Contribution of Individual and Neighborhood Factors to Racial Disparities in Respiratory Outcomes

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 ONLINE DATA SUPPLEMENT

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<u>**1. Statistical analysis**</u>

Descriptive analyses were used to examine means and standard deviations or proportions and counts. The unadjusted differences between blacks and whites with regards to demographic, COPD-related risk factors, neighborhood risk factors and respiratory outcomes were examined using t-tests and chi-squared tests for continuous and categorical variables respectively. To assess the impact of different sets of covariates on the association between race and outcome, we used linear regression for the continuous outcomes and negative binomial regression for the count outcome with follow-up days as offset in the latter, based on generalized linear mixed models with random intercept for study site. We regressed respiratory outcomes on race, with an initial model **(Model 1)** adjusting for individual characteristics (age, gender, smoking history, pack-years, BMI, depression, marital status, COPD status). We then both separately and sequentially adjusted for individual-level SES (income, education) and neighborhood SES (poverty rate, educational attainment, unemployment rate, median household income, ADI and food access). In the first sequential adjustment, we first adjusted for individual-level SES **(Model 2)** followed by adjustment for neighborhood-level SES **(Model 3)**. In the second sequence, we switched the order, adjusting for neighborhood SES first followed by individual SES **(Table S1)**. Each model provided a measure of the association between race and the outcome of interest. The difference in the strength of these measures, and the change after adding sequential variables, is then evaluated as the contribution of each set of variables to the black-white difference in COPD outcomes, using the "difference-method" within the framework of mediation analysis for multiple mediators. [1] In this type of analyses, "mediation proportion" is conceptualized as the proportional reduction in the exposure-outcome association from before and after the adjustment with mediators**.** In our

study, we first tested the mediation proportion based on individual-level SES factors alone (education, income). Next, we tested the additional mediation proportion by neighborhood-level SES factors by testing the proportional reduction in race-outcome association from individual-level SES adjusted model to the model that included neighborhood SES. Lastly, we tested the total mediation proportion by testing the proportional reduction in race-outcome association from the minimally adjusted model to the model that included both individual and neighborhood-level SES. We, then, replicated the procedure switching the order of sequence, with adjustment by neighborhood-level SES first. We allowed mediation proportion to exceed 100% where the signs of race-outcome associations were reversed following SES adjustment, as well as below 0% where there was proportional gain instead of reduction following SES adjustment The point estimates and 95% confidence interval of all our regression parameters, as well as the mediation proportion and its confidence intervals, were obtained using the recommended bootstrap approach [1] with 1000 replications.

Sensitivity analyses were conducted adjusting for site as a fixed effect and additionally adjusting models for individual parameters including baseline lung function and comorbidity count [2]; occupational exposure to hazardous vapor, gas, dust, or fumes [3]; and additional neighborhood factors including urban/rural status, region, and ambient pollution (particulate matter and ozone). Further, we tested for potential interaction between race and COPD status; and stratified models were shown separately for participants with COPD. In addition, we tested for variance inflation factor (VIF) to assess for potential collinearity of exposures. The VIF for our primary exposure of interest, race, in our fully adjusted model ranged 1.64~1.67; similarly, the VIF for individual and neighborhood SES variables ranged between 1.20 (minimum) to 2.74 (maximum).

All parameter estimates in our regression analysis, including mediation proportions and their confidence intervals, were generated based on bootstrap approach. [1] The threshold for statistical significance was $P < 0.05$ based on 95% confidence interval; all statistical analyses were performed using STATA v.15.1 (Stata Corp, College Station, TX).

Table E1. Association of race with respiratory outcomes and CT metrics, adjusted for neighborhood SES first and then individual SES.

