68 year old male with No Risk Factors

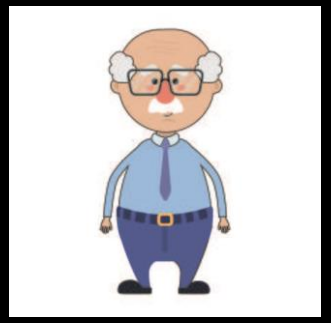
Should a Calcium Score be done for Risk Stratification?

Does it have incremental benefit ?
Will it change my clinical practice ?
Is it widely available & cost effective ?

68 year old male with No Risk Factors

What is his likelihood of having CVD in the next 10 years ?

- **68 yrs, Male**
- **Nonsmoker**
- **72 Kg, 165 cm**
- **BMI 26.4, Waist 88 cm**
- **TC 164, HDL 39, LDL 95; TGL 148 mg/dL**
- **BP 130/84 mm Hg**
- **BG: F 98, PP 136 mg/dL**



- **Framingham Risk score** (ATP III) **14.6%**

(Hard end points: 10 yr MI, CV death)

- **SCORE** (Europe – Low Risk) Death **4%**

  High Risk) Death **7%**

- **JBS3** (10 yr MI,Stroke) **20%**
- **QRisk 3** (10 yr MI, Stroke) **20%**
- **ASCVD** (ACC 10 yr ASCVD RE+) **16.3%**
- **WHO (ISH)** **10-20%**

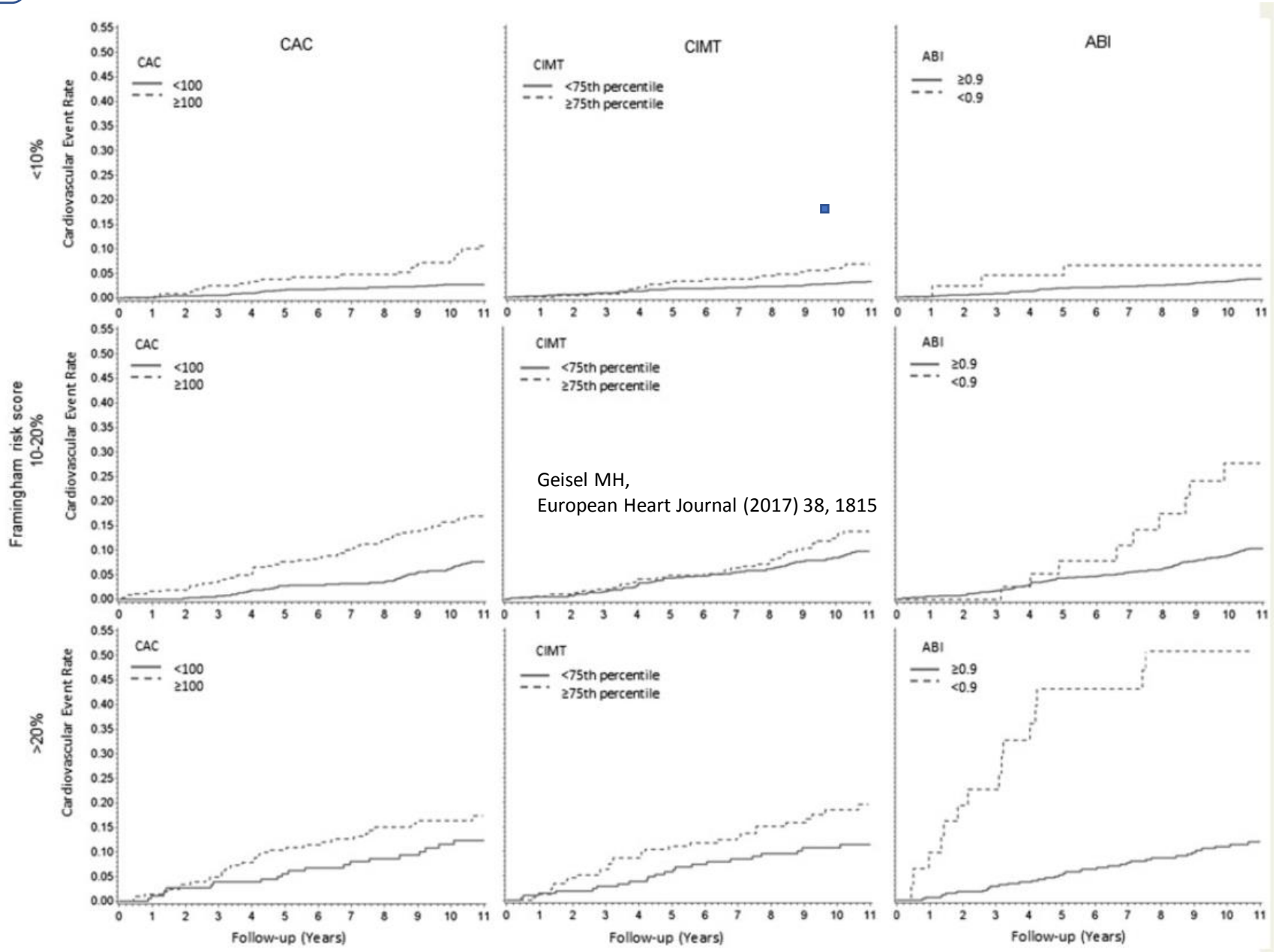
Tests for Subclinical Atherosclerosis

Heinz Nixdorf Recall study

CAC significantly improved the risk prediction in the **low & intermediate risk**

CIMT had a higher discriminative value for the **low risk**

ABI provided better discrimination for subjects with **high risk**



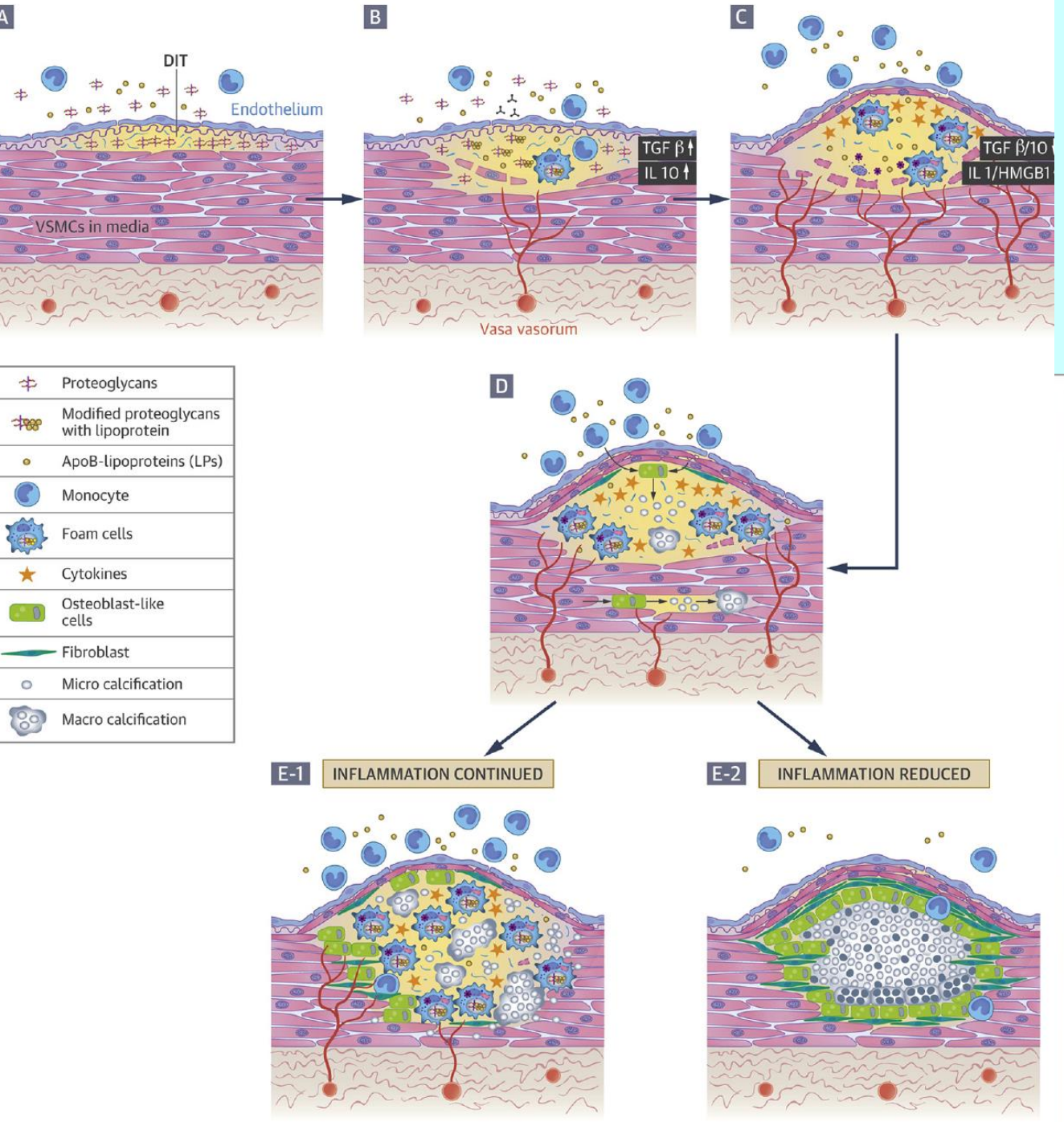
Intimal Ca is specific of Atherosclerosis

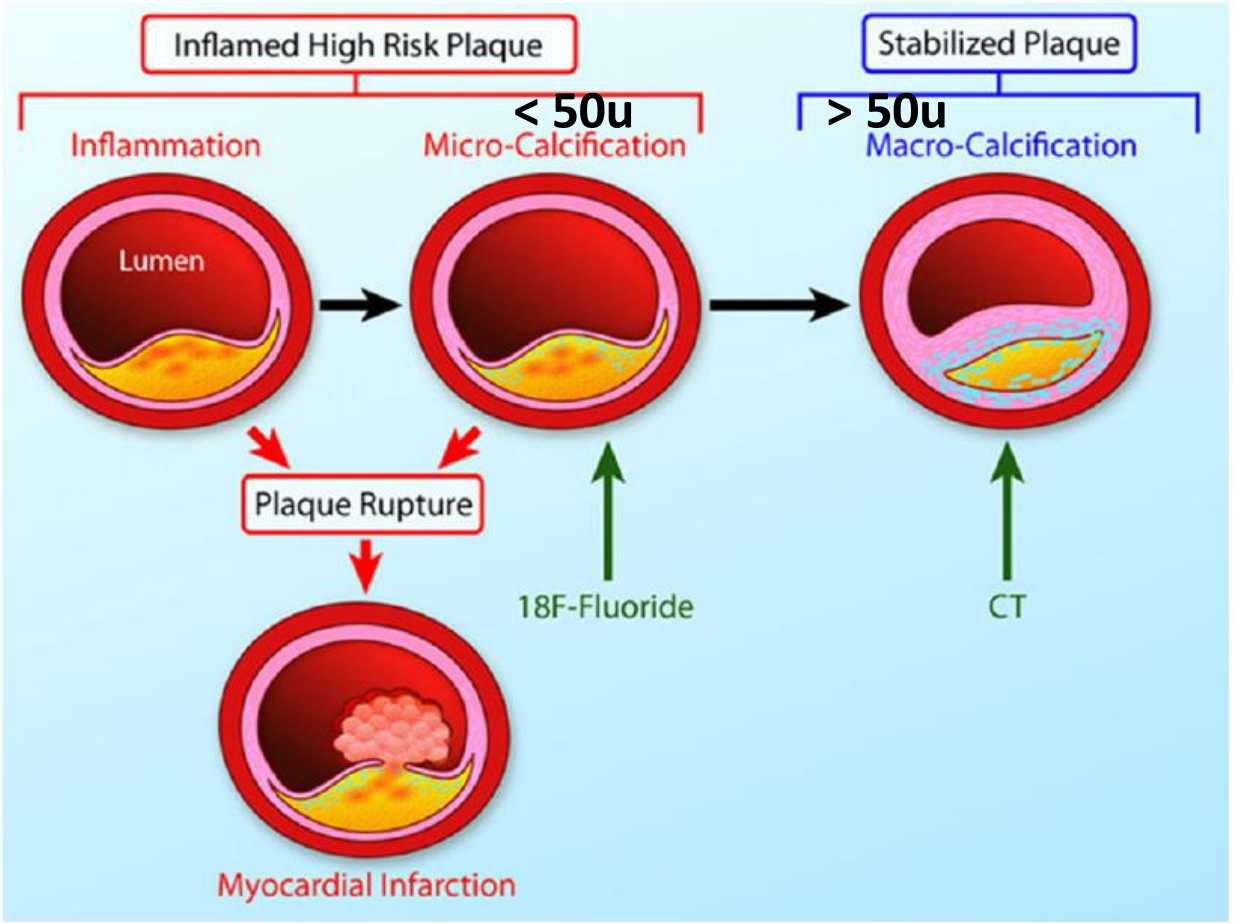
Not age related, Active, regulated process

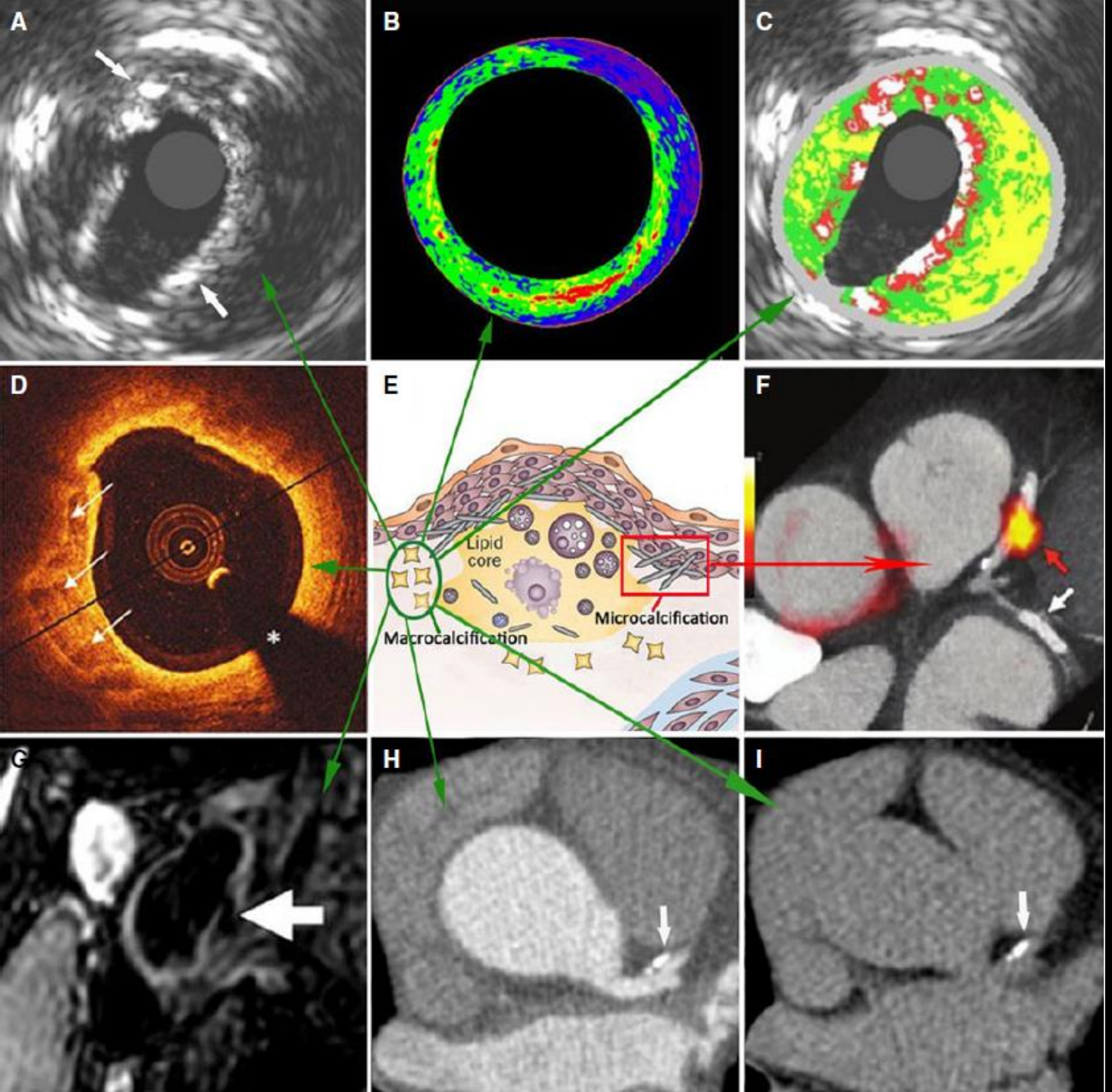
Starts early in atherogenesis,

Promoted by oxidative stress

VSMs > Osteoblast like cells







Multimodality Imaging of CAC

A: Grayscale IVUS image demonstrating a heavily calcified plaque

B: Integrated backscatter-IVUS image: Red: calcification, yellow: dense fibrosis, green: fibrosis, blue and purple: lipid pool

C: Virtual histology IVUS image: Plaque with dense calcifications (white)

D: Optical coherence tomography (OCT) image demonstrating CAC

E: Pathogenic processes demonstrating the atherosclerotic plaque, including lipid core & calcification

G: 3D Isotropic-Resolution Black-Blood MRI

H: Contrast-enhanced coronary CT angiography image demonstrating an area of calcium

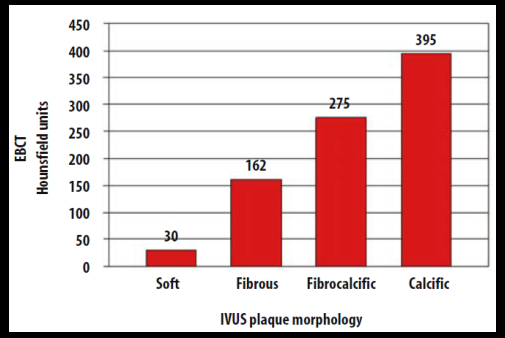
I: Non-contrast-enhanced calcium scoring image demonstrating an area of calcium

DETECTION OF CORONARY ARTERY CALCIUM

- **Chest X Ray, Fluoroscopy**
- **EBCT > MDCT**

Semi quantitiative – ordinal score

Quantitative – Agatston score (Ca volume/mass score)



Calcified plaque (130 HU) - density factor and area

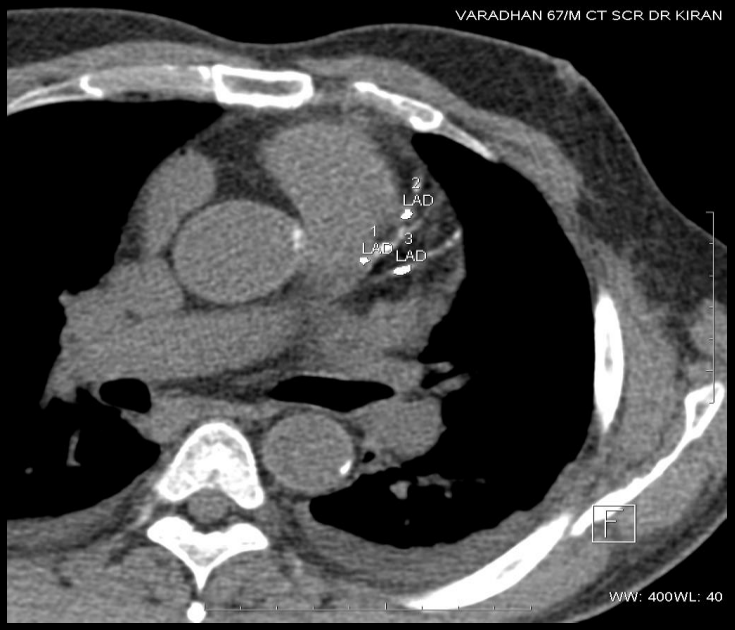
130-199 HU (1); 200-299 HU (2); 300-399 HU (3); 400 HU (4)

