Use of the Coronary Artery Calcium Score in Discussion of Initiation of Statin Therapy in Primary Prevention

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Abstract

Clinical guidelines for instituting pharmacotherapy for the primary prevention of atherosclerotic cardiovascular disease (ASCVD), specifically lipid management and aspirin, have long been based on absolute risk. However, lipid management in the current era remains challenging to both patients and clinicians in the setting of somewhat discordant recommendations from various organizations. All guidelines endorse the use of statins for primary prevention for those at sufficient absolute risk, and treatment recommendations are generally "risk-based" rather than exclusively targeting specific low-density lipoprotein cholesterol levels. Nonetheless, guidelines differ in relation to the risk threshold for initiation and the intensity of statin treatment. The key concept of the clinician-patient risk discussion introduced in the 2013 American College of Cardiology/American Heart Association cholesterol guidelines is a process that addresses the potential for ASCVD risk reduction with statin treatment, potential for adverse treatment effects, patient preferences, encouragement of heart-healthy lifestyle, and management of other risk factors. However, operationalizing the clinician-patient risk discussion requires effective communication of the most accurate and personalized risk information. In this article, we review our treatment approach for the appropriate use of coronary artery calcium testing in the intermediate-risk patient to guide shared decision making. The decision to initiate or intensify statin therapy may be uncertain across a broad range of estimated 10-year ASCVD risk of 5% to 20%, and coronary artery calcium testing can reclassify risk upward or downward in approximately 50% of this group to inform the risk discussion. We conclude with 2 case-based examples of uncertain risk and uncertain statin therapeutic benefit to illustrate execution of the clinician-patient risk discussion.

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The aim of this article is to review the 2013 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for the assessment of atherosclerotic cardiovascular disease (ASCVD) risk and the selection of patients for primary prevention with statin therapy for ASCVD risk reduction. We discuss the central tenet of the clinician-patient risk discussion, a process that addresses the potential for ASCVD risk reduction with statin treatment, the potential for adverse treatment effects, patient preferences, encouragement of heart-healthy lifestyle, and management of other risk factors. We review our treatment approach for the use of coronary artery calcium (CAC) measurements in selected patients to help facilitate a more informed risk discussion. Because atherosclerotic plaque burden is strongly linked to cardiovascular events, assessment of CAC can help patients and clinicians make decisions about matching intensity of preventive therapy to those at increased risk, while potentially offering more flexible treatment options in patients with low atherosclerotic burden. We conclude with 2 case-based examples of operationalizing the clinician-patient risk discussion in clinical practice.

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BURDEN OF ASCVD AND OPPORTUNITIES FOR PREVENTION

Atherosclerotic cardiovascular disease, including both coronary heart disease (CHD) and stroke, was the cause of approximately 1 in 3 deaths in the United States in

2014,[1] and more than a third of ASCVD deaths occurred among individuals younger than 75 years. Yet, modifiable factors may account for approximately 90% of CHD risk.[2] In their 2020 Strategic Impact Goal statement, the AHA described 7 health metrics (ie, body mass index [BMI; calculated as weight in kilograms divided by height in meters squared], physical activity, diet, smoking, total cholesterol, blood pressure, and blood glucose), collectively known as the Life's Simple 7 criteria, to serve as a marker of ideal cardiovascular health and a framework for decreasing the overall burden of ASCVD.[3]

Intensive risk factor modification and implementation of evidence-based therapies can regress or stabilize existing atherosclerotic plaques[4] and reduce ASCVD outcomes.[5] Some of the most effective interventions for ASCVD risk reduction are lifestyle modifications, which serve as the foundation for all prevention strategies. However, patients with established ASCVD (ie, secondary prevention) and individuals at higher risk for new-onset ASCVD (ie, primary prevention) warrant intensification of preventive efforts with pharmacotherapies (specifically lipid management and aspirin).

2013 ACC/AHA ASCVD RISK ESTIMATOR

For nearly 2 decades, clinical decisions for lipid-lowering pharmacotherapy in primary prevention have been predicated on an initial assessment of global absolute risk. For example, the Adult Treatment Panel III guidelines relied on an estimation of 10-year CHD risk using a version of the Framingham Risk Score.[6] More recently, the 2013 ACC/AHA risk assessment guidelines[7] endorse risk factor screening every 4 to 6 years for those aged 20 to 79 years and application of the race- and sex-specific Pooled Cohort Equations (PCE) in asymptomatic adults aged 40 to 79 years to estimate 10-year risk for a first "hard" ASCVD event (myocardial infarction and stroke).

Estimated ASCVD risk by the PCE is directly linked to the 2013 ACC/AHA cholesterol guidelines,[8] which identified 4 groups of patients that would likely benefit from moderate- to high-intensity statin therapy: (1) those with established clinical ASCVD, (2) those aged 40 to 75 years who have diabetes mellitus, (3) those with low-density lipoprotein cholesterol (LDL-C) levels of 190 mg/dL or higher (to convert to mmol/L, multiply by 0.0259), and (4) those aged 40 to 75 years who have LDL-C levels of 70 to 189 mg/dL and estimated 10-year risk of 7.5% or greater. Initiation of a moderate-intensity statin for those at 5% to 7.5% 10-year risk was also deemed reasonable.

