CHEST

Original Research

OBSTRUCTIVE LUNG DISEASES

Racial Differences in Quality of Life in Patients With COPD

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Background: **Although COPD is associated with significant health-related quality-of-life (HRQL) impairment, factors influencing HRQL in patients with COPD are not well understood, particularly in African Americans. We hypothesized that HRQL in COPD differs by race and sought to identify factors associated with those differences.**

Methods: **We analyzed 224 African American and 1,049 Caucasian subjects with COPD enrolled in the COPDGene (Genetic Epidemiology of COPD) Study whose conditions were classified as GOLD (Global Initiative for Chronic Obstructive Lung Disease) stages I to IV. HRQL and symptoms were compared using the St. George Respiratory Questionnaire (SGRQ) and the modified Medical Research Council Dyspnea (MMRC) scale. We constructed a mixed-effects linear regression model for SGRQ score.**

Results: **African Americans were younger and reported fewer pack-years of smoking, more current smoking, and less attained education than Caucasians; MMRC scores were higher ($P = .02$) as were SGRQ scores (mean score difference, 8.4; $P < .001$). In a general linear model of SGRQ total score after adjusting for factors such as age, sex, and pack-years of smoking, SGRQ total score was similar for African Americans and Caucasians who reported no COPD exacerbations in the prior year. However, for subjects with exacerbations, SGRQ total score was increased to a greater relative extent for African Americans than for Caucasians (1.89 points for each exacerbation, $P = .006$). For hospitalized exacerbations, the effect on SGRQ total score also was greater for African Americans (4.19 points, $P = .04$). Furthermore, a larger percentage of African Americans reported having had at least one exacerbation that required hospitalization in the prior year (32% vs 16%, $P < .001$).**

Conclusion: **In analyses that account for other variables that affect quality of life, HRQL is similar for African Americans and Caucasians with COPD without exacerbations but worse for African Americans who experience exacerbations, particularly hospitalized exacerbations.**

Trial registry: **ClinicalTrials.gov; No.: NCT00608764; URL: www.clinicaltrials.gov**

CHEST 2011; 140(5):1169–1176

Abbreviations: 6MWD = 6-min walk distance; COPDGene = Genetic Epidemiology of COPD; GOLD = Global Initiative for Obstructive Lung Disease; HRQL = health-related quality of life; MMRC = modified Medical Research Council; SGRQ = St. George Respiratory Questionnaire

Multiple studies have demonstrated significant impairment in the health-related quality of life (HRQL) in subjects with COPD.[1] The concept of HRQL relates to disparity between an individual's desired and real-life well being as influenced by his or her health.[2] Many factors have been reported to influence HRQL in COPD, including lung function, exercise capacity, depression, and level of education.[3,4] Little has been published, however, regarding the influence of race on HRQL. Until recently, many clinical trials have failed to enroll adequate numbers of African Americans to allow such an evaluation.

Data demonstrate both an increasing prevalence of COPD among African Americans and a significant increase in mortality.[5] There is also reason to believe that tobacco susceptibility[6] and response to inhaled therapies[7] may differ between African American and Caucasian subjects. Racial disparities in the treatment

of COPD[5] and in quality of life in other lung diseases, including cystic fibrosis[8] and asthma,[9] have been reported. We hypothesized that differences in HRQL and dyspnea exist in African American subjects with COPD recruited for the Genetic Epidemiology of COPD (COPDGene) Study.

Materials and Methods

Patient Selection

The COPDGene Study (www.copdgene.org) is an ongoing, National Heart, Lung, and Blood Institute-funded multicenter investigation of the genetic epidemiology of smoking-related lung disease and involved recruitment of subjects at 21 clinical centers (e-Appendix 1). Subjects were selected for participation based on the following criteria: aged 45 to 80 years; cigarette smoking ≥ 10 pack-years; and willingness to undergo study-related testing that included spirometry, CT scan of the chest, and blood collection for biomarker and genetic analysis.[10] Full inclusion and exclusion criteria have been described previously.[10] (Reasons for failure to enroll for this study by race are presented in e-Appendix 2. Approximately 77% of Caucasians and 69% of African Americans who were contacted successfully enrolled [$P < .0001$], with the largest difference coming from African Americans who were screened by phone but did not proceed with a study visit.) Subjects included in our analysis were from the first 2,500 data set from the COPDGene Study (April 2010) and included 1,273 subjects who met GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria[11] for stages I to IV fixed airflow obstruction with a postbronchodilator FEV_1/FVC ratio of ≤ 0.7. All participants provided written informed consent. This research protocol was approved by the institutional review board at each participating institution (e-Appendix 3).

