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Development and validation of asthma questionnaire for assessing and achieving best control in preschool-age children

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Abstract

Background: Several patient/caregiver-completed questionnaires have been utilized for assessment of asthma control. However, due to the diversity in medical/social circumstances, they may not be optimal for use in all countries. The Japanese pediatric asthma guideline (JPGL) aims at higher levels of control compared to other international guidelines, based on a strong social demand for best care. We developed a new control test to help meet that demand.

Methods: A 34-item working questionnaire was developed based on input from pediatric asthma specialists and the caregivers of preschool children with asthma. The questionnaire was administered to caregivers of 565 patients aged <6 years who had physician-diagnosed asthma or β_2 -agonist-responsive recurrent wheeze. Then, 6 questions for assessing JPGL-defined control levels were selected from the 34 questions by stepwise logistic regression methods using randomly

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selected questionnaires completed by two-thirds of the caregivers. We named that set of questions the Best Asthma Control Test for Preschoolers (Best ACT-P). Validation of Best ACT-P was performed using the remaining completed questionnaires.

Results: The 6 questions asked about the frequency/severity of cold-induced wheeze, nighttime awakening, exercise-induced symptoms and disruption of family life due to asthma in the past 4 weeks and hospitalization in the past 12 months. The 6-item logistic model showed good statistical fit, and the scores for the physicians' ratings of the asthma control differed significantly in the hypothetical direction.

Conclusions: Best ACT-P is a valid caregiver-completed questionnaire of asthma control in preschoolers in whom total control needs to be achieved.

Keywords

asthma; control; caregiver-completed questionnaire; control test; preschool children

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Introduction

Most childhood asthma starts in preschool age, and young children with asthma, compared with older children, have a greater risk of exacerbation, often induced by viral respiratory infections. In a longitudinal study, children with severe

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asthma already had a lower FEV1 at age 9 (1), suggesting that the deficit had developed at an earlier age. and early effective control of the disease may be vital to improve the long-term outcome. On the other hand, a significant portion of early wheezers commonly regress completely during the preschool years (2). Imprudent, prolonged asthma treatment of this group may lead to overuse of medication. Accurate assessment of the control level is critical for avoiding both over- and under-treatment.

Several easy-to-administer, patient/caregiver-completed questionnaires aimed at assessing asthma control have been developed (3-5) and are being used not only in the country of origin but in many other countries as well (6, 7). However, due to the diversity in medical and social circumstances, they may not be optimal for use in all countries. In fact, inconsistency has been reported (8, 9) between the childhood asthma control test (C-ACT) (4), a widely-used control test for children with asthma, and the Global Initiative for Asthma (GINA) (10) guideline-based asthma control measure. Medical delivery systems, socioeconomic status and cultural background may affect the assessment of control.

The Japanese pediatric asthma guideline (JPGL) was first published in 2000 and has been updated about every 3 years, with the most recent version released in 2012 (11). One of the major differences between JPGL and other international guidelines such as GINA (10) is the severity criteria. For an untreated patient with asthma, manifestation of asthma symptoms more than once a month, but less than once a week, is classified as mild persistent severity in the JPGL, which recommends starting anti-inflammatory treatment with a low-dose inhaled corticosteroid (ICS). JPGL also defines 'well-controlled' as asymptomatic normal functioning (Table E3), under the condition that close monitoring is properly performed to avoid overdosing (11). This is partly because of universal health coverage and the high expectation of the populace for optimal health in Japan. There remains a strong need for a simple—yet reliable—measurement tool to assess asthma control in young children, aiming for best control. While C-ACT (4) and TRACK (5) were developed to identify children whose asthma is inadequately controlled, a test to achieve a higher level of control may be useful (12). We have

developed and validated a standardized, caregiver-completed tool for assessing asthma control in young children based on JPGL. We have named it the Best Asthma Control Test for Preschoolers (Best ACT-P). This article details the development and cross-sectional validation of Best ACT-P.

