Can EQ-5D-5L discriminate the clinical severity of Asthma ?

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BACKGROUND:

The EQ-5D-5L is recommended as a health-related QOL assessment tool in cost-effectiveness analyses of health technologies conducted in many countries. However, as noted in a paper by Brazier et al. (2017), the EQ-5D-5L does not possess sufficient discriminative sensitivity for all diseases. Specifically, regarding respiratory diseases, the paper raises questions about the performance of the EQ-5D-5L, categorizing them as "problematic conditions."

OBJECTIVE:

This study aimed to investigate whether the EQ-5D-5L, commonly used in cost-effectiveness analyses for health technology assessments (HTAs),can discriminate the clinical severity of asthma.

METHODS:

A pre-screening survey was conducted via a large web-based disease panel to minimize bias related to asthma control status. Participants were categorized into "mild" and "moderate or severe" asthma groups. Recruitment continued until each group included 350 participants. Asthma severity was assessed using the Asthma Control Questionnaire (ACQ) -6, and the two clinical severity groups (well-controlled and poorly controlled groups) were classified based on a cutoff score of 1.5. Patient-reported outcome (PRO) was measured by the Asthma Quality of Life Questionnaire (AQLQ), and health-state utility value was measured by the EQ-5D-5L, whose response scores were converted into utility values using a Japanese value set. The comparison of the two measures was examined by correlation and the rate of decline by severity.

OUTCOME MEASURES:

ACQ-6: The ACQ-6 is a patient-reported outcome measure that was developed by Juniper et al. (1999) to measure asthma control status. The questionnaire comprises six questions rated on a Likert scale from 0 to 6, with the mean score for the six questions being the ACQ-6 score; a score of ≥1.5 indicates poor asthma control.

AQLQ: The AQLQ is an asthma-specific HRQoL scale that was developed by Juniper et al. (1992) and comprises 32 questions in four domains (activity limitation, symptoms, emotional functioning, and exposure to environmental stimuli). Each question is rated on a Likert scale with a 2-week recall period.

EQ-5D-5L: The EQ-5D-5L was introduced by the EuroQol Group in 2009 to improve the instrument's sensitivity and to reduce ceiling effects. The descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has 5 levels: no problems, slight problems, moderate problems, severe problems and extreme problems. The Japanese scoring algorithm was used to convert the EQ-5D-5L scores.

Ethical Procedures and Consent Formation:

This study was conducted in accordance with the Declaration of Helsinki. At the beginning of the study, participants were asked to read carefully an explanation of the purpose and methods of the study and to give their informed consent to it; only those who gave consent were able to respond to the survey.

Statistical Analysis:

Participating patients were divided into two groups based on the presence or absence of asthma control. The difference in HRQoL between these two groups was compared using a t-test. Multiple regression analysis was used to examine the effect of asthma severity on HRQoL score, controlled for demographic characteristics such as age and sex. STATA 18.0 was used for the statistical analyses.

RESULTS:

The screening survey revealed that 351 participants had "a cough lasting more than 3 weeks" and 330 participants "needed occasional oral steroid therapy more than twice a year." Those who had both or either of these conditions were included in this study as the "moderate or severe" group (n=358) and others as the "mild" group (n=352).

The mean ACQ-6 score for the entire sample was 0.90±0.93, with a mean ACQ-6 score of 0.57±0.68 for the mild group and 1.23±1.02 for the moderate or severe group. The good control group had ACQ-6 scores less than 1.5 and the poor control group ACQ-6 scores of 1.5 or more (**Table 1**).

Table 2 shows the results for HRQoL scores classified by ACQ-6 cutoff values. The mean AQLQ score for the entire sample was 5.91±1.01, ranging from 6.30±0.64 for the good control (<1.5 points) group to 4.77±1.02 for the poor control (≥1.5 points) group. Similar results were obtained for the four sub-items. The mean utility values of the EQ-5D-5L were 0.892±0.139 for the good control group and 0.789±0.180 for the poor control group.

The distributions of AQLQ scores, EQ-5D-5L utility values, and Visual Analog Scale scores are shown in **Figures 1**. Group comparisons by cutoff values of the ACQ-6 showed different distributions for all scales, but a ceiling effect was visually confirmed for the EQ-5D-5L. Furthermore, for each 1-unit decrease in ACQ-6 scores, HRQOL scores decreased gradually, but still only the EQ-5D-5L score showed a ceiling effect up to ACQ-6 scores of 3 or less. In other words, the total percentage of those who reported a full health ("11111") was 202 of 416 (48.6%) for an ACQ-6 of less than 1, 66 of 182 (36.3%) for an ACQ-6 of 1 to 2, and 16 of 89 (18.0%) for an ACQ-6 of 2 to 3.

Multiple regression analysis was performed to determine the effect of asthma severity on each HRQoL scale. As shown in **Tables 3**, asthma severity, as assessed by the ACQ-6, had a clear impact on the overall AQLQ and EQ-5D-5L utility values.