Race was determined by self-report. The designation "African American" was assigned if patients identified themselves as "black or African American." The designation "Caucasian" was assigned if patients identified themselves as "white." None of the subjects were Hispanic or Latino.

Data Collection and Exacerbation Determination

Demographic data, smoking, and medical history were collected through interview or self-administered questionnaires. Dyspnea was quantified using the five-point modified Medical Research Council (MMRC) dyspnea scale,[12] which asks respondents to rate dyspnea from 0 (absent) to 4 (dyspnea when dressing/undressing). The St. George Respiratory Questionnaire (SGRQ) is an HRQL obstructive lung disease-specific instrument with total and subscores ranging from 0 to 100. Higher scores correspond to worse HRQL.[13]

Self-reported acute exacerbation frequency was quantified with the following question: "Have you had a flare-up of your chest trouble in the last 12 months?" Zero exacerbations were recorded if the answer was no. If the answer was yes, the subject was prompted with the question, "How was the flare-up treated?" The respondent was allowed to describe between one and six episodes. If the respondent described that any of the following occurred during an episode, the episode was counted as one exacerbation: "took additional antibiotic or steroid medication which you keep at home," "consulted your doctor who prescribed additional antibiotic and/or steroid treatment but did not admit you to the hospital," or "admitted to hospital." Hence, the number of exacerbations for any respondent was zero to six (e-Appendix 4 contains the actual questionnaire used in this study).

Physiologic Testing

Patients underwent spirometry before and after the administration of short-acting bronchodilating medication (albuterol). All spirometric tracings were independently reviewed to ensure that American Thoracic Society criteria were met.[14]

Statistical Analyses

Statistical analyses were done with SAS/STAT, version 9.2 for Windows XP (SAS Institute Inc; Cary, North Carolina) software. Baseline comparisons between Caucasians and African Americans were done using Student *t* test (continuous variables) or Fisher exact test (categorical variables). We controlled for multiple comparisons using the false discovery rate procedure. Education was categorized into three levels: no high school graduation, high school graduation or equivalent, and education beyond high school.

Because of their clinical importance to quality of life, we examined the impact of race, age, sex, FEV_1 % predicted, pack-year smoking history, MMRC dyspnea score, 6-min walk distance (6MWD), education, current smoking status, and exacerbation frequency in the previous year on SGRQ total score using a mixed-effects linear regression model that included the clinical center of recruitment as a random effect in order to adjust for possible clustering effects within a center. In preliminary analyses, we also examined interactions between race and each of the other predictor variables in the regression model. Using a process of manual backward elimination, only an interaction between race and exacerbation frequency in the previous year was statistically meaningful. There was no interaction of race with this random center effect ($P = .44$), so we dropped this center-race interaction term from subsequent analyses. We examined the impact on SGRQ total score of the same predictor variables, including a random center effect but substituted history of hospitalized exacerbation for exacerbation frequency in the previous year. For all analyses, two-tailed tests were used. We considered $P < .05$ to be statistically significant.

Manuscript received November 6, 2010; revision accepted April 14, 2011.

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Funding/Support: The project was supported by the National Heart, Lung, and Blood Institute [award numbers U01HL089897 and U01HL089856]. The COPDGene project also is supported by the COPD Foundation through contributions made to an industry advisory board comprising AstraZeneca, Boehringer Ingelheim GmbH, Novartis Pharmaceuticals Corporation, and Sepracor Inc. Dr Han is supported by funding from the National Heart, Lung and Blood Institute [Grant K23 HL093351].

