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Relation of Socioeconomic Position With Ankle–Brachial Index

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Abstract

Potential upstream determinants of coronary heart disease (CHD) include life-course socioeconomic position (e.g., childhood socioeconomic circumstances, own education and occupation); however, several plausible biological mechanisms by which socioeconomic position (SEP) may influence CHD are poorly understood. Several CHD risk factors appear to be more strongly associated with SEP in women than in men; little is known as to whether any CHD risk factors may be more strongly associated with SEP in men. Objectives were to evaluate whether cumulative life-course SEP is associated with a measurement of subclinical atherosclerosis, the ankle–brachial index (ABI), in men and women. This study was a prospective analysis of 1,454 participants from the Framingham Heart Study Offspring Cohort (mean age 57 years, 53.8% women). Cumulative SEP was calculated by summing tertile scores for father's education, own education, and own occupation. ABI was dichotomized as low (≤ 1.1) and normal (> 1.1 to 1.4). After adjustment for age and CHD risk factors cumulative life-course SEP was associated with low ABI in men (odds ratio [OR] 2.04, 95% confidence interval [CI] 1.22 to 3.42, for low vs high cumulative SEP score) but not in women (OR 0.86, 95% CI 0.56 to 1.33). Associations with low ABI in men were substantially driven by their own education (OR 4.13, 95% CI 1.86 to 9.16, for lower vs higher than high school education). In conclusion, cumulative life-course SEP was associated with low ABI in men but not in women.

Very little is known about whether life-course socioeconomic position (SEP) is associated with the ankle–brachial index (ABI), a subclinical measurement of atherosclerosis. ABI is the ratio of systolic blood pressure in the ankle to systolic blood pressure in the arm. It is well recognized that ABI is a measurement of generalized atherosclerosis and that an ABI < 0.9 indicates peripheral arterial disease. In the Atherosclerosis Risk In Communities (ARIC)¹ study and in a systematic review including longitudinal studies from the United States and Europe,² low ABI was associated with increased incidence of total mortality, cardiovascular mortality, myocardial infarction, and stroke. The increased relative risks were shown to be independent of baseline cardiovascular disease and risk factors, suggesting that the ABI might have an independent role in predicting cardiovascular events. Consequently,

the primary objective of this study was to investigate whether cumulative life-course SEP is associated with ABI in the Framingham Offspring Study cohort independent of classic coronary heart disease (CHD) risk factors.

Methods

The Framingham Heart Study is a community-based observational cohort study initiated in 1948 to investigate risk factors for CHD. The present investigation was based on participants in the Framingham Offspring Study, which began in 1971 with recruitment of 5,124 United States men and women who were offspring (or spouses of offspring) of the original cohort of the Framingham Heart Study. The design and selection criteria of the Framingham Offspring Study have been described elsewhere.³ Participants were examined every 4 to 8 years, undergoing medical history, physical examination, anthropometry, and laboratory assessment of CHD risk factors at each examination, as previously described.³ Framingham Study participants signed informed consent and the Framingham Study is reviewed annually by the Boston University Medical Center institutional review board.

Childhood SEP was measured by father's educational attainment in primary analyses and father's occupation in secondary analyses. Father's education and occupation were obtained directly from the participants' fathers who were enrolled in the Framingham Heart Study original cohort from 1948 through 1950 (mean age 44 years, range 28 to 62). Father's education was categorized as 3 levels: lower than high school, completed high school, and higher than high school. Father's occupation was categorized as 3 levels: laborer, clerical/sales, and professional/executive/supervisory/technical. Young adulthood SEP was measured by own educational attainment, obtained directly from the Framingham Offspring Study participants at examinations 2 (1979 to 1982) and 3 (1984 to 1987). Education was categorized as 3 levels: 12, 13 to 16, and 17 years of education. Active professional-life SEP was measured as own occupation, ascertained at examination 2 (1979 to 1982), and categorized as 3 levels: laborer, homemaker/clerical/sales, and professional/executive/supervisory/technical. Analyses testing the accumulation-of-risk framework used a cumulative SEP score that was created by summing values for SEP at 3 successive life-course periods: childhood SEP (measured as father's education: lower than high school = 0, high school = 1, higher than high school = 2), young adulthood SEP (measured as own education: 12 years = 0, 13 to 16 years = 1, 17 years = 2), and active professional-life SEP (measured as own occupation: laborer = 0, clerical/sales/homemaker = 1, executive/professional/supervisory/technical = 2). Cumulative SEP score was categorized as low (score of 0 or 1), medium (score of 1 or 2), and high (score of 4 to 6) for analyses. Higher cutpoints were used for educational categories of offspring compared to fathers to account for secular trends of increased normative levels of education across generations.

