

Clinical Communications

Psychometric properties of the Asthma Control Test in 2 randomized clinical trials

Mark Kosinski, MSc^a, Linda Nelsen, MHS^b,
Avery A. Rizio, PhD^a, James Lay-Flurrie, MSc^c,
Robyn von Maltzahn, MSc^d, Loretta Jacques, PhD^e,
Michael Schatz, MD^f, Richard H. Stanford, PharmD^g, and
Henrik Svedsater, PhD^d

Clinical Implications

- Asthma Control Test measurement properties are robust in both a double-blind randomized controlled trial and an open-label, randomized effectiveness study. These study results provide empirical support for Asthma Control Test use as an end point in interventional trials of patients with asthma.

The Asthma Control Test (ACT) is a brief, 5-item, patient-completed questionnaire designed to allow standardized, quantitative assessment of asthma-related impairment.^{1,2} The ACT is mainly known as a clinical end point, yet little evidence supports its use in clinical trials. To evaluate the reliability, validity, and responsiveness of the ACT in randomized clinical trials, we performed analyses to estimate the psychometric properties of the ACT using data from 2 phase 3 clinical trials with different designs.

The data used in our analyses come from study HZA106829 (NCT01134042) and the Salford Lung Study in asthma (SLS Asthma [HZA115150/NCT01706198]) whose designs and primary findings have been published previously.^{3,4} HZA106829 was a 24-week, double-blind, double-dummy randomized controlled trial that compared the efficacy and safety of inhaled fluticasone furoate (FF)/vilanterol with inhaled FF and inhaled fluticasone propionate in patients aged 12 years or older ($n = 586$) with persistent asthma.³ SLS Asthma was a 12-month, open-label clinical trial conducted in UK primary care that evaluated the clinical effectiveness and safety of FF/vilanterol versus continuing usual care in adults (≥ 18 years old; $n = 4233$) with symptomatic asthma and taking regular maintenance inhaler therapy.⁴ A post hoc analysis plan was developed to describe all analyses that would be conducted. The measurement properties evaluated included reliability (internal consistency) of ACT scores, confirmation of the conceptual framework of ACT, convergent validity, known-groups validity, and responsiveness. Criterion measures used to evaluate the measurement properties of ACT included categories of lung function, severe asthma exacerbations, and asthma-related quality of life. Analyses were performed across treatment groups within each study.

The reliability of ACT scores at baseline and each follow-up time point for both studies are presented in Table I. At all time points across both studies, Cronbach alpha exceeded the minimum recommended standard of 0.70,⁵ (observed range, 0.74–0.88), indicating that the ACT items measure the same concept. Listwise deletion of ACT items resulted in slightly lower Cronbach coefficients, indicating that all 5 items are important

for measuring asthma control, and that all the items make an important contribution to the total ACT score.

The conceptual framework of ACT was confirmed through confirmatory factor analysis (Table II). The factor loadings observed across ACT items 1 to 5 were high at baseline (≥ 0.56) and final visit (≥ 0.77). Item-to-factor loadings were higher at final visit owing in part to increased variability in item responses compared with baseline. For both studies, the fit of ACT items to a 1-factor solution was acceptable at baseline and final visit, based on the majority of model-fit statistics exceeding the recommended values for model fit.

Convergent validity analyses demonstrated moderate effect size (0.3–0.5) to strong effect size (>0.5) correlations⁶ at baseline and final visit between ACT and Asthma Quality of Life Questionnaire (AQLQ) scores in both studies. As hypothesized, ACT scores had a higher Spearman rank correlation (r_s) with the AQLQ symptoms domain (0.66–0.84) than with other AQLQ domains (0.44–0.75). For study HZA106829, correlations between ACT scores at week 24 and a composite index of asthma daytime symptoms were moderate (-0.60 ; $P < .001$). For SLS Asthma, there were moderate but significant ($P < .001$) correlations between ACT scores and work impairment scores of the Work Productivity and Activity Impairment Questionnaire at baseline (-0.53) and at week 52 (-0.56), and strong correlations between ACT scores and activity limitation scores at baseline (-0.63) and at week 52 (-0.67 ; all $P < .001$). There were also moderate correlations between ACT scores and the European Quality of Life-5 Dimension Visual Analogue Scale at baseline (0.47) and week 52 (0.46; both $P < .001$) (see Table E1 in this article's Online Repository at www.jaci-inpractice.org).

