



Healthy lifestyle factors and incident heart disease and mortality in candidates for primary prevention with statin therapy



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ABSTRACT

Background: There are limited data on the use of healthy lifestyles among adults who are candidates for primary prevention of atherosclerotic cardiovascular disease (ASCVD) with statin therapy due to a 10-year predicted risk $\geq 7.5\%$. We determined the prevalence of healthy lifestyle factors and their association with incident ASCVD and all-cause mortality in the Reason for Geographic and Racial Differences in Stroke study participants ($n = 5709$). **Methods:** Lifestyle factors (non-obese waist circumference, physical activity ≥ 5 times-per-week, non-smoking, low saturated-fat-intake, highest Mediterranean diet score quartile) were assessed during an in-home examination and interviewer-administered questionnaires. Adjudicated incident ASCVD (nonfatal/fatal stroke, nonfatal myocardial infarction or coronary heart disease death) and all-cause mortality were identified through active participant follow-up.

Results: Overall, 5.1%, 28.9%, 36.9%, 21.7% and 7.5% had 0, 1, 2, 3, and ≥ 4 of the 5 healthy lifestyle factors studied. There were 377 incident ASCVD events (203 CHD events and 174 strokes) and 471 deaths during 5.8 and 6.0 median years of follow-up, respectively. ASCVD incidence rates (95% CI) per 1000-person-years associated with 0, 1, 2, 3 and ≥ 4 healthy lifestyles were 13.4 (7.3–19.5), 12.8 (10.4–15.2), 11.0 (9.0–12.9), 11.0 (8.3–13.7), and 8.7 (4.9–12.4), respectively. Mortality rates associated with 0, 1, 2, 3 and ≥ 4 healthy lifestyles were 20.6 (13.3–27.8), 15.9 (13.3–18.5), 13.1 (10.9–15.2), 12.6 (9.9–15.2) and 9.2 (5.3–13.2) per 1000-person-years, respectively. The use of more healthy lifestyles was associated with lower risks for ASCVD and mortality after multivariable adjustment.

Conclusion: Healthy lifestyles are underutilized among high-risk US adults and may substantially reduce their ASCVD risk.

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1. Introduction

The 2013 American College of Cardiology/American Heart Association (ACC/AHA) Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults recommends consideration of statin therapy for primary prevention of atherosclerotic cardiovascular disease (ASCVD) for individuals aged 40–79 years without a history of diabetes, with low-density-lipoprotein-cholesterol levels between 70 and 189 mg/dL, and a 10-year predicted ASCVD risk $\geq 7.5\%$ [1]. Prior analyses suggest that many more adults are eligible for statin therapy for the primary prevention of ASCVD using the 2013 ACC/AHA guidelines when compared to the 2001 Adults Treatment Panel III guidelines [2,3].

Observational studies and randomized controlled trials (RCTs) demonstrate that lifestyle modification reduces ASCVD risk [4,5]. In the 2013 ACC/AHA cholesterol treatment guideline, lifestyle modification (i.e., maintaining a heart healthy diet and healthy weight, regular exercise, tobacco smoking avoidance) is emphasized both prior to and in conjunction with the use of lipid-lowering medications [1]. A *New England Journal of Medicine* survey found that most physicians favored lifestyle modification before initiating statins when presented with the case of a 52-year old male who jogs frequently but has a 10-year predicted risk of 10.9% [6]. Few studies have assessed the prevalence of healthy lifestyle factors among adults recommended statins for primary prevention of ASCVD by the 2013 ACC/AHA cholesterol treatment guidelines. If high-risk individuals practice few healthy lifestyle factors, then increasing the number of healthy lifestyles may provide a large ASCVD and mortality risk reduction, possibly eliminating the need for statins in some individuals. Based on data from the population-based REasons for Geographic And Racial Differences in Stroke (REGARDS)

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cohort study, we estimated the prevalence of healthy lifestyle factors among candidates for primary prevention of ASCVD with statin therapy due to having a 10-year predicted risk $\geq 7.5\%$ [1]. Additionally, we determined the association of healthy lifestyles, individually and in combination, with incident ASCVD and all-cause mortality.

2. Methods

2.1. Study population

The REGARDS study has been described in detail previously [7]. Briefly, 30,239 adults aged ≥ 45 years were recruited between January 2003 and October 2007 from the 48 contiguous US states and District of Columbia. Residents of the “stroke buckle” (coastal North Carolina, South Carolina, and Georgia) and “stroke belt” (the remainder of North Carolina, South Carolina, and Georgia as well as Alabama, Mississippi, Tennessee, Arkansas and Louisiana) and blacks were oversampled by design. The inclusion criteria applied for the current analyses were chosen to identify candidates for primary prevention of ASCVD with statin therapy due to an estimated 10-year ASCVD risk $\geq 7.5\%$. Therefore, we excluded REGARDS participants aged ≥ 80 years, with a history of ASCVD (coronary heart disease [CHD], revascularization, or stroke), heart failure, atrial fibrillation, diabetes, or end-stage renal disease (ESRD), low-density-lipoprotein-cholesterol < 70 or ≥ 190 mg/dL, or taking statins at baseline (Fig. 1). Additionally, participants missing data on the Pooled Cohort risk equation components or with a 10-year predicted ASCVD risk $< 7.5\%$ were excluded leaving 5709 participants for our analyses [8]. At all participating centers, the Institutional Review Boards governing research in human subjects confirmed that the REGARDS study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. All participants provided written informed consent.

