

COSEHC global vascular risk management quality improvement program: rationale and design

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Background: The Consortium for Southeastern Hypertension Control (COSEHC) promotes global risk factor management in patients with metabolic syndrome. The COSEHC Global Vascular Risk Management Study (GVRM) intends to quantify these efforts on long-term patient outcomes. The objectives of this study were to present baseline demographics of patients enrolled in the GVRM, calculate a modified COSEHC risk score using 11 variables (COSEHC-11), and compare it with the original COSEHC-17 and Framingham, Prospective Cardiovascular Münster (PROCAM), and Systemic Coronary Risk Evaluation (SCORE) risk scores.

Methods: Deidentified electronic medical records of enrolled patients were used to calculate the risk scores. The ability of the COSEHC-11 score to predict the COSEHC-17 score was assessed by regression analysis. Raw risk scores were converted to probability estimates of fatal coronary heart disease (CHD) and compared with predicted risks from other algorithms.

Results: Of the 177,404 patients enrolled, 43,676 had data for all 11 variables. The COSEHC-11 score (mean \pm standard deviation) of these 43,676 patients was 31.75 ± 11.66 , implying a five-year fatal CHD risk of 1.4%. The COSEHC-11 score was highly predictive of the COSEHC-17 score ($R^2 = 0.93$; $P < 0.0001$) and correlated well with the SCORE algorithm.

Conclusion: The COSEHC-11 risk score is statistically similar to the COSEHC-17 risk score and should be a viable tool for evaluating its ability to predict five-year cardiovascular mortality in the coming years.

Keywords: cardiovascular risk, electronic medical records, metabolic syndrome

Introduction

Metabolic syndrome refers to a constellation of cardiovascular risk factors. Although several different definitions of metabolic syndrome exist,¹ the US National Cholesterol Education Program Adult Treatment Panel III defines metabolic syndrome as the presence of at least three of five core risk factors: abdominal obesity; insulin resistance, glucose intolerance, or drug treatment for elevated glucose levels; elevated blood pressure or antihypertensive drug treatment; low levels of high-density lipoprotein cholesterol (HDL-C); and elevated triglyceride levels.² Other factors commonly associated with the metabolic syndrome include vascular inflammation, presence of a prothrombotic state, physical inactivity, aging, and a genetic predisposition.³⁻⁵

Improved management of these risk factors is important because the metabolic syndrome strongly predicts the development of cardiovascular disease (CVD).⁶⁻⁸ In a large meta-analysis of 172,573 individuals enrolled in longitudinal studies, persons with metabolic syndrome had almost a twofold increased risk of experiencing a cardiovascular event or death compared with those without metabolic syndrome

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(summary risk ratio [RR], 1.78; 95% confidence interval: 1.58, 2.00).⁶ The risk remained significant even when adjusting for known cardiovascular risk factors or a history of CVD. Furthermore, there appears to be a gender effect such that women have a greater risk than men (summary RR, 2.63 versus 1.98; $P=0.09$)⁶ and a continuum of risk that increases with the number of metabolic syndrome components present.^{9,10}

While the American Heart Association and the American College of Cardiology¹¹ recommend using the Framingham Heart Study global risk assessment scoring system¹² for estimating an individual's 10-year risk of experiencing a fatal or nonfatal cardiovascular event, this approach has several limitations¹³ that are underscored by the more comprehensive global hypertension management guidelines put forth by the European Society of Hypertension and European Society of Cardiology.¹⁴ Although the Framingham scoring system includes the "standard" risk factors of smoking, blood pressure, total cholesterol, HDL-C, blood glucose, sex, and age, exclusion of other recognized risk factors such as left ventricular hypertrophy (LVH) limits its ability to discriminate sensitively between individuals at different levels of cardiovascular risk.¹⁵ Equally important, the generalized application of the Framingham risk score to both sexes and all racial and ethnic groups has been questioned, because the Framingham study was conducted among 5208 predominantly white, healthy individuals living in Framingham, Massachusetts.^{12,13,16} For example, in a study that assessed the multiethnic, multiracial applicability of the Framingham risk score, the score was found to be generally predictive for whites and blacks, but systematically overestimated five-year risk in Japanese American and Hispanic men and Native American women.¹² Other studies reported that the Framingham score also overestimates risk in patients from China,¹⁷ The Netherlands,¹⁸ and Ireland and France.¹⁹ To address these limitations, other risk scoring tools have been developed, including the Prospective Cardiovascular Münster (PROCAM) score, which estimates the 10-year risk of fatal and nonfatal cardiovascular events,²⁰ and the Systemic Coronary Risk Evaluation (SCORE) score, or Weibull algorithm,²¹ which estimates the 10-year risk of fatal cardiovascular events.