In support of known-groups validity, significant differences in mean ACT scores from study HZA106829 were observed across patient groups differing in percent-predicted FEV₁ ($\geq 80\%$, 50%– $<80\%$, and $<50\%$) in the hypothesized direction at baseline (F statistic [F] = 4.13 [degrees of freedom 2, 575]; $P = .017$) and week 24 (F = 17.18 [degrees of freedom 2, 472]; $P < .001$). In SLS Asthma, patients who had experienced 1 or more severe exacerbations in the previous year had significantly lower baseline ACT scores ($n = 1540$; mean, 15.04 ± 4.67) than patients with no severe exacerbations in the previous year ($n = 2692$; mean, 17.10 ± 4.14) (F = 219.93 [degrees of freedom 1, 4231]; $P < .001$).

In support of responsiveness, changes in ACT scores were found to be significantly correlated with changes in AQLQ, Work Productivity and Activity Impairment Questionnaire, and European Quality of Life-5 Dimension Visual Analogue Scale scores. Across both groups, significant ($P < .001$) correlations between changes in ACT scores and change in AQLQ domains ranged from 0.40 to 0.74. In SLS Asthma, there were significant ($P < .001$) moderate correlations between changes in ACT scores and changes in both percent work impairment ($r_s = -0.42$) and percent activity limitations ($r_s = -0.46$). In both studies, mean changes in ACT scores differed significantly (all $P < .001$) across AQLQ domains (see Table E2 in this article's Online Repository at www.jaci-inpractice.org). In study HZA106829, mean changes in ACT scores differed significantly for absolute FEV₁, global assessment of change in asthma symptoms, and change in rescue medication use (all $P < .001$).

TABLE I. Reliability (internal consistency) of overall ACT scale and with listwise deletion (Cronbach α)

Study	Time point	ACT scale	Cronbach α coefficient				
			With item deletion				
			1. Effect on productivity	2. Shortness of breath	3. Nighttime symptoms	4. Rescue medication use	5. Asthma control rating
HZA106829	Baseline (N = 587)	0.74	0.69	0.68	0.68	0.69	0.71
	Week 12 (N = 516)	0.85	0.82	0.81	0.81	0.82	0.82
	Week 24 (N = 479)	0.86	0.83	0.82	0.83	0.83	0.83
SLS Asthma	Baseline (N = 4232)	0.82	0.77	0.78	0.78	0.80	0.78
	Week 12 (N = 4097)	0.85	0.81	0.81	0.83	0.83	0.81
	Week 24 (N = 4026)	0.85	0.82	0.81	0.84	0.83	0.82
	Week 40 (N = 3935)	0.86	0.83	0.83	0.84	0.84	0.83
	Week 52 (N = 3863)	0.88	0.84	0.85	0.86	0.86	0.85

TABLE II. Confirmatory factor analysis of ACT items

Study	Time point	Factor loadings					Model-fit statistics		
		1. Effect on productivity	2. Shortness of breath	3. Nighttime symptoms	4. Rescue medication use	5. Asthma control rating	RMSEA	CFI	TLI
HZA106829	Baseline (N = 587)	0.65	0.69	0.69	0.65	0.56	0.033	0.997	0.994
	Week 24 (N = 479)	0.80	0.85	0.80	0.77	0.78	0.105	0.991	0.982
SLS Asthma	Baseline (N = 4232)	0.80	0.73	0.72	0.66	0.75	0.059	0.995	0.990
	Week 52 (N = 3863)	0.86	0.83	0.77	0.78	0.84	0.070	0.997	0.994

CFI, Comparative Fit Index; RMSEA, root mean square error of approximation; TLI, Tucker Lewis Index.

