

## **ONLINE DATA SUPPLEMENT**

**Oxygen desaturation in six-minute walk test is a risk factor for adverse outcomes in**

**COPD**

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**Table E1a. The coefficients from the full multivariable GEE regression model with robust standard errors estimating yearly decline in FEV1 in % predicted by oxygen desaturation during the 6MWT, adjusted for the confounders shown**

	Coeff	95% CI	p
Constant	0.514		
<b><i>Time (years)</i></b>	<b>-0.0087</b>	-0.012, -0.005	<0.001
<b><i>Desaturation</i></b>	<b>-0.0142</b>	-0.024, -0.004	<0.01
<b><i>Time * Desaturation</i></b>	<b>-0.0087</b>	<b>-0.016, -0.002</b>	<b>0.014</b>
Sex			
Men	-0.0021	-0.014, 0.010	0.730
Age per 10 year increase	0.0111	0.003, 0.020	0.011
Body composition at baseline			
Cachectic	0.0014	-0.015, 0.018	0.866
Obese	-0.0192	-0.039, 0.001	0.061
Smoking habits at baseline			
Daily-smoker	0.0031	-0.008, 0.014	0.57
FEV1 % predicted per 10% reduction	0.9115	0.867, 0.956	<0.001
Exacerbations last 12 months before baseline			
2 or more/yr	-0.0024	-0.018, 0.013	0.76
PaO2 at baseline, per kPa increase	-0.0022	-0.007, 0.002	0.35
Charlson comorbidity Score			
2	0.0025	-0.009, 0.014	0.69
3	0.0109	-0.007, 0.028	0.22
4+	-0.0116	-0.032, 0.009	0.27
6MWD per 10 meters increase at baseline	0.0010	0.0004, 0.002	<0.001
Height, per cm increase at baseline	0.0014	-0.008, 0.012	0.76
Weight, per kg increase at baseline	0.0095	0.003, 0.015	<0.01

The estimated mean yearly decline for the entire cohort is given by the time variable; -0.0087 (=0.9%) per year in percent predicted. The decline by desaturation is given by the time by desaturation interaction term: Those who did not desaturate have an estimated decline of the mean average -0.0087, whereas those who did desaturate have an estimated decline of  $-0.0087 + -0.0087 = 1.7\%$  reduction in FEV1 in percent predicted per year.

**Table E1b. The coefficients from the full multivariable GEE regression model with robust standard errors estimating yearly decline in FVC in % predicted by oxygen desaturation during the 6MWT, adjusted for the confounders shown**

	Coeff	95% CI	p
Constant	0.8147		
<b><i>Time (years)</i></b>	<b>-0.0170</b>	-0.022, -0.012	<0.001
<b><i>Desaturation</i></b>	<b>0.0149</b>	-0.032, 0.002	0.09
<b><i>Time * Desaturation</i></b>	<b>-0.0154</b>	<b>-0.028, -0.003</b>	<b>0.02</b>
Sex			
Men	0.0016	-0.016, 0.019	0.86
Age per 10 year increase at baseline	0.0126	0.001, 0.024	0.03
Body composition at baseline			
Cachectic	0.0011	-0.025, 0.027	0.93
Obese	-0.015	-0.045, 0.015	0.32
Smoking habits at baseline			
Daily-smoker	0.009	-0.007, 0.025	0.26
FVC per 10% reduction at baseline	0.8227	0.76, 0.88	<0.001
Exacerbations last 12 months before baseline			
2 or more/yr	0.0104	-0.015, 0.036	0.42
PaO2 at baseline, per kPa increase	-0.0017	-0.008, 0.005	0.61
Charlson comorbidity Score			
2	0.0070	-0.013, 0.027	0.49
3	0.0032	-0.019, 0.026	0.78
4+	-0.0233	-0.058, 0.011	0.18
6MWD per 10 meters increase at baseline	0.0016	0.001, 0.002	0.001
Height, per cm increase at baseline	-0.0023	-0.016, 0.012	0.75
Weight, per kg increase at baseline	0.0087	-0.001, 0.018	0.07

The mean yearly decline for the entire cohort is given by the time variable; -0.017 per year in percent predicted (=1.7%). The estimated decline among those who desaturate is given by the time by desaturation interaction term: Those who did not desaturate have an estimated decline of the mean average -0.017 (or 1.7%) whereas those who did desaturate had an estimated decline of  $-0.017 + -0.0154 = 3.2\%$  reduction in FVC in percent predicted per year.

