

## Life's Simple 7 and Peripheral Artery Disease: The Multi-Ethnic Study of Atherosclerosis



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**Introduction:** In 2010, the American Heart Association initiated Life's Simple 7 with the goal of significantly improving cardiovascular health by the year 2020. The association of Life's Simple 7 with risk of peripheral artery disease has not been thoroughly explored.

**Methods:** Racially diverse individuals from the Multi-Ethnic Study of Atherosclerosis (2000–2012) were followed for incident peripheral artery disease (ankle brachial index  $\leq 0.90$ ) and decline in ankle brachial index ( $\geq 0.15$ ) over approximately 10 years of follow-up. Cox and logistic regression were used to assess associations of individual Life's Simple 7 components (score 0–2) and overall Life's Simple 7 score (score 0–14) with incident peripheral artery disease and ankle brachial index decline, respectively, adjusted for age, sex, race/ethnicity, education, and income. Analyses were performed in 2016–2018.

**Results:** Of 5,529 participants, 251 (4.5%) developed incident peripheral artery disease; 419 (9.8%) of 4,267 participants experienced a decline in ankle brachial index. Each point higher for the overall Life's Simple 7 score was associated with a 17% lower rate of incident peripheral artery disease (hazard ratio=0.83, 95% CI=0.78, 0.88,  $p < 0.001$ ). Additionally, each point higher in overall Life's Simple 7 was associated with a 0.94-fold lower odds of decline in ankle brachial index (OR=0.94, 95% CI=0.87, 0.97,  $p = 0.003$ ). Four components (smoking, physical activity, glucose, and blood pressure) were associated with incident peripheral artery disease and two (smoking and glucose) with decline in ankle brachial index.

**Conclusions:** Better cardiovascular health as measured by Life's Simple 7 is associated with lower incidence of peripheral artery disease and less decline in ankle brachial index. Use of the Life's Simple 7 to target modifiable health behaviors may aid in decreasing the population burden of peripheral artery disease–related morbidity and mortality.

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## INTRODUCTION

Peripheral artery disease (PAD) is a significant public health problem, with approximately 8.5 million Americans currently affected.<sup>1</sup> Over 10 years, the risk of cardiovascular (CV) mortality in those with PAD is 4.2 times higher in men and 3.5 times higher in women compared with those without PAD.<sup>2</sup> In large meta-analyses, a low ankle brachial index (ABI; 0.90 or less), the standard clinical criterion for PAD diagnosis, was also associated with CV events and mortality, with approximately 1.5 to 2 times increased risk for myocardial infarction, stroke, CV mortality, and all-cause mortality when comparing those with low ABI with a normal ABI group (1.1–1.4).<sup>2,3</sup> Functional decline, intermittent claudication, critical leg ischemia, and amputation resulting from PAD affect quality of life and lead to increased morbidity.<sup>4–6</sup> As a result, useful preventive measures could decrease significant PAD-related morbidity and mortality.

In 2010, the American Heart Association's (AHA's) Strategic Planning Task Force and Statistics Committee designed the Life's Simple 7 (LS7) metric for monitoring the AHA's 2020 impact goal to improve CV health (CVH), which aims to improve the CVH of all Americans by 20% by the year 2020.<sup>7</sup> LS7 can be used to calculate an overall CVH score composed of an individual's values for modifiable CV risk factors (blood pressure [BP], glucose, and cholesterol), and CV-related health behaviors (physical activity, BMI, diet, and smoking). Adherence to ideal CVH defined by LS7 has been associated with lower risks of stroke,<sup>8</sup> diabetes,<sup>9</sup> heart failure,<sup>10</sup> and venous thromboembolism.<sup>11,12</sup> In the Jackson Heart Study, having scored poorly on three or more LS7 components was associated with increased odds of prevalent PAD in African Americans.<sup>13</sup> However, the extent to which this metric may be associated with preventing incident PAD or decline in ABI in a multi-ethnic population has not been fully established.

Thus, this investigation seeks to assess the association of the LS7 components and overall LS7, using a simple scoring method, with incident PAD and decline in ABI in non-Hispanic white, African American, Hispanic, and Asian men and women from the Multi-Ethnic Study of Atherosclerosis (MESA). Furthermore, this investigation seeks to determine whether these associations differed by race/ethnicity.