	Model 1 (Adjusted for Demographics and Individual Clinical Characteristics)	M1a (Mediation from Model 1 to Model 2; Mediation by Neighborhood SES) (%)	Model 2 (Model 1 Also Adjusted for Neighborhood SES)	M2a (Additional Mediation from Model 2 to Model 3; Mediation by Individual SES) (%)	Model 3 (Model 2 Also Adjusted for Individual SES)	M3a (Mediation from Model 1 to Model 3; Total Mediation by Neighborhood and Individual SES) (%)
COPD health related outcomes						
CAT*	**1.98 (1.13, 2.83)**	**32%**	**1.34 (0.41, 2.26)**	20%	**1.07 (0.14, 1.98)**	**46%**
mMRC*	**0.16 (0.05, 0.26)**	15%	**0.14 (0.02, 0.24)**	22%	0.11 (-0.02, 0.21)	**33%**
SGRQ overall*	**4.33 (2.28, 6.27)**	**31%**	**3.01 (0.96, 5.02)**	30%	2.10 (-0.08, 4.12)	**52%**
6MWD*	**-30.3 (-43.1, -17.9)**	**52%**	**-14.6 (-28.8, -1.4)**	36%	-9.3 (-23.2, 4.3)	**69%**
Total severe exacerbation count in past year **	**2.35 (1.75, 3.12)**	**34%**	**1.76 (1.27, 2.44)**	5%	**1.71 (1.24, 2.37)**	**37%**
CT metrics						
Pi10*	**0.016 (0.008, 0.024)**	13%	**0.014 (0.005, 0.023)**	3%	**0.013 (0.004, 0.023)**	16%
% emphysema*	**1.76 (0.69, 2.78)**	-10%	**1.93 (0.79, 3.02)**	1%	**1.90 (0.72, 2.99)**	-8%
% air trapping*	**3.32 (1.28, 5.09)**	16%	**2.77 (0.69, 4.67)**	11%	**2.47 (0.31, 4.40)**	26%

Notes: The regression analysis switched the order of M2 and M3 from our original model. *Entries represent mean differences (β) and their 95% confidence interval (CI) comparing blacks to whites. ** Entries represent incidence rate ratio and their 95% confidence interval (Cl) comparing blacks to whites. Model 1- adjusted participant's characteristics of age, gender, smoking history, pack-years, BMI, marital status, COPD status. Model 2 – Model 1 additionally adjusted for neighborhood SES (poverty rate, education, unemployment, median household income, Area Deprivation Index and Food Access) estimated at the census tract level using data from the 2010 US Census. Model 3 – Model 1 additionally adjusted for neighborhood SES (poverty rate, education, unemployment, median household income, Area Deprivation Index and Food Access) and participant SES (education, income). **Boldface entries indicate a statistically significant association with $P < 0.05$.**

Table E2. Association of race with respiratory outcomes and CT metrics, fixed site effect

	Model 1 (Adjusted for Demographics and Individual Clinical Characteristics)	M1a (Mediation from Model 1 to Model 2; Mediation by Individual SES) (%)	Model 2 (Model 1 Also Adjusted for Individual SES)	M2a (Additional Mediation from Model 2 to Model 3; Mediation by Neighborhood SES) (%)	Model 3 (Model 2 Also Adjusted for Neighborhood SES)	M3a (Mediation from Model 1 to Model 3; Total Mediation by Individual and Neighborhood SES) (%)
COPD health related outcomes						
CAT*	**1.90 (1.05, 2.75)**	**27%**	**1.38 (0.50, 2.25)**	25%	**1.04 (0.13, 1.97)**	**46%**
mMRC*	**0.13 (0.02, 0.23)**	**37%**	0.08 (-0.03, 0.18)	-2%	0.08 (-0.04, 0.20)	35%
SGRQ overall*	**4.09 (2.11, 5.90)**	**37%**	**2.59 (0.55, 4.51)**	26%	1.91 (-0.17, 3.90)	**53%**
6MWD*	**-30.9 (-44.0, -16.2)**	**33%**	**-20.8 (-34.2, -7.3)**	53%	-9.7 (-24.2, 5.1)	**68%**
Total severe exacerbation count in past year **	**2.27 (1.73, 3.11)**	7%	**2.14 (1.62, 2.93)**	32%	**1.67 (1.22, 2.39)**	**37%**
CT metrics						
Pi10*	**0.016 (0.008, 0.024)**	7%	**0.015 (0.007, 0.023)**	10%	**0.013 (0.005, 0.023)**	16%
% emphysema*	**1.69 (0.71, 2.71)**	-1%	**1.70 (0.73, 2.77)**	-9%	**1.85 (0.86, 2.93)**	-10%
% air trapping*	**3.02 (1.13, 4.99)**	13%	**2.62 (0.64, 4.66)**	14%	**2.25 (0.20, 4.32)**	25%

