Performance of the Asthma Impact on Quality of Life Scale (A-IQOLS) in diverse asthma research populations and demographic subgroups

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Background: The Asthma Impact on Quality of Life Scale (A-IQOLS) assesses the patient-perceived negative effect of asthma on quality of life. Its standard error of measurement is known; it has strong construct, convergent, and divergent validity; and it provides information that is unique among asthma outcome measures.

Objective: We sought to characterize the psychometric properties of the A-IQOLS and its suitability for use in demographically and clinically diverse adult asthmatic populations.

Methods: Data from participants in 5 independent asthma studies, with samples ranging from patients with well-controlled moderate asthma to patients with severe poorly controlled asthma, were pooled to determine the psychometric performance of A-IQOLS scores overall and in multiple demographic, disease status, and study subgroups.

Results: Pooled sample (n = 597) age averaged 45 years; 66% were female, 65% were white, 22% were African American, 11% were Hispanic, and 11% had a high school education or less. The rated importance of its underlying life dimensions and associations between A-IQOLS scores and lung function, symptom, Asthma Control Test, Juniper Mini Asthma Quality of Life Questionnaire, and Marks Asthma Quality of Life Questionnaire scores was very similar, regardless of patients' demographic and clinical characteristics. A-IQOLS scores discriminated among the individual study samples, as well as other patient-reported symptom and functional status measures. Distribution and anchor-based considerations suggest an A-IQOLS minimum clinically important difference in the vicinity of 0.50 and not less than 0.33 scale score units.

Conclusions: A-IQOLS is valid for research and potentially clinical use in demographically and clinically diverse patients. (J Allergy Clin Immunol 2018;■■■:■■■-■■■.)

Key words: *Asthma, quality of life, measurement/standardized measures, clinical outcomes, patient-centered outcomes*

Standardized core outcome measures used in asthma research include spirometry, asthma control, exacerbations, and health care use.[1] No measure of a patient's asthma-related physical, social, emotional, or role functions or quality of life (QoL) has been recommended as a core outcome. Recently, a measure is available that assesses the patient's perspective on the effect of asthma and its treatment on QoL.

The Asthma Impact on Quality of Life Scale (A-IQOLS) asks patients to rate the negative effect of their asthma on each of 16 research-based dimensions of QoL on a 5-point scale.[2] A-IQOLS summary scores (the average of the dimension ratings) are interpretable on the original rating scale. In the Asthma Quality of Life Impact Study (AQOLIS)'s test-retest study, A-IQOLS has strong content, convergent, and divergent validity, and its SEM was determined to be ±0.27. Participants in AQOLIS had diverse levels of asthma severity, a wide range in level of asthma control, and moderate racial and ethnic diversity. However, its size (n = 147) and composition did not support subgroup analyses to determine the generalizability of the A-IQOLS's psychometric properties to specific patient populations, such as those with low education, from specific racial/ethnic backgrounds, or with severe asthma.

In addition, A-IQOLS was administered as an ancillary measure in 4 additional independent asthma clinical trials that differed widely in target population, eligibility criteria, clinical intervention, and study design. Pooled baseline data from all 5 studies were analyzed to (1) determine whether the rated personal importance of the Flanagan Quality of Life Scale dimensions and psychometric performance of the A-IQOLS support its use in diverse demographic groups and clinical populations, (2) evaluate the A-IQOLS's sensitivity for differences in asthma severity and clinical status, (3) estimate the minimum clinically important within-patient score change, and (4) provide information to inform sample size and power estimates when planning future studies.

METHODS

This research was supported by grant HL119845 (Principal Investigator: S. R. Wilson) from the National Institutes of Health/National Heart, Lung, and

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Abbreviations used
ACT: Asthma Control Test
A-IQOLS: Asthma Impact on Quality of Life Scale
AQOLIS: Asthma Quality of Life Impact Study
ASUI: Asthma Symptom Utility Index
BTR: Prospective Observational Cohort Study of Biopredictors of Bronchial Thermoplasty Response in Patients with Severe Refractory Asthma
CPAP: Effect of [Continuous] Positive Airway Pressure on Reducing Airway Reactivity in Patients with Asthma
DASH: DASH Diet for Asthma
LASST: Long-acting Beta Agonist Step Down Study
Marks AQLQ: Marks Asthma Quality of Life Questionnaire
MID: Minimum clinically important difference
Mini-AQLQ: Juniper Mini Asthma Quality of Life Questionnaire
$PPFEV_1$: Percent predicted FEV_1
QoL: Quality of life

Blood Institute and is approved by the Sutter Health Institutional Review Board (SHIRB no. 14-06-327). All studies contributing data for the present analyses were approved by their respective institutional review boards. All subjects provided written consent.

Studies

The following studies contributed baseline data for pooled analysis:

- AQOLIS,[2]
- DASH Diet for Asthma (DASH) study,[3]
- Long-acting Beta Agonist Step-Down Study (LASST),[4]
- Prospective Observational Cohort Study of Biopredictors of Bronchial Thermoplasty Response in Patients with Severe Refractory Asthma (BTR),[5] and
- Effect of [Continuous] Positive Airway Pressure on Reducing Airway Reactivity in Patients with Asthma (CPAP) study.[6]

The eligibility criteria of LASST, AQOLIS, and BTR (see Table E1 in this article's Online Repository at www.jacionline.org) ensured that enrolled patients had persistent asthma and were prescribed asthma treatment at or greater than step 2.[7] Asthma in LASST patients was well controlled and relatively stable on combination inhaled corticosteroids and long-acting β-agonists (step 4 treatment). AQOLIS participants had persistent asthma (treatment steps 2-6), without regard to level of asthma control.[2] The DASH study targeted obese patients with poorly controlled asthma, and the CPAP study targeted patients with stable asthma and airway reactivity without regard to treatment step. BTR participants had severe asthma, which was defined as asthma that was uncontrolled despite high-dose inhaled corticosteroids plus long-acting β-agonists and/or other asthma controller medications (ie, step 5 or 6 antiasthma treatment), and were approved to undergo bronchial thermoplasty.

TABLE I. Demographic, health status, and QoL characteristics: Pooled and individual study samples

Measures	Pooled sample (n = 597) No. (%) or mean ± SD (range)	LASST (n = 227) No. (%) or mean ± SD (range)	AQOLIS (n = 152) No. (%) or mean ± SD (range)	CPAP study (n = 92) No. (%) or mean ± SD (range)	DASH study (n = 88) No. (%) or mean ± SD (range)	BTR (n = 38) No. (%) or mean ± SD (range)	*P* value: overall test of study differences
Demographic							
Age (y)*	44.8 ± 13.5 (18-84)	42.6 ± 13.2 (18-84)	49.3 ± 12.3 (21-70)	35.5 ± 11.0 (18-59)	51.5 ± 12.4 (20.5-70.5)	47.3 ± 12.2 (21.4-67.5)	**<.0001**
18-44 y	291 (48.7)	125 (55.1)	51 (33.6)	73 (79.3)	26 (29.5)	16 (42.1)	**<.0001**
45-59 y	208 (34.8)	74 (32.6)	64 (42.1)	19 (20.7)	37 (42.0)	14 (36.8)	
60 y	98 (16.4)	28 (12.3)	37 (24.3)	0 (0.0)	25 (28.4)	8 (21.1)	
Sex							.45
Female	396 (66.3)	153 (67.4)	97 (63.8)	58 (63.0)	58 (65.9)	30 (78.9)	
Male	201 (33.7)	74 (32.6)	55 (36.2)	34 (37.0)	30 (34.1)	8 (21.1)	
Race							**<.0001**
White	386 (64.9)	139 (61.2)	114 (75.0)	56 (60.9)	44 (50.6)	33 (89.2)	
Black/African American	129 (21.7)	70 (30.8)	22 (14.5)	24 (26.1)	10 (11.5)	3 (8.1)	
Asian	54 (9.1)	9 (4.0)	13 (8.6)	5 (5.4)	27 (31.0)	0 (0)	
Other	26 (4.4)	9 (4.0)	3 (2.0)	7 (7.6)	6 (6.9)	1 (2.7)	
Missing	*2 (0.3)*	*0 (0)*	*0 (0)*	*0 (0)*	*1 (1.1)*	*1 (2.6)*	
Ethnicity							.64
Hispanic	67 (11.2)	24 (10.6)	17 (11.2)	11 (12.0)	13 (14.8)	2 (5.4)	
Non-Hispanic	529 (88.8)	203 (89.4)	135 (88.8)	81 (88.0)	75 (85.2)	35 (94.6)	
Missing	*1 (0.2)*					*1 (2.6)*	
Education							**.02**
≤High school	64 (10.8)	31 (13.7)	8 (5.3)	13 (14.1)	7 (8.0)	5 (13.9)	
Some college	213 (35.8)	80 (35.2)	46 (30.3)	41 (44.6)	33 (37.5)	13 (36.1)	
≥4-y college degree	318 (53.4)	116 (51.1)	98 (64.5)	38 (41.3)	48 (54.5)	18 (50)	
Missing	*2 (0.3)*					*2 (5.3)*	
Treatment step†							**<.0001**
Step 1	39 (7.7)	0 (0)	0 (0)	—	39 (44.3)	0 (0)	
Step 2	24 (4.8)	0 (0)	16 (10.5)	—	8 (9.1)	0 (0)	
Step 3	35 (6.9)	0 (0)	23 (15.1)	—	12 (13.6)	0 (0)	
Step 4	296 (58.6)	227 (100)	64 (42.1)	—	5 (5.7)	0 (0)	

