

## Developing and Validating Prediction Models for Severe Exacerbations and Readmissions in Patients Hospitalized for COPD Exacerbation (SERCO) in China: a Prospective Observational Study

### Supplemental table S1. Geographic regions division of provinces

Region	Province
Northern	Beijing, Tianjin, Hebei, Shanxi, and Inner Mongolia.
Northeast	Heilongjiang, Jilin, and Liaoning.
Eastern	Shandong, Jiangsu, Shanghai, Zhejiang, Fujian, Anhui, and Jiangxi.
Southern	Guangdong, Guangxi, and Hainan.
Southwest	Sichuan, Yunnan, Guizhou, Chongqing, and Tibet.
Northwest	Xiangjiang, Gansu, Qinghai, Shannxi, and Ningxia.
Central	Henan, Hunan, and Hubei.

### Supplemental table S2. Candidate predictor parameters for models

- Sociodemographic characteristics
  - ✓ Age
  - ✓ Gender
  - ✓ Education
- COPD-related disease history
  - ✓ Smoking status
  - ✓ Ever diagnosed for COPD
  - ✓ Frequency of hospitalizations for AECOPD in the past 12 months
  - ✓ Ever regularly treated with long-acting bronchodilators
  - ✓ Ever regularly treated with inhaled corticosteroids
  - ✓ Home oxygen therapy
  - ✓ Pulmonary rehabilitation
- Comorbidity & Complication
  - ✓ Respiratory failure
  - ✓ Chronic cor pulmonale
  - ✓ Pulmonary arterial hypertension
  - ✓ Pneumonia
  - ✓ Lung cancer
  - ✓ Asthma
  - ✓ Coronary heart disease
  - ✓ Hypertension
  - ✓ Diabetes
- Treatment during hospitalization
  - ✓ Systemic corticosteroids
  - ✓ Antibiotic
  - ✓ Inhaled short-acting bronchodilators
  - ✓ Methylxanthine

- ✓ Expectorant
- ✓ Oxygen therapy
- clinical characteristics
  - ✓ Postbronchodilator FEV<sub>1</sub>%pred
  - ✓ CAT score at admission
  - ✓ mMRC at admission
  - ✓ BMI

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COPD=chronic obstructive pulmonary disease. AECOPD=acute exacerbations of chronic obstructive pulmonary disease. FEV<sub>1</sub>%pred=postbronchodilator percent predicted forced expiratory volume in 1 second. CAT= COPD assessment test. mMRC=modified British medical research council. BMI=body mass index.

**Supplemental table S3. P values of the interaction among the potential predictors**

	Age	Gender	Education	Smoking	Ever diagnosed for COPD	Frequency of hospitalizations for AECOPD in the past 12 months	Ever regularly treated with long-acting bronchodilators	Ever regularly treated with inhaled corticosteroids	Home oxygen therapy
Gender	0.374								
Education	0.314	0.168							
Smoking	0.398	0.055	0.136						
Ever diagnosed for COPD	0.789	0.654	0.195	0.164					
Frequency of hospitalizations for AECOPD in the past 12 months	0.518	0.081	0.653	0.062	0.107				
Ever regularly treated with long-acting bronchodilators	0.817	0.505	0.244	0.857	0.625	0.420			
Ever regularly treated with inhaled corticosteroids	0.604	0.061	0.115	0.526	0.957	0.638	0.667		
Home oxygen therapy	0.242	0.418	0.285	0.153	0.590	0.162	0.149	0.364	
Pulmonary rehabilitation	0.585	0.378	0.369	0.487	0.870	0.764	0.276	0.620	0.409
Respiratory failure	0.835	0.492	0.683	0.450	0.150	0.587	0.396	0.472	0.400
Chronic cor pulmonale	0.179	0.157	0.676	0.351	0.034	0.425	0.108	0.735	0.001
Pulmonary arterial hypertension	0.821	0.963	0.541	0.366	0.137	0.354	0.513	0.926	0.123
Pneumonia	0.509	0.699	0.967	0.681	0.884	0.583	0.502	0.281	0.611
Lung cancer	0.147	0.625	0.573	0.982	0.919	0.624	0.404	0.970	0.369
Asthma	0.401	0.709	0.289	0.268	0.907	0.600	0.017	0.336	0.347
Coronary heart disease	0.791	0.650	0.637	0.563	0.204	0.370	0.110	0.820	0.835
Hypertension	0.728	0.751	0.392	0.723	0.915	0.390	0.349	0.942	0.890
Diabetes	0.335	0.826	0.373	0.752	0.086	0.199	0.682	0.147	0.086