Methods

Development of the working questionnaire

Initial working questions were generated based on the replies of 20 caregivers of children (<6 y.o.) with symptomatic asthma to an open question of “Please describe the condition of your child when his/her asthma is bad”, and input from 7 pediatric allergy specialists. Then the questions were refined to develop a 34-item working questionnaire, including 21 questions on the frequency and severity of asthma-like symptoms, 5 on the effect of those symptoms on the child’s life, and 7 on asthma medication and health care use. A standard recall period of 4 weeks was decided for questions on symptoms in order to allow evaluation of recent asthma control, and 3 different recall periods of 4 weeks, 3 months and 1 year were decided for questions concerning severe exacerbations to assess the risk domain of asthma. A 5-point scale for the frequency of symptoms was decided based on the JPGL severity criteria (13, 14) (i.e., “none”, “once in 4 weeks”, “2–3 times in 4 weeks”, “every week” and “daily”). Another 5-point scale was employed for the frequency of severe exacerbation episodes in each recall period (i.e., “none”, “once”, “twice”, “3 times” and “4 times or more”) and 2 Likert scales were also used for the frequency (i.e., “none”, “occasionally”, “sometimes”, “often” and “always”) and the severity (i.e., “none”, “mild”, “slightly severe”, “severe” and “very severe”) of symptoms (Table E1).

Cross-sectional study design

A cross-sectional, nonrandomized study was conducted to identify and validate a subset of questions from the 34-item working questionnaire for inclusion in the final Best ACT-P. Study participants were recruited from 16 hospitals and 13

primary care clinics across Japan. Institutional review boards (IRB) at the participating hospitals approved the study. The Central IRB at Shimoshizu National Hospital approved the study to be performed at the clinics. All caregivers gave informed consent.

Caregivers of <6 y.o. children who met the study inclusion/exclusion criteria at the time of a visit, either scheduled or unscheduled, to a physician were invited to participate in the study. To avoid possible selection bias, the study physicians continuously invited caregivers to participate throughout the study period. Caregivers were eligible to participate if they were the main caregiver who took care of the child day and night and were able to understand and complete the questionnaire. Inclusion criteria for the children were a diagnosis of asthma or a history of 3 or more episodes of wheezing, shortness of breath or cough, at least one of which was relieved by an oral/inhaled beta2 agonist. The exclusion criteria were respiratory conditions not consistent with asthma, presence of other significant chronic disorders or congenital abnormalities, or enrollment in another clinical trial.

Data collection

Data were obtained from eligible caregivers and their physicians. During the child's visit to the physician, the caregiver completed the 34-item working questionnaire. Independently, the physician—blinded to the caregiver's questionnaire replies—completed a 10-item questionnaire (Table E2). The replies of the physicians were used to classify the control level of each child and to establish criterion (concurrent) validity. For determination of the control level based on the JPGL 2012 classifications (Table E3), 6 questions about the frequency of moderate/severe symptoms (Qs 1, 4 and 5), mild symptoms (Qs 2 and 3) and rescue use of a short-acting beta2 agonist (SABA) (Q6) were used. The frequency was graded from “none” to “daily” using a 4-point scale based on the JPGL severity criteria (11). Since the severity of symptoms is different in each question, we gave a graded score to each reply in order to fit the JPGL 2012 classifications. For moderate/severe symptoms, score 0 was given to “none”, score

5 to “none in previous 4 weeks but some in previous 3 months”, 10 to “once or more but less than 4 times during the past month”, 50 to “more than once per week, not daily” and 100 to “daily”. For mild symptoms and rescue use of SABA, 0 was given to “none”, 1 to “once or more but less than 4 times during the past month”, 10 to “more than once per week, not daily” and 50 to “daily”. The control level of each patient was then determined based on the sum of scores from the 6 questions as follows: 0, well-controlled; 1~9, partially controlled; 10~99, poorly controlled; and 100~, very poorly controlled. “Very poorly controlled” was defined to match the GINA classification of “uncontrolled”, although it is not defined in the control classifications in JPGL 2012.