Measurements of ABI were obtained at offspring examination 6 (1995 to 1998). Ankle-brachial systolic blood pressure measurements were performed by trained technicians according to standardized protocols.⁴ Systolic blood pressure was measured using an 8-MHz Doppler pen probe and an ultrasonic Doppler flow detector (Parks Medical Electronics, Inc., Aloha, Oregon) 2 times for each limb (right arm, left arm, right ankle, left ankle). ABI was then calculated for each leg as the ratio of average systolic blood pressure in the ankle divided by average systolic blood pressure in the arm with the higher blood pressure. The lower of the ABI values calculated for the left and right ankles was used for analyses. If ABI was missing for 1 ankle, data from the nonmissing ankle were used ($n = 8$ for the present investigation).

Emerging evidence has demonstrated increased risk for coronary and carotid atherosclerosis, coronary events, and cardiovascular disease mortality with ABI values up to 1.1.⁵⁻⁷

Consequently the ABI Collaboration defined normal ABI as > 1.1 to 1.4 .⁵ Therefore, ABI was dichotomized as low (ABI < 1.1) versus normal (ABI > 1.1 to 1.4) for the present investigation. However, additional analyses were carried out for women using a lower cut-point of 1.0 to define low ABI. This was done in light of recent evidence suggesting that normal ABI values may be intrinsically lower in healthy women than in men.⁸ Participants with ABI values > 1.4 were excluded because an ABI > 1.4 has been demonstrated to confer increased risk for cardiovascular and total mortality, possibly because of poor arterial compressibility resulting from stiffness and calcification.⁵ Because of a very small number of subjects ($n = 41$) with an ABI value < 0.9 (i.e., definite peripheral arterial disease), there was inadequate statistical power to carry out analyses with ABI dichotomized as < 0.9 versus > 0.9 to 1.4 .

All covariates were measured at offspring examination 6 (1995 to 1998). Smoking status (current, former, or never) was determined by self-report. Systolic blood pressure was calculated as the average of the clinic physician's 2 measurements of systolic blood pressure while a subject was seated. Body mass index was calculated as weight in kilograms divided by the square of height in meters. High-density lipoprotein (HDL) and total cholesterol concentrations were measured by automated enzymatic techniques.⁹ Participants were considered to have diabetes if they reported receiving treatment with insulin or a hypoglycemic agent or if they had fasting plasma glucose levels ≥ 126 mg/dl (7.0 mmol/L). Participants who were missing information on treatment status or fasting glucose were classified as having diabetes if they had a nonfasting glucose concentration ≥ 200 mg/dl (11.1 mmol/L), or a nonfasting glucose concentration from 126 to 200 mg/dl plus a history of diabetes, or if nonfasting glucose concentration was 126 to 200 mg/dl with a diabetes diagnosis at a subsequent Framingham examination. Use of antihypertensive and cholesterol-lowering medication was self-reported. Depressive symptomatology was measured using the Center for Epidemiologic Studies Depression scale (range 0 to 51).

There were 3,413 participants in the dataset who completed offspring examination 6, on which the present investigation was based. After implementation of exclusion criteria (details shown in Figure 1), the final sample was 1,454 (782 women and 672 men). Cardiovascular disease events (as part of exclusion criteria) were identified in participants since the onset of the Framingham Offspring Study (1971 to 1975) and included recognized myocardial infarction, coronary insufficiency, cerebrovascular events (including cerebral atherothrombotic infarction, cerebral embolism, intracerebral hemorrhage, subarachnoid hemorrhage, and other cerebrovascular accident), and congestive heart failure. Those excluded ($n = 1,913$) were more likely to be older (mean age 60.0 vs 57.2 years, respectively, $p < 0.0001$), to be taking antihypertensive medication (31.6% vs 23.5% , $p < 0.0001$) and cholesterol-lowering medication (15.2% vs 10.0% , $p < 0.0001$), and to be diabetic (11.3% vs 8.4% , $p = 0.006$). Included and excluded participants did not differ significantly for other variables including gender, body mass index, HDL/total cholesterol ratio, depression score, and current smoking.

