

Cost-effectiveness of Contemporary Statin Use Guidelines With or Without Coronary Artery Calcium Assessment in African American Individuals

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IMPORTANCE Clinical and economic consequences of statin treatment guidelines supplemented by targeted coronary artery calcium (CAC) assessment have not been evaluated in African American individuals, who are at increased risk for atherosclerotic cardiovascular disease and less likely than non-African American individuals to receive statin therapy.

OBJECTIVE To evaluate the cost-effectiveness of the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guideline without a recommendation for CAC assessment vs the 2018 ACC/AHA guideline recommendation for use of a non-O CAC score measured on one occasion to target generic-formulation, moderate-intensity statin treatment in African American individuals at risk for atherosclerotic cardiovascular disease.

DESIGN, SETTING, AND PARTICIPANTS A microsimulation model was designed to estimate life expectancy, quality of life, costs, and health outcomes over a lifetime horizon. African American-specific data from 472 participants in the Jackson Heart Study (JHS) at intermediate risk for atherosclerotic cardiovascular disease and other US population-specific data on individuals from published sources were used. Data analysis was conducted from November 11, 2018, to November 1, 2019.

MAIN OUTCOMES AND MEASURES Lifetime costs and quality-adjusted life-years (QALYs), discounted at 3% annually.

RESULTS In a model-based economic evaluation informed in part by follow-up data, the analysis was focused on 472 individuals in the JHS at intermediate risk for atherosclerotic cardiovascular disease; mean (SD) age was 63 (6.7) years. The sample included 243 women (51.5%) and 229 men (48.5%). Of these, 178 of 304 participants (58.6%) who underwent CAC assessment had a non-O CAC score. In the base-case scenario, implementation of 2013 ACC/AHA guidelines without CAC assessment provided a greater quality-adjusted life expectancy (0.0027 QALY) at a higher cost (\$428.97) compared with the 2018 ACC/AHA guideline strategy with CAC assessment, yielding an incremental cost-effectiveness ratio of \$158 325/QALY, which is considered to represent low-value care by the ACC/AHA definition. The 2018 ACC/AHA guideline strategy with CAC assessment provided greater quality-adjusted life expectancy at a lower cost compared with the 2013 ACC/AHA guidelines without CAC assessment when there was a strong patient preference to avoid use of daily medication therapy. In probability sensitivity analyses, the 2018 ACC/AHA guideline strategy with CAC assessment was cost-effective compared with the 2013 ACC/AHA guidelines without CAC assessment in 76% of simulations at a willingness-to-pay value of \$100 000/QALY when there was a preference to lose 2 weeks of perfect health to avoid 1 decade of daily therapy.

CONCLUSIONS AND RELEVANCE A CAC assessment-guided strategy for statin therapy appears to be cost-effective compared with initiating statin therapy in all African American individuals at intermediate risk for atherosclerotic cardiovascular disease and may provide greater quality-adjusted life expectancy at a lower cost than a non-CAC assessment-guided strategy when there is a strong patient preference to avoid the need for daily medication. Coronary artery calcium testing may play a role in shared decision-making regarding statin use.

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African American individuals have a greater incidence of atherosclerotic cardiovascular disease (ASCVD) compared with white individuals¹ yet are less likely to receive guideline-recommended statin therapy.² Beliefs regarding statin safety and effectiveness,² along with reports raising concerns about statin overtreatment owing to risk overestimation in African American and white individuals with predicted 10-year ASCVD risk of 7.5% or higher,³ may result in reluctance of patients to adhere to statin therapy. To this end, the 2018 American College of Cardiology/American Heart Association (ACC/AHA) guidelines⁴ recommend consideration of a non-0 coronary artery calcium (CAC) score to guide statin therapy for primary ASCVD prevention in adults with an intermediate risk for ASCVD and no other risk factors that automatically lead to statin therapy indication (eg, diabetes) (Figure 1).

The presence of CAC shown on computed tomographic (CT) scanning is used to more appropriately classify high- and low-risk individuals in guidelines for treatment compared with guideline recommendations that do not include CAC measurement,⁵⁻⁷ and patients' knowledge of the presence of CAC may improve adherence to statin therapy.⁸ Previous studies have suggested that CAC assessment may be cost-effective compared with assessments included in older guideline recommendations,⁹ particularly when use of daily statin therapy substantially affects quality of life (QOL).^{10,11} However, it is not known whether incorporation of CAC measurement in guideline recommendations is cost-effective among African American individuals, whose statin use patterns and disease epidemiologic factors differ from those of white Americans.