After the release of the 2013 guidelines, however, conflicting reports emerged regarding the accuracy of the ACC/AHA ASCVD risk estimator. Some studies found reasonable calibration in certain populations, particularly those with more social deprivation.[9,10] In contrast, other studies have found overestimation of risk (which could lead to overtreatment among many individuals unlikely to receive net benefit from preventive pharmacotherapies).[11-14] Furthermore, other studies pointed out concern for underestimation of risk (and potential for undertreatment) among individuals with unique risk factors (eg, autoimmune disease) not captured in current risk scoring models.[15] Attempts to incorporate additional information from novel risk factors into existing risk models is limited by understanding the prevalence of those risk factors in specific patient populations.[16]

In essence, these risk calculators work by estimating the average risk in a group of individuals who have similar risk factor profiles, but a given risk score is far more accurate for a population group than it is for any particular individual.[17,18]

CONCORDANCE AND DISCORDANCE IN LIPID GUIDELINES

Adding to the confusion, in 2016, the US Preventive Services Task Force (USPSTF) published their own recommendations for cholesterol management in primary prevention.[19] The USPSTF recommended, with moderate-grade evidence, that adults aged 40 to 75 years who had an estimated 10-year ASCVD risk of 10% or higher (by the PCE) and at least one major risk factor (ie, hypertension, diabetes, dyslipidemia, or smoking) should be offered a low- to moderate-intensity statin, with a weaker endorsement for the use of low- to

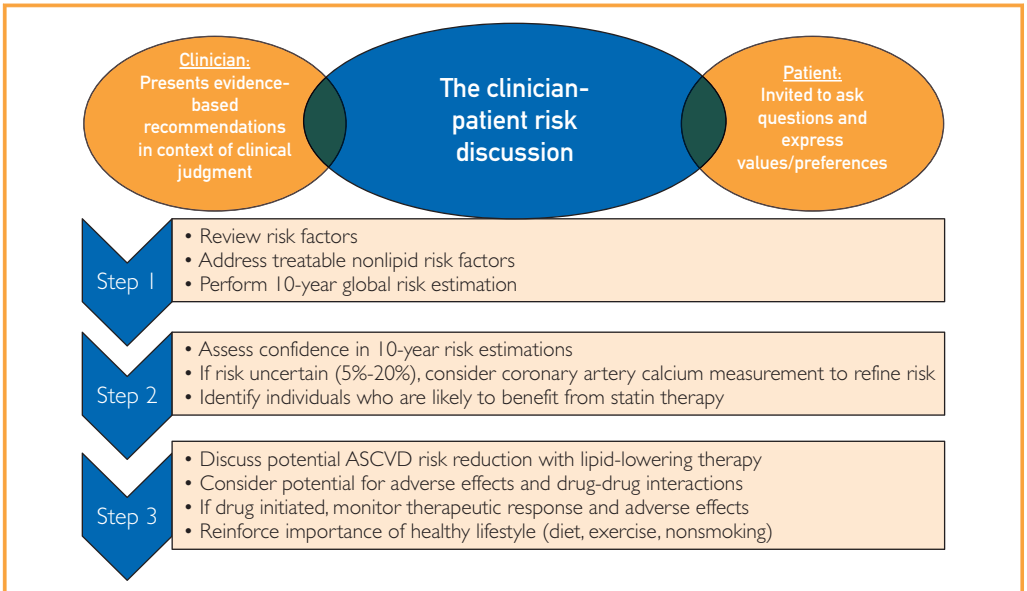

FIGURE 1. Core components of the clinician-patient risk discussion. ASCVD = atherosclerotic cardiovascular disease.

moderate-intensity statins for those with risk between 7.5% and 10%. They found insufficient evidence to make specific recommendations for adults older than 75 years. The US Department of Veterans Affairs also published their own recommendations in 2014,[20] which endorsed moderate-intensity statins for those with a 10-year risk of more than 12% and consideration of moderate-intensity statins for those with a 6% to 12% 10-year risk in the context of shared decision making.

Additionally, in 2014, the National Lipid Association (NLA) also published their recommendations for management of patients with dyslipidemia.[21] A key difference in the NLA statement was the consensus that non—high-density lipoprotein cholesterol (non—HDL-C) levels were a better risk marker and target for therapy than LDL-C levels. In addition, the NLA endorsed specific non—HDL-C and LDL-C targets based on risk categories for low-, moderate-, high-, and very high-risk individuals.[21] The Canadian Cardiovascular Society[22] and European[23,24] guidelines have slightly different risk scores and treatment recommendations as well.

Compared with the Adult Treatment Panel III recommendations, the 2013 ACC/AHA cholesterol guidelines expanded the number of individuals potentially eligible for statins by nearly 13 million.[25] Of these patients, approximately 9.3 million individuals would meet recommendations for statins by ACC/AHA criteria but not by the USPSTF criteria.[26] There may be some downsides of expanded statin eligibility including patient reluctance to take a medication for decades, concerns about possible adverse effects including myalgias[27] and new-onset diabetes,[28] costs (to the individual and society), and long-term treatment of some patients who are unlikely to benefit.

It is important to point out the similarities between the ACC/AHA, USPSTF, Veterans Affairs, and NLA guidelines. Notably, the majority of these guidelines endorse the use of statins for primary prevention of ASCVD for those at sufficient absolute risk, and treatment recommendations are generally risk-based rather than exclusively targeting specific LDL-C levels. Nonetheless, there are clear differences in relation to the risk threshold for statin initiation and the intensity of statin treatment, which understandably may generate confusion for both patients and clinicians.

CLINICIAN-PATIENT RISK DISCUSSION

Perhaps lost among the confusion between the various lipid guidelines, it is important to remember that the 2013 ACC/AHA lipid guidelines had advised a clinician-patient risk discussion before statin initiation.[8] The clinician-patient risk discussion, which requires effective communication of the most accurate and personalized risk information, may be the ideal way to bridge the gap between guidelines. This shared decision-making conversation should address potential for ASCVD risk reduction, potential for adverse effects, patient preferences in terms of their comfort with taking long-term preventive medications, encouragement of heart-healthy lifestyle, and management of other risk factors (Figure 1).[18,29]

The level of uncertainty that people will tolerate about their risk may vary from individual to individual, and this conversation should be part of the clinician-patient risk discussion. Some individuals at 7.5% or higher estimated 10-year risk and their physicians may have some level of uncertainty about their risk but still feel comfortable initiating statin therapy without further testing. A family history of premature ASCVD may be enough for some to guide the decision about statin and aspirin therapy. Conversely, some patients may be reluctant to take a medication for many years or may be concerned about possible adverse effects. A survey found that more than 8% of people were willing to trade as much as 2 years of life to avoid taking daily medication for ASCVD, while roughly 21% would trade between 1 week and 1 year of their lives.[30]

