Tip of the Iceberg: There is a REVOLUTION in Preventive Cardiology

Thomas D.Stuckey, MD, FACC
Medical Director, LeBauer-Brodie Center
Clinical Professor of Medicine, UNC School of Medicine

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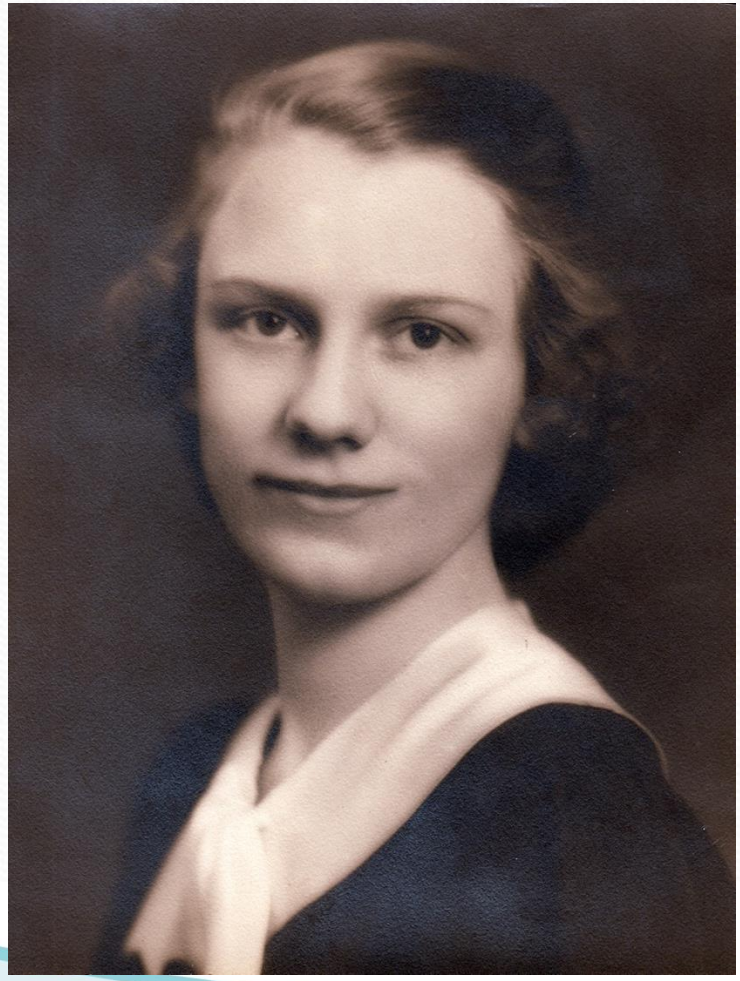
Disclosures

- Nothing to Disclose

Objectives

- What can imaging now tell us about cardiovascular risk
- What can we do to address cardiac risk
- What new targets are available to address cardiac risk



'Surely this was something to write about,' columnist Martha Long recalls thinking during treatment for a heart attack, 'and I tried to think of a really good lead'

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Olezarsen for Triglycerides

Before open label drug

Month after 1 dose of open label drug

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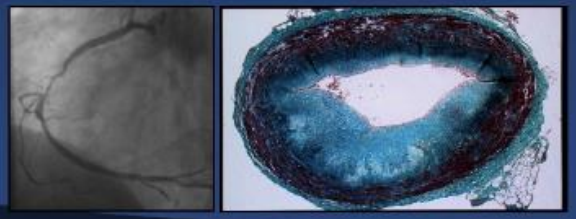
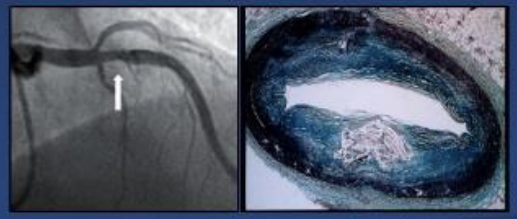
The Final Word

Ischemia, vulnerable plaque, prognosis and treatment

Symptoms of ischemia (angina, exertional dyspnea)	CV risk factors, inflammation, recent ACS
↓	↓
Ischemia ⟷	Vulnerable plaque
↓	↓
Treat to relieve symptoms (anti-anginal drugs, revasc)	Treat to prevent CV death, MI, ACS (APT, lipid lowering, revasc)





Mount Sinai Heart

Cardiovascular Research Foundation®

Slide. Gregg Stone

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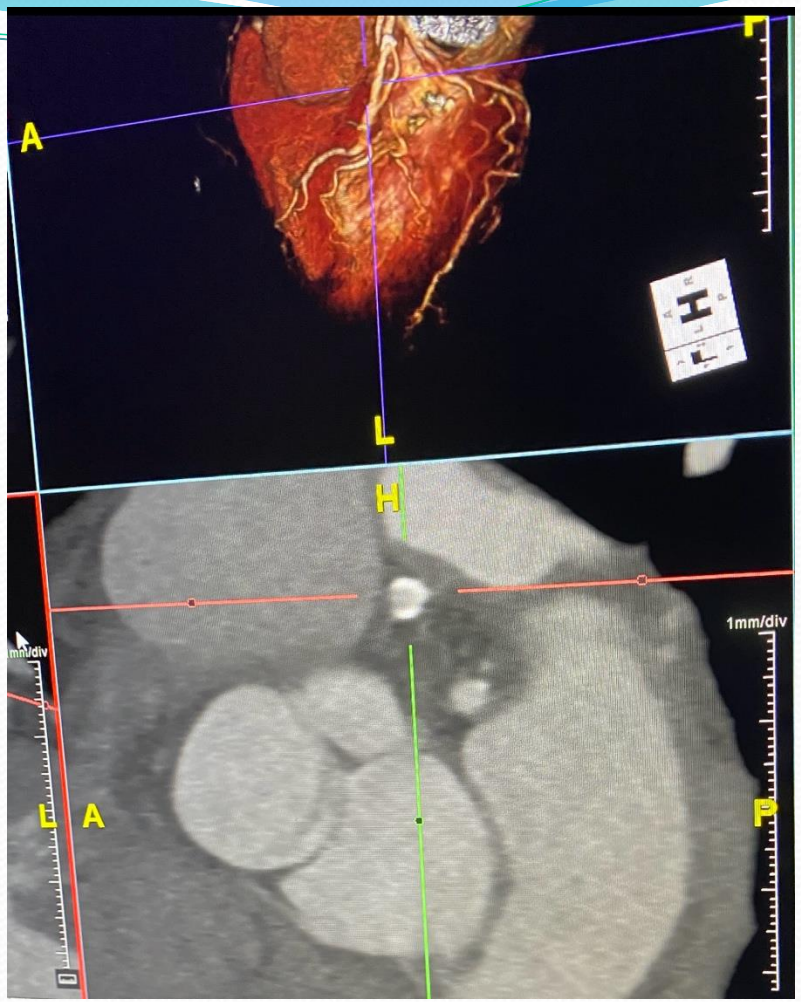
Table | Graph | Export Measur...

Artery	Lesion No	Score	Volume	Mean	Mas
Coronaries T	9	382	380		71.7
LM Total	0	0	0		0
LAD Total	4	116	120		20.9
LCX Total	1	160	129		29.6
RCA Total	4	106	131		21.2
Other Total	0	0	0		0
Total	9	382	380		71.7

Percentile Ranking: 74 (MESA)

Gender: Male Age: 67 Ethnicity: White

Patient size for mass score



Thomas Stuckey Calcium Score

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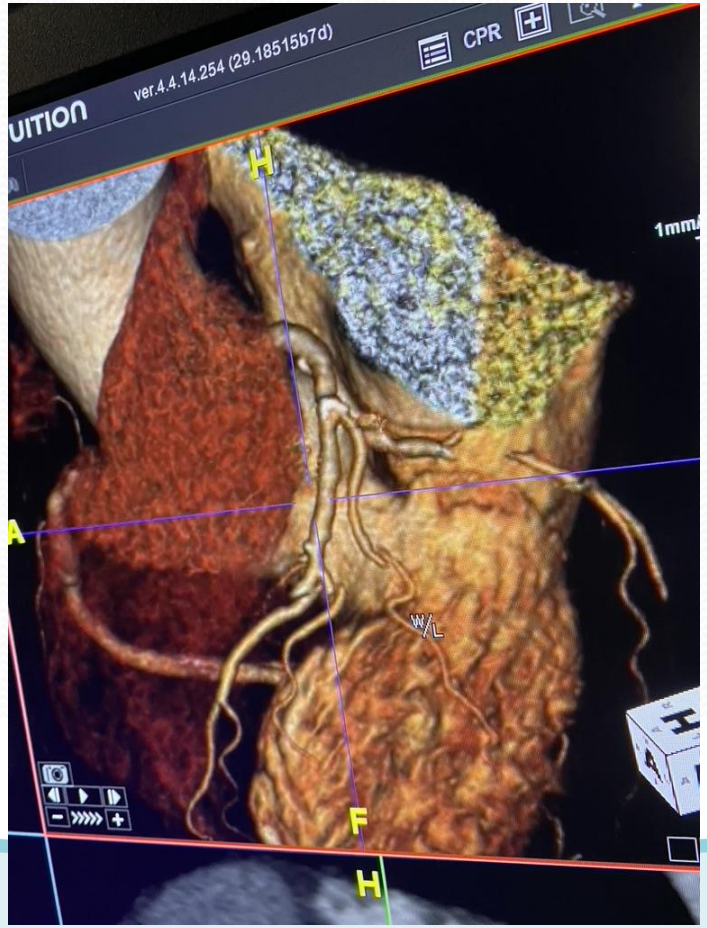

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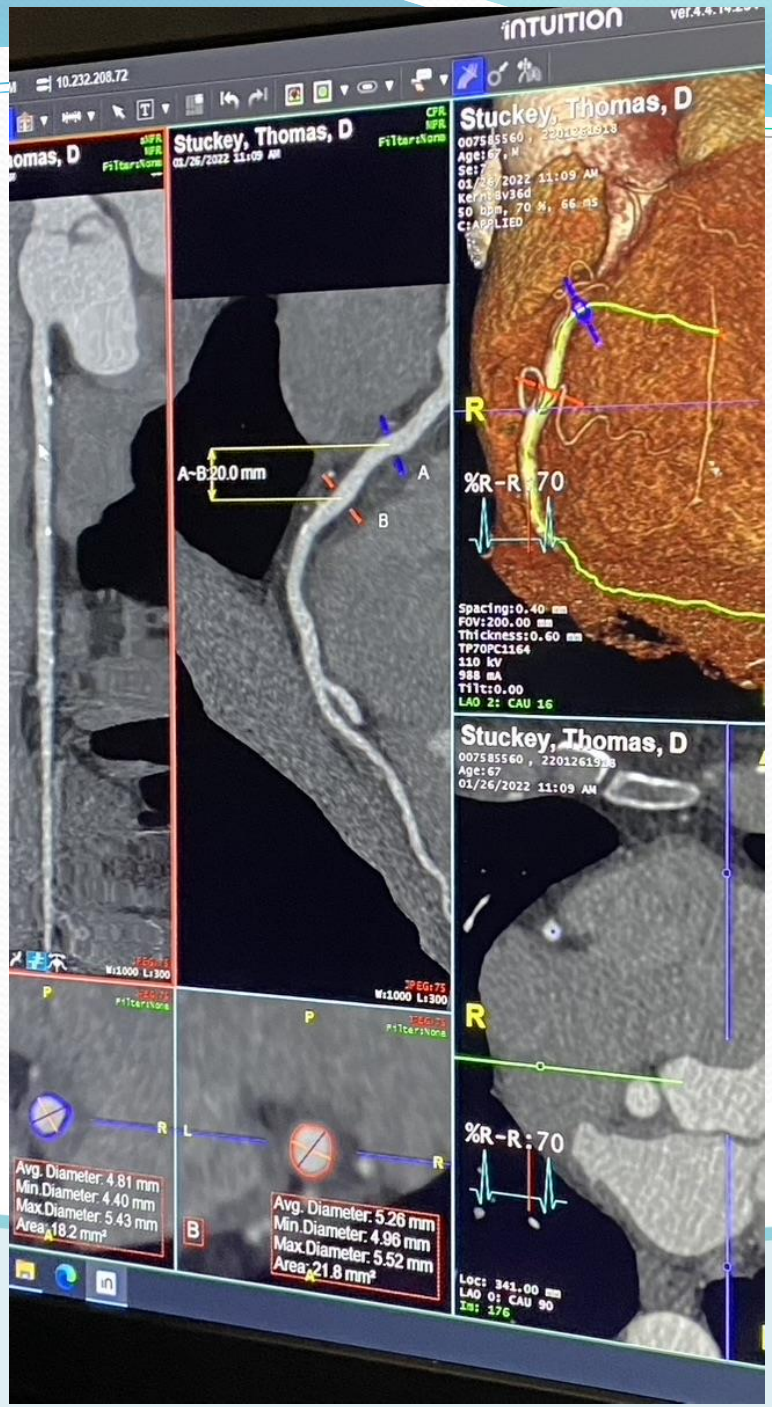
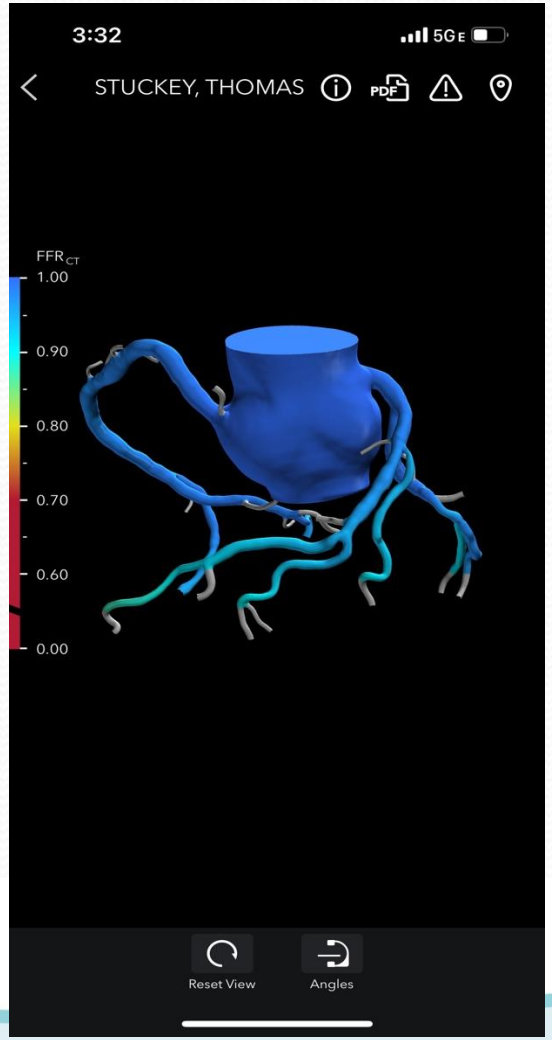

INTUITION
10.232.208.72
Stuckey, Thomas, D
A-B:20.0 mm
A
B
%R-R:70
Spacing:0.40 mm
FOV:200.00 mm
Thickness:0.60 mm
TP70PC1164
110 kV
988 mA
Tilt:0.00
LAO 2: CAU 16
Avg. Diameter: 4.81 mm
Min.Diameter: 4.40 mm
Max.Diameter: 5.43 mm
Area: 18.2 mm²
Avg. Diameter: 5.26 mm
Min.Diameter: 4.96 mm
Max.Diameter: 5.52 mm
Area: 21.8 mm²



Lp(a) 120 nmol/l - I am in a race for my own mortality

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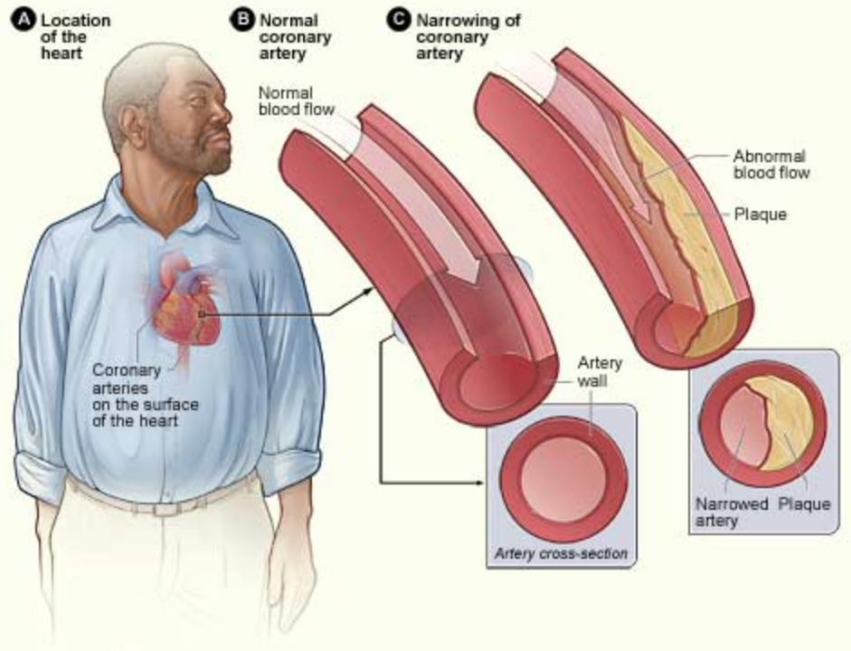
Would you want to know if you have Coronary Artery Disease?