In this study, we aimed to evaluate the cost-effectiveness of the ACC/AHA 2013 guidelines, which do not make a strong recommendation for CAC assessment,¹² vs the 2018 guidelines, which recommend CAC assessment using a non-0 CAC score in African American individuals at intermediate risk for ASCVD, prevalence and outcome data from the Jackson Heart Study (JHS). The JHS is a community-based, prospective study designed to identify risk factors for ASCVD and outcomes among African American individuals.^{13,14}

Methods

Data Sources and Study Population

Cost data, clinical event rates, probabilities, and QOL (utility) weights were obtained from peer-reviewed literature^{1,11,15-29} and from individual data collected in the JHS^{13,14} (Table 1). Data analysis for the present study was conducted from November 11, 2018, to November 1, 2019. The institutional review boards of Jackson State University, University of Mississippi Medical Center, and Tougaloo College approved the JHS and Massachusetts General Hospital approved the present analysis of data from JHS, and all participants provided written informed consent. Patients in the JHS received financial compensation. This study followed the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guideline.

Key Points

Question What is the cost-effectiveness of statin therapy guidelines with and without use of coronary artery calcium assessment in African American individuals at intermediate risk for atherosclerotic cardiovascular disease?

Findings In a model-based economic evaluation informed in part by follow-up data from 472 individuals, use of the 2018 American College of Cardiology/American Heart Association guideline strategy with coronary artery calcium assessment appeared to be cost-effective in most cases. The 2013 guidelines, which do not include coronary artery calcium assessment, provided a greater quality-adjusted life expectancy at a higher cost (\$428.97) compared with the 2018 guideline strategy; results appeared to be sensitive to the patient's preference to avoid use of daily medication therapy.

Meaning The results of this study suggest that the 2018 American College of Cardiology/American Heart Association statin allocation guidelines with coronary artery calcium assessment appear to be cost-effective for the primary prevention of atherosclerotic cardiovascular disease in African American individuals.

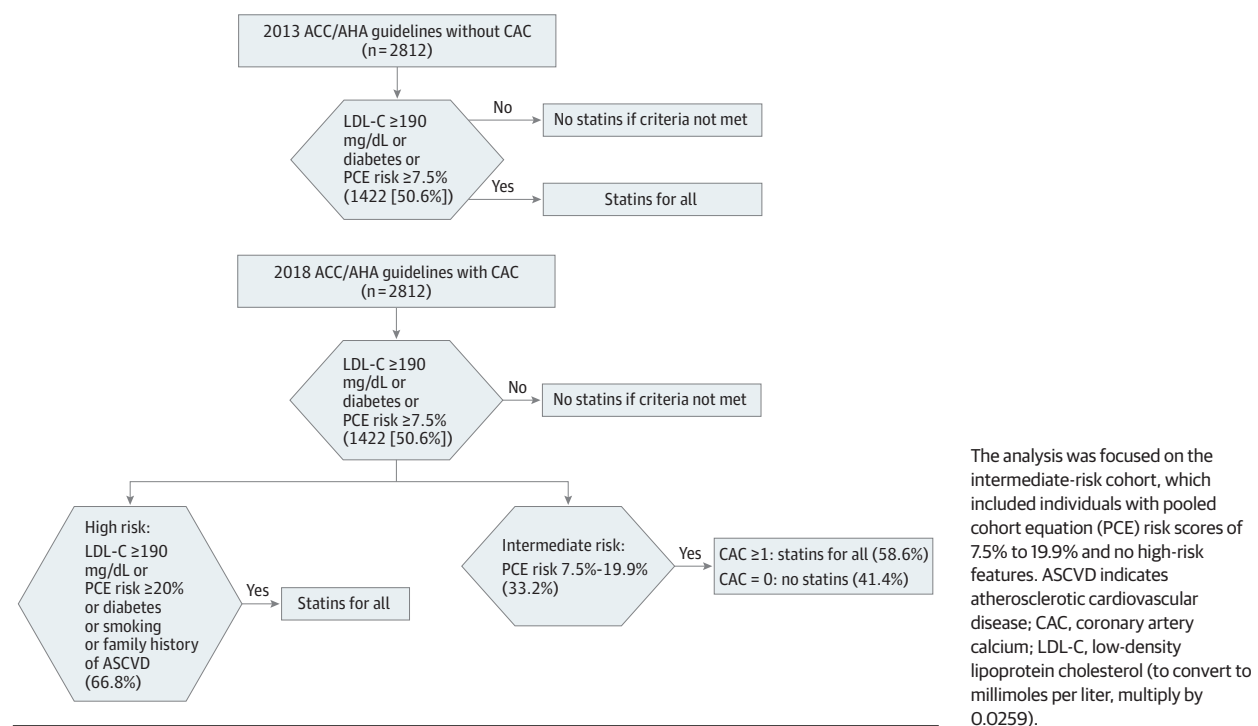
We determined the proportion of intermediate-risk individuals eligible for statin therapy, prevalence of non-0 CAC scores, and estimated incident ASCVD from a subpopulation of the JHS. For this study, we included 2812 participants aged 40 to 75 years without prevalent ASCVD who were not receiving statin treatment at the beginning of the JHS enrollment and had full data available on variables used to determine statin eligibility as described in prior work.³⁰ Statin eligibility was determined from data assessed at the baseline study visit (2000-2004). The CAC score measurement occurred at visit 2 (2005-2008). We assumed that a 0 CAC score at visit 2 implied a 0 CAC score at the baseline visit and a non-0 CAC score at visit 2 implied a non-0 CAC score at the baseline visit, as in prior work.³⁰

We matched the JHS population by age and sex to African American individuals from the 2009-2015 National Health and Nutrition Examination Survey³¹ to ensure a nationally representative sample of the US African American population. We then combined the weighted National Health and Nutrition Examination Survey population with 2018 US Census data³² to extrapolate per-person results to 7 272 372 intermediate-risk African American individuals aged 40 to 75 years based on 2018 US Census national estimates.