10-15 mins, 1 mSv, No contrast

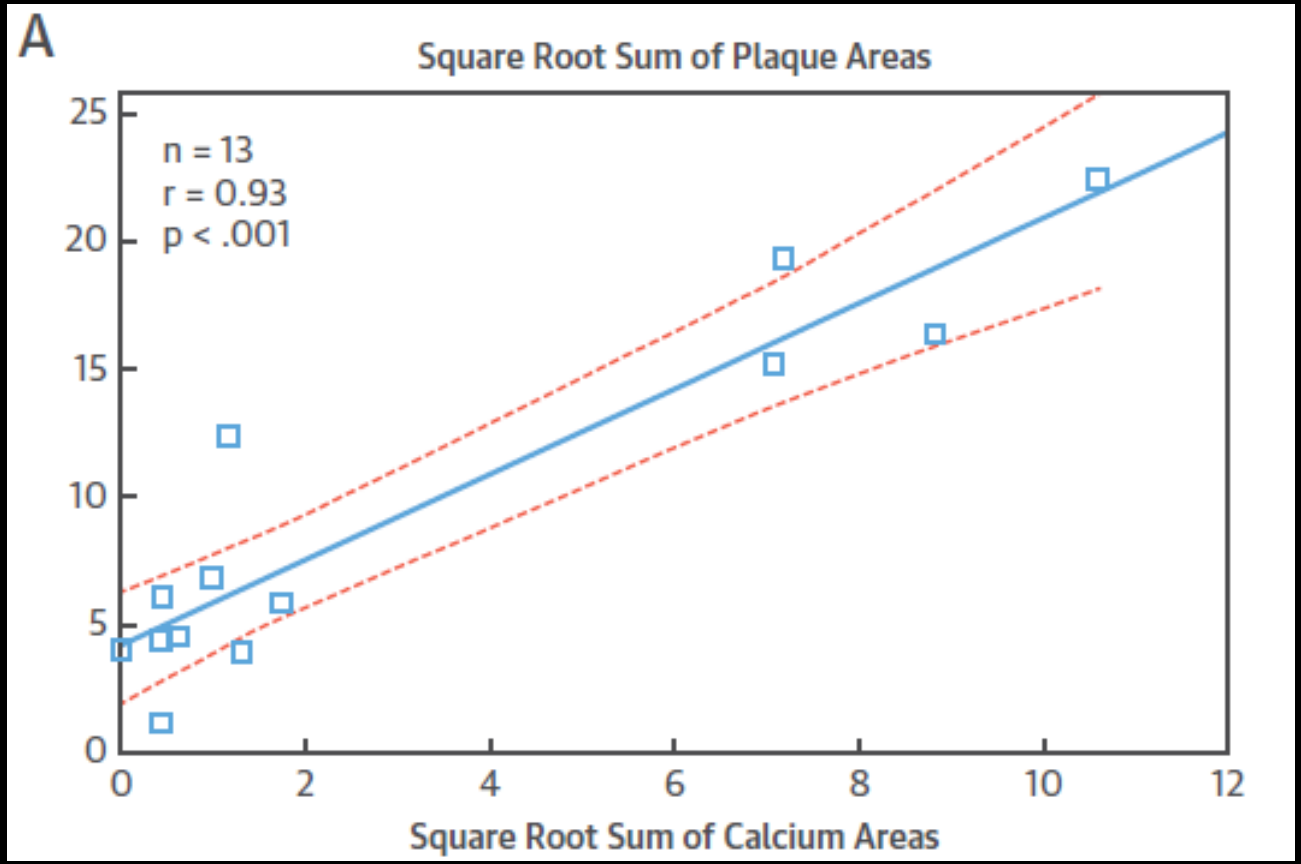
Sensitivity 88-100%, NPV 100%

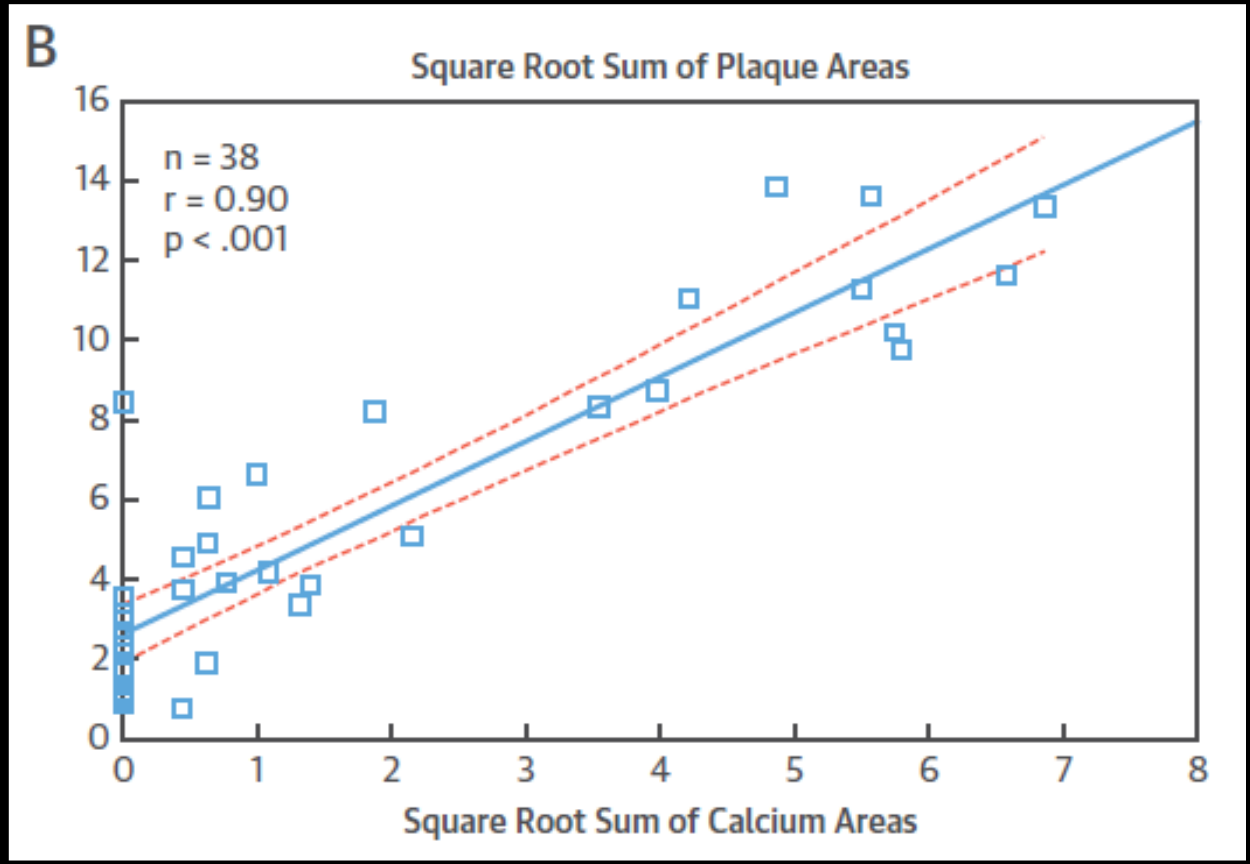
Predicts plaque volume (Disease burden)

not the lumen narrowing



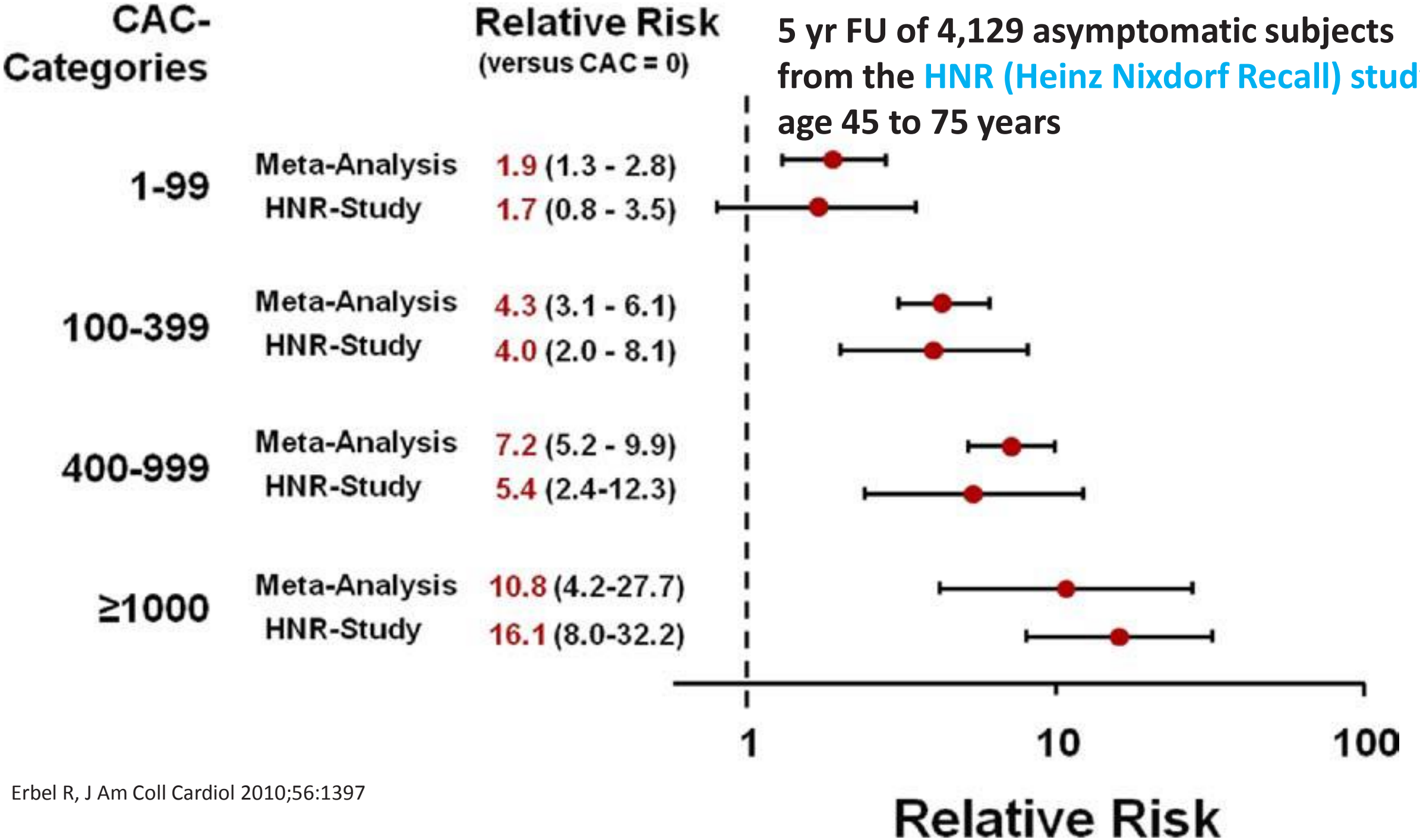
Coronary Calcium correlates with plaque burden





Rumbereger GA, Circulation. 1995;92:2157

5 yr FU of 4,129 asymptomatic subjects from the HNR (Heinz Nixdorf Recall) study age 45 to 75 years



Erbel R, J Am Coll Cardiol 2010;56:1397

Degree of CAC by CAC scores with clinical implications

CAC score	Percentile		Implication	p/a
0	0	56%	Very low risk for future CV events	0.4%
1-100	< 75	26%	Low risk for CV events	0.8%
101-400	76-90	18%	Increased risk for CV events	2.4%
> 400	> 90		Increased probability of ischemia	

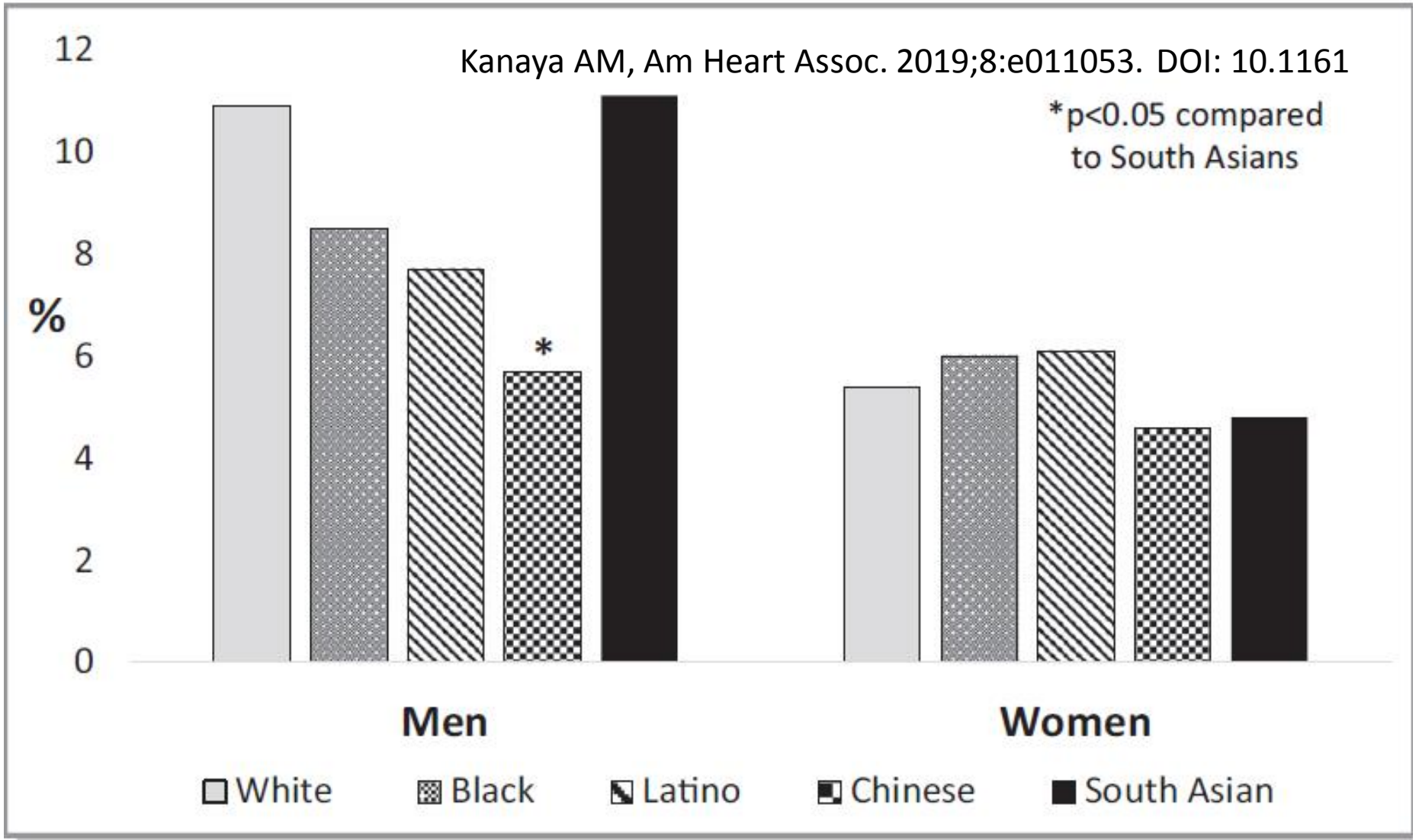
Incident CAC related to age, gender & ethnicity

23% in men 45 to 49 yrs of age to 67% in the 70 to 74 yrs

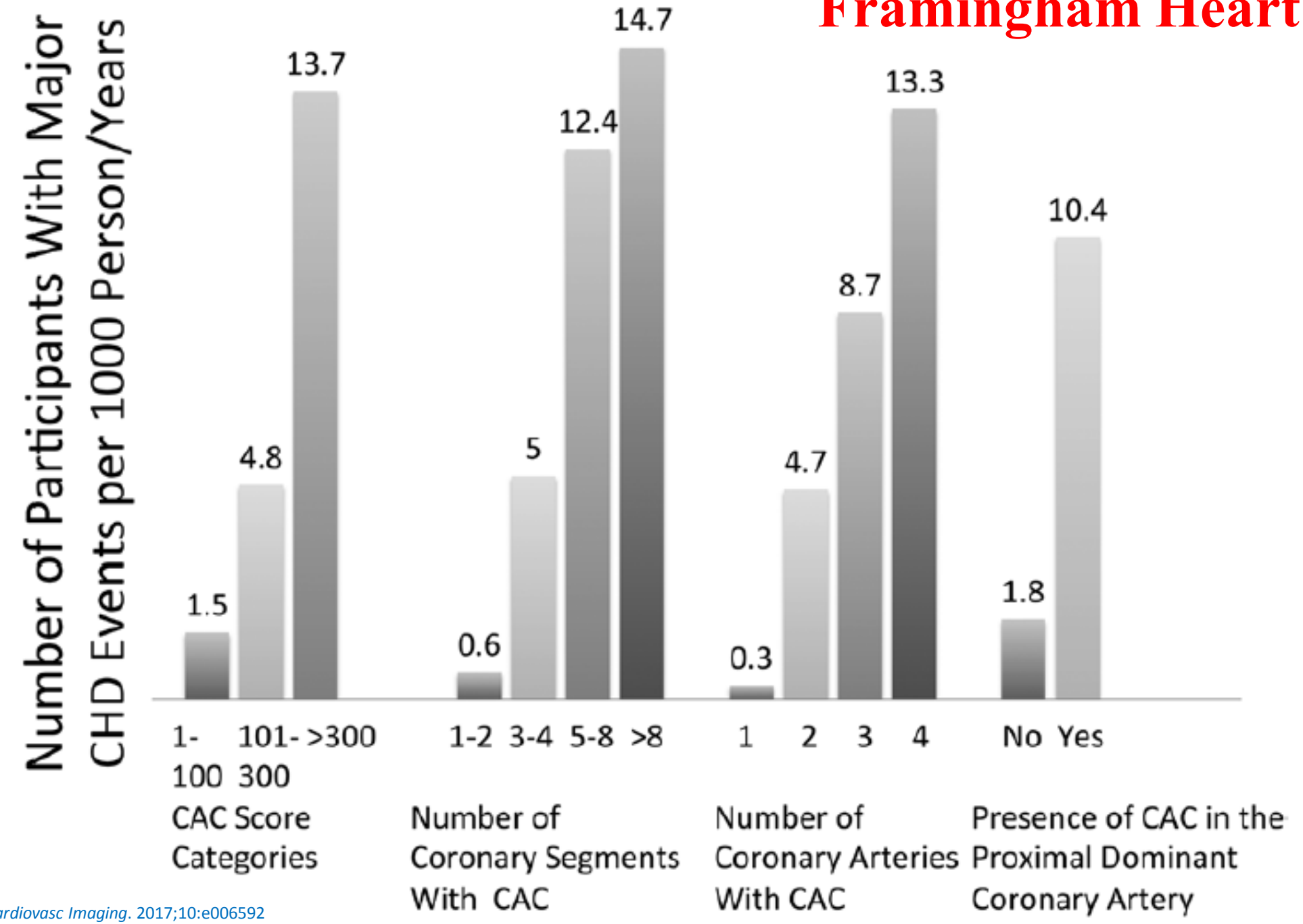
15% in women age 45 to 49 years to 43% age 70 to 74 yrs

MASALA (Mediators of Atherosclerosis in South Asians Living in America) study

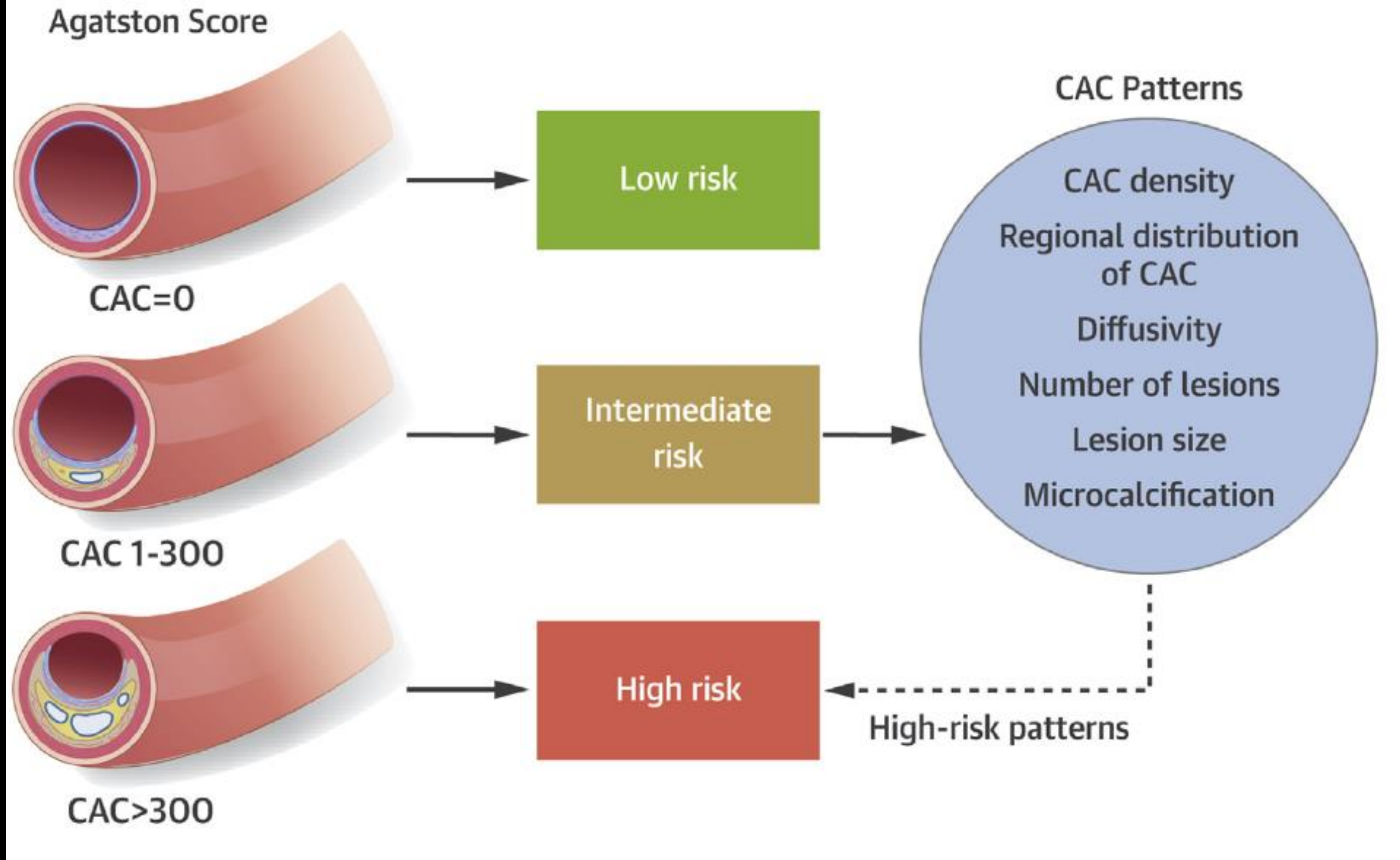
749 South Asians (SFO & Chicago) 56±10 (M) 54±8 (W)yrs at entry, CAC at baseline and at 5 yrs FU
749 Baseline CAC 0 44% (M) 77% (W) > at 5 yrs 26% & 75%



