Advances in the Management of Coronary Artery Disease Utilizing CCTA and CAC Scoring

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July 24, 2024

OPTUM®

Disclosures:

None

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
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PUBLISHED BY ELSEVIER

VOL. 78, NO. 22, 2021

CLINICAL PRACTICE GUIDELINE: FULL TEXT

2021 AHA/ACC/ASE/CHEST/SAEM/ SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain

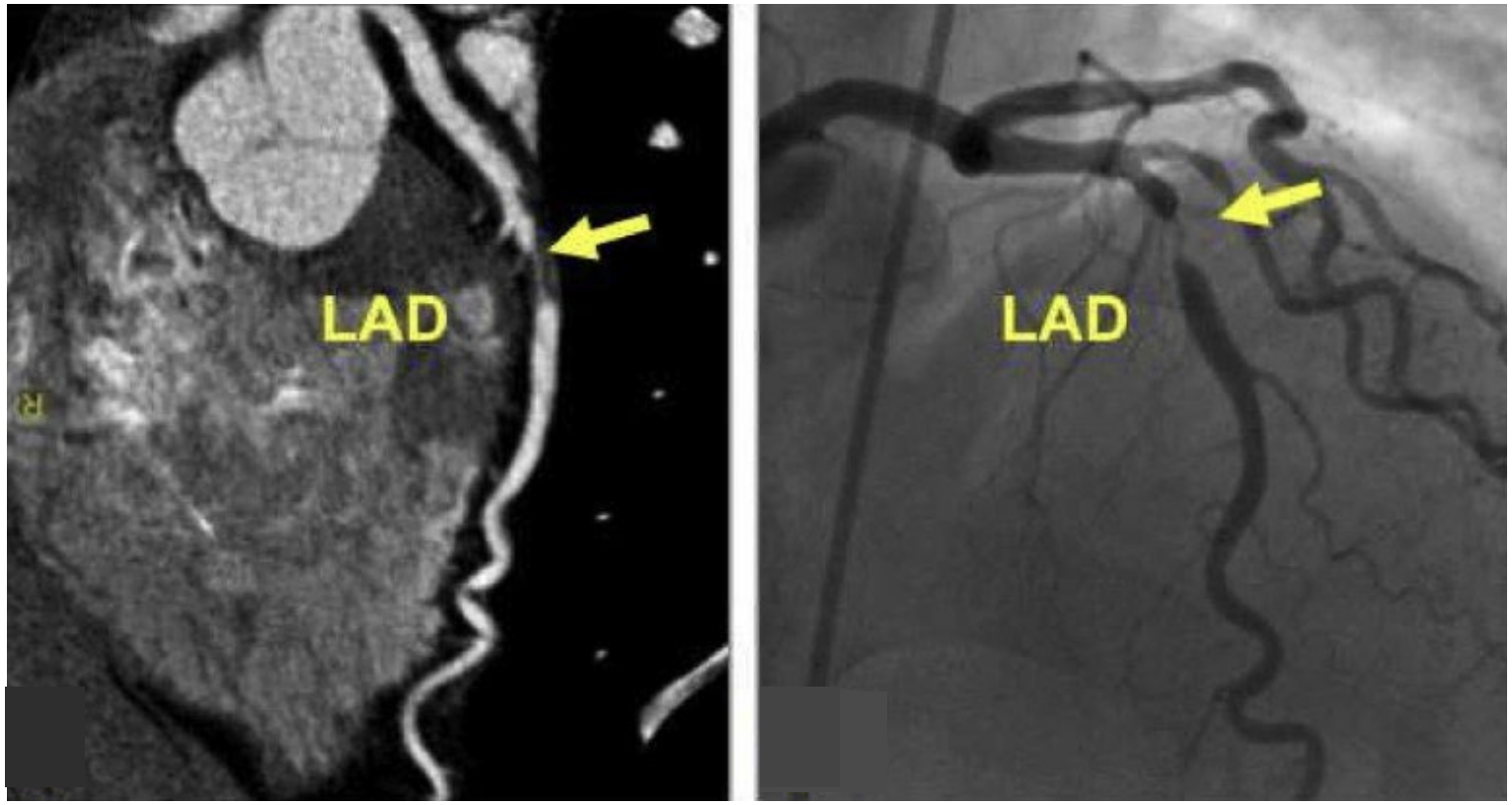
A Report of the American College of Cardiology/American Heart Association
Joint Committee on Clinical Practice Guidelines

CCTA

Recommendations for Intermediate-High Risk Patients With Stable Chest Pain and No Known CAD
Referenced studies that support the recommendations are summarized in Online Data Supplements 29 and 30.

COR	LOE	Recommendations
		Index Diagnostic Testing
		Anatomic Testing
1	A	1. For intermediate-high risk patients with stable chest pain and no known CAD, CCTA is effective for diagnosis of CAD, for risk stratification, and for guiding treatment decisions.[1-12]
		Stress Testing
1	B-R	2. For intermediate-high risk patients with stable chest pain and no known CAD, stress imaging (stress echocardiography, PET/SPECT MPI or CMR) is effective for diagnosis of myocardial ischemia and for estimating risk of MACE.[8,13-35]

CCTA is a noninvasive coronary angiogram.



CCTA

Cardiac Cath

Goals in evaluation stable chest pain:

1. Establish the presence or absence of CAD.

2. Establish the presence or absence of ischemia.

3. To stratify risk and to enable appropriate downstream therapeutic decision making of preventive care, medical therapy and or revascularization.

Stress test or CCTA?

The NEW ENGLAND JOURNAL of MEDICINE

SPECIALTIES TOPICS MULTIMEDIA CURRENT ISSUE LEARNING/CME AUTHOR CENTER PUBLICATIONS

ORIGINAL ARTICLE

Initial Invasive or Conservative Strategy for Stable Coronary Disease

Authors: David J. Maron, M.D., Judith S. Hochman, M.D., Harmony R. Reynolds, M.D., Sripal Bangalore, M.D., M.H.A., Sean M. O'Brien, Ph.D., William E. Boden, M.D., Bernard R. Chaitman, M.D., +49, for the ISCHEMIA Research Group* Author Info & Affiliations

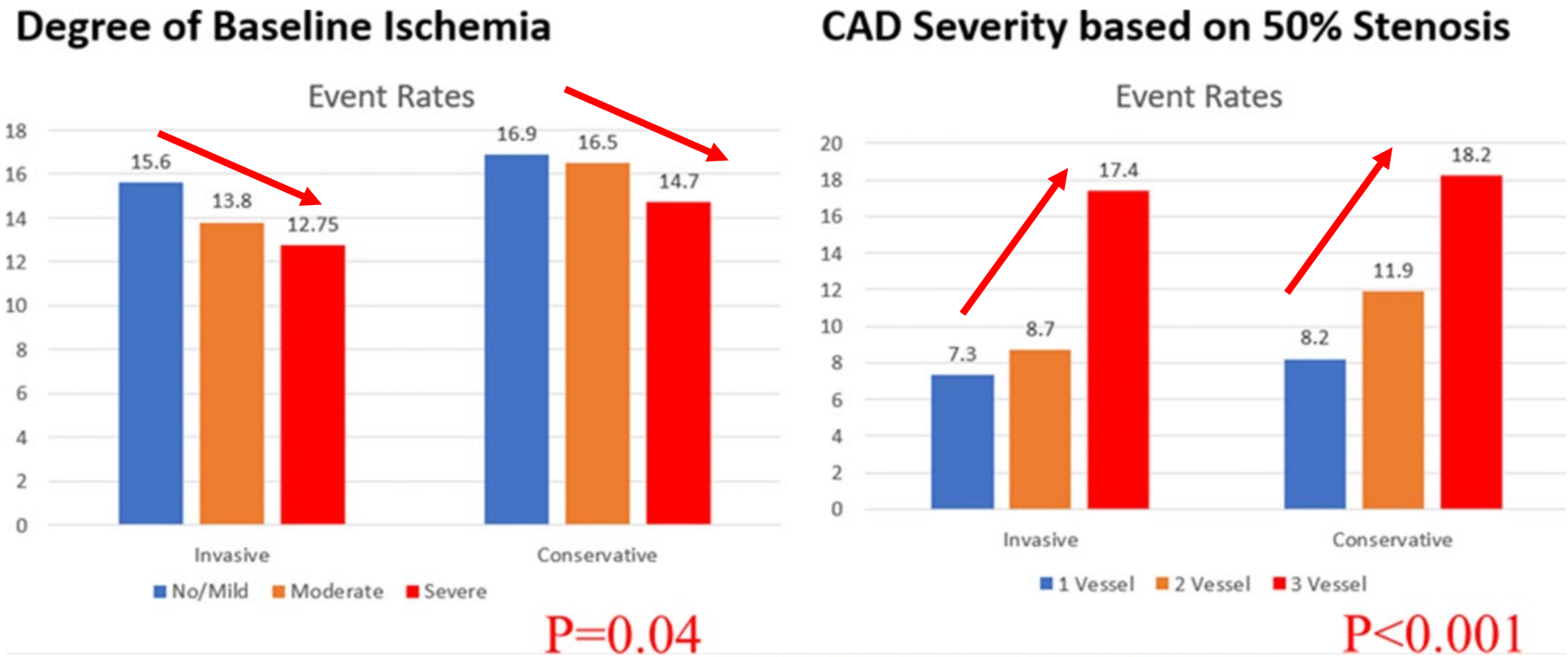
Published March 30, 2020 | N Engl J Med 2020;382:1395-1407 | DOI: 10.1056/NEJMoa1915922 | VOL. 382 NO. 15

- Stress test with moderate to severe ischemia.

- CCTA to confirm presence of CAD with >50% stenosis and rule out left main disease.

Assessing ischemic risk

ISCHEMIA Trial



N Engl J Med 2020; 382:1395-1407

Journal of Cardiovascular Computed Tomography 15 (2021) 110–111

Ischemia testing

Anatomy

Ischemia testing: Gatekeeper

385,000 patients 1100 US hospitals

High rate of false positives

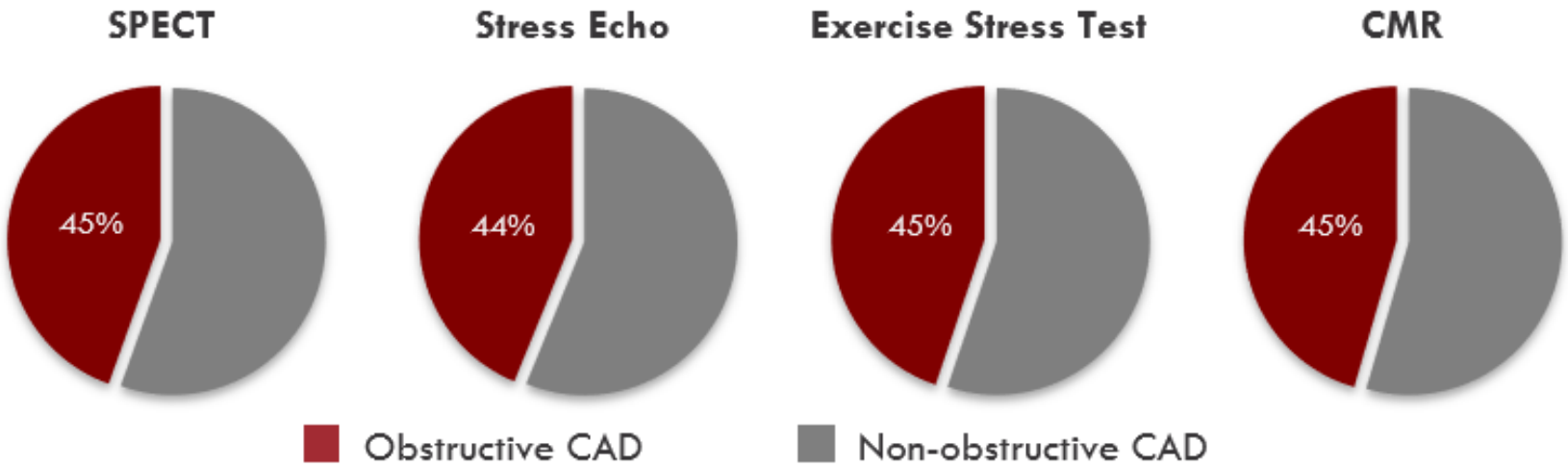
55% of patients sent for an elective ICA following a non-invasive test have no obstructive CAD[1]

High rate of false negatives

20-30% of patients will have a false negative result for obstructive CAD from a non-invasive test[2]

1. Patel, et al. N Engl J Med 2010. Patel, et al. AHJ 2014. Danad, et al. JAMA Cardiology 2017.
2. Arbab-Zadeh, Heart Int 2012. Yokota, et al. Neth Heart J 2018. Nakanishi, et al. J Nucl Cardiol 2018.

Ischemia testing: Gatekeeper

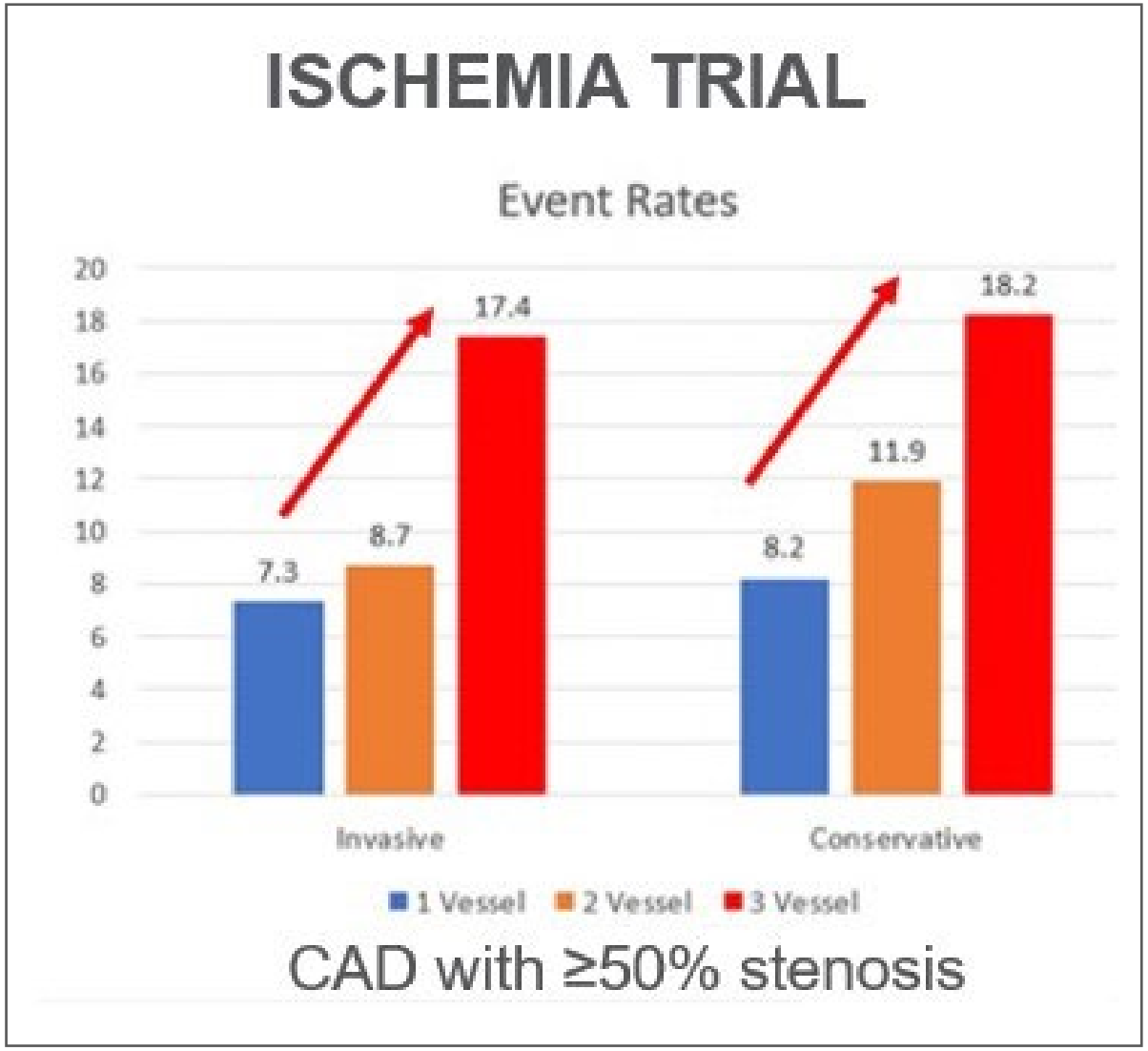


> 50% false positive for the detection of obstructive CAD. Regardless of the testing modality.

