BRIGHAM AND WOMEN'S HOSPITAL
| Heart & Vascular Center |

Asymptomatic Patient with CAC: Evaluation and Management

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Associate Director, Cardiovascular Imaging Program
Director, Cardiac Computed Tomography
Co-Director, Cardiovascular Imaging Training Program
Senior Physician, Preventive Cardiology
Brigham and Women's Hospital
Past-President, Society of Cardiovascular Computed Tomography
Chair-Elect, ACC Cardiovascular Imaging Section Leadership Council

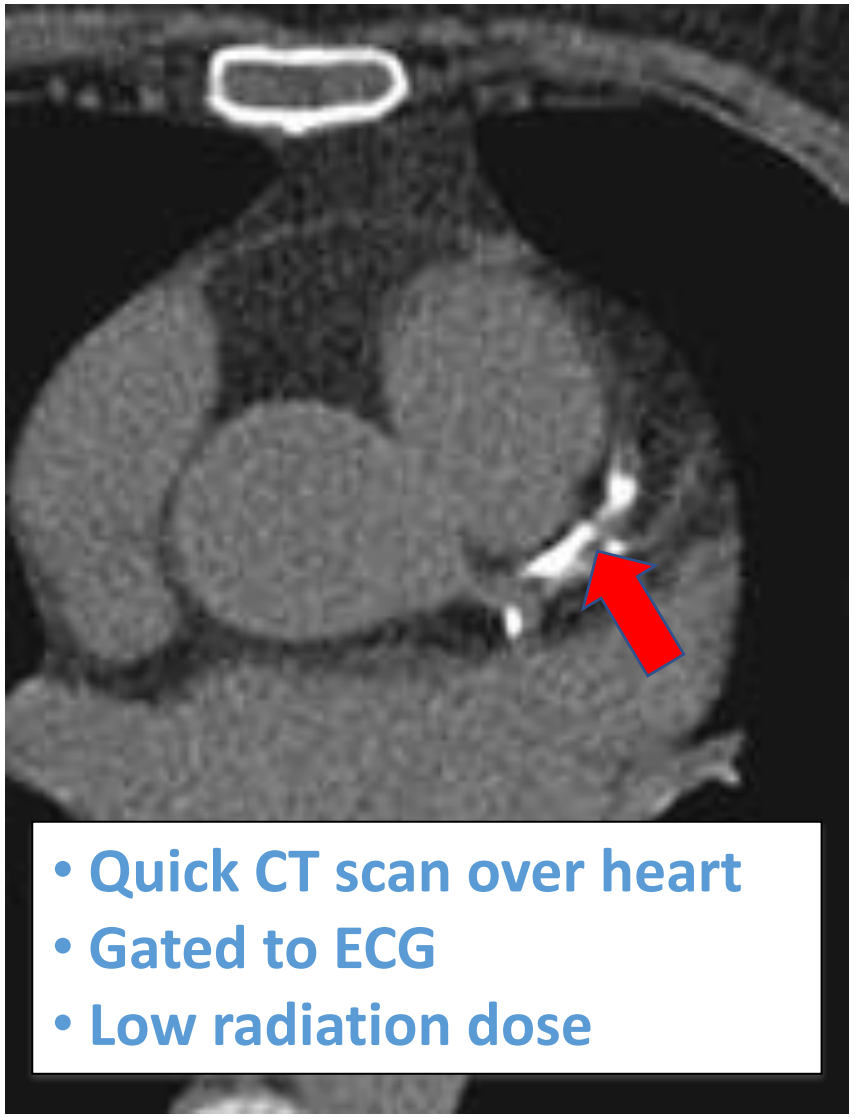
January 21, 2023

Your cardiology colleague who did not get to come to today's Cardiovascular Symposium India meeting, asks you the following questions:

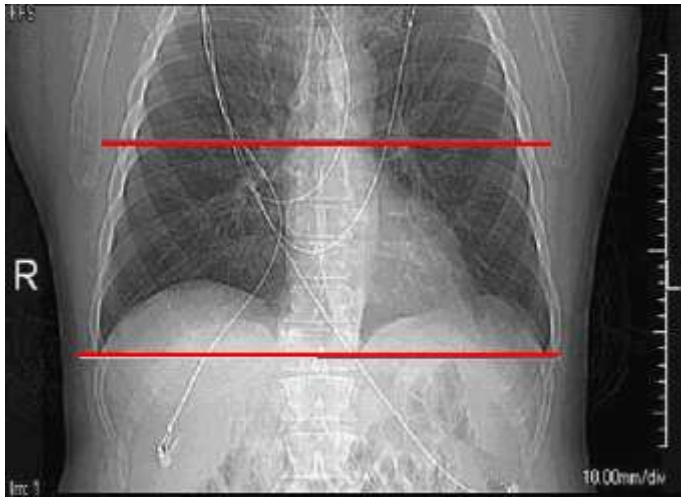
Most Common Questions:

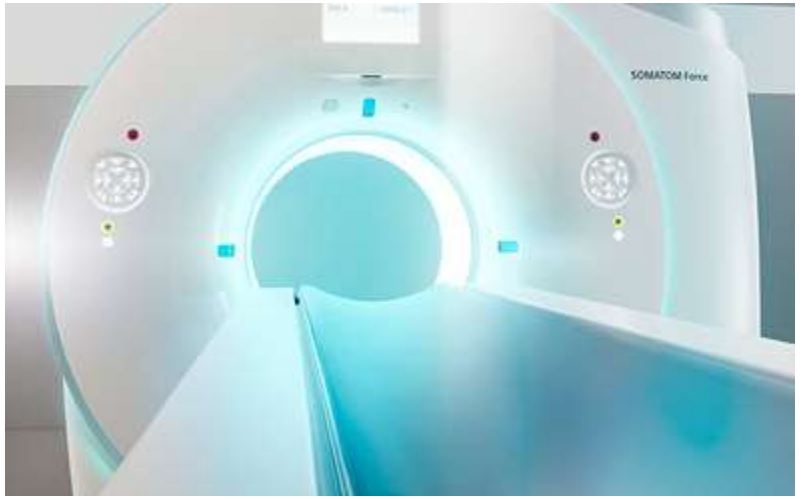
1. What is CAC….and how is this test done?
2. When is CAC testing useful ?
3. How does CAC enhance risk assessment ?
4. What medical therapy is needed ?
5. When is stress testing helpful ?
6. What if the patient has a prior chest CT…do I need CAC ?

Coronary Artery Calcium is Coronary Plaque



- Quick CT scan over heart
- Gated to ECG
- Low radiation dose





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CAC Testing in Guidelines

2018 Multisociety Cholesterol Guideline and 2019 ACC/AHA Prevention Guideline

Assessment of Cardiovascular Risk		
COR	**LOE**	**Recommendations**
IIa	B-NR	In intermediate-risk or selected borderline-risk adults, if the decision about statin use remains uncertain, it is reasonable to use a CAC score in the decision to withhold, postpone or initiate statin therapy.

2020 NLA Scientific Statement

The National Lipid Association scientific statement on coronary artery calcium scoring to guide preventive strategies for ASCVD risk reduction

Carl E. Orringer[a], Michael J. Blaha, Ron Blankstein, Matthew J. Budoff, Ronald B. Goldberg, Edward A. Gill, Kevin C. Maki, Laxmi Mehta, Terry A. Jacobson

2017 SCCT Expert Consensus

Guidelines

Clinical indications for coronary artery calcium scoring in asymptomatic patients: Expert consensus statement from the Society of Cardiovascular Computed Tomography

Harvey Hecht, MD, FSCCT [a,*], Michael J. Blaha, MD, MPH [b], Daniel S. Berman, MD, FSCCT [c], Khurram Nasir, MD, MPH, FSCCT [d], Matthew Budoff, MD, FSCCT [e], Jonathon Leipsic, MD, FSCCT [f], Ron Blankstein, MD, FSCCT [g], Jagat Narula, MD, PhD [a], John Rumberger, MD, FSCCT [h], Leslee J. Shaw, PhD, FSCCT [i]

2020 Endocrine Guideline

Clinical Practice Guideline

Lipid Management in Patients with Endocrine Disorders: An Endocrine Society Clinical Practice Guideline

Connie B. Newman,[1] Michael J. Blaha,[2] Jeffrey B. Boord,[3] Bertrand Cariou,[4] Alan Chait,[5] Henry G. Fein,[6] Henry N. Ginsberg,[7] Ira J. Goldberg,[1] M. Hassan Murad,[8] Savitha Subramanian,[5] and Lisa R. Tannock[9]

CAC Testing in Guidelines

2018 Multisociety Cholesterol Guideline and 2019 ACC/AHA Prevention Guideline

Assessment of Cardiovascular Risk		
COR	**LOE**	**Recommendations**
IIa	**B-NR**	**In intermediate-risk or selected borderline-risk adults, if the decision about statin use remains uncertain, it is reasonable to use a CAC score in the decision to withhold, postpone or initiate statin therapy.**