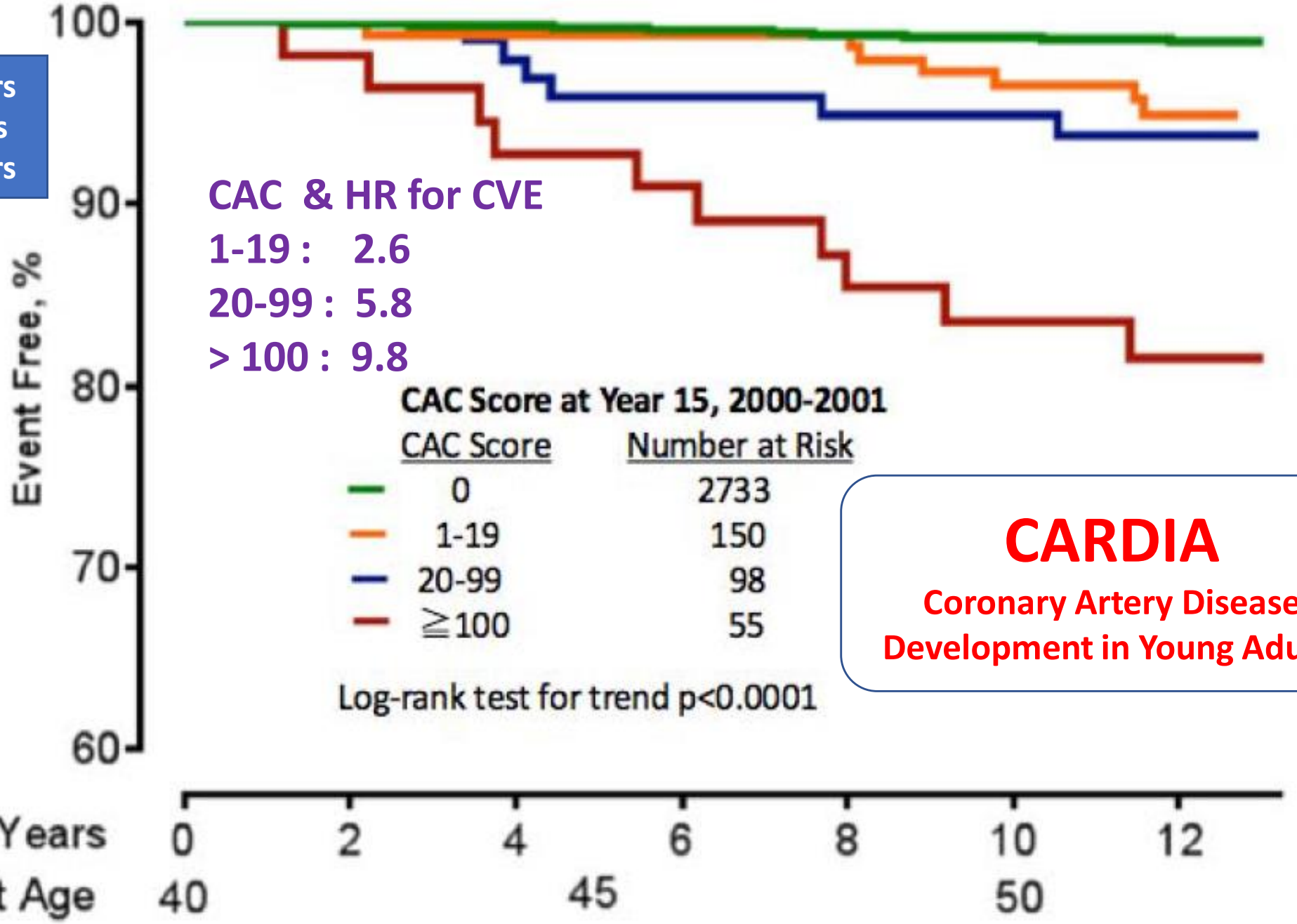
Framingham Heart Study



Ferencick M, *Circ Cardiovasc Imaging*. 2017;10:e006592


Agatston Score
CAC=0
CAC 1-300
CAC>300
Low risk
Intermediate risk
High risk
CAC Patterns
CAC density
Regional distribution of CAC
Diffusivity
Number of lesions
Lesion size
Microcalcification
High-risk patterns

10.2% at m age 40 yrs
20.1% at m age 45yrs
28.4% at m age 50 yrs



CARDIA

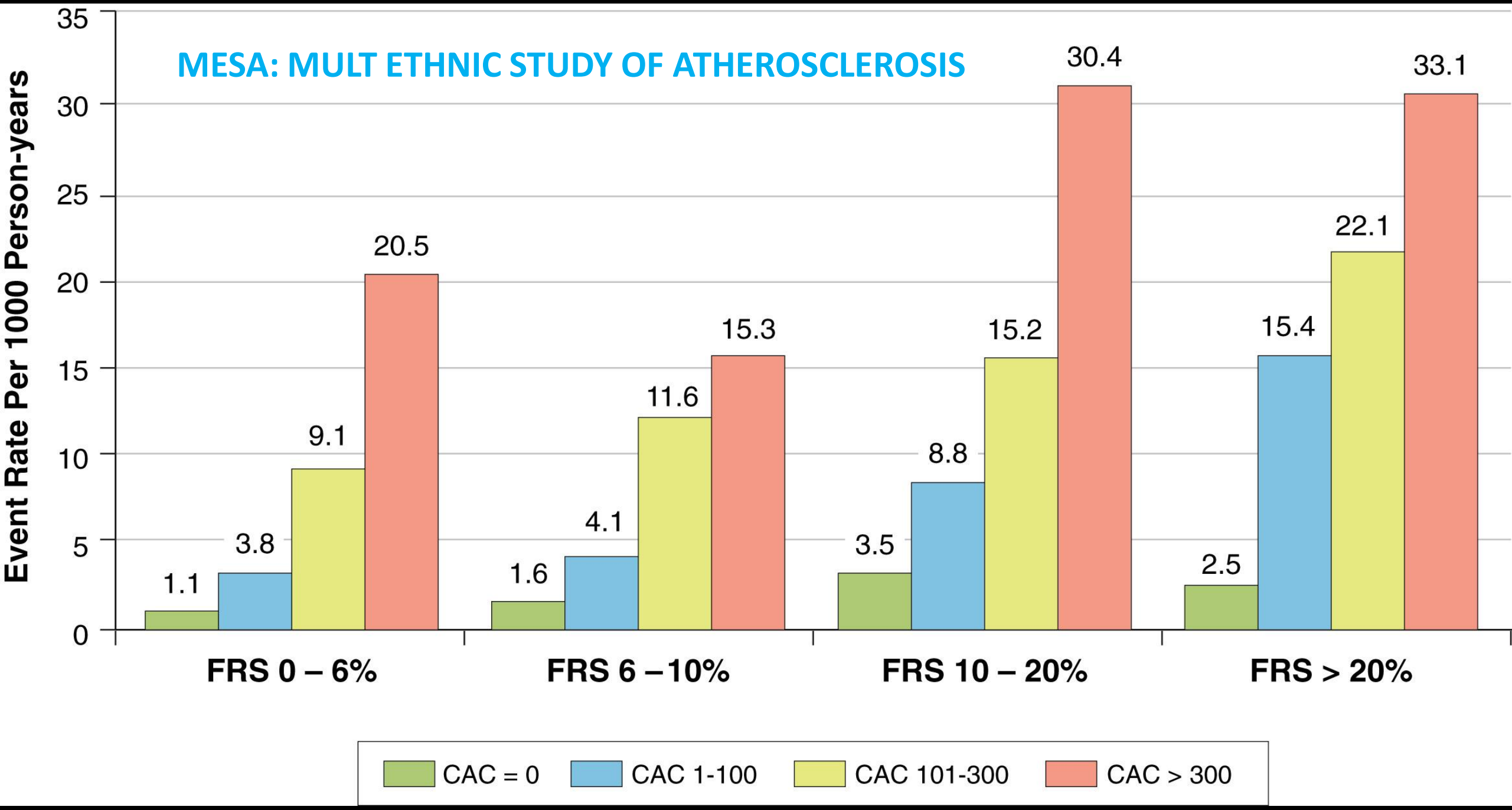
Coronary Artery Disease Development in Young Adults

Carr JJ, JAMA Cardiol. 2017;2(4):391

Prospective Observational Studies of the Coronary Artery Calcium Score

	MESA	HNR	Rotterdam	Framingham
Year CAC study started	2000-2002	2000-2003	1997-2000	2002-2005
Type of CT scan performed	EBCT at 3 centers, MDCT at 3 centers	EBCT	EBCT	MDCT
Number of participants	6,814	4,487	2,063*	3,238
Age range of participants, yrs (mean)	45-84 (62.2 ± 10.2)	45-74 (59 ± 8)	≥55 (71.1 ± 5.7)	Men >35, women >40 (49 ± 10.9)
Women	53%	53%	57%	54%
Systolic blood pressure, mm Hg	126.6 ± 21.5	133 ± 21	144 ± 21 men, 142 ± 21 women	124.0 ± 16.7
Total cholesterol, mg/dl	194.2 ± 35.7	231.2 ± 38.6	216.6 ± 34.8 men, 232.0 ± 34.8 women	206.0 ± 38.2
Current smoking	12%	23%	18% men, 15% women	26%
Previous CVD included or excluded	Clinical CVD excluded	Clinical CAD excluded†	Not excluded	Excluded from most analyses
Percentage with CAC >0 at baseline examination	Men 52%-70%, women 35%-45%‡	Men 82%, women 55%	91% overall (125)	Men 40.5%, women 20.6%

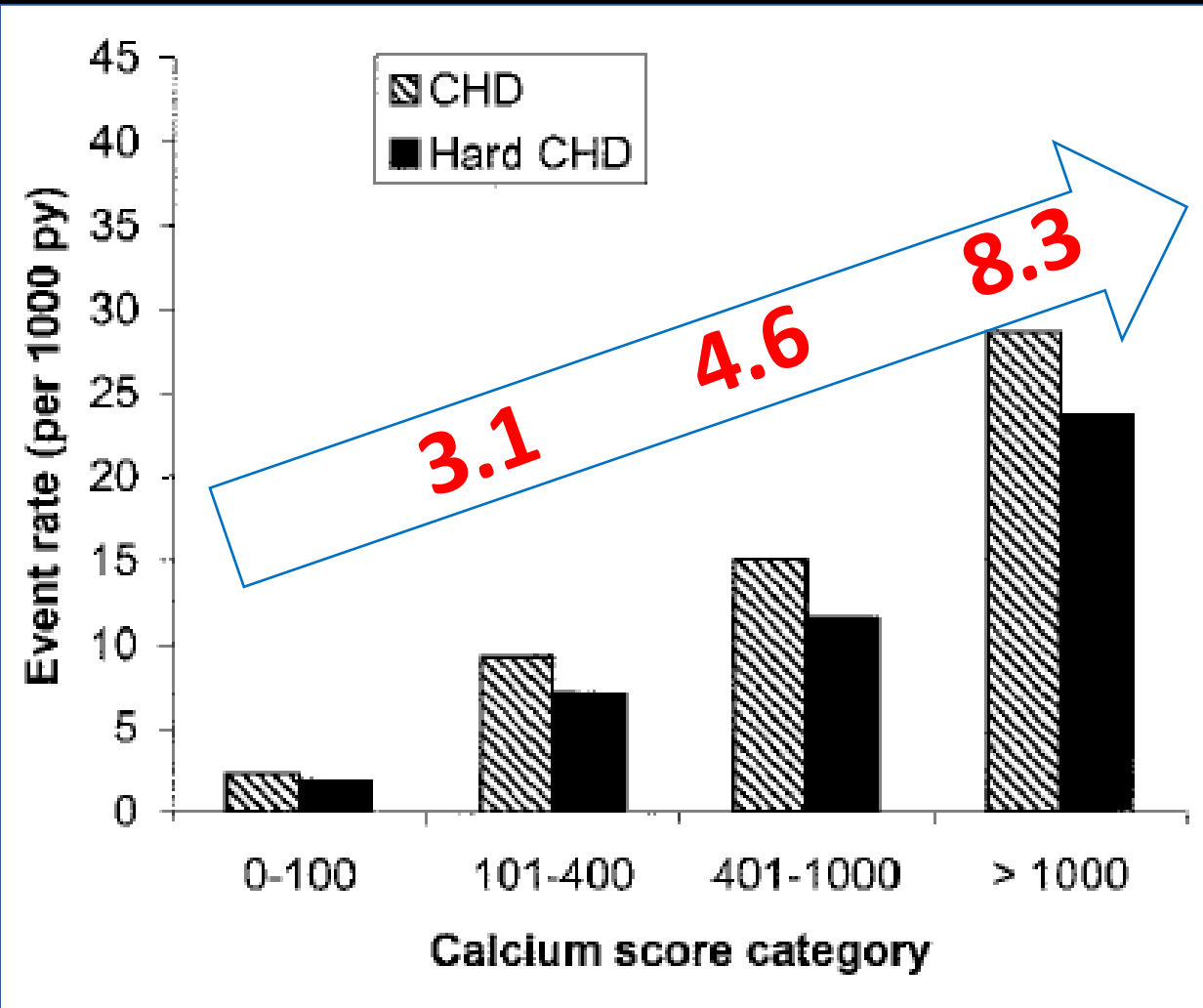
MESA: MULTI ETHNIC STUDY OF ATHEROSCLEROSIS; HNR: HEINZ NIXDORF RECALL

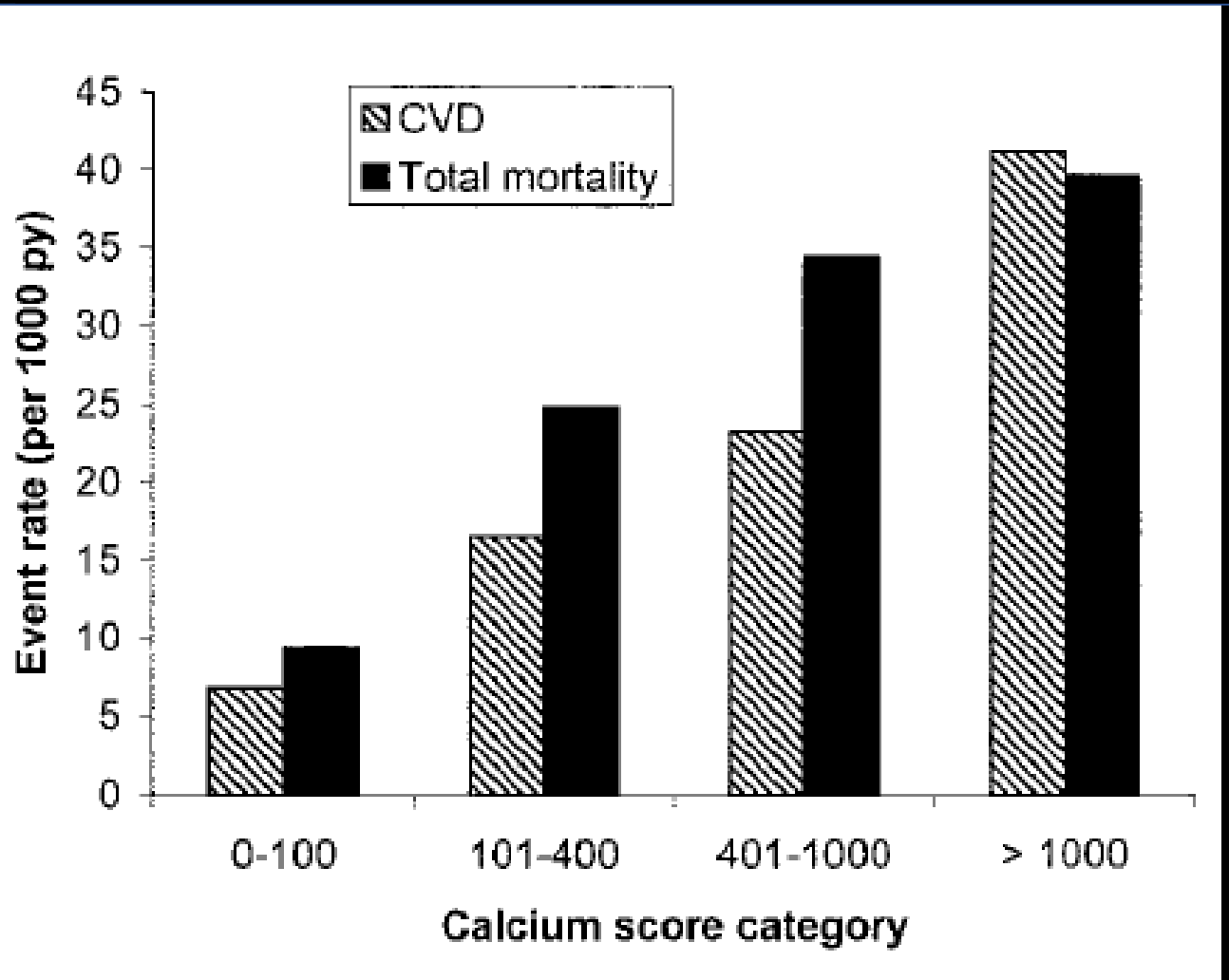

MESA: MULT ETHNIC STUDY OF ATHEROSCLEROSIS
Event Rate Per 1000 Person-years
35
30
25
20
15
10
5
0
1.1
3.8
9.1
20.5
1.6
4.1
11.6
15.3
3.5
8.8
15.2
30.4
2.5
15.4
22.1
33.1
FRS 0 – 6%
FRS 6 –10%
FRS 10 – 20%
FRS > 20%
CAC = 0
CAC 1-100
CAC 101-300
CAC > 300

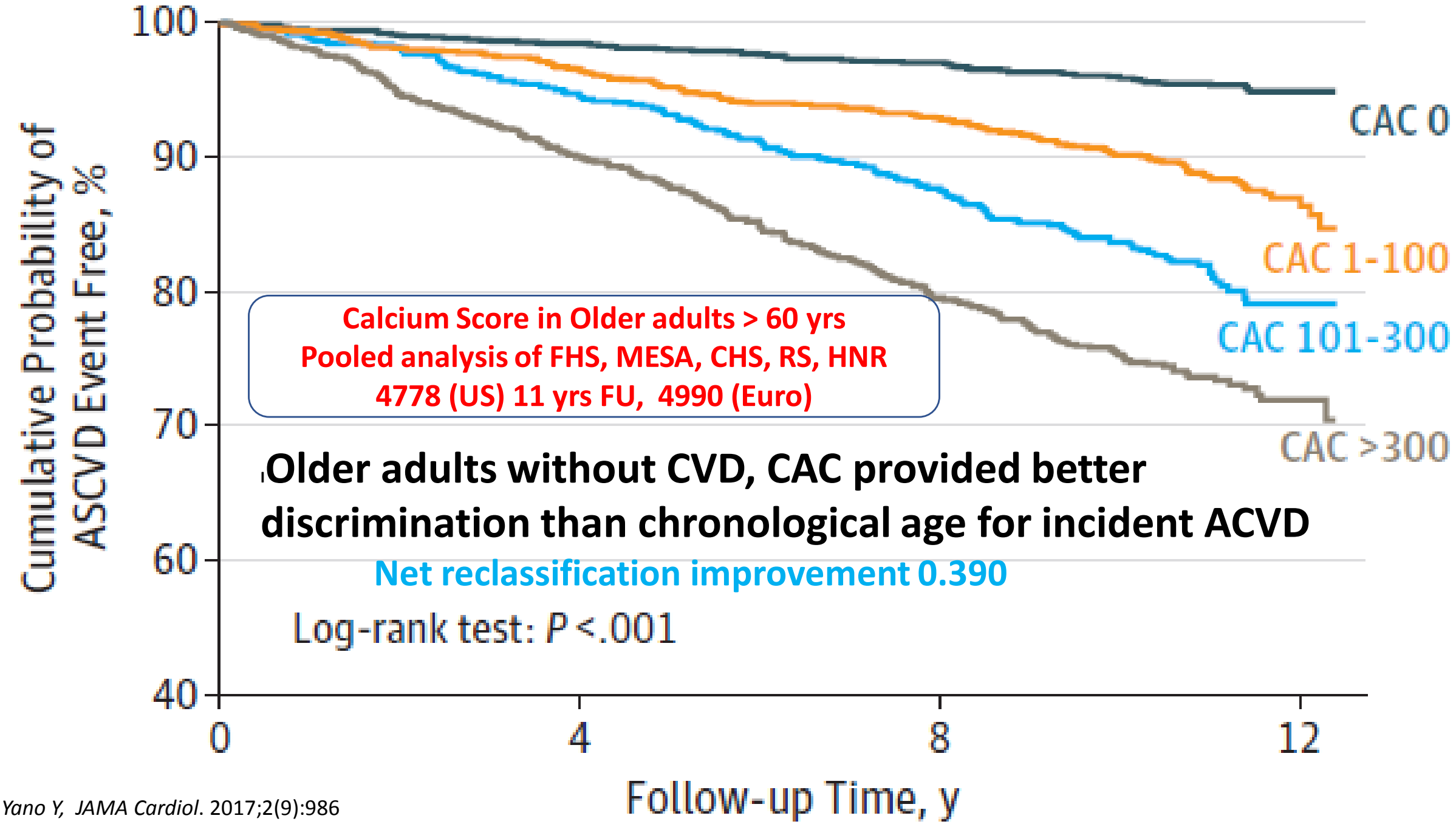
Could this benefit be seen in elderly ?

