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Psychometric Evaluation of a New Electronic Pediatric Asthma Symptom Diary

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BACKGROUND

- As part of the evaluation of treatments for pediatric asthma in clinical trials, patient-reported outcomes (PRO) measures facilitating self-report by children are needed that have been developed following the United States Food and Drug Administration guidance and ISPOR good research practices.[1-3]
- To meet this need, we developed an electronic pediatric asthma symptom diary (ePASD) to assess the severity of daily asthma symptoms and proximal impacts in children aged 6 to 11 years with mild to severe asthma.[4]
- The ePASD is uniquely designed to be administered via a digital application with visuals, sounds, and written and audible text, which minimizes the importance of reading skills on children's ability to self-report accurately and reduces the bias of proxy report.
- The ePASD includes the following:
  - A nighttime diary (completed each morning): 5 items assessing nocturnal asthma symptoms (cough, wheeze, difficulty breathing), nighttime awakening due to asthma, and rescue medication use
  - A daytime diary (completed each evening): 7 items assessing daytime asthma symptoms (cough, wheeze, chest pain/tightness, difficulty breathing), activity limitations, and rescue medication use

OBJECTIVE

- The objective of this study was to perform an initial psychometric evaluation of the ePASD in children aged 6 to 11 years with mild to severe asthma to evaluate the structure, scoring, reliability, and validity of the ePASD.

METHODS

- This study utilized a prospective, usual-care, noninterventional, longitudinal design.
- Eligible English-speaking pediatric patients aged 6 to 11 years with mild to severe asthma (as defined by the Global Initiative for Asthma guidelines[5]) and their primary caregivers were recruited through qualitative research facilities in the United States.
- The children and caregivers received training and completed asthma-specific clinical outcome assessment (COA) questionnaires at 2 study visits (Table 1).
- Factor analyses, inter-item correlations, and internal consistencies guided ePASD scoring. Reliability, construct validity, and discriminating ability were evaluated for ePASD items and candidate composite scores.
- All tests are two-tailed with an alpha of 0.01 (unless otherwise noted).

Table 1. Schedule of Key Events and COAs for ePASD Validation Analyses

Procedures	Screening	Study visit 1 Day 1	Study Day 1 to EOS Day −1	EOS visit
Screening, demographics (patient and caregiver), and medical history (patient)	X			
ePASD			p.m. and a.m.	
ACQ-5, ACQ-IA-5, ACQ-IA-6, C-ACT, PAQLQ(S), PGIS, and CGIS		X		X
PGIC and CGIC				X
HCRU			p.m.	
EOS surveys and exit interview				X

ACQ-5 = Asthma Control Questionnaire, Symptoms Only; ACQ-IA-5 = Asthma Control Questionnaire–Interviewer Administered, Symptoms Only; ACQ-IA-6 = Asthma Control Questionnaire–Interviewer Administered 6; C-ACT = Childhood Asthma Control Test; CGIC = Caregiver Global Impression of Change; CGIS = Caregiver Global Impression of Severity; EOS = end of study; HCRU = healthcare resource utilization; PAQLQ(S) = Pediatric Asthma Quality of Life Questionnaire–Standardized; PGIC = Patient Global Impression of Change; PGIS = Patient Global Impression of Severity.

RESULTS

- This study commenced on 3 March 2020, but due to the spread of coronavirus disease 2019 and its health risks to pediatric patients with asthma, the study was paused on 14 March 2020, with 24 participants having completed the study in person at that time. The study resumed on 7 April 2021 with virtual data-collection procedures (i.e., no in-person study visits) with 67 additional participants.
- 91 children (n = 58, 63.7% male) aged 6 to 11 years with mild (n = 26, n = 28.6%), moderate (n = 40, 44.0%), or severe (n = 25, 27.5%) asthma and their caregivers participated.
- The HCRU questionnaire was completed electronically by caregivers at the end of every day. No overnight hospital stays were reported, but 4 emergency room visits, 2 urgent care visits, and 8 unplanned doctor visits were reported over the course of the study.

