ORIGINAL ARTICLE
COPD

Association of low income with pulmonary disease progression in smokers with and without chronic obstructive pulmonary disease

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ABSTRACT Low socioeconomic status has been associated with chronic obstructive pulmonary disease (COPD) but little is known about its impact on disease progression. We assessed the association of income to symptoms, pulmonary disease severity and progression in smokers with and without COPD.

The COPDGene cohort of 4826 smokers who reported annual income in phase 2 was analysed. Those who reported annual income <USD 15 000 per year were "low-income" and the remainder "higher income". Baseline demographics, symptoms, computed tomography (CT) imaging, and 5-year change in spirometry and CT metrics were characterised by group.

The low income group was younger (55.7 *versus* 61.7, p<0.0001), had more current smokers (73% *versus* 36%, p<0.0001), higher rates of severe exacerbations (13% *versus* 7%, p<0.0001), more chronic bronchitis (22% *versus* 14%, p<0.0001), reduced access to preventative care and lower quality of life, but less emphysema (4.7% *versus* 6.2%, p<0.0001). After 5 years the low-income group had more smoking-related disease progression, without significant change in exacerbations or symptoms, than higher-income subjects. Low income was an independent predictor of decreasing forced expiratory volume in 1 s (FEV_1) (p=0.001) and increased airway disease (p=0.007) after adjusting for baseline FEV_1, age, sex, race, exposures and current smoking.

Income disparity beyond the effects of race and current smoking is an important factor for disease progression. Worldwide, poverty and its consequences: associated respiratory exposures, limited healthcare access, and inadequate education about smoking risks, may exacerbate chronic lung disease.

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Cite this article as: Lowe KE, Make BJ, Crapo JD, *et al.* Association of low income with pulmonary disease progression in smokers with and without chronic obstructive pulmonary disease. *ERJ Open Res* 2018; 4: 00069-2018 [https://doi.org/10.1183/23120541.00069-2018].

This article has supplementary material available from openres.ersjournals.com

Received: May 21 2018 | Accepted after revision: Sept 11 2018

Introduction

Socioeconomic status (SES) has a broad impact on health outcomes and longevity and encompasses a variety of factors including income, education, occupation, race and social status. Lower incomes are specifically associated with reduced life expectancy, although the effect varies across geographic regions [1]. The reduction in life expectancy associated with low income is significantly influenced by regional differences in health behaviours, especially smoking [1]. Race and sex, which are strongly associated with SES, have been identified as risk factors for more severe chronic obstructive pulmonary disease (COPD) [2–5]. COPD is linked to smoking and other respiratory exposures such as gases, smoke, fumes and dust commonly found in low-income jobs. Earlier published works regarding impacts of low income and SES focused on symptoms [6, 7], disease severity [6], racial disparities [8, 9] and COPD within a general population cohort [10]. However, the effect of low income as a factor in disease progression has not been assessed comprehensively.

The COPDGene study enrolled 10 192 smokers with and without COPD (phase 1) and characterised them with spirometry, chest computed tomography (CT) scans and symptoms. Subjects returned for a 5-year follow-up visit (phase 2) to assess disease progression by repeat spirometry, CT imaging and reported symptoms. During the phase 2 visit they provided information on their current annual income, insurance status and access to medications and health care.

We assumed income stability over the 5-year interval and postulated that the lowest income subjects (earning <USD 15 000 USD per year) would have worse respiratory symptoms and decreased quality of life. We also hypothesised that low income would be associated with worse outcomes over 5 years, specifically increasing spirometric obstruction and progression of pulmonary disease on CT scans.

Methods

Study population

COPDGene (Genetic Epidemiology of COPD) is a longitudinal cohort study at 21 clinical centres across the United States. Subjects were current and former smokers aged 45–80 years at entry, non-Hispanic white or African American subjects who reported smoking histories >10 pack-years and had no other lung disease except asthma [9]. All subjects provided documentation of informed consent in writing and the study was approved at each clinical centre by their local institutional review board. Details of the phase 1 study have been presented previously [9]. In phase 2 of the study during the years 2013–2017, subjects completed a 5-year return visit. At this second visit, subjects had a comprehensive examination including repeat spirometry, a 6-min walk test, questionnaires and a CT scan. Subjects included in this analysis are those who completed an in-person phase 2 visit, passed spirometry quality control at both visits and reported income during the phase 2 visit (see figure 1 for CONSORT diagram).

The low-income group in our analysis was defined as participants earning less than the United States federal minimum wage of USD 7.25 per hour. A person earning minimum wage working 40 h per week,

