

Blood Eosinophil Count Predicts Treatment Failure and Hospital

Readmission for COPD

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Table S1. Additional Baseline Patient Characteristics

Variable	Cohort 1 (N=6,416)	Cohort 2 (N=10,245)
Charlson comorbidity index		
≤1	4,023 (62.7)	6,199 (60.5)
2–4	1,344 (20.9)	1,730 (16.9)
5+	1,049 (16.3)	2,316 (22.6)
Maintenance therapy		
None	755 (11.8)	1,253 (12.2)
Short-acting BD only	592 (9.2)	687 (6.7)
Long-acting BD only	680 (10.6)	1,232 (12.0)
ICS+LABA	1,500 (23.4)	2,674 (26.1)
Triple therapy	2,889 (45.0)	4,399 (42.9)
Daily ICS dosage, median (IQR) ^a	361.7 (82.0–721.3)	393.5 (92.9–739.8)
≥1 SABA inhaler prescribed	4,687 (73.1)	7,594 (74.1)
≥1 SAMA inhaler prescribed	1,066 (16.6)	3,563 (34.8)
Cumulative average daily OCS dosage, median (IQR) ^b	1.5 (0.8–2.9)	0.4 (0.0–1.4)
Number of COPD exacerbations ^c		
0	0 (0)	0 (0)
1	520 (8.1)	2,348 (22.9)
2	2,331 (36.3)	2,325 (22.7)
3	1,155 (18.0)	1,831 (17.9)
≥4	2,410 (37.6)	3,741 (36.5)
Number of short-term OCS courses ^c		
0	0 (0)	4,796 (46.8)
1	1,946 (30.3)	2,332 (22.8)
2	1,225 (19.1)	1,215 (11.9)
3	945 (14.7)	753 (7.3)
≥4	2,300 (35.8)	1,149 (11.2)
mMRC dyspnoea score		
n	5,460	8,789
0	409 (7.5)	314 (3.6)
1	2,256 (41.3)	3,883 (44.2)
2	1,527 (28.0)	1,976 (22.5)
3	1,030 (18.9)	1,823 (20.7)
4	238 (4.4)	793 (9.0)

BD, bronchodilator; COPD, chronic obstructive pulmonary disease; ICS, inhaled

corticosteroids; IQR, interquartile range; LABA, long-acting β_2 -agonists; mMRC, modified

Medical Research Council; OCS, oral corticosteroids; SABA, short-acting β_2 -agonists;

SAMA, short-acting muscarinic antagonists.

Data expressed as n (%) unless otherwise noted.

^aICS dosage expressed as fluticasone propionate or equivalent (μg).

^bOCS dosage expressed as prednisolone or equivalent (mg).

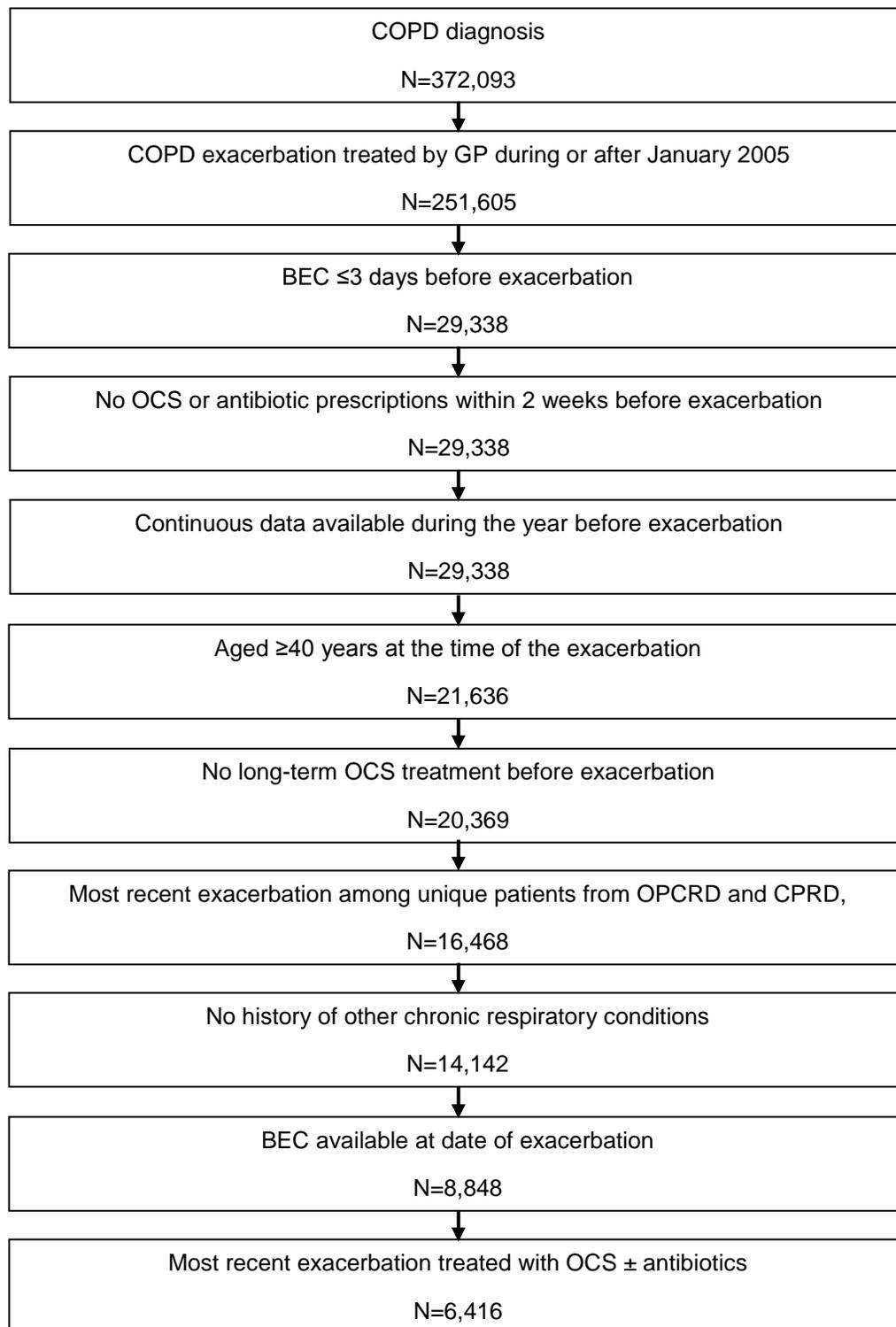
^cIncluding exacerbation on index date.

