Burden of disease associated with a COPD eosinophilic phenotype

Supplementary Material

Methods

Data source

For all patients, electronic medical records (EMRs) provided information on patient demographics, diagnoses and procedures with associated dates of services, laboratory results, prescriptions (including name, dosage and days of supply), and clinical measures. Insurance claims data provided information on emergency room (ER) visits, inpatient and outpatient visits, pharmacy dispensing with associated billed charges, and paid and copay amounts. Claims data was available for 50–60% of the EMR population. The analysis was conducted among the subset of patients with both EMR and claims information available.

Inclusion criteria

A diagnosis of COPD during the previous year was defined using the International Classification of Disease (ICD) codes: ICD-9-CM: 491.xx, 492.xx or 496.xx; or ICD-10-CM: J41.xx, J43.xx, or J44.xx.

Identification of COPD exacerbation population

The claims based algorithm used to identify exacerbation was as follows: A moderate exacerbation was defined as an outpatient or ER visit with a primary or secondary diagnosis of COPD (ICD-9-CM codes: 491.x, 492.x, or 496) and ≥1 dispensing for a systemic corticosteroid or antibiotic within seven days of the visit. A severe exacerbation was defined

as an inpatient hospital stay with a primary or secondary diagnosis of COPD (ICD-9-CM codes: 491.x, 492.x, or 496).
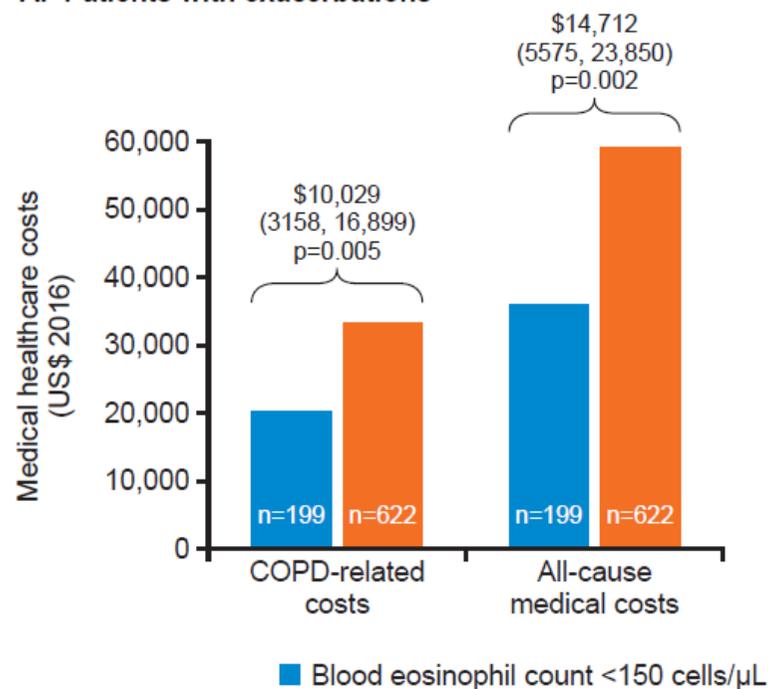
Sensitivity analysis

Due to the large number of covariates, a sensitivity analysis was conducted for the multivariate analysis using fewer variables (age, gender, insurance type, body mass index, blood pressure, year of index date, asthma, rheumatoid arthritis, respiratory infections, diabetes, cardiovascular disease, bacterial infections, Quan-Charlson comorbidity index, and triple therapy use).
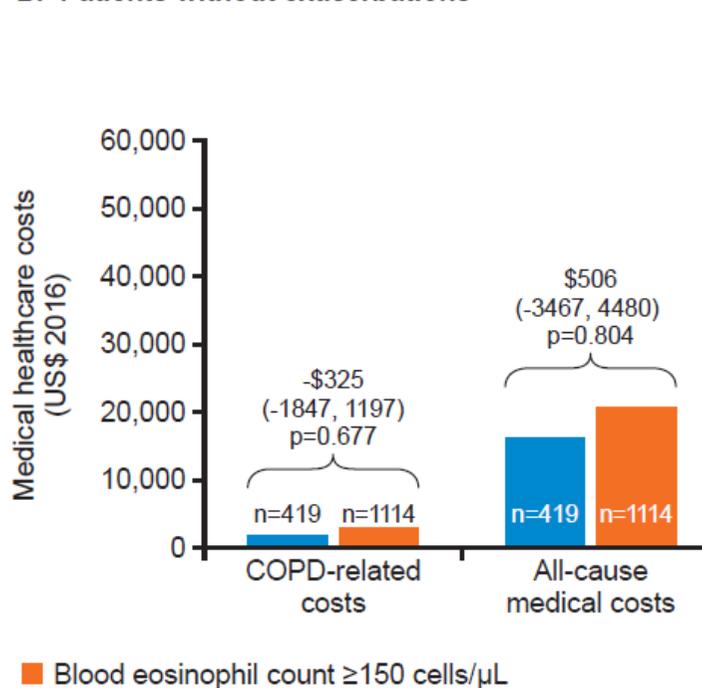
Results