2.2. Data collection

Baseline data were collected through a computer-assisted-telephone-interview, self-administered questionnaires and an in-home

examination. Information on age, race, sex, education, annual household income, co-morbid conditions [i.e., diabetes, atrial fibrillation, history of stroke, CHD or revascularization procedure, ESRD], antihypertensive medication use, cigarette smoking, and physical activity was self-reported during computer-assisted-telephone-interview administered by trained staff. Participants were asked to fast overnight prior to the in-home examination. During the examination, waist circumference and blood pressure were measured, blood and spot urine samples were collected, and an electrocardiogram was performed by trained technicians. Additionally, the names of all prescription and over-the-counter medications taken during the 2 weeks prior to the in-home visit were recorded based on pill bottle review. Following the in-home examination, participants were provided a Block 98 Food-Frequency Questionnaire to be completed and mailed to the REGARDS coordinating center [9].

Low-density-lipoprotein-cholesterol was calculated using the Friedewald equation for participants who fasted (≥ 8 h) prior to their in-home study visit [10]. Non-high-density-lipoprotein-cholesterol was calculated as total cholesterol minus high-density-lipoprotein-cholesterol for participants who did not fast ($n = 713$). High-sensitivity C-reactive protein (hs-CRP) was measured by particle-enhanced immunonephelometry. Elevated hs-CRP was defined as > 3.0 mg/L. The urinary albumin-to-creatinine ratio was calculated. Albuminuria was defined as an albumin-to-creatinine ratio ≥ 30 mg/g. Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation [11]. Reduced eGFR was defined as < 60 mL/min/1.73 m². Diabetes was defined by self-report of a prior diagnosis while not pregnant and the use of insulin or oral hypoglycemic medications, a fasting serum glucose ≥ 126 mg/dL, or a non-fasting serum glucose ≥ 200 mg/dL. Atrial fibrillation was defined by self-report or electrocardiogram evidence. Participants taking digoxin were considered to have heart failure. Baseline history of CHD was defined by a self-reported history of myocardial infarction or coronary revascularization procedure, or electrocardiogram evidence of myocardial infarction.

2.3. Lifestyle factors

Five lifestyle factors were evaluated: waist circumference, physical activity, cigarette smoking, percentage of calories consumed from saturated fat, and adherence to a Mediterranean-style diet. Waist circumference was chosen due to (1) having a stronger association with ASCVD risk than body mass index and (2) evidence that achieving weight reduction goals can improve ASCVD risk factors [12–15]. Waist circumference was measured midway between the lowest rib and the iliac crest while participants were standing. Abdominal obesity was defined by a waist circumference > 102 and > 88 cm for men and women, respectively. Physical activity was assessed using the question “How many times-per-week do you engage in intense physical activity, enough to work up a sweat?” with responses grouped as “none,” “1-to-4,” or “ ≥ 5 ” times. Current smoking was defined as responding “yes” to both of the following two questions: “Have you smoked at least 100 cigarettes in your lifetime?” and “Do you smoke cigarettes now, even occasionally?” Non-smoking was defined by answering “no” to either question. Thus, former and never smokers were categorized as non-smoking. The Food-Frequency Questionnaire was processed with NutritionQuest software. The average amount of daily calories consumed and dietary nutrients intake were estimated for the year before participants’ in-home visits. The percentage of average daily calories consumed from saturated fat was calculated by multiplying the grams of daily saturated fat intake by 9 cal per gram and dividing this product by average daily calories consumed. Low saturated fat intake, $< 7\%$, was defined according to the AHA’s recommended daily intake level for this component of a heart healthy diet [5]. Similar to methods described by Trichopoulos et al., a Mediterranean diet score was created from 14 all-inclusive food groups and nutrients using a monounsaturated-to-saturated-fats-ratio [16]. Quartiles

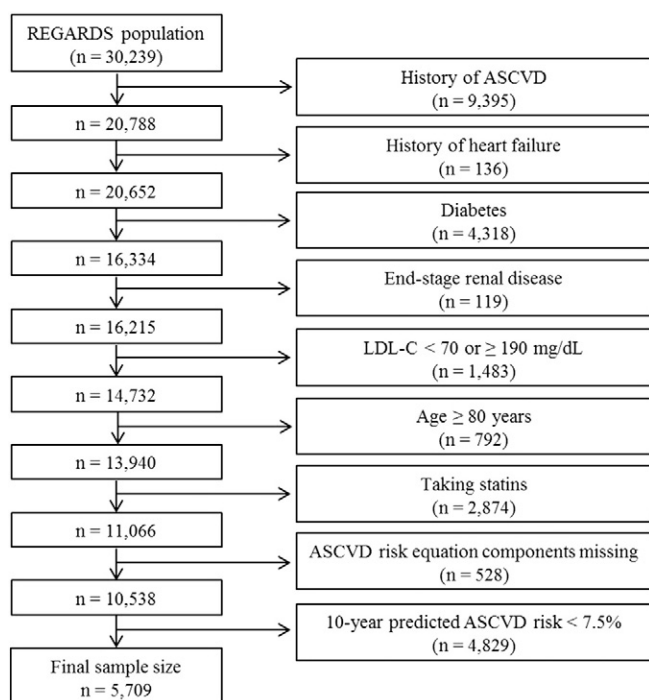


Fig. 1. Exclusion cascade for the analysis of healthy lifestyle factors with atherosclerotic cardiovascular disease and all-cause mortality in the REGARDS study ($n = 5709$). LDL-C: low-density lipoprotein cholesterol, ASCVD: atherosclerotic cardiovascular disease.

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