When the decision to treat with statins is uncertain after global risk assessment, additional factors can refine risk estimation and guide decision making. The 2014 NLA guidelines state that additional testing could be considered for some patients at moderate estimated risk to assist with decisions about risk stratification.[21] The 2013 ACC/AHA guidelines also allow for revising risk status upward if one of the following is present: family history of premature ASCVD, high-sensitivity C-reactive protein level of 2.0 mg/L or higher (to convert to nmol/L, multiply by 9.524), abnormal CAC score, or ankle-brachial index less than 0.9.[7] Among these factors, CAC score is now widely considered the superior marker for reclassification of risk.[31-33]

Prior studies have found that across a broad range of estimated 10-year risk of 5% to 20%, risk may be reclassified upward or downward by CAC testing in up to 50% in this group.[12,34]

CORONARY ARTERY CALCIUM TESTING

Refinement of ASCVD Risk Estimation

Coronary artery calcium is measured semiautomatically by noncontrast cardiac computed tomography (CT)[34] and typically quantified by the Agatston score,[35] which factors in the density and area of the calcium. Coronary artery calcium is a useful surrogate measure of total coronary atherosclerotic burden[36] and therefore "arterial age."[37] An elevated CAC score has been found in multiple epidemiological studies to be a robust predictor of future CHD,[38] stroke,[39] and ASCVD[40] events as well as non-CVD events,[41] independent of traditional ASCVD risk factors. The CAC score predicts risk even among patients estimated to be at low risk by global risk estimation.[42,43]

Global estimators of ASCVD risk are heavily weighted toward chronological age, yet "arterial" or "biological" age is not always concordant with chronological age. In addition to the role of CAC in upgrading risk in younger patients when extensive CAC is present, perhaps an equally important potential use of CAC testing may be for downgrading or "derisking" an older adult with a CAC score of zero who might otherwise be recommended for pharmacological therapy based on global risk estimation. A CAC score of zero corresponds to very low future event rates (in the range of ~1% per year) and is a potent negative (favorable) risk marker.[33,34,44] Three recent population-based studies found that among individuals eligible for statin therapy, a CAC score of zero was fairly common and was associated with a very low ASCVD rate of 2 to 5 events per 1000 patient-years.[12,45,46] The presence or absence of CAC can discriminate future ASCVD and mortality risk even among older adults (>70 years).[47-50]

Some clinicians may argue to avoid risk estimation equations altogether and consider

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the eligibility criteria for statin primary prevention clinical trials. However, a recent simulation of data from the Multi-Ethnic Study of Atherosclerosis (MESA) community-based cohort found that even among individuals with an indication for statin therapy based on eligibility criteria for 7 randomized clinical trials of statins for primary prevention, the absence of CAC (CAC score of zero) and the presence of extensive CAC (score >100) could risk stratify individuals into low and high ASCVD risk groups, respectively.[51] Thus, CAC is a useful tool to refine ASCVD risk and inform the clinician-patient risk discussion.

Global risk estimation equations are predicated on the basis of traditional risk factors that are typically measured at a single "snapshot" of time. In contrast, CAC is likely such a superior and potent marker of risk because it measures the disease (ie, coronary atherosclerosis) directly and integrates a lifetime of risk exposure from both measured and unmeasured factors (ie, genetics, environment, traditional and novel risk factors) (Figure 2).

The MESA CHD risk score, published in 2015, was the first to incorporate CAC scores into global risk assessment,[52] with the note that this score predicts 10-year risk for hard CHD, not total ASCVD; however, a MESA ASCVD score (CHD + stroke risk) is under development and should be available soon.

Who to Test?

The Society of Cardiovascular Computed Tomography recently published an expert consensus statement regarding clinical indications for CAC scoring.[34] In general, our treatment approach for CAC,[53] which is concordant with the Society of Cardiovascular Computed Tomography recommendations, is to consider CAC testing in the context of shared decision making among patients aged 45 to 75 years who are free of clinical ASCVD and deemed to be at intermediate risk or uncertain risk as follows:

- Patients with estimated 10-year risk of 5% to 20% in situations in which risk estimation or the decision for statin initiation, statin intensification, or potential other preventive therapies remains uncertain
- Patients with estimated 10-year risk of less than 5% but are suspected to be at elevated ASCVD risk because of a major risk factor not accounted for in the global risk equations such as erectile dysfunction, rheumatologic diseases, or family history of premature CHD
- Patients in whom statin therapy is indicated but who have intolerable adverse effects from statins or reluctance to take statin medication, to guide the need for alternative lipid-lowering strategies.

In general, CAC testing is not warranted in individuals with estimated very high risk (>20%) or very low risk (<5% with no other compelling risk factors), as the CAC score does not meaningfully alter risk estimation in these groups.[12] Although the CAC score does predict risk in the elderly (aged >75 years),[49] there is less data about its use in this age group for guiding statin treatment decisions, but it may be considered in selected cases.

Guiding Treatment Decisions

We present our simplified CAC-based treatment approach in Figure 3. The presence of an elevated CAC score places one into a higher-risk group than was predicted by risk factors and may facilitate a patient's decision

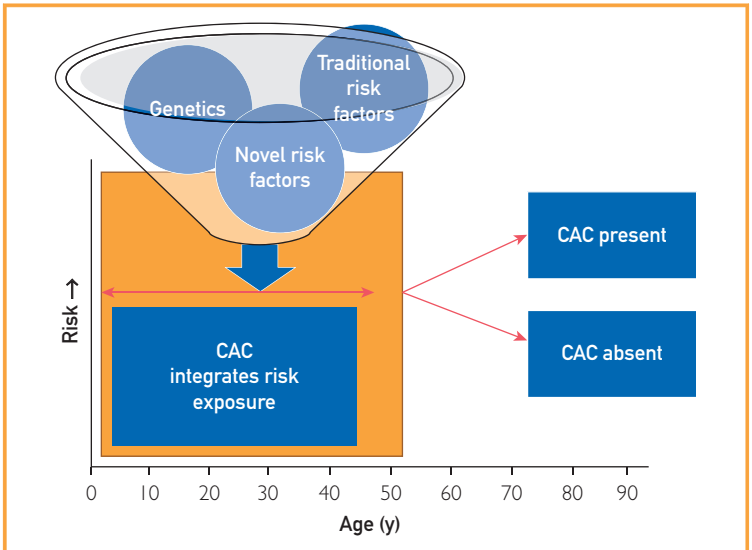

FIGURE 2. The coronary artery calcium (CAC) score integrates lifetime exposure of traditional and nontraditional risk factors for atherosclerotic cardiovascular disease.