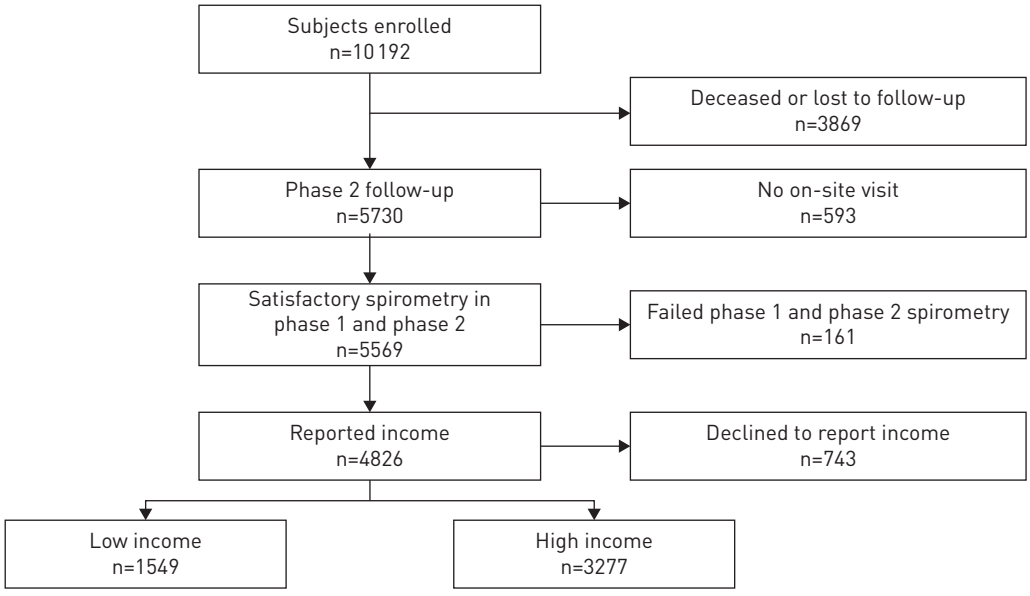

FIGURE 1 COPDGene consort diagram.

52 weeks per year (just over full time) would earn USD 15 080 before taxes. Any participant who reported earning more than USD 15 000 per year was categorised as higher income.

Aims

Our primary aim was to assess the role of low income as a predictor of disease progression for subjects with COPD and early smoking-related lung disease after correcting for the possible confounding variables of age, sex, race, current smoking, education, baseline function and pack-years. Disease progression variables included change in percentage emphysema, change in FEV_1 and change in gas trapping over a 5-year time period. Our secondary aim was to investigate the relationship of income to baseline patient variables including symptoms, spirometry and CT-based estimates of emphysema severity, airway wall thickness and gas trapping.

Questionnaires

Questionnaires in phase 1 included medical history, educational history, a modified American Thoracic Society respiratory questionnaire, the modified Medical Research Council (mMRC) dyspnoea score [11], St George's Respiratory Questionnaire (SGRQ) [12] and the Medical Outcomes Study 36-item short form survey (SF-36) [13]. In phase 2, the COPD Assessment Test (CAT) and a socioeconomic questionnaire were added. The socioeconomic questionnaire queried annual income, insurance status, home ownership and access to preventative care. Education was considered as a categorical variable, with high school or less *versus* any education beyond high school. Comorbid disease was self-reported on the medical history questionnaire. We calculated a nonweighted comorbidity score using the methodology of Putcha *et al.* [14], summing the number of comorbidities.

Functional evaluations

Function was evaluated using post-bronchodilator spirometry to determine forced expiratory volume in 1 s (FEV_1), forced vital capacity and 6-min walking distance (6MWD).

Radiographic measures

Inspiratory and expiratory CT scans were performed on all participants who consented. Details of the lung CT protocol and quantitative analysis have been reported elsewhere [15]. Inspiratory CT scans were analysed for emphysema as percentage low attenuation area at −950 Hounsfield Units (%LAA@-950HU) and adjusted lung density as well as for airway wall thickness. Expiratory CT scans were analysed for gas trapping using percentage low attenuation area at −856 Hounsfield Units (%LAA@-856HU). All CT scans were analysed using Thirona LungQ (Thirona, Nijmegen, the Netherlands).

Statistical analysis

Data were analysed using STATA 15.1 (StataCorp, College Station, TX, USA). Phase 1 to phase 2 changes were calculated for FEV_1, mMRC dyspnoea score, SGRQ total score and distance walked. The percentage emphysema, adjusted lung density, gas-trapping scores and airway wall thickness at phase 1 and phase 2 were used to calculate the 5-year difference in CT variables. Comparisons between groups with categorical variables were made using a Chi-squared test and continuous variables were compared with a two-tailed t-test. p-values <0.05 were considered significant. Multivariate linear regression was used to assess the independent effects of income and education on 1) baseline imaging measures of emphysema, gas trapping and airway wall thickness and 2) the 5-year change variables: FEV_1 % predicted, emphysema, gas trapping and airway wall thickness. Baseline models were fitted with age, race, sex, current smoking status, smoking pack-years, education and income; while change models added the baseline value of the change modelled (either FEV_1 % pred, emphysema, gas trapping or airway wall thickness). Statistically different demographic variables (table 1) and clinically significant variables were selected *a priori* for regression models.

Results

Demographics

4826 subjects self-reported annual income and other information about their socioeconomic situation. Of the full cohort, 1549 (32%) subjects reported an income of <USD 15 000 per year. The low-income participants were on average younger (55.7±7.4 years *versus* 61.7±8.5 years, $p<0.0001$), more likely to be current smokers (72.6% *versus* 35.5%, $p<0.0001$), had started smoking at an earlier age (16.7±5.1 years *versus* 17.2±4.1 years, $p=0.0016$), more likely to be using respiratory medications (42% *versus* 31%, $p<0.0001$) and were more likely to be African American (57% *versus* 16%, $p<0.0001$) (table 1). The two groups had similar smoking exposure (42.7±25.1 pack-years *versus* 42.6±22.7 pack-years, $p=0.8828$) at baseline. Spirometric disease severity was slightly worse in the low-income participants with mean FEV_1 78.4±23.2% pred compared to 80.4±23.0% pred in the higher-income group ($p=0.0042$). Distribution by Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage was similar between the two groups

