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Interpreting Hemoglobin A1C in Combination With Conventional Risk Factors for Prediction of Cardiovascular Risk

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Abstract

Background—Hemoglobin A1C (HbA1C) is associated with increased risk of cardiovascular events, but its use for prediction of cardiovascular disease (CVD) events in combination with conventional risk factors has not been well defined.

Methods and Results—To understand the effect of HbA1C on CVD risk in the context of other CVD risk factors, we analyzed HbA1C and other CVD risk factor measurements in 2000 individuals aged 40-79 years old without pre-existing diabetes or cardiovascular disease from the 2011-2012 NHANES survey. The resulting regression model was used to predict the HbA1C distribution based on individual patient characteristics. We then calculated post-test 10-year atherosclerotic cardiovascular disease (ASCVD) risk incorporating the actual versus predicted HbA1C, according to established methods, for a set of example scenarios. Age, gender, race/ethnicity and traditional cardiovascular risk factors were significant predictors of HbA1C in our model, with the expected HbA1C distribution being significantly higher in non-Hispanic black, non-Hispanic Asian and Hispanic individuals than non-Hispanic white/other individuals. Incorporating the expected HbA1C distribution into pretest ASCVD risk has a modest effect on post-test ASCVD risk. In the patient examples we assessed, having an HbA1C < 5.7% reduced post-test risk by 0.4%-2.0% points, whereas having an HbA1C ≥ 6.5% increased post-test risk by 1.0%-2.5% points, depending on the scenario. The post-test risk increase from having an HbA1C ≥ 6.5 % tends to approximate the risk increase from being five years older in age.

Conclusions—HbA1C has modest effects on predicted ASCVD risk when considered in the context of conventional risk factors.

Keywords

cardiovascular risk factors; cardiovascular disease prevention; hemoglobin A1C; primary prevention

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Prediction of cardiovascular disease (CVD) risk is important for clinical decision making, including whether or not to prescribe risk-reducing therapies such as statins or aspirin. Despite identification of novel, independent markers of risk, established risk prediction algorithms continue to rely on a set of conventional factors (age, gender, blood pressure, lipid levels, and smoking)(1). How to decide whether or not to include novel risk markers in risk assessment remains a topic of intense debate and research (1, 2).

One of the most contentious debates in CVD risk prediction centers around whether or not to incorporate a measure of glycemia, such as hemoglobin A1C (HbA1C), fasting glucose, or clinical diagnosis of diabetes (3, 4, 5). Blood glucose levels are clearly associated with CVD risk, including values that fall below the range that defines the presence of diabetes (4). In the most recent cardiovascular risk prediction equations, the "Pooled Cohort Risk Equations," released by the AHA/ACC in 2013, clinical diagnosis of diabetes, but not levels of glycemia, is incorporated (1). Actual levels of glycemia, as measured by HbA1C testing, may be a more precise measure of such risk and may be important even in individuals without diabetes. Accurately incorporating HbA1C into established risk prediction algorithms and interpreting the results, however, requires knowledge of the expected distribution of HbA1C, conditional on other CVD risk factors and demographic characteristics; post-test risk is increased more when the HbA1C value is higher than expected, and vice-versa (6).

We have previously developed methods to allow accurate assessment of the effect of incorporating another non-traditional CVD risk factor, coronary artery calcium, in the context of conventional risk factors (7). In our present study, we use similar methods to model the expected distribution of HbA1C in individuals without diabetes or cardiovascular disease, based on traditional cardiovascular disease risk factors, as well as race/ethnicity. We then demonstrate, using an Excel-based tool that integrates a patient's expected HbA1C distribution and their pretest 10-year ASCVD risk, how such information can be used to calculate 10-year ASCVD risk that incorporates HbA1C.

Methods

To understand the effects of HbA1C measurement on predicted CVD risk in the context of other CVD risk factors, we developed a linear regression model for expected HbA1C using gender, race/ethnicity and other traditional cardiovascular risk factors in the 2011-2012 National Health and Nutrition Examination Surveys (NHANES) sample. We then used the coefficient estimates from the model to establish a prediction equation, which allows calculation of the expected HbA1C distribution based on an individual patient's characteristics. Finally, we examined the impact of expected HbA1C distribution on 10-year ASCVD risk by calculating a post-test ASCVD risk estimate that incorporates the expected HbA1C distribution for an individual patient.

