Mass General Brigham
Heart and Vascular Institute

Advanced Cardiovascular Risk Detection
For the Critical Decades

HEART HOUSE ROUNDTABLES
AMERICAN COLLEGE of CARDIOLOGY

# Strengths & Gaps of Current Cardiovascular Risk Models


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# Disclosures

Research support: NIH, Amgen Inc, Novartis Inc, Nanox AI, Heartflow

Steering Committee:  CAVS (Novartis) ; Vesalius (Amgen)

Consultant: Caristo Inc, Hearflow Inc, Nanox AI, Siemens Inc, Novartis

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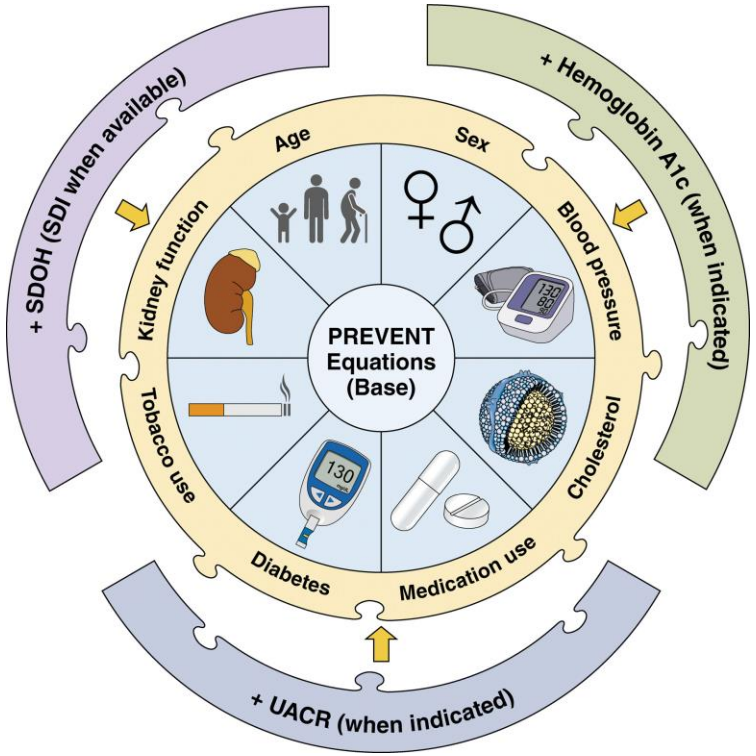
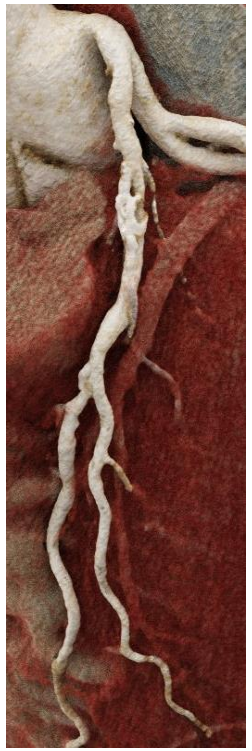
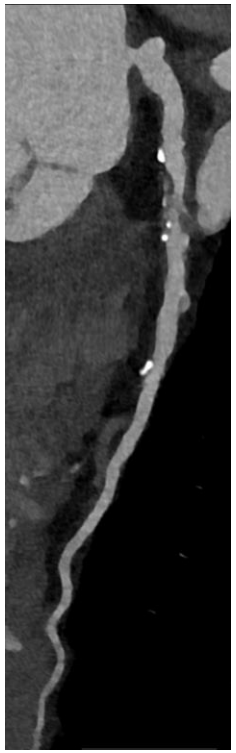
# Outline

