Published in final edited form as:

Am J Prev Med. 2018 November ; 55(5): 642–649. doi:10.1016/j.amepre.2018.06.021.

Life's Simple 7 and Peripheral Artery Disease Risk: The Atherosclerosis Risk in Communities Study

Parveen K. Garg, MD, MPH¹, Wesley T. O'Neal, MD, MPH², Yejin Mok, PhD, MPH³, Gerardo Heiss, PhD⁴, Joseph Coresh, MD, PhD³, and Kunihiro Matsushita, MD, PhD³

¹Division of Cardiology, University of Southern California Keck School of Medicine, Los Angeles, California ²Division of Cardiology, Emory University School of Medicine, Atlanta, Georgia

³Department of Epidemiology and the Welch Center for Prevention, Epidemiology, and Clinical Research, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland ⁴Department of Epidemiology, University of North Carolina Gillings School of Global Public Health, Chapel Hill, North Carolina

Abstract

Introduction: The American Heart Association's Life's Simple 7 includes seven metrics of ideal cardiovascular health to target for cardiovascular disease prevention. This study determined the relationship between Life's Simple 7 and incident peripheral artery disease in a biracial cohort of middle and older aged adults.

Methods: This analysis included 12,865 participants from the Atherosclerosis Risk in Communities study recruited between 1987 and 1989 (mean age=54 years, 55% women, 25% black) and free of peripheral artery disease or other cardiovascular disease at baseline. Overall, Life's Simple 7 score was calculated as the sum of the Life's Simple 7 component scores (two points if ideal, one point if intermediate, and zero if poor) and classified as inadequate (zero to four), average (five to nine), or optimal (ten to 14) cardiovascular health and linked to incident peripheral artery disease identified by hospital discharge diagnosis and leg revascularization. Analysis was conducted in 2017.

Results: A total of 434 incident peripheral artery disease cases occurred over a median follow-up of 24.4 years. Compared with the inadequate category ($n=1,008$), participants in the average ($n=8,395$) and optimal ($n=3,462$) categories each had a substantially lower risk of developing peripheral artery disease in a Cox proportional hazards model adjusted for potential confounders (hazard ratio=0.36, 95% CI=0.28, 0.46 for average, and hazard ratio=0.09, 95% CI=0.06, 0.15 for optimal). In a similar model, a one-point higher Life's Simple 7 score was associated with a 25% lower risk of incident peripheral artery disease (hazard ratio=0.75, 95% CI=0.72, 0.79).

Address correspondence to: Parveen K. Garg, MD, MPH, 1510 San Pablo St., Suite 322, Los Angeles CA 90033. parveeng@med.usc.edu.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

No financial disclosures were reported by the authors of this paper.

Conclusions: Better cardiovascular health, as defined by higher Life's Simple 7 score, is associated with a substantially lower risk of peripheral artery disease.

INTRODUCTION

Worldwide 200 million people are estimated to have peripheral artery disease (PAD).^{1,2} These individuals are at a much higher risk of cardiovascular and all-cause mortality compared with individuals without PAD.^{3,4} The mean 2-year estimated hospitalization costs per patient range from nearly \$7,500 in asymptomatic PAD to more than \$10,000 in those with a history of lower-limb amputation or revascularization.⁵

The American Heart Association (AHA) Strategic Planning Task Force and Statistics Committee developed a metric, termed the Life's Simple 7 (LS7), to promote ideal achievement of seven modifiable health behaviors and biological factors: untreated total cholesterol less than 200 mg/dL, untreated blood pressure less than 120/ less than 80 mmHg, untreated fasting blood glucose less than 100 mg/dL, physical activity (PA), ideal diet, nonsmoking, and BMI less than 25 kg/m².⁶ Ideal achievement of these metrics has been associated with improved cardiovascular disease (CVD)–free survival, including coronary heart disease (CHD), stroke, and heart failure (HF), and a reduction in healthcare costs.^{6–10} Compared with the 2010 impact goals, the committee broadened their reach to encompass all CVD, including PAD.

Although PAD and other CVDs share many common risk factors included in the LS7, the association of the combination of these LS7 metrics with incident PAD has not been reported. Nearly 40% of people with PAD have no concomitant coronary or cerebrovascular disease, suggesting the importance of specifically studying PAD in this context.¹¹ Considering the increased morbidity and mortality as well as healthcare costs associated with PAD, identifying strategies to reduce PAD incidence are important. This study quantifies the association between LS7 and incident PAD in the Atherosclerosis Risk in Communities (ARIC) study.

METHODS

Study Population

The ARIC study included 15,792 men and women aged 45–64 years enrolled from four U.S. communities in 1987–1989.¹² Trained interviewers administered a questionnaire to collect information on demographic characteristics, health behaviors, medical history, and medication use. Fasting blood samples were also collected. Participants were re-examined in 1990–1992, 1993–1995, 1996–1998, and 2011–2013. IRBs at each participating institution (University of Minnesota, Johns Hopkins University, Wake Forest University, University of North Carolina, and University of Mississippi Medical Center) approved the study and all participants gave written informed consent at each study visit.

