



Psychometric Validation of Angioedema Quality-Of-Life Questionnaire in Hereditary Angioedema: Results from the OASIS-HAE Study

Aaron Yarlas¹, Jakob B. Bjorner², Alexandra J. Feld², Cary Thurm², Regina Rendas-Baum²
¹Ionis, Carlsbad, CA, USA • www.ionis.com; ²QualityMetric, an IQVIA business, Johnston, RI, USA

BACKGROUND

- Hereditary angioedema (HAE) is a rare disorder characterized by disabling episodes of local skin swellings, painful abdominal attacks, and laryngeal attacks that can be life-threatening¹
- HAE attacks, independent of frequency, can have a significant negative impact on patients' activities of daily living and quality of life (QoL), particularly regarding school and work productivity, due to the unpredictability, pain, and severity of swelling²⁻⁵
- The Angioedema Quality of Life Questionnaire (AE-QoL) is a 17-item, disease-specific, 4-week recall, patient-reported questionnaire capturing the global impact of angioedema (AE) attacks on functioning and well-being^{1,6}
 - The AE-QoL has 4 domains: Functioning, Fatigue/Mood, Fears/Shame, and Nutrition
- The AE-QoL is validated in recurrent AE, but supportive psychometric evidence is sparse in HAE⁷

OBJECTIVE

- To evaluate the psychometric properties of the AE-QoL in patients with HAE participating in OASIS-HAE, a phase 3, double-blind, placebo-controlled study (NCT05139810)

