Coronary Artery Calcium Score

Unnecessary Tool or Ultimate Precision?

Courtesy of Kaveh Bookani, MD

Presented by Cason Christensen, MD



Agenda

- Background and History
- CAC vs Risk Factors/Scores
- CAC in Different Populations
- What do the guidelines say?



BACKGROUND

- ✓ CAD is a major cause of death in the United States and worldwide.
- ✓ Atherosclerosis begins early in life and progresses silently until clinical symptoms occur late in the disease.
- ✓ Coronary arterial calcification occurs almost exclusively in atherosclerotic plaques.
- ✓ Not all plaques are calcified but total atherosclerotic plaque burden is proportional to the total calcium burden. Generally thought to represent about 1/5 of plaque burden.
- ✓ CAC may be present with areas of minimal or severe disease, so it is suboptimal for site-specific detection of luminal stenosis.



Quantification of Coronary Artery Calcium Using Ultrafast Computed Tomography

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Miami Beach, Florida and Long Beach, California







HOW IS IT DONE?

- ✓ Multidetector row CT or EBCT
- ✓ Gated to diastole to minimize coronary motion.
- ✓ Typically, prospectively ECG-triggered scanning mode with 2.5- to 3.0-mm thick axial images.
- ✓ Quantity of calcium is scored as the area affected on the scan multiplied by a weighting factor depending on the Hounsfield unit density of the calcium deposits.
- ✓ Radiation dose is low, typical effective dose of 1.5 mSv ~ 1 to 2 mammograms performed on each breast

European Heart Journal

JOURNAL ARTICLE

Coronary calcification detected by electron-beam computed tomography and myocardial infarction. The Rotterdam Coronary Calcification Study

R. Vliegenthart, M. Oudkerk, B. Song, D.A.M. van der Kuip, A. Hofman, J.C.M. Witteman

European Heart Journal, Volume 23, Issue 20, 1 October 2002, Pages 1596–1603,

https://doi.org/10.1053/euhj.2002.3240

Published: 01 October 2002 Article history ▼

2013 participants, mean age 71 years



Table 4 Age-adjusted odds ratio of myocardial infarction in calcium score categories, for men and women, in two age strata

	Men			Women		
	n	Events	Odds ratio (95% CI)	n	Events	Odds ratio (95% CI)
<70 years						
Calcium score:						
0-100	176	9	1.0 (reference)	338	7	1.0 (reference)
101-500	111	8	1.4 (0.5–3.7)	108	3	1.3 (0.3-5.1)
501-1000	58	12	4.8 (1.9-12.2)	36	3	4.3 (1.0–17.8)
>1000	84	24	7.1 (3.1–16.5)	15	3	10.0 (2.3-44.2)
≥70 years						
Calcium score:						
0-100	120	10	1.0 (reference)	293	18	1.0 (reference)
101-500	156	25	2.0 (0.9-4.5)	158	11	1.3 (0.6-2.8)
501-1000	87	21	3.4 (1.5-7.6)	73	9	2.4 (1.0-5.5)
>1000	140	57	7.7(3.7-16.1)	60	9	3.8 (1.6-9.3)



Prognostic power of CAC for coronary events in asymptomatic patients

Study	Patients, N	Mean age, y	Follow-up, y	Calcium score cutoff	Comparator group for relative risk calculation	Relative risk (RR) ratio
Arad et al. [7]	1173	53	3.6	CAC > 160	CAC < 160	20.2
Park et al. [8]	967	67	6.4	CAC > 142.1	CAC < 3.7	4.9
Raggi et al. [9]	632	52	2.7	Top quartile	Lowest quartile	13
Wong et al. [10]	926	54	3.3	Top quartile (>270)	First quartile	8.8
Kondos et al. [11]	5635	51	3.1	CAC	No CAC	10.5
Greenland et al. [12]	1312	66	7.0	CAC > 300	No CAC	3.9
Shaw et al. [13]	10,377	53	5	CAC ≥ 400	CAC ≤ 10	8.4
Arad et al. [14]	5585	59	4.3	CAC ≥ 100	CAC < 100	10.7
Taylor et al. [15]	2000	40-50	3.0	CAC > 44	CAC = 0	11.8
Vliegenthart et al. [16]	1795	71	3.3	CAC > 1000 CAC 400-1000	CAC < 100 CAC < 100	8.3 4.6
Budoff et al. [17]	25,503	56	6.8	CAC > 400	CAC = 0	9.2
Lagoski et al. [18]	3601	45-84	3.75	CAC > 0	CAC = 0	6.5
Becker et al. [19]	1726	57.7	3.4	CAC > 400	CAC = 0	6.8 men 7.9 women
Detrano et al. [20]	6814	6.2	3.8	CAC > 300	CAC = 0	14.1
Erbel et al. [21]	4487	45–75	5	>75th percentile	<25th percentile	11.1 men 3.2 women
Taylor et al. [22]	1634	42	5.6	CAC > 0	CAC = 0	9.3

CAC and Framingham Risk Score equivalents

CAC	10-years event rate	FRS risk
0	1.1-1.7%	Very low
1-100	2.3-5.9%	Low
100-400	12.8-16.4%	Intermediate
>400	22.5-28.6%	High
>1000	37%	Very high