Systemic corticosteroids treatment during hospitalization	0.074	0.148	0.544	0.824	0.045	0.295	0.489	0.502	0.027
Antibiotic treatment during hospitalization	0.705	0.399	0.992	0.274	0.116	0.053	0.073	0.835	0.064
Inhaled short-acting bronchodilators treatment during hospitalization	0.611	0.450	0.492	0.626	0.253	0.778	0.799	0.483	0.064
Methylxanthine treatment during hospitalization	0.522	0.680	0.538	0.764	0.982	0.766	0.296	0.867	0.133
Expectorant treatment during hospitalization	0.400	0.364	0.224	0.429	0.491	0.543	0.503	0.993	0.874
Oxygen therapy	0.366	0.006	0.881	0.944	0.416	0.148	0.931	0.068	0.083
Postbronchodilator FEV <sub>1</sub> %pred	0.347	0.413	0.468	0.920	0.765	0.219	0.525	0.317	0.468
CAT score at admission	0.616	0.817	0.962	0.901	0.792	0.495	0.826	0.274	0.051
mMRC at admission	0.554	0.381	0.999	0.516	0.982	0.205	0.686	0.755	0.002
BMI	0.852	0.335	0.289	0.499	0.685	0.089	0.194	0.503	0.665

**Supplemental table S3. P values of the interaction among the potential predictors (Continued)**

	Pulmonary rehabilitation	Respiratory failure	Chronic cor pulmonale	Pulmonary arterial hypertension	Pneumonia	Lung cancer	Asthma	Coronary heart disease	Hypertension	Diabetes
Respiratory failure	0.743									
Chronic cor pulmonale	0.236	0.997								
Pulmonary arterial hypertension	0.038	0.660	0.503							
Pneumonia	0.076	0.612	0.782	0.879						
Lung cancer	0.598	0.897	0.763	0.764	0.314					
Asthma	0.819	0.675	0.633	0.581	0.852	0.966				
Coronary heart disease	0.957	0.686	0.225	0.460	0.503	0.327	0.974			
Hypertension	0.710	0.911	0.283	0.162	0.312	0.963	0.022	0.307		

Diabetes	0.348	0.044	0.149	0.148	0.641	0.088	0.194	0.501	0.299	
Systemic corticosteroids treatment during hospitalization	0.112	0.284	0.659	0.269	0.964	0.545	0.070	0.515	0.987	0.932
Antibiotic treatment during hospitalization	0.394	0.256	0.508	0.567	0.043	0.958	0.417	0.689	0.634	0.820
Inhaled short-acting bronchodilators treatment during hospitalization	0.709	0.123	0.052	0.711	0.105	0.601	0.082	0.268	0.461	0.033
Methylxanthine treatment during hospitalization	0.686	0.764	0.660	0.981	0.454	0.960	0.371	0.182	0.784	0.242
Expectorant treatment during hospitalization	0.274	0.110	0.011	0.113	0.906	0.958	0.114	0.543	0.832	0.980
Oxygen therapy	0.050	0.001	0.088	0.320	0.685	0.966	0.170	0.479	0.305	0.643
Postbronchodilator FEV <sub>1</sub> %pred	0.708	0.093	0.073	0.138	0.165	0.458	0.289	0.558	0.869	0.078
CAT score at admission	0.098	0.401	0.257	0.892	0.625	0.382	0.246	0.635	0.137	0.071
mMRC at admission	0.008	0.729	0.750	0.026	0.819	0.766	0.822	0.362	0.948	0.461
BMI	0.215	0.933	0.734	0.450	0.703	0.275	0.016	0.053	0.524	0.909

Supplemental table S3. P values of the interaction among the potential predictors (Continued)

	Systemic corticosteroids treatment during hospitalization	Antibiotic treatment during hospitalization	Inhaled short-acting bronchodilators treatment during hospitalization	Methylxanthine treatment during hospitalization	Expectorant treatment during hospitalization	Oxygen therapy	FEV <sub>1</sub> %pred	CAT score at admission	mMRC at admission
Antibiotic treatment during hospitalization	0.393								
Inhaled short-acting bronchodilators treatment during hospitalization	0.182	0.151							
Methylxanthine treatment during hospitalization	0.909	0.655	0.672						
Expectorant treatment during hospitalization	0.113	0.336	0.005	0.050					