Statistical Analysis

Incident ASCVD in the JHS, defined as a composite outcome of incident myocardial infarction (MI), ischemic stroke, or fatal coronary heart disease event consistent with outcomes assessed by the pooled cohort equations,³³ was assessed at a median 10-year (25th-75th percentile, 9.1-10.7 years) follow-up. Given the relatively small number of patients with strokes ($n = 63$) and MIs ($n = 60$) in the JHS cohort, we combined MIs and strokes to allow for reliable estimates of event rates. We constructed age-, sex-, and CAC score-adjusted Cox proportional hazards regression models to estimate hazard ratios for ASCVD in participants with available CAC data ($n = 1691$). We

Figure 1. Schematic Representation of Differences Between 2013 and 2018 American College of Cardiology/American Heart Association (ACC/AHA) Class Guideline Recommendations



subsequently estimated a baseline annualized event rate for incident ASCVD using generalized linear models with a Poisson distribution and log link function, while assuming rate ratios of age, sex, and CAC presence to be equal to the hazard ratios. We performed multiple imputations for CAC presence as implemented in R, using the MICE package with 38 imputations for 38% missing CAC data.³⁴ We limited our analyses of the JHS data to individuals at intermediate ASCVD risk without diabetes to match the relevant model population. The hazard ratios and baseline annual rate, together with their SEs, were entered into the model to specify parametric distributions for ASCVD event rates in probabilistic sensitivity analyses. Statistical analyses were performed using SAS, version 9.4 (SAS Institute Inc) and R, version 3.6.1 (R Project for Statistical Computing). Findings were considered significant at $P < .05$.

We developed a microsimulation model using TreeAge Pro 2017 (TreeAge Software) to simulate the clinical and economic outcomes of 2 strategies based on the 2013 ACC/AHA guidelines without CAC assessment and the 2018 ACC/AHA guideline recommendations with a one-time CAC assessment as a rule-out strategy. The major difference in the strategies was whether statin therapy was allocated to individuals at intermediate risk without diabetes who had an ASCVD risk score of 7.5% to 19.9% and a low-density lipoprotein cholesterol level less than 190 mg/dL (to convert to millimoles per liter, multiply by 0.0259). We focused our analysis on this intermediate-risk group and did not include patients at high risk for ASCVD or those who were ineligible for statin therapy. The following 2 strategies were considered (Figure 1):

1. Based on published guideline recommendations without CAC assessment from the 2013 ACC/AHA¹² that suggest treatment with statins for individuals aged 40 to 75 years without diabetes, low-density lipoprotein cholesterol level of 70 to 189 mg/dL, and estimated 10-year ASCVD risk greater than or equal to 7.5% calculated by the pooled cohort equations risk score estimator.³³
2. Based on published guideline recommendations including CAC assessment from the 2018 ACC/AHA⁴ that suggest treatment with statins for individuals aged 40 to 75 years without diabetes, low-density lipoprotein cholesterol level of 70 to 189 mg/dL, estimated 10-year ASCVD risk of 7.5% to 19.9%, and a non-0 CAC score.

Simulation Model

The simulation model estimated life expectancy, QOL, health outcomes, and costs over the remaining lifetime of each individual. In every yearly model cycle, each simulated individual faced an age-, sex-, and CAC-specific risk of incident ASCVD based on our analyses of the JHS data. These analyses were based on the 10-year follow-up period in the JHS, so, to extrapolate these risks for each simulated individual, we updated baseline age used in the ASCVD risk function every 10 years in the model and used the updated baseline age to calculate subsequent annual ASCVD risks. We estimated ASCVD case fatality from 1-year mortality rates of MI reported for African American individuals.¹ The risk of death in the first year after an ASCVD event was assumed to be 14% for men and 9% for women younger than 65 years. For those aged 65 years or

Table 1. Microsimulation Model Data on Statin Treatment Strategies Among Individuals Aged 40 to 75 Years Without Prevalent ASCVD