Data from an analysis of more than 385,000 patients at over 1,100 US hospitals

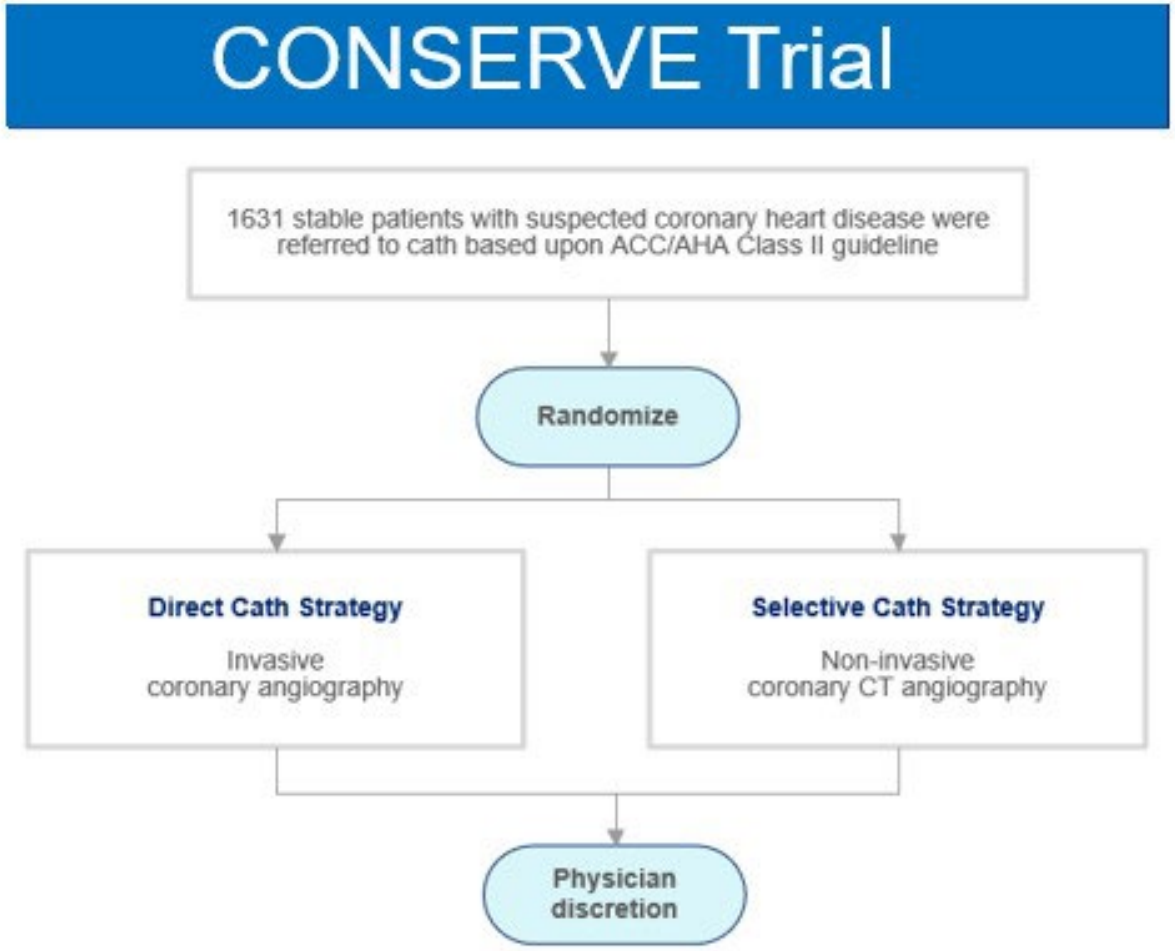
Patel, et al. N Engl J Med 2010. Patel, et al. AHJ 2014.

CCTA: Assessing ischemic risk



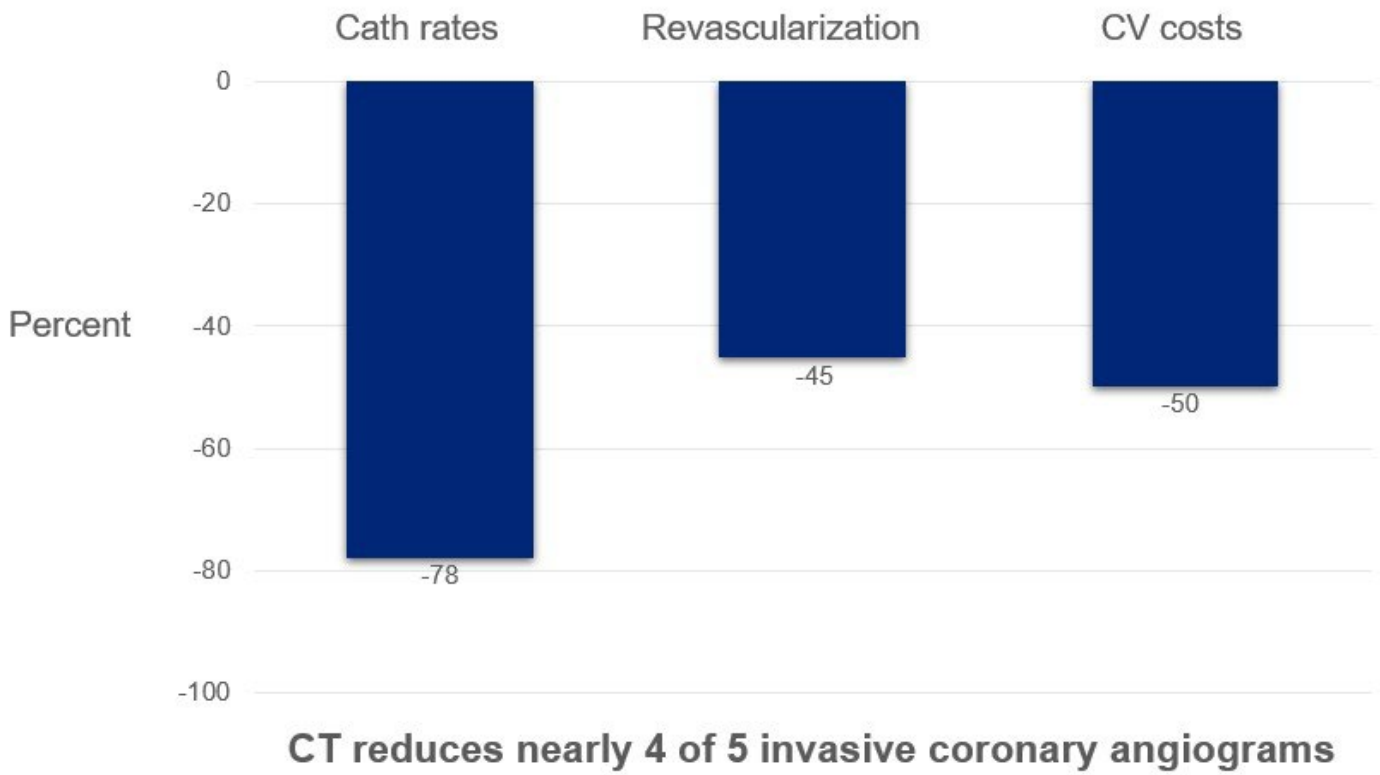
NEJM 382;15 April 9, 2020

CCTA: Gatekeeper.



Chang et al. JACC: VOL. 12, NO. 7, 2019

CONSERVE Trial



Chang et al. JACC: VOL. 12, NO. 7, 2019

CT or Invasive Coronary Angiography in Stable Chest Pain

The DISCHARGE Trial Group

3651 patients with stable chest pain were randomized to CCTA or ICA:

- 78% reduction in ICA in the CT group.
- 28% reduction in revascularization in the CT group.

Table 2. Results of Diagnostic Strategy during Initial Management.*

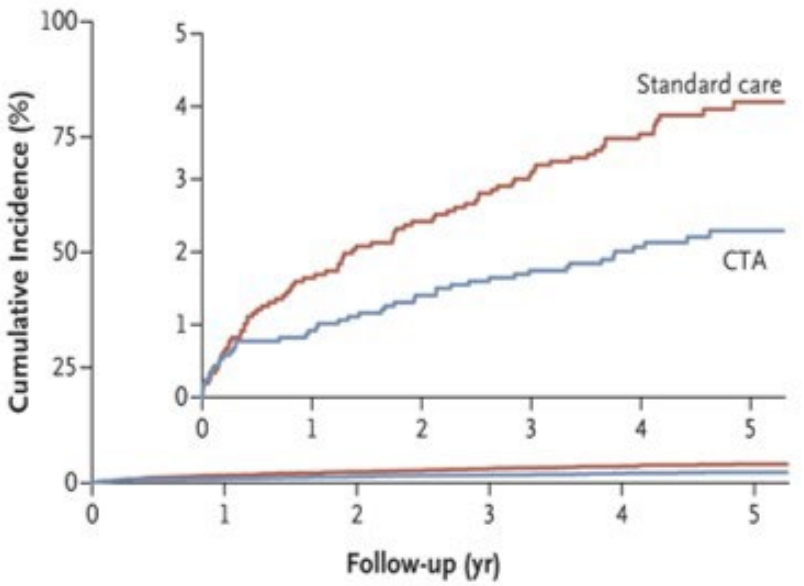
Result	Computed Tomography (N=1808)	Invasive Coronary Angiography (N=1753)
Median time from enrollment to initial intervention (IQR) — days†	3 (0–14)	12 (1–37)
Initial intervention — no. (%)		
CT	1782 (98.6)	31 (1.8)
ICA	20 (1.1)	1705 (97.3)
Did not have scheduled intervention	6 (0.3)	17 (1.0)
Diagnostic findings on assigned intervention — no. (%)‡		
Obstructive CAD: ≥50% stenosis	465 (25.7)	451 (25.7)
1 vessel	155 (8.6)	181 (10.3)
2 vessels	59 (3.3)	74 (4.2)
High-risk anatomy§	251 (13.9)	196 (11.2)
Nonobstructive CAD: 1–49% stenosis	655 (36.2)	393 (22.4)
No sign of CAD	573 (31.7)	877 (50.0)
Nondiagnostic result¶	103 (5.7)	5 (0.3)
CT performed during initial management — no. (%)	1784 (98.7)	35 (2.0)
ICA performed during initial management — no. (%)‖	404 (22.3)	1708 (97.4)
Type of access — no./total no. (%)		
Radial artery	343/404 (84.9)	1514/1708 (88.6)
Femoral artery	56/404 (13.9)	165/1708 (9.7)
Other artery or missing data**	5/404 (1.2)	29/1708 (1.7)
Invasive procedure performed during initial management — no. (%)††		
PCI	195 (10.8)	253 (14.4)
CABG	39 (2.2)	62 (3.5)

NEJM 386;17 April 28, 2022

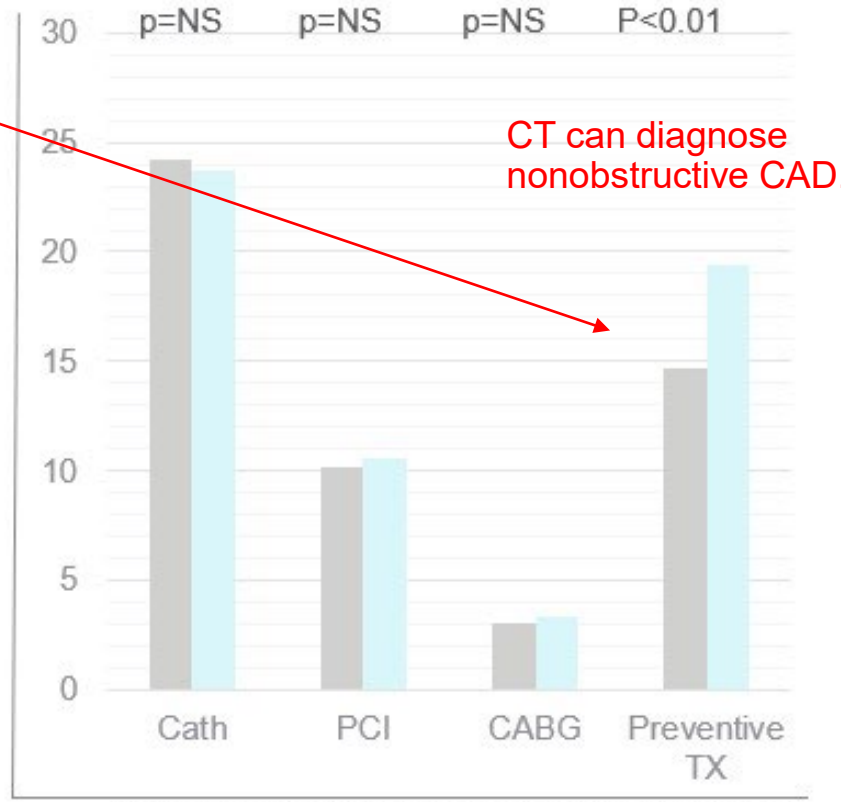
SCOT-HEART

Treating atherosclerosis improves outcomes

41% reduction in death / MI



- 4,146 patients undergoing SOC (n=2,073) vs. CT (n=2,073)
- 40% higher preventive therapies in CT arm



CT can diagnose nonobstructive CAD.

SCOT-HEART Investigators, Newby DE, Adamson PD, et al. Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. *N Engl J Med.* 2018;379(10):924-933.