## METHODS

### Study Sample

MESA participants were recruited from six field sites in the U.S.: Forsyth County, North Carolina (Wake Forest); Northern Manhattan/Bronx, New York (Columbia); Baltimore/Baltimore

County, Maryland (Johns Hopkins); St. Paul, Minnesota (University of Minnesota); Chicago, Illinois (Northwestern); and Los Angeles County, California (University of California, Los Angeles). Details of recruitment have been previously published.<sup>14</sup> Briefly, MESA recruited 6,814 men and women aged 45–84 years free of clinical CV disease, with the cohort comprising 53% women and a racial/ethnic composition of approximately 38% non-Hispanic white, 28% African American, 23% Hispanic, and 11% Asian, primarily of Chinese descent. Exclusion criteria included a self-reported medical history of heart attack, angina, CV procedures, heart failure, cerebrovascular disease, active treatment for cancer, or pregnancy. The baseline exam (Exam 1) occurred from 2000 to 2002, with Exam 2 from 2002 to 2004, Exam 3 from 2004 to 2005, Exam 4 from 2005 to 2007, and Exam 5 from 2010 to 2012. MESA complies with the Declaration of Helsinki, and IRBs at each field site, as well as the Coordinating Center (University of Washington, Seattle), approved the study.

### Measures

Systolic BP was measured in both the left and right brachial, dorsalis pedis, and posterior tibial arteries using a hand-held Doppler instrument with a 5-mHz probe. ABI was calculated for both the left and right sides as maximum systolic BP in the posterior tibial artery and dorsalis pedis, divided by the average of the left and right brachial pressures. As previous studies have shown a strong association between PAD and subclavian stenosis,<sup>15</sup> in the event that left and right brachial pressures differed by  $\geq 10$  mmHg, the higher of the brachial pressures was used. If a pulse was detected when the cuff was inflated to 300 mmHg, ABI was classified as incompressible. For these analyses, the lower of an individual's left and right leg ABI was used.

Incident PAD was defined as an ABI  $\leq 0.90$  at Exam 3 or Exam 5 and excluded participants with prevalent PAD (ABI  $\leq 0.90$ ) at the baseline exam; ABI  $> 1.4$  at Exams 1, 3, or 5; or without at least one follow-up ABI at Exam 3 or 5. An ABI  $> 1.4$  or incompressible is typically indicative of arterial stiffening caused by arterial medial calcification.<sup>16</sup> This may distort the accuracy of the ABI measure when evaluating lower extremity occlusive disease. Prior work has demonstrated that a significant change in ABI  $\geq 0.15$ <sup>17–19</sup> may be clinically significant progression of disease and not indicative of measurement error.<sup>20</sup> Thus, decline in ABI was defined as a decrease of  $\geq 0.15$  between Exam 1 and Exam 5, and excluded participants with missing ABI values at Exams 1, 5, or both exams. Participants with prevalent PAD (ABI  $\leq 0.90$ ) or ABI  $> 1.4$  were not excluded from the decline in ABI component of the analysis.

At Exam 1, baseline levels of LS7 metrics (smoking, BMI, physical activity, diet, BP, total cholesterol, and blood glucose) were measured and categorized into ideal, intermediate, and poor according to the AHA criteria<sup>7</sup> with modifications in MESA as previously reported.<sup>21</sup> Appendix Table 1 (available online) summarizes the definitions. Smoking status was assessed using questionnaires, and participants were classified as current smokers, former smokers who quit within the past 12 months, quitters  $> 12$  months ago, or never smokers. BMI was calculated from height and weight measurements performed by study personnel. Physical activity was measured using a detailed questionnaire adapted from the Cross-Cultural Activity Participation Study.<sup>22</sup> The questionnaire identifies the time and frequency spent in activities during a typical

week in the previous month using 28 questions including household chores; lawn/yard/garden/farm; care of children/adults; transportation; walking (not at work); dancing and sport activities; conditioning activities; leisure activities; and occupational and volunteer activities. Minutes of walking, conditioning, and leisure activities were also included as exercise, and the minutes of moderate and vigorous exercise were calculated from the questionnaire. For BP, three measurements were taken after participants were seated and had rested for 5 minutes. The average of the last two measurements was used for analysis. Total cholesterol and blood glucose levels were obtained from fasting blood samples.<sup>14</sup> Additionally, medication use in relation to BP, cholesterol, and glucose were verified by a medication inventory.

