

## Supporting information

**S1 Table: characteristics of COPD patients of the COBRA cohort**

Parameter	n *	All patients (n = 241)		Patients with 1 visit (n=78)		Patients with 2 visits (n = 163)		p value <sup>a</sup>	p value <sup>b</sup>	
		Visit 1	n *	Visit 1 only	n *	Visit 1	Visit 2			
Male sex – no. (%)	241	164 (68.1)	78	50 (64.1)	163	114 (69.9)	-	0.37	-	
Age (years)	241	63.1 ± 9.8	78	61.6 ± 11.4	163	63.8 ± 8.9	64.5 ± 9.0	0.14	-	
Caucasian origin – no. (%)	239	224 (93.7)	76	70 (92.1)	163	154 (94.5)	-	0.49	-	
Other origin – no. (%)	239	15 (6.3)	76	6 (7.9)	163	9 (5.5)	-	0.49	-	
<i>GOLD stages</i>										
GOLD I – no. (%)	238	54 (22.7)	75	24 (32.0)	159	28 (17.6)	28 (17.6)	<b>0.03</b>	0.99	
GOLD II – no. (%)	238	87 (36.5)	75	20 (26.6)	159	66 (41.5)	66 (41.5)	<b>0.03</b>	0.99	
GOLD III – no. (%)	238	53 (22.3)	75	14 (18.7)	159	38 (23.9)	36 (22.7)	<b>0.03</b>	0.99	
GOLD IV – no. (%)	238	44 (18.5)	75	17 (22.7)	159	27 (17.0)	29 (18.2)	<b>0.03</b>	0.99	
<i>Smoking history</i>										
Former smoker – no. (%)	241	149 (61.8)	78	41 (52.6)	163	108 (66.3)	108 (66.3)	<b>0.002</b>	1.00	
Packs per year in former smokers – no.	147	49.1 ± 23.9	39	49.7 ± 22.2	101	49.7 ± 25.1	49.9 ± 25.1	0.99	0.96	
Active smokers – no. (%)	241	84 (34.9)	78	30 (38.5)	163	54 (33.1)	54 (33.1)	<b>0.002</b>	1.00	
Packs per year in active smokers – no.	82	35.8 ± 21.7	28	35.1 ± 20.8	47	36.0 ± 23.8	34.9 ± 21.9	0.89	0.83	
Body Mass Index (kg per m <sup>2</sup> )	240	26.5 ± 6.1	77	25.7 ± 5.9	163	26.8 ± 6.2	-	0.21	-	
<i>Biology</i>										
Blood leukocytes (no. per mm <sup>3</sup> )	165	7500 (6500 - 8900)	43	7400 (6400 - 10000)	96	7350 (6500 - 8750)	7100 (6150 - 8150)	0.37	0.34	
Blood eosinophils (no. per mm <sup>3</sup> )	165	162 (104 - 230)	43	146 (94 - 213)	96	165 (103 - 225)	162 (117 - 244)	0.37	0.67	
With blood eosinophils ≥ 300 per mm <sup>3</sup> – no. (%)	165	27 (16.4)	43	4 (9.3)	96	17 (17.7)	12 (12.5)	0.21	0.32	
Blood neutrophils (no. per mm <sup>3</sup> )	163	4752 (3840 - 5950)	42	4479 (3782 - 6486)	95	4680 (3835 - 5950)	4560 (3843 - 5265)	0.74	0.39	
Blood lymphocytes (no. per mm <sup>3</sup> )	165	1830 (1406 - 2280)	43	1920 (1539 - 2438)	96	1648 (1302 - 2190)	1782 (1387 - 2184)	<b>0.04</b>	0.49	
Blood monocytes (no. per mm <sup>3</sup> )	161	560 (444 - 720)	40	603 (469 - 740)	96	532 (404 - 698)	555 (463 - 667)	<b>0.03</b>	0.25	
Hemoglobin – g per deciliter	115	14.4 ± 1.4	32	14.1 ± 1.6	72	14.6 ± 1.3	14.3 ± 1.4	0.10	0.25	
CRP – mg per Liter	112	7.6 ± 7.6	22	6.5 ± 4.6	73	7.8 ± 8.1	6.8 ± 7.5	0.35	0.47	
With CRP ≥ 3 mg per Liter – no. (%)	112	85 (75.9)	22	17 (77.3)	73	54 (74.0)	54 (74.0)	0.76	1.00	
<i>Blood gases</i>										
PaO <sub>2</sub> - mmHg	181	74.5 ± 14.1	57	74.8 ± 14.2	91	72.9 ± 13.7	74.7 ± 13.2	0.42	0.37	
PaCO <sub>2</sub> . mmHg	182	39.6 ± 4.8	57	40.0 ± 4.8	90	39.8 ± 4.9	40.0 ± 6.0	0.86	0.86	
pH	182	7.42 ± 0.03	57	7.41 ± 0.03	92	7.41 ± 0.03	7.41 ± 0.04	0.78	0.70	

