Relationship Between Lung Function Impairment and Health-Related Quality of Life in COPD and Interstitial Lung Disease

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e-Appendix 1.

Because of concern that hyperinflation and gas transfer defects were potential confounders of the relationships between lung function, diagnosis, and HRQL score, we performed supplementary analyses including diffusing capacity (DLCO) and ratio of inspiratory capacity to total lung capacity (IC/TLC) in our model. These variables were not included in the main model because the data was unavailable for over 20% of patients (n=107 (18.6%) for COPD, n=97 (24.0%) for ILD), and the data was not missing at random. Patients with missing data for IC/TLC ratio and/or DLCO were younger with lower lung function and worse HRQL scores. They were significantly less likely to have a cancer diagnosis and more likely to require supplemental oxygen at rest. In addition, the type of tissue collection performed was different compared to those with IC/TLC and DLCO data available.

When IC/TLC ratio and DLCO were added to the regression model, the magnitude of regression coefficient for diagnosis was slightly decreased, but SGRQ scores remained higher (9.22 points; 95% CI 5.68, 12.76) in ILD patients compared to those with COPD (n=774, e-Table 1). Similarly, in the SF-12 PCS model, inclusion of IC/TLC ratio and DLCO attenuated the magnitude of the regression coefficient for diagnosis, but SF-12 PCS scores were still on average 2.04 points (95% CI 0.08, 4.00) lower in ILD compared to COPD (n=765, e-Table 2). In addition, evidence for an interaction between diagnosis and FEV_1% persisted for both SGRQ (p<0.001) and SF-12 PCS (p=0.055) (e-Table 3).

e-Table 1. Relationship between chronic lung disease diagnosis, other predictors, and total SGRQ score after adjustment for diffusing capacity and hyperinflation

Variables[1]	Unadjusted β estimate	95% CI	p value	Adjusted β estimate[2]	95% CI	p value
Diagnosis (ILD vs COPD)	10.54	7.21, 13.86	<0.001	9.22	5.68, 12.76	<0.001
FEV_1 (% predicted)	-0.42	-0.48, -0.36	<0.001	-0.29	-0.37, -0.20	<0.001
Age (years)	-0.78	-0.94, -0.62	<0.001	-0.48	-0.64, -0.32	<0.001
Gender (M vs F)	-3.85	-7.18, -0.52	0.02	1.31	-1.57, 4.19	0.37
BMI (kg/m^2)	0.45	0.17, 0.73	0.002	0.51	0.25, 0.77	<0.001
Supplemental O_2 at rest (yes vs no)	14.84	11.57, 18.11	<0.001	5.64	2.84, 8.44	<0.001
IC/TLC ratio (%)	-0.31	-0.44, -0.17	<0.001	-0.03	-0.19, 0.13	0.72
Mean DLCO (mL/min/mmHg)	-1.72	-1.98, -1.47	<0.001	-1.11	-1.41, -0.81	<0.001

[1] Continuous variables (units): FEV_1 (% predicted), age (years), body mass index (BMI, kg/m^2), ratio of inspiratory capacity to total lung capacity (IC/TLC, %), diffusing capacity of the lung for carbon monoxide (DLCO, mL/min/mmHg). Categorical variables (coding): diagnosis (ILD=1 COPD=0), gender (male=1, female=0), supplemental oxygen requirement at rest (yes=1, no=0). In an additional regression model (results not shown), BMI was modeled as a categorical variable rather than a continuous variable, but this did not alter the regression coefficient estimates or their statistical significance.

[2] Adjusted regression coefficient estimates are adjusted for all variables listed in the table as well as race (Caucasian=1, non-Caucasian=0) and comorbidities (1=yes, 0=no) including angina, congestive heart failure, diabetes, renal failure, cancer diagnosis, and rheumatologic disease. For this multiple linear regression analysis, $r^2 = 0.44$, $\sigma = 17.92$. Compared with the original analysis, which included 976 observations, 774 observations that had complete data for IC/TLC ratio and mean DLCO were included in this supplemental analysis.

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e-Table 2. Relationship between chronic lung disease diagnosis, other predictors, and SF-12 PCS score after adjustment for diffusing capacity and hyperinflation

Variables[3]	Unadjusted β estimate	95% CI	p value	Adjusted β estimate[4]	95% CI	p value
FEV$_1$ (% predicted)	0.17	0.14, 0.20	<0.001	0.09	0.05, 0.14	<0.001
Diagnosis (ILD vs COPD)	-3.65	-5.35, -1.96	<0.001	-2.04	-4.00, -0.08	0.04
Age (years)	0.28	0.20, 0.37	<0.001	0.22	0.14, 0.31	<0.001
Gender (M vs F)	-0.01	-1.70, 1.67	0.99	-2.53	-4.13, -0.92	0.002
BMI (kg/m^2)	-0.19	-0.34, -0.05	0.008	-0.23	-0.38, -0.09	0.002
Supplemental O$_2$ at rest (yes vs no)	-6.93	-8.59, -5.27	<0.001	-3.14	-4.70, -1.59	<0.001
IC/TLC ratio (%)	0.11	0.04, 0.18	<0.001	-0.02	-0.11, 0.07	0.69
Mean DLCO (mL/min/mmHg)	0.75	0.61, 0.88	<0.001	0.62	0.45, 0.79	<0.001

[3] Continuous variables (units): FEV$_1$ (% predicted), age (years), body mass index (BMI, kg/m^2), ratio of inspiratory capacity to total lung capacity (IC/TLC, %), diffusing capacity of the lung for carbon monoxide (DLCO, mL/min/mmHg). Categorical variables (coding): diagnosis (ILD=1 COPD=0), gender (male=1, female=0), supplemental oxygen requirement at rest (yes=1, no=0). In an additional regression model (results not shown), BMI was modeled as a categorical variable rather than a continuous variable, but this did not alter the regression coefficient estimates or their statistical significance.