Diet assessment was performed using a validated 120-item food-frequency questionnaire modified from the Insulin Resistance Atherosclerosis Study instrument.<sup>23,24</sup> Diet was defined according to AHA criteria using five components of healthy diet (high intake of fruits and vegetables, fish, whole grains, low intake of sodium and sugar-sweetened beverages).<sup>7</sup> Of note, a coding error led to data being unavailable on the intake of 14 foods (fruit juice, dark/whole grains, fruit, salty snacks, other vegetables, leafy green vegetables, yogurt, potato, red meat, high fat and processed meat, high-fat dairy, desserts, cottage cheese, and legumes) in ~25% of MESA participants, the majority of whom were from two (Johns Hopkins and University of Minnesota) of six MESA field centers. Consequently, the data are not missing completely at random and may not be missing at random. To minimize biased analyses, imputation was conducted using sequential chained regression, implemented specifying multinomial or ordinal regression, with one model for all 14 items. Imputation models accounted for basic demographics, and other auxiliary variables were selected based on high correlation with the food-frequency questionnaire or serving size items. There were a few values imputed for the other four study sites, but these were in very small numbers (<10% of the imputed data). The imputed data set was used for this analysis.

This investigation used a previously defined scoring system<sup>12,21</sup> where points were assigned to each LS7 component and summed: ideal=2 points, intermediate=1 point, and poor=0 points, for a total score ranging from 0 to 14 points.<sup>25</sup> Study participants who scored 0–7 points were classified as having inadequate, those who scored 8–11 points were classified as having average, and participants who scored 12–14 points were classified as having optimum overall CVH.

Additional participant covariates were assessed by questionnaire at baseline and include participant age; sex; race/ethnicity; education (less than high school, high school graduate, some college, college graduate, or more than college graduate); and income (<\$50,000 and ≥\$50,000 per year).

### Statistical Analysis

Unadjusted participant characteristics including age, sex, race/ethnicity, highest level of education completed, income, and LS7 scores were compared for incident PAD and decline in ABI groups using ANOVA for continuous variables and chi-square tests for categorical variables. Poisson distribution; a log-link function; and an offset of ln(person-years) was used to calculate PAD incidence rates for LS7 individual component and overall CVH categories, using PROC GENMOD in SAS, version 9.3.

Each LS7 component was examined as a categorical variable: inadequate, average, and optimum. Overall LS7 score was assessed using the continuous 0–14 scale, as well as the overall categorical indications of inadequate, average, and optimum. Cox proportional hazard models were used to assess the association of individual LS7 components X overall LS7 with incident PAD. When defining incident PAD, time to event was the midpoint between exams at which the ABI was measured. To assess decline in ABI, logistic regression was performed after participants were dichotomized into those with ≥0.15 decline in ABI from Exam 1 to 5 versus those without. Models were adjusted for age, sex, race/ethnicity, education, and income. For models assessing decline in ABI, baseline ABI was included in the model.

Interactions of race/ethnicity X continuous LS7 score were assessed on a multiplicative scale for both incident PAD and decline in ABI outcomes, adjusted for age, sex, education, and income. A *p*-value <0.05 was used for statistical significance. All analyses were performed in 2016–2018 using SAS, version 9.3.

## RESULTS

A total of 5,529 participants had complete LS7 information and met inclusion criteria to assess incident PAD. During a median follow-up time of 9.2 years, a total of 251 (4.5%) participants developed incident PAD. For decline in ABI, 4,267 participants had an ABI measure at both Exams 1 and 5, as well as complete LS7 information. During a median follow-up time of 9.4 years, 419 (9.8%) participants had a decline of ≥0.15 in ABI. Baseline characteristics between those with and without incident PAD and those with and without a significant decline in ABI are presented in [Table 1](#). Compared with those without incident PAD, participants who developed incident PAD were older, more likely to be female, African American, have less than a high school education, income <\$50,000, have lower baseline ABI, and a lower total LS7 score. Participants who experienced a decline in their ABI were older, more likely to be African American, have less than a high school education, income <\$50,000, have lower baseline ABI and lower total LS7 score compared with those without a significant change in ABI.