## Risk scores and risk factors



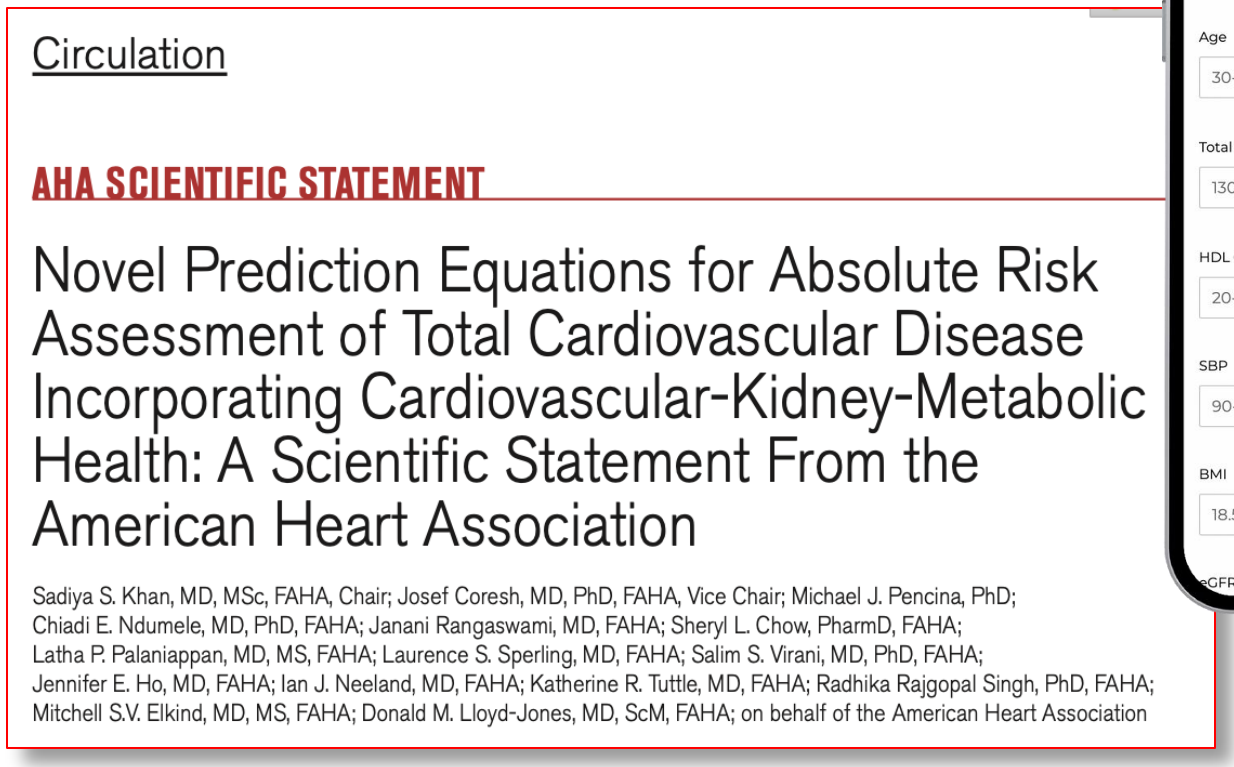

## Imaging based approaches





# Risk Scores

- Framingham Risk Score
- Pooled Cohort Equation
- PREVENT Risk Score

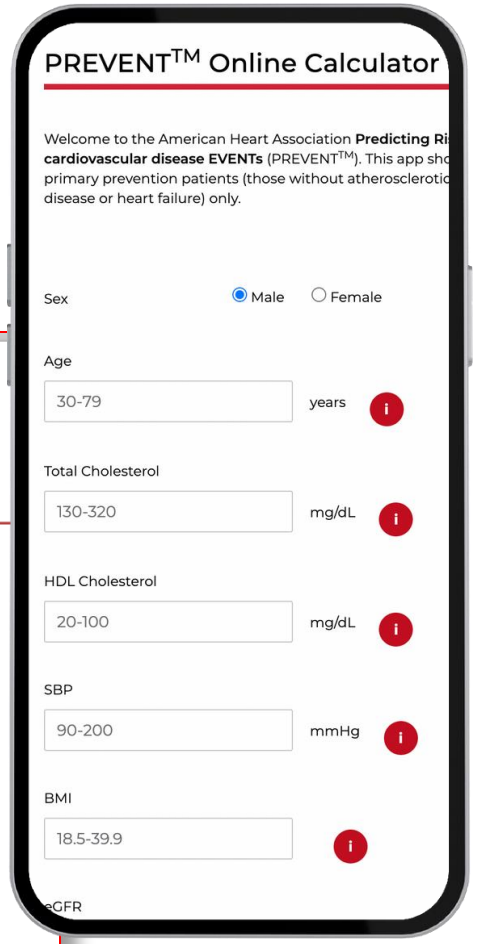


Circulation

AHA SCIENTIFIC STATEMENT

Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement From the American Heart Association