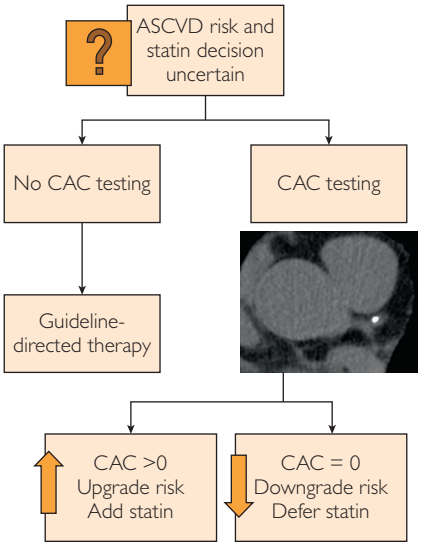

FIGURE 3. Coronary artery calcium (CAC) testing to guide the treatment decisions.

to start (and be adherent to) statin therapy. Conversely, the absence of CAC could meaningfully reclassify a patient downward into a lower-risk group to a level of risk at which the patient may feel comfortable with not starting statin therapy at that time.[12,31-33]

After reclassification of risk, many patients with a CAC score of zero may choose to defer statin therapy. For CAC scores of 1 through 99 or less than the 75th percentile, a moderate-intensity statin could be considered. A moderate- to high-intensity statin could be considered if the CAC is in the 75th or higher percentile or the CAC score is 100 through 299, and a high-intensity statin could be considered for CAC scores greater than 300 in the context of shared decision making with the patient.[34] The NLA guidelines also state that evidence of subclinical disease, including CAC score of 300 or higher or CAC in the 75th or greater percentile for age, sex, and ethnicity would upgrade an individual into a high-risk status.[21]

Risk stratification by CAC could even help guide shared decision making regarding decisions for antihypertensive therapy[54] or aspirin therapy.[55] Further work is needed to determine whether CAC measurement can help facilitate discussion regarding decisions for lipid-lowering therapy in addition to statins to achieve an LDL-C level of less than 70 mg/dL in these patients with very high CAC burden whose risk approaches that of patients eligible for secondary prevention.

Cost-effectiveness and Promotion of Medication Adherence

Cost-effectiveness analyses suggest that among intermediate-risk patients CAC testing is cost-effective for steering treatment toward those with measurable CAC, especially when considering the mild disutility of taking daily preventive medications.[56-58] Furthermore, knowledge of one's CAC score may influence behavioral motivation and medication adherence.[59] Patients with an elevated CAC score are more likely to initiate and continue pharmacological and lifestyle therapies for ASCVD prevention.[59-62]

Warranty Period

Patients may ask if and when their CAC test should be repeated. For an initial score of zero, it may be reasonable to rescan about 5 years after the initial test if the statin treatment decision is still uncertain,[34] although smokers, patients with diabetes, and those with evidence of atherosclerosis in other vascular beds (eg, aorta) have more rapid progression and might be considered for a rescan sooner.[63,64] Patients with an initial CAC score greater than zero (who would be advised to initiate statin therapy) do not require a repeated scan unless the finding of accelerated progression would help inform discussions about whether lipid-lowering therapy should be further intensified.[34] Patients should be counseled that although statin therapy reduces ASCVD events, statins do not decrease (and may even be associated with an increase in) the CAC score.

Test Cost, Radiation, and Limitations

Coronary artery calcium testing by noncontrast CT does not require fasting or intravenous access, takes approximately 10 to 15 minutes of procedure room time, costs $75 to $100 in many parts of the country, and is associated with a modest amount of radiation exposure (~1 mSv, roughly equivalent to that from a bilateral mammogram). One downside is the detection of incidental findings (most commonly noncalcified lung nodules) in about 4% to 8% of patients,[65]

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who may need follow-up CT to document stability; this issue can be reduced by limiting the field of view reconstructed and interpreted. Although CAC presence and severity is a potent marker of ASCVD risk and total atherosclerosis burden, CAC testing cannot directly inform the physician about noncalcified plaque or severity of coronary stenosis. Therefore, it is not recommended for evaluation of patients presenting with chest pain syndromes concerning for ischemic heart disease.

A patient with an elevated CAC score may ask about additional tests. Clinicians should counsel patients that an elevated CAC score in someone without symptoms should not prompt a referral for stress testing or coronary angiography. The EISNER (Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research) study[66] found that randomization to CAC scanning vs no scanning did not increase net downstream medical testing overall, with low-risk patients referred for less follow-up testing and high-risk patients tested more. Furthermore, randomization to CAC scanning was associated with modestly improved risk factor control.

Another caveat with CAC testing is that there is a lack of definitive clinical trial evidence that CAC-based treatment decision making is superior to traditional global risk assessment in reducing ASCVD outcomes. However, it is important to note that there have been no high-quality event-driven randomized clinical trials of any ASCVD risk assessment strategy including the PCE. Of note, a Cochrane review found insufficient evidence that providing ASCVD risk scores to patients can reduce ASCVD events either.[67] Unfortunately, although a CAC-based clinical trial has been proposed,[68] because of the low risk of patients not already qualifying for statin treatment and the cost involved for a large randomized controlled trial, it seems unlikely in the near future that a CAC-based clinical trial will be funded in the United States. In the Netherlands, the ongoing ROBINSCA (Risk or Benefit in Screening for Cardiovascular Diseases) clinical trial of CAC screening vs risk factor screening may offer future insight,[69] but in the meantime, approaches to ASCVD risk assessment may need to rely on the best evidence from observational studies.[68,70]

OPERATIONALIZING THE CLINICIAN-PATIENT RISK DISCUSSION: 2 CASE-BASED EXAMPLES

In this section, we illustrate execution of the clinician-patient risk discussion in 2 cases of uncertain risk and therapeutic benefit for statin primary prevention in clinical practice. In the first case, the patient has an elevated 10-year ASCVD risk largely driven by age, despite favorable levels of modifiable risk factors including normal lipid levels. In the second case, the patient has an elevated estimated 10-year ASCVD risk, largely driven by modifiable nonlipid factors.