Adjusted rates of PAD per 1,000 person-years were 17.8 for inadequate, 8.6 for average, and 4.1 for optimum CVH ([Table 2](#)). Each point higher on the continuous LS7 scale was associated with a 17% lower rate of incident PAD (hazard ratio [HR]=0.83, 95% CI=0.78, 0.88, *p*<0.001). Compared with inadequate CVH, participants with average and optimum health had a 49% lower rate (HR=0.51, 95% CI=0.38, 0.66, *p*<0.001) and a 76% lower rate (HR=0.24, 95% CI=0.10, 0.59, *p*<0.001) of incident PAD, respectively. Furthermore, each point higher on the continuous LS7 scale was associated with 0.94-fold lower odds of decline in ABI (OR=0.94, 95% CI=0.87, 0.97, *p*=0.003). Compared with those with inadequate CVH, participants with average

**Table 1.** Exam 1 (2000–2002) Characteristics and Life's Simple 7 Score by Incident PAD and Decline in the ABI in MESA

Characteristic	No incident PAD <sup>a</sup> (n=5,278)	Incident PAD <sup>a</sup> (n=251)	p-value	No decline in ABI <sup>b</sup> (n=3,848)	Decline in ABI <sup>b</sup> (n=419)	p-value
Age, years, M ± SD	61 ± 10	68 ± 9	<0.001	60 ± 9	63 ± 10	<0.001
Female, n (%)	2,756 (52)	155 (62)	0.003	2,026 (53)	213 (51)	0.48
Race/ethnicity, n (%)			<0.001			<0.001
Non-Hispanic white	2,145 (41)	82 (33)		1,592 (41)	169 (40)	
Chinese	676 (13)	18 (7)		495 (13)	34 (8)	
African American	1,309 (25)	105 (42)		945 (25)	136 (33)	
Hispanic	1,148 (22)	46 (18)		816 (21)	81 (19)	
Education, n (%)			0.002			0.003
≤High school	1,764 (33)	109 (43)		1,167 (30)	161 (38)	
Some college	1,503 (28)	70 (28)		1,123 (29)	103 (25)	
≥Bachelor's degree	2,010 (38)	72 (29)		1,558 (41)	155 (37)	
Income >\$50,000, n (%)	2,196 (43)	75 (32)	0.001	1,737 (46)	163 (41)	0.03
Life's Simple 7 Score <sup>c</sup>	8.5 ± 2.0	7.5 ± 2.2	<0.001	8.6 ± 2.1	8.2 ± 2.2	<0.001
Simple 7 categories, n (%)			<0.001			<0.001
Inadequate (0–7 points)	1,616 (31)	128 (51)		1,135 (30)	157 (38)	
Average (8–11 points)	3,279 (62)	118 (47)		2,408 (63)	242 (58)	
Optimum (12–14 points)	383 (7)	5 (2)		305 (8)	20 (5)	
Ankle Brachial Index ± SD	1.13 ± 0.09	1.05 ± 0.09	<0.001	1.12 ± 0.10	1.18 ± 0.13	<0.001

Note: Participant characteristics at Exam 1 (2000–2002) for those who developed incident PAD (ABI ≤0.9 any time after Exam 1) and/or experienced a decline in ABI (≥0.15 between Exam 1 [2002–2002] and Exam 5 [2010–2012]). Analyses include participants with complete information on Life's Simple 7 components. Boldface indicates statistical significance ( $p \leq 0.05$ ).

<sup>a</sup>Incident PAD removes participants with prevalent PAD (ABI ≤0.9) at Exam 1 and those with ABI >1.4 at Exams 1, 3, or 5.

<sup>b</sup>Decline in the ABI is defined as a decrease ≥0.15 in the ABI measure between Exam 1 and Exam 5.

<sup>c</sup>On a 0–14-point scale.

