Casus 1:

PCSK9-inhibitie bij atherosclerotisch vaatlijden

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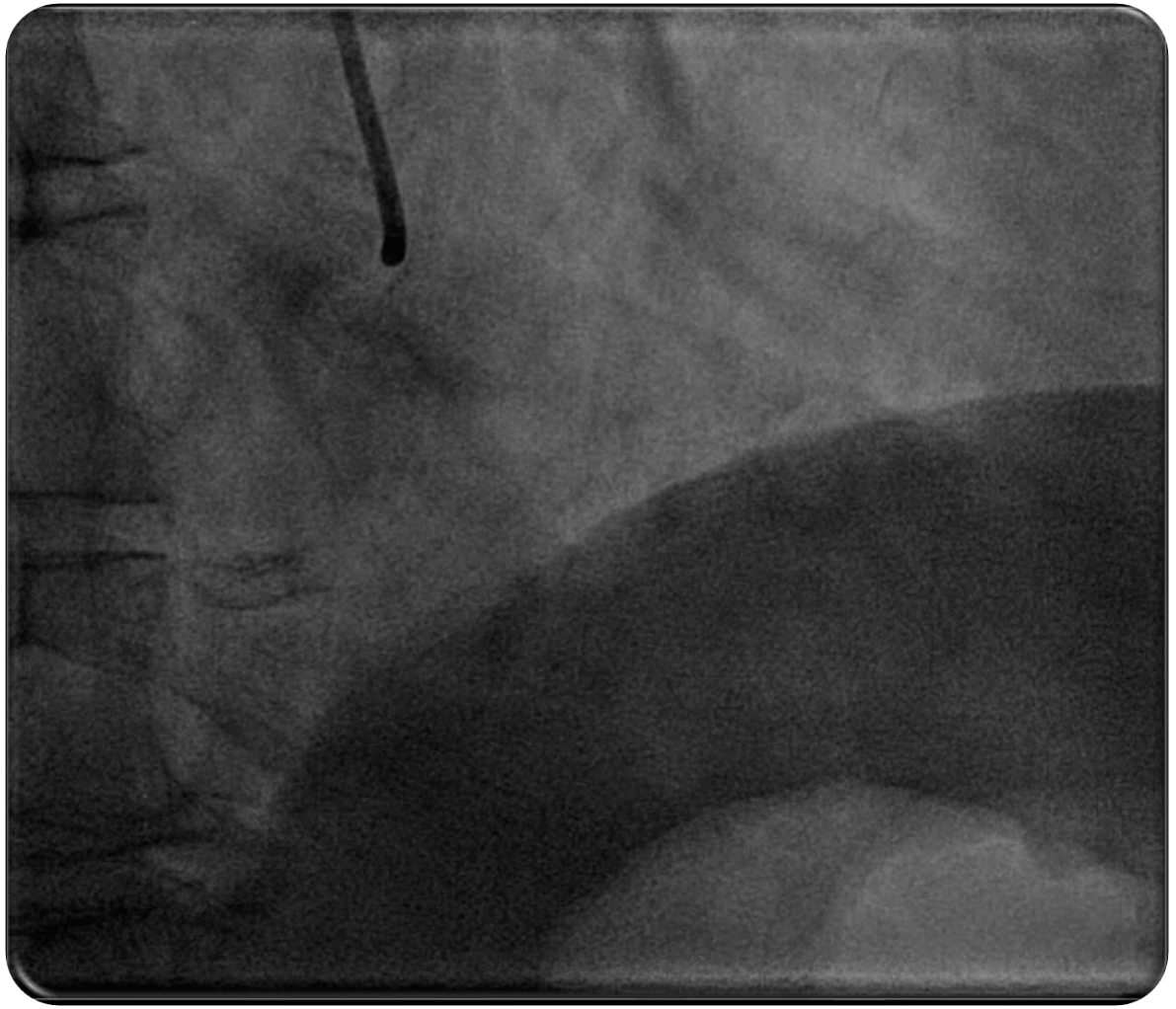
Disclosures

Geen

Casus



Man 49 jaar oud

- Herkenbare druk op de borst
- Inspanning, zakt in rust
- Laatste week “globus gevoel” in keel

Klinische parameters

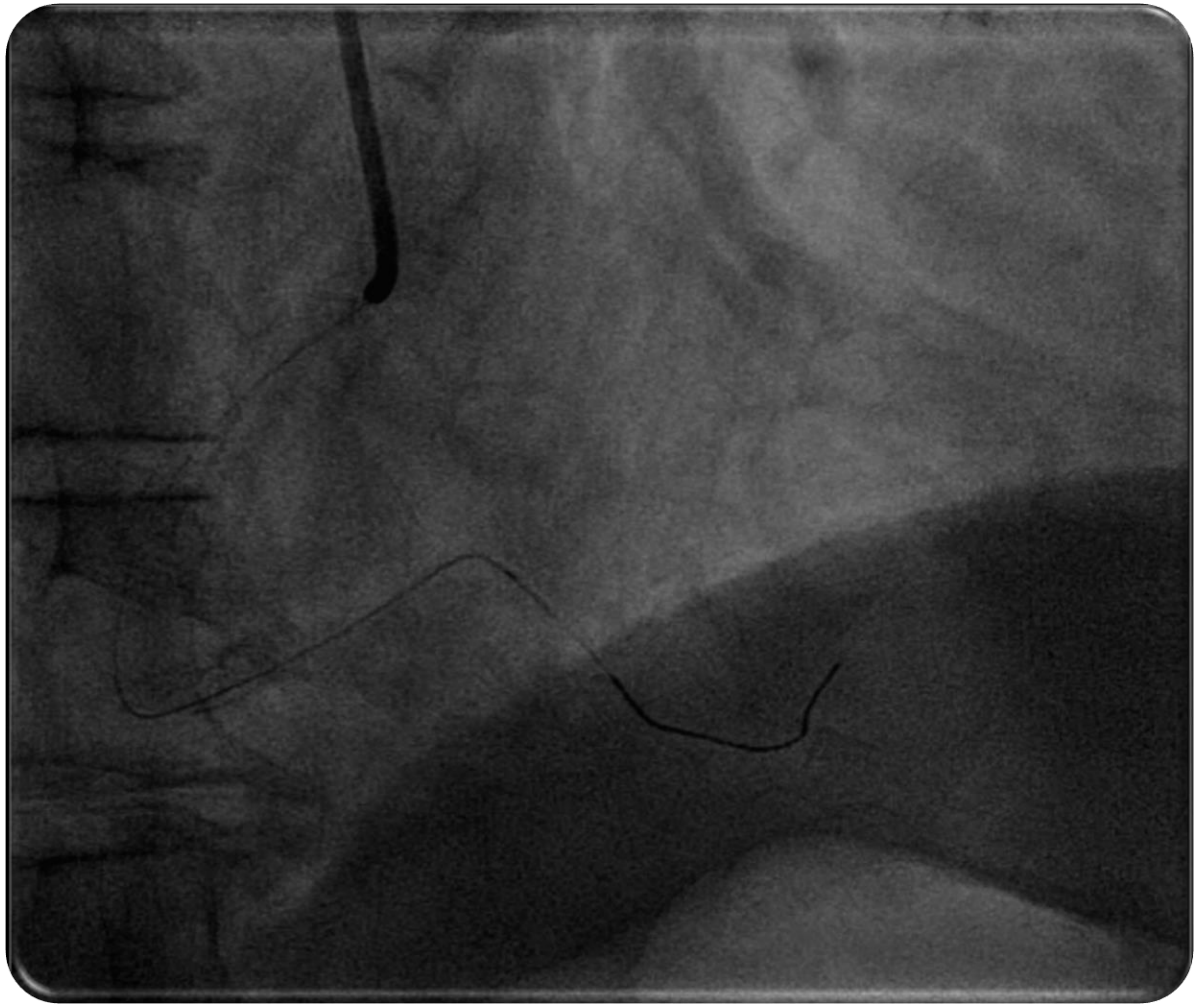
Voorgeschiedenis:
2022 Beperkt STEMI inferior waarvoor PCI RCA
Dyslipidemie

Risicofactoren: roken gestopt in 2021, dyslipidemie waarvoor statine, positieve familieanamnese: vader hartinfarct op 46 jarige leeftijd, broer van vader hartinfarct op 59 jarige leeftijd.

Huidige medicatie: acetylsalicylzuur, atorvastatine 40 mg, metoprolol gestopt in 2022 (bijwerkingen), ezetimbe gestopt (bijwerkingen), lisinopril 5 mg gestopt na echocardiogram

Stabiel angina pectoris (CSS 2)

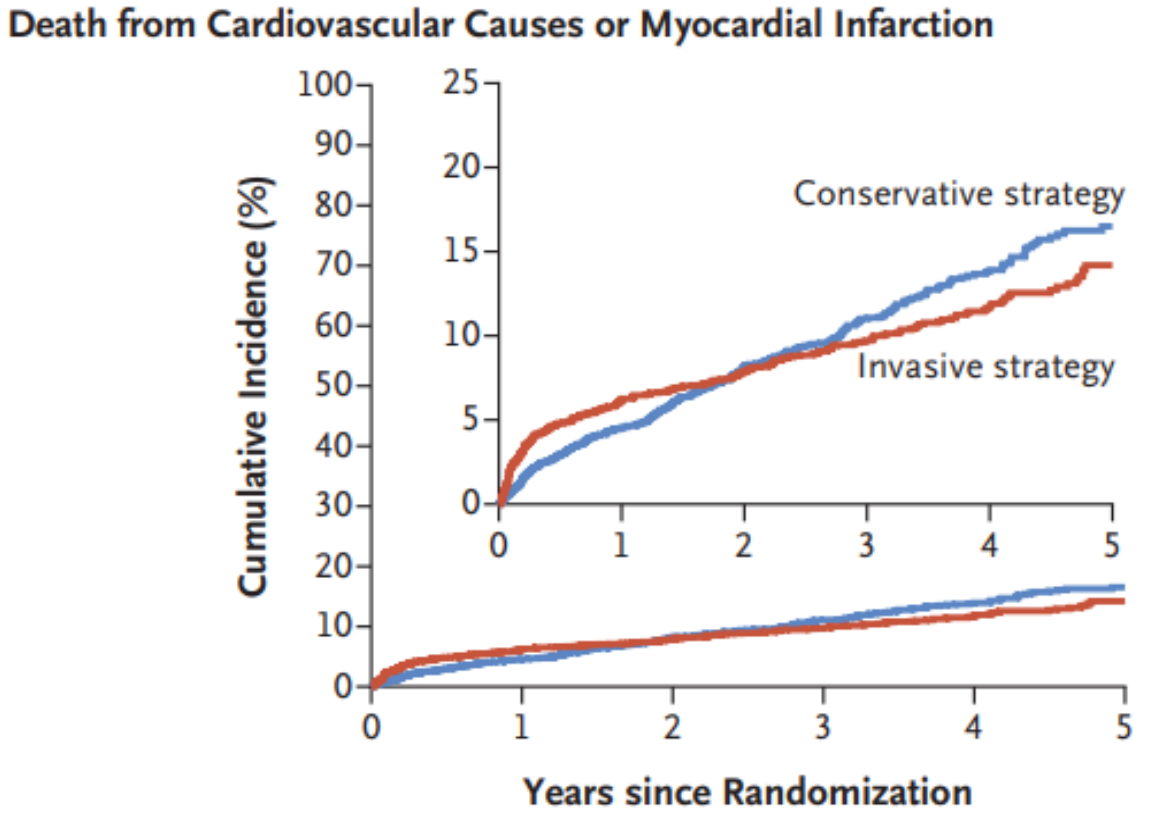
Start:
clopidogrel, isosorbidemononitraat, pantoprazol