Table S2. Baseline Patient Maintenance Therapy by Blood Eosinophil Count Category

		Blood eosinophil category (cells/μL)							
		<50	50–<150	150–<250	250–<350	350–<450	450–<550	550–<650	\geq650
Cohort 1		(n=275)	(n=2048)	(n=1768)	(n=1033)	(n=502)	(n=287)	(n=169)	(n=334)
Maintenance therapy	None	37 (13.5)	262 (12.8)	209 (11.8)	107 (10.4)	54 (10.8)	33 (11.5)	15 (8.9)	38 (11.4)
	Short-acting BD only	30 (10.9)	193 (9.4)	145 (8.2)	106 (10.3)	45 (9.0)	30 (10.5)	16 (9.5)	27 (8.1)
	Long-acting BD only	35 (12.7)	220 (10.7)	180 (10.2)	97 (9.4)	46 (9.2)	33 (11.5)	27 (16.0)	42 (12.6)
	ICS+LABA	58 (21.1)	451 (22.0)	440 (24.9)	240 (23.2)	118 (23.5)	69 (24.0)	37 (21.9)	87 (26.0)
	Triple therapy	115 (41.8)	922 (45.0)	794 (44.9)	483 (46.8)	239 (47.6)	122 (42.5)	74 (43.8)	140 (41.9)
ICS mean daily dosage	Median (IQR)	731.5 (114.8–1530.1)	786.9 (164.4–1528.8)	794.0 (246.6–1506.8)	746.9 (197.0–1479.5)	788.0 (163.9–1479.5)	731.5 (164.4–1315.1)	657.5 (164.4–1315.1)	739.7 (164.4–1475.4)
	Cohort 2		(n=734)	(n=3035)	(n=2794)	(n=1608)	(n=834)	(n=480)	(n=234)
Maintenance therapy	None	108 (14.7)	399 (13.1)	314 (11.2)	196 (12.2)	93 (11.2)	53 (11.0)	24 (10.3)	66 (12.5)
	Short-acting BD only	53 (7.2)	200 (6.6)	166 (5.9)	103 (6.4)	79 (9.5)	30 (6.3)	21 (9.0)	35 (6.7)
	Long-acting BD only	83 (11.3)	368 (12.1)	363 (13.0)	179 (11.1)	85 (10.2)	53 (11.0)	27 (11.5)	74 (14.1)
	ICS+LABA	200 (27.2)	778 (25.6)	696 (24.9)	447 (27.8)	209 (25.1)	126 (26.3)	61 (26.1)	157 (29.8)
	Triple therapy	290 (39.5)	1,290 (42.5)	1,255 (44.9)	683 (42.5)	368 (44.1)	218 (45.4)	101 (43.2)	194 (36.9)
ICS mean daily dosage	Median (IQR)	657.5 (54.8–1315.1)	723.3 (109.6–1479.5)	737.7 (164.4–1444.6)	710.4 (163.9–1315.1)	690.4 (164.4–1479.5)	657.5 (109.6–1315.1)	684.9 (137.0–1315.1)	657.5 (164.4–1479.5)