Parameter	Base-case value	Distribution	Source
Costs, 2017 US \$			
Cost of CT scan	183	No distribution	Medicare Physician Fee Schedule, ²⁵ 2017
Annual statin cost	84	No distribution	Red Book, ²⁹ 2017
Cost of annual follow-up post ASCVD	3917 (2611-6528)	γ	Lee et al, ²⁷ 2010
Medical costs for first-year nonfatal ASCVD events ^a	49 348	γ	O'Sullivan et al, ²⁴ 2011
Medical costs for fatal ASCVD event ^a	16 760	γ	O'Sullivan et al, ²⁴ 2011
Cost of mild statin adverse event	215 (196-326)	γ	Lee et al, ²⁷ 2010
Cost of major statin adverse event	8486 (6920-10 314)	γ	Lee et al, ²⁷ 2010
Annual diabetes cost ^a	4729	γ	Pandya et al, ²² 2015
Non-CVD health care cost	Age- and sex-specific table		Dieleman et al, ²³ 2016
Quality of life (utility)			
Asymptomatic individual	1		
Post-ASCVD event ^a	0.773	β	Sullivan and Ghushchyan, ²⁶ 2006
While asymptomatic and receiving daily statin therapy	0.996 (0.991-1.000)	β	Pletcher et al, ¹¹ 2014; Hutchins et al, ²⁸ 2015
Penalty of mild statin adverse event	-0.0055	No distribution	Lee et al, ²⁷ 2010
Penalty of major statin adverse event	-0.0383	No distribution	Lee et al, ²⁷ 2010
Events from literature			
Treatment outcome of statins, RR of incident ASCVD, statins vs placebo (95% CI)	0.79 (0.77-0.81)	Log-normal	Baigent, ¹⁸ 2005
Probability of first-year ASCVD related mortality after CHD event	Men <65 y, 14%; men >65 y, 25%; women <65 y, 9%; women >65 y, 30%	β	Mozaffarian et al, ¹ 2015
Mortality after ASCVD event, HR (95% CI)	1.90 (1.60-2.40)	Log-normal	Hooi et al, ¹⁷ 2004
Non-ASCVD death	Age- and sex-specific table		United States Life Tables ¹⁵ 2017; Global Burden of Disease Results Tool, ¹⁶ 2012
Probability of mild adverse event with statin, mean % ^a	4.7	β	Zhang et al, ¹⁹ 2013
Probability of major adverse event with statin, mean % ^a	0.006	β	Zhang et al, ¹⁹ 2013
Probability that major adverse event from statin is fatal, mean % ^a	0.09	β	Alsheikh-Ali et al, ²⁰ 2005
Annual odds for incident diabetes	0.017	No distribution	Ridker et al, ²¹ 2012
Diabetes, OR (95% CI)	1.28 (1.07-1.54)	Log-normal	Ridker et al, ²¹ 2012
Parameters from Jackson Heart Study			
Prevalence of non-0 CAC score in intermediate-risk individuals	58.6%	β	Jackson Heart Study
Baseline annualized event rate of ASCVD with CAC score of 0, mean per person-year (95% CI)	0.000057 (0.000047-0.000068)	Log-normal	Jackson Heart Study
ASCVD with non-0 CAC score vs 0 CAC, HR (95% CI)	2.58 (1.35-4.92)	Log-normal	Jackson Heart Study

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; CHD, coronary heart disease; CT, computed tomography; CVD, cardiovascular disease; HR, hazard ratio; OR, odds ratio; RR, relative risk.

^a A base-case value of ±15% was used to create upper and lower bounds because 95% CIs were not available from source data.

older, the first-year risk of death from ASCVD was estimated at 25% for men and 30% for women. By comparison, the risk of death in the first year after an ASCVD event in JHS was 23%. Cause of death was not classified in JHS; therefore, we used the published case fatality rate from the literature but performed a sensitivity analysis using JHS data. Data on death from causes other than ASCVD were derived from age- and sex-specific US life tables.^{15,16} The excess risk of death following 1 year from an ASCVD event was estimated using a hazard ratio for all-cause mortality in individuals with ASCVD obtained from the literature.¹⁷ Probabilities of clinical events, including ASCVD events, non-ASCVD-associated death, ASCVD-associated death, mild (myalgias or myopathy) and major (rhabdomyolysis) statin-associated adverse events, and fatal statin-associated adverse events, determined the transition to other

health states during each annual cycle. Health states included (1) well with statin, (2) well without statin, (3) post ASCVD event, and (4) death. We adjusted life expectancy by QOL (utility) weights (Table 1). Quality-of-life weights represent the overall well-being in each health state and range from 0 (death) to 1 (perfect health). We verified the internal validity of our model by comparing the model-predicted Kaplan-Meier survival curve for ASCVD incidence against observed 10-year ASCVD incidence data from the JHS cohort.