Rotterdam Study: 1795 asymptomatic, 62-85 yrs (m 71) m FU 3.3 yrs

Vliegenhart R, Circulation. 2005;112:572-577







Yano Y, JAMA Cardiol. 2017;2(9):986

Why try to refine CV Risk assessment in this elderly male with no symptoms & no risk factors ?

PREDICTION OF FUTURE CORONARY EVENTS
CV Risk factors (Risk based) ~ CAC score (Disease based)

The predictive power of cardiovascular risk factors decreases with age, partly because of selective survival and the influence of comorbidity on risk factor levels

Measuring CAC score instead of assessing cardiovascular risk factors may lead to an optimization of CHD prediction in older adults

CAC improves reclassification of risk status

HEINZ NIXDORF RECALL

4129 subjects,

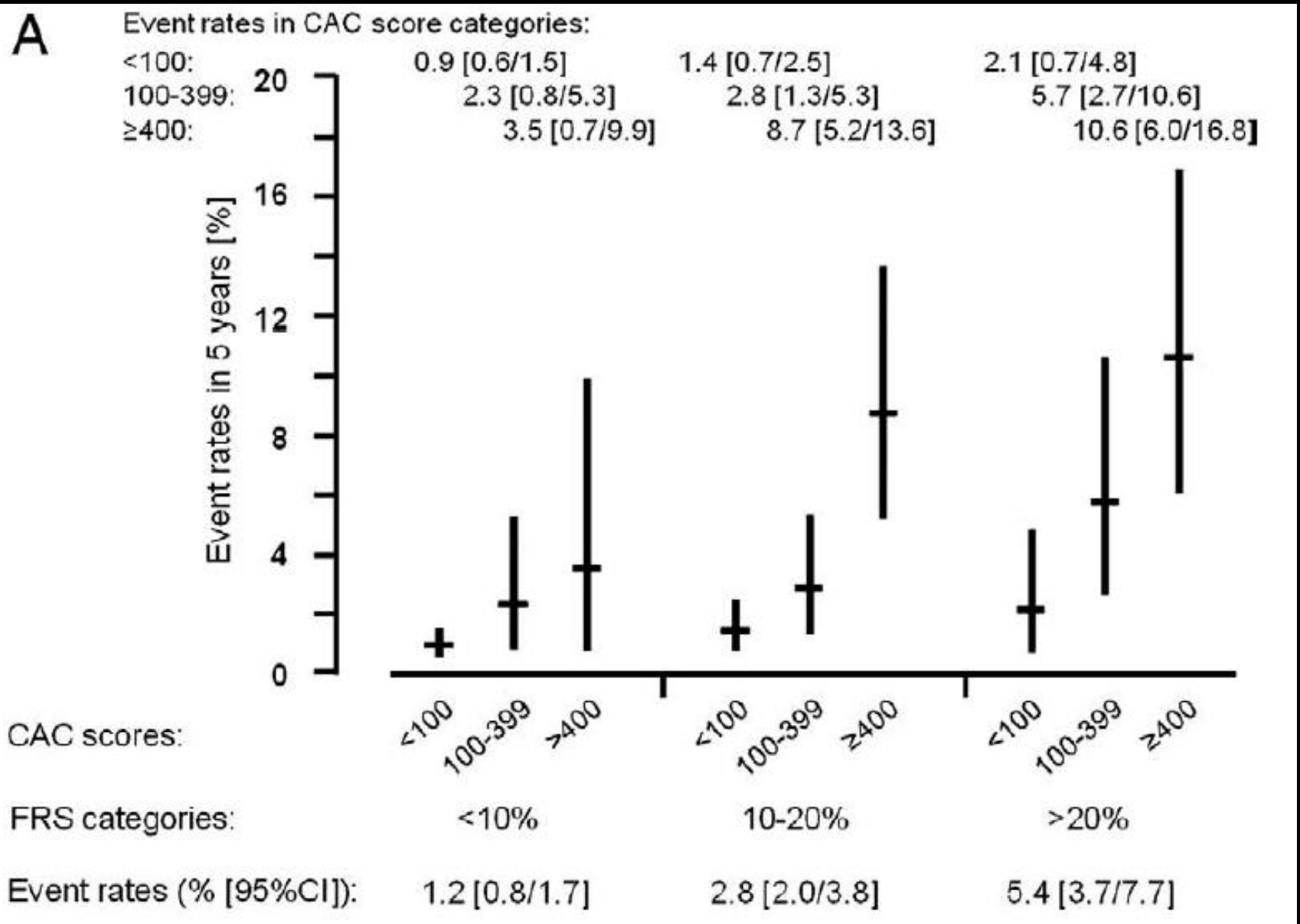
45-75 yrs, F 53%,

5 yrs Follow-up.

93 death + MI (2.3%)

Reclassifying Intermediate risk group to Low risk when CAC < 100 and High risk when CAC > 400, yielded a

net reclassification improvement of 21.7% and 30.6%



MESA The Mult-Ethnic Study of Atherosclerosis

MESA 10-Year CHD Risk with Coronary Artery Calcification

Back to CAC Tools

1. Gender	Male ◉	Female ○				
2. Age (45-85 years)	68	Years				
3. Coronary Artery Calcification		Agatston				
4. Race/Ethnicity	**Choose One**					
Caucasian	○					
Chinese	◉					
African American	○					
Hispanic	○					
5. Diabetes	Yes ○	No ◉				
6. Currently Smoke	Yes ○	No ◉				
7. Family History of Heart Attack (History in parents, siblings, or children)	Yes ○	No ◉				
8. Total Cholesterol	164	mg/dL	or	4.2	mmol/L	
9. HDL Cholesterol	39	mg/dL	or	1.0	mmol/L	
10. Systolic Blood Pressure	130	mmHg	or	17.3	kPa	
11. Lipid Lowering Medication	Yes ○	No ◉				
12. Hypertension Medication	Yes ○	No ◉				

Calculate 10-year CHD risk

The estimated 10-year risk of a CHD event for a person with this risk factor profile if we did not factor in their coronary calcium score would be 4.3%.

MESA The Mult-Ethnic Study of Atherosclerosis

MESA 10-Year CHD Risk with Coronary Artery Calcification

Back to CAC Tools

1. Gender	Male ◉	Female ○				
2. Age (45-85 years)	68	Years				
3. Coronary Artery Calcification	0	Agatston				
4. Race/Ethnicity	**Choose One**					
Caucasian	○					
Chinese	◉					
African American	○					
Hispanic	○					
5. Diabetes	Yes ○	No ◉				
6. Currently Smoke	Yes ○	No ◉				
7. Family History of Heart Attack (History in parents, siblings, or children)	Yes ○	No ◉				
8. Total Cholesterol	164	mg/dL	or	4.2	mmol/L	
9. HDL Cholesterol	39	mg/dL	or	1.0	mmol/L	
10. Systolic Blood Pressure	130	mmHg	or	17.3	kPa	
11. Lipid Lowering Medication	Yes ○	No ◉				
12. Hypertension Medication	Yes ○	No ◉				

Calculate 10-year CHD risk

The estimated 10-year risk of a CHD event for a person with this risk factor profile including coronary calcium is 1.7%. The estimated 10-year risk of a CHD event for a person with this risk factor profile if we did not factor in their coronary calcium score would be 4.3%

The Mult-Ethnic Study of Atherosclerosis

MESA 10-Year CHD Risk with Coronary Artery Calcification

Back to CAC Tools

1. Gender	Male ◉ Female ○				
2. Age (45-85 years)	68	Years			
3. Coronary Artery Calcification	180	Agatston			
4. Race/Ethnicity	**Choose One**				
	Caucasian ○				
	Chinese ◉				
	African American ○				
	Hispanic ○				
5. Diabetes	Yes ○	No ◉			
6. Currently Smoke	Yes ○	No ◉			
7. Family History of Heart Attack (History in parents, siblings, or children)	Yes ○	No ◉			
8. Total Cholesterol	164	mg/dL	or	4.2	mmol/L
9. HDL Cholesterol	39	mg/dL	or	1.0	mmol/L
10. Systolic Blood Pressure	130	mmHg	or	17.3	kPa
11. Lipid Lowering Medication	Yes ○	No ◉			
12. Hypertension Medication	Yes ○	No ◉			

Calculate 10-year CHD risk

The estimated 10-year risk of a CHD event for a person with this risk factor profile including coronary calcium is 7.0%. The estimated 10-year risk of a CHD event for a person with this risk factor profile if we did not factor in their coronary calcium score would be 4.3%.

The Mult-Ethnic Study of Atherosclerosis

MESA 10-Year CHD Risk with Coronary Artery Calcification

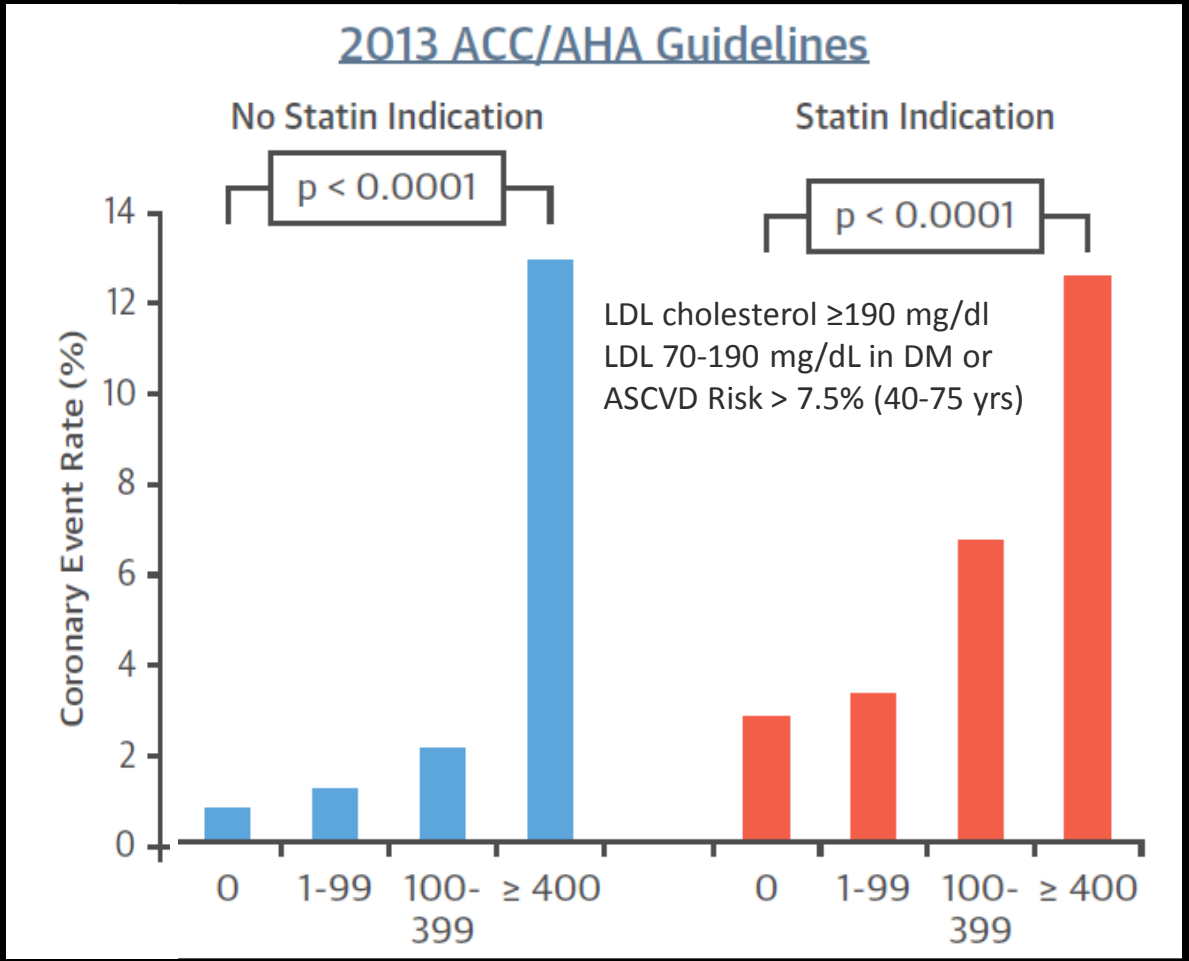
Back to CAC Tools

1. Gender	Male ◉ Female ○				
2. Age (45-85 years)	68	Years			
3. Coronary Artery Calcification	486	Agatston			
4. Race/Ethnicity	**Choose One**				
	Caucasian ○				
	Chinese ◉				
	African American ○				
	Hispanic ○				
5. Diabetes	Yes ○	No ◉			
6. Currently Smoke	Yes ○	No ◉			
7. Family History of Heart Attack (History in parents, siblings, or children)	Yes ○	No ◉			
8. Total Cholesterol	164	mg/dL	or	4.2	mmol/L
9. HDL Cholesterol	39	mg/dL	or	1.0	mmol/L
10. Systolic Blood Pressure	130	mmHg	or	17.3	kPa
11. Lipid Lowering Medication	Yes ○	No ◉			
12. Hypertension Medication	Yes ○	No ◉			

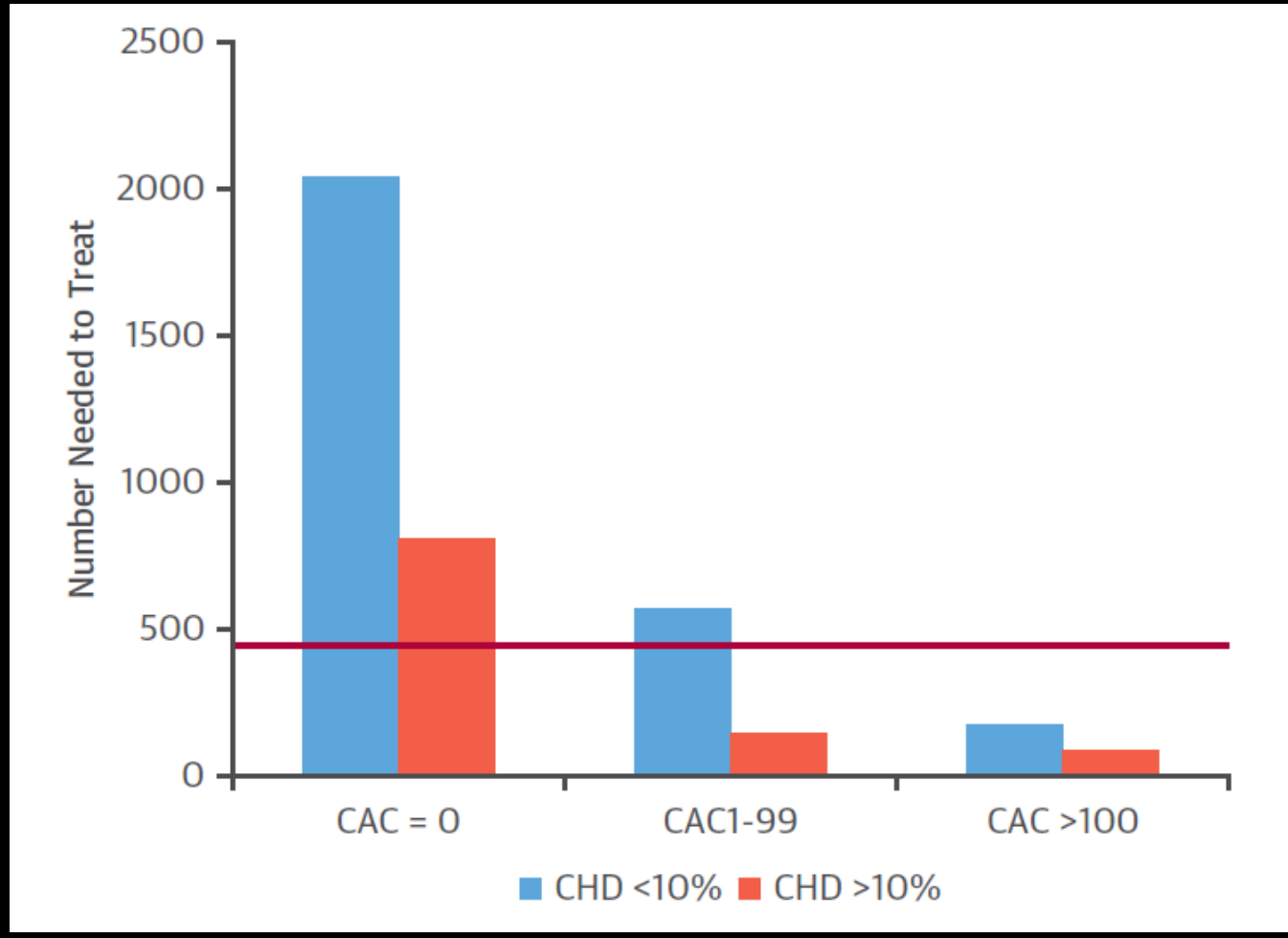
Calculate 10-year CHD risk

The estimated 10-year risk of a CHD event for a person with this risk factor profile including coronary calcium is 9.1%. The estimated 10-year risk of a CHD event for a person with this risk factor profile if we did not factor in their coronary calcium score would be 4.3%.

CAC could potentially modify therapies ……..



Cardiovascular Event Rate for
Heinz Nixdorf Recall Study Participants



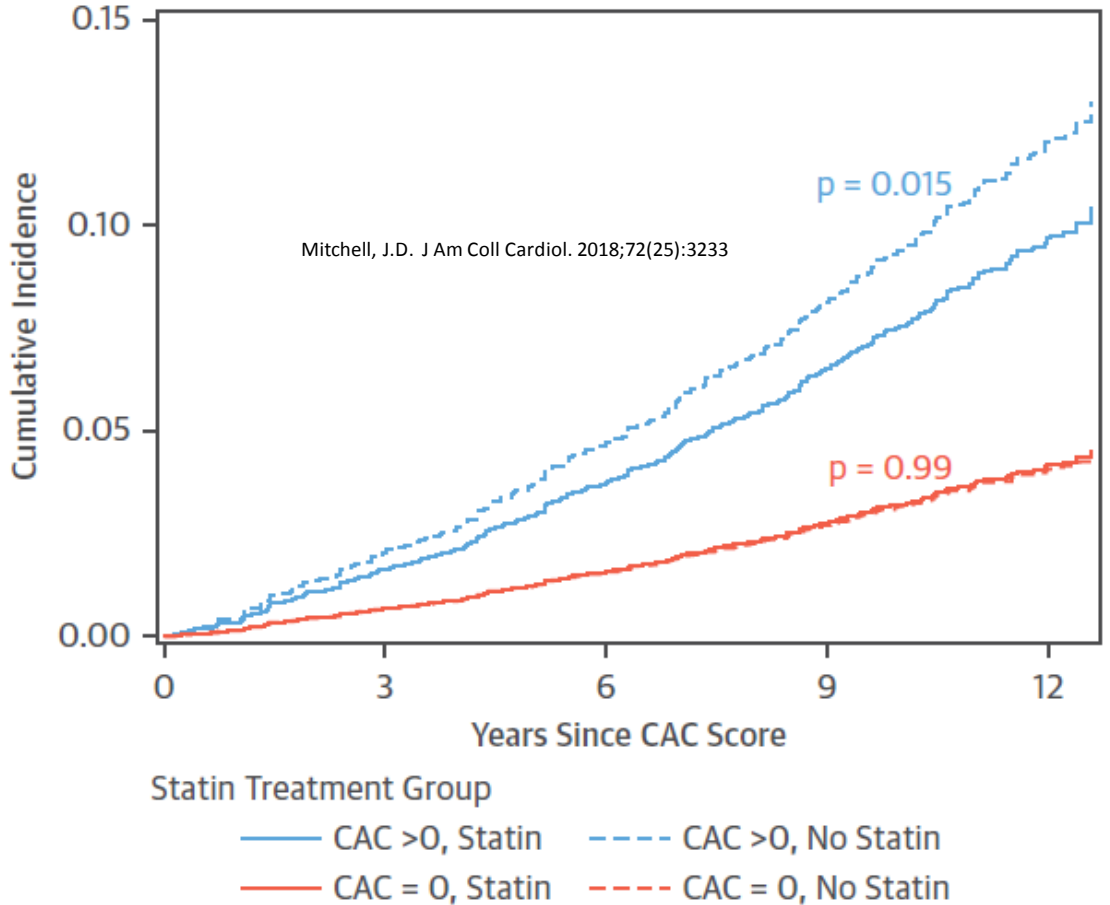
Estimated Risk and Benefit of Aspirin in Primary Prevention by Coronary Artery Calcium Score in Multi-Ethnic Study of Atherosclerosis Participants