Four other questions asked physicians about exacerbation episodes requiring hospitalization/systemic corticosteroid use in the past year, the JPGL-defined asthma severity level, the need for change in the controller medication, and the physician-judged control level. The replies to these 4 questions were used to validate Best ACT-P.

Statistical analysis

Data from the study were used to develop and then validate Best ACT-P. Two-thirds of the questionnaires that caregivers completed were randomly selected for use as the development dataset, and the remaining one-third were used as the validation dataset. Detailed methods for statistical analysis were described in Electronic repository (E: Statistical methods).

Validation of English translation

All questionnaires were administered in Japanese. A native English translator translated them into English. Then a native Japanese translator who was blind to the nature of the study translated the English version back into Japanese. Thereafter, the investigators who developed the questionnaire confirmed that there was no cultural bias between the original and translated questionnaires.

Results

Patient characteristics

Informed consent was obtained from 565 caregivers of preschool children with asthma. Fifty-three questionnaires were excluded because of incomplete replies or violation of the inclusion criteria. The remaining 512 questionnaires were randomly divided into 2 datasets, for development (n=341) and validation (n=170). Table 1 shows the demographic data for the patients and their caregivers, who completed the 34-item working questionnaire.

Item selection

Logistic regression analysis of the development questionnaire dataset identified 6 questions as meeting the selection criteria for assessment of good control (well-controlled/partially controlled vs. poorly controlled/very poorly controlled). The 6 questions were Q3 (wheezing episodes related to a common cold in 4 weeks), Q9 (nighttime awakening due to asthma symptoms in 4 weeks), Q12 (disruption of patient/family life due to asthma symptoms), Q17 (subjective severity of asthma symptoms), Q19 (subjective severity of exercise-induced symptoms) and Q29 (hospitalization events in the past year due to asthma) (Table 2). The 6-question logistic model showed good statistical fit and discriminant ability, with an AIC of 291.5, a *P* value of 0.964 in the Hosmer-Lemeshow goodness-of-fit test, and an AUC of 0.8873 (Fig. 1a). The 6 selected questions were evaluated for meaning, relevance to the ideal concept of control in young children and language clarity by the study group, and they were accepted as the components of the Best ACT-P questionnaire. The questionnaire was then tested further in the development and validation datasets.

Internal consistency

Cronbach's coefficient α for the 6-item Best ACT-p was 0.796 and 0.774 in the development and validation datasets, respectively, and satisfied the recommended minimum level of 0.7.

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Assessment accuracy

The assessment accuracy of the entire scale across all scores (0-24) provided an area under the ROC curve (AUC) of 0.8873 (95% confidence interval: 0.8485 to 0.9199) and 0.8604 (95% confidence interval: 0.8049 to 0.9159) for the development and validation datasets, respectively (Fig. 1). Then the performance of Best ACT-P in screening control levels defined in JPGL were tested and a cutoff score of 21 provided the best balance between sensitivity and specificity and the best discrimination between children with controlled and uncontrolled symptoms based on the AUC for both datasets, respectively (Table 3).

Next, we examined the ability of Best-ACT-P to discriminate “well-controlled” from the other levels of control. The AUC remained high at 0.8802 (95% confidence interval: 0.8427 to 0.9177) and 0.9050 (95% confidence interval: 0.8640 to 0.9460) in the development and validation datasets, respectively. A cutoff score of 23 provided the best balance between sensitivity and specificity and the best discrimination between children with well-controlled and the other levels based on the AUC in both datasets (Table E4).

We also tested whether Best-ACT-P can differentiate “very poorly controlled” from the other levels of control and found that the AUC for this analysis was also high, 0.905 (95% confidence interval: 0.8640 to 0.9460) for the development dataset. A cutoff score of 18 provided the best balance between sensitivity and specificity and the best discrimination between children with very poorly controlled and the other levels based on the AUC in both datasets (Table E5).

