Online Supplement:

Results

The baseline characteristics and longitudinal changes were similar when the CB+ group of 172 subjects meeting the strict definition was extended to all 220 subjects presenting with chronic phlegm production.**(Table S1)** Similar results on lung function decline (ml FEV_1/yr), frequent exacerbations and mortality were observed when the CB+ group was extended to the 220 subjects with chronic phlegm production (β -30.6ml; 95%CI -51.2;-10.08ml ; p=0.004, OR 3.82; 95% CI 2.64-5.53; p<0.001 and HR 1.26; 95%CI 1.01-1.59; p=0.043 respectively). When evaluating the impact of having chronic phlegm production but not meeting the strict definition in these 48 participants, we observed that they did not significantly differ from the CB- control group regarding FEV_1-decline (ml/yr) and mortality (β -8.2; 95%CI -44.2;27.8; p=0.656 and HR 1.04; 95%CI 0.69;1.58; p=0.845 respectively), but the risk of frequent exacerbations was significantly threefold increased (OR 3.26; 95% CI 1.64-6.47; p=0.001). Since interpretable lung function measurements were missing at baseline in 330 subjects, we evaluated the impact on the different outcomes. The association between chronic bronchitis and the frequent exacerbator phenotype was OR 3.51; 95%CI 2.01-6.10; p<0.001 in COPD subjects without interpretable spirometry at baseline and OR 3.65; 95% CI 2.03-6.56, p<0.001 in COPD subjects with interpretable spirometry at baseline, both adjusted for age, sex and packyears of cigarette smoking. The association between chronic bronchitis and the risk of all-cause death was HR 1.11; 95% CI 0.77-1.61; p=0.581 in COPD subjects without interpretable spirometry at baseline and HR 1.41; 95% CI 1.00-2.00; p=0.053 in COPD subjects with interpretable spirometry at baseline, both adjusted for age, sex and packyears of cigarette smoking.

Table S1: Baseline characteristics and longitudinal changes of the total population (n=972).

	COPD, CB- (n=752)	COPD+phlegm (n=220)	
			COPD, CB+ (n=172)
Age (years)	70.5 (15.2)	74.3 (12.2)	74.1 (13.6)
Males	380 (50.5%)	123 (55.9%)	96 (55.8%)
Smoking status			
Never smoker	134 (17.8%)	24 (10.9%)	17 (9.9%)
Former smoker	407 (54.1%)	119 (54.1%)	89 (51.7%)
Current smoker	211 (28.1%)	77 (35.0%)	66 (38.4%)
Pack-years cigarette smoking	23.0 (41.2)	29.8 (33.7)	30.6 (35.1)
Height (m)	1.69 (0.14)	1.68 (0.12)	1.68 (0.12)
Weight (kg)	76.7 (18.8)	75.2 (18.8)	74.8 (17.3)
BMI (kg/m²)	26.6 (5.3)	26.0 (5.7)	26.0 (5.5)
FEV_1 (l)	3.1 (1.6)	2.8 (1.3)	2.9 (1.4)
FEV_1 (% predicted)	82.0 (26.7)	68.6 (27.0)	70.5 (27.8)
FVC (l)	2.0 (1.1)	1.7 (0.9)	1.8 (0.9)
FVC (% predicted)	101.0 (29.5)	89.1 (31.9)	91.9 (33.0)
FEV_1/FVC (%)	65.4 (7.0)	61.5 (10.4)	61.0 (10.0)
Quality of life (%)	80.0 (21.9)	71.9 (34.4)	71.9 (31.3)
Longitudinal changes:			
Exacerbation rate (#/yr)	0.33 (0.85)	0.95 (1.77)	0.99 (1.78)
Lung function decline (ml/yr)	-35 (54)	-55 (74)	-57 (82)

Categorical variables are expressed as numbers (percentage). Values of continuous variables are expressed as median (interquartile range). Packyears were missing in 50 subjects, height/weight/BMI in 46 subjects and quality of life in 12 subjects.

Abbreviations: BMI = body mass index; CB= chronic bronchitis; COPD= Chronic Obstructive Pulmonary Disease

Table S2: Association between chronic bronchitis and lung function decline (ml/yr), stratified according to severity of airflow limitation.

	Model 1 (n=270)			Model 2 (n=259)		
	β	**95% CI**	**p-value**	**β**	**95% CI**	**p-value**
COPD≥80%FEV1 with chronic bronchitis	-45.3	-82.1;-8.5	0.016	-50.2	-89.2;-11.2	0.012
COPD<80%FEV1 with chronic bronchitis	-39.1	-65.0;-13.3	0.003	-39.1	-65.7;-12.5	0.004

Lung function decline per year was calculated by dividing the difference of two forced expiratory volume in 1 second (FEV1, in mL)-measurements by the years between the two measurements.

Model 1: age and sex adjusted

Model 2: adjusted for age, sex and packyears of cigarette smoking.

Abbreviations: β= unstandardized bèta-coefficient of millilitres lung function decline per year; CI= Confidence Interval; COPD= Chronic Obstructive Pulmonary Disease

Table S3: Association between chronic bronchitis and the frequent exacerbator phenotype, stratified according to severity of airflow limitation.

	Model 1 (n=594)			Model 2 (n=564)		
	OR	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
COPD≥80%FEV1 with chronic bronchitis	1.65	0.45-6.04	0.451	1.71	0.45-6.41	0.429
COPD<80%FEV1 with chronic bronchitis	4.09	2.08-8.05	<0.001	3.97	1.99-7.94	<0.001

Model 1: age and sex adjusted

Model 2: adjusted for age, sex and packyears of cigarette smoking.

Abbreviations: CI= Confidence Interval; COPD= Chronic Obstructive Pulmonary Disease; OR= Odds Ratio

Table S4 : Association between chronic bronchitis and the risk of all-cause death in COPD, stratified according to severity of airflow limitation.

	Model 1 (n=594)			Model 2 (n=564)		
	HR	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
COPD≥80%FEV1 with chronic bronchitis	1.22	0.63-2.36	0.563	1.22	0.62-2.40	0.566
COPD<80%FEV1 with chronic bronchitis	1.49	1.00-2.23	0.050	1.39	0.92-2.10	0.117

Model 1: age and sex adjusted

Model 2: adjusted for age, sex and packyears of cigarette smoking.

Abbreviations: CI= Confidence Interval; COPD= Chronic Obstructive Pulmonary Disease; HR= Hazard Ratio

Table S5 : Causes of death (n=351) in the COPD study population according to chronic bronchitis (CB) status.

		COPD, CB-		COPD, CB+	
		n	% of total	n	% of total
Pulmonary mortality		25	9.7	17	18.5
Mainly	COPD	18	6.9	12	13.0
	Pneumonia	6	2.3	4	4.3
Cardiovascular mortality		95	36.7	34	37.0
Mainly	Sudden (cardiac) death	24	9.3	11	12.0
	Stroke	21	8.1	5	5.4
	Heart failure	18	6.9	5	5.4
	Cardiac arrest	9	3.5	3	3.3
	Acute myocardial infarction	8	3.1	3	3.3
	Chronic ischaemic heart disease	5	1.9	2	2.2
Cancer mortality		79	30.5	20	21.7
Mainly	Malignant neoplasm of bronchus and lung	32	12.4	13	14.1
Other mortality		60	23.2	21	22.8
Mainly	Dementia	18	6.9	3	3.3
	Other ill-defined and unspecified causes	14	5.4	4	4.3
	Fracture of femur	5	1.9	3	3.3
	Total:	259		92	