After excluding participants with PAD (defined below) or other CVD, including CHD, HF, and stroke, at baseline ($n=2,113$), those with missing data for any of the LS7 components ($n=718$), and participants with race other than white or African American or the few African

American participants from Minneapolis, Minnesota, and Washington County, Maryland ($n=96$) who were excluded because of the small number of participants, the remaining sample size was 12,865. The current study is a prospective analysis of these participants to determine the relationship of the LS7, assessed at baseline, and incident PAD. Follow-up time was defined as the time from the baseline visit to PAD development, death, loss to follow-up, or end of follow-up (December 31, 2014).

Measures

Cigarette smoking status was categorized as current, former, or never. Former smokers were further classified according to quit date (>12 vs ≤ 12 months). Field center staff directly measured weight and standing height, and BMI was calculated as measured weight in kilograms divided by standing height in meters squared. Systolic blood pressure and diastolic blood pressure were measured three times and the average of the last two measurements were used. Total blood cholesterol concentration was assessed by enzymatic procedures.¹³ Blood glucose levels were measured by the modified hexokinase/glucose-6-phosphate dehydrogenase method.

PA was measured using the modified Baecke questionnaire, which defines three semi-continuous indices ranging from one (low) to five (high) for PA in sports, during leisure time, and at work.^{14,15} Responses were subsequently converted to minutes per week of moderate or vigorous exercise based on METs value and number of months annually a participant partook in the activity.¹⁶

Usual dietary intake was determined using a previously validated 66-item food-frequency questionnaire administered by trained interviewers to improve accuracy and completeness.^{17,18} The healthy diet score was calculated as the sum of the scores for each of the five individual components included in the AHA definition for an ideal diet: fruits and vegetables 4.5 cups per day, fish two or more 3.5 ounce servings per week, fiber-rich whole grains three or more 1 ounce-equivalent servings per day, sodium $<1,500$ mg per day, and sugar-sweetened beverages 450 kcal (36 ounces) per week (Appendix Table 1).⁶

Each individual component was categorized as poor, intermediate, or ideal according to the AHA's LS7 criteria (Appendix Table 2).⁶ An overall LS7 score ranging from zero to 14 was calculated as the sum of the LS7 component scores (two points for ideal, one point for intermediate, and zero for poor). This score was classified as inadequate (zero to four), average (five to nine), or optimal (ten to 14) cardiovascular health based on prior study.¹⁰

The presence of PAD at baseline was determined by an ankle-brachial index (ABI) ≤ 0.9 , intermittent claudication based on Rose Questionnaire, or self-reported history of leg revascularization. The ABI was measured by trained technicians on nearly all participants at Visit 1 (96%) and on selected participants at Visits 3 ($n=4,197$) and 4 ($n=5,882$). The ABI was defined as the ratio of a single ankle systolic blood pressure in one leg to a single brachial blood pressure. The Rose Questionnaire was used to evaluate whether participants had developed intermittent claudication, which was defined as exertional leg pain relieved within 10 minutes by resting.¹⁹

Given the caveats of ABI measurement and that the Rose Questionnaire was not administered beyond the time Visit 4 ended, PAD incidence was defined as a hospital discharge diagnosis which was available throughout the study follow-up. ARIC conducted active surveillance of local hospitals and regularly contacted every participant and his/her family to get data on all hospitalizations. A trained abstractor obtained and recorded all ICD-9 hospital discharge diagnoses when a hospitalization occurred. Specifically, all records with an ICD-9 code 440.2 (atherosclerosis of native arteries and extremities), 440.3 (atherosclerosis of bypass graft of the extremities), 440.4 (chronic total occlusion artery extremities), 84.1x (lower-extremity amputation), 38.18 (leg endarterectomy), 39.25 (aorto-iliac-femoral bypass), 39.29 (leg bypass surgery), and 39.50 (percutaneous transluminal angioplasty of non-coronary vessels) qualified as hospitalized PAD.

All covariates were assessed at Visit 1 and Visit 3 and included age (years), gender, race, ARIC field center, education level (high school or less, some college, and college or more), alcohol consumption (drinks/week), medication use (anti-diabetic, antihypertensive, aspirin, and lipid-lowering therapy), electrocardiogram-defined left ventricular hypertrophy (LVH),²⁰ CHD, HF, and stroke.

Medication use (anti-diabetic, antihypertensive, aspirin, and lipid-lowering therapy) was ascertained by asking participants to bring containers of current medications. CHD was defined as a self-reported history of physician diagnosed myocardial infarction, prior coronary revascularization, or a previous myocardial infarction by electrocardiogram. HF was defined as the reported use of HF medication or the presence of HF according the Gothenburg criteria.²¹ Stroke was defined as a self-reported history of physician diagnosed stroke.