Criterion-based validity

The Best ACT-P scores for the JPGL-defined classifications of asthma control differed significantly among the 4 groups of children (well-controlled, partially controlled, poorly controlled, very poorly controlled) in the development ($F=114.1$, $P<0.0001$) and validation ($F=38.47$, $P<0.0001$) datasets. A linear trend test confirmed the hypothetical direction, with the highest score for well-controlled and the lowest for very poorly controlled in the development (slope= -1.538 ,

$R^2=0.462$, $P<0.0001$) and validation (slope= -1.53 , $R^2=0.2981$, $P<0.0001$) datasets (Fig 2a, 2b). Similar trends were observed for the physicians' ratings of control (Table E6), JPGSL-defined asthma severity levels (Table E7), physician-recommended changes to therapy with asthma controller medications (Table E8) and frequency of exacerbation events that required hospitalization or systemic corticosteroid use in the previous year (Table E9).

Discussion

Patient or caregiver-completed questionnaires for asthma control, such as C-ACT for children aged 4–11 years (4) and TRACK for children aged <5 years (5), are very useful for assessing control levels, especially in identifying poorly controlled patients. But as the goal of asthma treatment is to achieve total control of the disease, a test designed to assess success or failure in achieving that goal would be useful. Accordingly, we developed the present control test, Best ACT-P

Best ACT-P, consisting of 6 questions, was demonstrated to have good internal consistency, with Cronbach's coefficients of 0.796 and 0.774, and good discriminant ability for incomplete control, with AUCs of 0.8873 and 0.8604, for the development and validation datasets, respectively. Those coefficients are comparable to the 0.880 reported for TRACK (5). In addition, Best ACT-P showed good discrimination of totally controlled asthma from the insufficiently controlled levels, and showed its usefulness in accurately assessing poorly controlled asthma.

Recently, TRACK was validated in Spain (15) and Turkey (16), and we also considered translating and validating it in Japan. However, our specialists concluded that differences in the medical environment might interfere with the use of TRACK in Japan. TRACK tries to detect asthma exacerbation by asking about the use of oral corticosteroids, as shown in Q5 (17), but oral corticosteroids are often avoided due to possible ineffectiveness in young children (18) and, in Japan, the need for hospitalization for close monitoring is high. Actually, in this study, our working questionnaire included questions asking about the use of oral corticosteroids, but they were not statistically selected for inclusion in Best

ACT-P. Instead, a question asking about hospitalization was included. Although the indications for asthma hospitalization may differ among countries, hospitalization clearly implies severe exacerbation.

Diagnosis of asthma in preschool children is not easy, and use of the word “asthma” has been carefully avoided for this age group (19). Criteria for preschool wheezing disorders remain to be established (20). One limitation of our study lies in this context. The inclusion criteria for this study were physician-diagnosed asthma or recurrent wheezing with proven beta-agonist responsiveness. This may not be sufficient for a proper diagnosis of “asthma”, and our study population thus may be contaminated with non-asthma cases. However, this was a multi-center study, and the study subjects were recruited among patients who had been treated as asthma cases by the study pediatricians. Since guidelines recommend early step-down of asthma treatment in young children, it is highly probable that patients who had been followed up and were still on medication at the time of inclusion in the study were true asthma cases. In addition, after initial differential diagnosis, pediatricians have to treat young children with problematic recurrent wheezing regardless of future outcomes (20). Best ACT-P may be useful in this regard as well.

In conclusion, we have developed Best ACT-P, a valid caregiver-completed questionnaire of asthma control in preschoolers that may be useful for assessing and monitoring patients in whom total control is needed. Validation studies of Best ACT-P are necessary for it to be used widely around the world.

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Conflicts of Interest

T. Fujisawa reports receiving grant support through his institution from GlaxoSmithKline, Kaketsuken and Pfizer Inc., and lecture fees from GlaxoSmithKline, MSD and Kyorin Pharmaceuticals.

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Figure legends

Figure 1 Receiver operating characteristic (ROC) curves of Best ACT-P scores to discriminate “well-controlled”/“partially controlled” patients and “poorly controlled”/“very poorly controlled” patients based on the JPGL 2012 control classifications in the development (a) and validation (b) databases.