Supplementary Figure 1 Sensitivity analysis of COPD-related and all-cause annual medical costs for patients with blood eosinophil counts <150 cells/μL and ≥150 cells/μL, and with exacerbations (A) or without exacerbations (B).
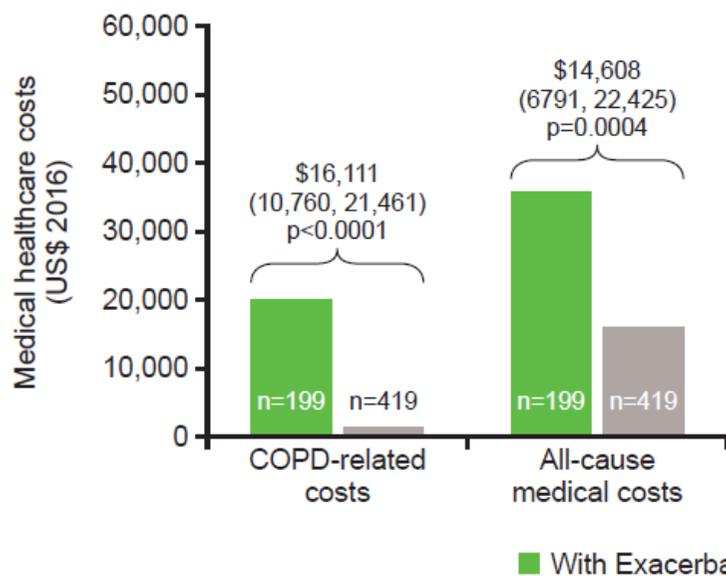

Notes: Numbers show adjusted* cost differences, 95% confidence intervals, and adjusted p values. *Adjusting for age, gender, insurance type, BMI, blood pressure, year of index date, asthma, rheumatoid arthritis, respiratory infections, diabetes, cardiovascular disease, bacterial infections, CCI score, and triple therapy use. **Abbreviations:** BMI, body mass index; CCI, Quan-Charlson comorbidity index; COPD, chronic obstructive pulmonary disease

Supplementary Figure 2 Sensitivity analysis of COPD-related and all-cause annual medical costs for patients with and without exacerbations, and with blood eosinophil count <150 cells/µL (A) or ≥150 cells/µL (B).
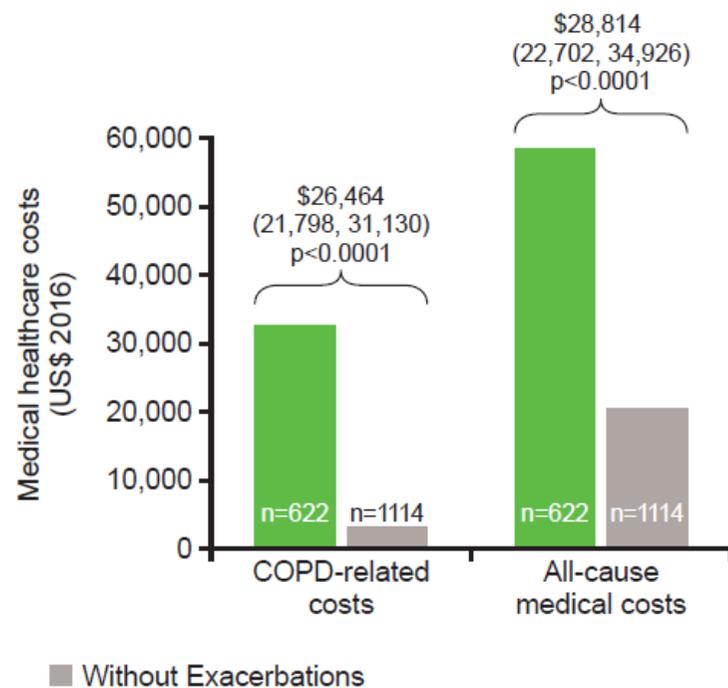