[4] Adjusted regression coefficient estimates are adjusted for all variables listed in the table as well as race (Caucasian=1, non-Caucasian=0) and comorbidities (1=yes, 0=no) including angina, congestive heart failure, diabetes, renal failure, cancer diagnosis, and rheumatologic disease. For this multiple linear regression analysis, $r^2 =$ 0.31, σ = 9.93. Compared with the original analysis, which included 965 observations, 765 observations that had complete data for IC/TLC ratio and mean DLCO were included in this supplemental analysis.

e-Table 3. Relationship between FEV$_1$ % predicted and HRQL score varies by chronic lung disease diagnosis after adjustment for hyperinflation and diffusing capacity

Outcome	Diagnosis	Adjusted β estimate for FEV$_1$ % predicted*	95% CI	p value for interaction term
SGRQ score	ILD	-0.11	-0.24, 0.01	<0.001
	COPD	-0.35	-0.44, -0.26	
SF-12 PCS score	ILD	0.04	-0.03, 0.11	0.055
	COPD	0.11	0.06, 0.16	

*Regression coefficient estimates are adjusted for age, body mass index, gender, race, requirement for supplemental oxygen, inspiratory capacity to total lung capacity ratio, diffusing capacity, and comorbidities including angina, congestive heart failure, diabetes, renal failure, cancer diagnosis, and rheumatologic disease.

e-Table 4. Relationship between chronic lung disease diagnosis, other predictors, and total SGRQ score using FVC % predicted

Variables[5]	Unadjusted β estimate	95% CI	p value	Adjusted β estimate[6]	95% CI	p value
Diagnosis (ILD vs COPD)	11.34	8.36, 14.31	<0.001	3.87	1.13, 6.60	0.006
FVC (% predicted)	-0.61	-0.67, -0.55	<0.001	-0.44	-0.51, -0.38	<0.001
Age (years)	-0.85	-0.99, -0.71	<0.001	-0.35	-0.48, -0.21	<0.001
Gender (M vs F)	-3.64	-6.65, -0.63	0.02	-2.07	-4.50, 0.36	0.09
BMI (kg/m^2)	0.31	0.05, 0.56	0.02	0.16	-0.06, 0.38	0.16
Supplemental O_2 at rest (yes vs no)	15.72	12.86, 18.57	<0.001	8.34	5.81, 10.88	<0.001

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[5] Continuous variables (units): forced vital capacity (FVC, % predicted), age (years), body mass index (BMI, kg/m^2). Categorical variables (coding): diagnosis (ILD=1 COPD=0), gender (male=1, female=0), supplemental oxygen requirement at rest (yes=1, no=0). In an additional regression model (results not shown), BMI was modeled as a categorical variable rather than a continuous variable, but this did not alter the regression coefficient estimates or their statistical significance.

[6] Adjusted regression coefficient estimates are adjusted for all variables listed in the table as well as race (Caucasian=1, non-Caucasian=0) and comorbidities (1=yes, 0=no) including angina, congestive heart failure, diabetes, renal failure, cancer diagnosis, and rheumatologic disease. This multiple linear regression analysis included 976 observations for which complete data were available ($r^2 = 0.39$, $\sigma = 18.93$).

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e-Table 5. Relationship between chronic lung disease diagnosis, other predictors, and SF-12 PCS score using FVC % predicted

Variables[7]	Unadjusted β estimate	95% CI	p value	Adjusted β estimate[8]	95% CI	p value
Diagnosis (ILD vs COPD)	-3.60	-5.10, -2.11	<0.001	-0.24	-1.72, 1.25	0.76
FVC (% predicted)	0.24	0.21, 0.27	<0.001	0.17	0.14, 0.21	<0.001
Age (years)	0.30	0.23, 0.38	<0.001	0.13	0.06, 0.20	<0.001
Gender (M vs F)	0.003	-1.49, 1.49	0.99	-0.48	-1.80, 0.84	0.48
BMI (kg/m^2)	-0.16	-0.29, -0.04	0.01	-0.11	-0.23, 0.01	0.07
Supplemental O$_2$ at rest (yes vs no)	-6.82	-8.24, -5.39	<0.001	-4.02	-5.39, -2.64	<0.001

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[7] Continuous variables (units): forced vital capacity (FVC, % predicted), age (years), body mass index (BMI, kg/m^2). Categorical variables (coding): diagnosis (ILD=1 COPD=0), gender (male=1, female=0), supplemental oxygen requirement at rest (yes=1, no=2). In an additional regression model (results not shown), BMI was modeled as a categorical variable rather than a continuous variable, but this did not alter the regression coefficient estimates or their statistical significance.

[8] Adjusted regression coefficient estimates are adjusted for all variables listed in the table as well as race (Caucasian=1, non-Caucasian=0) and comorbidities (1=yes, 0=no) including angina, congestive heart failure, diabetes, renal failure, cancer diagnosis, and rheumatologic disease. This multiple linear regression analysis included 965 observations for which complete data were available ($r^2 = 0.26$, $\sigma = 10.23$).