Oxygen therapy	0.605	0.053	0.441	0.721	0.719				
Postbronchodilator FEV <sub>1</sub> %pred	0.330	0.063	0.308	0.072	0.599	0.100			
CAT score at admission	0.784	0.428	0.232	0.338	0.810	0.651	0.386		
mMRC at admission	0.382	0.952	0.846	0.676	0.215	0.112	0.704	0.205	
BMI	0.133	0.411	0.104	0.421	0.611	0.861	0.087	0.237	0.489

COPD= chronic obstructive pulmonary disease. AECOPD=acute exacerbations of chronic obstructive pulmonary disease. FEV<sub>1</sub>%pred= percent predicted forced expiratory volume in 1 second. CAT= COPD assessment test. mMRC= modified British medical research council. BMI= body mass index.

**Supplemental table S4. Coefficients and P values of candidate predictor in the full model**

Candidate predictor parameters	Coefficient	P-value
Age	-0.002	0.837
Gender	0.074	0.829
Education	0.528	0.001
Smoking status	-0.333	0.080
Ever diagnosed for COPD	0.846	0.002
Frequency of hospitalizations for AECOPD in the past 12 months	0.182	0.002
Ever regularly treated with long-acting bronchodilators	0.418	0.024
Ever regularly treated with inhaled corticosteroids	0.290	0.343
Home oxygen therapy	0.584	0.398
Pulmonary rehabilitation	-0.278	0.756
Respiratory failure	0.379	0.282
Chronic cor pulmonale	1.081	0.009
Pulmonary arterial hypertension	-14.141	0.973
Pneumonia	-0.278	0.698
Lung cancer	-0.057	0.924
Asthma	-0.900	0.514
Coronary heart disease	0.227	0.204
Hypertension	-0.126	0.475
Diabetes	-0.755	0.163
Systemic corticosteroids treatment	0.567	0.089
Antibiotic treatment	0.120	0.770
Inhaled short-acting bronchodilators treatment	-0.340	0.093
Methylxanthine treatment	0.919	<0.001
Expectorant treatment	0.689	0.032
Oxygen therapy	0.146	0.527
GOLD 2	1.133	0.017
GOLD 3	0.942	0.046
GOLD 4	1.136	0.019
CAT score at admission	-0.018	0.132
mMRC at admission	0.064	0.540
BMI	-0.054	0.022
Ever diagnosed for COPD * Chronic cor pulmonale	-0.552	0.195
Home oxygen therapy * Chronic cor pulmonale	-0.351	0.393
Pulmonary rehabilitation * Pulmonary arterial hypertension	-0.781	0.473
Ever regularly treated with long-acting bronchodilators * Asthma	0.478	0.300
Asthma * Hypertension	0.810	0.078
Respiratory failure * Diabetes	0.121	0.826
Ever diagnosed for COPD * Systemic corticosteroids treatment	-0.628	0.100
Home oxygen therapy * Systemic corticosteroids treatment	-0.486	0.232
Pneumonia * Antibiotic treatment	0.273	0.710
Diabetes * Inhaled short-acting bronchodilators treatment	1.345	0.020

Chronic cor pulmonale * Expectorant treatment	0.789	0.020
Inhaled short-acting bronchodilators treatment * Expectorant treatment	-0.629	0.069
Gender * Home oxygen therapy	-0.384	0.331
Pulmonary rehabilitation * Home oxygen therapy	0.998	0.216
Respiratory failure * Home oxygen therapy	-0.909	0.020
Home oxygen therapy * mMRC at admission	0.513	0.305
Pulmonary rehabilitation * mMRC at admission	-0.372	0.106
Pulmonary arterial hypertension * mMRC at admission	12.828	0.381
BMI * Asthma	0.024	0.682

COPD=chronic obstructive pulmonary disease. AECOPD=acute exacerbations of chronic obstructive pulmonary disease. GOLD=global initiative for chronic obstructive lung disease. CAT= COPD assessment test. mMRC=modified British medical research council. BMI=body mass index.