**Table E2. The coefficients from the full multivariable GEE regression model with robust standard errors estimating yearly decline in fat free mass index (FFMI) by oxygen desaturation during the 6MWT, adjusted for the confounders shown**

	Coeff	95% CI	p
Constant	13.58		
<b><i>Time (years)</i></b>	<b>-0.028</b>	-0.08, 0.02	0.27
<b><i>Desaturation</i></b>	<b>-0.012</b>	-0.27, 0.25	0.93
<b><i>Time * Desaturation</i></b>	<b>-0.152</b>	<b>-0.28, -0.03</b>	<b>0.02</b>
Sex			
Men	4.444	4.23, 4.66	<0.001
Age per 10 year increase at baseline	-0.5242	-0.69, -0.36	<0.001
Body composition at baseline			
Cachectic	-1.242	-1.54, -0.94	<0.001
Obese	-0.763	-1.14, -0.38	<0.001
Smoking habits at baseline			
Daily-smoker	0.025	-0.18, 0.23	0.81
FEV1 per 10% reduction at baseline	1.14	0.26, 2.02	0.01
Exacerbations last 12 months before baseline			
2 or more/yr	-0.20	-0.51, 0.12	0.22
PaO2 at baseline, per kPa increase	-0.02	-0.13, 0.08	0.66
Charlson comorbidity Score			
2	0.04	-0.19, 0.28	0.72
3	0.18	-0.15, 0.51	0.29
4+	0.17	-0.28, 0.62	0.46
6MWD per 10 meters increase at baseline	0.01	0.0005, 0.03	0.04
Height, per cm increase at baseline	-1.12	-1.32, -0.93	<0.001
Weight, per kg increase at baseline	1.48	1.34, 1.61	<0.001

The mean yearly decline in FFMI for the entire cohort is given by the time variable; -0.028 kg/m<sup>2</sup> per year. The decline among those who desaturate is given by the time by desaturation interaction term: Those who did not desaturate have an estimated decline of the mean average -0.028 kg/m<sup>2</sup> whereas those who desaturate have an estimated decline of -0.028 + -0.152 = -0.180 kg/m<sup>2</sup> in yearly reduction in FFMI.

**Table E3. Sensitivity analyses for different definitions of desaturation and all outcomes. Comparing the definition used in the paper with two other definitions, one stricter and one milder.**

	Mortality*			Exacerbations #			Change in FEV1 †			Change in FVC †			Change in FFMI †		
	HR	95 CI	p	IRR	95 CI	p	Coeff	95 CI	p	Coeff	95 CI	p	Coeff	95 CI	p
SpO2 < 90% post test AND > 4% reduction (n= 86, 23%) used as definition in paper	2.7	1.2, 5.7	0.01	1.6	1.2, 2.2	<0.01	-0.009	-0.016, -0.002	0.01	-0.015	-0.028, -0.003	0.02	-0.152	-0.28, -0.03	0.02
< 6% reduction (n= 65, 18%)	2.2	1.1, 5.2	0.03	1.2	0.9, 1.7	0.24	-0.005	-0.010, -0.001	0.13	-0.008	-0.02, 0.004	0.21	-0.133	-0.25, -0.02	0.024
SpO2 < 90% OR 4% reduction (n= 139, 38%)	3.1	1.5, 6.3	0.002	1.2	0.9, 1.6	0.16	-0.008	-0.015, -0.002	0.01	-0.016	-0.025, -0.006	0.002	-0.129	-0.23, -0.02	0.017

\*Cox regression model

# Negative binomial regression

† GEE regression model