Additional possible indications for CAC testing in 2023:

- **Patients who require improved risk assessment**
- **Patients who are statin averse or statin intolerant**
- **Patients in whom uncertainty on intensity of therapy**

CAC Testing in Guidelines

STATE-OF-THE-ART REVIEW

JACC CV Imaging 2022

Major Global Coronary Artery Calcium Guidelines

Ilana S. Golub, BS, Orly G. Termeie, BS, Stephanie Kristo, BS, Lucia P. Schroeder, BS, Suvasini Lakshmanan, MD, Ahmed M. Shafter, MD, Luay Hussein, MD, Dhiran Verghese, MD, Jairo Aldana-Bitar, MD, Venkat S. Manubolu, MD, Matthew J. Budoff, MD

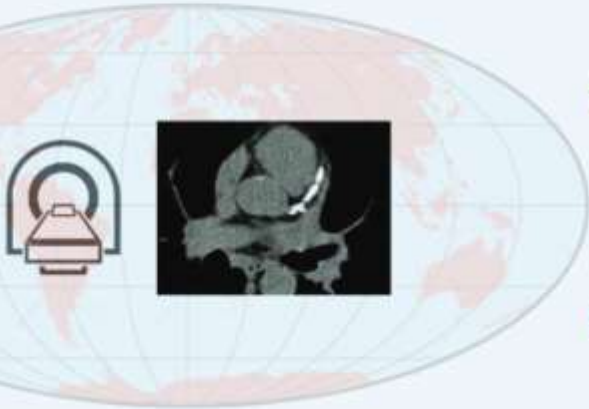
Major Worldwide Coronary Artery Calcium Guidelines

- CAC as an arbitrator of statin use on intermediate risk.

- CAC as a tool for adjudicating statin allocation.
- For CAC scoring among all asymptomatic patients with suggested ECG changes for ischemia.

- CAC as an arbitrator of statin use on intermediate risk.

- CAC as a prognostic tool in intermediate- to high-risk individuals.
- Local studies suggested.



- CAC scoring to up-classify or down-classify their risk (T1DM <35 yrs old, T2DM <50 yrs old), with diabetes mellitus duration <10 years and without other risk factors.

- CAC as a risk assessing tool, risk reclassification and therapy determinator.
- Indicated in low risk with strong family history or other concern features.
- High risk reluctant to accept treatment, CAC is indicated.

- CAC as an arbitrator for aspirin allocation.

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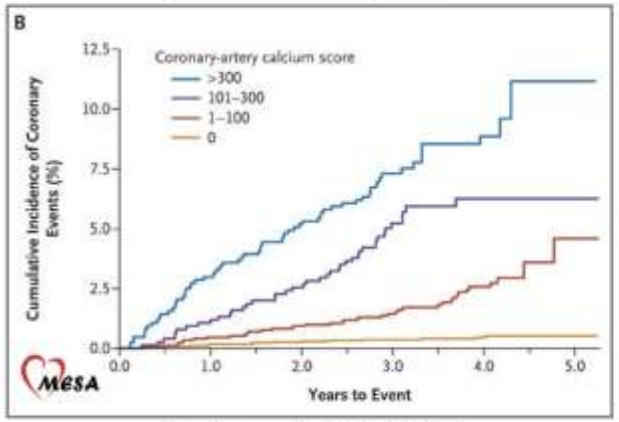
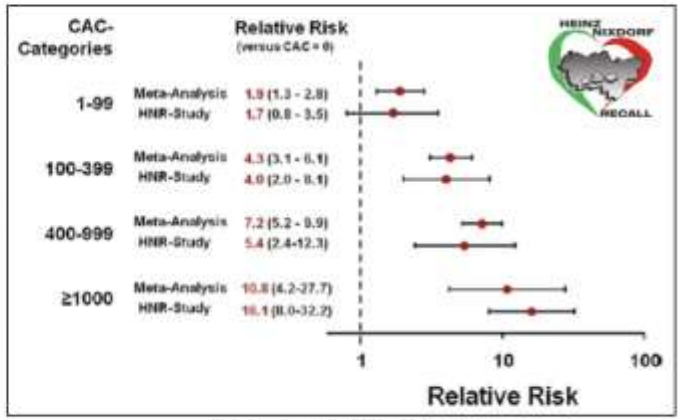
levated . → igher \isk of vents

Multi-Ethnic Study of Atherosclerosis



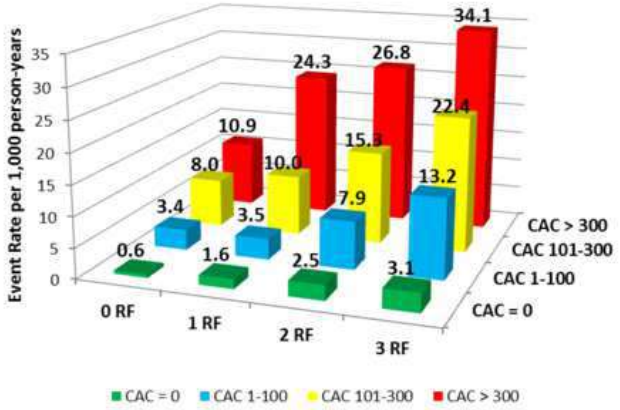
(Detrano, NEJM 2008)

Heinz Nixdorf Recall Study



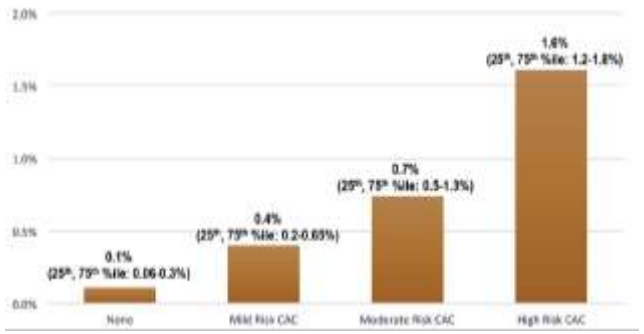
(Erbel, JACC 2010)

Silverman et al, EHJ 2014



Median Annual MACE

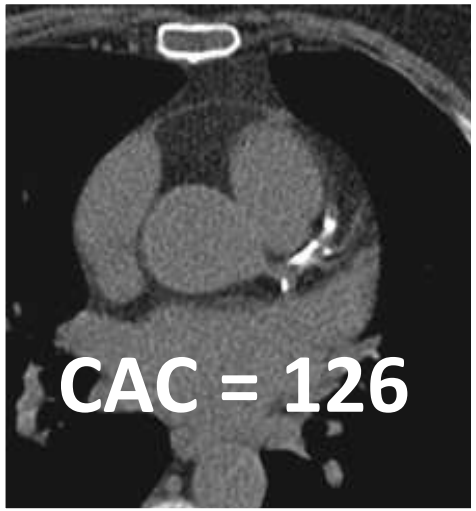
(Pooled data, SCCT CAC Statement, 2017)



Increased Risk of:

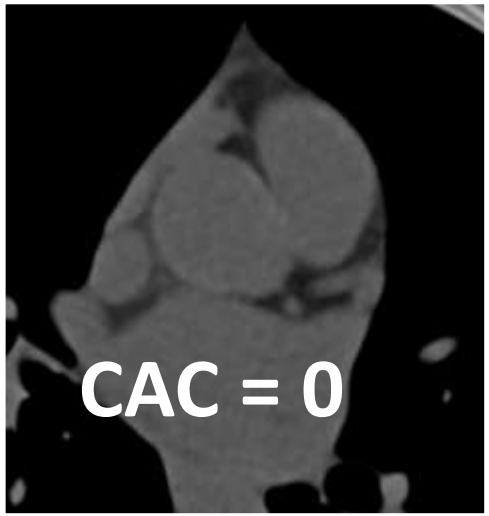
- All cause death
- CV death
- Non CV death
- MI
- CVA
- Coronary revascularization
- Heart failure
- Atrial fibrillation
- Valvular disease (MAC,AVC)

Elevated CAC → Higher Risk of Events



- Increased risk is proportional to amount of CAC
- Risk is incremental to traditional risk factors

CAC=0 Low Event Rates



- Concept of a “negative risk marker”
- CAC=0 not risk of zero, but risk *may* be low enough that Rx can be deferred

Blaha, Blankstein, Nasir JACC 2019

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Applying the 2018 ACC/AHA cholesterol guideline