Age-adjusted means and proportions were calculated for baseline covariates and compared across cumulative SEP categories. Multivariable logistic regression analyses evaluated associations between cumulative SEP (categorized as low [score of 0 or 1], medium [score of 1 or 2], and high [score of 4 to 6] as described earlier) and ABI (< 1.1 vs > 1.1 to 1.4 for primary analyses, < 1.0 vs > 1.0 to 1.4 for secondary analyses in women). All analyses were adjusted for age. Subsequent models were also adjusted for the CHD risk factors smoking, body mass index, systolic blood pressure, total/HDL cholesterol ratio, antihypertensive medication, cholesterol-lowering medication, depressive symptomatology, and diabetes. Further analyses of individual SEP measurements (father's education, own education, own occupation) in relation to ABI were performed to evaluate whether SEP at any of these life-

course periods particularly contributed to associations of cumulative SEP with ABI. These latter analyses were adjusted for age with subsequent adjustment for other individual SEP measurements and final adjustment for the CHD risk factors described earlier. All analyses performed were gender-specific because there was evidence of effect modification by gender ($p = 0.01$ for interaction between cumulative SEP score and gender). Generalized estimating equations were used to account for clustering of outcomes by family. Pearson correlation coefficients and variance inflation factors were used to evaluate colinearity, and no evidence of colinearity was found. The 3 primary SEP variables (father's education, own education, and own occupation) were not correlated highly enough to be of concern when simultaneously including all 3 in a single multivariable model (pairwise correlation coefficients ranged from 0.25 to 0.51). Power analyses were performed using PS Power and Sample Size Calculation 3.0.2 (Dupont and Plummer, Vanderbilt University, Nashville, Tennessee) according to methods for cohort studies with dichotomous outcomes.^{10,11}

Results

Participants in the study sample had a mean age of 57 years (range 38 to 80) and 53.8% were women. Mean ABIs $\pm$ SDs were 1.16 ± 0.10 in men and 1.09 ± 0.10 in women ($p < 0.0001$). Prevalences of low ABI defined as ≤ 1.1 were 21% in men and 49% in women; low ABI defined as ≤ 1.0 demonstrated prevalences of 4.8% in men and 16% in women. In age-adjusted analyses in men lower cumulative SEP was associated with older age, lower ABI, higher body mass index, lower HDL cholesterol, higher total/HDL cholesterol ratio, higher prevalence of current smoking, and higher depression score. In women lower cumulative SEP was associated with older age, higher body mass index, lower HDL cholesterol, higher total/HDL cholesterol ratio, higher prevalence of diabetes and current smoking, and higher depression score (Table 1). In addition, R^2 from univariate linear regression analyses showed that cumulative SEP explained 1.4% of the variance in ABI in men and 0.7% of the variance in women. Examples of the contribution of other specific CHD risk factors to the variance (R^2) in ABI were smoking (5.5% in men, 3.0% in women), hypertension medication (2.9% in men, 1.8% in women), systolic blood pressure (1.5% in men, 4.1% in women), and diabetes (1.3% in men, 0.1% in women).

Age-adjusted logistic regression analyses showed that lower cumulative SEP across the life course was associated with greater prevalence of low ABI in men (odds ratio [OR] 2.00, 95% confidence interval [CI] 1.28 to 3.14, for low vs high cumulative SEP score) and not in women (OR 0.94, 95% CI 0.63 to 1.38; Table 2). Further adjustment for CHD risk factors did not attenuate the association in men (OR 2.04, 95% CI 1.22 to 3.42). In analyses of individual SEP measurements own education was associated with low ABI in men with associations remaining after adjustment for age, other SEP measurements, and CHD risk factors (OR 4.13, 95% CI 1.86 to 9.16, for ≤ 12 years of education vs ≥ 17 years; Table 3). Own occupation was also associated with low ABI in men in age-adjusted analyses. Further adjustment for other SEP measurements and CHD risk factors attenuated the association for the laborer category (OR 1.22, 95% CI 0.70 to 2.11) but not for the homemaker/clerical/sales category (OR 1.92, 95% CI 1.01 to 3.62). No significant associations were observed between father's education and ABI in men (Table 3). In women no association was observed between own education and ABI (OR 1.23, 95% CI 0.76 to 2.00) or between own occupation and ABI (OR 1.36, 95% CI 0.76 to 2.41; Table 4). However, father's education in the lower-than-high-school category was weakly associated with a lower prevalence of low ABI after adjustment for other SEP measurements and CHD risk factors (Table 4). Additional analyses with low ABI alternatively defined as ≤ 1.0 in women revealed somewhat higher effect sizes; however, associations were still not statistically significant (supplementary Tables 1 and 2, available online). Patterns of association for cumulative SEP when using father's occupation as the measurement of childhood SEP were similar to results

obtained when father's education was used (supplementary Table 3, available online). In addition, associations between father's occupation and ABI were not significant in men or women (data not shown), similar to analyses using father's education.

