

Socioeconomic Status and Incidence of Hospitalization With Lower-Extremity Peripheral Artery Disease: Atherosclerosis Risk in Communities Study

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Background—Compared to coronary heart disease, heart failure, and stroke, the relationship between low socioeconomic status (SES) and peripheral artery disease (PAD) is less well established. We examined the association between SES and incidence of hospitalization with PAD and explored whether this association can be explained by traditional cardiovascular risk factors and healthcare access.

Methods and Results—A total of 12 517 participants in the Atherosclerosis Risk in Communities (ARIC) Study (1987–1989) with no prior PAD were examined. Individual-level SES was assessed from household income (low <\$12 000/year, medium \$12 000 to \$24 999/year, and high ≥\$25 000/year [double to approximate to values in 2016]) and educational attainment (<high school, high school, and >high school), and area-level SES from area deprivation index (quintiles). During a median follow-up of 23.6 (Interquartile range 19.6–24.5) years, 433 participants had a hospitalization with PAD. In Cox proportional hazards regression analysis, the demographically adjusted hazard ratio was 2.42 (1.81–3.23) for low household income, 2.08 (1.60–2.69) for low educational attainment, and 2.18 (1.35–3.53) for most deprived neighborhoods, compared to their high-SES counterparts. After adjustment for traditional cardiovascular risk factors and health care access, the associations were attenuated but remained significant, particularly for income and education. Results were consistent when stratified by race (*P*-values for interaction >0.2 for all SES parameters).

Conclusions—Low individual- and area-level SES are strong predictors of hospitalization with PAD, in part due to increased prevalence of cardiovascular risk factors and poor access to care in these groups. Additional risk factors may also need to be identified and acted on to eliminate SES disparities in PAD hospitalization. (*J Am Heart Assoc.* 2017;6:e004995. DOI: 10.1161/JAHA.116.004995.)

Key Words: epidemiology • peripheral artery disease • socioeconomic position

Socioeconomic status (SES) is a major determinant of cardiovascular disease (CVD). Studies have consistently demonstrated increased risk of various CVD subtypes, such as coronary heart disease, heart failure, stroke, and mortality

in low-SES groups as compared with high-SES groups.^{1–4} Accordingly, the American Heart Association highlights that identifying and understanding social determinants of CVD are pivotal for reducing death and disability due to CVD.⁵

In this context, the association between low SES and peripheral artery disease (PAD) is less understood. Previous studies examining this association have been inconsistent.^{6–11} Importantly, all of those studies were cross-sectional and could not discuss the temporality of the association. PAD can result in devastating and unique consequences, including leg pain, ulcer, and amputation as well as premature death, and its prevalence is likely to increase in the United States.^{12,13} Therefore, specific investigation of the impact of SES on future PAD risk would be important. Also, such an investigation might be helpful in identifying high-risk groups for PAD, which can be targeted for screening or prevention of PAD and PAD-related complications.

Therefore, we aim to examine the association between SES and hospitalization with PAD in a prospective cohort study.

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Accompanying Tables S1 through S14 and Figures S1 and S2 are available at <http://jaha.ahajournals.org/content/6/8/e004995/DC1/embed/inline-supplementary-material-1.pdf>

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We examined a few individual-level (household income and educational attainment) and area-level (area deprivation index [ADI]) measures of SES. We also sought to understand whether this association can be explained by traditional cardiovascular risk factors and healthcare access.

Methods

Study Population

We used the data from the Atherosclerosis Risk in Communities (ARIC) Study, which is a large, prospective, community-based study originally focusing on the etiology and natural history of atherosclerosis and CVD. Detailed descriptions of the ARIC study design and objectives have been published elsewhere.¹⁴ Briefly, the study cohort is comprised of 15 792 participants who were aged 45 to 64 years at baseline in 1987-1989. Participants were recruited from 4 US communities: Forsyth County, NC; Jackson, MS; suburbs of Minneapolis, MN; and Washington County, MD. Four follow-up visits (visits 2-5) took place from 1990 to 1992, 1993 to 1995, 1996 to 1998, and 2011 to 2013, respectively. Institutional review boards at each site approved all procedures, and all study participants provided written informed consent.

Of the 15 792 participants, we excluded participants with prevalent clinical PAD at baseline (n=635). In addition, we excluded participants with coronary heart disease (n=766), heart failure (n=752), and stroke (n=284), leaving 13 685 participants free of CVD at baseline. Of these participants, those who were neither white nor black (n=17), few blacks in the Minnesota and Washington County sites (n=31), those with missing information on SES measures (household income [n=802] and educational attainment [n=25]), and covariates of interest (n=393) at visit 1 (1987-1989) were excluded. The final analytic sample comprised 12 517 participants.

Socioeconomic Status

Our a priori primary exposures were individual-level SES parameters, annual household income, and educational attainment. Information on both SES measures was self-reported by participants at baseline. Household income was categorized into 3 levels: less than \$12 000/year, \$12 000/year to \$24 999/year, and \$25 000/year or more in 1987-1989. For reference, \$1 in 1987-1989 corresponds to ≈\$2 in 2016.¹⁵ Educational attainment was also categorized into 3 levels: less than high school, high school or equivalent such as vocational training, and more than high school such as college, graduate, or some professional degree.

As a secondary exposure, area-level SES was assessed using ADI, which represents socioeconomic deprivation experienced by a neighborhood (at census block group level or 9-digit ZIP

code). ADI scores were calculated from participants' addresses using the Singh method.¹⁶ This involved summing 17 census indicators (Table S1) weighted by the Singh factor score coefficients for each indicator.^{16,17} The distribution of ADI values was examined, and neighborhoods were sorted into quintiles (5 equal groups) by increasing ADI. Higher ADI values indicate higher levels of deprivation.

Incident Peripheral Artery Disease Hospitalization

Incident PAD hospitalization was the primary outcome of the study. We defined PAD hospitalization as hospitalizations with a discharge diagnosis related to lower-extremity PAD. In line with previous literature,^{18,19} we used the following ICD codes: 440.20 (atherosclerosis of native arteries of the extremities, unspecified); 440.21 (atherosclerosis of native arteries of the extremities with intermittent claudication); 440.22 (atherosclerosis of native arteries of the extremities with rest pain); 440.23 (atherosclerosis of native arteries of the extremities with ulceration); 440.24 (atherosclerosis of native arteries of the extremities with gangrene); 440.29 (other atherosclerosis of native arteries of the extremities); 440.3 (atherosclerosis of bypass graft of the extremities); 440.8 (atherosclerosis of other specified arteries); 38.18 (endarterectomy), 39.25 (aorta-iliac-femoral bypass), 39.29 (other [peripheral] vascular shunt or bypass), and 39.50 (angioplasty). Details on ICD codes used for PAD hospitalization assessment is provided in Table S2. Critical limb ischemia (CLI), a severe form of PAD, was a secondary outcome of this study and was defined as cases with 440.22, 440.23, 440.24 or those with PAD who had ICD codes for amputation, ulcer, or gangrene. Participants were followed through December 31, 2012 for incidence of PAD hospitalization (including CLI). Follow-up information was available for all included participants.

Other Covariates

Age, sex, race, smoking, alcohol consumption, and physical activity were self-reported by the participants. BMI was calculated as weight (in kilograms) divided by the square of height (in meters). Systolic and diastolic blood pressures were estimated by averaging the second and third of 3 blood pressure measurements (in mm Hg). Antihypertensive and cholesterol-lowering medication use was self-reported. Diabetes mellitus was defined as self-reported physician diagnosis, current use of glucose-lowering medications, fasting blood glucose greater than or equal to 126 mg/dL (7.0 mmol/L), or random blood glucose greater than 200 mg/dL (11.1 mmol/L).²⁰ Glomerular filtration rate was estimated from a participant's serum creatinine, age, sex, and race using the Chronic Kidney Disease Epidemiology Collaboration equation.²¹ Participants self-reported information on

their health insurance status and frequency of routine healthcare visits.