Impact of Statins on Cardiovascular Outcomes

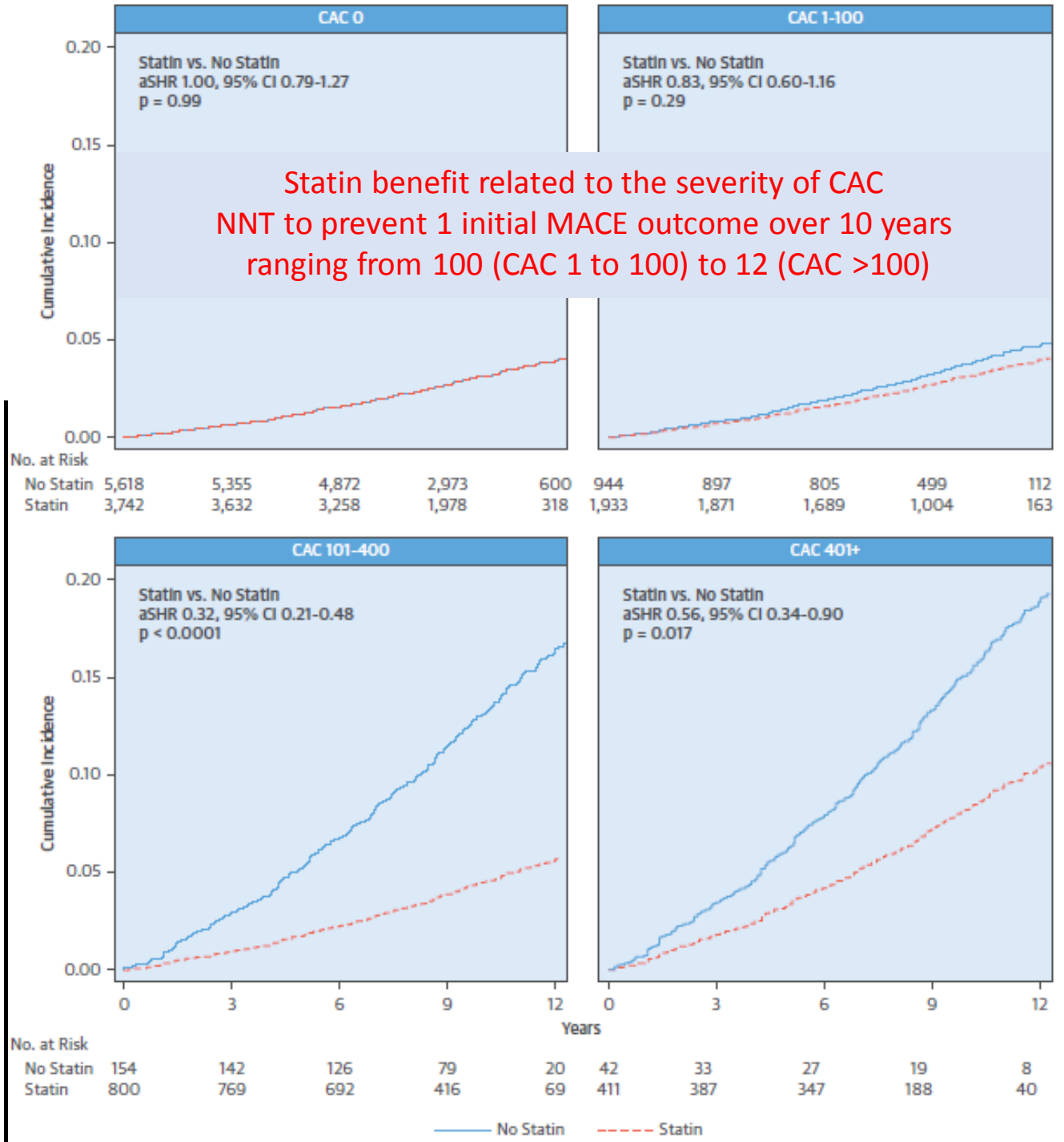
Following Coronary Artery Calcium Scoring

13,644 patients (m age 50 yrs; 71% men) FU m 9.4 years.

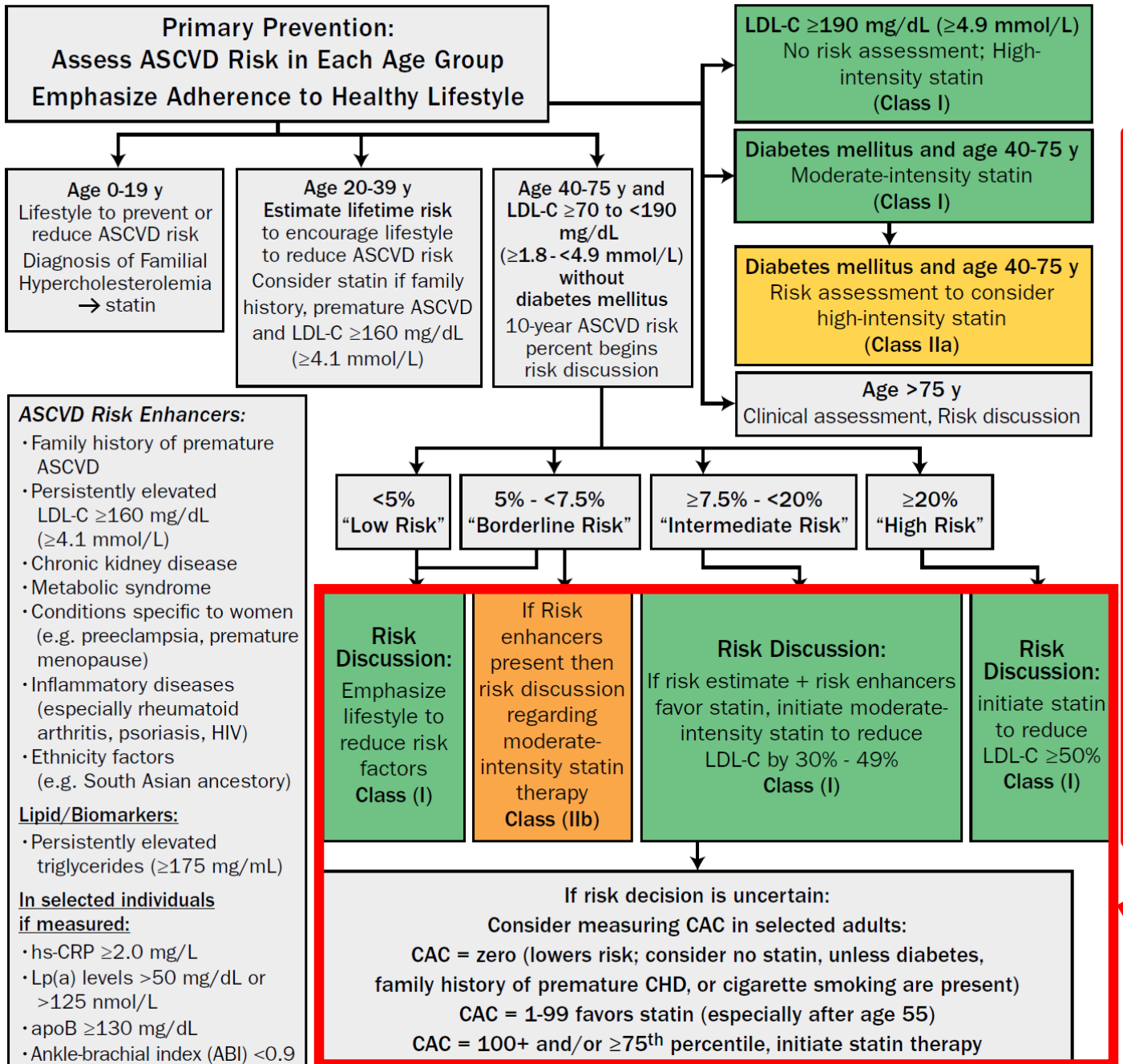
Statin therapy ↓ risk MACE in patients with CAC (HR 0.76) but not in patients without CAC (HR 1.00)

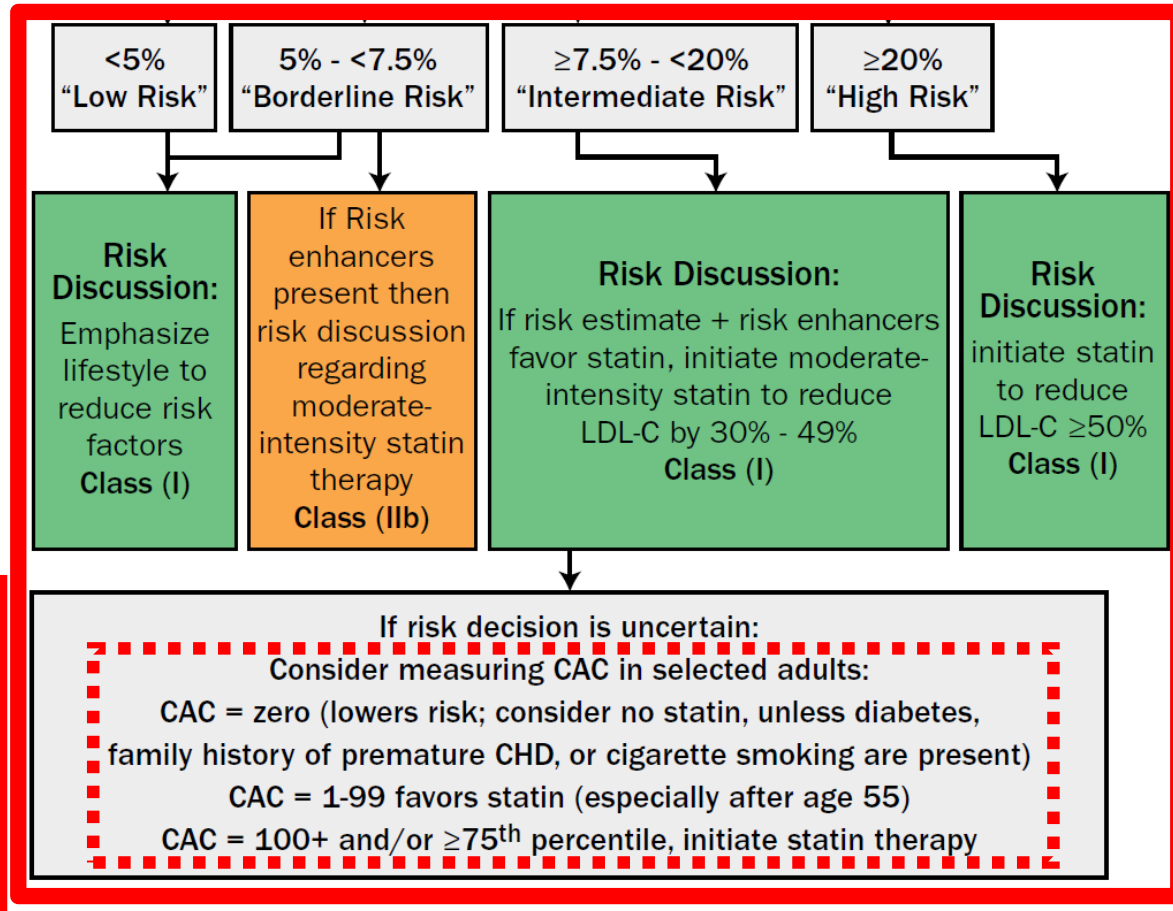


Statin benefit related to the severity of CAC
NNT to prevent 1 initial MACE outcome over 10 years ranging from 100 (CAC 1 to 100) to 12 (CAC >100)



Primary Prevention





I would prefer to do Calcium Scoring for him ……

Robust data from asymptomatic subjects

Incremental value for CVD Risk prediction

Helps the physician to reclassify the risk status

Starting or deferring preventive therapies

Motivates subjects to adopt LSM

Not time consuming

Reproducible

Less expensive

Low radiation (< 1 mSv)

CAC may be considered in …….

- Atypical symptoms, Functional testing not possible or False positive result is likely, baseline ECG changes (ST T / LBBB)
- Women with atypical symptoms
- Suspected ACS in Emergency Department
- In patients with T2 Diabetes Mellitus
- Family H/O premature CAD
- To motivate individuals to adhere to lifestyle (Diet/Tobacco)

CAC as a gatekeeper in ACS

- **204 patients presenting to ED for chest pain**
- **Prevalence of CAD 56%**
- **Of 93 patients with 0 CAC, ACS confirmed in 3**
- **The diagnostic performance of the dichotomized CAC score was: accuracy 56%, sensitivity 89%, specificity 51%, PPV 23% and NPV 97% The area-under-the-curve (AUC) of CAC for predicting ACS was 0.75, with no reliable cut-off.**

Hinzpeter R, Am J Em Med. 2017: 35;1565

Prevalence and Prognostic Implications of Coronary Artery Calcification in Low-Risk Women: A Meta-analysis

DHS, Dallas Heart Study; FHS, Framingham Heart Study; HNR, Heinz Nixdorf Recall; MESA, Multi-Ethnic Study of Atherosclerosis RS, Rotterdam Study

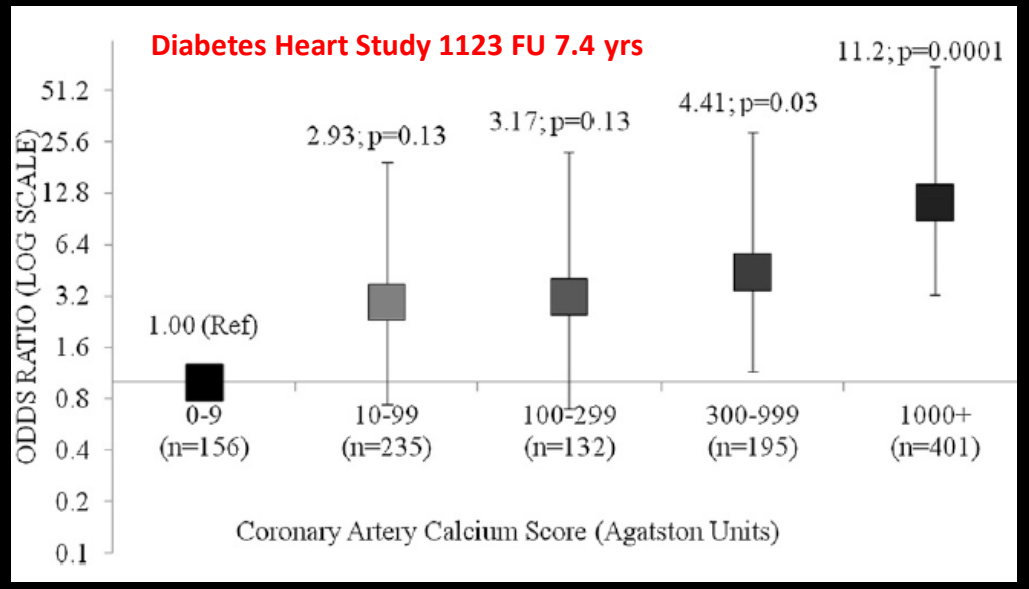
6739 women with low ASCVD risk (<7.5 % at 10 yrs) from the 5 studies, m. age 44 to 63 yrs CAC was present in 36.1%. Median follow-up ranged from 7.0 to 11.6 years

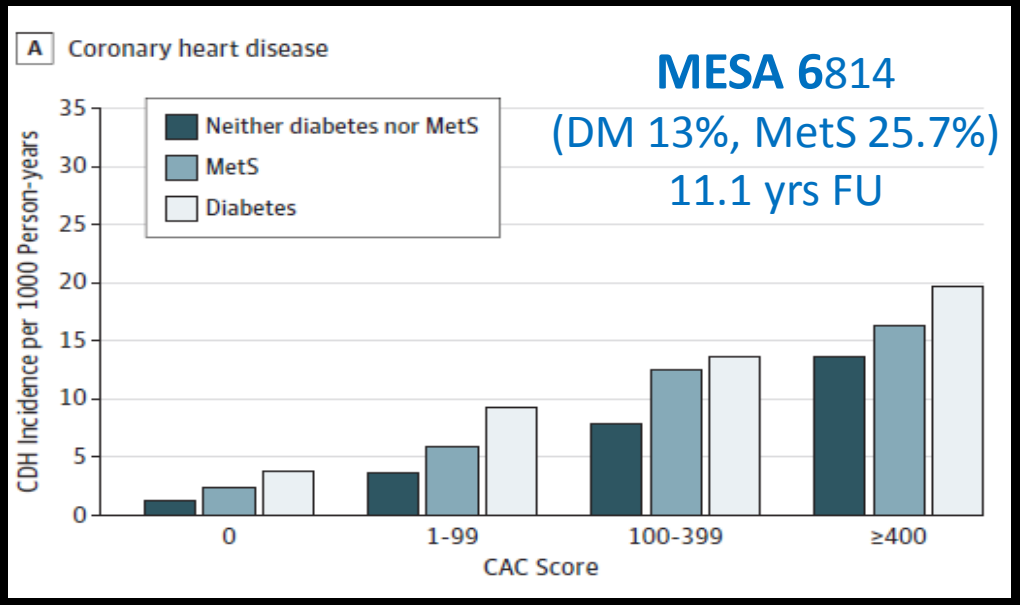
Kavousi M, JAMA. 2016;316(20):2126

	Hazard Ratio (95% CI) for ASCVD[a]			
Cohort	Continuous CAC[b]	CAC Presence (CAC >0) vs CAC Absence (CAC = 0)	CAC >0-100 vs CAC Absence	CAC >100 vs CAC Absence
DHS	1.70 (1.27-2.28)	4.92 (1.28-18.92)	4.35 (1.10-17.25)	14.08 (2.23-89.03)
FHS	1.24 (1.00-1.54)	1.44 (0.55-3.82)	0.84 (0.25-2.84)	3.75 (1.16-12.17)
HNR	1.28 (1.11-1.47)	2.23 (1.12-4.45)	1.79 (0.85-3.76)	4.24 (1.79-10.04)
MESA	1.29 (1.15-1.44)	1.93 (1.14-3.26)	1.25 (0.64-2.41)	3.78 (1.98-7.18)
RS	1.20 (0.98-1.47)	1.82 (0.60-5.47)	1.59 (0.51-4.99)	2.67 (0.73-9.79)
Fixed effects	1.29 (1.20-1.39)	2.04 (1.44-2.90)	1.53 (1.02-2.29)	4.02 (2.61-6.19)
I^2, %[c]	1.2	0.0	0.0	0.0
P value for I^2	.40	.68	.45	.69

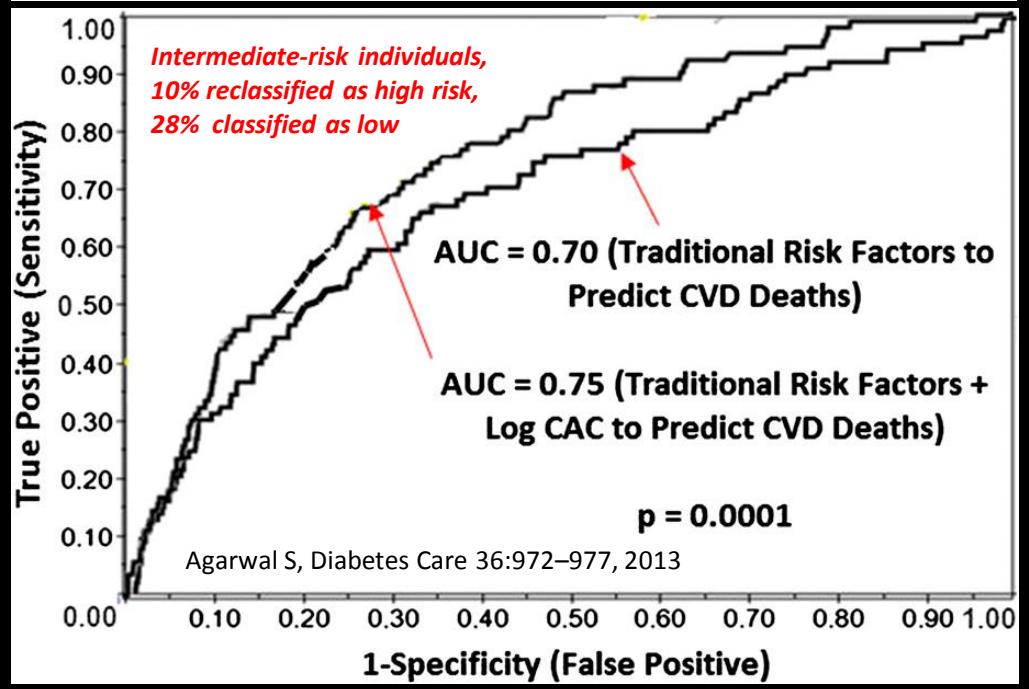
Addition of CAC to traditional risk factors improved the C statistic from 0.73 to 0.77; NRI 0.20 for ASCVD prediction

CAC Score in patients with T2DM

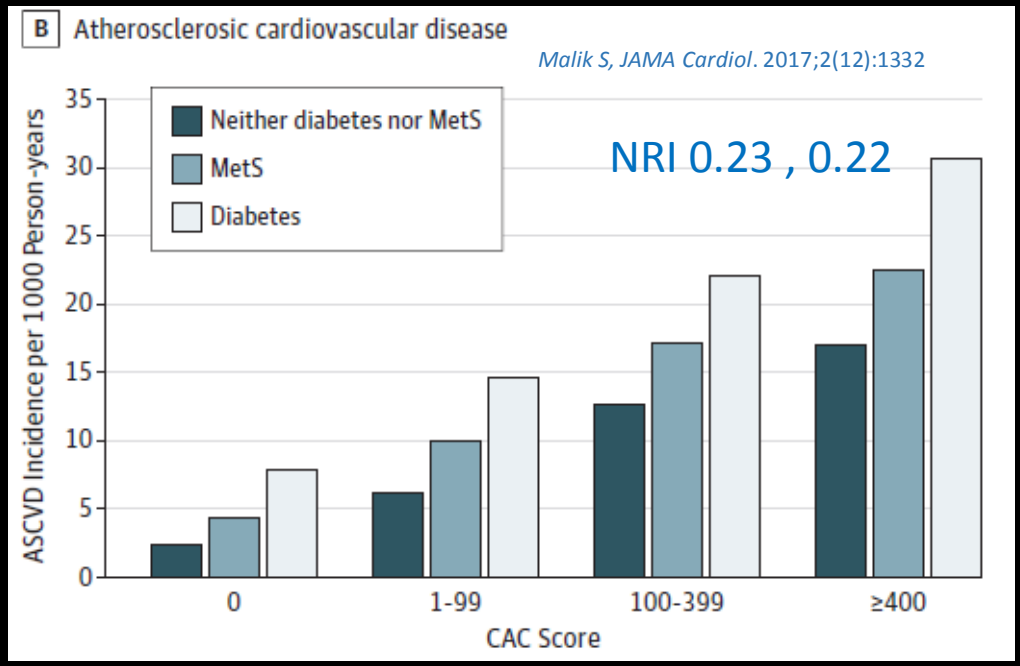




MESA 6814
(DM 13%, MetS 25.7%)
11.1 yrs FU



Agarwal S, Diabetes Care 36:972–977, 2013



Malik S, JAMA Cardiol. 2017;2(12):1332

NRI 0.23 , 0.22

Should we repeat the CAC after sometime ?