Study sample

NHANES is a stratified, multistage probability sample of the civilian, non-institutionalized U.S. population that includes an interview component (questionnaire data) and laboratory

examination. The National Center for Health Statistics (NCHS), a branch of the Centers for Disease Control and Prevention, releases data from the continuous NHANES in 2-year cycles. NHANES protocols are approved by the NCHS institutional review board and informed consent is received from all participants.

We used the data released for the 2011-2012 2-year survey period in this analysis. We limited our population to 2000 non-pregnant individuals aged 40 to 79 years who were not missing data on HbA1C, systolic blood pressure, total cholesterol, HDL cholesterol, smoking or hypertension treatment status. We also excluded those who self-reported a previous diagnosis of diabetes, congestive heart failure, coronary artery disease, angina, heart attack, or stroke. We used svy commands in Stata, along with the examination sample weights, to account for the complex survey design of NHANES. Standard errors were estimated with Taylor series linearization.

Measurement of HbA1C and CVD risk factors

Hemoglobin A1C was measured in venous whole blood specimens and processed using high-performance liquid chromatography on either the Tosoh G7 Automated HPLC Analyzer at the Fairview-University Medical Center in Minneapolis, MN or the Tosoh Automated Analyzer HLC-723G8 at the University of Missouri-Columbia (Tosoh Medics, Inc., San Francisco, CA). Total cholesterol and HDL-cholesterol were measured in blood serum specimens and processed using a Roche/Hitachi Modular P Chemistry Analyzer (Roche Diagnostics, Indianapolis, IN). Average systolic blood pressure was defined as the average of three consecutive systolic blood pressure measurements. If one of the three initial systolic blood pressure readings was missing, the fourth measurement was used for calculation of the average. The methods used for data collection and processing are described in detail in the examination and laboratory procedure manuals available on the NHANES website.

Current hypertensive medication use and smoking status were determined using the Blood Pressure, Cholesterol and Smoking-Cigarette Use questionnaire data. Participants that self-reported taking prescribed medication for high blood pressure were defined as being on hypertensive medication and participants that self-reported smoking within the past 30 days were defined as current smokers.

Racial/ethnic demographic information was available in six categories: “Mexican-American”, “Other Hispanic”, “Non-Hispanic White”, “Non-Hispanic Black,” “Non-Hispanic Asian” and “Other- Including Multi-racial.” We combined the categories “Mexican-American” and “Other Hispanic” to create the group “Hispanic.” The category “Other- Including Multi-racial” contained 44 individuals, so we included those individuals in the “Non-Hispanic White” category and renamed it “Non-Hispanic White/Other” for the summary statistics and regression analysis.

Regression analysis and model selection

We used linear regression analysis to model the expected distribution of HbA1C within the analytic population. We specified a set of candidate predictor variables from the information that a primary care provider would have available to calculate predicted 10-year ASCVD

risk. Thus, our set of candidate predictor variables included age, gender, race/ethnicity, total cholesterol, HDL cholesterol, systolic blood pressure, smoking status and hypertension treatment status.

Given the large number of potential interaction terms and functional forms of our candidate predictor variables, we chose to use an unbiased model selection process with 10-fold cross-validation (8, 9, 10) that tested models with all possible combinations of predictors, with up to 2 pairwise interactions (0, 1 or 2) and up to 1 quadratic term (0 or 1) for each continuous variable. For example, a model could either exclude or include age as a linear term (*0*age or 1*age*), and could include interaction terms with any or all of the other predictor variables (age*total cholesterol, age*HDL cholesterol, age*systolic blood pressure, age*current smoker, age*male, age*Hispanic, age*non-Hispanic black, age*non-Hispanic Asian, age*hypertension medication). Finally, a model could also include a quadratic term for a given predictor variable (*age*age*).

