SUPPLEMENTAL MATERIAL

1) Supplemental Figure

2) Excel tool screenshots

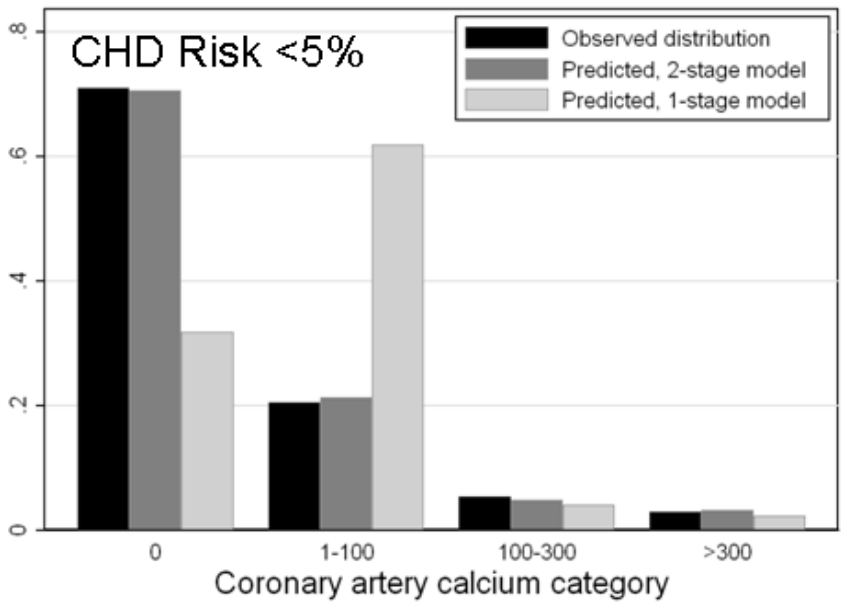
3) Supplemental Table 1

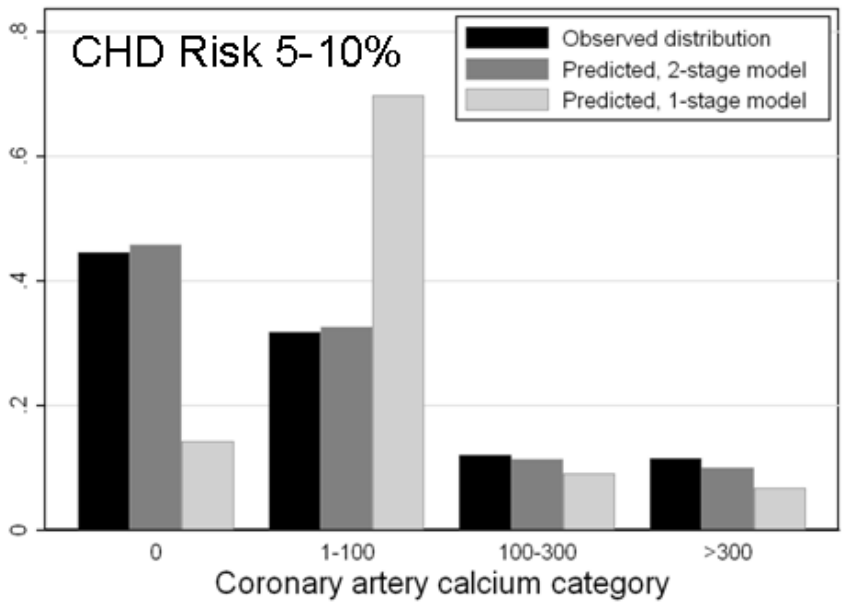
4) Supplemental Table 2

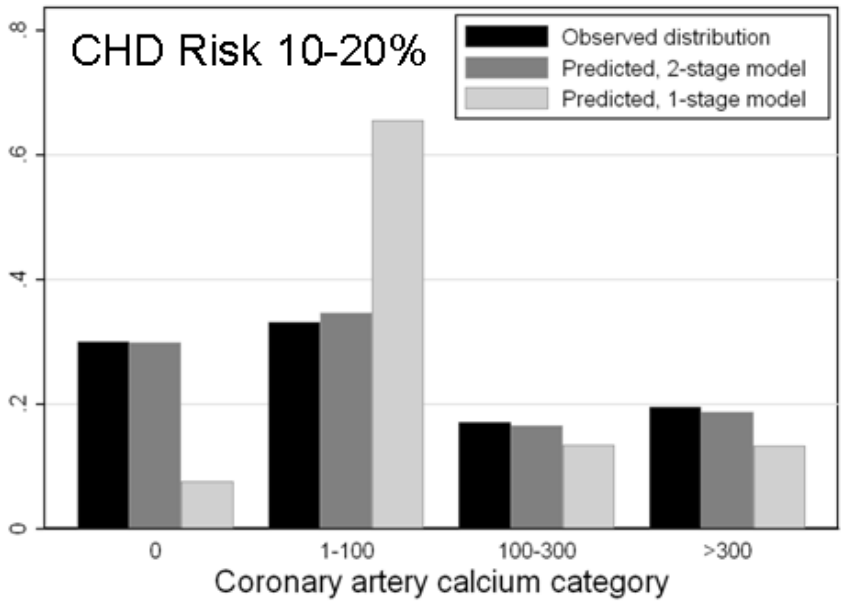
FIGURE LEGEND

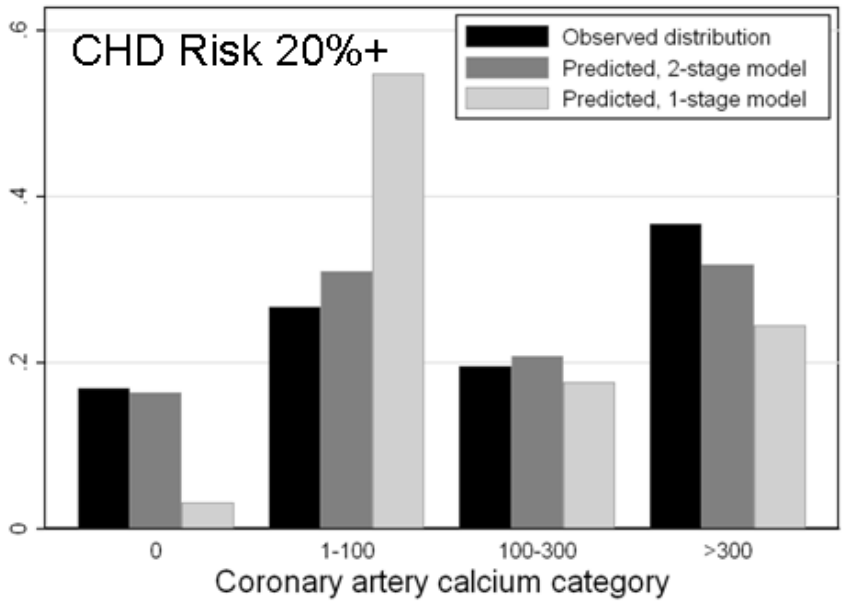
Supplemental Figure. Observed and Predicted Coronary Artery Calcium Score Distributions Across Different Levels of Coronary Heart Disease Risk.

Each bar chart shows 1) The observed distribution of coronary artery calcium (CAC) scores, 2) The expected distribution of scores given the participants' coronary heart disease (CHD) risk factors using the two-stage modeling approach described in the Methods (Model 3), and 3) The expected distribution of scores given the same CHD risk factor predictors but using a one-stage modeling approach (linear regression with log(CAC+1) as the outcome). Four bar charts are provided, stratifying the MESA study population by level of CHD risk (10-year Framingham Risk Score). The two-stage modeling approach predicts a CAC distribution that closely matches the observed distribution; the one-stage approach does not.

