An Exploratory Study on Test-Retest Reliability and Responsiveness of Respiratory Bolt-ons for EQ-5D-5L in Obstructive Airway Diseases

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BACKGROUND

❖In an earlier study, we observed nullified ceiling effects and small increases in sensitivity of EQ-5D-5L by adding 2 respiratory bolt-ons developed by Hoogendoorn in a prospective cohort of patients with chronic obstructive airway diseases (OAD) comprising of asthma & chronic obstructive pulmonary disease (COPD)[1-4].

AIM

❖In the present study, we examined the effects of these respiratory bolt-ons on the responsiveness and test-retest reliability of EQ-5D-5L.

METHODS

❖Consenting consecutive patients ≥ 21 years old (n=120) with physician-diagnosed asthma &/or COPD who enrolled in the earlier study & returned for their follow-up were interviewed using the *St George Respiratory Questionnaire (SGRQ)*, ***EQ-5D-5L standard (5L)***, and ***2 respiratory bolt-ons (R1, R2)*** tagged to 5L.

❖ **R1** was "***limitations in physical activities due to shortness of breath"***; **R2** was "***breathing problems***".

❖ Based on SGRQ assessments, we assigned patients into "*better*", "*stable*" and "*worse*" groups.

❖ The "***stable***" group was used to test the reliability of item scores and level sum score (LSS), and EQ index using intra-class correlation coefficient (ICC) or Cohen's Kappa (k).

❖ The "***better***" and "***worse/stable***" groups were used to test the responsiveness of the EQ measures using the standardized effect size (SES) values & c-statistics from receiver operating curve (ROC) analyses.

❖ We derived 5L utilities using the Singapore value set, and those of 5L+R1 and 5L+R2 using the Hoogendoorn's model based on Dutch value set.

Under each heading, please tick the ONE box that best describes your health TODAY.

R1: Limitations in physical activities due to shortness of breath

(e.g., climbing stairs, going for a walk, carrying things, gardening, doing housework)

- I have no problems doing physical activities due to my shortness of breath. ❑
- I have slight problems doing physical activities due to my shortness of breath. ❑
- I have moderate problems doing physical activities due to my shortness of breath. ❑
- I have severe problems doing physical activities due to my shortness of breath. ❑
- I am unable to do physical activities due to my shortness of breath. ❑

R2: Breathing problems (e.g., shortness of breath, wheezing, coughing, sputum)

- I have no breathing problems. ❑
- I have slight breathing problems. ❑
- I have moderate breathing problems. ❑
- I have severe breathing problems. ❑
- I have extreme breathing problems. ❑

	R1	R2
Intercept	-0.019	-0.025
Mobility 2	-0.044	-0.087
Mobility 3	-0.134	-0.120
Mobility 4	-0.194	-0.213
Mobility 5	-0.258	-0.290
Self-care 2	-0.024	-0.056
Self-care 3	-0.024	-0.056
Self-care 4	-0.112	-0.135
Self-care 5	-0.141	-0.135
Usual activities 2	-0.009	0
Usual activities 3	-0.009	0
Usual activities 4	-0.161	-0.177
Usual activities 5	-0.187	-0.177
Pain/discomfort 2	-0.064	-0.085
Pain/discomfort 3	-0.105	-0.085
Pain/discomfort 4	-0.353	-0.330
Pain/discomfort 5	-0.415	-0.434
Anxiety/depression 2	-0.081	-0.085
Anxiety/depression 3	-0.153	-0.160
Anxiety/depression 4	-0.393	-0.325
Anxiety/depression 5	-0.493	-0.390
Respiratory dimension 2	-0.020	-0.086
Respiratory dimension 3	-0.055	-0.086
Respiratory dimension 4	-0.087	-0.219
Respiratory dimension 5	-0.135	-0.327

Figure 1: 5 items in EQ-5D, respiratory bolt-ons (R1 & R2) and coefficients adapted from Hoogendoorn's mathematical model[4]

RESULTS

❖ 120 patients (mean age 56 years; standard deviation [sd]: 17); 60.0% male; 56.7% Chinese) completed baseline and follow-up assessments at mean time interval of 2.8 months (sd: 1.7). Table 1 shows the clinical profile of the follow-up cohort.

❖ 43.3% & 33.3% being rated as "better" and "stable", respectively.