Stabiel coronairlijden

N = 5.179
Bewezen ischemie

Randomisatie
- Initieel invasief
- Medicamenteuze therapie



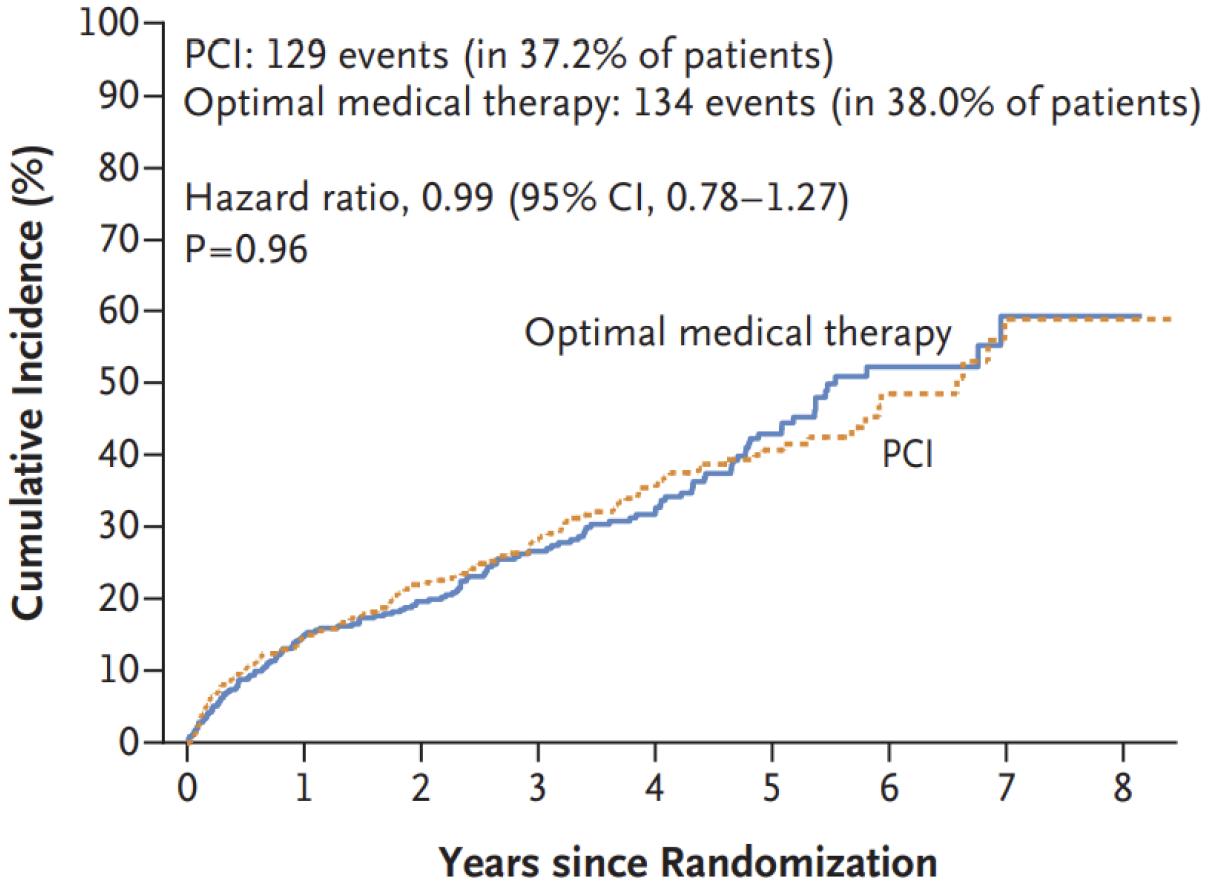
No. at Risk

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

ISCHEMIA Research Group NEJM 2020

N = 700

- LVEF ≤ 35%
- Obstructief coronairlijden
- Aangetoonde viabiliteit



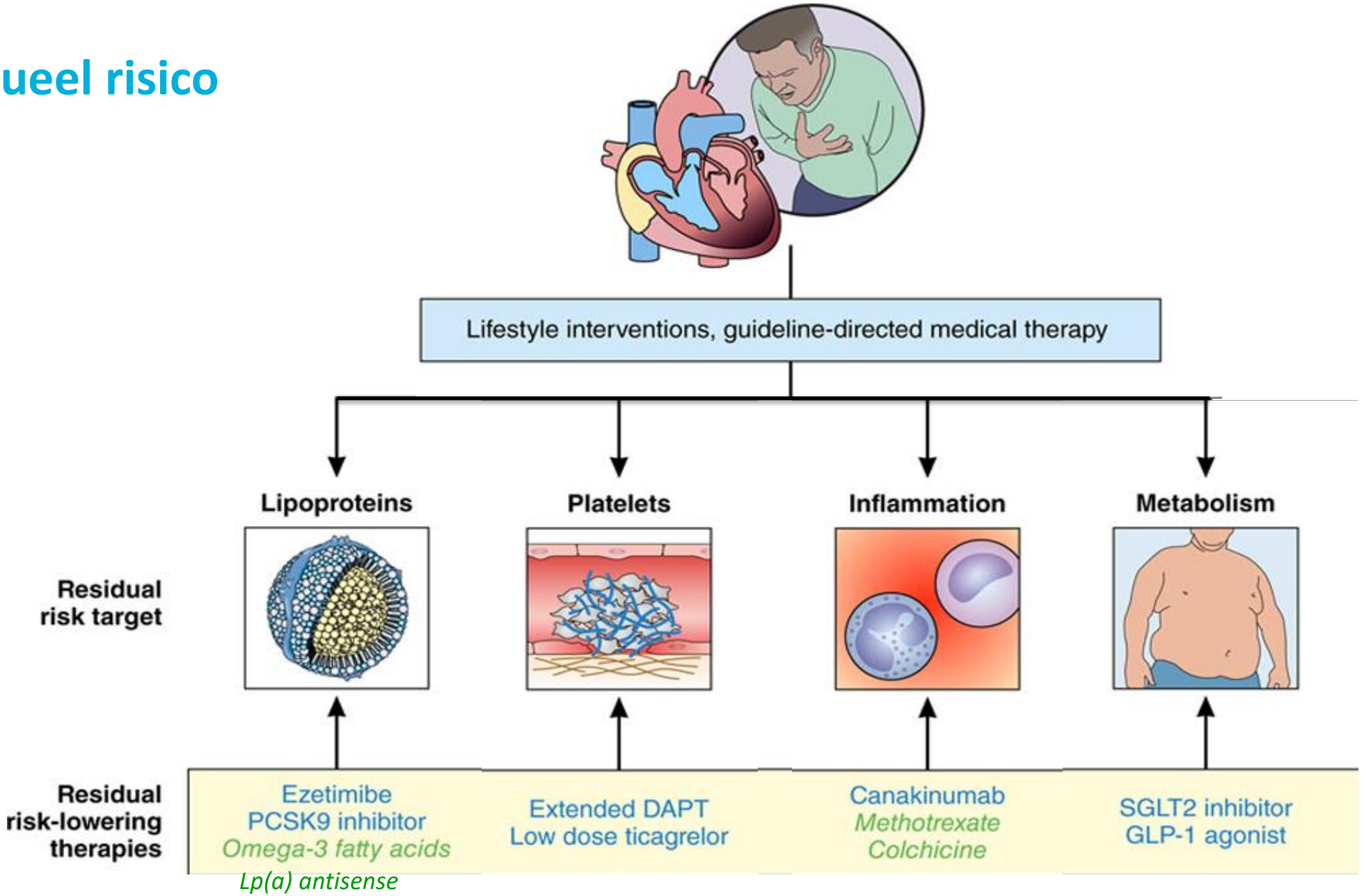
No. at Risk

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.