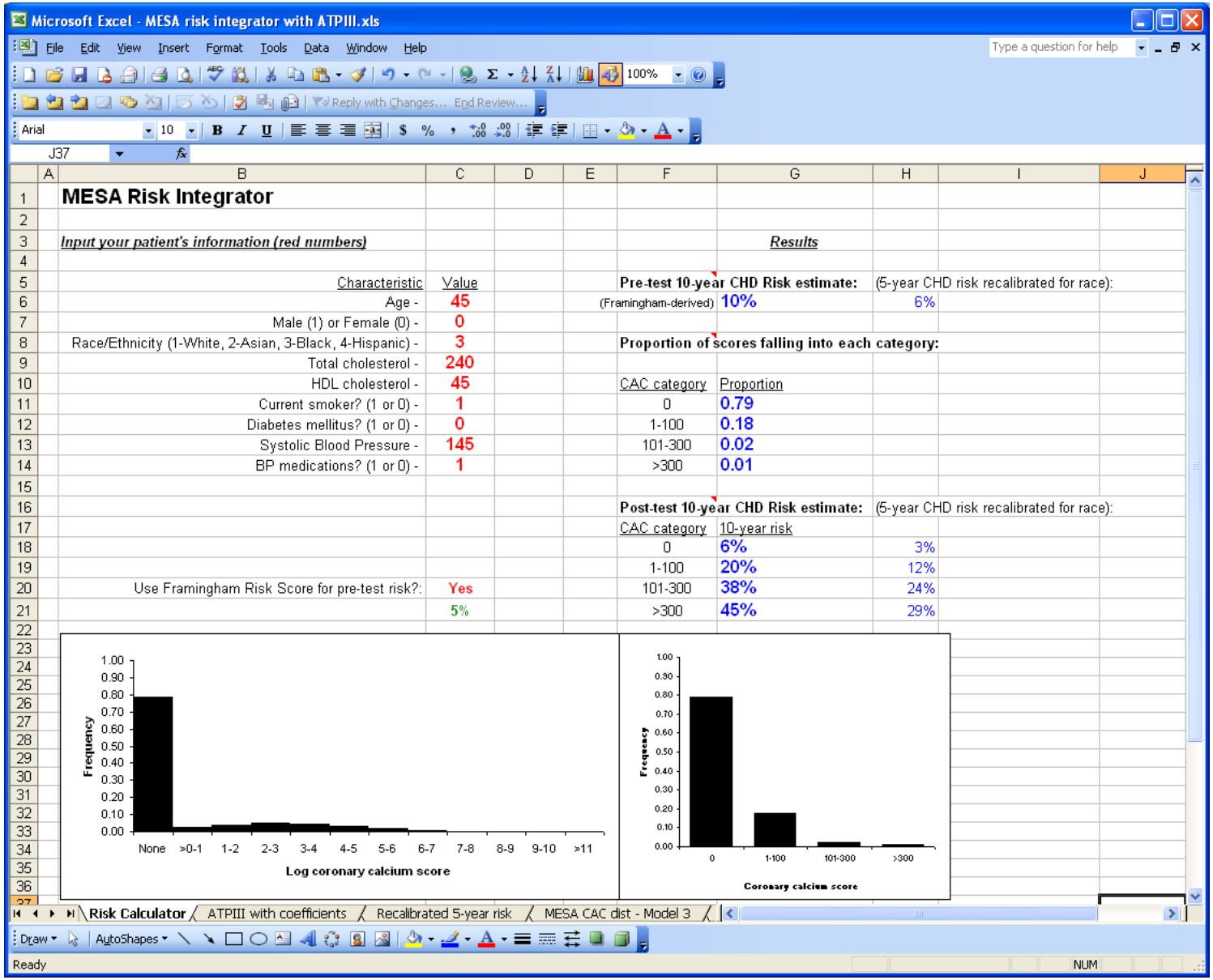

CHD Risk <5%
Observed distribution
Predicted, 2-stage model
Predicted, 1-stage model
0
.2
.4
.6
.8
0
1-100
100-300
>300
Coronary artery calcium category


CHD Risk 5-10%
Observed distribution
Predicted, 2-stage model
Predicted, 1-stage model
0
.2
.4
.6
.8
0
1-100
100-300
>300
Coronary artery calcium category