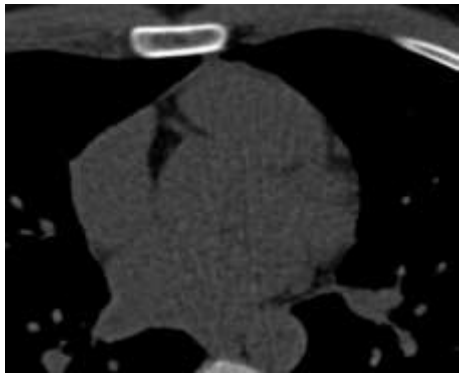
- Calculated 10-year ASCVD risk
- Consider risk enhancing factors

- Patient – Physician Discussion on role of statins

Uncertainty about risk

Preference to avoid statin therapy

Consider CAC Scan



- ✓ If CAC=0, treatment with statin may be withheld or delayed, except in cigarette smokers, strong family history of premature ASCVD

- ✓ If CAC 1 to 99: favors statin therapy, especially in those ≥55 years of age
- ✓ If CAC ≥100 or ≥75th percentile, statin therapy is indicated

Treatment Recommendations: Severe CAC

- **Aggressive LDL-C Lowering**: High intensity statin / ezetimibe / PCSK9i / (Bempedoic acid)
- **Antiplatelet agents**: ASA ; ? Antithrombotic therapy – rivaroxaban 2.5mg bid
- **Blood pressure lowering** (<120/80)
- **If diabetes/obesity**: GLP1-RA
- **In selected patients**: Icosapent Ethyl ; ↓ inflammation
- **Future options**: ↓Lp(a)

Dietary Changes

Exercise

Weight Loss

Avoid tobacco

Stress management

Diabetes management

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CAC and CCTA Used to Enrich Risk

CAC>100

Trial Design

- At least 13,000 high-risk patients with atherosclerosis or diabetes but no prior MI or stroke
- High LDL-C or non-HDL-C despite optimized lipid lowering therapy

RANDOMIZED
DOUBLE BLIND

Evolocumab SC
140 mg Q2W

Placebo SC
Q2W

Event-driven trial
Minimum f/up ≥4 yrs

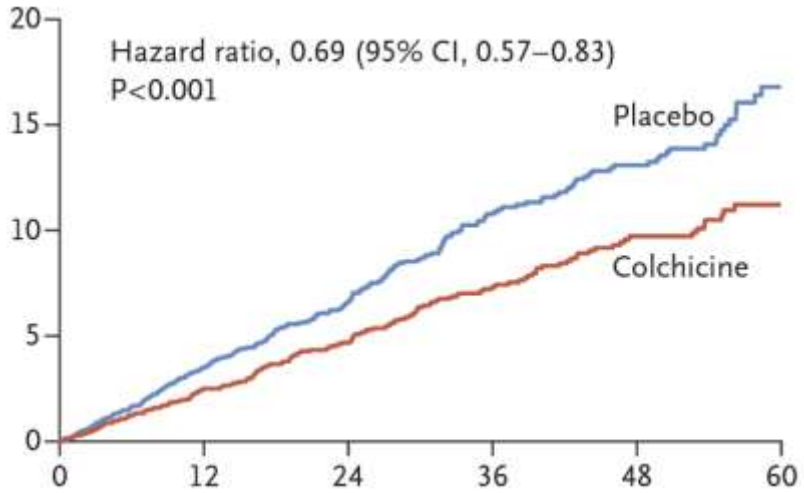
Primary Composite Endpoints:
- Coronary heart disease death, MI, or ischemic stroke
- Coronary heart disease death, MI, ischemic stroke, or ischemia-driven revasc

Vesalius-CV

LoDoCo2 Trial (NEJM 2020)

TRIAL POPULATION

Patients 35 to 82 years of age were eligible if they had any evidence of coronary disease on invasive coronary angiography or computed tomography angiography or a coronary-artery calcium score of at least 400 Agatston units on a coronary-artery calcium scan. Patients were required to have been



ORIGINAL ARTICLE

Colchicine in Patients with Chronic Coronary Disease

S.M. Nidorf, A.T.L. Fiolet, A. Mosterd, J.W. Eikelboom, A. Schut, T.S.J. Opstal, S.H.K. The, X.-F. Xu, M.A. Ireland, T. Lenderink, D. Latchem, P. Hoogslag, A. Jerzewski, P. Nierop, A. Whelan, R. Hendriks, H. Swart, J. Schaap, A.F.M. Kuijper, M.W.J. van Hessen, P. Saklani, I. Tan, A.G. Thompson, A. Morton, C. Judkins, W.A. Bax, M. Dirksen, M. Alings, G.J. Hankey, C.A. Budgeon, J.G.P. Tijssen, J.H. Cornel, and P.L. Thompson, for the LoDoCo2 Trial Investigators*

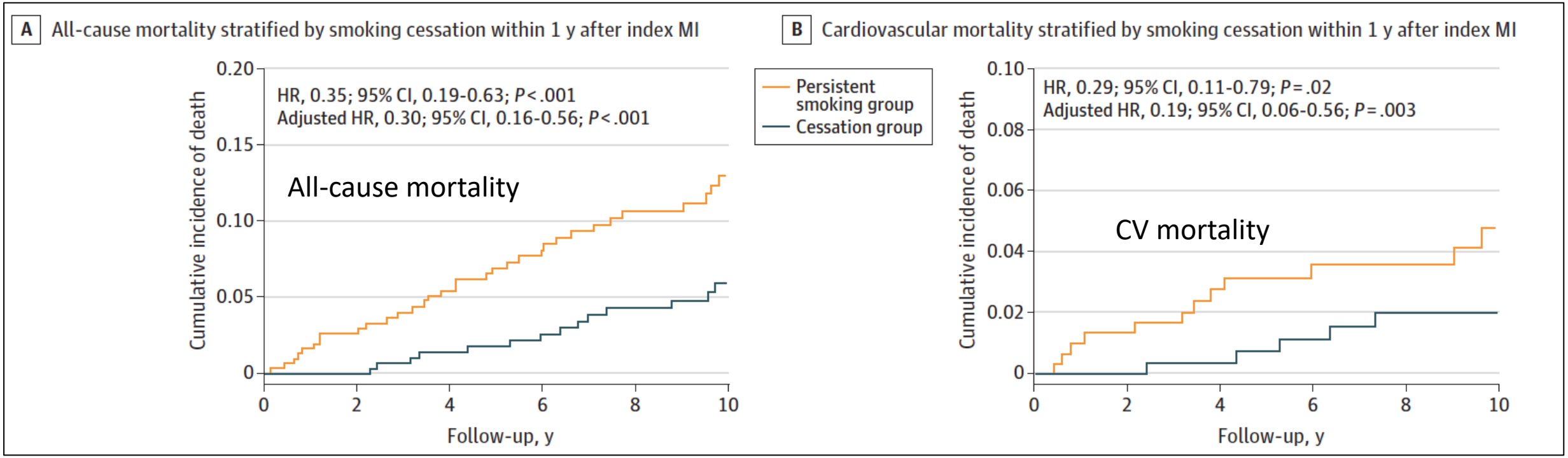
Identification of plaque enhances prevention!

<u>When CAC identified</u>:

↑rate initiation/continuation of aspirin, lipid lowering Rx, blood pressure lowering Rx, increase in exercise, dietary changes

(Gupta et al, JACC CV Imaging, 2017)

62% of smokers continue to smoke post MI
If quit >70% lower all-cause and cardiovascular mortality



JAMA Network Open

Original Investigation | Cardiology

Association of Smoking Cessation and Survival Among Young Adults With Myocardial Infarction in the Partners YOUNG-MI Registry

David W. Biery, AB; Adam N. Berman, MD; Avinainder Singh, MBBS, MMSc; Sanjay Divakaran, MD; Ersilia M. DeFilippis, MD; Bradley L. Collins, MD; Ankur Gupta, MD, PhD; Amber Fatima, MBBS; Arman Qamar, MD; Josh Klein, BS; Jon Hainer, BS; Michael J. Blaha, MD, MPH; Marcelo F. Di Carli, MD; Khurram Nasir, MD, MPH; Deepak L. Bhatt, MD, MPH; Ron Blankstein, MD

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Considerations for Stress Testing

1. Most Do Not Require Any Stress Testing

"There is no evidence to support the benefit of performing stress testing, or invasive coronary arteriography in asymptomatic individuals with high coronary calcium scores."