**S1 Table (continued)**

<i>Respiratory function</i>									
Pre-bronchodilator FEV <sub>1</sub> (% predicted)	233	59.6 ± 24.3	72	63.0 ± 27.7	144	56.6 ± 21.7	56.1 ± 21.7	0.10	0.84
Post-bronchodilator FEV <sub>1</sub> (% predicted)	171	63.7 ± 25.8	53	71.3 ± 30.4	70	56.6 ± 22.8	56.5 ± 21.5	<b>0.005</b>	0.98
With fixed airflow obstruction – no. (%) <sup>c</sup>	176	143 (81.3)	55	34 (61.8)	70	65 (92.9)	65 (92.9)	<b>&lt; 0.0001</b>	1.00
Pre-bronchodilator FVC (% predicted)	233	86.6 ± 21.3	73	86.1 ± 21.9	142	85.0 ± 20.4	84.0 ± 20.4	0.73	0.68
Post-bronchodilator FVC (% predicted)	169	91.5 ± 21.1	51	91.9 ± 21.5	69	91.0 ± 20.4	88.8 ± 21.1	0.83	0.54
Pre-bronchodilator FEV <sub>1</sub> / FVC (% predicted)	235	53.5 ± 15.3	74	57.0 ± 16.7	144	51.4 ± 14.0	51.7 ± 14.2	<b>0.01</b>	0.89
Post-bronchodilator FEV <sub>1</sub> / FVC (% predicted)	176	53.9 ± 16.2	55	60.6 ± 17.3	70	47.2 ± 14.4	48.4 ± 14.7	<b>&lt; 0.0001</b>	0.62
FRC - %	124	137.8 ± 38.3	49	131.5 ± 31.7	37	140.9 ± 43.4	139.9 ± 41.5	0.27	0.92
RV - %	135	156.4 ± 53.0	53	150.7 ± 43.1	41	165.9 ± 62.9	154.7 ± 56.6	0.19	0.41
TLC - %	137	113.8 ± 19.2	55	112.0 ± 16.9	42	114.1 ± 21.7	112.4 ± 19.5	0.60	0.70
DLCO - %	115	59.0 ± 21.7	46	63.9 ± 21.6	34	49.5 ± 18.8	49.9 ± 18.8	<b>0.003</b>	0.94
<i>Symptoms</i>									
With cough – no. (%)	241	97 (40.2)	78	27 (34.6)	163	70 (42.9)	56 (34.4)	0.22	0.12
With wheezing – no. (%)	241	32 (13.3)	78	14 (17.9)	163	18 (11.0)	16 (9.8)	0.14	0.72
With emphysema no. (%) <sup>d</sup>	241	92 (38.2)	78	28 (35.9)	163	64 (39.3)	64 (39.3)	0.62	1.00
With exacerbations in the previous 12 months - no. (%)	241	128 (53.1)	78	39 (50.0)	163	89 (54.6)	62 (38.0)	0.51	<b>0.003</b>
Exacerbations in the previous 12 months - no.	241	1.44 ± 0.16	78	1.26 ± 0.22	163	1.52 ± 0.21	1.46 ± 0.23	0.12	0.72
Unscheduled medical visits in the previous 12 months - no.	241	1.19 ± 0.17	78	0.96 ± 0.23	163	1.29 ± 0.22	1.08 ± 0.16	<b>0.03</b>	0.09
Hospitalizations for COPD in the previous 12 months – no.	241	0.32 ± 0.05	78	0.41 ± 0.11	163	0.27 ± 0.05	0.19 ± 0.06	0.10	0.17
<i>Comorbidities</i>									
Cardiovascular – no. (%)	241	103 (42.7)	78	32 (41.0)	163	71 (43.6)	-	0.71	-
Hypertension – no. (%)	241	67 (27.8)	78	21 (26.9)	163	46 (28.2)	-	0.84	-
Dyslipidemia – no. (%)	241	58 (24.1)	78	14 (17.9)	163	44 (27.0)	-	0.13	-
Diabetes – no. (%)	241	28 (11.6)	78	7 (9.0)	163	21 (12.9)	-	0.38	-
Sinusitis – no. (%)	241	27 (11.2)	78	7 (9.0)	163	20 (12.3)	-	0.45	-
Allergic rhinitis – no. (%)	241	38 (15.8)	78	12 (15.4)	163	26 (15.9)	-	0.92	-
Obstructive sleep apnea – no. (%)	241	22 (9.1)	78	4 (5.1)	163	18 (11.0)	-	0.14	-
Gastro Esophageal Reflux – no. (%)	241	70 (29.0)	78	21 (26.9)	163	49 (30.1)	-	0.62	-
Bronchial dilatation – no. (%)	241	11 (4.6)	78	3 (3.8)	163	8 (4.9)	-	0.72	-