Statistical Analysis

Baseline characteristics were compared across LS7 health categories (inadequate, average, or optimal). Categorical variables were reported as frequency and percentage whereas continuous variables were reported as mean (SD). Kaplan–Meier estimates were used to plot the cumulative incidence of PAD by LS7 categories (e.g., poor, intermediate, optimal). Cox proportional hazards models were used to compute the hazard ratios (HRs) and 95% CIs for incident PAD across overall LS7 score categories (optimal or average versus inadequate) and per one-unit higher overall LS7 score (i.e., a shift from poor to intermediate, or intermediate to ideal for any one of the seven components). Multivariable models were constructed as follows: Model 1 adjusted for age, sex, race, education, and ARIC study site; Model 2 adjusted for Model 1 covariates, alcohol consumption, aspirin, and LVH. HRs for incident PAD for each individual LS7 component (referent category=poor) were computed, using a single model with all LS7 components included simultaneously. Effect modification by sex and race was evaluated using a stratification technique and comparing models with and without interaction terms.

Because data for all LS7 components were available at baseline and Visit 3, the authors determined how changes in LS7 score between these two visits affected PAD risk. Change in LS7 score was defined as a change in overall LS7 score categories (referent category=no change). Multivariable models were constructed as above with additional adjustment for

baseline LS7 score. Participants with complete data for both study visits and free of PAD at Visit 3 were eligible for this analysis. The test statistic developed by Grambsch and Therneau²² was used to test the proportional hazards assumption, and this was not violated in these analyses. Statistical significance for all comparisons including interactions was defined as $p < 0.05$. Analyses were conducted in 2017. SAS, version 9.4 was used for all analyses.

RESULTS

A total of 12,865 participants free of baseline PAD or other CVD were included. Mean age was 54 (SD=5.7) years, 25% were black, and 55% female. The mean LS7 score at baseline was 7.9 (SD=2.3, black: 6.8 [SD=2.3], white: 8.3 [SD=2.2], $p < 0.001$). Sociodemographic and clinical characteristics across baseline LS7 categories are compared in Table 1. Older age, male sex, black race, less education, and LVH were all associated with poorer cardiovascular health, whereas current alcohol use and aspirin use were associated with better cardiovascular health.

A total of 434 (3.4%) participants developed PAD over a median follow-up of 24.4 years. Cumulative incidence of PAD according to LS7 category differed significantly (Figure 1). After adjustment for age, sex, race, education, study site, alcohol use, aspirin, and LVH, participants in the average and optimal categories had a 64% and 91% respective lower risk of developing PAD compared with those in the inadequate category (HR=0.36, 95% CI 0.28, 0.46 for average and HR=0.09, 95% CI=0.06, 0.15 for optimal; Table 2). A one-point higher LS7 score was associated with a 25% lower risk of incident PAD (HR=0.75, 95% CI=0.72, 0.79).

The most common ideal health components in the study population were blood glucose (56%) and PA (60%) whereas an ideal healthy dietary pattern was the least common (6%). Table 3 shows the risk of incident PAD according to the individual LS7 components, expressed as poor, intermediate, or ideal, evaluated in the same model. Compared with participants in the poor category of their respective components, those with ideal total cholesterol, either intermediate or ideal levels of blood pressure, fasting glucose, and smoking, or intermediate BMI were at a significantly lower risk of incident PAD in multivariate adjusted analysis (Table 3). The strongest associations were observed with ideal levels of blood pressure (HR=0.37, 95% CI=0.28, 0.50), fasting blood glucose (HR=0.20, 95% CI=0.16, 0.26), and smoking (HR=0.23, 95% CI=0.18, 0.29). Better levels of PA or the healthy diet score were not associated with a lower risk of incident PAD (Table 3).

The adjusted risk of incident PAD by both LS7 health category and per one-point improvement in the LS7 score were stronger in women (Appendix Table 3). Associations did not significantly differ in race-stratified analyses (Appendix Table 3).

Appendix Table 4 shows that a worsening in overall LS7 score category over time was associated with a higher risk of incident PAD (HR=1.50, 95% CI=1.11, 2.02). Amongst participants with an average LS7 score at baseline, PAD risk was significantly impacted by a change in overall LS7 score category in either direction (Appendix Table 4). Improving to

the optimal category was associated with a 50% lower risk of PAD (HR=0.50, 95% CI=0.29, 0.89) whereas worsening to the poor category was associated with an over twofold higher risk of PAD (HR=2.36, 95% CI=1.65, 3.39).