***Table 1**: Clinical characteristics of the 120 patients.*

	N (%)
Charlson comorbidity index	
>1	57 (47.5)
1	63 (52.5)
Obstructive airway disease	
COPD predominant	39 (32.5)
Asthma predominant	81 (67.5)
Disease duration, years	
≥ 10	59 (49.2)
<10	61 (50.8)
Exacerbation past 1 year*	
Yes	47 (39.2)
No	73 (60.8)
MRC severity grade	
> 0	66 (55.0)
0	54 (45.0)
Predicted FEV1, %	
< 80	71 (59.2)
≥ 80	49 (40.8)
S60 seconds sit-to-stand, count	
< 20	38 (31.7)
≥ 20	82 (68.3)
Handgrip, kg	
< 25	59 (49.2)
≥ 25	61 (50.8)

FEV1: forced expiratory volume in 1st second;
MRC: Medical Research Council dyspnea scale.
**exacerbations requiring emergency department visit and/or hospitalization in past 1 year.*

❖ Lower proportions reporting "*no problems*" in respiratory bolt-on items than EQ-5D items (Table 2)

❖ Higher kappa values of respiratory bolt-on than EQ-5D items.

***Table 2**: Response distributions of the EQ-5D Items & respiratory bolt-ons and Cohen's Kappa results.*

	N (%)	*Kappa
MOBILITY		**0.63**
no problems, n(%)	138 (75.0)	
SELF-CARE		**0.64**
no problems, n(%)	159 (86.4)	
USUAL ACTIVITY		**0.55**
no problems, n(%)	138 (75.0)	
PAIN / DISCOMFORT		**0.47**
no problems, n(%)	105 (57.1)	
ANIXIETY / DEPRESSION		**0.45**
no problems, n(%)	143 (77.7)	
RESPIRATORY BOLT-ON R1		**0.78**
no problems, n(%)	80 (43.5)	
RESPIRATORY BOLT-ON R2		**0.74**
no problems, n(%)	70 (38.0)	
RESPIRATORY BOLT-ON R1R2		-
no problems, n(%)	57 (31.0)	

**sample size of stable patients =44; all p<0.001*

❖ ICC trended higher in respiratory bolt-ons for LSS & EQ index (Table 3).

***Table 3**: ICC of EQ measures in EQ-5D standard & respiratory bolt-ons among patients with stable SGRQ status (n=44)*

	5L	5L+R1	5L+R2	5L+R1R2
LSS	0.74 (0.57-0.85)	0.81 (0.68-0.89)	0.80 (0.67-0.89)	0.85 (0.74-0.92)
EQ INDEX	0.76 (0.59-0.86)	0.77 (0.62-0.87)	0.79 (0.64-0.88)	-

(): 95% CI; 5L: EQ-5D-5L standard; n: sample size of patients with stable SGRQ status

❖ SES values were higher in respiratory bolt-ons for LSS & EQ index except in EQ index for 5L+R1R2 (Table 4).

❖ Mean C-statistics were highest in respiratory bolt-on (either one or combined) for LSS & EQ index (Table 4).

***Table 4**: SES values & mean C-statistics of EQ measures in 5L & respiratory bolt-ons of better vs stable/worse SGRQ status*

	5L	5L+R1	5L+R2	5L+R1R2
SES values				
LSS	-0.57 (-0.78--0.32)	-0.62 (-0.85--0.40)	-0.73 (-0.97--0.48)	-0.75 (-0.98--0.51)
EQ INDEX	0.58 (0.33-0.84)	0.55 (0.27-0.80)	0.80 (0.46-1.09)	-
C-statistics				
LSS	0.754	0.796	0.805	***0.833***
EQ INDEX	0.762	0.748	***0.777***	-

(): 95% CI; 5L: EQ-5D-5L standard; SES: standardized effect size
Highest mean C-statistics highlighted in bold red for each EQ measure.

CONCLUSIONS

The addition of respiratory bolt-ons improved the reliability and responsiveness of EQ-5D-5L and some of the improvements may be clinically significant.

References

1. *Guerra S. Asthma and chronic obstructive pulmonary disease. Curr Opin Allergy Clin Immunol. 2009;9(5):409-16.*
2. *Efthymiadou O, Mossman J, Kanavos P. Health related quality of life aspects not captured by EQ-5D-5L: Results from an international survey of patients. Health Policy. 2019;123(2):159-65.*
3. *Hoogendoorn M, Jowett S, Dickens AP, Jordan R, Enocson A, Adab P, et al. Performance of the EQ-5D-5L Plus Respiratory Bolt-On in the Birmingham Chronic Obstructive Pulmonary Disease Cohort Study. Value Health. 2021;24(11):1667-75.*
4. *Hoogendoorn M, Oppe M, Boland MRS, Goossens LMA, Stolk EA, Rutten-van Mölken M. Exploring the Impact of Adding a Respiratory Dimension to the EQ-5D-5L. Med Decis Making. 2019;39(4):393-404.*

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