- CAC scores increased by about 20% to 25% per year
- 20% of subjects with CAC 0 progressed to CAC > 0 within 4 to 5 yrs
- Those with “double zero,”(CAC 0 both at baseline & after 5 yrs) have the best outlook (10-year risk of only 1.4%)
- Repeat scan not of value for those who already have a double-zero CAC or have already been classified at high risk because of CAC
- Statin therapy > CAC increases despite reduction of clinical events promotes healing

Who would benefit from CCS ?

ACC 2018

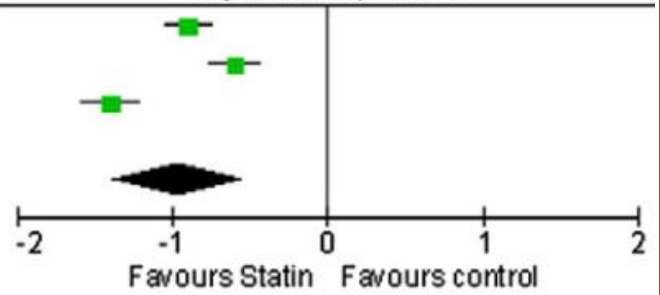
- **RISK PREDICTION:** Middle-aged asymptomatic adults (40-55 yrs) with intermediate risk (7.5 – 20% 10 yrs) or borderline risk (5-7.5%) with factors that increase their ASCVD risk.
- Patients reluctant to initiate statin or restart it after discontinuation for statin associated symptoms
- *Older patients (men 55 to 80; women 60-80 years old) with low burden of risk factors who question whether they would benefit from statin therapy*

Who would not need it ?

- Men < 40 yrs, Women < 50 yrs (detectable calcium unlikely)
- Low risk (< 5%) by clinical risk scoring (in the absence of F H/O premature CAD)
- High risk by clinical risk scoring
- Symptomatic / Diagnosed CAD
- Previously positive CAC study

Study or Subgroup	Statin Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Raggi (12)	2.4	0.9	218	3.3	0.8	257	33.7%	-0.90 [-1.05, -0.75]
Schmermund (13)	2.2	0.9	175	2.8	0.7	191	33.5%	-0.60 [-0.77, -0.43]
Terry (14)	1.9	0.4	30	3.3	0.4	32	32.8%	-1.40 [-1.60, -1.20]
Total (95% CI)			**423**			**480**	**100.0%**	**-0.96 [-1.39, -0.54]**

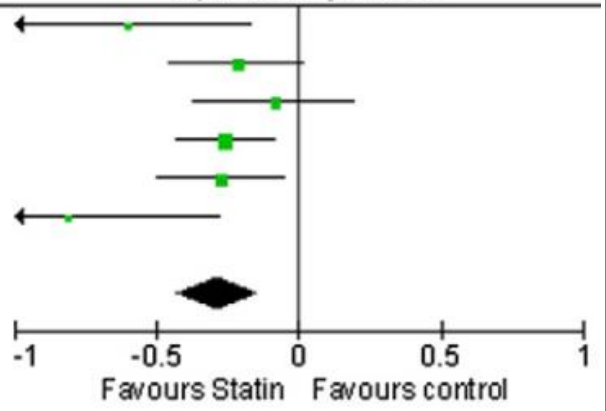
Heterogeneity: Tau² = 0.13; Chi² = 36.59, df = 2 (P < 0.00001); I² = 95%
Test for overall effect: Z = 4.44 (P < 0.00001)



LDL

Study or Subgroup	Statin Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Brown (15)	-0.7	5.3	38	2.1	3.9	46	8.6%	-0.61 [-1.04, -0.17]
Herd (16)	0.5	9.1	129	2.5	9.2	132	19.9%	-0.22 [-0.46, 0.03]
Mizuno (17)	0.055	0.27	90	0.078	0.27	98	16.3%	-0.08 [-0.37, 0.20]
Nissen (1)	0.6	5.1	253	1.9	4.9	249	27.6%	-0.26 [-0.44, -0.08]
Waters (2)	0.05	0.13	146	0.09	0.16	153	21.5%	-0.27 [-0.50, -0.05]
Yamada (18)	-1.4	11.6	26	7.6	10.3	32	6.1%	-0.81 [-1.35, -0.27]
Total (95% CI)			**682**			**710**	**100.0%**	**-0.29 [-0.43, -0.15]**

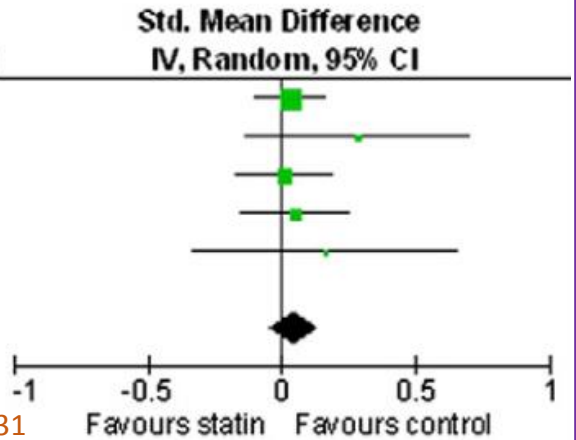
Heterogeneity: Tau² = 0.01; Chi² = 7.94, df = 5 (P = 0.16); I² = 37%
Test for overall effect: Z = 3.97 (P < 0.0001)



Atheroma

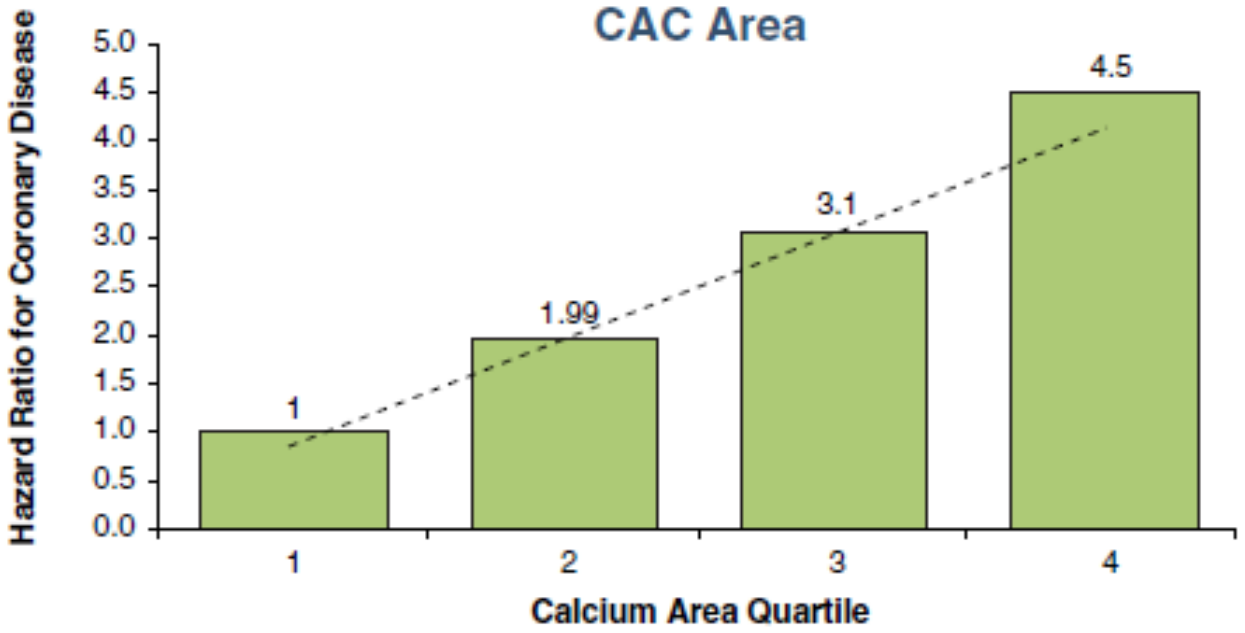
Study or Subgroup	Statin Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Arad (10)	38	75	417	36	58	431	46.3%	0.03 [-0.10, 0.16]
Houslay (11)	0.234	0.231	39	0.167	0.238	49	4.7%	0.28 [-0.14, 0.71]
Raggi (12)	20.1	30.8	218	19.8	34.8	257	25.7%	0.01 [-0.17, 0.19]
Schmermund (13)	27	40.5	175	25	42.3	191	19.9%	0.05 [-0.16, 0.25]
Terry (14)	69	582	30	-27	601	32	3.4%	0.16 [-0.34, 0.66]
Total (95% CI)			**879**			**960**	**100.0%**	**0.04 [-0.05, 0.14]**

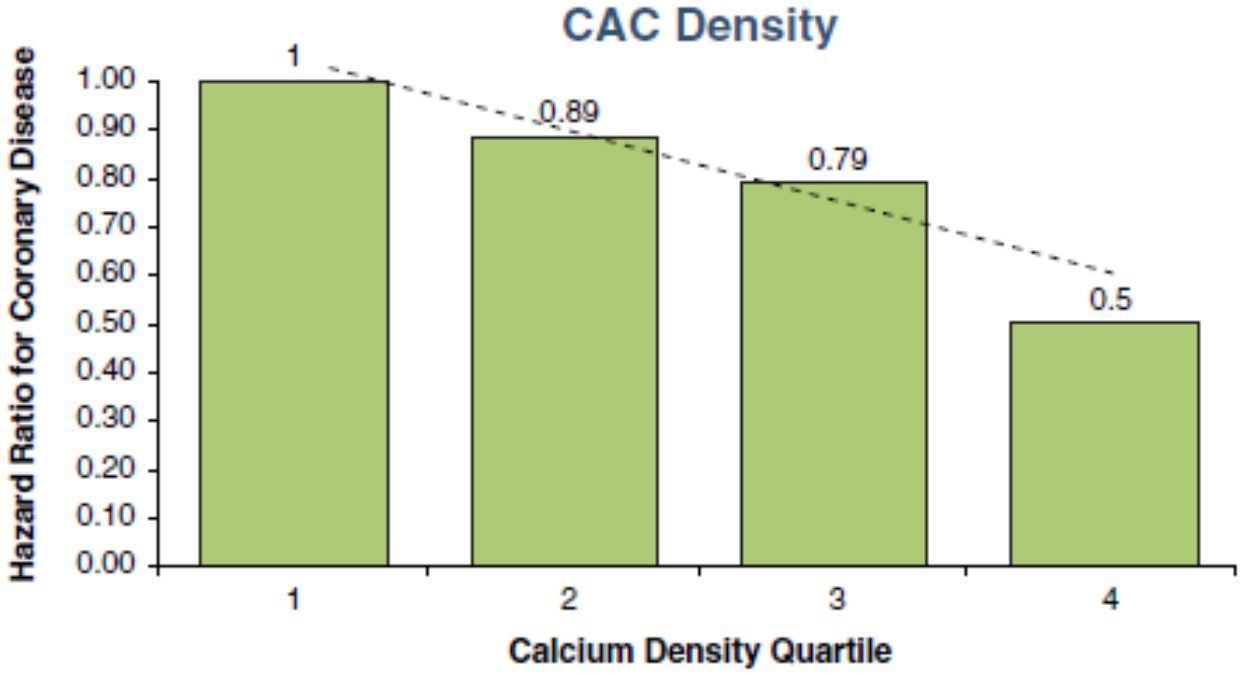
Heterogeneity: Tau² = 0.00; Chi² = 1.62, df = 4 (P = 0.81); I² = 0%
Test for overall effect: Z = 0.95 (P = 0.34)



CAC score

Y. Henein, International Journal of Cardiology 153 (2011) 31





Patients with stable angina often have higher CAC scores than patients with acute coronary events

Statins increase Agatston CAC scores through delipidation and therefore increase calcium density

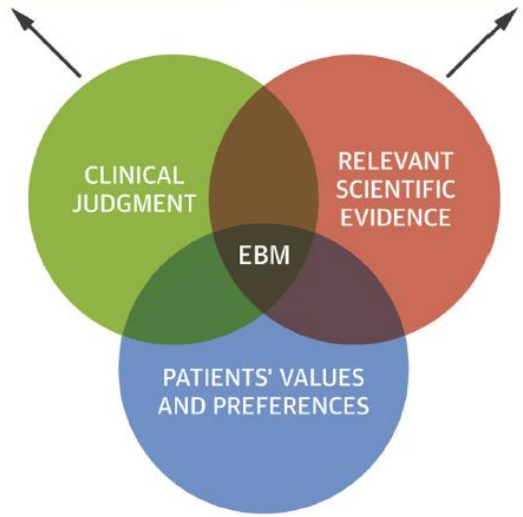
Using 10-year ASCVD risk estimate plus coronary artery calcium (CAC) score to guide statin therapy

Greenland, P, J Am Coll Cardiol. 2018;72(4):434

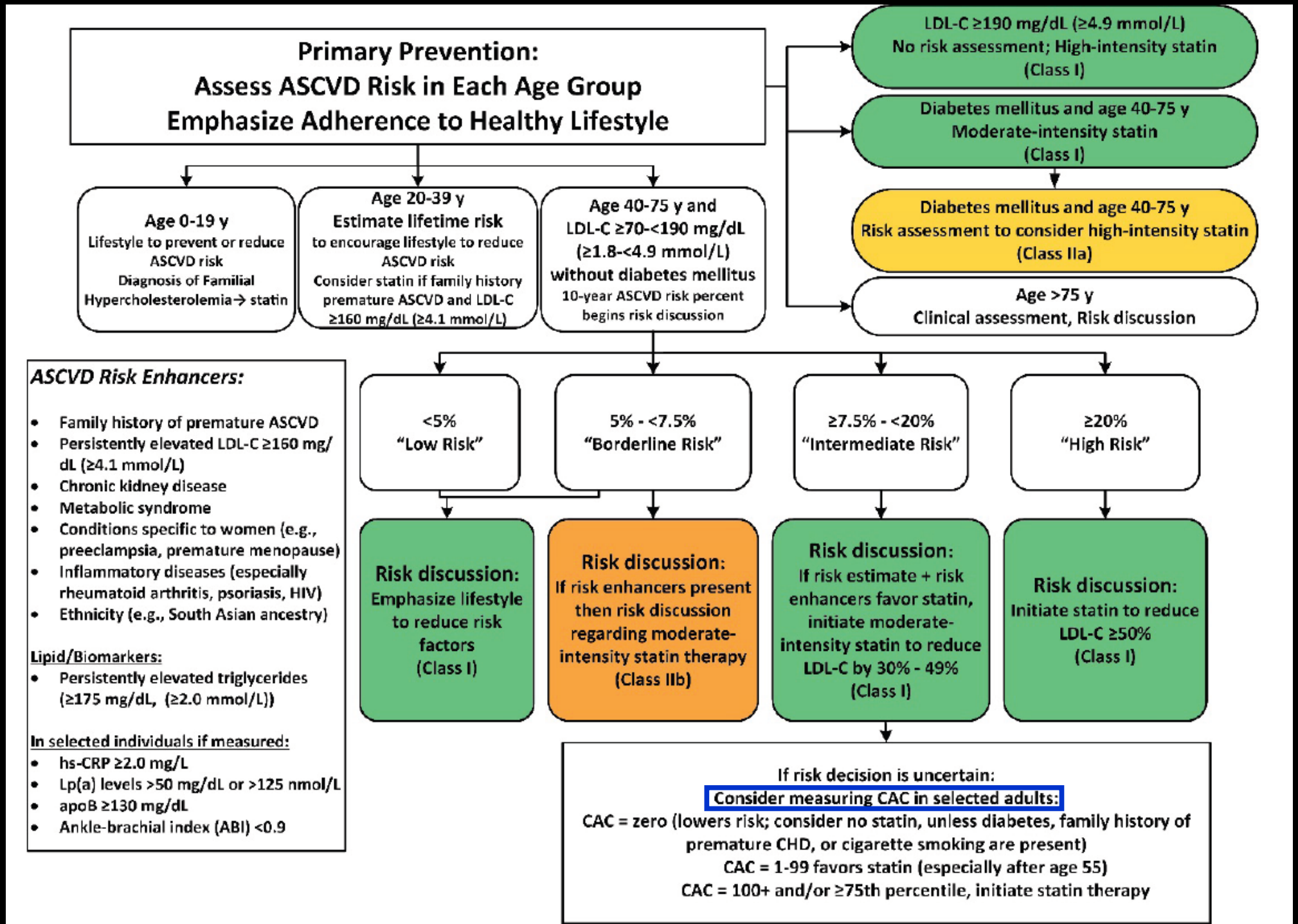
Patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimate:	<5%	5-7.5%	>7.5-20%	>20%
Consulting ASCVD risk estimate alone	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Consulting ASCVD risk estimate + CAC				
If CAC score =0	Statin not recommended	Statin not recommended	Statin not recommended	Recommend statin
If CAC score >0	Statin not recommended	Consider for statin	Recommend statin	Recommend statin
Does CAC score modify treatment plan?	✗ CAC not effective for this population	✓ CAC can reclassify risk up or down	✓ CAC can reclassify risk up or down	✗ CAC not effective for this population

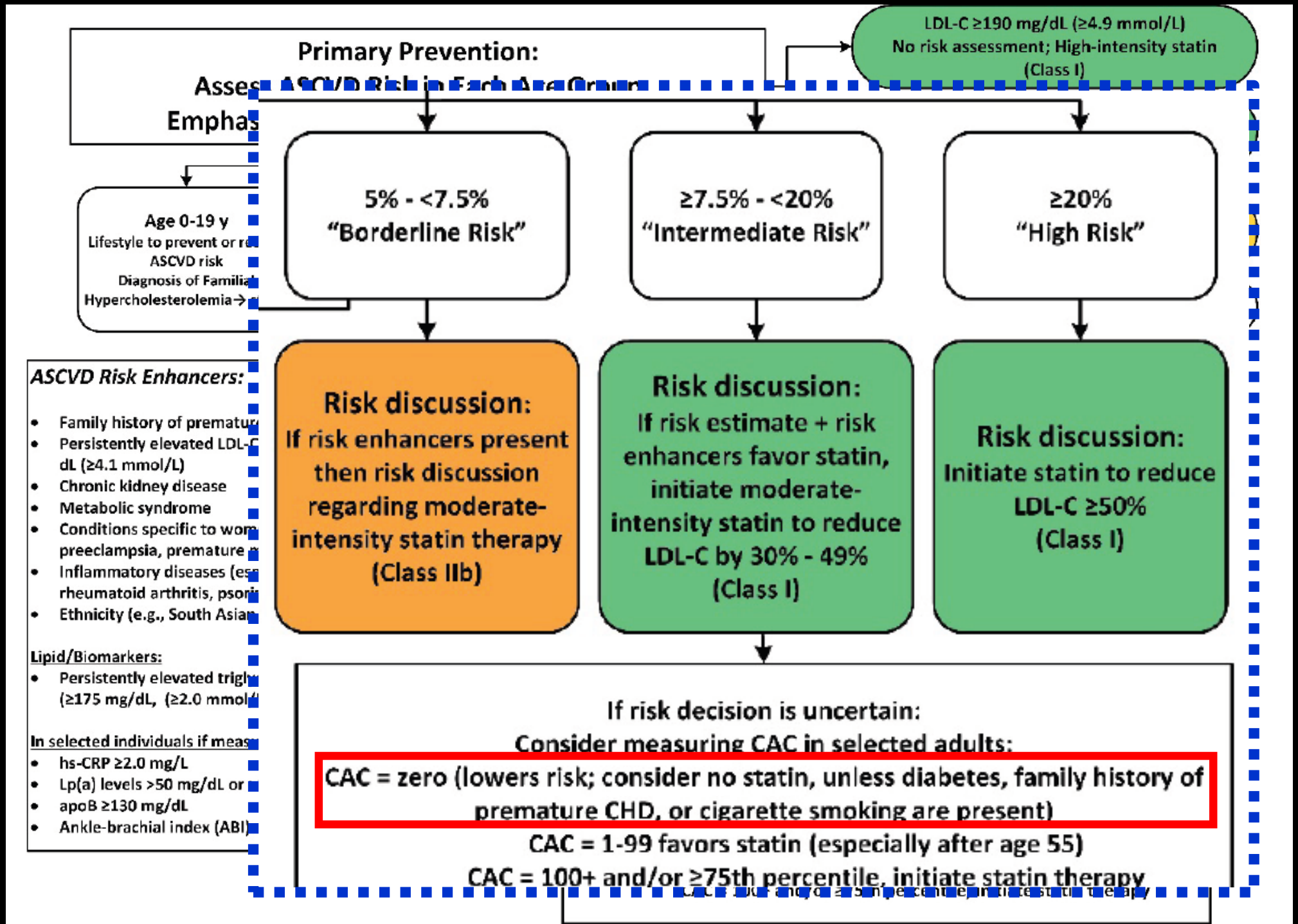
PROVIDER PREFERENCE FOR CAC	
PRO	CAC is near pathognomonic for CAD, can be measured non-invasively at low cost, and has been strongly associated with risk for atherosclerotic cardiovascular disease events in rigorous observational studies.
CON	Widespread CAC testing could expose low risk persons to unnecessary radiation, secondary testing, cost, and we cannot know if measuring CAC will lead to therapeutic changes that improve outcomes in the absence of a RCT confirming benefit.