REVIVED NEJM 2022

Residueel risico



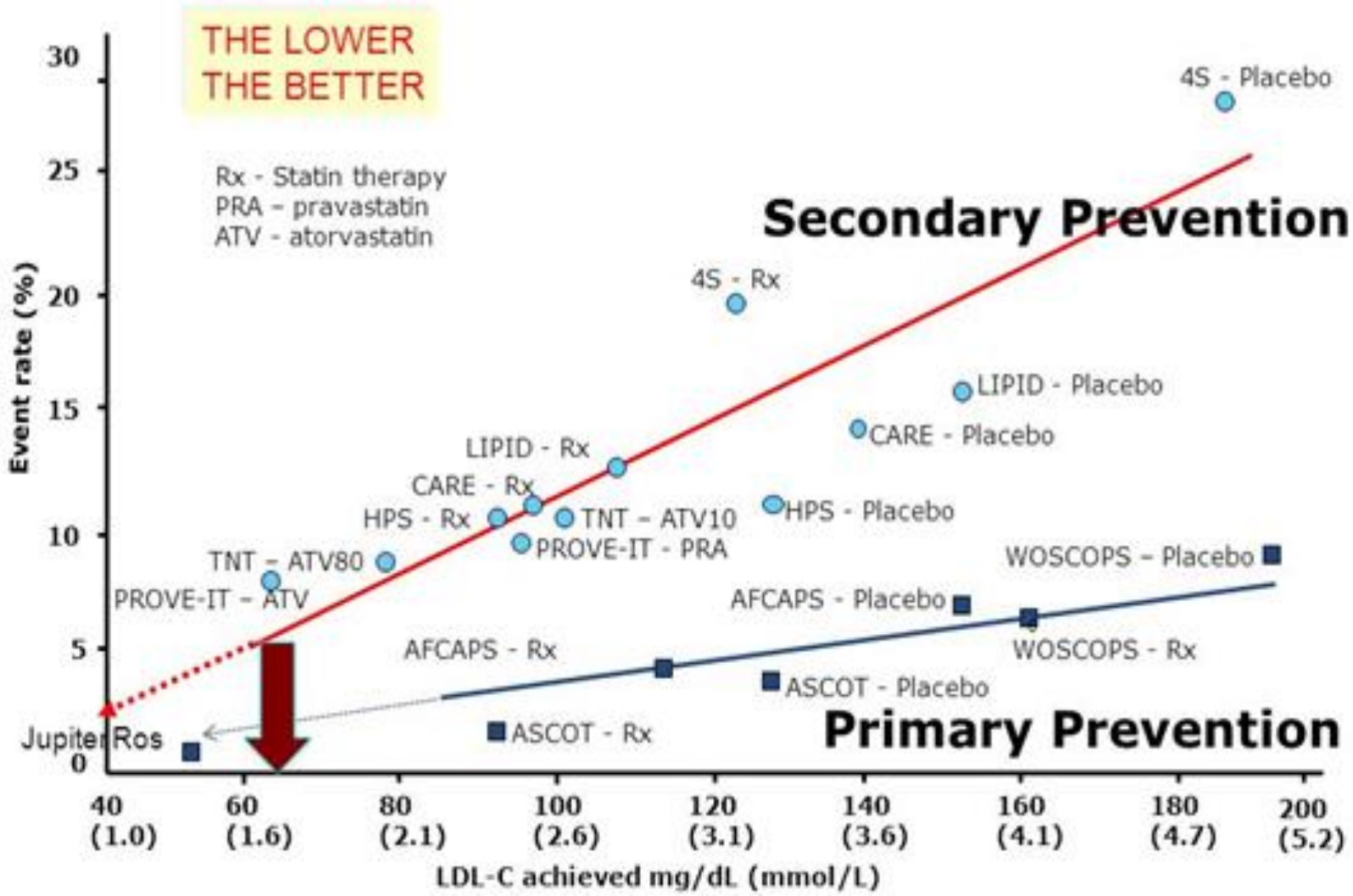
Adapted/modified from Patel et al. Circulation. 2018;137:2551–2553

Klinische parameters (2)

Laboratoriumonderzoek (atorvastatine 40 mg)

Totaal cholesterol	4.4 mmol/l
LDL-c	2.7 mmol/l
HDL-c	1.2 mmol/l
Triglyceriden	1.52 mmol/l
Lipoproteïne(a)	175 nmol/l

Lipiden – CV risico



LaRosa JC et al. N Engl J Med 2005;352:e-version

Interactieve poll

Wat is het percentage afname in het cardiovasculaire risico bij elke daling van 1 mmol/l LDL-cholesterol?

A. 5%

B. 12%

C. 20%

D. 50%

Wat is het percentage afname in het cardiovasculaire risico bij elke daling van 1 mmol/l LDL-cholesterol?

C. 20%

Iedere mmol/l daling in LDL-cholesterol geeft een daling van ruim 20% in cardiovasculair risico*

*Lancet 2015

LDL-cholesterol: The lower the better

I A

In secondary prevention for patients at very-high risk,[c] an LDL-C reduction of ≥50% from baseline[d] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL) are recommended.[33–35,119,120]

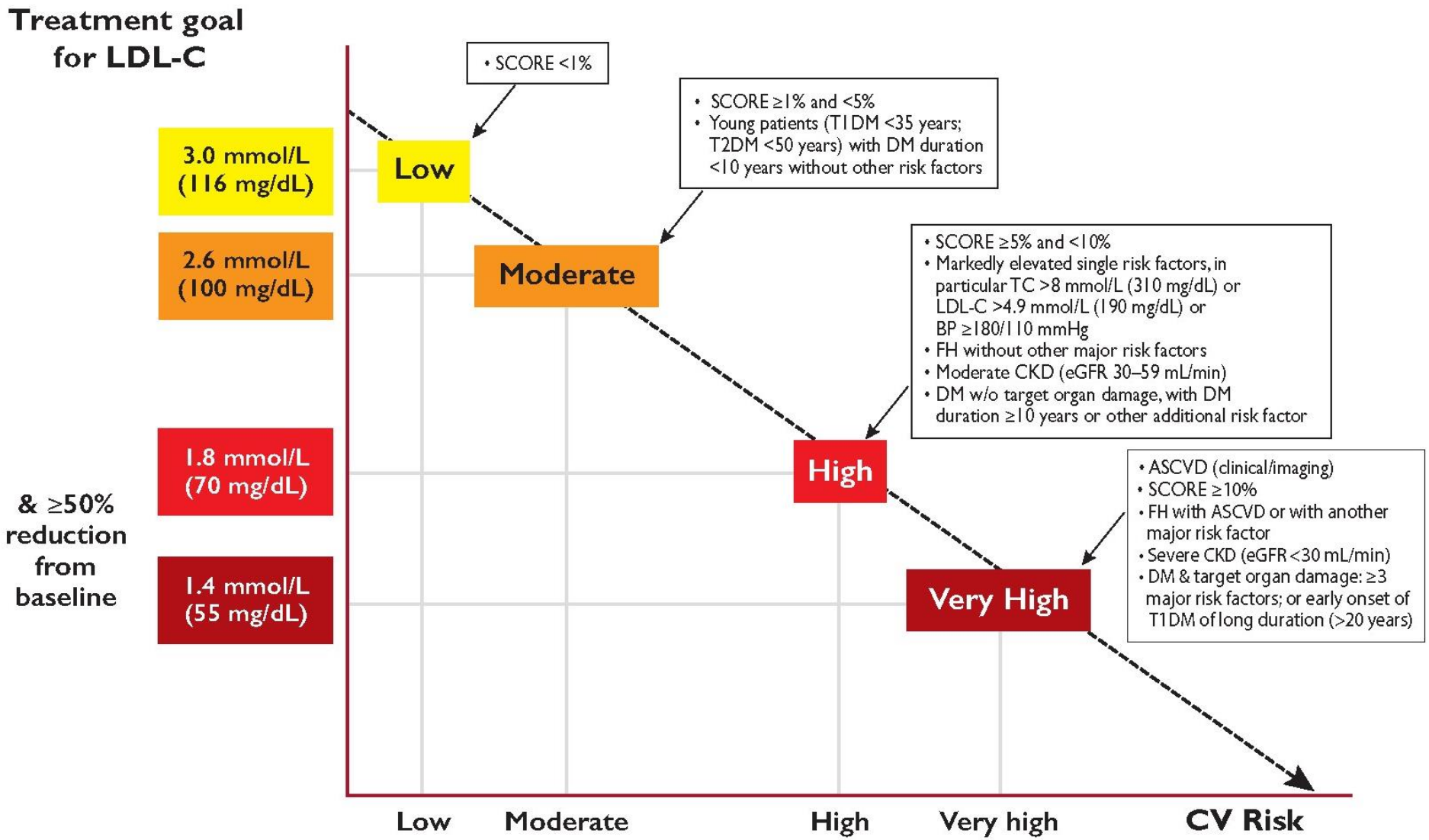
I A

For secondary prevention, patients at very-high risk not achieving LDL-C <1.4 mmol/L after 4–6 weeks of maximum-tolerated statin and ezetimibe therapy, a combination with a PCSK9 inhibitor is recommended.[119,120]

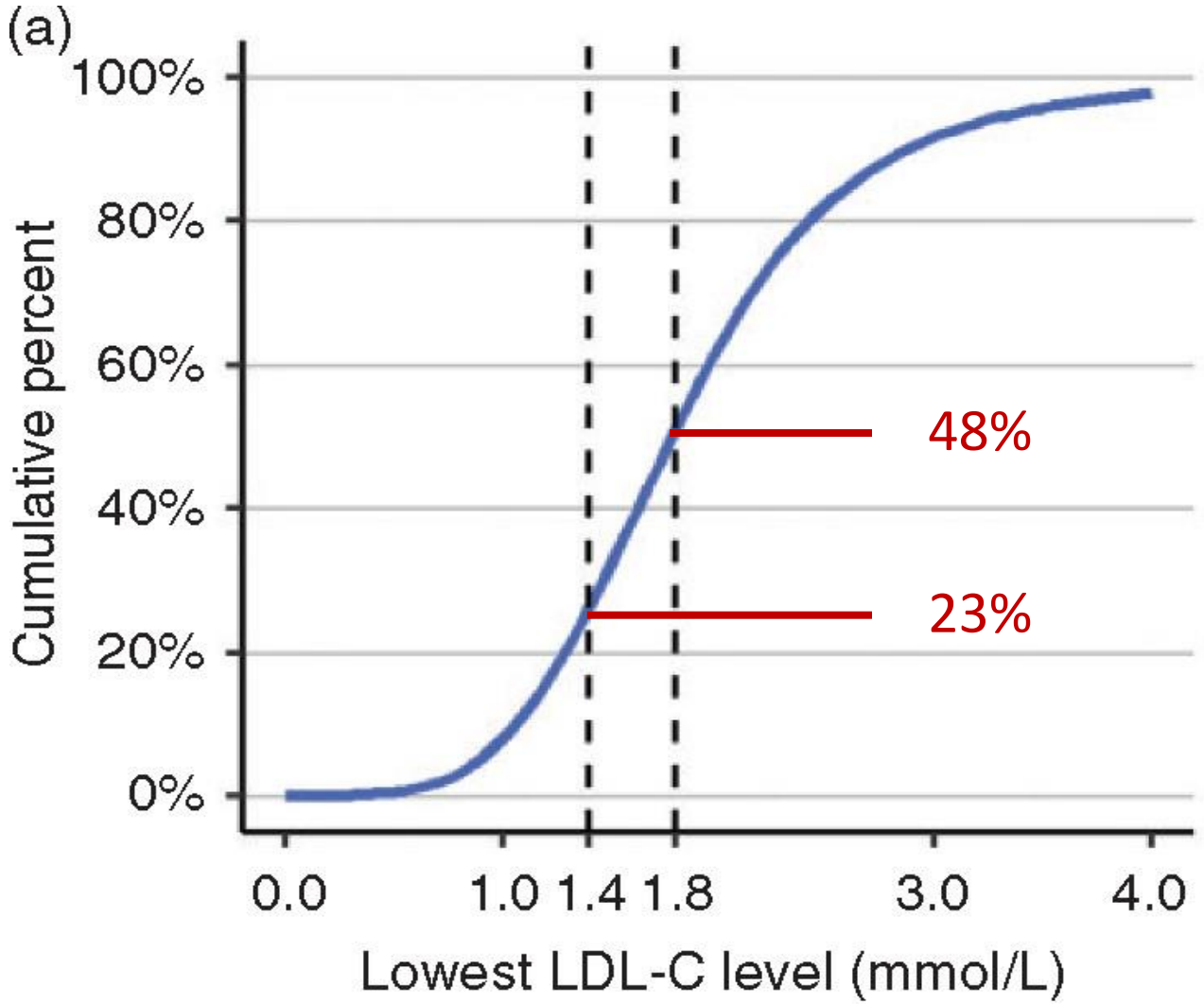
IIb B

For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]