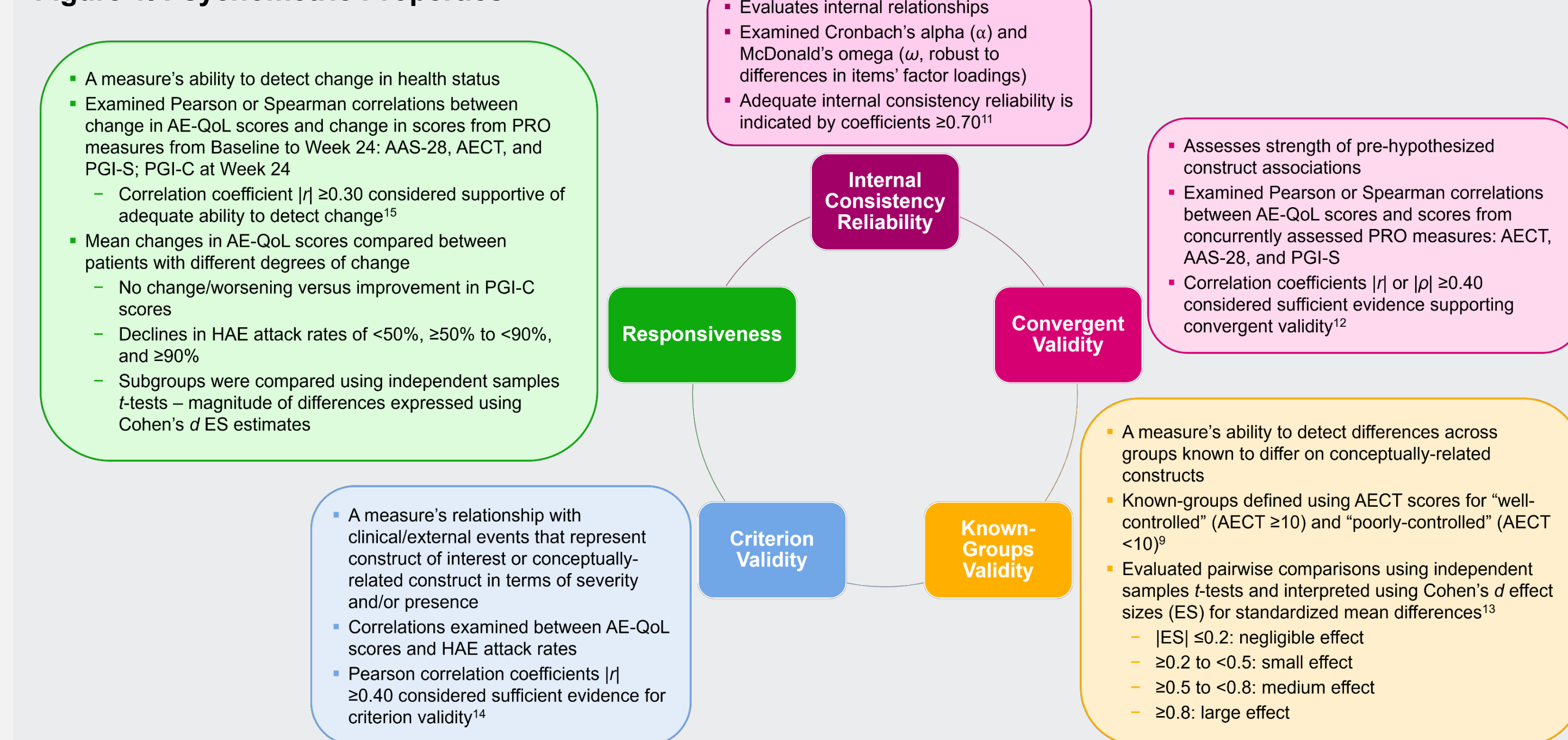
METHODS

Data Source: In the phase 3 OASIS-HAE study, 90 patients were randomized to and received donidalorsen 80 mg or placebo subcutaneously over 24 weeks. All patients were included in these analyses, pooled across treatment arms

Patient-Reported Outcome Assessments (Administered at Baseline [Week 0] and Week 24)

- AE-QoL: 0-100 scaled total and domain scores – lower scores indicate better QoL
- Angioedema Control Test (AECT): 4-item, patient-reported measure of AE symptom frequency/severity in the past month. Scores range 0-16, with higher scores indicating greater control, and scores ≥ 10 indicating well-controlled disease^{8,9}
- 28-day Angioedema Activity Score daily-diary (AAS-28): 5-item, self-reported measure of AE episode frequency/severity, averaged for a 28-day period, higher scores indicate greater disease severity¹⁰
- Patient Global Impression of Severity (PGI-S): Single-item, patient-reported measure of current HAE severity
- Patient Global Impression of Change (PGI-C): Single-item, patient-reported measure of change in HAE-related health
- Investigator-confirmed number of HAE attacks (i.e., HAE attack): Events, separated by 24-hour symptom-free intervals, characterized by signs or symptoms consistent with an attack in ≥ 1 pre-specified bodily locations
 - HAE attack rate calculated as number of attacks occurring during each 28-day interval, starting on study Day 1