Statistical Analysis

We compared baseline characteristics of study population by household income and educational attainment level using ANOVA (for continuous variables) and Pearson chi-squared test (for categorical variables). In addition, we also reported baseline characteristics by quintiles of ADI. Kaplan-Meier curves were created to compare the cumulative probability of remaining free of PAD-related hospitalization for each category of household income and educational attainment. For individual-level SES, with high household income and high educational attainment as a reference groups, Cox proportional hazards regression models were used to calculate hazard ratios (HRs) and 95% CIs for incident PAD hospitalization. The assumption of proportionality was confirmed by using generalized linear regression of the scaled Schoenfeld residuals on functions of time to test for a nonzero slope (Figure S1). For area-level SES, with least-deprived neighborhoods as the reference group (ie, highest ADI quintile), multilevel mixed-effects parametric survival models were used to calculate HR and 95% CI for incident PAD hospitalization. Two-level (individual clustered within 381 ecological units at baseline) exponential survival model with random effect for ADI was used. Multiple models were constructed to adjust for potential confounders and to explore mediating pathways that may link SES measures to PAD. Model 1 adjusted for age, sex, race, and ARIC field center (demographic confounders). In model 2, we additionally adjusted for major CVD risk factors including current smoking, current alcohol use, physical activity index (sport), BMI, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, cholesterol-lowering medication use, and diabetes mellitus (lifestyle and clinical mediators). Model 3 further adjusted for healthcare access, ie, health insurance status and frequency of routine healthcare visits (social mediators). With covariates in the fully adjusted model, the Harrell C statistic was 0.83, 0.82, and 0.83 for income, education, and ADI, respectively. The Cox proportional hazard model also fit the observed data reasonably well (Figure S2).

It is known that a high number of blacks disproportionately have low SES.²²⁻²⁴ Therefore, we tested the interaction between SES and race for PAD hospitalization risk and also present stratified analysis by race. We also explored the role of SES in the race-PAD relationship by examining whether and to what extent SES attenuates the association between race and risk of hospitalization with PAD. In addition, because the coexistence of low household income and low educational attainment may be necessary to have an impact on adverse

health outcomes,²⁵ we tested interaction between household income and educational attainment as well.

We performed a number of additional analyses. First, to test robustness of our findings, in our primary analysis we excluded people with prevalent PAD, defined as ankle-brachial index <0.9 at baseline. People with leg symptoms may have difficulty with full-time employment and consequently might have low income. Thus, to limit the possibility of reverse causation in the association between household income and incident PAD hospitalization, we examined their association after excluding participants who had symptoms of PAD at baseline and who developed PAD within first 2 years after the start of follow-up. Given that education is generally achieved in early adult life, reverse causation for educational attainment seems unlikely. Second, although we used relevant cutoffs for household income, there were fewer participants in the low-income category. Thus, to have more equal distribution of participants across income categories, we examined the robustness of our findings for other cutoffs for household income level: <\$16 000/year (low) (n=2567), \$16 000/year to \$34 999/year (medium) (n=4112), and ≥\$35 000/year (high) (n=5838).²⁶ Third, we examined the association between SES measures and PAD hospitalization while accounting for chronic psychological stress (available at visit 2), another potential mediator. Chronic psychological stress was measured using 21-item Maastricht Questionnaire, which assesses vital exhaustion.²⁷ Responses from these items (0=no, 1=don't know, and 2=yes) were summed to obtain a score for psychological stress (higher score indicating increased psychological stress). Finally, to assess robustness of findings for non-CLI events, we examined association between SES measures and non-CLI events.

A 2-tailed *P*-value of <0.05 (2-sided) was considered statistically significant. All analyses were conducted using Stata version 14.0 (College Station, TX).

Results

Baseline Characteristics

Baseline characteristics of the study population are presented according to household income and educational attainment level in Table 1. Participants in low-income households (<\$12 000/year) were more likely to be older, female, and of black ancestry compared with participants in high-income households (≥\$25 000/year). Similarly, the proportions of participants currently smoking, using antihypertensive medication, having diabetes mellitus, no health insurance, and no routine visits to seek health care were higher in low-income households compared to those in high-income households. Participants in low-income households on average had higher BMI, total cholesterol, systolic and diastolic blood pressure, and

Table 1. Baseline Characteristics of ARIC Study Population at Visit 1 (1987–1989) by Level of Household Income and Educational Attainment*

	Income Level			Educational Attainment		
	Low	Medium	High	Low	Medium	High
	<\$12 000/y	\$12 000/y to \$24 999/y	≥\$25 000/y	<High School	High School/Equivalent	>High School
N	1707	2719	8091	2674	5190	4653
Age, y	55.5±5.9	55.1±5.8	53.1±5.5	55.6±5.6	53.7±5.6	53.1±5.7
Sex, male, n (%)	475 (27.8)	1065 (39.2)	4086 (50.5)	1162 (45.1)	1971 (39.6)	2261 (50.6)
Race, black, n (%)	1117 (65.4)	922 (33.9)	927 (11.5)	1138 (44.2)	810 (16.3)	917 (20.5)
Current smoking, n (%)	574 (33.6)	727 (26.7)	1848 (22.8)	835 (32.4)	1305 (26.2)	877 (19.6)
Current alcohol intake, n (%)	545 (31.9)	1209 (44.5)	5501 (69.9)	954 (37.0)	2955 (59.3)	3071 (68.7)
Physical activity (sports index)	2.2±0.7	2.3±0.7	2.6±0.8	2.2±0.7	2.4±0.8	2.6±0.8
BMI, kg/m ²	29.2±6.5	28.0±5.5	26.9±4.6	28.7±5.8	27.3±5.1	26.9±4.7
Systolic blood pressure, mm Hg	127.9±21.4	123.6±19.1	117.9±16.7	125.8±19.8	120.0±18.1	118.1±16.9
Diastolic blood pressure, mm Hg	76.6±12.4	74.4±11.6	72.5±10.3	75.3±12.0	73.0±10.8	73.1±10.7
Antihypertension medicine use, n (%)	618 (36.2)	793 (29.2)	1665 (20.6)	864 (33.5)	1175 (23.6)	940 (21.0)
Diabetes mellitus, n (%)	338 (19.8)	351 (12.9)	575 (7.1)	418 (16.2)	462 (9.3)	334 (7.5)
Total cholesterol, mmol/L	5.7±1.2	5.6±1.1	5.5±1.0	5.6±1.1	5.6±1.1	5.4±1.0
High-density lipoprotein, mmol/L	1.40±0.4	1.36±0.4	1.33±0.4	1.33±0.4	1.34±0.4	1.36±0.4
Cholesterol-lowering medication use (yes), n (%) [†]	205 (2.6)	63 (2.3)	39 (2.3)	108 (2.3)	133 (2.6)	66 (2.5)
Ankle-brachial index	1.13±0.1	1.14±0.1	1.14±0.1	1.13±0.1	1.14±0.1	1.15±0.1
Estimated GFR, mL/(min·1.73 m ²)	106.7±19.6	103.6±15.7	101.6±13.4	103.9±17.2	102.5±14.2	102.4±14.6
Health insurance (no), n (%)	616 (36.1)	315 (11.6)	190 (2.3)	594 (22.2)	343 (6.6)	184 (3.9)
Routine visits to seek health care, n (%)						
No	568 (33.3)	884 (32.5)	2149 (26.5)	973 (36.4)	1609 (31.0)	1109 (21.9)
Less than once per year	342 (20.0)	642 (23.6)	2758 (34.1)	579 (21.6)	1520 (29.3)	1643 (35.3)
Once or more per year	797 (46.7)	1193 (43.9)	3184 (39.3)	1122 (41.9)	2061 (39.7)	1991 (42.8)

ARIC indicates Atherosclerosis Risk in Communities Study; GFR, glomerular filtration rate; PAD, peripheral artery disease.

*All comparisons had $P < 0.001$ except high-density lipoprotein for education with P of 0.005 and cholesterol-lowering medication use with P of 0.75 for household income and 0.73 for educational attainment.

