Arteriosclerosis, Thrombosis, and Vascular Biology



JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Arterioscler. Thromb. Vasc. Biol. 2006;26;411-416; originally published online Dec 1, 2005;

DOI: 10.1161/01.ATV.0000198245.16342.3d

Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association. 7272 Greenville Avenue, Dallas, TX 72514

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Socioeconomic Differences in Progression of Carotid Intima-Media Thickness in the Atherosclerosis Risk in Communities Study

Nalini Ranjit, Ana V. Diez-Roux, Lloyd Chambless, David R. Jacobs Jr, F. Javier Nieto, Moyses Szklo

Objective—To examine the association of socioeconomic factors with progression of carotid intimal-medial thickness (IMT) in middle-aged adults. Cross-sectional associations of IMT with socioeconomic status (SES) have been demonstrated in middle-aged cohorts. It is unclear whether these factors are associated with progression of IMT.

Methods and Results—We examined IMT progression over 9 years among a middle-aged cohort of 12 085 black and white subjects free of cardiovascular disease recruited from 4 US sites participating in the Atherosclerosis Risk in Communities (ARIC) study. Baseline IMT was inversely related to SES among whites and blacks. Repeated measures regression models of IMT progression showed moderate inverse relationships of IMT progression with income in whites so that the difference in 5-year IMT progression rates between the highest and lowest categories was −11.5 μm (CI, −17.4 to −5.6). In contrast, among blacks, this gradient is reversed, with an 11.1 μm (CI, −0.1 to 22.3) difference in 5-year progression between highest and lowest income category. Generally, similar patterns were observed for other socioeconomic indicators. Patterns were not accounted for by baseline cardiovascular risk factors.

Conclusions—SES is inversely related to IMT progression in middle-aged whites but positively related to IMT progression among middle-aged blacks. These differences do not appear to be attributable to selective attrition or higher IMT among blacks at baseline. (Arterioscler Thromb Vasc Biol. 2006;26:411-416.)

Key Words: IMT progression ■ socioeconomic status ■ race differences ■ ARIC ■ repeated measures regression

Tltrasound-assessed intimal-medial thickness (IMT) of the carotid arteries has been used as a marker of subclinical atherosclerosis in several ongoing populationbased studies and has been shown to be associated with prevalent and incident cardiovascular disease (CVD) and with CVD risk factors. 1-5 Investigating factors associated with the early atherosclerotic process may contribute to a greater understanding of the process of atherosclerosis itself and differentiate factors associated with progression of atherosclerotic lesions from those related to their clinical expression. In previous analyses, we documented inverse crosssectional associations between socioeconomic indicators and mean carotid intimal-medial wall thickness in white and black men and women free of clinical atherosclerotic disease participating in the baseline examination of the Atherosclerosis Risk in Communities (ARIC) study.6 Similar associations were reported for middle-aged men living in Kuopio, Finland.⁷ To our knowledge, only 1 study has examined the longitudinal association of socioeconomic factors with atherosclerosis progression; however, that study was limited to middle-aged white men.8 Using data from the ARIC study,

we examined socioeconomic differences in 9-year progression of subclinical atherosclerosis, as assessed by the IMT of the common carotid arterial wall, in a population-based sample of middle-aged men and women living in 4 US communities.

Materials and Methods

Study Population and Sources of Data

The ARIC study is a prospective investigation of clinical and subclinical atherosclerosis in 4 US communities (Forsyth County, NC; Jackson, Miss; the northwestern suburbs of Minneapolis, Minn; and Washington County, Md). The ARIC cohort is composed of 15 792 persons 45 to 64 years of age at the time of the baseline interview, selected by probability sampling in the 4 communities. White subjects were recruited from North Carolina, Maryland, and Minnesota. The majority of black subjects was recruited from Mississippi and North Carolina. The baseline examination of the ARIC cohort took place between 1987 and 1989. The first, second, and third follow-up exams were performed ≈3 years later (1990 to 1992), 6 years later (1993 to 1995), and 9 years later (1996 to 1998), respectively.

Ultrasound assessment of carotid wall thickness was performed on all cohort participants attending the baseline visit and the first

Original received February 1, 2005; final version accepted November 17, 2005.

