the last 4 weeks?	□	□	□	□	□
Q. 02	How often did your child have coughing in the last 4 weeks?	□	□	□	□	□
Q. 03	How often did your child have wheezing and/or whistling during a common cold in the last 4 weeks?	□	□	□	□	□
Q. 04	How often did your child have coughing during a common cold in the last 4 weeks?	□	□	□	□	□
Q. 05	How often did your child have coughing, wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□

The following questions are about the frequency of intense (strong) asthma symptoms occurring with dyspnea (shortness of breath) that your child has had in the last 4 weeks. Answer all questions even though some appear to be similar or repeated.

		None	Once in 4 weeks	2-3 times in 4 weeks	Every week	Daily
Q. 06	How often did your child breathe hard with shoulders rising and falling even at rest in the last 4 weeks?	□	□	□	□	□
Q. 07	How often did your child appear to have difficulty breathing due to coughing, wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□
Q. 08	How often did wheezing and/or whistling keep your child from playing and eating meals in the last 4 weeks?	□	□	□	□	□

The following questions are about the frequency of asthma symptoms that your child has had at night and morning in the last 4 weeks. Even though questions may appear to be similar or repeated, answer all questions.

		None	Once in 4 weeks	2-3 times in 4 weeks	Every week	Daily
Q. 09	How often did your child not sleep well due to nighttime coughing, wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□
Q. 10	How often was your child unable to sleep at night or did your child wake in the early morning due to coughing, wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□
Q. 11	How often did your child wake due to nighttime coughing, wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□

The following questions are about the frequency of disruption of daily life due to asthma symptoms that your child has had in the last 4 weeks. Even though questions may appear to be similar or repeated, answer all questions.

		None	Once in 4 weeks	2-3 times in 4 weeks	Every week	Daily
Q. 12	How often did your child have to be absent from a childcare center or kindergarten or you have to change your family schedule due to your child's wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□
Q. 13	How often were you prevented from doing household tasks and work due to your child's wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□
Q. 14	How often were you unable to sleep at night due to your child's wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□

The following questions are about the frequency of asthma symptoms triggered by slight stimulation that your child has had in the last 4 weeks. Even though questions may appear to be similar or repeated, answer all questions

		None	Once in 4 weeks	2-3 times in 4 weeks	Every week	Daily
Q. 15	How often did your child have coughing, wheezing and/or whistling when romping, running around, or crying intensely in the last 4 weeks?	□	□	□	□	□
Q. 16	How often did your child have coughing, wheezing and/or whistling after breathing smoke from cigarettes/fireworks, etc., dust, or cold air in the last 4 weeks?	□	□	□	□	□

The following questions are about the severity of asthma symptoms that your child has had in the last 4 weeks. Even though questions may appear to be similar or repeated, answer all questions.

		None	Mild	Slightly severe	Severe	Very severe
Q. 17	How severe has your child's coughing, wheezing and/or whistling been in the last 4 weeks?	□	□	□	□	□
Q. 18	How severe has nighttime coughing, wheezing and/or whistling been in the last 4 weeks?	□	□	□	□	□
Q. 19	How severe has coughing, wheezing and/or whistling been when your child was romping, running around, or crying intensely in the last 4 weeks?	□	□	□	□	□

The following questions are about how often your child had to be treated for asthma in the last 4 weeks. Even though questions may appear to be similar or repeated, answer all questions.

		None	Once in 4 weeks	2-3 times in 4 weeks	Every week	Daily
Q. 20	How often did your child require medication – oral medication, inhalation, tape, etc. – for asthma attacks due to coughing, wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□
Q. 21	How often did your child require inhaled medication for asthma attacks due to coughing, wheezing and/or whistling in the last 4 weeks? Note: For cases of medication for asthma attacks taken or inhaled continuously for several days, count the frequency as "once."	□	□	□	□	□

The following questions are about how often treatment for intense asthma attacks was required for your child in the last 4 weeks. Even though questions may appear to be similar or repeated, answer all questions.

		None	Once	Twice	3 times	4 times or more
Q. 22	How often was your child hospitalized for wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□
Q. 23	How often was your child administered oral steroids – Predonin, Rinderon, Decadron, etc. – in the last 4 weeks?	□	□	□	□	□
Q. 24	How often did your child have unscheduled visits to medical institutions – unscheduled visits in the daytime, after-hours such as at night or on holidays – due to wheezing and/or whistling in the last 4 week?	□	□	□	□	□
Q. 25	How often was your child administered drip infusions or injections for wheezing and/or whistling at outpatient clinics in the last 4 weeks? Note: For cases of steroids taken or inhaled continuously for several days, count the frequency as "once."	□	□	□	□	□

The following questions are about how often visiting an emergency room or hospitalization was required for your child in the last 3 months or 1 year. Even though questions may appear to be similar or repeated, answer all questions.

