Correspondence Between Symptoms and Preference-Based Health Status Measures in the Standardized Treatment Of Pulmonary Exacerbations (STOP) Study

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Study Aims

- We conducted a sub-study of the **S**tandardized **T**reatment **O**f **P**ulmonary exacerbations (STOP) Study in order to perform future cost- and comparative effectiveness analyses on cystic fibrosis (CF) patients
- *Primary aim of the STOP study was to assess feasibility of conducting interventional studies to develop pulmonary exacerbation (PE) treatment guidelines*
- Aim 1 (sub-study): Assess the responsiveness of the European Quality of Life Scale (EQ-5D) to treatment for CF patients
- Aim 2 (sub-study): Map patients' responses to a subset of the Cystic Fibrosis Respiratory Symptom Diary- Chronic Respiratory Infection Symptom Score (CFRSD-CRISS) items to EQ-5D and evaluate the validity of this algorithm

Methods

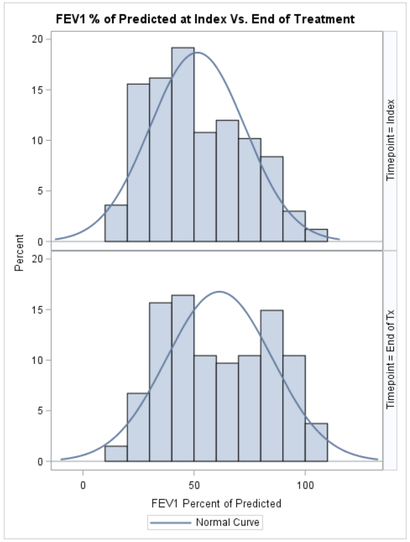
- STOP Study was a multi-center, prospective, observational study following CF patients admitted to the hospital to treat pulmonary exacerbations (PE)
- CRISS questionnaire consists of 8 items assessing *symptoms* such as difficulty breathing, feeling feverish and tired, and cough severity
- EQ-5D questionnaire consists of 5 items assessing *health status measures* such as pain, anxiety/depression, and ability to move, perform self-care, and usual activities
- CRISS and EQ-5D were self-reported by patients on:
  - Day of initial pulmonary exacerbation (index visit)
  - Day 7
  - End of treatment/Day 28
- We evaluated the change in FEV1 % Predicted, CRISS and EQ-5D and correlations between these over the three time points
- We created an age-stratified training set and performed multivariate linear regression with backward selection to evaluate associations between EQ-5D and CRISS items, adjusting for clinical and demographic variables
- Created separate regression models at each time point

Results

Table 1. Demographic and Clinical Variables at Index Pulmonary Exacerbation Visit

	Whole cohort n=220	Cohort with ≥3 measures EQ-5D and CRISS measures on same day (n=169)	50% cohort training (n=84)	50% cohort validation (n=85)
Age ≤18	42 (19%)	33 (20%)	16 (19%)	17 (20%)
Age >18-29	116 (53%)	84 (50%)	48 (57%)	36 (42%)
Age ≥30	62 (28%)	52 (31%)	20 (24%)	32 (38%)
Female	124 (56%)	100 (59%)	50 (60%)	50 (60%)
White Race	210 (95%)	162 (96%)	78 (93%)	84 (99%)
Non-White Race	10 (5%)	7 (4%)	6 (7%)	1 (1%)
Patient covered under parent's insurance	69 (36%)	54 (36%)	29 (39%)	25 (33%)
FEV1 Percent of Predicted: Mean ± Std. Dev, (n)				
Day 0	51% ± 22% (203)	51% ± 22% (157)	50% ± 21% (79)	53% ± 22% (78)
End of Treatment Day	62% ± 23% (167)	62% ± 24% (125)	61% ± 25% (64)	62% ± 23% (61)
Change in FEV1 % Predicted from Day 0 to End of Tx	9.4% ± 10% (156)	9.2% ± 9% (129)	10% ± 10% (64)	8.4% ± 9% (65)
Patient-Reported Outcomes: Mean ± Std. Dev				
EQ-5D Summary Score at Index Visit (Range 0 to 1; Higher=Better)	0.81 ± 0.12 (207)	0.80 ± 0.12	0.81 ± 0.12	0.79 ± 0.12
CRISS at Index Visit (Range 0 to 100; Lower=Better)	47 ± 11 (207)	48 ± 11	49 ± 10	48 ± 11
Change in EQ-5D Summary Score from Index Visit to End of Tx (Higher=Better; minimally important difference=0.074)	0.09 ± 0.11 (169)	0.09 ± 0.11	0.10 ± 0.12	0.08 ± 0.11
Change in CRISS from Index Visit to End of Tx (Lower=Better; minimally important difference=11 points)	-24 ± 15 (168)	-24 ± 15 (168)	-25 ± 16 (83)	-23 ± 14 (85)

Results (Continued)



Change in FEV1 % Predicted Versus Change in Summary EQ-5D from Index PE Visit to End of Treatment