Statin treatment resulted in a 21% reduction in ASCVD risk (relative risk, 0.79) based on a Cholesterol Treatment Trialists' meta-analysis.¹⁸ We included a 4.7% mild adverse event rate, a 0.006% major adverse event rate,¹⁹ and a 0.09%²⁰ death rate associated with major adverse events (ie, a conditional probability of 9 of every 10 000 individuals with a major ad-

verse event) with statin therapy permanently discontinued following either mild or major adverse events. Given the risk of type 2 diabetes due to statin therapy,²¹ we accounted for the reduction in QOL and increase in costs associated with statin-induced type 2 diabetes.²² We used the baseline risk (annual odds, 0.017) and odds ratio (1.28) from the JUPITER trial²¹ to estimate the excess risk of statin-induced type 2 diabetes for patients receiving statin therapy compared with those not receiving statin therapy in our simulation model, which was adjusted for statin adherence; in the model, patients did not discontinue therapy if they experienced statin-induced diabetes. Adherence to statin treatment was assumed at 67% in the first year, 53% in the second year, and 50% in the third year.²² In the base-case scenario, we did not assume an increase in statin adherence with a non-0 CAC score.

Costs were considered from the health care sector perspective and were adjusted to 2017 US dollars, using the medical component of the consumer price indexes accounting for inflation.³⁵ The health care sector perspective was chosen similar to previous analyses.^{11,36,37} Base-case simulations included unrelated health care costs recommended by the Second Panel on Cost-effectiveness in Health and Medicine,³⁸ the direct costs of ASCVD events and CAC testing, and cost of statins. We included age- and sex-specific baseline cost of non-cardiovascular health care.²³ We determined the relative frequencies of coronary heart disease events and ischemic strokes from the JHS cohort and estimated the weighted average of costs for fatal and nonfatal ASCVD based on 2007 cost data.²⁴ We assumed a base-case cost of \$183 for CAC measurement based on the Medicare Physician Fee Schedule for 2017 for a noncontrast CT scan²⁵ and considered a range of costs in sensitivity analyses. Moderate-intensity statin therapy, including atorvastatin, 20 mg (\$123/y), and simvastatin, 40 mg (\$44/y), were assumed to be given in equal proportions to individuals at intermediate risk. The base-case cost of \$84/y was estimated as the weighted average of the lowest 2016 *Red Book* wholesale acquisition costs for generic formulation of statins.²⁹ Given that all strategies tested required a general practitioner visit or laboratory fees for lipid levels, we did not include these costs. For the base-case scenario, we assumed that results of the CAC score would be communicated with a telephone call but included an additional visit to discuss CT scan results in a sensitivity analysis.

Quality of life for incident ASCVD was estimated from the EuroQOL 5 Dimensions questionnaire.²⁶ We calculated a weighted average of QOL decrement post MI (0.778) and stroke (0.768) based on relative frequencies of coronary heart disease and stroke events in the JHS cohort. The annual QOL decrement for statin treatment for the base-case analysis was considered 0.00384 life-years—equivalent to losing 2 weeks of perfect health to avoid 1 decade of daily use of medication.¹¹ We modeled mild statin adverse events as QOL decrements by 2 days and major statin adverse events as QOL decrements by 2 weeks of lost healthy life.²⁷ The QOL penalty for statin use is applied every year, whereas adverse events are considered a one-time event because patients discontinue statin therapy after occurrence of a mild or major adverse event.

We calculated quality-adjusted life-years (QALYs), life-time costs, and incremental cost-effectiveness ratios (ICERs). Costs and QALYs were discounted at a recommended US 3% discount rate.³⁹ We considered an ICER less than \$50 000/QALY gained as high-value care, \$50 000/QALY to \$150 000/QALY as intermediate-value care, and greater than \$150 000/QALY as low-value care per ACC/AHA conventions on cost-effectiveness and value.⁴⁰

We performed probabilistic sensitivity analysis using second-order Monte Carlo simulations to assess uncertainty in model parameters by drawing 1000 random samples for second-order uncertainty from each of the prespecified model parameter distributions (Table 1) and repeating the process over 100 000 simulations for each strategy for first-order uncertainty.⁴¹ We evaluated the probability that a strategy was cost-effective using cost-effectiveness acceptability curves for willingness-to-pay values between \$0 and \$200 000/QALY.

We varied the reduction in QOL associated with daily medication intake (0-0.009), annual cost of statins (\$50-\$1000), cost of CT scanning (\$50-\$400), ASCVD risk reduction with statin treatment (15%-24%), increased rate of adherence among individuals with a non-0 CAC score (0%-49%), prevalence of non-0 CAC score (40%-80%), reduction in QOL associated with an ASCVD event (0.10-0.40), and risk of death in the first year after ASCVD. We considered the association between incidental findings noted on CT scans and overall costs and QOL^{42,43} and included the cost of an additional visit to discuss CT scan results⁴⁴ in sensitivity analyses.