(Continued)

TABLE I. *(Continued)*

Measures	Pooled sample (n = 597) No. (%) or mean ± SD (range)	LASST (n = 227) No. (%) or mean ± SD (range)	AQOLIS (n = 152) No. (%) or mean ± SD (range)	CPAP study (n = 92) No. (%) or mean ± SD (range)	DASH study (n = 88) No. (%) or mean ± SD (range)	BTR (n = 38) No. (%) or mean ± SD (range)	*P* value: overall test of study differences
Step 5	92 (18.2)	0 (0)	48 (31.6)	—	24 (27.3)	20 (52.6)	
Step 6	19 (3.8)	0 (0)	1 (0.7)	—	0 (0)	18 (47.4)	
Asthma status							
$PPFEV_1$‡	88.6 ± 17.0 (34.9-154.3)	91.6 ± 13.4 (69.3-154.3)	87.2 ± 18.7 (37.0-151.0)	89.3 ± 10.9 (74.6-134.6)	89.8 ± 19.6 (41.5-129.9)	69.2 ± 24.4 (34.9-137.6)	**<.0001**
ACT score§	19.6 ± 4.8 (5-25)	22.9 ± 1.7 (20-25)	18.8 ± 4.0 (10-25)	20.8 ± 3.3 (9-25)	14.9 ± 3.7 (7-22)	10.5 ± 4.3 (5-22)	**<.0001**‖
ASUI score	0.86 ± 0.15 (0.20-1)¶	0.94 ± 0.07 (0.64-1)	0.81 ± 0.17 (0.20-1)	0.89 ± 0.12 (0.28-1)	0.81 ± 0.14 (0.44-1)¶	0.60 ± 0.13 (0.36-0.89)¶	**<.0001**
Mini-AQLQ, symptom Score#	5.4 ± 1.1 (1.0-7)¶	6.0 ± 0.42 (4.2-6.3)¶	5.2 ± 1.2 (2.2-7)	5.6 ± 0.7 (1.9-6.3)¶	5.2 ± 1.3 (1.8-7)	3.2 ± 1.2 (1-5.9)	**<.0001**
Mini-AQLQ, total score#	5.5 ± 1.1 (1.2-7)**	6.0 ± 0.5 (3.5-6.4)**	5.4 ± 1.1 (2.9-6.9)	5.4 ± 0.9 (2.5-6.4)**	5.2 ± 1.1 (1.9-7)	3.2 ± 1.2 (1.2-6.1)	**<.0001**
Marks AQLQ††	12.2 ± 12.0 (0-65)**	5.8 ± 6.5 (0-40)	14.2 ± 12.1 (0-65)	13.5 ± 12.5 (0-54)	15.3 ± 9.6 (0.1-44.1)**	33.0 ± 10.8 (7.9-50.6)**	**<.0001**
QoL							
A-IQOLS‡‡	1.43 ± 0.68 (1-4.94)	1.22 ± 0.56 (1-4.94)	1.36 ± 0.45 (1-3.94)	1.43 ± 0.73 (1-4.50)	1.56 ± 0.60 (1-3.25)	2.67 ± 0.87 (1.13-4.38)	**<.0001**§§

Values in boldface indicate statistical significance. Italics for "Missing" rows indicate that the proportions of patients with missing data are not included in the calculation of proportions of patients for whom the information on that characteristic is available (ie, not missing).

ACT, Asthma Control Test (well-controlled, 20-25; poorly controlled, 16-29; very poorly controlled, 5-15); *A-IQOLS*, Asthma Impact on Quality of Life Scale (1 = no negative effect at all to 5 = extremely negative effect); *ASUI*, Asthma Symptom Utility Index (0 = worst possible symptoms to 1 = best state/no symptoms); *Juniper Mini-AQLQ*, Juniper Mini-Asthma Quality of Life Questionnaire (total score 1 = totally limited to 7 = not at all limited and symptom subscale [1 = symptoms all of the time to 7 = symptoms none of the time]); and *Marks AQLQ*, Asthma Quality of Life Questionnaire (0 = less negative effect on functional status to 80 = very severe negative effect on functional status).

*For AQOLIS, age was as of the patient's last birthday. For the DASH study, age was the difference between the date of the baseline visit and the patient's birth date divided by 365.25. For LASST, the CPAP study, and BTR, age at enrollment was available to the nearest tenth of a year.

†The patients' pharmacotherapy regimens were documented in all except the CPAP study.

‡In the CPAP study lung function was measured 0 to 2 weeks before the baseline questionnaire was administered. One AQOLIS, 2 DASH study, and 5 BTR participants were missing a lung function value.

§In the DASH study the ACT was used for telephone eligibility screening.

‖After controlling for age, sex, race, ethnicity, and education, the overall test of group ACT score differences remained significant ($P < .0001$), as did all pairwise study comparisons (all $P < .0001$). Pooled sample size in these analyses was 593. The resultant least-square ACT score means (LASST, 23.0; AQOLIS, 18.7; CPAP study, 20.9; DASH study, 14.9; and BTR, 10.5) were virtually the same as the unadjusted means.

¶Pearson correlation between ASUI and Mini-AQLQ symptom scores in the AQOLIS sample was 0.81. Linear regression was used to impute ASUI scores from Juniper symptom scores in the DASH study and BTR samples and to impute Mini-AQLQ symptom scores in the LASST sample and CPAP study samples from their ASUI scores.

#BTR used the full-length standardized Juniper AQLQ questionnaire.

**Pearson correlation between the Mini-AQLQ total score and the Marks AQLQ score in the AQOLIS sample was −0.80. Linear regression was used to impute Marks AQLQ scores for DASH study and BTR samples from their Juniper total scores and to impute Juniper total scores in the LASST and CPAP studies from their Marks scores.

††One CPAP study participant was missing a Marks AQLQ score.

‡‡A subject's standard A-IQOLS summary score was defined as $S = \frac{\sum_{d=1}^{n} r_d}{n}$, where r_d is their rating of the effect of asthma on dimension d, and n is the number of dimensions rated, typically 16.

§§After controlling for age, sex, race, ethnicity, and education, the P value was less than .0001. After further controlling for ACT score, the P value was less than .0001; least-square means for A-IQOLS scores were as follows: LASST, 1.4; AQOLIS, 1.3; CPAP study, 1.5; DASH study, 1.3; and BTR, 2.2. All pairwise study comparisons with BTR were significant ($P < .0001$). Other pairwise study comparisons were not significant.

Data

Baseline data were available for 597 patients (AQOLIS, n = 152; LASST, n = 227; CPAP study, n = 92; and BTR, n = 38).

Treatment step. Pharmacotherapy regimens were documented in all but the CPAP study and were classified by step per US treatment guidelines.[7]

Lung function. Baseline lung function was assessed before and after bronchodilator use by using American Thoracic Society–recommended procedures and equipment.[8] Race-specific norms were used to determine percent predicted FEV_1 ($PPFEV_1$) values.

Asthma control. All studies administered the Asthma Control Test (ACT).[9]

Symptoms. The Asthma Symptom Utility Index (ASUI)[10] was administered in LASST, the CPAP study, and AQOLIS. Juniper Mini-Asthma Quality of Life (Mini-AQLQ) symptom subscale[11] scores were available for AQOLIS, the DASH study, and BTR.

