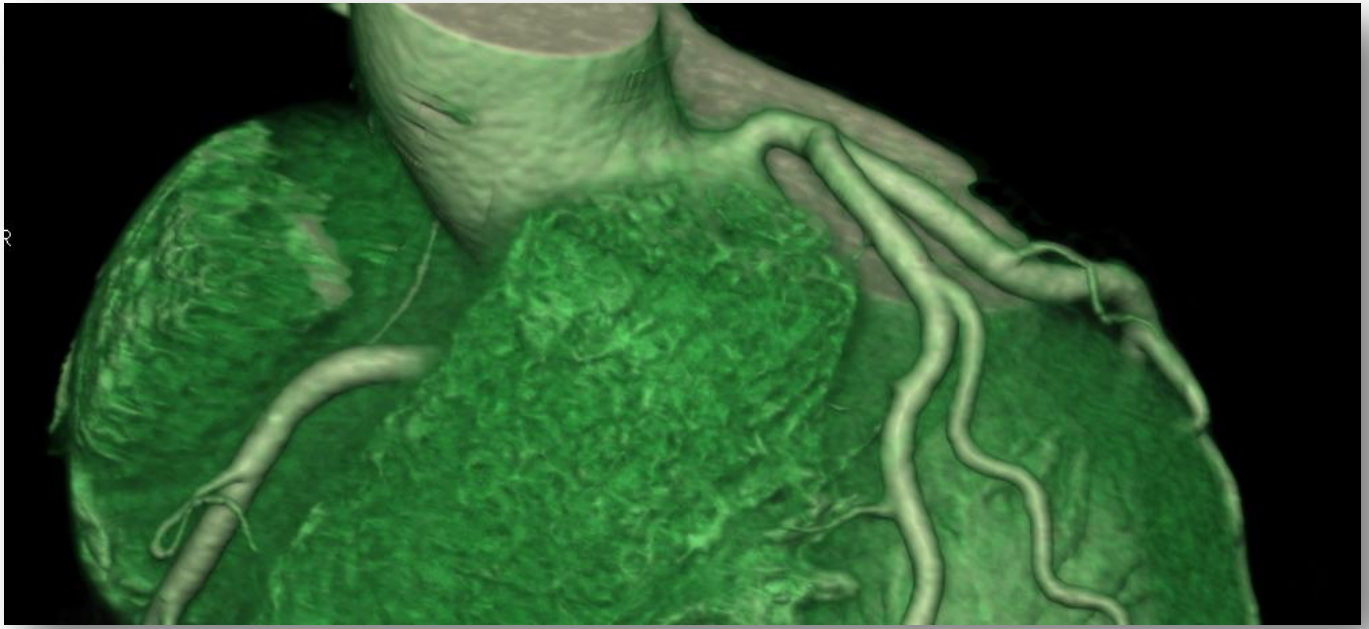
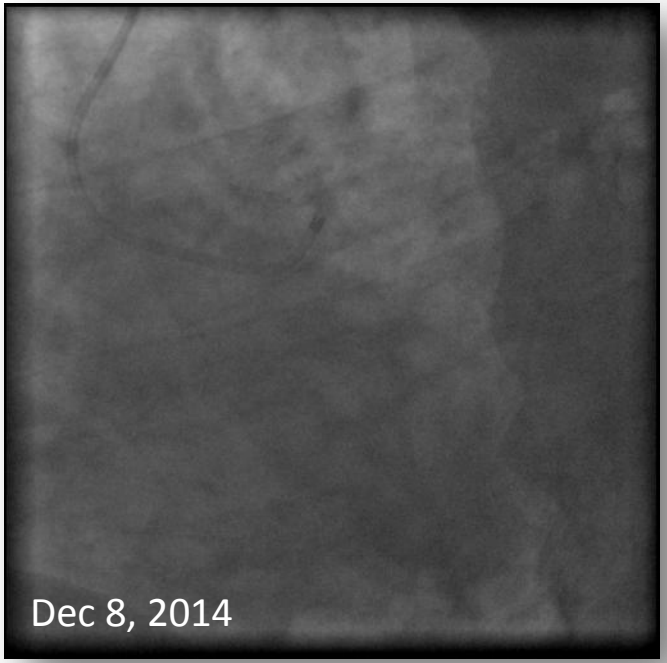
What Cardiac CT can teach us about prevention



Stephan Achenbach, FESC
University of Erlangen, Germany

We all know the problem



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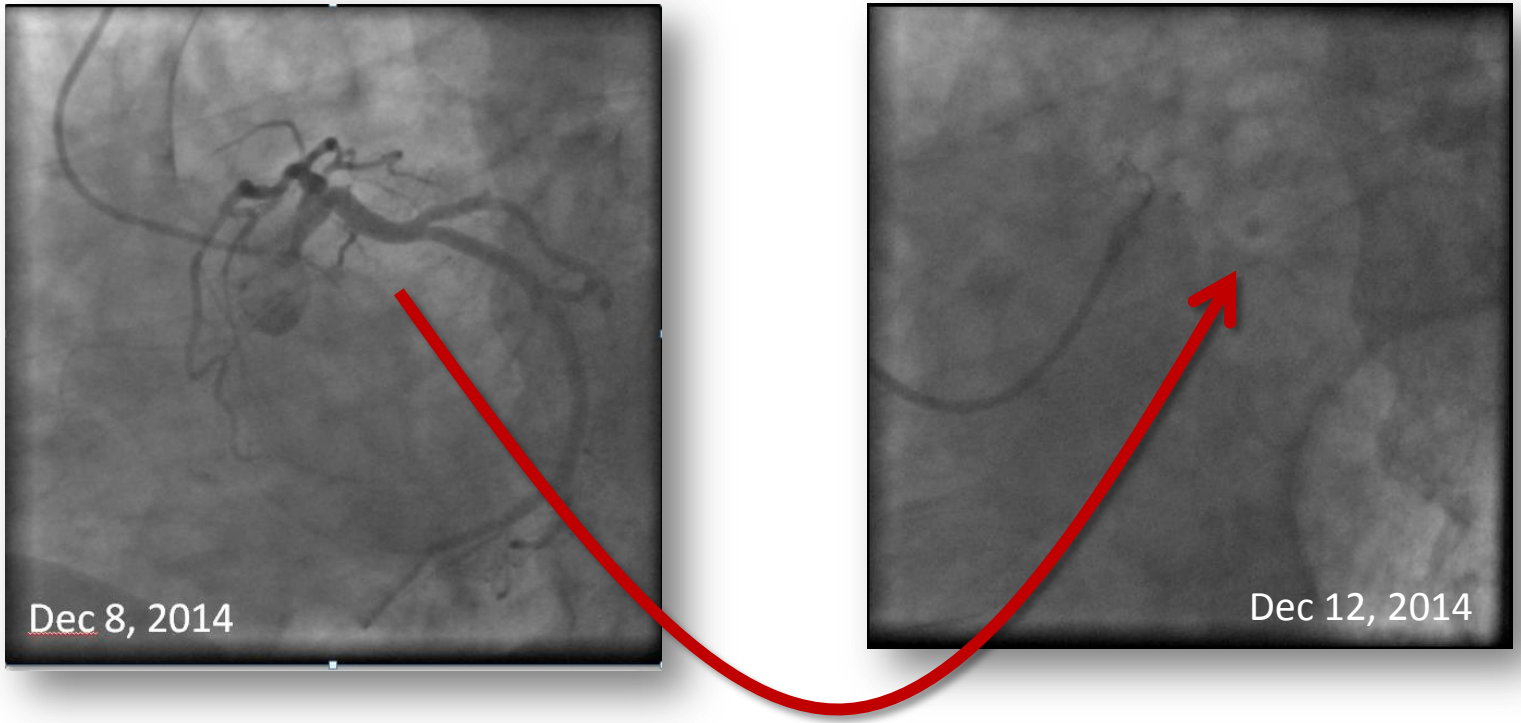
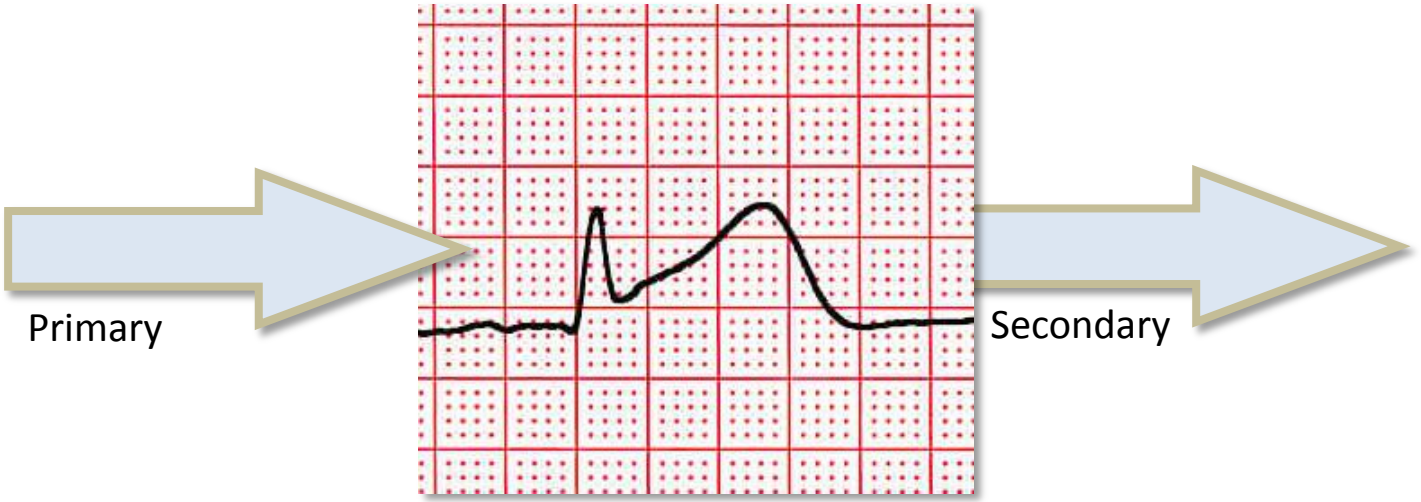


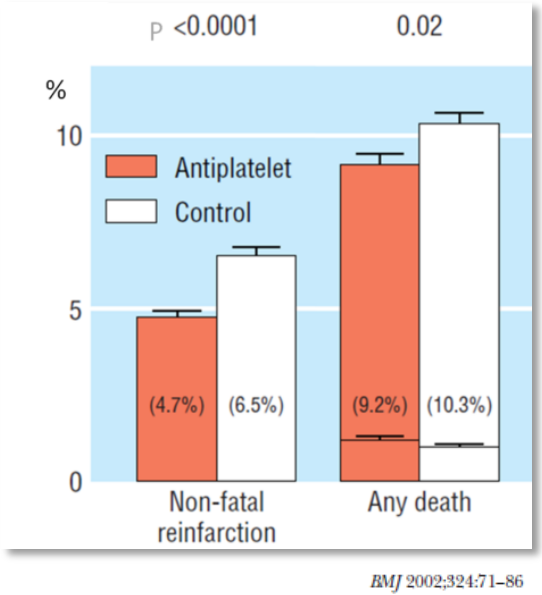
We all know the problem

- Acute coronary syndromes are caused by plaque rupture
- 50% happen suddenly without relevant prior symptoms
- Primary prevention would be important to avoid events and deaths

Prevention



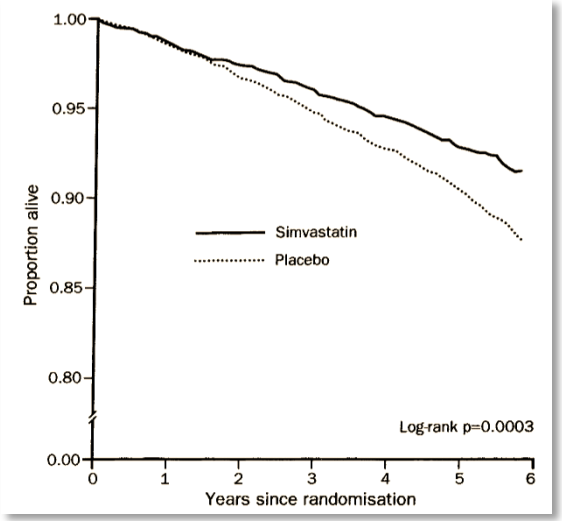
Secondary Prevention



BMJ 2002;324:71–86

Aspirin after MI
(n = 135 000, 2 years)

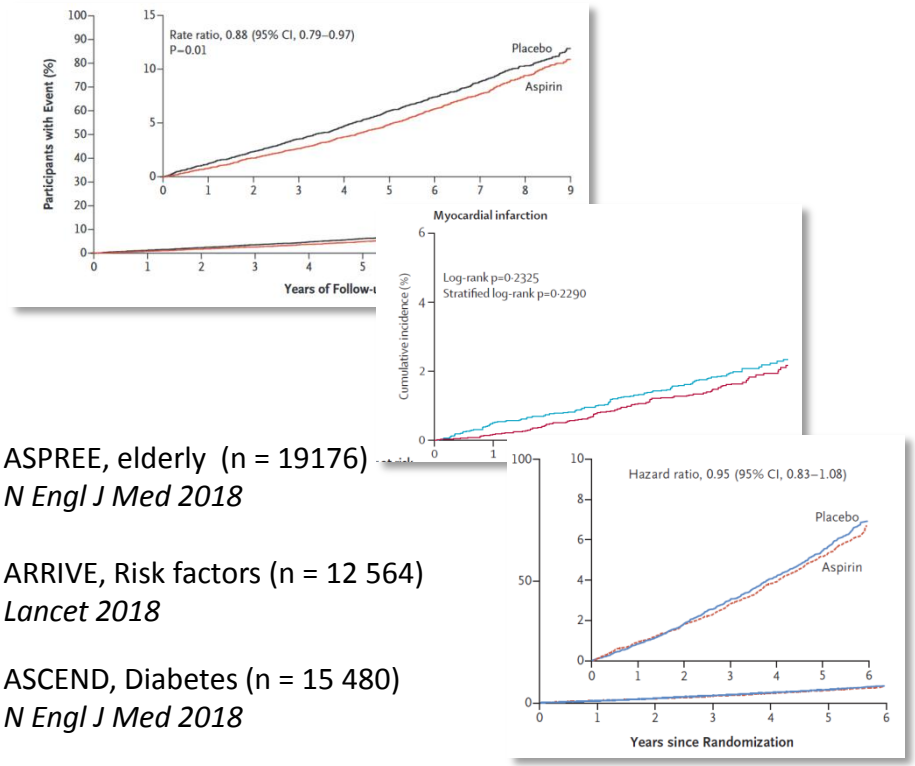
Number needed to treat:
100 for 2 years to prevent 1 death



SSSS: Simvastatin in 4444 patients with MI (80%) or current angina (20%), 5 years

Number needed to treat:
100 for 1.5 years to prevent 1 death

Primary Prevention: Difficult.