**Supplemental table S5. Cutoff of predicted risk, sensitivity, specificity, positive predictive value, and negative predictive value of SERCO model**

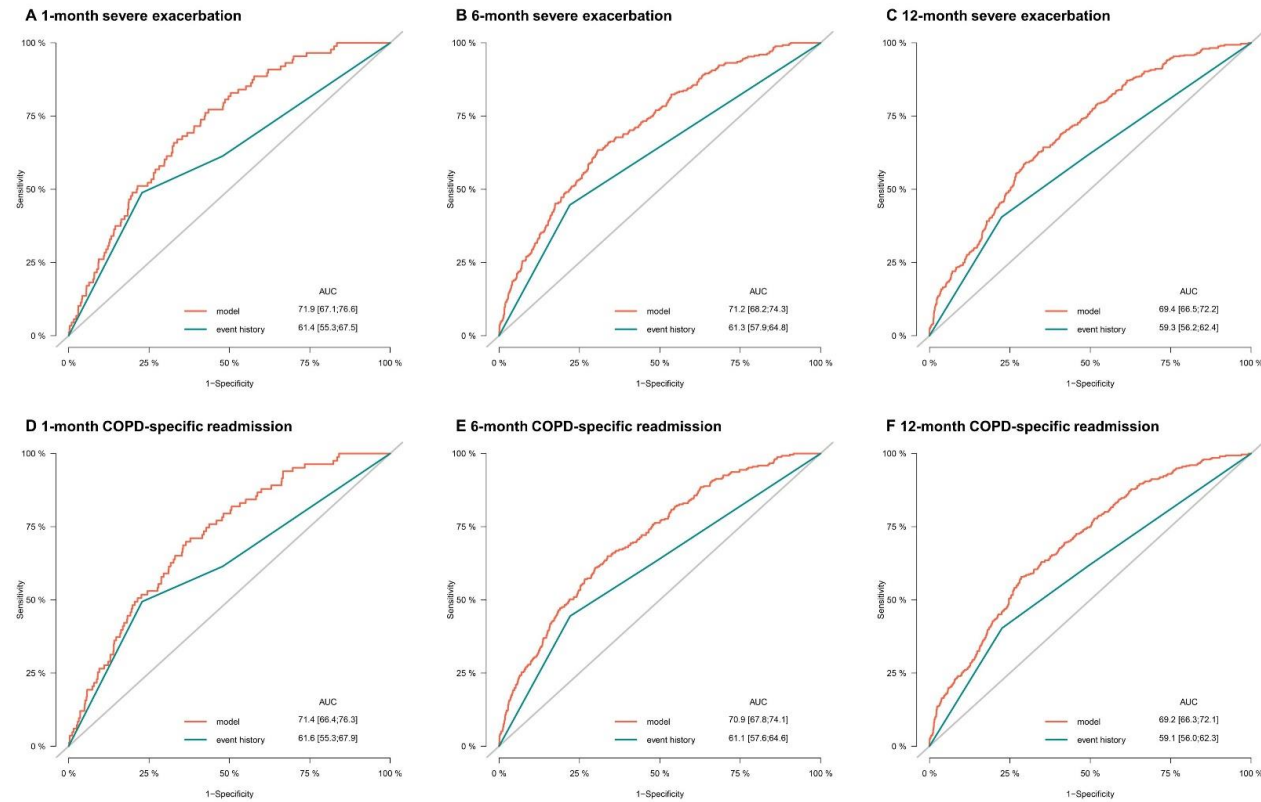
	Cutoff (%)	Sensitivity	Specificity	Positive predictive value	Negative predictive value
<b>Severe exacerbation</b>					
1-month	1.8	0.767	0.565	0.039	0.990
6-month	9.2	0.630	0.685	0.131	0.961
12-month	16.0	0.600	0.693	0.171	0.942
<b>COPD-specific readmission</b>					
1-month	1.8	0.694	0.635	0.039	0.990
6-month	8.0	0.645	0.652	0.119	0.961
12-month	15.9	0.586	0.706	0.171	0.943

COPD=chronic obstructive pulmonary disease.