ESC guideline 2019



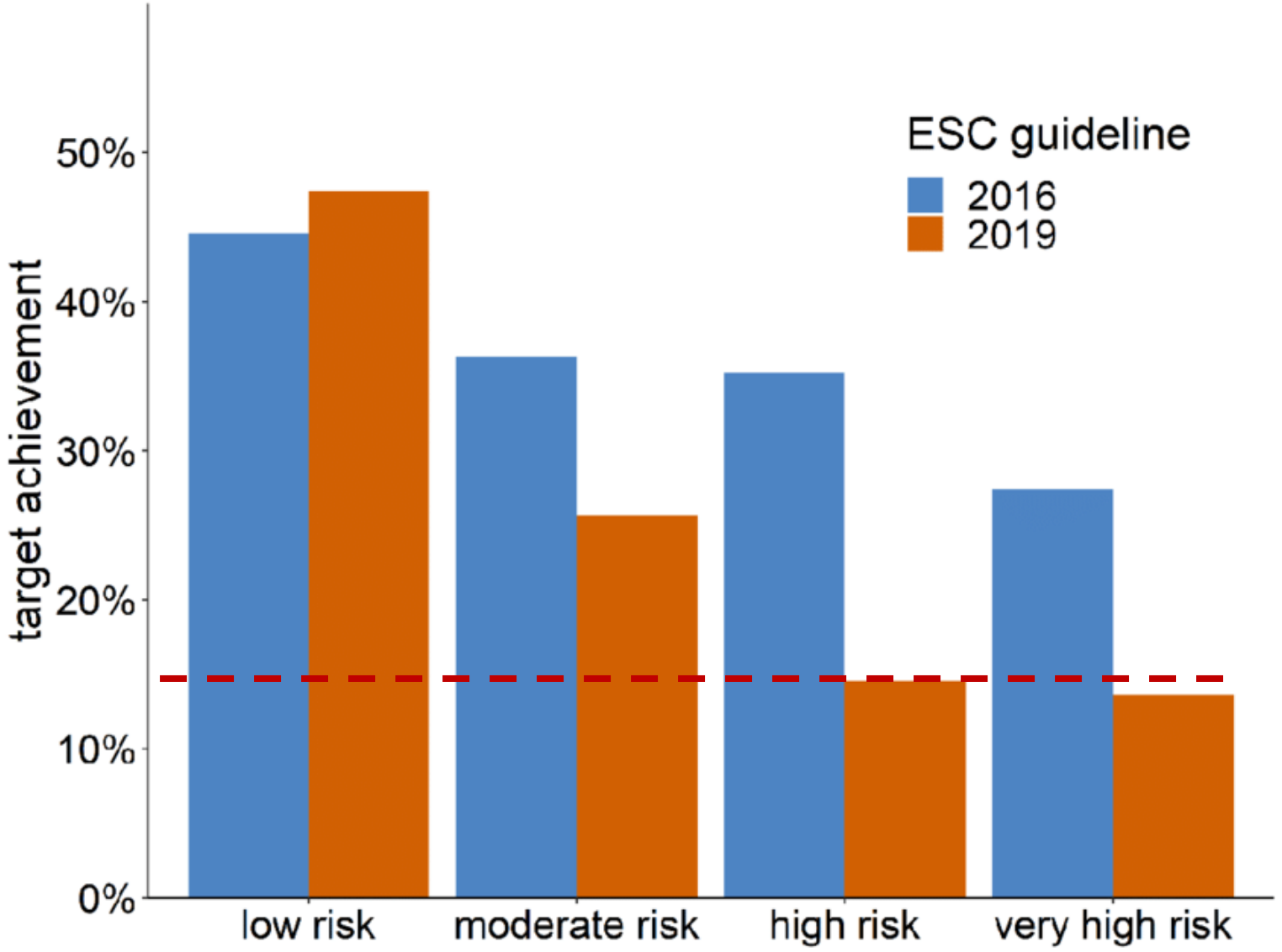
ESC guideline 2019



N = 10,071 na PCI
T= 1 jaar

Harris et al, Eur. J. Prev. Cardiol. 2021

N = 8060
Eerste lijn



Meier et al; Journal of Clinical Medicine July 2020

Veelgehoorde opmerkingen..

Patiënt

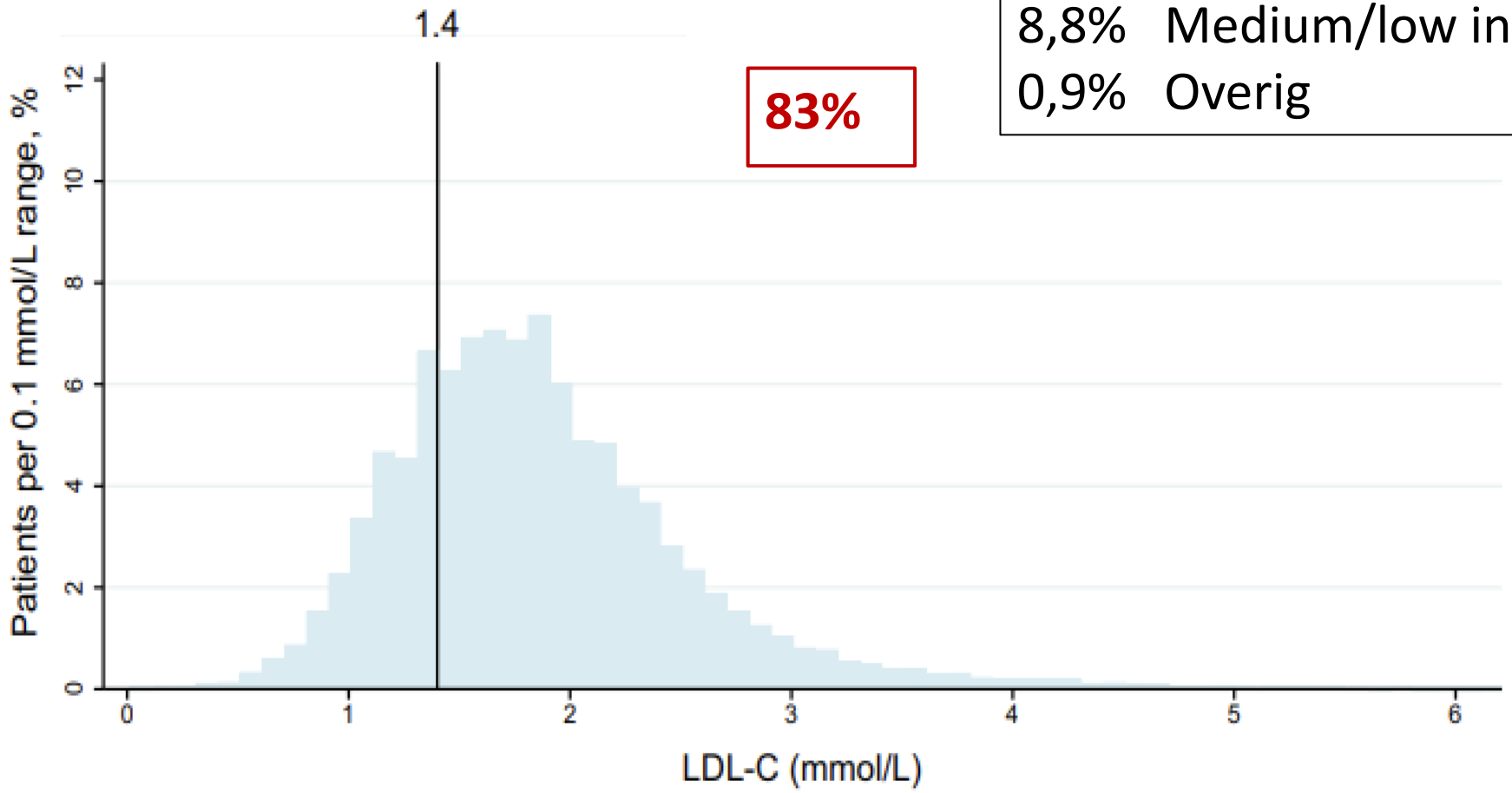
“Dokter, ik wil het eerst zelf proberen. Ik ben nu gemotiveerd om af te vallen”

- **0.2 mmol/l LDL reductie per 10 kg gewichtsverlies**
- Effect van fysieke inspanning op het LDL is zelfs kleiner

Dokter

- Laat de huisarts / de cardioloog het LDL-c instellen

N = 25.466



83%

6-10 weken na MI

86,6% Mono- High intensity statine (HIS)