ASPREE, elderly (n = 19176)
N Engl J Med 2018

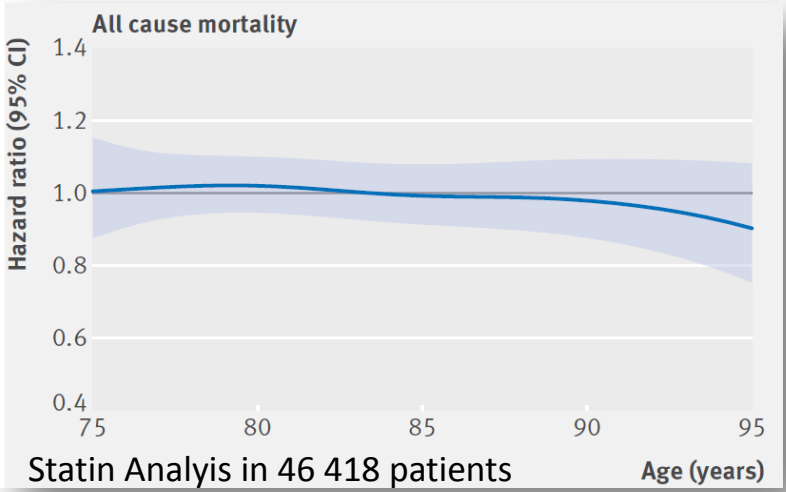
ARRIVE, Risk factors (n = 12 564)
Lancet 2018

ASCEND, Diabetes (n = 15 480)
N Engl J Med 2018

=> No significant net benefit of Aspirin in primary prevention

Statins for primary prevention of cardiovascular events and mortality in old and very old adults with and without type 2 diabetes: retrospective cohort study *BMJ* 2018;362:k3359

Rafel Ramos,[1-4] Marc Comas-Cufí,[1,2] Ruth Martí-Lluch,[1-3] Elisabeth Balló,[1-4] Anna Ponjoan,[1-3] Lia Alves-Cabratosa,[1,2] Jordi Blanch,[1,2] Jaume Marrugat,[5,6] Roberto Elosua,[5,6] María Grau,[5,6] Marc Elosua-Bayes,[1,2] Luis García-Ortiz,[7] Maria Garcia-Gil[2-4]

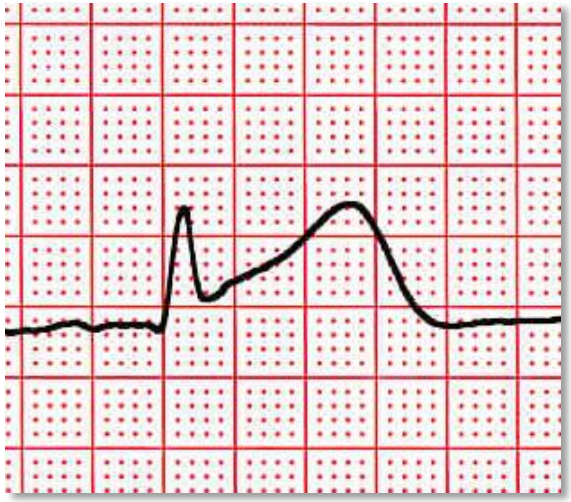


Statin Analyis in 46 418 patients

No mortality benefit of statins in primary prevention

Primary Prevention: Difficult.

Primary prevention would be important to avoid first coronary events



If patients are selected according to risk factors:

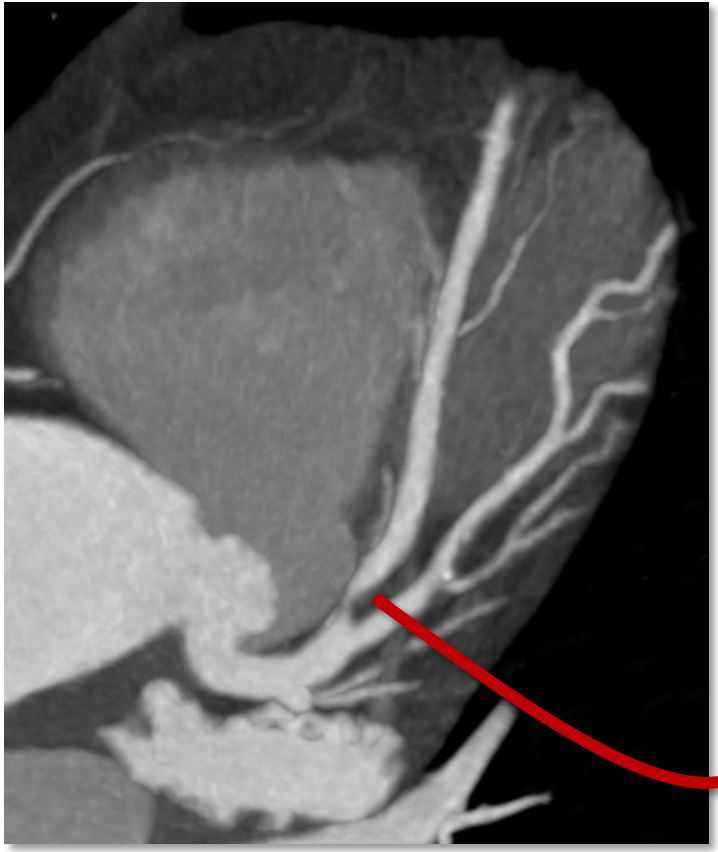
Statins only recommended for high-risk and very-high-risk individuals

Aspirin **not** recommended for primary prevention

Antiplatelet therapy is not recommended in individuals without CVD due to the increased risk of major bleeding.	III	B

2016 European Guidelines on cardiovascular disease prevention in clinical practice

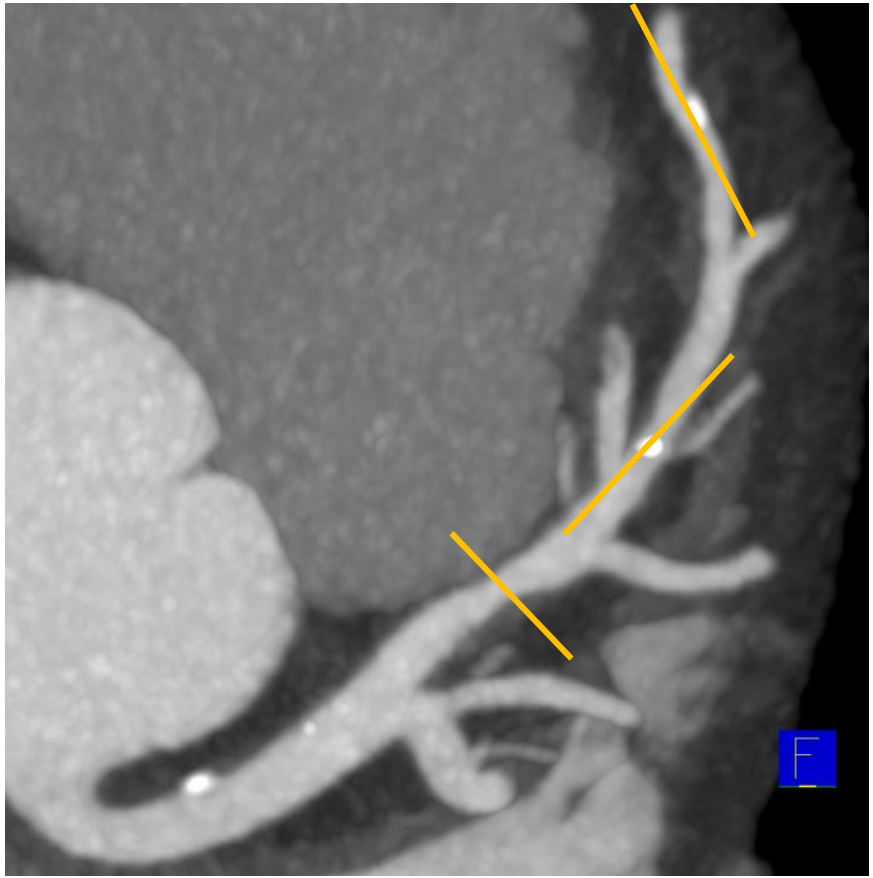
Cardiac Computed Tomography

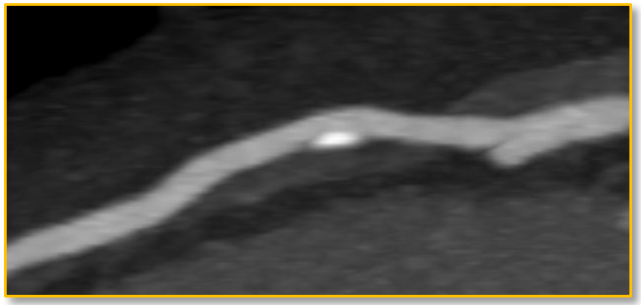


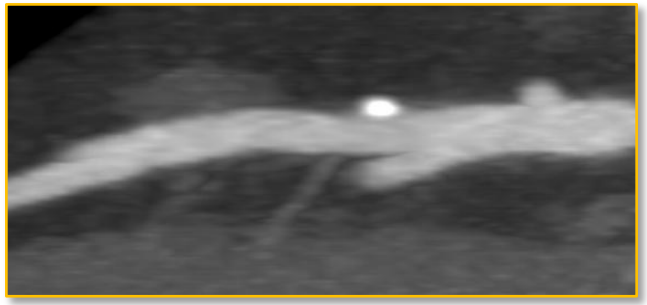
Well established to detect and rule out coronary stenoses

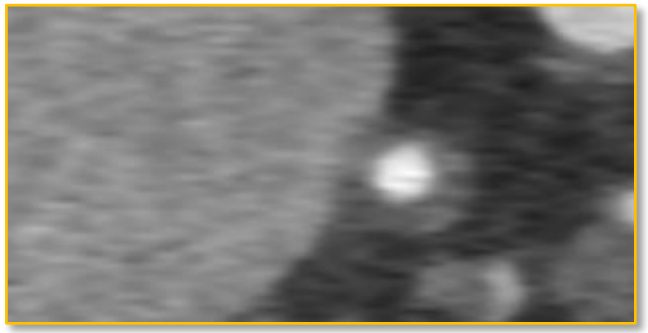
ESC Guidelines:
Suspected CAD
Acute chest pain

Cardiac Computed Tomography

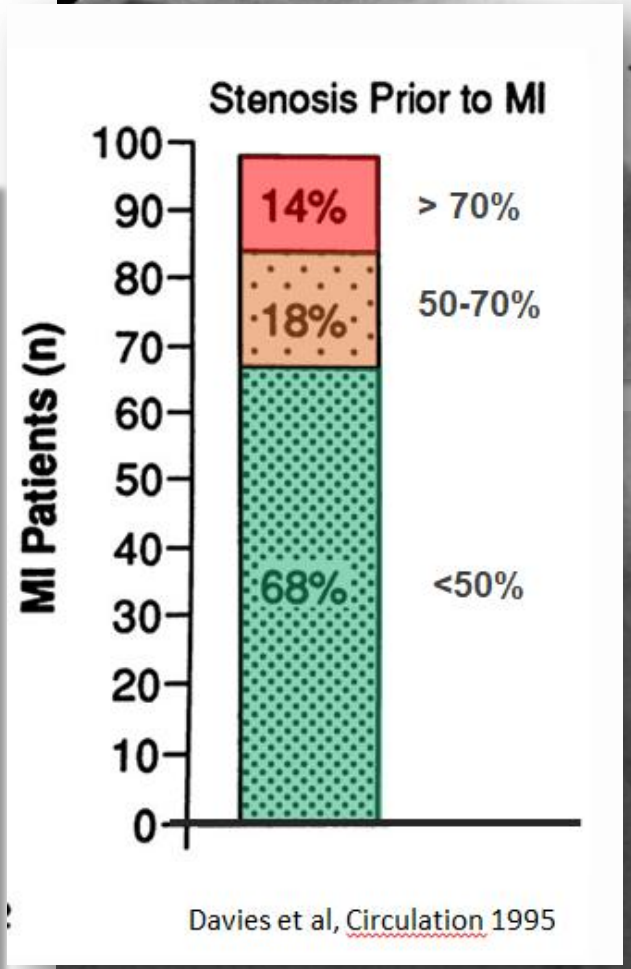






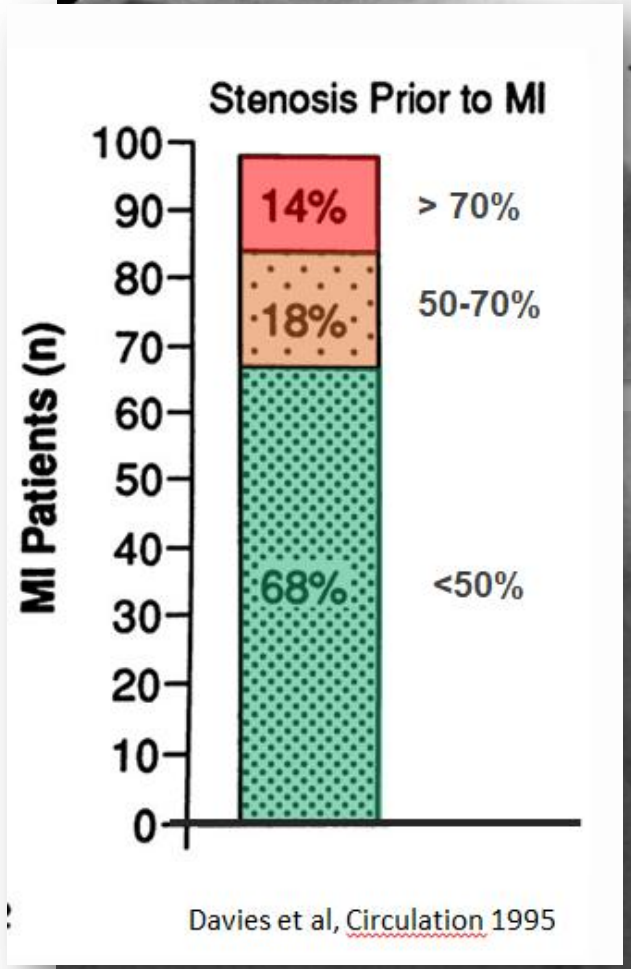


Plaque


Stenosis Prior to MI
MI Patients (n)
100
90
80
70
60
50
40
30
20
10
0
14%
> 70%
18%
50-70%
68%
<50%
Davies et al, Circulation 1995

