



Gepersonaliseerd lipidenmanagement op basis van (imaging) biomarkers

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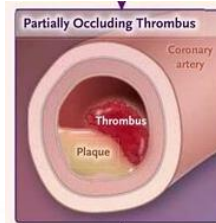
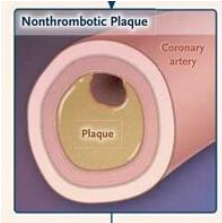


Disclosures

Voor presentatie mogelijk relevante relaties	
Sponsoring of onderzoeksgeld:	Geen
Honorarium of andere (financiële) vergoeding:	Geen
Aandeelhouder:	N.V.T.
Andere relatie, namelijk ...	N.V.



Coronary artery disease



Chronic stable angina

Acute coronary syndrome

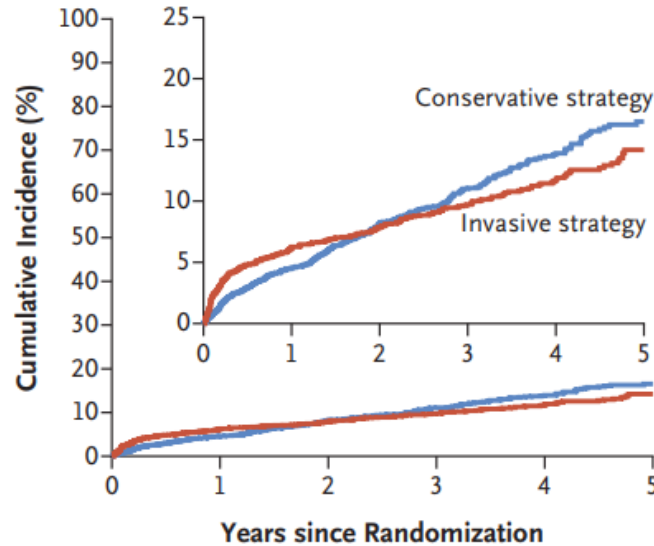
- Unstable angina
- Non-ST-segment-elevation MI

ST-segment-elevation MI

Stabiel obstructief coronairlijden + bewezen ischemie

N = 5,179

Death from Cardiovascular Causes or Myocardial Infarction

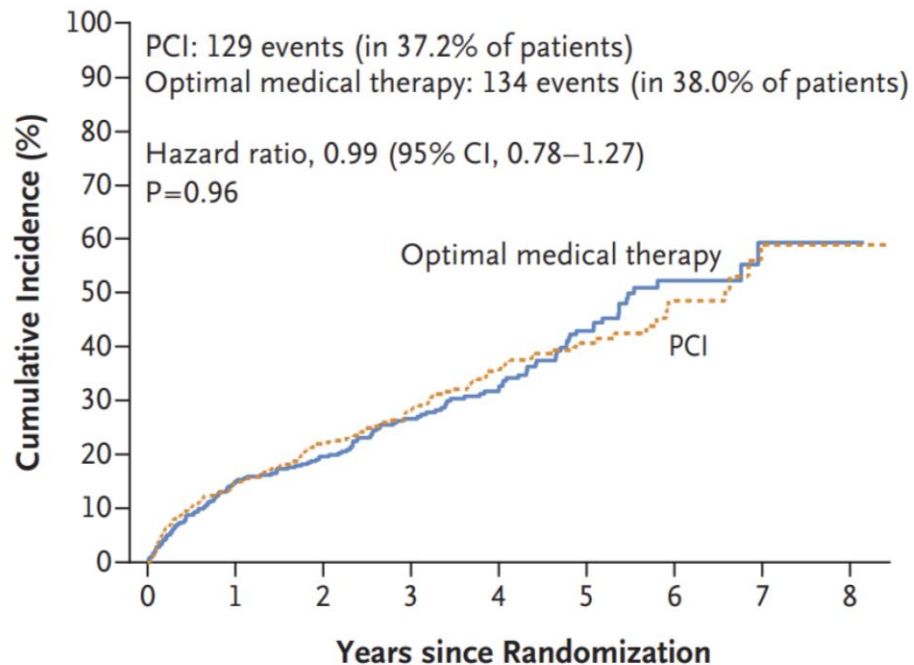


No. at Risk

Conservative strategy	2591	2453	1933	1325	746	298
Invasive strategy	2588	2383	1933	1314	742	282

N = 700

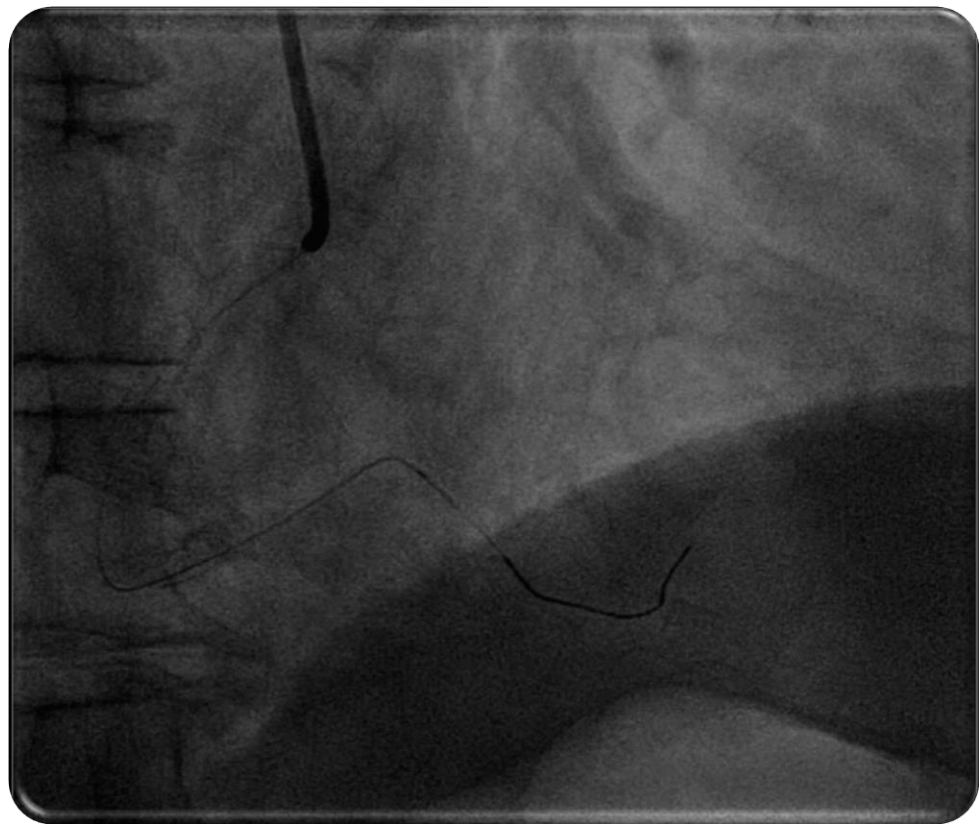
- LVEF \leq 35%
- Obstructief coronairlijden
- Aangetoonde viabiliteit



No. at Risk

PCI	347	295	262	179	130	80	32	14	3
Optimal medical therapy	353	299	276	191	142	82	33	10	1

Figure 1. Primary Outcome of Death from Any Cause or Hospitalization for Heart Failure.