Disease-specific health status. Asthma symptoms and impairment in patients' physical, social, emotional, and/or role functions were assessed based on the Mini-AQLQ score[11] in AQOLIS, the DASH study, and the CPAP study; the Juniper standardized AQLQ in BTR; and the Marks Asthma Quality of Life Questionnaire (Marks AQLQ)[12] in AQOLIS, LASST, and the CPAP study.

A-IQOLS. A-IQOLS[2] was self-administered by patients, requiring less than 5 minutes (typically 3-4 minutes). It asks the following: "Over the past four weeks, how much did your asthma negatively affect your life in each of the following areas?" Respondents were instructed to "Consider the effects of the asthma itself, the asthma medications you use, and anything you did to avoid, treat, or get medical care for asthma symptoms." Ratings were obtained on each of 16 life dimensions[13,14] on a 5-point, unidirectional, Likert-type scale: 1, no negative effect at all; 2, slightly negative effect; 3, moderately negative effect; 4, very negative effect; and 5, extremely negative effect.

One study (AQOLIS) added the following question assessing the overall effects of asthma: "In the past four weeks, how much did your asthma negatively affect your life overall" at both test and retest assessments? Responses used A-IQOLS' 5-point negative effect rating scale.

Flanagan Quality of Life Scale dimension importance questionnaire. The personal importance of each of the Flanagan Quality of Life Scale dimensions[13] plus the Burckhardt addition of independence was determined in all 5 asthma studies. Respondents were asked the following: "At this time in your life, how important is each of the following areas to you?" Ratings were obtained on a 5-point scale: 1, not at all important; 2, only slightly important; 3, moderately important; 4, important; and 5, very important. The importance questionnaire has no summary score.

Statistical analysis

Sample characteristics. Means ± SDs or proportions, as appropriate, were calculated for patients' characteristics for the pooled sample, each constituent study, and the demographic subgroups defined by age, sex, race, ethnicity, education, and ACT score category. Subgroup differences were evaluated by using *t* tests and linear regression methods.

QoL dimension importance. The mean (SD) rated importance of each QoL dimension, and the proportion of patients rating each dimension as important/very important was determined for the pooled sample and demographic subgroups.

Asthma outcome measure scoring. All standardized asthma outcome measures were scored and scaled by using their published algorithms: ACT,[9] ASUI,[15] Marks AQLQ,[16] Juniper AQLQ,[11,17,18] and A-IQOLS.[2]

The A-IQOLS summary score is shown as follows: $S = \frac{\sum_{d=1}^{n} r_d}{n}$, where r_d is the subject's asthma negative effect rating for each dimension *(d)* and the number of dimensions actually rated *(n)*.[2] Dimension importance ratings do not have to be obtained to score the A-IQOLS. Importance weighted and unweighted A-IQOLS scores were highly correlated ($r = 0.99$) and had similar correlations with other asthma outcome measures.

Convergent and divergent validity. Pearson correlations between A-IQOLS summary scores and other asthma outcome measures were determined for the pooled sample and demographic subgroups. The strength of the correlations *(r)* was interpreted as follows: very weak, 0.00 to 0.19; weak, 0.20 to 0.39; moderate, 0.40 to 0.59; strong, 0.60 to 0.79; and very strong, 0.80 to 1.0.[19] The R^2 value estimates the proportion of common variance between any 2 measures.

Internal consistency reliability. The standardized coefficient α was calculated to characterize the internal consistency of the A-IQOLS dimension ratings.

Sensitivity to differences in asthma status. An overall test of difference among the 5 studies on each asthma outcome was performed, as were various pairwise comparisons. No specific study differences were hypothesized, and hence no adjustment was made for multiple pairwise comparisons.

Association between change in overall asthma effect rating and change in A-IQOLS score. Linear regression and descriptive analyses were used to estimate the size of the change in A-IQOLS score associated with a 1-category change in the rated overall negative effect of asthma in the AQOLIS sample.

Estimation of the minimum clinically important difference. The minimum clinically important difference (MID) is the smallest change in a score that patients perceive as beneficial (or detrimental) that would mandate, in the absence of other considerations (eg, side effects and excessive cost), a change in the patient's management.[20] The MID defines cut points in change scores that distinguish between improvement, stability, and worsening. The definition of the MID presumes that the difference is large enough to be a true difference but not the result of measurement error.

A triangulation approach, as recommended by Leidy et al[21] was used to estimate the MID of the A-IQOLS from the following: (1) distribution-based considerations[22,23] using Wyrwich et al's suggested value of 1 SEM,[24] McHorney and Tarlov's suggested value of 1.96 SEM,[25] and intermediate values that represent the smallest score changes that constitute a true difference with 80% and 67% probability (1.81 and 1.15 SEM, respectively), and one half the measure's SD[26] and (2) an anchor-based estimation approach determining the magnitude of the A-IQOLS score change that was associated, by using linear regression, with a 1-category change in the patient's rating of the overall negative effect of asthma between test and retest in AQOLIS.

All statistical analyses were performed with SAS software (version 9.2; SAS Institute, Cary, NC). A significance level of .05 was used throughout.

RESULTS

Sample demographic characteristics

Mean age of participants was approximately 45 ± 14 years; 66% were female 65% were white, 22% were black, 9% were Asian, 4% were another race, and 11% were Hispanic (Table I). Approximately 11% had a high school education or less, 36% had some college, and 53% had a 4-year college or advanced degree.

As expected based on eligibility criteria, the 5 studies had diverse asthma outcome status ($P < .0001$, Table I) and constituted a very heterogeneous population of patients with persistent asthma. Demographically, they differed in age, education level, and race but not sex or ethnicity. BTR patients, who all had severe refractory asthma, had significantly worse lung function ($PPFEV_1$) than the other samples, which was similar to values reported for adult patients categorized as exacerbation prone in the Severe Asthma Research Program 3 severe asthma cohort.[27] BTR patients also had higher symptom levels (ASUI and Juniper AQLQ Symptom scores), worse asthma control (ACT scores), greater impairment in functional status (Mini-AQLQ total and Marks AQLQ scores), and higher A-IQOLS scores (greater negative effect) compared with the other 4 studies (Table II and see Fig E1 in this article's Online Repository at www.jacionline.org). Conversely, LASST patients, who were selected for good asthma control, had better status on all asthma measures than patients from the other 4 studies. Results for the combined AQOLIS and CPAP samples are also presented (Table II) because they are the most similar samples, and results for this composite might be useful for planning future studies with similar eligibility requirements.

The AQOLIS, CPAP study, and DASH study samples fell between the LASST and BTR samples on all 7 asthma outcomes (see Fig E1). Of the 3, the DASH study was the most distinct, with numerically but not necessarily significantly worse status on all asthma outcome measures, except symptoms. The AQOLIS and CPAP study samples varied in their positions relative to the DASH study sample, depending on which asthma outcome measure was considered. A-IQOLS scores differed significantly between the AQOLIS and DASH study samples and between the combined AQOLIS/CPAP study and DASH study samples, but ASUI, Mini-AQLQ total and symptom, and Marks AQLQ scores did not. By contrast, ASUI and Mini-AQLQ symptom scores differed significantly between the CPAP study sample and both the DASH study and AQOLIS, whereas Mini-AQLQ total, Marks AQLQ, and A-IQOLS scores did not.

Perceived importance of QoL dimensions

From 60% to 97% of patients in the pooled sample rated 15 of the individual QoL dimensions as personally important/very important, and 56% rated 12 or more of the 16 dimensions as personally important/very important (Fig 1, *A*). Only dimension

TABLE II. Statistical significance (*P* values) of tests of pairwise mean differences between studies* on all asthma measures

Measures	LASST vs BTR	AQOLIS vs BTR	CPAP study vs BTR	AQOLIS/ CPAP study vs BTR	DASH study vs BTR	LASST vs AQOLIS	LASST vs CPAP study	LASST vs AQOLIS/ CPAP study	LASST vs DASH study	AQOLIS vs DASH study	CPAP study vs DASH study	AQOLIS/ CPAP study vs DASH study	CPAP study vs AQOLIS
$PPFEV_1$†	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**.009**	.25	**.02**	.37	.24	.85	.38	.32
ACT score	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**
ASUI‡	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**.0003**	**<.0001**	**<.0001**	.94	**<.0001**	.06	**<.0001**
Mini-AQLQ symptom score§	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**.004**	**<.0001**	**<.0001**	.95	**.001**	.13	**.0003**
Mini-AQLQ total score‖	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	.29	.18	.19	.66
Marks AQLQ¶#	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	.40	.22	.26	.58
A-IQOLS**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**.02**	**.003**	**.002**	**<.0001**	**.01**	.16	**.02**	.35

Values in boldface indicate statistical significance.
*Study sample size: LASST, n = 227; AQOLIS, n = 152; CPAP study, n = 92; DASH study, n = 88; and BTR, n = 38.
†One AQOLIS, 2 DASH study, and 5 BTR participants were missing a lung function value.
‡ASUI scores imputed from Mini-AQLQ symptom scores for DASH study and BTR samples.
§Mini-AQLQ symptom scores were imputed from ASUI scores for LASST and CPAP study samples.
‖Mini-AQLQ total scores were imputed from Marks AQLQ scores for LASST and CPAP study samples.
¶Marks AQLQ score is missing for 1 CPAP study participant.
#Marks AQLQ scores were imputed from Juniper total scores for DASH study and BTR samples.
**A subject's standard A-IQOLS summary score was defined as $S = \frac{\sum_{d=1}^{n} r_d}{n}$, where r_d is their rating of the effect of asthma on dimension d, and n is the number of dimensions rated, typically 16.