Notes: Fixed effect for study site was specified in all models. *Entries represent mean differences (β) and their 95% confidence interval (CI) comparing black to white. ** Entries represent incidence rate ratio and their 95% confidence interval (Cl) comparing black to white. Model 1- adjusted participant's characteristics of age, gender, smoking history, pack-years, BMI, marital status, COPD status, study site. Model 2 – Model 1 additionally adjusted for participant SES (education, income). Model 3 – Model 1 additionally adjusted for participant SES and neighborhood SES (poverty rate, education, unemployment, median household income, Area Deprivation Index and Food Access) estimated at the census tract level using data from the 2010 US Census. **Boldface entries indicate a statistically significant association $P < 0.05$.**

Table E3. Association of race with respiratory outcomes and CT metrics, adjusted for baseline lung function and comorbidity

	Model 1 (Adjusted for Demographics and Individual Clinical Characteristics)	M1a (Mediation from Model 1 to Model 2; Mediation by Individual SES) (%)	Model 2 (Model 1 Also Adjusted for Individual SES)	M2a (Additional Mediation from Model 2 to Model 3; Mediation by Neighborhood SES) (%)	Model 3 (Model 2 Also Adjusted for Neighborhood SES)	M3a (Mediation from Model 1 to Model 3; Total Mediation by Individual and Neighborhood SES) (%)
COPD health related outcomes						
CAT*	**1.45 (0.62, 2.24)**	**30%**	**1.02 (0.20, 1.84)**	21%	0.81 (-0.06, 1.72)	**44%**
mMRC*	**0.11 (0.00, 0.21)**	**31%**	0.08 (-0.03, 0.18)	-19%	0.09 (-0.02, 0.20)	17%
SGRQ overall*	**2.90 (1.18, 4.65)**	**41%**	1.70 (-0.14, 3.40)	12%	1.50 (-0.41, 3.34)	**48%**
6MWD*	**-24.6 (-36.7, -13.1)**	**35%**	**-16.0 (-28.1, -4.0)**	**57%**	-6.9 (-19.3, 7.2)	**72%**
Total severe exacerbation count in past year **	**2.21 (1.63, 2.90)**	6%	**2.11 (1.56, 2.77)**	**30%**	**1.69 (1.22, 2.28)**	**34%**
Pi10*	**0.014 (0.007, 0.022)**	3%	**0.013 (0.006, 0.021)**	4%	**0.013 (0.005, 0.021)**	7%
% emphysema*	**1.71 (0.85, 2.57)**	-7%	**1.83 (0.94, 2.73)**	-14%	**2.09 (1.16, 3.03)**	-22%
% air trapping*	**3.02 (1.45, 4.63)**	4%	**2.89 (1.30, 4.53)**	3%	**2.80 (1.07, 4.60)**	8%

Notes: The regression analysis was adjusted for FEV1 % predicted and comorbidity count in all models. *Entries represent mean differences (β) and their 95% confidence interval (CI) comparing blacks to whites. ** Entries represent incidence rate ratio and their 95% confidence interval (Cl) comparing blacks to whites. Model 1- adjusted participant's characteristics of age, gender, smoking history, pack-years, BMI, marital status, COPD status, FEV1 % predicted, and comorbidity count. Model 2 – Model 1 additionally adjusted for participant SES (education, income). Model 3 – Model 1 additionally adjusted for participant SES and neighborhood SES (poverty rate, education, unemployment, median household income, Area Deprivation Index and Food Access) estimated at the census tract level using data from the 2010 US Census. **Boldface entries indicate a statistically significant association *P* <0.05.**