Results

Baseline Characteristics

The baseline characteristics of the JHS subpopulation included in this analysis have been published.³⁰ We focused the present analysis on 472 intermediate-risk individuals with a mean (SD) age of 63 (6.7) years; 178 of 304 individuals (58.6%) who received CAC assessment had a non-0 CAC score (eTable 1 in the [Supplement](#)). The sample included 243 women (51.5%) and 229 men (48.5%). The model predicted 5- and 10-year ASCVD-free survival probabilities that fell within the 95% log-log CI of the JHS data. The observed 5-year ASCVD-free survival probabilities were 97.3% (95% CI, 95.3%-98.5%) in the JHS vs 96.7% in our model. The observed 10-year ASCVD-free survival probability was 93.9% (95% CI, 91.0%-95.8%) in the JHS vs 93.6% in our model (eFigure in the [Supplement](#)).

Cost-effectiveness Analysis

Per the 2013 ACC/AHA guideline strategy vs the 2018 ACC/AHA guideline strategy, a greater proportion of individuals had indications for statin therapy with the 2013 guidelines (100% vs 58.6%) and were receiving the medications (67% vs 39%) (Table 2). Fewer ASCVD events (26.86% vs 27.54%) but more statin-associated adverse events (3.14% vs 1.84%) occurred during use of the 2013 ACC/AHA guidelines compared with the 2018 ACC/AHA guidelines (Table 2). Probabilistic sensitivity analyses suggested that the 2018 ACC/AHA guidelines with CAC assessment were cost-effective in 81% of simulations using

Table 2. Lifetime Per-Person Events, Costs, QALYs, and ICERs in the Base-Case Analysis^a

Strategy	Proportion of individuals, %		Statin		ASCVD events ^b	Life expectancy, y	QALYs	Total lifetime costs, \$	Incremental costs/QALY (95% credible interval) ^c
	Eligible for statins	Statins in the first year	Associated adverse events ^a	Costs, \$					
2018 ACC/AHA with CAC assessment	58.6	39	0.0184	359.46	0.2754	17.8181	17.5445	266 404	Reference
2013 ACC/AHA without CAC assessment	100	67	0.0314	684.44	0.2686	17.8358	17.5472	266 833	\$158 325 (\$11 544/QALY to 2013 guidelines dominated by 2018 guidelines)

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; ICERs, incremental cost-effectiveness ratios; QALYs, quality-adjusted life-years.

^a Future life-years, costs, and QALYs were discounted at 3%/y.

^b Values indicate proportion of individuals who experience an outcome in their lifetime.

^c Ninety-five percent credible from probabilistic sensitivity analysis.

willingness-to-pay values of \$50 000/QALY, 76% of those using \$100 000/QALY, and 72% of simulations using \$150 000/QALY when the QOL for patients who were asymptomatic and receiving daily statin therapy was 0.996 and a non-0 CAC score did not appear to affect adherence to therapy (Figure 2A). However, the strategies resulted in similar costs and outcomes when there was no QOL penalty for statin use as societal willingness-to-pay increased (Figure 2C).

In our base-case simulations, we projected that the 2013 ACC/AHA guidelines without CAC assessment provided a per-person greater quality-adjusted life expectancy (0.0027 QALY), albeit at a greater cost (\$428.97), with an ICER of \$158 325/QALY compared with the 2018 ACC/AHA guideline strategy with CAC assessment, representing low-value care per the ACC/AHA definition (Table 2).⁴⁰ On a national population scale, there would be approximately 19 635 QALYs gained at an incremental cost of \$3.1 billion using the 2013 ACC/AHA guidelines instead of the 2018 guidelines.

One-Way Sensitivity Analyses

In one-way sensitivity analyses, the 2018 ACC/AHA guidelines with CAC assessment strategy had greater or equal health gains and lower costs than the 2013 ACC/AHA guidelines without CAC assessment when the patient's QOL while they were asymptomatic and receiving daily statin therapy was 0.991 (equivalent to losing approximately ≥ 5 weeks to avoid 1 decade of daily therapy), if statin efficacy was lower (ie, ASCVD relative risk reduction of 15%), if adherence to daily statin therapy increased when a non-0 CAC score was reported (ie, by $\geq 10\%$), with lower CAC prevalence (ie, 40%), or if the QOL penalty following an ASCVD event was low (ie, 0.90 with QOL while asymptomatic and receiving statin therapy) (eTable 2 in the Supplement). The QALY decrement attributable to daily statin use was 0.013 (QALY gain of 0.0027 QALY with a QOL measure of 0.996 while the patient was asymptomatic and receiving daily statin therapy vs 0.016 QALY with no QOL penalty), representing 83% of the base-case QALY difference between the 2018 and 2013 ACC/AHA guidelines.