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e-Table 6. Relationship between FVC % predicted and HRQL score varies by chronic lung disease diagnosis

Outcome	Diagnosis	Adjusted β estimate for FVC % predicted*	95% CI	p value for interaction term
SGRQ score	ILD	-0.31	-0.41, -0.20	0.001
	COPD	-0.51	-0.59, -0.43	
SF-12 PCS score	ILD	0.11	0.05, 0.17	0.005
	COPD	0.21	0.17, 0.25	

*Regression coefficient estimates are adjusted for age, body mass index, gender, race, requirement for supplemental oxygen, and comorbidities including angina, congestive heart failure, diabetes, renal failure, cancer diagnosis, and rheumatologic disease.

e-Table 7. Relationship between chronic lung disease diagnosis, other predictors, and SGRQ symptoms component score

Variables[9]	Unadjusted β estimate	95% CI	p value	Adjusted β estimate[10]	95% CI	p value
Diagnosis (ILD vs COPD)	12.62	9.52, 15.71	<0.001	15.62	12.31, 19.10	<0.001
FEV_1 (% predicted)	-0.27	-0.33, 0.21	<0.001	-0.34	-0.41, -0.28	<0.001
Age (years)	-0.65	-0.81, -0.50	<0.001	-0.25	-0.48, 0.09	0.002
Gender (M vs F)	1.57	-1.58, 4.72	0.33	2.09	-0.75, 4.94	0.15
BMI (kg/m^2)	0.46	0.19, 0.73	0.001	0.28	0.02, 0.54	0.03
Supplemental O_2 at rest (yes vs no)	7.98	4.87, 11.10	<0.001	2.06	-0.92, 5.04	0.18

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[9] Continuous variables (units): FEV_1 (% predicted), age (years), body mass index (BMI, kg/m^2). Categorical variables (coding): diagnosis (ILD=1 COPD=0), gender (male=1, female=0), supplemental oxygen requirement at rest (yes=1, no=0). In an additional regression model (results not shown), BMI was modeled as a categorical variable rather than a continuous variable, but this did not alter the regression coefficient estimates or their statistical significance.

[10] Adjusted regression coefficient estimates are adjusted for all variables listed in the table as well as race (Caucasian=1, non-Caucasian=0) and comorbidities (1=yes, 0=no) including angina, congestive heart failure, diabetes, renal failure, cancer diagnosis, and rheumatologic disease. This multiple linear regression analysis included 976 observations for which complete data were available ($r^2 = 0.22$, $\sigma = 22.19$).

e-Table 8. Relationship between chronic lung disease diagnosis, other predictors, and SGRQ activity component score

| Variables[11]	Unadjusted β estimate	95% CI	p value	Adjusted β estimate[12]	95% CI	p value
Diagnosis (ILD vs COPD)	11.13	7.15, 15.10	<0.001	16.67	12.94, 20.41	<0.001
FEV$_1$ (% predicted)	-0.62	-0.69, -0.55	<0.001	-0.65	-0.72, -0.58	<0.001
Age (years)	-1.02	-1.21, -0.83	<0.001	-0.17	-0.34, 0.002	0.05
Gender (M vs F)	-7.79	-11.74, -3.84	<0.001	-6.46	-9.51, -3.41	<0.001
BMI (kg/m^2)	0.41	0.07, 0.75	0.02	0.48	0.20, 0.76	0.001
Supplemental O$_2$ at rest (yes vs no)	21.12	17.42, 24.93	<0.001	9.55	6.36, 12.74	<0.001

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[11] Continuous variables (units): FEV$_1$ (% predicted), age (years), body mass index (BMI, kg/m^2). Categorical variables (coding): diagnosis (ILD=1 COPD=0), gender (male=1, female=0), supplemental oxygen requirement at rest (yes=1, no=0). In an additional regression model (results not shown), BMI was modeled as a categorical variable rather than a continuous variable, but this did not alter the regression coefficient estimates or their statistical significance.

[12] Adjusted regression coefficient estimates are adjusted for all variables listed in the table as well as race (Caucasian=1, non-Caucasian=0) and comorbidities (1=yes, 0=no) including angina, congestive heart failure, diabetes, renal failure, cancer diagnosis, and rheumatologic disease. This multiple linear regression analysis included 976 observations for which complete data were available ($r^2 = 0.44$, $\sigma = 23.79$).

e-Table 9. Relationship between chronic lung disease diagnosis, other predictors, and SGRQ impacts component score

Variables[13]	Unadjusted β estimate	95% CI	p value	Adjusted β estimate[14]	95% CI	p value
Diagnosis (ILD vs COPD)	10.80	7.87, 13.72	<0.001	14.27	11.33, 17.22	<0.001
FEV_1 (% predicted)	-0.39	-0.44, -0.34	<0.001	-0.39	-0.45, -0.34	<0.001
Age (years)	-0.82	-0.96, -0.68	<0.001	-0.27	-0.41, -0.14	<0.001
Gender (M vs F)	-2.86	-5.82, 0.09	0.06	-1.66	-4.06, 0.75	0.18
BMI (kg/m^2)	0.19	-0.06, 0.44	0.14	0.10	-0.12, 0.33	0.36
Supplemental O_2 at rest (yes vs no)	15.27	12.47, 18.08	<0.001	7.85	5.34, 10.37	<0.001

[13] Continuous variables (units): FEV_1 (% predicted), age (years), body mass index (BMI, kg/m^2). Categorical variables (coding): diagnosis (ILD=1 COPD=0), gender (male=1, female=0), supplemental oxygen requirement at rest (yes=1, no=0). In an additional regression model (results not shown), BMI was modeled as a categorical variable rather than a continuous variable, but this did not alter the regression coefficient estimates or their statistical significance.