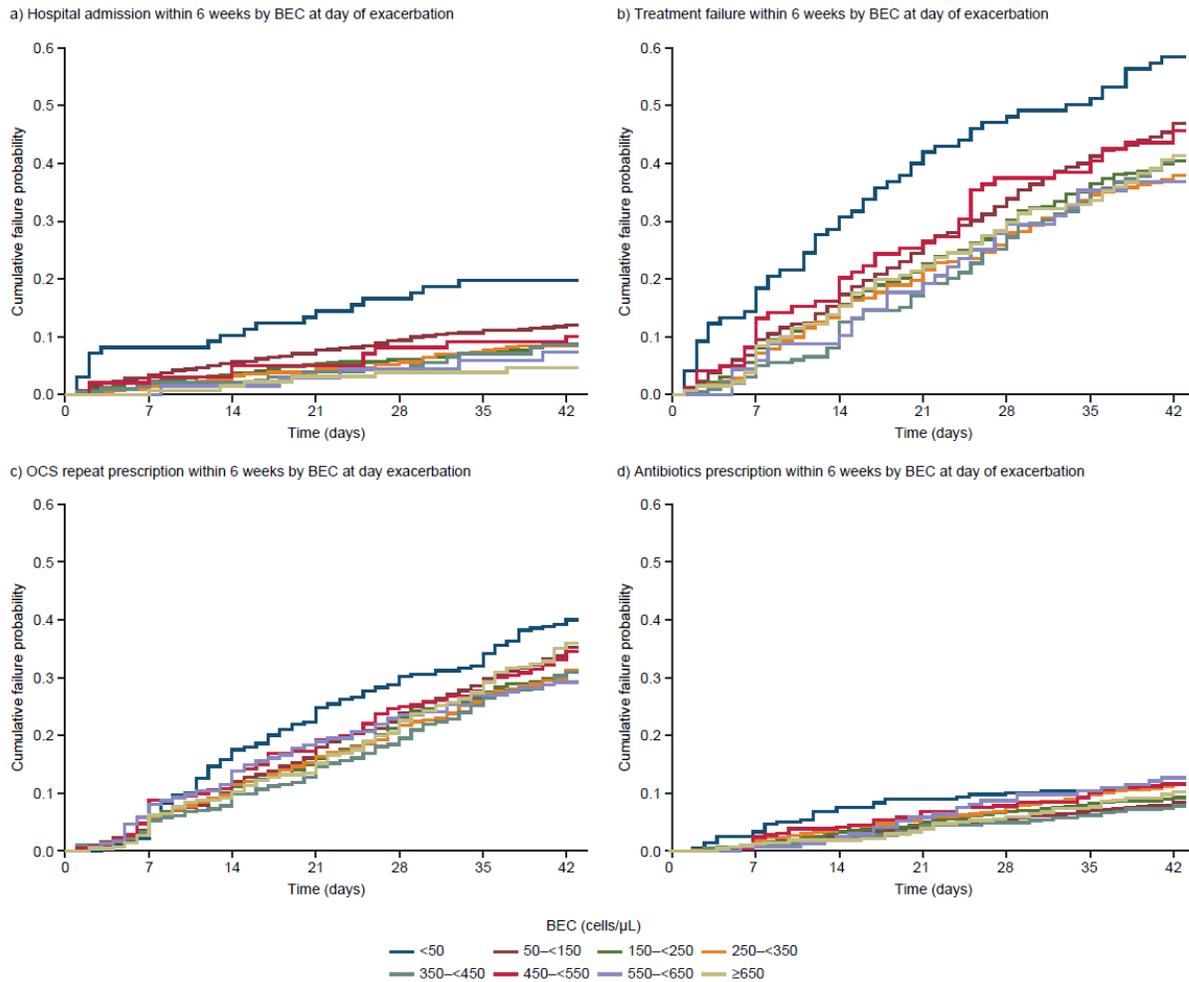
BD, bronchodilator; ICS, inhaled corticosteroids; IQR, interquartile range; LABA, long-acting β_2 -agonists.

Figure S1. Cohort 1 Patient Flow Diagram



BEC, blood eosinophil counts; CPRD, Clinical Practice Research Datalink; COPD, chronic obstructive pulmonary disease; GP, general practitioner; OCS, oral corticosteroids; OPCR, Optimum Patient Care Research Database.