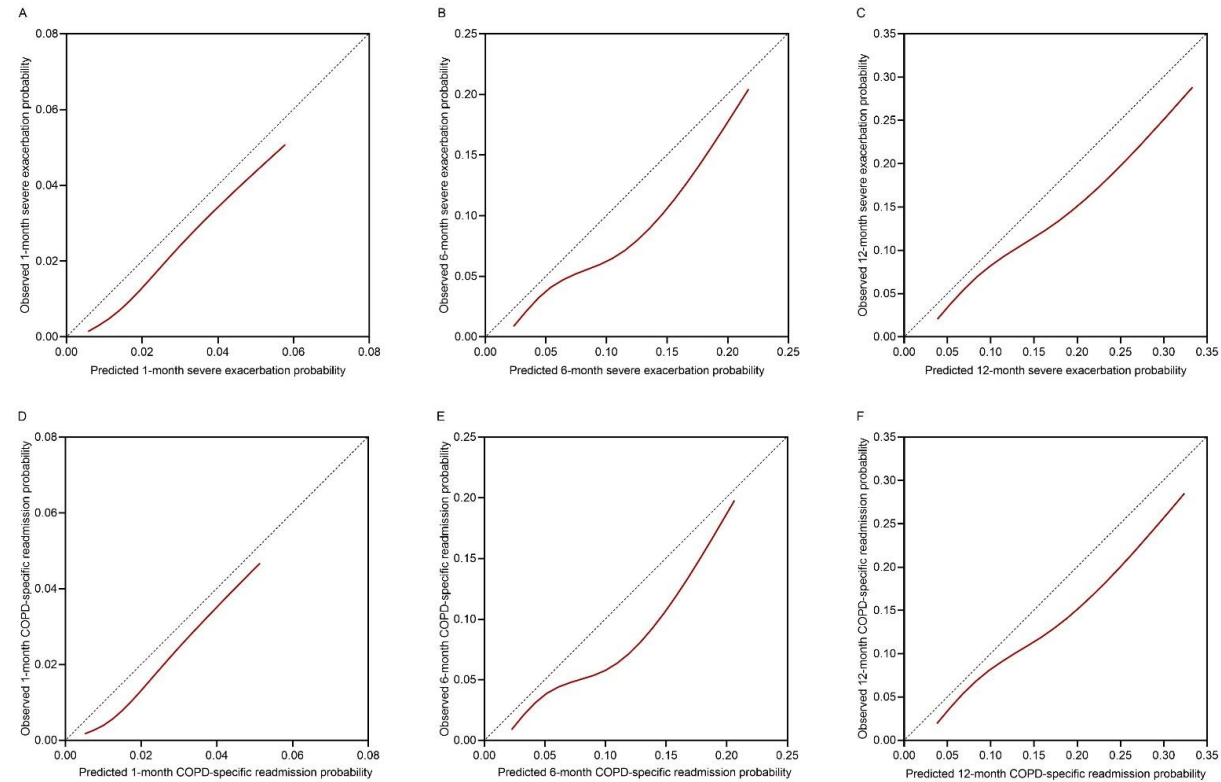
**Table S6. Slope and intercept of the calibration in external validation cohort before and after adjustment**

	Before slope and intercept adjustment		After slope and intercept adjustment	
	Slope	Intercept	Slope	Intercept
<b>Severe exacerbation</b>				
1-month	0.526 (-0.058 to 1.110)	0.011 (-0.011 to 0.033)	0.676 (-0.116 to 1.468)	0.010 (-0.013 to 0.033)
6-month	0.359 (-0.068 to 0.787)	0.045 (-0.015 to 0.105)	0.429 (-0.058 to 0.915)	0.045 (-0.012 to 0.102)
12-month	0.309 (-0.112 to 0.736)	0.069 (-0.023 to 0.161)	0.427 (-0.123 to 0.977)	0.056 (-0.044 to 0.156)
<b>COPD-specific readmission</b>				
1-month	0.541 (-0.148 to 1.230)	0.012 (-0.012 to 0.035)	0.675 (-0.134 to 1.484)	0.012 (-0.010 to 0.033)
6-month	0.345 (-0.138 to 0.829)	0.047 (-0.018 to 0.112)	0.385 (-0.140 to 0.909)	0.050 (-0.012 to 0.110)
12-month	0.328 (-0.073 to 0.728)	0.067 (-0.017 to 0.151)	0.437 (-0.063 to 0.938)	0.056 (-0.034 to 0.148)