		None	Once	Twice	3 times	4 times or more
Q. 26	How often did your child have unscheduled visits to medical institutions – unscheduled visits in the daytime, after-hours such as at night or on holidays – due to wheezing and/or whistling in the last 3 months?	□	□	□	□	□
Q. 27	How often was your child hospitalized for wheezing and/or whistling in the last 3 months?	□	□	□	□	□
Q. 28	How often did your child have unscheduled visits to medical institutions – unscheduled visits in the daytime, after-hours such as at night or on holidays – due to wheezing and/or whistling in the last 1 year?	□	□	□	□	□
Q. 29	How often was your child hospitalized for wheezing and/or whistling in the last 1 year?	□	□	□	□	□

The following questions are about how often your child has had asthma-related symptoms in the last 4 weeks. Even though questions may appear to be similar or repeated, answer all questions.

		None	Occasionally	Sometimes	Often	Always
Q. 30	How often did your child have wheezing and/or whistling when breathing out in the last 4 weeks?	□	□	□	□	□
Q. 31	How often did your child have coughing in the last 4 weeks?	□	□	□	□	□
Q. 32	How often did your child have wheezing and/or whistling during a common cold in the last 4 weeks?	□	□	□	□	□
Q. 33	How often did your child have coughing during a common cold in the last 4 weeks?	□	□	□	□	□
Q. 34	How often did your child have coughing, wheezing and/or whistling in the last 4 weeks?	□	□	□	□	□

Supplementary Table 3　Physician's questionnaire assessing asthma control

Q1　How often have obvious asthma symptoms associated with dyspnea or continuing for one or more days occurred?

(1) none for 3 months or longer; (2) none within 1 month but any within 3 months; (3) once or more but less than 4 times in the past month; (4) 4 times or more in the past month

Q2　How often did mild asthma symptoms such as coughing or wheezing of short duration occur in the last 4 weeks?

(1) none; (2) once or more but less than 4 times in the past month; (3) more than once per week, not daily; (4) daily

Q3　How often did symptoms suggesting airway hyperresponsiveness triggered by intense crying, hard laughing, romping, etc., occur in the past 4 weeks?

(1) none; (2) once or more but less than 4 times in the past month; (3) more than once per week, not daily; (4) daily

Q4　How often was the child patient's daily living disturbed by asthma in the past 4 weeks?

(1) none; (2) once or more but less than 4 times in the past month; (3) more than once per week, not daily; (4) daily

Q5　How often did the child patient wake up during the night due to coughing or wheezing in the past 4 weeks?

(1) none; (2) once or more but less than 4 times in the past month; (3) more than once per week, not daily; (4) daily

Q6　How often did you use β2-stimulator to treat asthma in the past 4 weeks?

(1) none; (2) once or more but less than 4 times in the past month; (3) more than once per week, not daily; (4) daily

Q7　How often was the child patient hospitalized or treated with systemic steroids – oral and/or intravenous – for asthma exacerbation in the past year?

(1) none; (2) 1 time; (3) 2 times; (4) 3 times or more

Q8　Overall, what is the severity (based on symptoms regardless of treatment) of the patient? Note: Use JPGL2008 criteria.

(1) intermittent; (2) mild persistent; (3) moderate persistent; (4) severe persistent

Q9　Did you change the controller medication on this visit?

(1) stepped down; (2) no change; (3) stepped up

Q10　Overall, how has the child patient's asthma control been in the past 4 weeks? Note: Base this answer on criteria you consider appropriate.

(1)　well-controlled; (2) partially controlled; (3) poorly controlled; (4) not controlled

Supplementary Table 4 JPGL classification of asthma control in children aged 0–15 years

	Totally controlled[a]	Well controlled[a]	Uncontrolled[a]
Minor asthma symptoms[b]	None	≥1x/mo, <1x/wk	≥1x/wk
Major asthma symptoms[c]	None	None	≥1x/mo
Limitation of activities	None	None (or minimal)	≥1x/mo
Rescue use of SABA	None	≥1x/mo, <1x/wk	≥1x/wk

a. Current control status is assessed based on asthma-related symptoms during the previous 4 weeks.

b. Minor asthma symptoms: transient/short-lasting wheeze or cough after exercise, laughing/crying, or at wake-up, and night-time cough of short duration without awakening.

c. Major asthma symptoms: severe cough or wheeze with dyspnea lasting/recurring day and night.

JPGL = Japanese Pediatric Guidelines for the treatment and management of bronchialAsthma;
SABA = short acting beta2 adrenergic agonists.