We assessed model performance using the cross-validated R^2 and identified the top twenty models. The cross-validated R^2 is preferable to the unadjusted R^2 because adding predictor variables will not automatically cause an increase in the value of the statistic; this allows us to compare the performance of models with different total numbers of predictor variables. Furthermore, the cross-validation process utilizes subsets of the data as "training sets" to calculate many sets of coefficient estimates (in our case, ten sets) and then compares each set of predicted HbA1C values (from the ten sets of coefficient estimates) to actual HbA1C values in an unused subset of the data (the "validation set"). The cross-validated R^2 will increase as the correlation between average predicted HbA1C values and the actual HbA1C values increases, but will be subject to a penalty if the variation in predicted HbA1C values across the training sets is large. The cross-validated R^2 and coefficient estimates for the final model are presented in the results section. We also show two alternate models for the sake of comparison: one with demographic variables (age, gender and race/ethnicity) as the only predictors and one with 10-year ASCVD risk as the sole predictor of expected HbA1C.

We then calculated the estimated prevalence of HbA1C in the categories <5.7%, 5.7 to <6.5%, and ≥6.5% using the final model's regression coefficients. These categories represent the generally accepted clinical definitions of normal HbA1C (<5.7%), pre-diabetes or borderline diabetes (5.7% to <6.5%), and frank diabetes mellitus (≥6.5%).

In the final step of our analysis we combined "pretest" 10-year ASCVD risk and expected HbA1C distribution to yield a single post-test risk for each HbA1C category. We calculated 10-year ASCVD risk for all individuals in our sample using the 2013 ACC/AHA Pooled Cohort Risk Equations and defined this as the "pretest risk." In order to calculate the post-test risk, we assumed that the pretest risk represented an average of people with different HbA1C scores, weighted by the probability of having an HbA1C value in each category. The relative risks in each HbA1C category were assumed to differ according to adjusted hazard ratio estimates from Emerging Risk Factors Collaboration (4): HbA1C <5.7%: 1.0 (reference category); 5.7% to <6.5%: 1.25; and ≥6.5%: 1.43. These hazard ratios were adjusted for age, gender, smoking status, systolic blood pressure, total cholesterol and HDL cholesterol.

We present the post-test risk for a selection of individuals with varying demographic and clinical profiles. For interested readers, we created an Excel-based calculator to calculate pretest 10-year ASCVD risk (using the Pooled Cohort equations), expected HbA1C distribution and post-test 10-year ASCVD risk for patients with a set of user-defined inputs, including age, gender, race/ethnicity, systolic blood pressure, total cholesterol, HDL cholesterol, current smoking and hypertension treatment status.

Results

Of the 9756 total NHANES participants, 7,388 were excluded based on age (< 40 years or > 79 years), confirmed pregnancy, history of congestive heart failure, coronary artery disease, angina, stroke, or diabetes mellitus. Another 368 were excluded due to missing HbA1C or other input data used in the calculation of ASCVD risk, leaving an analysis sample of 2000 participants. Of these, 52% female, 20.8% Hispanic, 39.3% non-Hispanic white/other, 26% non-Hispanic African-American, and 14% non-Hispanic Asian. Both HbA1c values and other risk factor levels differed across race/ethnicity and gender (Table 1). The proportion of individuals with HbA1C ≥6.5% is also shown in Table 1 to highlight the possible cases of undiagnosed diabetes stratified by race/ethnicity and gender. In this analytic population of non-diabetic individuals, non-Hispanic black females and males have the highest proportion of individuals with HbA1C ≥6.5% at 7.6% and 6.7%, respectively.

We examined the top twenty models (ranked by cross-validated R^2) chosen through the unbiased model selection process. The predictor variables age, systolic blood pressure, total cholesterol, HDL cholesterol, and race/ethnicity (Hispanic, non-Hispanic black, and non-Hispanic Asian indicators) appeared in all top twenty models. Of note, current hypertension treatment was not a significant predictor of HbA1C distribution in any of the top twenty models. The “cross-validation selector”, or the top performing model, included the predictor variables age, systolic blood pressure, total cholesterol, HDL cholesterol, race/ethnicity, gender, HDL^2, and the interaction terms age*total cholesterol and HDL*non-Hispanic Asian. However, for the sake of parsimony, we have chosen to present a model without quadratic or interaction terms as our final model (Table 2). Although gender and smoking status did not appear in all top twenty models, we chose to include them in the final model for consistency with the cardiovascular risk prediction equations.