Figure S2. Kaplan-Meier Curves for the Unadjusted Association Between Blood Eosinophil Counts Recorded on the Day of an OCS-Treated Exacerbation and Time to First Outcome Event Within 6 Weeks (Cohort 1)



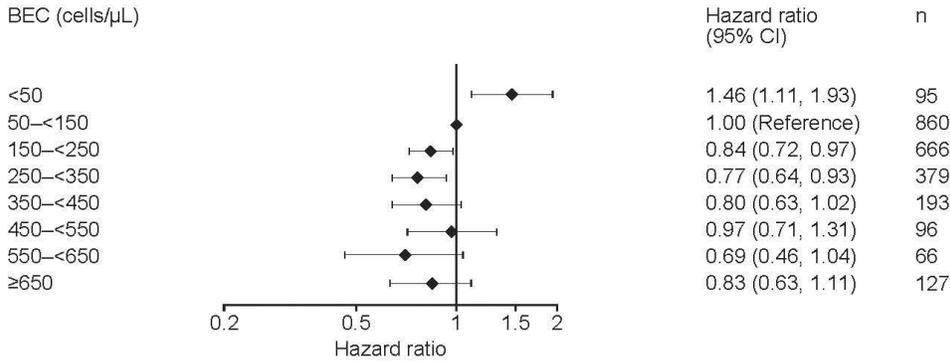
Panel a: Hospital admission. Panel b: Treatment failure. Panel c: OCS prescription.
 Panel d: Antibiotic prescription.

BEC, blood eosinophil counts; OCS, oral corticosteroids.

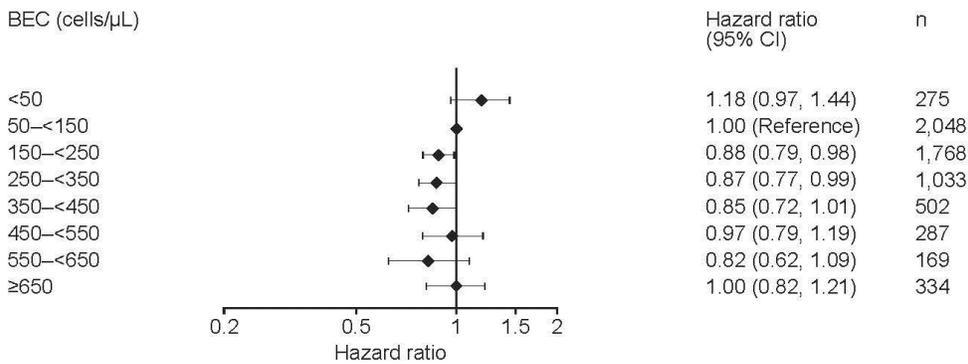
BEC are classified in incremental categories with 50–<150 cells/ μ L as the reference category.

Figure S3. Association Between Blood Eosinophil Counts Recorded on the Day of an OCS-Treated Exacerbation and Treatment Failure Within 6 Weeks (Cohort 1)

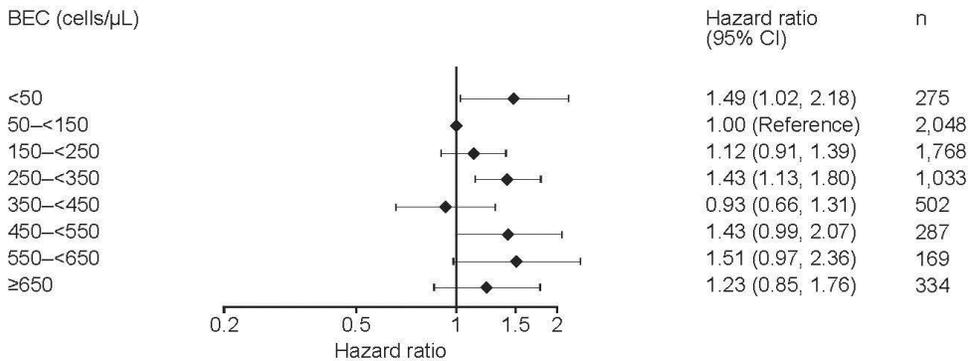
a) Treatment failure within 6 weeks by BEC at day of exacerbation



b) OCS repeat prescription within 6 weeks by BEC at day of exacerbation



c) Antibiotics prescription within 6 weeks by BEC at day of exacerbation

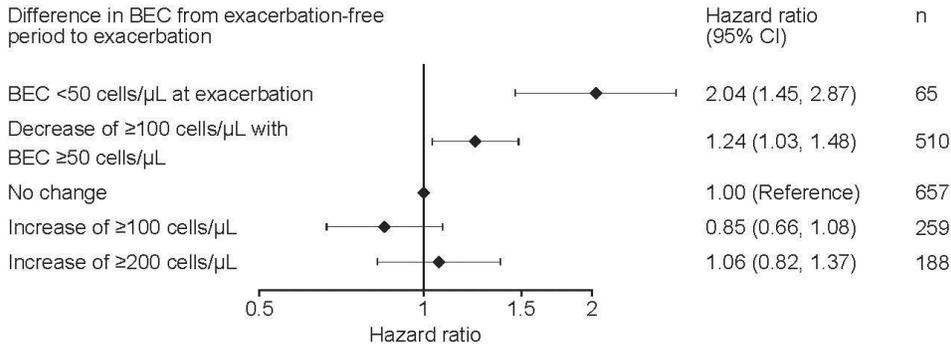


Panel a: Overall treatment failure (N=2,482). Panel b: Treatment failure defined as a repeat OCS prescription (N=6,416). Panel c: Treatment failure defined as an antibiotic prescription (N=6,416).

