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Patient-Reported Outcomes in Non-Small Cell Lung Cancer: Psychometric Evaluation of the PROMIS PF-SF 8c and NSCLC-SAQ in Two Phase 3 Clinical Trials

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OBJECTIVE

- Evaluate **reliability**, **validity**, and **meaningful change thresholds** of two patient-reported outcome (PRO) measures in non-small cell lung cancer (NSCLC):
  - Patient-Reported Outcomes Measurement Information System (PROMIS®) Physical Function (PF) short form (SF) 8c (Rose et al., 2008)
  - Non-Small Cell Lung Cancer Symptom Assessment Questionnaire (NSCLC-SAQ; McCarrier et al., 2016; Bushnell et al., 2021)

METHODS

Data Sources

- Data from the PAPILLON trial (NCT04538664) were used for the PROMIS PF-SF 8c analyses
  - Included participants with epidermal growth factor receptor (EGFR) Exon 20 insertion mutated NSCLC
- Data from the MARIPOSA-2 trial (NCT04487080) were used for the NSCLC-SAQ analyses
  - Included participants with EGFR exon19del or exon18 L858R mutated locally advanced or metastatic NSCLC

Reference and Anchor Measures

- European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire-Core 30 items (EORTC-QLQ-C30; Aaronson et al., 1993)
- Eastern Cooperative Oncology Group Performance Status (ECOG; Oken et al., 1982)
- EQ-5D-5L (Herdman et al., 2011): anchor for PROMIS PF-SF 8c
- Patient global impression of severity (PGIS) and patient global impression of change (PGIC) items: anchors for NSCLC-SAQ

Analyses

- Expected relationships between the target PRO measures and relevant study variables were prespecified
- Internal consistency reliability was assessed via Cronbach's alpha
- Validity evidence was generated via
  - Cross-sectional correlations between the target measures and reference variables (**convergent and discriminant validity** evidence)
  - Analysis of variance of target PRO scores by clinically meaningful groups (**known groups validity** evidence)
  - Correlations of target PRO change scores with reference variable change scores (**ability to detect change**)
- **Meaningful change thresholds** were estimated using anchor-based and distribution-based analyses

RESULTS

- Internal consistency was sufficiently high
  - PROMIS PF-SF 8c alpha = 0.89
  - NSCLC-SAQ alpha = 0.77
- Convergent and discriminant correlations conformed to *a priori* expectations with reference variables
- Known groups validity evidence showed significant differences across clinically meaningful groups
- Correlations between change in PROMIS PF-SF 8c scores and change in reference variables conformed to *a priori* expectations (Table 2)
- Anchor-based methods established meaningful worsening thresholds
  - PROMIS PF-SF 8c: decrease of 6 – 7 points
  - NSCLC-SAQ: increase of 2.5 points

TABLE 1: Demographic and descriptive statistics of analysis sets

Variable	MARIPOSA-2 NSCLC-SAQ (N = 615)	PAPILLON PROMIS PF-SF 8c (N = 300)
Age (years)		
Mean (SD)	60.75 (10.3)	59.7 (12.0)
Median	62	62
Q1, Q3	54, 68	53,68
Min, max	23, 84	27,92
Age group (years)		
<65 years	379 (61.6%)	184 (61.3%)
>=65 years	236 (38.4%)	116 (38.7%)
Sex		
Female	383 (62.3%)	173 (57.7%)
Male	232 (37.7%)	127 (42.3%)
Race		
American Indian or Alaska Native	4 (0.7%)	3 (1.0%)
Asian	303 (49.3%)	185 (61.7%)
Black or African-American	7 (1.1%)	2 (0.7%)
White	286 (46.5%)	120 (34.0%)
Multiple	2 (0.3%)	1 (0.3%)
Not Reported	9 (1.5%)	5 (1.7%)
Unknown	4 (0.7%)	2 (0.7%)
Ethnicity		
Hispanic or Latino	53 (8.6%)	20 (6.7%)
Not Hispanic or Latino	547 (88.9%)	277 (92.3%)
Not Reported	7 (1.1%)	2 (0.7%)
Unknown	8 (1.3%)	1 (0.3%)

