

# Understanding racial differences of COPD patients with an ecological model: two large cohort studies in the US and Korea

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## Abstract

**Background:** There are limited data about the racial difference in the characteristics of chronic obstructive pulmonary disease (COPD) patients who are treated at clinics. We aimed to compare sociodemographic and clinical characteristics between US and Korean COPD patients using large-scale nationwide COPD cohorts.

**Methods:** We used the baseline demographic and clinical data of COPD patients aged 45 years or older with at least a 10 pack-per year smoking history from the Korean COPD Subtype Study (KOCOSS,  $n = 1686$ ) cohort (2012–2018) and phase I (2008–2011) of the US Genetic Epidemiology of COPD (COPDGene) study ( $n = 4477$ , 3461 were non-Hispanic whites [NHW], and 1016 were African Americans [AA]).

**Results:** Compared to NHW, AA had a significantly lower adjusted prevalence ratio (aPR) of cough >3 months (aPR: 0.67; 95% CI [confidence interval]: 0.60–0.75) and phlegm >3 months (aPR: 0.78, 95% CI: 0.70–0.86), but higher aPR of dyspnea (modified Medical Round Council scale  $\geq 2$ ) (aPR: 1.22; 95% CI: 1.15–1.29), short six-minute walk distance (<350m) (aPR: 1.98; 95% CI: 1.81–2.14), and poor quality of life (aPR: 1.10; 95% CI: 1.05–1.15). Compared to NHW, Koreans had a significantly lower aPR of cough >3 months (aPR: 0.53; 95% CI: 0.47–0.59), phlegm >3 months (aPR: 0.75; 95% CI: 0.67–0.82), dyspnea (aPR: 0.72; 95% CI: 0.66–0.79), and moderate-to-severe acute exacerbation in the previous year (aPR: 0.73; 95% CI: 0.65–0.82). NHW had the highest burden related to chronic bronchitis symptoms and cardiovascular diseases related to comorbidities.

**Conclusion:** There are substantial differences in sociodemographic characteristics, clinical presentation, and comorbidities between COPD patients from the KOCOSS and COPDGene, which might be caused by interactions between various intrapersonal, interpersonal, and environmental factors of the ecological model. Thus, a broader and more comprehensive approach would be necessary to understand the racial differences of COPD patients.

**Keywords:** chronic obstructive pulmonary disease, cohort, ecological model, racial difference

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## Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most common non-communicable diseases worldwide, and its global burden is increasing,<sup>1</sup> especially in Asian countries.<sup>2</sup> COPD is characterized by persistent respiratory symptoms and airflow limitation,<sup>3</sup> but the clinical presentations of COPD appear to be substantially different depending on the race of the patient.<sup>4</sup>

Several *post hoc* analyses of therapeutic interventions showed different clinical characteristics between Asian and overall populations.<sup>5,6</sup> Asian patients were more likely to be men, have a lower body mass index (BMI), and experience more severe airflow limitation than overall populations.<sup>4–6</sup> However, most of the studies which compared racial differences were based on the results of therapeutic interventional trials or

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population-based observational studies. These studies may not reflect the characteristics of COPD patients who are treated at clinics.

We hypothesized that sociodemographic and clinical characteristics in COPD patients are different by race. In this study, we aimed to compare sociodemographic and clinical characteristics between US and Korean COPD patients using large-scale nationwide COPD cohorts in each country.

## Methods

### Study population

We used the baseline demographic and clinical data from the Korean COPD Subgroup Study (KOCOSS) cohort (2012–2018) and phase I (2008–2011) of the US Genetic Epidemiology of COPD (COPDGene) study. The KOCOSS is a multicenter cohort study of COPD patients of tertiary hospitals in South Korea.<sup>7</sup> The COPDGene study is a multicenter cohort study of non-hispanic whites (NHW) and African Americans (AA) with at least a 10 pack-year smoking history in the US.<sup>8,9</sup>

For our analysis, we included patient data of adults aged 45 years or older with at least a 10 pack per-year smoking history and whose post-bronchodilator forced expiratory volume in 1 s (FEV<sub>1</sub>)/forced vital capacity was <0.7. The KOCOSS included 1686 Korean participants, and the COPDGene study included 4477 participants, of which 3461 were NHW, and 1016 were AA.