8, "Participation in activities relating to local and national government and public affairs," was considered important/very important by fewer than half of the patients (23%). No importance ratings were missing.

The dimension importance patterns were very similar for men and women and patients of all ages, races, ethnicities, and education levels (see Fig E2 in this article's Online Repository at www.jacionline.org), with the exception that younger subjects on average considered "Having and raising children" (dimension 4) to be less important than older subjects.

Despite similar mean importance rating patterns across demographic subgroups, there was substantial individual variability. To characterize this, the absolute difference between each subject's importance rating on a given dimension and the dimension's overall mean importance rating was calculated and summed across the 16 dimensions. The mean of the individual deviations was 12.8 (SD, 3.7). Subjects' summed differences ranged from 4.9 (a subject with importance ratings similar to the sample average ratings) to 35.0 (a subject with a ≥2-point average deviation from the sample mean dimension importance ratings). Demographic characteristics together accounted for only 2% of the variance in deviations; 98% was due to other (undetermined) individual differences and measurement errors. Only increasing age was significantly associated with greater deviation ($P = .03$).

Negative effect of asthma: A-IQOLS summary scores

A-IQOLS scores and dimension ratings. Missing A-IQOLS ratings were rare: only 3 of 597 patients omitted 1 and only 1 patient omitted 2 dimension-negative effect ratings.

In the pooled sample and the individual study samples, the dimensions of "Health/safety" and "Active recreation" were most negatively affected by the patient's asthma and its treatment, with "Work," "Material well-being," "Independence," and "Socializing" somewhat more negatively affected than the remaining 10 dimensions (Fig 1, *B*). BTR (severe asthma) patients reported substantially greater negative effects on all QoL dimensions than those of the other study samples, and greater negative effects on the "Work," "Socializing," "Health/safety," and "Active recreation dimensions" relative to the other 10 dimension than the other studies. There was substantial individual variation in the dimensions perceived to be most negatively affected by their asthma (eg, 59.1% of patients considered the negative effect to be as great or greater on ≥1 of the other dimensions than on any of the 6 most commonly affected dimensions).

Demographic subgroup A-IQOLS score comparisons. A-IQOLS scores did not differ significantly as a function of age, sex, race, or ethnicity (see Table E2 in this article's Online Repository at www.jacionline.org) but differed significantly by level of education (ie, greater negative effect of asthma in those with high school education or less) and treatment step (greater negative effect at higher treatment step). These associations ($P = .02$ and $P < .0001$, respectively) persisted after controlling for ACT score ($P = .008$ and $P = <.0001$). Thus the greater perceived negative effects of asthma and its treatment among patients with more intense treatment regimens, lower education, or both are not explained by subgroup differences in level of disease control but might be due to their functional impairments or the cost, inconvenience, or side effects of asthma treatment.

Correlations between A-IQOLS scores and other outcomes (convergent and divergent validity)

A-IQOLS scores were significantly correlated with all other asthma outcome measures (Table III). Although statistically significant, the correlation between $PPFEV_1$ and A-IQOLS score was very weak ($r = -0.13$). For all other asthma outcomes, the correlations were highly significant ($P < .0001$) but ranged from very weak (ASUI) to moderate (ACT and Marks AQLQ) and

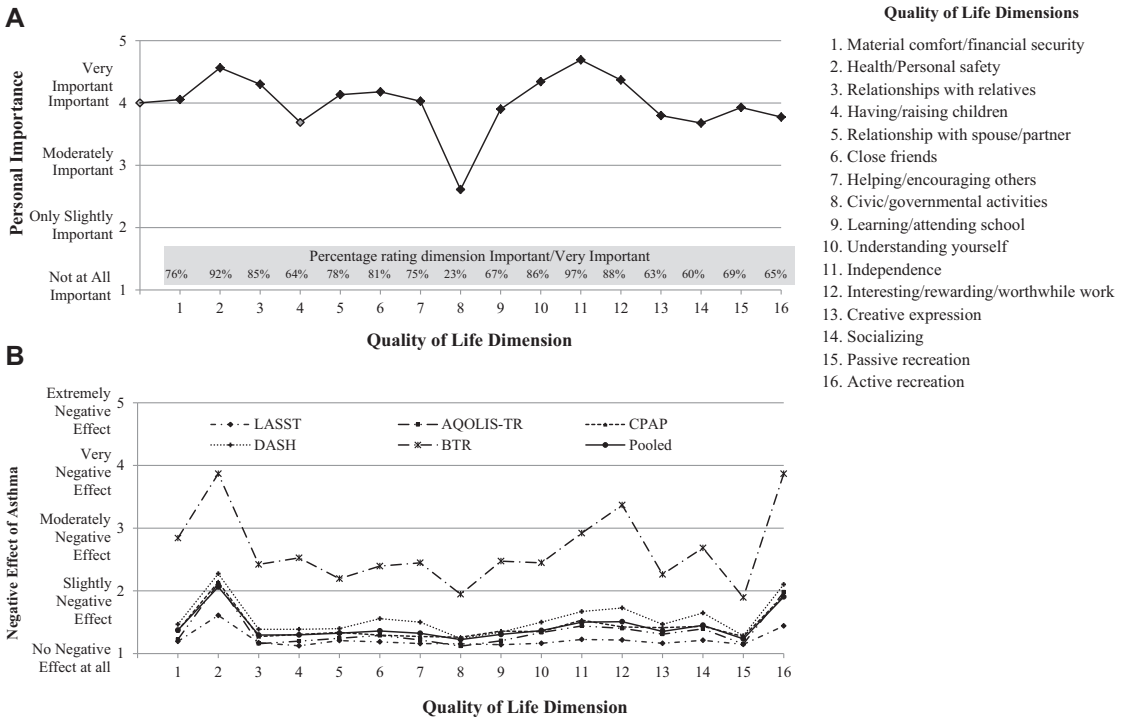

FIG 1. A, Mean ratings of the importance of each QoL dimension: pooled sample (n = 597). **B,** Mean A-IQOLS ratings of negative effect of asthma on each QoL dimension: pooled and by study sample.

strong (Mini-AQLQ). In all cases the shared/common variance (R^2) between the A-IQOLS score and the other asthma measures was 48% or less, confirming, as previously reported for the AQOLIS sample,[2] that the A-IQOLS provides substantial unique information not provided by the other measures.

In all age groups, male and female subjects, Hispanic and non-Hispanic subjects, all racial groups, and those at different levels of education, associations between A-IQOLS scores and other asthma outcome measures were statistically significant, and their absolute and relative magnitudes, as well as their R^2 values, were similar to those in the pooled sample as a whole (see Table E3 in this article's Online Repository at www.jacionline.org). The only exception was that the correlations between the A-IQOLS score and $PPFEV_1$ tended to be lower and not statistically significant in numerically smaller subgroups, which also tended to be less heterogeneous than the pooled sample as a whole on both measures.

Estimation of the MID. The SEM of the A-IQOLS score averaged across all score levels was determined previously to be 0.27.[2] One recommended estimate of the MID based on its distributional properties (ie, its SEM) is ±1.96 SEM,[25] which yields an MID of 0.54 for A-IQOLS score. This criterion provides 95% probability that a change of this magnitude or greater is a true change (ie, statistically reliable). An alternative criterion (±1 SEM) yields an estimated MID of 0.27[24] but less assurance that the change is real. Other levels of assurance can be considered as well. For example, the smallest A-IQOLS score change that constitutes a true change with 80% probability would be ±1.81 SEM (MID = ±0.49) or, if only 67% probability was acceptable, ±1.15 SEM (MID = ±0.31).