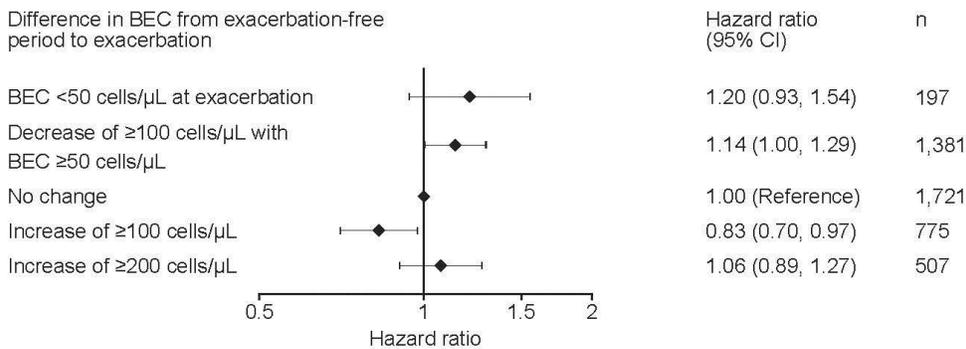
BEC, blood eosinophil counts; CI, confidence interval; OCS, oral corticosteroids.

Figure S4. Association Between Change in Blood Eosinophil Counts from an Exacerbation-Free Period to Index Exacerbation Date and Treatment Failure Within 6 Weeks (Cohort 1)

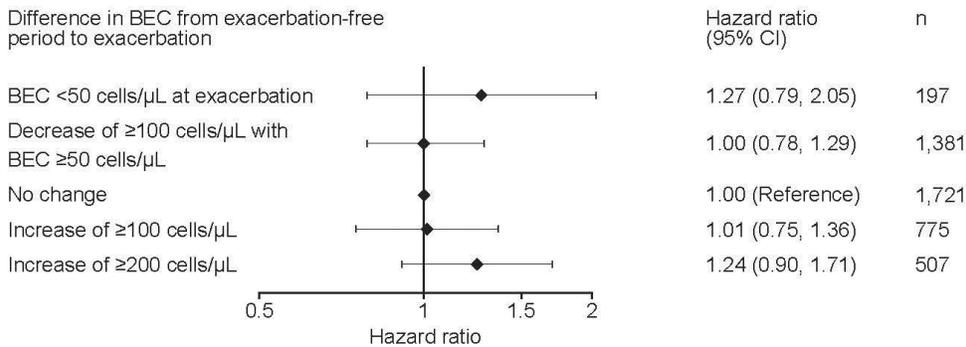
a) Treatment failure within 6 weeks by BEC at exacerbation vs. exacerbation-free period



b) OCS repeat prescription within 6 weeks by BEC at exacerbation vs. exacerbation-free period



c) Antibiotics prescription within 6 weeks by BEC at exacerbation vs. exacerbation-free period



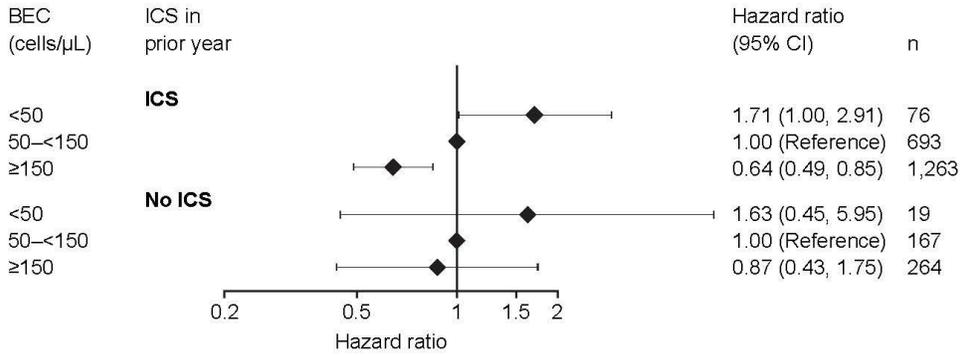
Panel a: Overall treatment failure. Panel b: Treatment failure defined as a repeat OCS prescription. Panel c: Treatment failure defined as an antibiotic prescription.

BEC, blood eosinophil counts; CI, confidence interval; OCS, oral corticosteroids.