Discussion

Life-course cumulative SEP was inversely associated with low ABI, an indicator of subclinical atherosclerosis, in men and not in women. The effect in men appeared to be largely due to early adulthood SEP measured as participants' education compared to childhood SEP or active professional-life SEP. Adjustment for CHD risk factors did not attenuate the association in men, suggesting these may not be explanatory mechanisms. Few studies have investigated associations of cumulative SEP in relation to ABI. Carson et al¹² reported inverse associations between cumulative SEP and peripheral arterial disease (ABI <0.9) in middle-aged white men (n = 4,284) and women (n = 5,170) of the ARIC. Similar to our findings, they found that SEP in the young adulthood period was associated more strongly with peripheral arterial disease than in the childhood or older adulthood periods. Furthermore, associations of SEP with peripheral arterial disease were found in men and women, whereas our study did not find associations in women.

In previous publications evaluating relations between adulthood SEP only (rather than cumulative SEP) and ABI, studies in developed countries have shown generally similar findings to our study. Fowkes et al¹³ demonstrated in a cross-sectional survey of participants 55 to 74 years old in the Edinburgh Artery Study that mean ABI decreased consistently with decreasing educational level in men and not in women. Rooks et al¹⁴ found inverse associations between various measurements of adulthood SEP (education, income, home ownership, and financial assets) and ABI in an elderly population of black and white men and women (n = 3,075). However, after adjustment for race, age, household family size, marital status, and study site, associations between education and low ABI persisted in men but not in women. Another study of 1,025 subjects in the Chianti area of Italy reported significantly lower age-adjusted mean ABIs in men but not in women with low education versus high education.¹⁵

Because there were large SEP gradients in some of the strongest risk factors for peripheral arterial disease (smoking and diabetes), lack of associations in women was somewhat surprising although consistent with other studies focused on associations of adulthood SEP with ABI.^{13–15} One potential explanation is that the use of inappropriate cutpoints for defining low ABI in women may have contributed to null findings. There is evidence that ABI values are intrinsically lower in women compared to men⁸ even after adjustment for height (which is suggested to contribute to the lower ABI observed in women).¹³ McDermott et al⁶ found evidence of excess coronary and carotid atherosclerosis with an ABI value up to 1.1 in men but only with an ABI value up to 1.0 in women. In our analyses, using lower ABI cutpoints (1.0 instead of 1.1) to define low ABI somewhat increased effect sizes for associations between SEP and ABI in women; however, these effects were small and not statistically significant.

In our investigation measurements of childhood SEP (father's education and father's occupation) were not associated with low ABI with the exception of a slight positive association between father's education and low ABI in women. To the best of our knowledge the association between childhood SEP and subclinical atherosclerosis measured as ABI has rarely been examined. However, inverse associations between childhood SEP and clinically manifest CHD are more established and consistently observed.^{16,17} In the present investigation those who were excluded from analyses because of cardiovascular disease were more likely to have lower childhood SEP and low ABI (data not shown)

compared to those included. This may have led to an underestimation of an association between childhood SEP and low ABI in the study sample.

There is evidence suggesting that the effect of SEP on subclinical and clinically manifest CHD is partly mediated through CHD risk factors.^{18–21} In this investigation adjustment for CHD risk factors did not attenuate the associations observed, similar to results from several previous studies reporting on associations between SEP and subclinical atherosclerosis.^{22–25} Carson et al¹² reported that none of the risk factors tested in their study was a strong or moderate mediator of the association between SEP and peripheral arterial disease (ABI <0.9). However, it is important to note that methodologic biases may arise because of statistical adjustment for potential mediators and confounders.²⁶ Other potential risk factors not accounted for in this study may also play a role in the association between SEP and atherosclerosis development such as novel CHD risk markers,²⁷ psychosocial stressors,²⁸ and genetic susceptibility.²⁹

A strength of this investigation was that measurements of childhood SEP were assessed directly from the participants' parents. Thus this measurement was less likely to be subject to measurement error compared to studies that obtained measurements of childhood SEP retrospectively through personal recall by participants.¹⁶ Furthermore, rigorous quality assurance and quality control methods were used in this study to ensure high-quality measurements of outcomes and covariates.