CORONARY ARTERY CALCIUM
Evidence Hierarchy
✗ Systematic Reviews & Meta-Analyses of RCTs
✗ Randomized Controlled Trials (RCTs)
✓ Cohort Studies
✓ Case-Control Studies
✓ Cross-Sectional Surveys
✓ Case Reports
✓ Perspectives



McEvoy, J.W. et al. J Am Coll Cardiol Img. 2016;9(8):994-1002.


Primary Prevention:
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle
LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin
(Class I)
Diabetes mellitus and age 40-75 y
Moderate-intensity statin
(Class I)
Diabetes mellitus and age 40-75 y
Risk assessment to consider high-intensity statin
(Class IIa)
Age >75 y
Clinical assessment, Risk discussion
Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia→ statin
Age 20-39 y
Estimate lifetime risk
to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)
Age 40-75 y and
LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L)
without diabetes mellitus
10-year ASCVD risk percent begins risk discussion
ASCVD Risk Enhancers:
Family history of premature ASCVD
Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
Chronic kidney disease
Metabolic syndrome
Conditions specific to women (e.g., preeclampsia, premature menopause)
Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
Ethnicity (e.g., South Asian ancestry)
Lipid/Biomarkers:
Persistently elevated triglycerides (≥175 mg/dL, (≥2.0 mmol/L))
In selected individuals if measured:
hs-CRP ≥2.0 mg/L
Lp(a) levels >50 mg/dL or >125 nmol/L
apoB ≥130 mg/dL
Ankle-brachial index (ABI) <0.9
<5%
"Low Risk"
5% - <7.5%
"Borderline Risk"
≥7.5% - <20%
"Intermediate Risk"
≥20%
"High Risk"
Risk discussion:
Emphasize lifestyle to reduce risk factors
(Class I)
Risk discussion:
If risk enhancers present then risk discussion regarding moderate-intensity statin therapy
(Class IIb)
Risk discussion:
If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49%
(Class I)
Risk discussion:
Initiate statin to reduce LDL-C ≥50%
(Class I)
If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy


Primary Prevention:
LDL-C ≥190 mg/dL (≥4.9 mmol/L)
No risk assessment; High-intensity statin
(Class I)
Age 0-19 y
5% - <7.5%
"Borderline Risk"
≥7.5% - <20%
"Intermediate Risk"
≥20%
"High Risk"
ASCVD Risk Enhancers:
Risk discussion:
If risk enhancers present then risk discussion regarding moderate-intensity statin therapy
(Class IIb)
Risk discussion:
If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49%
(Class I)
Risk discussion:
Initiate statin to reduce LDL-C ≥50%
(Class I)
Lipid/Biomarkers:
In selected individuals if meas
hs-CRP ≥2.0 mg/L
Lp(a) levels >50 mg/dL or
apoB ≥130 mg/dL
Ankle-brachial index (ABI)
If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy

What do the Experts say ?

2012 ACC/AHA Risk Assessment: If, after quantitative risk assessment using **traditional risk factors**, a risk-based treatment **decision is uncertain**, CAC score may be considered to inform treatment decision making. Class IIb, LOE: B

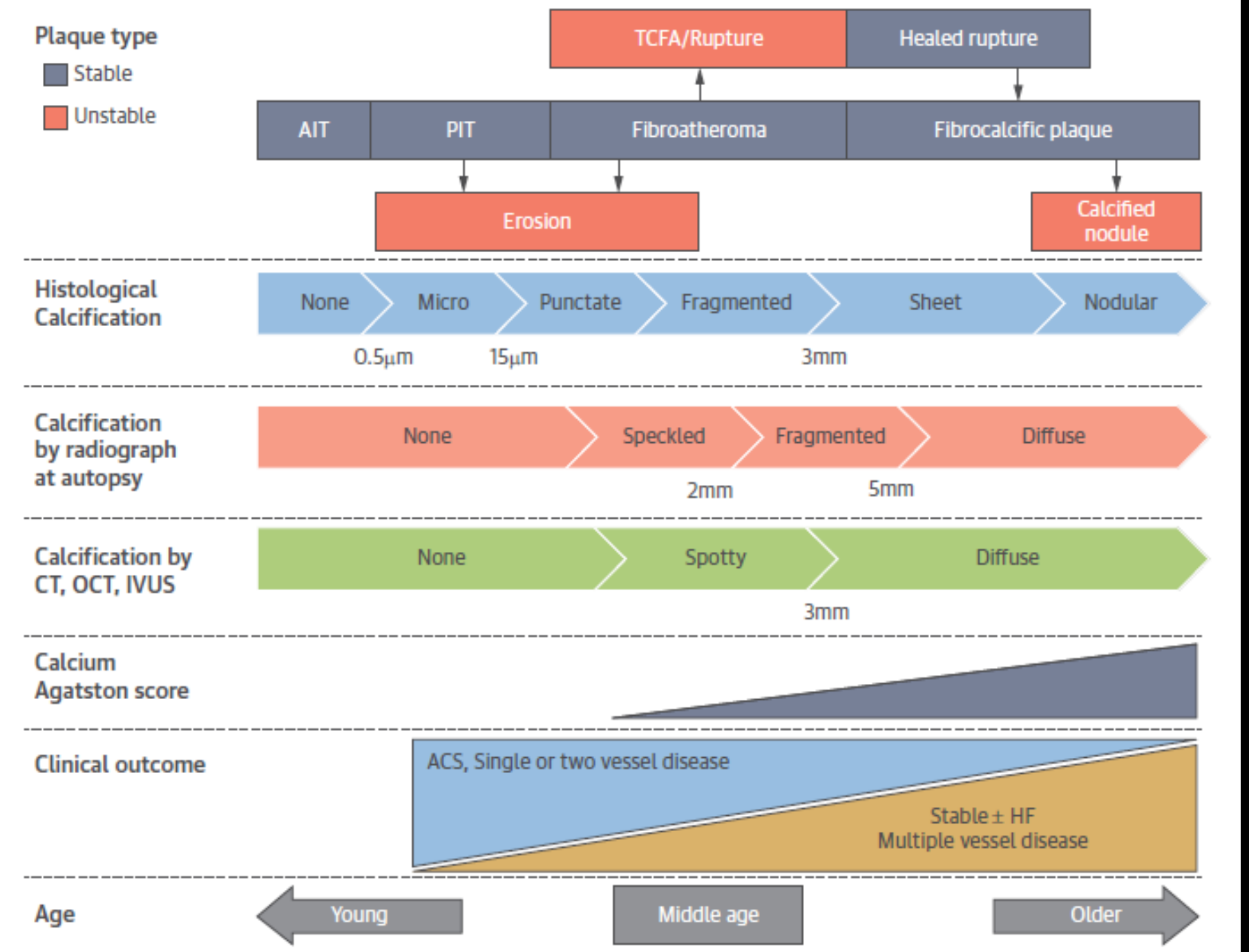
2016 European Guidelines on CVD prevention: CAC scoring may be considered as a **risk modifier in CV risk assessment.** Class IIb, LOE B

2017 Society of Cardiovascular CT Expert Consensus: It is appropriate to perform CAC testing in the context of **shared decision making** for asymptomatic individuals without clinical ASCVD who are **40–75 years of age in the 5%–20% ten-year ASCVD risk group** and selectively in the < 5% ASCVD risk group, such as those with a **family history of premature CAD**

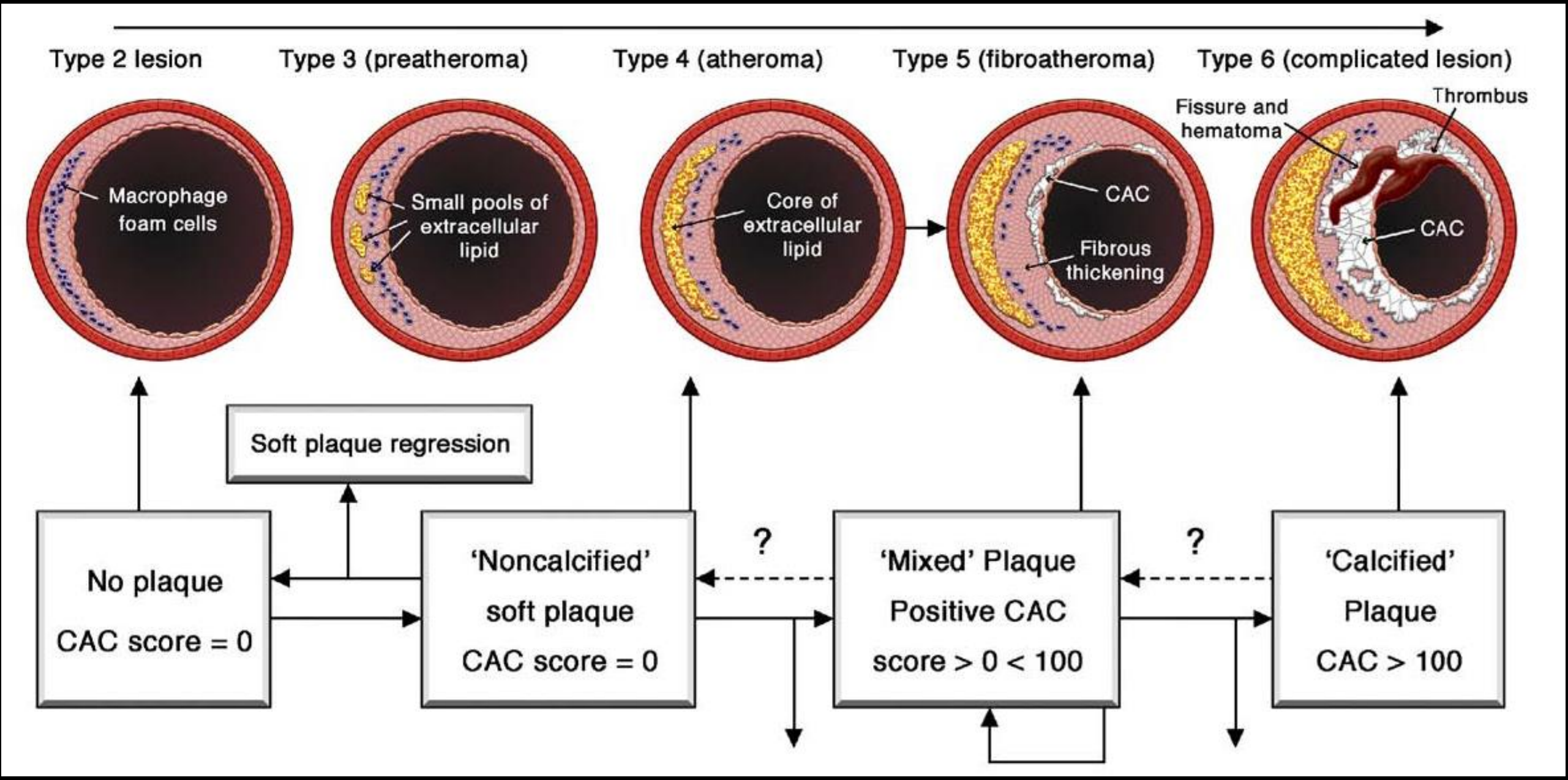
2018 USPTF: In asymptomatic adults, the **current evidence is insufficient to assess the balance of benefits and harms** of adding CAC score to traditionalrisk assessment for CVDprevention. Class I

CAC - Caveats

- **CAC correlates with disease burden but not the luminal narrowing**
- **Trying to correlate symptoms with CAC is not advisable**
- **Noncalcified lesions may cause symptoms including ACS**
- **May miss the diagnosis of Microvascular disease**
- **Low clinical risk > Low yield; High clinical risk > No need**
- **Radiation exposure**
- **Time, money, and effort spent**
- **Incidental findings requiring FU CT**



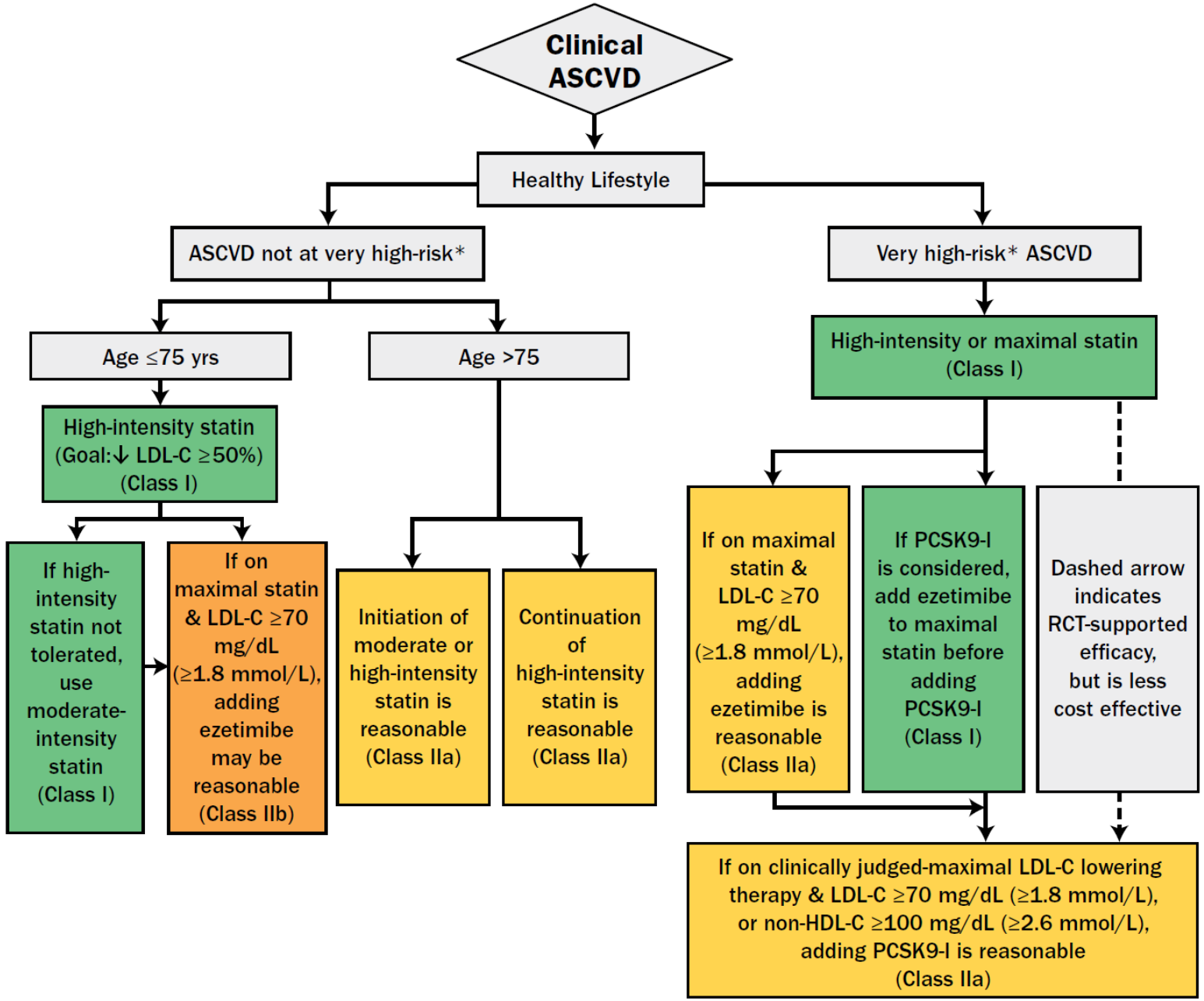
Mori, H. et al. J Am Coll Cardiol Img. 2018;11(1):127-42.


Type 2 lesion
Type 3 (preatheroma)
Type 4 (atheroma)
Type 5 (fibroatheroma)
Type 6 (complicated lesion)
Macrophage foam cells
Small pools of extracellular lipid
Core of extracellular lipid
CAC
Fibrous thickening
Fissure and hematoma
Thrombus
CAC
Soft plaque regression
No plaque
CAC score = 0
'Noncalcified' soft plaque
CAC score = 0
?
'Mixed' Plaque
Positive CAC
score > 0 < 100
?
'Calcified' Plaque
CAC > 100

COR	LOE	Recommendations
I	B-NR	1. For adults 40 to 75 years of age, clinicians should routinely assess traditional cardiovascular risk factors and calculate 10-year risk of ASCVD by using the pooled cohort equations (PCE) (S2.2-1, S2.2-2).
IIa	B-NR	2. For adults 20 to 39 years of age, it is reasonable to assess traditional ASCVD risk factors at least every 4 to 6 years (S2.2-1–S2.2-3).
IIa	B-NR	3. 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 (e.g., statin therapy) (S2.2-4–S2.2-14).
IIa	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 (e.g., statin therapy) remain uncertain, it is reasonable to measure a coronary artery calcium score to guide clinician–patient risk discussion (S2.2-15–S2.2-31).
IIb	B-NR	5. For adults 20 to 39 years of age and for those 40 to 59 years of age who have <7.5% 10-year ASCVD risk, estimating lifetime or 30-year ASCVD risk may be considered (S2.2-1, S2.2-2, S2.2-32–S2.2-35).

	High-Intensity	Moderate-Intensity	Low-Intensity
LDL-C Lowering†	≥50%	30% to 49%	<30%
Statins	Atorvastatin (40 mg‡) 80 mg Rosuvastatin 20 (40 mg)	Atorvastatin 10 mg (20 mg) Rosuvastatin (5 mg) 10 mg Simvastatin 20–40 mg§	Simvastatin 10 mg
	–	Pravastatin 40 mg (80 mg) Lovastatin 40 mg (80 mg) Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 1–4 mg	Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg

Secondary Prevention in Patients with Clinical ASCVD



Major ASCVD Events
Recent acute coronary syndrome (within the past 12 months)
History of myocardial infarction (other than recent acute coronary syndrome event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ankle brachial index <0.85, or previous revascularization or amputation)
High-Risk Conditions
Age ≥65 years
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or PCI outside of the major ASCVD event(s)
Diabetes Mellitus
Hypertension
Chronic kidney disease (eGFR 15-59 mL/min/1.73 m^2)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL (≥2.6 mmol/L)) despite maximally tolerated statin therapy and ezetimibe
History of congestive heart failure

RISK ENHANCING FACTORS

- **Family history of premature ASCVD;** (males <55 years; females <65 years)
- **Primary hypercholesterolemia** (LDL-C 160-189 mg/dL (4.1- 4.8 mmol/L); non-HDL-C 190-219 mg/dL (4.9-5.6 mmol/L).
- **Metabolic syndrome** (increased waist circumference, elevated TG (>175 mg/dL, elevated BP, elevated glucose, low HDL-C (<40 mg/dL in men, <50 mg/dL in women) are factors; tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15- 59 ml/min per 1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions** such as psoriasis, rheumatoid arthritis (RA) or human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS)
- **History of premature menopause (before age 40) and history of pregnancy-associated conditions that increase later ASCVD risk such as pre-eclampsia**
- **High-risk ethnicities** (e.g. South Asian ancestry)
- **Lipid/Biomarkers:** Associated with increased ASCVD risk

  -Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dl);

  -If measured:

  - **High-sensitivity C-reactive protein** - (≥2.0 mg/L)
  - **Elevated lipoprotein (a)** - A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥ 50 mg/dL or ≥125 nmol/L constitutes a risk enhancing factor especially at higher levels of Lp(a).
  - **Elevated apo B ≥130 mg/dL** - A relative indication for its measurement would be triglyceride ≥ 200 mg/dL. A level ≥ 130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk enhancing factor.
  - **ABI <0.9**

Why not to do Calcium score for him?