DISCUSSION

In this population-based cohort without known CVD the AHA's LS7 healthy lifestyle metric was associated with a markedly lower risk of incident PAD. Individuals with average and optimal CV health had a 64% and 91% respective lower risk of developing PAD compared with those with inadequate health. Associations were even stronger in women. More importantly, a difference of only one component of the LS7 by one level (i.e., poor to intermediate or intermediate to ideal) was associated with a 21% lower risk of PAD. The magnitude of observed PAD risk reduction associated with improved cardiovascular health in this study was similar or even stronger to that seen in prior studies focusing on either CHD or stroke risk.^{7-9,23}

No prior reports have specifically looked at LS7 scores and risk of incident PAD. Amongst Framingham Offspring Study participants, a higher cardiovascular health score was associated with a lower risk of both prevalent subclinical disease including low ABI and incident composite CVD including new onset of intermittent claudication; however, only 1.5% of participants met criteria for subclinical disease as defined by a low ABI and less than 10% of CVD events were due to intermittent claudication.²⁴ The risk of PAD, as defined by a low ABI, according to LS7 metrics was specifically evaluated in a cross-sectional analysis of 4,400 African Americans participating in the Jackson Heart Study.²⁵ Approximately 40% had poor health for at least three different LS7 metrics and these individuals had a 34% increased adjusted odds for PAD compared with the rest of the study participants. Higher blood pressure, higher total cholesterol, and lower PA were each associated with an increased prevalence of PAD in this analysis.²⁵

Better health status for tobacco use, blood pressure, total cholesterol, and fasting glucose were all associated with a lower risk of PAD and are consistent with prior literature documenting hypertension, diabetes, smoking, and hyperlipidemia as established risk factors for the development of PAD.²⁶⁻³¹ Interestingly, intermediate BMI also protected against incident PAD. Ideal BMI was also associated with a lower risk of incident PAD to a similar magnitude as intermediate BMI but findings lost significance in fully adjusted models. These findings are in contrast to multiple prior studies suggesting that a lower BMI has either no association with PAD or is associated with an increased PAD risk.^{27,31-36} Conflicting findings may have been because of the fact that results were less affected by residual confounding from chronic illness seen in older cohorts with cardiac comorbidities. In a study of adults aged 65 years or older, BMI was inversely associated with prevalent PAD and not associated with incident PAD; however, among never smokers in good health, higher BMI was associated with an increased risk of both prevalent and incident PAD.³⁷ Similar results were reported when the BMI was calculated using these participants' weight at the age of 50 years, based on self-recall, instead of from the baseline visit.³⁷

A consistent association between PA levels with risk of PAD is not supported by prior studies.^{27,38–42} Although lower PA is associated with more prevalent PAD, these studies are limited because individuals with PAD have lower PA levels as a result of their disease.^{40–42} More importantly, except for one study demonstrating an association between higher intentional activity and lower risk of an incident low ABI, PA has not been prospectively associated with lower incident PAD.^{27,38,39}

Compared with poor diet, neither intermediate diet nor ideal diet was associated with lower risk of PAD in this study. Although a small randomized trial reported that the Mediterranean diet led to a significantly lower risk for development of symptomatic PAD compared with the control arm, several other studies have shown conflicting results for a relationship between consumption of either fruits and vegetables or overall fiber intake with a lower risk of incident PAD.^{43,44}

Lower-extremity PAD is associated with a substantial clinical and economic burden. Eight million people in the U.S. are estimated to have PAD.¹ Symptomatic PAD requiring hospitalization is associated with a 5-year mortality rate that approaches 25%.⁴⁵ Domestic PAD-related healthcare costs are comparable to those for cardiac arrhythmias, HF, and cerebrovascular disease and annual PAD-related Medicare costs alone are estimated at \$4 billion.⁴⁶ The LS7 was designed to improve the overall cardiovascular health of all Americans by targeting seven modifiable cardiovascular risk factors in an effort to reduce incident CVD.⁶ Findings presented here suggest that even small improvements in LS7 health behaviors and risk factors can have a sizeable impact on reducing PAD incidence and significantly lower the healthcare burden associated with this disease.

Limitations

This study has limitations. Low ABI was not included as an endpoint so findings do not apply to asymptomatic PAD. Symptomatic PAD that did not require hospitalization was also not included. Consequently, the actual incidence rate of PAD was underestimated. However, it is important to quantify the association of LS7 with severe PAD cases because their impact on patients and medical expenditure is substantial. The food-frequency questionnaire is not ideal for assessing dietary intake, especially sodium, and this may have affected assessment of dietary factors and risk of PAD. The associations of diet and exercise with incident PAD may have been masked, as people with known poor scores for cholesterol, blood pressure, and glucose possibly were more likely to report favorable levels of these lifestyle behaviors. Finally, this is an observational study and the presence of residual confounding cannot be excluded.

Future studies should focus on better understanding the relationship of dietary patterns on risk of PAD. Although results from the PREDIMED trial were significant, the symptomatic PAD endpoint was an exploratory, non-prespecified analysis.⁴³ Randomized trials specifically designed with PAD as the major endpoint are needed. Additionally, formal evaluation of the impact of population-based interventions to improve LS7 health behaviors and risk factors on decreasing PAD incidence is also needed.