Several limitations of this study should be noted. Subjects in this study population were predominantly of European descent (representing the demographics of the city of Framingham, Massachusetts at study onset); thus results from this study are not necessarily generalizable to other races and ethnicities. Furthermore, primary analyses on lifecourse SEP included only 3 measurements: father's education, own education, and own occupation. Additional measurements (such as SEP during in utero period) or more comprehensive measurements (such as multiple measurements of occupation throughout the life course) of lifecourse SEP would provide richer data on the potential contributions of life-course SEP to low ABI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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References

1. Weatherley BD, Nelson JJ, Heiss G, Chambless LE, Sharrett AR, Nieto FJ, Folsom AR, Rosamond WD. The association of the ankle-brachial index with incident coronary heart disease: the Atherosclerosis Risk In Communities (ARIC) study, 1987–2001. *BMC Cardiovasc Disord*. 2007; 7:3–13. [PubMed: 17227586]

2. Heald CL, Fowkes FG, Murray GD, Price JF. Ankle Brachial Index Collaboration. Risk of mortality and cardiovascular disease associated with the ankle-brachial index: systematic review. *Atherosclerosis*. 2006; 189:61–69. [PubMed: 16620828]
3. Kannel WB, Feinleib M, McNamara PM, Garrison RJ, Castelli WP. An investigation of coronary heart disease in families. The Framingham Offspring Study. *Am J Epidemiol*. 1979; 110:281–290. [PubMed: 474565]
4. Murabito JM, Guo CY, Fox CS, D'Agostino RB. Heritability of the ankle-brachial index: the Framingham Offspring Study. *Am J Epidemiol*. 2006; 164:963–968. [PubMed: 16928729]
5. Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, Folsom AR, Hirsch AT, Dramaix M, deBacker G, Wautrecht JC, Kornitzer M, Newman AB, Cushman M, Sutton-Tyrrell K, Lee AJ, Price JF, d'Agostino RB, Murabito JM, Norman PE, Jamrozik K, Curb JD, Masaki KH, Rodriguez BL, Dekker JM, Bouter LM, Heine RJ, Nijpels G, Stehouwer CD, Ferrucci L, McDermott MM, Stoffers HE, Hooi JD, Knottnerus JA, Ogren M, Hedblad B, Witteman JC, Breteler MM, Hunink MG, Hofman A, Criqui MH, Langer RD, Fronek A, Hiatt WR, Hamman R, Resnick HE, Guralnik J, Resnick HE, Guralnik J, McDermott MM. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. *JAMA*. 2008; 300:197–208. [PubMed: 18612117]
6. McDermott MM, Liu K, Criqui MH, Ruth K, Goff D, Saad MF, Wu C, Homma S, Sharrett AR. Ankle-brachial index and subclinical cardiac and carotid disease: the multi-ethnic study of atherosclerosis. *Am J Epidemiol*. 2005; 162:33–41. [PubMed: 15961584]
7. O'Hare AM, Katz R, Shlipak MG, Cushman M, Newman AB. Mortality and cardiovascular risk across the ankle-arm index spectrum: results from the Cardiovascular Health Study. *Circulation*. 2006; 113:388–393. [PubMed: 16432070]
8. Aboyans V, Criqui MH, McClelland RL, Allison MA, McDermott MM, Goff DC Jr, Manolio TA. Intrinsic contribution of gender and ethnicity to normal ankle-brachial index values: the Multi-Ethnic Study of Atherosclerosis (MESA). *J Vasc Surg*. 2007; 45:319–327. [PubMed: 17264011]
9. McNamara JR, Schaefer EJ. Automated enzymatic standardized lipid analyses for plasma and lipoprotein fractions. *Clin Chim Acta*. 1987; 166:1–8. [PubMed: 3608193]
10. Casagrande JT, Pike MC. An improved approximate formula for calculating sample sizes for comparing two binomial distributions. *Biometrics*. 1978; 34:483–486. [PubMed: 719125]
11. Fleiss, JL. *Statistical Methods for Rates and Proportions*. New York: John Wiley; 1981. p. 38–46.
12. Carson AP, Rose KM, Catellier DJ, Kaufman JS, Wyatt SB, Diez-Roux AV, Heiss G. Cumulative socioeconomic status across the life course and subclinical atherosclerosis. *Ann Epidemiol*. 2007; 17:296–303. [PubMed: 17027292]
13. Fowkes FG, Housley E, Cawood EH, Macintyre CC, Ruckley CV, Prescott RJ. Edinburgh Artery Study: prevalence of asymptomatic and symptomatic peripheral arterial disease in the general population. *Int J Epidemiol*. 1991; 20:384–392. [PubMed: 1917239]
14. Rooks RN, Simonsick EM, Miles T, Newman A, Kritchevsky SB, Schulz R, Harris T. The association of race and socioeconomic status with cardiovascular disease indicators among older adults in the health, aging, and body composition study. *J Gerontol B Psychol Sci Soc Sci*. 2002; 57:S247–S256. [PubMed: 12084794]
15. Coppin AK, Ferrucci L, Lauretani F, Phillips C, Chang M, Bandinelli S, Guralnik JM. Low socioeconomic status and disability in old age: evidence from the In Chianti study for the mediating role of physiological impairments. *J Gerontol A Biol Sci Med Sci*. 2006; 61:86–91. [PubMed: 16456198]
16. Galobardes B, Smith GD, Lynch JW. Systematic review of the influence of childhood socioeconomic circumstances on risk for cardiovascular disease in adulthood. *Ann Epidemiol*. 2006; 16:91–104. [PubMed: 16257232]
17. Loucks EB, Lynch JW, Pilote L, Fuhrer R, Almeida ND, Richard H, Agha G, Murabito JM, Benjamin EJ. Life-course socioeconomic position and incidence of coronary heart disease: the Framingham Offspring Study. *Am J Epidemiol*. 2009; 169:829–836. [PubMed: 19179358]
18. Dragano N, Verde PE, Moebus S, Stang A, Schmermund A, Roggenbuck U, Möhlenkamp S, Peter R, Jöckel KH, Erbel R, Siegrist J. Heinz Nixdorf Recall Study. Subclinical coronary atherosclerosis is more pronounced in men and women with lower socio-economic status:

- associations in a population-based study. Coronary atherosclerosis and social status. *Eur J Cardiovasc Prev Rehabil.* 2007; 14:568–574. [PubMed: 17667649]
19. Harald K, Pajunen P, Jousilahti P, Koskinen S, Vartiainen E, Salomaa V. Modifiable risk factors have an impact on socio-economic differences in coronary heart disease events. *Scand Cardiovasc J.* 2006; 40:87–95. [PubMed: 16608778]
 20. Nordstrom CK, Diez Roux AV, Jackson SA, Gardin JM. Cardiovascular Health Study. The association of personal and neighborhood socioeconomic indicators with subclinical cardiovascular disease in an elderly cohort. *The Cardiovascular Health Study. Soc Sci Med.* 2004; 59:2139–2147. [PubMed: 15351479]
 21. Yan LL, Liu K, Daviglus ML, Colangelo LA, Kiefe CI, Sidney S, Matthews KA, Greenland P. Education, 15-year risk factor progression, and coronary artery calcium in young adulthood and early middle age: the Coronary Artery Risk Development in Young Adults study. *JAMA.* 2006; 295:1793–1800. [PubMed: 16622141]
 22. Gallo LC, Matthews KA, Kuller LH, Sutton-Tyrrell K, Edmundowicz D. Educational attainment and coronary and aortic calcification in postmenopausal women. *Psychosom Med.* 2001; 63:925–935. [PubMed: 11719631]
 23. Lutsey PL, Diez Roux AV, Jacobs DR Jr, Burke GL, Harman J, Shea S, Folsom AR. Associations of acculturation and socioeconomic status with subclinical cardiovascular disease in the multi-ethnic study of atherosclerosis. *Am J Public Health.* 2008; 98:1963–1970. [PubMed: 18511718]
 24. Lynch J, Kaplan GA, Salonen R, Salonen JT. Socioeconomic status and progression of carotid atherosclerosis. Prospective evidence from the Kuopio Ischemic Heart Disease Risk Factor Study. *Arterioscler Thromb Vasc Biol.* 1997; 17:513–519. [PubMed: 9102170]
 25. Ranjit N, Diez-Roux AV, Chambless L, Jacobs DR Jr, Nieto FJ, Szklo M. Socioeconomic differences in progression of carotid intima-media thickness in the Atherosclerosis Risk in Communities study. *Arterioscler Thromb Vasc Biol.* 2006; 26:411–416. [PubMed: 16322533]
 26. Cole SR, Hernán MA. Fallibility in estimating direct effects. *Int J Epidemiol.* 2002; 31:163–165. [PubMed: 11914314]
 27. Allison MA, Criqui MH, McClelland RL, Scott JM, McDermott MM, Liu K, Folsom AR, Bertoni AG, Sharrett AR, Homma S, Kori S. The effect of novel cardiovascular risk factors on the ethnic-specific odds for peripheral arterial disease in the Multi-Ethnic Study of Atherosclerosis (MESA). *J Am Coll Cardiol.* 2006; 48:1190–1197. [PubMed: 16979004]
 28. Lynch J, Smith GD. A life course approach to chronic disease epidemiology. *Annu Rev Public Health.* 2005; 26:1–35. [PubMed: 15760279]
 29. Trichopoulos A, Yiannakouris N, Bamia C, Benetou V, Trichopoulos D, Ordovas JM. Genetic predisposition, nongenetic risk factors, and coronary infarct. *Arch Intern Med.* 2008; 168:891–896. [PubMed: 18443266]

Figure 1.