Table E4. Association of race with respiratory outcomes and CT metrics, adjusting for occupational exposure

	Model 1 (Adjusted for Demographics and Individual Clinical Characteristics)	M1a (Mediation from Model 1 to Model 2; Mediation by Individual SES) (%)	Model 2 (Model 1 Also Adjusted for Individual SES)	M2a (Additional Mediation from Model 2 to Model 3; Mediation by Neighborhood SES) (%)	Model 3 (Model 2 Also Adjusted for Neighborhood SES)	M3a (Mediation from Model 1 to Model 3; Total Mediation by Individual and Neighborhood SES) (%)
COPD health related outcomes						
CAT*	**1.98 (1.05, 2.76)**	**30%**	**1.38 (0.50, 2.27)**	27%	**1.00 (0.05, 1.94)**	**49%**
mMRC*	**0.16 (0.04, 0.26)**	**32%**	0.11 (-0.01, 0.21)	5%	0.10 (-0.03, 0.21)	36%
SGRQ overall*	**4.33 (2.49, 6.10)**	**36%**	**2.76 (0.86, 4.55)**	26%	2.05 (-0.02, 4.02)	**53%**
6MWD*	**-30.3 (-44.9, -18.0)**	**32%**	**-20.7 (-34.6, -7.7)**	**52%**	-9.9 (-24.4, 3.1)	**67%**
Total severe exacerbation count in past year **	**2.35 (1.74, 3.08)**	8%	**2.19 (1.63, 2.91)**	**32%**	**1.71 (1.22, 2.38)**	**38%**
CT metrics						
Pi10*	**0.016 (0.008, 0.024)**	7%	**0.015 (0.007, 0.023)**	11%	**0.013 (0.005, 0.021)**	17%
% emphysema*	**1.76 (0.69, 2.65)**	6%	**1.65 (0.63, 2.63)**	-9%	**1.79 (0.73, 2.85)**	-2%
% air trapping*	**3.32 (1.21, 5.20)**	**16%**	**2.77 (0.72, 4.81)**	16%	**2.33 (0.10, 4.47)**	30%

Notes: Occupational exposure variable (1: exposed to hazardous vapor, gas, dust, or fumes at his/her longest job, 0: not exposed) was included as a part of individual SES adjustment. *Entries represent mean differences (β) and their 95% confidence interval (CI) comparing black to white. ** Entries represent incidence rate ratio and their 95% confidence interval (Cl) comparing black to white. Model 1- adjusted participant's characteristics of age, gender, smoking history, pack-years, BMI, marital status, COPD status. Model 2 – Model 1 additionally adjusted for participant SES (education, income). Model 3 – Model 1 additionally adjusted for participant SES and neighborhood SES (the principal component score of the five continuous neighborhood SES variables and Food Access) estimated at the census tract level using data from the 2010 US Census. **Boldface entries indicate a statistically significant association *P* < 0.05.**

Table E5. Association of race with respiratory outcomes and CT metrics, adjusting for rural/urban status

