

Supplementary tables

Table 1 Univariate analysis of predictors for COPD exacerbations according to p-value rank

Baseline variable	HR	95% CI
<i><u>Baseline variables with $P < 0.001$</u></i>		
Reliever use		
During the day	1.08	1.06–1.10
Reliever use during the night	1.11	1.06–1.15
No. of inhalations per day	1.06	1.05–1.07
Lung function parameters		
Pre-bronchodilator FEV ₁ /FVC ratio (per 10% increase), %	0.80	0.76–0.85
Pre-bronchodilator FEV ₁ (per 10% increase in % predicted)	0.80	0.75–0.84
Post-bronchodilator FEV ₁ (per 10% increase in % predicted)	0.83	0.79–0.87
FEV ₁ reversibility (per 10% increase)	0.72	0.60–0.85
Morning PEF (10% predicted) ^a	0.86	0.82–0.90
Evening PEF (10% predicted) ^a	0.87	0.84–0.91
SGRQ scores (per 10-point increase)		
Total score	1.10	1.06–1.14
Activity score	1.11	1.07–1.15
Impact score	1.06	1.03–1.09
Symptom score	1.06	1.03–1.10
Number of exacerbations in the previous year		
2 vs 1	1.43	1.25–1.65
3 vs 1	1.71	1.40–2.09
4 vs 1	1.76	1.34–2.31
> 4 vs 1	2.22	1.67–2.96
Number of COPD maintenance medications at study entry ^a		
1 vs 0	1.15	0.96–1.39
2 vs 0	1.54	1.31–1.82
3 vs 0	1.94	1.62–2.32
BCSS score (0–4)	1.29	1.18–1.40
MMRC scale score		
3 vs 2	0.33	0.08–1.34
4 vs 2	0.36	0.09–1.42
5 vs 2	0.48	0.12–1.91
Unknown vs 2	0.55	0.13–2.26
Pulse (per 10-bmp increase)	1.12	1.06–1.18
Sex (female vs male)	1.25	1.11–1.41
<i><u>Baseline variables with $0.001 < P < 0.01$</u></i>		
Depression or anxiety (presence vs absence)	1.24	1.07–1.44
<i><u>Baseline variables with $0.01 < P < 0.05$</u></i>		
Smoking history (per increase of 10 pack-years)	1.03	1.01–1.05
Gastroesophageal reflux disease (presence vs	1.22	1.04–1.44

absence)		
Cardiac-related comorbidity (presence vs absence)	1.19	1.02–1.39
BMI (per 1-kg/m ² increase)	0.99	0.98–1.00
Total symptom score (0–4)	1.03	1.00–1.06
<i><u>Baseline variables with $P \geq 0.05$</u></i>		
No. of comorbidities		
1 vs none	1.12	0.97–1.29
2 vs none	1.21	1.02–1.43
>2 vs none	1.28	1.03–1.60
Smoking status (current vs ex-smoker)	0.89	0.79–1.01
PEF variability	1.36	0.92–2.01
Age (per 10-year increase)	1.05	0.98–1.12
Diastolic BP (mm Hg)	1.00	0.99–1.00
Sleep symptom score (0–4)	1.04	0.97–1.11
Comedication with ACEI or angiotensin II antagonist (yes vs no)	0.93	0.81–1.07
Time since first COPD symptoms (per 10-year increase)	1.04	0.96–1.13
Diabetes (presence vs absence)	1.07	0.88–1.31
Comedication with statin (yes vs no)	1.05	0.89–1.23
Presence of hypertension (yes vs no)	0.98	0.87–1.10
Sputum symptom score (0–4)	1.01	0.94–1.08
Cough symptom score (0–4)	1.00	0.93–1.07
Systolic BP (mm Hg)	1.00	1.00–1.00

Notes: ^aNumber of COPD maintenance medications at study entry: 0 = no maintenance treatment with LA (long-acting β_2 -agonists, long-acting antimuscarinics, and theophylline), ICS, or other daily treatments (ie, short-acting [β_2 -agonist or antimuscarinic] bronchodilators only), 1 = one maintenance medication, 2 = two maintenance medications, 3 = three or more maintenance medications. Data from.^{15–17}

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; BCSS, Breathlessness, Cough, and Sputum Scale; CI, confidence interval; HR, hazard ratio; ICS, inhaled corticosteroids; LA, long-acting bronchodilators; MMRC, Modified Medical Research Council; SGRQ, St George's Respiratory Questionnaire; vs, versus.

