SUPPLEMENTAL MATERIAL

1) Supplemental Figure

2) Excel tool screenshots

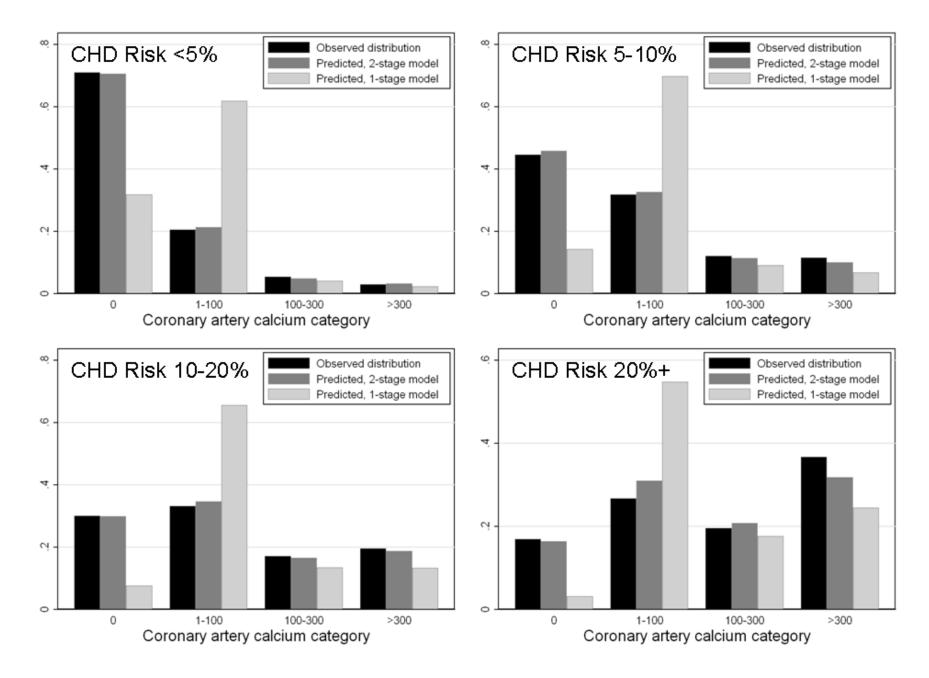
3) Supplemental Table 1

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 does not.



Excel Tool output - Example 5 from Table 4

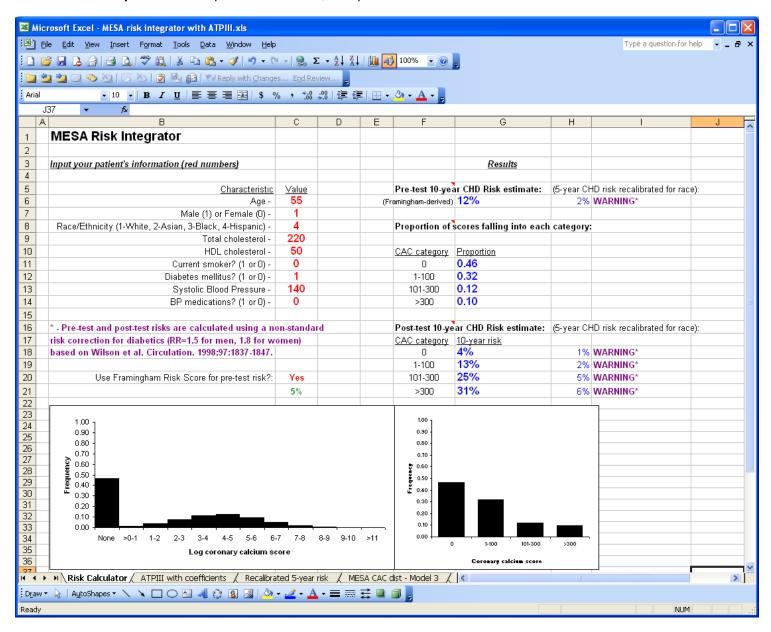
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6	Age -	45 0		(Framingham-de	rved) IU%	6%		
7	Male (1) or Female (0) - Race/Ethnicity (1-White, 2-Asian, 3-Black, 4-Hispanic) -	3		Dronartia	n of scores falling into ea	ch catoger	•	
9	Total cholesterol -	240		Fiopoluo	n or scores failing into ea	cii category	•	
10	HDL cholesterol -	45		CAC cater	ory Proportion			
11	Current smoker? (1 or 0) -	1		0,10 00100	0.79			
12	Diabetes mellitus? (1 or 0) -	0 0		1-100	0.18			
13	Systolic Blood Pressure -	145		101-30				
14	BP medications? (1 or 0) -	1		>300	0.01			=
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19				1-100	20%	12%		
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24	1.00			1.00				
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Excel Tool output - For Example 6 from Table 4