Na infarct

- Ongeveer 50% van deze patiënten heeft bijkomende, (significante) “non-culprit” laesies
- Een deel van deze patiënten zal een recidief myocardinfarct krijgen
- Echter.... een deel ook niet

“Stabiel coronairlijden”

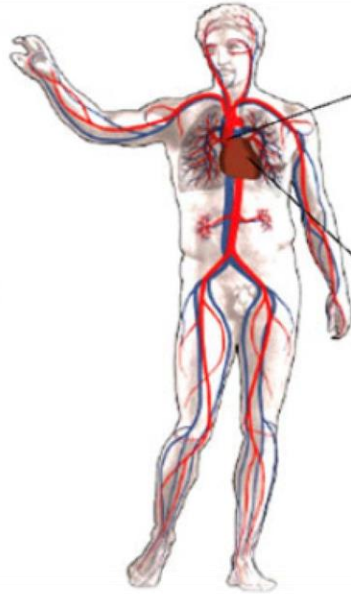
- Een deel van de patiënten zal later alsnog een infarct krijgen

Vulnerable patient

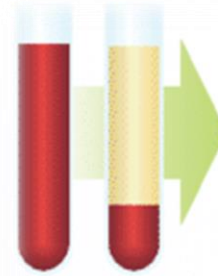
Hypertension
Diabetes
Lipids
Obesity
Thrombosis
Inflammation
Immune response
Gut microbiome

Smoking
Diet
Exercise
Stress
Socioeconomics

Omics
Imaging



Vulnerable blood



Serological markers

Inflammation
blood coagulation
Extracellular-matrix remodelling
Oxidative stress
Myocyte injury/stress



The vulnerable plaque



Visualizing

Thrombus formation
Neo-vascularization
Inflammation
Calcification
Morphological features

**Near future risk at
Individual level**

Imaging & risk stratification

Offer diagnostic testing

No diagnostic testing mandated

Coronary CTA^f

Choice of the test based on clinical likelihood, patient characteristics and preference, availability, as well as local expertise^d

Testing for ischaemia (imaging testing preferred)

Invasive angiography (with iwFR/FFR)^e

Very low

Clinical likelihood of obstructive CAD

Very high

I

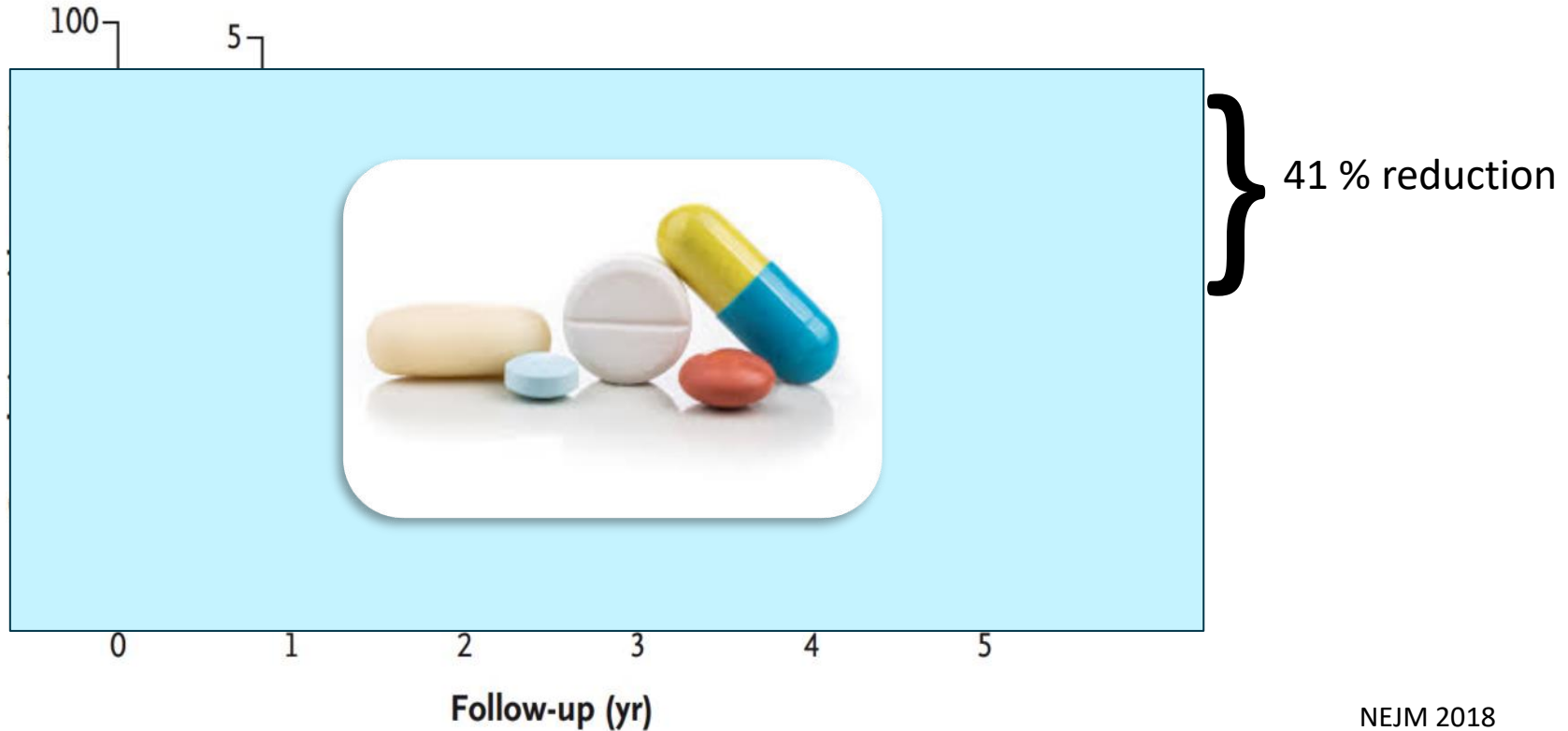
CT calciumscore



Calcium score	Interpretation	Risk of myocardial infarction/stroke at 10 years
0	Very low risk	<1%
1–100	Low risk	<10%
101–400	Moderate risk	10–20%
101–400 and >75th percentile	Moderately high risk	15–20%
>400	High risk	>20%