Case 1

Mr J is a 65-year-old white man who has been in good health and has no current symptoms. He is a lifetime nonsmoker and enjoys running 4 times a week. His diet is mostly vegetarian, but he will eat salmon twice a week. He has a normal BMI of 23, untreated systolic blood pressure of 118 mm Hg, no diabetes, and no family history of premature ASCVD. Laboratory studies revealed a total cholesterol level of 160 mg/dL(to convert to mmol/L, multiply by 0.0259), HDL-C level of 50 mg/dL (to convert to mmol/L, multiply by 0.0259), triglyceride level of 150 mg/dL (to convert to mmol/L, multiply by 0.0113), and LDL-C level of 80 mg/dL. He saw his physician for consultation regarding his cardiovascular risk. His physician estimated his 10-year ASCVD risk (using the PCE), which was 9.5%. A clinician-patient risk discussion was initiated.

Mr J felt uncomfortable with taking a cholesterol-lowering medication when his total cholesterol is "low," and he was worried about potential of muscle-related problems that might affect his running. In the context of shared decision making, Mr J expressed a desire for more information to help refine his risk, and his physician referred him for CAC testing.

Mr J's 10-year risk exceeds 7.5%; thus, initiation of a moderate- to high-intensity statin was discussed as part of the clinician-patient risk discussion. Given his older age of 65 years, even if all of his risk factors were optimal, his 10-year risk would still reach 9%. Furthermore, in the absence of any other major ASCVD risk factors, he did not meet statin treatment eligibility criteria suggested by the USPSTF. His global risk

estimated by the PCE did not take into account his absence of a family history of premature CHD, normal BMI, healthy diet, and regular physical activity. In this context of a 10-year risk between 5% and 20% and uncertainty of risk, the use of CAC testing would be useful to facilitate the risk discussion.

Mr J's CAC testing revealed a score of zero, which placed him in the <25th or lower percentile for age, sex, and race. Using the MESA CHD risk score (which incorporates both his traditional risk factors and his CAC score), his estimated 10-year risk for CHD events would be only 2%. Mr J decided to defer statin therapy for now and continue to follow his heart-healthy lifestyle.

Several population-based studies have documented how a CAC score of zero could potentially provide information that moves an individual from a risk level at which treatment is generally recommended to a lower risk level at which treatment may be deferred. In the MESA trial, 41% of individuals recommended for any statin therapy had a CAC score of zero with an ASCVD event rate of 5.2 per 1000 person-years, and for those recommended for a moderate-intensity statin treatment, 57% had a CAC score of zero with an ASCVD event rate of only 1.5 per 1000 person-years.[12] Among individuals eligible for statin therapy by ACC/AHA guidelines in the Framingham Heart Study, 33% had a CAC score of zero with a 10-year ASCVD event rate of only 1.6%.[45] Similarly, in the Heinz Nixdorf Recall Study (conducted in Germany), among those for whom statin treatment was indicated per the ACC/AHA guidelines, the coronary event rate ranged from 2.7 per 1000 person-years for those with a CAC score of zero to 9.1 per 1000 person-years for those with a CAC score of 100 of more.[46] Although these ASCVD event rates were not zero among patients with a CAC score of zero (ie, low risk does not equate to no risk), they were below the previous threshold estimated by PCE and may alter a patient's decision to take statins.

Taking into account Mr J's lower estimated ASCVD risk after CAC testing, the disutility of taking a pill every day that he is less likely to benefit from, and his personal preferences, it is reasonable to forgo statin therapy for the next few years in this circumstance. A repeated CAC scan might be considered in about 5 years if the ASCVD risk estimation and the decision for statin therapy is still uncertain.

Case 2

Mrs M is a 45-year-old African American woman with hypertension, which is being treated. She is a current smoker and is sedentary. She has no family history of premature ASCVD. As an office manager and mother of 4 young children, Mrs M reports having a busy life with increased stress levels. Most of her meals are eaten at fast food establishments in between carpooling to her children's various extracurricular activities. She is free of cardiovascular symptoms. Her office blood pressure was 148/92 mm Hg, her BMI was 36, and her blood glucose level was 110 mg/dL (to convert to mmol/L, multiply by 0.0555). Total cholesterol and HDL-C levels were 180 and 60 mg/dL, respectively. Her clinician initiated a conversation with her about her cardiovascular risk. Her estimated 10-year ASCVD risk is 7% (by PCE) and lifetime risk is 50%.

Mrs M is in the intermediate-risk group of 5% to 7.5% short-term (10-year) risk in which a moderate-intensity statin could be considered. However, if she was a nonsmoker and had controlled blood pressure on her antihypertensive therapy (systolic blood pressure of 128 mm Hg), her estimated 10-year risk would be less than 2%. Certainly statin therapy is not the only intervention for aggressive ASCVD risk reduction. Her main modifiable risks at this time are smoking, blood pressure control, weight management, and glucose control. She also has much room for improvement in terms of diet, physical activity, and stress reduction to mitigate her substantial lifetime risk.

Mrs M was also wary of taking additional medications and expressed a desire to work on lifestyle changes first. A CAC test was suggested to refine her risk, given her smoking history, but the patient declined. She was reluctant to take a statin at this time regardless of what her CAC score might be. She expressed motivation at improving her lifestyle. Her antihypertensive regimen was adjusted to achieve better blood pressure control; advice and assistance were given for tobacco cessation and stress management. Activity tracking with a pedometer was recommended, with a goal of more than 10,000 steps a day. She was encouraged to follow a Dietary Approach to Stop Hypertension

(DASH) or Mediterranean-style healthy diet pattern and to track caloric intake through a daily food diary.