In an effort to develop a more accurate and valid risk score for predicting CVD mortality in the southeastern US, a region with a highly diverse population and a historically higher prevalence of CVD and CVD-related mortality,^{22,23} the Consortium for Southeastern Hypertension Control (COSEHC) developed an alternative global approach to

screening and scoring patients for cardiovascular risk. The COSEHC risk tool includes 17 risk factors and is based on the cardiovascular risk score published by the Individual Data ANalysis of Antihypertensive intervention trials (INDANA) database study,²⁴ which included 11 variables.^{25,26} The INDANA algorithm calculates the five-year risk of death from CVD. It was derived with data from eight large randomized trials ($n = 48,088$), all of which assessed antihypertensive drugs versus no intervention and reported mortality by intention to treat. Furthermore, the trials were multinational, which enhanced generalizability, and because follow-up in these trials was stringent, the risk estimators developed were precise.

To validate the discriminative value of the COSEHC risk tool in predicting CVD mortality in the diverse population of the southeastern US, the Global Vascular Risk Management (GVRM) study was initiated. This large-scale prospective study was designed to determine the sensitivity of the COSEHC risk tool. The GVRM also seeks to determine if the COSEHC risk tool can be useful in improving quality of care in the management of vascular disease and the metabolic syndrome by providing benchmarking data on treatment patterns and outcomes to participating COSEHC Cardiovascular Centers of ExcellenceTM and in assessing the effect of COSEHC-designated treatment goals²⁶ on patient outcomes at five years.

In this article, the demographic profile and risk factor prevalence of the GVRM study population at baseline are presented, the development of the COSEHC-11 risk score tool is described, and the COSEHC-11 score is compared with the original COSEHC-17 risk score tool, as well as the Framingham, PROCAM, and SCORE (Weibull) risk score algorithms.

Methods

Study design

The GVRM study is a voluntary, observational, prospective quality improvement initiative conducted at eight COSEHC Cardiovascular Centers of Excellence. The Centers of Excellence network, established in 1998, represents a cooperative initiative of expert health care providers who partner with local health, consumer, employer, and academic groups to develop programs that focus on the treatment, clinical research, and prevention of metabolic syndrome-related CVD. Data were derived from patients who were aged ≥ 18 years and met one or more of the following criteria: at least one predefined International Classification of Diseases, 9th Revision (ICD-9) code corresponding to CVD

or risk factors, treatment at a cardiac or vascular-related clinic or department of a participating Center of Excellence, or treatment at a noncardiac-related outpatient clinic associated with a cardiac-related Current Procedural Terminology code. Because this is an observational study, all patients from each participating center are treated per the standard of care for their respective conditions, and no predefined visits, medical or laboratory tests, procedures, or interventions are required.

The 11 variables used in calculating the modified COSEHC-11 risk score are listed in Table 1. Additional variables of interest include those required to calculate the original COSEHC-17 risk score (Table 1). Of the 11 variables necessary to calculate the modified COSEHC score, age, sex, smoking status, and family history of coronary heart disease (CHD) are collected only once; all other data are updated on a quarterly basis from the individual centers and submitted to COSEHC.

Study duration and outcomes

A five-year prospective study is planned from a baseline data date of February 4, 2010. The main outcome measures are cardiovascular morbidity and mortality, including the development of CHD, congestive heart failure, stroke, transient ischemic attack, abdominal aortic aneurysm, myocardial infarction, death, renal failure, and diabetic retinopathy.

Data flow and management

The GVRM study was approved at a central level by the Copernicus Group Institutional Review Board (Research Triangle Park, NC). Individual patient electronic medical records from participating COSEHC Centers of Excellence sites are submitted to the COSEHC Coordinating Center at the Wake Forest University School of Medicine on a quarterly basis. The Coordinating Center includes a scientific advisory board to provide guidance on data interpretation and analytic review. The cutoff for inclusion of data in the baseline analysis was February 4, 2010. The Coordinating Center maintains a master electronic medical record for each patient, which includes all treatments, laboratory records, and clinical events. In order to comply with all local and federal privacy acts, including Health Insurance Portability and Accountability Act requirements, all patient-level data are deidentified prior to analysis. The deidentification process involves assigning each unique patient record a deidentified key that consists of a three-character center ID and a sequential number from 1 to n and the conversion of all calendar dates to days since date of birth. Deidentified data are sent for analysis to ICON Clinical Research (North Wales, PA) along with the patient's unique key, age, sex, and ethnic background (white, black, Hispanic, other). These data include converted visit dates expressed in terms of days

Table 1 Variables included in the original COSEHC, modified COSEHC, Framingham, SCORE (Weibull), and PROCAM cardiovascular risk scores

Variable	Modified COSEHC	Original COSEHC ²⁵	Framingham Heart Study ¹²	SCORE ²¹	PROCAM ²⁰
Age, years					
Sex					
Total cholesterol, mmol/L					
HDL-C, mmol/L					
LDL-C, mmol/L					
Triglycerides, mmol/L					
Systolic blood pressure, mmHg					
Smoking status (yes or no)					
Diabetes mellitus, ^a mmol/L					
Diabetes mellitus (yes or no)					
Family history of premature CHD ^b (yes or no)					
ECG-confirmed LVH (yes or no)					
Height, inches					
Serum creatinine, μ mol/L					
Homocysteine, μ mol/L					
Prior MI (yes or no)					
Prior stroke (yes or no)					

Notes: Grey shading indicates the variable is included in the calculation of the risk score. ^aDiabetes diagnosis based on fasting blood glucose >6.66 mmol/L listed in electronic medical record; ^bFor COSEHC score, required only for males aged <60 years.