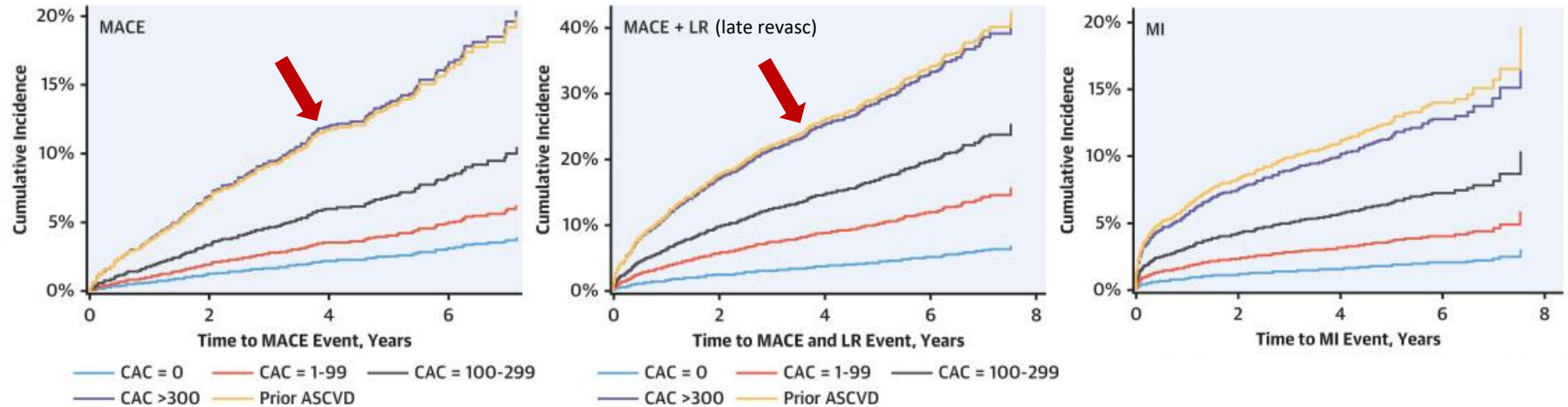
Scot-Heart study: N 4146

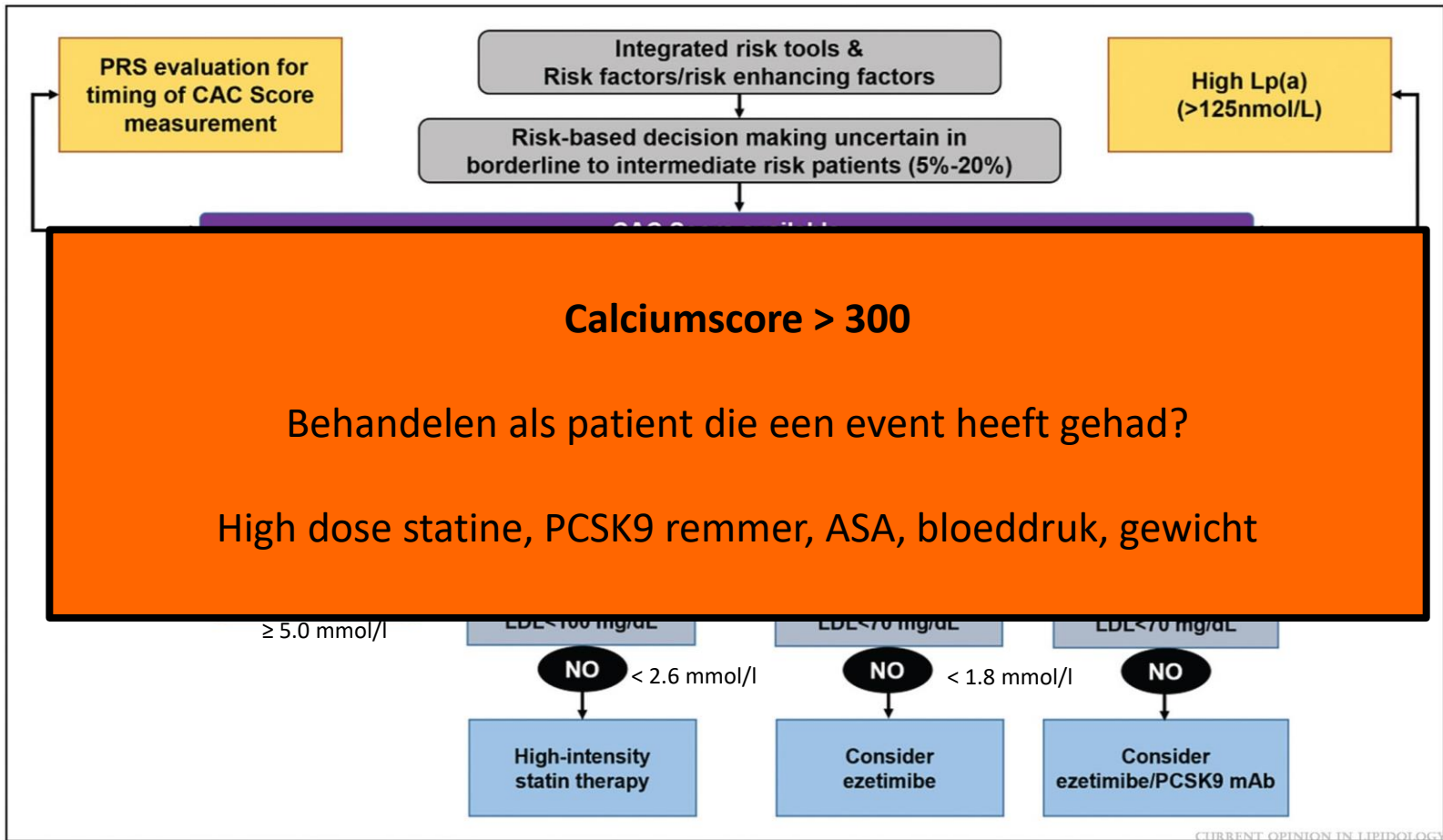
Death from Coronary Heart Disease or Nonfatal Myocardial Infarction