### Data collection

Baseline sociodemographic information includes age, sex, smoking history, BMI, and education level. Overweight was defined as BMI  $\geq 25.0$  kg/m<sup>2</sup> and BMI  $\geq 23.0$  kg/m<sup>2</sup> for the NHW and AA and Koreans, respectively.<sup>10</sup> In terms of clinical characteristics, symptoms [cough >3 months, phlegm >3 months, and modified medical round council (mMRC) scale], acute exacerbations in the previous year, six-minute walk distance, and severity of airflow limitation were included. The severity of airflow limitation was defined based on post-bronchodilator forced expiratory volume in 1 s (FEV<sub>1</sub>) as mild (FEV<sub>1</sub>  $\geq 80\%$  predicted), moderate (50%  $\leq$  FEV<sub>1</sub> < 80% predicted), or severe-to-very severe (FEV<sub>1</sub> < 50% predicted).<sup>3</sup> Comorbidities included cardiovascular disease, diabetes, gastroesophageal reflux, and osteoporosis. Quality of life was also

assessed using the St George's Respiratory Questionnaire (SGQR) in the COPDGene or the COPD-specific version of SGRQ (SGRQ-C) in the KOCOSS. It is well known that the SGRQ-C score is equivalent to the original SGRQ.<sup>11</sup>

### Ethics and consent

Study protocols of the KOCOSS and COPDGene were approved by the institutional review board (IRB) of each participating hospital. Written informed consent was obtained from all patients of both studies. Ethical approval for this study was obtained from the institutional review board of the Samsung Medical Center (no. 2014-06-132).

### Statistical analysis

Continuous and categorical variables were compared among the three groups using analysis of variance and  $\chi^2$  tests, respectively. To compare the clinical characteristics by race, we generated all the variables as bivariate outcomes and conducted multivariable logistic regression models. Then we calculated prevalence ratios (PRs) using the predicted proportion from logistic regression. In this analysis, we adjusted for age, sex, BMI category (underweight, normal, overweight, obese, and unknown), smoking status (former and current), and post-bronchodilator FEV<sub>1</sub> < 50% predicted. In addition, we conducted a subgroup analysis by the severity of airflow limitations (mild-to-moderate *versus* severe-to-very severe) in all the characteristics. *p* values < 0.05 were considered significant, and two-sided tests were used in all calculations. Statistical analyses were performed using STATA 14.0 (StataCorp LP, College Station, TX, USA).

## Results

### Sociodemographic and clinical characteristics

As shown in Table 1, Koreans in the KOCOSS were older and were more likely to be men than NHW and AA in the COPDGene study (*p* < 0.01 for both). The ratio of men to women among current smokers was highest in Koreans (24.8) and lowest in NHW (1.3) (*p* < 0.01). The mean BMI of NHW and AA was similar, while the BMI of Koreans was significantly lower (NHW *versus* AA *versus* Koreans, 27.9 *versus* 27.9 *versus* 22.3 kg/m<sup>2</sup>, *p* < 0.01). Koreans had the lowest educational status, and NHW had the highest (NHW *versus*

AA versus Koreans, 34.4 versus 59.0 versus 86.5%,  $p < 0.01$ ). The KOCOSS data showed a pulmonary tuberculosis prevalence of 24% (these data were not available in the COPDGene data).

Compared to NHW, AA had a significantly lower aPR of cough  $>3$  months (aPR: 0.67; 95% CI [confidence interval]: 0.60–0.75) and phlegm  $>3$  months (aPR: 0.78, 95% CI: 0.70–0.86), but higher aPR of dyspnea (mMRC  $\geq 2$ ) (aPR: 1.22; 95% CI: 1.15–1.29), short six-minute walk distance ( $<350$  m) (aPR: 1.98; 95% CI: 1.81–2.14), and poor quality of life (SGQR total score  $\geq 25$ ) (aPR: 1.10; 95% CI: 1.05–1.15). Compared to NHW, Koreans had a significantly lower aPR of cough  $>3$  months (aPR: 0.53; 95% CI: 0.47–0.59), phlegm  $>3$  months (aPR: 0.75; 95% CI: 0.67–0.82), dyspnea (aPR: 0.72; 95% CI: 0.66–0.79), moderate-to-severe AE in the previous year (aPR: 0.73; 95% CI: 0.65–0.82), and severe-to-very severe COPD (aPR: 0.50; 95% CI: 0.44–0.55). Korean COPD patients had poorer quality of life (SGQR-C total score  $\geq 25$ ) (aPR: 1.07; 95% CI: 1.01–1.12) compared to NHW (Table 2).