8,8% Medium/low intensity statine

0,9% Overig

Allahyari et al; European Heart Journal 2020

Interactieve poll

Vraag

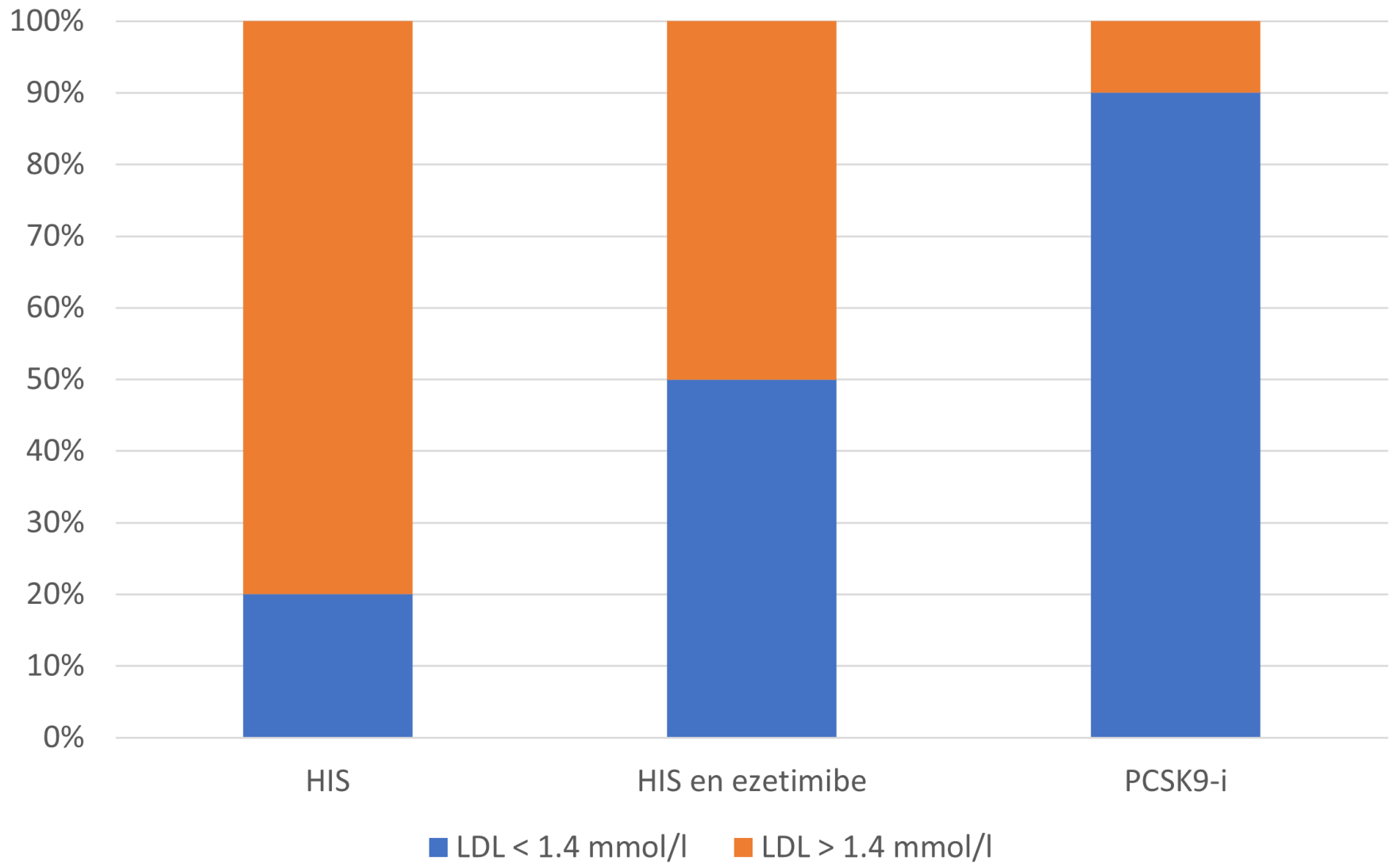
Welk antwoord(en) is/zijn juist volgens de huidige ESC-richtlijn?

A. LDL-c target in “very high risk” patiënten is < 1.8 mmol/l

B. PCSK9-remmer wordt aanbevolen indien het LDL-c target met enkel maximaal getolereerde statine niet gehaald wordt

C. Het streef LDL-c in onze casus is < 1.4 mmol/l

D. Alle bovenstaande antwoorden zijn niet juist



Allahyari et al. Eur Heart J. 2020

Recommendations	Class[a]	Level[b]
It is recommended that a high-intensity statin is prescribed up to the highest tolerated dose to reach the goals set for the specific level of risk.[32,34,38]	I	A
If the goals[c] are not achieved with the maximum tolerated dose of a statin, combination with ezetimibe is recommended.[33]	I	B
For primary prevention patients at very-high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor may be considered.	IIb	C
For secondary prevention, patients at very-high risk not achieving their goal[c] on a maximum tolerated dose of a statin and ezetimibe, a combination with a PCSK9 inhibitor is recommended.[119,120]	I	A

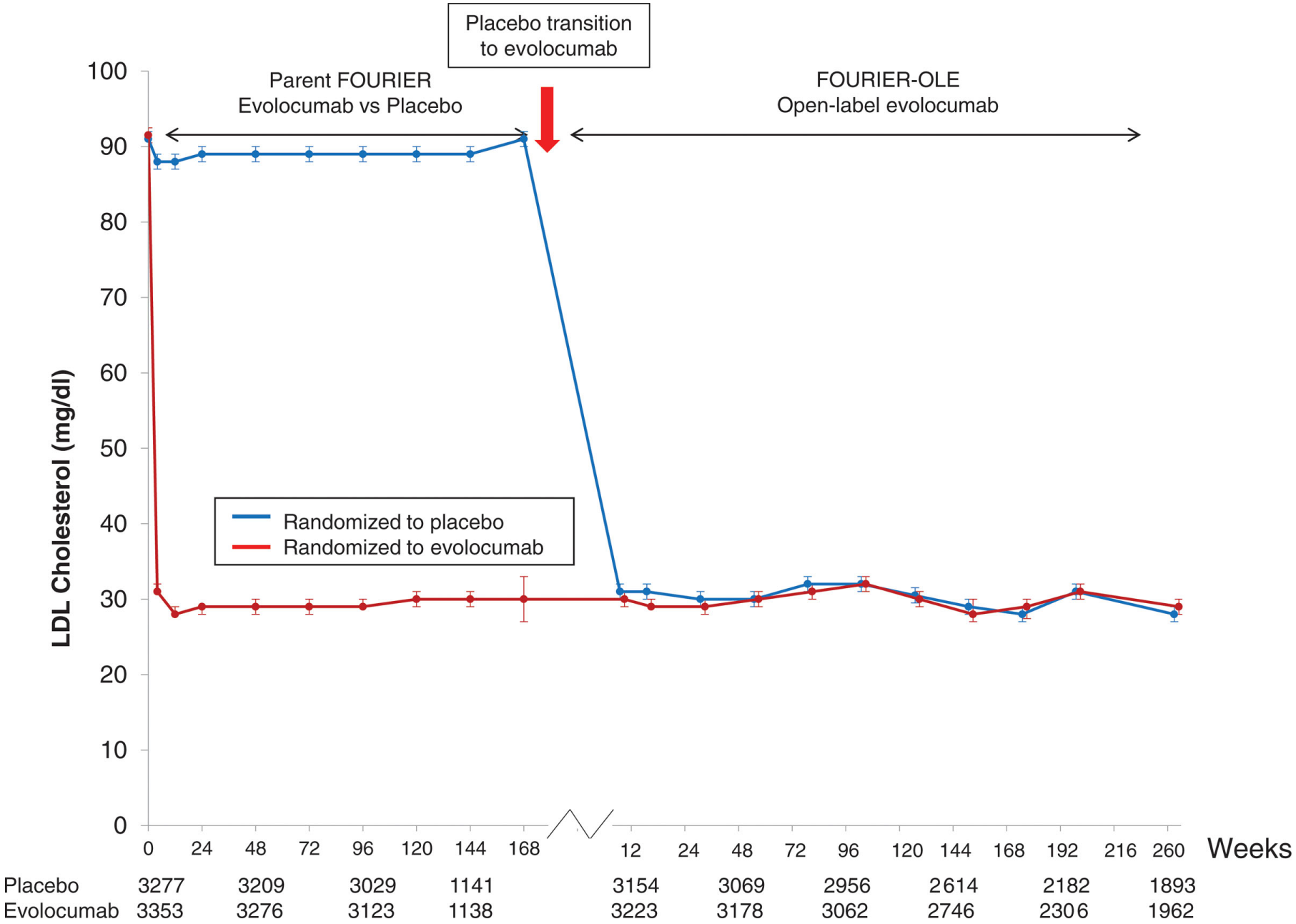
ESC guideline 2019

Long-Term Evolocumab in Patients with Established Atherosclerotic Cardiovascular Disease

Running Title: *O'Donoghue et al.; Long-term evolocumab in cardiovascular disease*

Michelle L. O'Donoghue MD MPH[1]; Robert P. Giugliano MD SM[1]; Stephen D. Wiviott MD[1]; Dan Atar MD[2,3]; Anthony Keech MBBS[4]; Julia F. Kuder MA[1]; KyungAh Im PhD[1]; Sabina A. Murphy MPH[1]; Jose H. Flores-Arredondo MD[5]; J. Antonio G. López MD[5]; Mary Elliott-Davey MSc[6]; Bei Wang PhD[5]; Maria Laura Monsalvo MD[5]; Siddique Abbasi MD[5]; Marc S. Sabatine MD MPH[1]