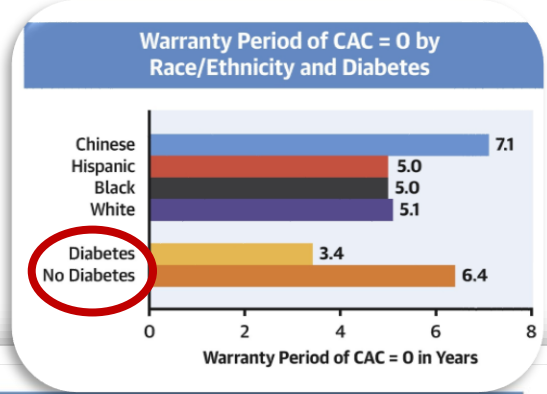
CT calciumscore en CV risk

N = 4.511 zonder doorgemaakt event
Cohort met een doorgemaakt event

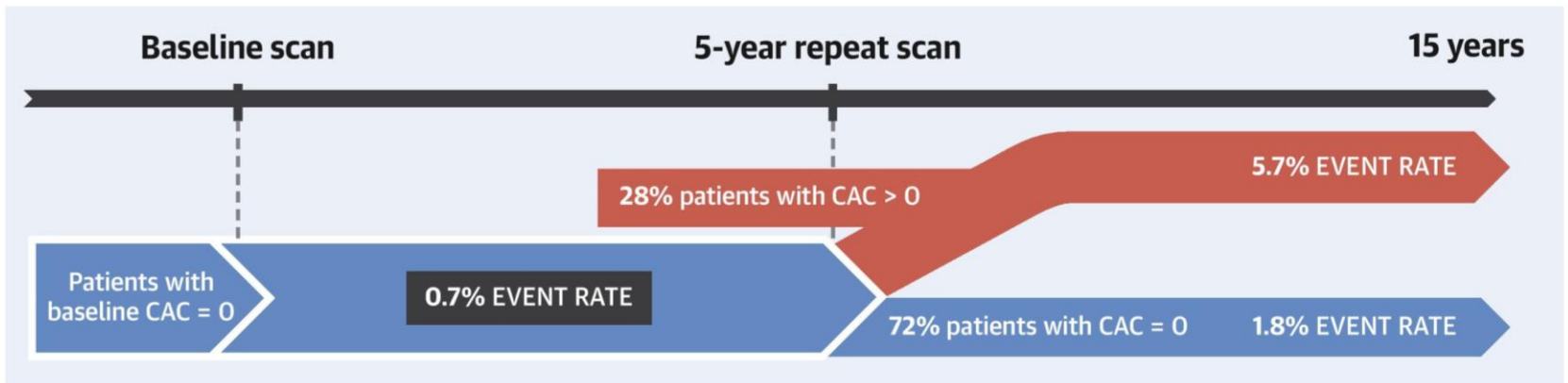




“Geldigheid”



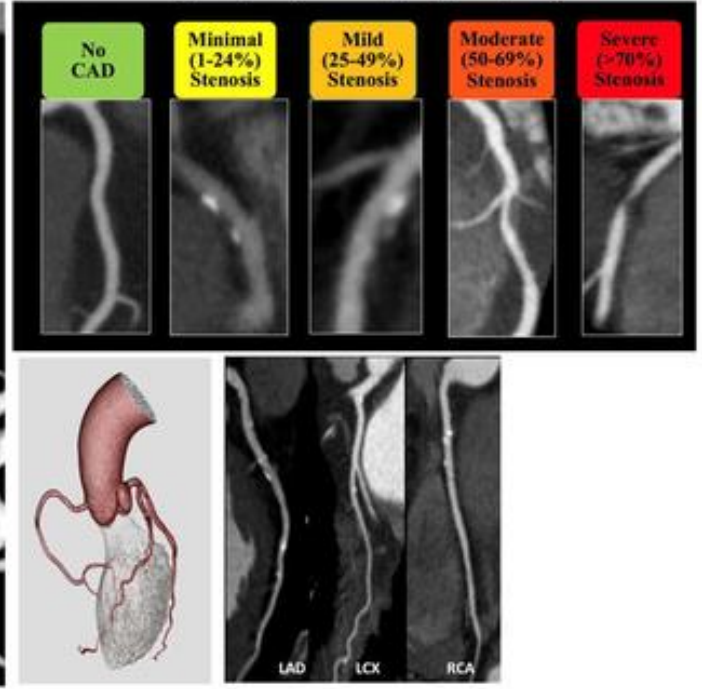
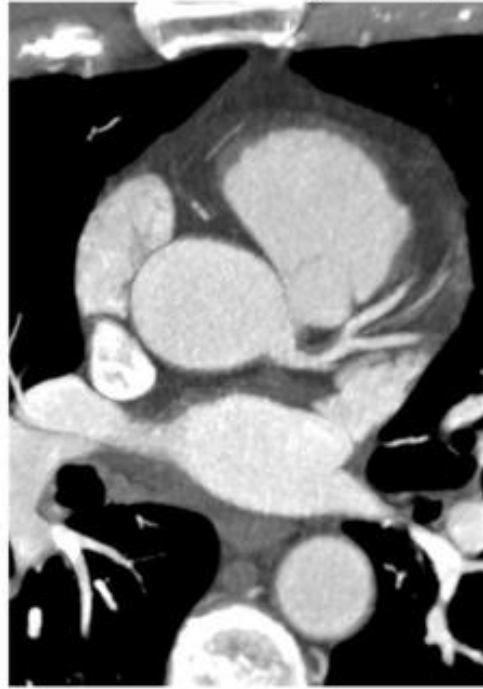
CHD Events Before and After 5-Year Repeat Scan