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Arterioscler Thromb Vasc Biol. is available at http://www.atvbaha.org

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follow-up visit. At the second follow-up (≈6 years after baseline), ultrasound scans were offered to all Jackson and Forsyth participants but only to a random half of Washington County and Minneapolis participants. The remaining participants from these 2 counties were evaluated at the third follow-up, as were participants in Jackson and in Forsyth County who had not had a second follow-up. In addition, all black participants at the Forsyth County center and a randomly chosen half of other participants in Jackson and Forsyth Counties were evaluated. Thus, most respondents, by design, have 1 measure from the second and third follow-up exams, in addition to 2 measures from the baseline and first follow-up visits. The ultrasound measurements of the ARIC study are based on validated techniques10 and used a scanning protocol common to the 4 field centers11 and standardized central reading of scans.12 IMT was measured at the far wall of designated 1-cm lengths of the common carotid arteries (CCAs), the carotid bifurcation, and the internal carotid arteries (ICAs) as the mean of as many 1-mm-apart intima-to-media distances as were available.13-14 Although IMT of the near wall was also measured, the nature of ultrasound reflection off the near compared with the far wall resulted in much more missing data from the near wall measurements. For this reason, ARIC and other studies elected to use almost exclusively the far wall data in analyses. Maximum likelihood techniques for linear mixed models were used to adjust for carotid site-specific reader differences and measurement drift across visits.15 Because of a change of scanning and reading equipment midway through the second follow-up, follow-up measurements had to be corrected statistically to ensure comparability of measurements across visits. 15 Statistical correction resulted in reliable repeat measurements of IMT for the CCA but not for the internal carotid or the carotid bifurcation. Hence, this report only examines IMT progression in the left or right CCAs.

Information on income, education, and neighborhood characteristics was obtained from the baseline interview of the ARIC study. Participants were asked to select their total combined family income from a list of 8 categories. Four race-specific categories of income were constructed, corresponding roughly to race-specific quartiles. Information on highest grade or year of school completed was used to group participants into 4 categories: (1) less than high school, (2) high school or vocational school, (3) incomplete college, and (4) college completed. Neighborhood characteristics were summarized in a cumulative score constructed by combining 6 variables for block-groups obtained from the 1990 Census. These variables represent neighborhood income and wealth, neighborhood education, and neighborhood occupation. Deviations from the mean across all blocks were computed and used to derive z scores, which were then summed to obtain the neighborhood summary score. Racespecific quartiles of this cumulated score were used in the analyses. Race-specific categories were used for income and neighborhood score because of important differences in the distribution of these variables by race. In addition, a fourth variable, combined socioeconomic score ranging from 0 to 9, was constructed as the sum of category positions on each available socioeconomic measure (with the lowest category coded as 0 and the highest as 3 for each

Cardiovascular risk factors at baseline shown to be associated with progression of common carotid IMT in the ARIC study¹⁵ were examined as covariates in analyses of socioeconomic differences. These include diabetes at baseline (defined as fasting glucose of ≥126 mg/dL, a nonfasting level of ≥200 mg/dL, a self-reported physician diagnosis, or ongoing treatment), smoking status at baseline, high-density lipoprotein cholesterol, fibrinogen, white blood cell count, and pulse pressure. Details of these measures have been described previously.⁵

Of the 15 792 persons participating in the baseline examination of the ARIC study, 48 were excluded because they were neither black nor white. Black participants residing in the Minnesota and Washington sites (n=55) were also excluded because small numbers made site- and race-specific results unreliable. To examine progression of subclinical disease in asymptomatic persons, an additional 2031 participants with a history of clinical coronary heart disease at baseline were also excluded, leaving a total of 13 658 participants.

The sample was further restricted to the 12 085 participants with \geq 2 measures of IMT on the same side during the study period. A total of 12.4% of this sample had IMT measures for all 4 waves, 20.5% had IMT measures for only 2 waves, and 67% had 3 IMT measures. Of the 12 085 participants, 686 (6%) had missing information on baseline income, 15 (<.01%) had missing information on education, and 1220 (10%) had missing information on neighborhood score. The 12 085 participants yielded a total of 66 298 side-specific repeat IMT measures for the longitudinal analysis.

Statistical Methods

Graphical analyses were initially used to explore race and sex differences in baseline IMT and IMT progression as well as cohort effects. Baseline IMT varied by sex and race, with higher mean levels in men and in blacks. Progression of IMT varied by race but not by sex, with lower progression rates for blacks. There was no evidence of cohort effects (results not shown). Consequently, all analyses were stratified by race and adjusted for sex and age at baseline.