[†]Additional 94 participants were missing information on cholesterol-lowering medication use.

lower physical activity index and ankle-brachial index. There was no statistically significant difference in cholesterol-lowering medication use across household income groups. The distribution of participant characteristics across levels of educational attainment was similar to the distribution of participant characteristics across levels of household income. Similar patterns were observed across ADI quintiles as well except for age with an inverse U-shaped pattern (Table S3).

Individual-Level Socioeconomic Status and Incident Peripheral Artery Disease Hospitalization

During a median follow-up of 23.6 years (interquartile interval 19.6–24.5 years), 433 participants had hospitalizations with a

diagnosis of PAD. The Kaplan-Meier curve indicated cumulative probability of survival free from PAD-related hospitalization was lowest in the low-household-income and low-educational-attainment groups (Figure) ($P < 0.001$ from log-rank test for both household income and educational attainment). Even after adjustment for age, sex, and race center, the risk of hospitalization with PAD in the group with lowest household income was approximately double compared with the group with high household income (HR=2.42, 95%CI 1.81–3.23, model 1 in Table 2). Similarly, the risk was 2-fold higher in the low-educational-attainment group (HR=2.08, 95%CI 1.60–2.69) compared with high-educational-attainment group. Also the medium group for income and education showed increased risk of hospitalization with

PAD. With further adjustment for potential mediators including major CVD risk factors (model 2) and factors related to healthcare access (model 3), associations of low household income and low educational attainment with risk of hospitalization with PAD were attenuated but remained statistically significant. Medium income demonstrated a significantly increased risk of hospitalization with PAD even in models 2 and 3 as well. Similar results were obtained when analysis was stratified by race (Table S4). There was no statistical interaction observed between race and SES (P for interaction=0.85 for household income and 0.82 for educational attainment in model 3) and between household income and educational attainment (P for interaction=0.62) for the risk of PAD. Although the association between race and incident PAD hospitalization remained statistically significant, both annual household income and educational attainment attenuated about 21% and 8% of this association, respectively (Table S5).

Area-Level Socioeconomic Status and Incident Peripheral Artery Disease Hospitalization

In the age, sex, and race-center-adjusted model (model 1), people in the most deprived neighborhoods (ie, highest quintile of ADI) had \approx 2-fold higher likelihood of incident PAD hospitalization (HR 2.18, 95%CI 1.35-3.53) compared with those in the least deprived neighborhoods (ie, lowest quintile of ADI) (Table 3). This association attenuated, although point estimates were similar to point estimates for low household income or low educational attainment, further adjustment for major CVD risk factors (model 2) and factors related to healthcare access (model 3). When analysis was stratified by race, although the pattern was somewhat variable, incidence of hospitalization with PAD tended to be higher in deprived neighborhoods compared with least-deprived neighborhoods in both whites and blacks (Table S6). No statistical interaction was observed between race and ADI (P for interaction=0.35 in model 3). Similar to individual-level SES measures, ADI attenuated about 27% of the association between race and incident PAD hospitalization (Table S5).

Additional Analyses

Analysis of redefined household income levels (ie, <\$16 000/year [low], \$16 000/year to \$34 999/year [medium], and \geq \$35 000/year [high]) supported our primary analyses (Table S7). The associations of SES individual- and area-level measures with CLI ($n=161$) were essentially similar to their associations with incident PAD hospitalization (Tables S8 and S9). After excluding participants with intermittent claudication at baseline and those who developed PAD within the first 2 years of the start of follow-up, the association between household income level and incident PAD hospitalization was

well in line with our main results (Table S10). Association between SES measures and incident PAD hospitalization was significant when additionally adjusted for chronic psychological stress (Tables S11 and S12). Low SES was also associated with non-CLI events in a demographically adjusted model, although this association was not significant when adjusted for major CVD risk factors and factors related to healthcare access (Tables S13 and S14).

Discussion

In this prospective cohort study with more than 12 000 middle-aged US adults, we found that individual- and area-level SES, assessed as household income, educational attainment, or area deprivation index, is associated with risk of hospitalization with PAD with \approx 2-fold higher risk between their lowest and highest categories, after accounting for demographic factors. Although there was some attenuation, adjusting for traditional CVD risk factors as well as factors related to healthcare access did not fully explain this association. The associations were consistent in whites and blacks, and there was no interaction between household income and educational attainment.

Several prior studies have cross-sectionally investigated the association between SES measures and PAD and obtained conflicting results.⁶⁻¹¹ This study expands current knowledge in a number of aspects. First, using a long follow-up (23.6 years) of a relatively large study population (>250 000 person-years), including a large number of blacks, the present study found a strong association between SES and future risk of hospitalization with PAD. Second, this association was robust and similar across various measures of SES and across race, suggesting that people with low income, low education, or living in deprived neighborhoods are at a higher risk of hospitalization with PAD regardless of their races. Third, our results suggest that traditional risk factors and access to health care are important factors in this association, but it is likely that some other factors still play a role. Finally, we confirmed the same patterns for CLI, a devastating clinical condition with extremely high risk of death or leg amputation.¹²

There are several potential mechanisms behind the SES-PAD association. High prevalence of traditional CVD risk factors in low-SES groups is a potential mechanism.²⁸ Healthcare access might also explain excess risk of hospitalization with PAD in low-SES groups. More people in low SES than high SES lack health insurance and do not routinely seek care, which may mean they have more advanced PAD at the time of first diagnosis.²⁹ Indeed, in our study, prevalence of traditional CVD risk factors, lack of health insurance, and limited or no visit to seek routine care was high in low-SES groups, and the adjustment for these factors attenuated the association between SES and incidence of hospitalization with

