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# Socioeconomic Status is Positively Associated with Percent Emphysema on CT Scan. The MESA Lung Study

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## Abstract

**Rationale and Objectives—**Higher socioeconomic status (SES) has been associated with lower respiratory mortality and better lung function, but whether a similar gradient exists for computed tomography (CT) measures of subclinical emphysema is unknown.

**Materials and Methods—**The Multi-Ethnic Study of Atherosclerosis (MESA) recruited African American, Chinese, Hispanic, and white participants, ages 45–84 years, without clinical cardiovascular disease, from 6 US sites in 2000–2002. The MESA Lung Study assessed percent emphysema, defined based on the proportion of pixels below an attenuation threshold of 910 HU from lung windows of cardiac CT scans. Generalized linear models were adjusted for demographic characteristics, height, body mass index, history of respiratory illness, occupational and residential exposures, tobacco use, and CT scanner type.



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**Results—**Among 3,706 participants with a mean age of 61 (±10), the median value for percent emphysema was 18 (interquartile range=20). Compared with those who did not complete high school, participants with a graduate degree had a higher percent emphysema (difference of 4; $p < 0.001$). Income and wealth were also positively associated with percent emphysema. In contrast, higher SES was associated with better lung function. Descriptive and subgroup analyses were used to explore potential explanations for divergent results, including the possibility that suboptimal inspiration during CT scanning would decrease percent emphysema, making the lungs appear healthier when effort is relatively poor.

**Conclusion—**While SES indicators were positively associated with subclinical emphysema detectable on CT scan, this unexpected association may highlight potential bias due to effort-dependence of both CT measures and spirometry.

### Keywords

Chronic Obstructive Pulmonary Disease; Emphysema; Socioeconomic Status; Epidemiology

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Socioeconomic disparities for respiratory mortality may be comparable to or larger than disparities for other major causes of death (1–3). A strong socioeconomic gradient has also been observed for subclinical respiratory health measures such as lung function (4–6). Suggested mechanisms for such an association include not only smoking and tobacco exposure (7), but also occupational and neighborhood exposures (8), obesity (9), and stress (10).

Socioeconomic status (SES) may also be associated with subclinical emphysema measured with computed tomography (CT), but no previous studies have assessed this relationship in a large, population-based sample. Subclinical emphysema is moderately correlated with but distinct from impaired lung function. We hypothesized that greater educational attainment, income, and wealth would be associated with less emphysema-like patterns on CT scans.

## MATERIALS AND METHODS

### Setting and Subjects

The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective cohort study designed to investigate prevalence, correlates and progression of subclinical cardiovascular disease (11). The study enrolled 6,814 men and women from six communities in the United States: Forsyth County, NC; Northern Manhattan and the Bronx, NY; Baltimore City and Baltimore County, MD; St. Paul, MN; Chicago, IL; and Los Angeles, CA. Participants were between ages 45 and 84 when recruited in 2000–2002. Exclusion criteria included clinical cardiovascular disease, any cardiovascular procedure, weight over 136 kg, pregnancy, or impediment to long-term participation. The protocols of MESA and all studies described herein were approved by Institutional Review Boards at all collaborating institutions and the National Heart, Lung, and Blood Institute.

The MESA Lung Study identified 4,484 MESA participants for recruitment based on prior consent to genetic analyses, availability of baseline measures of endothelial function, and attendance at an examination in 2004–2006. A total of 3,706 participants enrolled in the MESA Lung Study and had complete CT, spirometry, and SES data.

### CT Measures of Lung Density

CT scans were performed under a standardized protocol on multidetector and electron beam scanners during the baseline visit in 2000–2002 (12). Quantitative measures of emphysema were performed on lung fields of cardiac CT scans, which imaged approximately 70% of the lung volume, from the carina to the lung bases. Two cardiac CT scans were performed on each participant on separate breath-holds at full inspiration: participants were instructed to take a deep breath and hold it during each scan. The scan with higher air volume was used for analyses, except in cases of discordant scan quality control score in which case the higher quality scan was used (13). Emphysema measures from cardiac scans correlated with those from full-lung scans from the same MESA participants (e.g., 0.93 on multidetector scanners) (13).