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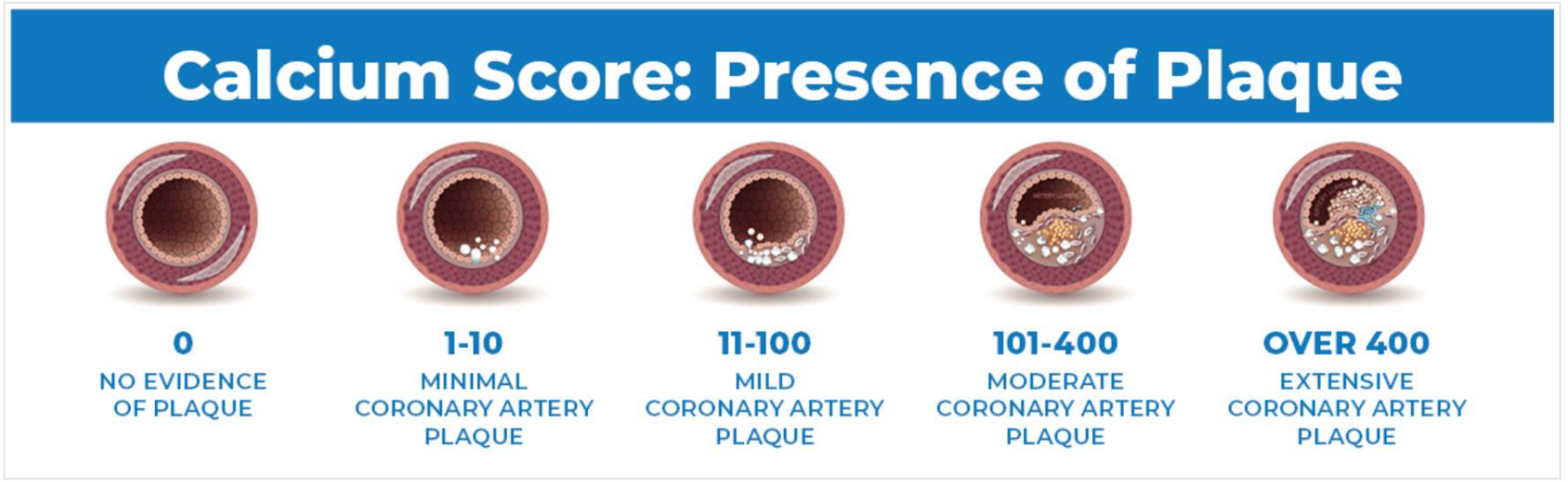
What are the clinical implications of the presence and absence of CAC?



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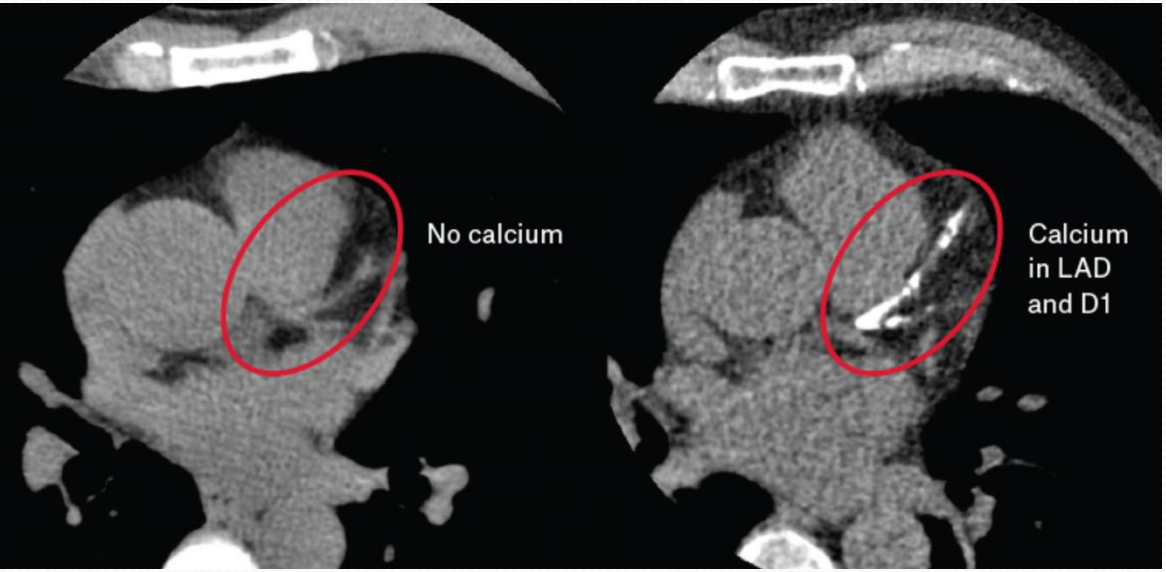
What is coronary artery **Calcium Score Scan (CAC)**?



- **Rapid CT scan of heart**
- **Does not require contrast**
- **No prep is required**
- **“Inexpensive”**
- **Low radiation dose**
- **Powerful prognostic data**

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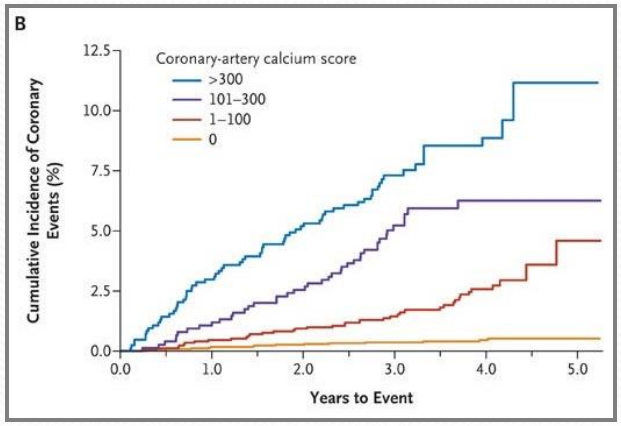
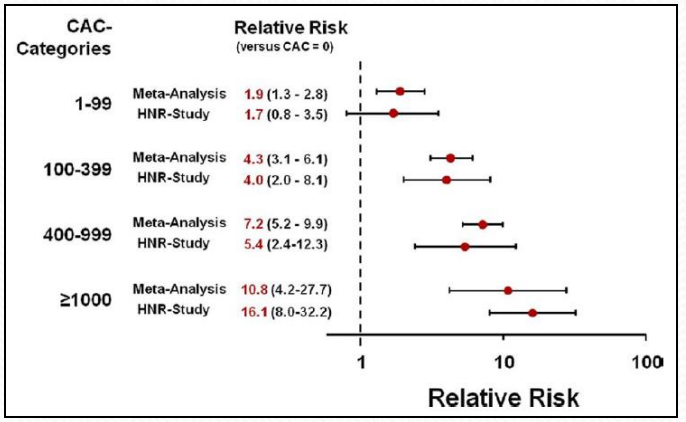
Elevated Calcium Score -> Elevated Risk

Multi-Ethnic Study of Atherosclerosis (MESA)



(Detrano, NEJM 2008)

Heinz Nixdorf Recall Study



(Erbel, JACC 2010)

- CAC 0 -> 0.1%/year event rate
- Risk increased by 10x if severe CAC present
- Adds to traditional risk factors/reclassifies CVD risk

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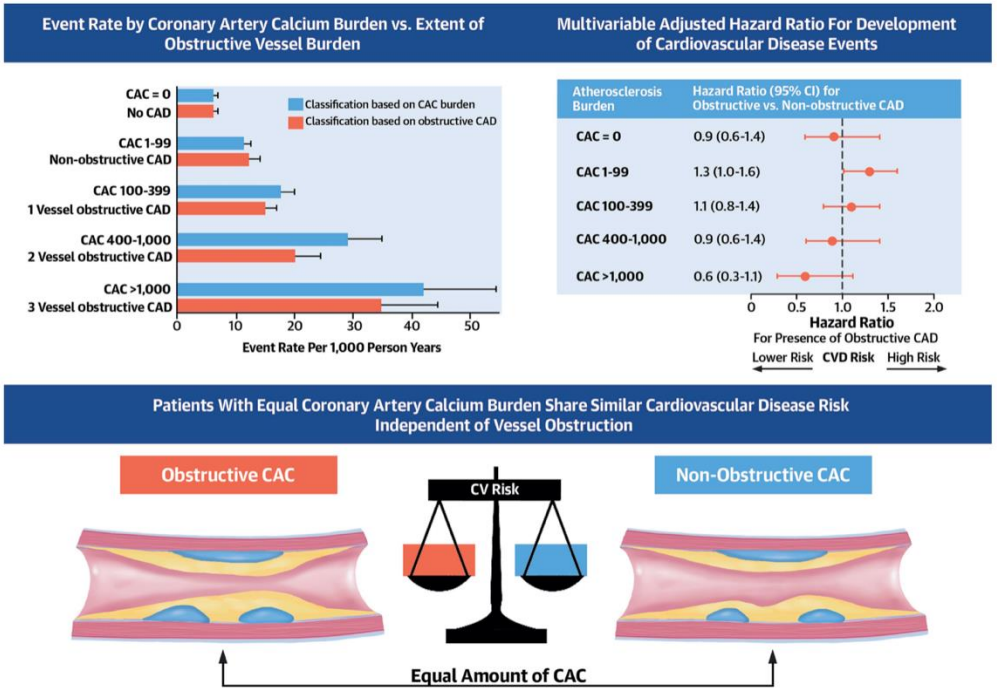
Plaque burden, not stenosis is the major predictor of CV risk

Impact of Plaque Burden Versus Stenosis on Ischemic Events in Patients With Coronary Atherosclerosis JACC 2020

Martin Bødtker Mortensen, Omar Dzaye, Flemming Hald Steffensen, Hans Erik Bøtker, Jonathon Leipsic, Bjarne Linde Nørgaard

23,279 patients from Western Denmark Heart Registry



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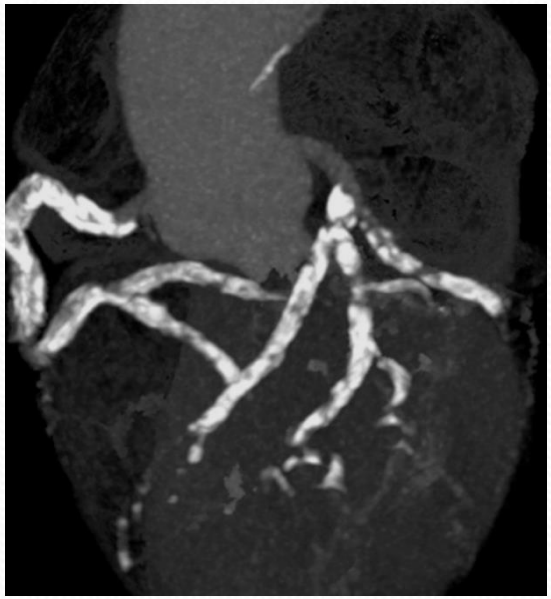
What to do if CAC is high?

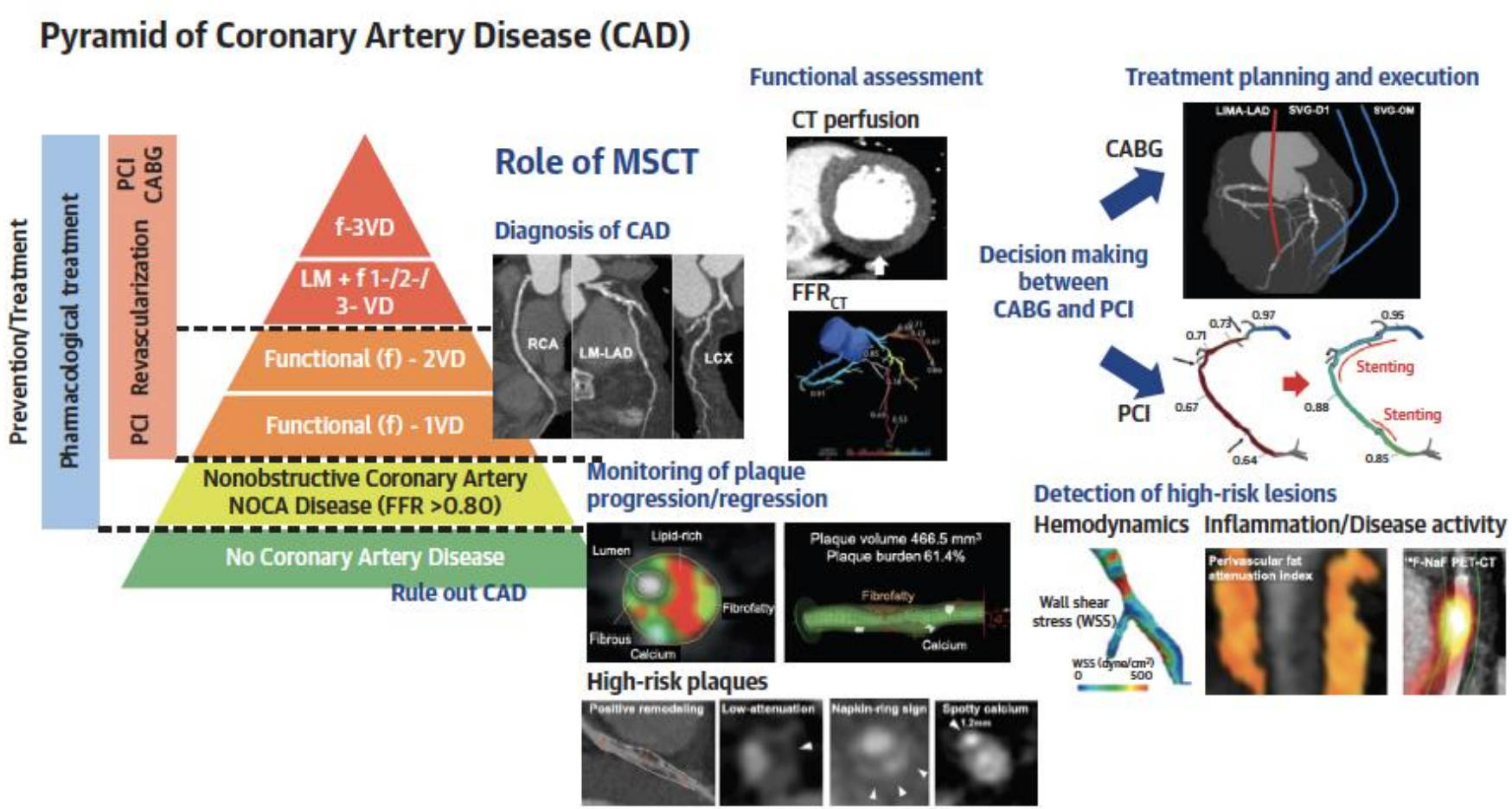
Treat same as you would for other high-risk pts:

- ✓ Aggressive prevention: statin(add on lipid lowering agent) & aspirin
- ✓ Lifestyle changes

- ✓ Most will not need any other testing, especially if active lifestyle and no Sx



CENTRAL ILLUSTRATION The Pyramid of Coronary Artery Disease and the Diagnostic Role of Multislice Computed Tomography



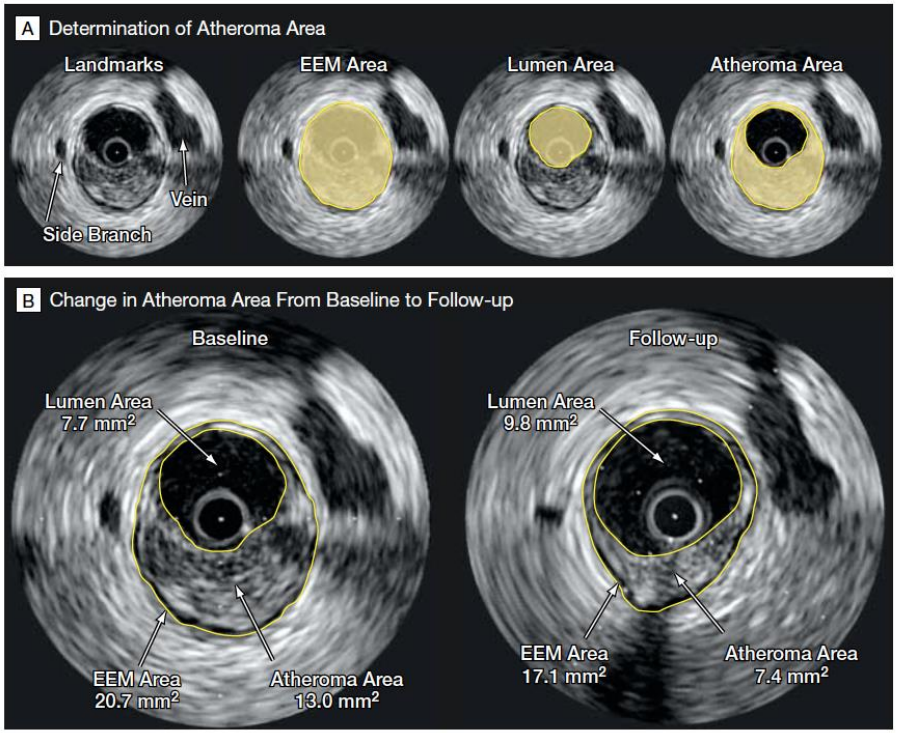
Serruys, P.W. et al. J Am Coll Cardiol. 2021;78(7):713-736.

Testing for Vulnerable Plaque

- Calcium scoring
- Coronary CTA
- Noninvasive FFR
- CT Pet
- Nirs IVUS
- OCT

High Versus Low intensity Statin Impact

Figure 3. Intravascular Ultrasound Images at Baseline and Follow-up



A, Atheroma area is calculated by subtracting the lumen area from the area of the external elastic membrane (EEM). B, Patient randomized to 80 mg of atorvastatin. There is substantial reduction in atheroma area (from 13.0 to 7.4 mm²). A lesser increase in lumen area is noted (from 7.7 to 9.8 mm²). See video at http://jama.com/cgi/content/full/291/9/1071/DC1.