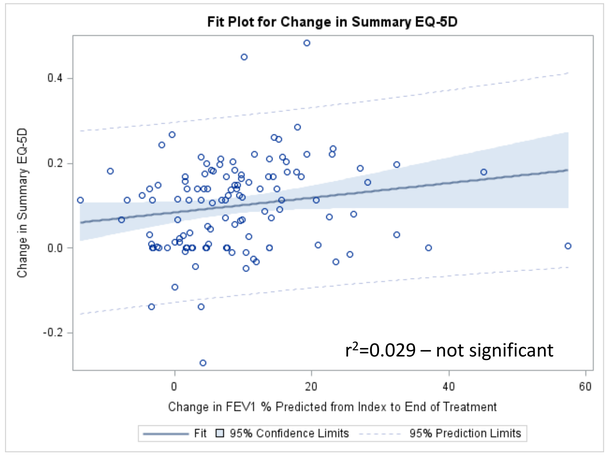
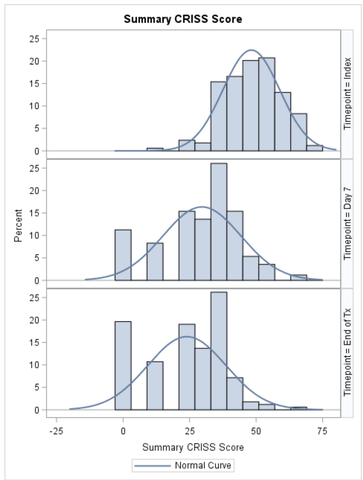


Table 2. Correlations Between EQ-5D and CRISS Items at Index Pulmonary Exacerbation Visit Day

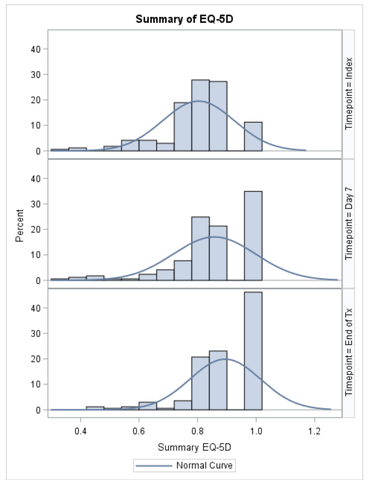
EQ-5D/CRISS Item	Trouble Breathing	Feverish	Tired	Chills	Cough	Mucus Quantity	Chest Tightness	Wheezing	Summary CRISS
Mobility	0.40	0.26	0.18	0.13	0.12	0.06	0.22	0.18	0.27
Self-Care	0.24	0.34	0.15	0.32	0.06	0.02	0.07	0.16	0.18
Usual Activities	0.42	0.27	0.34	0.01	0.27	0.15	0.33	0.31	0.39
Pain/Discomfort	0.28	0.33	0.35	0.36	0.20	0.13	0.40	0.34	0.43
Anxiety/ Depression	0.26	0.01	0.19	0.02	0.09	0.13	0.12	0.13	0.22
Summary EQ-5D	-0.49	-0.37	-0.37	-0.29	-0.25	-0.12	-0.36	-0.34	-0.46

- **Correlations between EQ-5D and CRISS items at day 7 and end of treatment/day 28 assessments weaker than correlations at index day assessment**

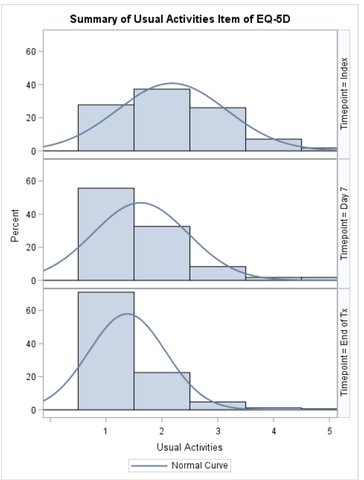
Change in Patient-Reported Outcomes Over Time



Improved Health (Lower CRISS)
Range: 0 = No Symptoms to 100 = Maximum Symptoms



Improved Health (Higher EQ-5D)
Range: 0 = Death to 1.0 = Perfect Health



Improved Health (Lower Score)
Range: 1 = "No problems with usual activities" to
5 = "Unable to do usual activities"

Conclusions and Next Steps

- In this population of CF patients with pulmonary exacerbations, we did not observe a strong correlation between the change in EQ-5D and the percent predicted FEV1 over time
  - The EQ-5D sub-item of "problems with usual activities" showed the most improvement over time.
- CRISS symptom items, while slightly to modestly correlated with EQ-5D items on the day of the index pulmonary exacerbation visit, are not strong predictors and therefore cannot be used interchangeably to measure preference-based health status
- We planned to use the validation dataset to test the predictive models and evaluate associations between EQ-5D and CRISS items at each time point, but poor fits in the training data may preclude this aim
- Future studies should consider using the full CFRSD (8 items more than CRISS with detailed questions about symptom severity and timing) in order to improve prediction