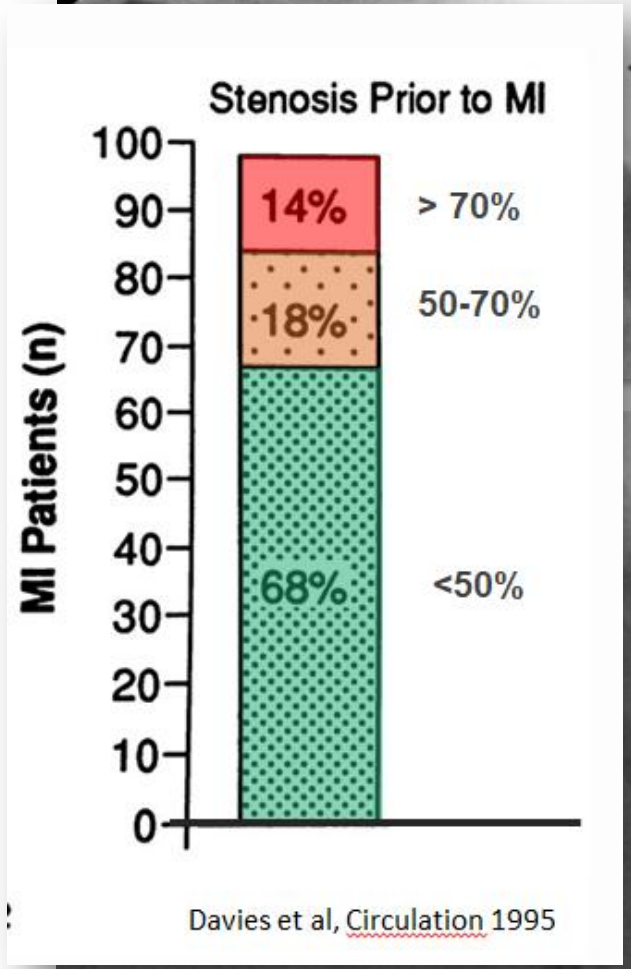
Plaque

- Majority of infarctions are caused by lesions that are not high-grade.
- 32% of MI caused by high-grade stenoses.



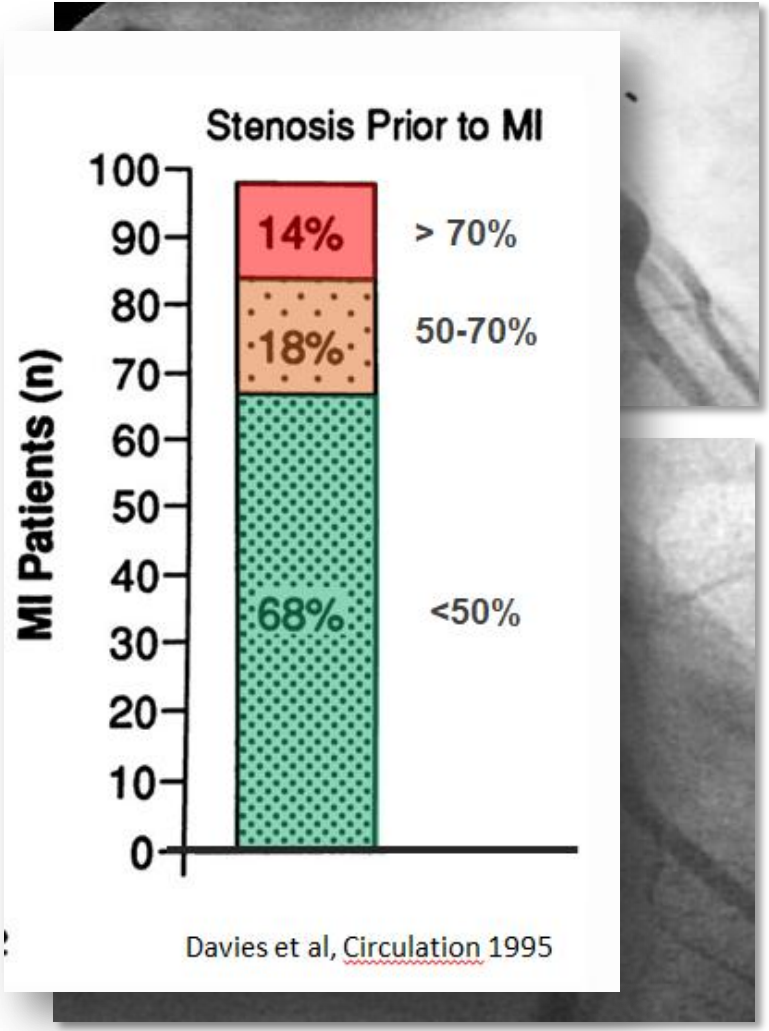
Plaque

- Majority of infarctions are caused by lesions that are not high-grade.
- 32% of MI caused by high-grade stenoses.
- In the population, there are **a lot** more lesions that are „mild“ than there are high- grade stenoses.



Plaque

- Majority of infarctions are caused by lesions that are not high-grade.
- 32% of MI caused by high-grade stenoses.
- In the population, there are **a lot** more lesions that are „mild“ than there are high- grade stenoses.
- A single high-grade stenosis is much more dangerous than a single mild lesion



Plaque vs. Stenosis

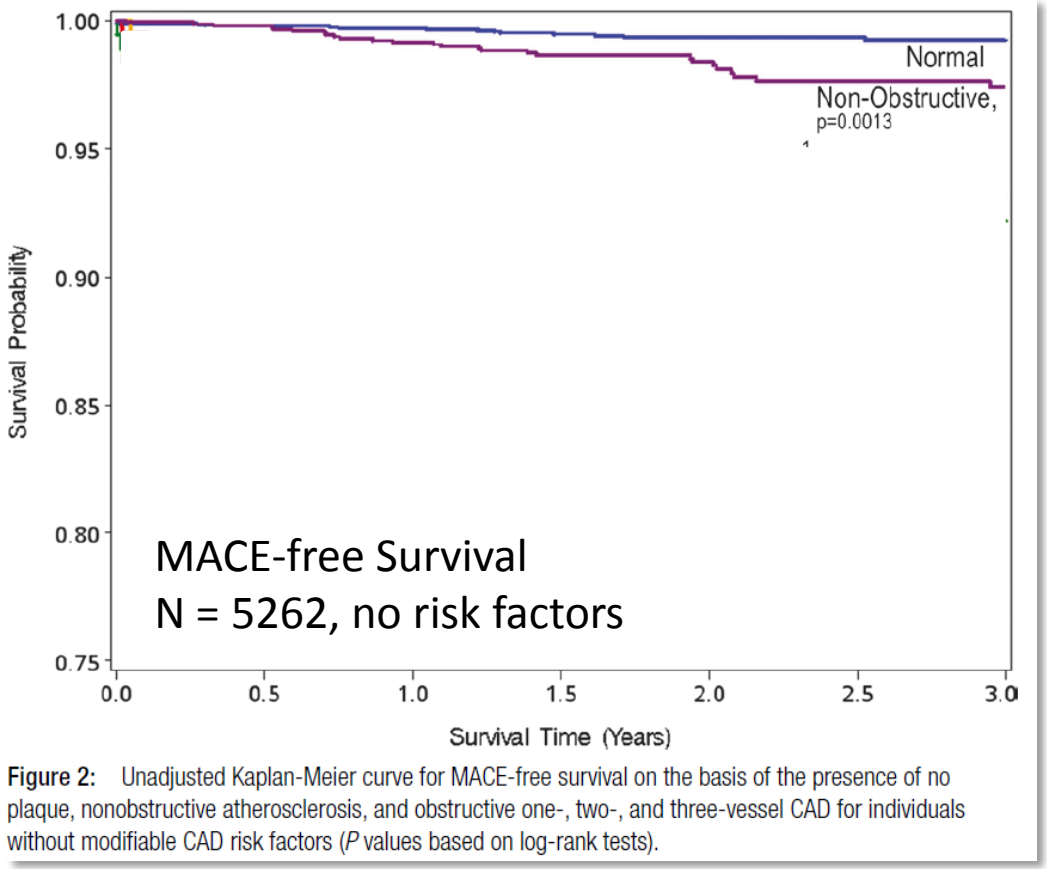
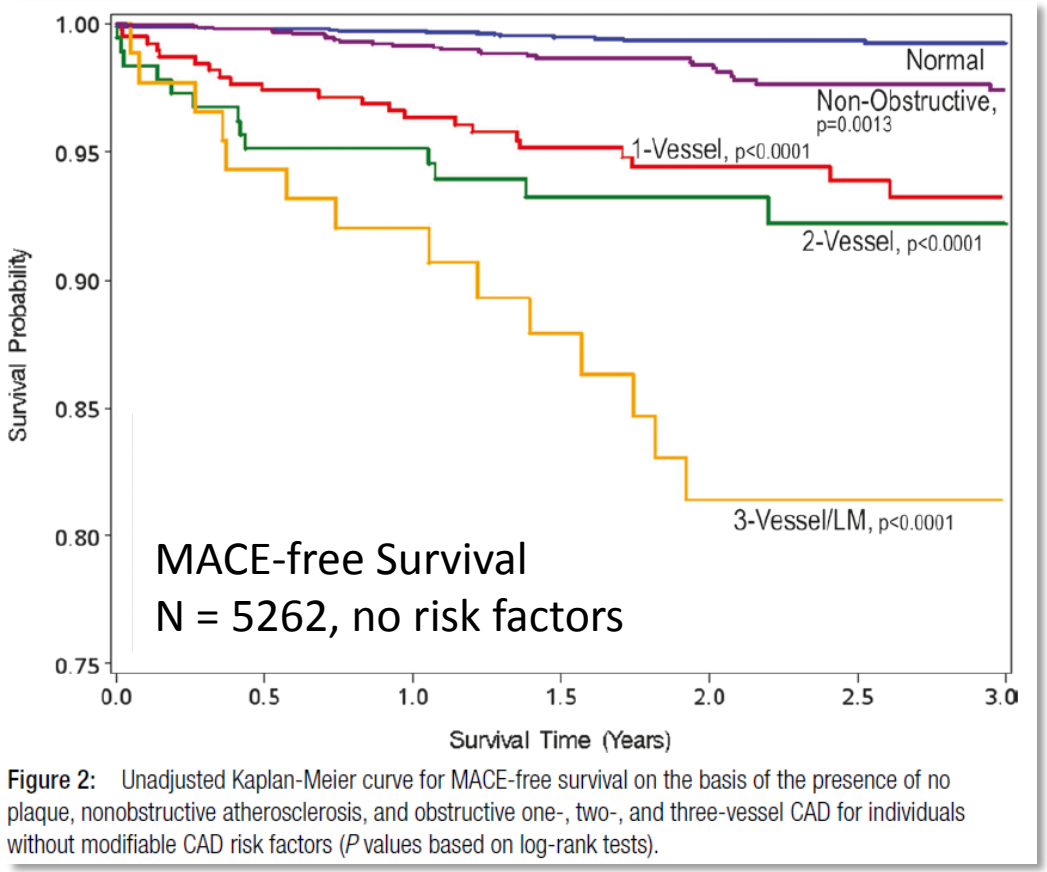


Figure 2: Unadjusted Kaplan-Meier curve for MACE-free survival on the basis of the presence of no plaque, nonobstructive atherosclerosis, and obstructive one-, two-, and three-vessel CAD for individuals without modifiable CAD risk factors (*P* values based on log-rank tests).