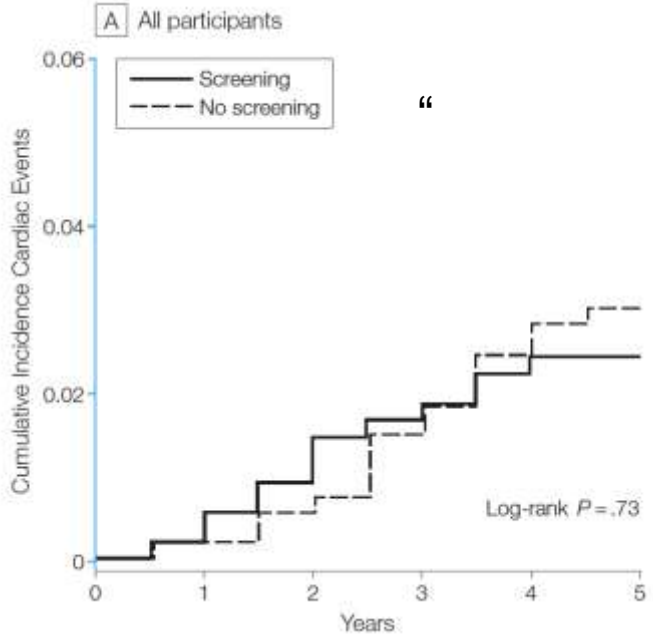
NLA CAC Scientific Statement, 2021

Considerations for Stress Testing

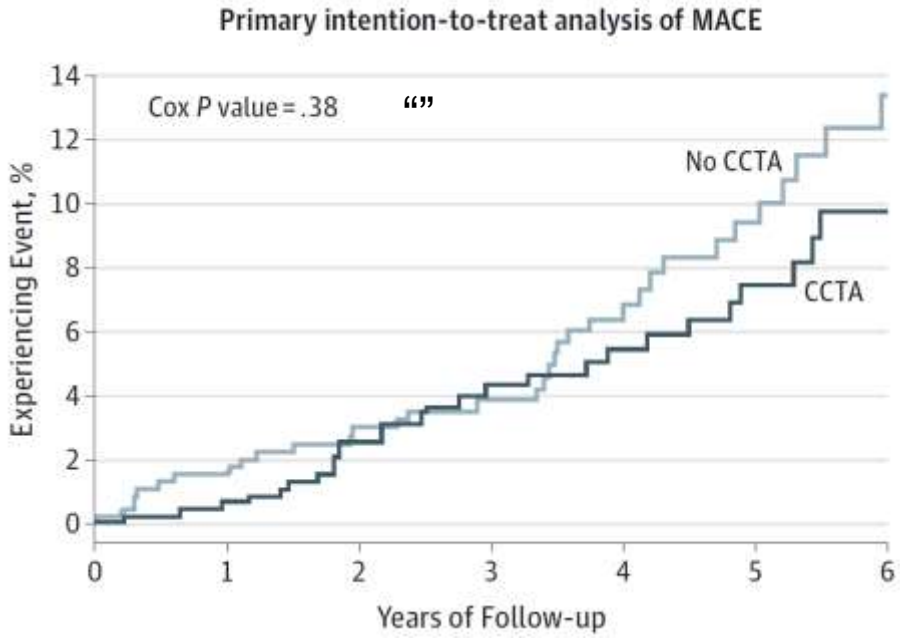
1. Most Do Not Require Any Stress Testing

(No benefit of testing asymptomatic pts)

Cardiac Outcomes After Screening for Asymptomatic Coronary Artery Disease in Patients With Type 2 Diabetes
The DIAD Study: A Randomized Controlled Trial



Effect of Screening for Coronary Artery Disease Using CT Angiography on Mortality and Cardiac Events in High-Risk Patients With Diabetes
The FACTOR-64 Randomized Clinical Trial



Considerations for Stress Testing

1. Most Do Not Require Any Stress Testing

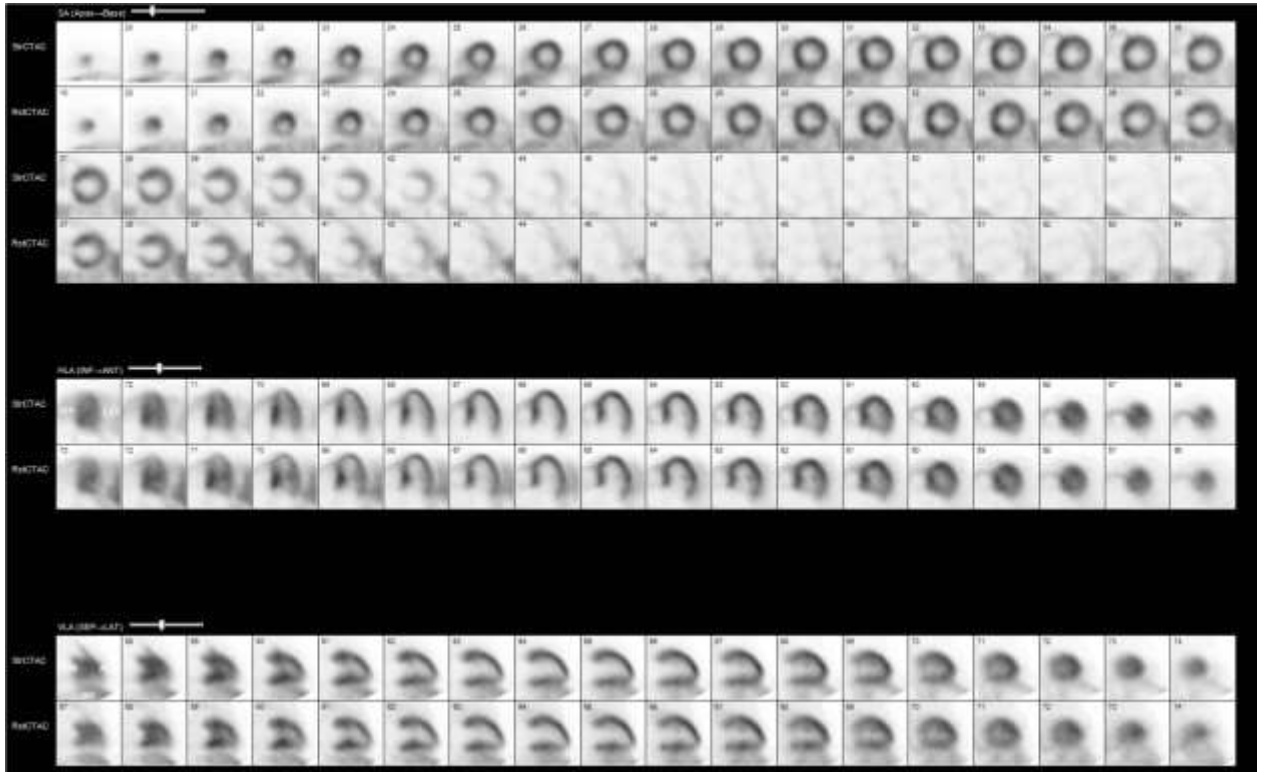
2. If severe CAC AND unclear if symptoms, can consider exercise treadmill testing