Nissen et al, JAMA, 2004

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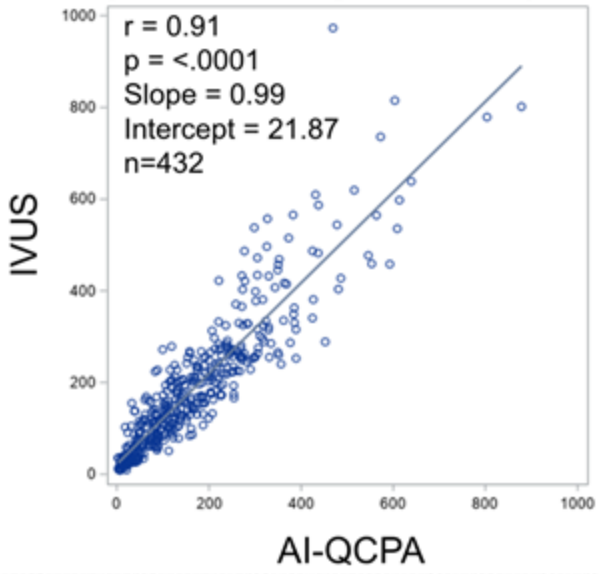
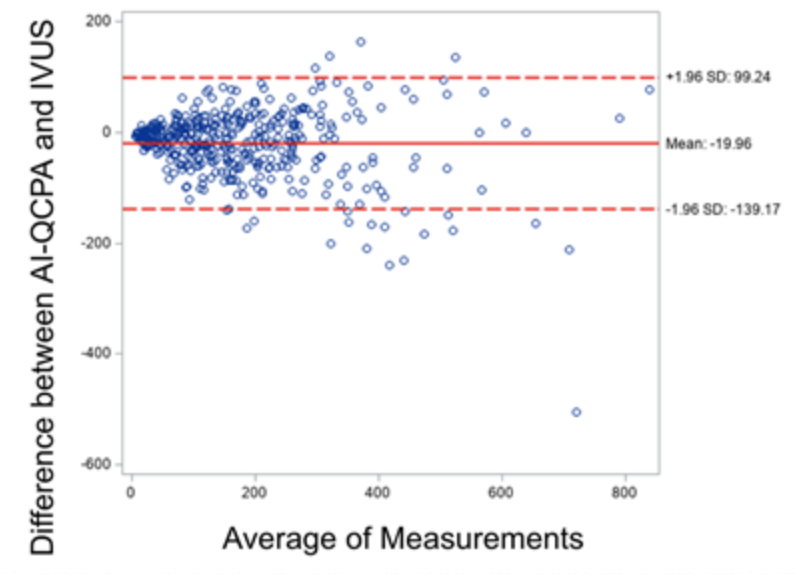
Total Plaque Volume Per Lesion

Scatterplot with Slope



Bland-Altman Analysis



Narula, Stuckey, et al SCCT 2023

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Plaque: Quantified and Characterized

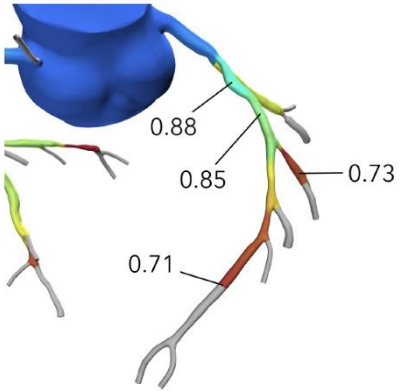
Case Example: Serial lesions with diffuse non-calcified and calcified plaque in proximal LAD.

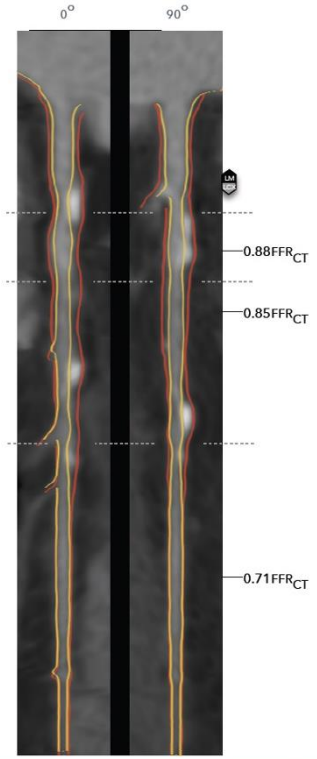
LAD Plaque overview

CORONARY SYSTEM (including branches)	TOTAL PLAQUE MM^3	CALCIFIED PLAQUE	NON-CALCIFIED PLAQUE	LOW ATTENUATION PLAQUE
Left Main	3	0	3	0
Left Anterior Descending	273	50	223	8
Total	276	50	226	8

Quantitative plaque is provided on vessels > 1.8 mm.

VESSEL BOUNDARY
- outer wall boundary
- lumen boundary





LAP (Low attenutation Plaque) and PR (positive remodeling)

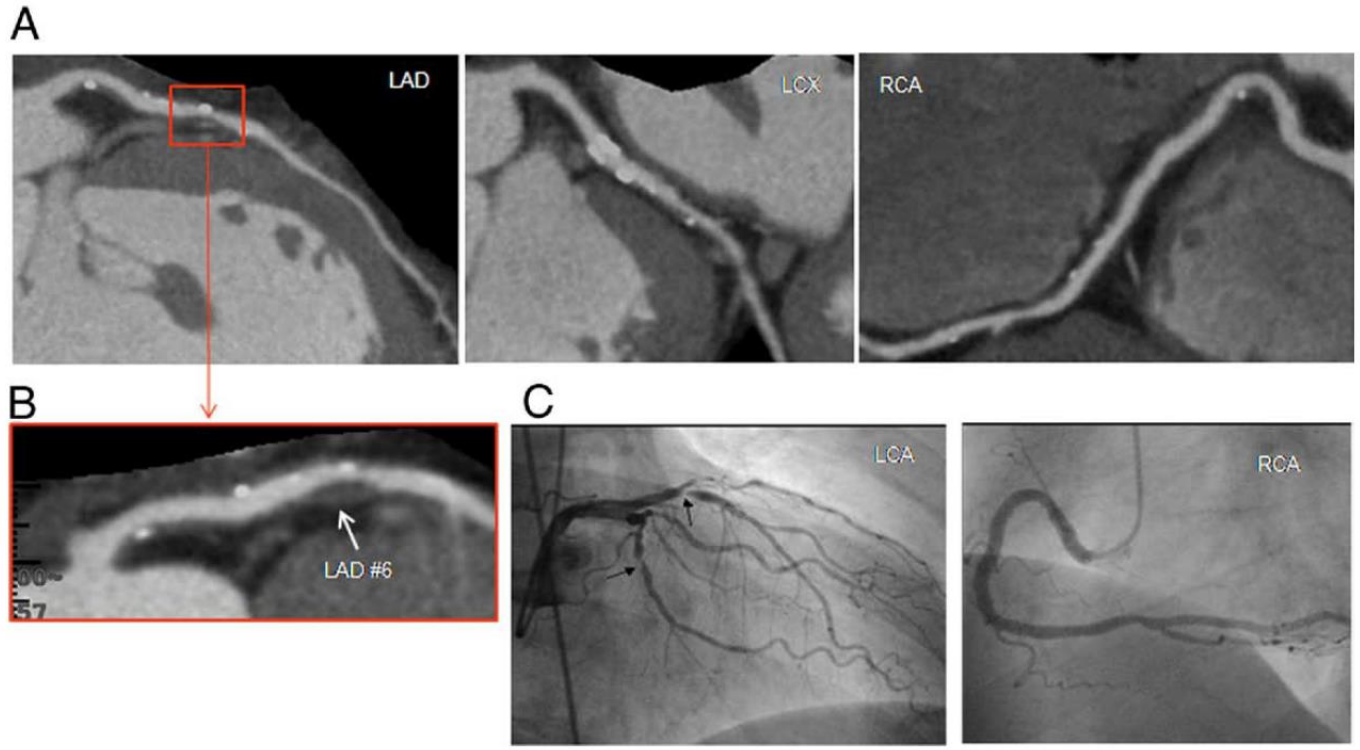


Figure 2 **Example of a Patient With ACS 6 Months After CT Angiography**

(A) Curved multiplanar reformation images of left anterior descending artery (LAD), left circumflex artery (LCX), and right coronary artery (RCA). **(B)** Positive remodeling, low-attenuation plaque, and spotty calcification were detected in LAD #6 on coronary computed tomography (CT) angiography. **(C)** Acute coronary syndrome (ACS) occurred 6 months after CT angiography. LAD #6 was determined as the culprit lesion based on invasive coronary angiogram findings. Please note the location of the lesion proximal to the first septal branch, both in CT angiography before the event and coronary angiogram after the event when the patient was brought to the catheterization laboratory for percutaneous coronary intervention. LCA = left coronary artery.

Motoyama et al. J Am Coll Cardiol 2009;54:49-57

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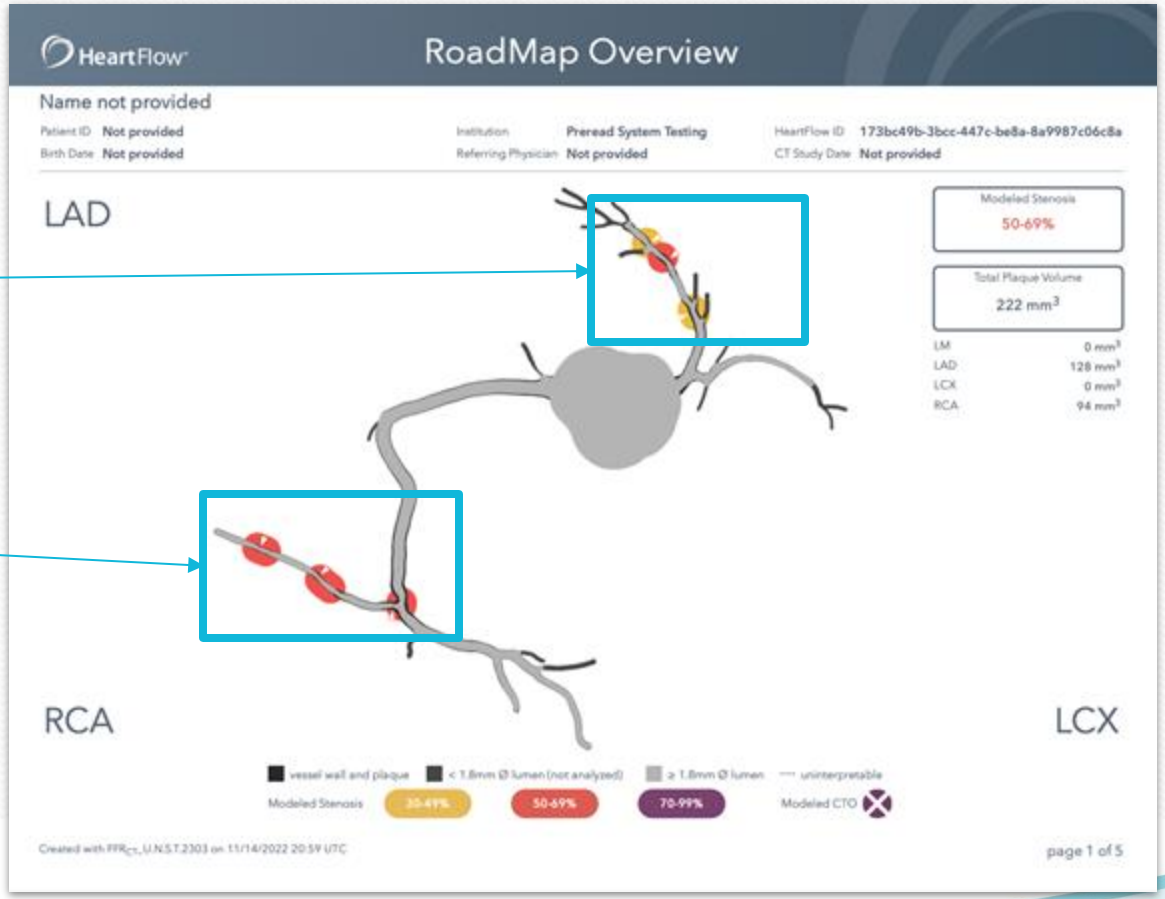
Example

Serial stenoses from 30-69% in LAD

50-69% PDA/PLB bifurcation stenosis and serial PDA stenoses



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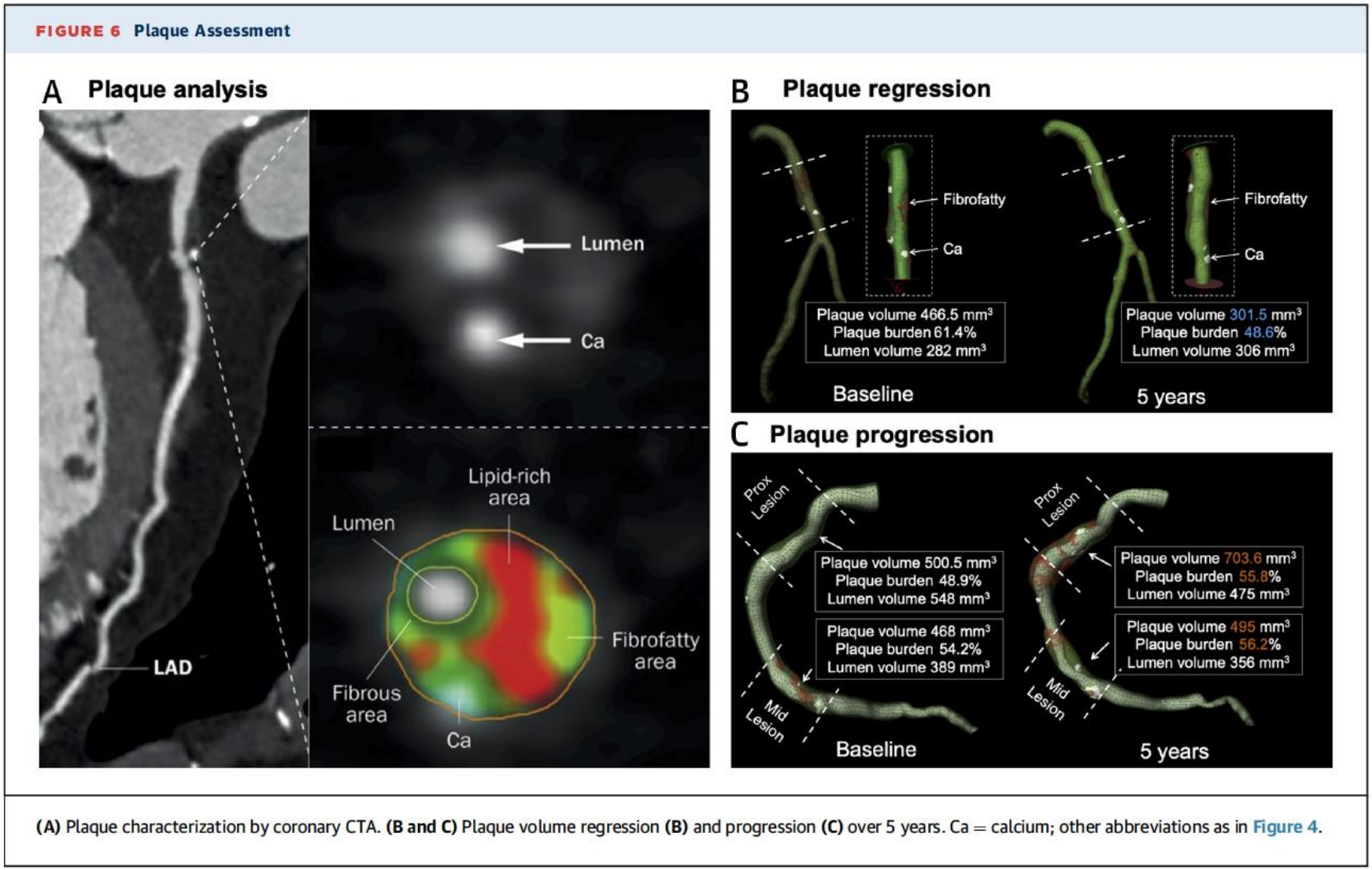
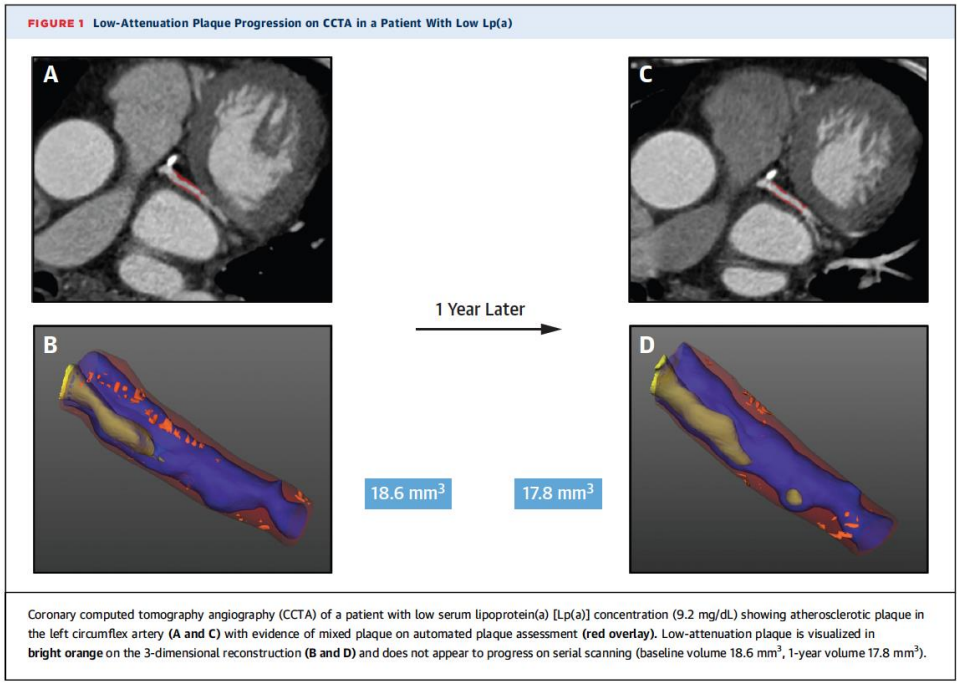
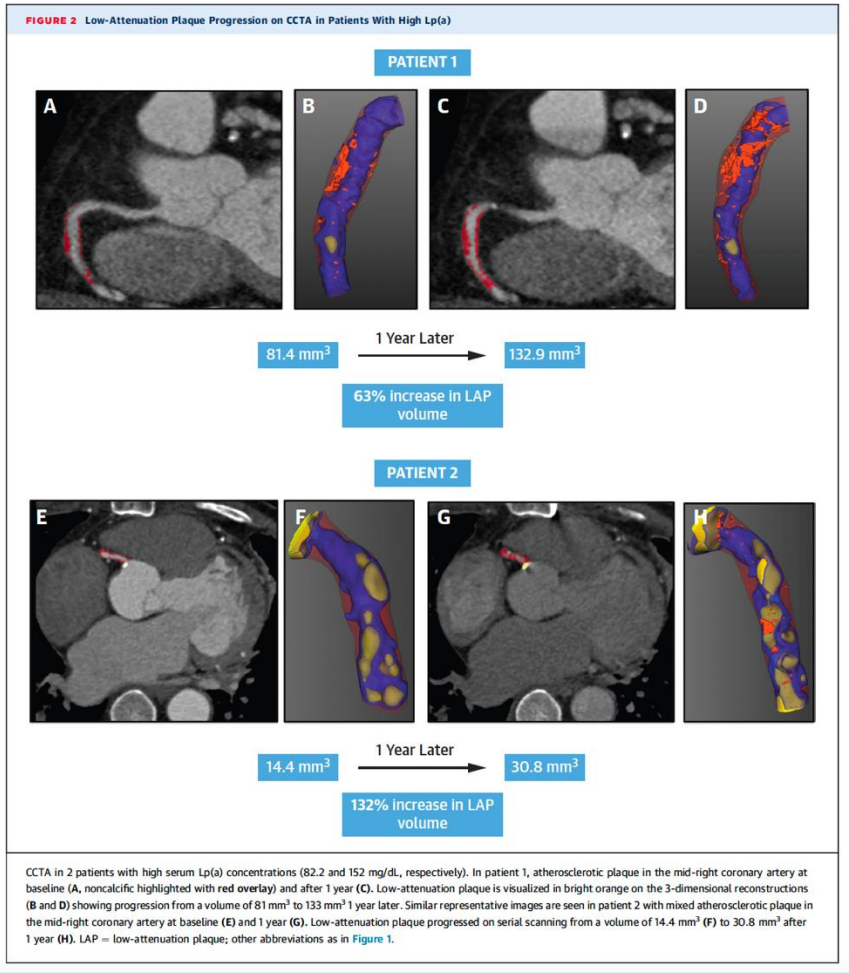


(A) Plaque characterization by coronary CTA. **(B and C)** Plaque volume regression **(B)** and progression **(C)** over 5 years. Ca = calcium; other abbreviations as in Figure 4.