Table 2 Backwards selection model by Cox regression analysis of predictors for severe COPD exacerbations for all patients,¹⁵⁻¹⁷ replacing the pre-bronchodilator FEV₁/FVC ratio with post-bronchodilator FEV₁^a

Baseline variables	HR	95% CI	Overall P-value
Number of COPD maintenance medications at study entry ^b			
3 vs 1-2	1.43	1.23-1.67	< 0.001
4 vs 1-2	1.82	1.52-2.17	
Reliever use, no. of inhalations per day			
5-10 vs 5	1.33	0.97-1.38	< 0.001
≥10 vs 5	1.77	1.42-2.14	
Exacerbations during the previous year			
2 vs 1	1.44	1.24-1.68	< 0.001
3-4 vs 1	1.67	1.38-2.02	
>4 vs 1	2.04	1.41-2.97	
Post-bronchodilator FEV ₁ , % predicted			
30-49% vs ≥50%	1.16	0.97-1.38	< 0.001
<30% vs ≥50%	1.75	1.42-2.14	
Sex, female vs male	1.30	1.13-1.50	< 0.001

Notes: ^aBackward selection starting with all predictors and recursively removing those with $P < 0.001$. ^bNumber of COPD maintenance medications at study entry: 0 = no maintenance treatment with LA (long-acting β_2 -agonists, long-acting antimuscarinics, and theophylline), ICS, or other daily treatments (ie, short-acting [β_2 -agonist or antimuscarinic] bronchodilators only), 1 = one maintenance medication, 2 = two maintenance medications, 3 = three or more maintenance medications.

Abbreviations: CI, confidence interval; HR, hazard ratio; ICS, inhaled corticosteroid; LA, long-acting bronchodilator; vs, versus.

Table 3 Risk score formula for COPD exacerbation in the next 6 months, replacing the pre-bronchodilator FEV₁/FVC ratio with post-bronchodilator FEV₁

Baseline variable	Score
Sex	
Male	–
Female	10
Number of COPD maintenance medications ^a	
0–1	–
2	13
3	22
Number of exacerbations in previous year	
1	–
2	13
3–4	19
>4	26
Post-bronchodilator FEV ₁ , % predicted	
≥50%	–
30–49%	6
<30%	21
Reliever use, no. of inhalations/day	
<5	–
5–10	10
<u>≥10</u>	<u>21</u>

Notes: ^aNumber of COPD maintenance medications at study entry: 0 = no maintenance treatment with LA (long-acting β_2 -agonists, long-acting antimuscarinics, and theophylline), ICS, or other daily treatments (ie, short-acting [β_2 -agonist or antimuscarinic] bronchodilators only), 1 = one maintenance medication, 2 = two maintenance medications, 3 = three or more maintenance medications.

Abbreviations: ICS, inhaled corticosteroid; LA, long-acting bronchodilator.