Regarding comorbidities, AA had a significantly lower aPR of dyslipidemia (aPR: 0.80; 95% CI: 0.72–0.88), gastro-esophageal reflux (aPR: 0.64; 95% CI: 0.55–0.73), and osteoporosis (aPR: 0.47; 95% CI: 0.34–0.60), but had a higher aPR of hypertension (aPR: 1.34; 95% CI: 1.25–1.42) and diabetes mellitus (aPR: 1.63; 95% CI: 1.33–1.94) compared to NHW. Koreans had a significantly lower aPR of hypertension (aPR: 0.81; 95% CI: 0.74–0.88), dyslipidemia (aPR: 0.24; 95% CI: 0.20–0.27), myocardial infarction (aPR: 0.45; 95% CI: 0.33–0.57), peripheral vascular disease (aPR: 0.34; 95% CI: 0.19–0.50), gastro-esophageal reflux (aPR: 0.35; 95% CI: 0.29–0.41), and osteoporosis (aPR: 0.42; 95% CI: 0.29–0.54) and had a higher aPR of diabetes mellitus (aPR: 1.61; 95% CI: 1.34–1.88), compared to NHW (Table 2). When we conducted additional analysis using COPD severity (mild-to-moderate or severe-to-very severe), the results were similar (Supplemental Table 1).

## Discussion

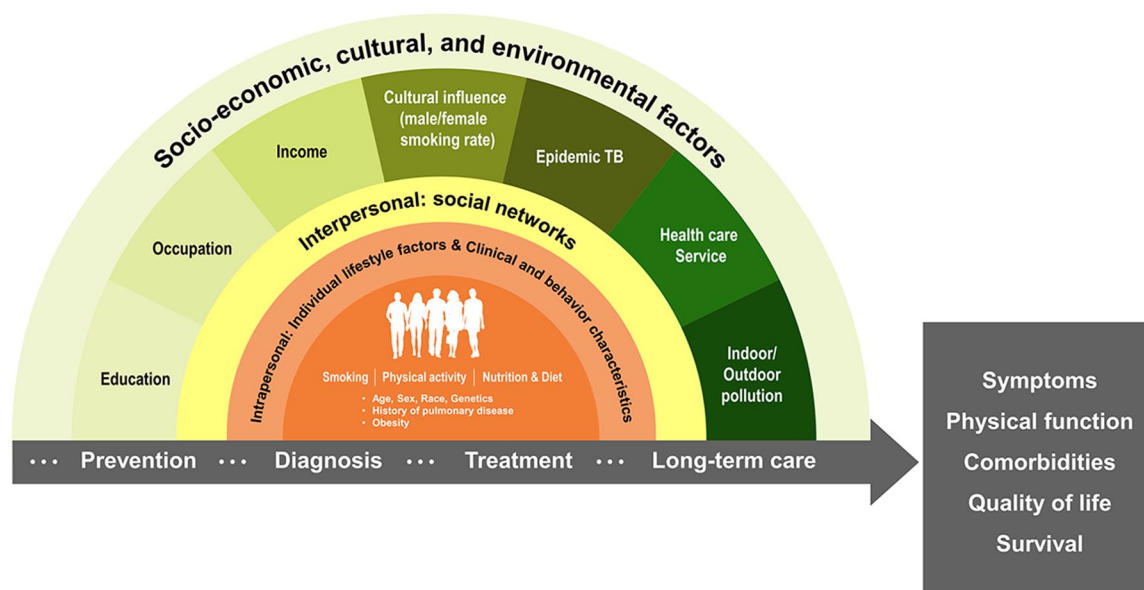
The analysis of the COPDGene registry from the US and the KOCOSS registry from Korea showed that sociodemographic and clinical characteristics were significantly different between COPD patients from two cohorts. Among the three racial groups, NHW had the highest-burden related to

chronic bronchitis symptoms and cardiovascular diseases related to comorbidities. In comparison, AA were most likely to be current smokers, reported more dyspnea, and had worse exercise capacity. Korean COPD patients were more likely to be men, older, and underweight compared to the NHW and AA COPD patients. They were also least likely to have symptoms and comorbidities except for diabetes. These findings were consistent irrespective of COPD severity.