In summary, ACT scores showed significant correlations with other clinical and patient-reported measures of asthma control. Only weak correlations were observed between ACT scores and lung function, supporting the view that both lung function and ACT scores are important in the clinical assessment of asthma and together may help achieve better asthma control among patients, compared with assessments focused solely on lung function or ACT scores.⁷ The strength and directionality of relationships between the ACT and other outcomes, such as quality of life, were consistent with other studies investigating correlations between ACT scores and scores from related asthma-control measures.^{8,9} This study demonstrates that the ACT is a viable patient-reported outcome to measure asthma control as an end point in trials of asthma treatment.

Acknowledgements

Editorial support for manuscript development (in the form of medical writing support) was provided by Joanna Wilson, PhD, and Fraser Shearer, MSc, of Gardiner-Caldwell Communications (Macclesfield, UK), and was funded by GlaxoSmithKline plc.. Trademarks are owned by or licensed to the GlaxoSmithKline group of companies.

^aOptum, Johnston, RI^bValue Evidence and Outcomes, GlaxoSmithKline plc, Collegeville, Pa^cClinical Statistics, GlaxoSmithKline plc, Uxbridge, United Kingdom^dValue Evidence and Outcomes, GlaxoSmithKline plc, London, United Kingdom^eClinical Sciences, GlaxoSmithKline plc, Uxbridge, United Kingdom^fKaiser Permanente, San Diego, Calif^gAESARA Inc, Chapel Hill, NCData sharing statement: Information on GlaxoSmithKline's data sharing commitments and requesting access to anonymized individual participant data and associated documents can be found at www.clinicalstudydatarequest.com.

This study (HO-17-18331) was funded by GlaxoSmithKline plc.. The data analyzed in the study were derived from trials funded by GlaxoSmithKline plc. (HZA106829/NCT01134042 and HZA115150/NCT01706198).

Conflicts of interest: L. Nelsen, R. V. Maltzahn, L. Jacques, and H. Svedsater are employees of and shareholders in GlaxoSmithKline plc. R. H. Stanford and J. Lay-Flurrie are former employees of GlaxoSmithKline plc, and were employees and shareholders during the time of the study. M. Kosinski and A. A. Rizio are employees of Optum, which provides consulting and other research services to pharmaceutical, device, government, and nongovernment organizations. M. Schatz is Editor-in-chief of the *Journal of Allergy and Clinical Immunology: In Practice* but was not involved in editorial decisions related to this manuscript.

Received for publication December 4, 2019; revised July 14, 2020; accepted for publication July 26, 2020.

Available online ■■

Corresponding author: Mark Kosinski, MSc, Optum, 1301 Atwood Ave, Ste 311—North, Johnston, RI 02919. E-mail: mkosinski@qualitymetric.com.

2213-2198

© 2020 American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaip.2020.07.040>

REFERENCES

- Nathan RA, Sorkness CA, Kosinski MA, Schatz M, Li JT, Marcus P, et al. Development of the Asthma Control Test: a survey for assessing asthma control. *J Allergy Clin Immunol* 2004;113:59-65.
- Schatz M, Kosinski M, Yarlas AS, Hanlon J, Watson ME, Jhingran P. The minimally important difference of the Asthma Control Test. *J Allergy Clin Immunol* 2009;124:719-23.
- O'Byrne PM, Bleecker ER, Bateman ED, Busse WW, Woodcock A, Forth R, et al. Once-daily fluticasone furoate alone or combined with vilanterol in persistent asthma. *Eur Respir J* 2014;43:773-82.
- Woodcock A, Vestbo J, Bakerly ND, New J, Martin Gibson J, McCorkindale S, et al. Effectiveness of fluticasone furoate plus vilanterol on asthma control in clinical practice: an open-label, parallel group, randomised controlled trial. *Lancet* 2017;390:2247-55.
- Nunnally JC, Bernstein IH. *Psychometric Theory*. 3rd ed. New York, NY: McGraw-Hill; 1994.
- Cohen J. *Statistical Power Analysis for the Behavioural Sciences*. 2nd ed. New York, NY: Lawrence-Erlbaum Associates; 1988.