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DOI: 10.1378/chest.10-2869

Results

A comparison of baseline demographics by race is shown in Table 1. Eighteen percent of the cohort (224 of 1,273 subjects) were African American. African American subjects in the study were younger than Caucasian subjects (60 vs 65 years, $P < .001$) but exhibited comparable lung function. African Americans reported fewer pack-years of smoking (54 vs 42, $P < .001$), significantly shorter 6MWD (381 vs 298 m, $P < .001$) despite similar height, and less education than Caucasians ($P < .001$). A greater proportion of African Americans were current smokers (32% vs 54%, $P < .001$).

In Table 2, comparisons of symptom and HRQL measures by race are reported. African American subjects had significantly higher (worse) SGRQ total and subscores than Caucasian subjects, with differences ranging between approximately 5 and 10 points, exceeding the minimal clinically important difference for SGRQ in COPD of 4.[17] Analysis of MMRC also indicated greater levels of dyspnea in African American subjects ($P = .02$). No significant difference in exacerbation frequency was seen ($P = .47$); however, the percentage of African American subjects who experienced at least one hospitalized exacerbation in the previous year was greater than that for Caucasian subjects (32% vs 16%, $P < .001$).

Results of the first mixed-effects linear regression model for SGRQ total score are shown in Table 3. Factors that were significantly associated with worse HRQL were greater pack-year smoking history, younger age, lower FEV_1 % predicted, and greater dyspnea as measured by MMRC. The number of exacerbations per subject in the prior year also was significantly associated with higher SGRQ total score. Race was not an independent predictor of SGRQ total score. However, a significant interaction between exacerbation frequency and race was seen such that African Americans experienced even higher SGRQ scores for each additional exacerbation. Because more African Americans experienced a hospitalized exacerbation, we hypothesized that greater exacerbation severity is responsible for the greater impact of exacerbations on HRQL seen in these subjects. Therefore, we developed a second mixed-effects linear regression model where we substituted history of hospitalized exacerbations for total exacerbations in the previous year. Again, we detected a statistically significant race-exacerbation interaction: African American subjects with a hospitalized exacerbation had a 4.2 higher adjusted SGRQ score ($P = .04$) than Caucasian subjects with a hospitalized exacerbation (Table 4).

Discussion

COPD is an important health problem for African Americans. Death rates for African Americans with COPD increased more rapidly than for Caucasians between 1980 and 2000.[18] COPD also has been cited as a predictor of global decline in HRQL in African American middle-aged adults; however, the factors influencing HRQL in this patient population have been underexamined.[19] Here, we report that in simple group comparisons, African Americans had worse dyspnea and HRQL than did Caucasians. Our general linear model for SGRQ, however, reveals that the relationship between race and HRQL is complex. When we accounted for other factors that affect quality of life (age, sex, FEV_1 % predicted, pack-year smoking history, MMRC dyspnea score, 6MWD, education, current smoking status, and exacerbation frequency in the previous year), SGRQ total score actually was similar for African Americans and Caucasians without exacerbations. For subjects who experienced exacerbations, SGRQ score was increased to a greater relative extent for African Americans than for Caucasians. A significant effect on SGRQ score also was seen after substituting a history of hospitalized

Table 1—*Baseline Demographics by Race*

Variable	Caucasian	African American	*t* (*df*)	*P* Value
Age, y	65 ± 8.3	60 ± 8.7	−8.35 (314)	< .001[a]
FEV_1 % predicted	56 ± 23.8	55 ± 21.2	−0.61 (354)	.54
Pack-y smoking history	54 ± 26.9	42 ± 22.3	−7.34 (375)	< .001[a]
Current smokers	336 (32)	121 (54)	NA	< .001[a]
Women	484 (46)	113 (50)	NA	.27
BMI, kg/m^2	27.8 ± 6.0	27.8 ± 6.2	0.07 (318)	.94
Height, cm	170 ± 9.7	170 ± 9.5	0.13 (330)	.90
6-min walk distance, m	381 ± 135.2	298 ± 119.4	−9.25 (356)	< .001[a]
Education				
Less than HS	91 (9)	60 (27)	NA	< .001[a]
Graduated HS	267 (25)	63 (28)		
More than HS	691 (66)	101 (45)		