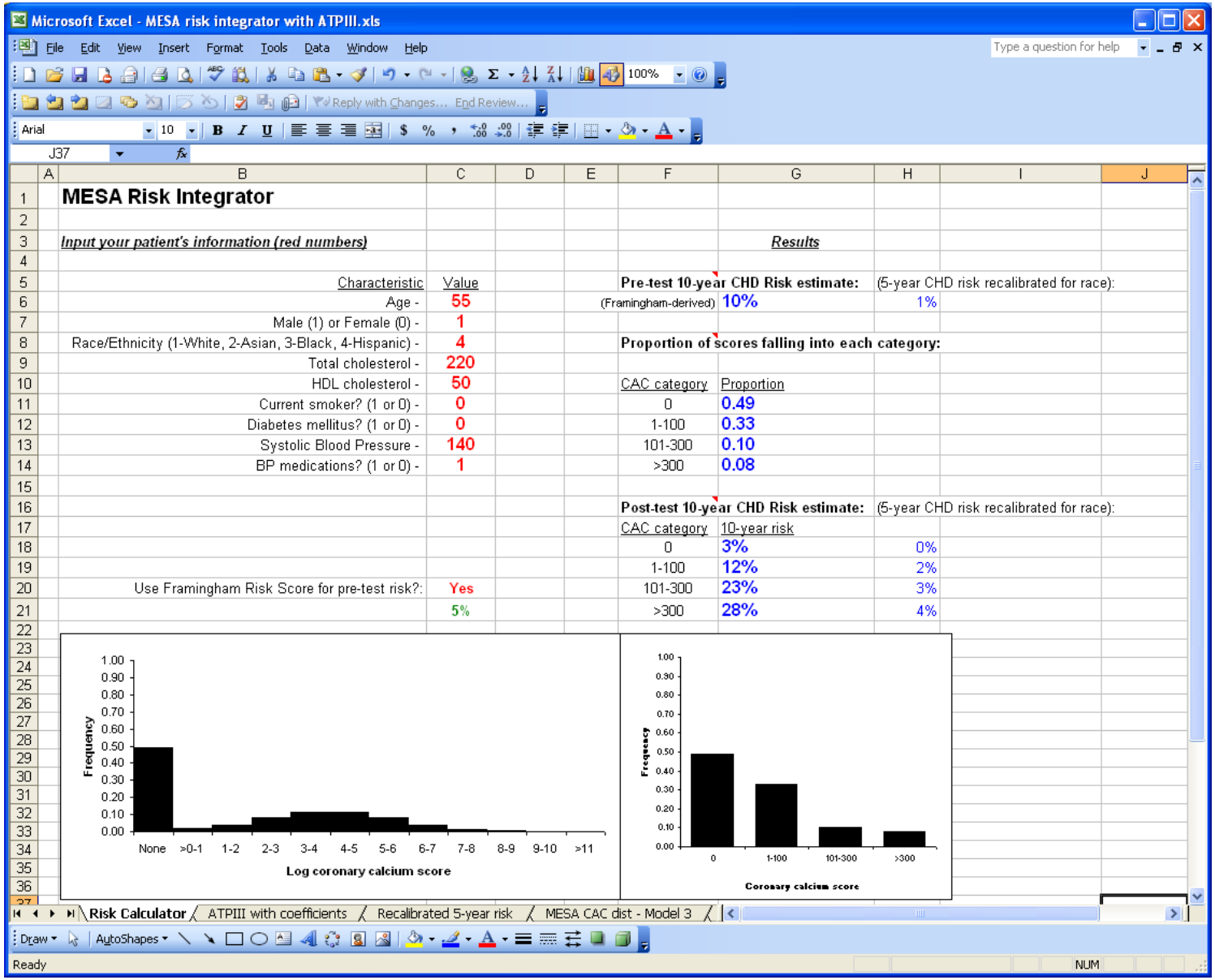

CHD Risk 10-20%
Observed distribution
Predicted, 2-stage model
Predicted, 1-stage model
0
.2
.4
.6
.8
0
1-100
100-300
>300
Coronary artery calcium category


CHD Risk 20%+