TABLE 1 Demographics and baseline disease severity

	Low-income smokers (<USD 15000 per year)	Higher-income smokers (>USD 15000 per year)	p-value
Subjects n	1549	3277	
Age years	55.7±7.4	61.7±8.5)	<0.0001
African American	57	16	<0.0001
Male	49	52	0.031
BMI kg·m^{-2}	29.1±6.7	29.1±5.7	0.95
More than high-school education	45	77	<0.0001
ATS pack-years	42.5±25.0	42.2±22.6	0.66
Age started smoking years	16.7±5.1	17.2±4.1	0.0016
Current smoking status	73	36	<0.0001
Using respiratory medications	42	31	<0.0001
FEV_1 % pred	78.4±23.2	80.4±23.0	0.0042
FVC % pred	87.7±17.8	89.6±16.5	0.0002
FEV_1/FVC	0.70±0.14	0.68±0.14	0.0003
Percentage emphysema LAA@-950 HU	4.68±7.6	6.24±8.9	<0.0001
Percentage gas trapping LAA@-856 HU	19.3±17.9	20.5±17.8	0.0652
Airway wall thickness mm	1.063±0.231	1.018±0.211	<0.0001

Data are presented as mean±SD or %, unless otherwise stated. BMI: body mass index; ATS: American Thoracic Society; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LAA: low-attenuation areas.

(figure 2) with increased prevalence of preserved ratio impaired spirometry (PRISm) subjects in the low-income group and a small increase of GOLD stage 1 in the higher income group [16].

Symptoms, comorbid disease and quality of life

Symptoms were reported in both the phase 1 and phase 2 visits (table 2). Low-income subjects had significantly more symptoms (chronic bronchitis 22% *versus* 14%, severe exacerbations 13% *versus* 7%, mMRC dyspnoea score ⩾2 49% *versus* 28%) in phase 1 with similar results in phase 2. Low-income subjects scored higher (worse) on the CAT in phase 2, with a mean±SD score of 15.0±9.2, compared to 10.5±7.7 for higher-income subjects. Self-report of diabetes, congestive heart failure and stroke were significantly higher at baseline in the low-income group, while cancer, osteoarthritis, high cholesterol, hay fever and gastro-oesophageal reflux disease were significantly lower. Coronary artery disease, obesity, stomach ulcers, peripheral vascular disease, sleep apnoea and hypertension were not significantly different between groups. The overall comorbidity score was significantly lower in the low income group (online supplementary table S1). The low-income group had a mean SGRQ total score of 31.7±23.3 *versus* 19.3±18.8 in phase 1 and 31.8±23.16 *versus* 19.6±19.0 when assessed at their phase 2 visit, with higher

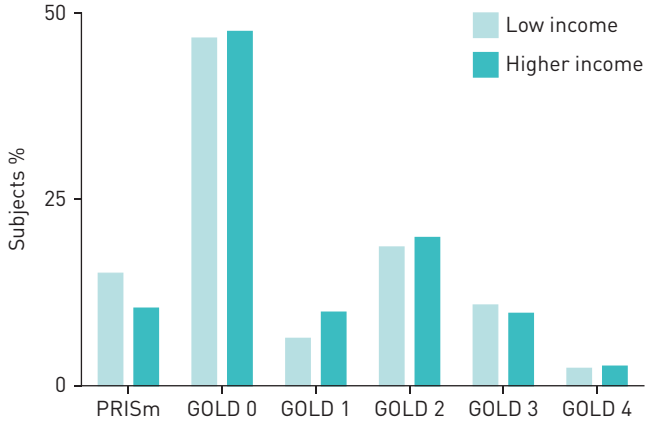

FIGURE 2 Income status by Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage. Higher- and low-income status was identified for phase 2 subjects who reported annual income based on income >USD 15 000 (higher) and <USD 15000 (low). Percentage of subjects in higher- and low-income categories is shown for each GOLD stage. In general, the distribution of income status is similar across the GOLD stages except for an excess of low-income subjects in the preserved ratio impaired spirometry group and fewer in GOLD stage 1.

TABLE 2 Symptoms, function and quality of life

	Low-income smokers (<USD 15 000 per year)	Higher-income smokers (>USD 15 000 per year)	p-value
Phase 1			
Chronic bronchitis	22	14	<0.0001
mMRC score	1.58±1.46	0.93±1.24	<0.0001
mMRC score >2	49	28	<0.0001
Severe exacerbation within the past year	13	7	<0.0001
SGRQ total	31.74±23.3	19.3±18.8	<0.0001
6MWD feet	1297±381	1486±352	<0.0001
SF-36 PCS	42.0±11.2	47.1±10.0	<0.0001
SF-36 MCS	45.95±12.6	52.4±9.8	<0.0001
Phase 2			
Chronic bronchitis	20	13	<0.0001
mMRC	1.64±1.51	0.99±1.29	<0.0001
mMRC score >2	52	31	<0.0001
Severe exacerbation within the past year	14	7	<0.0001
SGRQ total	31.79±23.1	19.6±19.0	<0.0001
6MWD feet	1168±438	1356±420	<0.0001
SF-36 PCS	39.9±11.4	45.3±10.6	<0.0001
SF-36 MCS	48.0±11.7	53.6±9.5	<0.0001
CAT score	15.0±9.2	10.5±7.7	<0.0001

Data are presented as % or mean±SD, unless otherwise stated. mMRC: modified Medical Research Council; SGRQ: St George's Respiratory Questionnaire; 6MWD: 6-min walking distance; SF-36: Medical Outcomes Study 36-item short-form questionnaire; PCS: physical component summary; MCS: mental component summary; CAT: Chronic Obstructive Pulmonary Disease Assesment Test.