Another distributional approach to estimating the MID is to use one half the SD of the measure. The A-IQOLS score SD in the pooled sample (0.68; Table I) yields an estimated MID of 0.34.

An anchor-based approach to estimating the MID uses self-reported change (eg, a patient's perception that the negative effects of asthma had increased, decreased, or remained the same) over a given time period. Reliance on a single item reporting perceived change has been criticized on methodologic grounds and might not provide new information because the results of many such studies turn out to yield an MID value close to one half the SD of the measure.[26] In AQOLIS, however, patients were asked for an overall rating of the negative effect of asthma on their life at both test and retest assessments, allowing direct determination of change rather than retrospective report. By using simple linear regression, a 1-category change in the patient's overall assessment was associated with a 0.23-point change in A-IQOLS summary score.

Considering these various estimates, it appears reasonable to consider the A-IQOLS score's MID conservatively to be approximately one half scale score point (0.50) and possibly somewhat less if one is willing to accept less assurance that the change exceeds statistical variability.

A-IQOLS' internal consistency reliability. The standardized coefficient α is reported commonly, even though it is not informative regarding measurement reliability. Standardized coefficient α values of A-IQOLS scores were high in the pooled sample as a whole (α = 0.97) and in all demographic subgroups (α = 0.94-0.98).

DISCUSSION

We evaluated the psychometric properties of the A-IQOLS in 5 asthma studies constituting a large heterogeneous population, representing multiple demographic subgroups and asthma severities. The dimensions underlying the A-IQOLS were personally important for substantial proportions of patients in

TABLE III. Correlations and shared variances between A-IQOLS scores and other asthma measures: Pooled sample (n = 597)

Variable	A-IQOLS score		
	*r**	*P* value	R^2
$PPFEV_1$†	−0.13	.002	0.02
ACT score	−0.50	<.0001	0.25
ASUI score‡	−0.33	<.0001	0.11
Mini-AQLQ, symptom score§	−0.64	<.0001	0.41
Mini-AQLQ, total score§	−0.70	<.0001	0.48
Marks AQLQ‡‖	0.50	<.0001	0.25

*Pearson product-moment correlation.
†Pooled sample size, n = 589; 1 AQOLIS, 2 DASH study, and 5 BTR participants were missing a baseline $PPFEV_1$ value.
‡Pooled results for LASST, AQOLIS, and CPAP study samples only. When ASUI scores were imputed from Mini-AQLQ Symptom scores, results were as follows: $r = -0.51$ and $R^2 = 0.26$. When Marks AQLQ scores were imputed from Mini-AQLQ total scores, results were as follows: $r = 0.62$ and $R^2 = 0.38$.
§Pooled Mini-AQLQ results for AQOLIS, DASH study, and BTR samples only. AQOLIS and the DASH study used the Mini-AQLQ; BTR used the standardized Juniper AQLQ. When Mini-AQLQ total scores were imputed from Marks AQLQ scores, results were as follows: $r = -0.62$ and $R^2 = 0.38$. When Mini-AQLQ Symptom scores were imputed from ASUI scores, results were as follows: $r = -0.54$ and $R^2 = 0.29$.
‖One CPAP study participant was missing the Marks AQLQ score.

all demographic subgroups. These findings reinforce the content and construct validity of the A-IQOLS score for use in diverse populations. Similar ratings of which dimensions are important, similar associations between A-IQOLS scores and other asthma outcome measures, and similar standardized coefficient α values in all subgroups suggest that patients, including those with low education, had a similar understanding of the dimension descriptions and rating task.

A strength of the A-IQOLS is that subjects can characterize the negative effects of asthma in light of how important each dimension is to them. The similarity of the mean dimension importance ratings across sex, race, and ethnic subgroups shows the general relevance of the dimensions. However, the validity and utility of the A-IQOLS do not depend on whether a subject's priorities are similar to others' priorities or whether the subject's priorities remain stable over time.

The question posed to respondents by the A-IQOLS differs substantially from the questions posed in instruments conventionally referred to as asthma-related QoL measures. A number of A-IQOLS dimensions also are not represented by items in other instruments or in the item bank of a newer measure: the RAND-IAQL.[28] When choosing items to include in disease-specific QoL measures, it has been common practice to pretest a pool of items and eliminate those that relate to domains that are affected in smaller proportion of respondents, are less strongly correlated with other items, or both.[28,29] This practice reduces instrument length and administration time and tends to increase internal consistency reliability. However, it can compromise content validity by narrowing the range of disease effects that are assessed. The modest shared variances between the A-IQOLS and the Juniper and Marks AQLQ measures are likely due to the smaller number of life dimensions assessed by the latter measures. The construct validity of the IQOLS template requires including all dimensions of life, and because the A-IQOLS administration time is already brief, there is no need to exclude dimensions less commonly affected.

BTR patients, all of whom had severe asthma refractory to intensive asthma pharmacotherapy and who had been approved to undergo bronchial thermoplasty, typically believed their asthma was having an effect between "slightly negative" and "moderately negative" on most dimensions and a very negative effect on their overall health and safety (A-IQOLS score mean ± SD, 2.67 ± 0.87). Patients with moderate persistent asthma that was stable and well controlled (LASST) typically believed their asthma had very little negative effect on their life (mean, 1.22; only slightly greater than "no negative effect at all"). Those with asthma that was not well controlled (eg, DASH study patients) typically believed that its negative effect was about halfway between "no negative effect at all" and a "slightly negative effect." The relatively low mean A-IQOLS scores of the DASH study patients might seem surprising because the functional consequences and risks of poorly controlled asthma can be important. However, A-IQOLS scores indicate that how much the patient believes asthma affects his or her life, which perspective might be influenced by their overall QoL or other circumstances. Other life problems might overshadow the effects of asthma. In all these groups, however, the situation of individual patients varies substantially. Scores of 3.25 or greater were observed in all study groups, and scores of 4.38 or greater were observed in BTR, the CPAP study, and LASST.

In summary, the A-IQOLS, which is based on a comprehensive set of empirically derived dimensions of QoL, accommodates variation in individual priorities, yields reliable information on how and how much asthma negatively affects patients' lives and is associated with other asthma outcomes but provides unique information, has a score range that makes it useful across the full spectrum of asthma severity and control, requires only a few minutes to administer, and is not copyrighted. The underlying IQOLS template (dimensions, stem question, and rating scale) can be easily modified for use in other diseases/conditions, assuming their psychometric performance, when evaluated, supports such use.

Measurement reliability and the MID

Lydick and Epstein[22] noted that any change in a QoL measure can be considered clinically significant in that it represents the patient's perception of an altered health outcome. However, this proposition needs to be tempered. The evidence presented here suggests that the minimum clinically important within-person change (MID) of the A-IQOLS score is approximately 0.50 but that somewhat smaller changes (between one third and one half a scale score point) might be informative, whereas smaller changes are more likely to be caused by measurement error. As with any new measure, it will take time and experience with its response to clinical interventions to clarify the clinical importance of within-person A-IQOLS score changes.[22]

Use of the results to inform sample size and power calculations

When planning studies in which the A-IQOLS might be a primary or secondary outcome measure, the information provided in Table I and Table E2 can be used to estimate sample size requirements or determine statistical power.

Limitations and future directions

A-IQOLS scores are sensitive to sample differences and are correlated with other asthma outcome measures. Changes in asthma control are significantly associated with changes in A-IQOLS scores,[2] providing grounds for optimism regarding its suitability as an outcome measure in clinical research and regarding the suitability of the IQOLS approach more generally for assessing the patient-perceived negative effect of other medical conditions. However, A-IQOLS sensitivity to experimental group differences has not yet been directly evaluated.

The present study populations do not exhaust the demographic or clinical diversity of patients in which the A-IQOLS or any measure using the A-IQOLS template might be used. The basic IQOLS stem question, dimension descriptions, and response scale already have been translated into many languages and national variants of those languages for an international clinical trial in another respiratory disease. Simply inserting the relevant translations of the word asthma into these language versions will yield a corresponding translation of the A-IQOLS. Further information is available from the corresponding author.

Conclusions

The A-IQOLS measures the patient-perceived effect of asthma and its treatment on the patient's life. The dimensions of life underlying the A-IQOLS are important across adults of both sexes; all age groups; white, African American, and Asian ancestry; Hispanics and non-Hispanics; and all levels of education, but their importance varies greatly between subjects. A-IQOLS scores are significantly associated with standardized measures of symptom and disease control in all of these demographic subgroups and can be recommended for use in those groups. A-IQOLS scores discriminate between asthmatic patients with different levels of disease control and severity at least as well as functional status or asthma-specific QoL measures but yield unique information.