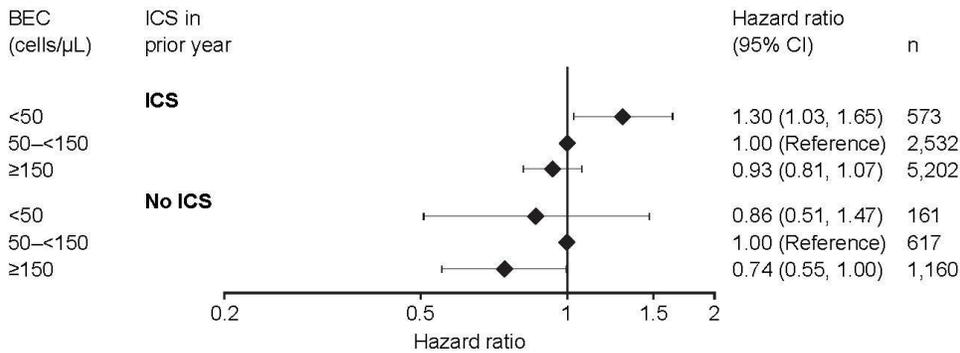
An exacerbation-free period is defined as at least 4 weeks before any COPD exacerbations.

Figure S5. Association Between Blood Eosinophil Counts and Hospital Admission Within 6 Weeks (Cohort 1) or Readmission Within 4 Weeks (Cohort 2) Stratified by ICS Treatment in the Prior Year

a) Hospital admission within 6 weeks by BEC at day of exacerbation



b) Hospital readmission within 4 weeks by BEC during exacerbation-free period in prior year

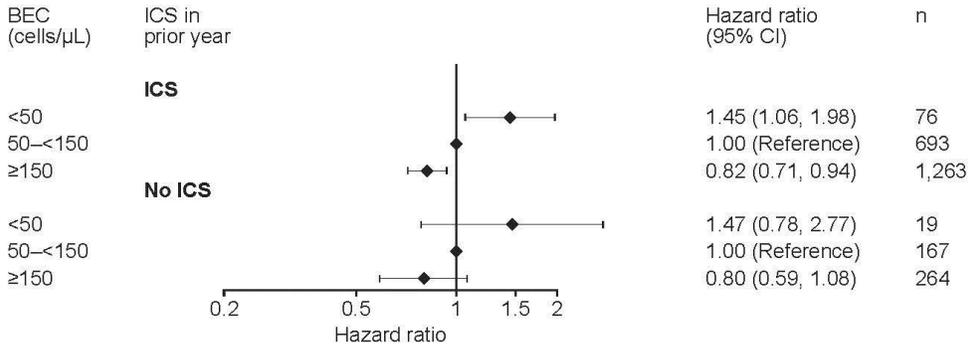


Panel a: Association between BEC recorded on the day of an exacerbation and hospital admission within 6 weeks for Cohort 1. Panel b: Association between BEC recorded during stable disease (no exacerbations within 4 weeks) and hospital readmission within 6 weeks for Cohort 2.

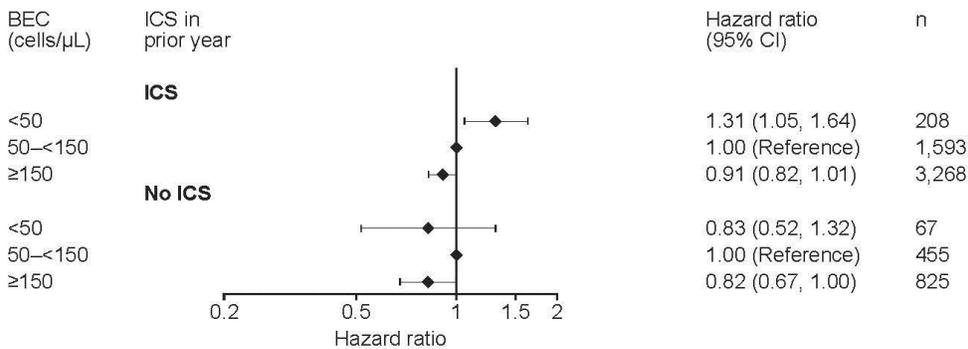
BEC, blood eosinophil counts; CI, confidence interval; ICS, inhaled corticosteroids.