Journal of Cardiovascular Computed Tomography 18 (2024) 233–242

Contents lists available at ScienceDirect

Journal of Cardiovascular Computed Tomography

journal homepage: www.JournalofCardiovascularCT.com

VOLUME 18, ISSUE 3
MAY/JUN 2024
ISSN 1934-5925

Research paper

Changes in use of preventive medications after assessment of chest pain by coronary computed tomography angiography: A meta-analysis

Giuliano Generoso [a], Vikram Agarwal [b], Leslee J. Shaw [c], Rhanderson Cardoso [b], Ron Blankstein [b], Marcio S. Bittencourt [d,*]

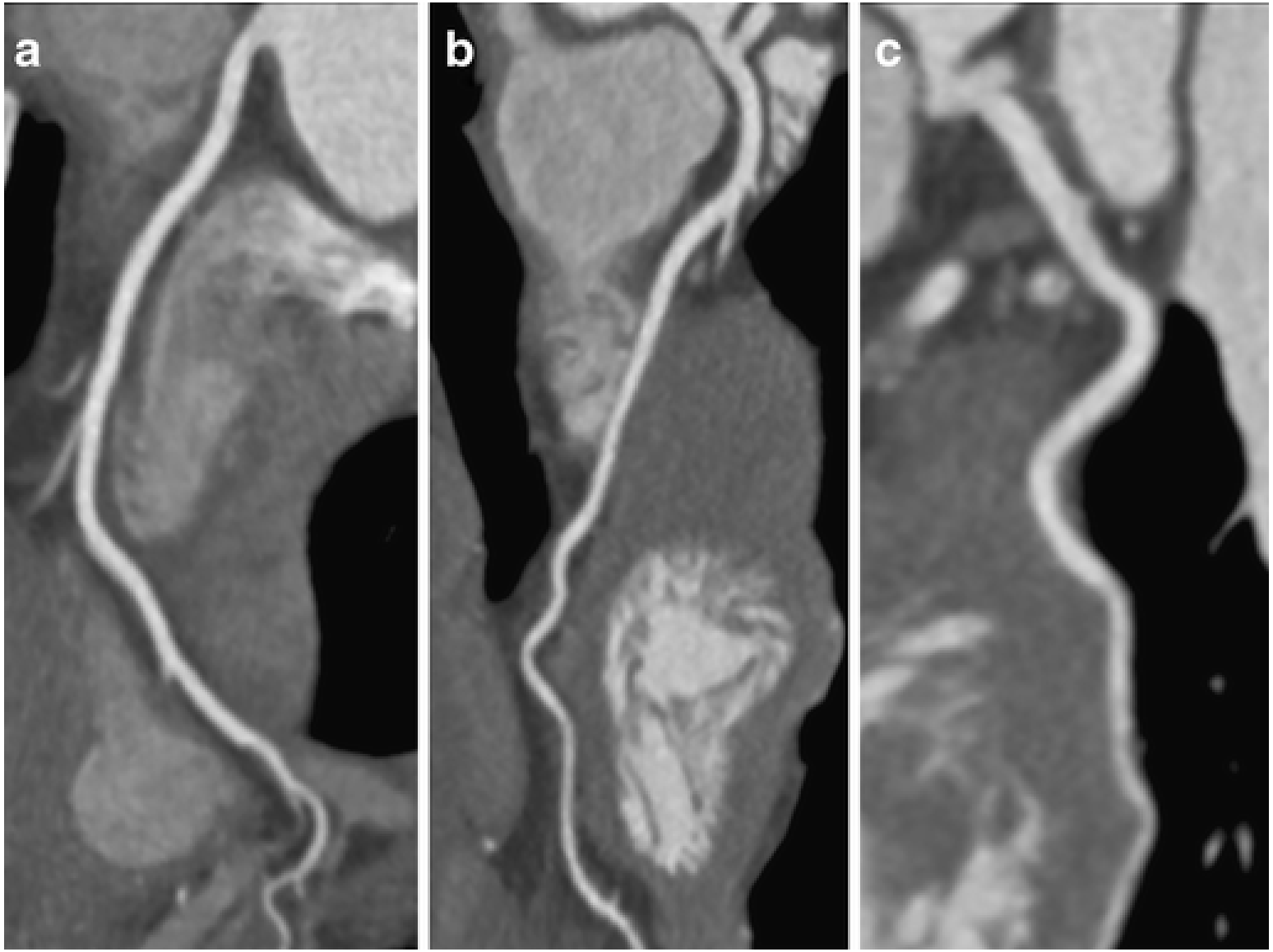
Baseline characteristics: Eight studies were included in the first analysis, with a total of **106,930 patients**, including 42,812 (40 %) who underwent CCTA exam and 64,118 (60 %) who underwent functional testing.

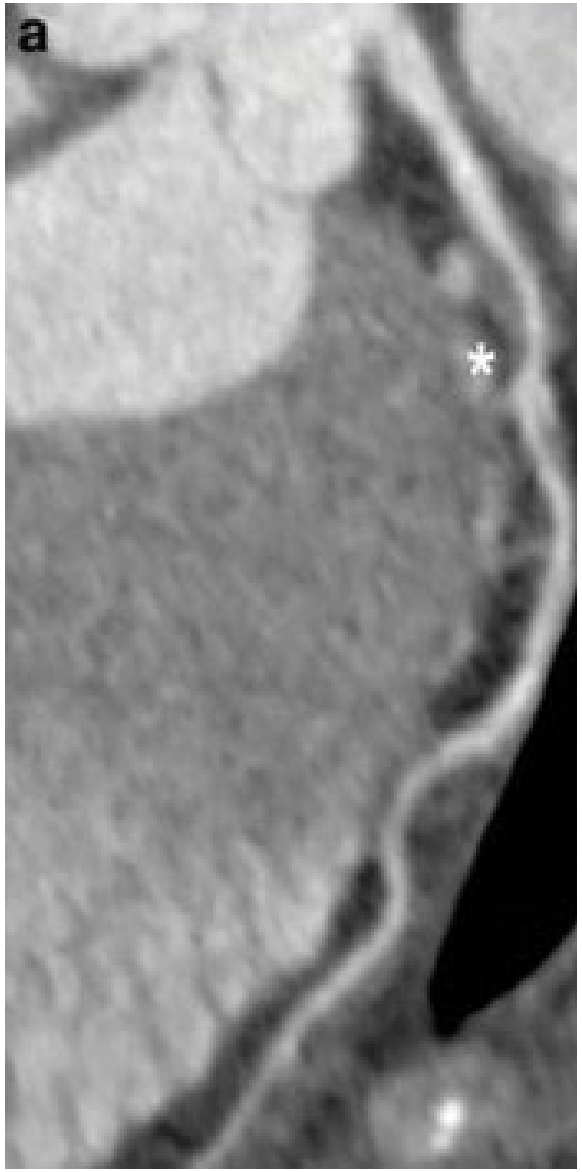
There were 66 % more statin prescription and 74 % more aspirin given to patients undergoing CCTA versus functional testing.

Coronary CT Angiography

- Defines the presence or absence of CAD. ~~Stress test~~
- Excellent gatekeeper for invasive cardiac catheterization. ~~Stress test~~
- Better outcomes when compared to usual care.

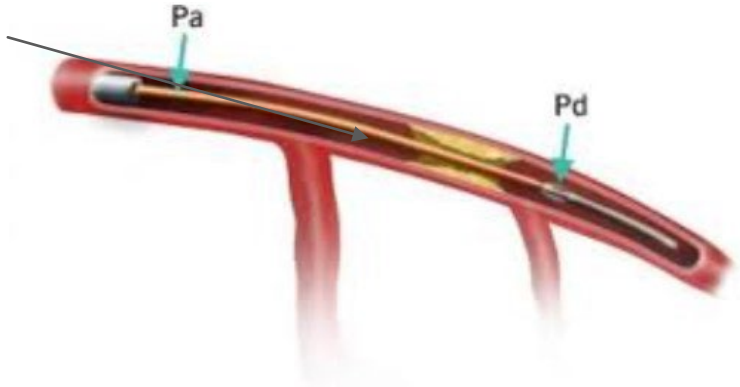
Normal CT coronary angiogram





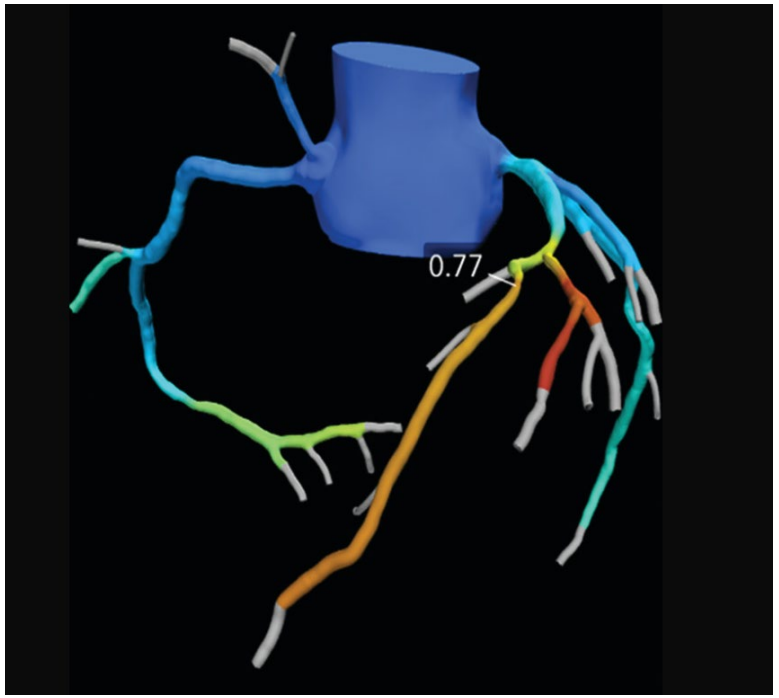
Is the stenosis causing ischemia?

Invasive FFR



≤ 0.8 is abnormal

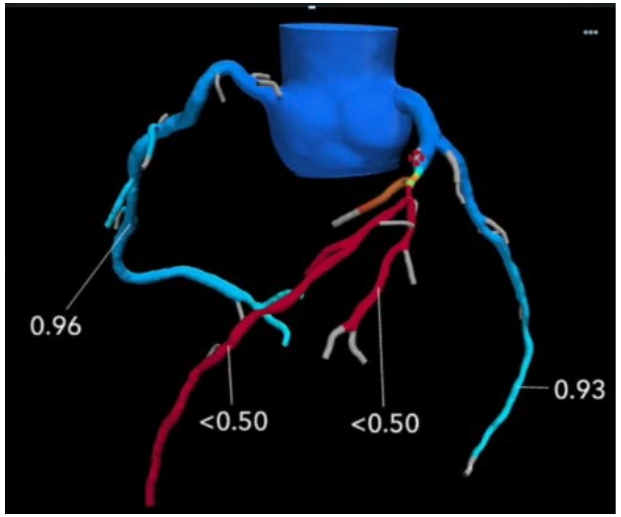
FFR_{CT}

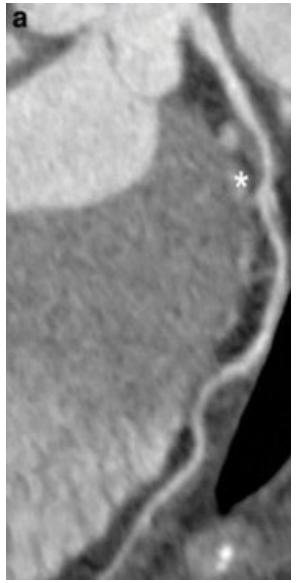


CCTA

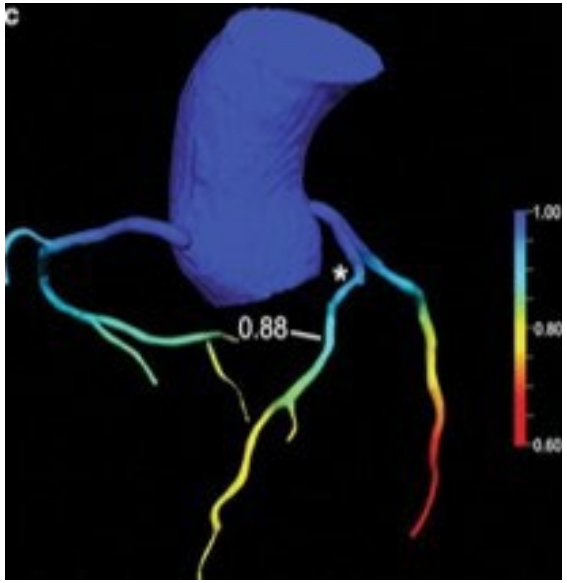
FFR_{CT}

≤0.8
Ischemia positive





>0.8
Ischemia negative



CCTA: FFR_{CT} to assess the presence of ischemia

Stenosis

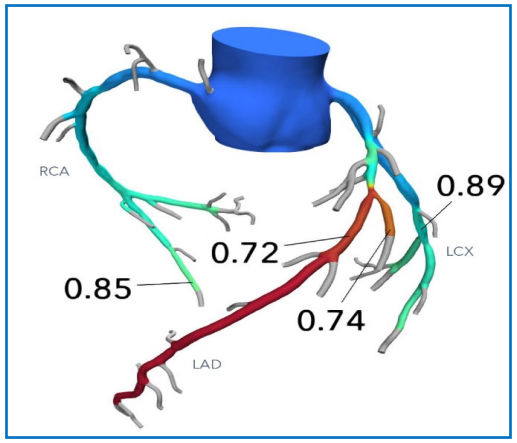
<40%

40-90%

>90%

FFRct
> 0.8

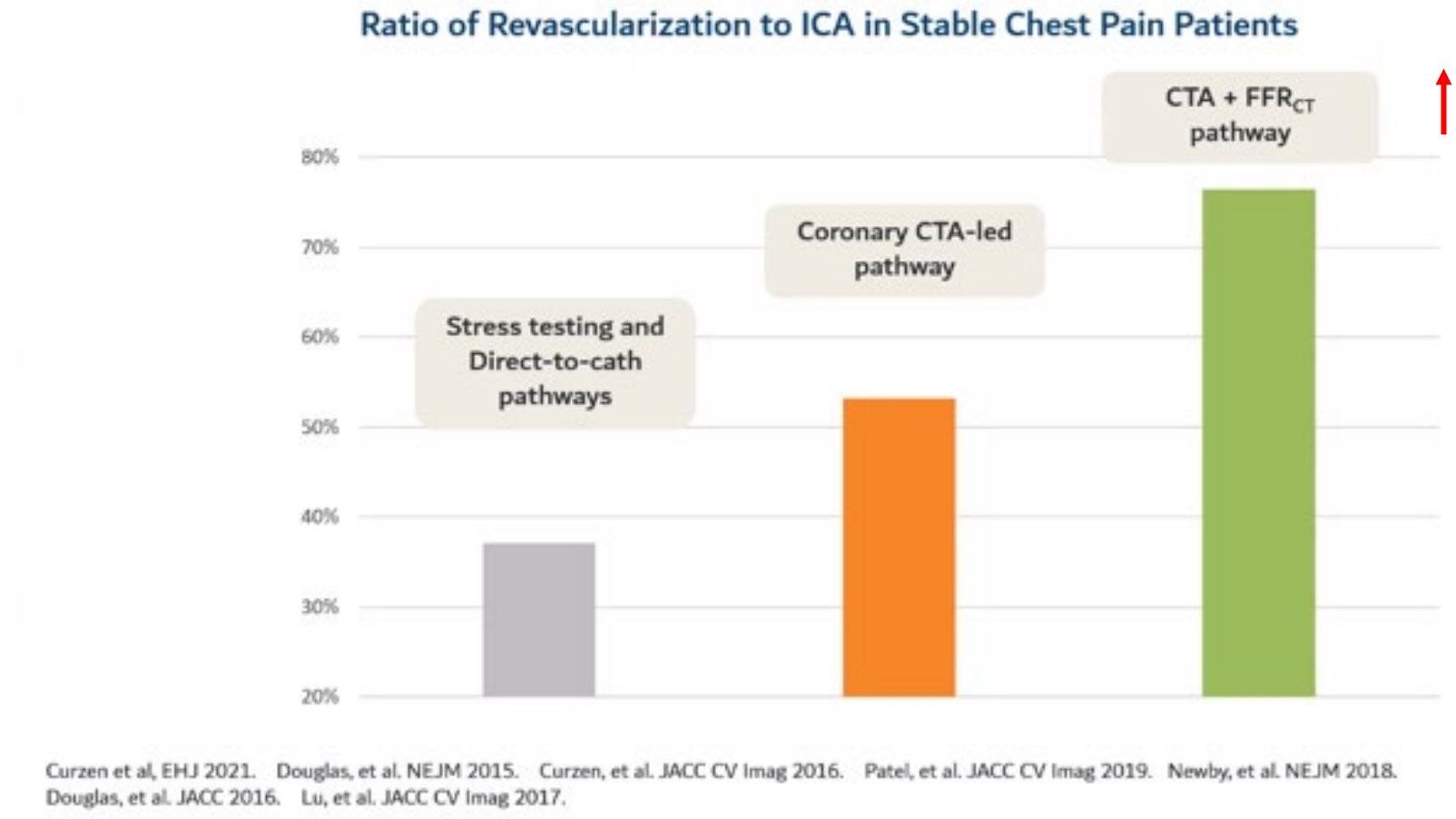
FFRct
≤0.8



Med Rx

Consider ICA

Coronary CTA + FFR_{CT} is the only non-invasive cardiac pathway to provide both anatomical and lesion-specific functional information in a single patient encounter.



Curzen et al, EHJ 2021. Douglas, et al. NEJM 2015. Curzen, et al. JACC CV Imag 2016. Patel, et al. JACC CV Imag 2019. Newby, et al. NEJM 2018. Douglas, et al. JACC 2016. Lu, et al. JACC CV Imag 2017.

Coronary CT Angiography

- Defines the presence or absence of CAD.
- Excellent gatekeeper for invasive cardiac catheterization.
- Better outcomes when compared to usual care.
- CCTA is the only noninvasive cardiac test to provide both anatomical and lesion-specific functional information in a single patient encounter.