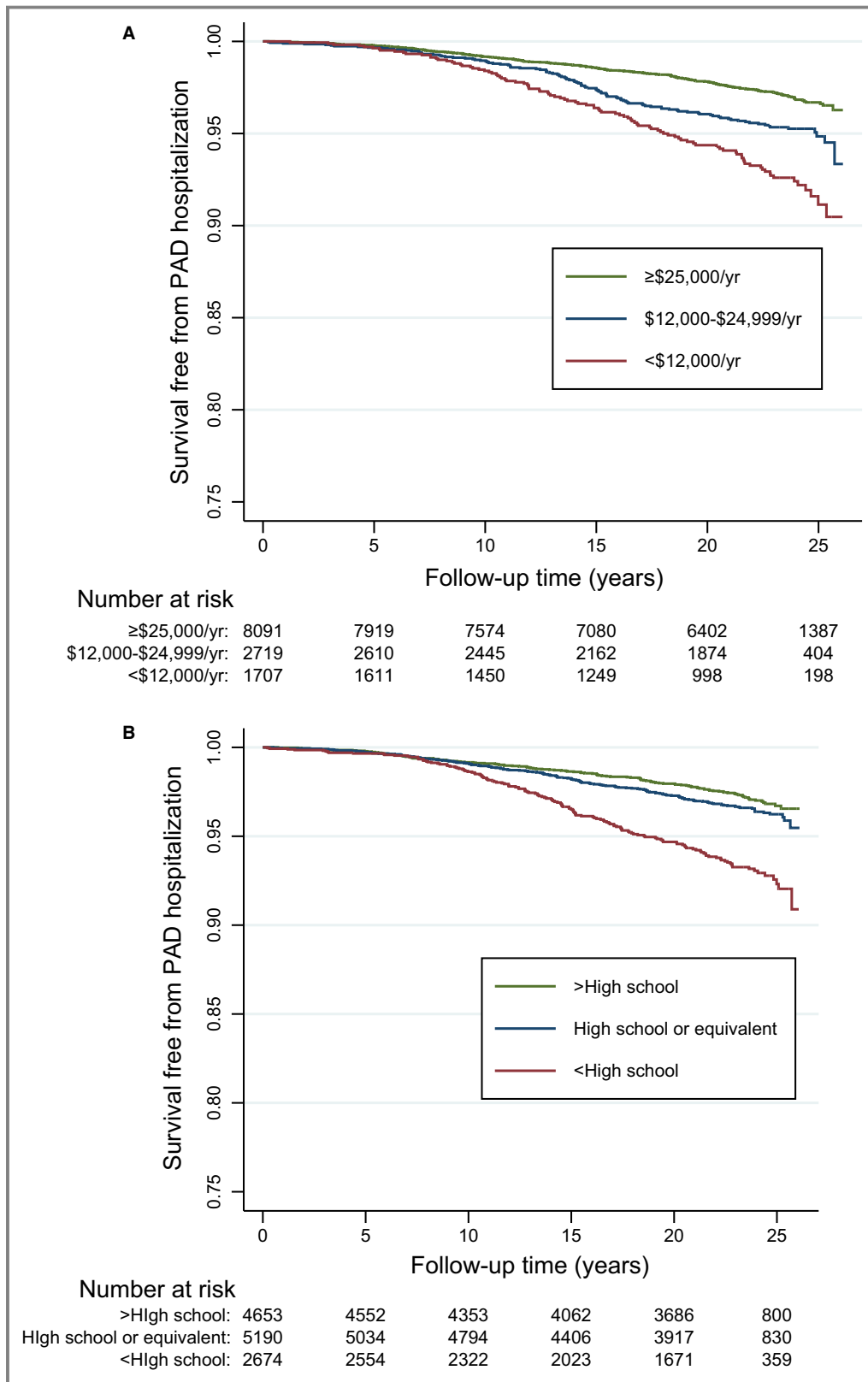


Figure. Kaplan-Meier curves showing cumulative probability of survival free from hospitalization with PAD by (A) annual household income and (B) educational attainment level. PAD indicates peripheral artery disease.

Table 2. Association Between Household Income and Educational Attainment Level and Incidence of Hospitalization With PAD

	Household Income			P-Trend
	High	Medium	Low	
	≥\$25 000/y (n=8091)	\$12 000/y to \$24 999/y (n=2719)	<\$12 000/y (n=1707)	
Events, n (%)	2.8 (223)	4.0 (110)	5.9 (100)	
Model 1, HR (95%CI)	(Ref)	1.53 (1.20-1.95)	2.42 (1.81-3.23)	<0.001
Model 2, HR (95%CI)	(Ref)	1.32 (1.03-1.69)	1.64 (1.21-2.20)	0.001
Model 3, HR (95%CI)	(Ref)	1.29 (1.01-1.66)	1.54 (1.13-2.10)	0.004
	Educational Attainment			P-Trend
	High	Medium	Low	
	(>High School) (n=4653)	(High School/Equivalent) (n=5190)	(<High School) (n=2674)	
Events, n (%)	2.6 (123)	3.1 (162)	5.5 (148)	
Model 1, HR (95%CI)	(Ref)	1.27 (1.00-1.61)	2.08 (1.60-2.69)	<0.001
Model 2, HR (95%CI)	(Ref)	1.05 (0.82-1.33)	1.42 (1.08-1.85)	0.01
Model 3, HR (95%CI)	(Ref)	1.04 (0.81-1.32)	1.36 (1.04-1.79)	0.03

Model 1: age, sex, race-center. Model 2: model 1+current smoking, current alcohol intake, physical activity (sport index), BMI, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes mellitus, total cholesterol, high-density lipoprotein cholesterol, cholesterol-lowering medication use, estimated glomerular filtration rate. Model 3: model 2+health insurance status, frequency of routine healthcare visit. CI indicates confidence interval; HR, hazard ratio; PAD, peripheral artery disease; Ref, reference value.

PAD. However, because adjustment for these factors did not completely attenuate this association, other factors may still play a role. Other plausible factors linking SES to PAD includes chronic psychological stress and limited health literacy. Chronic psychological stress is often higher in low-SES groups (as also seen in our study: Tables S10 and S11) and is shown to be associated with atherosclerosis (possibly via chronic inflammation).^{30,31} Limited health literacy in the low-SES groups might influence their health-seeking behaviors (eg, when and where to seek care, adherence to medication) and thus might also explain some of the excess risk of hospitalizations with PAD in low-SES groups.^{32,33}

In our study the association between ADI and hospitalization with PAD was not statistically significant after adjustment for CVD risk factors. This kind of weaker association for area-level SES parameters compared to individual-level parameters has been seen in previous studies.³⁴⁻³⁶ This pattern has been attributed to less granular and precise assessment of individual characteristics when using area-level SES.³⁷ Of note, ADI did not reach significance due to wide 95% CIs, but its point estimates for most- versus least-deprived neighborhood were similar to the point estimates for the association of low income and low education with PAD hospitalization in each model.

Table 3. Association Between Area Deprivation Index and Incidence of Hospitalization With PAD in Participants Free of PAD at Baseline

	Area Deprivation Index*					P-Trend
	Quintile 1 (Least Deprived)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (Most Deprived)	
	29.3 to 96.0 (n=2452)	96.1 to 101.7 (n=2460)	101.8 to 107.2 (n=2480)	107.3 to 112.5 (n=2405)	112.6 to 127.5 (n=2445)	
Events, % (n)	2.4 (59)	3.6 (89)	2.9 (73)	3.5 (84)	3.9 (120)	
Model 1, HR (95%CI)	(Ref)	1.51 (1.08-2.12)	1.31 (0.92-1.87)	1.57 (1.02-2.42)	2.18 (1.35-3.53)	0.008
Model 2, HR (95%CI)	(Ref)	1.27 (0.91-1.78)	1.05 (0.73-1.49)	1.29 (0.86-1.93)	1.39 (0.85-2.26)	0.33
Model 3, HR (95%CI)	(Ref)	1.27 (0.91-1.78)	1.03 (0.72-1.47)	1.27 (0.85-1.91)	1.33 (0.81-2.17)	0.42

Model 1: age, sex, race-center. Model 2: model 1+current smoking, current alcohol intake, physical activity (sport index), BMI, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes mellitus, total cholesterol, high-density lipoprotein cholesterol, cholesterol-lowering medication use, estimated glomerular filtration rate. Model 3: model 2+health insurance status, frequency of routine healthcare visits. CI indicates confidence interval; HR, hazards ratio; PAD, peripheral artery disease Ref, reference value. *Additional 275 participants were missing information on area deprivation index at baseline.

Higher risk of PAD in blacks compared with whites has been widely reported,²²⁻²⁴ and low SES is considered a contributing factor of this racial disparity. Indeed, the adjustment for SES attenuated the association between race and hospitalization with PAD in our study. Nonetheless, to fully address racial disparity in PAD, SES parameters other than what were evaluated in the current study, and non-SES factors such as genetics should be explored.

Our findings have a number of public health practice and research implications. Although screening for PAD using ankle-brachial index is controversial, a few clinical guidelines recommend ankle-brachial index measurement in older adults or middle-aged adults with traditional risk factors, but none of them take into account SES.³⁸ Our findings suggest that those at low SES are at high risk of PAD and thus may be a reasonable target for PAD screening. Nonetheless, the cost-effectiveness of such an approach needs to be investigated. Major CVD risk factors are known to be influenced by SES, and our findings reconfirm the importance of these risk factors behind the SES-PAD relationship. Thus, although it may be hard to intervene on SES itself, our findings suggest that traditional risk factors play an important role in SES-PAD association, and their control may be beneficial in reducing SES disparities in hospitalization with PAD. However, current prevention and management of CVD risk factors mostly take place in the healthcare setting, whereas people in low-SES groups often have limited healthcare access. Thus, it would be necessary to implement community-level interventions such as the National Implementation and Dissemination for Chronic Disease Prevention,³⁹ focusing on community-level improvement of physical activity, tobacco control, and access to disease management opportunities. Nonetheless, because the adjustment for traditional risk factors and healthcare access did not completely attenuate the SES-PAD hospitalization relationship in our study, examination of other mediators such as psychosocial factors (eg, chronic stress, health literacy) would be of importance.