Cardiovascular Risk among Stable Individuals Suspected of Having Coronary Artery Disease with No Modifiable Risk Factors: Results from an International Multicenter Study of 5262 Patients[1]

Plaque vs. Stenosis



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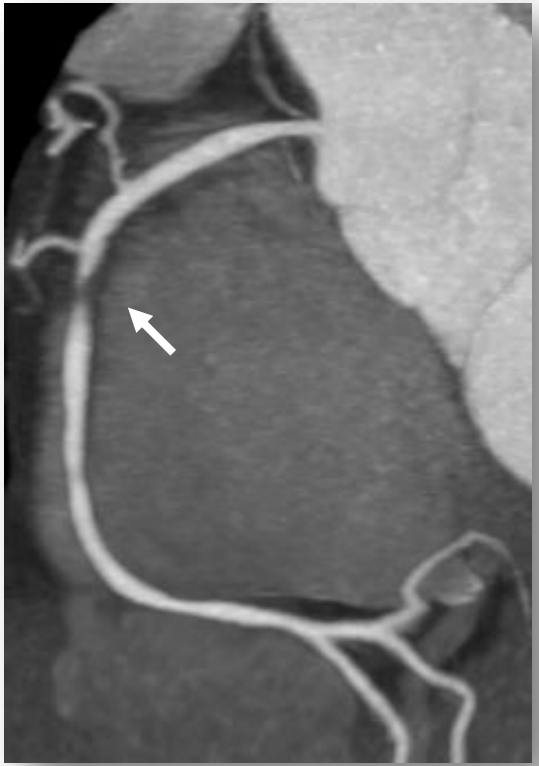

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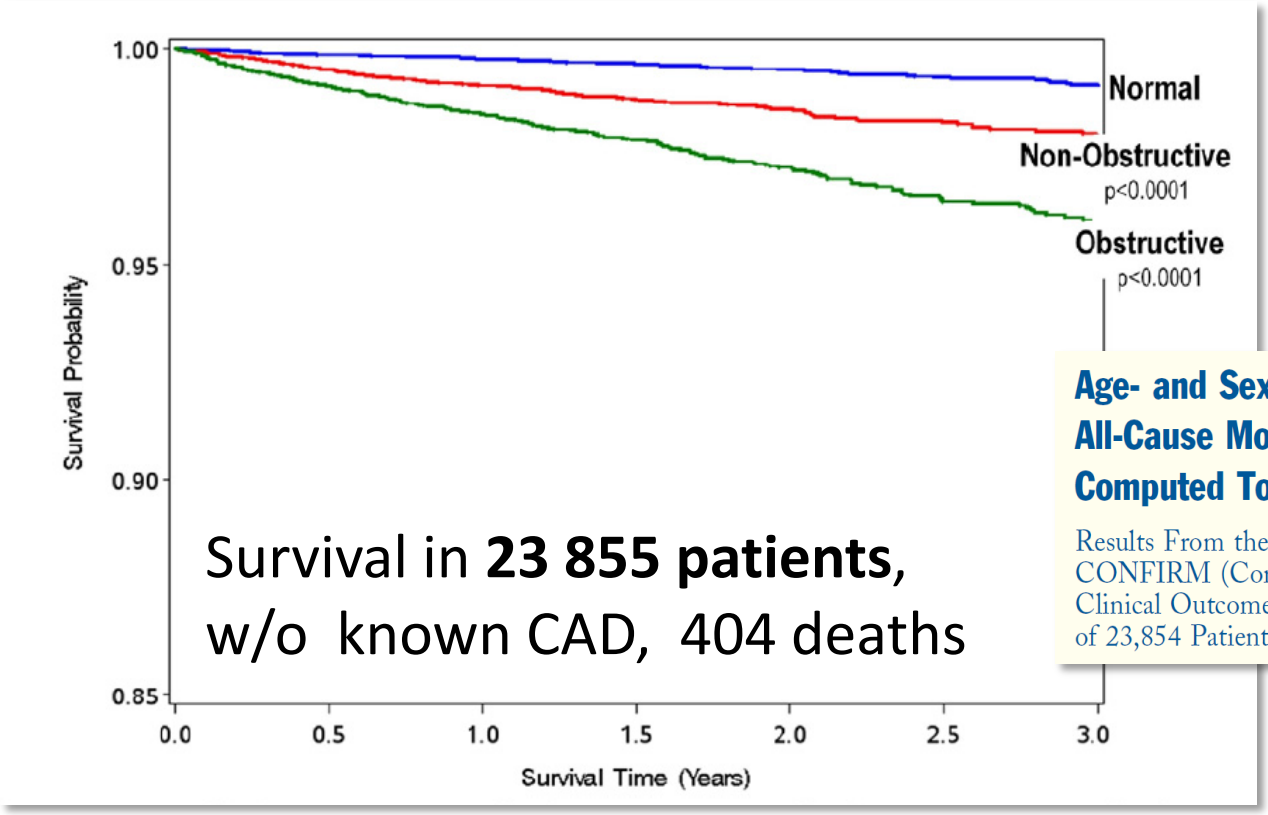


Survival in **23 855 patients**, w/o known CAD, 404 deaths

Age- and Sex-Related Differences in All-Cause Mortality Risk Based on Coronary Computed Tomography Angiography Findings

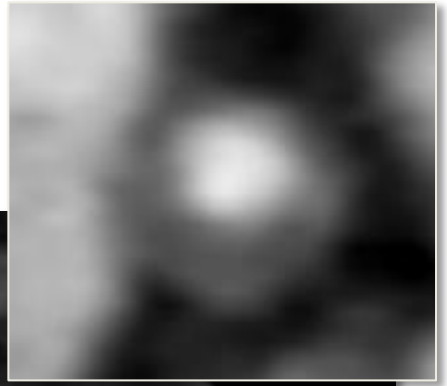
Results From the International Multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry) of 23,854 Patients Without Known Coronary Artery Disease

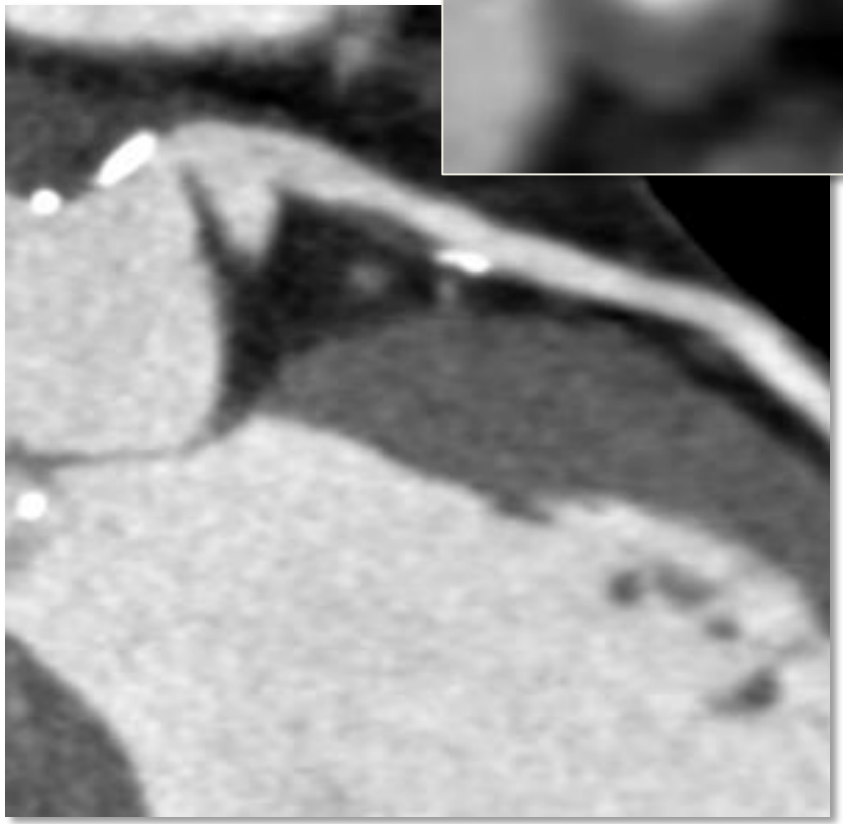
J Am Coll Cardiol 2011

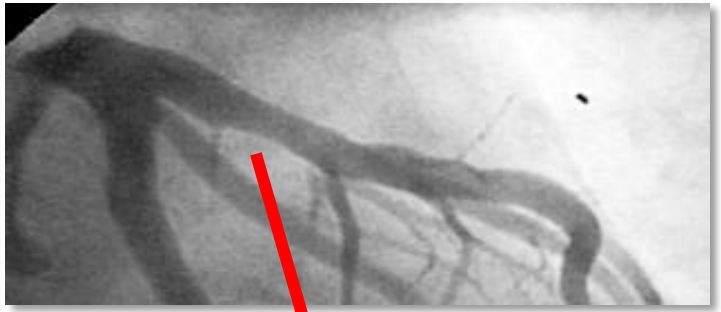
Plaque vs. Stenosis

1) Stenosis is a very powerful marker of risk.

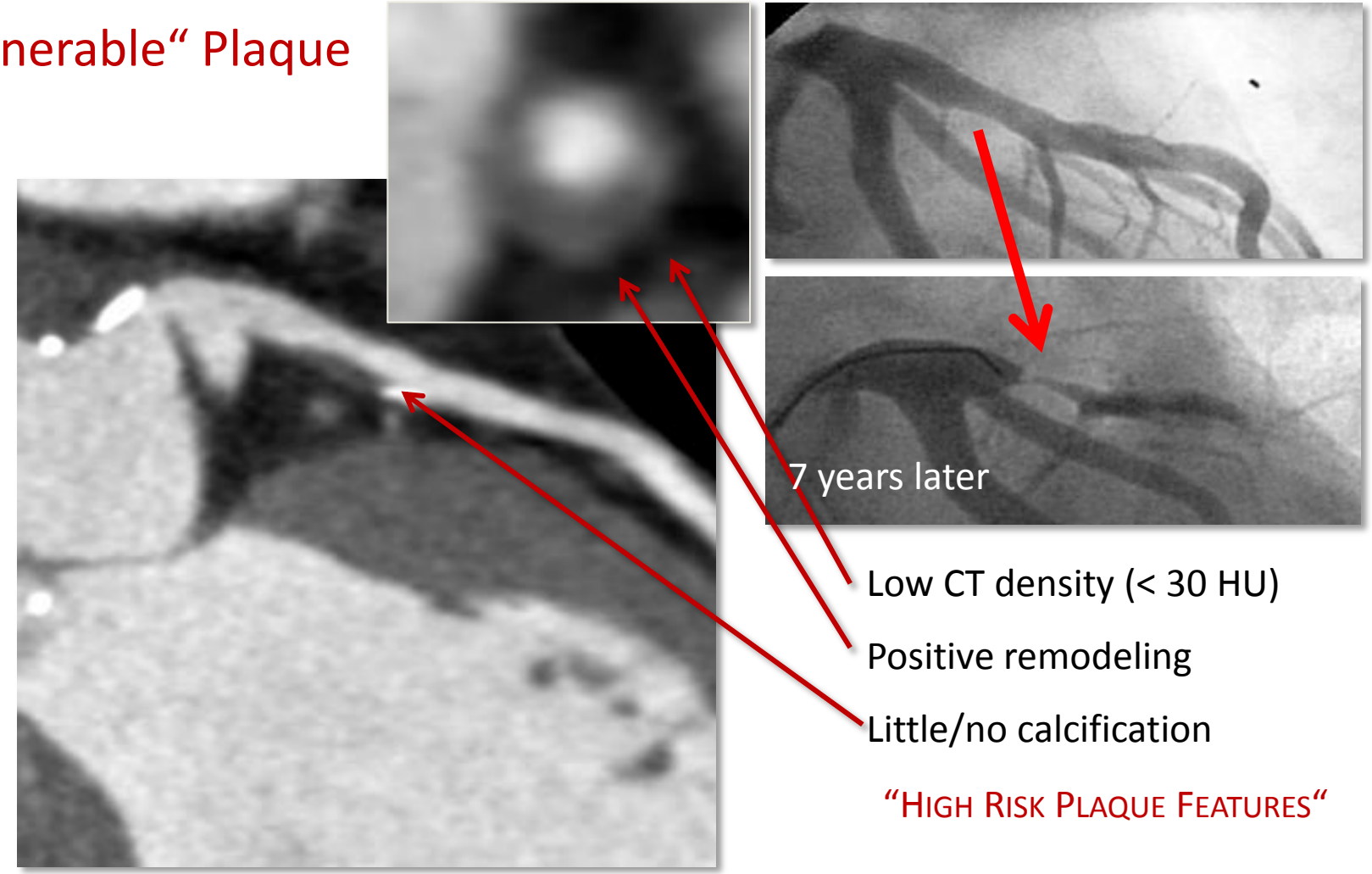
“Vulnerable“ Plaque







“Vulnerable“ Plaque



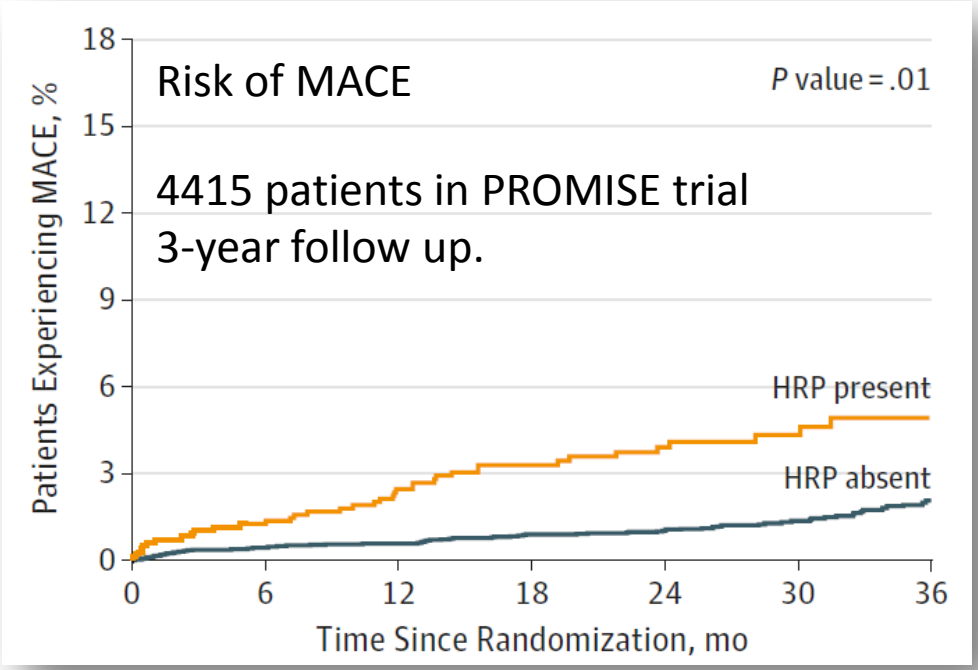
Low CT density (< 30 HU)