Associations of socioeconomic indicators with baseline IMT and progression of IMT over time were estimated by fitting mixed models¹⁶ to repeat measures data pooled across visits. Models included age at baseline, sex, time since baseline, study center, side of measurement (whether the IMT measure was obtained from the left or right side), and socioeconomic status (SES) at baseline. A time-by-SES interaction was included to allow progression to differ by socioeconomic categories and to test the statistical significance of any differences observed. Initial analyses showed that IMT progression over time varied by side of measurement; hence, an interaction term for time by side of measurement was added to reflect this. However, all results presented here are averaged over left and right side. Interactions of time with sex and baseline age were found to be nonsignificant and were not included. A random intercept and random time component (random slope) for each person were included to allow for interindividual differences and to account for correlation between repeat measures within an individual over time. Additionally, a variance component was included to allow for correlation of measures across sides within individuals. Although no standard procedures exist for assessing model sufficiency for the growth models used here, an examination of residuals in the basic fixed-effects models did not signal any obvious problems with the model fit. Random effects were fitted with minimal assumptions as to the form of the variance-covariance matrix.

Income, education, neighborhood score, and combined score were examined in separate models. Socioeconomic indicators were investigated as categorical variables to investigate dose-response relationships. The regression models described above were used to estimate age- and sex-adjusted mean IMT at baseline and mean annual change in IMT over the 9-year follow-up for each race by categories of income, education, and neighborhood characteristics. Models were rerun after including cardiovascular risk factors. To evaluate the possible impact of selective attrition, models were refitted using early follow-up data (2 repeat measures). To evaluate the impact of excluding participants with clinical atherosclerotic disease at baseline, models were fitted without excluding these cases. Analyses were also repeated after restricting the range of baseline IMT for blacks to assess the influence of very high IMT values at baseline.

Results

Black participants were more likely than white participants to be in the lower categories of socioeconomic characteristics (Table 1). Within race groups, males of both races had a more favorable socioeconomic distribution than women. Mean baseline IMT was higher in men than in women, with mean IMT for males exceeding that for females of the same race, by $50 \mu m$ for blacks and $60 \mu m$ for whites. Mean IMT in blacks exceeded mean IMT in whites by $50 \mu m$ in men and by $60 \mu m$ in women. Although 5-year progression was generally

TABLE 1. Sociodemographic Characteristics at Baseline, Mean IMT at Baseline, and IMT Progression in the 12 085 Participants Included in the Analyses, the ARIC Study, 1987–1998

	Men		Women	
	White (n=4213)	Black (n=1075)	White (n=4952)	Black (n=1845)
Mean age (SD) at baseline in years	54.4 (5.7)	53.3 (5.9)	53.9 (5.7)	53.0 (5.7)
Annual family income (% distribution)				
<\$12 000	3.0	27.4	7.9	42.8
\$12 000–24 999	14.8	31.1	21.2	30.1
\$25 000–34 999	18.8	15.7	20.0	12.9
\$35 000–49 999	25.8	14.6	21.9	8.3
≥\$50 000	37.6	11.2	29.1	5.9
Missing	3.5	10.3	4.9	10.0
Education (% distribution)				
Incomplete high school	15.0	39.0	14.2	37.0
High school or vocational school	40.0	26.9	51.0	29.3
Incomplete college	16.0	11.1	18.2	10.0
Complete college	16.0	8.2	10.5	8.4
Graduate or professional school	14.0	14.8	6.0	15.3
Missing	0.1	0.5	0	0.1
Median neighborhood score (25th, 75th percentile)	2.4 (0.03, 5.0)	-3.0 (-6.1, -0.1)	2.3 (0.0, 4.9)	-4.5 (-6.5, -1.6)
Mean combined SES score (range 0-9)	5.05 (2.57)	4.77 (2.66)	4.44 (2.44)	4.19 (2.78)
Mean No. of IMT measures	2.90 (0.53)	2.97 (0.67)	2.92 (0.54)	2.95 (0.65)
Estimated mean IMT at baseline in $\mu\text{m},$ at 54 years of age†	641.1 (2.17)	690.0 (7.00)	582.0 (1.57)	640.2 (5.04)
Estimated mean 5-year change n IMT in μ m†	45.8 (1.77)	35.8 (3.44)	46.8 (1.35)	37.3 (2.37)

†Mean IMT at 54 years of age and 5-year changes in IMT are estimated from mixed models for IMT, with adjustment for baseline age and field center, and are averaged over side.

similar in men and women, it was greater in whites than in blacks (5-year increase in IMT of \approx 46 μ m in whites and \approx 37 μ m in blacks). The sample distribution of demographic and socioeconomic indicators across examinations (data not shown) does not change significantly over the course of the study, aside from a small drift toward higher socioeconomic categories for both races as follow-up progresses, likely reflecting greater deaths and losses to follow-up in the lower socioeconomic groups.