At a willingness-to-pay threshold less than \$50 000/QALY (the high-value designation per the ACC/AHA), a shift in the optimal decision from 2018 ACC/AHA guidelines with CAC assessment to 2013 ACC/AHA guidelines without CAC assess-

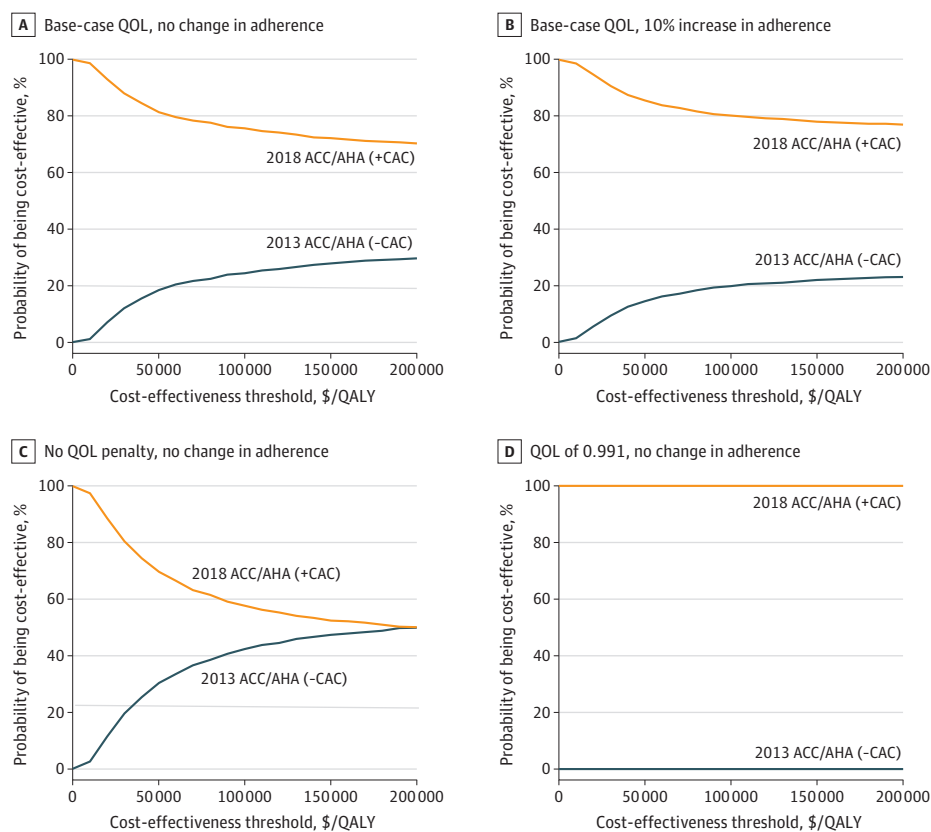
ment would occur if there was no QOL penalty associated with use of daily statin medication. In most other cases, the 2013 ACC/AHA guideline without CAC assessment represented intermediate- to low-value care; a prevalence of non-0 CAC scores varying from 40% to 80% altered the ICER from the 2018 ACC/AHA guideline dominating to an ICER of \$53 993/QALY for the 2013 guidelines; varying the annual statin cost from \$50 to \$1000 altered the ICER of the 2013 guideline from \$102 455/QALY to \$1 480 375/QALY.

Discussion

In this study, we evaluated the cost-effectiveness of contemporary strategies for primary prevention of ASCVD using data from an intermediate-risk, community-based cohort of African American participants from the JHS. We found that allocation of generic-formulation, moderate-intensity statin therapy based on the 2018 ACC/AHA guidelines with a single CAC measurement to guide statin treatment appeared to likely be cost-effective compared with the 2013 ACC/AHA guidelines without CAC measurement only when incorporating a QOL penalty owing to daily use of statin medications (ie, QOL impairments that are associated with the act of taking a pill daily as opposed to QOL outcomes associated with adverse events). When the QOL penalty for use of daily therapy was equivalent to losing 5 weeks or more of perfect health to avoid 1 decade of daily therapy, the 2018 guidelines, which recommend CAC assessment, appeared to have greater effectiveness and lower cost compared with the 2013 guidelines. When the QOL penalty of daily therapy was equivalent to losing at least 2 weeks of perfect health to avoid 1 decade of daily therapy (our base-case assumption), the 2013 ACC/AHA guideline strategy led to what appeared to be slightly better health outcomes measured using QALYs, albeit at greater cost, resulting in low-value care (incremental cost-effectiveness ratio $> \$150 000/\text{QALY}$).⁴⁰ Assuming no QOL penalty for daily therapy, the 2013 guidelines had a favorable incremental cost-effectiveness ratio of \$24 003/QALY.