We acknowledge the contributions of the investigators, staff, participants, oversight committees, funders, and institutions/research networks involved in the LASST, AQOLIS, CPAP study, DASH study, and BTR, which provided the data used in the present analyses. We also acknowledge the helpful suggestions regarding data analyses and their interpretation provided by Lauress Wise, PhD (educational measurement and statistics), and Lan Xiao, PhD (biostatistics).

Clinical implications: The A-IQOLS assesses the negative effect of asthma on QoL from the patient's perspective and is suitable as an asthma outcome measure in diverse demographic and clinical populations.

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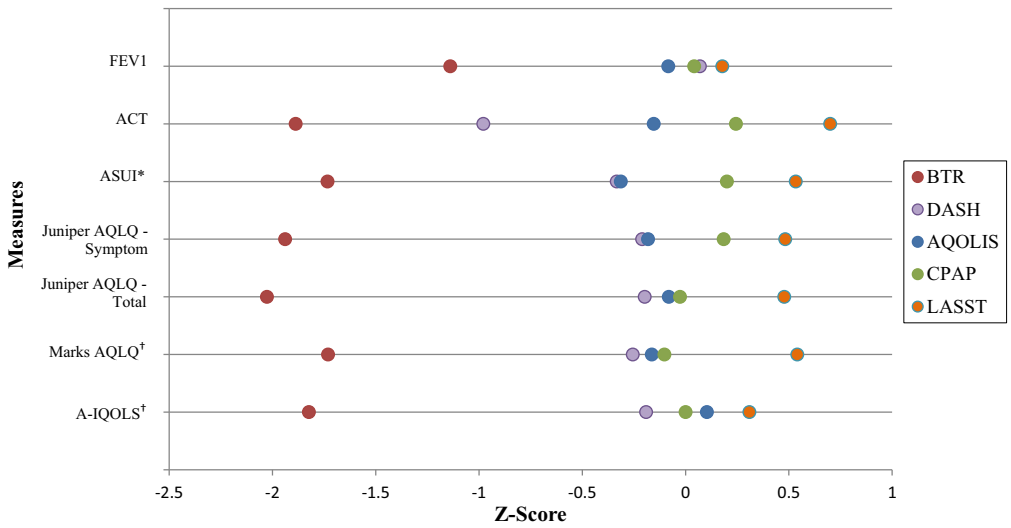

*ASUI and Juniper Symptom Z-scores of AQOLIS group were shifted by +0.02 in order to visually discriminate data points.
† On the Marks AQLQ and A-IQOLS, higher scores indicate worse asthma status/effect. Scores on both measures have been inverted in this figure to be consistent with the orientation of the other measures.

FIG E1. Study means on asthma measures in relation to pooled sample mean (*z* scores based on pooled sample SD).

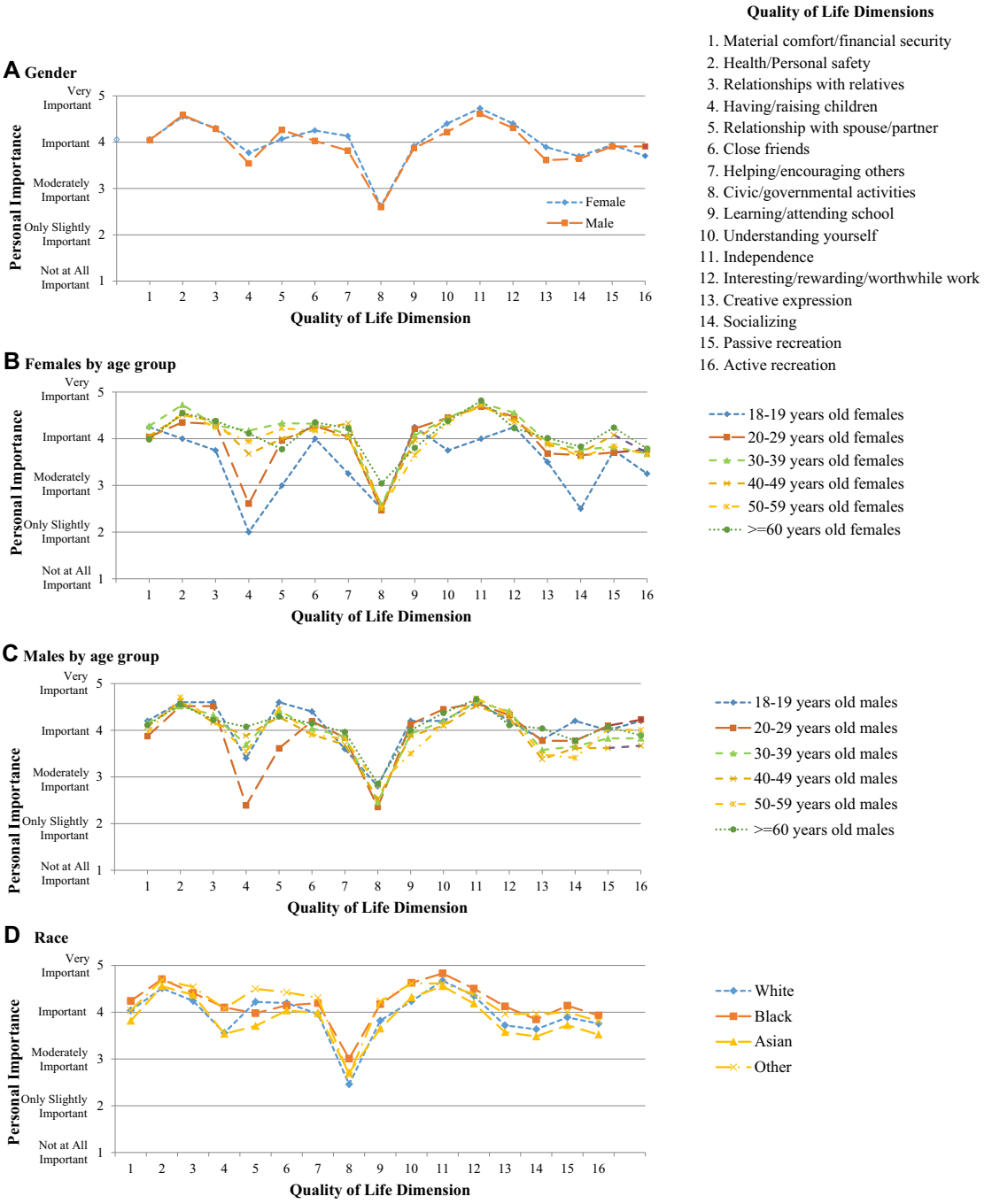

FIG E2. Mean ratings of the importance of each QoL dimension by subgroup. **A,** Sex. **B,** Female subjects by age group. **C,** Male subjects by age group. **D,** Race. **E,** Ethnicity. **F,** Level of education.

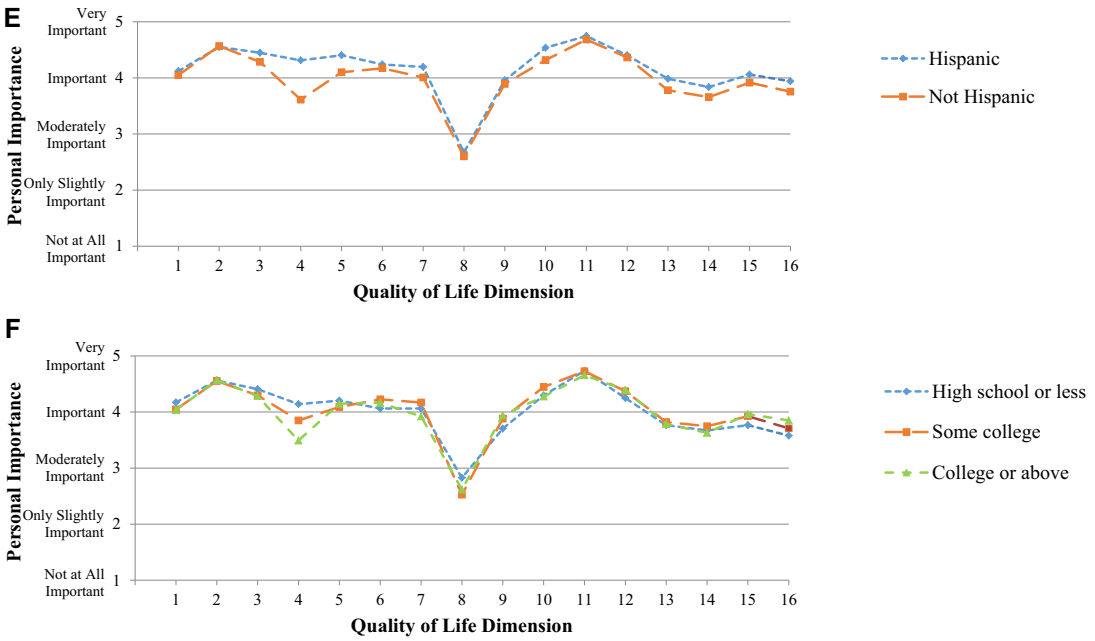

FIG E2. *(Continued).*

TABLE E1. Characteristics of the 5 asthma studies contributing to the pooled sample (n = 597)

