

Supplemental Table 1. Sensitivities and Specificities for CAC and Functional Testing

	Sensitivity (95% CI)			Specificity (95% CI)		
	CAC Testing	Functional testing	p-value	CAC Testing	Functional testing	p-value
All-cause death/MI/UA						
Abnormal: (CAC>0; FT=mild/moderate/severe)	84.2% (76.9–90.0)	43.2% (34.6–52.1)	<0.001	35.2% (33.8–36.7)	78.6% (77.4–79.8)	<0.001
Abnormal: (CAC>100; FT=moderate/severe)	60.9% (52.1–69.2)	36.4% (28.2–45.2)	<0.001	67.3% (65.9–68.8)	88.1% (87.1–89.0)	<0.001
Abnormal: (CAC>400; FT=severe)	30.8% (23.1–39.4)	26.5% (19.2–34.9)	0.498	85.3% (84.2–86.4)	92.6% (91.8–93.4)	<0.001
Cardiovascular death/MI/UA						
Abnormal: (CAC>0; FT=mild/moderate/severe)	86.8% (78.8–92.6)	48.1% (38.4–58.0)	<0.001	35.2% (33.7–36.7)	78.6% (77.4–79.8)	<0.001
Abnormal: (CAC>100; FT=moderate/severe)	63.2% (53.3–72.4)	40.7% (31.4–50.6)	0.001	67.2% (65.8–68.7)	88.0% (87.0–89.0)	<0.001
Abnormal: (CAC>400; FT=severe)	33.0% (24.2–42.8)	28.7% (20.4–38.2)	0.555	85.3% (84.1–86.3)	92.6% (91.8–93.3)	<0.001
Cardiovascular death/MI						
Abnormal: (CAC>0; FT=mild/moderate/severe)	83.0% (70.2–91.9)	33.3% (22.7–45.4)	<0.001	34.8% (33.4–36.3)	78.1% (76.9–79.3)	<0.001
Abnormal: (CAC>100; FT=moderate/severe)	50.9% (36.8–64.9)	26.4% (16.7–38.1)	0.008	66.7% (65.2–68.1)	87.6% (86.6–88.5)	<0.001
Abnormal: (CAC>400; FT=severe)	24.5% (13.8–38.3)	19.4% (11.1–30.5)	0.517	84.9% (83.8–88.3)	92.3% (91.4–93.0)	<0.001

MI indicates myocardial infarction; UA, unstable angina.

Supplemental Table 2: Alternative Cutpoints for CAC—Frequency of Test Findings and Association With Clinical Events for CAC Testing

Initial Test Results	CAC Testing (N=4209)				Functional Testing (N=4602)			
	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P-value	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P-value
All-cause death/MI/UA								
Normal (CAC 0, FT = normal)	1457/4209 (34.6)	21/1457 (1.44)			3588/4602 (78.0)	75/3588 (2.1)		
Mild (CAC 1-99, FT = mild)	1340/4209 (31.8)	31/1340 (2.31)	1.51 (0.86–2.64)	0.149	432/4602 (9.4)	9/432 (2.1)	0.94 (0.47–1.89)	0.867
Moderate (CAC 100-300, FT moderate)	621/4209 (14.8)	32/621 (5.15)	3.18 (1.80–5.62)	<0.001	217/4602 (4.7)	13/217 (6.0)	2.65 (1.46–4.83)	0.001
Severe (CAC >300, FT Severe)	791/4209 (18.8)	49/791 (6.19)	3.42 (1.95–5.99)	<0.001	365/4602 (7.9)	35/365 (9.6)	3.88 (2.58–5.85)	<0.001
Cardiovascular death/MI/UA								
Normal (CAC 0, FT = normal)	1457/4209 (34.6)	14/1457 (0.96)			3588/4602 (78.0)	56/3588 (1.6)		
Mild (CAC 1-99, FT = mild)	1340/4209 (31.8)	25/1340 (1.87)	1.84 (0.95–3.56)	0.070	432/4602 (9.4)	8/432 (1.9)	1.11 (0.53–2.34)	0.783
Moderate (CAC 100-300, FT moderate)	621/4209 (14.8)	27/621 (4.35)	4.08 (2.10–7.93)	<0.001	217/4602 (4.7)	13/217 (6.0)	3.50 (1.89–6.48)	<0.001
Severe (CAC >300, FT Severe)	791/4209 (18.8)	40/791 (5.06)	4.29 (2.22–8.30)	<0.001	365/4602 (7.9)	31/365 (8.5)	4.59 (2.93–7.19)	<0.001
Cardiovascular death/MI								
Normal (CAC <0, FT = normal)	1457/4209 (34.6)	9/1457 (0.62)			3588/4602 (78.0)	48/3588 (1.3)		
Mild (CAC 1-99, FT = mild)	1340/4209 (31.8)	17/1340 (1.27)	1.77 (0.78–4.02)	0.171	432/4602 (9.4)	5/432 (1.2)	0.81 (0.32–2.04)	0.654
Moderate (CAC 100-300, FT moderate)	621/4209 (14.8)	11/621 (1.77)	2.17 (0.87–5.41)	0.095	217/4602 (4.7)	5/217 (2.3)	1.53 (0.60–3.90)	0.368

SUPPLEMENTAL TABLES
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Initial Test Results	CAC Testing (N=4209)				Functional Testing (N=4602)			
	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P-value	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P-value
Severe (CAC >300, FT Severe)	791/4209 (18.8)	16/791 (2.02)	2.00 (0.82–4.89)	0.130	365/4602 (7.9)	14/365 (3.8)	2.13 (1.16–3.91)	0.014

* Hazard ratios (HR) adjusted for age, sex, CAD risk equivalent (history of either diabetes mellitus, peripheral artery disease, or cerebrovascular disease), and the prespecification of the intended functional test (if randomly assigned to the functional testing arm).