Previous cost-effectiveness analyses have evaluated different statin allocation approaches for primary prevention of ASCVD in several cohorts. In a cost-effectiveness analysis from

Figure 2. Association of Quality-of-Life (QOL) Penalty Assigned for Daily Statin Therapy and Adherence in Patients With Non-O Coronary Artery Calcium (CAC) Score With Cost-effectiveness



The curves show the probability that each strategy is cost-effective at varying willingness-to-pay values for different scenarios of statin QOL penalty. A, Base-case QOL value of 0.996 while the patient is asymptomatic and receiving daily statin therapy with no change in adherence with non-O CAC score. B, Base-case QOL value of 0.996 while the patient is asymptomatic and receiving daily statin therapy with a 10% increase in adherence with non-O CAC score. C, No QOL penalty of daily statin therapy and no change in adherence with non-O CAC score. D, Quality-of-life value of 0.991 while the patient is asymptomatic and receiving daily statin therapy and no change in adherence with non-O CAC score. For example, in the probabilistic sensitivity analysis using the base-case assumption of the 0.996 QOL value, while the patient is asymptomatic and receiving daily statin therapy (A), the preferred strategy at a willingness-to-pay value of \$0 per quality-adjusted life-year (QALY) gained was the 2018 ACC/AHA guidelines in 100% of the simulations; the 2018 ACC/AHA guidelines were preferred in 81% of the \$50 000/QALY willingness-to-pay simulations, 76% of the \$100 000/QALY simulations, and 72% of the \$150 000/QALY simulations. ACC/AHA indicates American College of Cardiology/American Heart Association.

the Multiethnic Study of Atherosclerosis, a treat-all strategy was preferred over a strategy in which individuals with a non-O CAC score were treated with statins when statins were inexpensive and there was no QOL penalty given for daily medication therapy.¹¹ However, when statin assumptions were less favorable, allocation of treatment based on a non-O CAC score strategy was generally preferred. Similarly, Roberts and colleagues⁹ suggested that allocating statin therapy on the basis of the CAC score was more cost-effective than treating all intermediate-risk (classified by Framingham risk score) individuals after considering adverse effects, the QOL penalty assigned for daily statin therapy, and enhanced treatment adherence associated with CAC testing. Other cost-effectiveness analyses incorporating the 2013 ACC/AHA guidelines have suggested that broad treatment with statins is cost-effective,^{45,46} even in populations with a lower predicted ASCVD risk compared with our study cohort.²² Hong and colleagues⁴⁷ noted that a CAC assessment-guided strategy appeared to result in

similar costs and QALYs as a guideline-alone-based strategy in individuals eligible for statin therapy with an ASCVD risk greater than 5%. In those studies, the cost-effectiveness profile of CAC assessment was most favorable in populations with an estimated ASCVD risk of 5.0% to 7.5%. We extended these results to an African American population, using contemporary guideline recommendations that incorporate CAC assessment as a rule-out strategy for individuals with an estimated ASCVD risk between 7.5% and 19.9%. The QOL penalty associated with daily statin use played an important role in this and previous cost-effectiveness analyses, suggesting that CAC assessment may be used to aid in decisions on initiation of statin therapy for individuals who have a strong preference not to take a statin medication daily.

Limitations

This study has limitations. This analysis was based on several African American-specific factors, including statin eligi-

bility, CAC assessment prevalence, and event rates from the JHS, and the findings approximate rates in other diverse populations.^{5,48} However, guideline recommendations and screening for the presence of CAC could have different implications in other groups and may not apply to individuals who are already receiving statin treatment. With the JHS design, CAC assessment was performed on a healthier subset of the JHS population³⁰ and it is possible that the hazard of ASCVD associated with a non-0 CAC score could underestimate the true hazard rate in the population. Furthermore, 18.1% of the participants had initiated statin treatment by visit 3 and incident ASCVD rates may underestimate the true rate in an untreated population. We combined the coronary heart disease and stroke event rates to obtain reliable estimates of ASCVD event rates; however, QOL and costs capture the outcomes of both coronary heart disease and stroke events proportionally. This research was based on a decision analysis model using assumptions for model parameters. While we conducted probabilistic sensitivity analyses for the main parameters tested in our decision analysis model, distributions tested may not be representative of the values in the general population. We obtained cost data from older studies and, while true costs may have changed, alteration of cost parameters did not appear to be influential in our sensitivity analyses. Furthermore, although we incorporated a QOL penalty from use of daily medication, we did not account for changes in QOL when patient preferences are

included or when the decision-making process is viewed as burdensome. In addition, to our knowledge, earlier studies did not examine the perceived burden of daily medication therapy in primarily African American populations, although one report suggested that daily therapy with a preventive medication is viewed as more burdensome by nonwhite compared with white individuals.²⁸ Future studies should examine the association between daily statin use and African Americans' QOL. If providing CAC scoring information improves statin adherence or acceptability in African American individuals, then our base-case findings might have understated the cost-effectiveness of the 2018 guidelines.

Conclusions

In this model of asymptomatic African American adults at intermediate risk for ASCVD, contemporary 2018 ACC/AHA primary prevention guidelines including CAC assessment provided an apparently greater quality-adjusted life expectancy at a lower cost than a strategy without recommended CAC assessment when there was a strong patient preference to avoid use of daily medication therapy. A shared decision-making conversation regarding primary ASCVD prevention should gauge patients' preferences before consideration of CAC assessment for intermediate-risk individuals who prefer not to receive daily medication therapy.

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