Sadiya S. Khan, MD, MSc, FAHA, Chair; Josef Coresh, MD, PhD, FAHA, Vice Chair; Michael J. Pencina, PhD; Chiadi E. Ndumele, MD, PhD, FAHA; Janani Rangaswami, MD, FAHA; Sheryl L. Chow, PharmD, FAHA; Latha P. Palaniappan, MD, MS, FAHA; Laurence S. Sperling, MD, FAHA; Salim S. Virani, MD, PhD, FAHA; Jennifer E. Ho, MD, FAHA; Ian J. Neeland, MD, FAHA; Katherine R. Tuttle, MD, FAHA; Radhika Rajgopal Singh, PhD, FAHA; Mitchell S.V. Elkind, MD, MS, FAHA; Donald M. Lloyd-Jones, MD, ScM, FAHA; on behalf of the American Heart Association




professional.heart.org/prevent

# PREVENT Equations Overview

## Population

CKD Prognosis Consortium

MESA

CHS

JACKSON HEART STUDY

FRAMINGHAM HEART STUDY

CARDIA

ARIC

Optum

Geisinger

## Predictors

- Base: SBP (and tx status), total cholesterol, HDL cholesterol, diabetes, smoking, eGFR, statin
- BMI
- Add-on: UACR, HbA1c, SDI

## Outcomes

- CVD: composite of ASCVD (nonfatal MI or CHD death, fatal or nonfatal stroke) and HF
- ASCVD, HF

**Does not include:**
**- Lp(a), hsCRP, imaging**

# The American Heart Association PREVENT™ Online Calculator

Welcome to the American Heart Association **Predicting Risk of cardiovascular disease EVENTs** (PREVENT™). This app should be used for primary prevention patients (those without atherosclerotic cardiovascular disease or heart failure) only.

Diabetes ○ No ○ Yes

Sex

Age

57

Total Ch

210

HDL Ch

55

SBP

132 mmHg

BMI

28

eGFR

62

HbA1C ○ No ○ Yes

Zip Code (for estimating social deprivation index [SDI]) ○ No ○ Yes

Calculate Reset

○ Risk of CVD ○ Risk of ASCVD ○ Risk of Heart Failure

## Risk scores

- Population based approach
- Thresholds for considering treatment / initiate discussion

# Limitations of Risk Scores in Young

## Cardiovascular Risk and Statin Eligibility of Young Adults After an MI (JACC 2018)

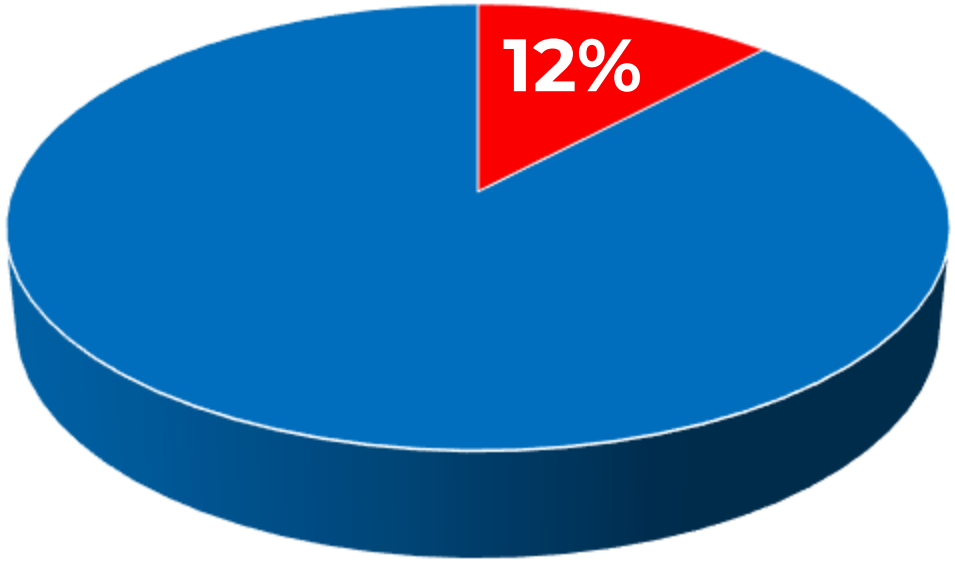
### Partners YOUNG-MI Registry

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]

**YOUNG MI Registry: (age <50)**

**~90% have underlying risk factors → most classified as low risk**

**Lipid lowering therapy use prior to MI ~ 12%**



# Atherosclerosis is highly prevalent among asymptomatic individuals

**SCAPIS Study (age 50-64)**

Bergstorm et al, Circulation 2021
25,182 individuals in Sweden
Plaque **42%**
Stenosis 5%