ABI, ankle brachial index; MESA, Multi-Ethnic Study of Atherosclerosis; PAD, peripheral artery disease.

and optimum health had a 0.84-fold lower odds (95% CI=0.58, 0.93,  $p=0.01$ ) and a 0.54-fold lower odds (95% CI=0.32, 0.90,  $p=0.02$ ) of decline in ABI over the follow-up period, respectively.

Adjusted PAD incidence rates varied across inadequate, average, and optimum categories for each individual LS7

component (Figure 1), with the highest rates in the inadequate category for all components. These associations appeared strongest for smoking, physical activity, glucose, and BP. Furthermore, after adjusting for age, sex, race/ethnicity, income, education, and using the inadequate category as the reference group for each individual LS7

**Table 2.** Associations of Life's Simple 7 With Incident PAD and Decline in the ABI in MESA

Variable	PAD incidence rate <sup>a</sup> (per 1,000 person-years)	Incident PAD <sup>b</sup> (n=5,529)		Decline in ABI <sup>c</sup> (n=4,461)	
		HR (95% CI)	p-value	OR (95% CI)	p-value
Per 1 point higher	—	0.83 (0.78, 0.88)	<0.001	0.94 (0.87, 0.97)	0.003
Categories					
Inadequate (0–7 points)	17.8	1.00 (ref)		1.00 (ref)	
Average (8–11 points)	8.6	0.51 (0.38, 0.66)	<0.001	0.84 (0.58, 0.93)	0.01
Optimum (12–14 points)	4.1	0.24 (0.10, 0.59)	<0.001	0.54 (0.32, 0.90)	0.02

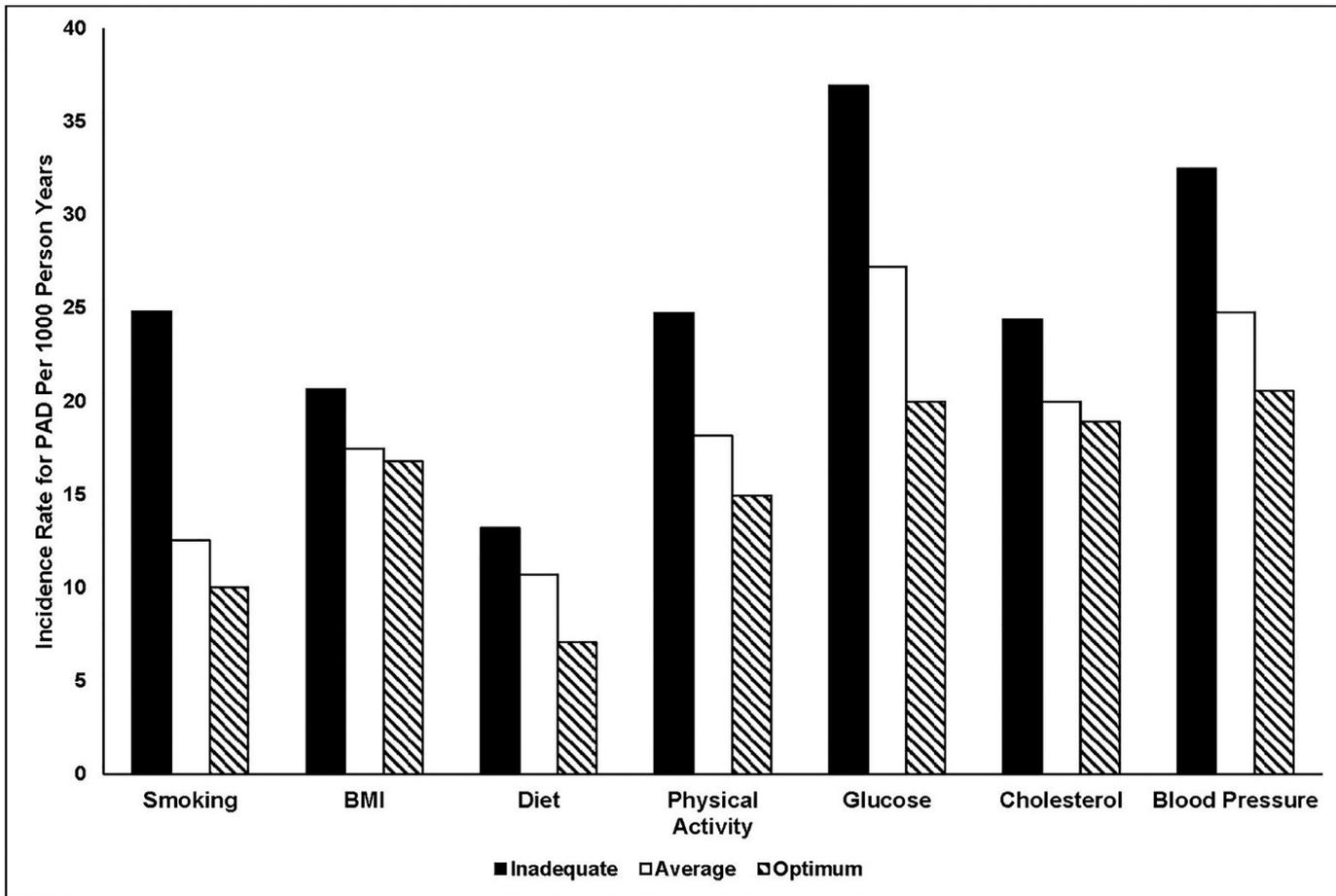
Note: Presented are the incident rates (per 1,000 person-years); HRs for incident PAD (ABI ≤0.9 any time after Exam 1); and ORs for experiencing a decline in ABI (≥0.15 between Exam 1 [2002–2002] and Exam 5 [2010–2012]). All models were adjusted for age, sex, and race/ethnicity. Boldface indicates statistical significance ( $p \leq 0.05$ ).