Abbreviations: CHD, coronary heart disease; COSEHC, Consortium for Southeastern Hypertension Control; ECG, electrocardiogram; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVH, left ventricular hypertrophy; MI, myocardial infarction; PROCAM, Prospective Cardiovascular Münster; SCORE, Systemic Coronary Risk Evaluation.

since birth. The data will never be “reidentified,” and ICON will never have access to actual calendar dates.

Statistical methods

The COSEHC-11 risk score is an additive score calculated using separate algorithms for men and women. The individual scoring elements are for age (five-year ranges), smoking status (with differential scores for each age range), systolic blood pressure ranges, laboratory test score ranges, and patient history variables. The final COSEHC-11 score is the sum of each of these individual scoring elements. The primary baseline analysis for this article involved the calculation of the COSEHC-11 risk score and included only those patients with all 11 required data elements. An exception for this requirement was made for women and men aged >59 years with missing data for family history of myocardial infarction. This exception is made because the COSEHC risk score only uses premature family CHD for male patients aged <60 years. For the current report, the following applies: if a patient had multiple visits during the six months prior to the end of the baseline period (February 4, 2010), data from the last visit were used; if laboratory values or blood pressure readings were missing from the last visit, data from the most recent prior visit were used, with a maximum carry-forward time of 12 months; and patient history variables (ie, smoking and diabetes status, family CHD history, and LVH) had unlimited carry-forward times.

The impact of using <11 variables to estimate the modified COSEHC-11 risk score was gauged by including patients with incomplete data. Only patients with ≥ 8 of 11 variables were considered for this analysis. Three methods of data imputation were used to improve the accuracy of the modified COSEHC risk score. The first imputation method increased the amount of time that laboratory and blood pressure values were carried forward to replace missing values; thus, instead of the original cutoff time of 12 months, unlimited carry-forward was used. The second imputation augmented the results of the first imputation with pharmacy data. When patients were missing data for diabetes status, we checked for the presence of diabetes-specific medications (ie, insulin detemir, insulin glargine, human recombinant insulin, insulin lispro, metformin, pioglitazone, and rosiglitazone). Patients with at least one of these medications had their diabetes status changed from “missing” to “diabetic.” Lastly, multiple imputations were implemented using SAS[®] PROC MI (SAS Institute, Inc., Cary, NC) with the Markov chain Monte Carlo (MCMC) method. The MCMC method can be used when some of the missing variables (eg, laboratory tests) have

arbitrarily missing patterns.²⁷ MCMC simulation constructs a Markov chain that is long enough for the distribution of the elements to stabilize to a stationary distribution (the distribution of interest). Through repeated simulations of the steps of this chain, the method simulates draws from the distribution of interest.²⁷ This allows for simulations from a wide range of distributions without being computationally burdensome.²⁸ For the COSEHC dataset, a set of mean and covariance priors were created using data from site 4 ($n = 1319$), which had complete data on all patients and good laboratory test compliance. These priors were used by the MCMC algorithm to improve its imputation.

To validate the modified COSEHC score, a regression analysis was used to estimate the full COSEHC-17 score using the modified COSEHC-11 score as a predictor. To perform this analysis, the original COSEHC-17 risk score was calculated for the subgroup of patients with complete data for all COSEHC-17 variables. The modified COSEHC-11 risk score was also calculated for this subgroup. The modified COSEHC-11 risk score was used as the only predictor for the full COSEHC-17 risk score using linear regression. This analysis was performed to demonstrate that the COSEHC-11 risk score could serve as a proxy for the full COSEHC-17 risk score. In addition, we used the results from this regression analysis to transform the modified COSEHC-11 risk score into an estimated CHD event probability and to characterize the distribution of CHD event risk within the study population.

To compare the modified COSEHC risk score and its resulting event probability with other risk indices, the subset of patients who had complete data for all 11 variables to calculate Framingham, PROCAM, and SCORE (Weibull) risk scores was used. These risk scores were calculated using both the nonimputed and multiple imputation datasets. It should be noted that the SCORE (Weibull) risk score predicts the 10-year risk of fatal CHD events, whereas the Framingham and PROCAM risk indices predict both fatal and nonfatal events over 10 years. Table 1 lists the required data elements for each risk score. All data are reported as mean \pm 1 standard deviation (SD) of the mean.