Patients might be offered CAC testing to refine their risk and decide to decline; if the test results are not going to change the management decisions for the patient, then this is also part of the shared decision-making conversation. Mrs M currently meets only poor or intermediate metrics for nearly all of the Life Simple 7 criteria and clearly has multiple areas to work on through intensification of lifestyle and pharmacological therapies to strive toward obtainment of ideal cardiovascular health. Coronary artery calcium testing might be offered to her again in the future if her risk remains uncertain.

PUTTING IT ALL TOGETHER: THE ABCDE APPROACH

A comprehensive "ABCDE" approach[71] is one way to provide a consistent and comprehensive organizational method for managing cardiovascular risk and promotion of ideal cardiovascular health,[3] personalized for the individual patient. The very first step of this approach is "A: Assessment of risk" through the PCE and initiating the clinician-patient risk discussion. coronary artery calcium testing can be considered when risk is uncertain after global risk assessment. Further patient discussions regarding "A: Antiplatelet therapy," "B: Blood pressure management," "C: Cholesterol management," "C: Cigarette smoking cessation," "D: Diet," "D: Diabetes prevention or management," and "E: Exercise" directly stem from risk assessment and guideline-directed therapy.

RECOMMENDATIONS

Risk estimation using the PCE is a helpful starting point in the clinician-patient risk discussion for preventive therapy. As part of shared decision making, guidelines support offering CAC testing for advanced risk assessment in a wide variety of circumstances when either the patient or the clinician feel uncertain about whether to initiate (or intensify) lipid-lowering therapy. Personalized risk assessment allows the opportunity to engage in a more sophisticated patient-centered risk discussion during which patient preferences, competing medical risks, polypharmacy, and the disutility of taking medications can be considered. A healthy environment and lifestyle and striving toward meeting ideal cardiovascular health should remain the foundation of all efforts at ASCVD risk reduction.

Abbreviations and Acronyms: **ACC** = American College of Cardiology; **AHA** = American Heart Association; **ASCVD** = atherosclerotic cardiovascular disease; **BMI** = body mass index; **CAC** = coronary artery calcium; **CHD** = coronary heart disease; **CT** = computed tomography; **HDL-C** = high-density lipoprotein cholesterol; **LDL-C** = low-density lipoprotein cholesterol; **MESA** = Multi-Ethnic Study of Atherosclerosis; **NLA** = National Lipid Association; **PCE** = Pooled Cohort risk equations; **USPSTF** = US Preventive Services Task Force

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REFERENCES

1. Benjamin EJ, Blaha MJ, Chiuve SE, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2017 update: a report from the American Heart Association [published corrections appear in *Circulation*. 2017;135(10):e646 and *Circulation*. 2017;136(10):e196]. *Circulation*. 2017;135(10):e146-e603.
2. Yusuf S, Hawken S, Ounpuu S, et al; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. 2004;364(9438):937-952.
3. Lloyd-Jones DM, Hong Y, Labarthe D, et al; American Heart Association Strategic Planning Task Force and Statistics Committee. 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.
4. Robinson JG, Gidding SS. Curing atherosclerosis should be the next major cardiovascular prevention goal. *J Am Coll Cardiol*. 2014;63(25, pt A):2779-2785.
5. Cholesterol Treatment Trialists' (CTT) Collaborators. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of