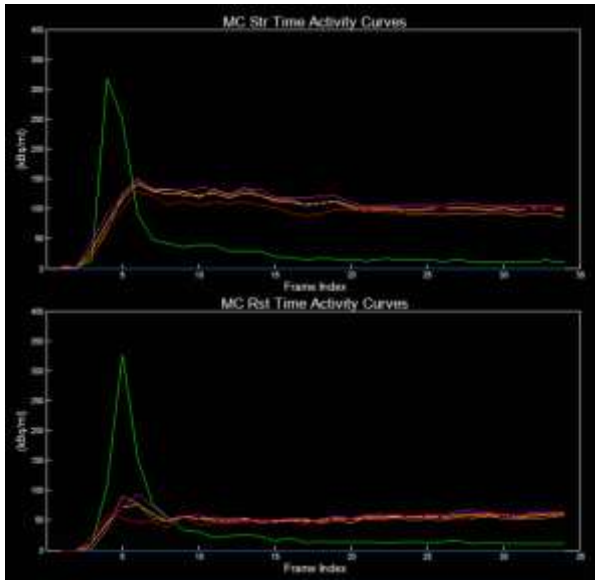
“

3. Do not send for invasive angiography

4. PET MPI most reassuring if normal

PET MPI in 63 yo F with severe CAC





Global Results

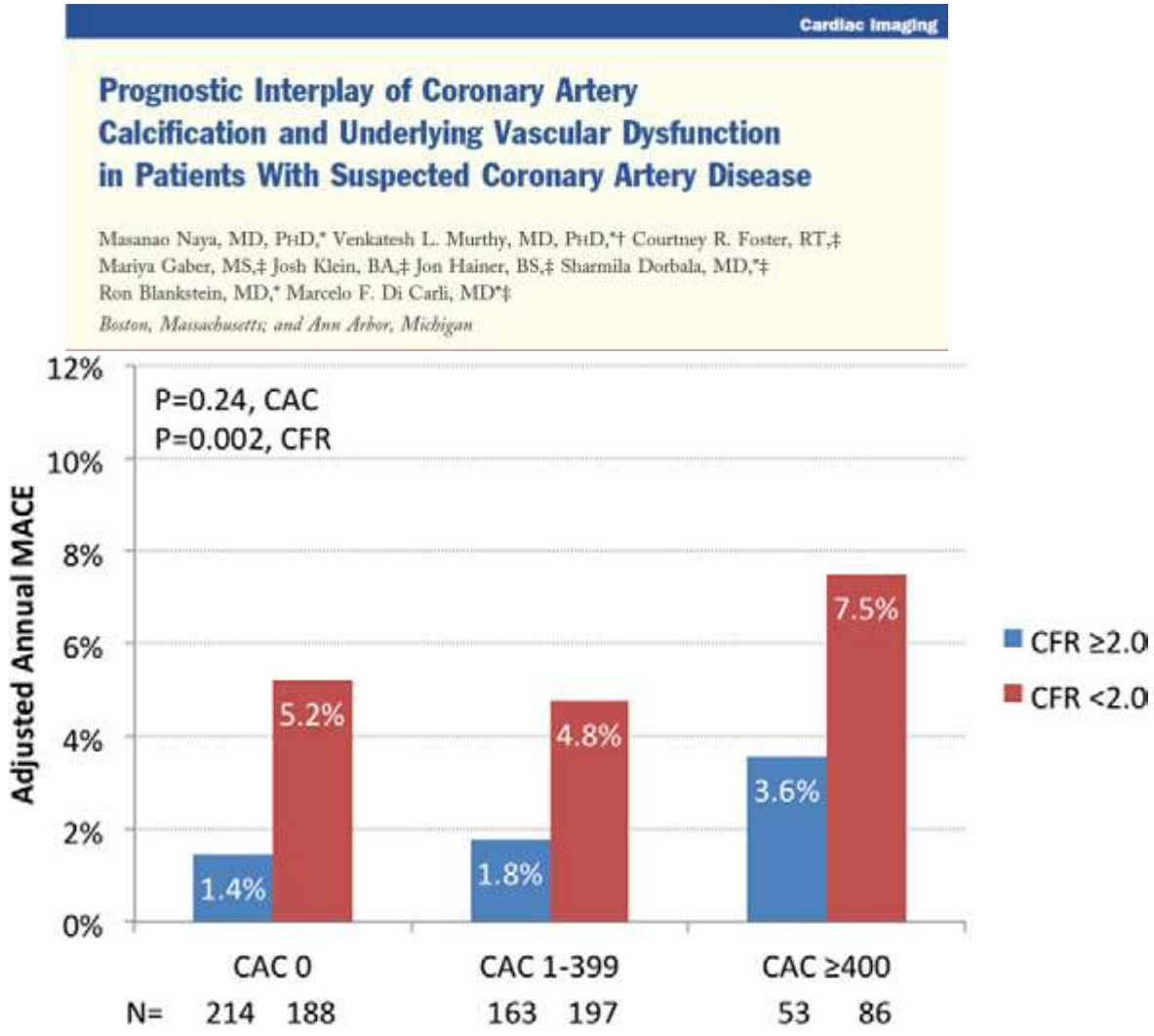
Region	Mean Flow (ml/min/g) MC Str	MC Rst	MC Str	MC Rst	Reserve
LAD	90 %	88 %	2.65	0.99	2.67
LCX	77 %	76 %	2.62	0.96	2.73
RCA	84 %	81 %	2.11	0.79	2.68
TOT	84 %	82 %	2.48	0.92	2.70

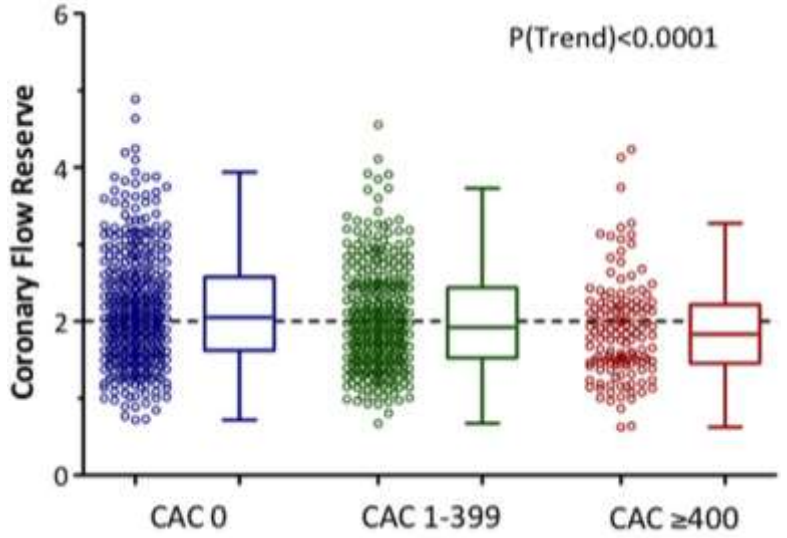
Algorithm (MC Str): INVIA N-13 ROI 1:1
Algorithm (MC Rst): INVIA N-13 ROI 1:1

Normal Myocardial Blood Flow (MBF) Reserve:

1. **Good prognosis**
2. **Low likelihood of obstructive 3vz**

CAC and Myocardial Blood Flow Reserve: Complementary Role





MACE:

- cardiac death
- myocardial infarction
- Late revascularization,
- hospitalization for heart failure

Low yield of Detecting Ischemia in Asymptomatic Individuals with CAC

CACS and the Frequency of Stress-Induced Myocardial Ischemia During MPI

A Meta-Analysis

Chirag Bavishi, MD, MPH, Edgar Argulian, MD, Saurav Chatterjee, MD, Alan Rozanski, MD

6 studies ; 2123 pts

In asymptomatic patients, ischemia < 10%

TABLE 2 Pooled Prevalence and Odds Ratio for Ischemia by CAC Categories From 6 Major Studies*

CAC Categories	Patients (n)	Pooled Prevalence of Ischemia (%)	Range of Ischemia (%)	Pooled Odds Ratio (95% CI)
0	487	6.6	0.0-24.1	Reference
1-100	529	8.5	2.1-50.0	1.7 (1.04-2.2)
101-399	513	10.5	4.0-63.6	3.3 (1.4-8.2)
≥400	594	23.6	12.4-57.1	6.9 (3.5-13.4)

Limitation: includes both symptomatic and asymptomatic individuals

Is adding B-blockers helpful ?

β-Blocker Use and Clinical Outcomes in Stable Outpatients With and Without Coronary Artery Disease

Sripal Bangalore, MD, MHA
Ph. Gabriel Steg, MD
Prakash Deedwania, MD
Kevin Crowley, MS
Kim A. Eagle, MD
Shinya Goto, MD, PhD
E. Magnus Ohman, MD
Christopher P. Cannon, MD
Sidney C. Smith Jr, MD
Uwe Zeymer, MD
Elaine B. Hoffman, PhD
Franz H. Messerli, MD
Deepak L. Bhatt, MD, MPH
for the REACH Registry Investigators

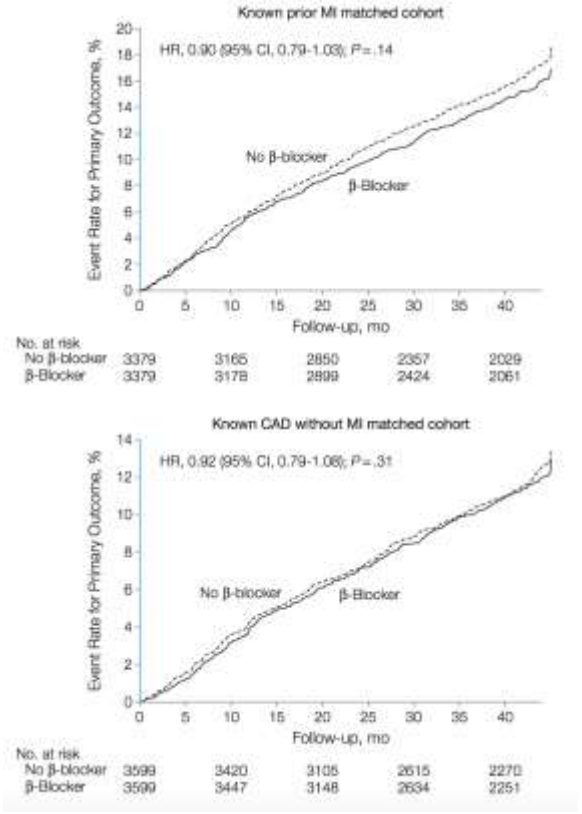
Context β-Blockers remain the standard of care after a myocardial infarction (MI). However, the benefit of β-blocker use in patients with coronary artery disease (CAD) but no history of MI, those with a remote history of MI, and those with only risk factors for CAD is unclear.

Objective To assess the association of β-blocker use with cardiovascular events in stable patients with a prior history of MI, in those with CAD but no history of MI, and in those with only risk factors for CAD.