7. Sullivan PW, Ghushchyan VH, Marvel J, Barrett YC, Fuhlbrigge AL. Association between pulmonary function and asthma symptoms. *J Allergy Clin Immunol Pract* 2019;7:2319-25.
8. Nguyen VN, Chavannes N, Le LT, Price D. The Asthma Control Test (ACT) as an alternative tool to Global Initiative for Asthma (GINA) guideline criteria for assessing asthma control in Vietnamese outpatients. *Prim Care Respir J* 2012;21:85-9.
9. Rodrigo GJ, Arcos JP, Nannini LJ, Neffen H, Broin MG, Contrera M, et al. Reliability and factor analysis of the Spanish version of the asthma control test. *Ann Allergy Asthma Immunol* 2008;100:17-22.

ONLINE REPOSITORY

TABLE E1. Test of convergent validity: Correlations between ACT and other outcomes

Criterion Measures	HZA106829				SLS Asthma			
	Baseline		Week 24		Baseline		Week 52	
	N	r_s	N	r_s	N	r_s	N	r_s
AQLQ activity limitations domain	583	0.52*	477	0.67*	4232	0.72*	3863	0.75*
AQLQ symptoms domain	583	0.66*	477	0.81*	4232	0.81*	3863	0.84*
AQLQ emotional function domain	583	0.48*	476	0.64*	4232	0.64*	3863	0.69*
AQLQ environment stimuli domain	583	0.44*	477	0.58*	4232	0.54*	3863	0.61*
AQLQ total score	583	0.61*	476	0.76*	4232	0.79*	3863	0.82*
Percent-predicted FEV ₁ at baseline	578	0.10†	475	0.10‡	NA	NA	NA	NA
Number of daytime asthma symptoms§	NA	NA	344	−0.60*	NA	NA	NA	NA
WPAI percent overall work impairment	NA	NA	NA	NA	1992	−0.53*	1850	−0.56*
WPAI percent overall activity limitations	NA	NA	NA	NA	4232	−0.63*	3860	−0.67*
EQ-5D VAS	NA	NA	NA	NA	4232	0.47*	3863	0.46*

EQ-5D VAS, European Quality of Life-5 Dimension Visual Analogue Scale; NA, not applicable; r_s , Spearman's rank correlation; WPAI, Work Productivity and Activity Impairment Questionnaire.

* $P < .001$.

† $P = .172$.

‡ $P = .0223$.

§Number of daytime asthma symptoms represents the total number of daytime asthma symptoms reported in daily diaries during the week preceding week 24 ACT assessment.

||Overall work impairment scores are calculated only for those employed at the time of survey administration.

TABLE E2. Tests of responsiveness: Correlation between change in ACT and change in other outcomes

Change in variable*	HZA106829		SLS Asthma	
	N	r_s	N	r_s
AQLQ activity limitations domain	474	0.56†	3863	0.60†
AQLQ symptoms domain	474	0.72†	3863	0.74†
AQLQ emotional function domain	473	0.56†	3863	0.57†
AQLQ environment stimuli domain	474	0.50†	3863	0.40†
AQLQ total score	473	0.69†	3863	0.70†
Percent-predicted FEV ₁ at baseline	468	0.24†	NA	NA
WPAI percent overall work impairment	NA	NA	1605	−0.42†
WPAI percent overall activity limitations	NA	NA	3860	−0.46†
EQ-5D VAS	NA	NA	3863	0.26†

AQLQ, Asthma Quality of Life Questionnaire; EQ-5D VAS, European Quality of Life-5 Dimension Visual Analogue Scale; NA, not applicable; r_s , Spearman rank correlation; WPAI, Work Productivity and Activity Impairment Questionnaire.

*Change for variables was assessed from baseline to week 24 in HZA106829, and from baseline to week 52 in SLS Asthma.

† $P < .0001$.