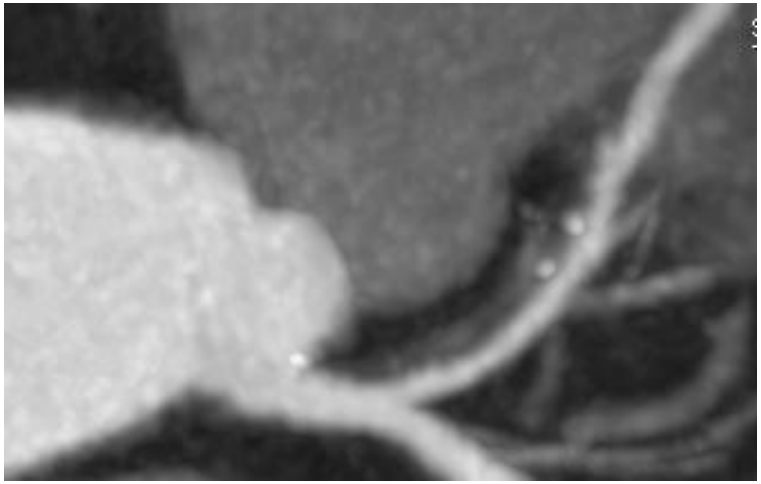
Positive remodeling

Little/no calcification

“High Risk Plaque Features“

“Vulnerable“ Plaque





YES: High-risk plaque significantly higher risk

BUT: Only 6% of patients with high-risk plaque developed MACE

JAMA Cardiology | Original Investigation

Use of High-Risk Coronary Atherosclerotic Plaque Detection for Risk Stratification of Patients With Stable Chest Pain
A Secondary Analysis of the PROMISE Randomized Clinical Trial

Maros Ferencik, MD, PhD, MCR; Thomas Mayrhofer, PhD; Daniel O. Bittner, MD; Hamed Emami, MD; Stefan B. Puchner, MD; Michael T. Lu, MD, MPH; Nandini M. Meyersohn, MD; Alexander V. Ivanov, BS; Elizabeth C. Adami, BS; Manesh R. Patel, MD; Daniel B. Mark, MD, MPH; James E. Udelson, MD; Kerry L. Lee, PhD; Pamela S. Douglas, MD; Udo Hoffmann, MD, MPH

JAMA Cardiol. 2018;3(2):144-152.

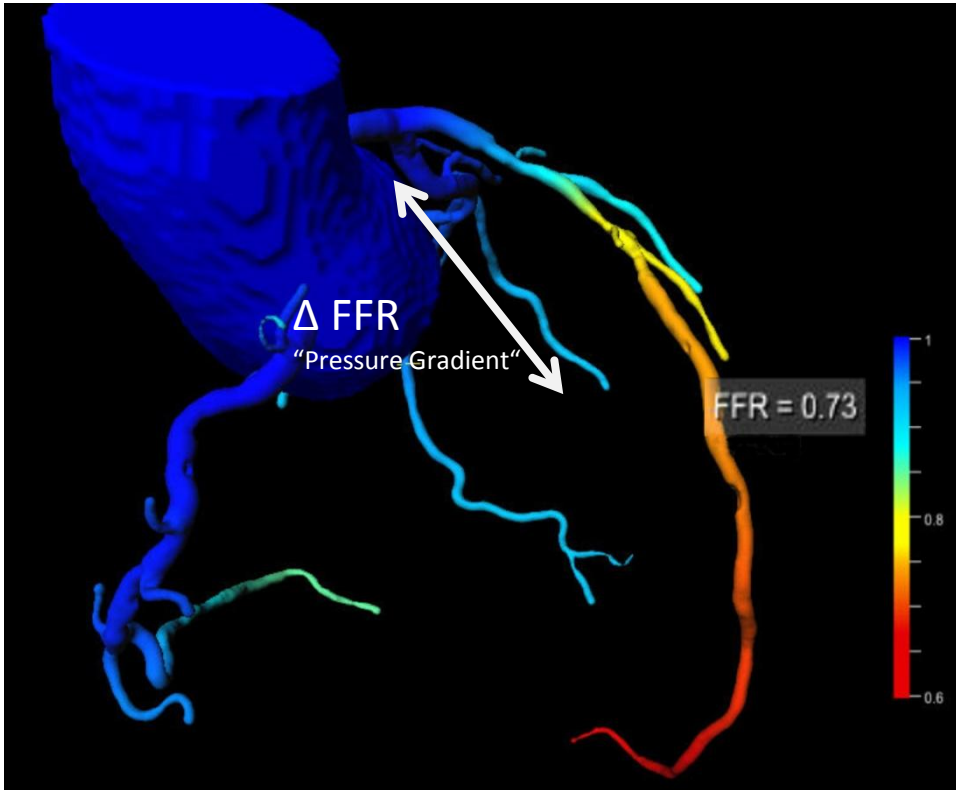
“Vulnerable“ Plaque

1) Stenosis is a powerful marker of risk

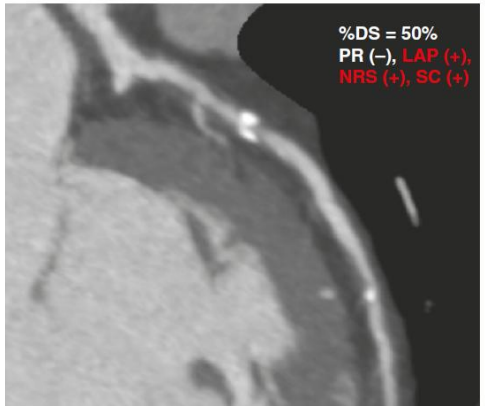
2) Presence of plaque is a marker of risk, but the typical “vulnerable plaque“ features are not very helpful (low specificity)

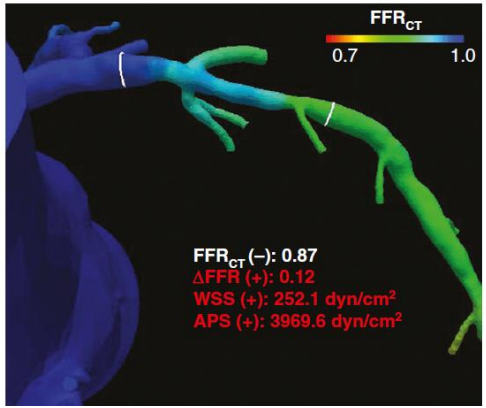
Vulnerable Plaque Characteristics

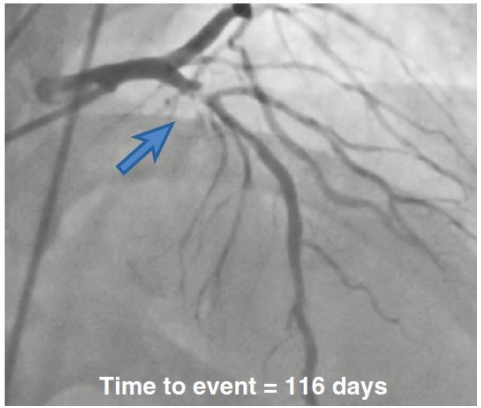
CT can be used to simulate flow and pressure in the coronary arteries (FFR_{CT})



Vulnerable Plaque Characteristics

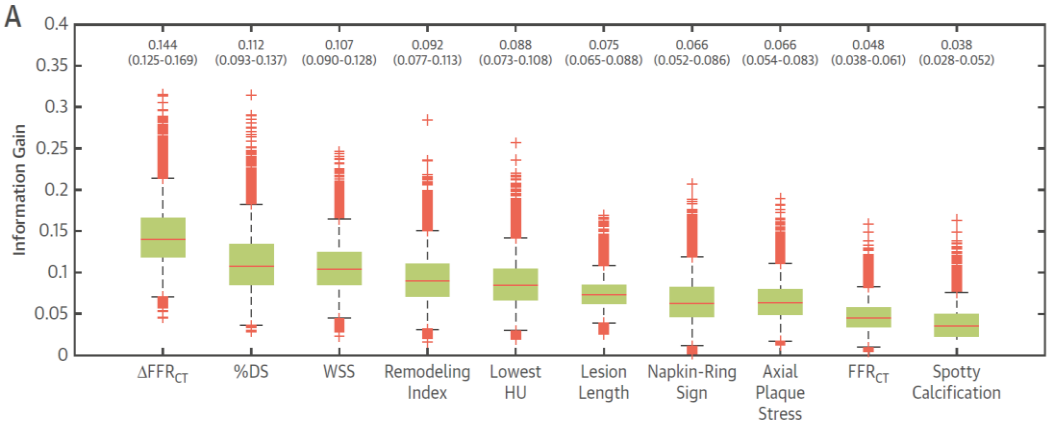






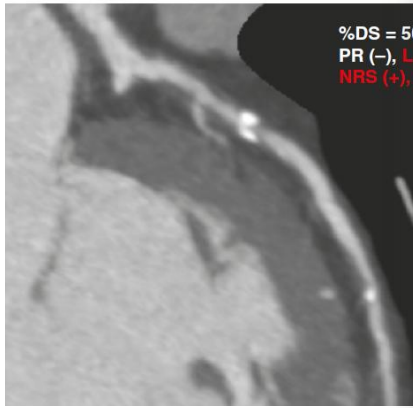
150 non culprit lesions
vs.
66 culprit lesions

Wall Shear Stress
&
Pressure Gradient



Lee JM et al, JACC Img (epub aheab of print)

Vulnerable Plaque Characteris



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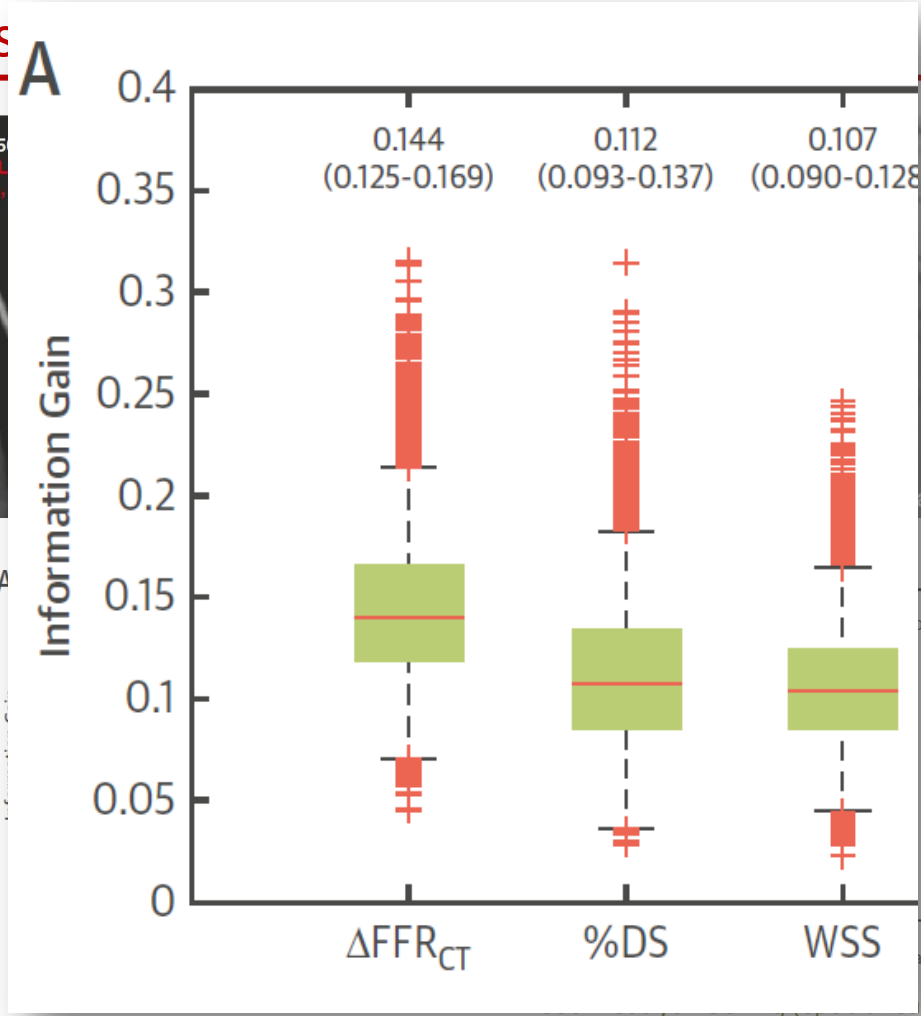
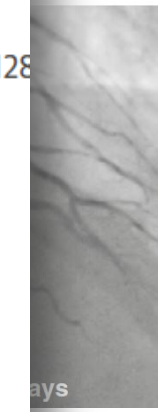
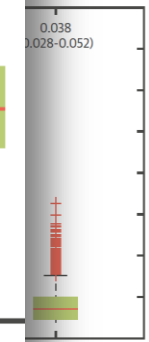




