

TABLE E1 Baseline demographic and clinical characteristics of participants who consented versus did not consent to participate in the 8-year follow-up

Parameter	Not Consented for 8-year follow-up		Consented for 8-year follow-up (N=1555)	p-value**
	Died by Year 3 (N=211)	Alive or LTFU* at Year 3 (N=398)		
Baseline Demographic and Clinical Characteristics				
Mean (SD) age, y	66 (6)	63 (7)	63 (7)	0.968
Male, %	70	66	64	0.451
Mean (SD) post-BD FEV ₁ , L	1.11 (0.47)	1.28 (0.49)	1.40 (0.52)	<0.001
Mean (SD) post-BD FEV ₁ , % predicted	41 (15)	46 (16)	50 (16)	<0.001
FEV ₁ /FVC ratio	0.42 (0.12)	0.45 (0.12)	0.45 (0.11)	0.774
GOLD II/III/IV, %	27/47/26	40/43/17	48/41/11	<0.001
GOLD 2017 A/B/C/D, %	10/12/21/58	14/15/22/49	26/12/25/36	<0.001
Mean (SD) 6MWD, m	303 (126)	318 (109)	391 (117)	<0.001
Mean (SD) Emphysema, PD15 [†] , g/L	46 (26)	49 (27)	53 (26)	0.016

Mean (SD) BODE index	4.4 (2.3)	3.8 (2.1)	2.8 (2.0)	<0.001
Mean (SD) SGRQ total score	54 (18)	54 (17)	46 (18)	<0.001
COPD hospitalisation history, %	28	12	14	0.376
Frequent exacerbation history, %	27	24	20	0.097
Cardiovascular history, %	46	30	32	0.457
Depression symptoms, %	32	37	23	<0.001
Asthma history, %	24	23	23	0.970
Diabetes history, %	17	7	10	0.073
Clinical Characteristics at Year 3				
Mean (SD) post-BD FEV ₁ , L	n/a	1.20 (0.50)	1.33 (0.54)	0.001
Mean (SD) post-BD FEV ₁ , % predicted	n/a	44 (16)	47 (16)	0.007
Mean (SD) FEV ₁ decline during main study, (mL/yr)	n/a	35 (44)	26 (40)	<0.001
Mean (SD) 6MWD, m	n/a	308 (131)	384 (128)	<0.001
Mean (SD) Emphysema, PD15 [¶] , g/L	n/a	45 (25)	51 (28)	0.006
Mean (SD) BODE index	n/a	4.0 (2.3)	3.1 (2.2)	<0.001

Mean (SD) SGRQ total score	n/a	54 (18)	46 (19)	<0.001
COPD hospitalisation during main study, %	n/a	24	31	0.003
Frequent exacerbations (FE) all 3 years of main study, %	n/a	17	12	0.015

*LTFU (lost to follow-up) includes 19 who were lost during the main study plus the 379 who did not consent for participation in the 8-year follow-up after Year 3.

**Comparison between consented participants and non-consented participants who were not confirmed to have died by Year 3.

†PD15: lowest 15th percentile of lung density.

6MWD: 6-minute walk distance; BD: bronchodilator; BODE: body mass index, obstruction, dyspnoea, and exercise; COPD: chronic obstructive pulmonary disease; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; SD: standard deviation; SGRQ: St. George's Respiratory Questionnaire.

TABLE E2 Correlations (Spearman’s Rho) between disease activity markers and baseline measurements

Variable description	1yr chg, FEV ₁	FEV ₁ decline, 3yr	1yr chg, PD15	PD15 decline, 3yr	1yr chg, BODE	3yr chg, BODE	COPD Hosp, Year 1	COPD Hosp, 3 Years	Freq Exbs, Year 1	1yr chg, SGRQ	3yr chg, SGRQ	Systemic Inflamm. Markers
BASELINE DEMOGRAPHICS												
Age	0.01	0.05	0.07	0.07	-0.02	0.06	0.06	0.08	0.02	0.06	0.08	0.04
Sex (+ Female; – Male)	0.02	0.05	-0.04	-0.25	-0.02	-0.01	-0.03	-0.01	0.09	-0.01	0.02	-0.04
Weight	0.03	0.02	0.07	0.48	-0.04	-0.10	-0.07	-0.10	-0.08	0.01	-0.07	0.12
Body Mass Index	0.04	0.06	0.08	0.47	-0.05	-0.11	-0.06	-0.07	-0.02	0.00	-0.07	0.14
Fat free mass	0.01	-0.01	0.05	0.41	0.00	-0.08	-0.06	-0.10	-0.12	0.01	-0.07	0.04
Fat free mass index	0.02	0.04	0.06	0.44	0.00	-0.07	-0.04	-0.06	-0.08	0.01	-0.06	0.11
Percent body fat	0.06	0.06	0.01	0.05	-0.08	-0.05	0.00	0.02	0.10	-0.03	-0.02	0.10
Pack-year history	-0.06	-0.08	0.04	0.07	-0.01	0.05	0.03	0.02	-0.02	0.02	0.03	0.13
Current smoker	-0.01	-0.11	-0.04	-0.25	0.02	0.03	-0.03	-0.01	-0.02	0.01	0.03	0.08
BASELINE SYMPTOMS												
Chronic bronchitis	0.02	-0.02	-0.04	-0.03	-0.01	-0.03	0.02	0.03	0.00	-0.07	-0.10	0.07