**Miami Heart Study (age 50-64)**

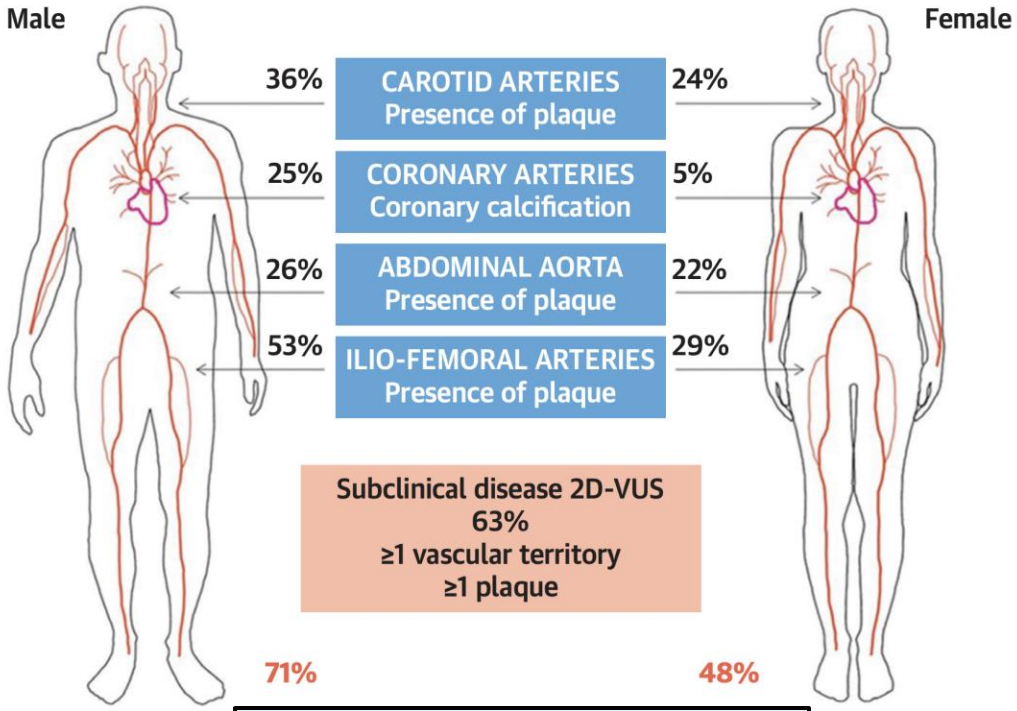
Nasir et al, JACC CV Imaging, 2021
2,459 individuals in Miami
Plaque **49%**
Stenosis 6%

**MESA (age 45-84)**

NEJM, 2008
6,814 individuals in US
Plaque ~**50%**

**PESA Study (age 40-54)**

Fernández-Friera, Circulation 2015
4184 participants in Spain
CAC + Ultrasound
Plaque **63%**




Mean age 46; 63% male

# Plaque in YOUNG individuals

## CAC Consortium

JAMA Network | Open

Original Investigation | Cardiology

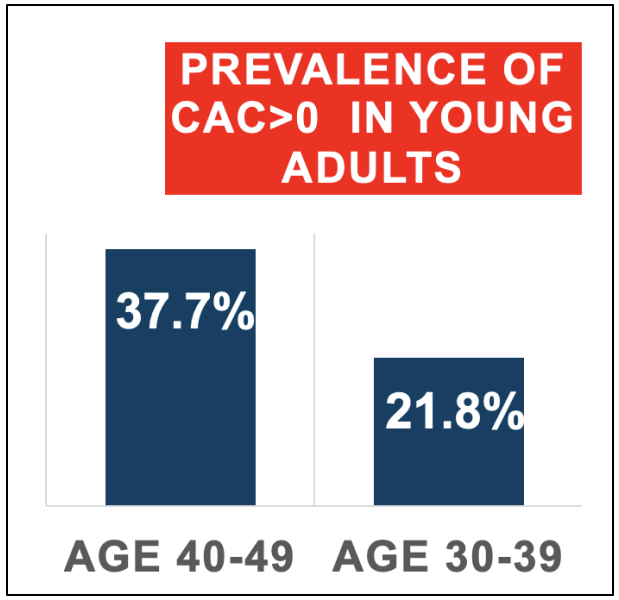
**Association of Coronary Artery Calcium With Long-term, Cause-Specific Mortality Among Young Adults**

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** age 30-49 referred for CAC testing