CAC vs Risk Factors/Scores





Circulation: Cardiovascular Imaging

Volume 5, Issue 4, July 2012; Pages 467-473 https://doi.org/10.1161/CIRCIMAGING:111.964528



ORIGINAL ARTICLE

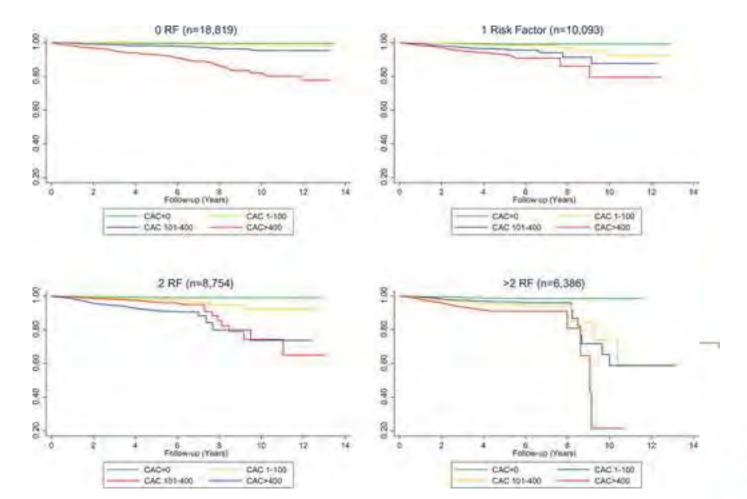
Interplay of Coronary Artery Calcification and Traditional Risk Factors for the Prediction of All-Cause Mortality in Asymptomatic Individuals

Khurram Nasir, MD, MPH, Jonathan Rubin, MD, Michael J. Blaha, MD, MPH, Leslee J. Shaw, PhD, Ron Blankstein, MD, Juan J. Rivera, MD, MPH, Atif N. Khan, MD, Daniel Berman, MD, Paolo Raggi, MD, Tracy Callister, MD, John A. Rumberger, MD, PhD, James Min, MD, Steve R. Jones, MD, Roger S. Blumenthal, MD, and Matthew J. Budoff, MD

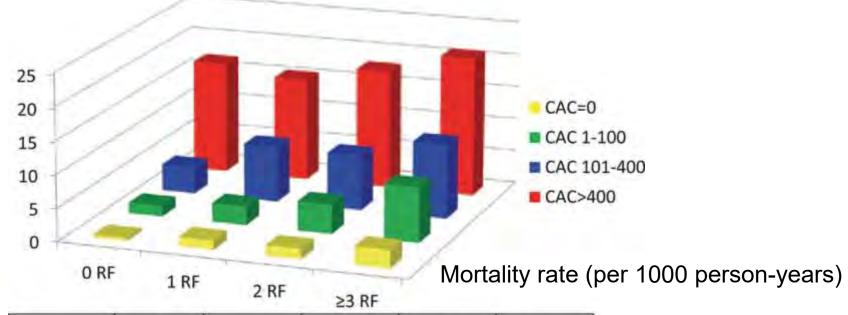
Cohort of 44,052 asymptomatic individuals

RFs: (1) current smoking, (2) HLD, (3) DM, (4) HTN, and (5) FHx of CAD.

Followed for 5.6±2.6 years all-cause mortality.







	0 RF	1 RF	2 RF	≥3RF	Total
CAC=0	9,805	4,558	3,322	2,123	19,898
CAC 1-100	5,994	3,250	2,913	2,204	14,181
CAC 101-400	1,883	1,301	1,371	1,184	5,739
CAC>400	1,047	984	1,148	1,055	4,234
Total	18,819	10,093	8,754	6,386	44,052



Imaging of Coronary Calcium

Coronary Risk Stratification, Discrimination, and Reclassification Improvement Based on Quantification of Subclinical Coronary Atherosclerosis

The Heinz Nixdorf Recall Study

Raimund Erbel, MD,* Stefan Möhlenkamp, MD,* Susanne Moebus, PhD,† Axel Schmermund, MD,‡ Nils Lehmann, PhD,† Andreas Stang, MD,§ Nico Dragano, PhD,|| Dietrich Grönemeyer, MD,¶ Rainer Seibel, MD,# Hagen Kälsch, MD,* Martina Bröcker-Preuss, PhD,** Klaus Mann, MD,** Johannes Siegrist, MD,|| Karl-Heinz Jöckel, PhD,† for the Heinz Nixdorf Recall Study Investigative Group Essen, Frankfurt am Main, Halle, Düsseldorf, Witten, and Mülheim, Germany

4,129 subjects, Age 45 to 75 years, 53% female



Reclassification Accounting for CAC Scores

Classification According to the FRS	Low	Intermediate	High	Total No.
6%-20%				
Participants with events				
Low, <6% in 10 yrs	7	0	0	7
Intermediate, 6%-20% in 10 yrs	27	12	18	57
High, >20% in 10 yrs	0	0	29	29
Total number with events	34	12	47	93
Participants without events				
Low, <6% in 10 yrs	933	0	0	933
Intermediate, 6%-20% in 10 yrs	1,870	479	246	2,595
High, >20% in 10 yrs	0	0	508	508
Total number without events	2,803	479	754	4,036
Net reclassification improvement		30.6% (p < 0.	0001)	