Serruys et al. J Am Coll Cardiol 2021;78:713-76

Progression of Low Attenuation Plaque
191 Patients with similar baseline plaque burden





Kaiser et al. J Am Coll Cardiol 2022;79:223-33.

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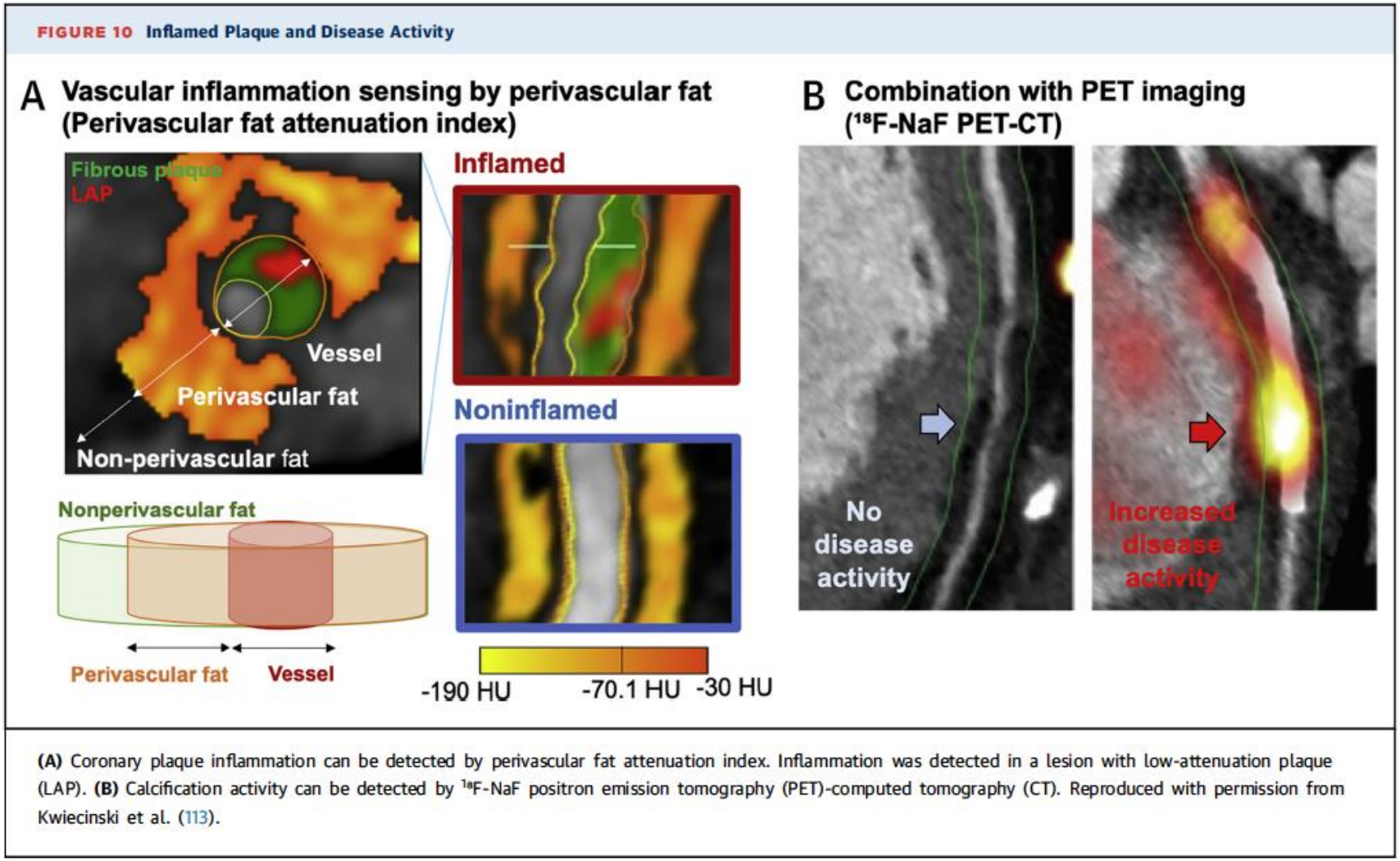
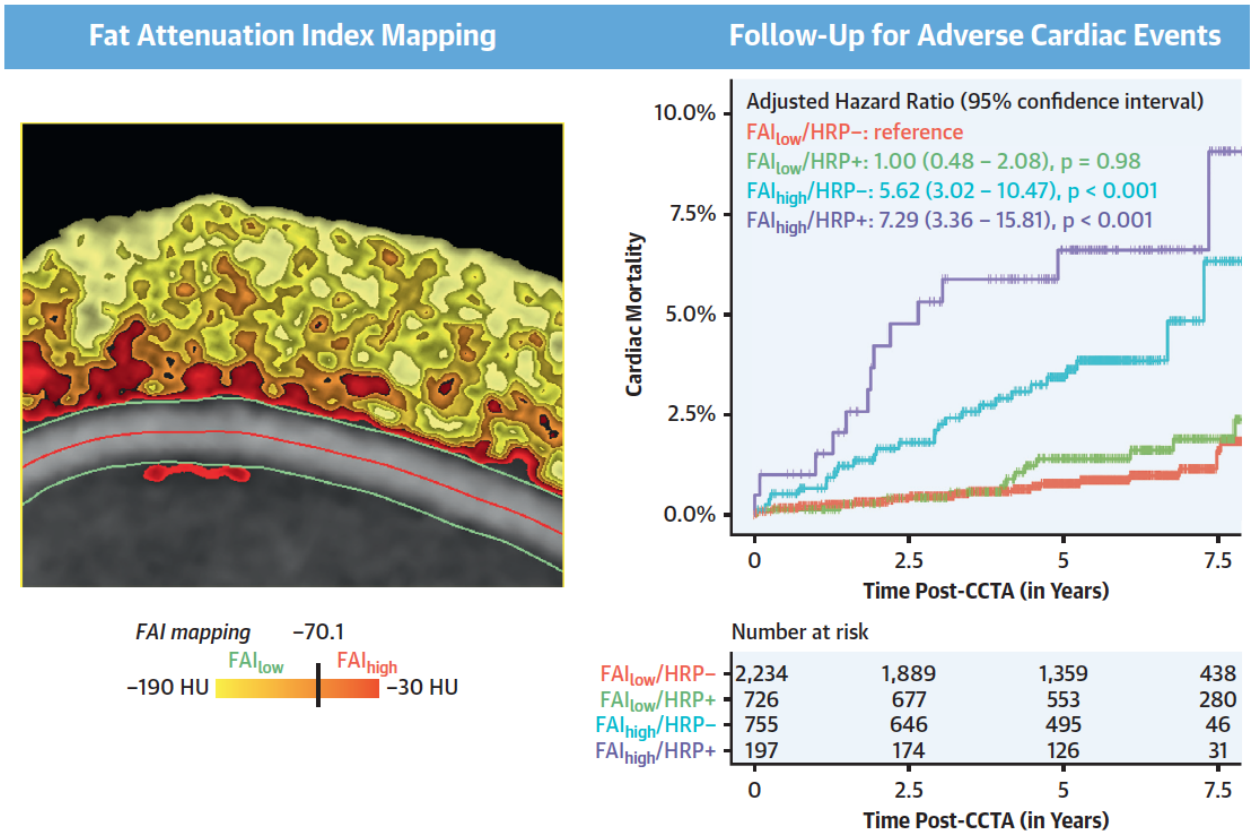


Serruys et al. J Am Coll Cardiol 2021;78:713-36

Perivascular Fat Attenuation Index Mapping

FIGURE 1 Perivascular FAI Stratifies the Risk Associated With HRP Features



(A) A visual example of pericoronary Fat Attenuation Index (FAI) mapping. **(B)** Unadjusted Kaplan-Meier curves with adjusted hazard ratios for patients stratified based on FAI around the right coronary artery (cutoff: -70.1 HU) and high-risk plaque (HRP) presence, illustrating how FAI mapping identifies distinct risk groups among HRP+ and HRP- patients. CCTA = coronary computed tomography angiography.

Oikonomou et al. J Am Coll Cardiol 2020;76:755-7

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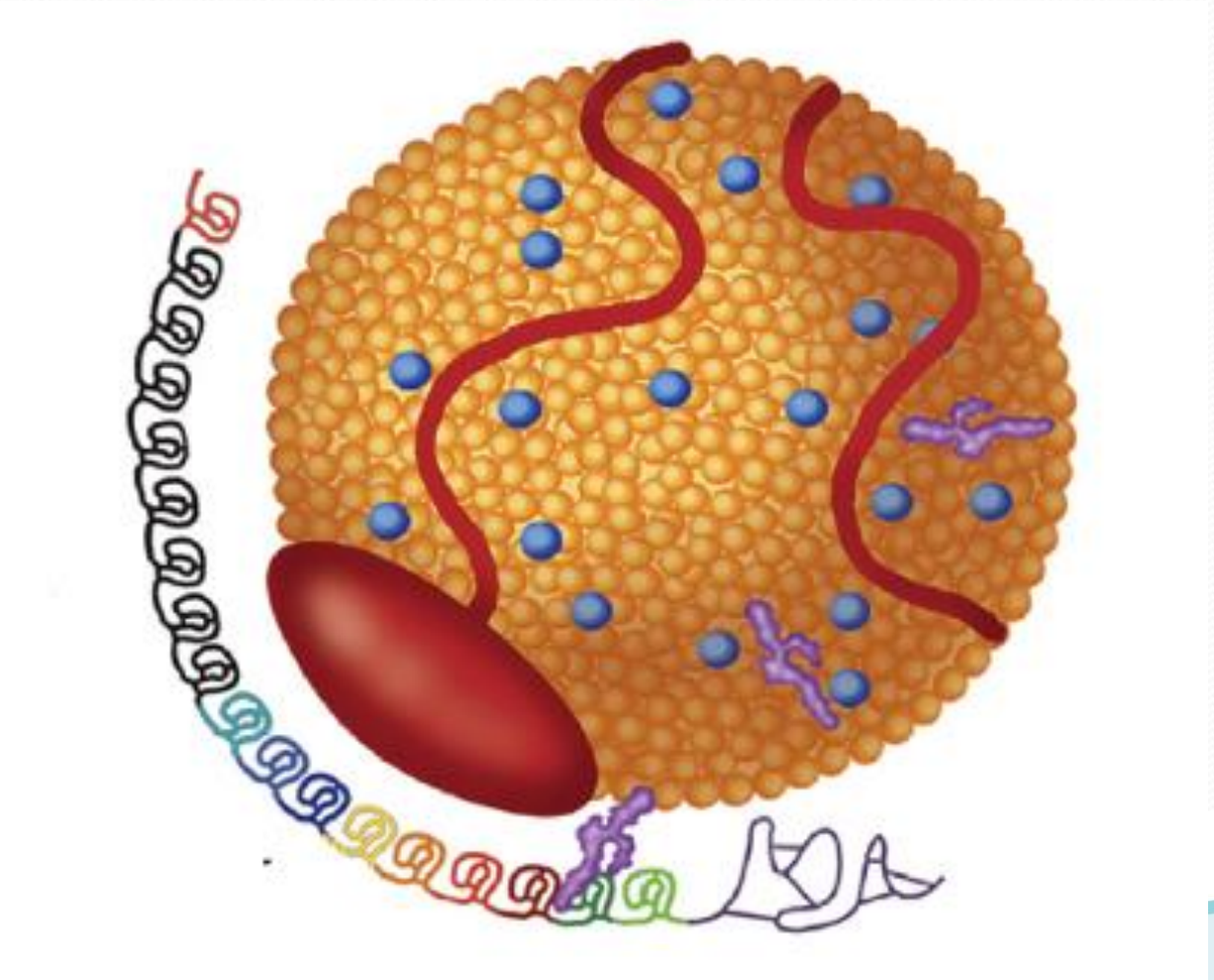
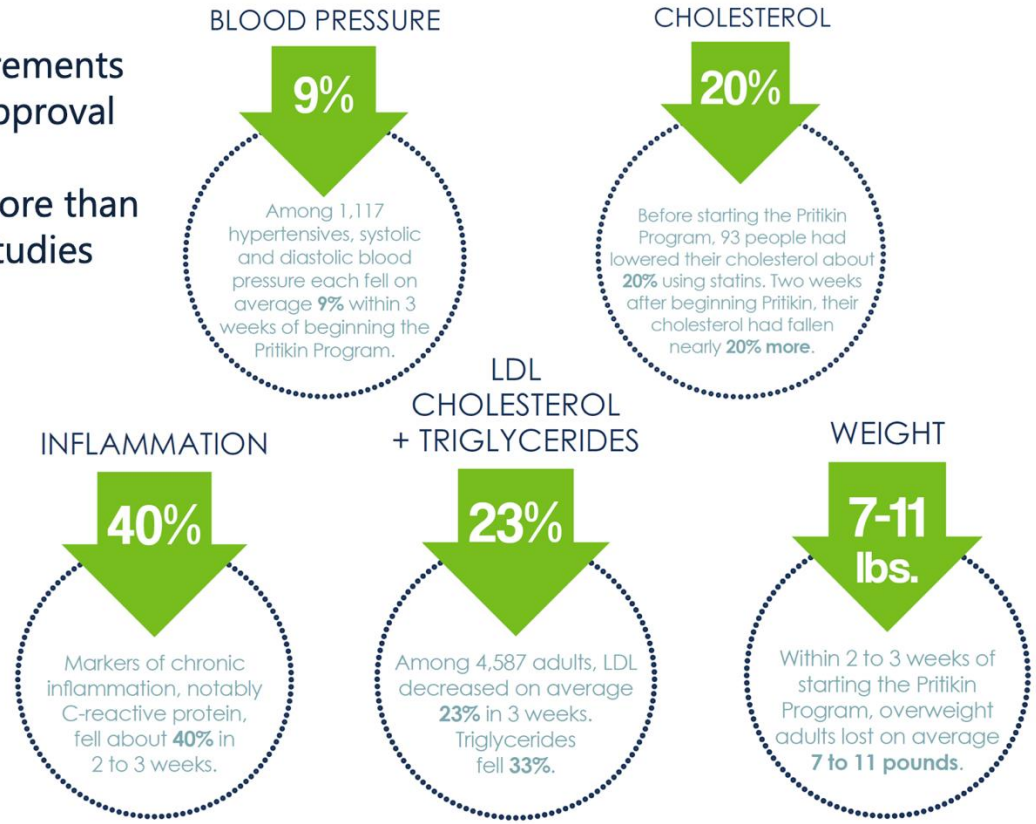
Addressing Cardiac Risk



Results of the Pritikin Program

- Meets the rigorous requirements necessary for Medicare approval
- Results documented in more than 100 published scientific studies



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THE SIX PILLARS OF LIFESTYLE MEDICINE

The aim of lifestyle medicine is to redesign health delivery to rely on therapeutic lifestyle interventions as a primary modality to treat, prevent, manage, and reverse chronic cardiometabolic conditions.