Design, Setting, and Patients Longitudinal, observational study of patients in the Reduction of Atherothrombosis for Continued Health (REACH) registry who were divided into 3 cohorts: known prior MI (n=14 043), known CAD without MI (n=12 012), or those with CAD risk factors only (n=18 653). Propensity score matching was used for the primary analyses. The last follow-up data collection was April 2009.

Main Outcome Measures The primary outcome was a composite of cardiovascular death, nonfatal MI, or nonfatal stroke. The secondary outcome was the primary outcome plus hospitalization for atherothrombotic events or a revascularization procedure.

Results Among the 44 708 patients, 21 860 were included in the propensity score–matched analysis. With a median follow-up of 44 months (interquartile range, 35-45



"the use of b-blockers was not associated with a lower risk of composite cardiovascular events."

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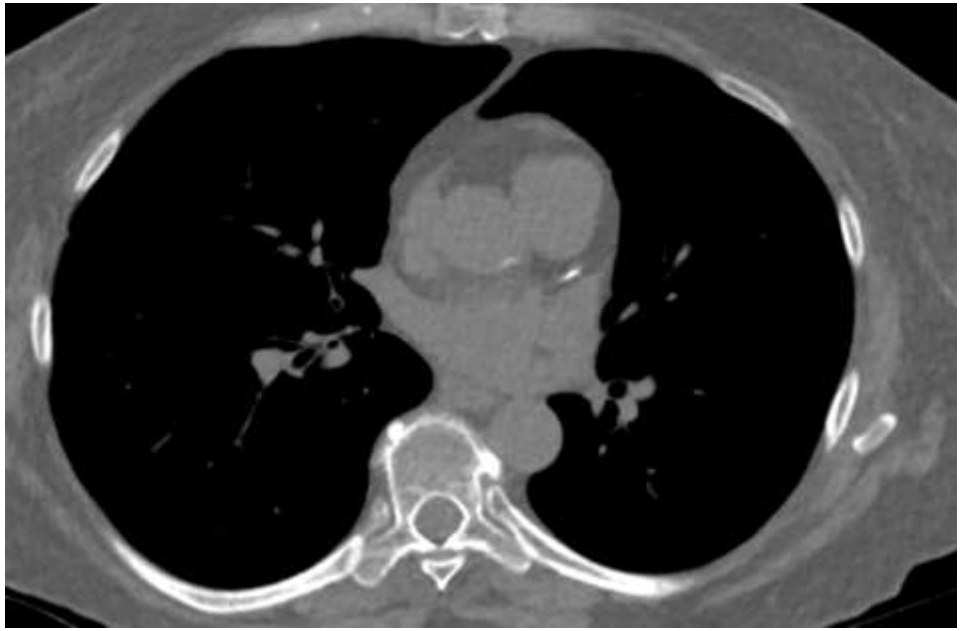
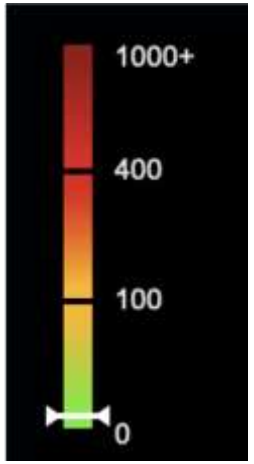
CAC Can Often Be Identified on Images Already Acquired

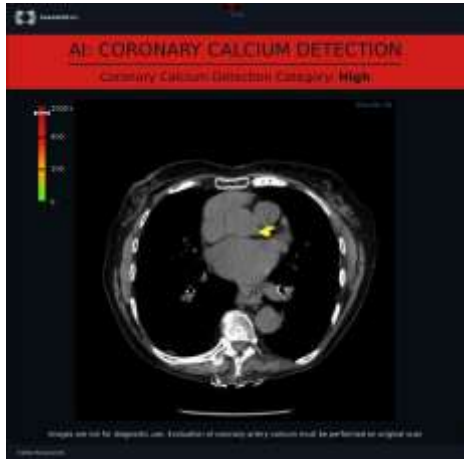


Prior chest CT can be used to estimate presence and amount of CAC (although this is often not reported)

Even if no score….knowing if mild/moderate/severe amount of CAC may be sufficient

In the future AI used detection of CAC may enhance detection





Extensive Coronary Artery Calcifications

No Longer Primary Prevention!

Ron Blankstein, MD,[a] Y. Chandrashekhar, MD[b]

It is well established that the overall amount of coronary plaque—which can be estimated by measuring the coronary artery calcium score (CAC)—directly correlates with the risk of future cardiovascular events, myocardial infarction, and stroke (1,2); absence of calcium predicts very low risk and its presence identifies a cohort with increased risk—this holds across a multiple populations of variable risk including FH (3), DM including the younger type I patient (4) and across a range of risk factor severity (5).

The predictive value for risk increases proportionally with higher CAC scores, but where the group with the highest risk begins is unclear - CAC ≥100 Agatston units (AU) or ≥75th percentile (for age and sex) are considered higher risk and might become a statin indication in the right context, but there may sometimes be a dissociation between the 2 indices (CAC ≥100 Agatston units (AU) or ≥75th percentile),

data that among individuals without cardiovascular disease who have a borderline (5.0% to 7.5%) or intermediate (7.5% to 20%) 10-year risk of atherosclerotic cardiovascular disease (ASCVD) events, the presence of any CAC can be used to identify those who are more likely to benefit from statin therapy (12).

However, the landscape of preventive cardiology has changed significantly in the last several years, and there are now several new effective pharmacological agents that can be added on top of statin therapy, including PCSK9 inhibitors, icosapent ethyl, low-dose antithrombotic therapies, and new agents to treat diabetes (13). Furthermore, current on-going clinical trials are evaluating new therapies to lower triglycerides, low-density lipoprotein cholesterol, and lipoprotein (a). Although there is substantial excitement about the resurgence of multiple new therapeutic options for the prevention of cardiovascular events,

Take Home Points:

- Patients with elevated CAC have increased risk
- Intensity of preventive measures based on amount of CAC & other risk factors:
  - ✓ Lifestyle therapies for all
  - ✓ LDL lowering
  - ✓ Consider ASA if severe CAC
  - ✓ GLP1RA if overweight/DM
- No further testing required if asymptomatic
- If uncertain regarding symptoms → ETT
- If stress test → exercise preferred

  (PET with quantitative MBFR if available)

Thank You

Extra Slides: CAC in Young

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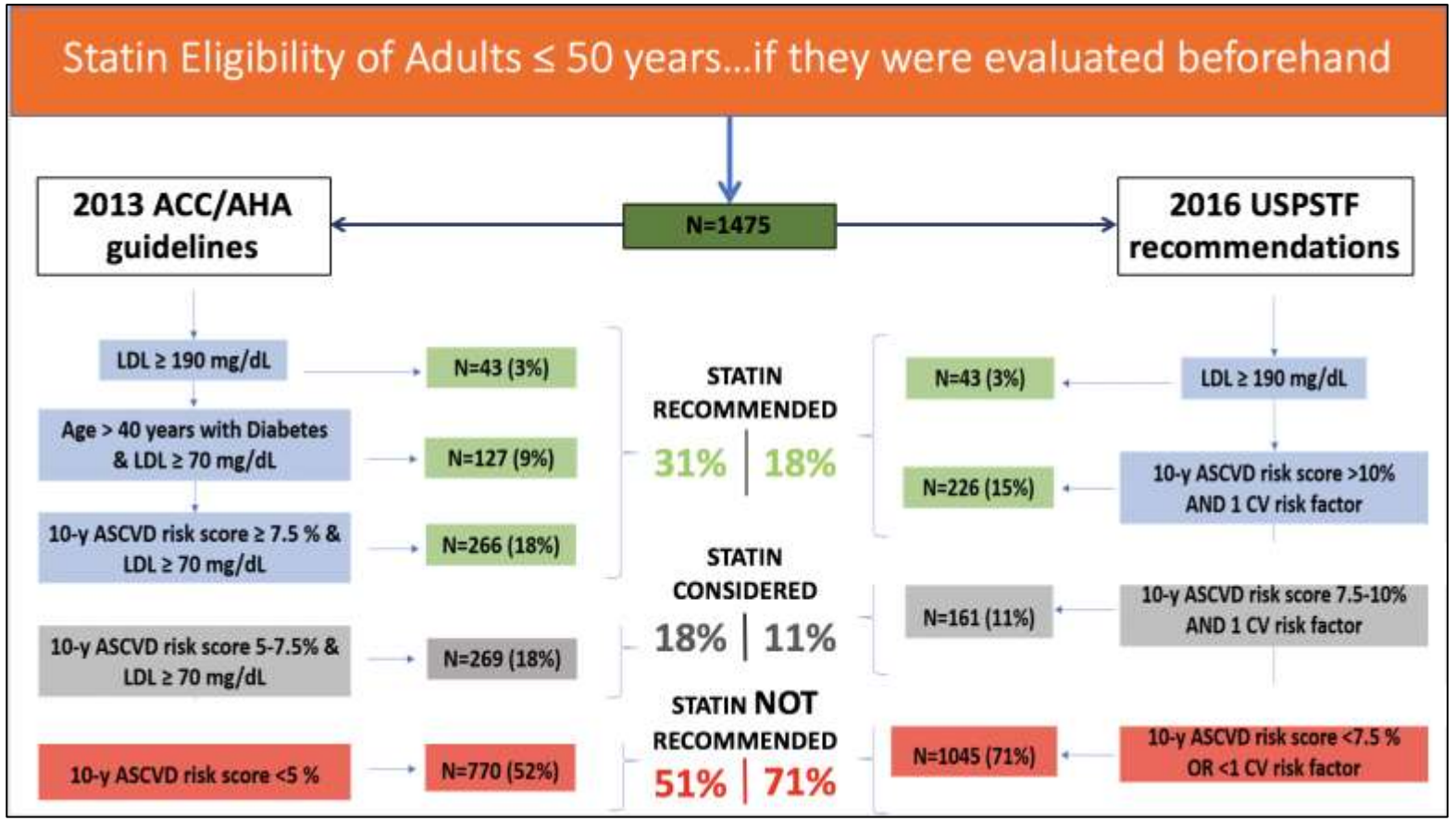
Cardiovascular Risk and Statin Eligibility of Young Adults After an MI