Stable chest pain with no known CAD:

Which patients should be referred for a coronary CT angiogram?

Answer: Whenever you're considering a stress test!

- PTP >15%: Int-High Risk
  - Testing is Beneficial
- PTP ≤15%: Low Risk

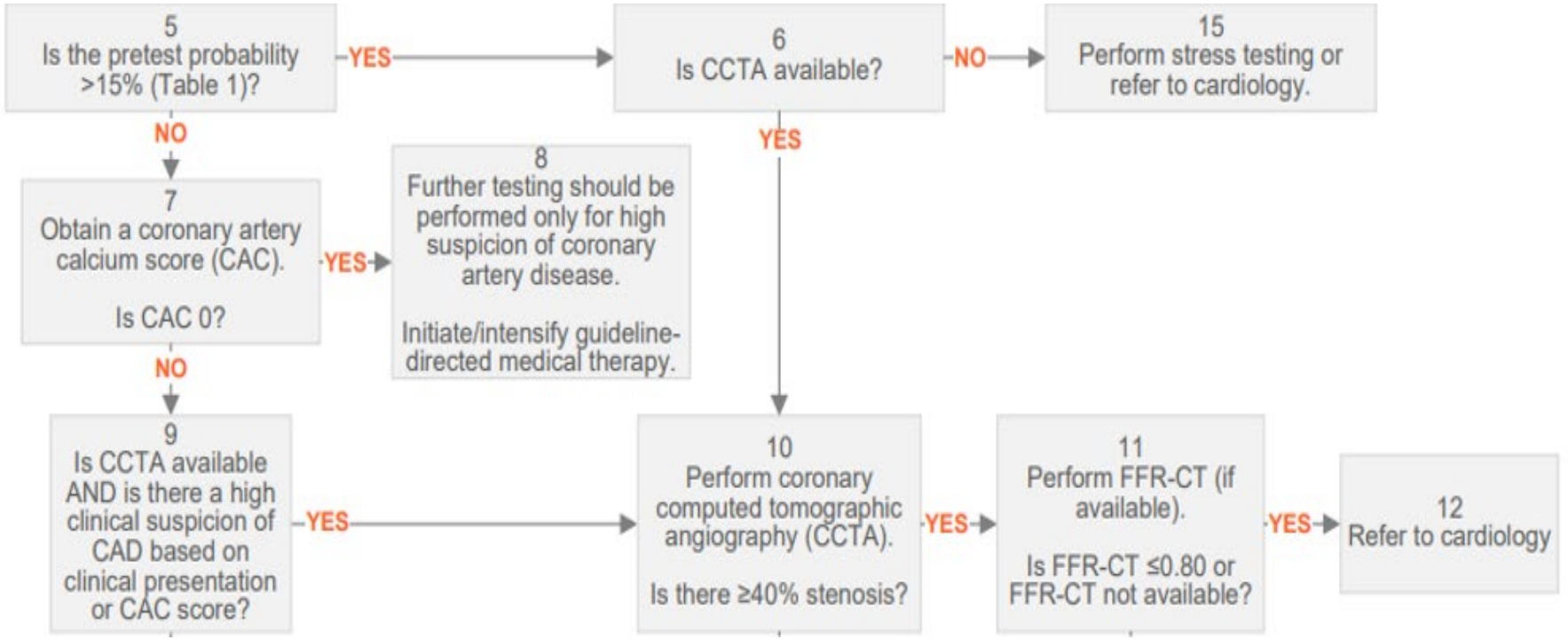
Testing Not Routinely Needed in Low-Risk Patients

Pretest Probabilities of Obstructive CAD in Symptomatic Patients
(A) according to age, sex, and symptoms;
(B) according to age, sex, symptoms, and CAC

Age, y	Chest Pain		Dyspnea	
	Men	Women	Men	Women
30–39	≤4	≤5	0	3
40–49	≤22	≤10	12	3
50–59	≤32	≤13	20	9
60–69	≤44	≤16	27	14
70+	≤52	≤27	32	12

Gulati et al 2021 Chest Pain Guideline

Stable chest pain with no known CAD



Coronary CT Angiography

Contraindications:

- Serious contrast reactions
- Stage IV CKD (GFR <30)

Potential issues:

- Presence of arrhythmia
- Heart rate control
- Significant coronary artery calcification
- Stents

Local CT scanner technology

Chest pain

Treating symptoms, ischemia and stenosis.

Managing the disease process

Assessing and treating atherosclerosis

ASCVD Risk & Management

CAC score vs. Plaque analysis

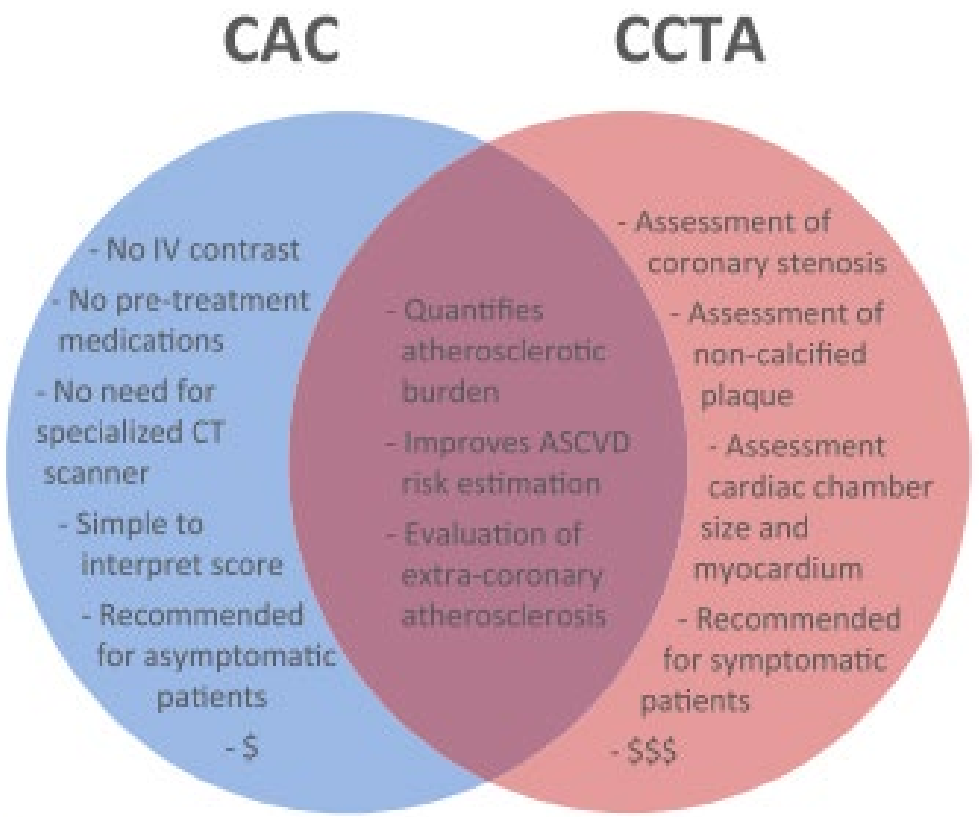
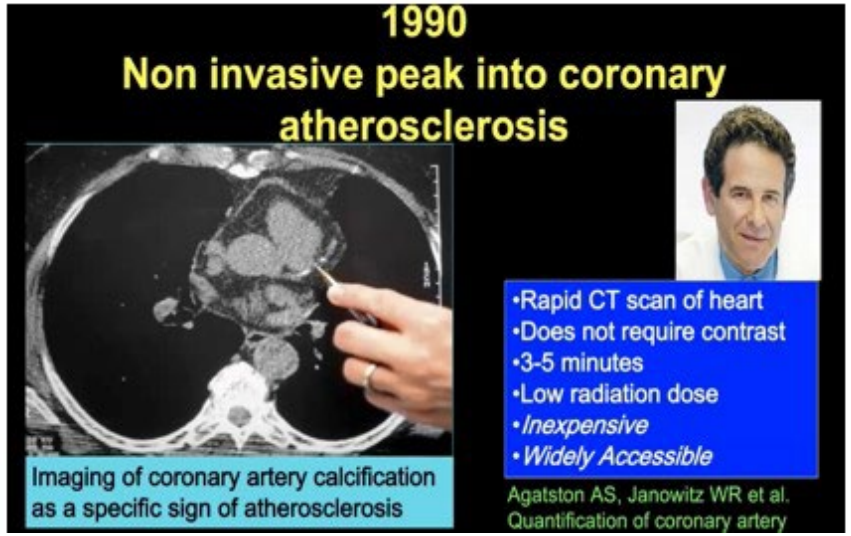


Fig. 1. Venn Diagram for Differences and Similarities Between Coronary Artery Calcium and Coronary computed tomography angiography.

Journal of Cardiovascular Computed Tomography 18 (2024) 113–119

Coronary artery calcium scoring



JACC Vol. 15, No. 4
March 15, 1990:827–32

Quantification of Coronary Artery Calcium Using Ultrafast Computed Tomography

ARTHUR S. AGATSTON, MD, FACC, WARREN R. JANOWITZ, MD,
FRANK J. HILDNER, MD, FACC, NOEL R. ZUSMER, MD, MANUEL VIAMONTE, JR., MD,
ROBERT DETRANO, MD, PHD
Miami Beach, Florida and Long Beach, California

2018 Cholesterol Guidelines

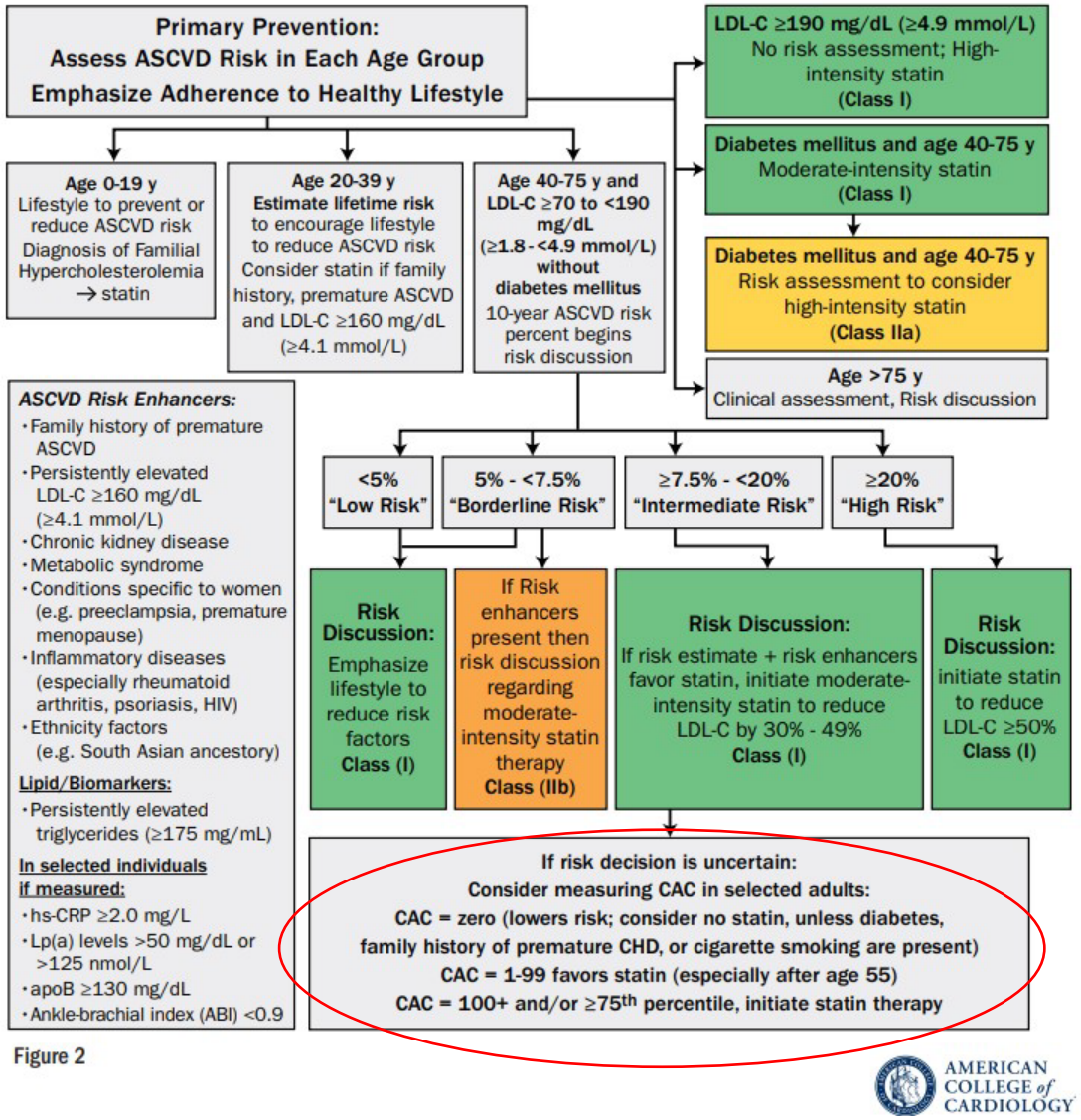
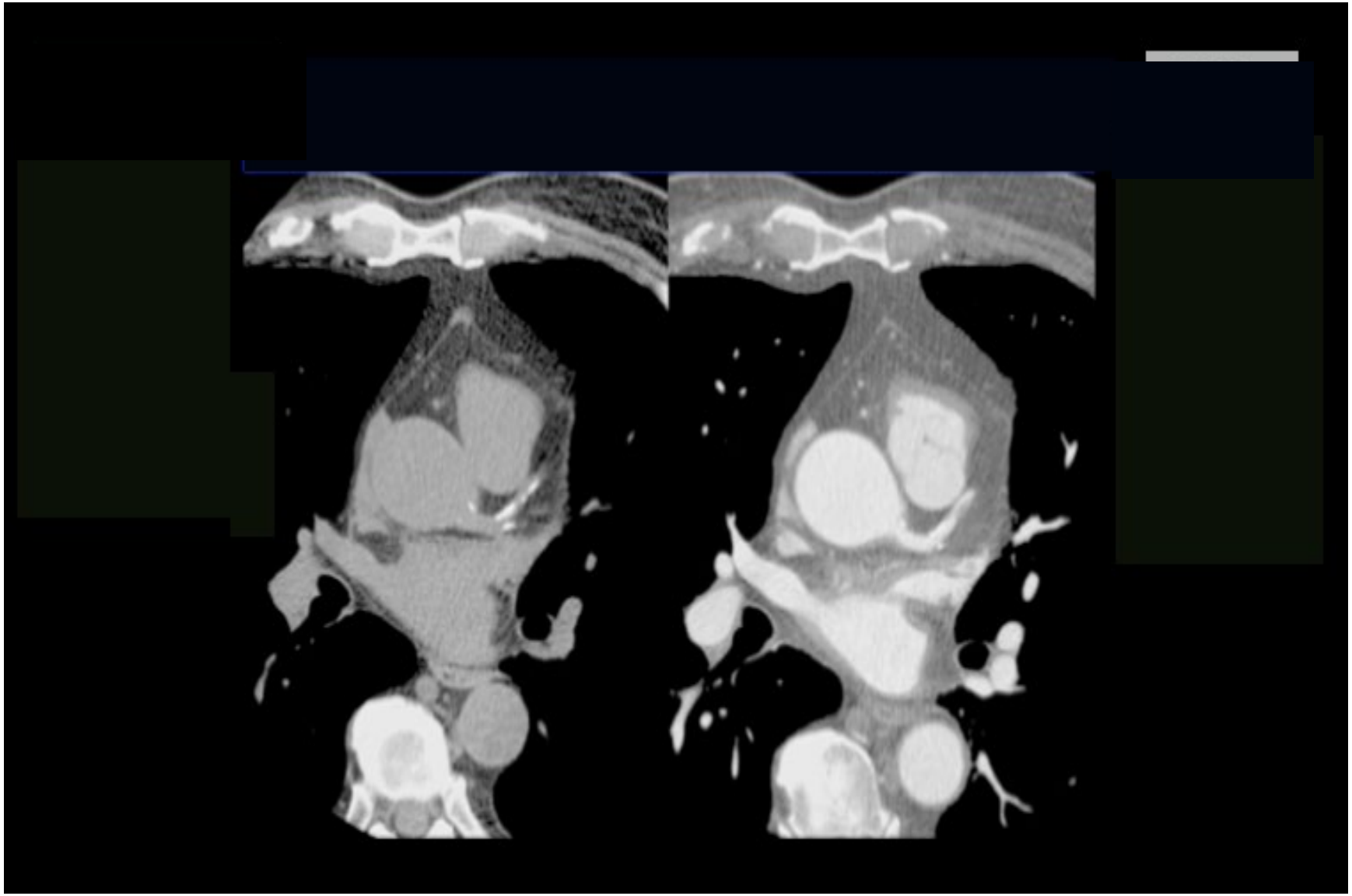