Exclusion criteria and final sample size for the present investigation from the Framingham Heart Offspring Study cohort in the United States (1971 to 1998). CVD = cardiovascular disease.

Table 1

Age-adjusted characteristics according to cumulative life course socioeconomic position, Framingham Heart Study Offspring cohort, United States (1971 to 1998)

	Cumulative SEP Score		
	0 or 1	2 or 3	4–6
Men	192 (28.6%)	189 (28.1%)	291 (43.3%)
Age (years) *	58.9 (57.63–60.2)	56.3 (55.1–57.6)	55.6 (54.7–56.5)
Mean ankle–brachial index	1.15 (1.14–1.16)	1.15 (1.14–1.17)	1.17 (1.16–1.19)
Body mass index (kg/m ²)	29.0 (28.3–29.6)	29.0 (28.3–29.6)	28.2 (27.7–28.8)
Systolic blood pressure (mm Hg)	128.1 (125.9–130.3)	129.6 (127.4–131.7)	128.5 (126.8–130.3)
High-density lipoprotein cholesterol (mg/dl)	42.9 (41.1–44.8)	43.1 (41.3–44.9)	45.3 (43.8–46.8)
Total/high-density lipoprotein cholesterol ratio	5.1 (4.8–5.4)	5.4 (5.1–5.8)	4.7 (4.4–5.0)
Antihypertensive medication use	23.4% (17.8–30.0)	26.9% (20.9–34.0)	22.1% (17.6–27.5)
Cholesterol-lowering medication	11.4% (7.6–16.6)	12.3% (8.3–17.8)	10.4% (7.3–14.5)
Diabetes mellitus	9.4% (6.0–14.4)	7.2% (4.3–11.8)	8.4% (5.7–12.3)
Current smoker	15.4% (10.9–21.4)	19.5% (14.4–25.9)	10.0% (7.0–13.9)
Depression score	5.3 (4.3–6.2)	5.3 (4.4–6.3)	3.9 (3.1–4.7)
Women	230 (29.4%)	318 (40.7%)	234 (29.9%)
Age (years) *	61.1 (60.0–62.3)	56.1 (55.1–57.0)	55.9 (54.8–57.1)
Mean ankle–brachial index	1.08 (1.07–1.10)	1.09 (1.08–1.11)	1.09 (1.08–1.11)
Body mass index (kg/m ²)	27.9 (27.1–28.6)	27.6 (27.0–28.3)	26.4 (25.7–27.2)
Systolic blood pressure (mm Hg)	126.1 (123.8–128.5)	126.4 (124.4–128.3)	124.0 (121.8–126.3)
High-density lipoprotein cholesterol (mg/dl)	56.8 (54.7–58.9)	57.5 (55.7–59.2)	60.9 (58.9–62.9)
Total/high-density lipoprotein cholesterol ratio	4.1 (3.9–4.2)	4.0 (3.9–4.2)	3.7 (3.6–3.9)
Antihypertensive medication use	23.9% (18.7–30.0)	22.3% (17.9–27.4)	14.9% (10.8–20.2)
Cholesterol-lowering medication	8.8% (5.8–13.2)	6.2% (4.0–9.5)	6.4% (3.9–10.4)
Diabetes mellitus	7.9% (5.0–12.1)	7.4% (4.9–10.9)	4.5% (2.5–8.1)
Current smoker	25.2% (19.8–31.5)	16.2% (12.6–20.7)	11.5% (8.0–16.2)
Depression score	8.5 (7.4–9.6)	6.5 (5.6–7.5)	5.2 (4.1–6.3)

Data are expressed as mean or percent prevalence (95% confidence interval).

* Calculated using bivariate analysis.

Table 2

Odds ratios for association between life-course socioeconomic position and low ankle–brachial index defined as ankle–brachial index 1.10, Framingham Heart Study Offspring cohort, United States (1971 to 1998)

	Cumulative SEP Score	Subjects	Number of Events With ABI	1.1 (%)	Model Adjustment			
					Model 1*		Model 2†	
					OR	95% CI	OR	95% CI
Men								
0 or 1		192		52 (27.1%)	2.00	1.28–3.14	2.04	1.22–3.42
2 or 3		189		45 (23.8%)	1.81	1.13–2.92	1.51	0.87–2.62
4–6		291		42 (14.4%)	1.00		1.00	
Women								
0 or 1		230		117 (50.9%)	0.94	0.63–1.38	0.86	0.56–1.33
2 or 3		318		153 (48.1%)	0.93	0.67–1.31	0.94	0.65–1.36
4–6		234		117 (50.0%)	1.00		1.00	

* Adjusted for age.