We have included an online appendix containing the coefficient estimates for all top twenty models for the convenience of readers (Appendix A, Tables 1-2). We created a worksheet in the Excel-based calculator that uses the “cross-validation selector” coefficients, instead of the “final model” coefficients, to calculate expected HbA1C prevalence and post-test ASCVD risk. In addition, we have included a worksheet that contains a side-by-side comparison of the “final model” and “cross-validation selector” predictions of expected HbA1C and post-test ASCVD risk.

The final model included age, gender, race/ethnicity, current smoking, systolic blood pressure, total cholesterol, and HDL cholesterol as significant predictors of HbA1C (Table 2; cross-validated R^2 of 0.0735). The race/ethnicity variables Hispanic, non-Hispanic black and non-Hispanic Asian were significant predictors of increased HbA1C. ASCVD risk alone

was a significant predictor of HbA1C but explained very little variation in HbA1C (Table 2; cross-validated R^2 of 0.0174). The model that included only age, gender and race/ethnicity as predictor variables also explained little variation in HbA1C compared to the final model (Table 2; cross-validated R^2 of 0.0235).

Using the final model, we find that expected HbA1C distribution has a modest effect on post-test ASCVD risk in patients with intermediate pretest ASCVD risk (Table 3). Individuals in racial/ethnic groups with higher expected HbA1C distributions had lower elevations in post-test risk with an HbA1C measurement of ≥ 6.5% compared to non-Hispanic white/other individuals (shaded rows); for example, Patients 2 and 3 in Table 3 both had an increase of 1.7 percentage points in post-test risk with an HbA1C ≥ 6.5% (relative increase of 23%). In comparison, Patient 1's post-test risk was raised 2.0 percentage points with an HbA1C ≥ 6.5% (relative increase of 27%). Although the expected distribution of HbA1C was much higher for non-Hispanic Asian, non-Hispanic black and Hispanic patients (e.g. Patients 2-4), the resulting post-test risk was similar to that of non-Hispanic white patients (e.g. Patient 1). Patient 4 has the same clinical profile as Patients 1-3, but has a higher pretest risk due to the use of different Pooled Cohort equations for non-Hispanic black individuals (1). While the pretest risk is substantially higher for Patient 4 compared to Patients 1-3, the expected HbA1C distribution is comparable to Patient's 2 and 3. A clinical profile with values within normal ranges (total cholesterol/HDL cholesterol: 195/55 mg/dL; systolic blood pressure: 135 mmHg) was chosen to demonstrate the elevated pretest risk, expected HbA1C and post-test risk in individuals who may not have been previously considered for ASCVD primary prevention.

Increasing age was a strong predictor of increased expected HbA1C. Table 4 illustrates the effect of age on pretest risk, expected HbA1C and post-test risk using an example patient profile with age ranging from 45 years to 75 years in increments of 5. In this patient profile, having an HbA1C ≥ 6.5% results in a post-test risk that is approximately equivalent to the pretest risk of an identical patient five years older in age. For example, clinical scenario 2 (age 50) results in a post-test risk of 6.0% with an HbA1C ≥ 6.5% (relative increase of 28%); subsequently, clinical scenario 3 (age 55) results in a pretest risk of 6.0%, which is a 28% increase from the pretest risk in clinical scenario 2 (4.7%). This holds true through the entire age range.

Discussion

We have shown that the expected HbA1C distribution varies based on individual clinical characteristics and that incorporating the predicted HbA1C distribution has a modest effect on post-test 10-year ASCVD risk. As expected, age, gender and other conventional CVD factors were important in predicting the expected distribution of HbA1C; however, higher ASCVD risk does not necessarily correlate with higher expected HbA1C and vice versa. Integrating information from HbA1C with information from other CVD risk factors helps understand the implications of using this measurement for risk prediction; from our investigations, the post-test risk increase from having an HbA1C ≥ 6.5 % tends to approximate the risk increase from being five years older in age.