FIGURE 1: ePDF & eCDF of PROMIS PF-SF 8c change scores by change in EQ-5D-5L usual activities item from baseline

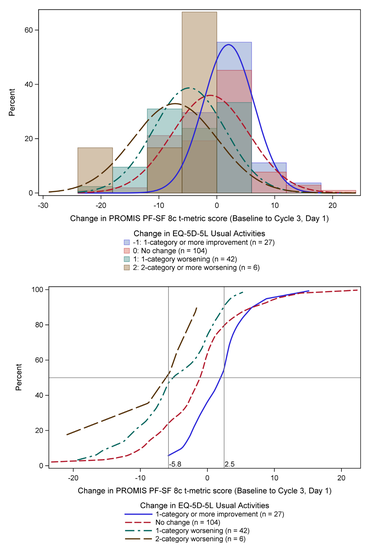

FIGURE 2: ePDF & eCDF of NSCLC-SAQ change scores by change in PGIS from baseline

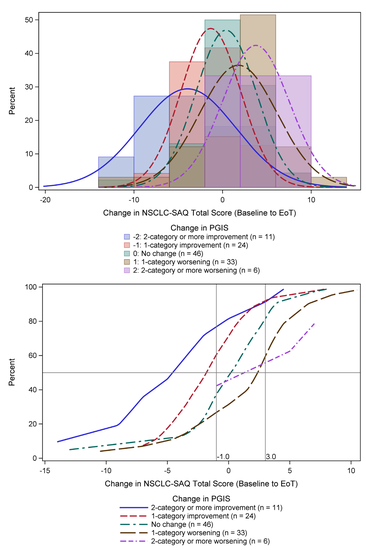

TABLE 2: Change score correlations among PROMIS PF-SF 8c, NSCLC-SAQ, and reference variables

Reference Variable	PROMIS PF-SF 8c *Positive change scores = Better outcome*						NSCLC-SAQ *Negative change scores = Better outcome*					
	Change 1 (Cycle 3 Day 1 - Baseline)			Change 2 (EoT - Baseline)			Change1 (Cycle 3 Day 1 - Baseline)			Change2 (EoT - Baseline)		
	N	r		N	r		N	r		N	r	
EORTC-QLQ-C30												
Physical Function	274	0.50	***	134	0.73	***	500	-0.48	***	214	-0.47	***
Role Function	274	0.42	***	134	0.66	***	500	-0.39	***	215	-0.59	***
Emotional Function	274	0.25	***	134	0.38	***	499	-0.42	***	216	-0.46	***
Global	274	0.32	***	134	0.50	***	499	-0.55	***	216	-0.59	***
Fatigue	274	-0.37	***	134	-0.54	***	500	0.58	***	216	0.72	***
Pain	274	-0.25	***	134	-0.45	***	500	0.53	***	216	0.54	***
Dyspnea	274	-0.19	**	134	-0.25	**	500	0.48	***	216	0.65	***
Appetite loss	274	-0.20	***	134	-0.29	***	499	0.57	***	216	0.64	***
Diarrhea	273	-0.03		134	-0.20	*	499	0.08		216	0.11	
Financial difficulties	274	-0.15	*	134	-0.27	**	499	0.25	***	215	0.30	***
EQ-5D-5L VAS	273	0.28	***	133	0.48	***	483	-0.45	***	210	-0.39	***

Notes. EORTC-QLQ-C30 = European Organization for Research and Treatment of Cancer-Quality of Life Questionnaire-Core 30 items. EQ-5D-5L VAS = EuroQOL-5 Dimensions-5 Levels Visual Analog Scale.
*p<.05, **p<.01, ***p<.001

KEY TAKEAWAY

PROMIS PF-SF 8c and NSCLC-SAQ are reliable and valid measures of physical function and NSCLC symptom severity, respectively, for people living with NSCLC.

CONCLUSIONS

Results from this study support the validity of these instruments in NSCLC and aid the interpretation of clinically meaningful change in scores over time.

Estimated thresholds for meaningful worsening were a decrease of 6 to 7 points on PROMIS PF and an increase of 2.5 points on NSCLC-SAQ Total Score.

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DISCLOSURES

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