It is important to acknowledge limitations of the present study. First, our case ascertainment relied on hospitalized cases, and thus, we were likely to miss mild cases that were treated in outpatient settings. This may raise a concern that our findings may be biased by lower hospitalization threshold in lower SES because of severe disease manifestation due to access to care, patterns of medical care utilization, and management of PAD.⁴⁰⁻⁴² However, the associations remained significant even after accounting for health insurance status and frequency of medical care utilization. Nonetheless, PAD cases requiring hospitalizations have poor prognosis and quality of life and are important drivers of medical expenditure related to PAD^{43,44}; thus, our findings for PAD-related hospitalizations are of value. Second, we did not

have information on some details about hospital admission (eg, direct inpatient versus admissions from emergency department or types of hospitals such as safety net hospitals) with PAD. This might have provided a clue to whether low-SES individuals with PAD were more likely to receive care in an emergent setting. Third, we lacked detailed information on barriers in accessing healthcare (eg, distance to health center and availability of transportation) and quality of care (eg, number of specialized physicians and physician-to-population ratio), which may have been useful in understanding the role of rural/urban differences in access to care in the SES-PAD association. Finally, the ARIC study consists of data from 4 US communities, and thus, our findings may not be generalizable to the entire US population. However, risk factor profiles in ARIC participants are similar to those reported in other population-based US studies.⁴⁵ The strengths of this study, however, include the prospective design, large number of outcomes, rigorous measurement of a number of CVD risk factors, and detailed assessment of PAD-related hospitalization utilizing comprehensive and adjudicated surveillance data for clinical events.

In conclusion, low individual- and area-level SES, assessed as household income, educational attainment, and area deprivation, are strongly associated with future risk of hospitalization with PAD. Disproportionate distribution of CVD risk factors and access to care across SES groups explained part of the excess risk of PAD hospitalization in low-SES groups but did not fully explain this association. Our study highlights low SES as an underrecognized risk group for PAD hospitalization. Further studies are needed to identify other factors responsible for the remaining excess risk of PAD hospitalization in low-SES groups.

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had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. Vart conceived the study and formulated the analysis plan with Coresh and Matsushita. Vart analyzed the data and interpreted results with Matsushita. Matsushita, Kwak, and Ballew helped in data acquisition. All authors reviewed and revised it critically for important intellectual content. All authors approved the manuscript version to be published.

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Supplemental Material

Table S1. List of 17 indicators of socioeconomic status used to obtain Area Deprivation Index

No.	List of indicators
1	Percent of the population aged 25 and older with less than 9 years of education
2	Percent of the population aged 25 and older with at least a high school diploma
3	Percent employed persons aged 16 and older in white-collar occupations
4	Median family income in US dollars
5	Income disparity
6	Median home value in US dollars
7	Median gross rent in US dollars
8	Median monthly mortgage in US dollars
9	Percent of owner-occupied housing units
10	Percent of civilian labor force population aged 16 years and older who are unemployed
11	Percent of families below federal poverty level
12	Percent of the population below 150% of the federal poverty threshold
13	Percent of single-parent households with children less than 18 years of age
14	Percent of households without a motor vehicle
15	Percent of households without a telephone
16	Percent of occupied housing units without complete plumbing
17	Percent of households with more than 1 person per room

Table S2. Description of ICD codes used for PAD hospitalization assessment

No.	ICD code	Description	Number of cases*
1	440.20	Atherosclerosis of native arteries of the extremities, unspecified	117
2	440.21	Atherosclerosis of native arteries of the extremities with intermittent claudication	103
3	440.22	Atherosclerosis of native arteries of the extremities with rest pain	30
4	440.23	Atherosclerosis of native arteries of the extremities with ulceration	38
5	440.24	Atherosclerosis of native arteries of the extremities with gangrene	87
6	440.29	Other atherosclerosis of native arteries of the extremities	11
7	440.3	Atherosclerosis of bypass graft of the extremities	2
8	440.8	Atherosclerosis of other specified arteries	12
9	38.18	Endarterectomy	35
10	39.25	Aorta-iliac-femoral bypass	39
11	39.29	Other (peripheral) vascular shunt or bypass	99
12	39.50	Angioplasty	150

*290 PAD cases had more than one ICD code

Table S3. Baseline characteristics of ARIC study population at visit 1 (1987-1989) by quintile of area deprivation index

	Area deprivation index*				
	Quintile 1 (Least deprived)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (Most deprived)
N	2,637	2,564	2,539	2,374	2,128
Age (years)	53.4 ± 5.7	53.8 ± 5.6	54.4 ± 5.7	54.0 ± 5.8	53.8 ± 5.7
Sex (male), % (n)	44.6 (5,394)	53.6 (232)	53.6 (232)	53.6 (232)	53.6 (232)
Race (African-American), % (n)	0.9 (24)	3.9 (101)	8.8 (223)	23.9 (567)	94.2 (2,005)
Household income (<\$12,000/yr), % (n)	2.0 (53)	5.4 (138)	8.9 (226)	11.8 (281)	45.3 (963)
Education (<high school), % (n)	6.3 (166)	12.8 (329)	19.1 (484)	25.9 (614)	47.3 (1,006)
Current smoking, % (n)	21.5 (567)	23.8 (610)	26.6 (674)	24.2 (575)	30.5 (649)
Current alcohol intake, % (n)	78.9 (2,081)	67.4 (1,728)	58.3 (1,480)	49.8 (1,183)	30.6 (652)
Physical activity (sports index)	2.6 ± 0.8	2.6 ± 0.8	2.4 ± 0.8	2.4 ± 0.8	2.1 ± 0.7
Body mass index (kg/m²)	26.3 ± 4.3	26.8 ± 4.7	27.2 ± 4.9	27.7 ± 5.2	29.6 ± 6.2
Systolic blood pressure (mmHg)	116.8 ± 16.5	118.3 ± 16.6	119.8 ± 17.5	120.3 ± 17.6	128.9 ± 21.4
Diastolic blood pressure (mmHg)	71.9 ± 9.8	72.1 ± 9.9	72.3 ± 10.5	72.9 ± 10.9	79.5 ± 12.3
Anti-hypertension medication use, % (n)	16.9 (445)	21.2 (543)	21.7 (551)	27.5 (653)	38.5 (820)
Diabetes, % (n)	5.7 (149)	8.6 (221)	9.6 (244)	10.5 (249)	17.8 (378)
Total cholesterol (mmol/L)	5.4 ± 1.0	5.5 ± 1.0	5.6 ± 1.0	5.6 ± 1.1	5.6 ± 1.2
High density lipoprotein (mmol/L)	1.38 ± 0.4	1.32 ± 0.4	1.31 ± 0.4	1.31 ± 0.4	1.43 ± 0.5
Ankle-brachial index	1.15 ± 0.1	1.14 ± 0.1	1.15 ± 0.1	1.15 ± 0.1	1.14 ± 0.1
Estimated GFR (ml/min/1.73m²)	99.9 ± 12.2	100.7 ± 12.8	100.9 ± 13.1	102.6 ± 15.4	110.9 ± 19.2
Health insurance (No), % (n)	1.9 (47)	4.1 (102)	4.5 (111)	8.1 (196)	26.0 (637)
Routine visits to seek health care					
No	23.1 (566)	27.3 (671)	31.0 (770)	35.0 (842)	26.9 (659)
Less than once per year	36.3 (891)	34.5 (849)	29.7 (736)	28.9 (694)	20.7 (506)
Once or more per year	40.6 (995)	38.2 (940)	39.3 (974)	36.1 (869)	52.3 (1,280)

Abbreviations: ARIC= Atherosclerosis Risk in Communities Study, GFR=glomerular filtration rate

*p for difference was <0.001 for all variables except for ankle-brachial index where p for difference was 0.002

Table S4. Association between household income and educational attainment level and incidence of hospitalization with PAD by race*