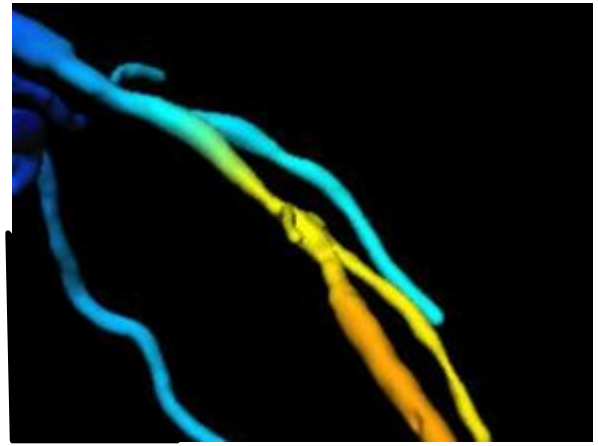


b of print)

Vulnerable Plaque Characteristics

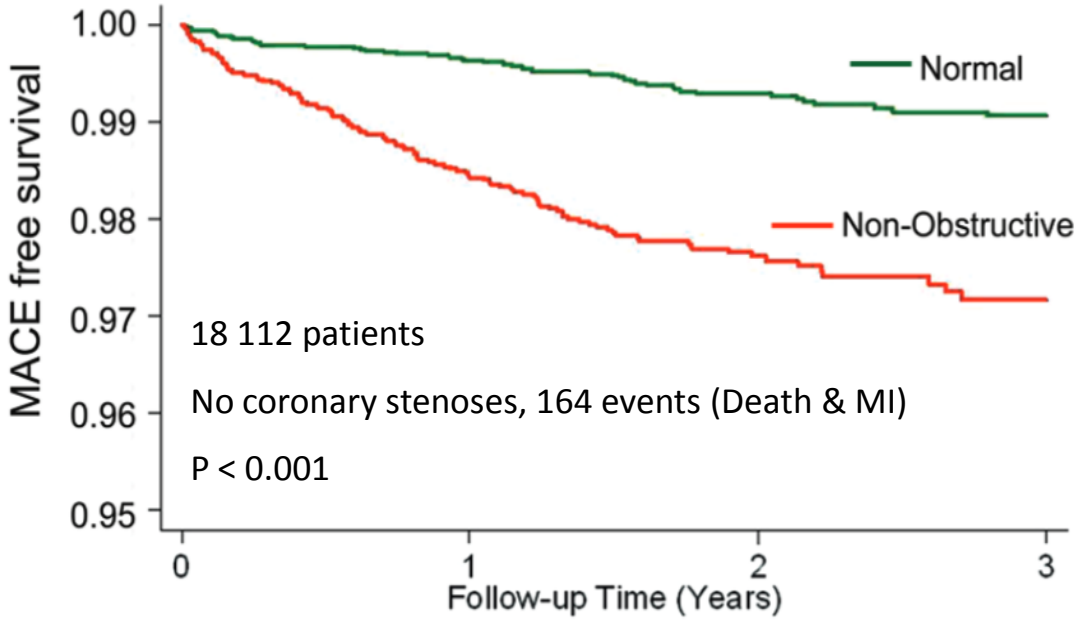
1) Stenosis is a powerful marker of risk

2) Presence of plaque is a marker of risk, but the typical "vulnerable plaque" features are not very helpful (low specificity)



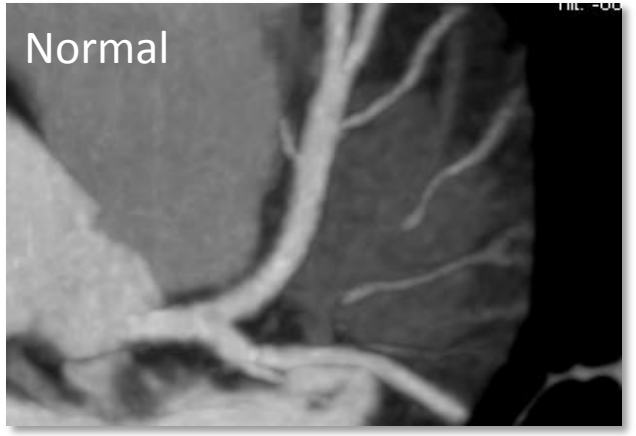
Men vs. Women

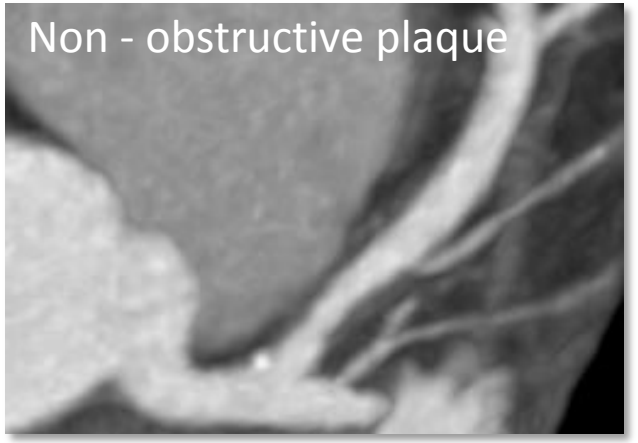
Men vs. Women



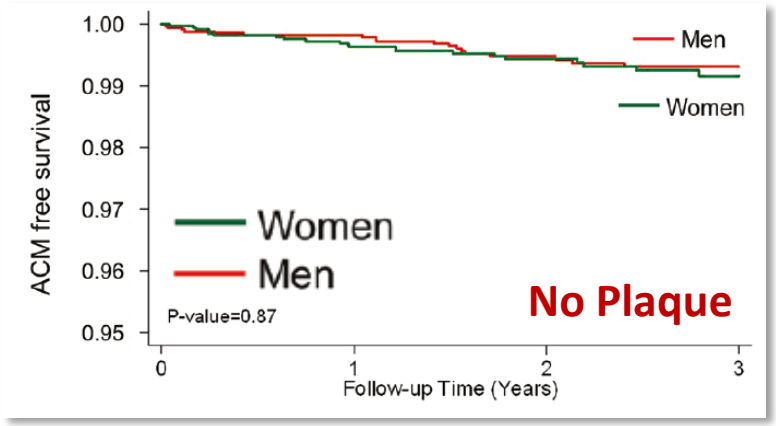
Sex-based Prognostic Implications of Nonobstructive Coronary Artery Disease: Results from the International Multicenter CONFIRM Study[1]

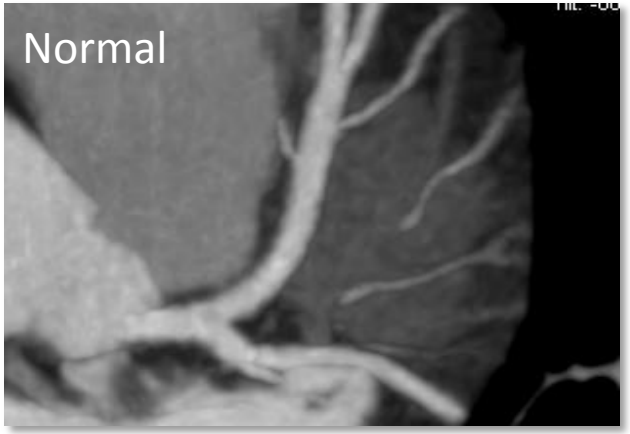
Leipsic et al, Radiology 2013

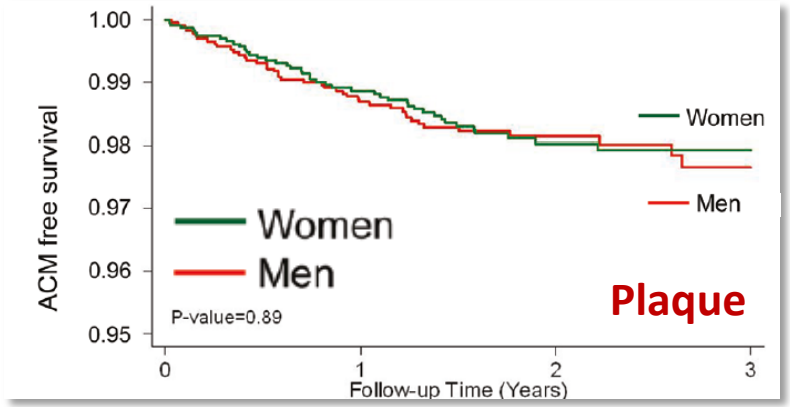


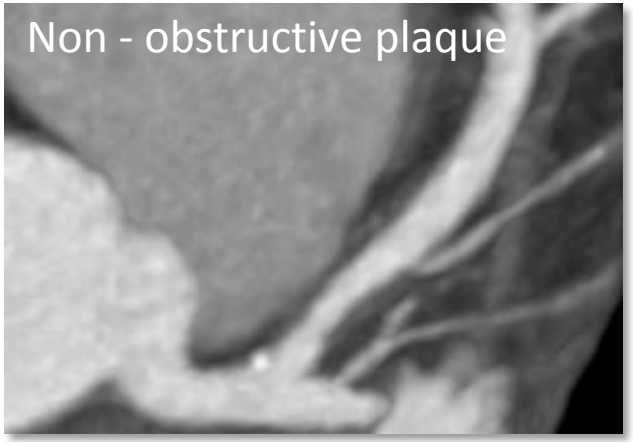


Men vs. Women


1.00
0.99
0.98
0.97
0.96
0.95
ACM free survival
0
1
2
3
Follow-up Time (Years)
Men
Women
Women
Men
P-value=0.87
No Plaque


Normal


1.00
0.99
0.98
0.97
0.96
0.95
ACM free survival
0
1
2
3
Follow-up Time (Years)
Women
Men
Women
Men
P-value=0.89
Plaque


Non - obstructive plaque

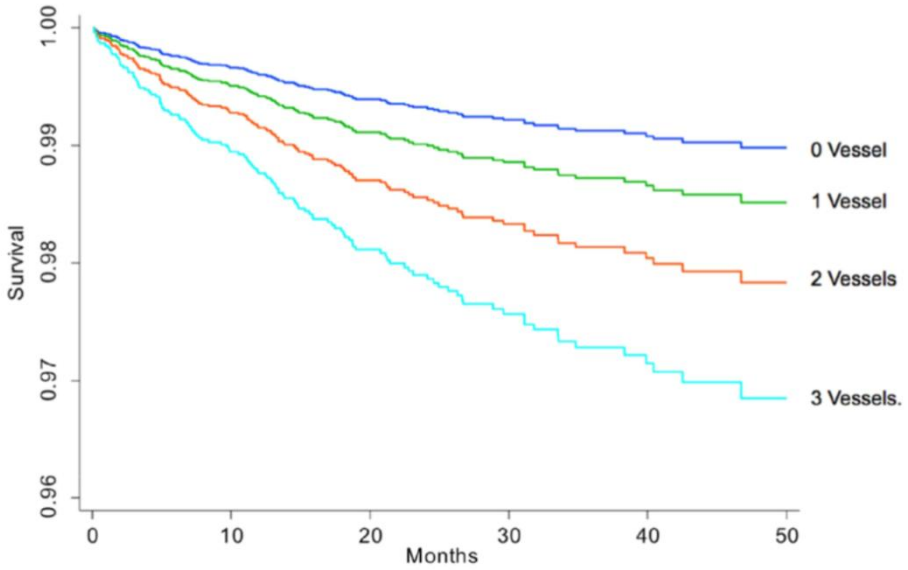
Men vs. Women

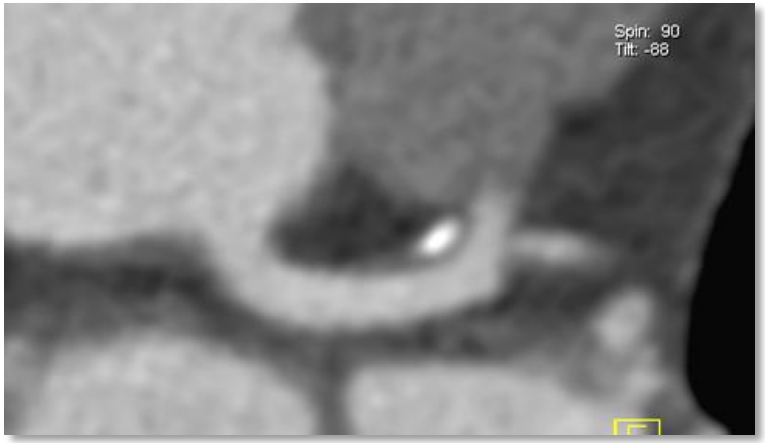
1) Stenosis is a powerful marker of risk

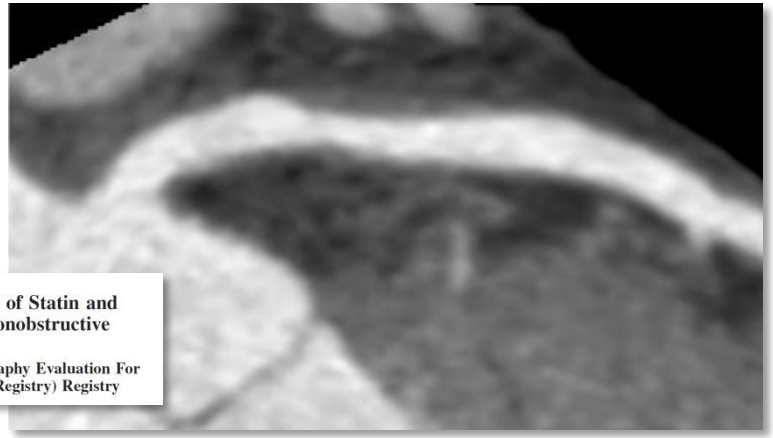
2) Presence of plaque is a marker of risk, but the typical “vulnerable plaque“ features are not very helpful