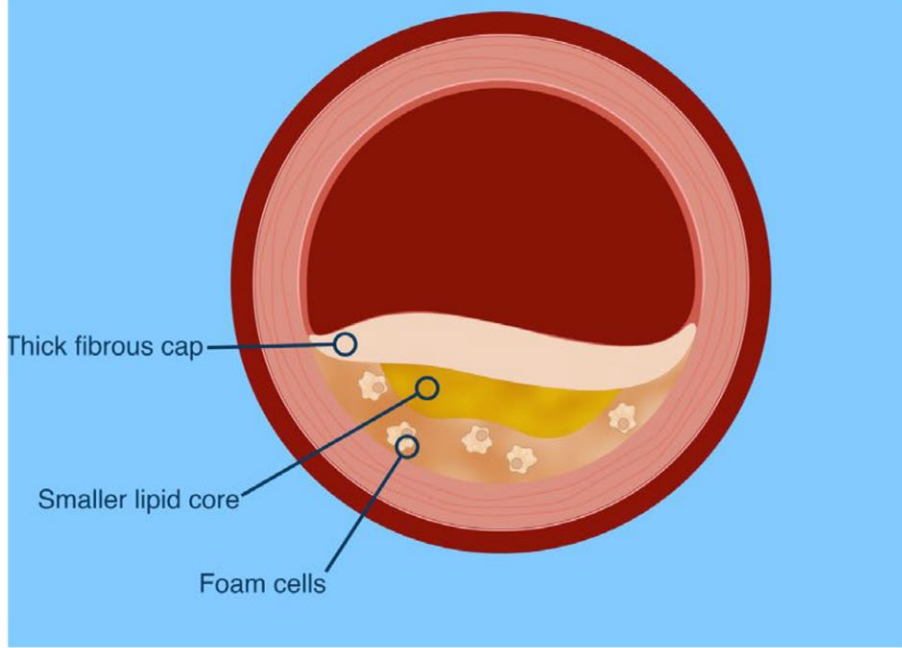
Coronary Calcium



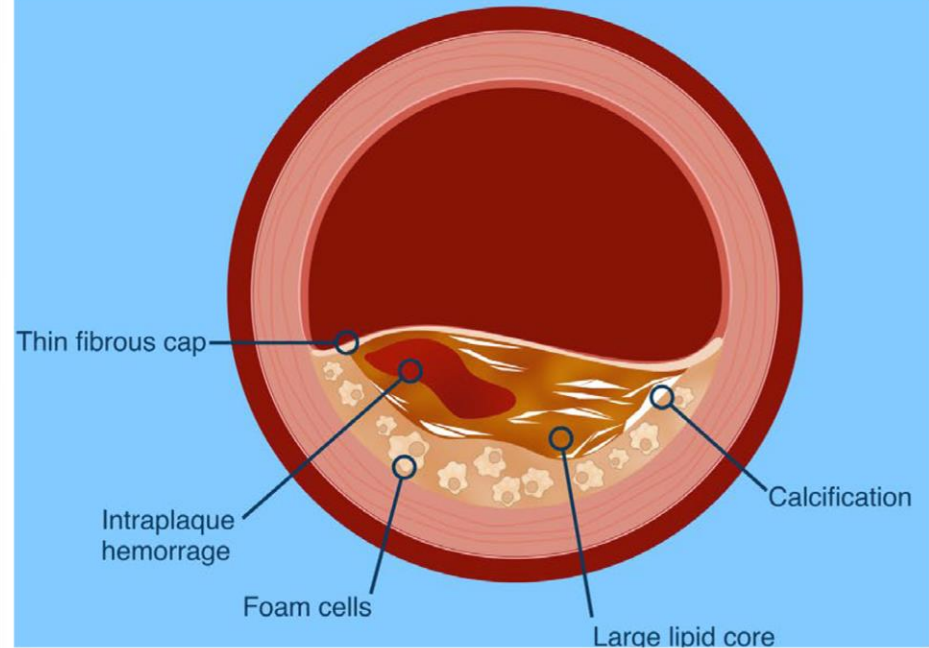
Coronary Computed Tomography Angiography



Stable plaque

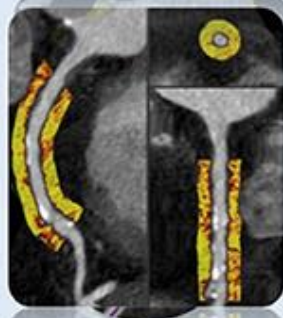
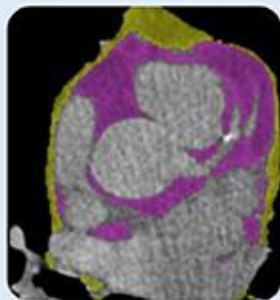


Vulnerable plaque



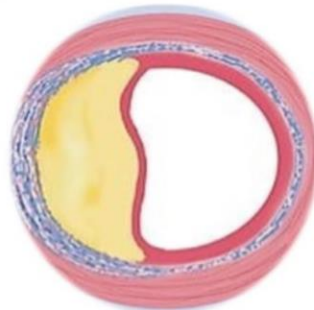
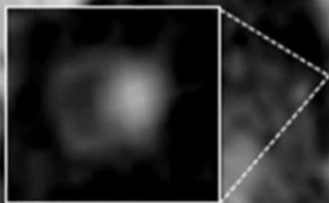
Precision imaging

Epicardial adipose tissue (EAT)

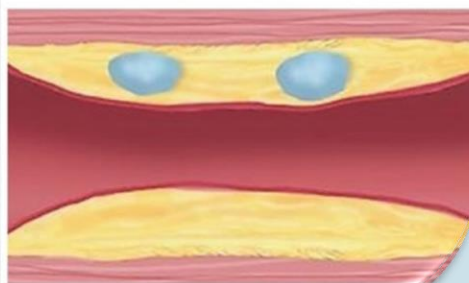
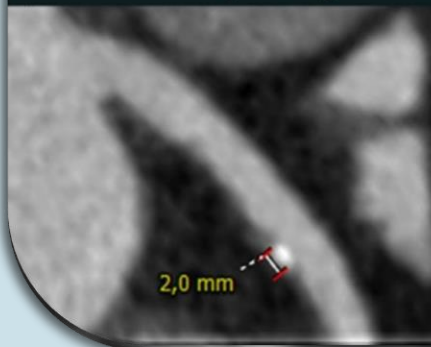


Pericoronary adipose tissue (PCAT)