Table 4.4 Reclassification of FRS risk by Coronary Artery Calcium (CAC): primary prevention outcome studies

Study	FRS risk	Reclassified	Patients, N	Age,	Follow-up,
MESA	0-6%	11.6%	5878	62.2	5.8
[20]	6-20%	54.4%			
	>20%	35.8%			
		NRI 25%			
Heinz	<10%	15.0%	4487	45–75	5.0
Nixdorf	10-20%	65.6%			
[21]	>20%	34.2%			
		NRI 22.4%			
Rotterdam [27]	<10%	12%	2028	69.6	9.2
	10-20%	52%			
	>20%	34%			
		NRI 19%			



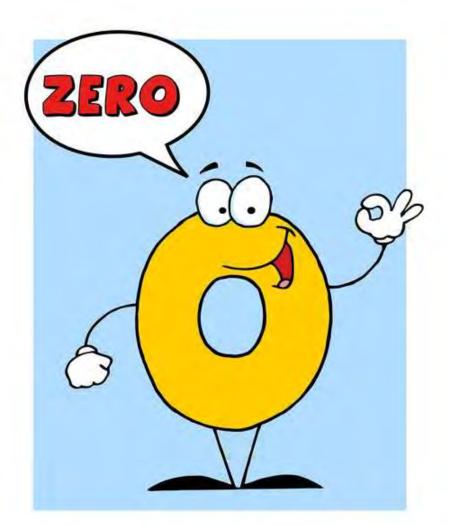
FRS	CAC >300	NNS
0-2.5%	1.7%	59.7
2.6-5%	4.4%	22.7
5.1-7.5%	7.5%	13.4
7.6-10%	13.1%	7.6
10.1-15%	15.6%	6.4
15.1-20%	24%	4.2
>20%	30%	3.3

Okwuosa et al. J Am Coll Cardiol. 2011;57:1838–45.



Use CAC for risk stratification while view traditional risk factors as potentially treatable targets.







Absence of Coronary Artery Calcification and All-Cause Mortality

Michael Blaha, MD, MPH,* Matthew J. Budoff, MD,† Leslee J. Shaw, PhD,‡ Faisal Khosa, MD,§ John A. Rumberger, MD, PhD,|| Daniel Berman, MD,¶ Tracy Callister, MD,# Paolo Raggi, MD,‡ Roger S. Blumenthal, MD,* Khurram Nasir, MD, MPH**

Baltimore, Maryland; Torrance and Los Angeles, California; Atlanta, Georgia; Boston, Massachusetts; Princeton, New Jersey; and Hendersonville, Tennessee

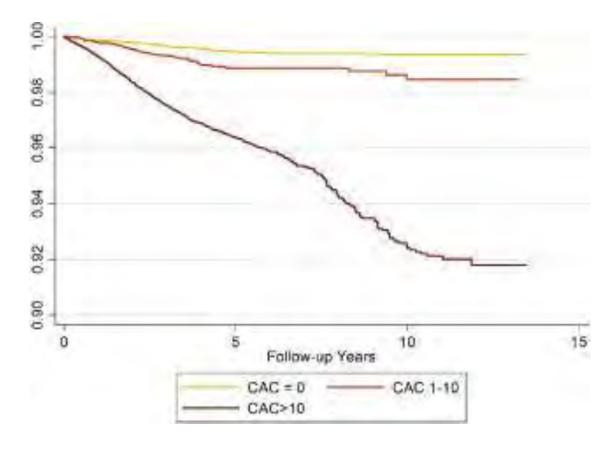
Combined cohort of 44,052 asymptomatic individuals



Table 2. All-Cause Mortality Rates by CAC Scores in Overall Population

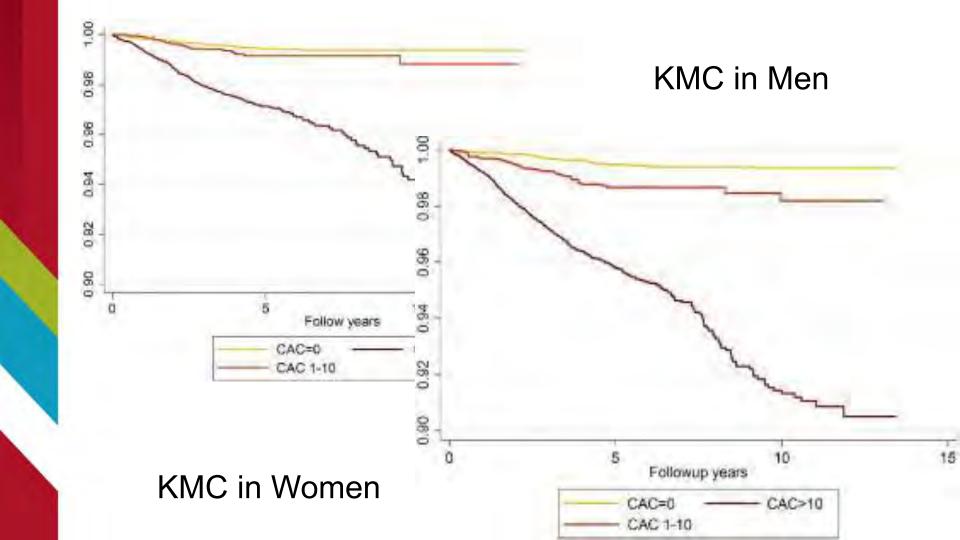
	No. of Patients	No. of Events	Rate/1,000 Person-Yrs at Risk	95% CI for Rate
CAC = 0	19,898(45%)	104(0.52%)	0.87	0.72-1.05
CAC 1 to	5,388(12%)	58(1.06%)	1.92	1.48-2.48
CAC >10	18,766(43%)	739(3.96%)	7.48	6.95-8.04
Total	44,052(100%)	901(2.05%)	3.62	3.39-3.89