Our analysis is an intermediate step towards the larger goal of evaluating the clinical utility of HbA1C measurement for cardiovascular risk assessment. Although we found only modest effects on predicted risk and a high-quality meta-analysis found only small improvements in the C-statistic and integrative discrimination index and no change in net reclassification improvement (4), these measures alone are unable to fully evaluate for the clinical utility of HbA1C. Such an evaluation will require use of a decision-analytic framework that assess the costs, risks, and benefits by taking into account the cost of obtaining the additional information, health impact (e.g. incidence and severity of the disease or quality of life) and clinical decisions that might change with measurement of the risk factor (e.g. preventative therapies or treatments) (11). Hemoglobin A1C testing is inexpensive and has few direct adverse effects, so it is possible that even small changes in risk prediction may be valuable enough to warrant measurement; our next step is to perform such modeling, as we have done previously for coronary artery calcium scanning (12).

Results of cost-effectiveness analyses are often highly sensitive to changes in underlying population prevalence of a biomarker or condition, especially when evaluating screening or primary prevention strategies (6, 12). Furthermore, prevalence of biomarkers often varies between subpopulations, whether those are defined by demographic variables such as race/ethnicity and age, or a cluster of clinical characteristics, such as individuals with metabolic syndrome. Therefore, it is important for modelers to build in these subpopulation differences in biomarker prevalence in order to obtain valid model outputs. The results we have presented here represent a necessary intermediate step prior to conducting these more comprehensive analyses assessing the utility of HbA1C testing in ASCVD primary prevention as well as the larger question of universal screening for abnormal blood glucose levels.

Previous studies have observed differences in average HbA1C levels between non-Hispanic whites, non-Hispanic blacks and Hispanic-Americans, specifically Mexican-Americans (13, 14, 15). In a longitudinal analysis of the ARIC cohort, Selvin et al. observed elevated baseline HbA1C in blacks compared to whites and found that HbA1C was an equally strong predictor of cardiovascular outcomes for blacks and whites (13). Hispanic and non-Hispanic Asian populations have similarly elevated population HbA1C levels, but the connection between increased HbA1C and ASCVD outcomes has not been well-defined in population cohort studies in the United States. In the interim, non-traditional CVD biomarkers with expected distributions that vary across racial/ethnic groups can be combined, using our approach, with pretest estimates from established risk prediction models to help improve individualization of risk estimation in less well-studied populations.

A limitation of our analysis is the cross-sectional nature of NHANES, such that our predicted risk calculations rely on hazard ratios derived from a meta-analysis of 24 studies, 101,280 participants and 4,267 CVD cases and are adjusted for age, gender, smoking status, systolic blood pressure, total cholesterol and HDL cholesterol (4). We believe that they represent the most accurate reflection of the average increase in ASCVD risk associated with increased HbA1C currently available; however, if new evidence shows different relationships between HbA1C and ASCVD outcomes in non-Hispanic Asian or Hispanic

populations, our model could be updated to include different hazard ratios for these populations.

We tailored our analysis to the parameters used to establish the Pooled Cohort Equations. We only included individuals aged 40 to 79 years in our sample; therefore, the tool should not be used in individuals of other ages, especially adults aged 20-39 years, in whom characteristics other than age and race/ethnicity may play a larger role in expected HbA1C distribution.

Similarly, we did not examine the role of lipid-lowering medication in the relationship between CVD risk factors and expected HbA1C distribution because this is not considered a traditional CVD risk factor. Recent analyses suggest a small but significant increase in HbA1C and incident diabetes in individuals treated with statins (16, 17). A potential next step could be to expand our analysis to examine the impact of statin treatment on the prognostic value of A1C testing.