Observed distribution
Predicted, 2-stage model
Predicted, 1-stage model
0
.2
.4
.6
0
1-100
100-300
>300
Coronary artery calcium category

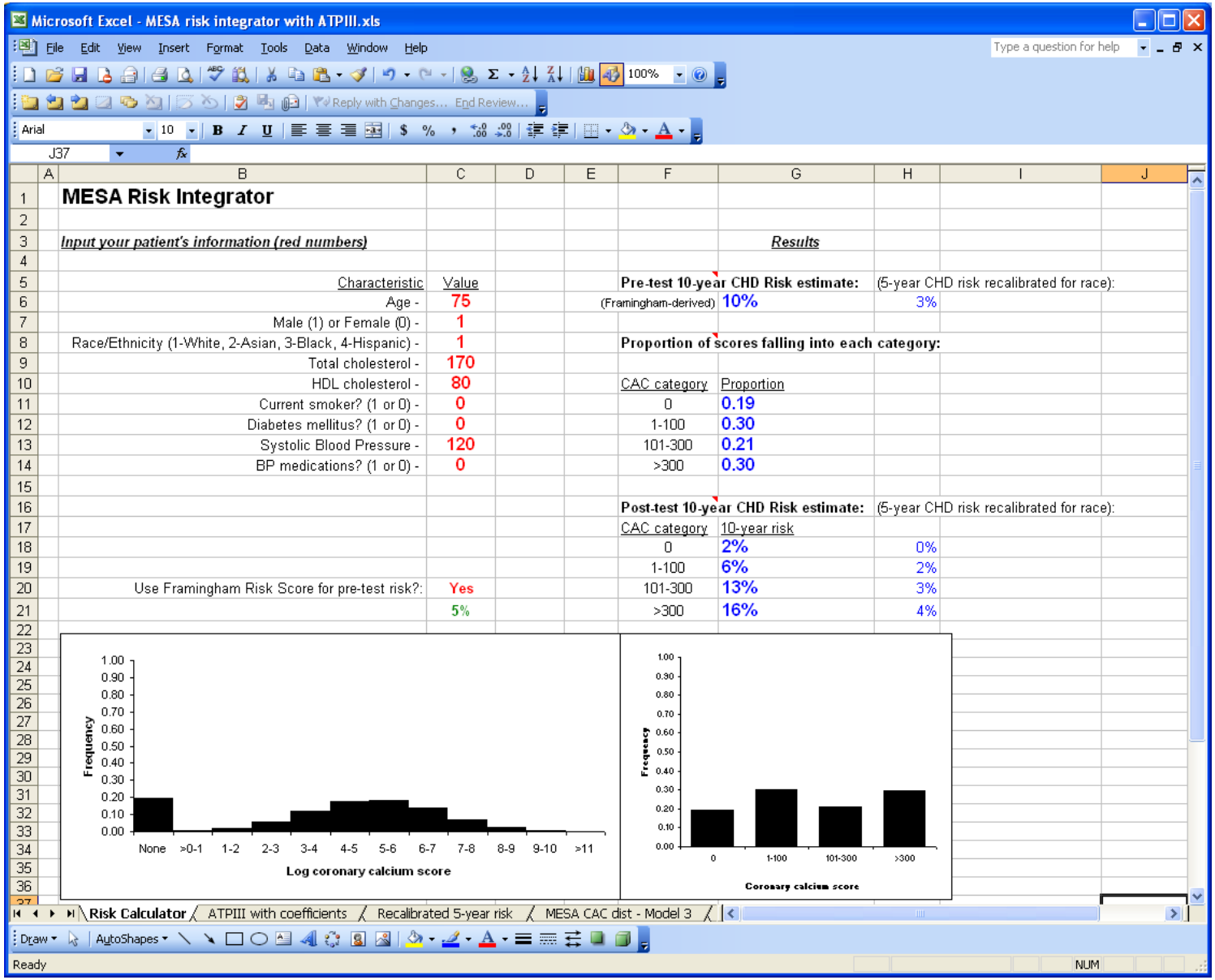
Excel Tool output - Example 5 from Table 4