Kaplan-Meier Survival Curve According to CAC Scores
Total population





Clinicians should not down classify risk in patients who have coronary artery calcium scores of zero but who are persistent cigarette smokers, have diabetes, have a family history of ASCVD, or, possibly, have chronic inflammatory conditions.

In the presence of these conditions, a coronary artery calcium of zero does not rule out risk from noncalcified plaque or increased risk of thrombosis.



VOL. 14, NO. 5, 2021

ORIGINAL RESEARCH

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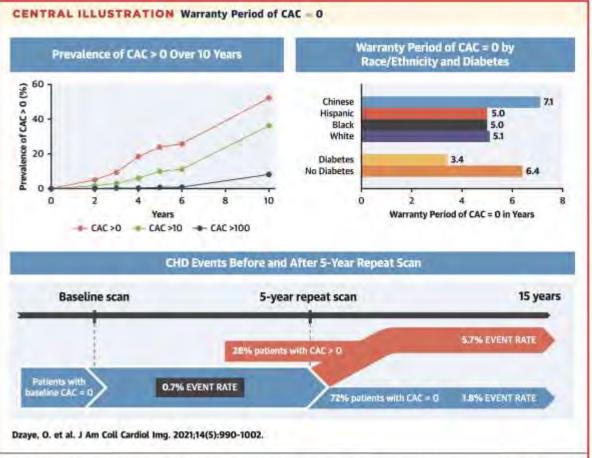
Warranty Period of a Calcium Score of Zero

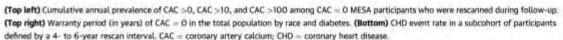


Comprehensive Analysis From MESA

Omar Dzaye, MD, PhD, B, Czeina A. Dardari, MS, Miguel Cainzos-Achirica, MD, MPH, PhD, Ron Blankstein, MD, Arthur S. Agatston, MD, Matthias Duebgen, MD, Joseph Yeboah, MD, MSc, Moyses Szklo, MD, Matthew J. Budoff, MD, Joao A.C. Lima, MD, MBA, Roger S. Blumenthal, MD, Khurram Nasir, MD, MPH, MSc, Michael J. Blaha, MD, MPH









FOLLOW-UP BASED ON CAC SCORE

- CAC of 0 at baseline Among patients with a baseline CAC score of 0, we use their baseline ASCVD risk to determine when repeat CAC testing should be performed. A repeat scan is done if it may change treatment recommendations. The following ASCVD risk categories determine when the repeat scan should be done:
 - . In patients at low 10-year ASCVD risk (<5 percent), we repeat CAC scanning in five to seven years.
 - In patients at intermediate risk for ASCVD (5 to 10 percent), we repeat CAC scanning in three to five years.
 - In patients with diabetes, we repeat CAC scanning in three years.

This approach was recommended by the authors of a Multiethnic Study of Atherosclerosis (MESA) study of 3116 individuals with baseline CAC score of 0 who underwent repeat CAC scanning [51]. Among study participants, the time for conversion to CAC > 0 varied according to baseline ASCVD risk and particularly the presence of diabetes.





March 27, 2008

N Engl J Med 2008; 358:1336-1345

DOI: 10.1056/NEJMoa072100

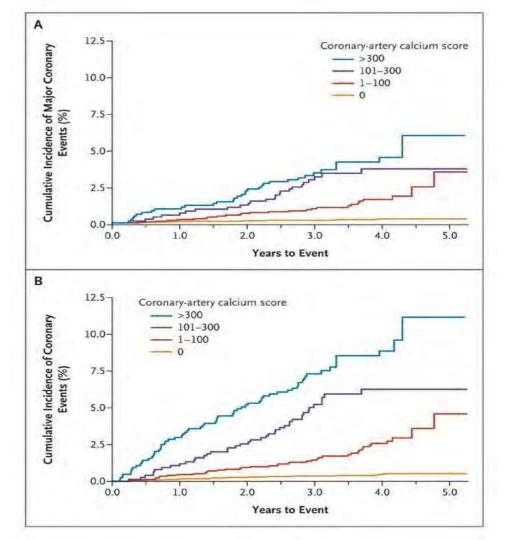
Coronary Calcium as a Predictor of Coronary Events in Four Racial or Ethnic Groups