Partners YOUNG-MI Registry

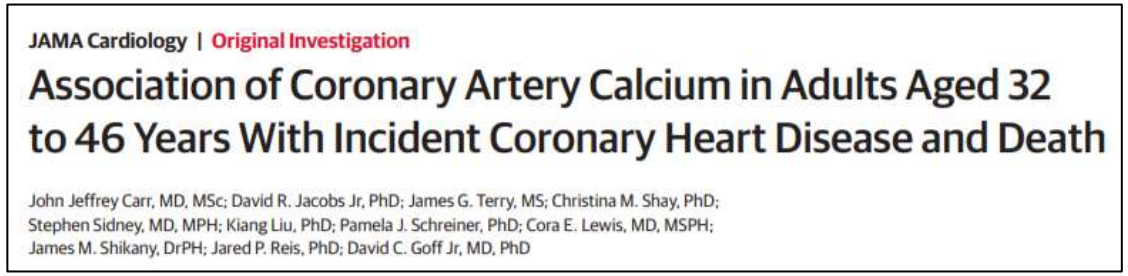
Avinainder Singh, MBBS,[a] Bradley L. Collins, BA,[a] Ankur Gupta, MD, PhD,[a] Amber Fatima, MBBS,[b] Arman Qamar, MD,[c] David Biery, BS,[a] Julio Baez,[a] Mary Cawley,[a] Josh Klein, BS,[a] Jon Hainer, BS,[a] Jorge Plutzky, MD,[c] Christopher P. Cannon, MD,[c] Khurram Nasir, MD, MPH,[d] Marcelo F. Di Carli, MD,[a] Deepak L. Bhatt, MD, MPH,[c] Ron Blankstein, MD[a]



Majority of young adults who experienced MI under the age of 50 would not have been eligible for statin therapy prior to their MI

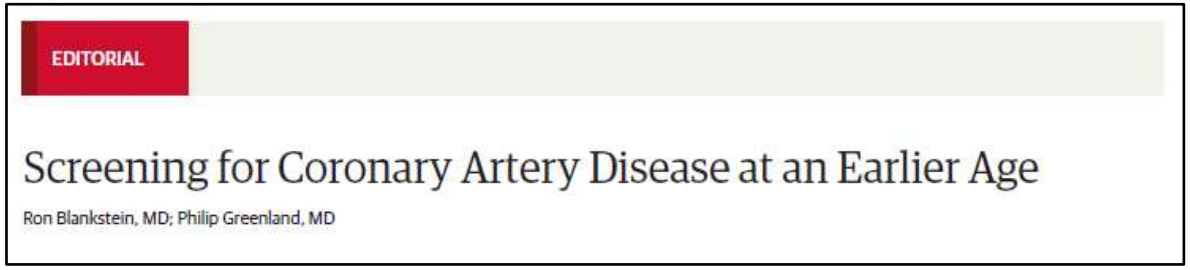
JACC 2018

Is there a role for selective CAC testing in Young Patients ?


JAMA Cardiology | Original Investigation

Association of Coronary Artery Calcium in Adults Aged 32 to 46 Years With Incident Coronary Heart Disease and Death

John Jeffrey Carr, MD, MSc; David R. Jacobs Jr, PhD; James G. Terry, MS; Christina M. Shay, PhD; Stephen Sidney, MD, MPH; Kiang Liu, PhD; Pamela J. Schreiner, PhD; Cora E. Lewis, MD, MSPH; James M. Shikany, DrPH; Jared P. Reis, PhD; David C. Goff Jr, MD, PhD


EDITORIAL

Screening for Coronary Artery Disease at an Earlier Age

Ron Blankstein, MD; Philip Greenland, MD

- Presence of <u>any</u> plaque → higher risk of CHD events.
- Individuals aged 32-46 in CARDIA: only <u>10%</u> have CAC → this increases to nearly <u>30%</u> by age 42-56.
- If use risk factors to define a high risk group→ <u>45%</u> of young individuals had CAC (Number needed to scan to identify CAC = 2.2)

JAMA Network | Open

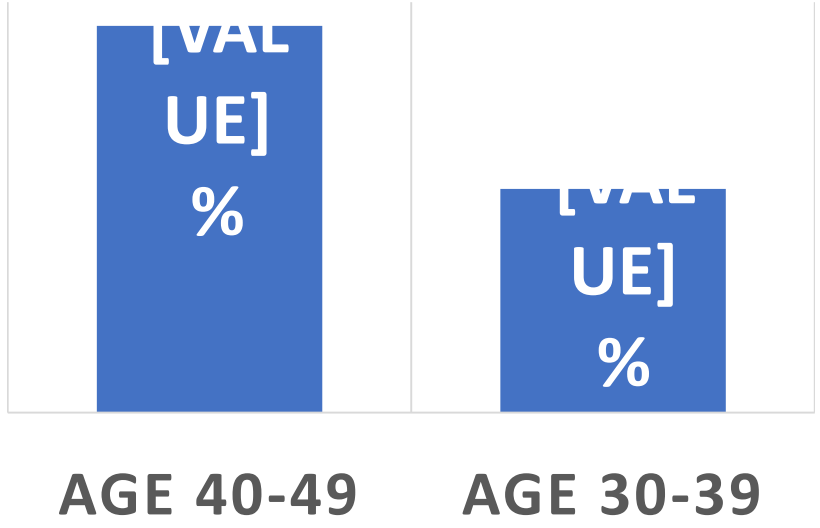
Original Investigation | Cardiology

Association of Coronary Artery Calcium With Long-term, Cause-Specific Mortality Among Young Adults

Michael D. Miedema, MD, MPH; Zeina A. Dardari, MS; Khurram Nasir, MD; Ron Blankstein, MD; Thomas Knickelbine, MD; Sandra Oberembt, PA-C; Leslee Shaw, PhD; John Rumberger, MD, PhD; Erin D. Michos, MD, MHS; Alan Rozanski, MD; Daniel S. Berman, MD; Matthew J. Budoff, MD; Michael J. Blaha, MD, MPH

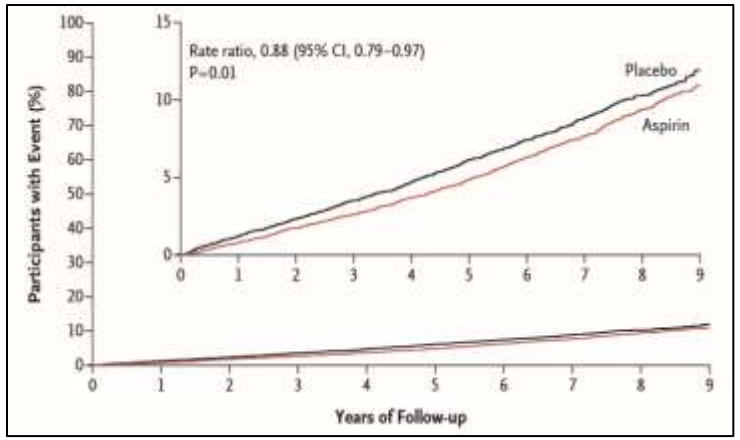
- 22 346 adults aged 30-49 referred for CAC testing.
- 34% had CAC (7% with CAC>100)
- CAC → higher risk of CHD, CVD and all-cause death