3) Once plaque is present, women are no different from men

Influence of Treatment







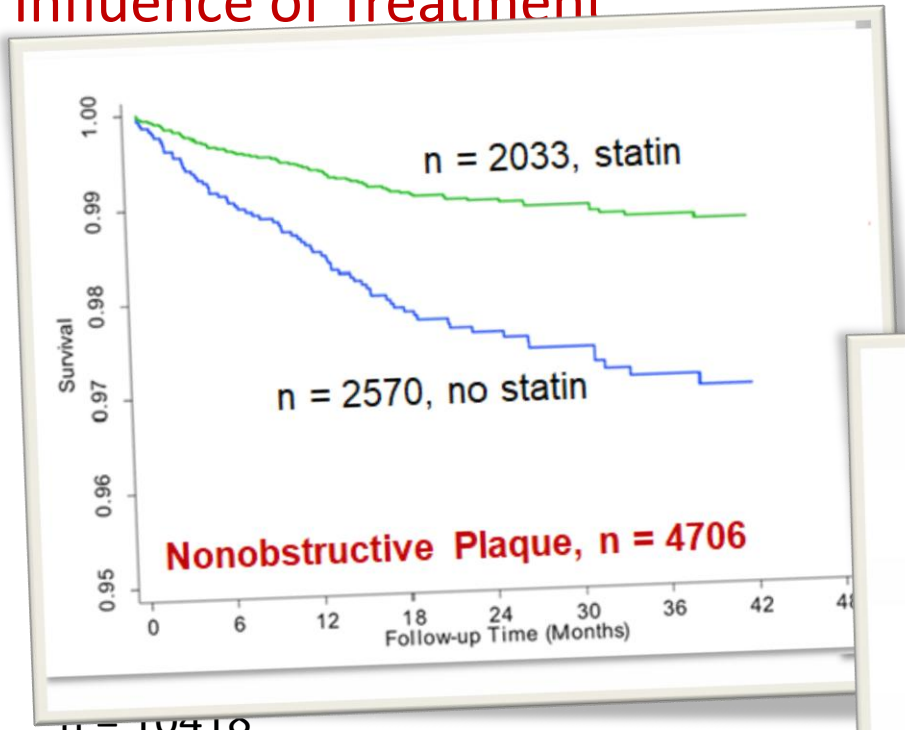
n = 10418
Patients without stenoses

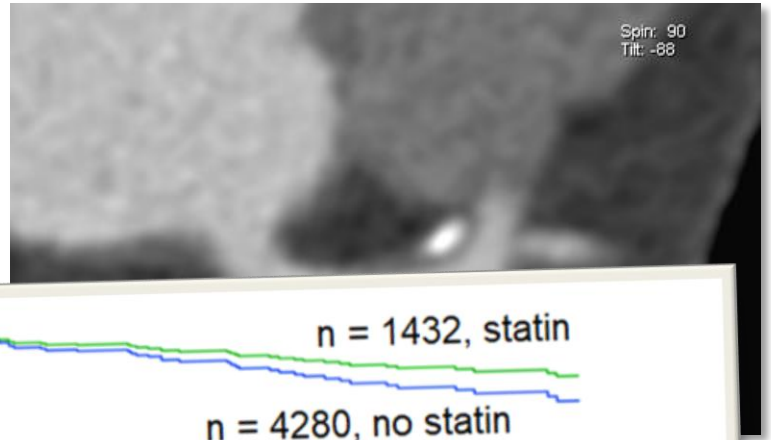
Each segment with plaque increased mortality by 6%.

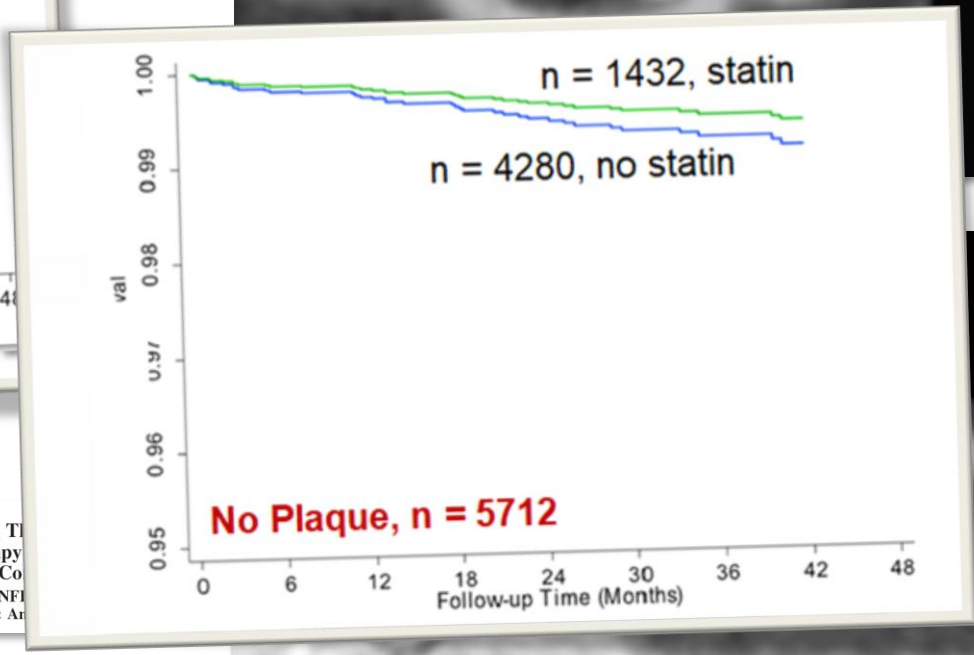
Prognostic and Therapeutic Implications of Statin and Aspirin Therapy in Individuals With Nonobstructive Coronary Artery Disease

Results From the CONFIRM (Coronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter Registry) Registry

Influence of Treatment







n = 10418

Patients without stenoses

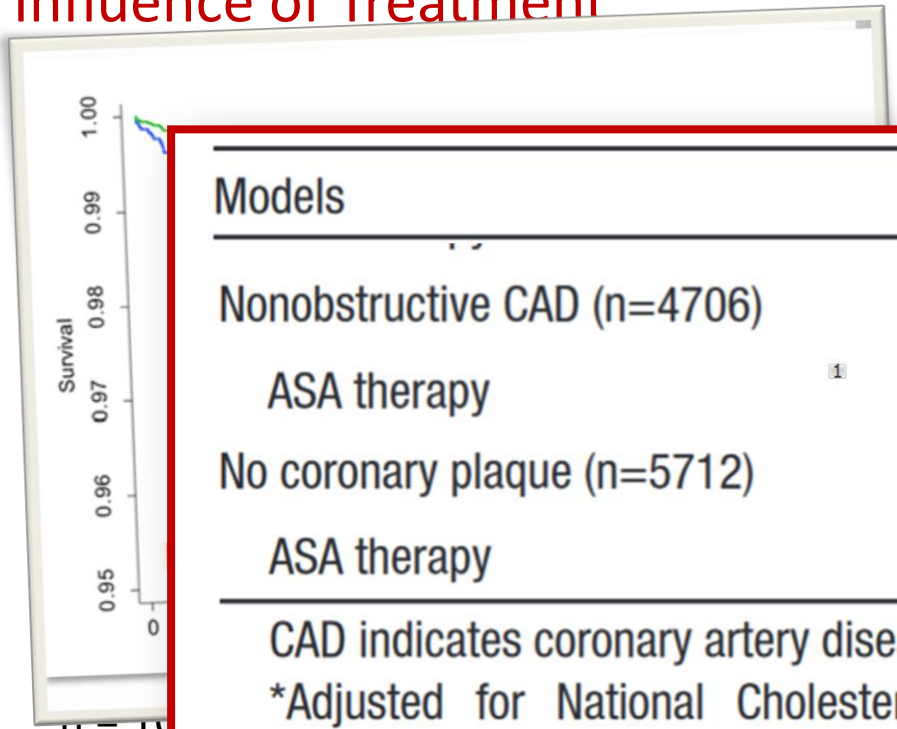
Each segment with plaque increased mortality by 6%.

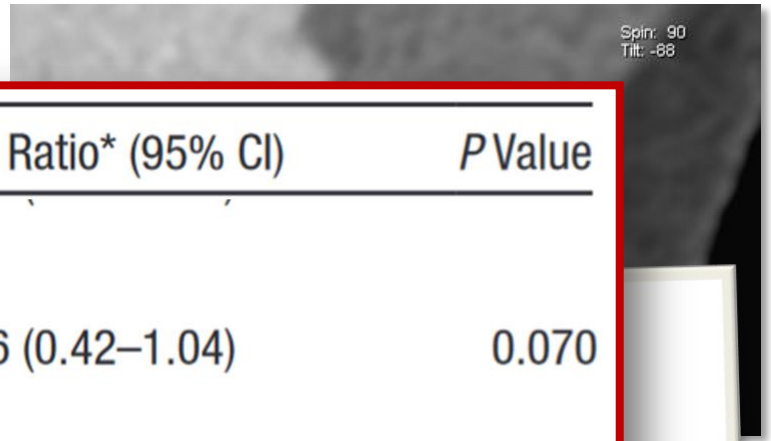
Influence of Treatment

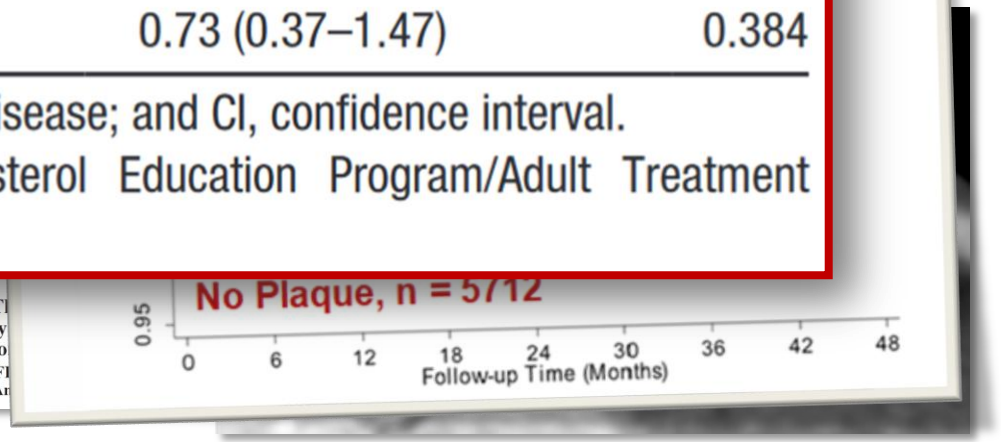
Models	Hazard Ratio* (95% CI)	*P* Value
Nonobstructive CAD (n=4706)		
ASA therapy	0.66 (0.42–1.04)	0.070
No coronary plaque (n=5712)		
ASA therapy	0.73 (0.37–1.47)	0.384

CAD indicates coronary artery disease; and CI, confidence interval.

*Adjusted for National Cholesterol Education Program/Adult Treatment Program III risk.



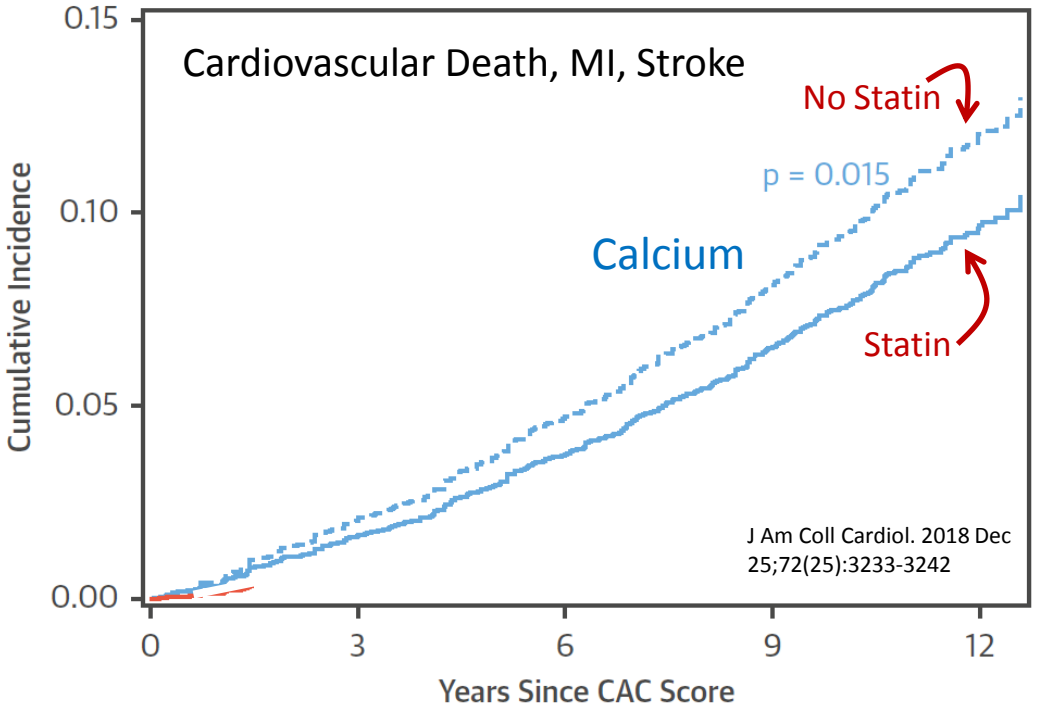




Patien

Each segment with plaque increased mortality by 6%.