	Model 1 (Adjusted for Demographics and Individual Clinical Characteristics)	M1a (Mediation from Model 1 to Model 2; Mediation by Individual SES) (%)	Model 2 (Model 1 Also Adjusted for Individual SES)	M2a (Additional Mediation from Model 2 to Model 3; Mediation by Neighborhood SES) (%)	Model 3 (Model 2 Also Adjusted for Neighborhood SES)	M3a (Mediation from Model 1 to Model 3; Total Mediation by Individual and Neighborhood SES) (%)
COPD health related outcomes						
CAT*	**1.90 (1.03, 2.71)**	**30%**	**1.34 (0.45, 2.19)**	**27%**	**0.97 (0.04, 1.86)**	**49%**
mMRC*	**0.15 (0.04, 0.25)**	**33%**	0.10 (-0.01, 0.20)	-0%	0.10 (-0.02, 0.21)	33%
SGRQ overall*	**4.27 (2.23, 6.10)**	**37%**	**2.70 (0.63, 4.58)**	24%	2.05 (-0.08, 4.01)	**52%**
6MWD*	**-31.7 (-44.7, -17.6)**	**33%**	**-21.4 (-34.5, -7.9)**	**51%**	-10.5 (-24.8, 4.2)	**67%**
Total severe exacerbation count in past year **	**2.39 (1.82, 3.29)**	7%	**2.24 (1.70, 3.08)**	**31%**	**1.74 (1.26, 2.48)**	**36%**
CT metrics						
Pi10*	**0.016 (0.008, 0.024)**	7%	**0.015 (0.007, 0.023)**	9%	**0.013 (0.005, 0.022)**	16%
% emphysema*	**1.66 (0.66, 2.67)**	0%	**1.66 (0.69, 2.71)**	-13%	**1.87 (0.83, 2.94)**	-12%
% air trapping*	**3.21 (1.28, 5.24)**	14%	**2.77 (0.73, 4.76)**	11%	**2.46 (0.41, 4.58)**	23%

Notes: Rural/urban status, as defined by US Census 2010 designation and linked to our participants through their FIPS code, was included as a covariate in all models. *Entries represent mean differences (β) and their 95% confidence interval (CI) comparing blacks to whites. ** Entries represent incidence rate ratio and their 95% confidence interval (CI) comparing blacks to whites. Model 1- adjusted participant's characteristics of age, gender, smoking history, pack-years, BMI, marital status, COPD status. Model 2 – Model 1 additionally adjusted for participant SES (education, income). Model 3 – Model 1 additionally adjusted for participant SES and neighborhood SES (poverty rate, education, unemployment, median household income, Area Deprivation Index and Food Access) estimated at the census tract level using data from the 2010 US Census. **Boldface entries indicate a statistically significant association *P* <0.05.**

Table E6. Association of race with respiratory outcomes and CT metrics, adjusting for region (Northeast, Midwest, South, West)

	Model 1 (Adjusted for Demographics and Individual Clinical Characteristics)	M1a (Mediation from Model 1 to Model 2; Mediation by Individual SES) (%)	Model 2 (Model 1 Also Adjusted for Individual SES)	M2a (Additional Mediation from Model 2 to Model 3; Mediation by Neighborhood SES) (%)	Model 3 (Model 2 Also Adjusted for Neighborhood SES)	M3a (Mediation from Model 1 to Model 3; Total Mediation by Individual and Neighborhood SES) (%)
COPD health related outcomes						
CAT*	**1.94 (1.09, 2.76)**	**28%**	**1.40 (0.52, 2.26)**	**28%**	**1.02 (0.12, 1.93)**	**48%**
mMRC*	**0.16 (0.04, 0.25)**	**28%**	0.11 (-0.01, 0.20)	3%	0.11 (-0.02, 0.22)	30%
SGRQ overall*	**4.34 (2.35, 6.13)**	**34%**	**2.86 (0.85, 4.74)**	25%	2.14 (-0.00, 4.08)	**51%**
6MWD*	**-30.3 (-43.4, -16.2)**	**34%**	**-20.2 (-33.6, -6.8)**	**55%**	-9.1 (-23.6, 5.7)	**70%**
Total severe exacerbation count in past year **	**2.30 (1.78, 3.12)**	7%	**2.16 (1.65, 2.93)**	**31%**	**1.70 (1.23, 2.40)**	**37%**
CT metrics						
Pi10*	**0.016 (0.008, 0.024)**	7%	**0.015 (0.007, 0.023)**	10%	**0.013 (0.005, 0.022)**	16%
% emphysema*	**1.72 (0.76, 2.70)**	-1%	**1.73 (0.76, 2.76)**	-8%	**1.88 (0.88, 2.91)**	-9%
% air trapping*	**3.33 (1.43, 5.27)**	13%	**2.91 (0.90, 4.87)**	15%	**2.48 (0.38, 4.50)**	25%