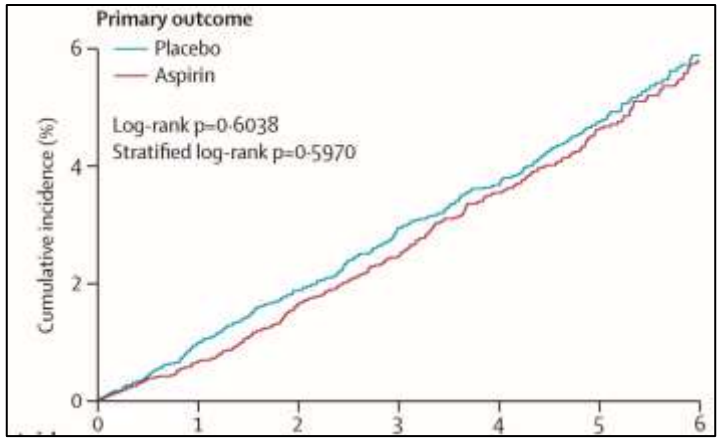
PREVALENCE OF CAC>0 IN YOUNG ADULTS

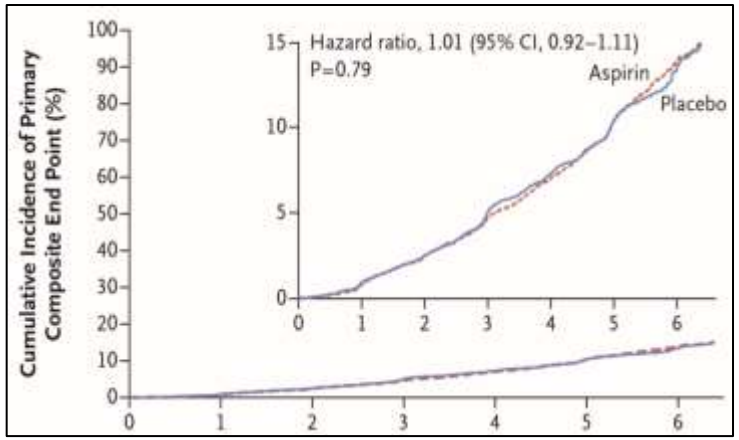


ASA

New Trials: Aspirin for Primary Prevention



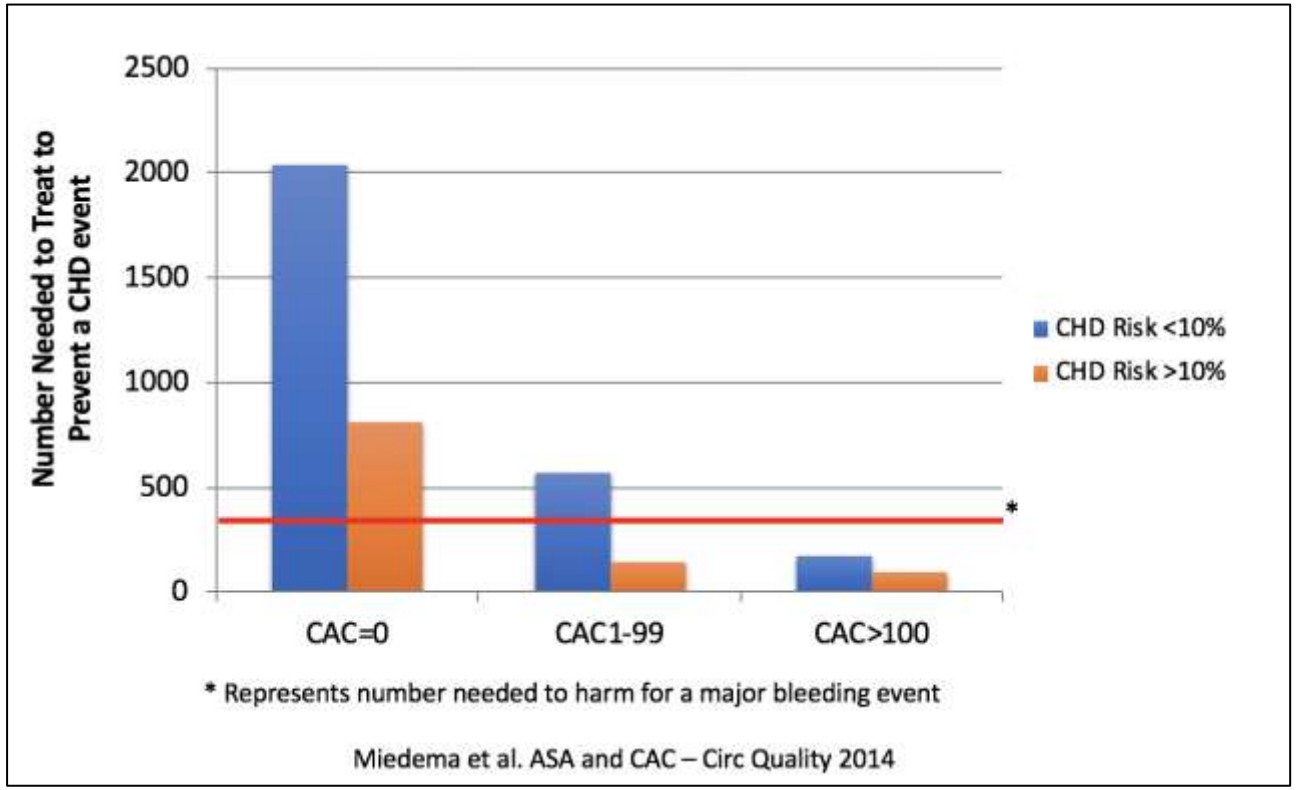




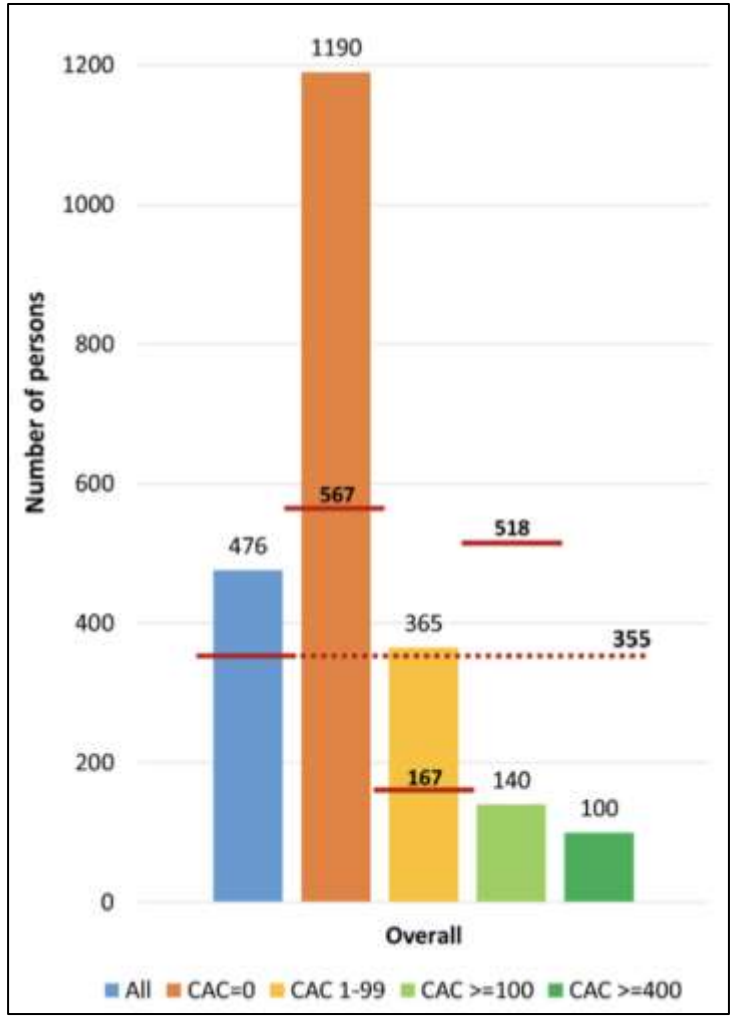
ASCEND	ARRIVE	ASPREE, 2018
15,480 **with diabetes** and no evident CVD.	12,546 with Moderate CVD risk **w/o DM** or high risk of GI bleeding	19,114 adults > 70 yr with no cardiovascular disease.
100 mg of aspirin vs. placebo	100 mg aspirin vs. placebo	100 mg aspirin vs. placebo
Reduction in vascular events was **counterbalanced by bleeding**	**No difference** in a composite of CV death, MI, UA, CVA, or TIA. With **increased risk of bleeding**	Aspirin did **not prolong disability** free survival but **increased major** hemorrhage
N Engl J Med. 2018;379:1529-39	Lancet. 2018;392:1036-46	N Engl J Med 2018; 379:1509-1518

CAC → valuable tool for aspirin therapy allocation

Modeling Benefit and Risk of Aspirin



Miedema et al, Circ Quality 2014



Cainzos-Achirica et al, Circulation 2020