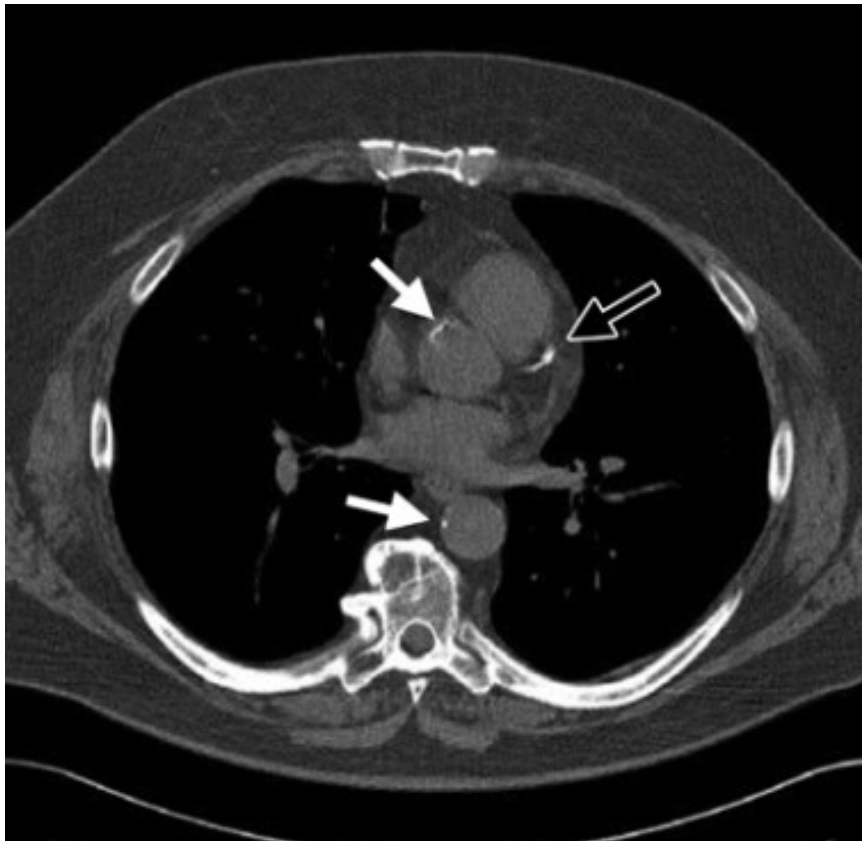
Figure 2

AMERICAN COLLEGE of CARDIOLOGY



Noncontrast Iodine contrast

Non-gated screening chest CT



2016:
12.7 million chest CTs in the US
57,000 CAC scores

NOTIFY- 1 Project

Stanford Health Care System

- Objective was to evaluate the effect of notifying clinicians and patients of incidental CAC on statin initiation.

- Screened 2113 patients who had non-gated chest CT without a previous diagnosis of ASCVD and not on a statin.

- **Resulted in a 51 % increased use of statin.**

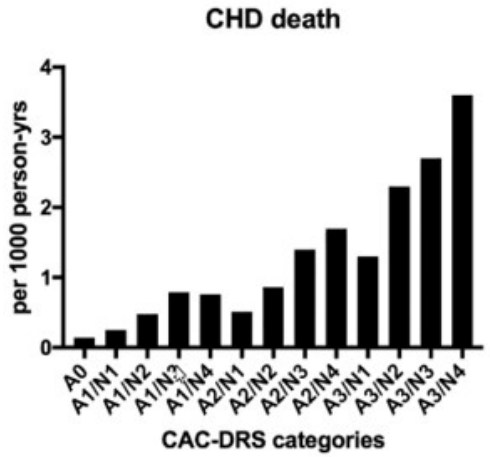
Artery	Lesions	Volume / mm³	Equiv. Mass / mg	Score
LM	2	23.1	4.05	25.3
LAD	3	251.1	46.37	291.0
CX	0	0.0	0.00	0.0
RCA	5	97.0	17.39	103.7
Ca	0	0.0	0.00	0.0
Total	10	371.3	67.80	420.0

CAC 1-99: Mild

CAC 100-299: Moderate

CAC >300: Severe

N = number of vessels involved



High coronary artery calcium score: ≥75th percentile.

MESA The Multi-Ethnic Study of Atherosclerosis

Back to MESA CAC

Input your age, select your gender and race/ethnicity, input (optionally) your observed calcium score and click "Calculate".

Age (45-84): 67

Gender: female

Race/Ethnicity: white

Observed Agatston Calcium Score (optional): 420

Calculate

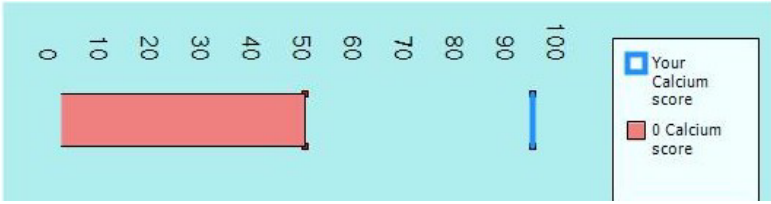
The estimated probability of a non-zero calcium score for a white female of age 67 is 52 %.

Percentiles and Calcium Scores for: white female of age 67

25th	50th	75th	90th
0	3	75	286

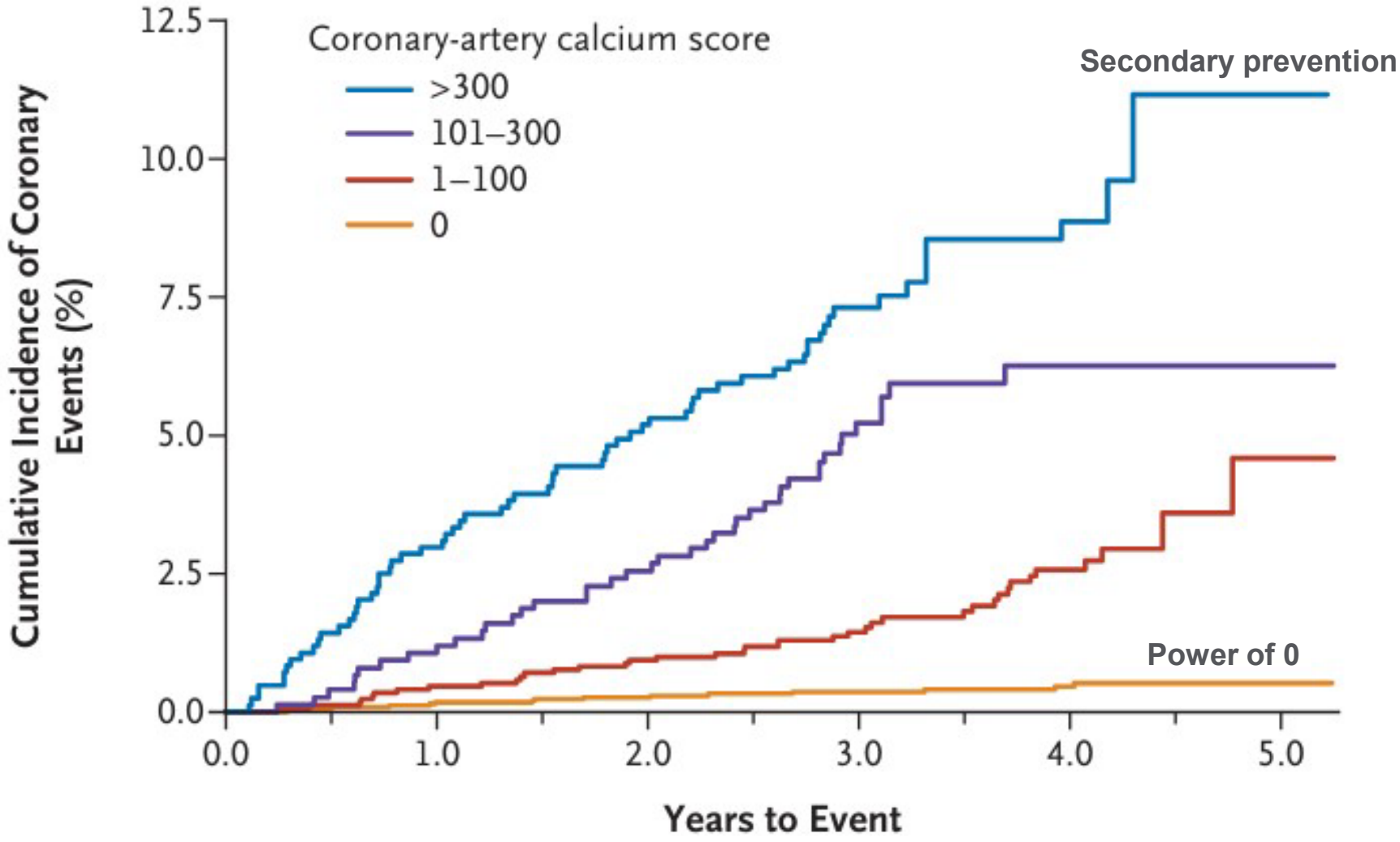
The observed calcium score of is at percentile 93 for subjects of the same age, gender, and race/ethnicity who are free of clinical cardiovascular disease and treated diabetes.

Chart 1: Percentiles

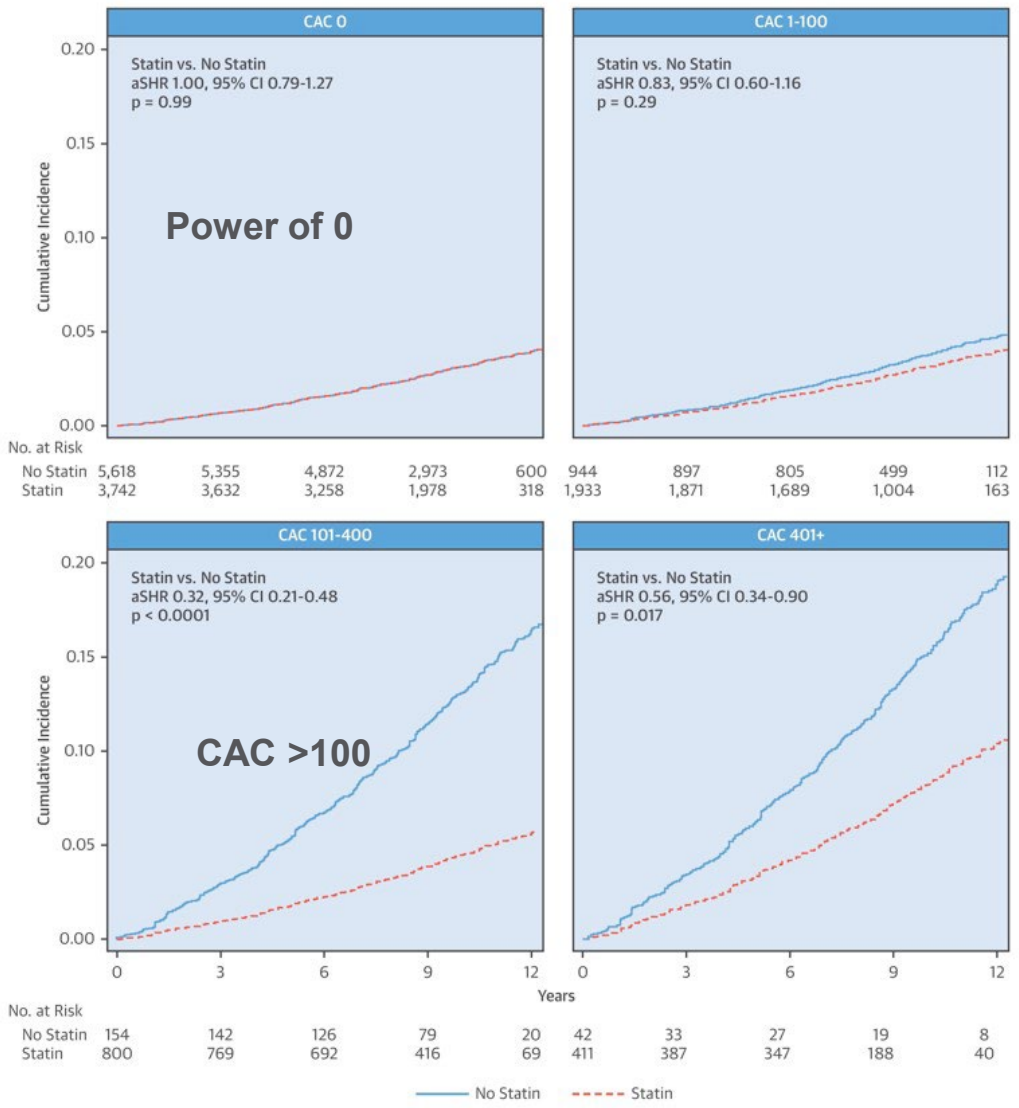


Optum Health Education™

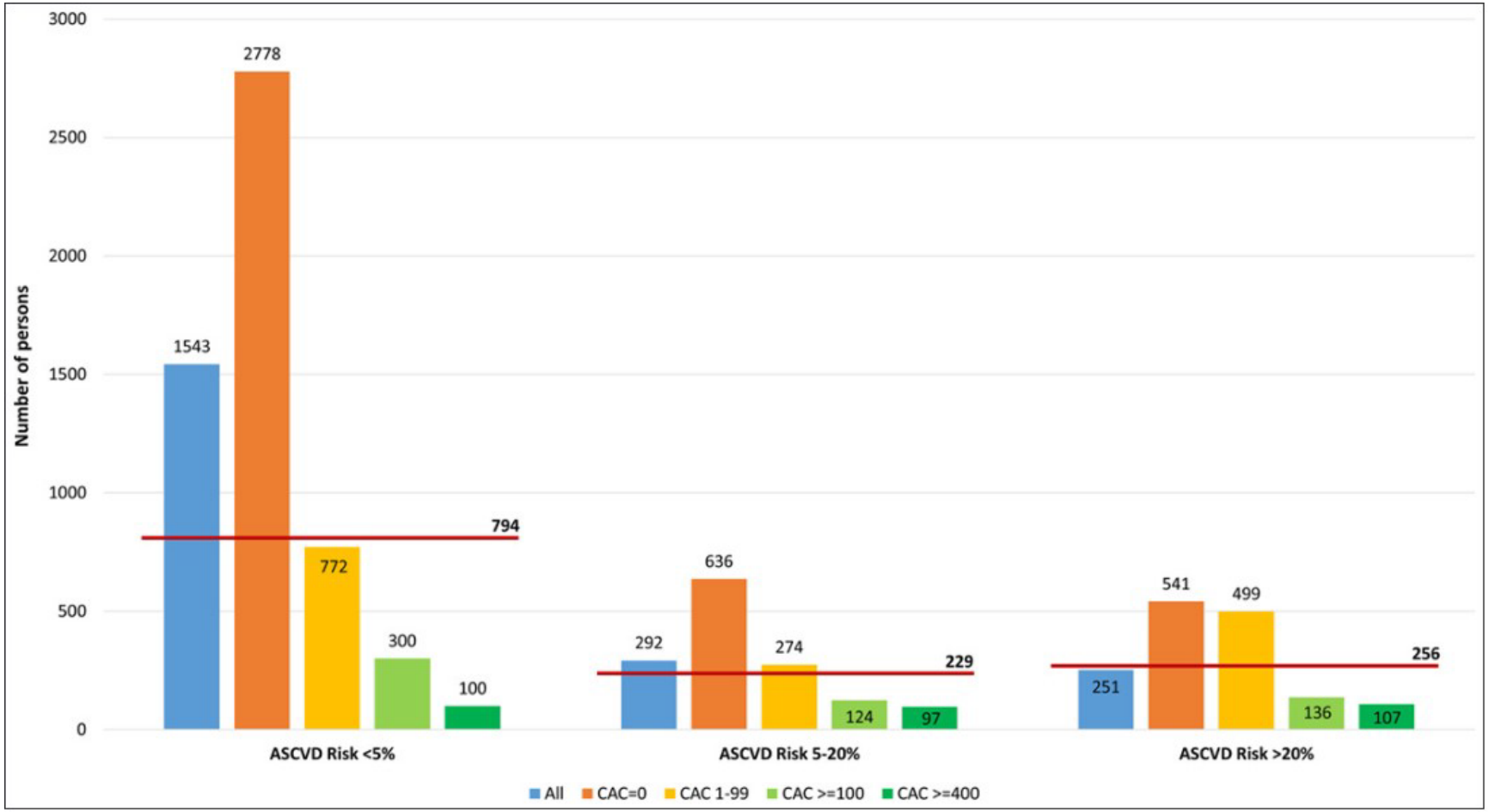
MESA Study NEJM 2008;358:1336-45



CENTRAL ILLUSTRATION: Cumulative Incidence of MACE Stratified by Statin Treatment and CAC Severity