SGRQ score indicating lower quality of life. Both the mental and physical component scores of the SF-36 were significantly lower (worse) in the low-income group at both time points.

Detailed analysis of respiratory medications is presented in online supplementary table S2. The low-income subjects report significantly more use of short-acting (37% *versus* 25%, p<0.0001) and long-acting medications (25% *versus* 21%, p=0.003) than higher-income subjects, probably in response to higher rates of respiratory symptoms.

Socioeconomic status

5-year follow-up phase 2 COPDGene visits were performed after implementation of the Affordable Care Act in the United States. In spite of that expansion of insurance coverage, 8% of low-income subjects lacked health insurance, compared to 2.4% of higher-income subjects (table 3). Low-income subjects were less likely to receive preventive care and more likely to seek care in emergency rooms (12% *versus* 3%) than higher-income subjects. In addition, educational background differed significantly, with 45% of the low-income group reporting education beyond a high school diploma compared to 77% of the higher-income group. Subjects reported stretching medications and limiting physician visits because of costs and income (table 4). Low-income subjects were twice as likely to not have gone to a doctor or not filled a prescription due to cost than higher income subjects. Low-income subjects used one or more cost-saving strategies significantly more often than higher-income subjects (25% *versus* 14%).

Baseline CT parameters

Emphysema and wall area percentage at the baseline visit showed differences based on income group, with less emphysema (4.68±7.6% *versus* 6.24±8.9%, p<0.0001) in the low-income group while airway wall thickness was greater (1.063±0.23 *versus* 1.018±0.21, p<0.0001) in the low-income subjects (table 1). Gas trapping was not significantly different at baseline. In multivariate linear regression models, income and educational level were highly significantly predictors of emphysema and segmental airway wall thickness at baseline, while education, but not income, was a significant factor for gas trapping (table 5). Exposures to dust and fumes were tested separately in the baseline models and were not significant predictors of baseline emphysema or gas trapping, but dust exposure was a significant factor for airway wall thickness (online supplementary tables) and income remained significant. Race was significant in all models, but after adjusting for income, African Americans had less emphysema, gas trapping and

TABLE 3 Socioeconomic factors beyond income

	Low-income smokers (<USD 15 000 per year)	Higher-income smokers (>USD 15 000 per year)	p-value
Education beyond high school	45	77	<0.0001
Residence			
Own home	19	70	<0.0001
Rent	59	22	<0.0001
Lack a permanent home	5	0.5	<0.0001
Have health insurance	90	97	<0.0001
Access to preventative care			
Get preventative care from doctor/clinic	88	97	<0.0001
Get preventative care from emergency room	8	1	<0.0001
Do not get preventative care	4	2	<0.0001
Lack a primary-care physician	9	3	<0.0001
Have access to internet	55	89	<0.0001
Exposures			
Worked in a dusty job	54	40	<0.0001
Worked in a fumes-related job	49	45	<0.0001

Data are presented as %, unless otherwise stated.

airway wall thickness. Although we adjusted for disease severity by FEV_1 in the models, the distribution of African Americans by GOLD stage differed from non-Hispanic white subjects with less severe disease. African Americans had greater proportions in GOLD 0 and PRISm categories (online supplementary figure S1).

Disease progression

At the 5-year visit there were no significant differences in change in dyspnoea, quality of life by the SGRQ total score or 6MWD between low-income and higher income groups (table 6). However, the low-income group showed greater progression in emphysema (0.68±3.7%) *versus* 0.06±3.95%, p<0.0001), gas trapping (2.31±9.5% *versus* 0.62±8.2%, p<0.0001) and FEV_1 (−3.26±12.9% pred *versus* −1.40±10.1% pred, p<0.0001). Change in airway wall thickness (−0.0061±0.137 *versus* −0.0025±0.108, p=0.409) was not significantly different.

Multivariate linear regression modelling for change outcomes (FEV_1, emphysema, gas trapping and airway disease using airway wall thickness) with baseline level of the outcome, age, sex, race, smoking status, pack-years and FEV_1 % pred (table 7) showed that low income was a significant predictor of disease progression in models for FEV_1 and airway wall thickness, but income was not a significant predictor of change in gas trapping or emphysema. Low income predicted worsening FEV_1 and increased airway wall thickness.

TABLE 4 Accommodation to healthcare costs

	Low-income smokers (<USD 15 000 per year)	Higher-income smokers (>USD 15 000 per year)	p-value
In the last year, because of the expense or lack of coverage, have you ...			
Not gone to your doctor when you needed to	11	5	<0.0001
Not filled a prescription	10	6	<0.0001
Stretched out a prescription medication by taking less of it or less often than it was prescribed	9	7	0.005
Not gone to the hospital when you needed to	6	1	<0.0001
Gone to an emergency room to be treated	9	2	<0.0001
One or more of the above	25	14	<0.0001

Data are presented as %, unless otherwise stated.