Age, sex, smoking history, and education were significantly different among NHW, AA, and Korean COPD patients. This might be due to the rapid entry into an aging society and the predominantly high prevalence of male smokers in Korea.<sup>12,13</sup> While women smoke at nearly the same rate as men in western countries, the 2019 Organization for Economic Cooperation and Development (OECD) data indicated that less than 5% of Korean women smoke.<sup>13</sup> This high smoking rate is associated with low educational attainment, which is a well-known risk factor for COPD.<sup>14</sup> In addition, Korean COPD patients had significantly lower BMI, which would be associated with nutrition and diet habit. These sociodemographic characteristics might interact with different prevalences of comorbidities as a COPD risk factor; a relatively high incidence of tuberculosis and a low prevalence of asthma in Korea, resulting in racial differences in clinical phenotype.<sup>4,15</sup> Compared to NHW, AA are known to have a higher prevalence of childhood asthma.<sup>16</sup> This might account for the relatively young age in AA in this study.

Regarding symptoms, NHW had more symptoms including cough and sputum than AA, suggesting the chronic bronchitis type of COPD would be predominant among the NHW COPD patients; whereas AA were younger and current smokers with lower education levels, more dyspnea, and poor exercise capacity, which was similar to the previous study.<sup>17</sup> Compared to NHW and AA of the COPDGene, Koreans of the KOCOSS had significantly milder symptoms including cough, sputum, dyspnea, fewer previous exacerbations, and had fewer cardiovascular comorbidities, irrespective of COPD severity (Supplemental Table 1). Less symptom burden and lower exacerbation rate in patients from the KOCOSS might be attributed to relatively easy access to medical care.

We found that the comorbidity profile is different among groups. NHW had the highest



**Figure 1.** The ecological model of chronic obstructive pulmonary disease development and outcome adapted from Dahlgren and Whitehead (1991).<sup>22</sup>

burden of cardiovascular comorbidities and osteoporosis, while AA had comorbidity patterns driven by hypertension and diabetes mellitus, and Koreans had the lowest burden of comorbidities, except for diabetes mellitus. Given that COPD is often regarded as part of multimorbidity particularly in the elderly and these comorbidities are associated with COPD poor outcomes,<sup>18,19</sup> different strategies among races may be required for optimal management of COPD-related comorbidities.

A simple model is hardly applicable to explain racial differences in sociodemographic and clinical characteristics of COPD patients from the two cohorts. Considering individual, interpersonal, social, and cultural factors are interactively linked in a complex manner, an ecological model comprehensively addressing these factors is necessary (Figure 1). The specific composition of individual, interpersonal, social, and cultural risk factors of COPD might be linked to the healthcare system in each country, further compounding differences by race in disease burden and presentation such as symptoms, physical function, and comorbidities (Figure 1). Or some of the differences in clinical features might be due to inter-racial genetic differences.<sup>20</sup> Finally, environmental factors such as indoor/outdoor pollution levels, which continue to have a significant effect on the rates of COPD in Asia,<sup>21</sup> might contribute to racial differences in our study.

There are several limitations to this study. First, both cohorts were hospital based, so participants would not represent COPD patients in each country studied. However, both cohorts were nationwide studies recruiting patients from multiple hospitals across each respective country. However, further study with a representative sample would be necessary to confirm the study findings. Second, the analysis was retrospective in nature, so all factors in ecological models such as indoor/outdoor pollution or genetics were not available. Third, because the two cohorts were conducted a few years apart, racial differences of some symptoms, quality of life, and outcomes might be due to different therapeutic approaches over time.

In conclusion, there are substantial differences in sociodemographic characteristics, clinical presentation, and comorbidities between COPD patients from the COPDGene and KOCOSS, which might be caused by interactions between various intrapersonal, interpersonal, and environmental factors of the ecological model. Thus, a broader and more comprehensive approach linking research-oriented clinical centers to national health registries or air pollution surveillance data would be necessary to understand the racial differences of COPD patients and to develop clinical guidelines for COPD prevention, diagnosis, treatment, and long-term care in the precision medicine era. Furthermore, it would be necessary to develop