individual data from 27 randomised trials. *Lancet*. 2012; 380(9841):581-590.
6. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA*. 2001;285(19):2486-2497.
7. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [published correction appears in *Circulation*. 2014;129(25, suppl 2):S74-S75]. *Circulation*. 2014;129(25, suppl 2):S49-S73.
8. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [published corrections appear in *Circulation*. 2014;129(25, suppl 2):S46–S48 and *Circulation*. 2015;132(25):e396]. *Circulation*. 2014;129(25, suppl 2):S1-S45.
9. Colantonio LD, Richman JS, Carson AP, et al. Performance of the atherosclerotic cardiovascular disease Pooled Cohort risk equations by social deprivation status. *J Am Heart Assoc*. 2017;6(3):e005676.
10. Muntner P, Colantonio LD, Cushman M, et al. Validation of the atherosclerotic cardiovascular disease Pooled Cohort risk equations. *JAMA*. 2014;311(14):1406-1415.
11. DeFilippis AP, Young R, Carrubba CJ, et al. An analysis of calibration and discrimination among multiple cardiovascular risk scores in a modern multiethnic cohort. *Ann Intern Med*. 2015; 162(4):266-275.
12. Nasir K, Bittencourt MS, Blaha MJ, et al. Implications of coronary artery calcium testing among statin candidates according to American College of Cardiology/American Heart Association cholesterol management guidelines: MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol*. 2015;66(15): 1657-1668.
13. Emdin CA, Khera AV, Natarajan P, et al. Evaluation of the Pooled Cohort Equations for prediction of cardiovascular risk in a contemporary prospective cohort. *Am J Cardiol*. 2017; 119(6):881-885.
14. Rana JS, Tabada GH, Solomon MD, et al. Accuracy of the atherosclerotic cardiovascular risk equation in a large contemporary, multiethnic population. *J Am Coll Cardiol*. 2016;67(18): 2118-2130.
15. Amin NP, Martin SS, Blaha MJ, Nasir K, Blumenthal RS, Michos ED. Headed in the right direction but at risk for miscalculation: a critical appraisal of the 2013 ACC/AHA risk assessment guidelines. *J Am Coll Cardiol*. 2014;63(25, pt A):2789-2794.
16. Kooter AJ, Kostense PJ, Groenewold J, Thijs A, Sattar N, Smulders YM. Integrating information from novel risk factors with calculated risks: the critical impact of risk factor prevalence. *Circulation*. 2011;124(6):741-745.
17. McEvoy JW, Diamond GA, Detrano RC, et al. Risk and the physics of clinical prediction. *Am J Cardiol*. 2014;113(8): 1429-1435.
18. Pender A, Lloyd-Jones DM, Stone NJ, Greenland P. Refining statin prescribing in lower-risk individuals: informing risk/benefit decisions. *J Am Coll Cardiol*. 2016;68(15):1690-1697.
19. US Preventive Services Taskforce. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. *JAMA*. 2016; 316(19):1997-2007.
20. Downs JR, O'Malley PG. Management of dyslipidemia for cardiovascular disease risk reduction: synopsis of the 2014 U.S. Department of Veterans Affairs and U.S. Department of Defense clinical practice guideline. *Ann Intern Med*. 2015;163(4): 291-297.
21. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 1-executive summary. *J Clin Lipidol*. 2014; 8(5):473-488.
22. Anderson TJ, Grégoire J, Hegele RA, et al. 2012 Update of the Canadian Cardiovascular Society guidelines for the diagnosis and treatment of dyslipidemia for the prevention of cardiovascular disease in the adult. *Can J Cardiol*. 2013; 29(2):151-167.
23. Catapano AL, Graham I, De Backer G, et al. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias [published correction appears in *Eur Heart J*, April 24, 2017: https://doi.org/10.1093/eurheartj/ehx180]. *Eur Heart J*. 2016;37(39): 2999-3058.
24. JBS3 Board. Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3). *Heart*. 2014; 100(suppl 2):ii1-ii67.
25. Pencina MJ, Navar-Boggan AM, D'Agostino RB Sr, et al. Application of new cholesterol guidelines to a population-based sample. *N Engl J Med*. 2014;370(15):1422-1431.
26. Pagidipati NJ, Navar AM, Mulder H, Sniderman AD, Peterson ED, Pencina MJ. Comparison of recommended eligibility for primary prevention statin therapy based on the US Preventive Services Task Force recommendations vs the ACC/AHA guidelines. *JAMA*. 2017;317(15):1563-1567.
27. Fernandez G, Spatz ES, Jablecki C, Phillips PS. Statin myopathy: a common dilemma not reflected in clinical trials. *Cleve Clin J Med*. 2011;78(6):393-403.
28. Sattar N, Preiss D, Murray HM, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. *Lancet*. 2010;375(9716):735-742.
29. Martin SS, Sperling LS, Blaha MJ, et al. Clinician-patient risk discussion for atherosclerotic cardiovascular disease prevention: importance to implementation of the 2013 ACC/AHA guidelines. *J Am Coll Cardiol*. 2015;65(13):1361-1368.
30. Hutchins R, Viera AJ, Sheridan SL, Pignone MP. Quantifying the utility of taking pills for cardiovascular prevention. *Circ Cardiovasc Qual Outcomes*. 2015;8(2):155-163.
31. Yeboah J, Young R, McClelland RL, et al. Utility of nontraditional risk markers in atherosclerotic cardiovascular disease risk assessment. *J Am Coll Cardiol*. 2016;67(2):139-147.
32. Yeboah J, McClelland RL, Polonsky TS, et al. Comparison of novel risk markers for improvement in cardiovascular risk assessment in intermediate-risk individuals. *JAMA*. 2012; 308(8):788-795.
33. Blaha MJ, Cainzos-Achirica M, Greenland P, et al. Role of coronary artery calcium score of zero and other negative risk markers for cardiovascular disease: the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation*. 2016;133(9):849-858.
34. Hecht H, Blaha MJ, Berman DS, et al. Clinical indications for coronary artery calcium scoring in asymptomatic patients: expert consensus statement from the Society of Cardiovascular Computed Tomography. *J Cardiovasc Comput Tomogr*. 2017; 11(2):157-168.
35. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol*. 1990;15(4):827-832.
36. Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area: a histopathologic correlative study. *Circulation*. 1995; 92(8):2157-2162.
37. McClelland RL, Nasir K, Budoff M, Blumenthal RS, Kronmal RA. Arterial age as a function of coronary artery calcium (from the Multi-Ethnic Study of Atherosclerosis [MESA]). *Am J Cardiol*. 2009;103(1):59-63.
38. Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med*. 2008;358(13):1336-1345.