TABLE 5 Adjusted relationships of income to baseline computed tomography measures

	Coefficient (95% CI)	p>|t|
Baseline emphysema	Model R^2 0.3287	
Baseline FEV_1	−5.91 (−6.24– −5.58)	<0.0001
Height	0.15 (0.11–0.18)	<0.0001
Current smoking	−2.95 (−3.47– −2.44)	<0.0001
Female	−4.16 (−4.80– −3.53)	<0.0001
Age at recruitment	−0.075 (−0.11– −0.042)	<0.0001
Education beyond high school	−0.91 (−1.42– −0.40)	<0.0001
Lower income	−0.82 (−1.37– −0.27)	0.004
African American	−2.21 (−2.81– −1.61)	<0.0001
Smoking pack-years	0.012 (0.0023–0.022)	0.015
Baseline gas trapping	Model R^2 0.4874	
Baseline FEV_1	−14.67 (−15.30– −14.03)	<0.0001
Height	0.39 (0.33–0.46)	<0.0001
Current smoking	−3.92 (−4.93– −2.92)	<0.0001
Female	−9.78 (−11.02– −8.54)	<0.0001
Age at recruitment	0.74 (0.011–0.14)	0.022
Education beyond high school	−1.38 (−2.36– −0.37)	0.007
Lower income	1.00 (−0.089–2.10)	0.072
African American	−5.19 (−6.40– −3.99)	<0.0001
Smoking pack-years	0.023 (0.0031–0.042)	0.023
Baseline airway wall thickness	Model R^2 0.2928	
Baseline FEV_1	−0.10 (−0.11– −0.095)	<0.0001
Height	0.0036 (0.0027–0.0045)	<0.0001
Current smoking	0.080 (0.066– 0.094)	<0.0001
Female	−0.18 (−0.20– −0.17)	<0.0001
Age at recruitment	−0.0020 (−0.0028– −0.0011)	<0.0001
Education beyond high school	−0.018 (−0.032– −0.0048)	0.008
Lower income	0.021 (0.0062– 0.036)	0.005
African American	−0.07 (−0.083– −0.051)	<0.0001
Smoking pack-years	0.00069 (0.00042–0.00095)	<0.0001

FEV_1: forced expiratory volume in 1 s.

TABLE 6 Income status and 5-year change in spirometry, dyspnoea, health-related quality of life and imaging characteristics

	Low-income smokers (<USD 15 000 per year)	Higher-income smokers (>USD 15 000 per year)	p-value
FEV_1 % pred	−3.26±12.9	−1.40±10.1	<0.0001
FEV_1 mL	−225.6±342	−202.1±280	0.0115
FEV_1 mL per year	−40.0±61.5	−35.9±50.0	0.0142
Loss of >300 mL in FEV_1 n (%)	570 (36.8%)	1055 (32.19%)	0.002
mMRC dyspnoea score[#]	0.0575±1.43	0.0649±1.14	0.87
SGRQ total score	0.0442±19.5	0.298±13.2	0.6
Distance walked feet[¶]	−130±401	−128±335	0.82
Adjusted lung density[+]	−1.90±12.1	−0.35±11.5	0.0003
Emphysema[+] %	0.677±3.74	0.06±3.95	<0.0001
Gas trapping[§] %	2.31±9.52	0.623±8.17	<0.0001
Airway wall thickness mm	−0.0061±0.137	−0.0025±0.108	0.409
Current smokers	−0.0051	−0.017	0.083
Former smokers	−0.0086	0.0051	0.0291

Data are presented as mean±SD, unless otherwise stated. FEV_1: forced expiratory volume in 1 s; mMRC: modified Medical Research Council; SGRQ: St George's Respiratory Questionnaire. [#]: n=1547 (low income), n=3271 (higher income); [¶]: n=1503 (low income), n=3234 (higher income); [+]: n=1085 (low income), n=2489 (higher income); [§]: n=828 (low income), n=2133 (higher income).

TABLE 7 Associations of income and education to disease progression

	Coefficient (95% CI)	p-value
Change in FEV_1 mL	Model R^2 0.0660	
Baseline FEV_1 % pred	−2.78 (−3.13– −2.41)	<0.0001
Current smoking	−51.36 (−70.99– −31.73)	<0.0001
Female	68.47 (51.85–85.09)	<0.0001
Age at recruitment	−0.39 (−1.54–0.77)	0.51
Education beyond high school	−7.96 (−27.00–11.08)	0.41
Low income	−36.58 (−57.23– −15.93)	0.001
African American race	49.21 (27.48–70.93)	<0.0001
Smoking pack-years	−0.89 (−1.27– −0.51)	<0.0001
Change in emphysema	Model R^2 0.0925	
Baseline emphysema	−0.017 (−0.035–0.00073)	0.060
Baseline FEV_1 % pred	−0.051 (−0.058– −0.045)	<0.0001
Current smoking	0.68 (0.39–0.98)	<0.0001
Female	−0.039 (−0.29–0.21)	0.76
Age at recruitment	−0.0057 (−0.023–0.011)	0.51
Education beyond high school	0.21 (−0.075–0.49)	0.15
Low income	0.14 (−0.17–0.45)	0.39
African American race	0.31 (−0.019–0.64)	0.065
Smoking pack-years	0.0051 (−0.00070–0.011)	0.085
Change in airway wall thickness	Model R^2 0.1121	
Baseline airway wall thickness	−0.20 (−0.22– −0.18)	<0.0001
Baseline FEV_1 % pred	−0.00018 (−0.00036– −0.0000048)	0.044
Current smoking	0.0060 (−0.0029–0.015)	0.185
Female	−0.022 (−0.030– −0.014)	<0.0001
Age at recruitment	0.00070 (0.00019–0.0012)	0.008
Education beyond high school	−0.0013 (−0.0099–0.0073)	0.76
Low income	0.013 (0.0036–0.022)	0.007
African American race	−0.015 (−0.025– −0.0050)	0.003
Smoking pack-years	0.00013 (−0.000042–0.00031)	0.136

FEV_1: forced expiratory volume in 1 s.