Notes: Numbers show adjusted* cost differences, 95% confidence intervals, and adjusted p values. *Adjusting for age, gender, insurance type, BMI, blood pressure, year of index date, asthma, rheumatoid arthritis, respiratory infections, diabetes, cardiovascular disease, bacterial infections, CCI score, and triple therapy use. **Abbreviations:** BMI, body mass index; CCI, Quan-Charlson comorbidity index; COPD, chronic obstructive pulmonary disease

Supplementary Figure 3 Multivariate analysis of COPD-related and all-cause annual medical costs for patients with blood eosinophil counts <300 cells/μL and ≥300 cells/μL, and with exacerbations (A) or without exacerbations (B).

Notes: Numbers show adjusted* cost differences, 95% confidence intervals, and adjusted p values. *Adjusting for age, gender, insurance type, BMI, blood pressure, calendar year, asthma, malignant neoplasm of respiratory and intrathoracic system, rheumatoid arthritis, Crohn's disease, systemic lupus erythematosus, multiple sclerosis, allergic rhinitis, respiratory infections, chronic sinusitis, diabetes, cardiovascular disease, acute sinusitis, atopic dermatitis, eosinophilic granulomatosis with polyangiitis, nasal polyps, hypereosinophilic syndrome, eosinophilic esophagitis, bacterial infections, CCI score, and triple therapy use. **Abbreviations:** BMI, body mass index; CCI, Quan-Charlson comorbidity index; COPD, chronic obstructive pulmonary disease
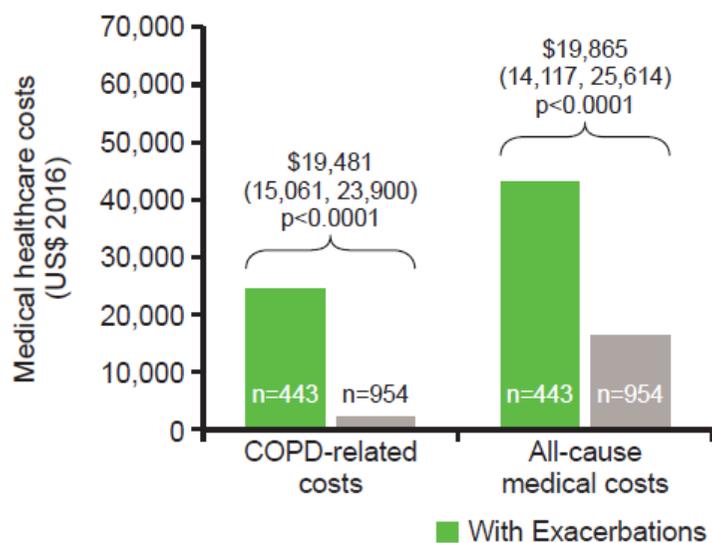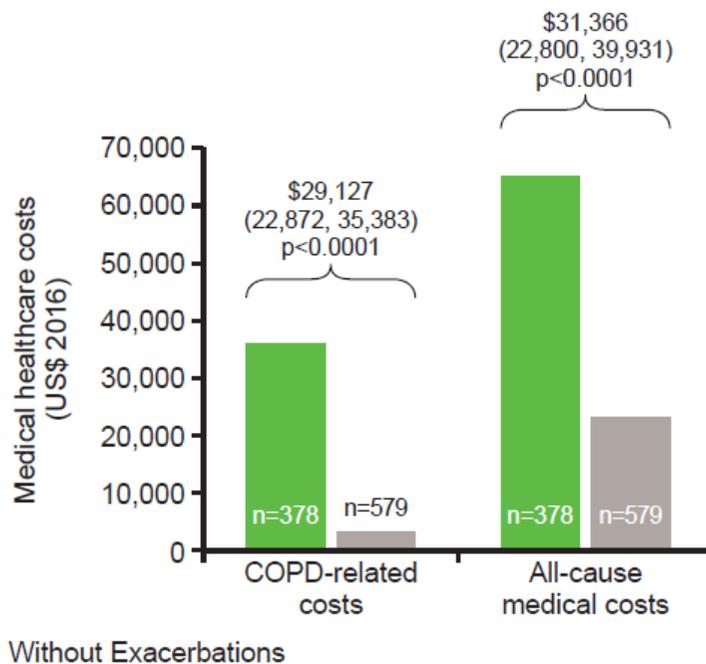
Supplementary Figure 4 Multivariate analysis of COPD-related and all-cause annual medical costs for patients with and without exacerbations, and with blood eosinophil count <300 cells/µL (A) or ≥300 cells/µL (B).