Figure 2 Box and whisker plots of Best ACT-P scores with JPGL classifications of control in the development dataset (a) and validation dataset (b). The bottom of the box plot indicates the 25th percentile, the middle indicates the median and the top indicates the 75th percentile of the data. The lower end of a whisker indicates the 2.5th percentile, and the top end indicates the 97.5th percentile. Outliers are plotted as dots.

Table 1. Demographic data of caregivers and their children.

	Development dataset (n=342)	Validation dataset (n=170)
Age in months	44.6 (6 - 71)	42.7 (10 – 71)
Gender (M/F/not stated)	208/104/20	113/57/10
Person who completed the questionnaire		
Mother	323 (94.4%)	160 (94.1%)
Father	10 (2.5%)	9 (5.3%)
Grandparent	8 (2.3%)	1 (0.6%)
Other	1 (0.3%)	0 (0%)

Table 2. Summary of logistic regression analysis on 6 questions selected for Best ACT-P.

Question and reply options	Adjusted odds ratio	95% confidence interval		P
Q3: How often did your child have wheezing and/or whistling during a common cold in the last 4 weeks? A3: None, Once in 4 weeks, 2-3 times in 4 weeks, Every week, Daily	2.003	1.277	3.141	0.0025
Q9: How often did your child not sleep well due to nighttime coughing, wheezing and/or whistling in the last 4 weeks? A9: None, Once in 4 weeks, 2-3 times in 4 weeks, Every week, Daily	1.918	1.092	3.366	0.0234
Q12: 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? A12: None, Once in 4 weeks, 2-3 times in 4 weeks, Every week, Daily	3.501	1.486	8.248	0.0042
Q17: How severe has your child's coughing, wheezing and/or whistling been in the last 4 weeks? A17: None, Mild, Slightly severe, Severe, Very severe	2.253	1.359	3.735	0.0016
Q19: How severe has coughing, wheezing and/or whistling been when your child was romping, running around, or crying intensely in the last 4 weeks? A19: None, Mild, Slightly severe, Severe, Very severe	1.816	1.070	3.083	0.0272
Q29: How often was your child hospitalized for wheezing and/or whistling in the last <u>1 year</u> ? A29: Not once, Once, 2 times, 3 times, 4 times or more	1.695	1.108	2.593	0.0150

Table 3. Evaluation of cutoff scores of Best ACT-P: well-controlled/partially controlled v.s. poorly controlled/ very poorly controlled.

Cutoff point	Sensitivity	Specificity	PPV	NPV	Correctly assessed
Development dataset					
<18	0.482	0.978	0.969	0.574	0.689
<19	0.623	0.943	0.939	0.641	0.756
<20	0.728	0.894	0.906	0.701	0.797
<21	0.834	0.830	0.873	0.781	0.832
<22	0.904	0.605	0.762	0.819	0.780
<23	0.949	0.359	0.675	0.836	0.703
Validation dataset					
<18	0.462	0.969	0.961	0.521	0.653
<19	0.566	0.953	0.952	0.570	0.712
<20	0.726	0.891	0.917	0.663	0.788
<21	0.802	0.734	0.833	0.691	0.776
<22	0.896	0.625	0.798	0.784	0.794
<23	0.962	0.453	0.745	0.879	0.771