Table 2 presents associations of socioeconomic variables with baseline IMT (adjusted to 54 years of age, the average age of the cohort at baseline) and 5-year progression in IMT by race. In both races, socioeconomic position showed a graded and negative association with baseline IMT, such that low socioeconomic position is associated with thicker IMT at baseline. The direction of this effect is common across races, although the magnitude differs across race and socioeconomic measure. Socioeconomic position was also associated with IMT progression although the direction of the association is different in whites and blacks. For whites, the lowest category of income is associated with the highest rate of IMT progression, 11.5 μ m/5 years higher than is seen in the highest income category (P for linear trend <0.005). A similar graded pattern is present for the combined score and less so for education, with P values for linear trend at 0.08 and 0.2, respectively. No patterns were observed for neighborhood score. However, in the case of blacks, a consistent positive association between socioeconomic position and IMT progression appears. This is strongest in the case of the neighborhood score, with a difference of 16.7 in 5-year progression rate between the highest and lowest quartiles, but the effect is consistent and substantial for all other socioeconomic variables. In analyses stratified by center, the positive association between socioeconomic indicators and IMT progression was present in Forsyth and Jackson blacks (data not shown).

Overall, associations of socioeconomic indicators with IMT progression are only slightly weakened after additional adjustment for cardiovascular risk factors (Table 3). For example, the income difference for whites is reduced from -11.5 to $-9.1~\mu m$, whereas the neighborhood score difference for blacks drops from 16.7 to 14.9 μm . The inclusion of multiple variables in the model results in larger SEs, but point estimates do not change substantially after risk factor adjustment.

To assess sensitivity of our results to selective attrition, exclusion of persons with prevalent CVD at baseline and baseline IMT levels, analyses were repeated on various selected subsamples of the entire data (Table 4). The obtained results were robust, with the direction and magnitude of effects persisting across most of the various sensitivity analyses, particularly for whites. In blacks, the positive

TABLE 2. Mean Baseline IMT and IMT Progression by Socioeconomic Characteristics at Baseline in Whites and Blacks, the ARIC Study, 1987–1998*

	IMT at Baseline (in μ m)		Five-Year Change in IMT (in μ m)	
	Whites	Blacks	Whites	Blacks
Income†				
First (lowest) category (L1)	622.0 (2.8)	682.0 (5.8)	53.3 (2.3)	30.7 (4.4)
Second category	624.1 (3.0)	673.9 (5.6)	43.5 (2.5)	35.1 (4.2)
Third category	621.1 (2.8)	669.0 (6.4)	46.4 (2.3)	39.9 (4.8)
Fourth (highest) category (L4)	615.7 (2.4)	662.3 (5.1)	41.7 (1.9)	41.8 (3.6)
L4-L1 (highest-lowest) difference	-6.3(3.7)	-19.6 (7.7)	-11.5 (3.0)	11.1 (5.7)
P value for L4-L1 difference	0.0889	0.0111	0.0001	0.0522
P value for trend	0.048	0.0095	0.0008	0.039
Education				
<high (l1)<="" school="" td=""><td>633.3 (3.5)</td><td>684.7 (4.3)</td><td>48.5 (3.0)</td><td>30.8 (3.3)</td></high>	633.3 (3.5)	684.7 (4.3)	48.5 (3.0)	30.8 (3.3)
High school/vocational school	621.6 (1.9)	660.2 (5.1)	47.1 (1.6)	42.5 (3.7)
Incomplete college	618.8 (3.2)	671.9 (8.2)	46.2 (2.6)	35.6 (5.9)
College completed (L4)	605.8 (2.7)	658.0 (5.5)	44.0 (2.2)	39.8 (4.0)
L4-L1 (highest-lowest) difference	-27.2(4.4)	-26.7 (6.9)	-4.5(3.7)	9.0 (5.1)
P value for L4-L1 difference	< 0.0001	0.0001	0.2	0.08
P value for trend	< 0.0001	0.0005	0.2	0.13
Neighborhood score				
First quartile (L1)	626.1 (2.9)	678.4 (5.6)	46.3 (2.5)	27.7 (4.2)
Second quartile	620.2 (2.8)	679.3 (5.5)	47.3 (2.4)	30.6 (4.2)
Third quartile	619.2 (2.7)	664.0 (5.5)	49.5 (2.3)	44.8 (4.1)
Fourth quartile (L4)	612.4 (2.6)	660.2 (5.3)	44.8 (2.2)	44.4 (3.9)
L4-L1 (highest-lowest) difference	-13.7(3.9)	-18.2 (7.6)	-1.5(3.3)	16.7 (5.7)
P value for L4-L1 difference	0.0005	0.0163	0.6	0.004
P value for trend	0.0007	0.0038	0.8	0.0005
Combined socioeconomic score				
Mean IMT difference per unit decrease in score	-2.8(0.6)	-4.0 (1.1)	-0.9(0.5)	2.1 (0.8)
P value for linear trend	< 0.0001	0.0002	0.08	0.007