Figure 1. Psychometric Properties



RESULTS

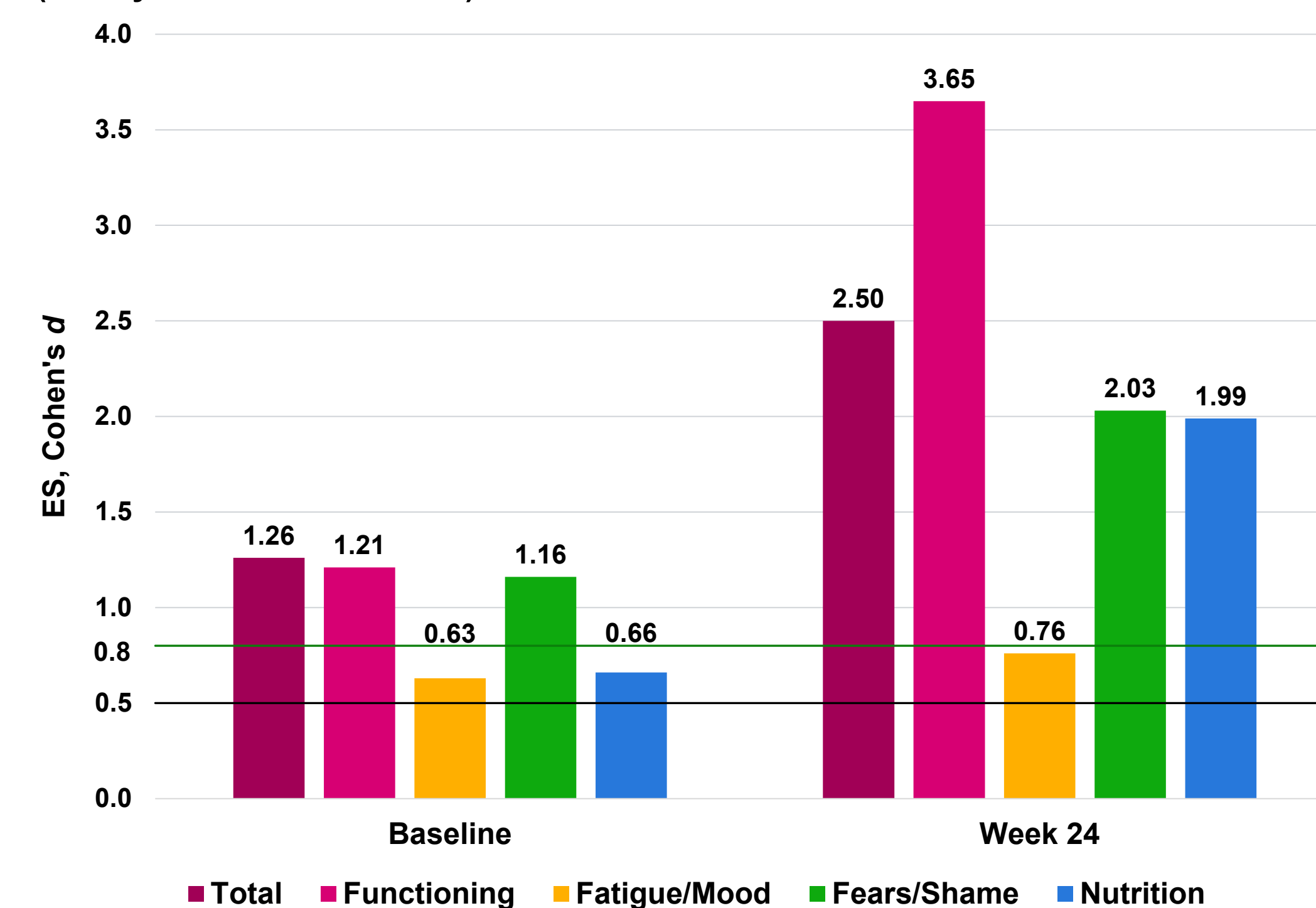
Reliability

- AE-QoL total score had excellent internal consistency (Cronbach's α : 0.90 and 0.94; McDonald's ω : 0.93 and 0.97, at Baseline and Week 24, respectively). Internal consistency reliability was adequate to excellent for AE-QoL domains (both α and $\omega \geq 0.70$), except for the Nutrition domain at Baseline ($\alpha = 0.65$; $\omega = 0.64$)

Construct Validity

- Convergent validity supported by correlations ≥ 0.40 between AE-QoL total and most domain scores and scores on AAS-28, AECT, and PGI-S at Week 24 (Table 1)
- Strong correlations ($r \geq 0.55$) between AE-QoL total and most domain scores and HAE attack rate at Week 24 provided evidence supporting criterion validity (Table 1)
 - As the only exception, Fatigue/Mood domain showed weak correlations with HAE attack rate and scores on AAS-28, AECT, and PGI-S
- Known-groups validity supported by substantial differences in mean AE-QoL scores between well-controlled (AECT ≥ 10) and poorly-controlled (AECT < 10) disease subgroups at Baseline and at Week 24 (Figure 2)
 - All AE-QoL total and domain mean scores were significantly higher in patients with poorly-controlled disease than those with well-controlled disease (total scores: all $p < 0.001$; domain scores: all $p < 0.05$)
 - ES for pairwise differences between the well- and poorly-controlled groups were very large for AE-QoL total scores at both timepoints
 - Fatigue/Mood domain scores at both timepoints and Nutrition domain scores at Baseline showed medium-sized mean differences between well- and poorly-controlled groups. All other AE-QoL domain score differences were very large at both timepoints

Figure 2. Known-Groups Validity: Cohen's *d* ES for Mean Differences in AE-QoL Scores for Subgroups with AECT ≥ 10 (Well-Controlled Disease) and AECT < 10 (Poorly-Controlled Disease) at Baseline and Week 24