Results

Baseline demographics

A total of 177,404 patients from eight participating COSEHC centers were found to be eligible for inclusion in the GVRM study and represent the baseline population. Of these patients, 70,567 had at least 8 out of 11 required COSEHC variables present in their electronic medical record, including 43,676

who had complete data for all 11 variables. Table 2 presents the characteristics of the 70,567 patients with eight or more data elements complete. Of these 70,567 patients, the mean age was 60 years and 54% were women. Diabetes mellitus was present in 35% of the 65,391 patients for whom the status was available. The most commonly missing data elements among this group were for ethnicity, family CHD history, and clinical diagnosis of LVH. Of the 18,725 patients whose race or ethnicity was known, 70% were white, 20% were black, 1% were Hispanic, and 8% were classified as other.

COSEHC-11 scores

COSEHC-11 scores were calculated for the 43,676 patients with complete baseline data for all 11 variables. As can be seen in Table 3, data completeness varied across the centers, with the proportion of patients for whom complete baseline data were available for all 11 variables ranging from 0.3% (center 7) to 63.4% (center 3). Among the 43,676 patients with complete data, the mean COSEHC-11 score was 31.75 ± 11.66 . The range across the centers was 30.93

to 36.85. One interesting finding is the relative stability of the SD across sites and between the individual sites and the total cohort (Table 3).

Table 3 also displays the COSEHC-11 scores that result from the three methods of data imputation. The first method of imputation, with no limit on carry-forward time, resulted in the availability of 43,861 patients for analysis, an increase of 185 patients over no imputation. The relatively small number of additional patients is consistent with the availability of complete laboratory and blood pressure records for most patients (Table 2). The second method of imputation (pharmacy imputation of diabetes medications), which could only add patients with diabetes, added no additional patients. While there were 5176 patients with a missing diabetes history, patients with no diabetes records were typically missing other patient history variables in addition to their diabetes status. Thus, the imputation using pharmacy records did not produce any new complete records, although it did find 79 patients from this group with a positive history of diabetes-specific medications.

The MCMC method of imputation increased the sample size from 43,676 to 70,567. The average COSEHC-11 score in the imputed group decreased slightly from 31.75 ± 11.66 to 31.24 ± 11.24 (Table 3). Center 7, which had the fewest number of patients with available data for all 11 variables, showed the largest change in risk score upon imputation, decreasing from 36.85 ± 11.13 to 32.12 ± 10.94 . Of the five sites having ≥ 1000 patients with complete data for all 11 variables, multiple imputation changed the average COSEHC-11 score by <1 point.

Table 2 Baseline demographics of the 70,567 patients with ≥ 8 COSEHC-11 variables

Variables	Descriptive statistic	N ^a
Age, years	60 ± 14	70,567
Women, n (%)	38,238 (54%)	70,567
Race/ethnicity		
White, n (%)	13,159 (70%)	18,725
Black, n (%)	3755 (20%)	18,725
Hispanic, n (%)	105 (1%)	18,725
Other, n (%)	1560 (8%)	18,725
Clinical history		
Current smoker, n (%)	14,793 (27%)	55,002
Diabetes mellitus, n (%)	22,895 (35%)	65,391
Premature CHD in family, n (%)	9920 (40%)	25,070
Left ventricular hypertrophy, n (%)	6284 (12%)	52,334
Clinical and laboratory values ^b		
Systolic blood pressure, mmHg	129 ± 17	70,036
Diastolic blood pressure, mmHg	77 ± 11	70,032
Total cholesterol, mmol/L ^c	4.8 ± 1.1	69,949
HDL-C, mmol/L ^c	1.2 ± 0.3	69,363
LDL-C, mmol/L ^c	2.8 ± 0.9	69,474
Triglycerides, mmol/L ^d	1.7 ± 1.0	70,384

Notes: Age and clinical and laboratory values are presented as mean \pm standard deviation. ^aThe total number of patients available for each variable is $<70,567$, reflecting missing data for the various elements. The exception is age and sex, which were required for all patients; ^bAll values are from the last recorded assessment. If the last assessment occurred >12 months before the last visit, the results were not used; ^cTo convert total, HDL-C and LDL-C levels from mmol/L to mg/dL, multiply by 38.61; ^dTo convert triglycerides from mmol/L to mg/dL, multiply by 88.50.

Abbreviations: CHD, coronary heart disease; COSEHC, Consortium of Southeastern Hypertension Control; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Comparison of COSEHC-11 and COSEHC-17 scores

Figure 1 shows the results of a linear regression model of the more comprehensive COSEHC-17 score using the COSEHC-11 score as the predictor. This regression was performed on the subset of 735 patients who had available data for all 17 COSEHC variables except homocysteine. (Homocysteine levels were available for only one patient in this cohort and were therefore excluded as a required variable.) The COSEHC-11 coefficient was a statistically significant predictor of the COSEHC-17 score ($P < 0.0001$; $R^2 = 0.93$). This suggests that the COSEHC-11 risk score is highly correlated with the full COSEHC-17 risk score, and that a simple linear transformation of the COSEHC-11 score can yield a good approximation of the full COSEHC-17 risk score, and therefore, cardiovascular event probability.