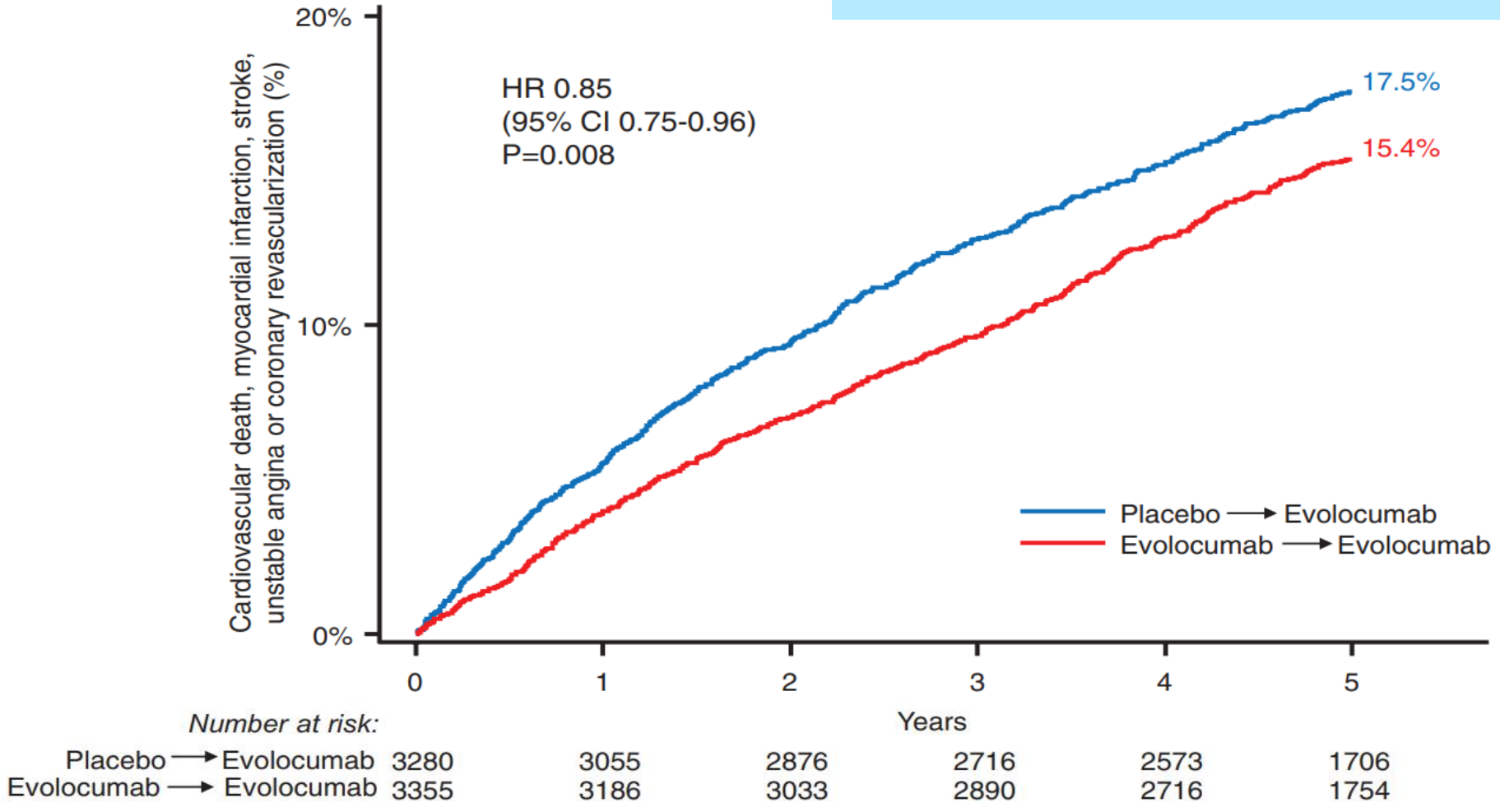
FOURIER-OLE; O'Donoghue et al, Circulation 2022



O'Donoghue et al, Circulation 2022

FOURIER-OLE

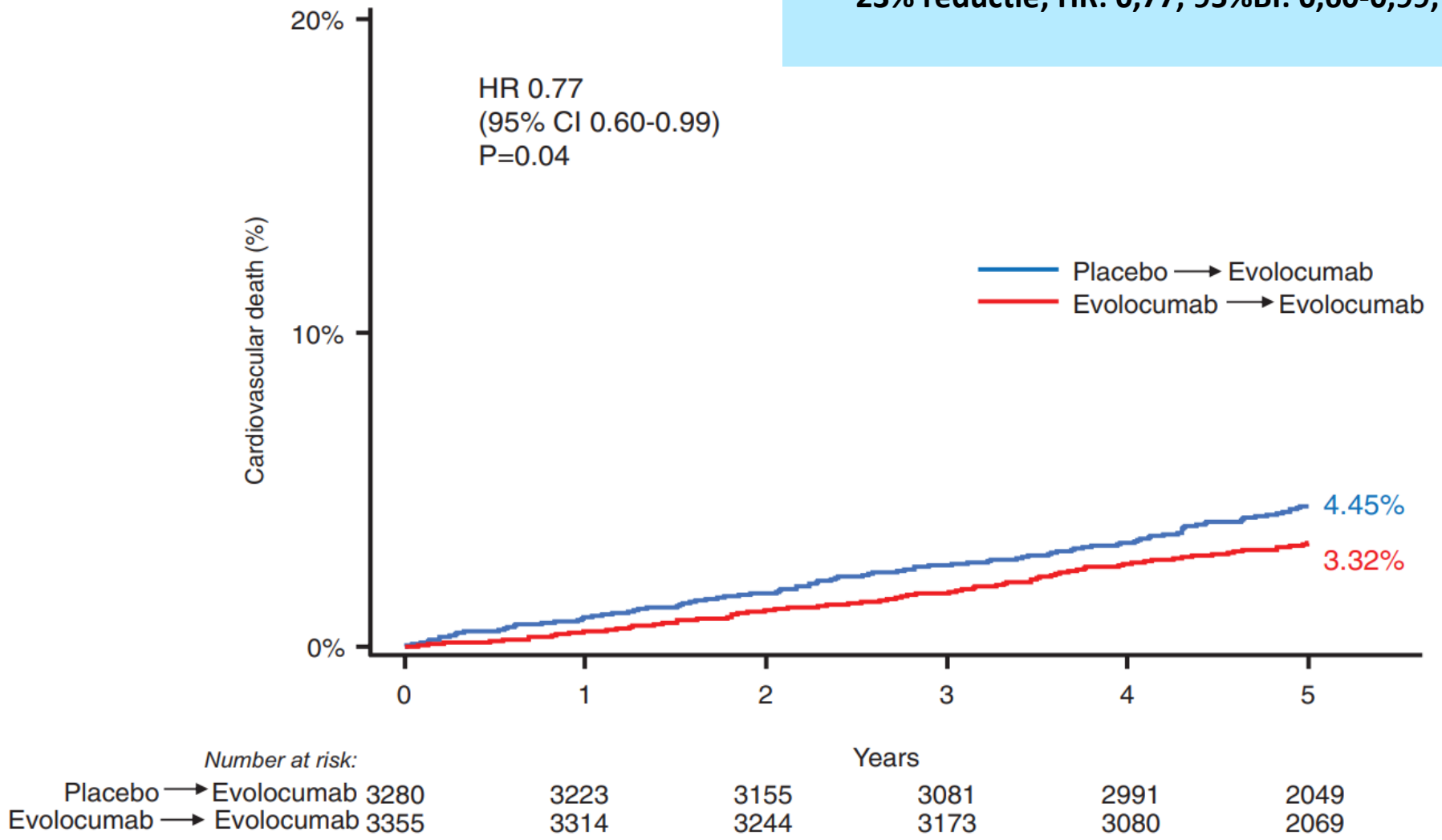
15% reductie; HR: 0,85; 95%BI: 0,75-0,96; P=0,008