In conclusion, the results presented in this analysis represent a necessary intermediate step prior to conducting a full cost-effectiveness analysis of HbA1C testing in ASCVD primary prevention. Although the costs of HbA1C testing are low and potential consequences of testing appear benign, the net comparative effectiveness and efficiency (cost-effectiveness) of this approach for guiding HbA1C testing has not been proven. Future randomized, controlled trials of an integrated screening and targeted prevention strategy or careful modeling of expected benefits, harms, and costs are necessary to fully assess the potential implications of this strategy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Characteristics of 2011-2012 NHANES study participants

	Male (n=969)				Female (n=1031)			
	Hispanic (n=212)	**NH* White/Other (n=380)**	**NH Black (n=240)**	**NH Asian (n=137)**	**Hispanic (n=204)**	**NH White/Other (n=405)**	**NH Black (n=280)**	**NH Asian (n=142)**
Age (years)	51.0 ± 9.3	54.3 ± 9.5	54.0 ± 9.1	52.2 ± 9.6	52.4 ± 9.7	56.0 ± 10.2	52.6 ± 9.1	53.7±9.7
SBP (mmHg)*	125 ± 15	124 ± 15	130 ± 18	124 ± 16	121 ± 17	122 ± 16	126 ± 20	123±16
TC (mg/dL)*	202 ± 41	203 ± 39	194 ± 37	201 ± 35	207 ± 37	215 ± 39	206 ± 39	204 ± 38
HDL (mg/dL)*	45 ± 12	49 ± 14	52 ± 15	47 ± 13	55 ± 13	61 ± 17	62 ± 18	59 ± 13
Smoker (%)‡	24 ± 3	24 ± 2	29 ± 2	15 ± 3	8 ± 2	16 ± 2	18 ± 3	2 ± 1
HTN meds (%)‡	16 ± 3	24 ± 2	32 ± 2	18 ± 4	19 ± 3	26 ± 3	38 ± 3	15 ± 2
10-yr ASCVD risk (%)	7.5 ± 7.8	8.6 ± 7.1	10.2 ± 7.4	7.6 ± 7.8	3.9 ± 7.2	5.0 ± 6.5	5.3 ± 6.1	3.8 ± 6.5
HbA1C (%)	5.7 ± 0.9	5.5 ± 0.6	5.7 ± 0.8	5.7 ± 0.7	5.7 ± 0.6	5.5 ± 0.4	5.7 ± 0.7	5.7 ± 0.9
Individuals with HbA1C ≥ 6.5% (%) ‡	4.6 ± 0.01	3.7 ± 0.01	6.7 ± 0.01	5.7± 0.01	5.6± 0.01	2.7 ± 0.01	7.6± 0.02	4.3± 0.01

Values are means ± standard deviation (except where otherwise noted)

*NH, Non-Hispanic; SBP, systolic blood pressure; TC, total cholesterol; HDL, high-density lipoprotein cholesterol

‡current smoker, hypertension medication (HTN), and proportion of individuals with HbA1C ≥ 6.5% are prevalence estimates ± linearized standard errors

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Table 2

Predictors of HbA1C

Model Predictors	ASCVD risk only	Demographic predictors only	Final model
	Coefficient (95% CI)*	**Coefficient (95% CI)***	**Coefficient (95% CI)***
Pretest ASCVD risk	**1.48** (1.15, 1.80)		
Age, per 10 years		**0.091** (0.059, 0.124)	**0.102** (0.072, 0.132)
Hispanic‡		**0.207** (0.097, 0.316)	**0.186** (0.072, 0.300)
Non-Hispanic black‡		**0.209** (0.094, 0.324)	**0.223** (0.112, 0.334)
Non-Hispanic Asian‡		**0.214** (0.060, 0.367)	**0.226** (0.007, 0.380)
Male (1=Yes)		**0.046** (−0.036, 0.127)	**−0.043** (−0.112, 0.026)
Current Smoker (1=Yes)			**0.112** (−0.010, 0.235)
SBP, per 10 mmHg			**0.022** (0.001, 0.043)
TC, per 10 mg/dL			**0.016** (0.009, 0.023)
HDL, per 10 mg/dL			**−0.076** (−0.106, −0.047)
Constant	**5.46** (5.40, 5.52)	**4.98** (4.78, 5.19)	**4.76** (4.54, 4.98)
Cross-validated R^2	**0.0174**	**0.0235**	**0.0735**

The standard deviation of the residuals for the final model is 0.63995.