### Supplemental figure S1. Discriminative ability of prediction model compared with event history

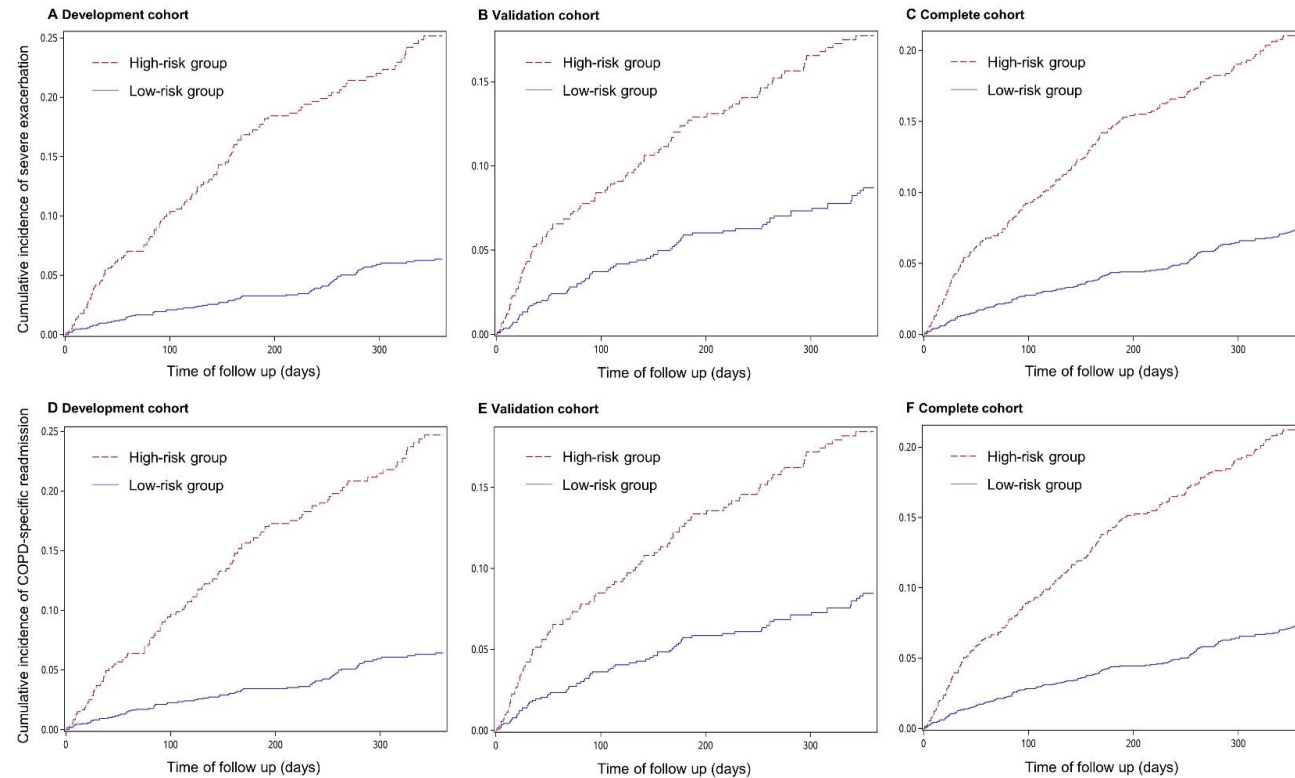
Receiver operating characteristic (ROC) curves and area-under-the-curve (AUC) of the prediction models for predicting the probability of severe exacerbation at 1 month (A), 6 months (B), and 12 months (C), and COPD-specific readmission (D, E, and F) compared with event history. Event history was the history of severe exacerbations in the past 12 months. COPD=chronic obstructive pulmonary disease.



**Supplemental figure S2. Calibration plots of observed and predicted probability in the internal validation cohort before slope and intercept adjustment**

Calibration plot comparing per quintile average predicted and observed probability of severe exacerbation at 1 month (A), 6 months (B), and 12 months (C), and COPD-specific readmission (D, E, and F). Perfect agreement is shown by the black dashed line. Error bars represent 95% CI.

COPD=chronic obstructive pulmonary disease. CI= confidential interval.



### Supplemental figure S3. Cumulative incidence by risk groups

Cumulative incidence curves for severe exacerbation in development cohort (A), validation cohort (B), and complete set (C), and COPD-specific readmission (D, E, and F) by risk groups. Participants were stratified into high-risk and low-risk groups by the model-predicted probability of 12-month severe exacerbation and COPD-specific readmission with the cutoff point at 16%.

COPD=chronic obstructive pulmonary disease.