CONCLUSIONS

In this large cohort of middle-aged U.S. adults, the AHA's LS7 metric, developed to measure and promote cardiovascular health, was associated with a substantially lower risk of PAD. These findings should further support efforts to improve the population's cardiovascular health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS

The authors thank the staff and participants of the Atherosclerosis Risk in Communities study for their important contributions. This study was funded in whole or in part with federal funds from the National Heart, Lung, and Blood Institute; NIH; and HHS under Contract nos. (HHSN268201700001I, HHSN268201700003I, HHSN268201700005I, HHSN268201700004I, HHSN268201700002I).

References

1. Go AS, Mozaffarian D, Roger VL, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Executive summary: heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation*. 2013;127(1):143–152. 10.1161/CIR.0b013e318282ab8f. [PubMed: 23283859]
2. Fowkes FG, Rudan D, Rudan I, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *Lancet*. 2013;382(9901):1329–1340. 10.1016/S0140-6736(13)61249-0. [PubMed: 23915883]
3. Ankle Brachial Index Collaboration, Fowkes FG, Murray GD, et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. *JAMA*. 2008;300(2):197–208. 10.1001/jama.300.2.197. [PubMed: 18612117]
4. 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(1):61–69. 10.1016/j.atherosclerosis.2006.03.011. [PubMed: 16620828]
5. Mahoney EM, Wang K, Keo HH, REACH Registry Investigators, et al. Vascular hospitalization rates and costs in patients with peripheral artery disease in the United States. *Circ Cardiovasc Qual Outcomes*. 2010;3(6):642–651. 10.1161/CIRCOUTCOMES.109.930735. [PubMed: 20940249]
6. Lloyd-Jones DM, Hong Y, Labarthe D, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic impact goal through 2020 and beyond. *Circulation*. 2010;121(4):586–613. 10.1161/CIRCULATIONAHA.109.192703. [PubMed: 20089546]
7. Folsom AR, Yatsuya H, Nettleton JA, Lutsey PL, Cushman M, Rosamond WD. Community prevalence of ideal cardiovascular health, by the American Heart Association definition, and relationship with cardiovascular disease incidence. *J Am Coll Cardiol*. 2011;57(16):1690–1696. 10.1016/j.jacc.2010.11.041. [PubMed: 21492767]
8. Kulshreshtha A, Vaccarino V, Judd S, et al. Life's Simple 7 and risk of incident stroke: REasons for Geographic And Racial Differences in Stroke (REGARDS) Study. *Stroke*. 2013;44(7):1909–1914. 10.1161/STROKEAHA.111.000352. [PubMed: 23743971]
9. Ford ES, Greenlund KJ, Hong Y. Ideal cardiovascular health and mortality from all causes and diseases of the circulatory system among adults in the United States. *Circulation*. 2012;125(8):987–995. 10.1161/CIRCULATIONAHA.111.049122. [PubMed: 22291126]
10. Folsom AR, Shah AM, Lutsey PL, et al. American Heart Association's Life's Simple 7: avoiding heart failure and preserving cardiac structure and function. *Am J Med*. 2015;128(9):970–976. 10.1016/j.amjmed.2015.03.027. [PubMed: 25908393]