Table 3 Average COSEHC-11 score by site calculated with and without imputation

	Site 1	Site 2	Site 3	Site 4	Site 5	Site 6	Site 7	Site 8	Total
Total population^a	2822	62,222	31,946	1319	4865	34,867	4930	34,433	177,404
No imputation									
Total available for analysis	1420	11,420	20,239	737	939	6047	13	2861	43,676
COSEHC score	31.94 (9.08)	31.95 (10.76)	30.93 (12.65)	31.07 (9.53)	35.90 (9.97)	31.18 (11.08)	36.85 (11.13)	36.60 (9.46)	31.75 (11.66)
Unlimited carry-forward^b									
Total available for analysis	1420	11,420	20,239	737	1124	6047	13	2861	43,861
COSEHC score	31.94 (9.08)	31.95 (10.76)	30.93 (12.65)	31.07 (9.53)	36.13 (9.70)	31.18 (11.08)	36.85 (11.13)	36.60 (9.46)	31.77 (11.65)
Pharmacy imputation^c									
Total available for analysis	1420	11,420	20,239	737	1124	6047	13	2861	43,861
COSEHC score	31.94 (9.08)	31.95 (10.76)	30.93 (12.65)	31.07 (9.53)	36.13 (9.70)	31.18 (11.08)	36.85 (11.13)	36.60 (9.46)	31.77 (11.65)
Multiple imputation^d									
Total available for analysis	1425	20,733	28,293	1127	2677	11,312	1963	3037	70,567
COSEHC score	31.94 (9.08)	31.72 (10.85)	29.95 (11.57)	30.65 (9.47)	34.01 (11.01)	31.26 (11.42)	32.12 (10.94)	36.75 (9.45)	31.24 (11.24)

Notes: All scores are presented as mean (standard deviation). ^aFor each site, total population includes all patients with \geq one visit in the eMR; ^bAccounts for laboratory and blood pressure values collected outside the original cutoff time of 12 months prior to inclusion; ^cAccounts for a missing history of diabetes from the eMR but the presence of diabetes-specific medications (insulin detemir, insulin glargine, human recombinant insulin, insulin lispro, metformin, pioglitazone, and rosiglitazone) in the pharmacy record; ^dAccounts for missing laboratory data from random visits using the Markov chain Monte Carlo method.

Abbreviations: COSEHC, Consortium for Southeastern Hypertension Control; eMR, electronic medical record.

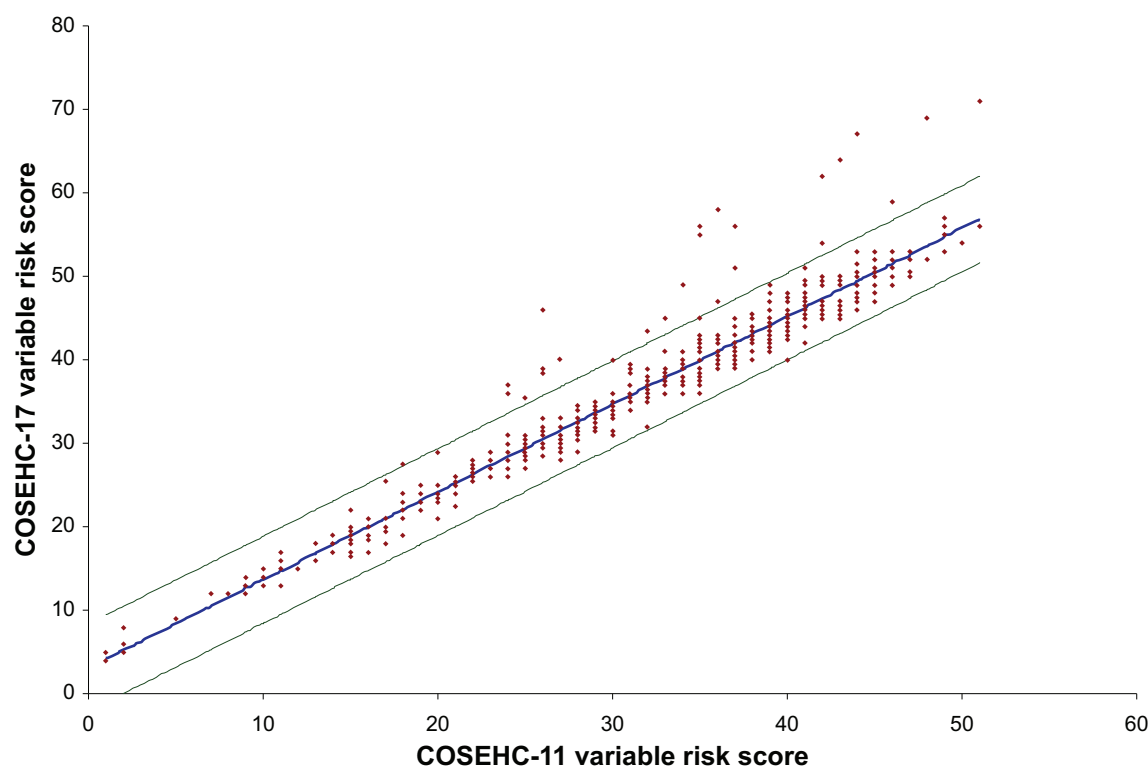


Figure 1 COSEHC-17 versus COSEHC-11 risk score scatter plot with regression line and 95% confidence limits. The solid blue line shows the ordinary least-squares regression line (intercept = 3.19; slope = 1.05; $R^2 = 0.93$; $P < 0.0001$). The thin green lines represent the 95% confidence bounds. The outliers above the 95% confidence limits included primarily patients with a history of stroke or myocardial infarction. These two variables, while heavily weighted in the COSEHC-17 score, were typically unreported in the electronic medical record system and were relatively uncommon even in the complete dataset.