[14] Adjusted regression coefficient estimates are adjusted for all variables listed in the table as well as race (Caucasian=1, non-Caucasian=0) and comorbidities (1=yes, 0=no) including angina, congestive heart failure, diabetes, renal failure, cancer diagnosis, and rheumatologic disease. This multiple linear regression analysis included 976 observations for which complete data were available ($r^2 = 0.37$, $\sigma = 18.77$).

e-Figure 1. Boxplot distribution of SGRQ scores by deciles of FEV_1 % predicted (n=981).
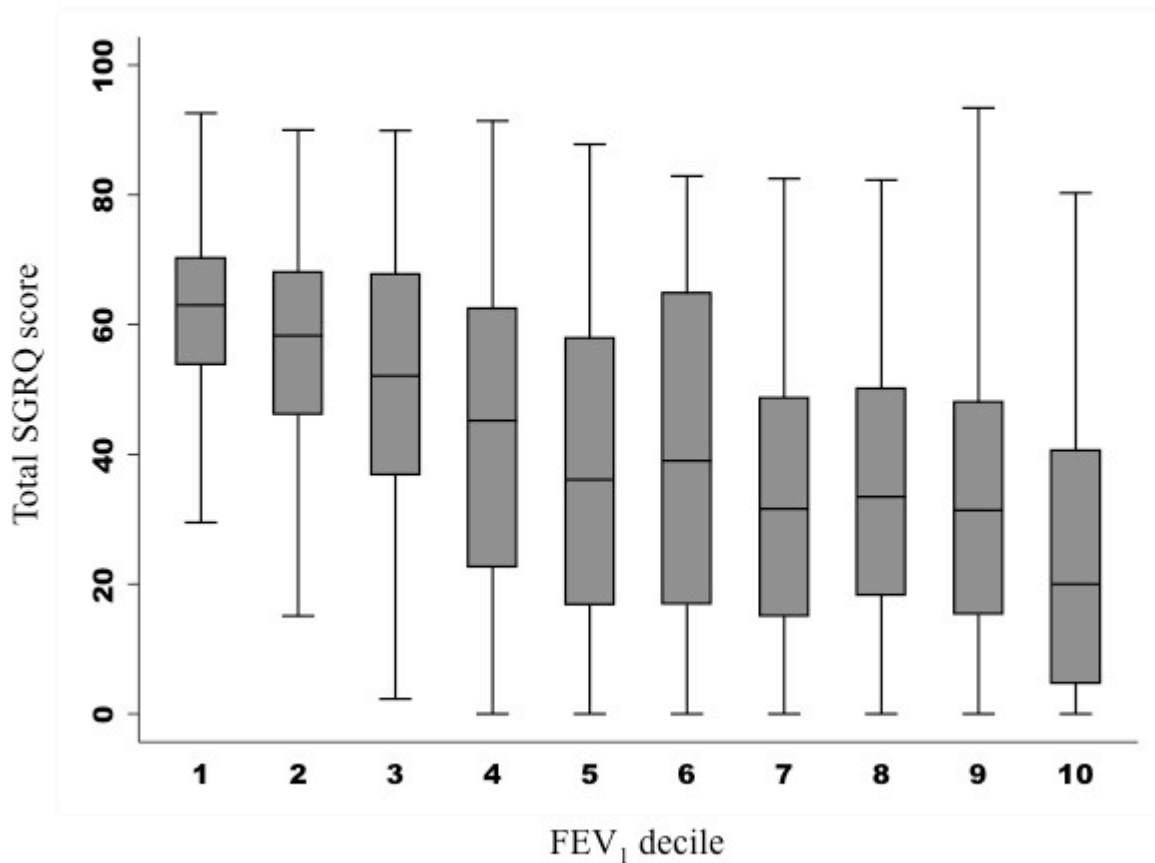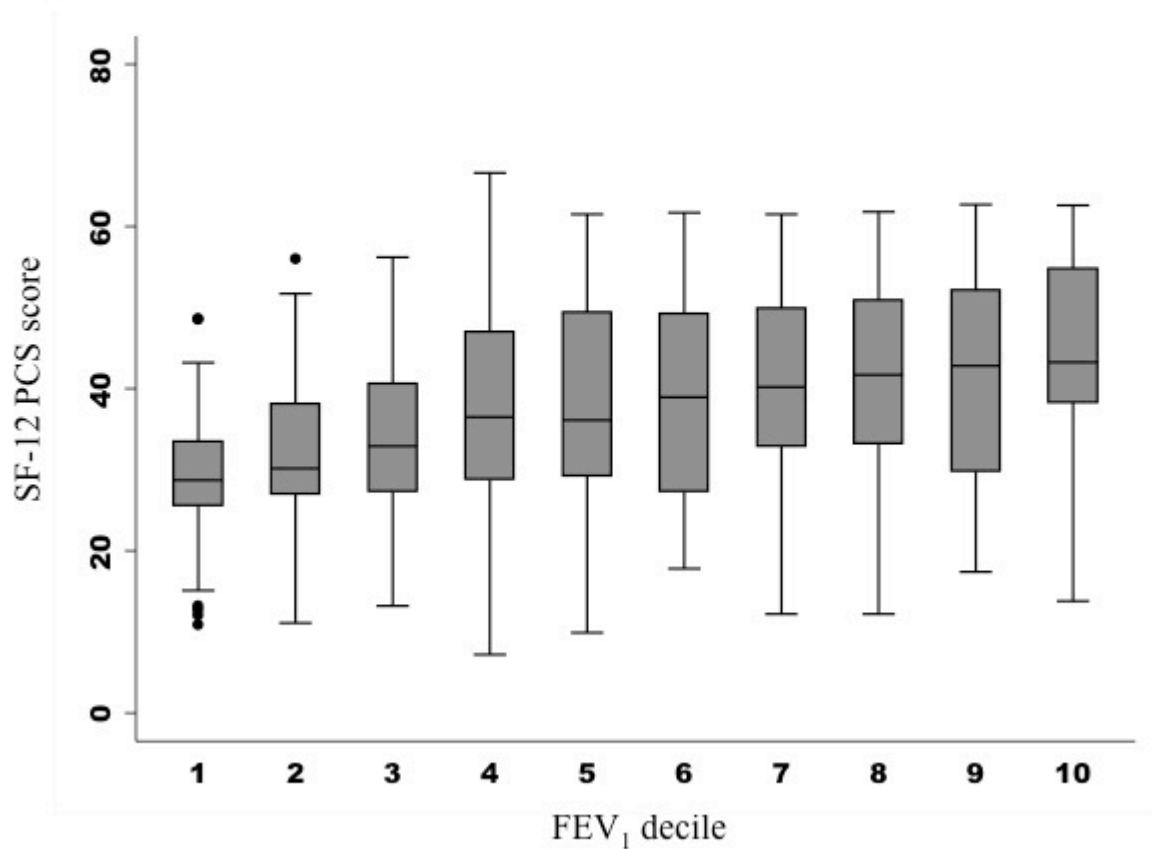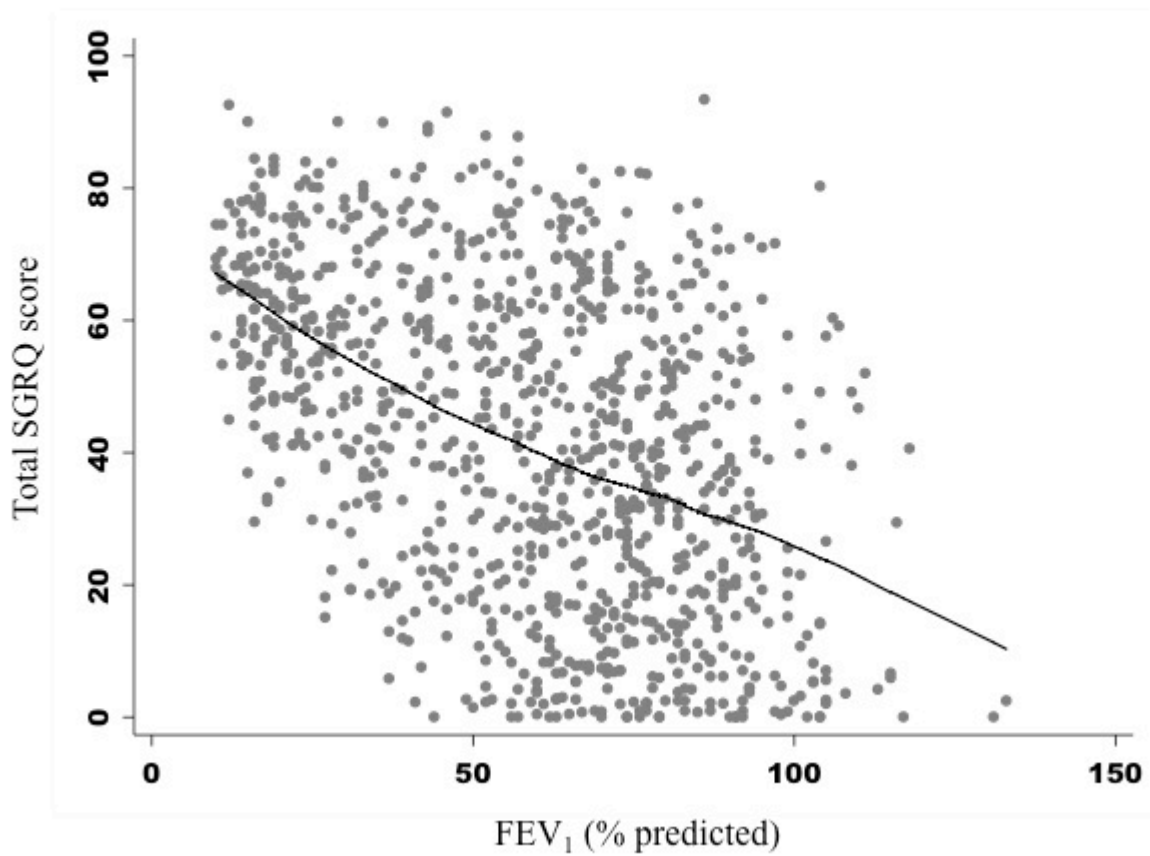