Excel Tool output - For Example 6 from Table 4



Excel Tool output - For Example 7 from Table 4



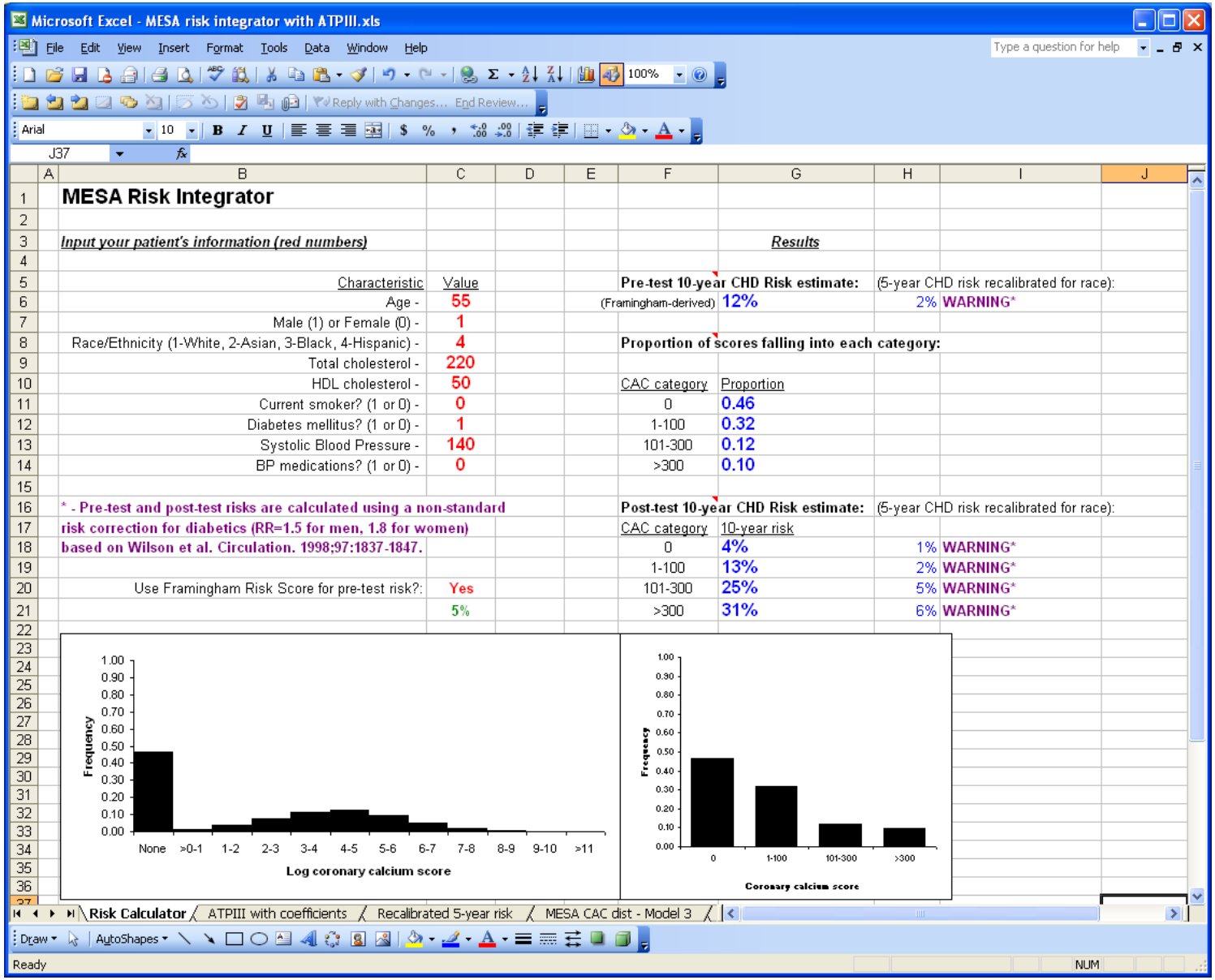
Microsoft Excel - MESA risk integrator with ATPIII.xls