Data are presented as mean ± SD or No. (%), unless otherwise indicated. *df* = degrees of freedom; HS = high school; NA = not applicable.
[a]These comparisons remain statistically significant after controlling for multiple comparisons using the false discovery rate procedure.[15,16]

Table 2—*Symptom and Quality-of-Life Scores by Race*

Variable	Caucasian	African American	*t* (*df*)	*P* Value
SGRQ				
Total score	34.8 ± 21.5	43.2 ± 23.8	4.89 (306)	< .001[a]
Activity subscore	50.5 ± 28.4	60.8 ± 29.7	4.73 (316)	< .001[a]
Impacts subscore	24.0 ± 19.9	32.2 ± 23.5	4.86 (296)	< .001[a]
Symptom subscore	40.5 ± 25.2	46.0 ± 25.3	2.95 (325)	.003[a]
MMRC dyspnea score			NA	.02[a]
0	284 (27)	45 (20)		
1	142 (14)	27 (12)		
2	158 (15)	35 (16)		
3	289 (28)	59 (27)		
4	167 (16)	55 (25)		
Exacerbation frequency[b]			NA	.47
0	691 (66)	141 (63)		
1	191 (18)	40 (18)		
2	82 (8)	21 (9)		
3	37 (4)	12 (5)		
4	27 (3)	3 (1)		
5	3 (0.3)	2 (1)		
6	18 (2)	5 (2)		
Hospitalized exacerbation[c]				
0	878 (84)	152 (68)	NA	< .001[a]
1	171 (16)	72 (32)	…	…

Data are presented as mean ± SD or No. (%), unless otherwise indicated. MMRC = modified Medical Research Council; SGRQ = St. George Respiratory Questionnaire. See Table 1 legend for expansion of other abbreviations.

[a]These comparisons remain statistically significant after controlling for multiple comparisons using the false discovery rate procedure.[15,16]

[b]Number of COPD exacerbations reported in the year prior to enrollment.

[c]COPD exacerbations associated with a hospitalization in the year prior to enrollment.

exacerbation into the model. Furthermore, hospitalized exacerbations were more frequent among African Americans than Caucasians in the sample. These data underscore the need for a better understanding of the prevention and treatment of exacerbations in the African American patient population.

In general, few other data exist on symptoms and HRQL in African Americans with COPD. Using the San Diego Shortness of Breath Questionnaire, Criner et al[20] reported on dyspnea in African American subjects with COPD treated with tiotropium. Although improvements in pulmonary function were noted, no significant improvement in dyspnea was detected with the intervention. In the present analysis, we report significantly greater dyspnea in African Americans despite similar lung function. It is possible that the experience of dyspnea may differ between the African American and the Caucasian patient populations. Alternatively, these data also could reflect a lack of sensitivity for questionnaires used to assess dyspnea in this patient subpopulation.

We also attempted to better understand the factors behind racial differences in HRQL by building a multivariate model to determine the importance of race in relation to other predictors, such as dyspnea. Previously, Chatila et al[21] analyzed 42 African American and 1,156 Caucasian subjects enrolled in the National Emphysema Treatment Trial. In that analysis, no significant difference in HRQL was found, although the population was limited to patients with severe emphysema, and thus, the results may not apply to patients with more moderate COPD. In the present patient population, one of the most interesting findings is the greater relative impact of exacerbations on HRQL for African Americans. Although no significant difference in the frequency of exacerbations was noted between African Americans and Caucasians, a larger percentage of African Americans reported hospitalized exacerbations. Hence, greater severity could account for the greater relative impact of exacerbations on HRQL. In fact, when examined in the multivariate model, a history of hospitalized exacerbations was associated with an even higher SGRQ score (4.2 points) for African Americans than for Caucasians, which exceeds the minimal clinically important difference for SGRQ of 4.[17]