Notes: The region (Northeast, Midwest, South, West), as defined by US Census and linked to our participants through their FIPS code, was included as a covariate in all models. *Entries represent mean differences (β) and their 95% confidence interval (CI) comparing blacks to whites. ** Entries represent incidence rate ratio and their 95% confidence interval (CI) comparing blacks to whites. Model 1- adjusted participant's characteristics of age, gender, smoking history, pack-years, BMI, marital status, COPD status. Model 2 – Model 1 additionally adjusted for participant SES (education, income). Model 3 – Model 1 additionally adjusted for participant SES and neighborhood SES (poverty rate, education, unemployment, median household income, Area Deprivation Index and Food Access) estimated at the census tract level using data from the 2010 US Census. **Boldface entries indicate a statistically significant association *P* <0.05.**

Table E7. Association of race with respiratory outcomes and CT metrics, adjusting for air pollution (PM2.5 & ozone)

	Model 1 (Adjusted for Demographics and Individual Clinical Characteristics)	M1a (Mediation from Model 1 to Model 2; Mediation by Individual SES) (%)	Model 2 (Model 1 Also Adjusted for Individual SES)	M2a (Additional Mediation from Model 2 to Model 3; Mediation by Neighborhood SES) (%)	Model 3 (Model 2 Also Adjusted for Neighborhood SES)	M3a (Mediation from Model 1 to Model 3; Total Mediation by Individual and Neighborhood SES) (%)
COPD health related outcomes						
CAT*	**1.27 (0.31, 2.24)**	**40%**	0.76 (-0.23, 1.76)	34%	0.50 (-0.55, 1.61)	**61%**
mMRC*	**0.15 (0.02, 0.27)**	**24%**	0.12 (-0.02, 0.23)	-1%	0.12 (-0.02, 0.23)	24%
SGRQ overall*	**3.79 (1.52, 6.05)**	**36%**	**2.43 (0.24, 4.69)**	34%	1.61 (-0.60, 4.07)	**58%**
6MWD*	**-21.9 (-35.5, -8.0)**	**40%**	-13.2 (-26.9, 0.4)	60%	-5.3 (-20.6, 8.8)	**76%**
Total severe exacerbation count in past year **	**2.29 (1.59, 3.26)**	4%	**2.22 (1.56, 3.19)**	**35%**	**1.69 (1.17, 2.47)**	**37%**
CT metrics						
Pi10*	**0.017 (0.008, 0.025)**	3%	**0.016 (0.008, 0.024)**	17%	**0.013 (0.004, 0.022)**	20%
% emphysema*	**1.98 (0.84, 3.10)**	-0%	**1.98 (0.81, 3.16)**	5%	**1.88 (0.68, 3.13)**	5%
% air trapping*	**3.29 (0.95, 5.41)**	11%	**2.94 (0.57, 5.07)**	20%	2.34 (-0.04, 4.47)	**29%**

Notes: A yearly average of ambient PM2.5 and ozone (corresponding to participants' address at the time of baseline recruitment) were included as covariates in all models. *Entries represent mean differences (β) and their 95% confidence interval (CI) comparing blacks to whites. ** Entries represent incidence rate ratio and their 95% confidence interval (Cl) comparing blacks to whites. Model 1- adjusted participant's characteristics of age, gender, smoking history, pack-years, BMI, marital status, COPD status. Model 2 – Model 1 additionally adjusted for participant SES (education, income). Model 3 – Model 1 additionally adjusted for participant SES and neighborhood SES (poverty rate, education, unemployment, median household income, Area Deprivation Index and Food Access) estimated at the census tract level using data from the 2010 US Census. **Boldface entries indicate a statistically significant association *P* <0.05.**

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