Robert Detrano, M.D., Ph.D., Alan D. Guerci, M.D., J. Jeffrey Carr, M.D., M.S.C.E., Diane E. Bild, M.D., M.P.H., Gregory Burke, M.D., Ph.D., Aaron R. Folsom, M.D., Kiang Liu, Ph.D., Steven Shea, M.D., Moyses Szklo, M.D., Dr.P.H., David A. Bluemke, M.D., Ph.D., Daniel H. O'Leary, M.D., Russell Tracy, Ph.D., Karol Watson, M.D., Ph.D., Nathan D. Wong, Ph.D., and Richard A. Kronmal, Ph.D.

MESA Study

6722 men and women, age 45 to 84 years 38.6% white, 27.6 black, 21.9% Hispanic, and 11.9% Chinese.











ORIGINAL INVESTIGATION

Coronary Artery Calcium Scores and Risk for Cardiovascular Events in Women Classified as "Low Risk" Based on Framingham Risk Score

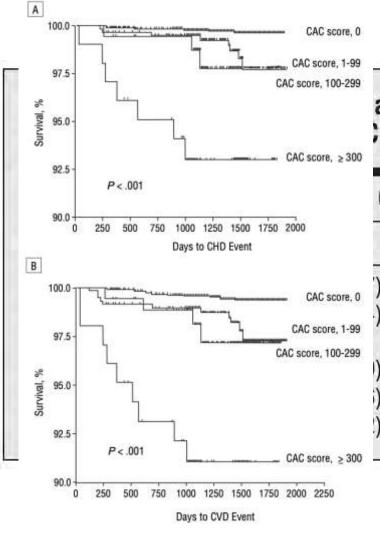
The Multi-Ethnic Study of Atherosclerosis (MESA)

Susan G. Lakoski, MD, MS; Philip Greenland, MD; Nathan D. Wong, PhD, MPH; Pamela J. Schreiner, PhD; David M. Herrington, MD, MHS; Richard A. Kronmal, PhD; Kiang Liu, PhD; Roger S. Blumenthal, MD



- 90% of women in MESA were classified as "low risk" based on FRS. The prevalence of CAC (CAC score > 0) in this "low-risk" subset was 32% (n = 870).
- Compared with women with no detectable CAC, low-risk women with a CAC score greater than 0 were at increased risk for CHD (hazard ratio, 6.5; 95% confidence interval, 2.6-16.4) and CVD events (hazard ratio, 5.2; 95% confidence interval, 2.5-10.8).
- Advanced CAC (CAC score > or = 300) was highly predictive of future CHD and CVD events compared with women with nondetectable CAC and identified a group of "low-risk" women with a 6.7% and 8.6% absolute CHD and CVD risk, respectively.





assified as "Low Risk" **CAC Score** 1-99 100-299 ≥300 255 (23) 90 (8) 68 (6) 22 (7) 78 (25) 7 (2) 44 (6) 145 (20) 21 (3) 111 (21) 20 (4) 9 (1) 589 (22) **176** (6) 105 (4)





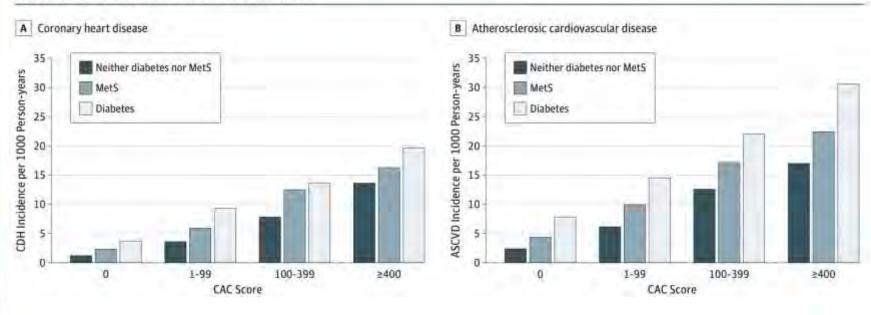
JAMA Cardiology | Original Investigation

Coronary Artery Calcium Score for Long-term Risk Classification in Individuals With Type 2 Diabetes and Metabolic Syndrome From the Multi-Ethnic Study of Atherosclerosis

Shaista Malik, MD, PhD, MPH; Yanglu Zhao, MD, MS; Matthew Budoff, MD; Khurram Nasir, MD; Roger S. Blumenthal, MD; Alain G. Bertoni, MD, MPH; Nathan D. Wong, PhD, MPH