Chronic cough	-0.01	-0.05		-0.07	-0.08		-0.02	0.04		0.08	0.10	0.08		-0.07	-0.06		0.16
MMRC dyspnoea	-0.02	-0.03		-0.03	0.03		-0.28	-0.13		0.23	0.26	0.19		-0.08	-0.04		0.23
SGRQ Total score	0.00	-0.04		-0.08	-0.01		-0.03	0.04		0.28	0.30	0.26		-0.24	-0.24		0.24
COMORBIDITIES																	
CV history (incl. hypertension)	0.07	0.03		0.02	0.10		-0.07	-0.01		0.00	-0.02	-0.03		-0.02	0.00		0.11
CV history (excl. hypertension)	0.02	0.01		0.00	0.09		-0.07	-0.01		0.03	0.05	0.01		-0.02	-0.06		0.09
Diastolic blood pressure	-0.01	0.00		-0.01	0.05		0.01	0.00		0.03	0.00	0.00		0.02	0.01		-0.03
Systolic blood pressure	0.03	0.05		0.00	0.04		-0.04	0.00		0.01	-0.04	-0.01		-0.03	0.00		0.00
Depression score	-0.02	-0.03		-0.01	-0.02		0.01	0.00		0.12	0.11	0.17		-0.08	-0.08		0.15
FACIT Fatigue score	0.01	0.02		0.06	0.01		0.02	-0.01		-0.21	-0.17	-0.19		0.07	0.12		-0.19
BASELINE LUNG FUNCTION																	
FEV ₁	-0.13	-0.10		0.08	0.15		0.03	-0.04		-0.24	-0.29	-0.27		-0.01	-0.09		-0.14
FEV ₁ %predicted	-0.14	-0.07		0.09	0.05		0.04	-0.01		-0.24	-0.27	-0.22		-0.01	-0.07		-0.15
FEV ₁ reversibility	-0.18	-0.12		0.01	0.01		0.02	0.00		-0.06	-0.01	-0.05		-0.03	-0.03		-0.01
FEV ₁ /FVC ratio	-0.01	0.06		0.09	0.10		0.00	-0.08		-0.17	-0.23	-0.17		-0.03	-0.14		-0.07
Inspiratory capacity	0.00	-0.15		0.01	0.18		0.01	-0.08		-0.16	-0.13	-0.19		0.01	-0.10		-0.12
Functional Residual Capacity	-0.05	-0.19		-0.01	-0.08		0.07	0.22		0.17	0.25	0.06		0.05	0.08		0.04

Residual volume	-0.03	-0.12		-0.02	-0.09		0.09	0.20		0.21	0.27	0.15		0.07	0.09		0.12
Total lung capacity	-0.05	-0.23		-0.01	0.03		0.06	0.13		0.10	0.15	-0.03		0.06	0.01		-0.03
Blood oxygen level	-0.01	0.03		0.03	0.00		0.01	-0.01		-0.19	-0.19	-0.12		0.01	-0.04		-0.13
6-minute walk distance	-0.02	-0.02		0.07	-0.05		0.13	0.05		-0.15	-0.18	-0.13		-0.04	0.01		-0.24
BODE Index	0.05	0.00		-0.08	-0.04		-0.25	-0.13		0.27	0.33	0.23		0.01	0.06		0.24
BASELINE IMAGING																	
Emphysema (PD15)	0.06	0.10		-0.17	-0.11		-0.07	-0.14		-0.12	-0.17	-0.12		-0.07	-0.13		-0.02
EXACERBATION HISTORY																	
Exacerbations, year prior to study	-0.01	-0.01		0.01	-0.02		0.00	0.03		0.23	0.24	0.37		0.00	0.02		0.10
COPD Hosp, year prior to study	0.00	-0.03		-0.07	-0.04		0.02	0.05		0.30	0.29	0.19		0.01	0.03		0.09
BASELINE INFLAMMATORY MARKERS																	
White blood count	0.02	-0.03		-0.04	-0.03		-0.04	0.00		0.08	0.08	0.09		-0.04	0.01		0.49
Neutrophil count	0.01	-0.05		-0.03	-0.01		-0.04	0.04		0.10	0.11	0.10		-0.03	0.02		0.50
Eosinophil count	0.01	0.03		0.03	0.04		-0.02	-0.06		-0.01	-0.03	0.05		0.00	0.02		0.08
High sensitivity CRP	-0.04	-0.01		0.01	0.13		-0.03	0.01		0.12	0.12	0.10		-0.02	-0.02		0.53
IL-6	-0.02	0.03		0.01	0.10		-0.04	-0.02		0.03	0.03	0.01		-0.04	-0.01		0.21

IL-8	-0.06	-0.02		0.01	-0.04		-0.01	0.01		0.02	0.05	0.01		-0.05	-0.02		0.06
Fibrinogen	-0.01	-0.02		0.06	0.10		0.00	0.05		0.10	0.10	0.12		0.02	0.01		0.49
SP-D	0.01	-0.04		-0.10	-0.11		-0.01	0.02		0.03	0.05	-0.01		-0.02	0.00		0.00
CC-16	0.00	0.05		0.00	0.08		-0.03	0.02		0.05	0.06	0.02		0.02	0.01		0.02
CCL-18	-0.01	-0.03		0.02	0.16		0.00	0.02		0.08	0.09	0.09		0.01	0.01		0.25

BODE: body mass index, obstruction, dyspnea, and exercise; CC-16: club cell protein 16; CCL-18: chemokine (C-C motif) ligand 18;

CRP: C-reactive protein; COPD: chronic obstructive pulmonary disease; CV: cardiovascular; FACIT: Functional Assessment of

Chronic Illness Therapy; FEV₁: forced expiratory volume in 1 second; FVC: forced vital capacity; IL-6: interleukin-6; IL-8:

interleukin-8; MMRC: modified Medical Research Council; PD15: lowest 15th percentile density method; SGRQ: St. George's

Respiratory Questionnaire; SP-D: surfactant protein-D;

Yr: year.