<sup>a</sup>Per 1-point increase on a 0–14-point scale.

<sup>b</sup>Removes those with ABI >1.4 at Exams 1, 3, and 5. Models were additionally adjusted for education and income.

<sup>c</sup>Decline in the ABI is defined as a decrease ≥0.15 in the ABI measure between Exam 1 and Exam 5. Models were additionally adjusted for education, income, and baseline ABI.

ABI, ankle brachial index; HR, hazard ratio; MESA, Multi-Ethnic Study of Atherosclerosis; PAD, peripheral artery disease.



**Figure 1.** Incidence rates of PAD by individual Life's Simple 7 components in MESA.

*Note:* This figure displays the age, sex, and race-ethnicity adjusted incidence rates for PAD by each component of Life's Simple 7. The y-axis displays the incidence rate for PAD per 1,000 person-years, whereas the x-axis displays the inadequate, average, and optimum categories for each of the Life's Simple 7 components.

MESA, Multi-Ethnic Study of Atherosclerosis; PAD, peripheral artery disease.

**Table 3.** Associations of Individual Life's Simple 7 Components With Incident PAD and Decline in ABI in MESA

Life's Simple 7 component	At risk for incident PAD, n/N	Incident PAD, <sup>a</sup> HR (95% CI)	Decline in ABI, <sup>b</sup> OR (95% CI)
<b>Smoking</b>			
Inadequate (current smoker)	49/696	1.00 (ref)	1.00 (ref)
Average (quit ≤12 months)	91/1,927	<b>0.53 (0.37, 0.77)</b>	<b>0.52 (0.37, 0.71)</b>
Optimum (never/quit >12 months)	111/2,906	<b>0.43 (0.30, 0.61)</b>	<b>0.45 (0.33, 0.61)</b>
<b>BMI</b>			
Inadequate (≥30)	89/1,723	1.00 (ref)	1.00 (ref)
Average (25–29.9)	97/2,183	0.85 (0.64, 1.15)	0.80 (0.62, 1.02)
Optimum (<25)	65/1,623	0.81 (0.57, 1.15)	0.93 (0.70, 1.23)
<b>Healthy diet score</b>			
Inadequate (0–1 components)	123/2,697	1.00 (ref)	1.00 (ref)
Average (2–3 components)	126/2,766	0.84 (0.64, 1.10)	0.95 (0.86, 1.19)
Optimum (4–5 components)	2/66	0.51 (0.13, 2.08)	1.17 (0.44, 3.07)
<b>Physical activity</b>			
Inadequate (none)	75/1,195	1.00 (ref)	1.00 (ref)
Average (<150 minutes/week)	45/960	0.75 (0.51, 1.10)	1.07 (0.76, 1.51)
Optimum (≥150 minutes/week)	131/3,374	<b>0.63 (0.47, 0.84)</b>	1.05 (0.80, 1.38)
<b>Glucose</b>			
Inadequate (≥126 mg/dL)	30/387	1.00 (ref)	1.00 (ref)
Average (100–125 mg/dL or treated to goal)	57/954	0.78 (0.49, 1.23)	0.51 (0.34, 0.78)
Optimum (<100 mg/dL)	164/4,188	<b>0.58 (0.38, 0.87)</b>	<b>0.47 (0.33, 0.68)</b>
<b>Total cholesterol</b>			
Inadequate (≥240 mg/dL)	30/520	1.00 (ref)	1.00 (ref)
Average (200–239 mg/dL or treated to goal)	112/2,383	0.81 (0.54, 1.22)	0.94 (0.65, 1.36)
Optimum (<200 mg/dL)	109/2,626	0.75 (0.49, 1.14)	0.95 (0.66, 1.37)