**S1 Table (continued)**

<i>Treatments</i>									
On SABA – no. (%)	231	144 (62.3)	70	33 (47.1)	158	110 (69.6)	115 (72.8)	<b>0.002</b>	0.54
On LABA alone – no. (%)	233	26 (11.2)	70	5 (7.1)	160	21 (13.1)	18 (11.2)	0.19	0.61
On LAMA alone – no. (%)	233	16 (6.9)	70	4 (5.7)	160	12 (7.5)	12 (7.5)	0.63	1.00
On ICS alone – no. (%)	233	4 (1.7)	70	1 (1.4)	160	3 (1.9)	3 (1.9)	0.82	1.00
Daily dose of ICS - µg of equivalents beclomethasone	119	1304 ± 669	28	1499 ± 811	77	1253 ± 633	1242 ± 626	0.11	0.92
On OCS – no. (%)	232	8 (3.4)	69	7 (10.1)	160	1 (0.6)	2 (1.2)	<b>0.0003</b>	0.57
Daily dose of prednisone (mg)	8	20.4 ± 10.9	7	22.6 ± 9.6	1	5	5	0.14	-
On LABA + LAMA – no. (%)	233	22 (9.4)	70	6 (8.6)	160	16 (10.0)	21 (13.1)	0.74	0.39
On LABA + LAMA + ICS – no. (%)	233	78 (33.5)	70	22 (31.4)	160	55 (34.4)	63 (39.4)	0.67	0.36
On anti-histamine – no. (%)	241	20 (8.3)	78	8 (10.3)	162	12 (7.4)	8 (4.9)	0.46	0.36
On theophylline – no. (%)	232	1 (0.4)	69	0 (0.0)	160	1 (0.6)	1 (0.6)	0.52	1.00
On gastro esophageal reflux inhibitors – no. (%)	241	56 (23.2)	78	17 (21.8)	163	39 (23.9)	29 (17.8)	0.72	0.18
On anti-hypertensive drugs – no. (%)	232	80 (34.5)	70	24 (34.3)	160	55 (34.4)	54 (33.7)	0.99	0.91
On statins – no. (%)	231	56 (24.2)	69	11 (15.9)	160	44 (27.5)	49 (30.6)	0.07	0.54
On fibrates – no. (%)	229	5 (2.2)	69	1 (1.4)	157	4 (2.5)	3 (1.9)	0.61	0.71
On anti-platelet aggregation – no. (%)	231	63 (27.3)	69	15 (21.7)	159	47 (29.6)	42 (26.4)	0.23	0.54
Other – no. (%)	227	102 (44.9)	68	20 (29.4)	157	81 (51.6)	75 (47.8)	<b>0.003</b>	0.50
On oxygen therapy – no. (%)	238	37 (15.5)	75	11 (14.7)	161	26 (16.1)	16 (9.9)	0.78	0.10
Adherence to treatments – no. (%)	224	203 (90.6)	64	55 (85.9)	155	144 (92.9)	143 (92.3)	0.11	0.83

Data are n (%), or means ± SD, or median (25-75 IQR), or means ± SEM, in case of number of exacerbations, of unscheduled hospital visits and hospitalizations for COPD in the previous 6 months

CRP = C reactive protein; FEV<sub>1</sub> = Forced Expiratory Volume in 1 second; FVC = Forced Vital Capacity; FRC = Functional Residual Capacity; RV = Residual Volume; TLC = Total Lung Capacity; DLCO = transfer factor of the lung for carbon monoxide; ICS = inhaled corticosteroids; SABA = short-acting β<sub>2</sub>-agonists; LABA = long-acting β<sub>2</sub>-agonists; OCS = oral corticosteroids; LAMA = long-lasting muscarinic antagonists.

\* denotes the number of patients with each available variable

<sup>a</sup> p ≤ 0.05, between COPD patients with 1 and 2 visits (n=78 and n=163, respectively) (Students' t test, or Mann-Whitney U-test, or Fisher exact test, 2-tailed, or Poisson test).

<sup>b</sup> p ≤ 0.05, between visits 1 and 2 for n=163 COPD patients (Students' t test, or Mann-Whitney U-test, or Fisher exact test, 2-tailed, or Poisson test).