Discussion

Individuals with an annual income at or below the US minimum wage level had significantly greater impacts of smoking-related disease. Although the low-income group had less emphysema at baseline, they showed greater disease progression over 5 years in FEV_1 and airway wall thickness. Current smoking was a clear factor predicting disease progression, but the effect of low income on disease progression remained after adjusting for current smoking. The adjusted difference in FEV_1 between the low and higher income groups was 37 mL greater loss in the low-income group. This is a similar magnitude of effect to the adjusted impact of current smoking on FEV_1 at 51 mL loss. These results suggest that low income is important and that factors other than continued smoking are involved in the relationship between low income and disease.

At baseline, low-income subjects had worse quality of life, worse dyspnoea, more chronic bronchitis and a shorter 6MWD, although smoking pack-years were not significantly different. Both current smoking and respiratory exacerbations requiring an emergency room visit or hospitalisation occurred twice as often in the low-income group relative to subjects reporting higher income. Our low-income group was similar in the distribution of disease severity to the higher-income subjects, but had more respiratory symptoms and had greater impairment in 6MWD, despite being significantly younger.

Factors that we considered to explain these results include that our low-income group reported less education, potentially impeding understanding of smoking risks; were less likely to have health insurance; and less likely to get preventative care from a doctor or clinic. In addition, they were more likely to have skipped medical visits or medications due to costs. Although they did report more respiratory exposures, the effect of those exposures on disease progression was not significant after adjusting for other factors. In addition, increased exposure to air pollution may play a role, but we do not have data available to assess that. Higher rates of respiratory medication use in the low-income group may be due to greater symptoms, or it may be the result of inadequate preventive and primary care.

Key social factors associated with low income and SES previously suggested to play a role in worse health include smoking, education, healthcare/insurance and unhealthy living conditions [17]. Smoking is much more prevalent in lower-income individuals [18] and CHETTY *et al.* [1] found local geographic variation in mortality that was associated with smoking behaviour. In the CHETTY *et al.* study, regional increased mortality linked to smoking behaviour was associated with heart disease and cancer, rather than increases in accidents, suicide or homicide. Others have identified associations between low SES and reduced lung function [6], increased hospitalisations [10] and increased mortality from respiratory disease [19]. In a systematic review, GERSHON *et al.* [7] identified consistently negative effects of low SES on COPD symptoms, morbidity and mortality. In that meta-analysis, measures of SES included income, education and occupation. They found that individuals of the lowest SES were twice as likely to have poor outcomes as the higher-income group. Comparing studies across multiple diseases, they found that the negative impact of SES was greatest in COPD relative to diabetes, heart disease, stroke and cancer. Our findings are consistent with these published results and add detail about access to care and impact of low income on decision-making to seek care and comply with treatment.

Our low-income group had a greater proportion of African Americans, but we did not find worse disease at baseline or greater progression in these subjects; in fact, we found less after adjusting for income. The role of race in COPD risk and progression remains unclear, potentially because of the complexities of SES and genetic factors that may influence risk of disease. EISNER *et al.* [6] in a study of insured health maintenance organisation subjects found that African Americans were not at increased risk of greater COPD severity after adjusting for demographics and physical characteristics. Our population varied in insurance status, but our results suggest that economics rather than race were the major factors predicting progression. African American subjects who experience exacerbations have worse quality of life than non-Hispanic white subjects with exacerbations [20], and they appear to have increased susceptibility to developing disease after smoking exposure [3], yet early work from the COPDGene study showed that African Americans had less emphysema than non-Hispanic white subjects adjusting for smoking pack-years, age and current smoking [4].

Education may influence decisions to continue smoking as well as interactions with the medical profession and compliance with treatment. A Norwegian study showed an association of lower educational level with greater emphysema but not airway wall thickness in COPD patients within a racially homogenous, rural population [21]. A previous COPDGene study relating parental COPD to risk of disease found that race was not significant, but education was an independent predictor of COPD [22]. Persistent smoking is associated with both lower income levels and lower educational attainments [18, 23]. Overall, the complex interplay of income, education, comorbidities and other factors increase the difficulty of defining solutions to continued smoking. The prominent role of continued smoking in low-income individuals suggests that strategies to improve outcomes must be linked to smoking cessation programmes. Smoking cessation programmes should be targeted to the needs and issues of low-income smokers.

Strengths of this study include the large cohort size, geographic diversity of the 21 clinical centres, extensive longitudinal clinical and radiographic data and the enhanced enrolment of African Americans. Limitations to generalisability include a US population that has unique and incomplete insurance coverage. Additionally, income level was documented at the phase 2 visit, not the initial visit when all of the other baseline variables were evaluated. While metrics of SES such as income and education have some stability over time [24], reverse causality cannot be excluded in this analysis. Those with faster disease progression may have been forced to retire, subsequently reducing their income from baseline to the reported level at the phase 2 visit. If they fell into the lowest category, this would bias the estimate of the difference between the low-income and the high-income group away from the null (overestimating the effect). However, the mean social security payment in the US is ~USD 16 000 per year and retirement will not necessarily result in a drop into the lowest income category.