CMHC Cardiometabolic Health Congress

AMERICAN COLLEGE OF Lifestyle Medicine

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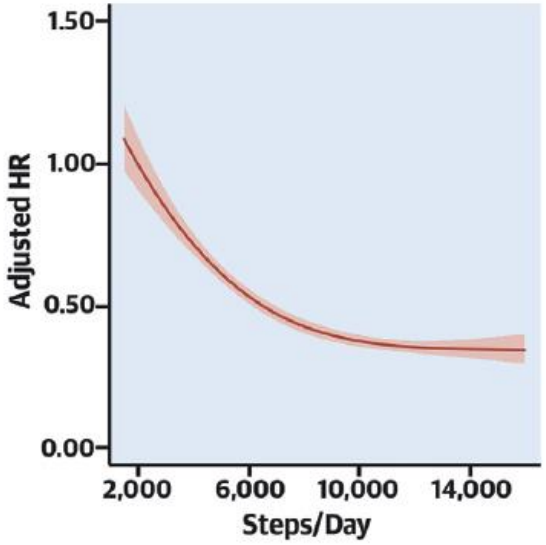
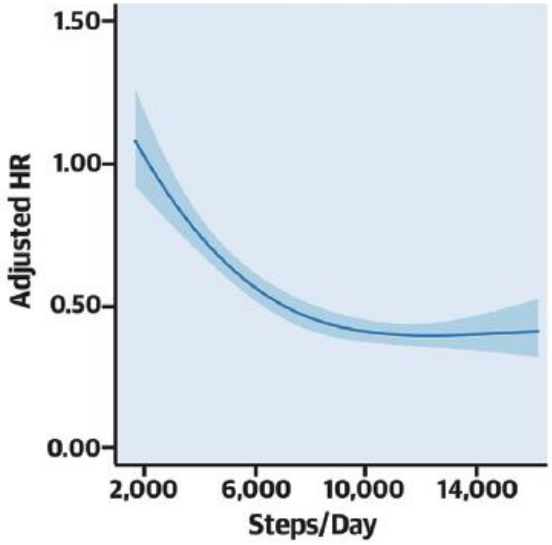
All-Cause Mortality



	Steps/day	Adjusted HR (95% CI)
Minimum dose	2,517	0.92 (0.84-0.99)
Optimum dose	8,763	0.40 (0.38-0.43)
Risk reduction at 16,000 steps	16,000	0.35 (0.30-0.40)

Incident CVD (Fatal and Nonfatal)



	Steps/day	Adjusted HR (95% CI)
Minimum dose	2,735	0.89 (0.79-0.99)
Optimum dose	7,126	0.49 (0.45-0.55)
Risk reduction at 16,000 steps	16,000	0.42 (0.33-0.53)

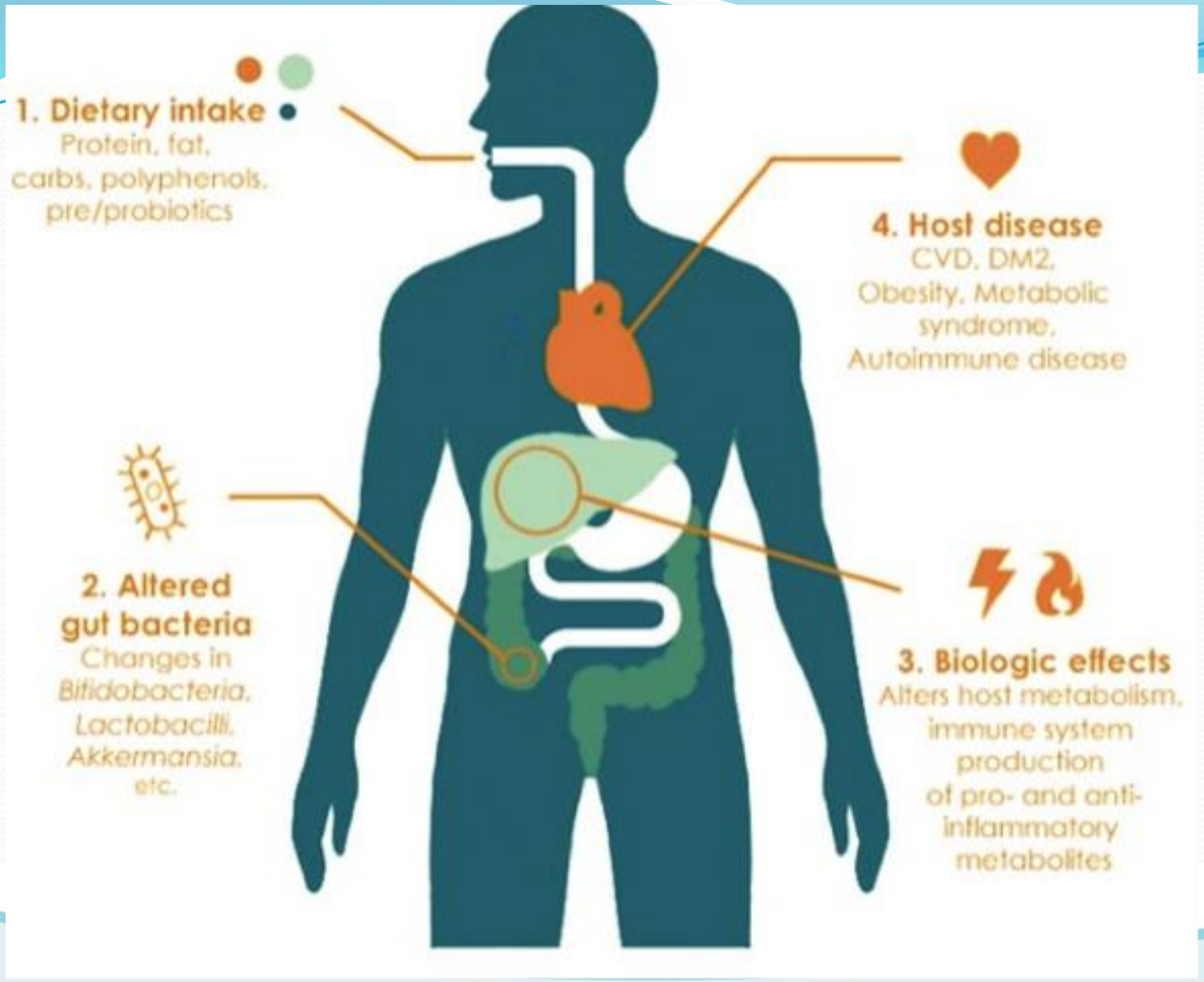
Step count targets were independent of:

Sex

Device wear location (wrist vs hip)

Additional health benefits with higher step cadence, irrespective of total step count

Stens NA, et al. J Am Coll Cardiol. 2023;82(15):1483-1494.


1. Dietary intake
Protein, fat, carbs, polyphenols, pre/probiotics
2. Altered gut bacteria
Changes in Bifidobacteria, Lactobacilli, Akkermansia, etc.
3. Biologic effects
Alters host metabolism, immune system production of pro- and anti-inflammatory metabolites
4. Host disease
CVD, DM2, Obesity, Metabolic syndrome, Autoimmune disease

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Heart & Vascular

CENTER FOR Prevention

We want to help you on your journey towards heart healthy living

MEET THE TEAM

Nurtrition and Exercise
Teaching Kitchen
Personalized Exercise and Nutrition Plans

Providers
Doctors, Pharmacists, Advanced Practice Providers

Coaching & Social Support
Health Coaches and Social Workers

Research
Access to new clinical trials

Who Can We Help?

- **Family history of early CV disease**
- **Elevated coronary calcium score**
- **Multiple Uncontrolled CV Risk Factors:**
  - Obesity
  - Hypertension
  - Hyperlipidemia
  - Diabetes
  - Pre-eclampsia
  - Premature menopause
  - Autoimmune disease
  - Tobacco Use

MedCenter Greensboro
3518 Drawbridge Pkwy, Greensboro, NC 27410

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Prevention Clinic

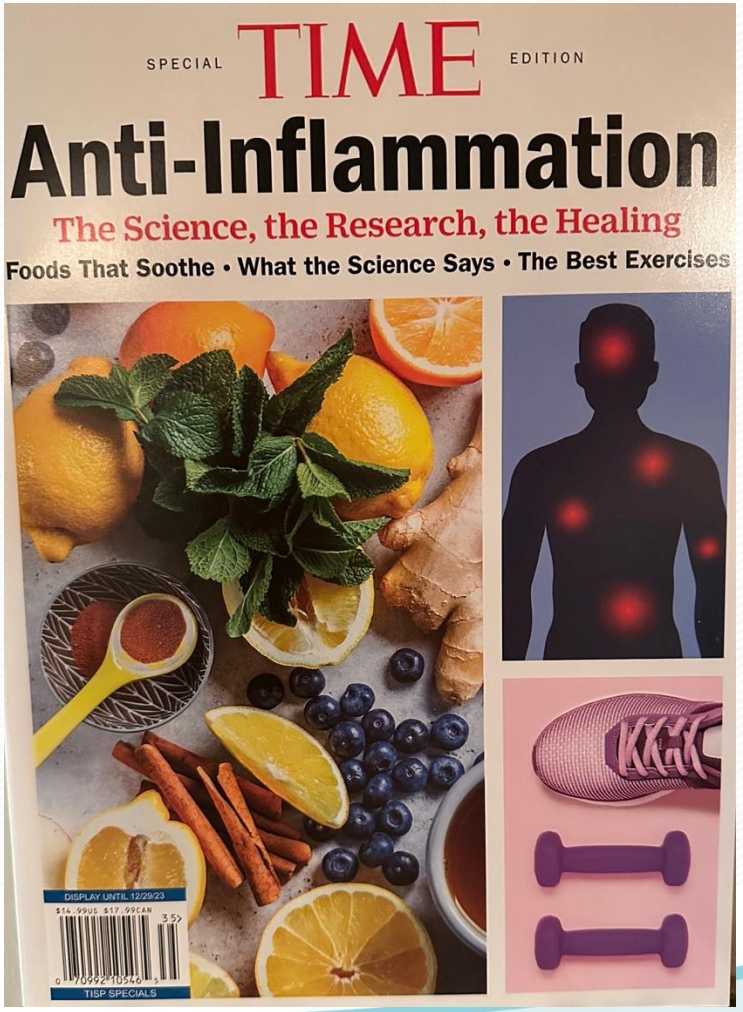
- Provides organized staff with expertise
- Focal point for patients and referring physicians
- Creates a one stop shop for access to innovative protocols
- Organizes referrals for complex patients
- Allows for group teaching of critical elements – dieticians, kitchens, group lessons
- Ideal entity for philanthropic support
- Higher percentage of patients at target
- mechanism to address primary prevention without occupying expert time

The New England
Journal of Medicine

VOLUME 343 AUGUST 24, 2000 NUMBER 8

EFFECTS OF ESTROGEN REPLACEMENT ON THE PROGRESSION OF CORONARY-ARTERY ATHEROSCLEROSIS

DAVID M. HERRINGTON, M.D., M.H.S., DAVID M. REBOUSSIN, PH.D., K. BRIDGET BROSNIHAN, PH.D., PENNY C. SHARP, ED.D., SALLY A. SHUMAKER, PH.D., THOMAS E. SNYDER, M.D., CURT D. FURBERG, M.D., PH.D., GLEN J. KOWALCHUK, M.D., THOMAS D. STUCKEY, M.D., WILLIAM J. ROGERS, M.D., DAVID H. GIVENS, M.D., AND DAVID WATERS, M.D.



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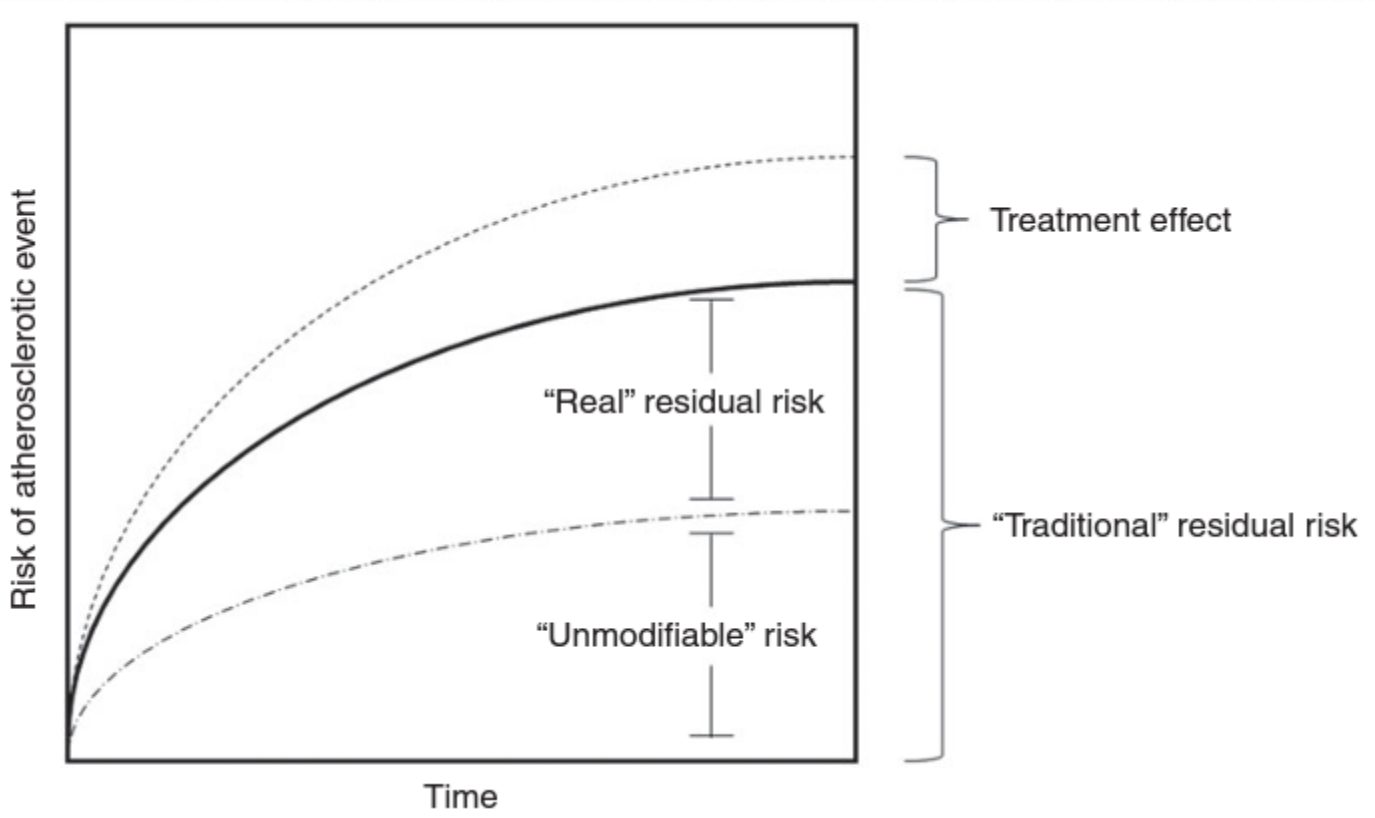
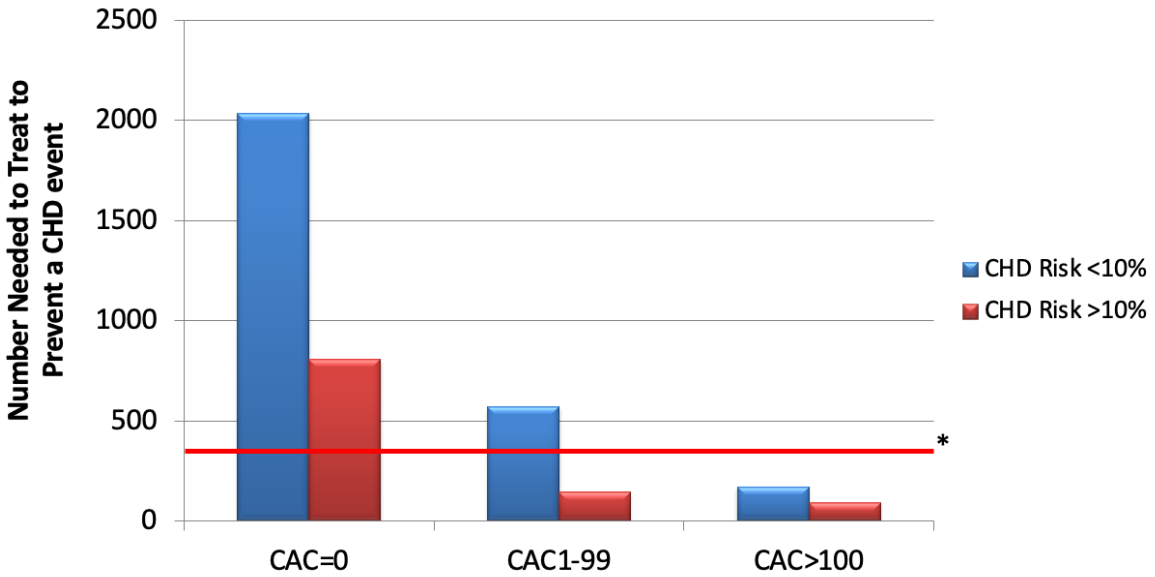
Addressing Residual Risk After Statin Treatment



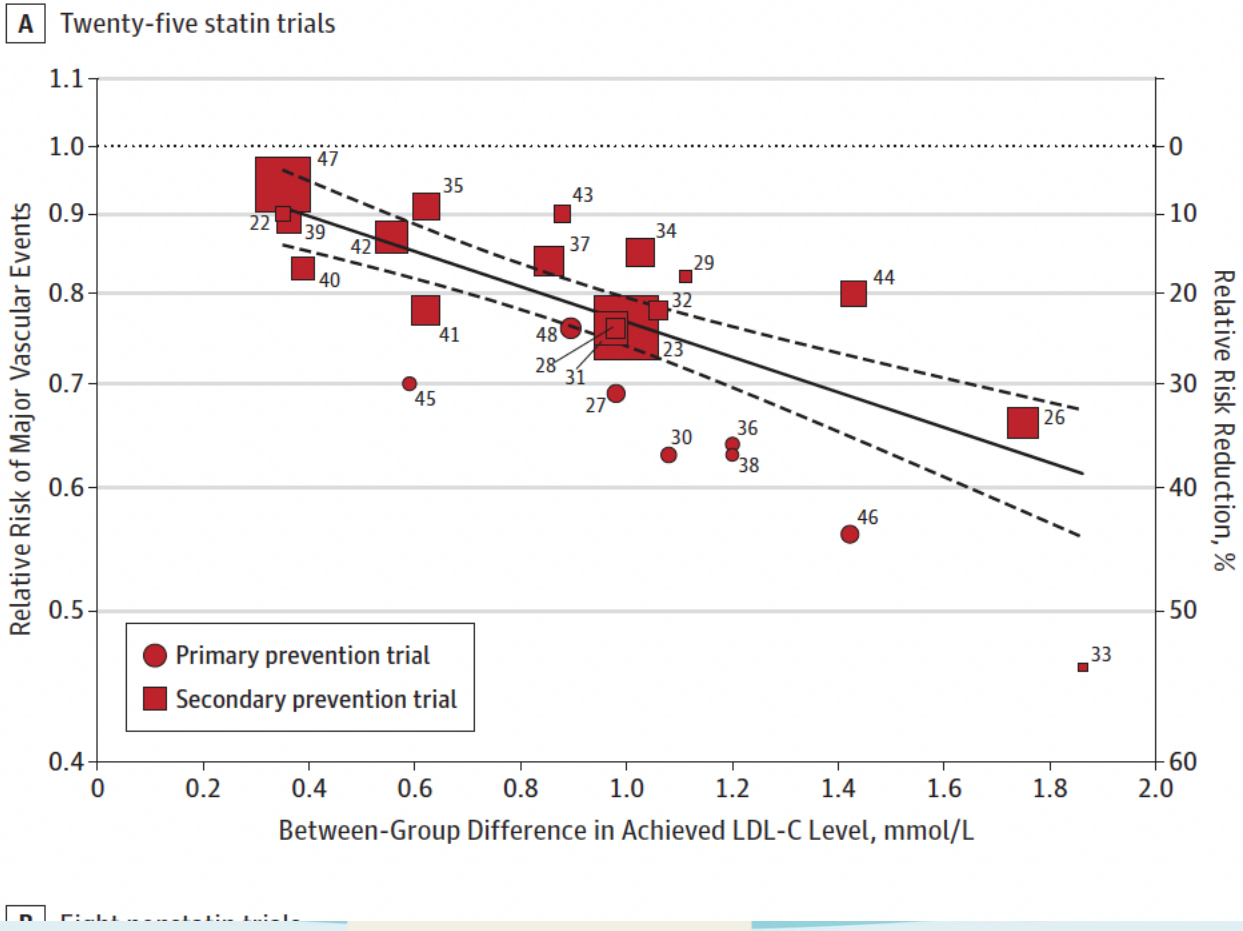
Risk/Benefits of ASA According to CAC



* Represents number needed to harm for a major bleeding event

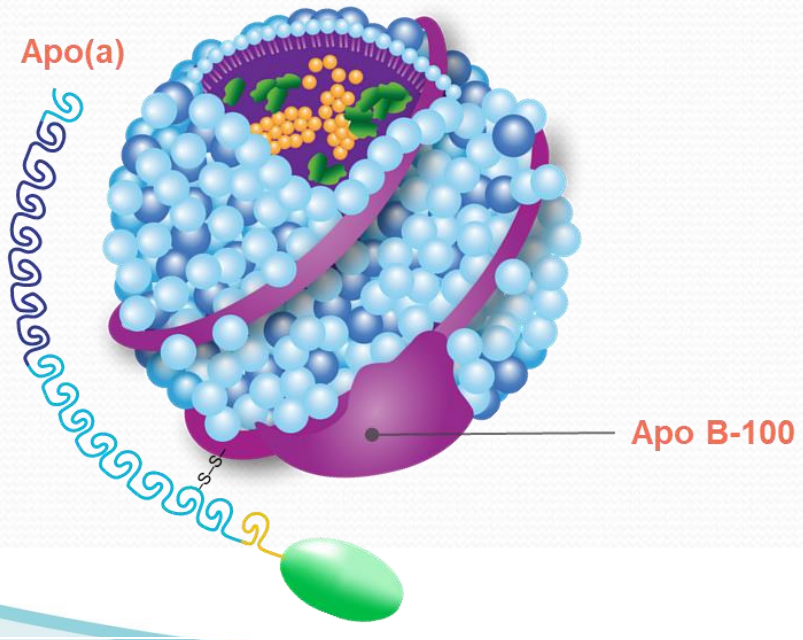
Miedema et al. ASA and CAC – Circ Quality 2014

Figure 2. Association of Between-Group Difference in Achieved Low-Density Lipoprotein Cholesterol (LDL-C) Levels and Risk of Major Vascular Events



Silverman et al. JAMA.2016;316(12):1289-1297.