Figure S6. Association Between Blood Eosinophil Counts and Treatment Failure Outcomes Within 6 Weeks, Stratified by ICS Treatment (Cohort 1)

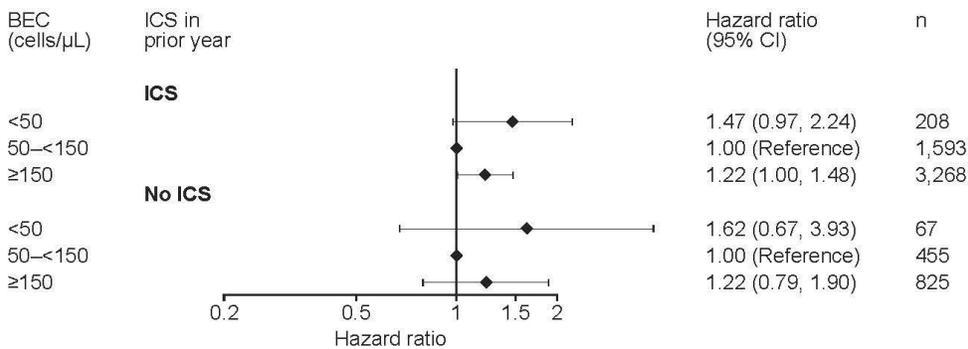
a) Treatment failure within 6 weeks by BEC at day of exacerbation



b) OCS repeat prescription within 6 weeks by BEC at day of exacerbation



c) Antibiotics prescription within 6 weeks by BEC at day of exacerbation

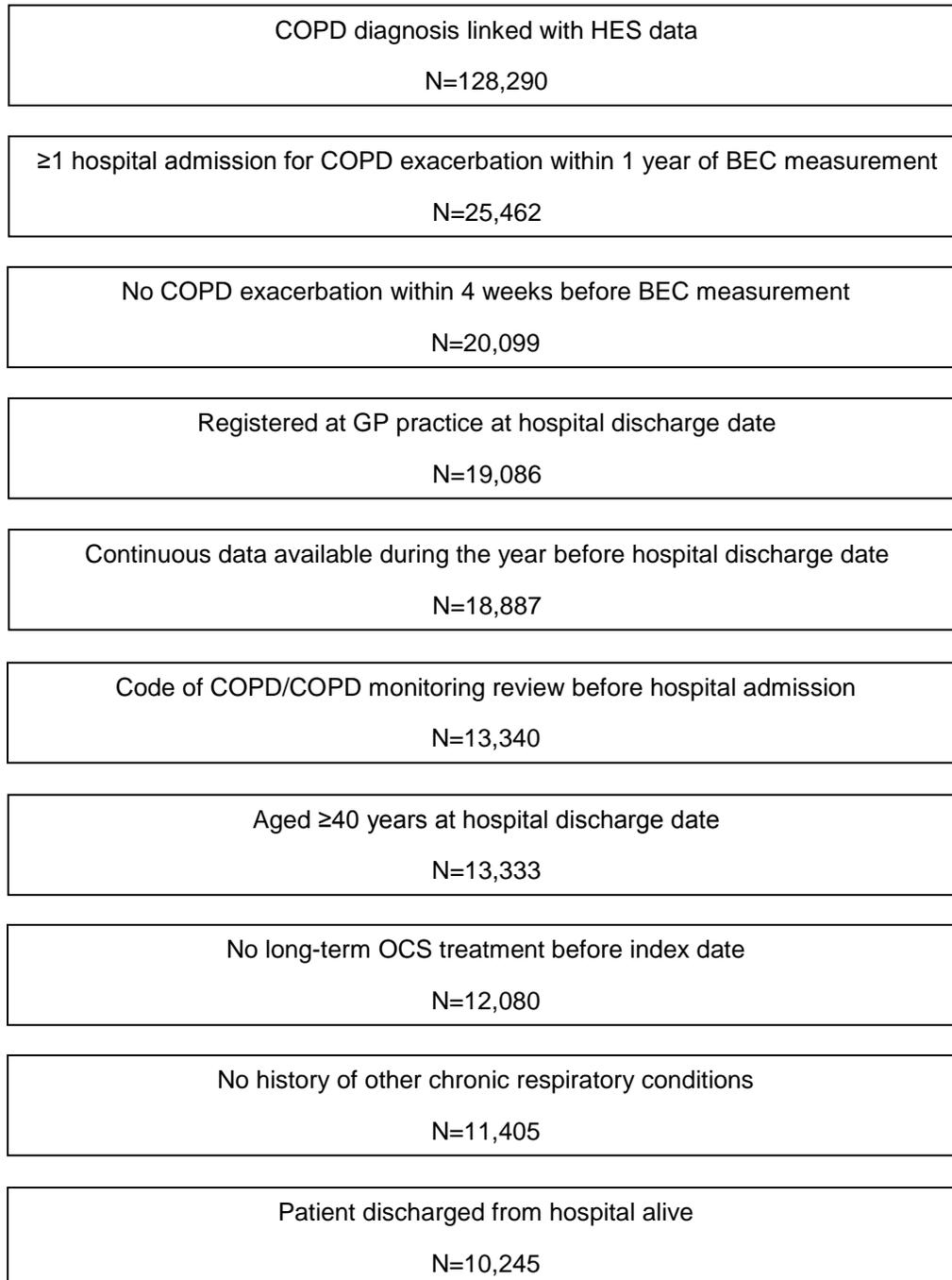


Panel a: Overall treatment failure. Panel b: Treatment failure defined as a repeat OCS prescription. Panel c: Treatment failure defined as an antibiotic prescription.