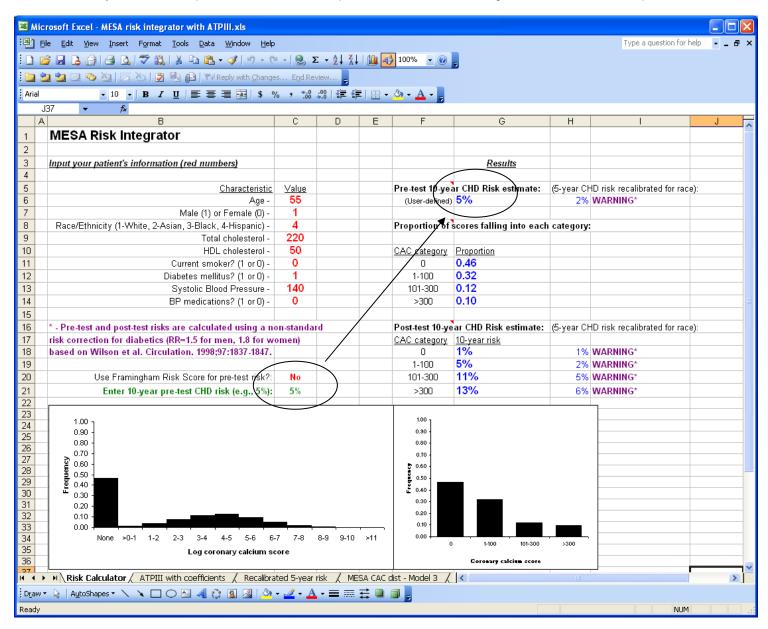
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6	Age -	55		(Fr	amingham-derived)	10%	1%		
7	Male (1) or Female (0) -								
3	Race/Ethnicity (1-White, 2-Asian, 3-Black, 4-Hispanic) -	4			Proportion of	scores falling into eac	h category:		
3	Total cholesterol -	220							
0	HDL cholesterol -	50			CAC category				
1	Current smoker? (1 or 0) -	0			0	0.49			
2	Diabetes mellitus? (1 or 0) -	0			1-100	0.33			
3	Systolic Blood Pressure -	140			101-300	0.10			
4	BP medications? (1 or 0) -	1			>300	0.08			
5									
6							(5-year CHI	D risk recalibrated for race	e):
7					CAC category				
8					0	3%	0%		
9					1-100	12%	2%		
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Excel Tool output - For Example 7 from Table 4

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6	Age -	75		(Framingham-derived		3%	TISK TECAIIDTALEU TOF TACE	
7	Male (1) or Female (0) -	1						
8	Race/Ethnicity (1-White, 2-Asian, 3-Black, 4-Hispanic) -	1		Proportion of	f scores falling into eac	h 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					ear CHD Risk estimate:	(5-year CHD	risk recalibrated for race	:):
17 18				CAC category	<u>10-year risk</u> 2%	0%		
10				1-100	2 % 6%	2%		
20	Use Framingham Risk Score for pre-test risk?:	Yes		101-300	13%	3%		
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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

	Logistic Regression for Coronary Calcium			Linear Regression for Coronary Calcium Extent (In(coronary calcium					
	Presence	(score>0)		score)) a					
Model	Odds ratio (95%	p-value	Cross-	Coefficients (95% CI)	Corresponding	p-value	Cross-		
- Predictors	CI)		validated		percent increase in		validated		
			C-statistic		natural CAC scores*		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 (-0.1230.015)	-7% (-12%1%)	.013			

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

* - 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

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

to estimate future risk: 11 examples using Model 3, with 5-year race/ethnicity recalibrated risk*

7 – 75 year old white man with		0:	.19	0%
SBP = 120 mmHg (no medication),	3%	1-100:	.30	2%
TC/HDL = 170/80 mg/dl		101-300:	.21	3%
		>300:	.30	4%
8 – 45 year old Asian woman with		0:	.68	Not available*
SBP = 155 mmHg on medication,	Not available*	1-100:	.27	Not available*
TC/HDL = 250/40 mg/dl who		101-300:	.04	Not available*
smokes		>300:	.02	Not available*
9 – 75 year old black man with		0:	.31	1%
SBP = 130 mmHg (no medication),	5%	1-100:	.34	4%
TC/HDL = 180/55		101-300:	.17	8%
		>300:	.18	9%
10 – 55 year old Hispanic woman		0:	.56	Not available*
with SBP = 160 mmHg on	Not available*	1-100:	.34	Not available*
medication, TC/HDL = 260/40		101-300:	.07	Not available*
mg/dl who smokes		>300:	.04	Not available*
11 – 80 year old white man with		0:	.06	1%
SBP = 130 mmHg on medication,	9%	1-100:	.22	4%
TC/HDL = 210/60 mg/dl		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 age² value, we used the age range to estimate the standard deviation (SD = range/4), and then used the following formula: average(age²) = (average(age))² + SD². 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 al²: 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