*Standard errors and 95% confidence intervals (CI) calculated using Taylor series linearization method

‡vs. non-Hispanic white/other (reference category)

Table 3

Effect of race/ethnicity on expected HbA1C and post-test 10-year ASCVD risk

Clinical scenario	Age (years)	Race/ ethnicity	Gender	Smoker?	TC/HDL (mg/dL)	SBP (mmHg)	Pretest ASCVD risk	HbA1C category	Proportion in HbA1C category	Post-test ASCVD risk
1	67	***Non-Hispanic white/other***	Female	Non-smoker	195/55	135 mmHg (untreated)	7.5 %	<5.7 %	0.54	6.7 %
								5.7 to <6.5 %	0.37	8.3 %
								≥6.5 %	0.09	9.5 %
2	67	***Hispanic***	Female	Non-smoker	195/55	135 mmHg (untreated)	7.5 %	<5.7 %	0.43	6.4 %
								5.7 to <6.5 %	0.43	8.1 %
								≥6.5 %	0.14	9.2 %
3	67	***Non-Hispanic Asian***	Female	Non-smoker	195/55	135 mmHg (untreated)	7.5 %	<5.7 %	0.40	6.4 %
								5.7 to <6.5 %	0.44	8.0 %
								≥6.5 %	0.16	9.2 %
4	67	***Non-Hispanic black***	Female	Non-smoker	195/55	135 mmHg (untreated)	10.2 %*	<5.7 %	0.40	8.6 %
								5.7 to <6.5 %	0.44	10.8 %
								≥6.5 %	0.16	12.4 %

* The different pretest 10-year ASCVD risk for the non-Hispanic black patient reflects the use of different ASCVD prediction equations for non-Hispanic black females and non-Hispanic white/other females.

Table 4

Effect of age on expected HbA1C distribution, pretest and post-test 10-year ASCVD risk

Clinical scenario	Age (years)	Race/ ethnicity	Gender	Smoker?	TC/HDL (mg/dL)	SBP (mmHg)	Pretest ASCVD risk	HbA1C category	Proportion in HbA1C category	Post-test ASCVD risk
1	***45***	NHB*	Male	Non-smoker	200/50	120 mmHg (untreated)	***3.7 %***	<5.7%	0.56	3.3 %
								5.7 to <6.5%	0.36	4.1 %
								≥6.5%	0.08	4.7 %
2	***50***	NHB	Male	Non-smoker	200/50	120 mmHg (untreated)	***4.7 %***	<5.7%	0.53	4.2 %
								5.7 to <6.5%	0.38	5.2 %
								≥6.5%	0.09	6.0 %
3	***55***	NHB	Male	Non-smoker	200/50	120 mmHg (untreated)	***6.0 %***	<5.7%	0.50	5.2 %
								5.7 to <6.5%	0.39	6.5 %
								≥6.5%	0.11	7.4 %
4	***60***	NHB	Male	Non-smoker	200/50	120 mmHg (untreated)	***7.3 %***	<5.7%	0.47	6.3 %
								5.7 to <6.5%	0.41	7.9 %
								≥6.5%	0.12	9.1 %
5	***65***	NHB	Male	Non-smoker	200/50	120 mmHg (untreated)	***8.9 %***	<5.7%	0.43	7.6 %
								5.7 to <6.5%	0.43	9.5 %
								≥6.5%	0.14	10.9 %
6	***70***	NHB	Male	Non-smoker	200/50	120 mmHg (untreated)	***10.6 %***	<5.7%	0.40	9.0 %
								5.7 to <6.5%	0.44	11.2 %
								≥6.5%	0.16	12.8 %

Clinical scenario	Age (years)	Race/ ethnicity	Gender	Smoker?	TC/HDL (mg/dL)	SBP (mmHg)	Pretest ASCVD risk	HbA1C category	Proportion in HbA1C category	Post-test ASCVD risk
7	***75***	NHB	Male	Non-smoker	200/50	120 mmHg (untreated)	***12.4 %***	<5.7%	0.37	10.4 %
								5.7 to <6.5%	0.45	13.0 %
								≥6.5%	0.18	14.9 %

* Non-Hispanic black