	Household income			p-trend
	High ≥\$25,000/yr	Medium \$12,000-\$24,999/yr	Low <\$12,000/yr	
Whites	n=7,164	n=1,797	n=590	
Events, n (%)	2.7 (194)	4.0 (72)	5.6 (33)	
Model 1, HR (95% CI)	(Ref.)	1.57 (1.19 – 2.08)	2.55 (1.72 – 3.77)	<0.001
Model 2, HR (95% CI)	(Ref.)	1.35 (1.01 – 1.79)	1.61 (1.07 – 2.42)	0.01
Model 3, HR (95% CI)	(Ref.)	1.35 (1.01 – 1.80)	1.64 (1.07 – 2.52)	0.01
African-Americans	n=927	n=922	n=1,117	
Events, n (%)	3.1 (29)	4.1 (38)	6.0 (67)	
Model 1, HR (95% CI)	(Ref.)	1.37 (0.84 – 2.23)	2.19 (1.38 – 3.48)	0.001
Model 2, HR (95% CI)	(Ref.)	1.23 (0.75 – 2.03)	1.63 (1.01 – 2.65)	0.04
Model 3, HR (95% CI)	(Ref.)	1.18 (0.72 – 1.95)	1.41 (0.85 – 2.35)	0.18
	Educational attainment			p-trend
	High (>high school)	Medium (high school/equivalent)	Low (<high school)	
Whites	n=3,713	n=4,345	n=1,493	
Events, n (%)	2.6 (96)	3.0 (131)	4.8 (72)	
Model 1, HR (95% CI)	(Ref.)	1.27 (0.97 – 1.64)	1.99 (1.44 – 2.77)	<0.001
Model 2, HR (95% CI)	(Ref.)	0.99 (0.76 – 1.30)	1.28 (0.91 – 1.79)	0.22
Model 3, HR (95% CI)	(Ref.)	0.99 (0.75 – 1.29)	1.26 (0.90 – 1.78)	0.25
African-Americans	n=940	n=845	n=1,181	
Events, n (%)	2.9 (27)	3.7 (31)	6.4 (76)	
Model 1, HR (95% CI)	(Ref.)	1.33 (0.79 – 2.23)	2.30 (1.47 – 3.61)	<0.001
Model 2, HR (95% CI)	(Ref.)	1.22 (0.71 – 2.07)	1.70 (1.07 – 2.71)	0.02
Model 3, HR (95% CI)	(Ref.)	1.17 (0.69 – 2.01)	1.56 (0.97 – 2.50)	0.05

Abbreviations: PAD=peripheral artery disease, HR= hazard ratio, CI=confidence interval

Model 1: Age, sex, study center

Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, estimate glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

*p for race-income interaction was 0.85 and race-education interaction was 0.82 (Model 3)

Table S5. Association between race and risk of PAD hospitalization in demographically adjusted model and when additionally adjusting for individual SES measures

	Race		p-value	% attenuation
	Whites (n=9,771)	African-Americans (n=2,966)		
Events, % (n)	3.1 (299)	4.5 (134)		
Model 1, HR (95% CI)	(Ref.)	2.33 (1.36 – 3.99)	0.002	NA
Model 2, HR (95% CI)	(Ref.)	1.87 (1.08 – 3.22)	0.024	21 (13 – 28)
Model 3, HR (95% CI)	(Ref.)	2.17 (1.26 – 3.71)	0.005	8 (3 – 13)
Model 4, HR (95% CI)	(Ref.)	1.82 (1.02 – 3.24)	0.044	27 (8 – 46)

Abbreviations: PAD=peripheral artery disease, HR= hazard ratio, CI=confidence interval

Model 1: Age, sex, study site

Model 2: Model 1 + annual household income

Model 3: Model 1 + educational attainment

Model 4: Model 1 + area deprivation index quintile

Table S6. Association between area deprivation index and risk of hospitalization with PAD in participants free of PAD at baseline by race*

	Area deprivation index**					p-trend
	Quintile 1 (Least deprived)	Quintile 2	Quintile 3	Quintile 4	Quintile 5 (Most deprived)	
Whites	(29.3 – 94.0) n=1,865	(94.1 – 99.3) n=1,911	(99.4 – 103.2) n=1,863	(103.3 – 108.9) n=1,899	(109.0 – 123.8) n=1,784	
Events, % (n)	2.3 (42)	3.5 (67)	3.4 (64)	3.4 (64)	3.1 (56)	
Model 1, HR (95% CI)	(Ref.)	1.61 (1.07 – 2.41)	1.53 (1.02 – 2.31)	1.66 (1.09 – 2.54)	1.64 (0.97 – 2.77)	0.05
Model 2, HR (95% CI)	(Ref.)	1.37 (0.92 – 2.03)	1.23 (0.82 – 1.83)	1.22 (0.80 – 1.86)	1.11 (0.69 – 1.79)	0.80
Model 3, HR (95% CI)	(Ref.)	1.37 (0.92 – 2.03)	1.23 (0.82 – 1.83)	1.22 (0.80 – 1.85)	1.11 (0.69 – 1.78)	0.83
African-Americans	(70.1 – 111.5) n=641	(111.9 – 115.6) n=587	(115.7 – 117.9) n=550	(118.1 – 119.4) n=573	(119.6 – 127.5) n=569	
Events, % (n)	2.9 (19)	3.6 (21)	5.6 (31)	4.0 (23)	6.7 (38)	
Model 1, HR (95% CI)	(Ref.)	1.20 (0.64 – 2.24)	1.89 (1.05 – 3.41)	1.33 (0.71 – 2.49)	2.27 (1.28 – 4.01)	0.01
Model 2, HR (95% CI)	(Ref.)	1.09 (0.58 – 2.04)	1.78 (0.97 – 3.25)	1.15 (0.61 – 2.18)	1.79 (1.00 – 3.21)	0.08
Model 3, HR (95% CI)	(Ref.)	1.08 (0.57 – 2.02)	1.68 (0.92 – 3.08)	1.04 (0.55 – 1.99)	1.68 (0.93 – 3.05)	0.14

Abbreviations: PAD= Peripheral artery disease, HR= Hazards ratio, CI=confidence interval

Model 1: Age, sex, site

Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, estimated glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

*p for race-area deprivation interaction was 0.35 (Model 3)

**Additional 275 participants were missing information on area deprivation index at baseline

Table S7. Association between household income and educational attainment level and incidence of CLI

	Household income			p-trend
	High ≥\$25,000/yr (n=8,091)	Medium \$12,000-\$24,999/yr (n=2,719)	Low <\$12,000/yr (n=1,707)	
Events, n (%)	0.8 (65)	1.4 (37)	3.5 (59)	
Model 1, HR (95% CI)	(Ref.)	1.40 (0.91 – 2.16)	3.09 (1.99 – 4.81)	<0.001
Model 2, HR (95% CI)	(Ref.)	1.25 (0.81 – 1.95)	2.24 (1.41 – 3.55)	<0.001
Model 3, HR (95% CI)	(Ref.)	1.22 (0.79 – 1.89)	1.96 (1.21 – 3.16)	0.01
	Educational attainment			p-trend
	High (>high school) (n=4,653)	Medium (high school/equivalent) (n=5,190)	Low (<high school) (n=2,674)	
Events, n (%)	0.8 (36)	1.1 (55)	2.6 (70)	
Model 1, HR (95% CI)	(Ref.)	1.52 (1.00 – 2.32)	2.60 (1.70 – 4.00)	<0.001
Model 2, HR (95% CI)	(Ref.)	1.29 (0.84 – 1.99)	1.85 (1.19 – 2.88)	0.01
Model 3, HR (95% CI)	(Ref.)	1.26 (0.82 – 1.95)	1.69 (1.08 – 2.66)	0.02

Abbreviations: CLI= critical limb ischemia, HR= hazard ratio, CI=confidence interval

Model 1: Age, sex, race-center

Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, estimated glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

Table S8. Association between area deprivation index and incidence of CLI

	Area deprivation index*					p-trend
	Quintile 1 (Least deprived) (29.3 – 96.0) (n=2,452)	Quintile 2 (96.1 – 101.7) (n=2,460)	Quintile 3 (101.8 – 107.2) (n=2,480)	Quintile 4 (107.3 – 112.5) (n=2,405)	Quintile 5 (Most deprived) (112.6 – 127.5) (n=2,445)	
Events, % (n)	0.5 (12)	0.9 (22)	1.0 (25)	1.2 (29)	2.8 (69)	
Model 1, HR (95% CI)	(Ref.)	1.86 (0.90 – 3.85)	2.10 (1.01 – 4.34)	2.35 (1.03 – 5.36)	2.95 (1.23 – 7.06)	0.02
Model 2, HR (95% CI)	(Ref.)	1.46 (0.71 – 3.00)	1.65 (0.80 – 3.41)	1.94 (0.86 – 4.38)	2.08 (0.87 – 5.00)	0.10
Model 3, HR (95% CI)	(Ref.)	1.45 (0.71 – 2.98)	1.62 (0.79 – 3.33)	1.92 (0.85 – 4.30)	1.94 (0.81 – 4.66)	0.13