Multiple factors could account for differences in exacerbation severity between African Americans and Caucasians, including cultural, socioeconomic, and biological influences. Data from others help us to better understand these findings. Sarrazin et al[22] reported that African American subjects admitted to Veterans Administration hospitals with COPD exacerbations were more likely to be admitted to the ICU and receive mechanical ventilation, supporting the conclusion that African Americans may be more prone

Table 3—*Mixed-Effects Linear Regression Model for SGRQ Total Score Using Exacerbation Frequency in the Prior Year (N = 1,255)*

Predictor Variable and Level	Estimate	SE	*P* Value
Pack-y smoking history	0.066	0.014	< .001
Age, y	−0.256	0.048	< .001
Annual exacerbation rate race interaction			
African American	1.887	0.688	.006
Caucasian	Ref	…	…
Annual exacerbation rate	1.928	0.327	< .001
FEV_1 % predicted	−0.111	0.019	< .001
Sex			
Female	−1.486	0.705	.04
Male	Ref	…	…
MMRC dyspnea score	8.489	0.310	< .001
Race			
African American	−0.672	1.213	.58
Caucasian	Ref	…	…
6-min walk distance, m	−0.026	0.004	< .001
Education level			
More than HS	−4.805	1.139	< .001
Graduated HS	−2.919	1.206	< .001
Less than HS	Ref	…	…
Current smoking			
Yes	2.754	0.817	< .001
No	Ref	…	…

This mixed-effects linear regression model included clinical center as a random effect to account for possible regional and other differences. Clinical center did affect SGRQ total score ($P < .001$). Of the 1,273 subjects in GOLD stages I to IV, six subjects did not answer the question about current smoking, and 12 subjects did not answer the questions from which the MMRC dyspnea score was derived. As a result, 1,255 subjects were used in this regression analysis. GOLD = Global Initiative for Obstructive Lung Disease; Ref = referent group. See Table 1 and 2 legends for expansion of other abbreviations.

to severe exacerbations. There are also some data to suggest racial disparities in treatment of COPD. Racial disparities in home oxygen prescriptions, influenza vaccination administration, and referral for smoking cessation all have been reported in COPD, which could contribute to greater severity of exacerbations.[23] A study of treatment of COPD exacerbations in the ED also reported that African American patients were more likely to be uninsured and less likely to have a primary-care provider than Caucasian patients.[24] Finally, socioeconomic disparities could affect treatment and subsequent severity of acute exacerbations in that lower socioeconomic status is a known predictor of lower lung function and is more common among African Americans.[5] Highest education level achieved is one way of assessing and controlling for the impact of differences in socioeconomic status.[25] We found that the highest level of education achieved was lower for African Americans, and this was a significant predictor of worse HRQL.

Age and smoking history were identified as significant predictors of HRQL and differ by race. Despite similar lung function impairment for African Americans, these patients reported fewer pack-years smoked and younger age than did Caucasians. A recent subgroup analysis of the UPLIFT (Understanding Potential Long-term Impacts on Function with Tiotropium) trial also demonstrated higher SGRQ in younger subjects with COPD, despite fewer pack-years smoked and similar FEV_1 % predicted.[26] Thus, the impact of COPD on HRQL may be greater when it develops at an age when subjects would normally be more active. These data also raise the question about whether African Americans may be more susceptible to the development of COPD. Others have previously reported that African Americans have less smoke exposure for similar levels of lung dysfunction.[21,27] Additionally, the severity of emphysema for African Americans in the National Emphysema Treatment Trial is less despite no difference in lung function, suggesting that African Americans may have relatively more airways disease. Thus, biologic differences, differences in environmental exposure, or differences in treatment all could contribute to racial HRQL differences.[21]

Table 4—*Mixed-Effects Linear Regression Model for SGRQ Total Score Using Hospitalized Exacerbation Frequency in the Prior Year (N = 1,255)*