1st decile: 10-21% predicted; 2nd decile: 22-31% predicted; 3rd decile: 32-43% predicted; 4th decile: 44-54% predicted; 5th decile: 55-62% predicted; 6th decile: 63-69% predicted; 7th decile: 70-75% predicted; 8th decile: 76-82% predicted; 9th decile: 83-90% predicted; 10th decile: 91-133% predicted

e-Figure 2. Boxplot distribution of SF-12 PCS scores by deciles of FEV_1 % predicted (n=967).
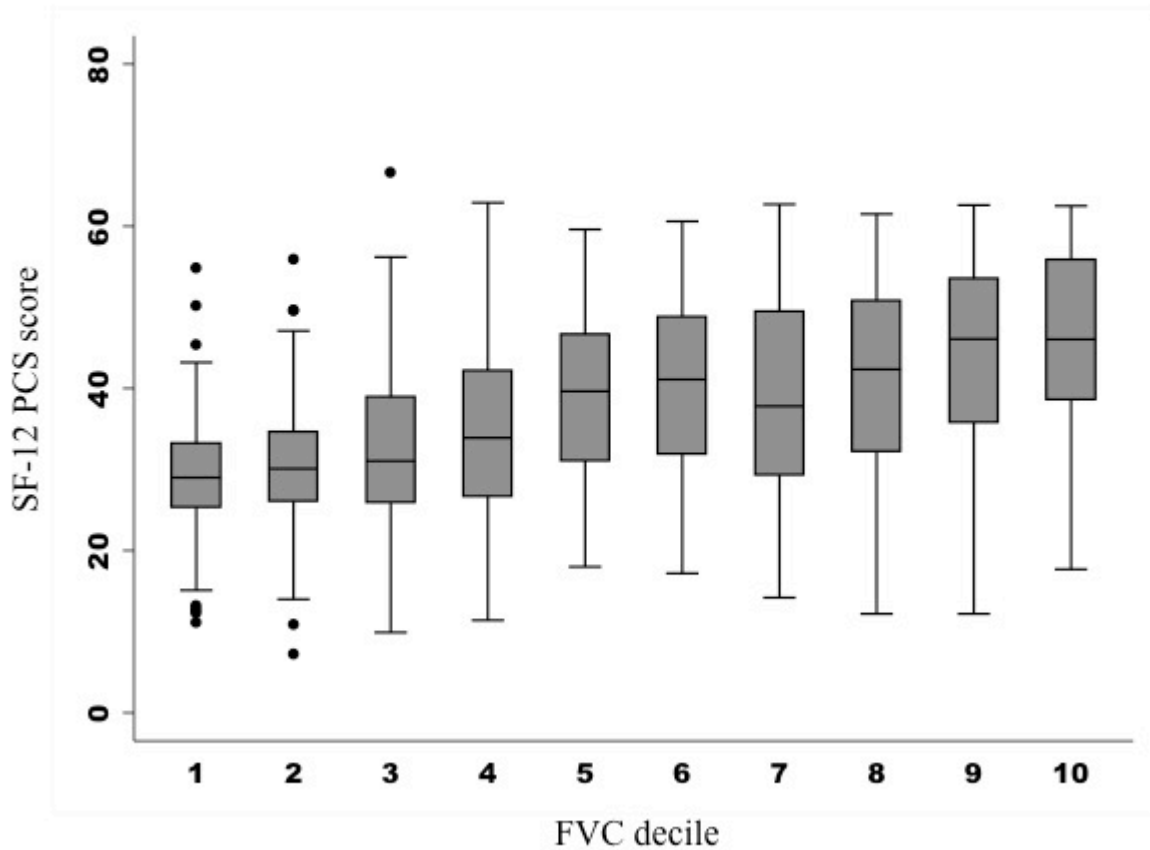

1st decile: 10-21% predicted; 2nd decile: 22-31% predicted; 3rd decile: 32-43% predicted; 4th decile: 44-54% predicted; 5th decile: 55-62% predicted; 6th decile: 63-69% predicted; 7th decile: 70-75% predicted; 8th decile: 76-82% predicted; 9th decile: 83-90% predicted; 10th decile: 91-133% predicted

e-Figure 3. LOWESS plot of total SGRQ score versus FEV_1 % predicted demonstrates a linear relationship (bandwidth 0.5).