39. Gibson AO, Blaha MJ, Arnan MK, et al. Coronary artery calcium and incident cerebrovascular events in an asymptomatic cohort: the MESA Study. *J Am Coll Cardiol Img*. 2014;7(11):1108-1115.
40. Blaha MJ, Budoff MJ, DeFilippis AP, et al. Associations between C-reactive protein, coronary artery calcium, and cardiovascular events: implications for the JUPITER population from MESA, a population-based cohort study. *Lancet*. 2011;378(9792):684-692.
41. Handy CE, Desai CS, Dardari ZA, et al. The association of coronary artery calcium with noncardiovascular disease: the Multi-Ethnic Study of Atherosclerosis. *J Am Coll Cardiol Img*. 2016;9(5):568-576.
42. Lakoski SG, Greenland P, Wong ND, et al. Coronary artery calcium scores and risk for cardiovascular events in women classified as "low risk" based on Framingham risk score: the Multi-Ethnic Study of Atherosclerosis (MESA). *Arch Intern Med*. 2007;167(22):2437-2442.
43. Kelkar AA, Schultz WM, Khosa F, et al. Long-term prognosis after coronary artery calcium scoring among low-intermediate risk women and men. *Circ Cardiovasc Imaging*. 2016;9(4):e003742.
44. Valenti V, Ó Hartaigh B, Heo R, et al. A 15-year warranty period for asymptomatic individuals without coronary artery calcium: a prospective follow-up of 9,715 individuals. *J Am Coll Cardiol Img*. 2015;8(8):900-909.
45. Pursnani A, Massaro JM, D'Agostino RB Sr, O'Donnell CJ, Hoffmann U. Guideline-based statin eligibility, coronary artery calcification, and cardiovascular events. *JAMA*. 2015;314(2):134-141.
46. Mahabadi AA, Möhlenkamp S, Lehmann N, et al; Heinz Nixdorf Recall Study Investigators. CAC score improves coronary and CV risk assessment above statin indication by ESC and AHA/ACC primary prevention guidelines. *J Am Coll Cardiol Img*. 2017;10(2):143-153.
47. Elias-Smale SE, Proença RV, Koller MT, et al. Coronary calcium score improves classification of coronary heart disease risk in the elderly: the Rotterdam study. *J Am Coll Cardiol*. 2010;56(17):1407-1414.
48. Mortensen MB, Fuster V, Muntendam P, et al. A simple disease-guided approach to personalize ACC/AHA-recommended statin allocation in elderly people: the BioImage Study. *J Am Coll Cardiol*. 2016;68(9):881-891.
49. Tota-Maharaj R, Blaha MJ, McEvoy JW, et al. Coronary artery calcium for the prediction of mortality in young adults <45 years old and elderly adults >75 years old. *Eur Heart J*. 2012;33(23):2955-2962.
50. Yano Y, O'Donnell CJ, Kuller L, et al. Association of coronary artery calcium score vs age with cardiovascular risk in older adults: an analysis of pooled population-based studies. *JAMA Cardiol*. 2017;2(9):986-994.
51. Mortensen MB, Falk E, Li D, et al. Statin trials, cardiovascular events, and coronary artery calcification: implications for a trial-based approach to statin therapy in MESA [published online ahead of print June 9, 2017]. *JACC Cardiovasc Imaging*.
52. McClelland RL, Jorgensen NW, Budoff M, et al. 10-Year coronary heart disease risk prediction using coronary artery calcium and traditional risk factors: derivation in the MESA (Multi-Ethnic Study of Atherosclerosis) with validation in the HNR (Heinz Nixdorf Recall) Study and the DHS (Dallas Heart Study). *J Am Coll Cardiol*. 2015;66(15):1643-1653.
53. Michos ED, Blumenthal RS, Mathews LM. My approach to using coronary artery calcium scoring in primary prevention of atherosclerotic cardiovascular disease. *Trends Cardiovasc Med*. 2016;26(2):205-206.
54. McEvoy JW, Martin SS, Dardari ZA, et al. Coronary artery calcium to guide a personalized risk-based approach to initiation and intensification of antihypertensive therapy. *Circulation*. 2017;135(2):153-165.
55. Miedema MD, Duprez DA, Misialek JR, et al. Use of coronary artery calcium testing to guide aspirin utilization for primary prevention: estimates from the Multi-Ethnic Study of Atherosclerosis. *Circ Cardiovasc Qual Outcomes*. 2014;7(3):453-460.
56. Pletcher MJ, Pignone M, Earnshaw S, et al. Using the coronary artery calcium score to guide statin therapy: a cost-effectiveness analysis. *Circ Cardiovasc Qual Outcomes*. 2014;7(2):276-284.
57. Roberts ET, Horne A, Martin SS, et al. Cost-effectiveness of coronary artery calcium testing for coronary heart and cardiovascular disease risk prediction to guide statin allocation: the Multi-Ethnic Study of Atherosclerosis (MESA). *PLoS One*. 2015;10(3):e0116377.
58. Hong JC, Blankstein R, Shaw LJ, et al. Implications of coronary artery calcium testing for treatment decisions among statin candidates according to the ACC/AHA cholesterol management guidelines: a cost-effectiveness analysis. *JACC Cardiovasc Imaging*. 2017;10(8):938-952.
59. Mamudu HM, Paul TK, Veeranki SP, Budoff M. The effects of coronary artery calcium screening on behavioral modification, risk perception, and medication adherence among asymptomatic adults: a systematic review. *Atherosclerosis*. 2014;236(2):338-350.
60. Nasir K, McClelland RL, Blumenthal RS, et al. Coronary artery calcium in relation to initiation and continuation of cardiovascular preventive medications: the Multi-Ethnic Study of Atherosclerosis (MESA). *Circ Cardiovasc Qual Outcomes*. 2010;3(3):228-235.
61. Taylor AJ, Bindeman J, Feuerstein I, et al. Community-based provision of statin and aspirin after the detection of coronary artery calcium within a community-based screening cohort. *J Am Coll Cardiol*. 2008;51(14):1337-1341.
62. Gupta A, Lau E, Varshney R, et al. The identification of calcified coronary plaque is associated with initiation and continuation of pharmacological and lifestyle preventive therapies: a systematic review and meta-analysis. *JACC Cardiovasc Imaging*. 2017;10(8):833-842.
63. Gassett AJ, Sheppard L, McClelland RL, et al. Risk factors for long-term coronary artery calcium progression in the Multi-Ethnic Study of Atherosclerosis. *J Am Heart Assoc*. 2015;4(8):e001726.
64. Al Rifai M, Cainzos-Achirica M, Blaha MJ. Establishing the warranty of a coronary artery calcium score of zero. *Atherosclerosis*. 2015;238(1):1-3.
65. Horton KM, Post WS, Blumenthal RS, Fishman EK. Prevalence of significant noncardiac findings on electron-beam computed tomography coronary artery calcium screening examinations. *Circulation*. 2002;106(5):532-534.
66. Rozanski A, Gransar H, Shaw LJ, et al. Impact of coronary artery calcium scanning on coronary risk factors and downstream testing: the EISNER (Early Identification of Subclinical Atherosclerosis by Noninvasive Imaging Research) prospective randomized trial. *J Am Coll Cardiol*. 2011;57(15):1622-1632.
67. Karmali KN, Persell SD, Perel P, Lloyd-Jones DM, Berendsen MA, Huffman MD. Risk scoring for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev*. 2017;3:CD006887.
68. McEvoy JW, Martin SS, Blaha MJ, et al. The case for and against a coronary artery calcium trial: means, motive, and opportunity. *JACC Cardiovasc Imaging*. 2016;9(8):994-1002.
69. Vonder M, van der Aalst CM, Vliegenthart R, et al. Coronary artery calcium imaging in the ROBINSCA trial: rationale, design, and technical background [published online ahead of print August 23, 2017]. *Acad Radiol*.
70. McEvoy JW, Blaha MJ. Coronary artery calcium testing: exploring the need for a randomized trial [editorial]. *Circ Cardiovasc Imaging*. 2014;7(4):578-580.
71. Kohli P, Whelton SP, Hsu S, et al. Clinician's guide to the updated ABCs of cardiovascular disease prevention. *J Am Heart Assoc*. 2014;3(5):e001098.