**34% had CAC**

**CAC → higher risk of CHD, CVD and all-cause death**




## CARDIA

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

**10% had CAC age 32-46 → 30% by age 42-56**

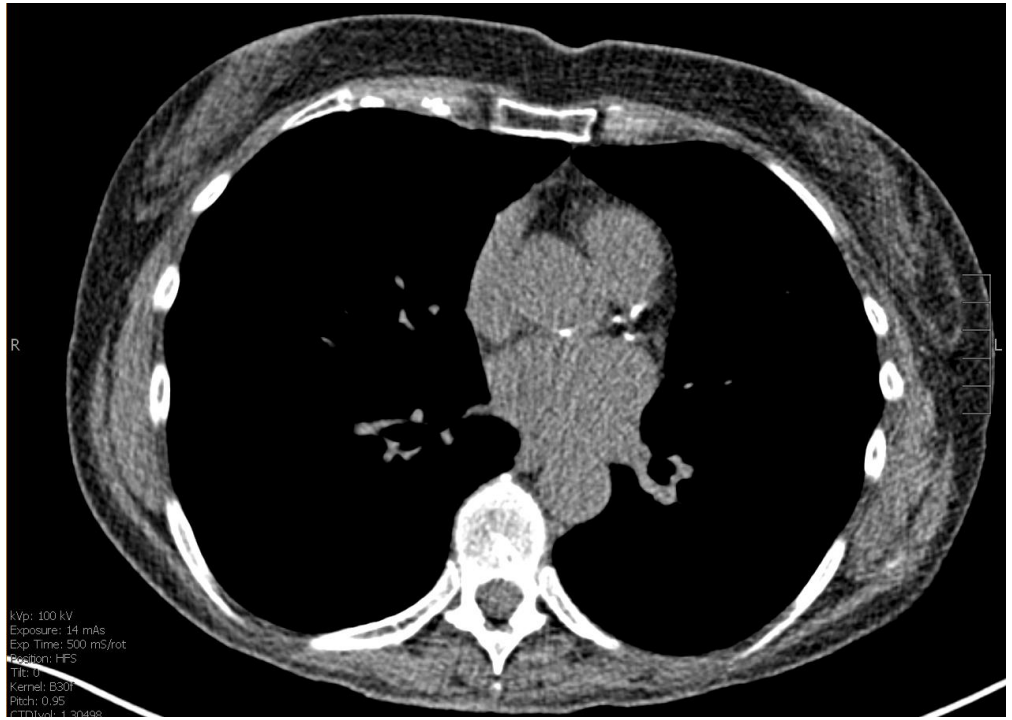
**If use risk factors to define a high-risk group → 45% had CAC**

**CAC → higher risk of CHD**

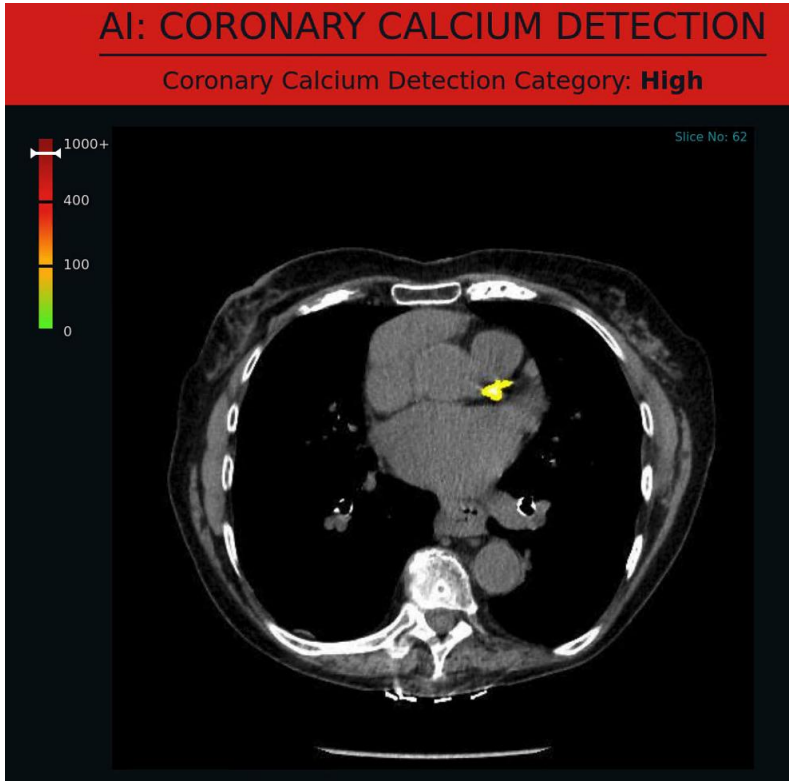
# Why is imaging plaque helpful?