Abbreviation: COSEHC, Consortium for Southeastern Hypertension Control.

Translation of COSEHC scores into probability of cardiovascular death

The distribution of the COSEHC-11 score by decile for the 43,676-member cohort is shown in Table 4. The median (ie, 50th percentile) score is 34, with a range of 0 to 62. The distribution of the estimated COSEHC-17 scores, calculated using the regression coefficients found in the Figure, are also presented, as is the corresponding probability of cardiovascular death. Thus, for the median COSEHC-11 score of 34, which equates to an estimated COSEHC-17 score of 38.92, the cardiovascular death probability is 1.4%. A method for converting both the COSEHC-11 and COSEHC-17 risk scores to cardiovascular death probability is shown in Table 5. Because the data are presented in a tabular form rather than as a continuous function, several closely spaced COSEHC scores may be inferred to yield the same event probability.

Comparison of COSEHC, Framingham, PROCAM, and SCORE (Weibull) risk scores

Table 6 shows a comparison of the COSEHC, Framingham, PROCAM, and high- and low-risk SCORE (Weibull) risk scores calculated for men and women using both the complete and imputed GVRM data cohorts. Because the other three risk indices have different data requirements, the nonimputed sample sizes were smaller for Framingham ($n = 23,683$), PROCAM ($n = 23,840$), and SCORE ($n = 23,787$). For the imputed data cohort, the sample sizes also varied slightly across the Framingham, PROCAM, and COSEHC indices

(Table 6). For all five risk scores, except PROCAM, the average man in the cohort had a higher risk than the average woman. The average Framingham scores reported for the full cohort correspond to a 10-year risk of fatal or nonfatal CHD events of 12.55% for men and 5.90% for women; in the imputed cohort, the risks are 11.93% and 5.47%, respectively. Using the PROCAM score, the probability of fatal or nonfatal CHD events in men was nearly two-fold higher than the probability calculated using the Framingham score, while the predicted risk in women was almost four-fold higher. The SCORE (Weibull) risk score has both a high- and low-risk algorithm, and both scores were calculated for all patients because the exponential functions used in this calculation imply that small changes in certain combinations of variables could create disproportionate changes in the final score. Upon multiple imputation and for both men and women, the 10-year risk of fatal CHD calculated using the SCORE low-risk algorithm is similar to the COSEHC-11 score, which predicts the five-year risk of fatal CHD. When the SCORE high-risk algorithm is used, the risk in men and women is roughly twice that calculated using the COSEHC-11 score (1.9-fold and 1.7-fold, respectively).

Table 7 shows the correlations between each of the five risk scores. The strongest correlations were between the COSEHC-11 and COSEHC-17 scores ($R^2 = 0.93$) and between the SCORE low- and high-risk algorithms ($R^2 = 0.99$). This is as expected because COSEHC-11 and COSEHC-17 and the SCORE algorithms assess the risk of the same endpoints (five-year fatal cardiac events for COSEHC and 10-year fatal cardiac events for SCORE). The correlation between scores that predict the risk of different endpoints was not as high. For example, the correlation between the COSEHC-11 risk score and the Framingham risk score, which assesses the 10-year risk of fatal and nonfatal cardiac events, was only 0.36. Although the Framingham and PROCAM scores both predict the 10-year risk of fatal and nonfatal cardiac events, their correlation was only 0.36. This poor correlation may be due to the fact that the variables included in the risk algorithms are different.

Discussion

In this analysis of 177,404 patients enrolled in the COSEHC GVRM study, 43,676 patients had complete data for all 11 risk factors that comprise the COSEHC-11 cardiovascular risk score, and an additional 26,891 had at least eight of the 11 required variables. The mean COSEHC-11 risk score for the 43,676 patients who had available data for all 11 variables was 31.75. The inclusion of multiple imputations to

Table 4 Translation of COSEHC-11 score to COSEHC-17 score

Percentile	COSEHC-11 score ^a	COSEHC-17 score ^b	Event probability ^c
0	0	3.19	0.04%
10	14	17.91	0.19%
20	21	25.26	0.51%
30	27	31.57	0.84%
40	31	35.77	1.40%
50	34	38.92	1.40%
60	36	41.03	2.30%
70	40	45.23	3.70%
80	42	47.33	3.70%
90	44	49.43	3.70%
100	62	68.35	24.50%

Notes: Given there are 43,676 patients with all data necessary to calculate the COSEHC-11 risk score, there are approximately 4367 patients per decile (eg, 4367 patients between percentiles 0 and 10). ^aCalculated for the 43,676 patients with complete COSEHC-11 data; ^bCalculated using the results of the logistic regression model ($\text{COSEHC-17} = 3.19480 + 1.05084 * \text{COSEHC-11}$); ^cFive-year risk of fatal coronary heart disease events.