^{*}Derived from mixed models controlling for sex, side of neck, side of neck by time, center, socioeconomic variable, and socioeconomic variable by time interaction. Baseline IMT values are adjusted to 54 years of age. Change estimates are averaged over side. *P* values presented for trend for categorical variables are tests for linear trend across successive categories.

relationship of progression with increasing SES was present even when analyses were restricted to measures collected at baseline and the first follow-up. There was no evidence that the relationship between SES and IMT progression differed by baseline IMT in blacks (P for interaction >0.8). When the sample is restricted to exclude blacks with IMT values above the 95th percentile for whites (n=2817), results are similar to those obtained in the full sample of blacks reported in Table 4.

Discussion

Although numerous studies have reported strong inverse associations of socioeconomic factors with clinical cardiovascular outcomes, ^{17–19} the relation of socioeconomic factors to early atherosclerotic disease has only recently begun to be examined. To our knowledge, ours is the first study to examine socioeconomic differences in the progression of IMT in a large, diverse, population-based sample in the United States. Among white participants, IMT progression

over the 9-year follow-up was inversely related to socioeconomic position, with the strongest associations observed for income. This pattern is consistent with studies based on clinical outcomes and with previous cross-sectional and longitudinal analyses documenting increased wall thickness and more rapid progression in the lower socioeconomic groups. 6-8 In contrast, among blacks, IMT progression over the follow-up was consistently and positively related to socioeconomic position, particularly as indexed by neighborhood characteristics, such that lower socioeconomic position was associated with a lower rate of progression from baseline IMT. These results contrast with cross-sectional results at baseline, which document increased IMT in blacks of lower socioeconomic position in the same cohort.

It is possible that this unexpected positive association of SES with IMT progression in blacks results from selective attrition attributable to death or loss to follow-up of low SES blacks with rapid IMT progression. However, logistic regres-

[†]Income cutoffs were at <\$7999 (28%), \$8000-\$15 999 (25%), \$16 000-\$24 999 (18%), and \geq \$25 000 (29%) for blacks; for whites, the cutoffs were at <\$24 999 (27%), \$25 000-\$34 000 (20%), \$35 000-\$49 999 (23%), and \geq \$50 000 (31%).

TABLE 3. Association of Socioeconomic Characteristics With IMT Progression in Whites and Blacks Before and After Adjustment for Risk Factors at Baseline

	Five-Year Change in IMT (in μ m)				
	Whites		Blacks		
	Model 1*	Model 2	Model 1	Model 2	
Income					
L4-L1 (highest-lowest) difference	-11.5 (3.0)	-9.1(3.1)	11.1 (5.7)	7.7 (6.0)	
P value for L4-L1 difference	0.0001	0.0031	0.05	>0.1	
Education					
L4-L1 (highest-lowest) difference	-4.5(3.7)	0.0 (3.8)	9.0 (5.1)	8.9 (5.4)	
P value for L4-L1 difference	>0.2	>0.9	0.08	0.10	
Neighborhood score					
L4-L1 (highest-lowest) difference	-1.5 (3.3)	-1.8 (3.4)	16.7 (5.7)	14.9 (6.0)	
P value for L4-L1 difference	>0.6	>0.6	0.0035	0.0126	
Combined socioeconomic score					
Mean IMT change per unit decrease in socioeconomic score	-0.9 (0.5)	-0.3 (0.5)	2.1 (0.8)	1.9 (0.8)	
P value for linear trend	0.07	>0.6	0.0070	0.0258	