	A	B	C	D	E	F	G	H	I	J
1		**MESA Risk Integrator**								
2										
3		***Input your patient's information (red numbers)***					***Results***			
4										
5		Characteristic	Value			**Pre-test 10-year CHD Risk estimate:**		(5-year CHD risk recalibrated for race):		
6		Age -	75			(Framingham-derived)	10%	3%		
7		Male (1) or Female (0) -	1							
8		Race/Ethnicity (1-White, 2-Asian, 3-Black, 4-Hispanic) -	1			**Proportion of scores falling into each category:**				
9		Total cholesterol -	170							
10		HDL cholesterol -	80			CAC category	Proportion			
11		Current smoker? (1 or 0) -	0			0	0.19			
12		Diabetes mellitus? (1 or 0) -	0			1-100	0.30			
13		Systolic Blood Pressure -	120			101-300	0.21			
14		BP medications? (1 or 0) -	0			>300	0.30			
15										
16						**Post-test 10-year CHD Risk estimate:**		(5-year CHD risk recalibrated for race):		
17						CAC category	10-year risk			
18						0	2%	0%		
19						1-100	6%	2%		
20		Use Framingham Risk Score for pre-test risk?:	Yes			101-300	13%	3%		
21			5%			>300	16%	4%		
22										

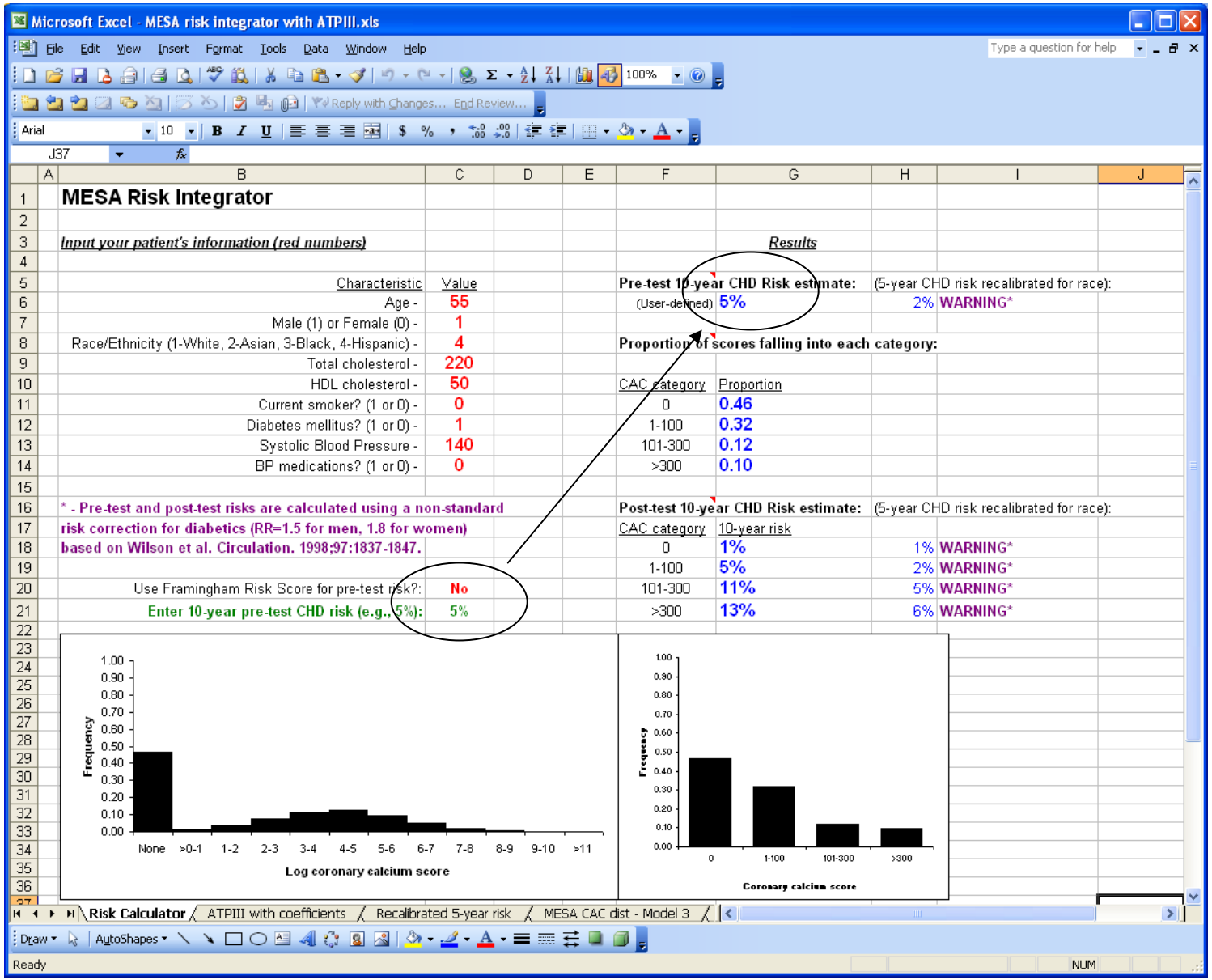
Risk Calculator | ATPIII with coefficients | Recalibrated 5-year risk | MESA CAC dist - Model 3