† Adjusted for age, smoking, body mass index, systolic blood pressure, total/high-density lipoprotein cholesterol ratio, antihypertensive medication, cholesterol-lowering medication, depressive symptomatology, and diabetes.

Table 3

Men—odds ratios for associations between socioeconomic position and low ankle–brachial index defined as ankle–brachial index 1.10, Framingham Heart Study Offspring cohort, United States (1971 to 1998)

SEP Measurement	SEP Level	Subjects	Number of Events With ABI 1.1 (%)	Model Adjustment					
				Model 1*		Model 2†		Model 3‡	
				OR	95% CI	OR	95% CI	OR	95% CI
Father's education	Lower than high school	331	72 (21.8%)	1.07	0.69–1.66	0.75	0.45–1.23	0.67	0.38–1.19
	High school	157	32 (20.4%)	1.2	0.71–2.04	0.96	0.54–1.71	1.00	0.52–1.92
	Higher than high school	184	35 (19.0%)	1.00		1.00		1.00	
Own education	12 years	216	59 (27.3%)	4.82	2.57–9.05	5.82	2.86–11.83	4.13	1.86–9.16
	13–16 years	270	67 (24.8%)	4.53	2.45–8.38	4.59	2.44–8.64	3.28	1.64–6.55
	17 years	186	13 (7.0%)	1.00		1.00		1.00	
Own occupation	Laborer	234	57 (24.3%)	1.55	1.02–2.35	0.92	0.57–1.50	1.22	0.70–2.11
	Homemaker, clerical, or sales	84	24 (28.6%)	1.91	1.10–3.32	1.40	0.79–2.51	1.92	1.01–3.62
	Professional, executive, supervisory, or technical	354	58 (16.4%)	1.00		1.00		1.00	

* Adjusted for age.

† Adjusted for age and other socioeconomic position measurements (i.e., socioeconomic position other than the exposure of interest; e.g., analyses on father's education are adjusted for own education and own occupation).

‡ Adjusted for age, other socioeconomic position measurements, smoking, body mass index, systolic blood pressure, total/high-density lipoprotein cholesterol ratio, antihypertensive medication, cholesterol-lowering medication, depressive symptomatology, and diabetes.

Table 4

Women—odds ratios for associations between socioeconomic position and low ankle–brachial index defined as ankle–brachial index 1.10, Framingham Heart Study Offspring cohort, United States (1971 to 1998)

SEP Measurement	SEP Level	Subjects	Number of Events With ABI 1.1 (%)	Model Adjustment					
				Model 1*		Model 2†		Model 3‡	
				OR	95% CI	OR	95% CI	OR	95% CI
Father's education	Lower than high school	388	185 (47.7%)	0.71	0.49–1.01	0.62	0.43–0.91	0.65	0.43–0.98
	High school	203	99 (48.8%)	0.86	0.58–1.29	0.85	0.56–1.28	0.94	0.60–1.47
	Higher than high school	191	103 (53.9%)	1.00		1.00		1.00	
Own education	12 years	333	173 (52.0%)	1.23	0.76–2.00	1.19	0.68–2.11	1.12	0.62–2.03
	13–16 years	355	172 (48.5%)	1.11	0.70–1.78	1.05	0.63–1.75	1.00	0.60–1.68
	17 years	94	42 (44.7%)	1.00		1.00		1.00	
Own occupation	Laborer	65	34 (52.3%)	1.36	0.76–2.41	1.42	0.75–2.68	1.12	0.56–2.23
	Homemaker, clerical, or sales	532	275 (51.7%)	1.40	1.00–1.96	1.40	0.79–2.51	1.31	0.87–1.98
	Professional, executive, supervisory, or technical	185	78 (42.2%)	1.00		1.00		1.00	

* Adjusted for age.

† Adjusted for age and other socioeconomic position measurements (i.e., socioeconomic position other than the exposure of interest; e.g., analyses on father's education are adjusted for own education and own occupation).

‡ Adjusted for age, other socioeconomic position measurements, smoking, body mass index, systolic blood pressure, total/high-density lipoprotein cholesterol ratio, antihypertensive medication, cholesterol-lowering medication, depressive symptomatology, and diabetes.