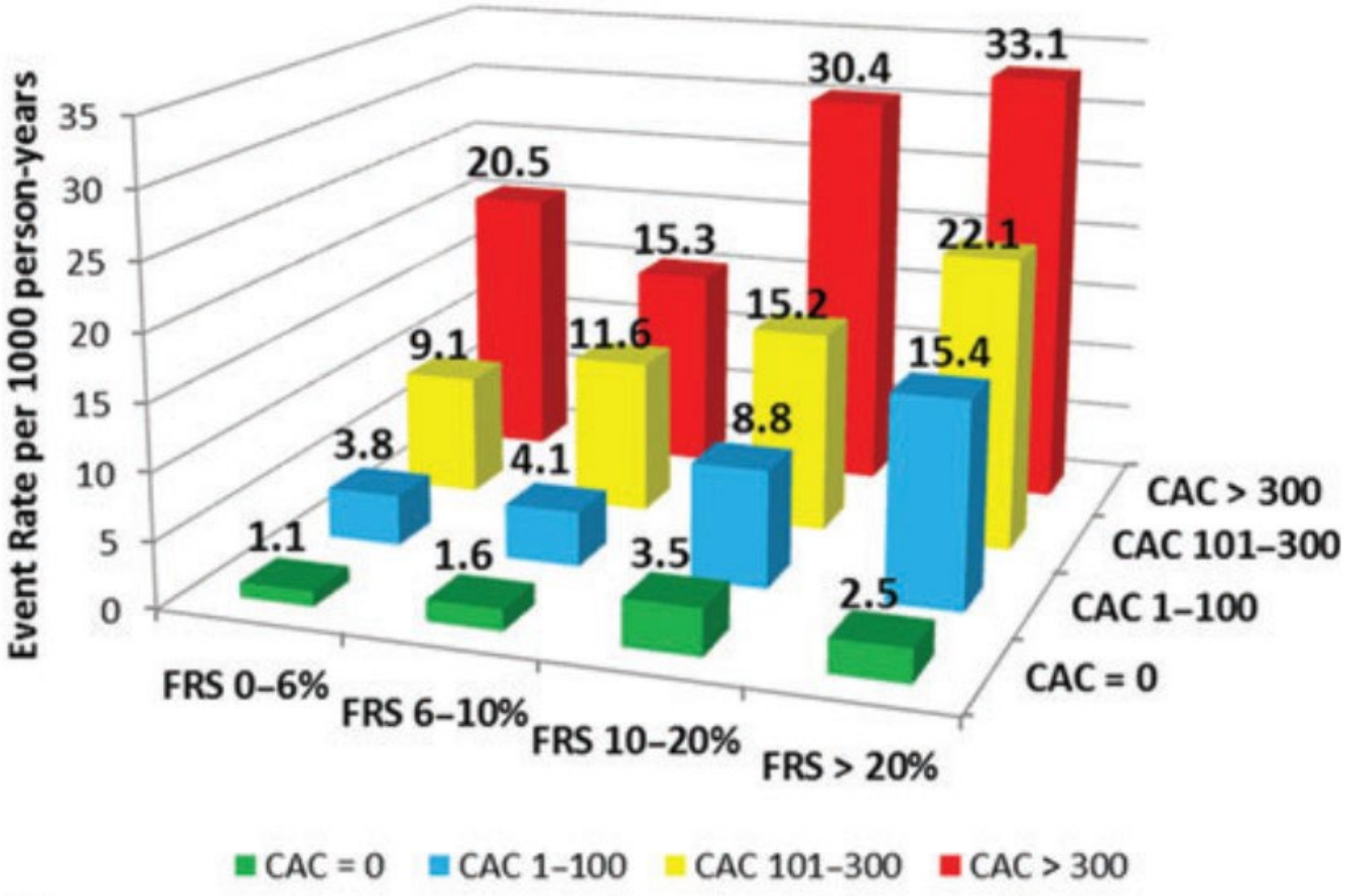
Mitchell, J.D. et al. J Am Coll Cardiol. 2018;72(25):3233-42.



Number needed to treat with aspirin during 5 years to prevent 1 CVD event and number needed to cause a major bleeding event, by estimated ASCVD risk and CAC.

Circulation

Volume 141, Issue 19, 12 May 2020: 1541-1553



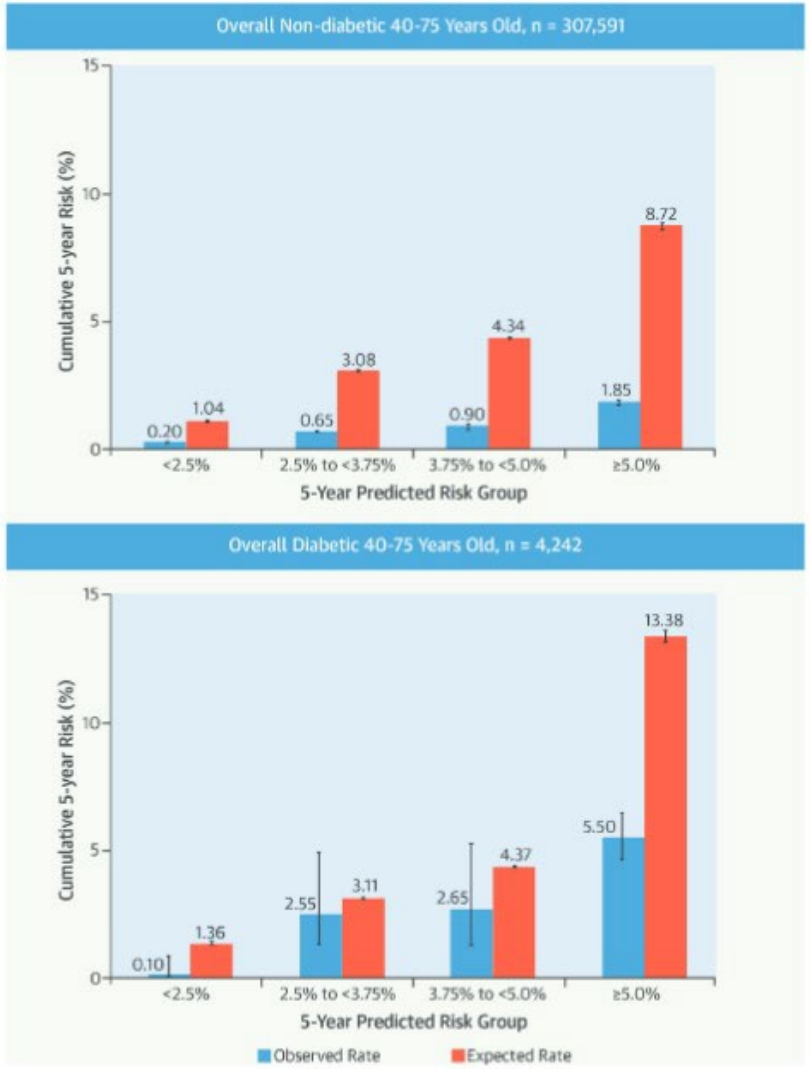
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 67, NO. 18, 2016

ISSN 0735-1097
http://dx.doi.org/10.1016/j.jacc.2016.02.055

Accuracy of the Atherosclerotic Cardiovascular Risk Equation in a Large Contemporary, Multiethnic Population

Jamal S. Rana, MD, PhD,[a,b,c] Grace H. Tabada, MPH,[b] Matthew D. Solomon, MD, PhD,[a,b,d] Joan C. Lo, MD,[b,c,e] Marc G. Jaffe, MD,[c,f] Sue Hee Sung, MPH,[b] Christie M. Ballantyne, MD,[g] Alan S. Go, MD[b,c,h,i]

CENTRAL ILLUSTRATION Cardiovascular Risk Prediction in Clinical Care: Comparison of Observed Versus Expected ASCVD Risks



Rana, J.S. et al. J Am Coll Cardiol. 2016;67(18):2118-30.

Observed 5-year risks of atherosclerotic cardiovascular disease (ASCVD) events within each predicted risk category in eligible adults 40 to 75 years of age are shown stratified according to diabetes status.

Chest pain: Low risk

CAC score →

Recommendations for Low-Risk Patients With Stable Chest Pain and No Known CAD Referenced studies that support the recommendations are summarized in Online Data Supplements 27 and 28.		
COR	**LOE**	**Recommendations**
1	**B-NR**	1. For patients with stable chest pain and no known CAD presenting to the outpatient clinic, a model to estimate pretest probability of obstructive CAD is effective to identify patients at low risk for obstructive CAD and favorable prognosis in whom additional diagnostic testing can be deferred.[1-5]
2a	**B-R**	2. For patients with stable chest pain and no known CAD categorized as low risk, CAC testing is reasonable as a first-line test for excluding calcified plaque and identifying patients with a low likelihood of obstructive CAD.[6-9]
2a	**B-NR**	3. For patients with stable chest pain and no known CAD categorized as low risk, exercise testing without imaging is reasonable as a first-line test for excluding myocardial ischemia and determining functional capacity in patients with an interpretable ECG.[10]

PROMISE Study

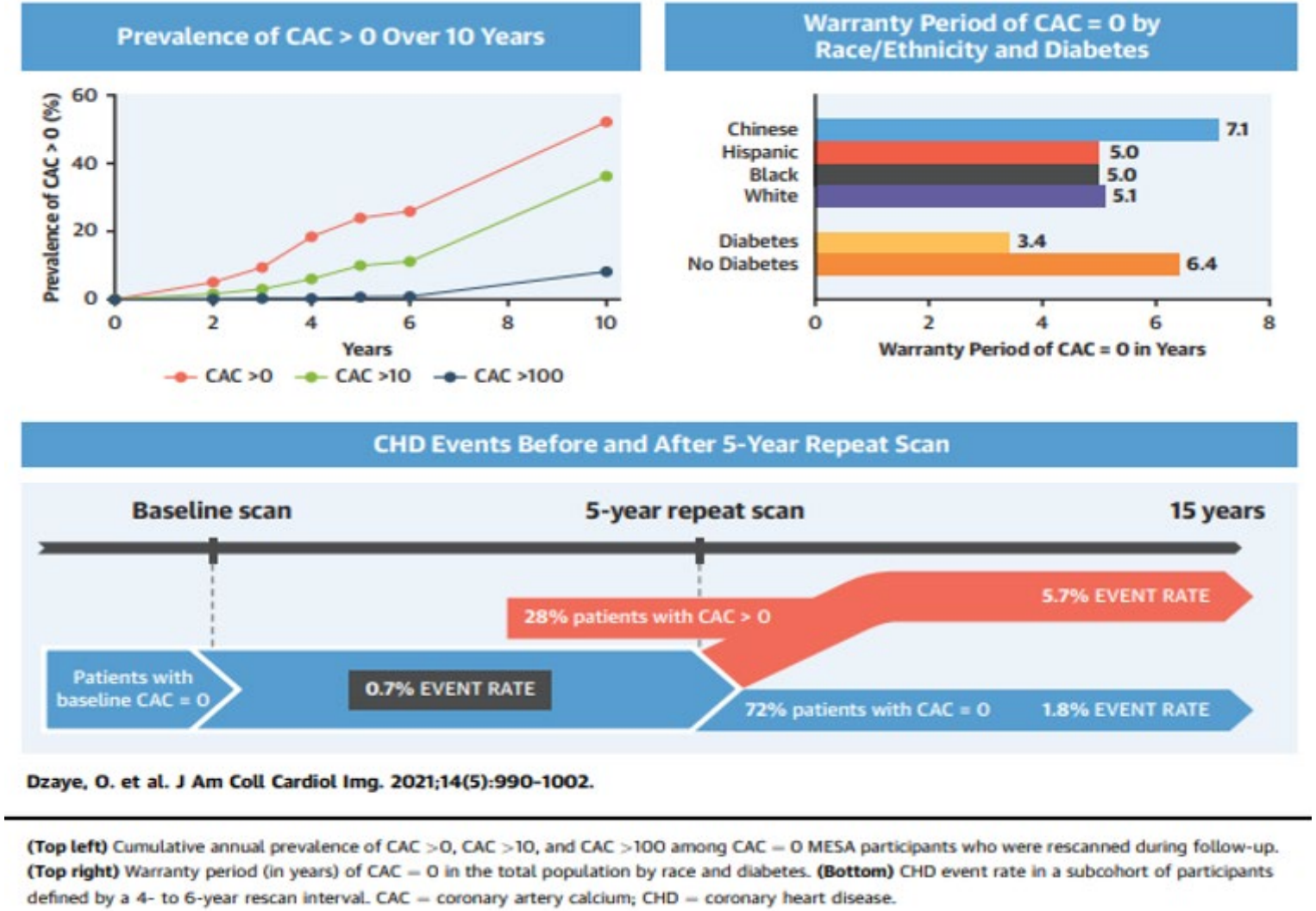
Prospective Multicenter Imaging Study for the Evaluation of Chest pain

Average age: 61
CAC 0 n=1457 (34.6%)

CAC score 0 → NPV >50% stenosis → **98.5%**

Budoff et al. *Circulation.* 2017;136:1993–2005.

CAC 0: When to repeat the scan.



Dzaye, O. et al. J Am Coll Cardiol Img. 2021;14(5):990-1002.

(Top left) Cumulative annual prevalence of CAC >0, CAC >10, and CAC >100 among CAC = 0 MESA participants who were rescanned during follow-up. **(Top right)** Warranty period (in years) of CAC = 0 in the total population by race and diabetes. **(Bottom)** CHD event rate in a subcohort of participants defined by a 4- to 6-year rescan interval. CAC = coronary artery calcium; CHD = coronary heart disease.

CAC scoring:

Low cost.
Accessible.

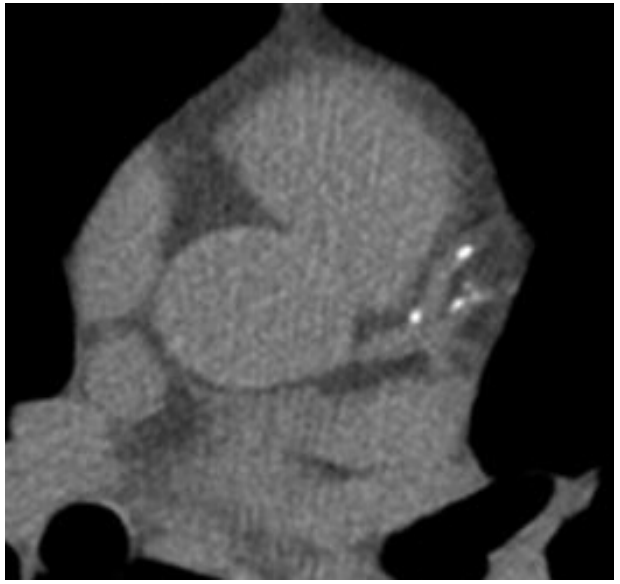
- Derisking. Risk calculators overestimate risk.
- CAC score > 100 is a powerful tool for the clinician and patient to institute statin and aspirin therapy.
- CAC score > 300. Secondary prevention LDL goals.