**Table 1.** Characteristics of COPD patients, with smoking history in the COPDGene and KOCOSS.

	COPDGene cohort		KOCOSS cohort	<i>p</i> Value
	NHW ( <i>n</i> =3461)	AA ( <i>n</i> =1016)	Koreans ( <i>n</i> =1686)	
Age, years	64.3 (8.3)	58.6 (8.2)	69.5 (7.6)	<0.01
Sex, male	1948 (56.3)	555 (54.6)	1641 (97.3)	<0.01
Smoking status				<0.01
Former	2185 (63.1)	351 (34.5)	1221 (72.4)	
Current	1276 (36.9)	665 (65.5)	465 (27.6)	
BMI, kg/m <sup>2</sup> ( <i>n</i> =6154)	27.9 (5.9)	27.9 (6.7)	22.3 (3.7)	<0.01
Education, high school or less ( <i>n</i> =6148)	1191 (34.4)	599 (59.0)	1447 (86.5)	<0.01
Symptoms				
Cough >3 months ( <i>n</i> =6025)	1486 (43.9)	368 (37.7)	357 (21.5)	<0.01
Phlegm >3 months ( <i>n</i> =5996)	1364 (40.5)	366 (37.7)	502 (30.3)	<0.01
mMRC ( <i>n</i> =6055)	1.9 (1.5)	2.1 (1.5)	1.4 (0.9)	<0.01
AE in the previous year				
≥1 or more moderate-to-severe AE	1295 (37.4)	384 (37.8)	377 (22.4)	<0.01
Six-minute walk distance, m ( <i>n</i> =5670)	387.4 (121.6)	336.7 (125.2)	389.7 (225.9)	<0.01
COPD group				<0.01
Mild	610 (17.6)	177 (17.4)	273 (16.2)	
Moderate	1442 (41.7)	482 (47.4)	931 (55.2)	
Severe	918 (26.5)	244 (24.0)	412 (24.4)	
Very severe	491 (14.2)	113 (11.1)	70 (4.2)	
Cardiovascular disease				
Hypertension ( <i>n</i> =6155)	1617 (46.7)	544 (53.5)	665 (39.6)	<0.01
Congestive heart failure ( <i>n</i> =6154)	154 (4.5)	51 (5.0)	56 (3.3)	0.07
Dyslipidemia ( <i>n</i> =6147)	1541 (44.5)	301 (29.6)	196 (11.7)	<0.01
Myocardial infarction ( <i>n</i> =6155)	286 (8.3)	59 (5.8)	81 (4.8)	<0.01
Peripheral vascular disease ( <i>n</i> =6153)	122 (3.5)	20 (2.0)	29 (1.7)	<0.01
Diabetes mellitus ( <i>n</i> =6156)	394 (11.4)	155 (15.3)	302 (18.0)	<0.01
Gastro-esophageal reflux ( <i>n</i> =6150)	1107 (32.0)	198 (19.5)	154 (9.2)	<0.01
Osteoporosis ( <i>n</i> =6153)	515 (14.9)	62 (6.1)	67 (4.0)	<0.01

*(Continued)*

**Table 1.** (Continued)

	COPDGene cohort		KOCOSS cohort	<i>p</i> Value
	NHW ( <i>n</i> = 3461)	AA ( <i>n</i> = 1016)	Koreans ( <i>n</i> = 1686)	
Quality of life ( <i>n</i> = 5495)				
Total score	35.9 (22.4)	40.1 (24.2)	36.0 (21.0)	<0.01
Symptoms	42.1 (25.7)	44.0 (26.3)	45.5 (20.7)	<0.01
Impacts	25.8 (21.1)	30.1 (24.0)	25.3 (19.6)	<0.01
Activity	50.6 (29.0)	55.5 (29.9)	48.0 (23.1)	<0.01

Variables were expressed as mean (SD) or number (%).

AA, African American; AE, acute exacerbation; BMI, body mass index; COPD, chronic obstructive pulmonary disease; COPDGene, US Genetic Epidemiology of COPD study; KOCOSS, Korean COPD Subtype Study; mMRC, modified Medical Round Council; NHW, non-Hispanic white.

