Original Article

Psychometric Properties of the Asthma Symptom Diary (ASD), a Diary for Use in Clinical Trials of Persistent Asthma

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What is already known about this topic? Asthma symptoms are highly variable, and symptom burden does not correlate well with clinical parameters. The asthma symptom diary was created with well-documented patient input.

What does this article add to our knowledge? This article documents the psychometric validation of a new valid and reliable patient-reported outcome asthma symptom measure.

How does this study impact current management guidelines? This study provides an asthma symptom measure that has well-documented content validity and good psychometric properties.

BACKGROUND: No currently available asthma symptom diary has sufficient validation to be recommended for use as a core asthma outcome measure.
OBJECTIVE: The objective of this study was to provide validation data for the 10-item asthma symptom diary (ASD).
METHODS: Data were collected in a 4-week prospective, observational study. Subjects completed 3 study visits, completing the ASD twice daily at home for 28 days. Psychometric properties in terms of dimensionality, reliability, validity, and responsiveness were assessed.
RESULTS: Data from 276 subjects were analyzed; mean age was 42.9 (standard deviation [SD] = 16.4) years, mean asthma duration was 23.3 (SD = 16.8) years, and 69.6% were female. Confirmatory factor and Rasch analysis supported the ASD as unidimensional and adequately measuring the spectrum of asthma symptom severity. High Cronbach's α (0.94) and intraclass correlation coefficients (0.89-0.95) supported reliability. A high correlation between the 7-day average ASD score and the Asthma Control Questionnaire (ACQ) total score ($r = 0.75$) and Asthma Quality of Life Questionnaire total scores ($r = -0.76$), and a moderate correlation with FEV_1% predicted ($r = -0.30$) supported convergent validity. Significant differences ($P < .001$) between groups classified by ACQ scores supported known-group validity. The 7-day average ASD scores were responsive to change, with significantly higher score changes ($P < .001$) in responders versus nonresponders. Minimally important differences were calculated and found to be in the range of 0.1-0.3.
CONCLUSION: Results of this study indicated that the ASD is a reliable and valid asthma symptom measure for use in adult and adolescent asthma patients to evaluate the effect of treatment on asthma in clinical trials. © 2015 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2015;■:■-■)

Key words: *Asthma; Symptoms; Patient-reported outcome; Psychometrics; Validity*

Asthma is a chronic respiratory illness characterized by airway remodeling, inflammation, and immunological hyperresponsiveness to allergens.[1] Approximately 300 million people worldwide suffer from this condition.[2] According to data from the 2011 National Health Interview Survey, asthma affected 17.5 million adults and 7.1 million children in the United States in 2009—a prevalence of 8.2% that has increased 1.2% annually

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Abbreviations used
ACQ- Asthma Control Questionnaire
AQLQ- Asthma Quality of Life Questionnaire
ASD- Asthma symptom diary
CDF- Cumulative distribution function
CFA- Confirmatory factor analysis
CFI- Comparative fit index
DIF- Differential item functioning
FEV_1- Forced expiratory volume in 1 second
ICC- Intraclass correlation coefficient
MID- Minimum important difference
PGIC- Patient global impression of change
PRO- Patient-reported outcome
RMSEA- Root mean square error of approximation
SD- Standard deviation
SEM- Standard error of measurement
WPAI- Work Productivity and Activity Impairment Questionnaire
WRMR- Weighted root mean square residual

between 2001 and 2009.[3] Uncontrolled asthmatics have been found to experience significantly reduced quality of life, as well as work productivity.[4] As the burden experienced by a patient as a result of a symptom does not correlate well with clinical measures,[5] direct patient reports, captured through patient-reported outcome (PRO) measures, are integral to defining asthma status and risk.[1,4] Asthma symptom diaries are recommended for research purposes, specifically for use in clinical trials to capture the variable nature of asthma symptoms. However, no currently available asthma symptom diary has sufficient evidence of validity to be recommended for use as a core asthma outcome measure.[6] A reliable and valid daily symptom diary may also be useful in clinical practice for patients with particularly severe or labile disease as it captures the variable nature of the disease and the patients' daily state on treatment.[1]

The aim of this study was to assess the validation properties of the Amgen asthma symptom diary (ASD). The original development of the ASD, involving qualitative concept elicitation and cognitive interviews with patients with asthma, is described in detail elsewhere.[7]