CAC scoring:

- Noncalcified plaque.
  - Younger patient.
  - Risk factors.

- Longitudinal management of plaque. Cannot follow CAC score.
  - All the things we do to treat plaque convert non-calcified plaque to calcified plaque.

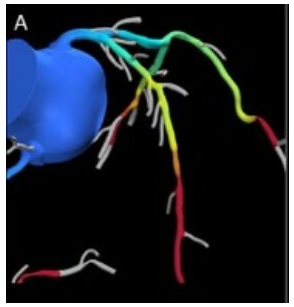
CCTA: Plaque analysis

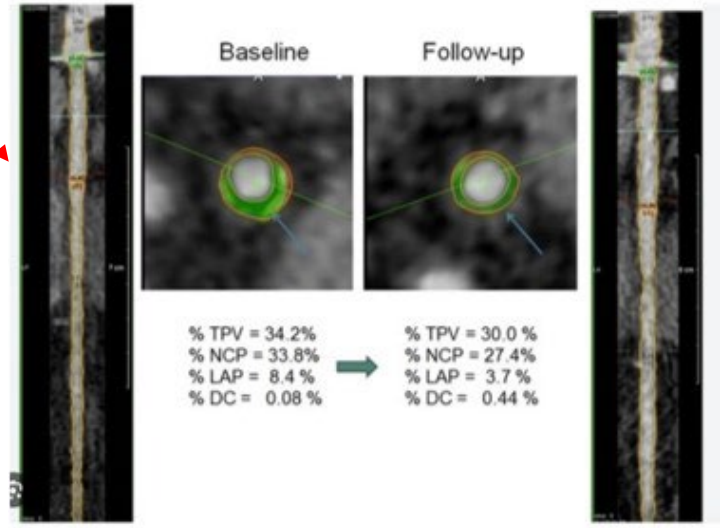


The presence of coronary calcium is atheroma…

But not all atheroma has calcium.

CCTA dataset





- Currently, primary CVD prevention relies upon risk stratification using population-based risk factors which are indirect surrogates of atherosclerosis.
  - Individuals with risk factors and no atherosclerosis are treated.
  - Fails to treat those with significant atherosclerosis and no risk factors.

- The current strategy cannot determine which individuals are inadequately treated despite effective risk factor management. Studies have shown that in a significant percentage of patients that there is plaque progression despite current guideline directed risk factor management.

- The argument against plaque analysis and possible CT follow-up: “what difference does it make, you’ll manage with statin and an aspirin.”

Medication	Target
Lipid Lowering	
Statins	LDL
Ezetimibe	LDL
PCSK9 Inhibitors	LDL
Bempedoic Acid	LDL
Inclisiran	LDL
Icosapent Ethyl	Triglycerides
Anti-Thrombotic / Anti-Platelet Agents	
Aspirin	Platelets
Rivaroxaban	Factor Xa
Clopidogrel	Platelets

Medication	Target
Cardiometabolic / Cardiorenal	
GLP1 Receptor Agonists	GLP1
GLP1 receptor / GIP Agonists	GLP1 and GIP
SGLT2 Inhibitors	SGLT2
Anti-Inflammatory	
Colchicine	Tubulin

In Development	
Lp(a) Lowering	Lipoprotein a

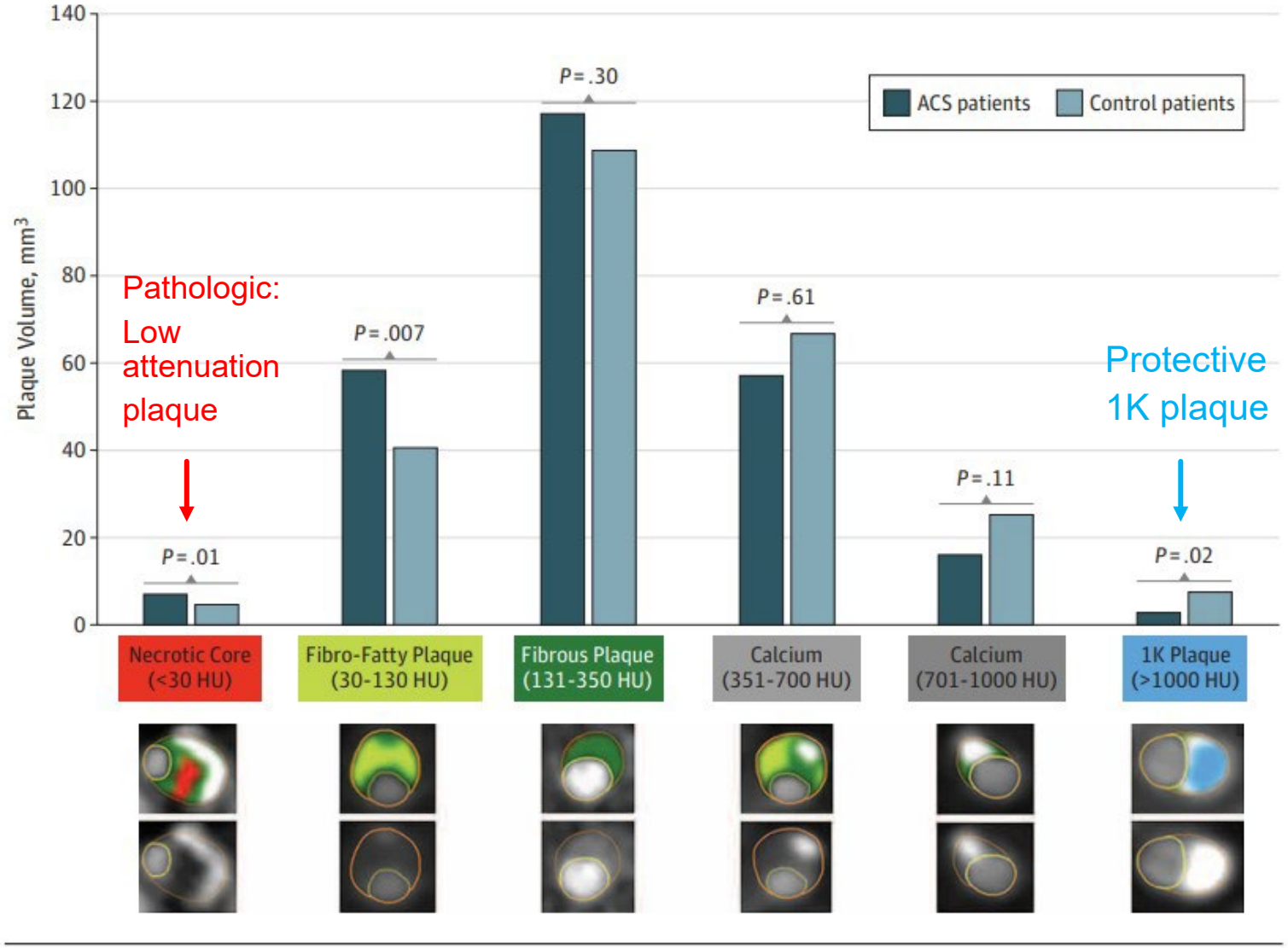
- Shift the paradigm from population-based risk tools to asking what is the individual patient's risk for having a myocardial infarction.
- >50% of patients with acute MI were unaware that they had CAD.
- 25-33% of myocardial infarctions will have a CAC 0.

Studies have confirmed:

- Low density noncalcified plaque is the strongest predictor of MI.
- Plaque progression is the strongest predictor of future major adverse CV events.
- Statins can convert non-calcified plaque into high density calcified plaque which is associated with decreased plaque progression and reduced risk.

- **Coronary CT is the only tool we have that can track how an atherosclerotic plaque is responding to treatment. Escalate treatment as needed.**

ICONIC



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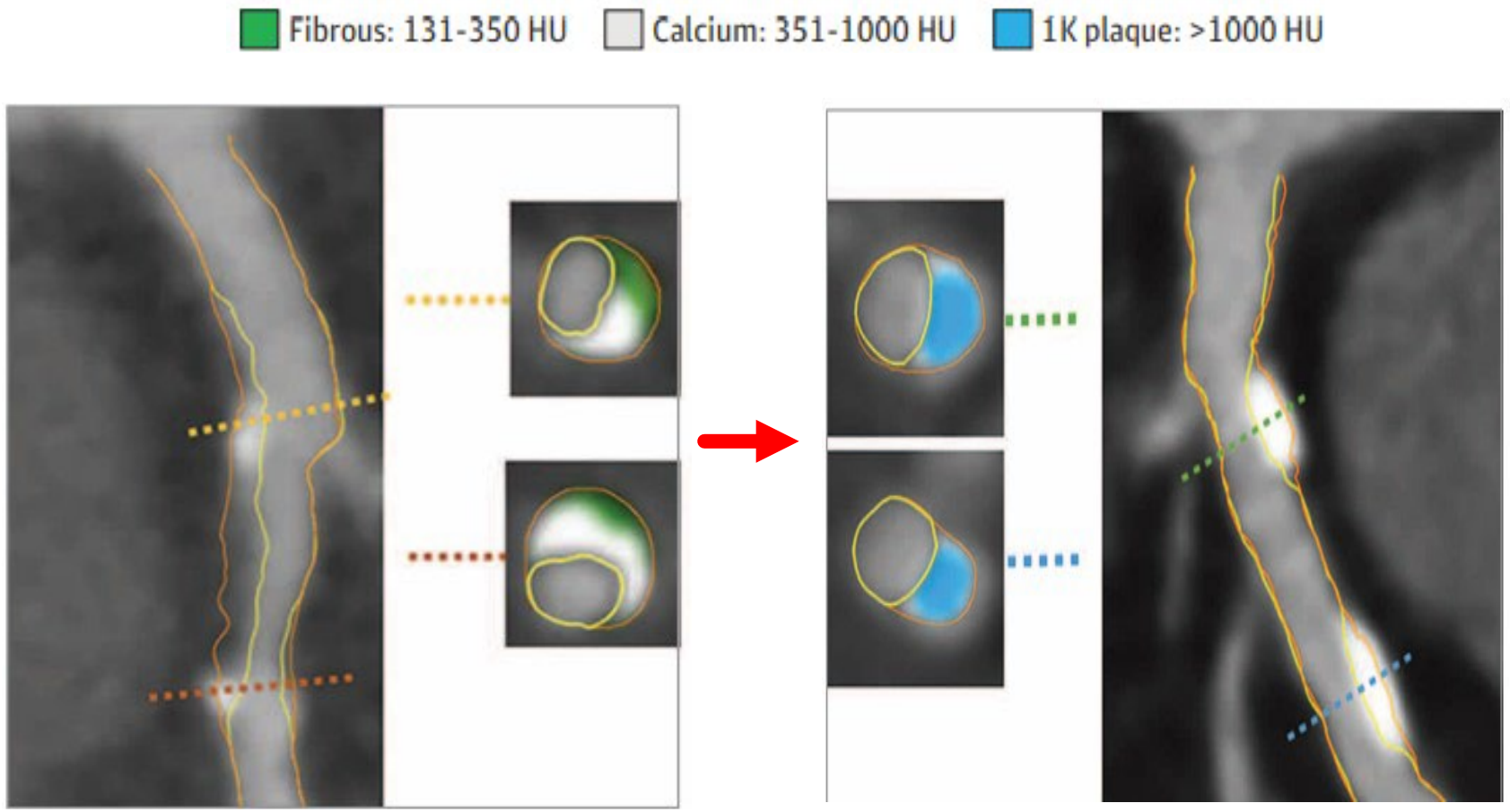
The goal is to convert dark plaque into bright plaque.