Image attenuation in Hounsfield Units (HU) was assessed using a modified Pulmonary Analysis Software Suite (14,15) at a single reading center. To correct for variations in scanner calibration and in the way different scanners handle scatter and beam hardening, we measured the attenuation of air outside the body, which should have a mean of −1,000 HU. The attenuation of each pixel in the lung regions was then corrected to have the value=measured pixel attenuation × (−1000/mean air attenuation). Percent emphysema was defined as the percentage of total voxels in the lung that fell below −910 HU, an attenuation threshold selected based upon pathology comparisons (16) and the generally mild degree of emphysema in this sample. The intraclass correlation coefficient (ICC) of percent emphysema on the 100% replicate sample was 0.94.

## Spirometry Measures of Lung Function

Spirometry was conducted in 2004–2006 in accordance with American Thoracic Society/ European Respiratory Society recommended guidelines (17) with all participants performing at least 3 acceptable maneuvers on a dry-rolling-sealed spirometer (18). Lung expiration time was defined according to American Thoracic Society/European Respiratory Society guidelines. Participant effort was reported subjectively by spirometry technicians. The ICC of both forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) on random 10% repeat testing was 0.99.

## Socioeconomic Measures

Participants were asked to report their educational attainment, annual household income, and household size, as well as ownership of a car, home, financial investments, or real estate investments. Education and per capita household income (income category midpoint divided by the household size (19)) were each grouped into five categories. We also developed a simple wealth index: four wealth indicators (car ownership, home ownership, financial investments, and real estate investments) were combined by adding one point for each indicator.

## Demographic Characteristics, Tobacco Use, and Other Covariates

Age, gender, race, ethnicity, country of birth, medical history, and environmental tobacco and occupational exposures (20) were self-reported, and height and weight were measured using standard techniques (described at http://www.mesa-nhlbi.org). Current smoking was defined as self-report of a cigarette in the last 30 days or urinary cotinine level at the time of CT exam greater than 100 ng/ml. Cotinine measurement was performed by immunoassay (Immulite 2000 Nicotine Metabolite Assay; Diagnostic Products Corp., Los Angeles, CA). Pack-years of cigarette smoking was calculated using standardized questionnaire items (20). Asthma was defined as self-report of physician-diagnosed asthma, restricted to symptom onset before age 45 years to avoid inclusion of chronic obstructive pulmonary disease misdiagnosed as asthma. Air pollution was assessed using a 20-year residential history and air pollution monitor values from the Environmental Protection Agency Aerometric Information Retrieval Service database to approximate the cumulative exposure to particles with a diameter smaller than 10 micrometers (21).

### Statistical Analysis

Generalized linear regression models with robust variance estimates were performed in Stata 10.0 (Stata Corp., College Station, TX). For percent emphysema, which was highly skewed, a gamma error distribution was used. Socioeconomic indicators were each analyzed as grouped linear variables with a range from 0 to 4 (See Appendix for alternative specifications). Coefficient values given in the tables thus represent the difference associated with each one-category increase; a larger contrast between the highest and lowest categories can be estimated by multiplying the coefficient by four. Multiple imputation was used to fill in missing data on covariates, mainly residential exposure to air pollution (N = 699), family history of emphysema (N = 380), and second hand smoke exposure at work (N = 434); all other covariates were missing for less than one percent. Five imputed datasets were created, and their results were recombined such that regression confidence intervals reflected uncertainty from missing covariate data (22).

All regression models were adjusted for age; sex; race/ethnicity; whether the participant was born in the US; height; body mass index (BMI); history of hay fever; history of asthma before age 45; family history of emphysema among siblings; occupational exposure to dust; residential exposure to air pollution; environmental tobacco exposure in the childhood home, adult home, or workplace; smoking status; and pack-years. Continuous covariates of age, height, BMI, and pack-years were modeled with linear and centered quadratic terms. Models of percent emphysema were adjusted for CT scanner type and, if multi-detector scanner, weight above 100 kg since the mAs was increased for these participants (12).