The information on income, education, comorbid disease, medication use and symptoms are all self-reported. Although verification of income and education would be ideal, it is uncommon to have that type of validation. Since subjects were offered the option to decline to answer these questions, we assume that responses are reflective of their social and economic situation. Although the lower comorbidity score in the low-income group may be accurate (possibly due to the lower average age), there may also be an ascertainment bias in that these subjects have reduced access to primary preventative care and may not have had an opportunity for physician diagnosis of asymptomatic conditions such as hypertension and high cholesterol. Additionally, while we have data on which medications subjects are prescribed, we do not have information on adherence, though our data on accommodations to healthcare costs suggest that low-income subjects may have lower adherence (more likely to not fill prescriptions, more likely to stretch out a prescription). Lower adherence rates may influence exacerbation rates and disease progression.

We chose to study the relationship of low income to a breadth of smokers both with and without spirometric COPD. Smoking impacts on the lung including emphysema, gas trapping and airway wall thickening are identified in smokers without obstruction [25]. We used CT metrics, reported symptoms and spirometry to provide a comprehensive analysis of baseline disease and progression.

The economic burden of smoking-related lung disease and COPD in the United States is sizeable, estimated to be USD 38.8 billion in 2005 [26]. As the third leading cause of death in the United States, there is value in improving outcomes of care for COPD. Worldwide, smoking and other respiratory exposures are common, and COPD is the fourth leading cause of death. Poverty and inadequate education are key issues to consider in order to reduce the burden of respiratory disease. Beyond smoking cessation, we identified a range of factors that could be addressed, including access to primary care and preventive care, access to health insurance and better information about health conditions. Although this study is based on data from the United States, similar associations of low SES to worse COPD have been identified in European cohorts, as well as around the world [7, 10, 21, 27]. Recognising and addressing the role of poverty in increased burden of disease, worse outcomes and more rapid disease progression represents an important strategy for all societies.

Author contributions: Concept: K.E. Lowe, E.A. Regan, J.D. Crapo and B.J. Make; data analysis: K.E. Lowe and E.A. Regan; manuscript development: K.E. Lowe, B.J. Make, J.D. Crapo, G.L. Kinney, J.E. Hokanson, V. Kim, A.S. Iyer, S.P. Bhatt, K.F. Hoth, K.E. Holm, R. Wise, M.G. Foreman, T.J. Stone and E.A. Regan; manuscript writing and editing: K.E. Lowe, B.J. Make, J.D. Crapo, J.E. Hokanson, G.L. Kinney, V. Kim, A.S. Iyer, S.P. Bhatt, K.F. Hoth, K.E. Holm, R. Wise, D. DeMeo, M.G. Foreman, T.J. Stone and E.A. Regan.

Conflict of interest: K.E. Lowe has nothing to disclose. B.J. Make reports grants and personal fees from AstraZeneca (international PI for multicentre clinical trial, medical advisory board, disease-state presentation, grant funds provided to and controlled by National Jewish Health); support from Spiration (reviewed clinical trial data, data and safety monitoring board); grants, personal fees and other support from GlaxoSmithKline (advisory board member, disease-state presentation, multicentre trial funds provided to and controlled by National Jewish Health); grants, personal fees and other support from Sunovian (medical board member, grant funds provided to and controlled by National Jewish Health); support for CME activity from Consensus Medical Education, Integrity Medical Education, Mt Sinai Medical Center, Web MD, Up-To-Date, National Jewish Health, SPIRE Learning, the American College of Chest Physicians, Projects in Knowledge, Hybrid Communications, Peer Review Institute, Cleveland Clinic, Medscape and Ult Medical Academy; personal fees from Novartis (medical advisory board, consultant); grants from National Heart, Lung and Blood Institute (grant funds provided to and controlled by National Jewish Health); personal fees from CSL Bering, Verona, Boehringer Ingelheim, Theravance and Circassia (medical advisory boards); and grants from Pearl (research funds provided to and controlled by National Jewish Health), all outside the submitted work. J.D. Crapo has nothing to disclose. G.L. Kinney has nothing to disclose. J.E. Hokanson has nothing to disclose. V. Kim reports personal fees from Medscape (peer reviewer), Gala Therapeutics (advisory board) and ABIM Critical Care Testwriting Committee (chairman), and grants from NHLBI (K23HL094696), outside the submitted work. A.S. Iyer reports grants from the Agency for Healthcare Research and Quality (K12 HS023009), outside the submitted work. S.P. Bhatt reports grants from NIH (K23HL133438) and ProterixBio (research grant to institution), during the conduct of the study. K.F. Hoth has nothing to disclose. K.E. Holm reports personal fees from AlphaNet, outside the submitted work. R. Wise reports grants from AstraZeneca/Medimmune, Boehringer Ingelheim, Teva, Pearl Therapeutics and GSK; and personal fees from AstraZeneca/Medimmune (data monitoring committee and consulting), Boehringer Ingelheim (steering committee and data monitoring committee), Contrafect (clinical end-point committee), Pulmonx (data safety monitoring committee), Roche (data monitoring committee), Spiration (steering committee), Sunovion (workshop and consulting), Teva, Circassia, Pneuma, Verona, Aradigm and Dinali (all for consulting), Merck (data monitoring committee), GSK (data monitoring committee and consulting) and Bonti (safety review committee), all outside the submitted work. Conflicts of interest for R. Wise are reported to and managed by Johns Hopkins University School of Medicine. D. DeMeo reports personal fees from Novartis and grants from NIH, outside the submitted work. M.G. Foreman has nothing to disclose. T.J. Stone has nothing to disclose. E.A. Regan has nothing to disclose.