Figure 1

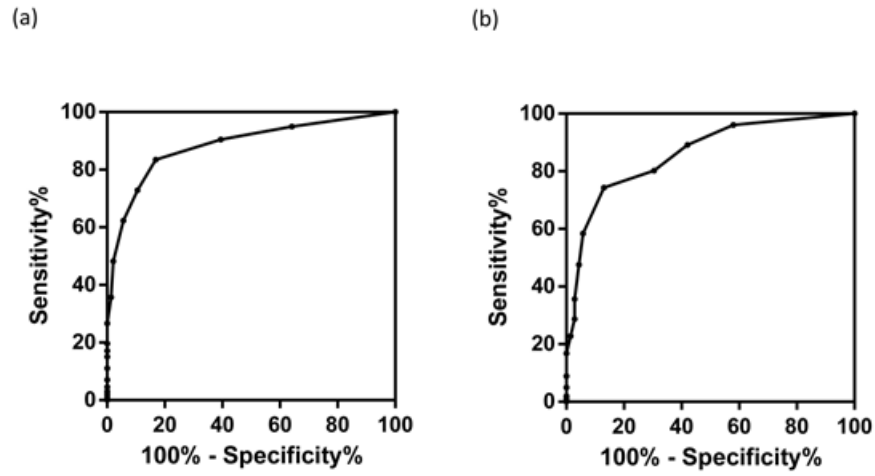


Figure 2

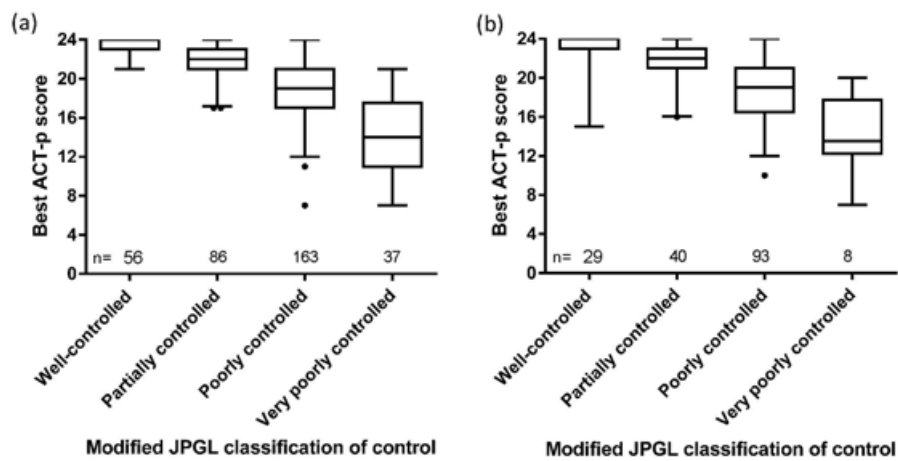


Table E1. The 34-item working questionnaire for caregivers

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 <u>3 months</u> ?	☐	☐	☐	☐	☐
Q. 27	How often was your child hospitalized for wheezing and/or whistling in the last <u>3 months</u> ?	☐	☐	☐	☐	☐
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 <u>1 year</u> ?	☐	☐	☐	☐	☐
Q. 29	How often was your child hospitalized for wheezing and/or whistling in the last <u>1 year</u> ?	☐	☐	☐	☐	☐

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?	☐	☐	☐	☐	☐

Table E2. Physician's questionnaire assessing asthma control

- Q. 1 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
- Q. 2 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
- Q. 3 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
- Q. 4 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
- Q. 5 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
- Q. 6 How often did you use β 2-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
- Q. 7 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
- Q. 8 Overall, what is the severity (based on symptoms regardless of treatment) of the patient?**
Note: Use JPGA2008 criteria.
(1) intermittent; (2) mild persistent; (3) moderate persistent; (4) severe persistent
- Q. 9 Did you change the controller medication on this visit?**
(1) stepped down; (2) no change; (3) stepped up
- Q. 10 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

Table E3. JPGL 2012 classifications of asthma control in children aged 0–15 years

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

#1 JPGL: Japanese Pediatric Guidelines for the treatment and management of bronchial asthma.

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

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

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

#5 SABA: short-acting beta2 adrenergic agonists.

Table E4. Evaluation of cutoff scores of Best ACT-P: well-controlled v.s. partially controlled /poorly controlled/ very poorly controlled.