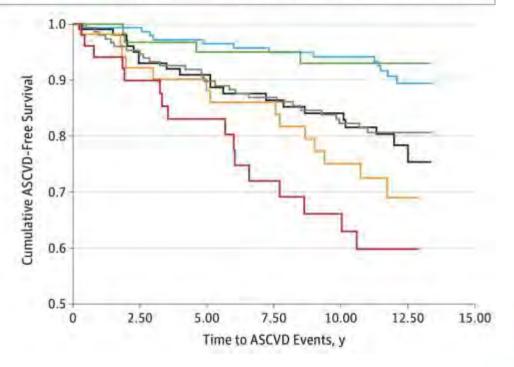


Figure 1. Incidence of Coronary Heart Disease (CHD) and Atherosclerotic Cardiovascular Disease (ASCVD) per 1000 Person-years by Disease Group and Coronary Artery Calcium (CAC) Score Categories





CAC score of 0 and diabetes duration <10 y
 CAC score of 1-399 and diabetes duration ≥10 y
 CAC score of 1-399 and diabetes duration <10 y
 CAC score of ≥400 and diabetes duration ≥10 y







European Heart Journal

JOURNAL ARTICLE

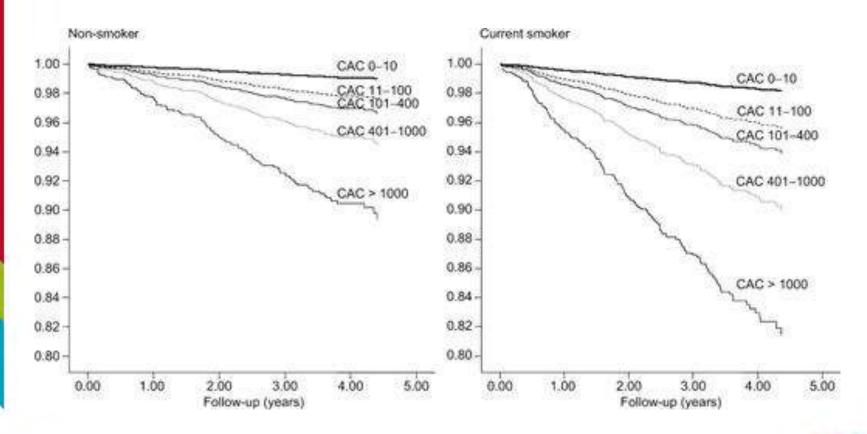
Leslee J. Shaw ™, Paolo Raggi, Tracy Q. Callister, Daniel S. Berman

European Heart Journal, Volume 27, Issue 8, April 2006, Pages 968–975, https://doi.org/10.1093/eurheartj/ehi750

Published: 27 January 2006 Article history ▼

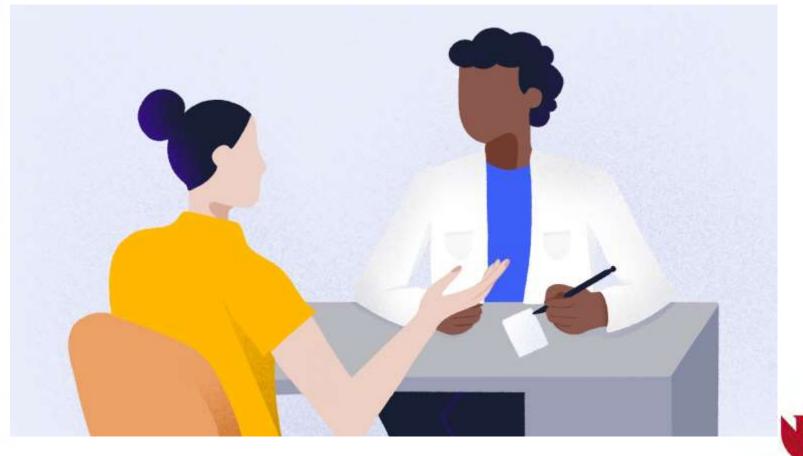
10,377 individuals, mean age 54 40% current smokers





Cox proportional hazard cumulative survival for smokers and non-smokers







American Journal of Cardiology

Effect of Patient Visualization of Coronary Calcium by Electron Beam
Computed Tomography on Changes in Beneficial Lifestyle Behaviors

Raza H. Orakzai, MD • Khurram Nasir, MD • Sarwar H. Orakzai, MD • Nove Kalia, MD • Ambarish Gopal, MD •
Kiran Musunuru, MD • Roger S. Blumenthal, MD • Mathew J. Budoff, MD 🙏 🖾 • Show less

Published: January 29, 2008 • DOI: https://doi.org/10.1016/j.amjcard.2007.11.059

- 980 asymptomatic patients
- Greater baseline CAC was strongly associated with initiation of ASA therapy, dietary changes, and increased exercise.

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When Does a Calcium Score Equate to Secondary Prevention?