- Imaging = ***actual*** presence of disease
- Compared to risk scores / genetics (PRS) improved discrimination, reclassificaiton, calibration
- Impact on physician + patient behavior
- Impact on outcomes
  - ↓ plaque progression (CAUGHT CAD, JAMA 2025)
  - ↓ events* (St Francis, DANCAVAS)

# Incidental Detection of Coronary Artery Calcium




Chest CT




AI Based Detection of CAC

ORIGINAL RESEARCH

Just published… JACC CV Imaging

# Prevalence and Prognostic Value of Incidentally Detected Coronary Artery Calcium Using Artificial Intelligence Among Individuals With Immune-Mediated Inflammatory Diseases

Brittany N. Weber, MD, PhD,[a,*] David W. Biery, AB,[a,b,*] Milena Petranovic, MD,[c] Stephanie A. Besser, MSAS, MSPA,[a] Daniel M. Huck, MD, MPH,[a,c] Arthur Shiyovich, MD,[a,c] Rhanderson Cardoso, MD,[a] Adam N. Berman, MD, MPH,[a,d] Camila V. Blair, MD,[a] Nayruti Trivedi, MS,[a] Micheal S. Garshick, MD,[e] Joseph Merola, MD,[f] Karen Costenbader, MD,[g] Leslee J. Shaw, PhD,[h] Khurram Nasir, MD, MPH,[i] Katherine P. Liao, MD,[g] Marcelo F. Di Carli, MD,[a,c] Ron Blankstein, MD[a,c]

**Among individuals with IMID, AI detection of CAC on chest CT:**

1. **Highly prevalent**
2. **Associated with adverse CV events**

**CENTRAL ILLUSTRATION** Prevalence and Prognostic Value of CAC-AI Among Individuals with IMIDs

## IMIDs are Associated With an Increased Risk of Cardiovascular Disease

Can we apply innovative solutions like CAC detected by AI to data that *already* exists in the medical record?

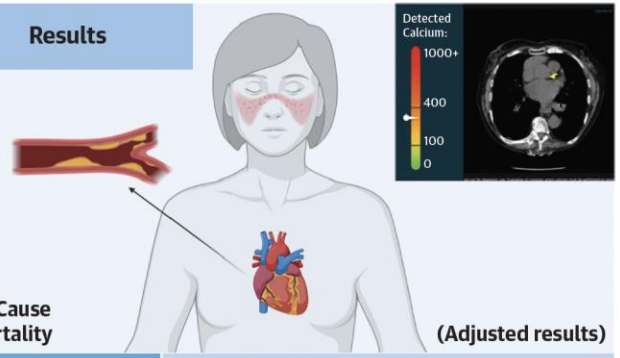

2,546 adults with RA, SLE, and PsO with incidental CAC identified by AI on routine, non-ECG-gated chest CTs performed between 2010-2020