Influence of Treatment



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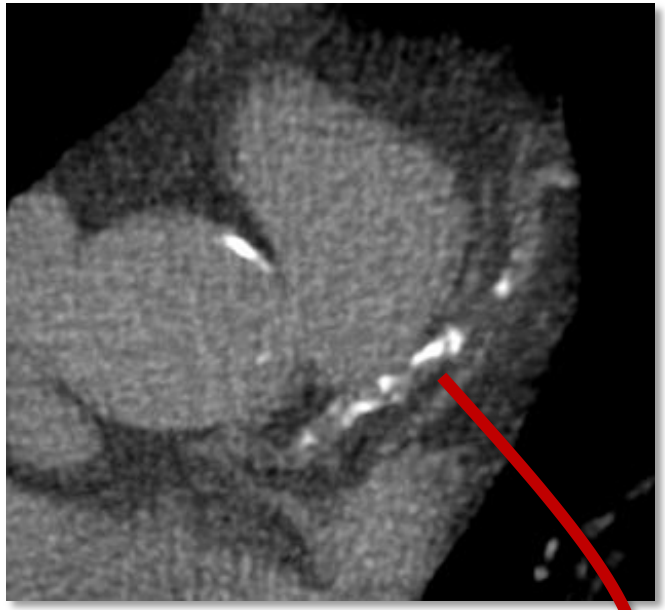
Impact of Statins on Cardiovascular Outcomes Following Coronary Artery Calcium Scoring

Joshua D. Mitchell, MD,[a] Nicole Fergestrom, MS,[b] Brian F. Gage, MD,[c] Robert Paisley, MD,[d] Patrick Moon, MD,[e] Eric Novak, MS,[a] Michael Cheezum, MD,[f] Leslee J. Shaw, PhD,[g] Todd C. Villines, MD[h]

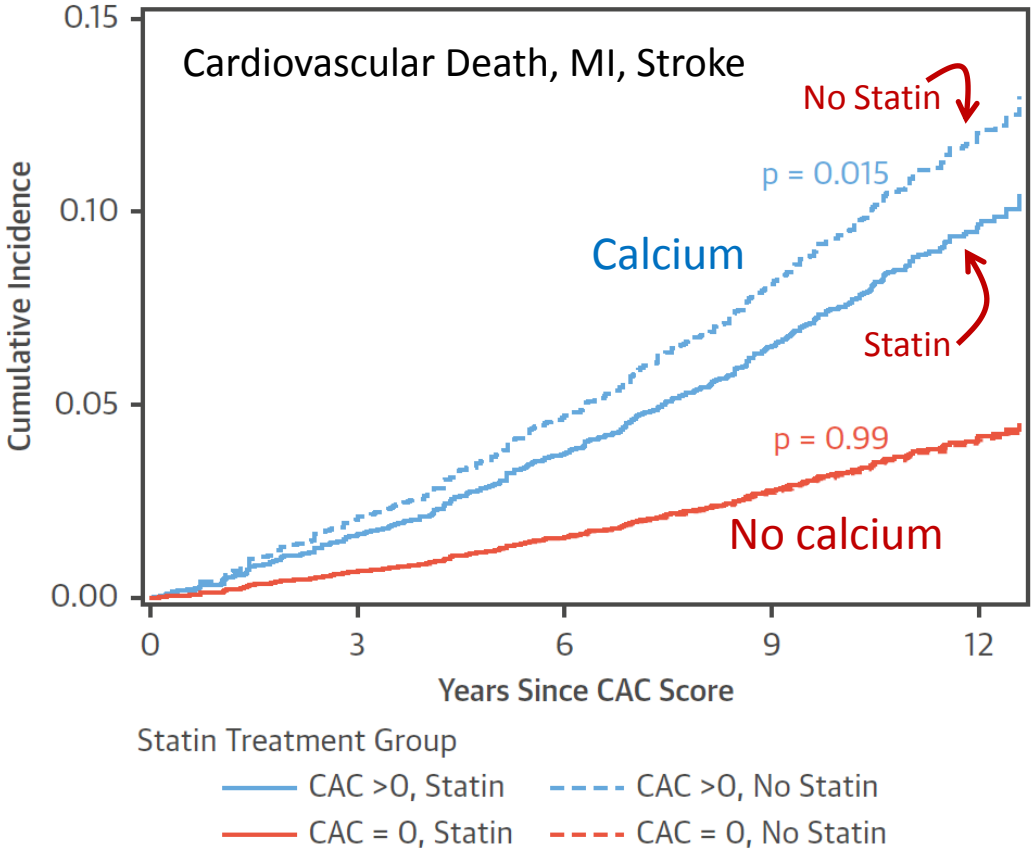


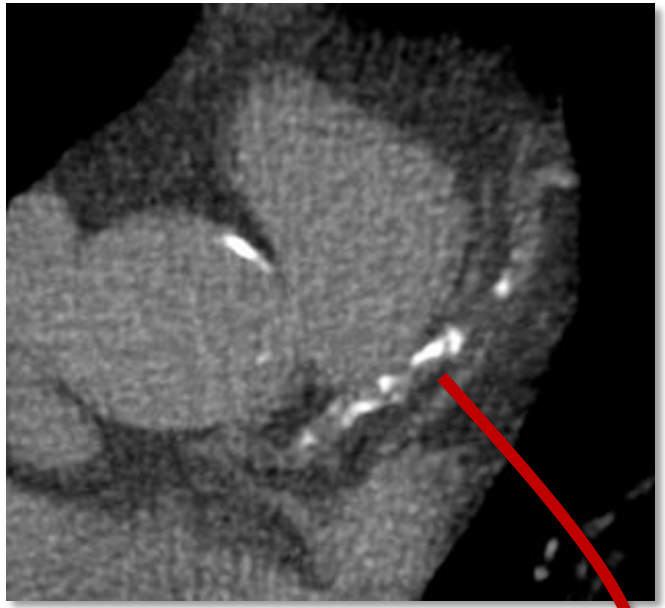
13 644 patients

Calcium Scoring

Follow-up 9 years

Influence of Treatment





13 644 patients

Calcium Scoring

Follow-up 9 years

Effect of Therapy

1) Stenosis is a powerful marker of risk

2) Presence of plaque is a marker of risk, but the typical “vulnerable plaque“ features are not very helpful

3) Once plaque is present, women are no different from men

4) Statins useful if plaque are present. Do not seem effective if no plaque is present.

Effect of Therapy

1) Stenosis is a powerful marker of risk

2) Presence of plaque is a marker of risk, but the typical “vulnerable plaque“ features are not very helpful

3) Once plaque is present, women are no different from men

4) Statins useful if plaque are present. Do not seem effective if no plaque is present.

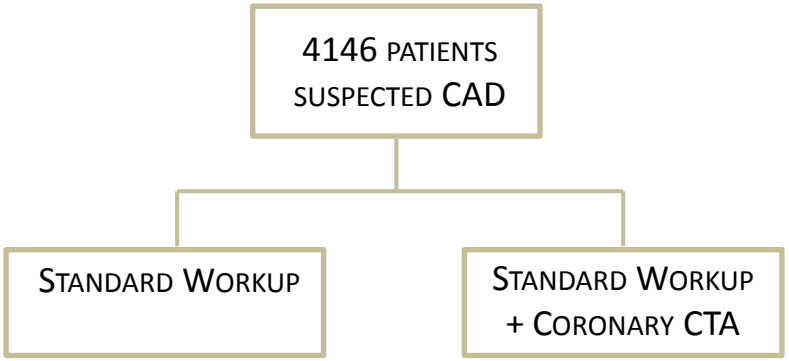
5) Reasonable to guide preventive treatment based on presence/absence of atherosclerosis

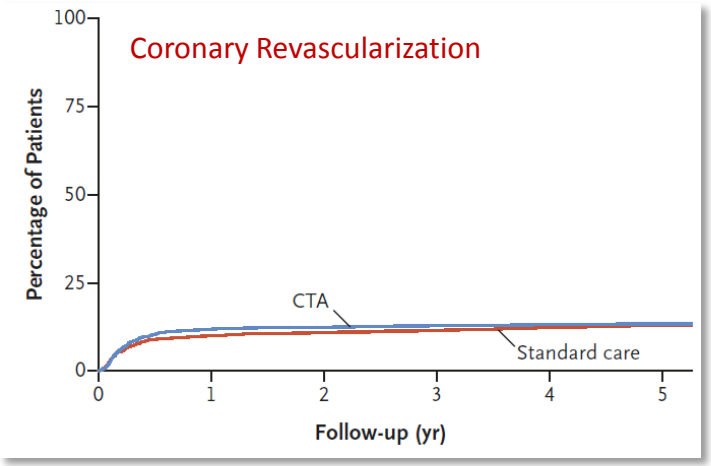
SCOT-Heart

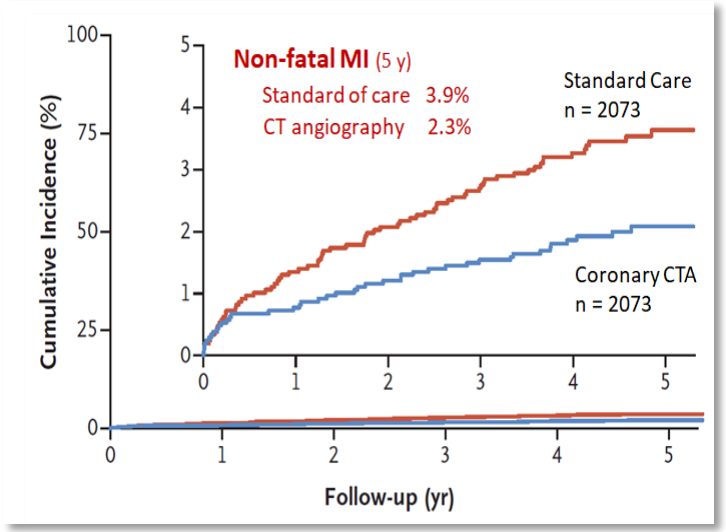
ORIGINAL ARTICLE

Coronary CT Angiography and 5-Year Risk of Myocardial Infarction

The SCOT-HEART Investigators*







SCOT-Heart

ORIGINAL ARTICLE

Coron

STAND

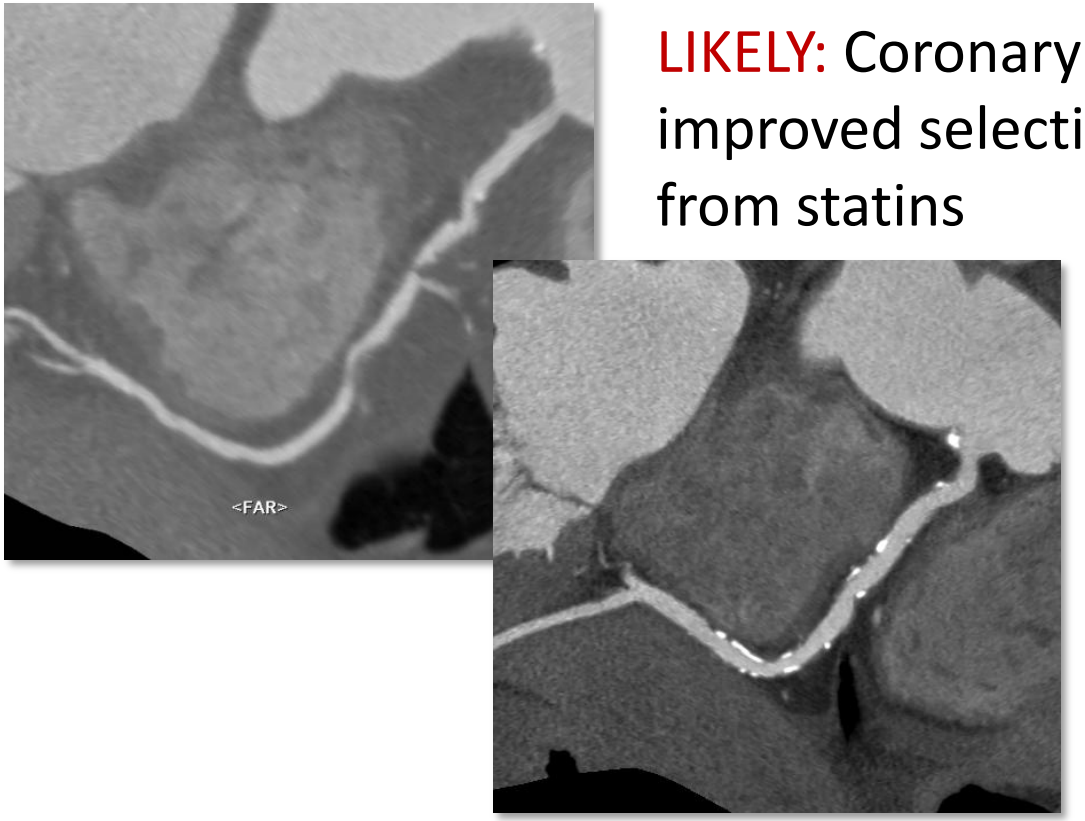
Coronary Revascularization

100
75
Patients

0
0 1 2 3 4 5
0 1 2 3 4 5
Follow-up (yr)

Preventive Medication	Started	Stopped
CTA	14%	4%
Standard	4%	0.4%

SCOT-Heart



LIKELY: Coronary atherosclerosis leads to improved selection of patients who benefit from statins

Suspected CAD:

If CT is available,

and patient is a good candidate

CT is a very good choice as diagnostic modality

Coronary Atherosclerosis and Outcome – Lessons Learned from CT

- ⇨ It is difficult to show a benefit of statins and aspirin in primary prevention
- ⇨ Aspirin not recommended
- ⇨ High prognostic relevance of stenoses / “pressure drop“
- ⇨ Some relevance of plaque (“vulnerable plaque“)
- ⇨ **Statins useful when plaque is present**
- ⇨ SCOT Heart: CT may be a good tool to work up suspected coronary artery disease