“Napkin-ring” sign



Spotty Calcifications



Acute plaque rupture or plaque erosion



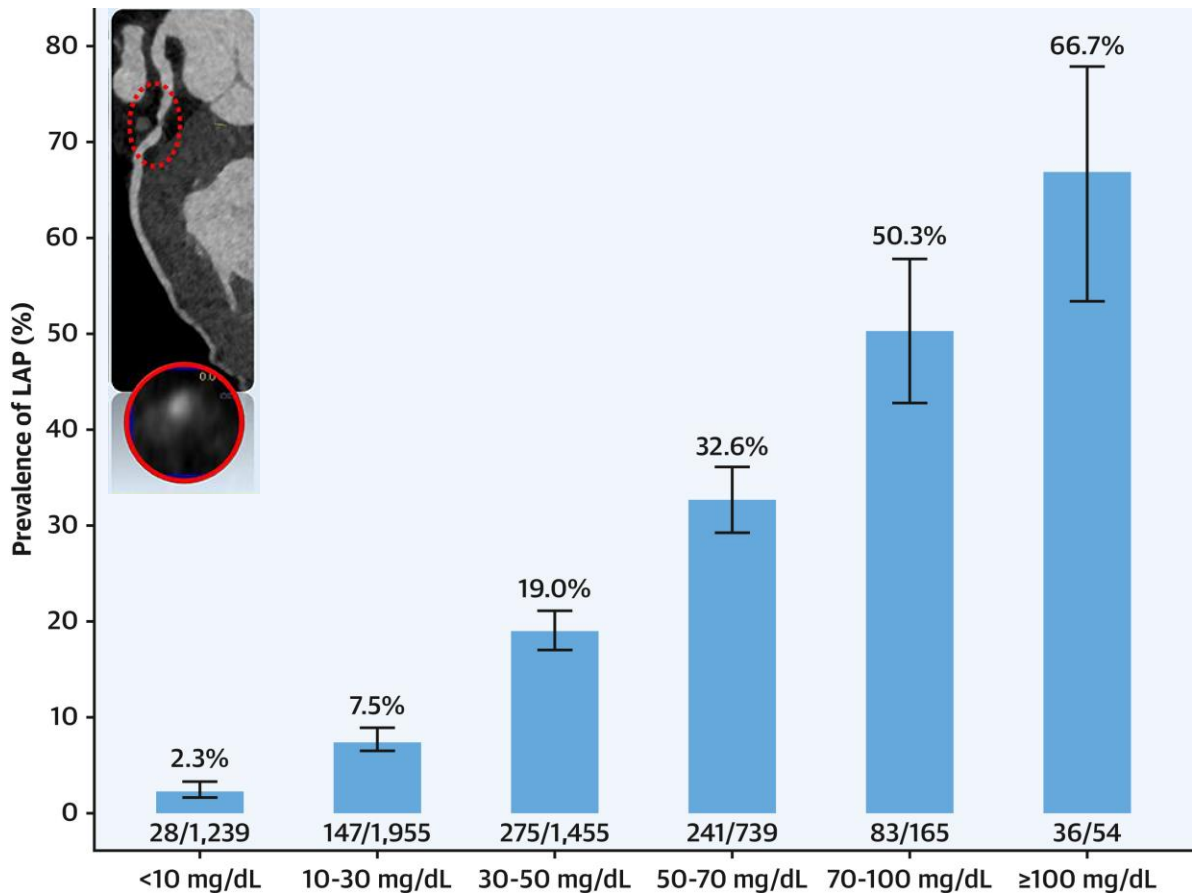
Acute coronary syndromes
Sudden cardiac death

High risk patient: verhoogd lipoproteïne(a)