Supplemental Table 3: Alternative Cutpoints for CAC—Frequency of Test Findings and Association With Clinical Events for CAC Testing

Initial Test Results	CAC Testing (N=4209)				Functional Testing (N=4602)			
	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P-value	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P-value
All-cause death/MI/UA								
Normal (CAC <10, FT = normal)	1831/4209 (43.5)	28/1831 (1.53)			3588/4602 (78.0)	75/3588 (2.1)		
Mild (CAC 10-99, FT = mild)	966/4209 (23.0)	24/966 (2.48)	1.52 (0.87–2.63)	0.139	432/4602 (9.4)	9/432 (2.1)	0.94 (0.47–1.89)	0.867
Moderate (CAC 100-400, FT moderate)	621/4209 (14.8)	32/621 (5.15)	3.02 (1.79–5.10)	<0.001	217/4602 (4.7)	13/217 (6.0)	2.65 (1.46–4.83)	0.001
Severe (CAC >400, FT Severe)	791/4209 (18.8)	49/791 (6.19)	3.24 (1.94–5.42)	<0.001	365/4602 (7.9)	35/365 (9.6)	3.88 (2.58–5.85)	<0.001
Cardiovascular death/MI/UA								
Normal (CAC <10, FT = normal)	1831/4209 (43.5)	18/1831 (0.98)			3588/4602 (78.0)	56/3588 (1.6)		
Mild (CAC 10-99, FT = mild)	966/4209 (23.0)	21/966 (2.17)	2.08 (1.10–3.94)	0.024	432/4602 (9.4)	8/432 (1.9)	1.11 (0.53–2.34)	0.783
Moderate (CAC 100-400, FT moderate)	621/4209 (14.8)	27/621 (4.35)	4.02 (2.17–7.44)	<0.001	217/4602 (4.7)	13/217 (6.0)	3.50 (1.89–6.48)	<0.001
Severe (CAC >400, FT Severe)	791/4209 (18.8)	40/791 (5.06)	4.25 (2.31–7.81)	<0.001	365/4602 (7.9)	31/365 (8.5)	4.59 (2.93–7.19)	<0.001
Cardiovascular death/MI								
Normal (CAC <10, FT = normal)	1831/4209 (43.5)	12/1831 (0.66)			3588/4602 (78.0)	48/3588 (1.3)		
Mild (CAC 10-99, FT = mild)	966/4209 (23.0)	14/966 (1.45)	1.88 (0.86–4.11)	0.155	432/4602 (9.4)	5/432 (1.2)	0.81 (0.32–2.04)	0.654
Moderate (CAC 100-400, FT moderate)	621/4209 (14.8)	11/621 (1.77)	2.08 (0.89–4.86)	0.089	217/4602 (4.7)	5/217 (2.3)	1.53 (0.60–3.90)	0.368

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Initial Test Results	CAC Testing (N=4209)				Functional Testing (N=4602)			
	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P-value	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P-value
Severe (CAC >400, FT Severe)	791/4209 (18.8)	16/791 (2.02)	1.92 (0.84–4.39)	0.122	365/4602 (7.9)	14/365 (3.8)	2.13 (1.16–3.91)	0.014

* Hazard ratios (HR) adjusted for age, sex, CAD risk equivalent (history of either diabetes mellitus, peripheral artery disease, or cerebrovascular disease), and the prespecification of the intended functional test (if randomly assigned to the functional testing arm).

Supplemental Table 4. Frequency of Abnormal and Normal Test Findings and Association With Clinical Events for Anatomic and

Initial Test Results	CAC Testing (N=4209)				Functional Testing (N=4602)			
	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P- value	Frequency n/N (%)	Event Rate n/N (%)	HR* (95% CI)	P-value
All-cause death/MI/UA								
Normal (CAC=0; FT=normal)	1457/4209 (34.62)	21/1457 (1.44)			3588/4602 (77.97)	75/3588 (2.09)		
Abnormal (CAC>0; FT=mild/moderate/severe)	2752/4209 (65.38)	112/2752 (4.07)	2.30 (1.41– 3.74)	0.001	1014/4602 (22.03)	57/1014 (5.62)	2.42 (1.70– 3.44)	<0.001
Cardiovascular death/MI/UA								
Normal (CAC=0; FT=normal)	1457/4209 (34.62)	14/1457 (0.96)			3588/4602 (77.97)	56/3588 (1.56)		
Abnormal (CAC>0; FT=mild/moderate/severe)	2752/4209 (65.38)	92/2752 (3.34)	2.86 (1.60– 5.13)	<0.001	1014/4602 (22.03)	52/1014 (5.13)	2.93 (2.00– 4.30)	<0.001
Cardiovascular death/MI								
Normal (CAC=0; FT=normal)	1457/4209 (34.62)	9/1457 (0.62)			3588/4602 (77.97)	48/3588 (1.34)		
Abnormal (CAC>0; FT=mild/moderate/severe)	2752/4209 (65.38)	44/2752 (1.60)	1.92 (0.90– 4.07)	0.090	1014/4602 (22.03)	24/1014 (2.37)	1.50 (0.91– 2.46)	0.112

Functional Testing.

MI indicates myocardial infarction; UA, unstable angina.

* Hazard ratios (HR) adjusted for age, sex, CAD risk equivalent (history of either diabetes mellitus, peripheral artery disease, or cerebrovascular disease), and the prespecification of the intended functional test (if randomly assigned to the functional testing arm).