## RESULTS

The 3,706 participants had an average age of 61; 25% were African American, 17% were Chinese, 23% were Hispanic and 36% were non-Hispanic Whites (Table 1). As expected, $FEV_1$/FVC ratio was negatively correlated with percent emphysema (r = −0.35).

### Socioeconomic Correlates of CT Lung Density

Contrary to our expectations, participants with higher SES were observed to have more emphysema-like patterns on their CT scans, as indicated by higher percent emphysema (Table 2). Each additional increment of education was associated with a 1.1 higher percent emphysema value; the corresponding difference between the highest and lowest education categories is 4.4. Associations of income and wealth with these CT measures were in the same direction (Table 2). A parallel analysis was conducted for the previously described measure alpha (23,24), likewise yielding significant associations that were in the opposite of the hypothesized direction (data not shown).

In contrast to the results for CT lung density, the socioeconomic gradient for lung function was in the expected direction: all statistically significant associations between socioeconomic indicators and lung function measures were positive (Table 2).

### Potential for Bias from Effort-Dependence

We considered several potential explanations for the divergence between our findings for CT and lung function measures (See Appendix). While none of these were conclusive, we found some suggestion that effort dependence of the two tests could partially explain divergent results. Inspiration below total lung capacity would artificially decrease lung function measures during spirometry, making the lungs appear less healthy; in contrast, during CT scanning such suboptimal inspiration would decrease percent emphysema (13), making the lungs appear healthier. All participants were coached to achieve full inspiration during spirometry by a certified spirometry technician and during CT scanning by a certified

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CT technician; however, it is likely that coaching of inspiration and coaching was not as intense for CT as for spirometry since inspiration has been long appreciated as a key component of valid spirometry but is only one of a number of components of CT scoring. In addition, CT scans were not spirometry-gated: CT scans and spirometry occurred at separate study visits. Measures of participant effort were available for spirometry, but not for CT scanning. Table 3 shows characteristics of participants who performed 6 seconds or more of expiratory time on spirometry, as compared with participants with inadequate expiratory time. Not surprisingly, FVC values were lower among those with inadequate expiratory time, and the $FEV_1$/FVC ratio was correspondingly higher. Those with lower expiratory time during spirometry also had lower indicators of socioeconomic status. Further, inadequate expiratory time during spirometry was associated with lower percent emphysema and lower air volume in the lungs on CT. Similar patterns were observed within each of the four racial/ethnic subgroups and when effort ratings by spirometry technicians were used instead of expiratory time. The observed associations between SES indicators and CT measures were attenuated slightly after adjustment for inadequate expiratory time during spirometry and low technician-rated spirometry effort (See Appendix).

## DISCUSSION

Contrary to our hypothesis, higher socioeconomic indicators were associated with more emphysema-like CT patterns. There are no prior studies with which to compare this result since epidemiologic studies that include CT measures of emphysema are, to date, few and almost all are case-control studies of chronic obstructive pulmonary disease (which may yield biased results for emphysema since they, by design, select on lung function). However, higher socioeconomic status did have the expected association with lung function consistent with prior studies.

Our study contributes to the literature on SES and respiratory health (5,25,26) by examining heterogeneity across multiple respiratory outcomes, SES indicators, and population subgroups. Previous studies have not examined the socioeconomic correlates of subclinical emphysema as measured by CT in a large, healthy cohort. However, we hypothesized that socioeconomic status would be negatively correlated with subclinical emphysema. However, in this cohort environmental tobacco smoke exposure in childhood has been linked with the low attenuation areas (24) considered in the current study, while the participants' own smoking history is associated with more high attenuation areas (29), suggesting that exposures may have a complicated relationship with lung development and disease over time.