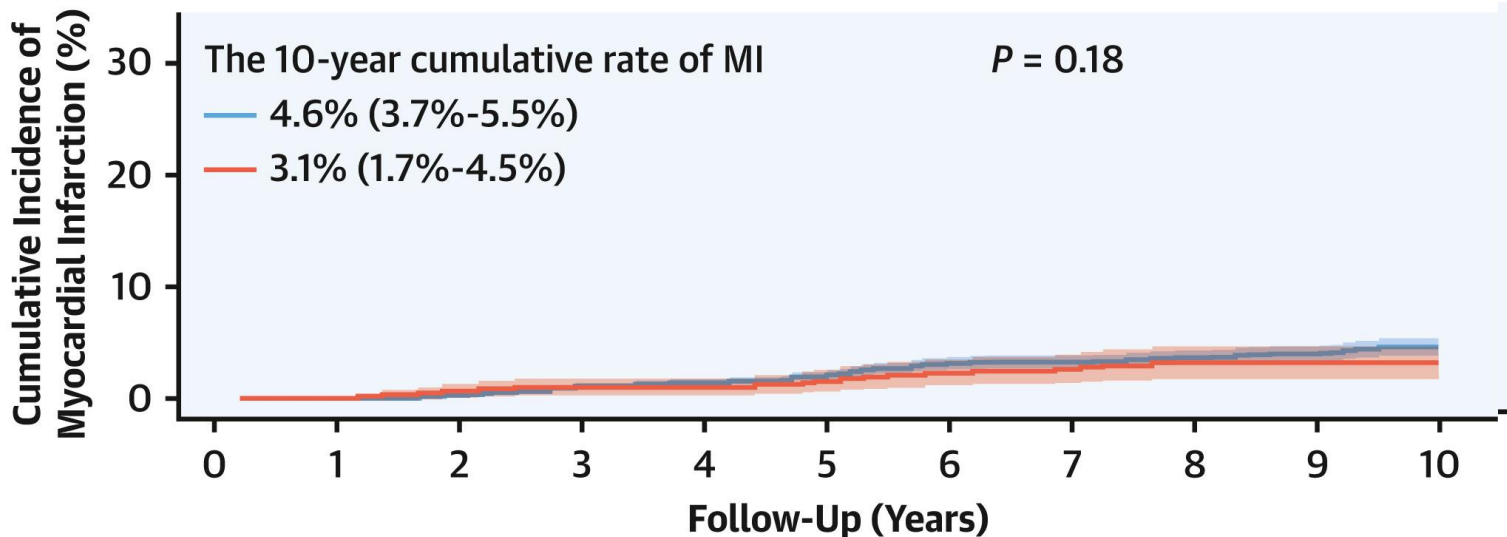
N = 5.607 + 1.122

CCAD

CT scan en FU: 8 y



C In Patients With Absence of LAP



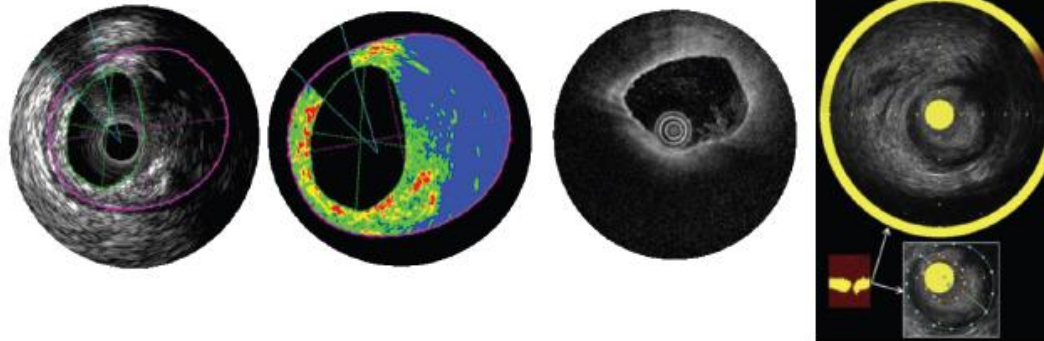
Number at risk

Follow-Up (Years)	0	1	2	3	4	5	6	7	8	9	10
Lp(a) <50 mg/dL	4,199	4,185	4,131	4,066	4,034	3,942	3,508	3,039	2,315	1,079	206
Lp(a) ≥50 mg/dL	598	594	589	582	576	571	562	553	547	493	219

Follow-Up (Years)

Invasive plaque karakterisatie

Modality	IVUS	IVUS-RF Analysis	OCT/OFDI	NIRS
Energy source	Ultrasound (20–60 MHz)	Ultrasound (20–40 MHz)	Near-infrared light	Near-Infrared light
Resolution	100–200 μm	100–200 μm	10–15 μm	NA
Penetration	8–10 mm	8–10 mm	2–3 mm	1–2 mm
Features of high-risk plaque	Eccentric pattern, outward remodeling, large plaque burden, large lipid core (echolucent core), spotty calcification	Plaque composition (fibrous, fibro-fatty, necrotic core, And calcification), large necrotic core (RF-IVUS-derived TCFA)	Thin fibrous cap, macrophage infiltration, neovascularization, large lipid core, spotty calcification	High lipid contents (high LCBI)
Limitation	Invasiveness, limited spatial resolution	Invasiveness, limited spatial resolution,	Invasiveness, limited tissue penetration, need for flushing	Invasiveness, limited tissue penetration



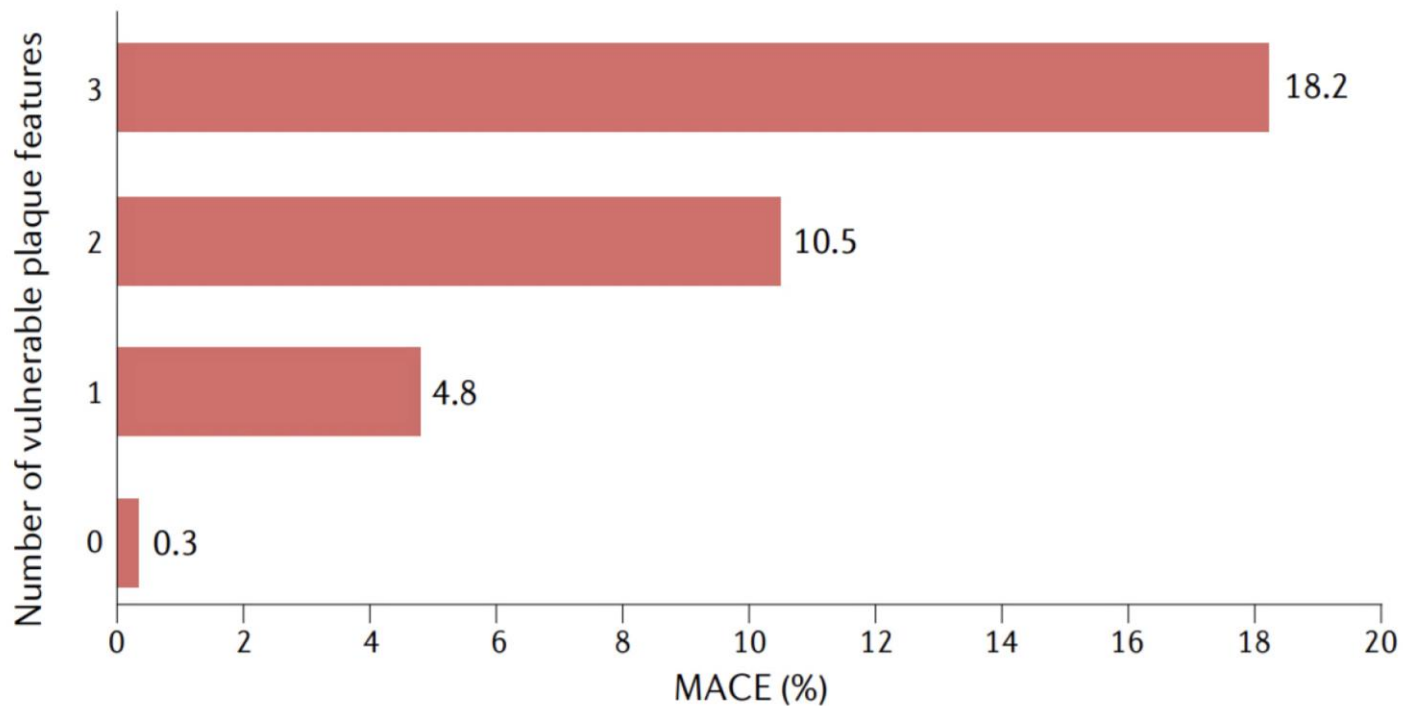
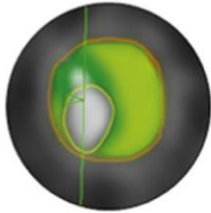


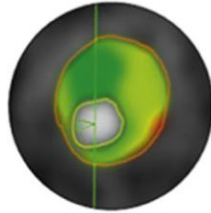
Fig. 8 | Vulnerable plaque features are associated with an increased risk of cardiac events. Data from the PROSPECT study³⁸ indicate that the greater the number of vulnerable features (plaque burden of $\geq 70\%$, minimal luminal area $\leq 4.0 \text{ mm}^2$ and virtual histology-defined thin-cap fibroatheroma), the greater the rate of non-culprit lesion-related major adverse cardiac events (MACE) at a median of 3.4 years of follow-up.