<b>Blood pressure</b>			
Inadequate (SBP ≥140 or DBP ≥90 mmHg)	99/1,304	1.00 (ref)	1.00 (ref)
Average (SBP 120–139 mmHg, DBP 80–89 mmHg, or treated to goal)	107/2,313	0.79 (0.60, 1.05)	0.93 (0.71, 1.22)
Optimum (SBP <120 mmHg and DBP <80 mmHg)	45/1,912	<b>0.64 (0.45, 0.93)</b>	0.85 (0.63, 1.15)

Note: Presented are the incident PAD cases; HRs for incident PAD (ABI ≤0.9 any time after Exam 1); and ORs for experiencing a decline in ABI [≥0.15 between Exam 1 (2002–2002) and Exam 5 (2010–2012)]. All models were adjusted for age, sex, and race/ethnicity. Boldface indicates statistical significance ( $p \leq 0.05$ ).

<sup>a</sup>Models were also adjusted for income and education.

<sup>b</sup>Models additionally were adjusted for income, education, and baseline ABI.

ABI, ankle brachial index; DBP, diastolic blood pressure; HR, hazard ratio; MESA, Multi-Ethnic Study of Atherosclerosis; PAD, peripheral artery disease; SBP, systolic blood pressure.

component, more optimal levels of smoking, physical activity, glucose, and BP were significantly associated with lower rates of incident PAD (Table 3). For decline in ABI, after adjusting for age, sex, race/ethnicity, income, education, and baseline ABI, more optimal levels of smoking, and glucose were significantly associated with lower odds of decline in ABI (Table 3). Categories of BMI, diet, and cholesterol were not associated with incident PAD or decline in ABI.

The strength of the continuous LS7 score X PAD association (Appendix Table 2, available online) differed marginally by race/ethnicity ( $p_{\text{interaction}}=0.04$ ) with the strongest associations found in non-Hispanic whites (HR=0.76, 95% CI=0.69, 0.85,  $p<0.001$ ) and Hispanics (HR=0.78, 95% CI=0.67, 0.91,  $p=0.001$ ). There were no significant interactions for decline in ABI ( $p_{\text{interaction}}=0.76$ ).

## DISCUSSION

In this prospective analysis of a multi-ethnic adult population-based cohort free of clinical CV disease at baseline, participants with higher LS7 scores of CVH were less likely to develop incident PAD or experience a decline in their ABI. Each one point higher on the LS7 score scale was associated with a lower rate of incident PAD and lower odds of decline in ABI (0.15 or more). Furthermore, participants with optimum and average CVH were significantly less likely to develop incident PAD or experience a decline in ABI over time compared with those with inadequate LS7 scores. These results were independent of age, sex, race/ethnicity, income, and education.