11. Bhatt DL, Steg PG, Ohman EM, REACH Registry Investigators, et al. International prevalence, recognition, and treatment of cardiovascular risk factors in outpatients with atherothrombosis. *JAMA*. 2006;295(2):180–189. 10.1001/jama.295.2.180. [PubMed: 16403930]
12. The ARIC Investigators. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. *Am J Epidemiol*. 1989;129(4):687–702. 10.1093/oxfordjournals.aje.a115184. [PubMed: 2646917]
13. Siedel J, Hagele EO, Ziegenhorn J, Wahlefeld AW. Reagent for the enzymatic determination of serum total cholesterol with improved lipolytic efficiency. *Clin Chem*. 1983;29(6):1075–1080. [PubMed: 6851096]
14. Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in epidemiological studies. *Am J Clin Nutr*. 1982;36(5):936–942. 10.1093/ajcn/36.5.936. [PubMed: 7137077]
15. Folsom AR, Arnett DK, Hutchinson RG, Liao F, Clegg LX, Cooper LS. Physical activity and incidence of coronary heart disease in middle-aged women and men. *Med Sci Sports Exerc*. 1997;29(7):901–909. 10.1097/00005768-199707000-00009. [PubMed: 9243489]
16. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc*. 2000;32(9S):S498–S504. 10.1097/00005768-200009001-00009. [PubMed: 10993420]
17. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. *Am J Epidemiol*. 1985;122(1):51–65. 10.1093/oxfordjournals.aje.a114086. [PubMed: 4014201]
18. Stevens J, Metcalf PA, Dennis BH, Tell GS, Shimakawa T, Folsom AR. Reliability of a food frequency questionnaire by ethnicity, gender, age and education. *Nutr Res*. 1996;16(5):735–745. 10.1016/0271-5317(96)00064-4.
19. Rose GA, Blackburn H, Gillum RF, Prineas RJ. *Cardiovascular Survey Methods*. Geneva: WHO; 1982.
20. Okwuosa TM, Soliman EZ, Lopez F, Williams KA, Alonso A, Ferdinand KC. Left ventricular hypertrophy and cardiovascular disease risk prediction and reclassification in blacks and whites: the Atherosclerosis Risk in Communities Study. *Am Heart J*. 2015;169(1):155–161. 10.1016/j.ahj.2014.09.013. [PubMed: 25497261]
21. Eriksson H, Caidahl K, Larsson B, et al. Cardiac and pulmonary causes of dyspnoea: validation of a scoring test for clinical-epidemiological use: the Study of Men Born in 1913. *Eur Heart J*. 1987;8(9):1007–1014. 10.1093/oxfordjournals.eurheartj.a062365. [PubMed: 3665952]
22. Grambsch P and Therneau T. Proportional hazards tests and diagnostics based on weighted residuals. *Biometrika*. 1994;81(3):515–526. 10.1093/biomet/81.3.515.
23. Dong C, Rundek T, Wright CB, Anwar Z, Elkind MS, Sacco RL. Ideal cardiovascular health predicts lower risks of myocardial infarction, stroke, and vascular death across whites, blacks, and Hispanics: the Northern Manhattan Study. *Circulation*. 2012;125(24):2975–2984. 10.1161/CIRCULATIONAHA.111.081083. [PubMed: 22619283]
24. Xanthakis V, Enserro DM, Murabito JM, et al. Ideal cardiovascular health: associations with biomarkers and subclinical disease and impact on incidence of cardiovascular disease in the Framingham Offspring Study. *Circulation*. 2014;130(19):1676–1683. 10.1161/CIRCULATIONAHA.114.009273. [PubMed: 25274000]
25. Collins TC, Slovut DP, Newton R, Jr., et al. Ideal cardiovascular health and peripheral artery disease in African Americans: results from the Jackson Heart Study. *Prev Med Rep*. 2017;7:20–25. 10.1016/j.pmedr.2017.05.005. [PubMed: 28593118]
26. Dormandy JA, Rutherford RB. Management of peripheral arterial disease (PAD). TASC Working Group. TransAtlantic InterSociety Consensus (TASC). *J Vasc Surg*. 2000;31(1 Pt 2):S1–S296. [PubMed: 10666287]
27. Hooi JD, Kester AD, Stoffers HE, Overdijk MM, van Ree JW, Knottnerus JA. Incidence of and risk factors for asymptomatic peripheral arterial occlusive disease: a longitudinal study. *Am J Epidemiol*. 2001;153(7):666–672. 10.1093/aje/153.7.666. [PubMed: 11282794]