Bias due to effort-dependence offers one potential explanation for the observed divergence between the socioeconomic gradients observed for CT-based lung density measures and lung function measures. If participants with lower educational attainment had systematically lower levels of effort or compliance with technician instructions, both CT scans and spirometry would have non-random measurement error. Suboptimal inspiration among low-SES participants would make these participants' CT measures appear healthier than they are, biasing the association of interest away from the hypothesized direction and toward the observed trend. The long-described association of socioeconomic status and lung function (4) may also be due in part to differential compliance and effort. Available measures of effort may be serving only as a crude proxy for the true confounder (e.g. intrinsic motivation to comply with test instructions in a clinical research setting; rapport between technician and participant), and future research is needed to assess this potential source of bias.

Our study had several important limitations. First, long-term health implications of percent emphysema measured on CT scan for a relatively healthy population like ours are unknown,

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although these data have been used to test other hypotheses (24,27–31). Second, this observational study among adults may be subject to survival or selection bias if participation was differential both by SES and by respiratory health. Third, there may be unmeasured or residual confounding. One such potential confounder is thoracic body fat, for which BMI is an imperfect measure. Also birth weight and gestational age were unavailable for this cohort. A fourth limitation is the large number of comparisons made in this study, which makes it difficult to rule out the role of chance in any one result. Given the interest in evaluating which associations were statistically significant, we did not make formal adjustment for multiple comparisons (32) but instead reported all main findings, positive and negative.

In conclusion, our results show evidence of socioeconomic patterning of clinical and subclinical lung disease in this large population sample of relatively healthy adults. CT measures of emphysema were positively associated with socioeconomic status; this unexpected association may also highlight a potential bias due to effort-dependence of both CT measures and lung function.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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**Table 1**

Participant Characteristics the MESA Lung Study, 2000–2006

| | mean (SD) or % | p25, median, p75 |
|---|---|---|
| Personal characteristics | | |
| Male, % | 49.4 | |
| Age, years | 61 (10) | 53, 61, 69 |
| Adult height, cm | 167 (10) | 159, 166, 174 |
| Body mass index | 28 (5) | 24, 27, 31 |
| Black, % | 25.3 | |
| Chinese, % | 16.6 | |
| Hispanic, % | 22.6 | |
| White, % | 35.5 | |
| Born outside of US, % | 36.6 | |
| Health and tobacco exposure history | | |
| Asthma before age 45, % | 8.1 | |
| Hay fever, % | 33.0 | |
| Family history of emphysema, % | 4.7 | |
| Never smoked cigarettes, % | 47.4 | |
| Current cigarette smoker, % | 15.3 | |
| Former cigarette smoker, % | 37.3 | |
| Pack-years for current/former cigarette smokers | 20 (29) | 3, 13, 29 |
| Lived with a smoker, % | 42.9 | |
| Second-hand tobacco exposure at work, % | 39.8 | |
| Occupational dust exposure, % | 36.6 | |
| Socioeconomic characteristics | | |
| Education, estimated years | 14 (4) | 12, 14, 16 |
| Annual household income, $1000s per person | 26 (20) | 11, 22, 38 |
| Employed, % | 52.4 | |
| Unemployed, % | 1.9 | |
| Home maker, % | 10.4 | |
| Retired, % | 35.2 | |
| Car ownership, % | 81.8 | |
| Home ownership, % | 66.1 | |
| Financial investments, % | 62.0 | |
| Real estate investments, % | 26.4 | |
| Wealth index, range 0 to 4 | 2.4 (1.3) | 1, 3, 3 |
| Lung density and lung function | | |
| Percent emphysema | 20 (13) | 9, 18, 29 |
| Percent predicted $FEV_1$ | 94 (18) | 83, 95, 105 |
| Percent predicted FVC | 96 (16) | 85, 95, 106 |
| Percent predicted FEV1/FVC ratio | 98 (11) | 93, 100, 105 |