Name	LASST*	AQOLIS	CPAP study	DASH study	BTR
Network/clinical sites(s)/PI(s)	Eighteen ALA Asthma Clinical Research Centers (L. Rogers)	Two Palo Alto Medical Foundation sites: Mountain View and Palo Alto (S. Wilson)	Eighteen ALA Asthma Clinical Research Centers (M. Busk and J. Holbrook)	Two Kaiser Health Care System sites: San Francisco and Hayward (J. Ma)	Five BTR research network sites (M. Castro)
Data Coordinating Center	Johns Hopkins Bloomberg School of Public Health	Palo Alto Medical Foundation Research Institute	Johns Hopkins Bloomberg School of Public Health	Palo Alto Medical Foundation Research Institute	Washington University, St Louis
Eligibility Criteria	≥18 y of age; asthma well controlled on combination therapy (ICS + LABA)	18-70 y of age; persistent asthma; sample stratified based on sex, race/ethnicity, and asthma therapy step	≥18 y of age; stable asthma; airways reactivity; no sleep disorder	18-70 y of age; uncontrolled persistent asthma; BMI, 18.5-39.9 kg/m^2; low-quality diet	≥18 y of age; severe refractory asthma; approved to undergo BT
Study design	56-wk 3-arm randomized, double-blind, 3-arm controlled trial *Interventions*: alternative step-down approaches	Observational test-retest study (3- to 5-wk interval) *Intervention*: None	16-wk 3-arm randomized, sham-controlled trial *Interventions*: <1, 5, or 10 cm H_2O CPAP	6-mo 2-arm controlled trial *Intervention*: DASH study dietary intervention vs usual care	Ongoing prospective cohort study *Intervention*: BT to reduce excess airway smooth muscle
Research hypotheses/purpose	• Discontinuing LABA while maintaining ICS dose will be inferior to continuing LABA and reducing ICS dose in rate of treatment failure • ICS step-down will not be inferior to stable ICS/LABA in rate of treatment failure	• Determine test-retest reliability and other psychometric properties of the A-IQOLS, a measure of patient-perceived effect of asthma on QoL	• CPAP will be associated with reduced airway reactivity	• Behavioral intervention to adopt the DASH study diet will improve asthma control relative to usual medical care	• Identify baseline clinical, physiologic, biologic, and imaging markers of BT response
ClinicalTrials.gov identifier	NCT01437995	NA	NCT01629823	NCT01725945	NCT01185275

ALA, American Lung Association; *BMI*, body mass index; *BT*, bronchial thermoplasty; *CPAP*, continuous positive airway pressure; *ICS*, inhaled corticosteroid; *LABA*, long-acting β-agonist; *PI*, principal Investigator.
*LASST included patients 12 to 17 years of age, as well as adults. Only adults were included in the present analyses.

TABLE E2. Baseline A-IQOLS scores (mean, SD, and range) in the pooled and separate LASST, AQOLIS-TR, CPAP study, DASH study, and BTR samples determined by using baseline sample characteristics

	Pooled samples (n = 597)		LASST (n = 227)		AQOLIS-TR (n = 152)		CPAP study (n = 92)		DASH study (n = 88)		BTR (n = 38)	
Characteristic	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value
Overall	1.43 ± 0.68 (1.00-4.94)	—	1.22 ± 0.56 (1.00-4.94)	—	1.36 ± 0.45 (1.0-3.94)	—	1.43 ± 0.73 (1.00-4.50)	—	1.56 ± 0.60 (1.00-3.25)	—	2.67 ± 0.87 (1.13-4.38)	—
Age (y)												
18-44	1.4 ± 0.65 (1-4.5)	.61	1.15 ± 0.27 (1-2.5)	.08	1.37 ± 0.41 (1-2.75)	.90	1.44 ± 0.73 (1-4.5)	.96	1.77 ± 0.71 (1-3.19)	.07	2.77 ± 0.91 (1.13-4.31)	.72
45-59	1.46 ± 0.73 (1-4.75)		1.33 ± 0.78 (1-4.75)		1.34 ± 0.47 (1-3.94)		1.43 ± 0.71 (1-3.69)		1.51 ± 0.588 (1-3.25)		2.63 ± 0.799 (1.44-4.25)	
60-70	1.45 ± 0.69 (1-4.94)		1.27 ± 0.76 (1-4.94)		1.39 ± 0.49 (1-2.81)		—		1.41 ± 0.43 (1-2.88)		2.52 ± 1.03 (1.44-4.38)	
Sex												
Female	1.43 ± 0.67 (1-4.94)	.86	1.22 ± 0.55 (1-4.94)	.91	1.4 ± 0.51 (1-3.94)	.18	1.28 ± 0.41 (1-3)	.01	1.53 ± 0.59 (1-3.19)	.60	2.68 ± 0.89 (1.13-4.38)	.85
Male	1.44 ± 0.71 (1-4.75)		1.23 ± 0.57 (1-4.75)		1.3 ± 0.33 (1-2.31)		1.7 ± 1.02 (1-4.5)		1.61 ± 0.63 (1-3.25)		2.62 ± 0.86 (1.44-3.81)	
Race (n = 595)*												
White	1.42 ± 0.66 (1-4.94)	.97	1.18 ± 0.42 (1-4.94)	.33	1.36 ± 0.44 (1-3.94)	.95	1.31 ± 0.59 (1-4.38)	.18	1.53 ± 0.56 (1-3.25)	.49	2.73 ± 0.89 (1.13-4.38)	.68
Black/African American	1.45 ± 0.8 (1-4.75)		1.3 ± 0.79 (1-4.75)		1.39 ± 0.54 (1-2.81)		1.69 ± 0.95 (1-4.5)		1.82 ± 0.69 (1-3.13)		2.42 ± 0.88 (1.44-3.13)	
Asian	1.43 ± 0.57 (1-3.13)		1.38 ± 0.54 (1-2.5)		1.31 ± 0.48 (1-2.75)		1.49 ± 0.85 (1-3)		1.5 ± 0.59 (1-3.13)		—	
Other	1.4 ± 0.58 (1-3.19)		1.1 ± 0.15 (1-1.38)		1.27 ± 0.16 (1.13-1.44)		1.53 ± 0.69 (1-2.69)		1.68 ± 0.84 (1-3.19)		1.94 ± 0 (1.94-1.94)	
Ethnicity (n = 596)†												
Hispanic	1.41 ± 0.67 (1-3.94)	.78	1.09 ± 0.12 (1-1.38)	.24	1.44 ± 0.7 (1-3.94)	.44	1.47 ± 0.78 (1-3.31)	.86	1.59 ± 0.6 (1-3.19)	.83	3.38 ± 0.37 (3.13-3.64)	.30
Non-Hispanic	1.43 ± 0.69 (1-4.94)		1.23 ± 0.59 (1-4.94)		1.35 ± 0.41 (1-2.81)		1.43 ± 0.72 (1-4.5)		1.55 ± 0.6 (1-3.25)		2.64 ± 0.89 (1.13-4.38)	
Education (n = 595)‡												
≤High school	1.64 ± 0.99 (1-4.94)	.02†§	1.4 ± 0.91 (1-4.94)	.07	1.41 ± 0.61 (1-2.81)	.90	1.67 ± 1.02 (1-4.38)	.35	1.82 ± 0.88 (1.13-3.19)	.44	3.15 ± 0.87 (2.19-4.38)	.55
Some college	1.44 ± 0.65 (1-4.75)		1.25 ± 0.63 (1-4.75)		1.38 ± 0.32 (1-2.19)		1.45 ± 0.61 (1-3.69)		1.5 ± 0.5 (1-3.13)		2.66 ± 0.76 (1.44-3.81)	
College or greater	1.38 ± 0.63 (1-4.5)		1.15 ± 0.34 (1-3.38)		1.35 ± 0.49 (1-3.94)		1.34 ± 0.72 (1-4.5)		1.56 ± 0.62 (1-3.25)		2.6 ± 0.98 (1.13-4.31)	
Treatment step (n = 505)												
Step 1	1.44 ± 0.46 (1-2.56)	<.0001§	—	—	—	.37	—	—	1.44 ± 0.46 (1-2.56)	.61	—	.15
Step 2	1.41 ± 0.42 (1-3)		—		1.26 ± 0.23 (1-1.81)		—		1.72 ± 0.56 (1.19-3)		—	
Step 3	1.37 ± 0.60 (1-3.25)		—		1.24 ± 0.32 (1-2.31)		—		1.62 ± 0.90 (1-3.25)		—	
Step 4	1.26 ± 0.53 (1-4.94)		1.22 ± 0.56 (1-4.94)		1.36 ± 0.41 (1-2.81)		—		1.60 ± 0.35 (1.13-2.0)		—	
Step 5	1.82 ± 0.88 (1-4.38)		—		1.45 ± 0.58 (1-3.94)		—		1.65 ± 0.68 (1-3.19)		2.93 ± 0.82 (1.75-4.38)	
Step 6	2.33 ± 0.86 (1.13-4.25)		—		1.44 ± 0 (1.44-1.44)		—		—		2.37 ± 0.86 (1.13-4.25)	
ACT												
Well-controlled (20-25)	1.23 ± 0.54 (1-4.94)	<.01	1.22 ± 0.56 (1-4.94)	—	1.15 ± 0.2 (1-2.06)	<.01	1.34 ± 0.7 (1-4.5)	.03	1.64 ± 0.79 (1-3.25)	.14	1.56 ± 0 (1.56-1.56)	.07