Item-Level Results and ePASD Structure

- The ePASD items displayed satisfactory test-retest reliability and acceptable construct validity.
- Despite the small sample size (N = 91), the confirmatory factor analysis results indicated that 5 ePASD composite scores were reasonable candidates for further evaluation. ePASD composite scores were computed as item averages, using the same 0-3 response scale as most ePASD items, with higher values reflecting worse symptoms and impacts.
  - Daytime Symptom score = average of Items D1 (Daytime Cough), D2 (Daytime Wheeze), D3 (Daytime Chest), and D4 (Daytime Breathing)
  - Daytime score = average of Items D1, D2, D3, D4, and D5 (Daytime Activities)
  - Nighttime Symptom score = average of Items N1 (Nighttime Cough), N2 (Nighttime Wheeze), and N3 (Nighttime Breathing)
  - Nighttime score = average of Items N1, N2, N3, and N4 (Nighttime Wakening)
  - Overall Symptom score = average of Items D1, N1, D2, N2, D3, N3, and D4

Composite-Level Reliability

- The internal consistencies indicated the item sets are strongly related and capable of supporting a unidimensional scoring structure but not redundant. From Day 2 through Day 6, alphas ranged from 0.73 (Nighttime Symptoms score) to 0.91 (Overall Symptoms score).
- Test-retest reliabilities (all intraclass correlation coefficients ≥ 0.63) were generally satisfactory with minor exceptions (Table 2).

Table 2. Test-Retest Reliability: ePASD Composite Scores

ePASD score	EOS Day −2 to EOS Day −1 ICC (95% CI), n PGIC = "The Same" (2)	EOS Day −2 to EOS Day −1 ICC (95% CI), n
Daytime Symptom score	0.60 (0.29-0.80), 44	0.63 (0.39-0.80), 61
Daytime score	0.60 (0.29-0.80), 44	0.64 (0.40-0.80), 61
Nighttime Symptom score	0.66 (0.36-0.83), 42	0.73 (0.53-0.85), 61
Nighttime score	0.65 (0.35-0.83), 42	0.70 (0.49-0.84), 61
Overall Symptom score	0.71 (0.44-0.86), 44	0.73 (0.53-0.85), 61

ICC = intraclass correlation coefficient.

Composite-Level Construct Validity

- Patterns of validity correlations generally supported the construct validity of ePASD composites (Table 3). As hypothesized: ePASD composite scores correlated relatively strongly with the ACQ-IA-5, ACQ-IA-6, and C-ACT; ePASD symptom scores correlated moderately to strongly with PAQLQ(S) Symptom scores (all correlations ≥ –0.46) and with ACQ scores (all correlations ≥ 0.42); most correlations between the ePASD composites and the PGIS are, in fact, moderate in size (0.30 ≤ r ≤ 0.49).
- Most of the change correlations for longitudinal construct validity are trivial (r < 0.10) and small (0.10 ≤ r ≤ 0.29) in size (Table 4), except for the moderate (0.30 ≤ r ≤ 0.49) correlations with the PGIC, which range from 0.32 with the ePASD Daytime score to 0.46 with the Nighttime Symptom score.

Composite-Level Known-Groups Validity

- Known-groups analyses supplied evidence of the discriminating ability of ePASD composite scores with all subgroup differences in the hypothesized direction (data not presented).
  - Participants classified as "Mild" at screening had better Day 1 ePASD scores compared with participants who were classified as "Severe" at screening (*P* > 0.01).
  - "Stable" participants (no changes in asthma medications in the last 2 weeks) at screening had better Day 1 ePASD scores compared with "Not stable" participants (those who required a medication change to improve asthma symptoms in the last 2 weeks) (*P* > 0.01).
  - At Day 1 and EOS Day −1, participants with C-ACT scores < 20 obtained worse ePASD composite scores compared with participants with C-ACT scores ≥ 20; the subgroup differences were statistically significant at both timepoints for the Daytime Symptom score, Nighttime score, and Overall Symptom score.