Lipoprotein A - A Sleeper



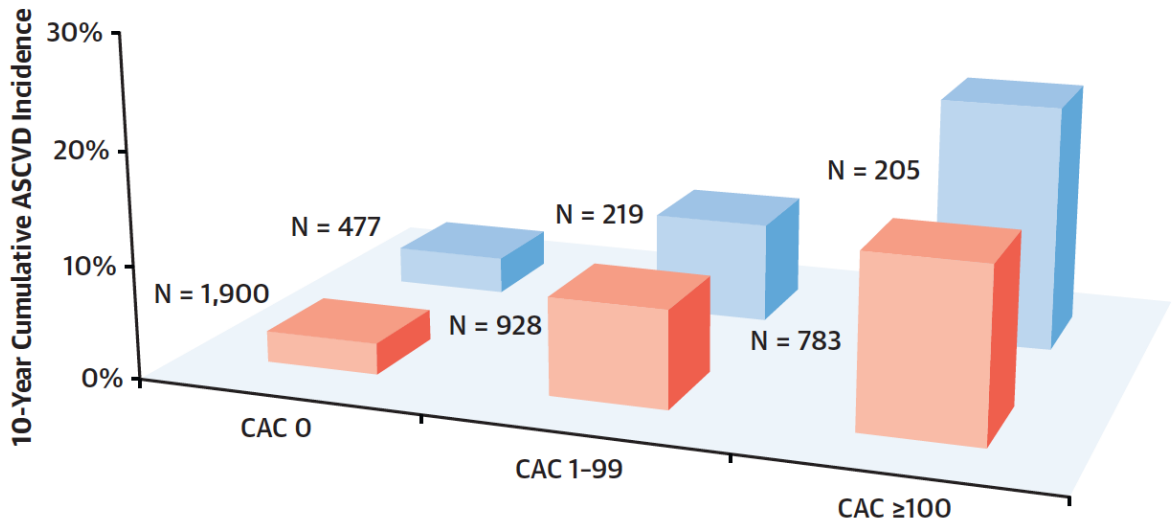
- More than 1.4 million individuals worldwide
- More than 70 million Americans
- 70-90% of the level is under genetic control
- Lifestyle and diet have no impact on this risk

LP(a) Recommendation

- "It is absolutely crucial that patients have their LP(a) level measured, particularly those with premature cardiovascular disease or strong family histories…..almost everybody should now have LP(a) measured, probably in their twenties, to know if they are at risk for ASCVD and can get proper guidance"

Multi-Ethnic Study of Atherosclerosis/Dallas Heart Study

FIGURE 1 10-Year ASCVD Incidence Across Lp(a) (Quintiles 1-4, Quintile 5) and CAC (0, 1-99, ≥100) Groups



	CAC 0	CAC 1-99	CAC ≥100
Lp(a) Quintile 5	3.4% (1.7%-5.0%)	9.0% (5.0%-13.0%)	22.0% (15.9%-28.0%)
Lp(a) Quintiles 1-4	2.8% (2.0%-3.6%)	8.6% (6.7%-10.6%)	15.1% (12.5%-17.8%)

Lp(a) Quintile 5 Lp(a) Quintiles 1-4

The highest 10-year atherosclerotic cardiovascular disease (ASCVD) incidence among MESA (Multi-Ethnic Study of Atherosclerosis) participants was seen in the lipoprotein(a) [Lp(a)] quintile 5 with coronary artery calcium (CAC) ≥100 group, while the lowest 10-year ASCVD incidence was seen in the Lp(a) quintiles 1 to 4 with the CAC = 0 group. A higher 10-year ASCVD incidence was apparent in the Lp(a) quintile 5 group when compared with Lp(a) quintiles 1 to 4 group only among participants with CAC ≥100.

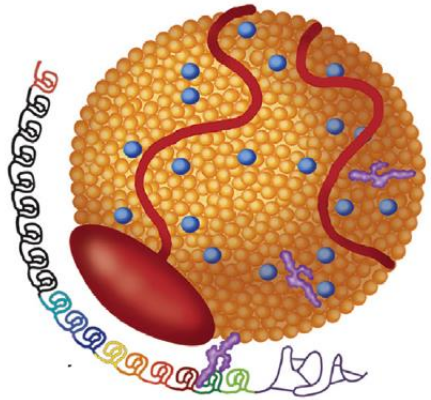
Mehta et al. J Am Coll Cardiol 2022;79:757-68

CENTRAL ILLUSTRATION Lipoprotein(a) Is Associated With Adverse Plaque Progression

191 Patients With Advanced Multivessel Coronary Artery Disease on Long-Term Guideline-Directed Preventive Therapies

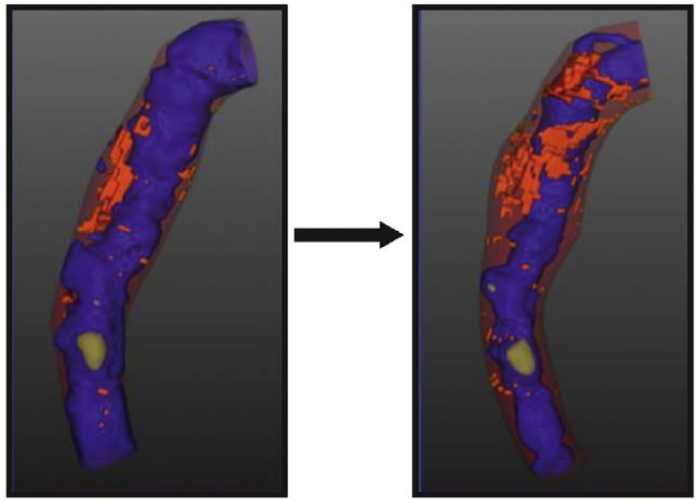
Lp(a) Measurement

Example patient Lp(a) concentration: 82.2 mg/dL



Repeat CCTA to Assess Plaque Progression

Low-attenuation plaque volume (orange regions) increased from 81.4 mm^3 to 132.9 mm^3



Elevated lipoprotein(a) is associated with accelerated progression of low-attenuation plaque, independent of traditional cardiovascular risk factors

Kaiser, Y. et al. J Am Coll Cardiol. 2022;79(3):223-233.

1.4 Billion Worldwide, More than 70 million Americans

Kaiser et al. J Am Coll Cardiol 2022;79:223-33

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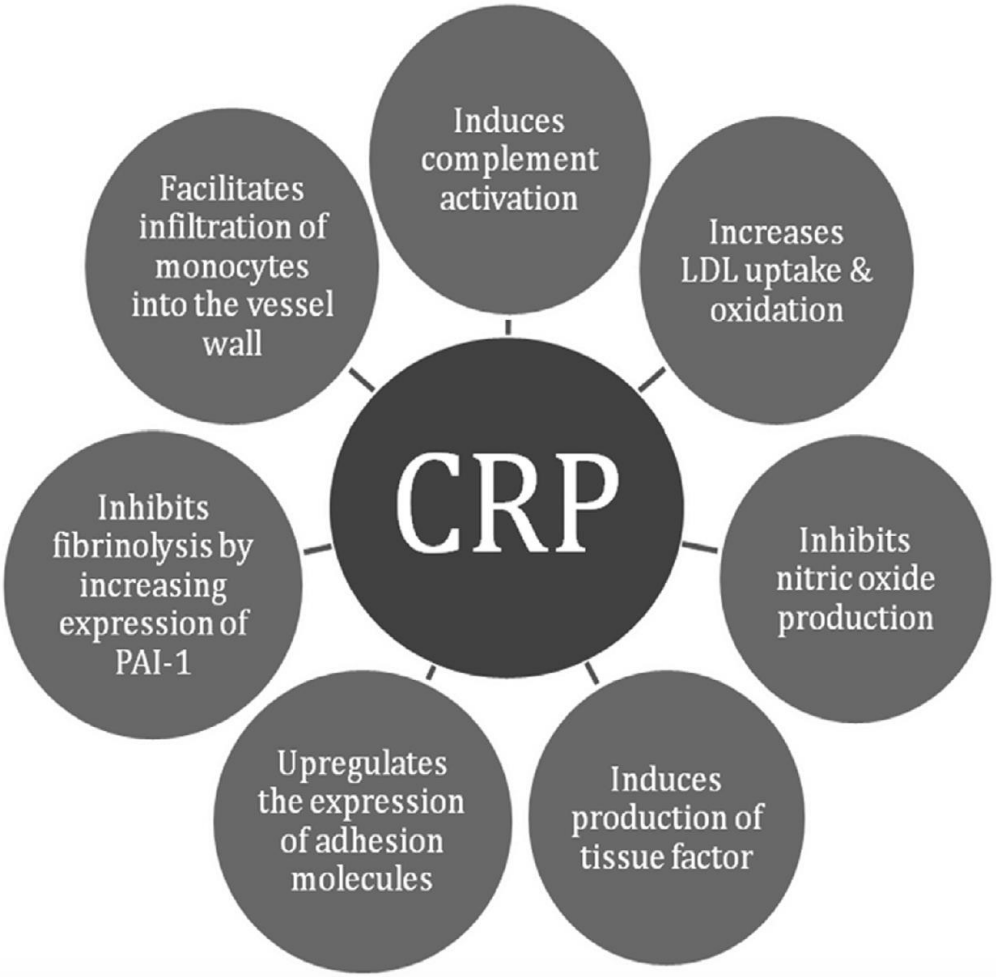
C-reactive protein, inflammation and coronary heart disease



Shrivastava et al. The Egyptian Heart Journal (2015) 67, 89–97

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Other Cardiac Risk Factor Targets

- Hypertension
- Obesity
- Triglyceride Rich Lipoproteins
- Smoking

Therapeutics

Before open label drug

Month after 1 dose of open label drug

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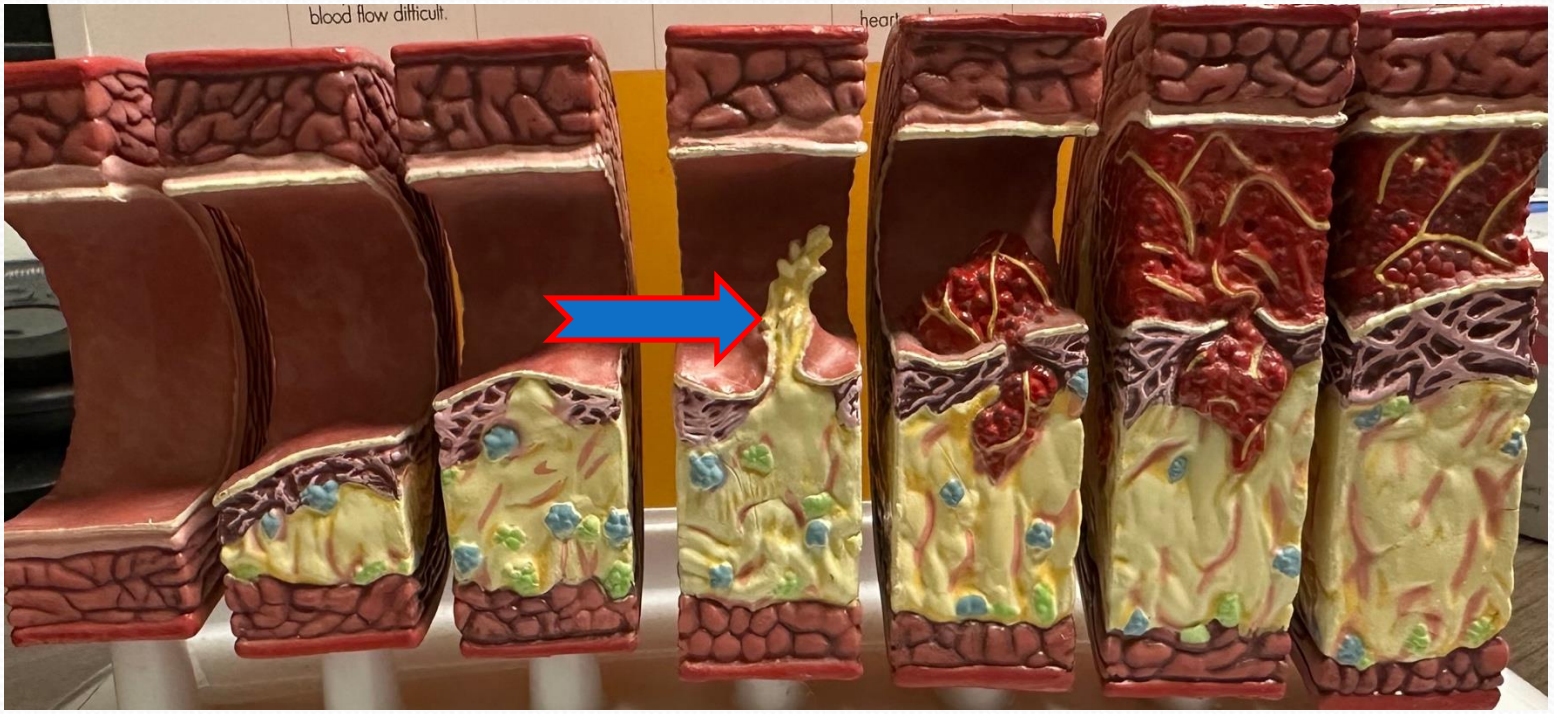
How does a Garden Variety Heart Attack Happen?
Plaque Rupture



Statins shrink the plaque and toughen up the surface lining. Aspirin reduces the potential for a clot

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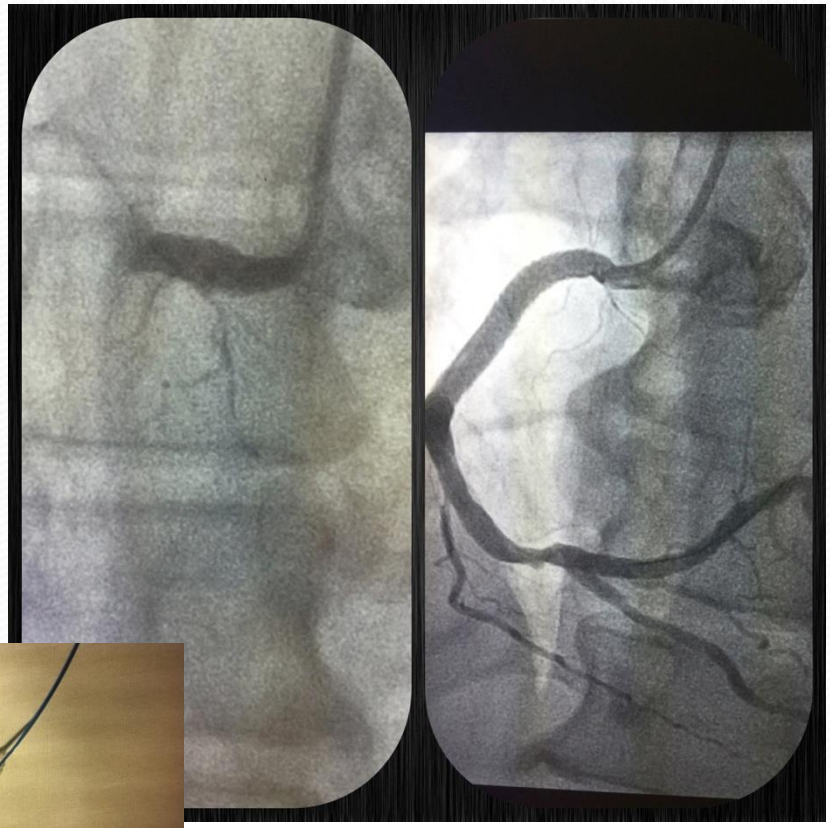
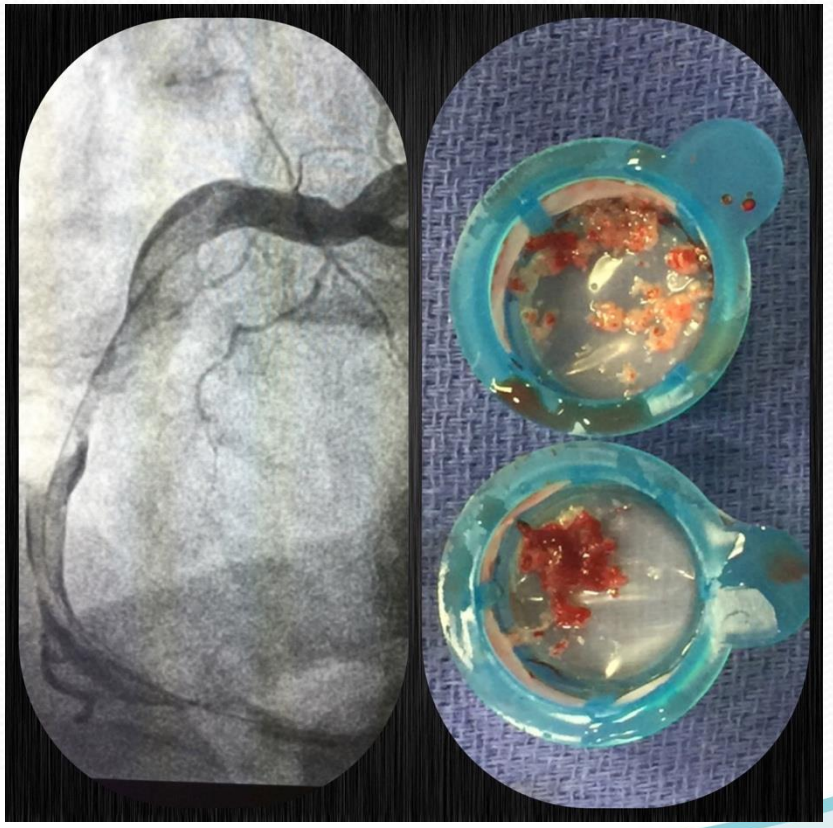
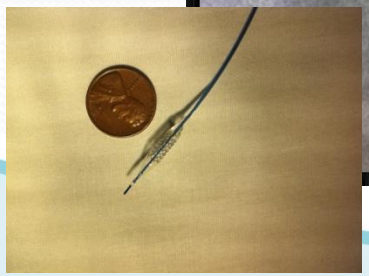
Garden Variety Heart Attack