Statin-naïve patients

Baseline

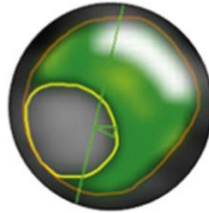


Follow-up

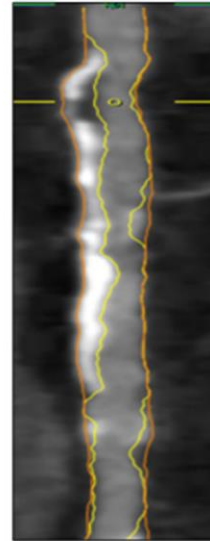
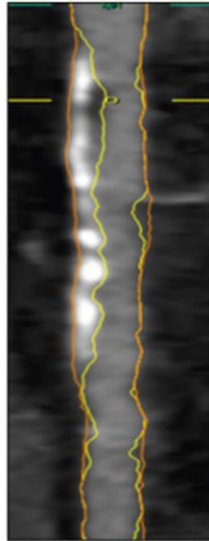
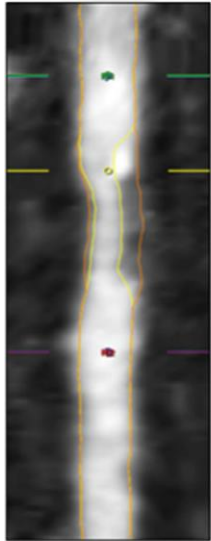
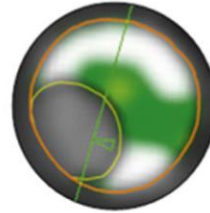


Statin-taking patients

Baseline



Follow-up



Plaque
composition

Dense calcium

Low-attenuation

Fibrous

Fibro-fatty

Table 1 | Randomized clinical trials of pharmacotherapy intensification for patients with non-culprit lesions

Study (year)	Cohort (number of patients)	Comparison (number of patients)	Therapy duration (weeks)	Change in LDL-C level (mg/dl)	Change in fibrous cap thickness (µm)	Change in lipid arc (degrees)	Change in maxLCBI _{4mm}	Ref.
YELLOW (2013)	Patients with multivessel CAD undergoing PCI and at least one non-target lesion (87)	Standard-of-care lipid-lowering therapy (43) versus rosuvastatin 40 mg daily (44)	7	Baseline 82.8 ± 26.9; follow-up 81.9 ± 27.9 versus baseline 79.1 ± 25.3; follow-up 58.4 ± 26.3 ^a ; P < 0.01	–	–	2.4 (–36.1 to 44.7) versus –149.1 (–210.9 to –42.9) ^b ; P < 0.01	130
EASY-FIT (2014)	Patients with untreated dyslipidaemia, unstable angina and an untreated, non-culprit lesion identified by OCT (60)	Atorvastatin 5 mg daily (30) versus atorvastatin 20 mg daily (30)	52	–44 (–63 to –29) versus –58 (–74 to –45) ^c ; P < 0.05	19 (–1 to 48) versus 73 (28 to 113) ^c ; P < 0.001	–10 (–20 to –5) versus –50 (–60 to –30) ^c ; P < 0.001	–	129
HUYGENS (2022)	Patients with non-STEMI and an untreated, non-culprit vulnerable plaque identified by OCT (161)	Placebo plus statin (81) versus evolocumab plus statin (80)	52	–55.3 ± 47.1 versus	21.5 (10.9–32.1)	–31.4 (–50.2	–	131
PACMAN-AMI (2022)	Patients undergoing PCI for acute MI and untreated, non-culprit lesions identified by NIRS-IVUS and OCT (300)	Placebo plus statin (152) versus alirocumab plus statin (148)	9				(–57.4 to) versus (–100.4 8.5) ^d ; P = 0.006	132

PCSK 9 remmer on top of statine:

- LDL lager
- Dikkere fibreuze cap
- Grotere “lipiden-kern”

CAD, coronary artery disease; LDL-C, LDL-cholesterol; maxLCBI_{4mm}, maximum 4-mm lipid core burden index; IVUS, intravascular ultrasonography; MI, myocardial infarction; NIRS, near-infrared spectroscopy; non-STEMI, non-ST-segment elevation myocardial infarction; OCT, optical coherence tomography; PCI, percutaneous coronary intervention. ^aMean ± standard deviation. ^bMedian (95% CI). ^cMedian (Q1, Q3). ^dMean (95% CI).

Preventive percutaneous coronary intervention versus optimal medical therapy alone for the treatment of vulnerable atherosclerotic coronary plaques (PREVENT): a multicentre, open-label, randomised controlled trial

Seung-Jung Park, Jung-Min Ahn*, Do-Yoon Kang, Sung-Cheol Yun, Young-Keun Ahn, Won-Jang Kim, Chang-Wook Nam, Jin-Ok Jeong, In-Ho Chae, Hiroki Shiomi, Hsien-Li Kao, Joo-Yong Hahn, Sung-Ho Her, Bong-Ki Lee, Tae Hoon Ahn, Ki-Yuk Chang, Jei Keon Chae, David Smyth, Gary S Mintz, Gregg W Stone, Duk-Woo Park, for the PREVENT Investigators†*

LET OP:

STABIEL AP > 80%

NON-FLOW-LIMITING NON-CULPRIT LESIONS (FFR >0.80)

N = 1606
Stabiel AP
FFR > 0.80

Moet je deze non-culprit High Risk Plaques dotteren

OF

Sneller en 'agressiever' de risicofactoren te behandelen?
(Niet allen high dose statine, PCSK9-i? LDL 2.3 mmol/l)

	Number at risk (number censored)							
Optimal medical therapy alone	803 (0)	765 (18)	710 (68)	544 (233)	432 (344)	308 (469)	198 (580)	61 (727)
Preventive percutaneous coronary intervention plus optimal medical therapy	803 (0)	792 (9)	745 (55)	570 (221)	450 (337)	320 (464)	198 (589)	77 (712)

Take home message

Huidige richtlijnen / risicostratificatie: Infarct – PCI versus geen infarct

~~Infarct (PCI)~~ =  = Infarct (PCI)

High Risk Patient

Take home message

Patient tailored approach → identificeren “High Risk Patient”

Risicostatificatie aan de hand van “Totaal Plaatje”

Comorbiditeit – Lab biomarkers - Imaging

Dank voor uw aandacht