Predictor Variable and Level	Estimate	SE	*P* Value
Pack-y smoking history	0.062	0.014	< .001
Age, y	−0.237	0.049	< .001
Hospitalized exacerbation race interaction			
African American	4.187	2.020	.04
Caucasian	Ref	…	…
Hospitalized exacerbation	4.748	1.059	< .001
FEV_1 % predicted	−0.117	0.019	< .001
Sex			
Female	−1.074	0.711	.13
Male	Ref	…	…
MMRC dyspnea score	8.760	0.309	< .001
Race			
African American	−0.882	1.232	.47
Caucasian	Ref	…	…
6-min walk distance, m	−0.025	0.004	< .001
Education level	−4.490	1.149	< .001
More than HS	−2.457	1.219	.04
Graduated HS	Ref	…	…
Less than HS			
Current smoking			
Yes	2.585	0.823	.002
No	Ref	…	…

This mixed-effects linear regression model included clinical center as a random effect to account for possible regional and other differences. Clinical center did affect SGRQ total score ($P < .001$). Of the 1,273 subjects in GOLD stages I to IV, six subjects did not answer the question about current smoking, and 12 subjects did not answer the questions from which MMRC dyspnea score was derived. As a result, 1,255 subjects were used in this regression analysis. See Table 1-3 legends for expansion of abbreviations.

Current smoking was another factor determined to be more common in African Americans and is associated with worse HRQL in the multivariate analysis. In general, the prevalence of smoking cessation is higher among Caucasians than African Americans, despite the fact that African Americans tend to be highly motivated to quit.[28-30] It has been suggested that African Americans may be more prone to nicotine dependence.[30] Finally, 6MWD was lower for African Americans despite similar height, BMI, and lung function; shorter distance is associated with higher SGRQ in the multivariate model. Correspondingly, the largest racial difference in SGRQ subscores was the activity subscore, which differed by ~10 points between African Americans and Caucasians. A good explanation for these findings is not readily apparent, although it is possible that exercise tolerance is more limited in African Americans because of greater dyspnea.

A strength of this analysis is the large number of patients included, particularly African American subjects. A potential limitation is that recruitment was based through academic institutions, and as such, it is possible that our results reflect a tertiary-care center bias. However, recruitment strategies at centers were quite diverse and included recruitment of patients through clinics as well as through direct-to-subject marketing and advertisement campaigns. Furthermore, to our knowledge, this is the largest cohort of African Americans in any such study to date and therefore is likely to reflect the diversity of US patients better than any other such study to date. Additionally, a larger number of African Americans who were contacted about the study did not complete the study, with the primary reason being a decision not to proceed with a study visit after the phone screening. This limitation may represent a cultural bias, but it is difficult to know how it may have biased the quality-of-life analysis. Another potential limitation of our analysis is that the data were not analyzed for or designed for the analysis of access to medical care, which could affect HRQL. Potential recall bias also could exist with respect to retrospective reporting of exacerbation frequency. However, a recent analysis compared patient recall for exacerbations against those detected through diary cards during the same time period, and no significant difference was found.[31] Furthermore, the ECLIPSE (Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points) study also recently reported that the best predictor of exacerbations that are prospectively assessed are patient-reported history of exacerbations in the year prior to study entry.[32] These publications provide support for the robustness of patient exacerbation frequency recall as an outcome measure.

In conclusion, the present data demonstrate that the impact of exacerbations on HRQL, particularly hospitalized exacerbations, is greater for African Americans than for Caucasians. Racial differences in disease biology, symptom perception, symptom reporting, and receipt of treatment all could potentially be contributing factors. It is clear that a better understanding of exacerbations and interventions aimed at improving the prevention and treatment of COPD exacerbations in the African American population is of particular importance.