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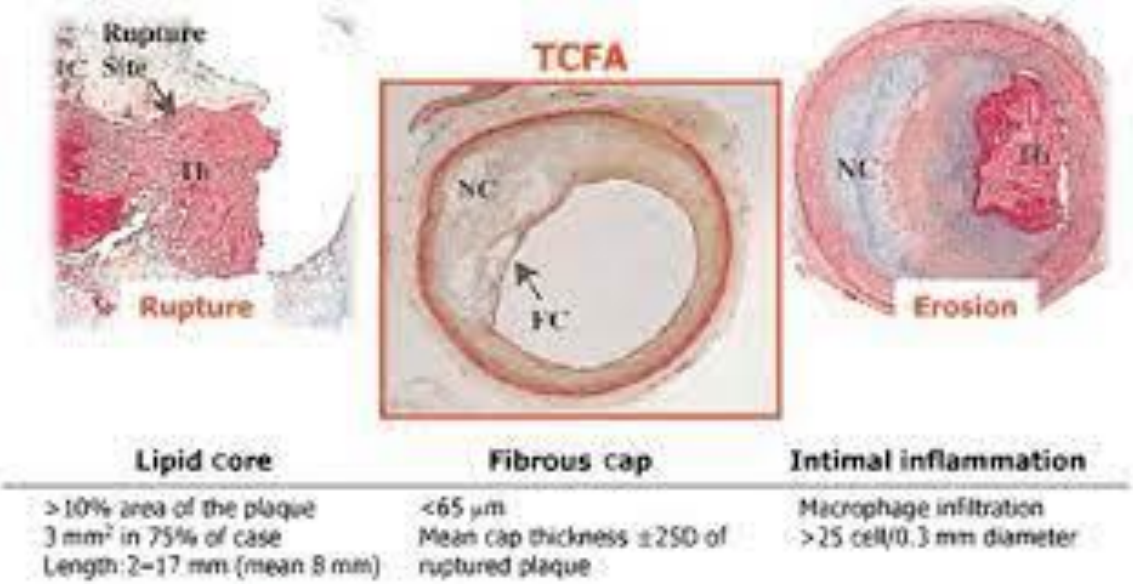
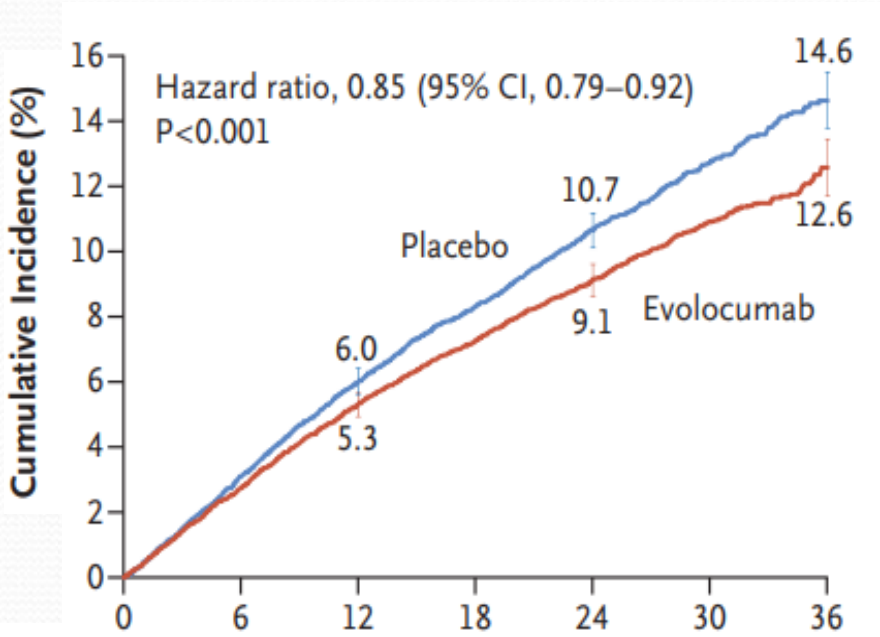
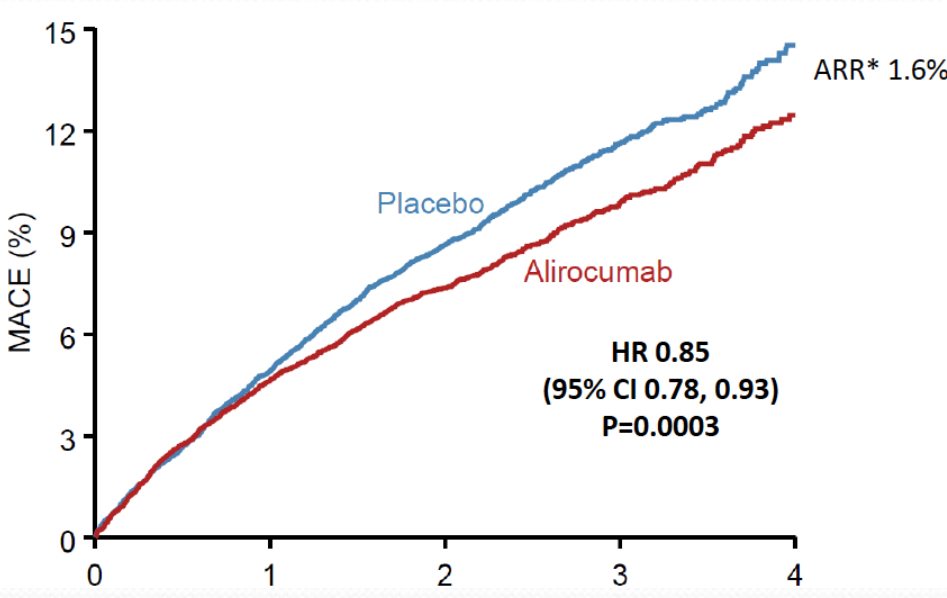
The Vulnerable Plaque



Thomas D. Stuckey, MD, FACC, FSCAI
Medical Director, LeBauer-Brodie Center
Clinical Professor of Medicine, UNC

PCSK-9 Inhibitors and Outcomes

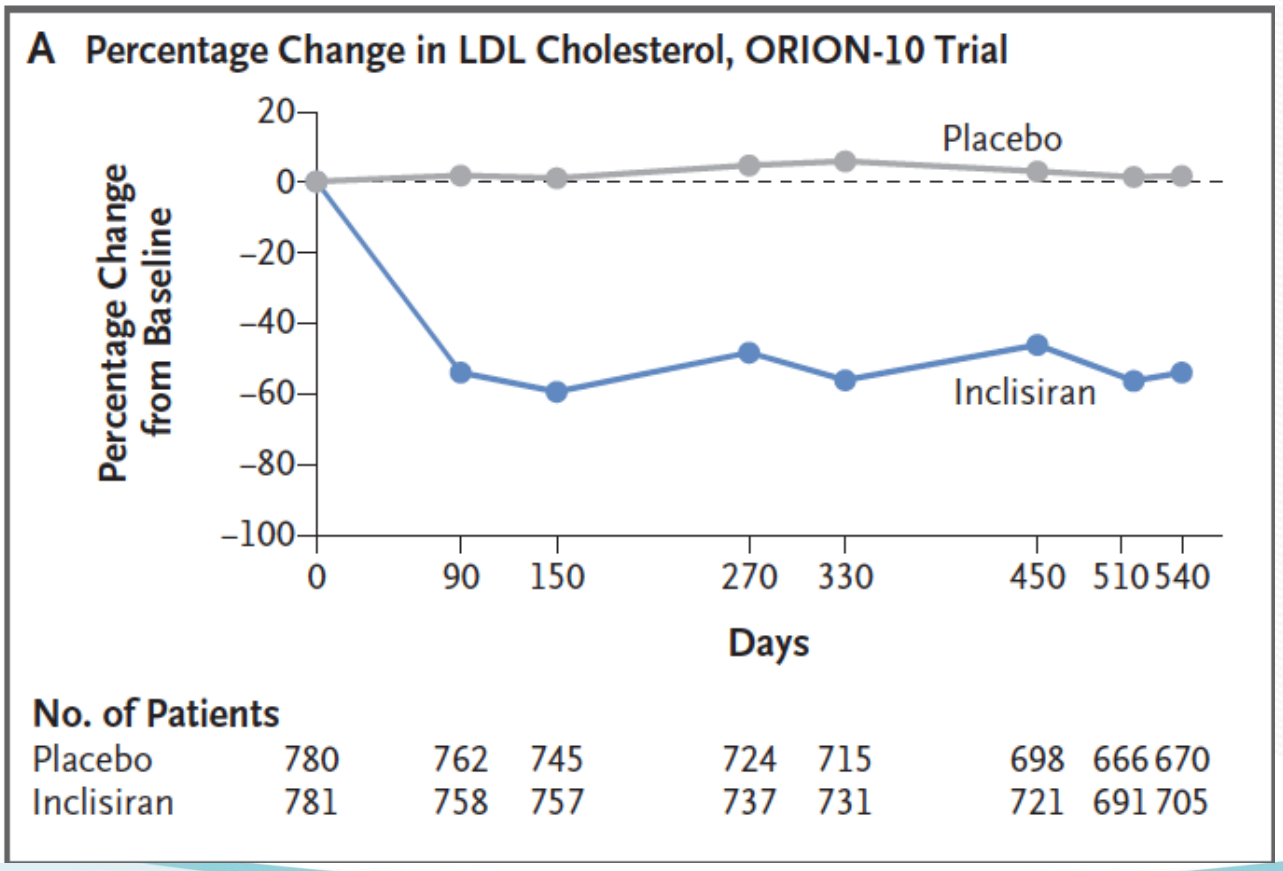




Sabatine MS et al. N Engl J Med 2018
Schwartz GG et al. N Engl J Med 2018

Pharmacologic Intervention with SiRna for LDL

Inclisiran



Ray et al. N Eng J Med 2020;382:1507-19.

PACMAN-AMI

JAMA | Original Investigation

Effect of Alirocumab Added to High-Intensity Statin Therapy on Coronary Atherosclerosis in Patients With Acute Myocardial Infarction The PACMAN-AMI Randomized Clinical Trial

Lorenz Räber, MD, PhD; Yasushi Ueki, MD, PhD; Tatsuhiko Otsuka, MD; Sylvain Losdat, PhD; Jonas D. Häner, MD; Jacob Lonborg, MD; Gregor Fahrni, MD; Juan F. Iglesias, MD; Robert-Jan van Geuns, MD, PhD; Anna S. Ondracek, MSc; Maria D. Radu Juul Jensen, MD, PhD; Christian Zanchin, MD, PhD; Stefan Stortecky, MD; David Spirk, MD; George C. M. Siontis, MD, PhD; Lanja Saleh, PhD; Christian M. Matter, MD; Joost Daemen, MD, PhD; François Mach, MD; Dik Heg, PhD; Stephan Windecker, MD; Thomas Engstrøm, MD, PhD; Irene M. Lang, MD; Konstantinos C. Koskinas, MD, MSc; for the PACMAN-AMI collaborators

Raber et al. JAMA 2022;327(18):1771-1781

Patients with AMI (N-STEMI/STEMI) undergoing coronary angiography & successful PCI of the infarct vessel & 2 non-infarct related arteries with angiographic evidence of atherosclerosis (20-50% DS)

Alirocumab PACMANAMI

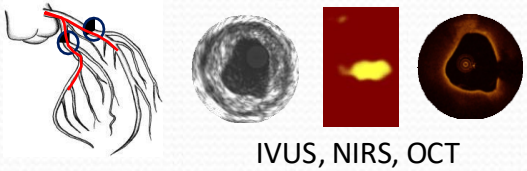
POC

No statin, LDL >125 mg/dL (>3.2 mmol/L)

On Statin, LDL >70 mg/dL (>1.8 mmol/L)

Enrollment of 300 Patients

Baseline



IVUS, NIRS, OCT

Baseline blood sampling

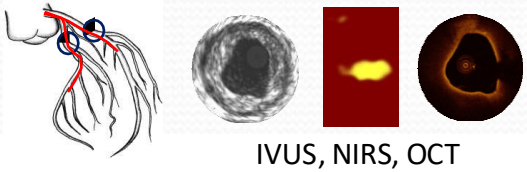
Alirocumab s.c. 150 mg / 2 weeks + Rosuvastatin 20 mg

R 1:1

Placebo s.c. / 2 weeks + Rosuvastatin 20 mg

Initiated <24 hrs after PCI

52 weeks



IVUS, NIRS, OCT

Blood sampling 4 weeks
3 visits, 4 phone calls
Blood sampling 52 weeks

Am Heart J 2021;238:33-44.

ENDPOINTS: Plaque burden, NIRS lipid, cap thickness

Raber et al. JAMA 2022; 327(18):1771-1781

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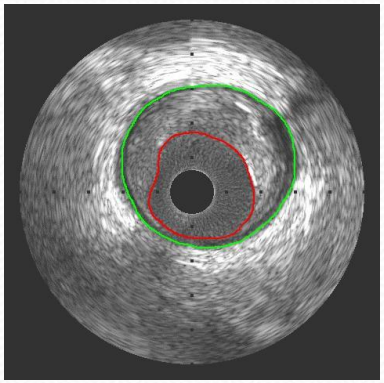
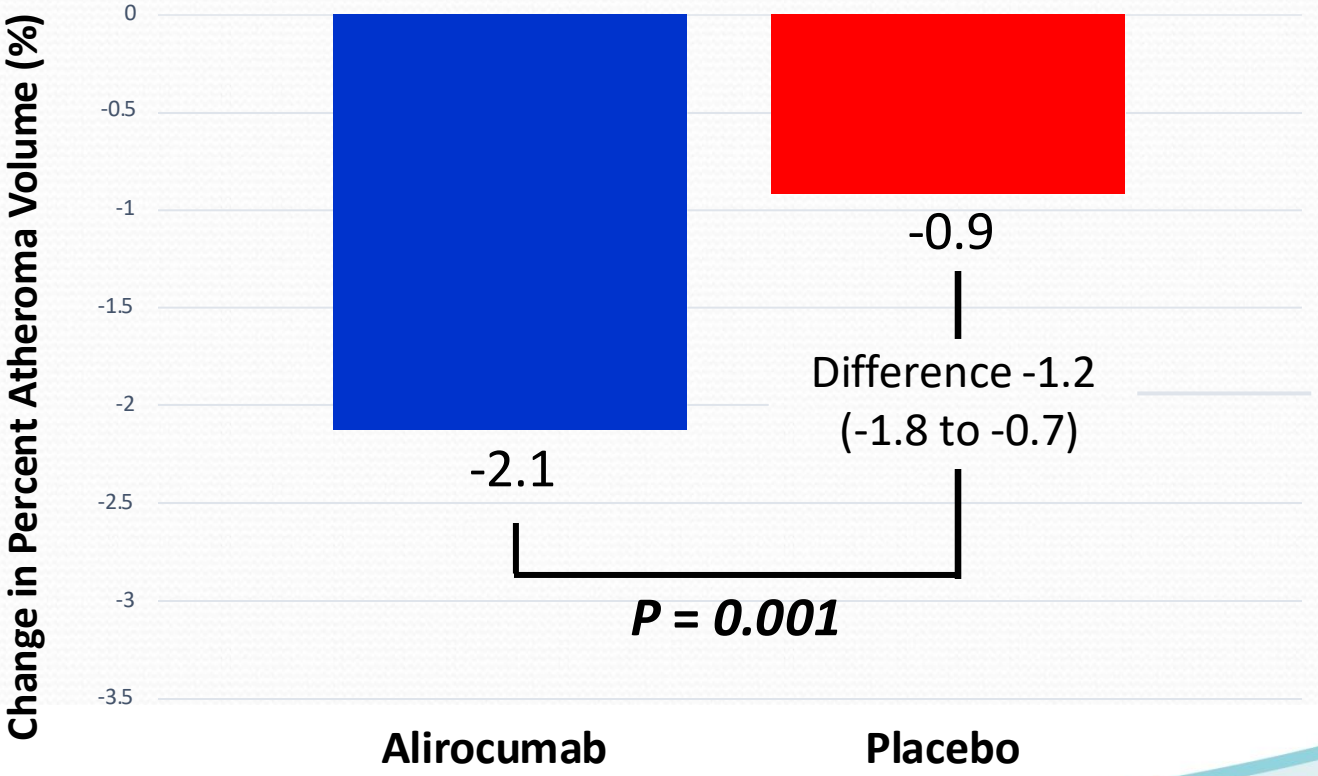
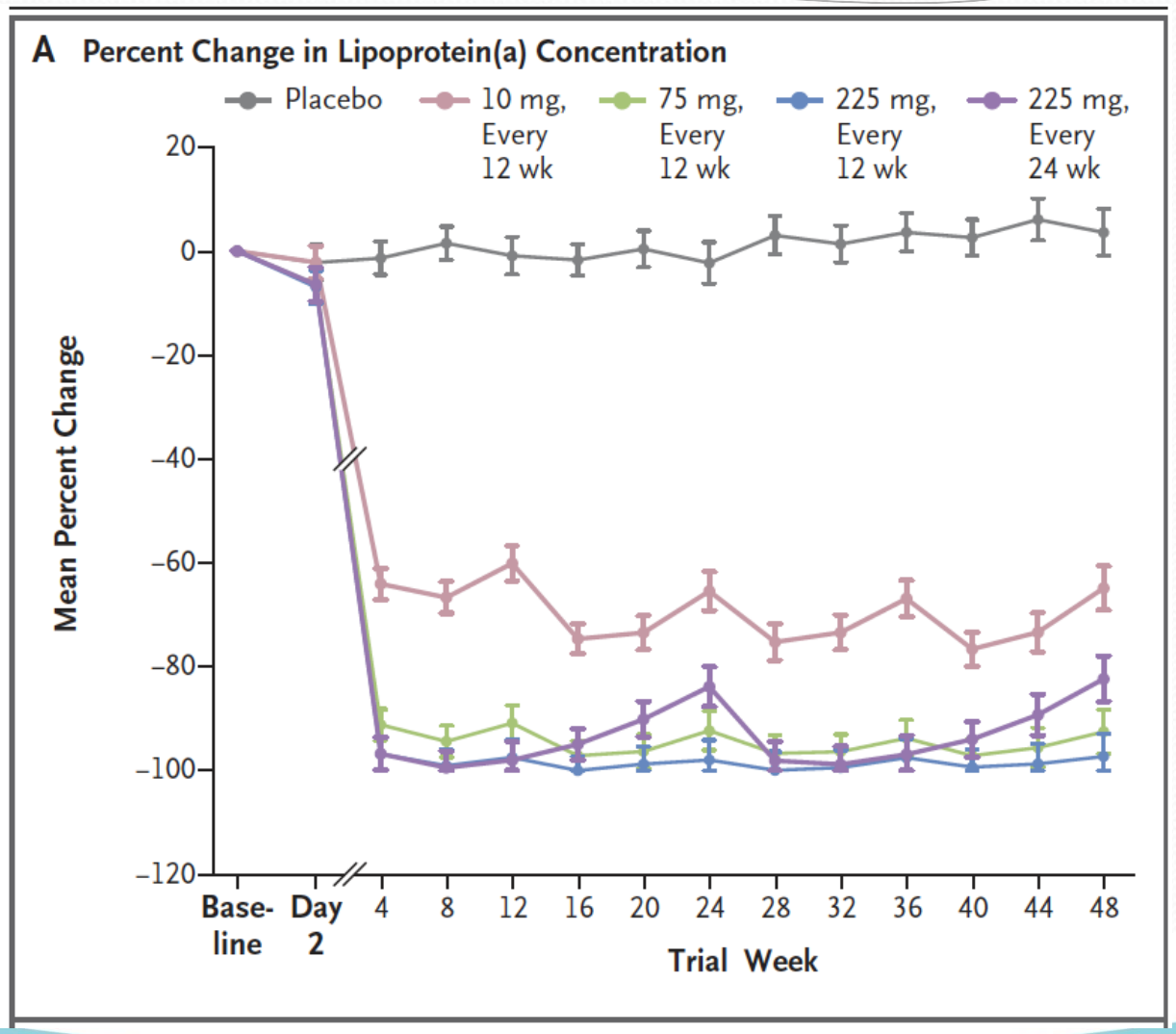
Primary EP:
Change in Percent Atheroma Volume (IVUS)