Insights From the Multinational CONFIRM Registry

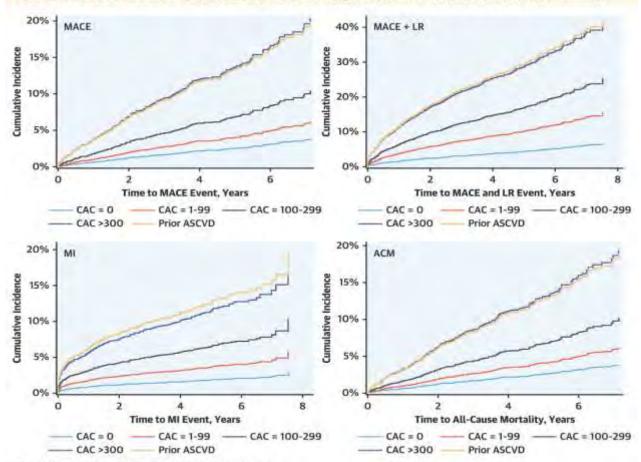
Matthew J. Budoff, MD, April Kinninger, MS, Heidi Gransar, MS, Stephan Achenbach, MD, Mouaz Al-Mallah, MD, Jeroen J. Bax, MD, Daniel S. Berman, MD, Filippo Cademartiri, MD, PhD, Tracy Q. Callister, MD, Hyuk-Jae Chang, MD, Benjamin J.W. Chow, MD, Ricardo C. Cury, MD, Gudrun Feuchtner, MD, Martin Hadamitzky, MD, Joerg Hausleiter, MD, Philipp A. Kaufmann, MD, Jonathon Leipsic, MD, Fay Y. Lin, MD, Yong-Jin Kim, MD, Hugo Marques, MD, PhD, Gianluca Pontone, MD, Ronen Rubinshtein, MD, Leslee J. Shaw, PhD, Todd C. Villines, MD, James K. Min, MD, on behalf of the CONFIRM Investigators

4,511 individuals without known CAD compared to 438 individuals with established ASCVD.

Mean age was 57.6 +/- 12.4years (56% male)



CENTRAL ILLUSTRATION Event Rates by CAC Score Categories for MACE Compared to Prior ASCVD Patients





Budoff MJ, et al. J Am Coll Cardiol Img. 2023;16(9):1181-1189.

What Guidelines Say?



Circulation

Volume 140, Issue 11, 10 September 2019; Pages e596-e646 https://doi.org/10.1161/CIP.0000000000000678



ACC/AHA CLINICAL PRACTICE GUIDELINE

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

Donna K. Arnett, PhD, MSPH, FAHA, Co-Chair, Roger S. Blumenthal, MD, FACC, FAHA, Co-Chair, Michelle A. Albert, MD, MPH, FAHA, Andrew B. Buroker, Esq, Zachary D. Goldberger, MD, MS, FACC, FAHA, Ellen J. Hahn, PhD, RN, Cheryl Dennison Himmelfarb, PhD, RN, ANP, FAHA, Amit Khera, MD, MSc, FACC, FAHA, Donald Lloyd-Jones, MD, SCM, FACC, FAHA, J. William McEvoy, MBBCh, MEd, MHS, Erin D. Michos, MD, MHS, FACC, FAHA, Michael D. Miedema, MD, MPH, Daniel Muñoz, MD, MPA, FACC, Sidney C. Smith Jr, MD, MACC, FAHA, Salim S. Virani, MD, PhD, FACC, FAHA, Kim A. Williams Sr, MD, MACC, FAHA, Joseph Yeboah, MD, MS, FACC, FAHA, and Boback Ziaeian, MD, PhD, FACC, FAHA



In intermediate-risk (≥7.5% to <20% 10-year lla B-NR Cholesterol Clinical Practice Guidelines.54.3-1

ASCVD risk) adults or selected borderline-risk (5% to <7.5% 10-year ASCVD risk) adults in whom a coronary artery calcium score is measured for the purpose of making a treatment decision, AND If the coronary artery calcium score is zero, it is reasonable to withhold statin therapy and reassess in 5 to 10 years, as long as higher-risk conditions are absent (eg, diabetes, family history of premature CHD, cigarette smoking); If coronary artery calcium score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥55 years of age; If coronary artery calcium score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy.54.3-28,54.3-34 Adapted from recommendations in the 2018



lla	B-NR	 In adults at borderline risk (5% to <7.5% 10-year ASCVD risk) or intermediate risk (≥7.5% to <20% 10-year ASCVD risk), it is reasonable to use additional risk-enhancing factors to guide decisions about preventive interventions (eg, statin therapy). 52.7-4-52.7-14
lla	B-NR	4. In adults at intermediate risk (≥7.5% to <20% 10-year ASCVD risk) or selected adults at borderline risk (5% to <7.5% 10- year ASCVD risk), if risk-based decisions for preventive interventions (eg, statin therapy) remain uncertain, it is reasonable to measure a coronary artery calcium score to guide clinician–patient risk discussion. 52.2-15-52.2-31