Ready

Excel Tool output - For Example 6 from Table 4, except with diabetes



Excel Tool output - For Example 6 from Table 4, except with diabetes; AND using a custom user-defined pre-test CHD risk estimate



Supplemental Table 1. Predictors of coronary calcium presence and extent – Model 4, all CHD risk factors but without race/ethnicity

Model - Predictors	Logistic Regression for Coronary Calcium Presence (score>0)			Linear Regression for Coronary Calcium Extent (ln(coronary calcium score)) among persons with a score>0			
	Odds ratio (95% CI)	p-value	Cross-validated C-statistic	Coefficients (95% CI)	Corresponding percent increase in natural CAC scores*	p-value	Cross-validated R^2
Model 4: All CHD risk factors (Model 3 but without race/ethnicity)*							
- Age, per 10 years	2.51 (2.36-2.68)	<.001	.778	0.61 (0.55-0.68)	85% (73%-97%)	<.001	.151
- Male (vs. female)	2.70 (1.39-3.05)	<.001		0.75 (0.62-0.87)	111% (86%-140%)	<.001	
- Total cholesterol, per 10 mg/dl	1.059 (1.042-1.077)	<.001		0.0084 (-0.009-0.025)	1% (-1%-3%)	.34	
- HDL cholesterol, per 10 mg/dl	0.893 (0.857-0.931)	<.001		0.0045 (-0.039-0.048)	0% (-4%-5%)	.84	
- Current smoker	1.44 (1.22-1.70)	<.001		0.19 (0.011-0.36)	21% (1%-44%)	.04	
- Diabetes mellitus	1.29 (1.08-1.53)	.004		0.36 (0.20-0.52)	43% (22%-68%)	<.001	
- Systolic blood pressure, per 10 mmHg	1.086 (1.046-1.127)	<.001		0.069 (0.030-0.109)	7% (3%-11%)	.001	
- Taking blood pressure medications	4.5 (2.2-9.3)	<.001		1.18 (0.46-1.90)	225% (58%-570%)	.001	
- BPmeds * SBP, per 10 mg/dl‖	0.914 (0.866-0.966)	.001		-0.069 (-0.123- -0.015)	-7% (-12%- -1%)	.013	

* - Additional model parameters required for estimating coronary calcium distribution (see Table 3) for Models 4 would be the intercept for the logistic models on the log-odds scale (-7.98017), intercepts for the linear regression model (-1.44688) and the standard deviation of the residuals for the linear model (1.684672).