e-Figure 4. LOWESS plot of SF-12 PCS score versus FEV$_1$ % predicted demonstrates a linear relationship (bandwidth 0.5).
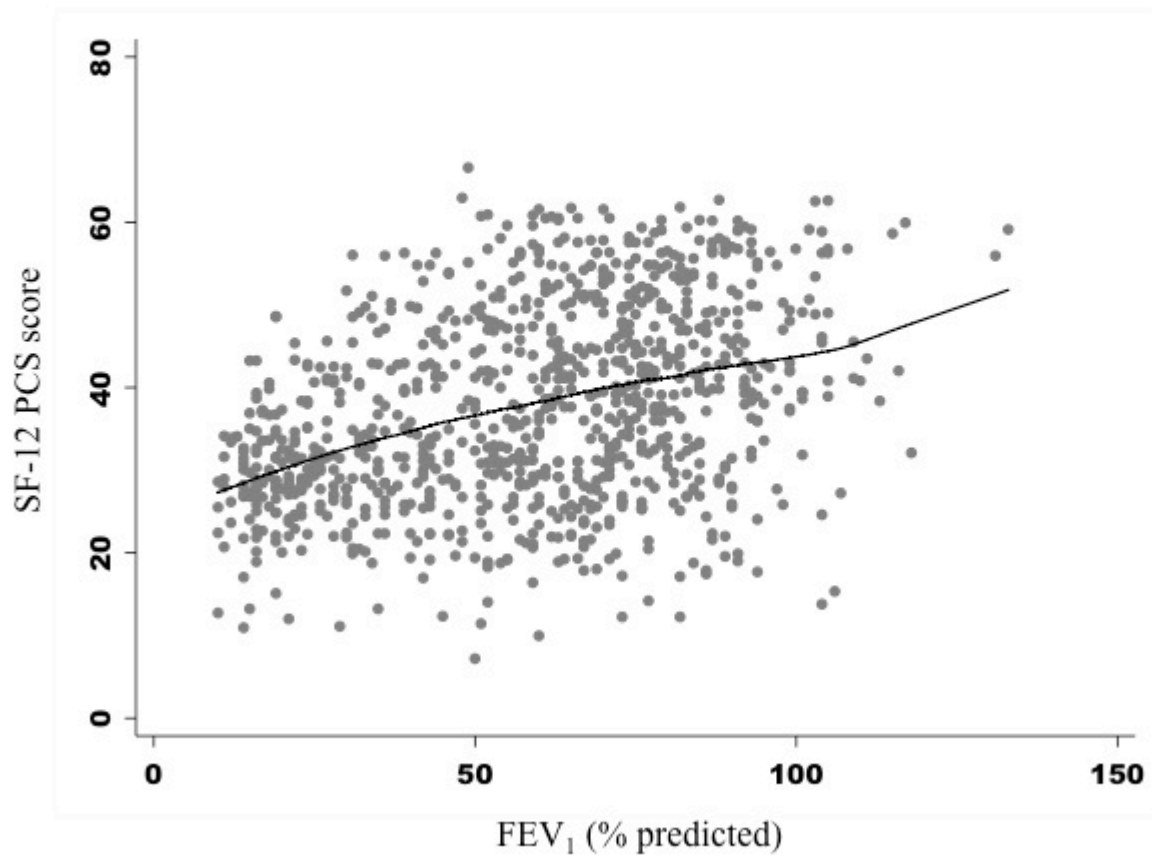
**e-Figure 5.** Boxplot distribution of SGRQ scores by deciles of FVC % predicted (n=981).
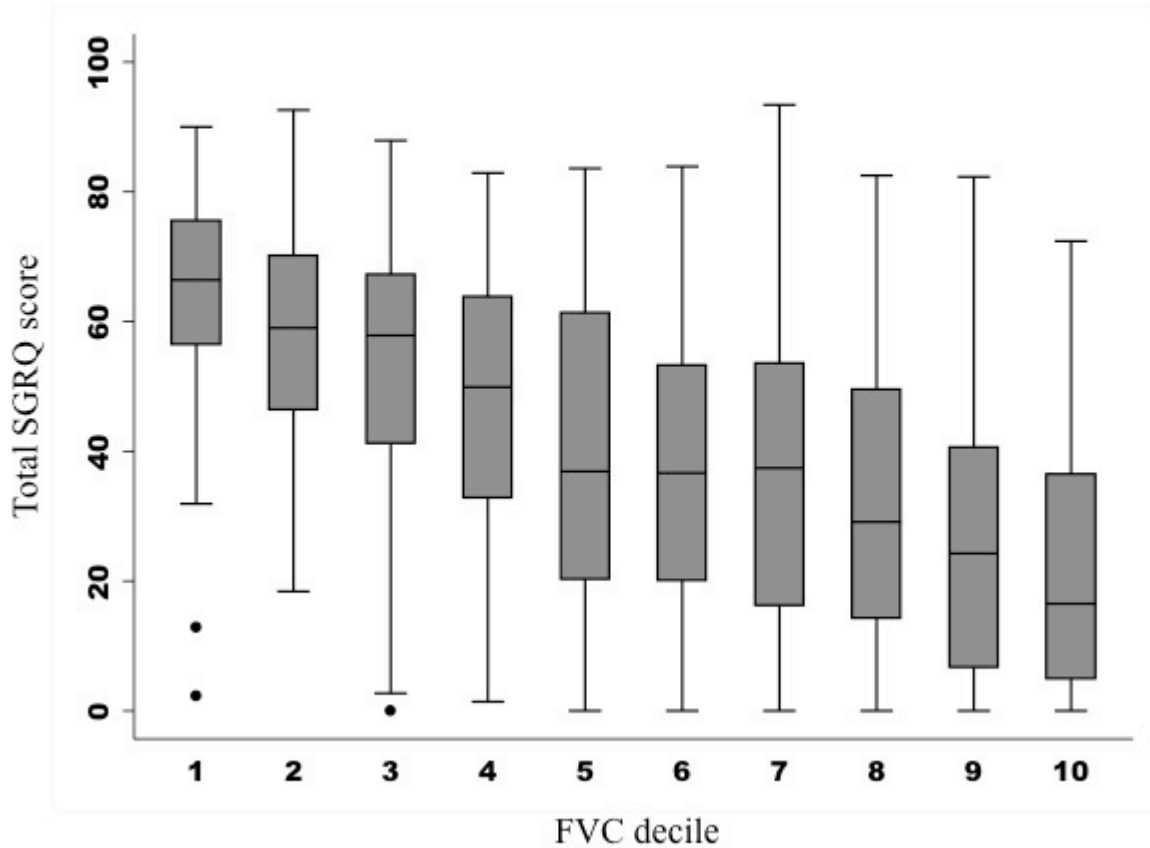
1st decile: 13-41% predicted; 2nd decile: 42-50% predicted; 3rd decile: 51-58% predicted; 4th decile: 59-64% predicted; 5th decile: 65-69% predicted; 6th decile: 70-75% predicted; 7th decile: 76-81% predicted; 8th decile: 82-87% predicted; 9th decile: 88-97% predicted; 10th decile: 98-139% predicted

e-Figure 6. Boxplot distribution of SF-12 PCS scores by deciles of FVC % predicted (n=967).