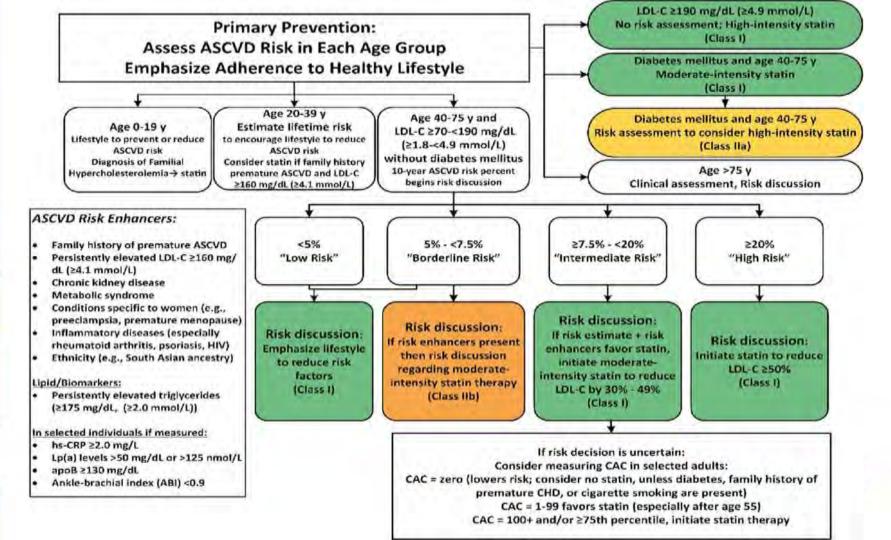


Table 6. Selected Examples of Candidates for Coronary Artery Calcium Measurement Who Might Benefit From Knowing Their Coronary Artery Calcium Score Is Zero (Table view)

Coronary Artery Calcium Measurement Candidates Who Might Benefit from Knowing Their Coronary Artery Calcium Score Is Zero

Patients reluctant to initiate statin who wish to understand their risk and potential for benefit more precisely

Patients concerned about need to reinstitute statin therapy after discontinuation for statin-associated symptoms

Older patients (men 55–80 y of age; women 60–80 y of age) with low burden of risk factors \$\frac{S4,3-53}{2}\$ who question whether they would benefit from statin therapy

Middle-aged adults (40–55 y of age) with PCE-calculated 10-year risk of ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group.





Contents lists available at ScienceDirect

Journal of Cardiovascular Computed Tomography

journal homepage: www.elsevier.com/locate/jcct

Guidelines

CAC-DRS: Coronary Artery Calcium Data and Reporting System. An expert consensus document of the Society of Cardiovascular Computed Tomography (SCCT)

Published: March 30, 2018 • DOI: https://doi.org/10.1016/j.jcct.2018.03.008 •



CAC-DRS category determined risk classifications and treatment recommendations.

a. Agatston Score	()		
	CAC Score	Risk	Treatment Recommendation
CAC-DRS 0	0	very low	statin generally not recommended*
CAC-DRS 1	1-99	mildly increased	moderate intensity statin
CAC-DRS 2	100-299	moderately increased	moderate to high intensity statin + ASA 81mg
CAC-DRS 3	> 300	moderately to severely increased	high intensity statin + ASA 81mg
b. Visual Score			
	CAC Score	Risk	Treatment Recommendation
CAC-DRS 0	0	very low	statin not recommended*
CAC-DRS 1	1	mildly increased	moderate intensity statin
CAC-DRS 2	2	moderately increased	moderate to high intensity statin + ASA 81mg
CAC-DRS 3	3	moderately to severely increased	high intensity statin + ASA 81mg

^{*}excluding familial hypercholesterolemia.

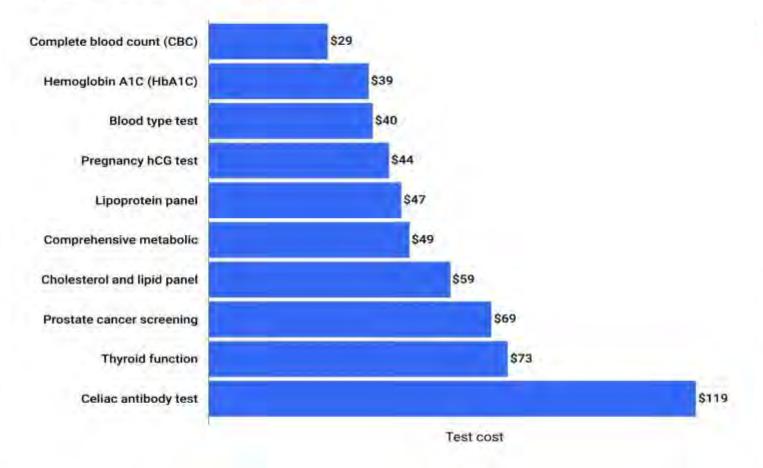
All dedicated CAC scans and all non-gated non-contrast chest CT scans irrespective of the indication.



\$50-400 Most insurances do not cover



Average Cost of Blood Work





Take Home Message

- ✓ CAC is simple and highly reproducible with low radiation.
- ✓ CAC offers direct assessment of the total burden of coronary calcified plaque
- ✓ CAC integrates the upstream effects of all risk and genetic factors over the life of an individual
- ✓ CAC overcome inherent challenges in one-time measures of individual risk factors which may be highly variable over time.
- ✓ CAC has high quality evidence as one of the strongest individual tests for determining long-term ASCVD risk.



Questions

What CAC is equates to secondary prevention?

- a. 100
- b. 1000
- c. 300
- d. 400



What is the "warranty period" of a CAC of zero; that is, when should someone with low 10-year ASCVD risk be rescanned?

- a. Never
- b. 5 years
- c. 1 year
- d. 10 years