Cutoff point	Sensitivity	Specificity	PPV	NPV	Correctly assessed
Development dataset					
<18	0.346	1.000	1.000	0.230	0.453
<19	0.462	1.000	1.000	0.267	0.550
<20	0.563	1.000	1.000	0.309	0.635
<21	0.661	0.964	0.990	0.358	0.711
<22	0.790	0.804	0.954	0.429	0.792
<23	0.902	0.589	0.918	0.541	0.851
Validation dataset					
<18	0.462	0.969	0.961	0.521	0.653
<19	0.566	0.953	0.952	0.570	0.712
<20	0.726	0.891	0.917	0.663	0.788
<21	0.802	0.734	0.833	0.691	0.776
<22	0.896	0.625	0.798	0.784	0.794
<23	0.962	0.453	0.745	0.879	0.771

Table E5. Evaluation of cutoff scores of Best ACT-P: Well-controlled/partially controlled/poory controlled v.s. very poorly controlled.

Cutoff point	Sensitivity	Specificity	PPV	NPV	Correctly assessed
Development dataset					
<18	0.800	0.766	0.247	0.976	0.769
<19	0.900	0.683	0.214	0.986	0.702
<20	0.967	0.587	0.184	0.995	0.620
<21	1.000	0.497	0.160	1.000	0.541
<22	1.000	0.359	0.130	1.000	0.415
<23	1.000	0.215	0.109	1.000	0.284
Validation dataset					
<18	0.938	0.753	0.283	0.991	0.771
<19	1.000	0.656	0.232	1.000	0.688
<20	1.000	0.539	0.184	1.000	0.582
<21	1.000	0.416	0.151	1.000	0.471
<22	1.000	0.286	0.127	1.000	0.353
<23	1.000	0.175	0.112	1.000	0.253

Table E6. Evaluation of the criterion-based validity of Best ACT-P: Physicians' ratings of control.

	Control rating				ANOVA		Test for linear trend	
	Well controlled	Partially controlled	Poorly controlled	Very poorly controlled	F	P value	R ²	P value
Development dataset								
n	72	160	91	19				
Best ACT-P score, mean (SD)	23.3 (1.1)	20.7 (2.7)	17.5 (3.4)	13.2 (4.0)	100.7	<0.0001	0.37	<0.0001
Validation dataset								
n	25	88	51	6				
Best ACT-P score, mean (SD)	22.7 (2.1)	21.1 (2.7)	17.7 (2.9)	12.0 (2.5)	43.8	<0.0001	0.31	<0.0001

Table E7. Evaluation of the criterion-based validity of Best ACT-P: 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	117	125	93	7				
Best ACT-P score, mean (SD)	22.3 (2.1)	19.5 (3.2)	18.1 (4.2)	12.9 (5.6)	42.4	<0.0001	0.13	<0.0001
Validation dataset								
n	60	63	42	5				
Best ACT-P score, mean (SD)	22.2 (2.2)	20.0 (2.6)	17.3 (3.7)	14.6 (5.7)	29.6	<0.0001	0.15	<0.0001

Table E8. Evaluation of the criterion-based validity of Best ACT-P: Recommended change in therapy.

	Physician's recommendation of change in therapy			ANOVA		Test for linear trend	
	Stepped-down therapy	No change in therapy	Stepped-up therapy	F	P value	R ²	P value
Development dataset							
n	24	253	65				
Best ACT-P score, mean (SD)	22.7 (1.8)	20.5 (3.4)	16.7 (3.7)	42.3	<0.0001	0.13	<0.0001
Validation dataset							
n	9	128	33				
Best ACT-P score, mean (SD)	22.4 (1.5)	20.6 (3.1)	16.6 (3.7)	42.4	<0.0001	0.11	<0.0001

Table E9. Evaluation of the criterion-based validity of Best ACT-P: Frequency of exacerbation.

	Number of exacerbations in the previous year				ANOVA		Test for linear trend	
	None	1 time	2 times	3 times or more	F	P value	R ²	P value
Development dataset								
n	204	81	25	32				
Best ACT-P score, mean (SD)	20.8 (3.1)	19.2 (4.1)	19.1 (3.7)	17.3 (4.7)	10.5	<0.0001	0.06	<0.0001
Validation dataset								
n	104	33	17	16				
Best ACT-P score, mean (SD)	20.6 (3.2)	19.9 (3.4)	18.2 (4.6)	17.7 (3.8)	5.1	0.002	0.07	0.0005