Table 3. Composite-Level Construct Validity Correlations

ePASD score	ACQ-IA-5	ACQ-IA-6	C-ACT	PAQLQ(S) Overall	PAQLQ(S) Activity Limitation	PAQLQ(S) Symptoms	PAQLQ(S) Emotional Function	PGIS	CGIS
Day 1 (n = 39-82)									
Daytime Symptom score	**0.42***	**0.44***	**−0.43***	**−0.61***	−0.59*	**−0.58***	−0.60*	**0.28**	0.28
Daytime score	**0.46***	**0.48***	**−0.40***	**−0.65***	−0.64*	**−0.61***	−0.63*	**0.31**	0.34*
Nighttime Symptom score	**0.47***	**0.49***	**−0.48***	**−0.57***	−0.58*	**−0.57***	−0.49*	**0.45***	0.35*
Nighttime score	**0.49***	**0.51***	**−0.52***	**−0.55***	−0.55*	**−0.57***	−0.47*	**0.48***	0.36*
Overall Symptom score	**0.48***	**0.50***	**−0.49***	**−0.64***	−0.64*	**−0.62***	−0.60*	**0.38***	0.34*
EOS Day −1 (n = 40-70)									
Daytime Symptom score	**0.42***	**0.43***	**−0.47***	**−0.48***	−0.46*	**−0.53***	−0.39*	**0.41***	0.33
Daytime score	**0.50***	**0.51***	**−0.45***	**−0.51***	−0.51*	−0.55*	−0.42*	**0.41***	0.34*
Nighttime Symptom score	**0.59***	**0.59***	**−0.33***	**−0.42***	−0.40*	**−0.46***	−0.33*	**0.27**	0.40*
Nighttime score	**0.60***	**0.60***	**−0.36***	**−0.43***	−0.42*	−0.47*	−0.35*	**0.30**	0.40*
Overall Symptom score	**0.48***	**0.49***	**−0.45***	**−0.48***	−0.45*	**−0.53***	−0.37*	**0.38***	0.37*

* *P* < 0.01.

Notes: EOS Day −1 ePASD data were correlated with EOS PAQLQ(S), C-ACT, ACQ-5, ACQ-IA-5, PGIS, and CGIS data. Correlation coefficients in **bold** were hypothesized to be relatively strong.

Table 4. Composite-Level Longitudinal Construct Validity Correlations

ePASD score	ACQ-IA-5	ACQ-IA-6	C-ACT	PAQLQ(S) Overall	PAQLQ(S) Activity Limitation	PAQLQ(S) Symptoms	PAQLQ(S) Emotional Function	PGIS	CGIS	PGIC	CGIC
Change from Day 1 to EOS Day −1 (n = 30-62)											
Daytime Symptom score	**−0.04**	**−0.02**	**−0.31**	**−0.09**	0.05	**−0.16**	−0.07	**0.06**	−0.09	**0.33**	0.14
Daytime score	**0.10**	**0.11**	**−0.27**	**−0.12**	−0.00	**−0.20**	−0.04	**0.08**	−0.05	**0.32**	0.14
Nighttime Symptom score	**0.10**	**0.09**	**−0.03**	**−0.16**	−0.06	**−0.19**	−0.04	**0.02**	0.22	**0.46***	0.32
Nighttime score	**0.11**	**0.09**	**−0.03**	**−0.13**	−0.05	**−0.16**	−0.03	**−0.00**	0.18	**0.42***	0.30
Overall Symptom score	**−0.08**	**−0.07**	**−0.21**	**−0.11**	0.02	**−0.16**	−0.08	**−0.01**	−0.03	**0.37***	0.17

* *P* < 0.01.

Note: Correlation coefficients in **bold** were hypothesized to be relatively strong. ePASD change was computed using study Day 1 and EOS Day −1 data; Day 1 and EOS data were used to compute change for the PAQLQ(S), C ACT, ACQ-5, ACQ-IA-5, PGIS, and CGIS.

DISCUSSION

- The findings of our initial psychometric evaluation support the reliability and validity of the ePASD items and composite scores.
- The distributional characteristics, factor analyses, reliability estimates, correlational analyses, and known-groups tests provided important information supporting the use of the ePASD, as well as the ability of young children with asthma to self-report symptoms and impacts.
- An important limitation is the lack of reported symptoms and impacts and minimal change demonstrated by the ePASD items and the supportive COAs. All of the COAs included in the study—the ePASD, ACQ-IA, C-ACT, PAQLQ(S), and global ratings—indicated that the children in the sample exhibited very few asthma-related symptoms and impacts at all timepoints, and consequently, demonstrated very little change over time, which explains the small and trivial longitudinal validity correlations and lack of support for responsiveness.
- Further evaluation of the ePASD in the context of a clinical trial is needed so that the longitudinal psychometric properties can be evaluated and meaningful change can be estimated.

CONCLUSIONS

- Our findings provide initial evidence that the ePASD is a reliable and valid measure of asthma symptoms in young children aged 6-11 years who may not be able to read independently and who have mild, moderate, or severe asthma.

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