66.5% female
Median age: 59 y

40.9% dyslipidemia
8.5% diabetes

CAC was present in ~1/2 of patients

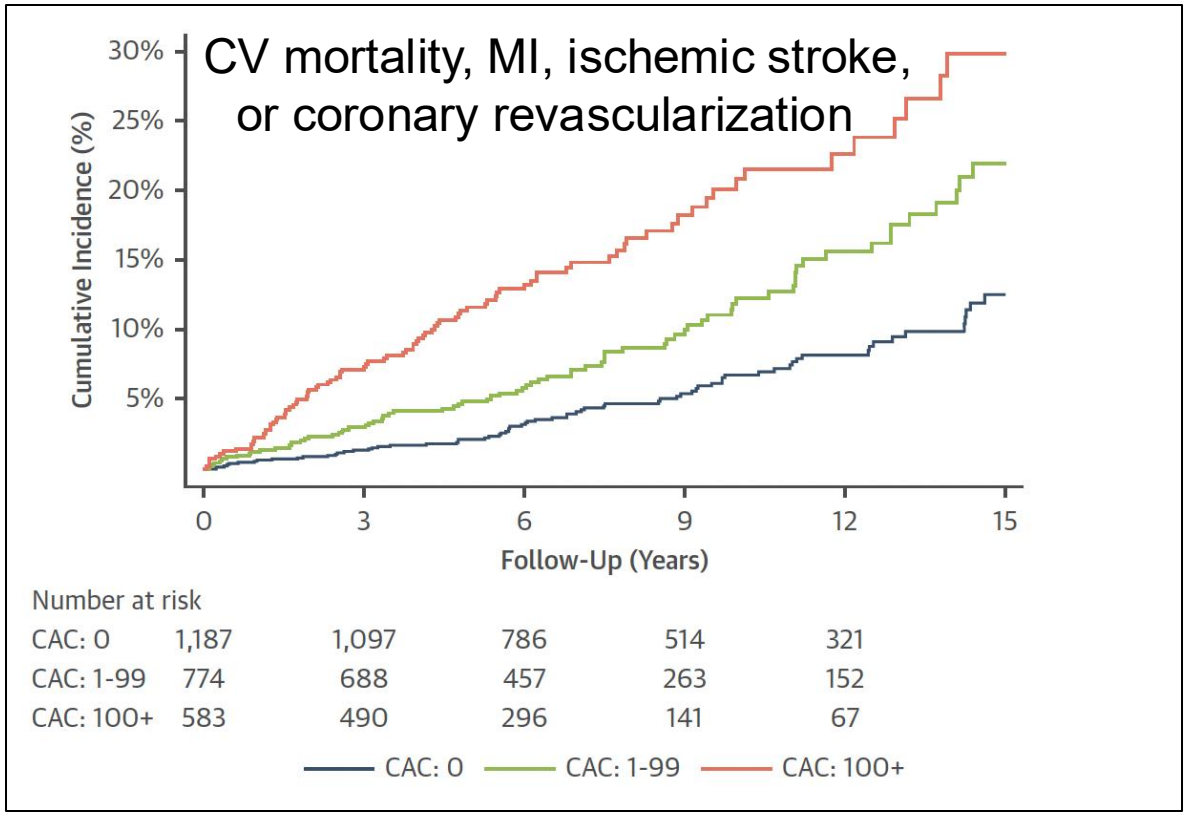
**Results**

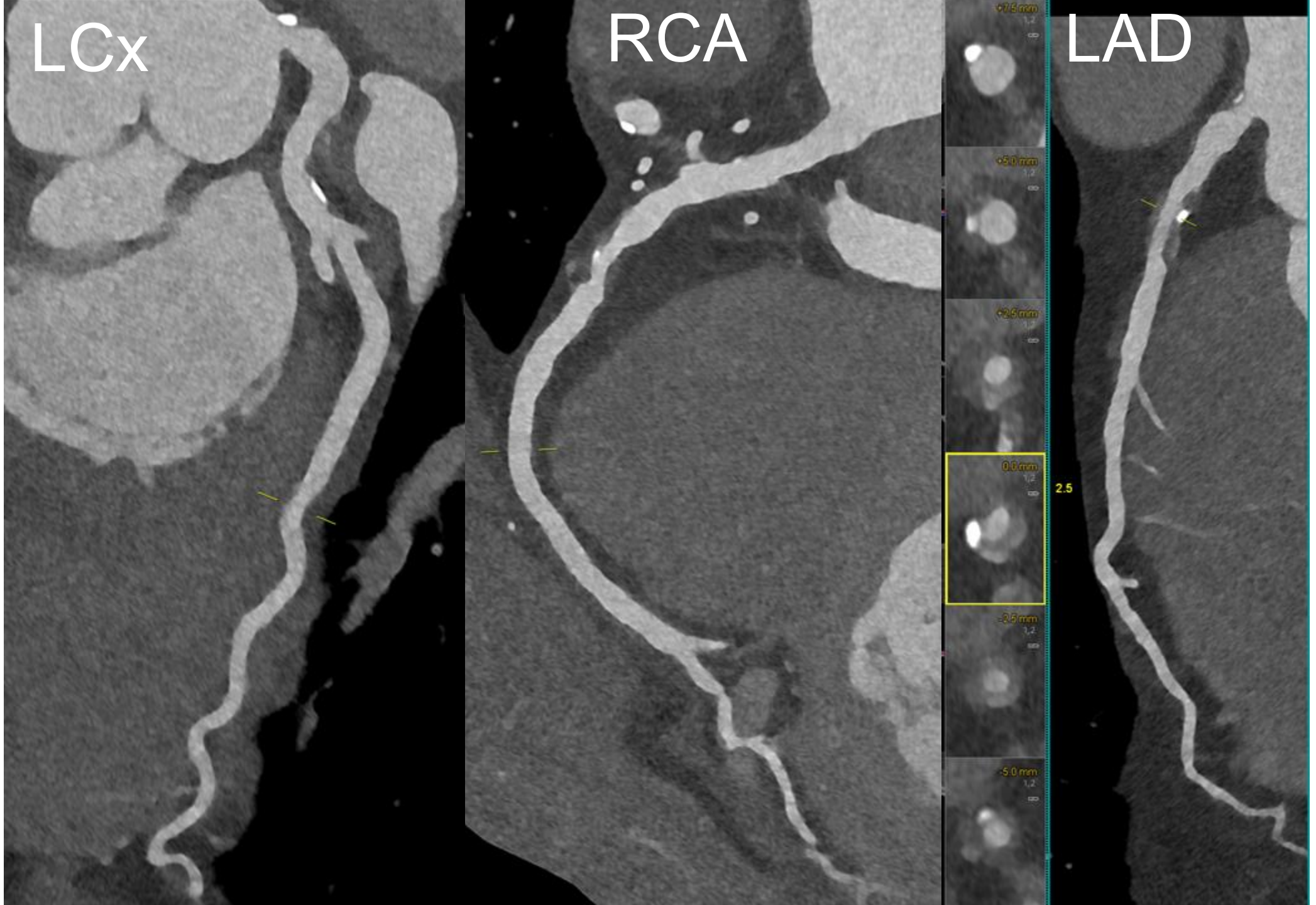



| All Cause Mortality | (Adjusted results) |
|---|---|
| AI CAC 1-99 | HR: 1.41 (*P* = 0.010) |
| AI CAC ≥100 | HR: 2.45 (*P* < 0.001) |

| MACE: | (Adjusted results) |
|---|---|
| AI CAC 1-99 | HR: 2.05 (*P* < 0.001) |
| AI CAC ≥100 | HR: 3.24 (*P* < 0.001) |