N Engl J Med 2022;387:1855-64.

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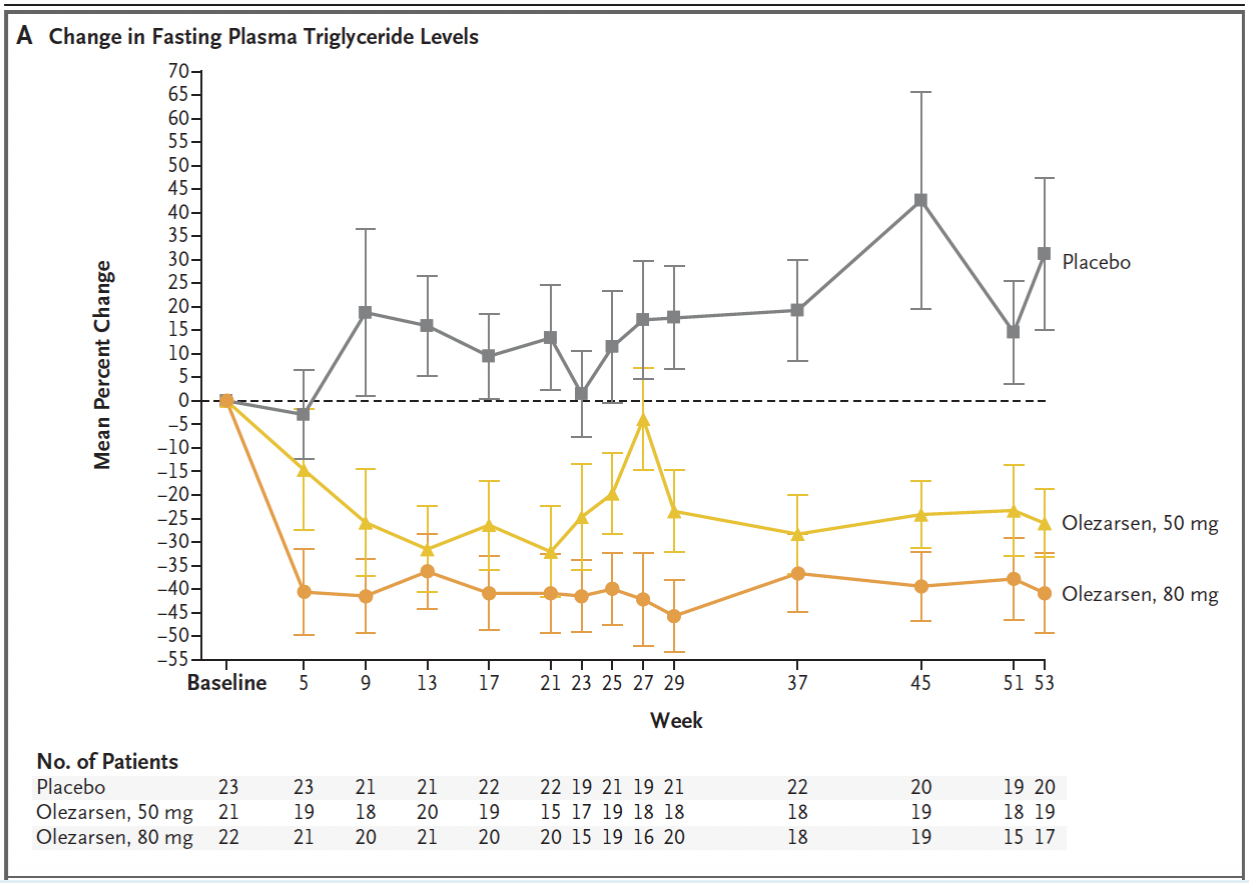
Olezarsen in Familial Chylomicronemia

The NEW ENGLAND JOURNAL of MEDICINE



N Engl J Med 2024;390:1781-92

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Icosapent Ethyl On LAP Regression – Evaporate Trial

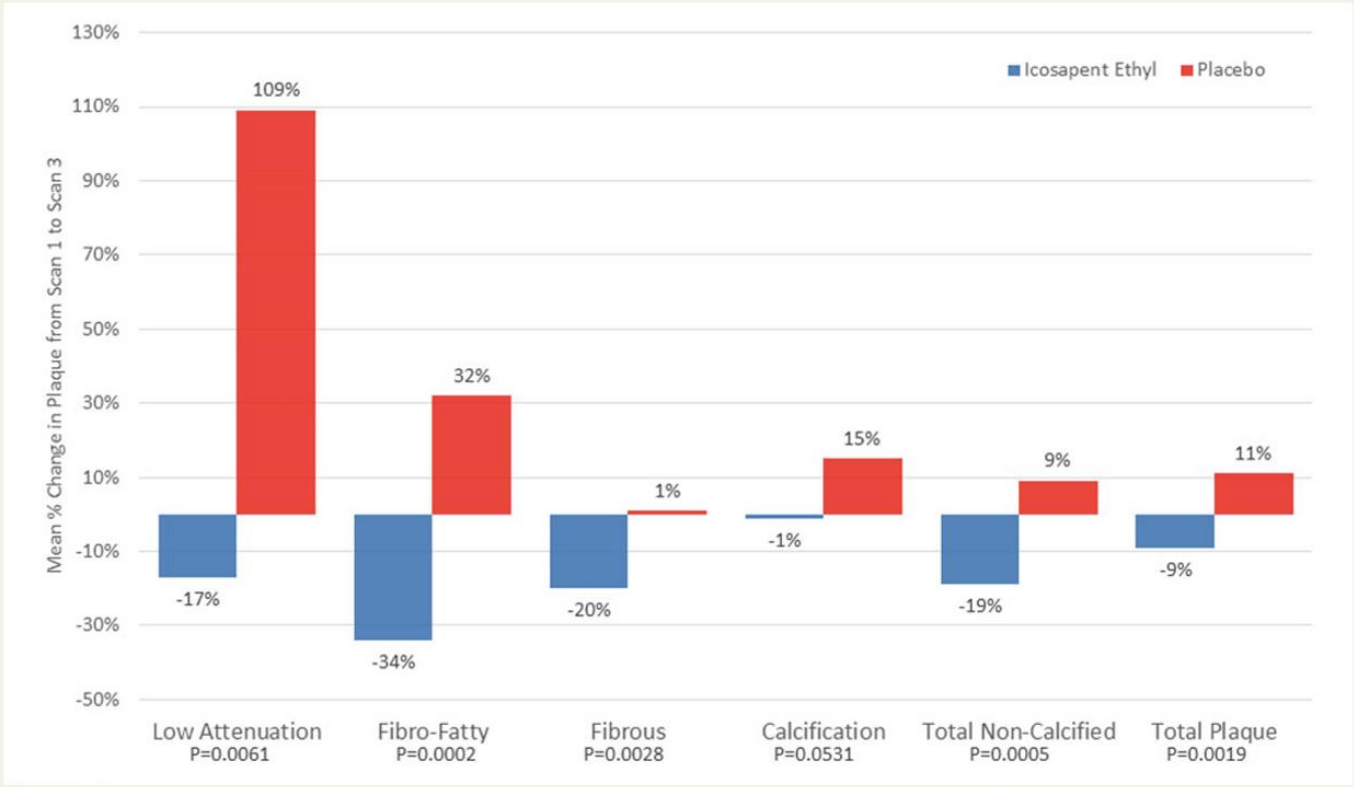

Figure 1 Mean plaque progression for each type of plaque composition measured on cardiovascular CT for the icosapent ethyl and placebo groups (icosapent ethyl group, $n = 31$ and placebo group, $n = 37$) after multivariable adjustment. Univariable analysis and multiple linear regression were used to examine the change in plaque levels between the cohorts. Multivariable models were adjusted by age, sex, diabetes status, hypertension, and baseline triglyceride levels. All statistical analyses report two-sided *P*-values for the outcomes. A *P*-value <0.048 was considered significant for the outcomes.

80 patients
Scanned at
18 months

Budoff et al. EHJ 2020;41:3925-3932

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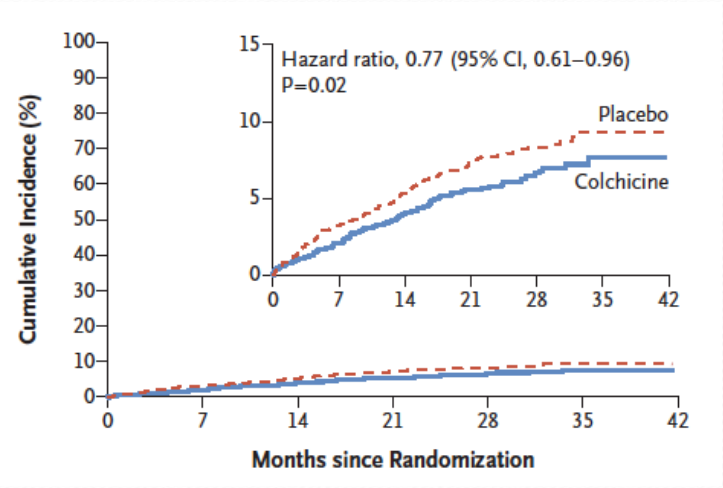
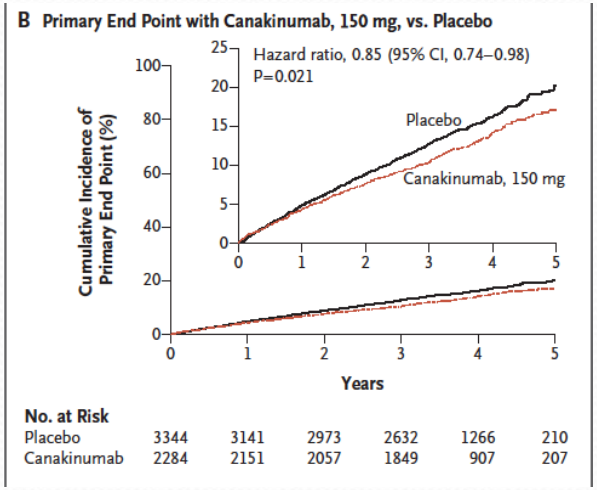
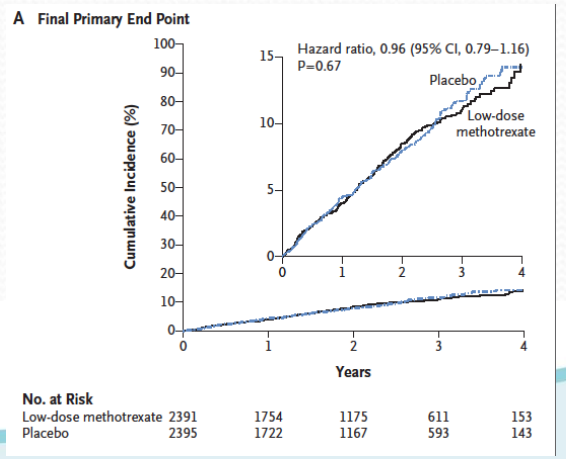
Colchicine, MTX, and Canakinumab





Ridker et al. NEJM 2017; 377:1119-1131.
Tardif et al. NEJM 2019; 381:2497-505
Ridker et al. NEJM 2019;380:752-762



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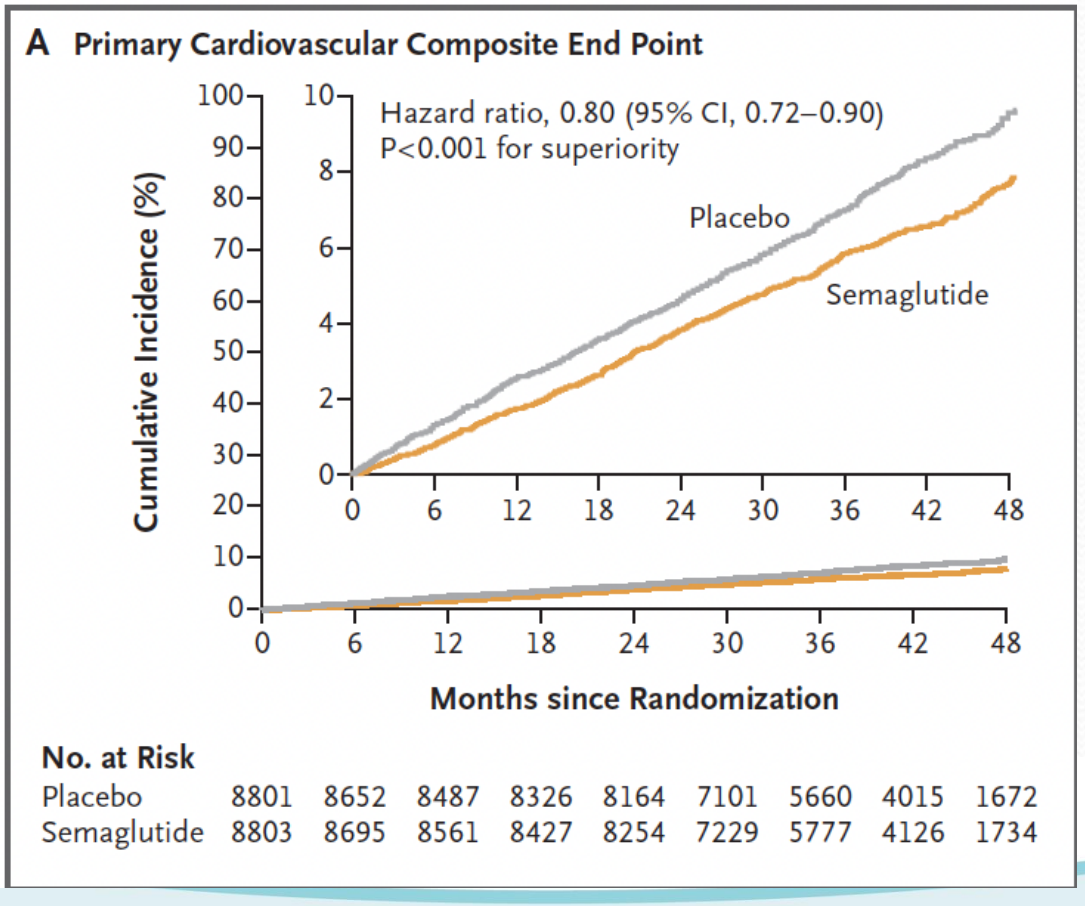
Semaglutide and Cardiovascular Mortality In Patients with Obesity and No Diabetes



Lincoff et all. N Engl J Med 2023;389:2221-32.

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Conclusions

- Vulnerable plaque results in unexpected ACS
- Life style changes are key to a healthy milieu, but multiple unidentified risk factors can elevate risk unexpectedly
- Imaging techniques for vulnerable plaque identification are improving rapidly, and can be obtained non invasively
- Targeted therapeutic options are developing rapidly
- A highly organized, strategic approach to preventive cardiovascular care is needed

THANK YOU