A. Blood eosinophil count <300 cells/µL

B. Blood eosinophil count ≥300 cells/µL

With Exacerbations   Without Exacerbations

Notes: Numbers show adjusted* cost differences, 95% confidence intervals, and adjusted p values. *Adjusting for age, gender, insurance type, BMI, blood pressure, calendar year, asthma, malignant neoplasm of respiratory and intrathoracic system, rheumatoid arthritis, Crohn's disease, systemic lupus erythematosus, multiple sclerosis, allergic rhinitis, respiratory infections, chronic sinusitis, diabetes, cardiovascular disease, acute sinusitis, atopic dermatitis, eosinophilic granulomatosis with polyangiitis, nasal polyps, hypereosinophilic syndrome, eosinophilic esophagitis, bacterial infections, CCI score, and triple therapy use. **Abbreviations:** BMI, body mass index; CCI, Quan-Charlson comorbidity index; COPD, chronic obstructive pulmonary disease

Supplementary Table Annual all-cause and COPD-related healthcare costs by blood eosinophil count cohort (2012–2015)

Healthcare costs ($US 2016), mean ± SD	2012 Patients with blood eosinophil count (N=773)		2013 Patients with blood eosinophil count (N=768)		2014 Patients with blood eosinophil count (N=788)		2015 Patients with blood eosinophil count (N=803)	
	Eosinophil count <150 cells/µL (n=225)	Eosinophil count ≥150 cells/µL (n=548)	Eosinophil count <150 cells/µL (n=206)	Eosinophil count ≥150 cells/µL (n=562)	Eosinophil count <150 cells/µL (n=213)	Eosinophil count ≥150 cells/µL (n=575)	Eosinophil count <150 cells/µL (n=211)	Eosinophil count ≥150 cells/µL (n=592)
All-Cause								
Total healthcare cost	**19,734 ± 30,469*****	**33,013 ± 57,368*****	**22,314 ± 47,245****	**35,980 ± 64,601****	**21,446 ± 40,819***	**32,517 ± 53,153***	**24,088 ± 49,430***	**35,427 ± 62,867***
Hospitalizations	**6796 ± 17,164****	**13,571 ± 35,000****	**5575 ±20,508****	**13,963 ± 44,717****	6918 ± 26,314	12,188 ± 30,639	8858 ± 32,218	13,732 ± 45,233
ER visits	415 ± 1327	648 ± 1736	**347 ±1183****	**1075 ± 4080****	1379 ± 4480	1700 ± 4017	1510 ± 3526	1831 ± 4867
Outpatient visits	**5285 ± 5765***	**6428 ± 6764***	5711 ± 10,445	6837 ± 8674	7741 ± 19,828	11,465 ± 28,703	**7116 ± 10,634*****	**12,633 ± 26,506*****
Other visits	**7237 ± 17,823****	**12,366 ± 27,195****	10,681 ± 32,025	14,104 ± 31,982	5409 ± 12,330	7164 ± 14,762	6604 ± 15,553	7231 ± 13,884
COPD-related								
Total healthcare cost	**4780 ± 10,711*****	**13,891 ± 33,664*****	7590 ± 30,029	13,088 ± 35,586	**6992 ± 18,230***	**11,495 ± 24,754***	10,620 ± 29,364	16,606 ± 47,337
Hospitalizations	**2781 ± 8599*****	**9744 ± 28,675*****	**3968 ± 18,488***	**9408 ± 32,346***	3783 ± 16,014	6997 ± 19,849	6853 ± 24,575	10,920 ± 41,958
ER visits	163 ± 947	195 ± 936	**52 ± 486***	**213 ± 1223***	702 ± 3199	636 ± 2369	586 ± 2099	867 ± 3459
Outpatient visits	756 ± 1584	1079 ± 1615	997 ± 3309	1151 ± 2681	**1163 ± 2354***	**1899 ± 5520***	1597 ± 5593	2538 ± 8662
Other visits	**1079 ± 2742*****	**2873 ± 8228*****	2572 ± 17,510	2316 ± 5706	1344 ± 4291	1963 ± 8647	1584 ± 5040	2281 ± 6722

Notes: Statistical significance is indicated as * p≤0.05, ** p≤0.01, *** p≤0.001

Abbreviations: COPD, chronic obstructive pulmonary disease; ER, emergency room; SD, standard deviation.