Supplemental Table 2. Using the coronary artery calcium score with conventional cardiovascular risk factors to estimate future risk: 11 examples using Model 3, with 5-year race/ethnicity recalibrated risk*

Clinical scenario‖	Pre-test 5-year CHD risk, recalibrated*	CAC score category	Proportion of CAC scores falling within the given category†	Post-test 5-year recalibrated risk* for each CAC score category‡
1 – 45 year old white man with SBP = 120 mmHg (no medication), TC/HDL = 160/60 mg/dl	0.6%	0:	.76	0%
		1-100:	.19	1%
		101-300:	.03	2%
		>300:	.02	3%
2 – 65 year old Asian woman with SBP = 110 mg/dl (no medication), TC/HDL = 160/80 mg/dl	Not available*	0:	.73	Not available*
		1-100:	.21	Not available*
		101-300:	.04	Not available*
		>300:	.02	Not available*
3 – 45 year old Hispanic woman with SBP = 150 mmHg (no medication), TC/HDL = 210/40 mg/dl who smokes	Not available*	0:	.84	Not available*
		1-100:	.14	Not available*
		101-300:	.01	Not available*
		>300:	.00	Not available*
4 – 60 year old white man with SBP = 120 mmHg (no medication), TC/HDL = 150/65 mg/dl	0.8%	0:	.47	0%
		1-100:	.31	1%
		101-300:	.12	2%
		>300:	.10	2%
5 - 45 year old black woman with SBP = 145 mmHg on medication, TC/HDL = 240/45 mg/dl who smokes	6%	0:	.79	3%
		1-100:	.18	12%
		101-300:	.02	24%
		>300:	.01	29%
6 – 55 year old Hispanic man with SBP = 140 mmHg on medication, TC/HDL = 220/50 mg/dl	1%	0:	.49	0%
		1-100:	.33	2%
		101-300:	.10	3%
		>300:	.08	4%

7 – 75 year old white man with SBP = 120 mmHg (no medication), TC/HDL = 170/80 mg/dl	3%	0:	.19	0%
		1-100:	.30	2%
		101-300:	.21	3%
		>300:	.30	4%
8 – 45 year old Asian woman with SBP = 155 mmHg on medication, TC/HDL = 250/40 mg/dl who smokes	Not available*	0:	.68	Not available*
		1-100:	.27	Not available*
		101-300:	.04	Not available*
		>300:	.02	Not available*
9 – 75 year old black man with SBP = 130 mmHg (no medication), TC/HDL = 180/55	5%	0:	.31	1%
		1-100:	.34	4%
		101-300:	.17	8%
		>300:	.18	9%
10 – 55 year old Hispanic woman with SBP = 160 mmHg on medication, TC/HDL = 260/40 mg/dl who smokes	Not available*	0:	.56	Not available*
		1-100:	.34	Not available*
		101-300:	.07	Not available*
		>300:	.04	Not available*
11 – 80 year old white man with SBP = 130 mmHg on medication, TC/HDL = 210/60 mg/dl	9%	0:	.06	1%
		1-100:	.22	4%
		101-300:	.22	9%
		>300:	.50	11%

* - The 5-year CHD risk, recalibrated for race/ethnicity, was obtained using estimates and methods from a published Framingham validation article(REF). All pre-test risk estimates use relative hazard estimates derived from Framingham (presented in Table 1 of the reference(REF)). Estimates for white men and white women use the average 5-year CHD rate and average CHD risk factor levels from Framinghm, but estimates for othe race/sex groups were "recalibrated" using race/sex-specific average 5-year CHD rates and risk factor averages, as described(REF). To obtain the average age^2 value, we used the age range to estimate the standard deviation (SD = range/4), and then used the following formula: average(age^2) = (average(age))^2 + SD^2. Values for black men and women were derived from the Atherosclerosis Risk in Communities (ARIC) Study; values for Asian men were derived from the Honolulu Heart Program; values for Hispanic men were derived from the Puerto Rico

Heart Program(REF). Note that our reference did not present results for Asian or Hispanic women, so these values are left missing in the table.

† - Uses model parameters from Table 2 (Model 3) and the two-step estimation procedure described in the Methods section. Results are identical to the last panel of Table 3.

‡ - Post-test risk estimates are calculated by assuming that the pre-test 10-year CHD risk estimate represents an average of persons with different CAC scores, weighted by the probability of having a CAC score in each category†. The risk in each category is calculated algebraically using these relative risk estimates from Detrano et al[2]: CAC=0: Reference; CAC=1-100: 3.61; CAC=101-300: 7.73; CAC>300: 9.67. Resulting risk scores are rounded to the nearest whole percentage. See Methods for details.

‖ - All possible combinations of risk factors cannot be described here; only selected scenarios are presented. Results for other clinical scenarios can be calculated using the Excel-based calculator available in the Online Materials. Where the risk factor level is not specified, we used SBP = 120, no blood pressure medications, TC = 160, HDL = 55, non-smoker, non-diabetic. Note: Pre- and Post-test risk cannot be calculated for diabetics; see Methods.

CHD – Coronary heart disease; CAC score – Coronary artery calcification score; SBP – systolic blood pressure; TC – Total cholesterol; HDLC – High density lipoprotein cholesterol