Supplementary Table 5 Cutoff scores of Best ACT-S: well controlled versus partially controlled/ poorly controlled/very poorly controlled

Cutoff point	Sensitivity	Specificity	PPV	NPV	Correctly assessed	Youden
Development dataset (n=243)						
22	1.000	0.316	0.497	1.000	0.592	0.316
23	0.937	0.385	0.507	0.900	0.607	0.321
24	0.911	0.462	0.533	0.885	0.643	0.373
25	0.861	0.556	0.567	0.855	0.679	0.416
26	0.785	0.684	0.626	0.825	0.724	0.469
27	0.671	0.795	0.688	0.782	0.745	0.466
28	0.456	0.889	0.735	0.707	0.714	0.345
Validation dataset (n=119)						
22	0.977	0.382	0.500	1.000	0.561	0.359
23	0.954	0.491	0.494	1.000	0.551	0.444
24	0.861	0.582	0.478	1.000	0.520	0.442
25	0.837	0.727	0.457	1.000	0.480	0.565
26	0.744	0.818	0.443	1.000	0.449	0.562
27	0.605	0.855	0.439		0.439	0.459
28	0.465	0.891	0.439		0.439	0.356

NPV = negative predictive value, PPV = positive predictive value.

Supplementary Table 6 Cutoff scores of Best ACT-S: well controlled/partially controlled/poorly controlled versus very poorly controlled

Cutoff point	Sensitivity	Specificity	PPV	NPV	Correctly assessed	Youden
Development dataset (n=243)						
17	0.625	0.957	0.385	0.984	0.944	0.5824
18	0.875	0.931	0.350	0.994	0.929	0.8059
19	0.875	0.915	0.304	0.994	0.913	0.7899
20	0.875	0.872	0.226	0.994	0.872	0.7473
21	0.875	0.840	0.189	0.994	0.842	0.7154
22	1	0.777	0.160	1.000	0.786	0.7766
Validation dataset (n=119)						
17	1.000	0.925	0.417	1.000	0.929	0.925
18	1.000	0.893	0.333	1.000	0.898	0.893
19	1.000	0.871	0.294	1.000	0.878	0.871
20	1.000	0.850	0.263	1.000	0.857	0.850
21	1.000	0.817	0.227	1.000	0.827	0.817
22	1.000	0.742	0.172	1.000	0.755	0.742

NPV = negative predictive value, PPV = positive predictive value.

Supplementary Table 7 Age group-stratified evaluation of the criterion-based validity of Best ACT-S: control levels

		Control levels Best ACT-S score, mean (SD), n				ANOVA		Test for linear trend	
		Well-controlled	Partially controlled	Poorly controlled	Very poorly controlled	F	P value	R^2	P value
Development dataset									
Age group (years)	6-9	26.5 (1.8), 38	25.4 (2.2), 21	20.9 (3.4), 32	15.8 (4.8), 5	42.7	<0.001	0.58	<0.001
	10-12	27.0 (1.6), 30	25.3 (2.5), 23	21.5 (3.6), 15	14.0 (-), 1	22.8	<0.001	0.51	<0.001
	13-15	26.0 (2.3), 11	26.2 (2.0), 13	22.2 (2.9), 5	14.0 (5.7), 2	16.4	<0.001	0.65	<0.001
Validation dataset									
Age group (years)	6-9	25.8 (2.4), 19	23.8 (3.3), 12	21.0 (4.3), 16	14.0 (2.8), 2	11.3	<0.001	0.43	<0.001
	10-12	27.0 (2.0), 14	25.3 (2.1), 8	21.1 (4.1), 10	13.3 (2.9), 3	23.5	<0.001	0.69	<0.001
	13-15	26.7 (0.9), 10	26.0 (1.7), 3	12.0 (-), 1	-	77.0	<0.001	0.93	<0.001

Supplementary Table 8 Evaluation of the criterion-based validity of Best ACT-S: JPGL-defined severity levels

	Severity				ANOVA		Test for linear trend	
	Intermittent	Mild persistent	Moderate persistent	Severe persistent	F	P value	R^2	P value
Development dataset								
n	126	45	21	6				
Best ACT-S score, mean (SD)	26.2 (2.2)	22.3 (3.5)	21.7(5.1)	16.5 (1.8)	40.6	<0.001	0.39	<0.001
Validation dataset								
n	59	24	9	3				
Best ACT-S score, mean (SD)	25.8 (2.5)	21.8 (3.7)	16.8 (4.3)	15.7 (8.1)	30.4	<0.001	0.50	<0.001

Supplementary Table 9　Evaluation of the criterion-based validity of Best ACT-S: exacerbations in the previous year

	N	Mean (SD)	P
Development dataset			
No exacerbations	177	24.9 (3.4)	<0.0001
Exacerbations	22	21.0 (5.6)	
Validation dataset			
No exacerbations	87	25.3 (0.6)	<0.0001
Exacerbations	8	16.1 (5.3)	

Supplementary Table 10　List of investigators

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