O'Donoghue et al, Circulation 2022

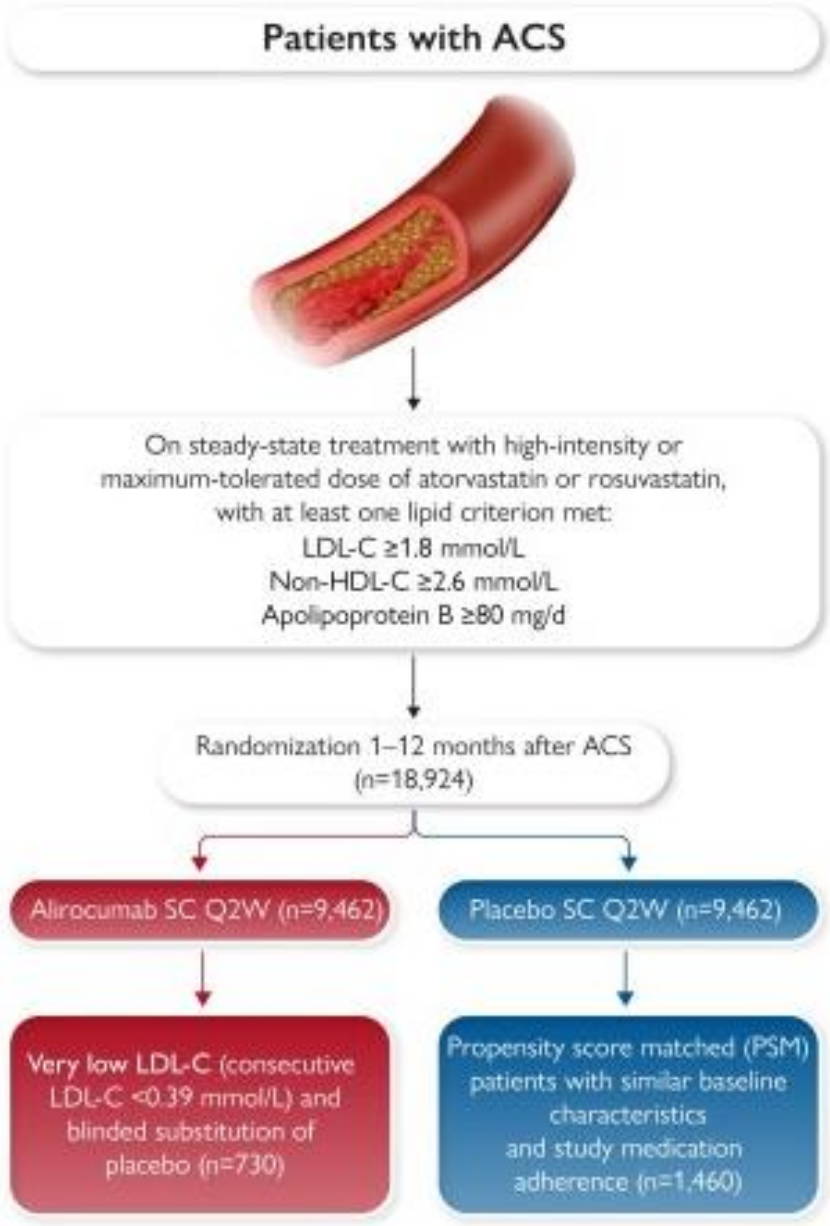
FOURIER-OLE

23% reductie; HR: 0,77; 95%BI: 0,60-0,99; P=0,04



O'Donoghue et al, Circulation 2022

ODYSSEY OUTCOMES trial



Schwartz et al, European Heart J 2023

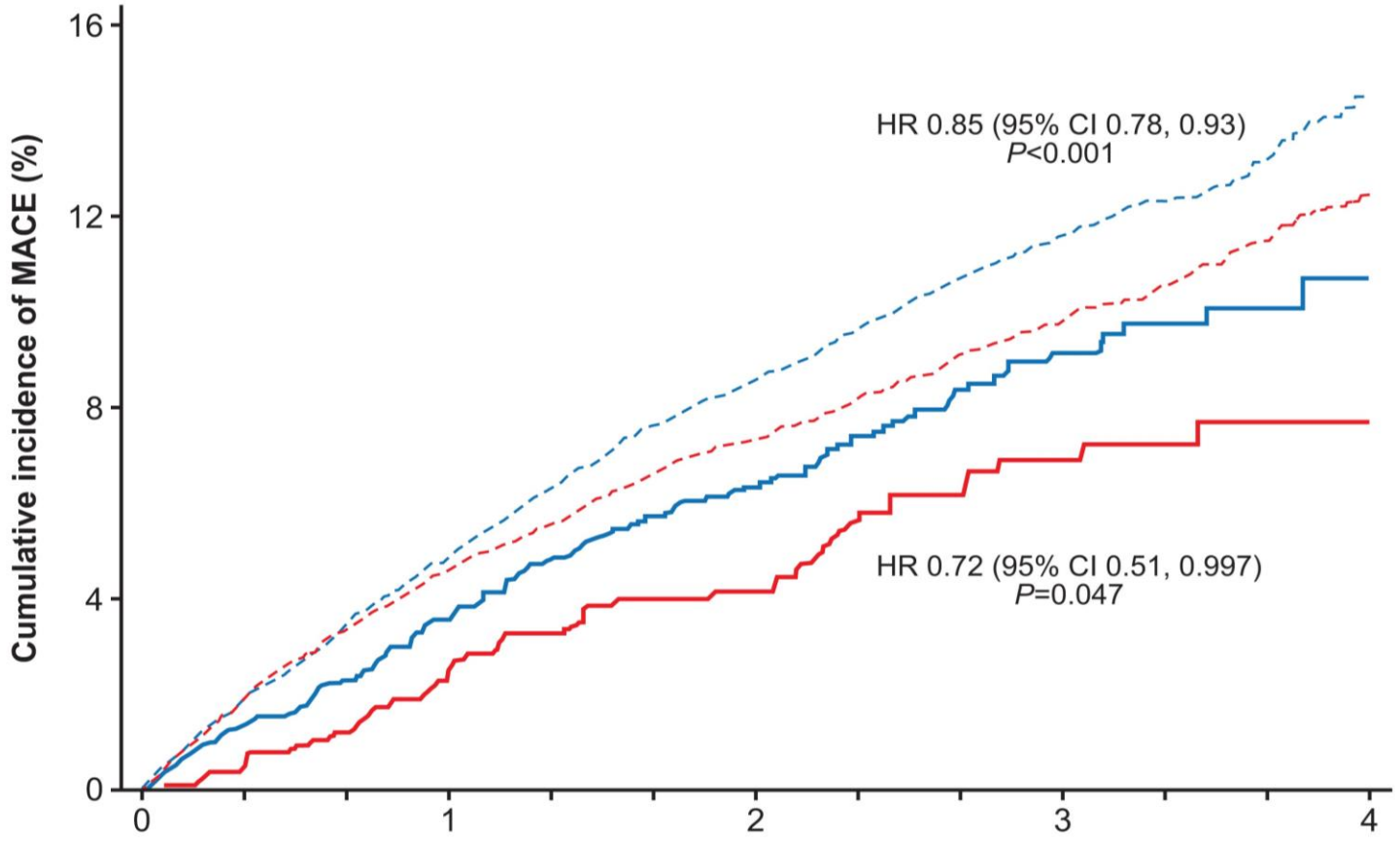
Legacy effect

Post hoc analyse

N = 730

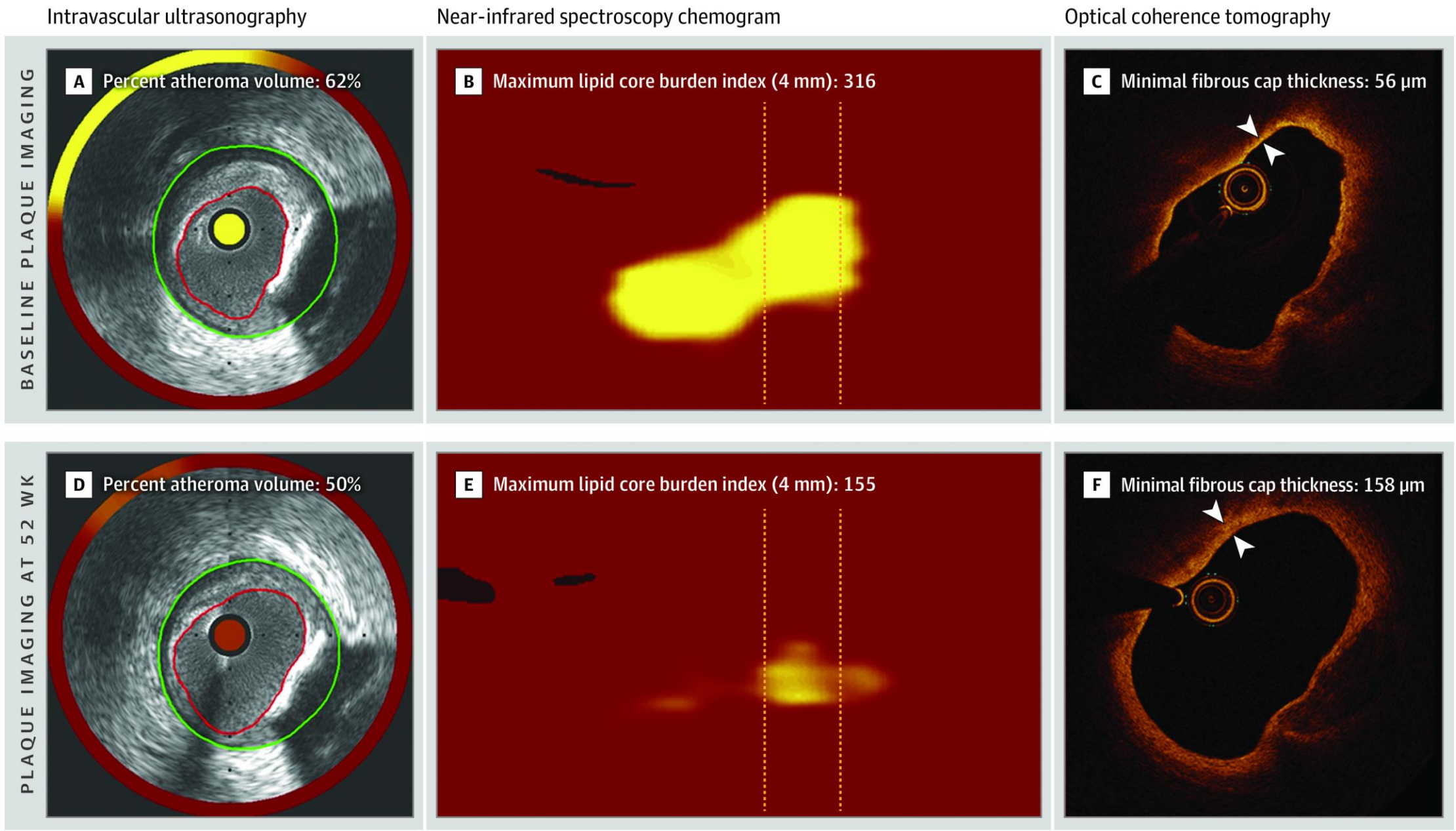
- LDL-C < 0.39 mmol/l
- 6 maanden

→ Blind placebo

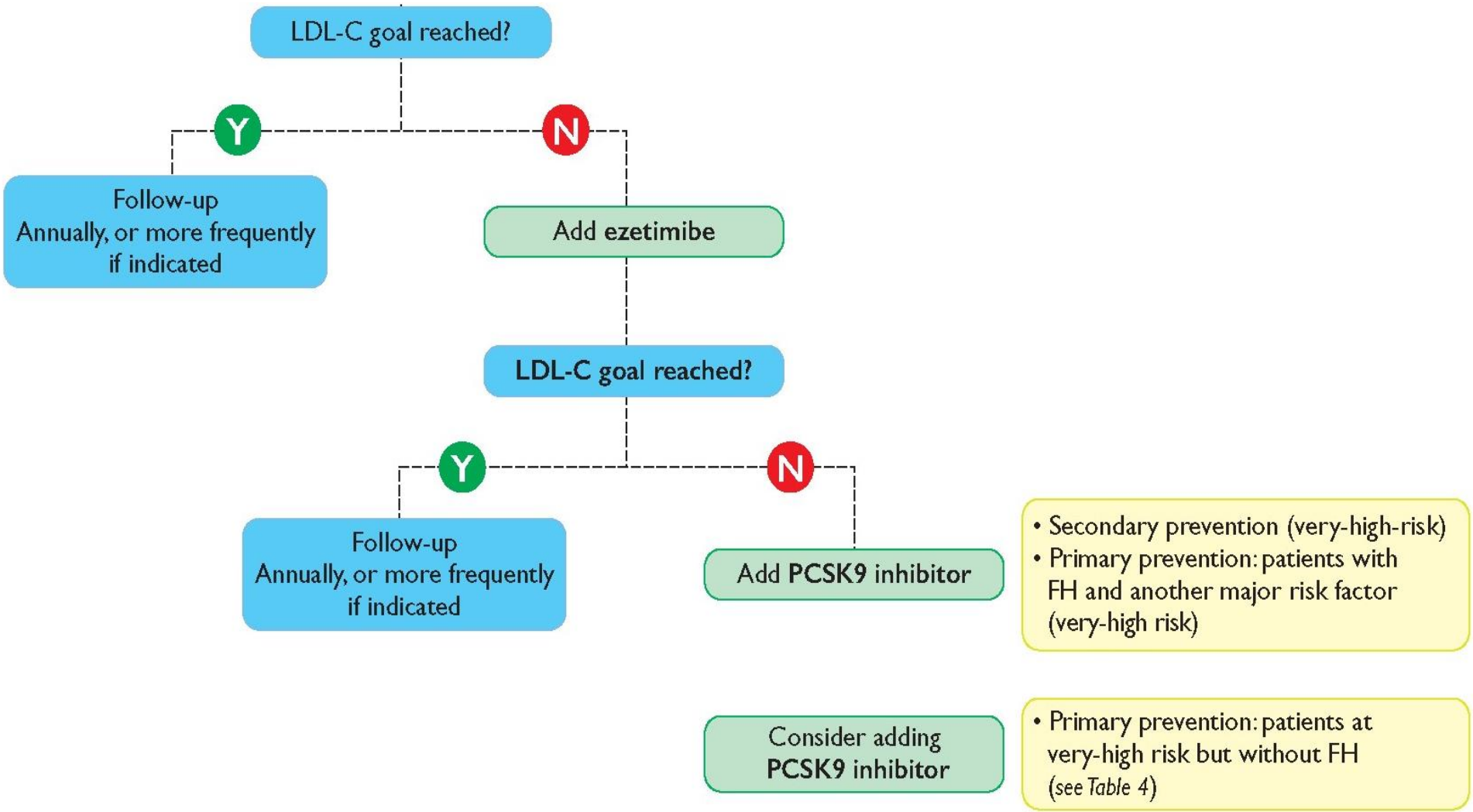


Number at risk					
Placebo (overall)	9462	8805	8201	3471	629
Alirocumab (overall)	9462	8846	8345	3574	653
Placebo (PSM)	1460	1359	1244	494	89
Alirocumab (very low LDL-C)	730	702	669	309	78