Abbreviations: CLI= critical limb ischemia, HR= hazards ratio, CI=confidence interval

Model 1: Age, sex, race-center

Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, estimated glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

*Additional 275 participants were missing information on area deprivation at baseline

Table S9. Association between income level and risk of PAD after excluding participants with PAD symptoms at baseline and who developed PAD within the first 2 years of follow-up

	Household income			p-trend
	High ≥\$25,000/yr (n=7,997)	Medium \$12,000-\$24,999/yr (n=2,663)	Low <\$12,000/yr (n=1,662)	
Events, % (n)	2.6 (212)	3.9 (105)	5.8 (96)	
Model 1, HR (95% CI)	(Ref.)	1.52 (1.18 – 1.95)	2.37 (1.77 – 3.18)	<0.001
Model 2, HR (95% CI)	(Ref.)	1.29 (1.01 – 1.67)	1.66 (1.23 – 2.23)	0.001
Model 3, HR (95% CI)	(Ref.)	1.27 (0.98 – 1.63)	1.57 (1.15 – 2.14)	0.01

Abbreviations: PAD=peripheral artery disease, HR= hazard ratio, CI=confidence interval

Model 1: Age, sex, race-center

Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, estimated glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

Table S10. Association between household income level (redefined: <\$16,000/yr (low), \$16,000-\$34,999/yr (medium) and ≥\$35,000/yr (high)) and risk of hospitalization with PAD in participants free of PAD at baseline

	Household income			p-trend
	High ≥\$35,000/yr (n=5,838)	Medium \$16,000-\$34,999/yr (n=4,112)	Low <\$16,000/yr (n=2,567)	
Events, % (n)	2.8 (163)	3.1 (126)	5.6 (144)	
Model 1, HR (95% CI)	(Ref.)	1.12 (0.88 – 1.43)	2.24 (1.70 – 2.94)	<0.001
Model 2, HR (95% CI)	(Ref.)	0.93 (0.73 – 1.19)	1.57 (1.18 – 2.09)	0.01
Model 3, HR (95% CI)	(Ref.)	0.92 (0.72 – 1.17)	1.49 (1.11 – 2.01)	0.02

Abbreviations: PAD= Peripheral artery disease, HR= hazard ratio, CI=confidence interval

Model 1: Age, sex, race-center

Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, estimated glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

Table S11: Association between household income, educational attainment and PAD hospitalization when additionally adjusting for chronic psychological stress in study population at visit 2

	Household income			p-trend
	High ≥\$25,000/yr (n=7,633)	Medium \$12,000-\$24,999/yr (n=2,440)	Low <\$12,000/yr (n=1,424)	
Depression score	6 (2 – 13)	10 (4 – 16)	13 (6 – 21)	
Events, n (%)	2.9 (221)	3.9 (95)	6.7 (95)	
Model 1, HR (95% CI)	(Ref.)	1.33 (1.03 – 1.74)	2.51 (1.86 – 3.40)	<0.001
Model 2, HR (95% CI)	(Ref.)	1.17 (0.89 – 1.53)	1.63 (1.19 – 2.24)	0.003
Model 3, HR (95% CI)	(Ref.)	1.17 (0.89 – 1.53)	1.64 (1.18 – 2.28)	0.004
	Educational attainment			p-trend
	High (>high school) (n=4,572)	Medium (high school/equivalent) (n=4,980)	Low (<high school) (n=2,395)	
Depression score	6 (2 – 12)	8 (4 – 15)	12 (6 – 20)	
Events, n (%)	2.7 (125)	3.2 (159)	5.9 (142)	
Model 1, HR (95% CI)	(Ref.)	1.32 (1.04 – 1.69)	2.22 (1.70 – 2.90)	<0.001
Model 2, HR (95% CI)	(Ref.)	1.07 (0.84 – 1.37)	1.52 (1.15 – 2.00)	0.004
Model 3, HR (95% CI)	(Ref.)	1.06 (0.83 – 1.36)	1.51 (1.14 – 2.00)	0.01

Abbreviations: PAD=peripheral artery disease, HR= hazard ratio, CI=confidence interval

Model 1: Age, sex, race-center

Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, **chronic psychological stress**, estimated glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

Table S12. Association between area deprivation index and incidence of PAD hospitalization when additionally adjusting for chronic psychological stress in study population at visit 2

	Area deprivation index*					p-trend
	Quintile 1 (Least deprived) (82.9 – 92.8) (n=2,415)	Quintile 2 (97.1 – 99.7) (n=2,447)	Quintile 3 (101.8 – 103.7) (n=2,335)	Quintile 4 (106.6 – 109.9) (n=2,295)	Quintile 5 (Most deprived) (115.6 – 119.4) (n=2,175)	
Events, % (n)	2.5 (60)	3.3 (81)	3.0 (71)	4.1 (95)	5.1 (110)	
Model 1, HR (95% CI)	(Ref.)	1.41 (0.99 – 2.02)	1.34 (0.93 – 1.92)	2.04 (1.42 – 2.94)	2.71 (1.66 – 4.42)	<0.001
Model 2, HR (95% CI)	(Ref.)	1.30 (0.91 – 1.85)	1.10 (0.77 – 1.59)	1.61 (1.11 – 2.33)	1.87 (1.14 – 3.08)	0.01
Model 3, HR (95% CI)	(Ref.)	1.28 (0.90 – 1.83)	1.10 (0.76 – 1.58)	1.59 (1.10 – 2.30)	1.86 (1.13 – 3.08)	0.02

Abbreviations: PAD= peripheral artery disease, HR= hazards ratio, CI=confidence interval

Model 1: Age, sex, race-center

Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, **chronic psychological stress**, estimated glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

*Additional 275 participants were missing information on area deprivation at baseline

Table S13. Association between household income and educational attainment level and incidence of non-CLI events

	Household income			p-trend
	High ≥\$25,000/yr (n=8,026)	Medium \$12,000-\$24,999/yr (n=2,682)	Low <\$12,000/yr (n=1,648)	
Events, n (%)	1.9 (158)	2.7 (73)	2.5 (41)	
Model 1, HR (95% CI)	(Ref.)	1.62 (1.21 – 2.18)	1.93 (1.29 – 2.88)	<0.001
Model 2, HR (95% CI)	(Ref.)	1.38 (1.02 – 1.86)	1.29 (0.85 – 1.94)	0.09
Model 3, HR (95% CI)	(Ref.)	1.37 (1.02 – 1.86)	1.30 (0.85 – 1.99)	0.09
	Educational attainment			p-trend
	High (>high school) (n=4,653)	Medium (high school/equivalent) (n=5,190)	Low (<high school) (n=2,674)	
Events, n (%)	1.9 (87)	2.1 (107)	3.0 (78)	
Model 1, HR (95% CI)	(Ref.)	1.18 (0.88 – 1.57)	1.84 (1.32 – 2.56)	<0.001
Model 2, HR (95% CI)	(Ref.)	0.95 (0.71 – 1.27)	1.22 (0.87 – 1.72)	0.32
Model 3, HR (95% CI)	(Ref.)	0.94 (0.71 – 1.26)	1.21 (0.85 – 1.71)	0.35

Abbreviations: CLI= critical limb ischemia, HR= hazard ratio, CI=confidence interval

Model 1: Age, sex, race-center

Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, estimated glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

Table S14. Association between area deprivation index and incidence of non-CLI events