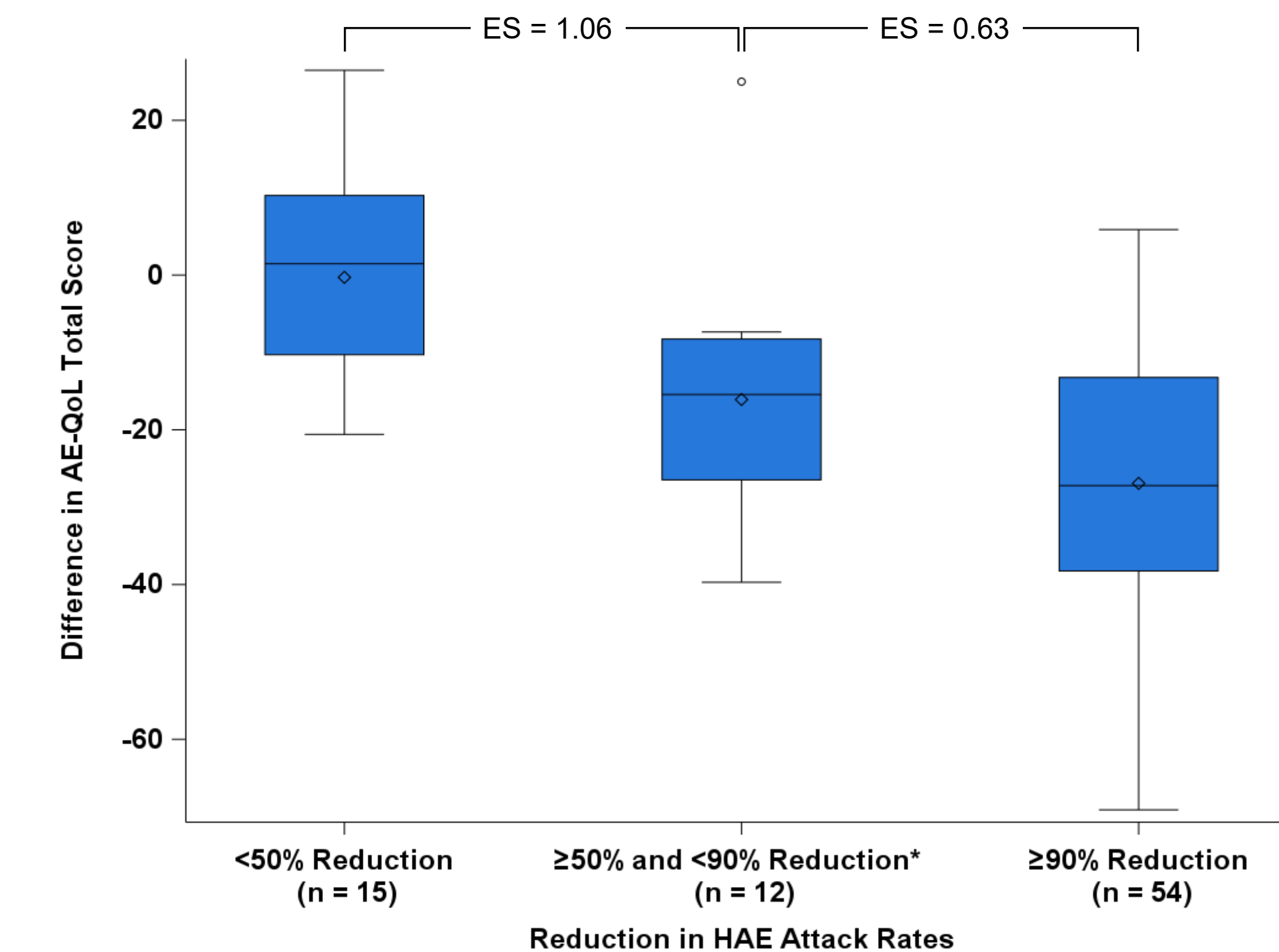


Abbreviations: AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; ES, effect size; HAE, hereditary angioedema
 Note: All differences were significant at p -values < 0.05 , based on independent samples t -test; no adjustments were made for multiplicity.
 Note: Medium ES ≥ 0.5 ; Large ES ≥ 0.8 .