Schwartz et al, European Heart J 2023



PACMAN AMI JAMA 2022



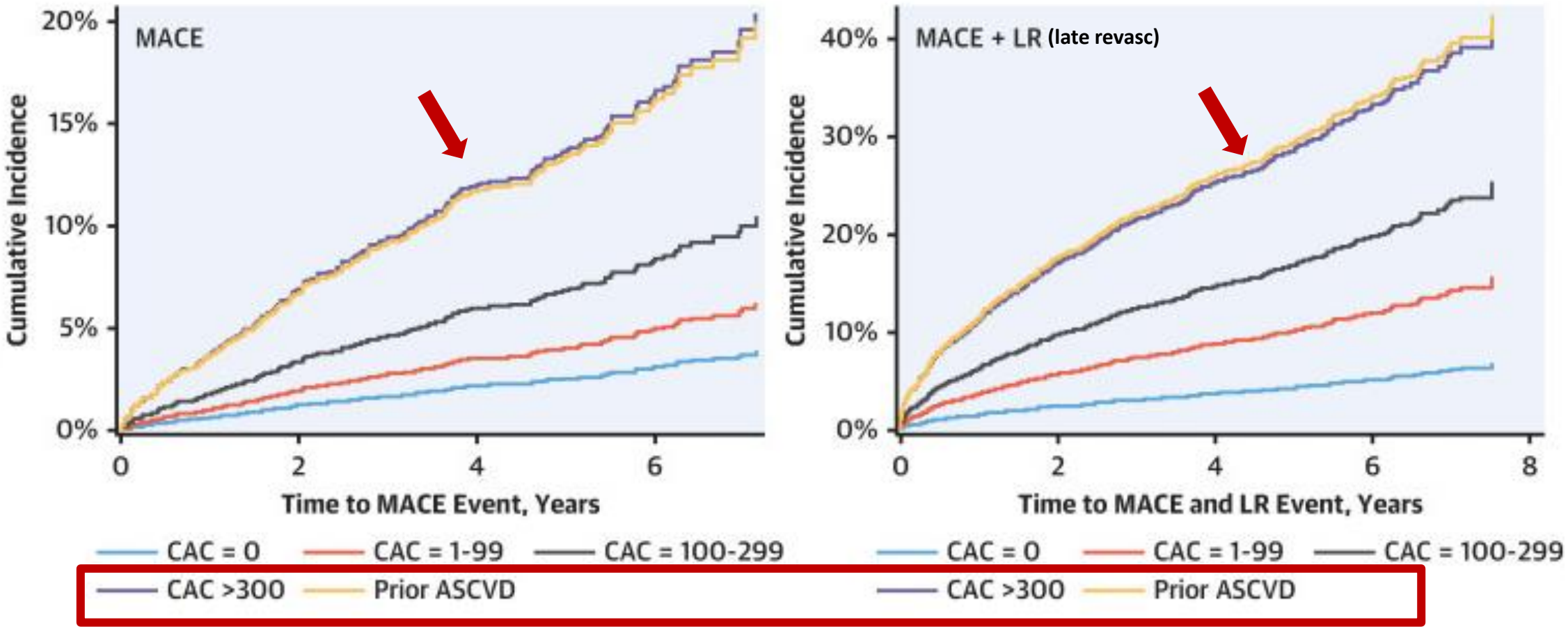
ESC guideline 2019

Recommendations	Class[a]	Level[b]
If the LDL-C goal is not achieved after 4–6 weeks with the maximally tolerated statin dose, combination with ezetimibe is recommended.[33]	I	B
If the LDL-C goal is not achieved after 4–6 weeks despite maximal tolerated statin therapy and ezetimibe, the addition of a PCSK9 inhibitor is recommended.[119,120]	I	B

ESC guideline 2019

CT calcium score and CV risk

N = 4.511 zonder event
Cohort met event in VG



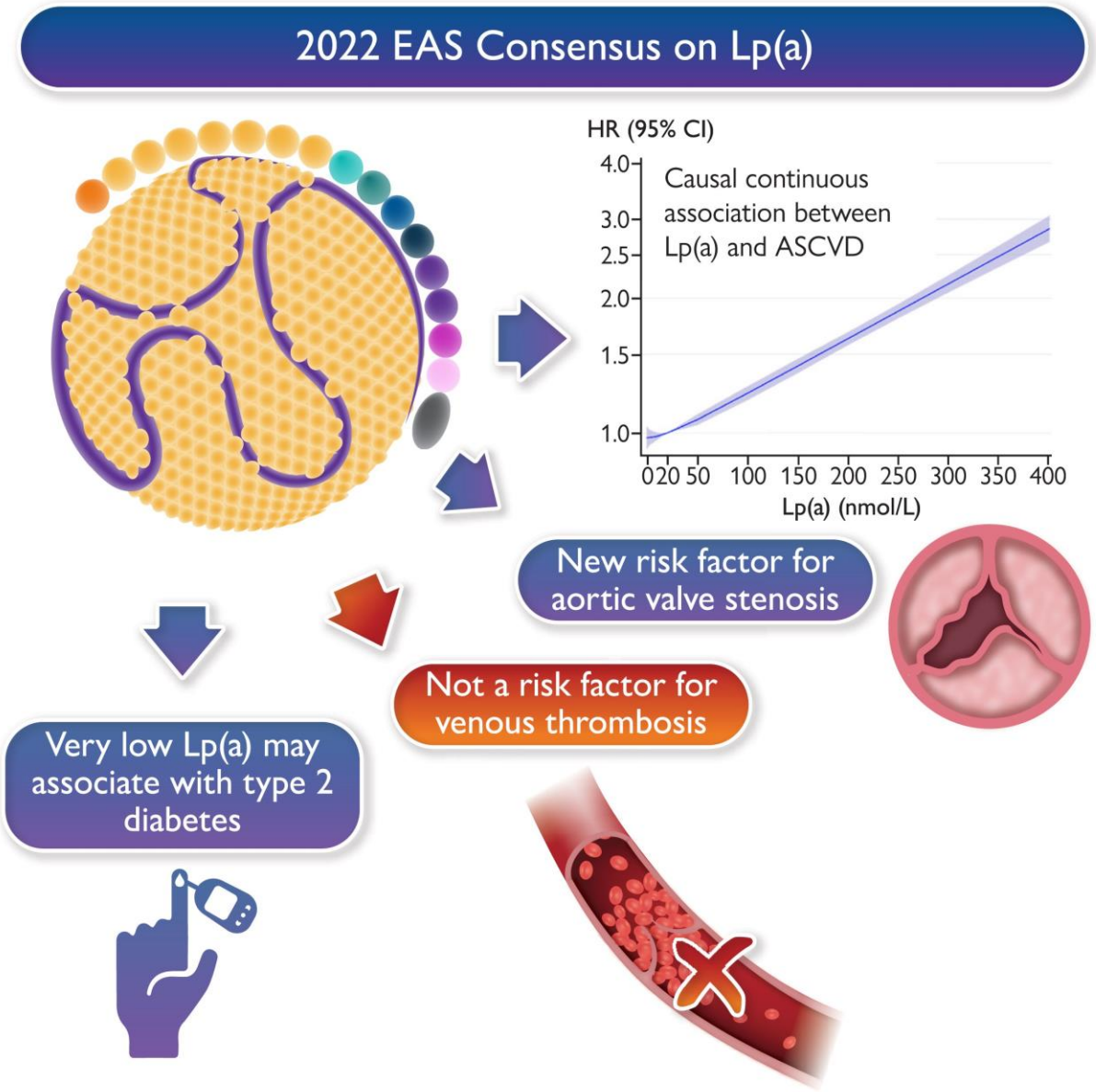
Budoff MJ, et al. J Am Coll Img. 2023; 11181-1189

	Ondergetekende, cardioloog of internist of kinderarts 'metabole ziekten', verklaart evolocumab te hebben voorgeschreven aan deze verzekerde:	kolom 1*	kolom 2*
1			XO
2	▪ Een doorgemaakt CVE + recidief CVE ▪ Een doorgemaakt CVE + diabetes type 2 ▪ Een CVE + statine-intolerantie ▪ Patiënten met FH		XO
3		36	XO

* Er is sprake van een ezetimib intolerantie (maximaal verdraagbare dosering is 0 mg) indien na minstens 4 weken onoverkomelijke bijwerkingen van ezetimib blijven bestaan.

Terug naar onze casus

- Eerder intolerantie voor simvastatine, rosuvastatine en bijwerkingen bij hogere dosis atorvastatine→ **atorvastatine 40 mg**
- Start met **ezetimibe 10 mg** → gestopt in verband met bijwerkingen na 4 weken
- Start **PCSK9 remmer → bijkomend voordeel: lipoproteïne(a) verlagend effect (20%)**
- Start colchicine



EAS

Lp(a) should be measured at least once in adults

Interpretation of Lp(a) concentration in the context of absolute global CVD risk

Intensified risk factor management by lifestyle modification and medications

Specific Lp(a)-lowering therapies in phase II/III trials

- **Olpasiran**
- **Pelacarsen**
- **Lepodisiran**

ESC European Society of Cardiology
European Heart Journal (2022) **43**, 3925–3946
https://doi.org/10.1093/eurheartj/ehac361

Wat kunnen we verbeteren?

- **Vroeg en agressiever optimaliseren lipidenprofiel**

  → indien LDL > 1.4 na 8-12 weken maximale statine/ezetimibe therapie→ start PCSK9-remmer

- **Richtlijnen synchroniseren** voor cardiologie, huisarts.. neurologie, vaatchirurgie