Acknowledgments

Author contributions: Drs Han and Foreman had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Dr Han: contributed to the data collection, analysis, and writing of the manuscript.
Dr Curran-Everett: contributed primarily to the data analysis and the statistical analysis, drafting, and review of intellectual content of the manuscript.
Dr Dransfield: contributed to the data collection and analysis and intellectual design of the analysis, review for important intellectual content, and approval of the final manuscript.
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Dr Zhang: contributed primarily to the data analysis and the statistical analysis, drafting, and review of intellectual content of the manuscript.
Dr Murphy: contributed primarily to the data analysis and the statistical analysis, drafting, and review of intellectual content of the manuscript.
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Dr Martinez: contributed to the data collection and analysis and intellectual design of the analysis, review for important intellectual content, and approval of the final manuscript.
Dr Westney: contributed to the data collection and analysis and intellectual design of the analysis, review for important intellectual content, and approval of the final manuscript.
Dr Foreman: contributed to the data collection, analysis, and writing of the manuscript.
Financial/nonfinancial disclosures: The authors have reported to *CHEST* the following conflicts of interest: In the past 3 years, Dr Han has participated in advisory boards for Boehringer Ingelheim GmbH, Pfizer, GlaxoSmithKline, Genentech, Novartis, and Medimmune. She has participated on speaker's bureaus for Boehringer Ingelheim GmbH, Pfizer, GlaxoSmithKline, the National Association for Continuing Education, and WebMD. She has consulted for Novartis and Nycomed, and has received royalties from UpToDate and ePocrates, Inc. In the past 3 years, Dr Dransfield has consulted for GlaxoSmithKline and Boehringer Ingelheim GmbH. His institution has received funds to conduct clinical research trials for GlaxoSmithKline and Boehringer Ingelheim GmbH. Over the past 3 years, Dr Make has participated in advisory boards, speaker bureaus, consultations, and multicenter clinical trials with funding from the National Heart, Lung, and Blood Institute; Abbott Laboratories; Astellas Pharma Inc; AstraZeneca;

Boehringer Ingelheim GmbH; Dey Pharma, LP; Embryon Inc; Forest Laboratories, Inc; GlaxoSmithKline; Nabi Biopharmaceuticals; Nycomed; Novartis Pharmaceuticals Corporation; Pfizer Inc; Respironics Inc; Merck/Schering-Plough; SeQual Technologies; and Talecris Biotherapeutics, Inc. Dr Martinez has served on advisory boards relating to COPD-related topics for GlaxoSmithKline; MedImmune, LLC; AstraZeneca; Merck & Co, Inc; Pearl Therapeutics Inc, Novartis Pharmaceuticals Corporation, United BioSource Corporation; Forest Laboratories, Inc; and Almirall, SA. He has consulted for Actelion Pharmaceuticals Ltd; Boehringer Ingelheim GmbH; Nycomed; Forest Laboratories; F. Hoffmann-La Roche Ltd; Bayer Corporation, Merck/Schering-Plough; Health Learning Systems; Talecris Biotherapeutics, Inc; Comgenex; fb Communications; BoomComm; and Actelion Pharmaceuticals Ltd. He has served on speaker's bureaus for GlaxoSmithKline; National Association for Continuing Education; Med-Ed; Potomac Center for Medical Education; Pfizer Inc; Boehringer Ingelheim GmbH; Merck/Schering-Plough; Vox Medica, Inc; American Lung Association; WebMD; ePocrates Inc; AstraZeneca; France Foundation; CME Incite; and Altana/Nycomed. His institution has received funds from Boehringer Ingelheim GmbH for a clinical trial. He has received royalties from Associates in Medical Marketing and Castle Connolly. He has developed educational materials for the France Foundation, HIT Global, and ePocrates Inc. He has served on steering committees for clinical trials supported by GlaxoSmithKline; Nycomed; Forest Laboratories, Inc; and Actelion Pharmaceuticals Ltd. Drs Curran-Everett, Criner, Zhang, Murphy, Hanzel, DeMeo, Regan, Westney, and Foreman have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Role of sponsors: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Heart, Lung, and Blood Institute or the National Institutes of Health. Neither the COPD Foundation nor any members of the industry advisory board composed of AstraZeneca, Boehringer Ingelheim GmbH, Novartis Pharmaceuticals Corp, or Sepracor Inc, had any input into the conduction or reporting of this analysis.

Additional information: The e-Appendixes can be found in the Online Supplement at http://chestjournal.chestpubs.org/content/140/5/1169/suppl/DC1.

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