Table1. Participants' demographic characteristics after adjustment for the ACQ-6 cutoff scores

		Overall (%)	1: ACQ <1.5 (%)	2: 1.5≤ACQ (%)
ACQ-6		0.90 (0.93)	0.57 (0.45)	2.20 (0.69)
Sex	Male	381 (53.7)	285 (54.1)	96 (52.5)
	Female	329 (46.3)	242 (45.9)	87 (47.5)
Age	20–29	6	4	2
	30–39	63	48	15
	40–49	184	140	44
	50–59	229	166	63
	60–69	174	130	44
	70 and over	54	39	15

Table2. Comparison of health-related quality of life scores by group

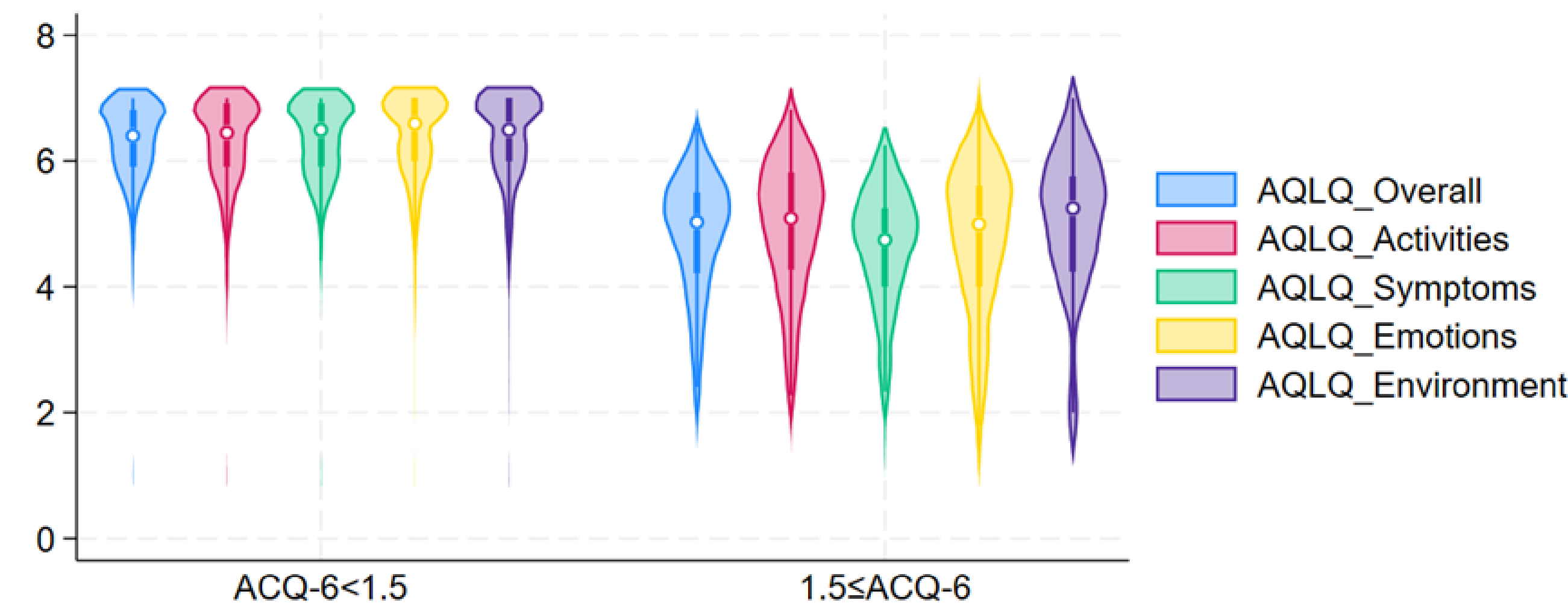|	Overall (n=710)	ACQ<1.5 (n=527)	1.5≤ACQ (n=183)	p
AQLQ scores				
Overall	5.91 (1.01)	6.30 (0.64)	4.77 (1.02)	<0.000
Activities	5.93 (1.02)	6.28 (0.74)	4.94 (1.09)	<0.000
Symptoms	5.87 (1.07)	6.31 (0.66)	4.59 (1.00)	<0.000
Emotions	5.90 (1.12)	6.32 (0.79)	4.67 (1.28)	<0.000
Environment	5.97 (1.13)	6.33 (0.79)	4.92 (1.30)	<0.000
EQ-5D-5L				
Utility values	0.866 (0.156)	0.892 (0.139)	0.789 (0.180)	<0.000
VAS scores	69.6 (23.0)	73.8 (21.2)	57.6 (23.9)	<0.000