Notes: $FEV_1$ indicates forced expiratory volume, 1 second; FVC, forced vital capacity; p25, $25^{th}$ percentile; p75, $75^{th}$ percentile; N = 3,706

## Table 2

Adjusted Associations of Education, Income, and Wealth with Computed Tomography Measures of Emphysema in the MESA Lung Study, 2000–2006

| | **Difference per SES category*** | |
|---|---|---|
| | **β (95% CI)** | **p-value** |
| Percent Emphysema | | |
| Education | **1.1 (0.8 to 1.5)** | **< 0.001** |
| Income | **0.4 (0.1 to 0.8)** | **0.012** |
| Wealth | **0.6 (0.3 to 1.0)** | **0.001** |
| $FEV_1$ (ml) | | |
| Education | **17 (5 to 29)** | **0.006** |
| Income | 7 (−5 to 19) | 0.269 |
| Wealth | **16 (3 to 29)** | **0.018** |
| FVC (ml) | | |
| Education | **25 (10 to 40)** | **0.001** |
| Income | 2 (−13 to 16) | 0.819 |
| Wealth | **18 (2 to 34)** | **0.030** |
| $FEV_1$/FVC Ratio (%) | | |
| Education | −0.1 (−0.3 to 0.2) | 0.544 |
| Income | 0.2 (−0.0 to 0.4) | 0.062 |
| Wealth | 0.2 (−0.1 to 0.4) | 0.221 |

Notes: $FEV_1$ indicates forced expiratory volume, 1 second; FVC, forced vital capacity; values shown are regression coefficients and 95% confidence intervals for an additional increment of a grouped linear variable with a range of 0 through 4 for education (less than a high school education; high school degree; some college; completed college; graduate degree), income (lowest quintile, < $9000 per person annually; highest quintile, > $40 000 per person annually) or wealth (no wealth indicators reported; only one indicator reported; two indicators reported; three indicators reported; car ownership, home ownership, financial investments, and real estate investments all reported); and the difference between extreme categories can be calculated by multiplying difference coefficient by 4; bold face font indicates statistical significance

*Models included adjustment for age; sex; race; ethnicity; whether the participant was born in the US; height; body mass index (BMI); history of hay fever; history of asthma before age 45; family history of emphysema among siblings; occupational exposure to dust; residential exposure to air pollution; environmental tobacco exposure in the childhood home, adult home, or workplace; smoking status; pack-years, and CT equipment type if applicable

## Table 3

Spirometry Effort Indicator Associated with Socioeconomic Indicators, Lung Function, and Computed Tomography Measures of Subclinical Respiratory Disease in the Multi-Ethnic Study of Atherosclerosis, 2000–2006

| | Acceptable expiratory time, ≥ 6 seconds | Insufficient expiratory time, < 6 seconds | Adjusted* difference (95% CI) |
|---|---|---|---|
| N | 3,602 | 102 | |
| Socioeconomic characteristics | | | |
| Education, estimated years | 14 | 12 | **0.8 (0.1 to 1.5)** |
| Annual household income, $1000s per person | 26 | 23 | 2.1(−0.9 to 5.1) |
| Wealth index, range 0 to 4 | 2.4 | 2.0 | 0.2 (0.0 to 0.4) |
| Lung function measures from spirometry | | | |
| Percent predicted $FEV_1$ | 94 | 93 | 2 (−2 to 6) |
| Percent predicted FVC | 96 | 83 | **14 (11 to 17)** |
| Percent predicted FEV1/FVC ratio | 98 | 111 | **−14 (−16 to −12)** |
| Low attenuation areas and air volume from CT | | | |
| Percent emphysema, median | 20 | 18 | **3.4 (1.5 to 5.4)** |
| Estimated air volume in lungs | 2333 | 2020 | **145 (52 to 239)** |

Notes: $FEV_1$ indicates forced expiratory volume, 1 second; FVC, forced vital capacity; values are means unless otherwise specified; bold face font indicates statistical significance

*Adjusted for age; sex; race; ethnicity; height; body mass index; and CT equipment type if applicable