High noncalcified plaque burden and no 1K plaque

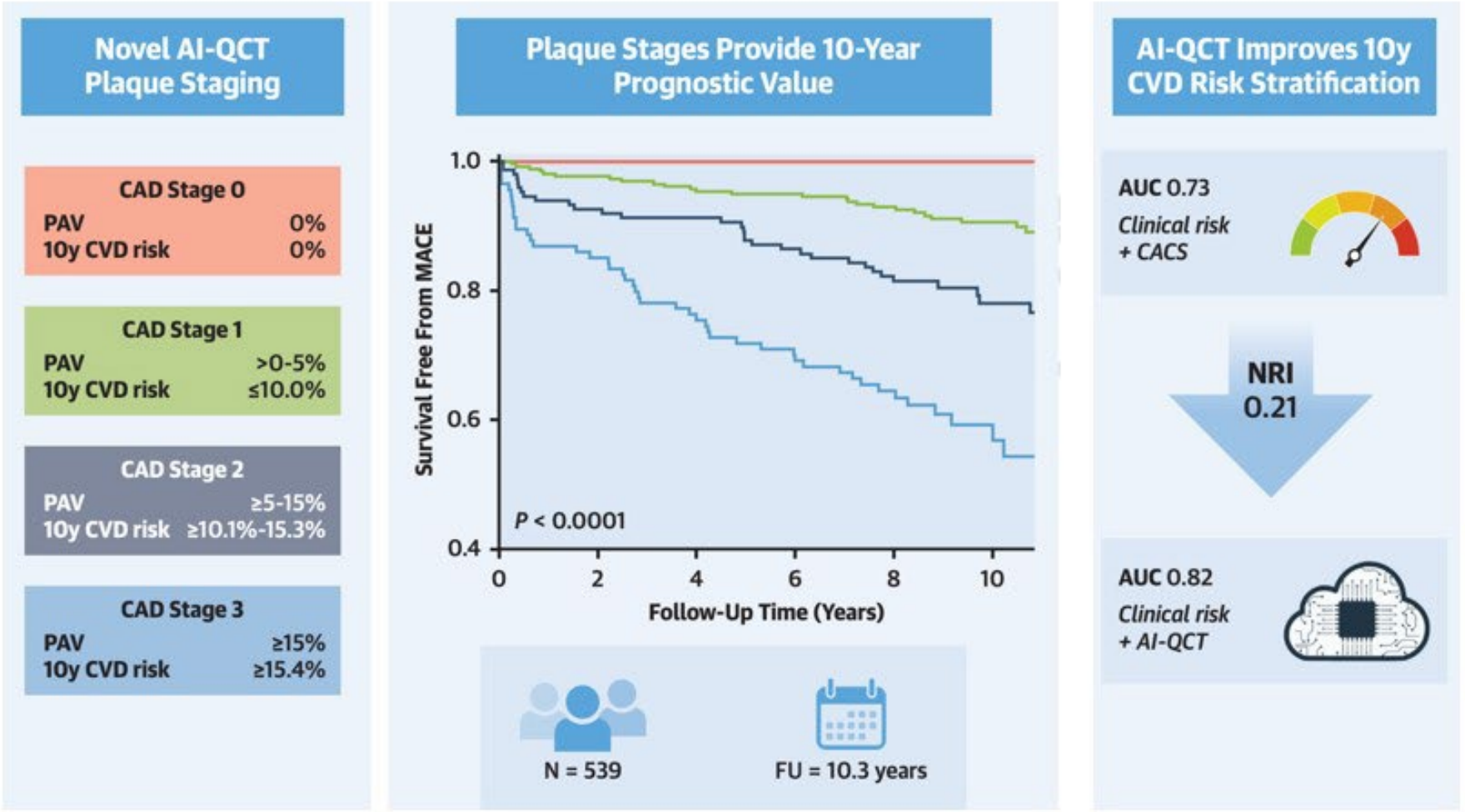
Pathologic: high risk

No noncalcified plaque and high 1K plaque burden

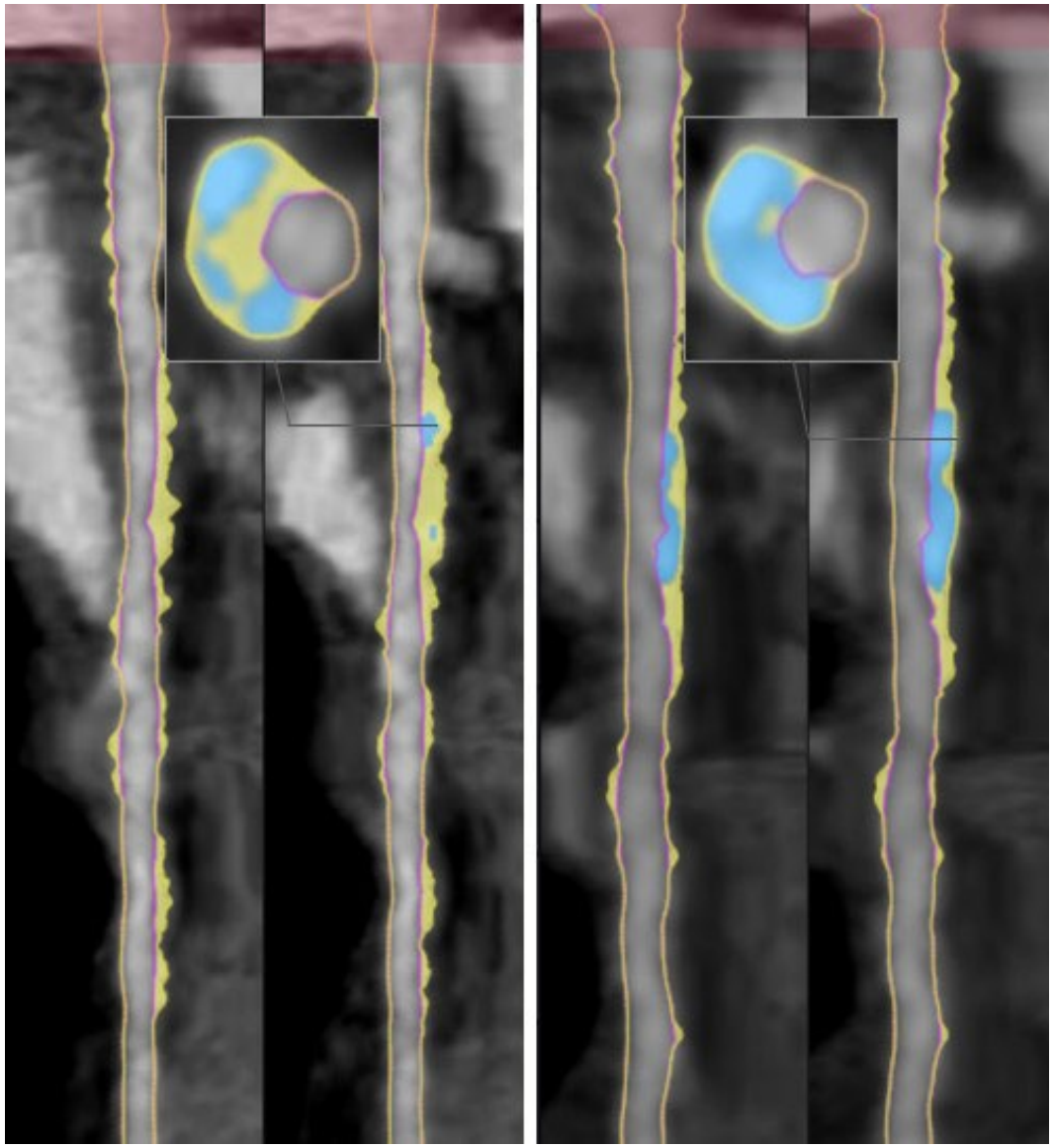
Protective

MACE Prediction:

- Plaque Stage is a better predictor of short- and long-term MACE events than:
  - Risk Score (ASCVD etc.).
  - Agatston Score.
  - Stenosis presence



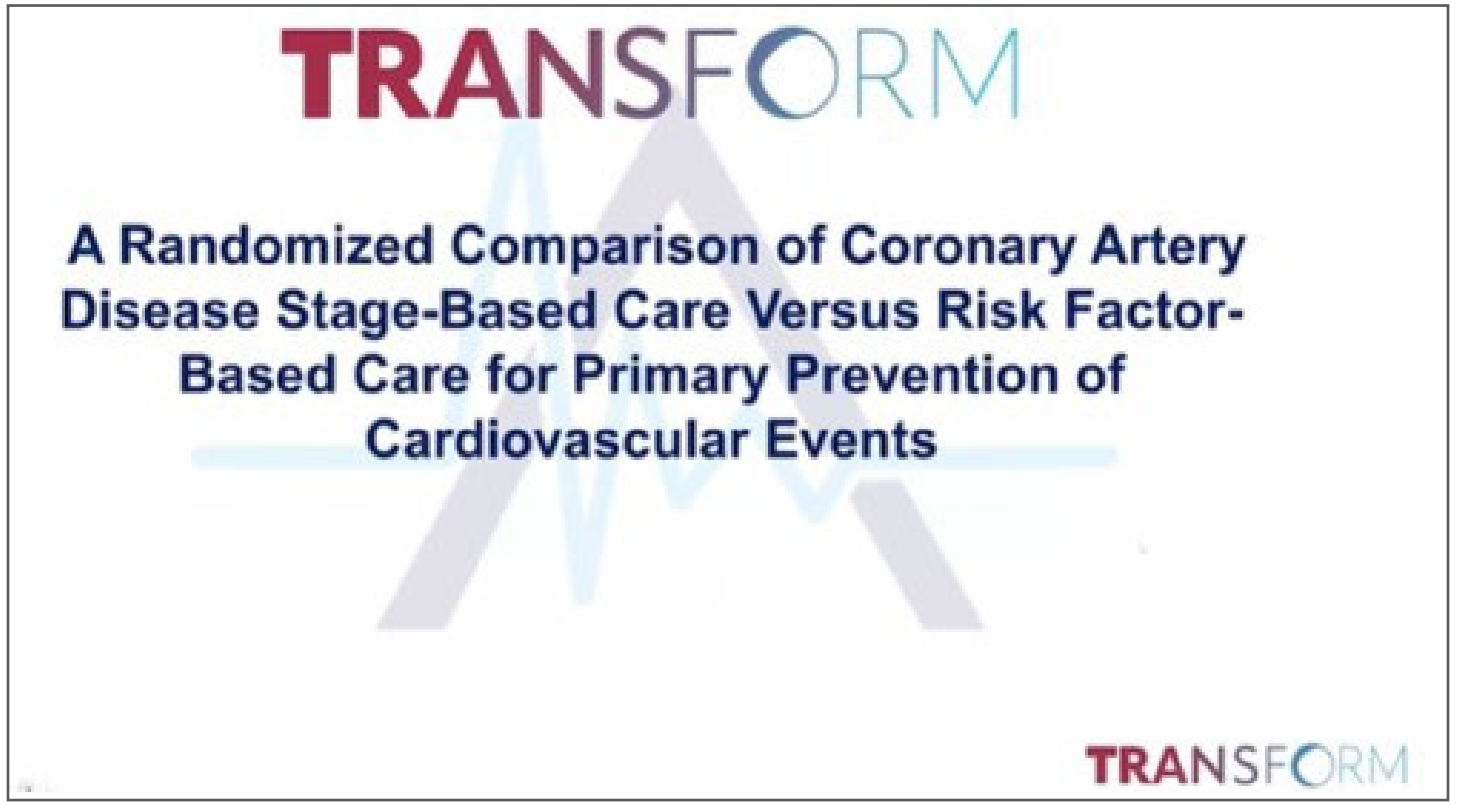
Nurmohamed et al JACC Imag 2023

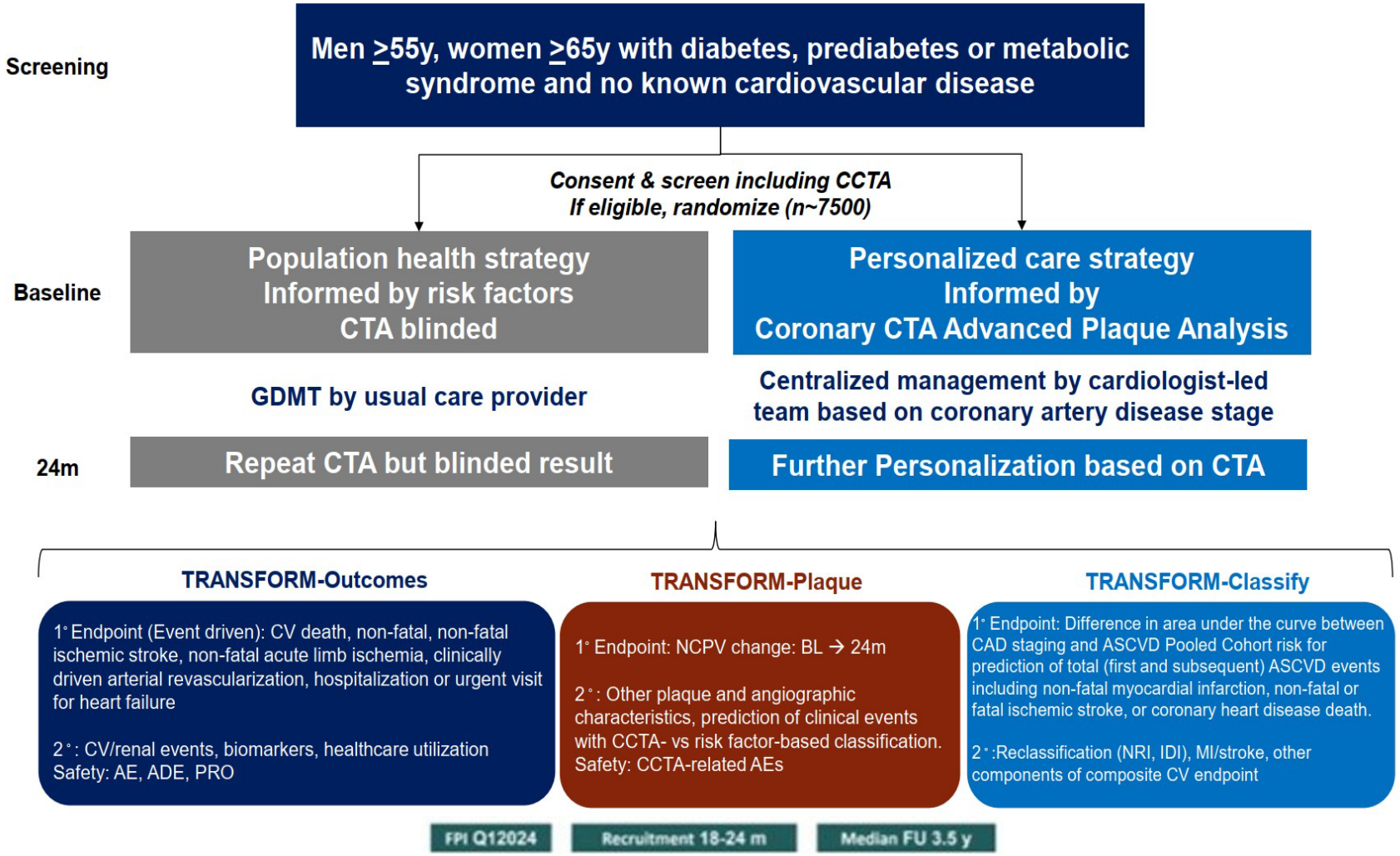


Baseline 3 years

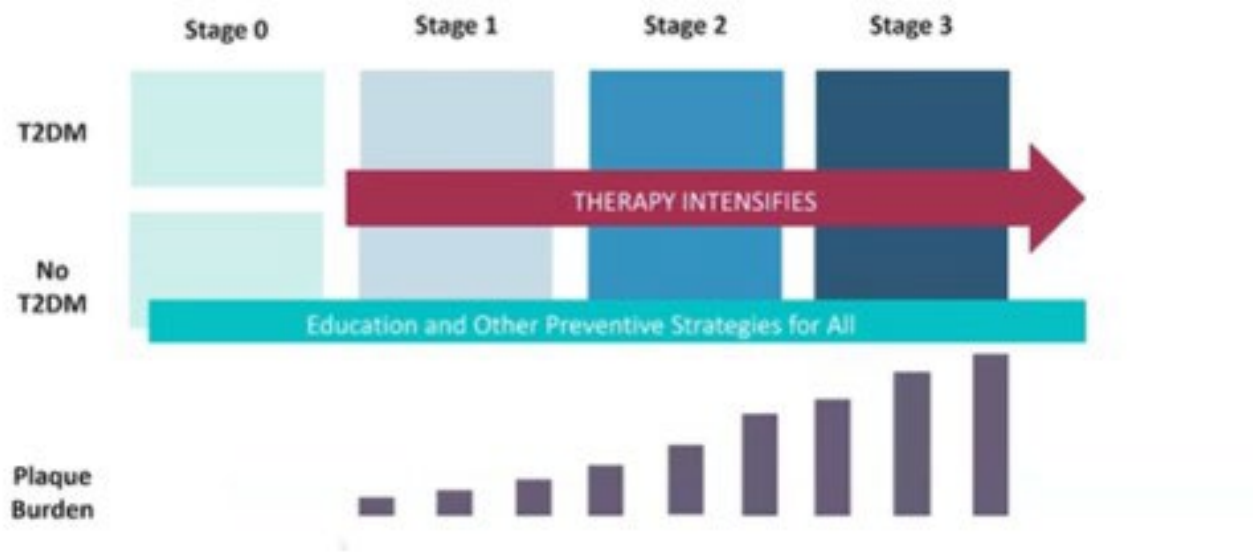
1. **Stabilization**: Halt New Disease Progression
2. **Transformation**: Convert to lower risk calcium

Stage	Baseline	Follow-up 3 years	Change
Total Plaque Volume	260.9 mm^3	255.5 mm^3	-2%
Non-calcified Plaque	139.9 mm^3	57.1 mm^3	-59%
Low Density Plaque	0.5 mm^3	0 mm^3	-100%
Calcified Plaque	121 mm^3	198.4 mm^3	+64%





CAD Stage-Based Intensification of Treatment



Target lipids, thrombosis, and inflammation

Cardiometabolic & Inflammatory Factors	Plaque volume			
	No CAD	*CAD Present*		
	Risk 0.6% per year	Risk 1.8% per year	Risk 3.6% per year	Risk 5.0% per year
	0	1	2	3
All	Usual RF management including statin therapy	Combination LLT to achieve LDL-C Goal < 70 mg/dL "PROVE IT"	Combination LLT to achieve LDL-C Goal < 50 mg/dL "IMPROVE IT" Aspirin	Combination LLT to achieve LDL-C Goal < 30 mg/dL "FOURIER" $P2Y_{12}$ monotherapy
If T2DM and/or Obesity		GLP-1 RA	GLP-1 RA **Sotagliflozin**	GLP-1 RA **Sotagliflozin**
If hsCRP ≥ 2.0 on maximum tolerated lipid lowering therapy				**Colchicine 0.5 mg**
Blood pressure, glucose control, smoking cessation	*Work with site PI and PCP to determine management approach including HBH prescribing medications to optimize BP and glucose control and to achieve smoking cessation*			

Sites will ...

- Get compensation starting from pre-screening efforts
- Gain access to participate in impactful academic output
- Be a part of a paradigm-changing study that will impact clinical practice for the better

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TRANSFORM

Final thoughts…

- CCTA is the test of choice for the evaluation of chest pain.
  - Ideally, there should be an explanation as to why a stress test is being ordered.

- CAC scoring is an excellent tool to stratify risk and can help convince a patient to take a statin. De-risking.

- Plaque analysis with serial coronary CTA as indicated?
  - It would seem to make sense that staging CAD and tracking the response to therapy would reduce risk.

  - Wait for the results of on-going trials – TRANSFORM.