	Area deprivation index*					p-trend
	Quintile 1 (Least deprived) (29.3 – 96.0) (n=2,452)	Quintile 2 (96.1 – 101.7) (n=2,460)	Quintile 3 (101.8 – 107.2) (n=2,480)	Quintile 4 (107.3 – 112.5) (n=2,405)	Quintile 5 (Most deprived) (112.6 – 127.5) (n=2,445)	
Events, % (n)	1.9 (47)	2.7 (67)	1.9 (48)	2.3 (55)	2.1 (51)	
Model 1, HR (95% CI)	(Ref.)	1.38 (0.93 – 2.07)	1.07 (0.69 – 1.66)	1.22 (0.74 – 2.02)	1.97 (1.03 – 3.79)	0.23
Model 2, HR (95% CI)	(Ref.)	1.19 (0.80 – 1.78)	0.84 (0.54 – 1.31)	1.00 (0.60 – 1.67)	1.19 (0.61 – 2.32)	0.82
Model 3, HR (95% CI)	(Ref.)	1.19 (0.80 – 1.78)	0.82 (0.53 – 1.28)	0.99 (0.59 – 1.64)	1.15 (0.59 – 2.24)	0.73

Abbreviations: CLI= critical limb ischemia, HR= hazards ratio, CI=confidence interval

Model 1: Age, sex, race-center

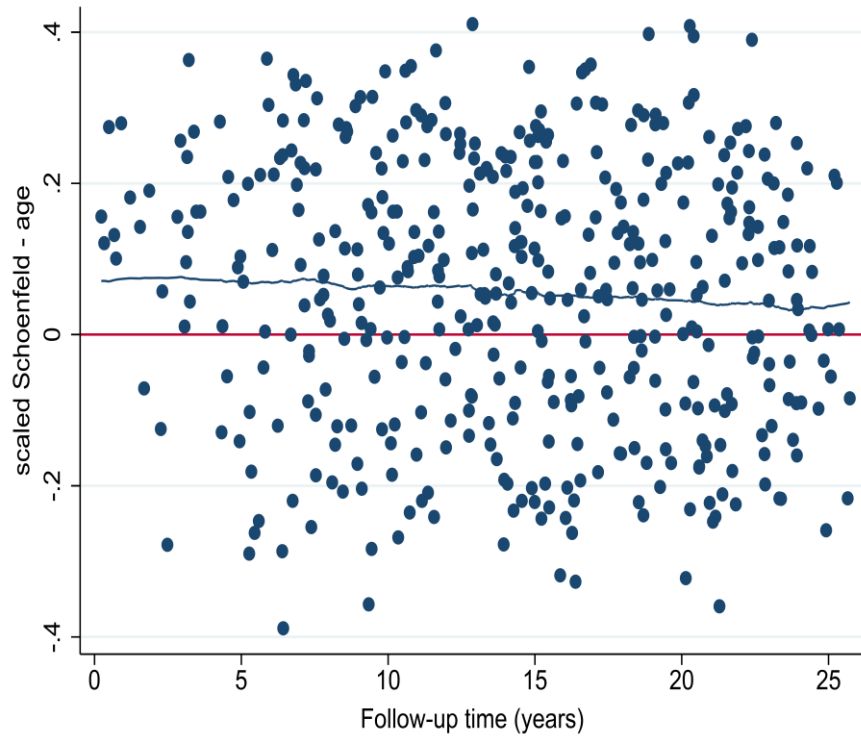
Model 2: Model 1 + current smoking, current alcohol intake, physical activity (sport index), body mass index, systolic blood pressure, diastolic blood pressure, antihypertensive medication use, diabetes, total cholesterol, high density lipoprotein cholesterol, cholesterol lowering medication use, estimated glomerular filtration rate

Model 3: Model 2 + health insurance status, frequency of routine health care visits

*Additional 275 participants were missing information on area deprivation at baseline

Figure S1. Test of proportional hazard assumption for (A) household income and (B) educational attainment

(A)



(B)

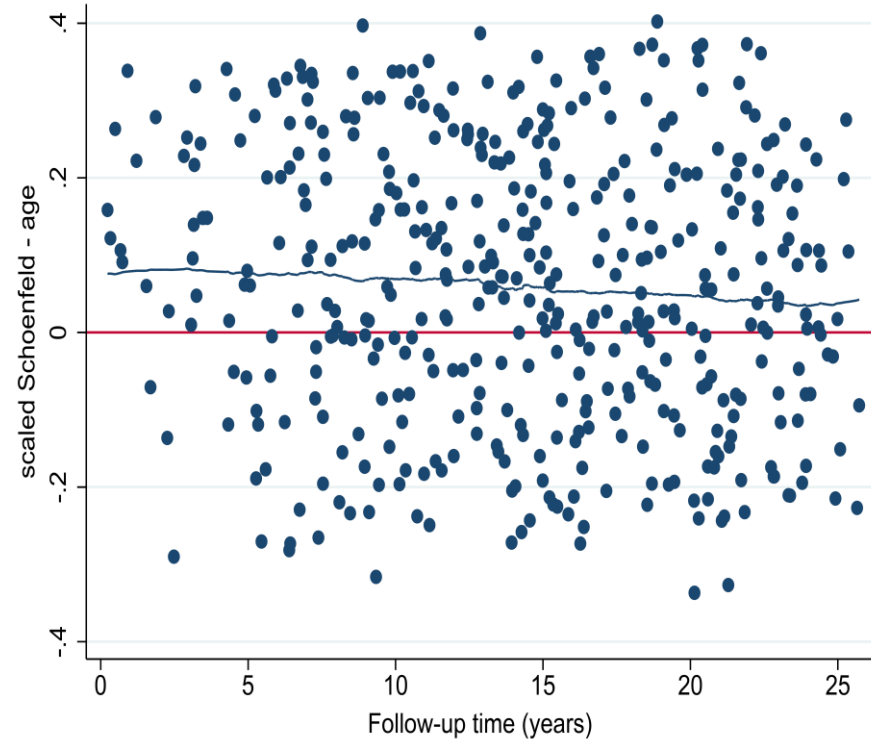
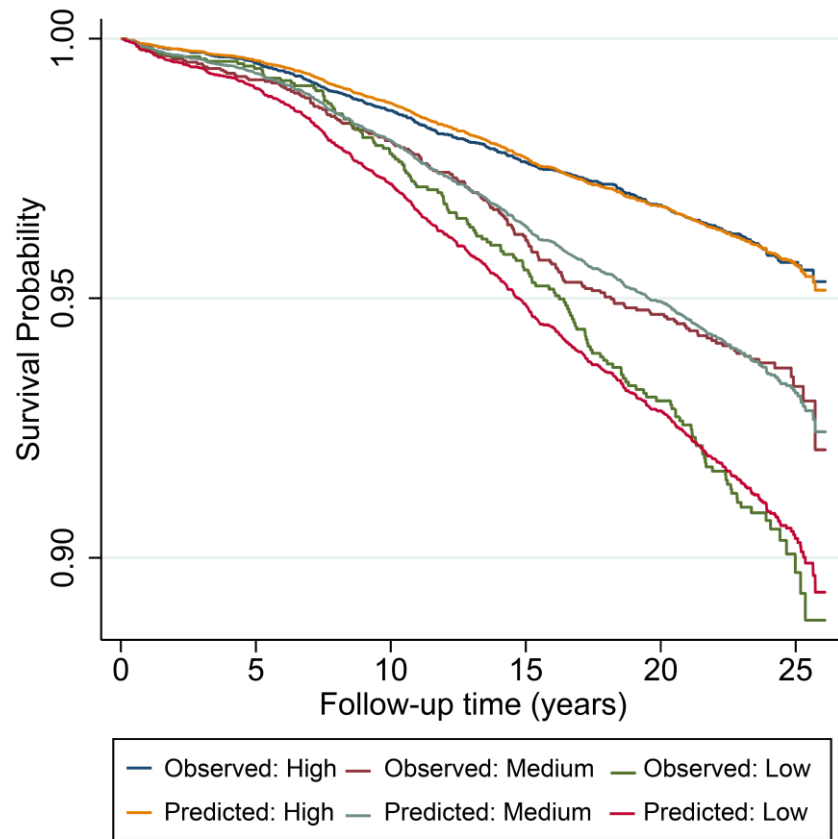


Figure S2. Goodness of fit of the Cox proportional hazards model to the observed data: (A) household income and (B) educational attainment

A)



B)