Supplementary figures

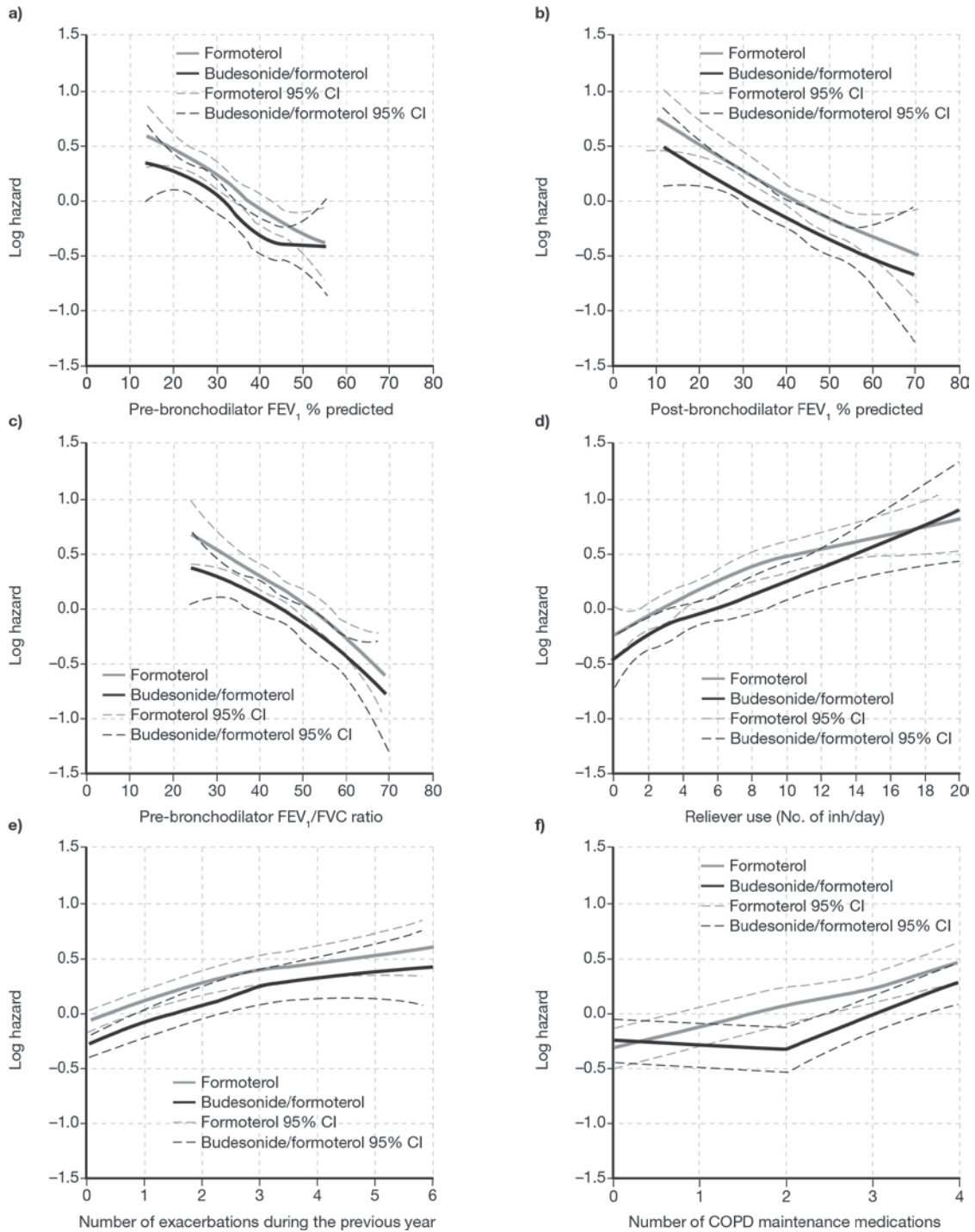


Figure 1 Baseline continuous variables (a) pre-bronchodilator FEV₁, (b) post-bronchodilator FEV₁, (c) pre-bronchodilator FEV₁/FVC ratio, (d) reliever use, (e) number of exacerbations in the previous year and (f) number of COPD maintenance medications as spline predictors for log

odds of a COPD exacerbation. Number of COPD maintenance medications at study entry: 0 = no maintenance treatment with LA (long-acting β_2 -agonists, long-acting antimuscarinics, and theophylline), ICS, or other daily treatments (i.e., short-acting [β_2 -agonist or antimuscarinic] bronchodilators only), 1 = one maintenance medication, 2 = two maintenance medications, 3 = three or more maintenance medications.

Abbreviations: CI, confidence interval; ICS, inhaled corticosteroid; LA, long-acting bronchodilator.

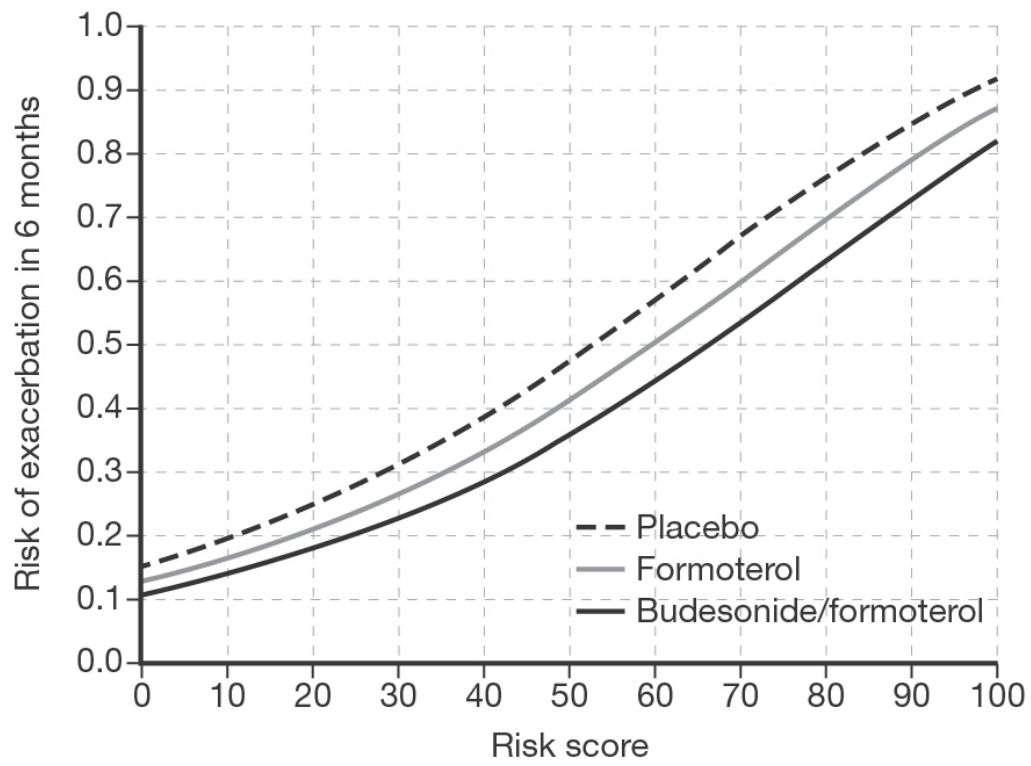


Figure 2 Risk of exacerbation of chronic obstructive pulmonary disease in 6 months based on baseline risk score for each treatment group with post-bronchodilator forced expiratory volume in 1 second.