Support statement: The project described was supported by award number U01 HL089897 and award number U01 HL089856 from the National Heart, Lung, and Blood Institute. 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. The COPDGene project is also supported by the COPD Foundation through contributions made to an Industry Advisory Board comprised of AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis, Pfizer, Siemens and Sunovion. Funding information for this article has been deposited with the Crossref Funder Registry.

References

1 Chetty R, Stepner M, Abraham S, *et al.* The association between income and life expectancy in the United States, 2001–2014. *JAMA* 2016; 315: 1750–1766.
2 Han MK, Curran-Everett D, Dransfield MT, *et al.* Racial differences in quality of life in patients with COPD. *Chest* 2011; 140: 1169–1176.
3 Dransfield MT, Davis JJ, Gerald LB, *et al.* Racial and gender differences in susceptibility to tobacco smoke among patients with chronic obstructive pulmonary disease. *Respir Med* 2006; 100: 1110–1116.
4 Hansel NN, Washko GR, Foreman MG, *et al.* Racial differences in CT phenotypes in COPD. *COPD* 2013; 10: 20–27.
5 McGhan R, Radcliff T, Fish R, *et al.* Predictors of rehospitalization and death after a severe exacerbation of COPD. *Chest* 2007; 132: 1748–1755.

6 Eisner MD, Blanc PD, Omachi TA, *et al.* Socioeconomic status, race and COPD health outcomes. *J Epidemiol Community Health* 2011; 65: 26–34.
7 Gershon AS, Dolmage TE, Stephenson A, *et al.* Chronic obstructive pulmonary disease and socioeconomic status: a systematic review. *COPD* 2012; 9: 216–226.
8 Dransfield MT, Bailey WC. COPD: racial disparities in susceptibility, treatment, and outcomes. *Clin Chest Med* 2006; 27: 463–471.
9 Regan EA, Hokanson JE, Murphy JR, *et al.* Genetic epidemiology of COPD (COPDGene) study design. *COPD* 2010; 7: 32–43.
10 Prescott E, Lange P, Vestbo J. Socioeconomic status, lung function and admission to hospital for COPD: results from the Copenhagen City Heart Study. *Eur Respir J* 1999; 13: 1109–1114.
11 Mahler DA, Wells CK. Evaluation of clinical methods for rating dyspnea. *Chest* 1988; 93: 580–586.
12 Jones PW. St. George's Respiratory Questionnaire: MCID. *COPD* 2005; 2: 75–79.
13 Jones PW, Nadeau G, Small M, *et al.* Characteristics of a COPD population categorised using the GOLD framework by health status and exacerbations. *Respir Med* 2014; 108: 129–135.
14 Putcha N, Puhan MA, Drummond MB, *et al.* A simplified score to quantify comorbidity in COPD. *PLoS One* 2014; 9: e114438.
15 Schroeder JD, McKenzie AS, Zach JA, *et al.* Relationships between airflow obstruction and quantitative CT measurements of emphysema, air trapping, and airways in subjects with and without chronic obstructive pulmonary disease. *AJR Am J Roentgenol* 2013; 201: W460–W470.
16 Wan ES, Castaldi PJ, Cho MH, *et al.* Epidemiology, genetics, and subtyping of preserved ratio impaired spirometry (PRISm) in COPDGene. *Respir Res* 2014; 15: 89.
17 Bull ER, Dombrowski SU, McCleary N, *et al.* Are interventions for low-income groups effective in changing healthy eating, physical activity and smoking behaviours? A systematic review and meta-analysis. *BMJ Open* 2014; 4: e006046.
18 Casetta B, Videla AJ, Bardach A, *et al.* Association between cigarette smoking prevalence and income level: a systematic review and meta-analysis. *Nicotine Tob Res* 2017; 19: 1401–1407.
19 Cournane S, Byrne D, Conway R, *et al.* Effect of social deprivation on the admission rate and outcomes of adult respiratory emergency admissions. *Respir Med* 2017; 125: 94–101.
20 Caraballo RS, Giovino GA, Pechacek TF, *et al.* Racial and ethnic differences in serum cotinine levels of cigarette smokers: Third National Health and Nutrition Examination Survey, 1988–1991. *JAMA* 1998; 280: 135–139.
21 Gjerdevik M, Grydeland TB, Washko GR, *et al.* The relationship of educational attainment with pulmonary emphysema and airway wall thickness. *Ann Am Thorac Soc* 2015; 12: 813–820.
22 Hersh CP, Hokanson JE, Lynch DA, *et al.* Family history is a risk factor for COPD. *Chest* 2011; 140: 343–350.
23 Hosseinpoor AR, Parker LA, Tursan d'Espaignet E, *et al.* Socioeconomic inequality in smoking in low-income and middle-income countries: results from the World Health Survey. *PLoS One* 2012; 7: e42843.
24 Miething A, Åberg Yngwe M. Stability and variability in income position over time: exploring their role in self-rated health in Swedish survey data. *BMC Public Health* 2014; 14: 1300.
25 Regan EA, Lynch DA, Curran-Everett D, *et al.* Clinical and radiologic disease in smokers with normal spirometry. *JAMA Intern Med* 2015; 175: 1539–1549.
26 Foster TS, Miller JD, Marton JP, *et al.* Assessment of the economic burden of COPD in the U.S.: a review and synthesis of the literature. *COPD* 2006; 3: 211–218.
27 Grigsby M, Siddharthan T, Chowdhury MA, *et al.* Socioeconomic status and COPD among low- and middle-income countries. *Int J Chron Obstruct Pulmon Dis* 2016; 11: 2497–2507.