1st decile: 13-41% predicted; 2nd decile: 42-50% predicted; 3rd decile: 51-58% predicted; 4th decile: 59-64% predicted; 5th decile: 65-69% predicted; 6th decile: 70-75% predicted; 7th decile: 76-81% predicted; 8th decile: 82-87% predicted; 9th decile: 88-97% predicted; 10th decile: 98-139% predicted
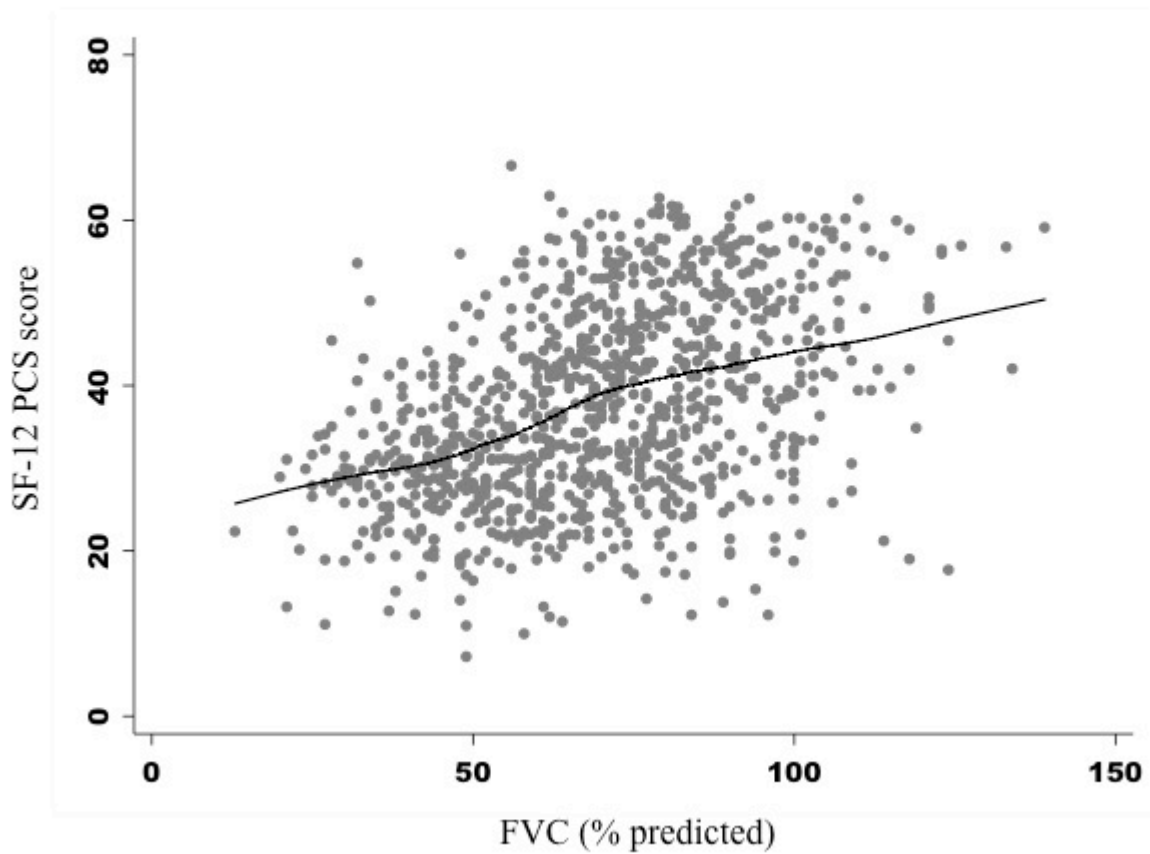
e-Figure 7. LOWESS plot of total SGRQ score versus FVC % predicted demonstrates a linear relationship (bandwidth 0.5).
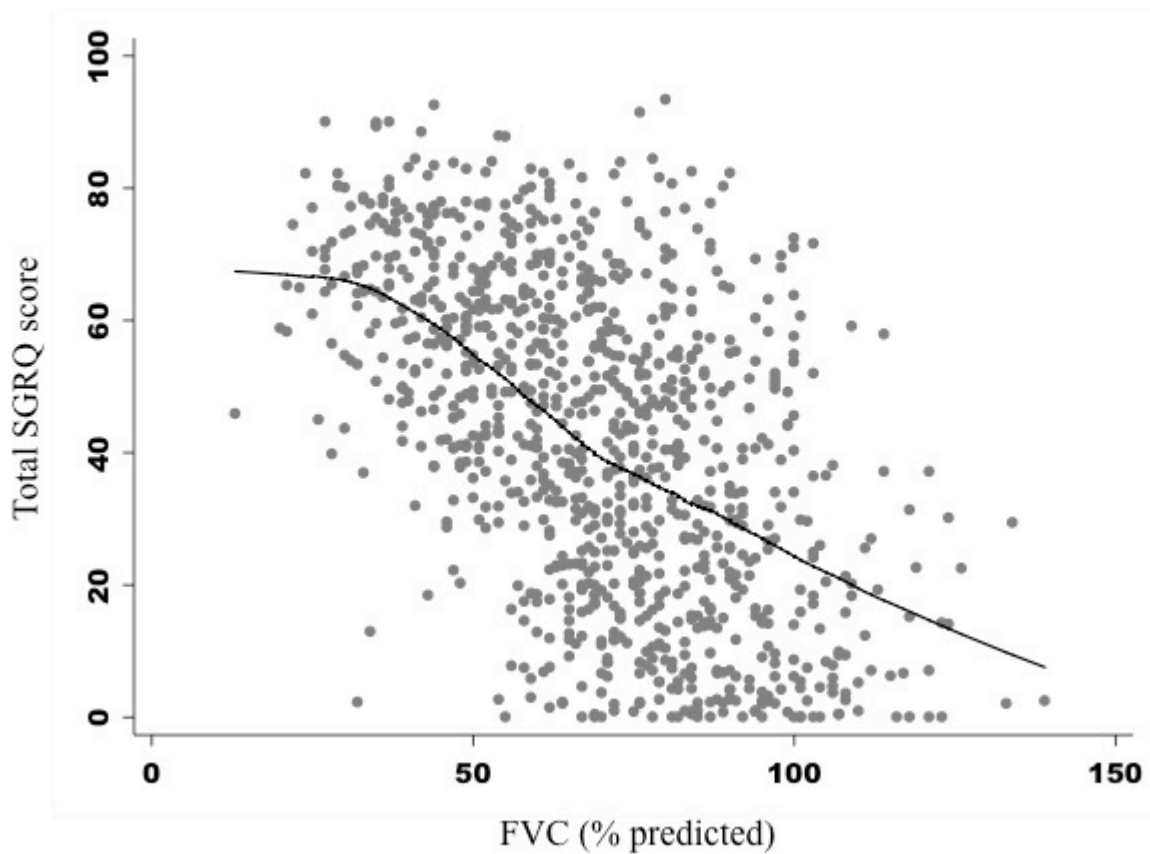
e-Figure 8. LOWESS plot of SF-12 PCS score versus FVC % predicted demonstrates a linear relationship (bandwidth 0.5).