The AHA's goal with the LS7 metric was to identify seven modifiable risk factors to optimize to promote and track individual and population progress in CVH improvement. The AHA goal "By 2020, to improve the cardiovascular health of all Americans by 20% while reducing deaths from cardiovascular diseases and stroke by 20%"<sup>27</sup> includes decreasing PAD-related death. PAD is associated with higher CV disease morbidity and mortality. For example, in a clinical vascular lab population, a significant decrease in ABI (0.15 or more) was found to be associated with greater CV and all-cause mortality.<sup>26</sup> Although an ABI change of 0.15 or more is routinely used by vascular specialists to track progression of PAD, screening with the ABI is not routinely performed in asymptomatic patients in primary care clinics.<sup>27</sup> Given that most individuals with PAD are asymptomatic,<sup>28</sup> a measurable decline in ABI without reaching the PAD threshold may still indicate a significant risk. As a result, many high-risk individuals may not receive

appropriate counseling and targeted therapies to reduce their CV risk. However, the results suggest that targeting the LS7 in adults should aid in preventing or slowing the progression of PAD.

Although higher overall LS7 scores were associated with lower rates of PAD and less decline in ABI, not all the individual LS7 components were significantly associated with these outcomes. In the analysis, LS7 categories for smoking, glucose level, BP, and physical activity were significantly associated with incident PAD. Not surprisingly, smoking and diabetes are consistently two of the strongest risk factors for the development of PAD.<sup>28</sup> Kennedy et al.<sup>17</sup> found that age, current cigarette use, diabetes, hypertension, and elevated cholesterol were associated with the development of PAD and decline in ABI. Additionally, lower levels of physical activity have been shown to be associated with prevalent PAD and worse outcomes in those with PAD.<sup>29</sup> Even though targeting all LS7 metrics would be ideal, choosing one or two of the highest-yield modifiable risks may be the only reasonable option in some individuals.

In the Jackson Heart Study, African Americans with three or more poor categories of the LS7 had 34% higher odds of having prevalent PAD.<sup>13</sup> In addition to an association in African Americans, the results in this investigation showed a significant prospective association between LS7 and incident PAD in Hispanics and non-Hispanic whites. Although the association was not statistically significant in Chinese Americans in MESA, this was likely due to the low number of incident PAD cases ( $n=18$ ). Additionally, the results for decline in ABI did not appear to differ across race/ethnicity. These results support the use of LS7 to prevent PAD and decline in ABI in multiple racial/ethnic groups, which is one of the stated goals from the AHA.<sup>7</sup> Previous studies of heart failure,<sup>10</sup> stroke,<sup>8</sup> diabetes,<sup>9</sup> and venous thromboembolism<sup>11,12,30</sup> showed robust associations of the LS7 across multiple racial/ethnic groups. The results are consistent with other publications demonstrating the powerful associations of the LS7 with prevention of multiple health outcomes. Important future directions include comparing the predictive capability of the LS7 score with more traditional risk factor assessment, such as the Framingham score or the more modern pooled cohort risk equations.<sup>31</sup>

## Limitations

There are limitations to this study. First, LS7 scores were assessed at baseline, and this investigation did not examine whether participants changed categories of LS7 after the baseline exam. Additionally, measures of physical activity and diet were self-reported and subject to recall

or reporting bias. The results demonstrating an association between physical activity and PAD may represent reverse causality. The ABI may not be sensitive to mild PAD, and those with mild PAD may be less physically active, while also being at greater risk of progressing to PAD severe enough to be detected by ABI. Furthermore, a scoring system was applied to the LS7 system not originally intended when introduced by the AHA. However, this scoring method was chosen for simplicity of implementation, interpretation, and consistency with other publications. Interpretation of the effect sizes should take this into consideration. Lastly, although MESA is a large, ethnically diverse population-based cohort study including participants from across the U.S., it was not designed to be nationally representative. A future study could examine if longitudinal improvement in LS7 scores confers a protective benefit against incident PAD. Strengths of the study include use of a large diverse population, lengthy follow-up time, and protocol-based measures of ABI.

## CONCLUSIONS

Higher scores on the AHA LS7 were associated with lower incident PAD and less decline in ABI. Preventive measures targeting LS7 components could assist with reducing PAD-related morbidity and mortality.

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## SUPPLEMENTAL MATERIAL

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