(Continued)

TABLE E2. *(Continued)*

Characteristic	Pooled samples (n = 597)		LASST (n = 227)		AQOLIS-TR (n = 152)		CPAP study (n = 92)		DASH study (n = 88)		BTR (n = 38)	
	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value	Mean ± SD (range)	*P* value
Poorly controlled (16-19)	1.5 ± 0.61 (1-4.31)		—		1.45 ± 0.56 (1-3.94)		1.57 ± 0.68 (1-3.69)		1.4 ± 0.43 (1-2.69)		2.13 ± 1.15 (1.13-4.31)	
Very poorly controlled (5-15)	1.99 ± 0.81 (1-4.38)		—		1.72 ± 0.48 (1-2.81)		2.1 ± 0.85 (1.19-3.31)		1.66 ± 0.66 (1-3.19)		2.81 ± 0.77 (1.44-4.38)	

ACT, Asthma Control Test (well-controlled, 20-25; poorly controlled, 16-29; and very poorly controlled, 5-15).

*One DASH study participant and 1 BTR participant were missing race information.

†One BTR participant was missing ethnicity information.

‡Two BTR participants were missing education information.

§Differences in A-IQOLS mean score by level of education and treatment step remained statistically significant after controlling for ACT score ($P = .008$ and $P < .0001$, respectively).

TABLE E3. Correlations *(r)* and shared variances *(R^2)* between subjects' A-IQOLs scores and other asthma outcome measures by age, sex, race, ethnicity, and education: Pooled sample (n = 597)

	Age									Sex					
	18-44 y (n = 291)			45-59 y (n = 208)			≥60 y (n = 98)			Female subjects (n = 396)			Male subjects (n = 201)		
Variable	***r****	***P* value**	***R^2***	***r****	***P* value**	***R^2***	***r****	***P* value**	***R^2***	***r****	***P* value**	***R^2***	***r****	***P* value**	***R^2***
$PPFEV_1$†	−0.27	<.0001	0.07	−0.01	.93	<0.01	−0.05	.62	<0.01	−0.12	.02	0.02	−0.13	.06	0.02
ACT score	−0.61	<.0001	0.37	−0.41	<.0001	0.17	−0.44	<.001	0.20	−0.54	<.0001	0.30	−0.42	<.0001	0.18
ASUI‡	−0.64	<.0001	0.4	−0.44	<.0001	0.19	−0.40	<.0001	0.16	−0.57	<.0001	0.32	−0.40	<.0001	0.16
Marks AQLQ§‖	0.67	<.0001	0.45	0.58	<.0001	0.34	0.55	<.0001	0.30	0.67	<.0001	0.45	0.52	<.0001	0.27
Mini-AQLQ: total score‖¶	−0.69	<.0001	0.48	−0.54	<.0001	0.3	−0.58	<.0001	0.34	−0.67	<.0001	0.45	−0.51	<.0001	0.26
Mini-AQLQ symptom score‡¶	−0.65	<.0001	0.42	−0.46	<.0001	0.21	−0.48	<.0001	0.23	−0.61	<.0001	0.37	−0.42	<.0001	0.18

	Race										Ethnicity				
	White (n = 386)			African American (n = 129)				Asian (n = 54)			Hispanic (n = 67)			Non-Hispanic (n = 529)		
Variable	***r****	***P* value**	***R^2***	***r****	***P* value**	***R^2***	***R^2*†**	***r****	***P* value**	***R^2***	***r****	***P* value**	***R^2***	***r****	***P* value**	***R^2***
$PPFEV_1$†	−0.19	.002	0.04	−0.02	.82	<0.01	—	−0.09	.54	0.01	<0.01	.998	<0.01	−0.14	.001	0.02
ACT score	−0.59	<.0001	0.35	−0.33	.0001	0.11	—	−0.43	.001	0.18	−0.60	<.0001	0.36	−0.49	<.0001	0.24
ASUI‡	−0.61	<.0001	0.37	−0.24	.007	0.06	—	−0.73	<.0001	0.53	−0.64	<.0001	0.41	−0.50	<.0001	0.25
Marks AQLQ§‖	0.69	<.0001	0.48	0.42	<.0001	0.18	—	0.74	<.0001	0.55	0.79	<.0001	0.62	0.60	<.0001	0.36
Mini-AQLQ total score‖¶	−0.70	<.0001	0.49	−0.40	<.0001	0.16	—	−0.69	<.0001	0.48	−0.72	<.0001	0.52	−0.61	<.0001	0.37
Mini-AQLQ symptom score‡¶	−0.64	<.0001	0.41	−0.25	.004	0.06	—	−0.70	<.0001	0.49	−0.65	<.0001	0.43	−0.53	<.0001	0.28

	Education								
	High school or less (n = 64)			Some college (n = 213)			College or greater (n = 318)		
Variable	***r****	***P* value**	***R^2***	***r****	***P* value**	***R^2***	***r****	***P* value**	***R^2***
$PPFEV_1$†	−0.10	.45	<0.01	−0.17	.02	0.03	−0.10	.09	0.01
ACT score	−0.44	.0003	0.19	−0.47	<.0001	0.22	−0.55	<.0001	0.30
ASUI‡	−0.47	<.0001	0.22	−0.45	<.0001	0.21	−0.58	<.0001	0.34
Marks AQLQ§‖	0.42	.0006	0.18	0.62	<.0001	0.38	0.70	<.0001	0.49
Mini-AQLQ total score‖¶	−0.46	.0002	0.21	−0.62	<.0001	0.38	−0.69	<.0001	0.47
Mini-AQLQ symptom score‡¶	−0.46	.0001	0.21	−0.51	<.0001	0.26	−0.61	<.0001	0.37

*Pearson product-moment correlation (equivalent to the square root of the R^2 value from the model y = x).

†Pooled sample size, n = 590; 1 AQOLIS, 2 DASH study, and 6 BTR participants were missing a baseline $PPFEV_1$ value.

‡Pearson correlation between the ASUI and the Mini-AQLQ symptom score in the AQOLIS sample was 0.81. Linear regression was used to impute ASUI scores from Juniper symptom scores in the DASH study and BTR samples and to impute Mini-AQLQ symptom scores in the LASST sample and CPAP study samples from their ASUI scores.

§One CPAP study participant is missing the Marks AQLQ score.

‖Pearson correlation between the Mini-AQLQ total score and the Marks AQLQ score in the AQOLIS sample was −0.80. Linear regression was used to impute Marks AQLQ scores for DASH study and BTR samples from their Juniper total scores and to impute Juniper total scores in the LASST and CPAP studies from their Marks scores.

¶AQOLIS and the DASH study used the Mini-AQLQ; BTR used the standardized Juniper AQLQ.