Responsiveness

- Responsiveness was supported by correlations ≥ 0.30 for changes (Baseline to Week 24) in AE-QoL total and most domain scores and changes in other PRO measures (Table 2)
 - Changes in the Fatigue/Mood domain score were not well correlated with changes in the selected PRO measures
- Further, analyses showed moderate-to-large differences in mean AE-QoL total scores across groups, defined by reduction of HAE attack rates ($< 50\%$, $\geq 50\%$ to $< 90\%$, and $\geq 90\%$) from Baseline to Week 24 (Figure 3)
 - Significant mean differences in AE-QoL total scores were observed for patients with different levels of reductions ($p < 0.001$)

Figure 3. Responsiveness: Differences in AE-QoL Total Scores for Patients with Different Levels of Reductions in HAE Attack Rates from Baseline to Week 24



Abbreviations: AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; ES, effect size; HAE, hereditary angioedema
 Note: Medium ES ≥ 0.5 ; Large ES ≥ 0.8 .

Table 1. Construct Validity: Pearson Correlations between AE-QoL Scores and AAS-28, AECT, PGI-S, and HAE Attack Rate[†] at Baseline and Week 24

AE-QoL Score	Convergent Validity						Criterion Validity	
	AAS-28		AECT		PGI-S*		HAE Attack Rate [†]	
	Baseline (N=62)	Week 24 (N=62)	Baseline (N=89)	Week 24 (N=85)	Baseline (N=86)	Week 24 (N=81)	Baseline (N=90)	Week 24 (N=81)
Total	0.39	0.51	-0.59	-0.77	0.37	0.63	0.34	0.65
Functioning	0.41	0.73	-0.62	-0.89	0.43	0.79	0.31	0.78
Fatigue/Mood	0.33	0.04	-0.32	-0.33	0.22	0.29	0.32	0.30
Fears/Shame	0.24	0.51	-0.53	-0.70	0.24	0.57	0.18	0.55
Nutrition	0.26	0.33	-0.32	-0.64	0.18	0.55	0.35	0.57

Abbreviations: AAS-28, Angioedema Activity Score – 28 days; AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; HAE, hereditary angioedema; PGI-S, Patient Global Impression of Severity
 * Spearman correlation coefficients
[†] HAE attack rate defined by the number of investigator-confirmed attacks per 4 week-period.
 Note: Bolded values indicate correlations $|r| \geq 0.40$ or $|p| \geq 0.40$.

Color	Interpretation
Green	$ r $ or $ p \geq 0.60$
Yellow	$0.40 \geq r $ or $ p < 0.60$
Orange	$ r $ or $ p < 0.40$

Table 2. Responsiveness: Pearson Correlations of Change in AE-QoL Scores with Change in AAS-28, Change in AECT, and Change in PGI-S from Baseline to Week 24, and with PGI-C at Week 24

AE-QoL Score	Baseline to Week 24			Week 24
	AAS-28 (N=49)	AECT (N=79)	PGI-S* (N=77)	PGI-C (N=81)
Total	0.40	-0.67	0.55	0.52
Functioning	0.39	-0.73	0.53	0.53
Fatigue/Mood	0.21	-0.28	0.28	0.15
Fears/Shame	0.30	-0.61	0.46	0.52
Nutrition	0.26	-0.39	0.37	0.43

Abbreviations: AAS-28, Angioedema Activity Score – 28 days; AECT, Angioedema Control Test; AE-QoL, Angioedema Quality of Life Questionnaire; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity
 * Spearman correlation coefficients
 Note: Bolded values indicate correlations $|r| \geq 0.30$ or $|p| \geq 0.30$.

Color	Interpretation
Green	$ r $ or $ p \geq 0.60$
Yellow	$0.30 \geq r $ or $ p < 0.60$
Orange	$ r $ or $ p < 0.30$

CONCLUSIONS

- Analyses provide strong evidence to support psychometric validity of the AE-QoL total score and Functioning, Fears/Shame, and Nutrition domains in patients with HAE, and generally support the construct validity, reliability, and responsiveness of the AE-QoL
 - However, for the Fatigue/Mood domain, the observed correlations were weak and did not support construct validity and responsiveness
- Weaker correlations with convergent/criterion measures at Baseline compared to Week 24 could be due to restricted range at Baseline, which can underestimate correlations
- Taken together with other evidence supporting its content validity,^{7,16} the AE-QoL appears to be fit-for purpose in clinical trials of patients with HAE
- This study provides support for use of the AE-QoL in the assessment of QoL among patients with HAE
 - These analyses support the use of both the total and most domain scores in this patient population

REFERENCES AND DISCLOSURES

This research was funded by Ionis. Please visit the QR code at the top of this poster to view additional disclosure and reference information.