METHODS

Study design

This study was a 4-week multicenter, prospective, observational study, in which treatment was provided at the discretion of the individual investigator. A total of 276 adult (≥18 years) and adolescent subjects (≥12 years) with clinically diagnosed persistent asthma were recruited. The study objective was to assess the psychometric properties of the ASD. At each study visit (visit 1 [baseline]: day 1; visit 2: day 14 ± 3 days [ie, day 11-day 17]; visit 3: day 28 ± 3 days [ie, day 25-day 31]), subjects completed the Asthma Control Questionnaire (ACQ),[8] the Asthma Quality of Life Questionnaire (AQLQ12+),[9] and the Work Productivity and Activity Impairment Questionnaire: Asthma (WPAI-Asthma).[10] At all 3 study visits, clinical site principal investigators or designees performed spirometry after the participant completed the ACQ. At visit 1, a baseline clinical form was completed that captured clinical variables as well as the clinician's global impression of control (CGIC). At visits 2 and 3, subjects completed the patient global impression of change (PGIC) to assess severity of asthma symptoms since the last study visit. A follow-up clinical form was completed at visits 2 and 3, and this captured adherence to the ASD, exacerbations, change in controller medication, and a clinician assessment of change in asthma control (CAC) since the previous visit (Figure E1, available in this article's Online Repository at www.jaci-inpractice.org). During the study, subjects completed the ASD at home on an electronic device twice daily (upon awakening before taking asthma medication and in the evening before retiring to bed), beginning on the evening of visit 1 (day 1) and continuing until visit 3 (day 28 ± 3 days). Further clinical visit details are available in Table E1 in this article's Online Repository at www.jaci-inpractice.org. Institutional Review Board approval was obtained before study initiation.

Description of the asthma symptom diary

The ASD was developed based on concept elicitation and cognitive interviews with patients with clinically diagnosed persistent asthma. Five morning questions (denoted as AM items) assess nighttime symptom severity in relation to wheezing, shortness of breath, cough, and chest tightness, and the frequency of nighttime awakening. An additional morning item assessed duration of nighttime awakening (Table 4 in Globe et al[7]). However, after an initial analysis of the data, this item was found to have considerable overlap with the frequency of nighttime awakening item. This finding was confirmed in the original qualitative patient interviews, and through consultation with clinical experts, the item was removed to leave 5 morning items. A further 5 evening questions (denoted as PM items) assess symptom severity in relation to wheezing, shortness of breath, cough, and chest tightness, and activity limitation since waking. Items are scored from "0" (no symptom, no nighttime awakening, or no activity limitation) to "4" (very severe symptom, unable to sleep, or extreme activity limitation). A daily ASD score is the mean of the 10 items, and the mean of 7 consecutive daily scores is calculated as the "7-day average ASD score." Responses for all 10 items are required to calculate the daily ASD score; otherwise, it is treated as missing. Compliance was captured electronically. For the 7-day average asthma symptom score, scoring is done with no imputation using the mean of at least 4 of the 7 daily ASD scores as a mean weekly item score. The 7-day average ASD score ranges from 0 to 4.

Patient global rating of change. The PGIC is a single-item measure of the perceived change in asthma course since the prior visit with 7 response categories from "extremely better," to "no change," to "extremely worse."[11,12]

Clinician global rating of change. The CGIC is a single-item measure of the clinician-rated change in the patient's asthma since the prior visit with 5 response categories: "much worse," "worse," "no change," "better," and "much better."[11]

Statistical analyses

Classical test theory[13] as well as modern psychometric theory,[14] including Rasch analysis, was used to examine the psychometric properties of the 10-item ASD. Table I describes the statistical analysis used.

Item performance. The performance of the 10 ASD items was evaluated by means of descriptive item statistics (mean, standard deviation [SD]), percentage of lowest and highest responses (floor and ceiling effects, respectively), and item frequency distribution at visit 1.

Confirmatory factor analysis. Confirmatory factor analysis (CFA)[15] was conducted using visit 1 data to assess whether the ASD items fit the hypothesized unidimensional construct using Mplus software (Muthén & Muthén, Los Angeles, Calif).[16] The CFA