Fig 1-A. Comparison of AQLQ and EQ-5D-5L utility grouped by the ACQ-6 cutoff value
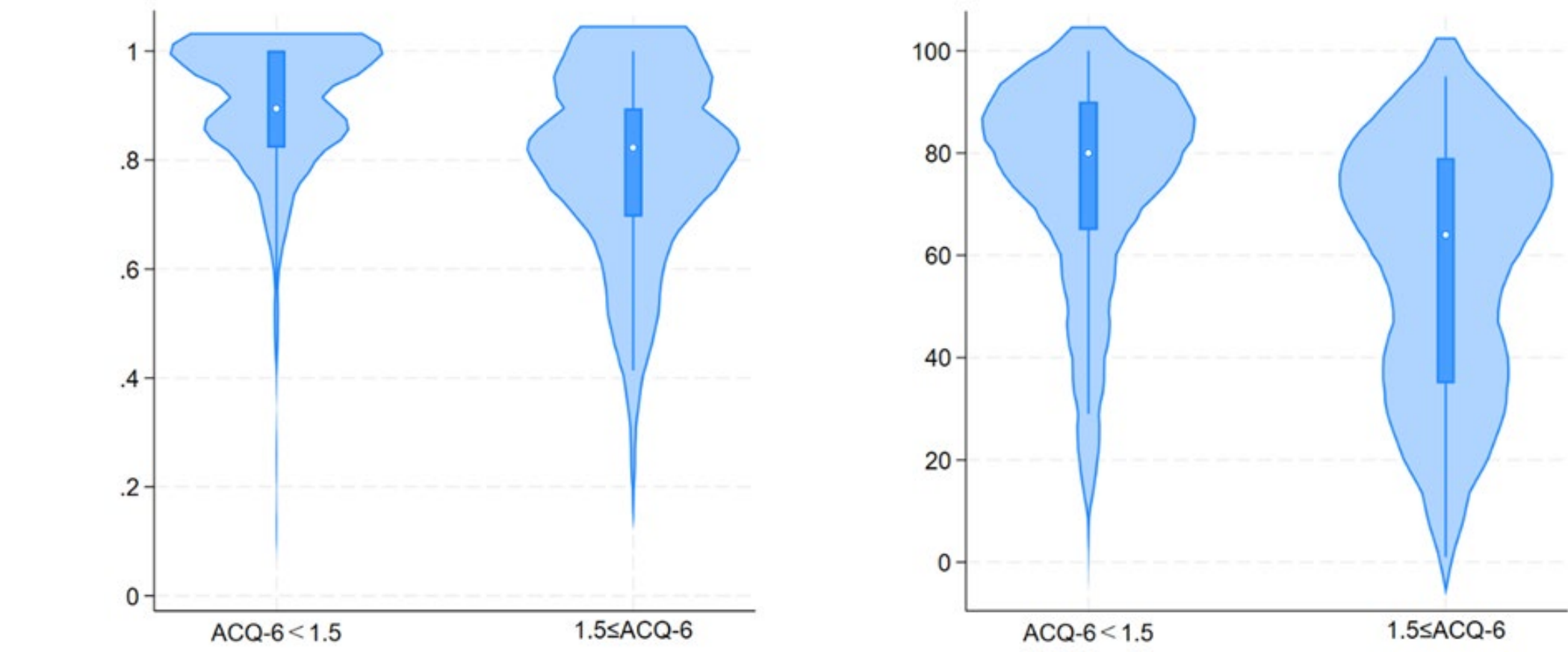

Fig 1-B. EQ-5D-5L (Left graph shows utility values, right graph shows VAS scores)

Table 3. Results of multiple regression analysis with the AQLQ score (upper) and EQ-5D-5L utility values (below) as the dependent variable

		Coefficient	P value	95% confidence interval	
Sex		−0.063	0.151	−0.149	0.023
Age (years)	20–29	0.029	0.521	−0.060	0.119
	30–39	0.072	0.105	−0.015	0.161
	40–49	−0.197	0.005	−0.336	−0.058
	50–59	−0.140	0.012	−0.250	−0.032
	60–69	−0.300	0.003	−0.495	−0.104
	70 and over	ref			
ACQ-6		−0.869	0.000	−0.921	−0.818
_cons		6.775	0.000	6.622	6.928

		Coefficient	P value	95% confidence interval	
Sex		0.0090	0.412	−0.012	0.031
Age (years)	20–29	−0.000	0.980	−0.022	0.022
	30–39	0.018	0.870	−0.020	0.024
	40–49	−0.070	0.000	−0.104	−0.035
	50–59	−0.046	0.001	−0.073	−0.019
	60–69	−0.039	0.116	−0.088	0.010
	70 and over	ref			
ACQ-6		−0.0500	0.000	−0.063	−0.037
_cons		0.9152	0.000	0.877	0.953

DISCUSSIONS:

This study is a large-scale survey of health-related quality of life among asthma patients in Japan. The EQ-5D-5L demonstrated a certain ceiling effect even in the "moderate or severe" group, indicating it lacks sufficient sensitivity to distinguish asthma severity compared to the AQLQ for asthma patients. This suggests that in HTA for asthma medications, consideration should be given to appropriate measurement tools to replace the EQ-5D-5L.

CONCLUSIONS:

The EQ-5D-5L may not fully capture asthma severity, suggesting caution is warranted when applying it in cost-effectiveness analysis for HTA.