- **Low clinical risk > Low yield**
- **High clinical risk > No need**
- **Radiation exposure**
- **Incidental findings requiring FU CT**
- **Time, money, and effort spent**

	Variables Included									
	FRS	ACC/AHA Pooled Cohort Equation	WHO/ISH Risk Prediction Charts	JBS3	SCORE CVD	QRISK	Reynolds	INTERHEART	China-PAR	MESA
Age	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Gender	✓	✓	✓	✓	✓	✓	×[a]	✓	✓	✓
Ethnicity	×	✓	×	✓	×	×	×	×	×	✓[b]
Region	×	×	×	✓[c]	✓[d]	✓[e]	×	×	✓[f]	×
History of diabetes	✓	✓	✓	✓	×	×	✓[g]	✓	✓	✓
Smoking history	✓	✓	✓	✓	✓	✓	✓	✓[h]	✓	✓
Family history of premature CVD	×	×	×	✓	×	✓[i]	✓[j]	✓[k]	✓	✓[l]
Atrial fibrillation	×	×	×	✓	×	×	×	×	×	×
Chronic kidney disease	×	×	×	✓	×	×	×	×	×	×
Rheumatoid arthritis	×	×	×	✓	×	×	×	×	×	×
Blood pressure treatment	✓	✓	×	✓	×	✓	×	×	✓	✓
Systolic blood pressure	✓	✓	✓	✓	✓	✓	✓	✓[m]	✓	✓
Body mass index	×	×	×	✓	×	✓	×	✓[n]	✓[o]	×
Apolipoprotein levels	×	×	×	×	×	×	×	✓[p]	×	×
Total cholesterol	✓	✓	✓	✓	✓	✓	✓	×	✓	✓
High-density lipoprotein cholesterol	✓	✓	×	✓	✓	✓	✓	×	✓	✓
Lipid-lowering treatment	×	×	×	×	×	×	×	×	✓	✓
High sensitivity C-reactive protein	×	×	×	×	×	×	✓	×	×	×
CAC score	×	×	×	×	×	×	×	×	×	✓
Psychosocial assessment	×	×	×	×	×	×	×	✓[q]	×	×

End Points Assessed

	FRS	ACC/AHA Pooled Cohort Equation	WHO/ISH Risk Prediction Charts	JBS3	SCORE CVD	QRISK	Reynolds	INTERHEART	China-PAR	MESA
CHD Death	✓	✓	×	✓	✓	✓	✓	×	✓	✓
Nonfatal MI	✓	✓	×	✓	×	✓	✓	✓[r]	✓	✓
Coronary insufficiency/angina	✓	×	×	✓	×	✓	×	×	×	×
Coronary revascularization	×	×	×	✓	×	✓	✓	×	×	✓
Arrhythmia	×	×	×	×	✓	×	×	×	×	×
Heart failure	✓	×	×	×	✓	×	×	×	×	×
Fatal/nonfatal stroke	✓[s]	✓	×	✓	✓	✓	✓[t]	×	✓	×
TIA	✓	×	×	✓	×	✓	×	×	×	×
Intermittent claudication	✓	×	×	✓	✓[u]	✓	×	×	×	×
Aortic aneurysm	×	×	×	×	✓	×	×	×	×	×
Cardiac resuscitation	×	×	×	×	×	×	×	×	×	✓

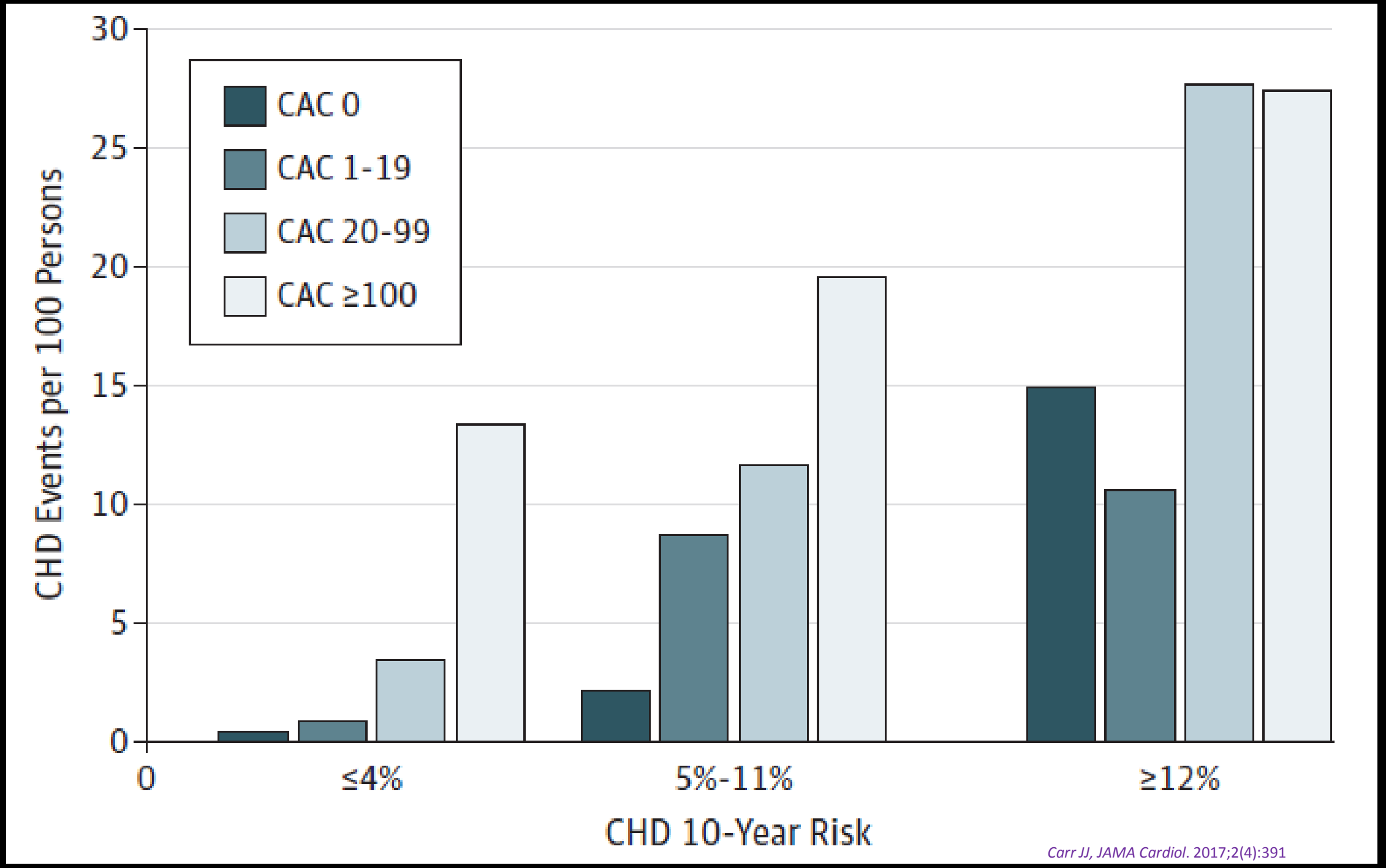
Imaging Coronary Artery Calcium

MODALITY	SPATIAL RESOLUTION
• CT SCAN	0.4 – 0.6 mm
• MRI	1.3 – 1.8 mm
• IVUS	100 – 200 µm
• OCT	15 – 20 µm
• NIR IMAGING	1 mm
• PET CT	3 – 5 mm

68 year old male with No Risk Factors

Should a Calcium Score be done for Risk Stratification?

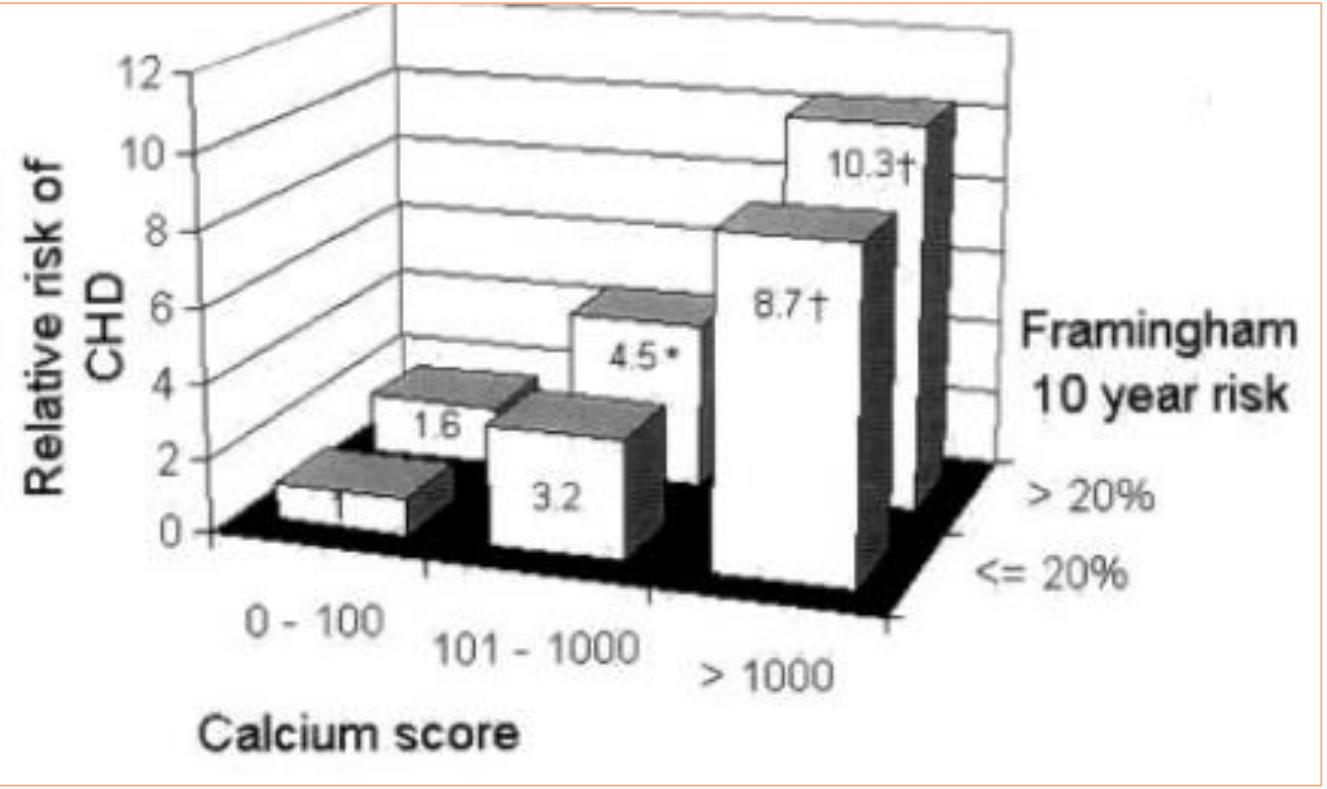
- **Is it worthwhile ?**
- **Does it have incremental benefit ?**
- **Will it change my clinical practice ?**
- **Can we have an easy access to it ?**
- **Is it cost effective ?**

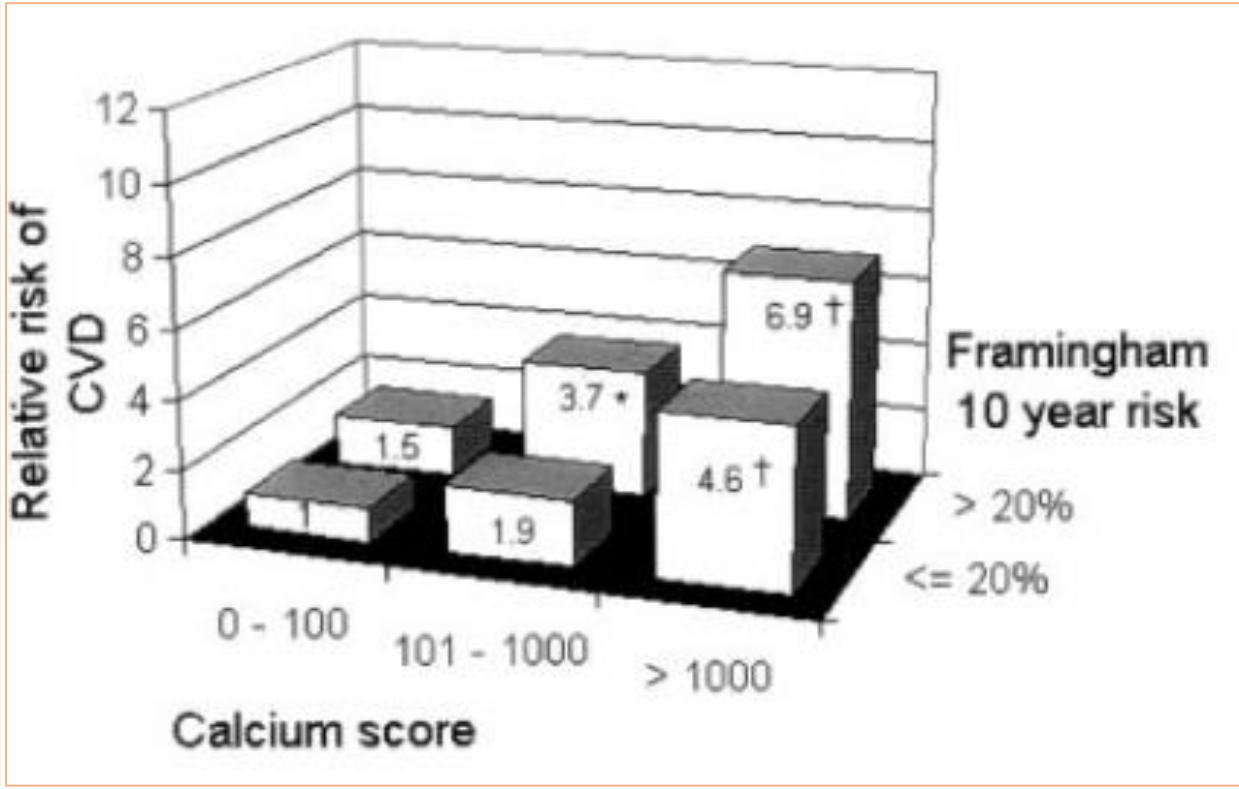


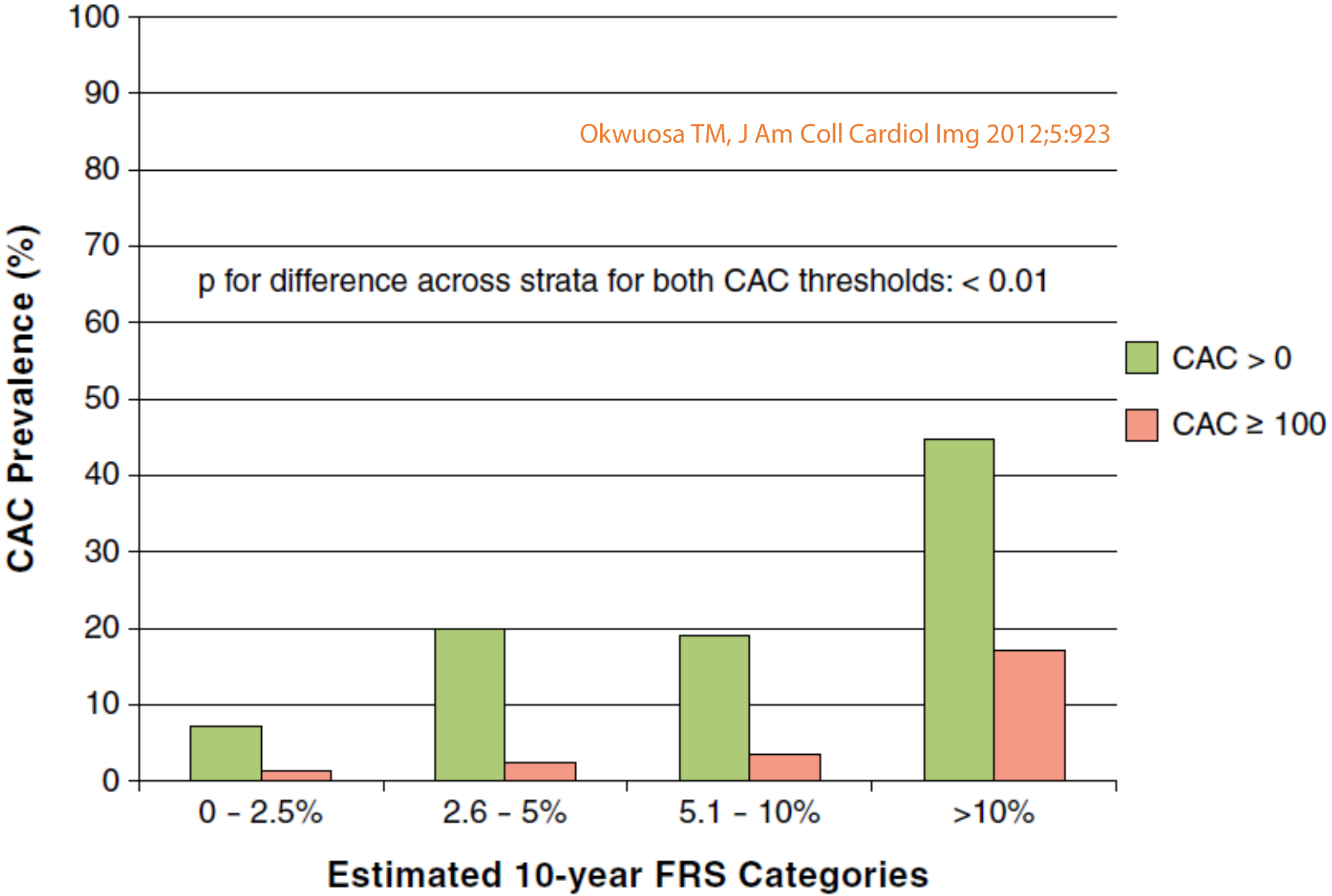
Carr JJ, JAMA Cardiol. 2017;2(4):391

Rotterdam Study – CAC score in Elderly

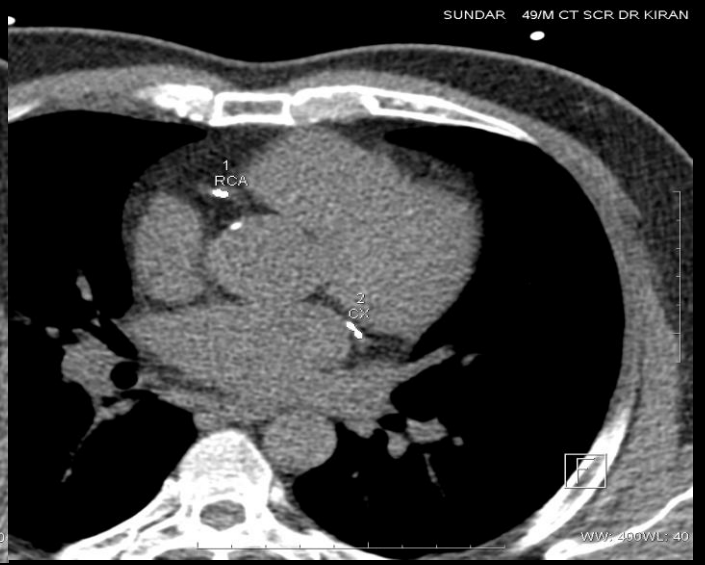
Vliegenhart R, Circulation. 2005;112:572-577

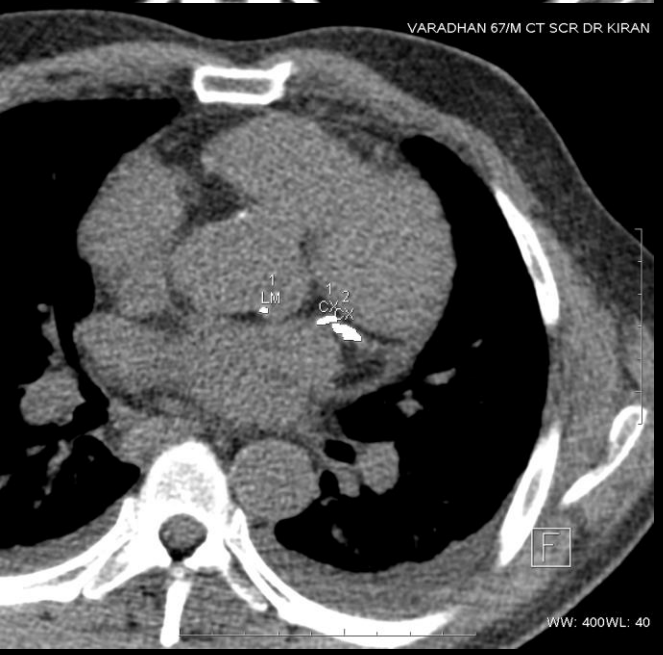





Okwuosa TM, J Am Coll Cardiol Img 2012;5:923
p for difference across strata for both CAC thresholds: < 0.01
CAC Prevalence (%)
100
90
80
70
60
50
40
30
20
10
0
CAC > 0
CAC ≥ 100
0 – 2.5%
2.6 – 5%
5.1 – 10%
>10%
Estimated 10-year FRS Categories

Coronary Artery Calcium – Agatston's Score





Threshold = 130 HU
(103.2 mg/cm³ CaHA)

Artery	Number of Lesions (1)	Volume [mm³] (3)	Equiv. Mass [mg CaHA] (4)	Calcium Score (2)
LM	1	73.6	17.19	92.3
LAD	4	55.8	9.56	49.4
CX	5	205.8	39.51	228.9
RCA	7	248.2	50.30	264.6
Total	17	583.3	116.56	635.2

(1) Lesion is volume based
(2) Equivalent Agatston score
(3) Isotropic interpolated volume
(4) Calibration Factor: 0.794

WW: 50WL: 200

Markers of Subclinical Atherosclerosis

Potential Predictors of future CV Events ?

- **CORONARY ARTERY CALCIFICATION**
- **CAROTID INTIMA-MEDIA THICKNESS**
- **ANKLE BRACHIAL INDEX**
- **PULSE WAVE VELOCITY**
- **SERUM LEVELS OF PROINFLAMMATORY & SOLUBLE ADHESION MOLECULES**