28. Joosten MM, Pai JK, Bertoia ML, et al. Associations between conventional cardiovascular risk factors and risk of peripheral artery disease in men. *JAMA*. 2012;308(16):1660–1667. 10.1001/jama.2012.13415. [PubMed: 23093164]
29. Murabito JM, D'Agostino RB, Silbershatz H, Wilson WF. Intermittent claudication. A risk profile from The Framingham Heart Study. *Circulation*. 1997;96(1):44–49. 10.1161/01.CIR.96.1.44. [PubMed: 9236415]
30. Bowlin SJ, Medalie JH, Flocke SA, Zyzanski SJ, Goldbourt U. Epidemiology of intermittent claudication in middle-aged men. *Am J Epidemiol*. 1994;140(5):418–430. 10.1093/oxfordjournals.aje.a117264. [PubMed: 8067334]
31. Ingolfsson IO, Sigurdsson G, Sigvaldason H, Thorgeirsson G, Sigfusson N. A marked decline in the prevalence and incidence of intermittent claudication in Icelandic men 1968–1986: a strong relationship to smoking and serum cholesterol—the Reykjavik Study. *J Clin Epidemiol*. 1994;47(11):1237–1243. 10.1016/0895-4356(94)90128-7. [PubMed: 7722559]
32. Newman AB, Siscovick DS, Manolio TA, et al. Ankle-arm index as a marker of atherosclerosis in the Cardiovascular Health Study. Cardiovascular Health Study (CHS) Collaborative Research Group. *Circulation*. 1993;88(3):837–845. 10.1161/01.CIR.88.3.837. [PubMed: 8353913]
33. Curb JD, Masaki K, Rodriguez BL, et al. Peripheral artery disease and cardiovascular risk factors in the elderly. The Honolulu Heart Program. *Arterioscler Thromb Vasc Biol*. 1996;16(12):1495–1500. 10.1161/01.ATV.16.12.1495. [PubMed: 8977454]
34. Criqui MH, Vargas V, Denenberg JO, et al. Ethnicity and peripheral arterial disease: the San Diego Population Study. *Circulation*. 2005;112(17):2703–2707. 10.1161/CIRCULATIONAHA.105.546507. [PubMed: 16246968]
35. Meijer WT, Grobbee DE, Hunink MG, Hofman A, Hoes AW. Determinants of peripheral arterial disease in the elderly: the Rotterdam study. *Arch Intern Med*. 2000;160(19):2934–2938. 10.1001/archinte.160.19.2934. [PubMed: 11041900]
36. Allison MA, Criqui MH, McClelland RL, et al. 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(6):1190–1197. 10.1016/j.jacc.2006.05.049. [PubMed: 16979004]
37. Ix JH, Biggs ML, Kizer JR, et al. Association of body mass index with peripheral arterial disease in older adults: the Cardiovascular Health Study. *Am J Epidemiol*. 2011;174(9):1036–1043. 10.1093/aje/kwr228. [PubMed: 21920948]
38. Tapp RJ, Balkau B, Shaw JE, Valensi P, Cailleau M, Eschwege E, DESIR Study Group. Association of glucose metabolism, smoking and cardiovascular risk factors with incident peripheral arterial disease: the DESIR study. *Atherosclerosis*. 2007;190(1):84–89. 10.1016/j.atherosclerosis.2006.02.017. [PubMed: 16674960]
39. Delaney JA, Jensky NE, Criqui MH, Whitt-Glover MC, Lima JA, Allison MA. The association between physical activity and both incident coronary artery calcification and ankle brachial index progression: the Multi-Ethnic Study of Atherosclerosis. *Atherosclerosis*. 2013;230(2):278–283. 10.1016/j.atherosclerosis.2013.07.045. [PubMed: 24075757]
40. Stein RA, Rockman CB, Guo Y, et al. Association between physical activity and peripheral artery disease and carotid artery stenosis in a self-referred population of 3 million adults. *Arterioscler Thromb Vasc Biol*. 2015;35(1):206–212. 10.1161/ATVBAHA.114.304161. [PubMed: 25359858]
41. Alzamora MT, Fores R, Baena-Diez JM, et al. The Peripheral Arterial disease study (PERART/SRTPER): prevalence and risk factor in the general population. *BioMed Central Public Health*. 2010;10:38 10.1186/1471-2458-10-38. [PubMed: 20529387]
42. Fowler B, Jamrozik K, Norman P, Allen Y. Prevalence of peripheral arterial disease: persistence of excess risk in former smokers. *Aust N Z J Public Health*. 2002;26(3):219–224. 10.1111/j.1467-842X.2002.tb00677.x. [PubMed: 12141616]
43. Ruiz-Canela M, Estruch R, Corella D, Salas-Salvadó J, Martínez-González MA. Association of Mediterranean diet with peripheral artery disease: the PREDIMED randomized trial. *JAMA*. 2014;311(4):415–417. 10.1001/jama.2013.280618. [PubMed: 24449321]
44. Ruiz-Canela M, Martínez-González MA. Lifestyle and dietary risk factors for peripheral artery disease. *Circ J*. 2014;78(3):553–559. 10.1253/circj.CJ-14-0062. [PubMed: 24492064]

45. Hirsch AT, Hartman L, Town RJ, Virnig BA. National health care costs of peripheral arterial disease in the Medicare population. *Vasc Med*. 2008;13(3):209–215. 10.1177/1358863X08089277. [PubMed: 18687757]
46. Mueller T, Hinterreiter F, Luft C, Poelz W, Haltmayer M, Dieplinger B. Mortality rates and mortality predictors in patients with symptomatic peripheral artery disease stratified according to age and diabetes. *J Vasc Sur*. 2014;59(5):1291–1299. 10.1016/j.jvs.2013.11.063.

Figure 1.
Cumulative incidence of peripheral artery disease by Life's Simple 7 Score.^a
^aCumulative incidence estimates are statistically different (log-rank $p < 0.001$).

Table 1.

Baseline Characteristics of ARIC Participants Without Known Cardiovascular Disease According to Life's Simple 7 Health Category^a

Characteristic	Inadequate LS7=0–4 (n=1,008)	Average LS7=5–9 (n=8,395)	Optimal LS7=10–14 (n=3,462)	P-value ^b
Age, years	55 ± 5.6	54 ± 5.7	53 ± 5.6	<0.001*
Male	423 (42)	4,061 (48)	1,266 (37)	<0.001*
Black	540 (54)	2,291 (27)	384 (11)	<0.001*
Education				<0.001*
High school or less	437 (43)	1,988 (24)	364 (11)	
Some college	371 (37)	3,570 (42)	1,367 (39)	
College or more	200 (20)	2,837 (34)	1,731 (50)	
Alcohol consumption				<0.001*
None	318 (32)	2,072 (25)	812 (23)	
Former	242 (24)	1,545 (18)	476 (14)	
Current	448 (44)	4,778 (57)	2,174 (63)	
Left ventricular hypertrophy	79 (8)	241 (3)	32 (1)	<0.001*
Aspirin use	392 (39)	3,768 (45)	1,627 (47)	<0.001*

Notes: Boldface indicates statistical significance (* $p < 0.001$).