Abbreviation: COSEHC, Consortium for Southeastern Hypertension Control.

Table 5 Event probabilities associated with ranges of COSEHC-11 and COSEHC-17 scores

COSEHC-17 lower bound		COSEHC-17 upper bound	Event probability ^a	Range	COSEHC-11 lower bound		COSEHC-11 upper bound	Event probability ^a	Range
0.00	to	4.99	0.04%	4.99	-3.04	to	1.71	0.04%	4.75
5.00	to	9.99	0.07%	4.99	1.72	to	6.47	0.07%	4.75
10.00	to	14.99	0.11%	4.99	6.48	to	11.22	0.11%	4.75
15.00	to	19.99	0.19%	4.99	11.23	to	15.98	0.19%	4.75
20.00	to	24.99	0.31%	4.99	15.99	to	20.74	0.31%	4.75
25.00	to	29.99	0.51%	4.99	20.75	to	25.50	0.51%	4.75
30.00	to	34.99	0.84%	4.99	25.51	to	30.26	0.84%	4.75
35.00	to	39.99	1.40%	4.99	30.27	to	35.01	1.40%	4.75
40.00	to	44.99	2.30%	4.99	35.02	to	39.77	2.30%	4.75
45.00	to	49.99	3.70%	4.99	39.78	to	44.53	3.70%	4.75
50.00	to	54.99	6.10%	4.99	44.54	to	49.29	6.10%	4.75
55.00	to	59.99	9.80%	4.99	49.30	to	54.05	9.80%	4.75
60.00	to	64.99	15.60%	4.99	54.06	to	58.81	15.60%	4.75
65.00	to	69.99	24.50%	4.99	58.82	to	63.56	24.50%	4.75
70.00	and up		37.90%		63.57	and up		37.90%	

Note: ^aProbability of fatal cardiovascular event over five years.

Abbreviation: COSEHC, Consortium for Southeastern Hypertension Control.

account for missing data points had a minimal impact on the mean COSEHC-11 risk score for the 70,567 patients who had at least eight of the 11 variables. In addition, linear regression analysis showed that the COSEHC-11 score was a significant predictor of the original, more comprehensive COSEHC-17 score. The high degree of correlation between the COSEHC-11 and 17 scores suggests that the simpler COSEHC-11 score is just as effective at predicting cardiovascular risk as the COSEHC-17 score, and can therefore be used to predict cardiovascular morbidity and mortality in patients whose electronic medical record may be lacking data for all 17 variables. Calculation of the Framingham, PROCAM, and high- and low-risk SCORE (Weibull) risk scores revealed that, for all but the PROCAM score, men have a higher predicted risk than women.

Aside from assessing achievement of COSEHC-recommended treatment goals and providing participating centers with benchmarking reports, one of the objectives of the GVRM study is to analyze the correlation between the COSEHC, Framingham,¹² PROCAM,²⁰ and SCORE (Weibull)²¹ coronary risk scores and the time to the first fatal (COSEHC, Framingham, PROCAM, and SCORE) or non-fatal (Framingham and PROCAM) coronary event over the five-year study duration to determine which score is most predictive for patients in the southeastern US. Although no single risk score is likely to be perfectly correlated with outcomes in all populations due to inherent variability, it is desirable to determine which score is most predictive for the majority of situations in a given population. Data suggest that the Framingham coronary risk score tends to overestimate risk,

Table 6 Cardiovascular event probability calculated using the COSEHC-11, Framingham, PROCAM, and SCORE (Weibull) risk scores

	Framingham ^a	PROCAM ^a	SCORE ^b low-risk	SCORE ^b high-risk	COSEHC-11 ^c
No imputation					
Men, n	11,006	11,163	11,136	11,136	16,951
Probability	12.55 (7.74)	20.07 (20.68)	2.48 (2.62)	4.96 (4.96)	3.15 (2.05)
Women, n	12,677	12,677	12,651	12,651	26,725
Probability	5.90 (5.84)	20.19 (22.22)	1.63 (2.31)	2.76 (3.76)	1.62 (1.81)
Multiple imputation^d					
Men, n	31,825	32,329	32,082	32,082	32,329
Probability	11.93 (7.79)	19.75 (21.52)	2.54 (2.86)	5.07 (5.38)	2.68 (2.06)
Women, n	38,238	38,238	38,013	38,013	38,238
Probability	5.47 (5.69)	19.68 (22.64)	1.62 (2.42)	2.75 (3.93)	1.65 (1.81)

Notes: All scores are presented as mean (standard deviation). ^aPredicts 10-year risk of fatal or nonfatal CHD events; ^bPredicts 10-year risk of fatal CHD events; ^cPredicts five-year risk of fatal CHD events; ^dAccounts for missing laboratory data from random visits using the Markov chain Monte Carlo method.