^{*}Model 1 includes sex, side, side by time, center, SES variable, and SES variable by time interaction. Model 2 adds cardiovascular risk factors at baseline (high-density lipoprotein cholesterol, smoking status, pulse pressure, diabetes, white blood cell count and fibrinogen) and their interactions with time.

sion models for attrition (data not shown) suggested that although in general, attrition was positively associated with low SES and last-measured IMT, there was little interaction evident between SES and IMT (ie, losses to follow-up did not appear to be selected on the basis of SES and IMT). Moreover, results were similar when analyses were restricted to the period between baseline and first follow-up measure (during which the amount of attrition was comparatively less than for the full follow-up) and when persons with prevalent CVD at baseline were not excluded. Another potential explanation for the inverse association of SES with progression in blacks is the high baseline IMT observed in low SES blacks at baseline, which may be associated with slower progression. However, previous published analyses of IMT progression in this sample 15 found that baseline IMT is not associated with rate of change of IMT. In addition, our findings were similar when blacks with IMT levels above the 95th percentile in whites were excluded from the analyses.

Another possible explanation for these seemingly paradoxical findings is that at the arbitrarily defined time of their entry into the ARIC cohort (45 to 64 years of age), blacks and whites as well as different socioeconomic groups within blacks are at very different stages in the natural history of atherosclerosis by virtue of their lifetime history of atherogenic exposures. It is plausible that socioeconomic effects on IMT are different at later than at earlier stages of the disease. Additionally, although the patterns that we observed did not change after adjustment for a set of baseline risk factors, it is also possible that race differences in the association of SES with progression are attributable to differential race and SES distributions of risk factors we did not investigate or changes over time in risk factors.

TABLE 4. Five-Year Changes in IMT by Selected Socioeconomic Variables, Under Various Scenarios: the ARIC Study, 1987–1998*

	Whites		Blacks	
	Income Difference (L4-L1) in IMT Progression	Neighborhood Score Difference (L4-L1) in IMT Progression	Income Difference (L4-L1) in IMT Progression	Neighborhood Score Difference (L4-L1) in IMT Progression
Full sample (data in Table 3)	-9.1 (3.1)	1.8 (3.4)	7.7 (6.0)	14.9 (6.0)
P value for L4-L1 difference	0.0031	0.5989	0.1971	0.0126
Restricted to baseline and first follow-up	-6.8(6.4)	-3.0 (6.9)	6.8 (14.0)	27.7 (13.9)
P value for L4-L1 difference	0.2893	0.6671	0.626	0.0467
Including respondents with prevalent CVD at baseline	-7.5(3.0)	-2.2(3.3)	7.8 (5.7)	14.0 (5.8)
P value for L4-L1 difference	0.0133	0.5049	0.1687	0.0156
Restricted to black participants $<$ 95th percentile of whites	1		4.1 (5.7)	15.3 (5.7)
P value for L4-L1 difference			0.4833	0.0076

^{*}Models include cardiovascular risk factors at baseline as in Table 3.

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Despite these limitations, the results strongly suggest that IMT progression is patterned by SES. Among whites, baseline IMT and progression of IMT over time were inversely associated with socioeconomic indicators. This patterning does not appear to be accounted for by baseline levels of cardiovascular risk factors shown previously to be associated with IMT progression, which suggests that other risk factors or changes in risk factors over time may play a role. Additional work on the mediators of the observed SES differences is needed. Regardless of the positive association between SES and IMT progression observed in blacks, the strong inverse association between socioeconomic position and IMT observed in the cross-sectional baseline analyses is suggestive of more rapid progression in the lower socioeconomic groups much earlier in the life course. A more complete understanding of the reasons for these socioeconomic differences, which may begin early in life, is likely to shed light on the etiology of atherosclerosis generally.

generalizable to US blacks as a whole.

Acknowledgments

These analyses were supported in part by R01-HL-64142 and P5-MD000206 (CHUMS). The Atherosclerosis Risk in Communities (ARIC) study is performed as a collaborative study supported by National Heart, Lung, and Blood Institute contracts N01-HC-55015, N01-HC-55016, N01-HC-55018, N01-HC-55019, N01-HC-55020, N01-HC-55021, and N01-HC-55022. The authors thank the staff and participants of the ARIC study for their important contributions.

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