^aContinuous variables are expressed as mean (SD). Categorical variables are N (%).

^bStatistical significance for categorical variables tested using the chi-square method and for continuous variables the analysis of variance procedure was used.

ARIC, Atherosclerosis Risk in Communities; LS7, Life's Simple 7

Table 2.

Associations Between Overall Life's Simple 7 Score and Incident Peripheral Artery Disease Among ARIC Participants^a

Variable	n PAD/N at risk	Incidence rate per 1,000 person years (95% CI) ^b	Model 1 ^c HR (95% CI)	Model 2 ^d HR (95% CI)
LS7 health categories				
Inadequate (0 to 4 points)	95/1,008	5.19 (4.25, 6.35)	1 (ref)	1 (ref)
Average (5 to 9 points)	309/8,395	1.13 (0.94, 1.36)	0.33 (0.26, 0.42)	0.36 (0.34, 0.56)
Optimal (10 to 14 points)	30/3,462	0.42 (0.29, 0.60)	0.08 (0.05, 0.13)	0.09 (0.09, 0.22)
LS7 score per unit increase	434/12,865	1.58 (1.44, 1.74)	0.74 (0.71, 0.77)	0.75 (0.75, 0.83)

^aResults of multivariable Cox proportional hazards models.

^bStandardized using the 2010 U.S. population.

^cModel 1 adjusted for age, sex, race, education, and ARIC study site.

^dModel 2 adjusted for Model 1 + alcohol consumption, aspirin, and left ventricular hypertrophy.

LS7, Life's Simple 7; PAD, peripheral artery disease; HR, hazard ratio; ARIC, Atherosclerosis Risk in Communities.

Table 3.

Associations Between Individual Life's Simple 7 Components and Incident Peripheral Artery Disease Among ARIC Participants^a

Component	n PAD/N at risk	Model 1 ^b HR (95% CI)	Model 2 ^c HR (95% CI)
Total cholesterol			
Poor	136/3,125	1 (ref)	1 (ref)
Intermediate	148/4,636	0.77 (0.61, 0.97)	0.81 (0.64, 1.03)
Ideal	150/5,104	0.73 (0.58, 0.93)	0.78 (0.61, 0.98)
Blood pressure			
Poor	133/2,102	1 (ref)	1 (ref)
Intermediate	206/5,435	0.60 (0.50, 0.79)	0.65 (0.52, 0.82)
Ideal	95/5,328	0.31 (0.25, 0.44)	0.37 (0.28, 0.50)
Blood glucose			
Poor	132/1,099	1 (ref)	1 (ref)
Intermediate	143/4,529	0.23 (0.18, 0.30)	0.24 (0.19, 0.30)
Ideal	159/7,237	0.18 (0.14, 0.23)	0.20 (0.16, 0.26)
Physical activity			
Poor	186/4,665	1 (ref)	1 (ref)
Intermediate	20/524	1.05 (0.66, 1.67)	1.36 (0.86, 2.18)
Ideal	228/7,676	0.83 (0.61, 1.02)	0.98 (0.79, 1.21)
Healthy diet score			
Poor	206/6,400	1 (ref)	1 (ref)
Intermediate	198/5,656	1.13 (0.93, 1.37)	1.11 (0.91, 1.35)
Ideal	30/809	1.28 (0.87, 1.89)	1.15 (0.77, 1.69)
Smoking			
Poor	186/3,212	1 (ref)	1 (ref)
Intermediate	132/4,098	0.40 (0.32, 0.51)	0.34 (0.27, 0.44)
Ideal	116/5,555	0.27 (0.21, 0.35)	0.23 (0.18, 0.29)
BMI			
Poor	160/3,350	1 (ref)	1 (ref)
Intermediate	163/5,109	0.64 (0.51, 0.80)	0.78 (0.62, 0.98)
Ideal	111/4,406	0.63 (0.49, 0.80)	0.83 (0.63, 1.08)

PAD, peripheral artery disease; HR, hazard ratio; LS7, Life's Simple 7; ARIC, Atherosclerosis Risk in Communities.

^aResults of multivariable Cox proportional hazards models.

^bModel 1 adjusted for age, sex, race, education, ARIC study site, alcohol consumption, aspirin, and left ventricular hypertrophy.

^cModel 2 adjusted for Model 1 + each individual LS7 component.