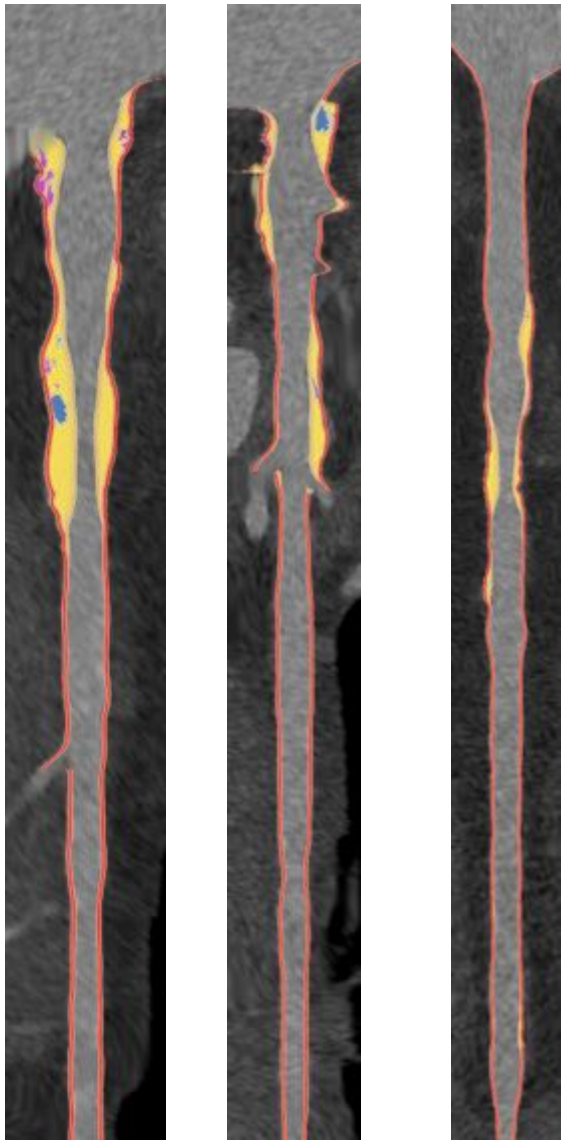
Calcified coronary plaque as detected by AI was associated with an increased risk of all-cause mortality, MACE, and recurrent nonfatal cardiovascular events among patients with PsO, RA, or SLE.




LCx
RCA
LAD
0.0 mm
2.5

# Quantitative Coronary Plaque Analysis

LAD LCx RCA



| Plaque Types | LM | LAD | LCX | RCA | Total |
|---|---|---|---|---|---|
| Calcified Plaque | 9 | 7 | 6 | 19 | 41 (9%) |
| Non Calcified Plaque | 123 | 101 | 58 | 114 | 396 (91%) |
| Low Attenuation Plaque | 20 | 2 | 3 | 15 | 40 (9%) |
| Total Plaque ($mm^3$) | 132 | 108 | 64 | 133 | 437 |

Quantitative plaque is provided on vessels > 1.8 mm.

# Coronary CTA for 1⁰ prevention: pros and cons

**☑ Advantages**

May be useful in individuals who may have a high burden of non-calcified plaque

Enhanced risk assessment

**Limitations**

More costly (vs. CAC)

Potential for excess downstream testing

**Stenosis Severity: ? Reassurance vs. Anxiety**

May provide reassurance (no obstructive CAD or concerning plaque) vs. anxiety (e.g. moderate stenosis)

# What are key gaps:

- ❤️ How can we leverage advances in AI to screen for incidental CAC when imaging already performed for other reasons
- ❤️ What is the best way to use available clinical data & risk scores to decide on which individuals may benefit from further imaging (CAC / CCTA) ?
- ❤️ How should we integrate clinical and imaging data to decide on the the role and intensity of various treatments, and identify individuals who may derive the greatest benefit from such therapies
- ❤️ Innovative trial design and registries to assess the impact of intervening in earlier stages of disease

# Thank you!

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