BEC, blood eosinophil counts; CI, confidence interval; ICS, inhaled corticosteroids; OCS, oral corticosteroids.

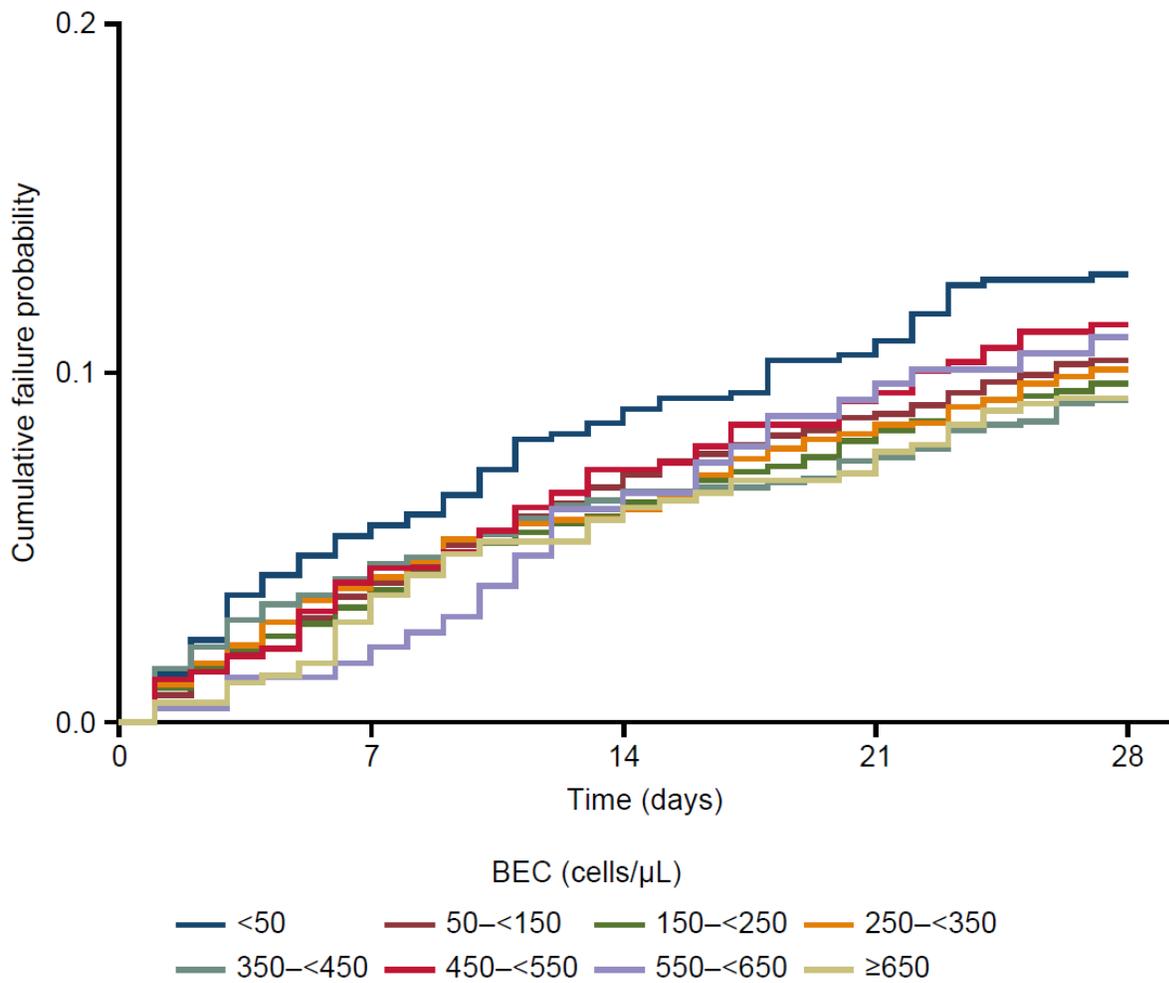
Reference range for BEC was 50–<150 cells/ μ L.

Figure S7. Cohort 2 Patient Flow Diagram



BEC, blood eosinophil counts; COPD, chronic obstructive pulmonary disease; GP, general practitioner; HES, Hospital Episode Statistics; OCS, oral corticosteroids.

Figure S8. Kaplan-Meier Curves for the Unadjusted Association Between Blood Eosinophil Counts Recorded During an Exacerbation-Free Period and Time to First Hospital Readmission for COPD Exacerbation (Cohort 2)



BEC, blood eosinophil counts; COPD, chronic obstructive pulmonary disease.

An exacerbation-free period was defined as at least 4 weeks before any COPD exacerbations.