**Table 2.** Adjusted prevalence ratios and 95% confidence intervals of clinical characteristics in all patients.

	COPDGene cohort		KOCOSS cohort
	NHW	AA	Koreans
		PR (95% CI)	PR (95% CI)
Age ≥65 years	Reference	0.61 (0.54, 0.68)	1.42 (1.34, 1.50)
Sex, male	Reference	0.98 (0.91, 1.04)	1.77 (1.71, 1.83)
Smoking status, current	Reference	1.52 (1.39, 1.65)	0.85 (0.76, 0.94)
Overweight or obese ( <i>n</i> = 6154)	Reference	0.95 (0.90, 1.00)	0.55 (0.50, 0.59)
Education, high school or less ( <i>n</i> = 6148)	Reference	1.64 (1.52, 1.77)	2.57 (2.43, 2.71)
Symptoms			
Cough >3 months ( <i>n</i> = 6111)	Reference	0.67 (0.60, 0.75)	0.53 (0.47, 0.59)
Phlegm >3 months ( <i>n</i> = 6082)	Reference	0.78 (0.70, 0.86)	0.75 (0.67, 0.82)
mMRC ≥2 ( <i>n</i> = 6131)	Reference	1.22 (1.15, 1.29)	0.72 (0.66, 0.79)
Moderate-to-severe AE in the previous year	Reference	1.05 (0.94, 1.16)	0.73 (0.65, 0.82)
Six-minute walk distance <350 m ( <i>n</i> = 5670)	Reference	1.98 (1.81, 2.14)	1.07 (0.94, 1.19)
Severe-to-very severe COPD	Reference	0.98 (0.89, 1.07)	0.50 (0.44, 0.55)
Cardiovascular disease			
Hypertension ( <i>n</i> = 6155)	Reference	1.34 (1.25, 1.42)	0.81 (0.74, 0.88)
Congestive heart failure ( <i>n</i> = 6145)	Reference	1.33 (0.89, 1.77)	0.77 (0.50, 1.03)
Dyslipidemia ( <i>n</i> = 6147)	Reference	0.80 (0.72, 0.88)	0.24 (0.20, 0.27)
Myocardial infarction ( <i>n</i> = 6155)	Reference	0.88 (0.63, 1.12)	0.45 (0.33, 0.57)
Peripheral vascular disease ( <i>n</i> = 6144)	Reference	0.70 (0.36, 1.04)	0.34 (0.19, 0.50)

(Continued)

**Table 2.** (Continued)

	COPDGene cohort		KOCOSS cohort
	NHW	AA	Koreans
		PR (95% CI)	PR (95% CI)
Diabetes mellitus ( <i>n</i> =6156)	<i>Reference</i>	1.63 [1.33, 1.94]	1.61 [1.34, 1.88]
Gastro-esophageal reflux ( <i>n</i> =6150)	<i>Reference</i>	0.64 [0.55, 0.73]	0.35 [0.29, 0.41]
Osteoporosis ( <i>n</i> =6153)	<i>Reference</i>	0.47 [0.34, 0.60]	0.42 [0.29, 0.54]
Poor quality of life* ( <i>n</i> =5571)	<i>Reference</i>	1.10 [1.05, 1.15]	1.07 [1.01, 1.12]

\*Defined as the St George's Respiratory Questionnaire (SGRQ) or COPD-specific version of SGRQ total score  $\geq 25$ . Adjusted for age, sex, BMI categories (underweight, normal, overweight, obese, and unknown), smoking (former, and current), post-bronchodilator FEV<sub>1</sub> <50% predicted.  
AA, African American; AE, acute exacerbation; CI, confidence interval; COPD, chronic obstructive pulmonary disease; COPDGene, US Genetic Epidemiology of COPD; KOCOSS, Korean COPD Subtype Study; mMRC, modified Medical Round Council; NHW, non-Hispanic white; PR, prevalence ratio.

local guidelines reflecting racial differences of COPD patients and provide more personalized care for COPD.

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### Author contributions

HYP, HL, JC, and KHY were responsible for the conception and design of the study. HYP, HL, DK, JC, and KHY undertook the analysis and interpretation of the data. HYP, HL, DK, DDS, JC, and KHY drafted the manuscript. HYP, HL, HSC, YHR, KSJ, DDS, JC, and KHY made a critical revision of the manuscript. All authors read and approved the final manuscript.

### Conflict of interest statement

The authors declare that there is no conflict of interest.

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COPDGene cohort. The COPDGene study (NCT00608764) is also supported by the COPD Foundation through contributions made to an industry advisory committee composed of Astra Zeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, and Sunovion.

### Ethics approval and consent to participate

Consent to participate in this study was obtained from each subject in the KOCOSS and COPDGene. Ethics approval for this study was obtained from the institutional review board of Samsung Medical Center (no. 2014-06-132).

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### Availability of data and material

All data extracted in this study are included in this article.

### Supplemental material

Supplemental material for this article is available online.

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