Abbreviations: CHD, coronary heart disease; COSEHC, Consortium for Southeastern Hypertension Control; PROCAM, Prospective Cardiovascular Münster; SCORE, Systemic Coronary Risk Evaluation.

Table 7 Correlation between the COSEHC-11, COSEHC-17, Framingham, PROCAM, and SCORE (low- and high-risk algorithms) risk scores

	COSEHC-11 ^a	COSEHC-17 ^a	Framingham ^b	PROCAM ^b	SCORE (Weibull) ^c low-risk	SCORE (Weibull) ^c high-risk
COSEHC-11 ^a	1.00					
COSEHC-17 ^a	0.93	1.00				
Framingham ^b	0.36	0.35	1.00			
PROCAM ^b	0.37	0.39	0.36	1.00		
SCORE (Weibull) ^c low-risk	0.52	0.49	0.15	0.27	1.00	
SCORE (Weibull) ^c high-risk	0.52	0.48	0.11	0.24	0.99	1.00

Notes: Correlation was calculated using multiple regression analysis. ^aPredicts the five-year risk of fatal CHD events; ^bPredicts the 10-year risk of fatal and nonfatal CHD events; ^cPredicts the 10-year risk of fatal CHD events.

Abbreviations: CHD, coronary heart disease; COSEHC, Consortium for Southeastern Hypertension Control; PROCAM, Prospective Cardiovascular Münster; SCORE, Systemic Coronary Risk Evaluation.

particularly in nonwhite populations due to the derivation of the score from a primarily white cohort.^{12,13,16–19,29–31} Although the PROCAM and SCORE (Weibull) coronary risk scores were partly developed to address the limitations of the Framingham cardiovascular risk score, external validation data suggest that the PROCAM and SCORE (Weibull) risk scores also tend to overestimate coronary risk.^{18,19,31–33}

In the current era of rising health care costs and the increased pressure to provide adequate health care coverage for all persons, it is important to identify a patient's true risk of coronary events correctly. For example, if a risk score systematically overestimates cardiovascular risk, then health care resources will be unnecessarily used and patients may be exposed to potentially unnecessary treatments.²⁹ Conversely, if a risk score systematically underestimates cardiovascular risk, patients will be less likely to receive appropriate treatment, and resource utilization may increase due to the occurrence of more acute events. Thus, identification of a region-specific, accurate coronary risk score is desirable.

A unique aspect of the COSEHC GVRM study is the use of electronic medical records and the ease of data collection and validation. Using data from the patient's actual medical record and not that recorded on a study-specific report form is more representative of the care patients receive in the "real world." Another strength of the COSEHC GVRM study is that it includes only patients enrolled at COSEHC Centers of Excellence. Thus, it provides a unique tool for directly assessing the population living in the southeastern US, which has a different racial and ethnic composition compared with other areas of the US.

The COSEHC GVRM study does have several limitations. Although not proven, physicians at COSEHC Centers of Excellence may provide better care for their patients,

and thus, the risk observed in the GVRM study cohort may underestimate the risk observed in the general population. This possibility is reflected in the high frequency of patients with controlled blood pressure (mean systolic blood pressure of 129 ± 17 mmHg) and lipid levels (mean plasma total cholesterol 4.8 ± 1.1 mmol/L [184 ± 42 mg/dL], HDL-C 1.2 ± 0.3 mmol/L [47 ± 13 mg/dL], and triglyceride levels 1.7 ± 1.0 mmol/L [151 ± 87 mg/dL]) at study baseline. The ability to obtain certain patient demographics and clinical history variables from electronic medical records, including ethnicity, premature family CHD, history of LVH, smoking, and diabetes, can be difficult and is dependent on the electronic medical record system design, the effort of clinicians to report patient history, and, in some cases, the ability and willingness of patients to self-report history and demographic data. For example, family CHD history and LVH history are difficult to observe because they are not represented by an ICD-9 code and may only appear in a free-text comment area. Furthermore, the lack of a standardized definition of history of premature family CHD among providers, and it not being considered clinically important for older patients, suggests it may go unreported. In addition, while performance of echocardiography is typically reported in an electronic medical record, the objective test results defining LVH are not always included. Finally, as is true for any nonrandomized registry study, the influence of recruitment bias cannot be known.

In conclusion, these baseline data from the COSEHC GVRM study show there is excellent correlation between the original COSEHC-17 and the modified COSEHC-11 cardiovascular risk scores ($P < 0.0001$; $R^2 = 0.93$). Follow-up data collected over the next five years will demonstrate the predictive ability of the COSEHC cardiovascular risk score

relative to the more widely used Framingham, PROCAM, and SCORE (Weibull) risk scores among patients in the southeastern US.

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Disclosure

The authors report no conflicts of interest in this work.

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