TERAPIA CON INIBITORI DEL PCSK9 DOPO SCA: IN QUALI PAZIENTI?

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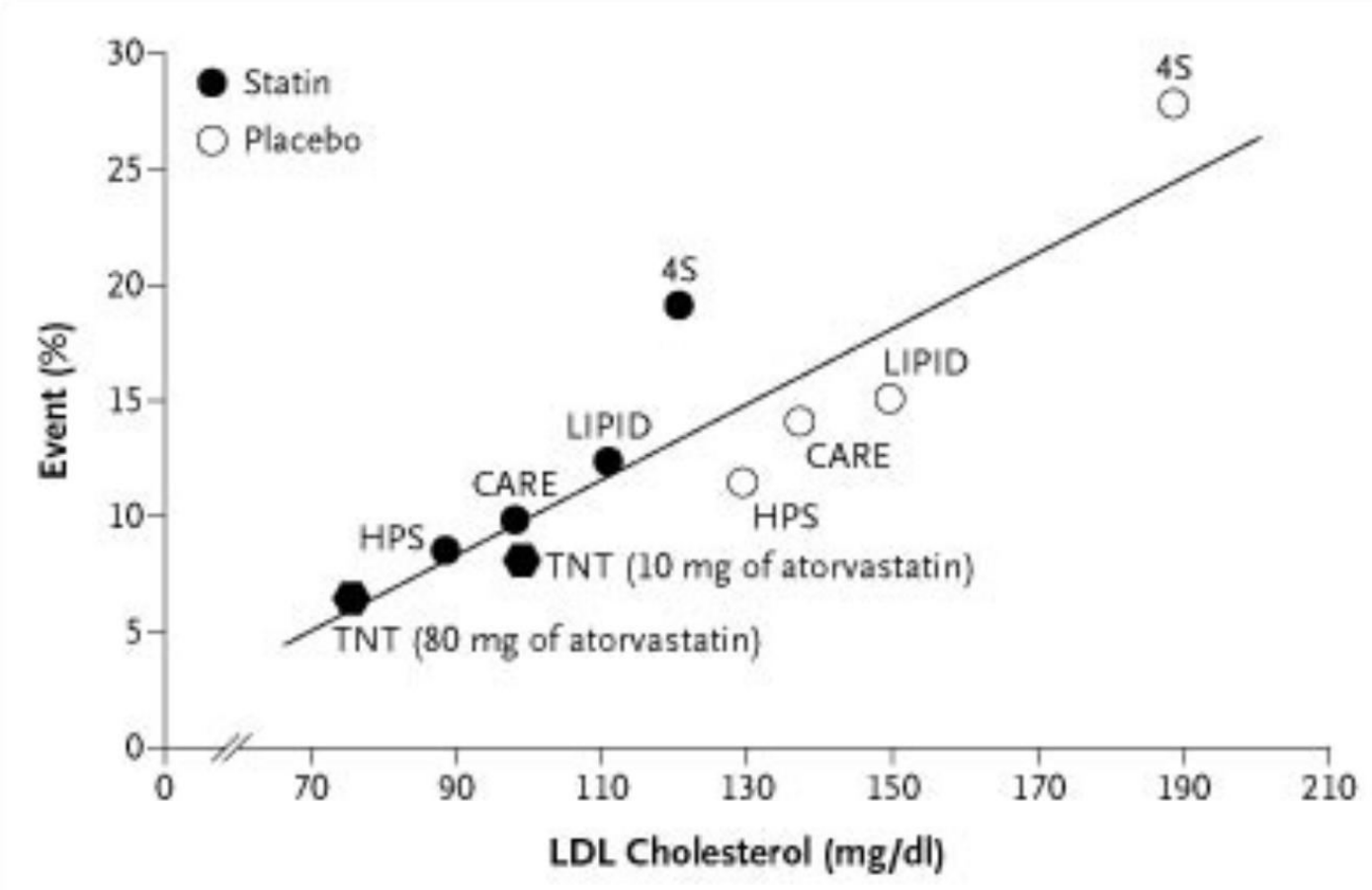
Università Humanitas
IRCCS Istituto Clinico Humanitas

Linear Relationship Between LDL-C and Event Rate

Statin Therapy in Secondary-Prevention Studies



LaRosa JC et al. N Engl J Med 2005; 352:1425-1435

PCSK9 Inhibitors

Evolocumab, Alirocumab

Proprotein convertase subtilisin/kexin type 9 (**PCSK9**) → **degradation of LDLr**

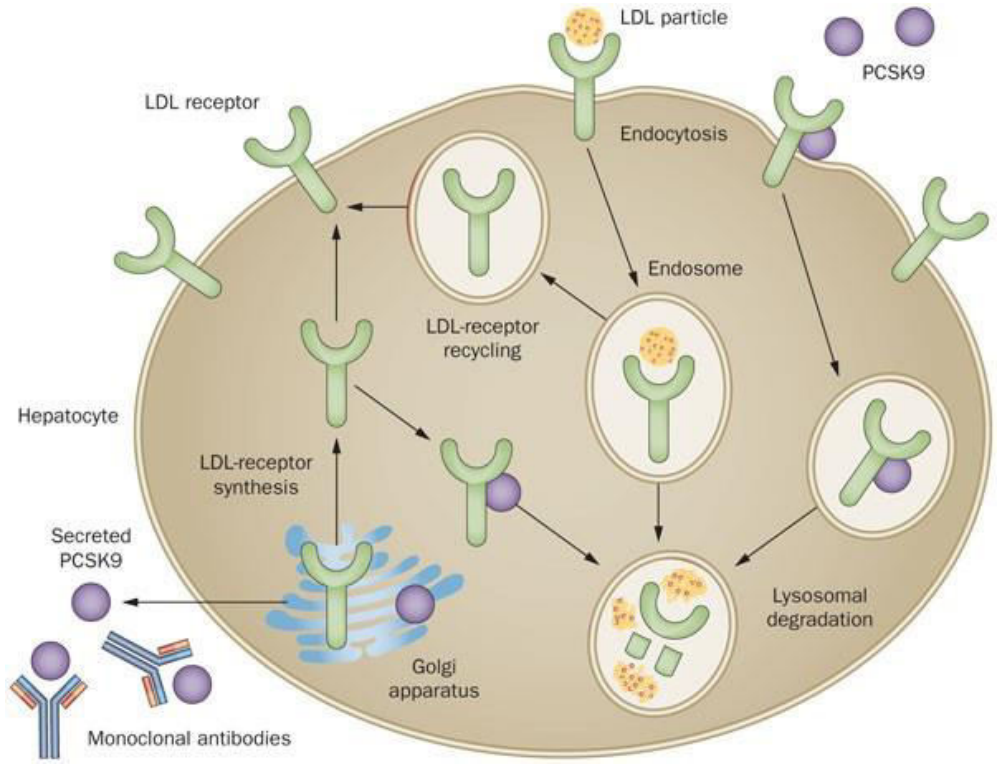
- Binds to LDL receptor → lysosome

MOA: **Antibodies inactivate PCSK9**

↓ LDL receptor degradation

↑ LDL receptors on hepatocytes

↓ LDL cholesterol in plasma

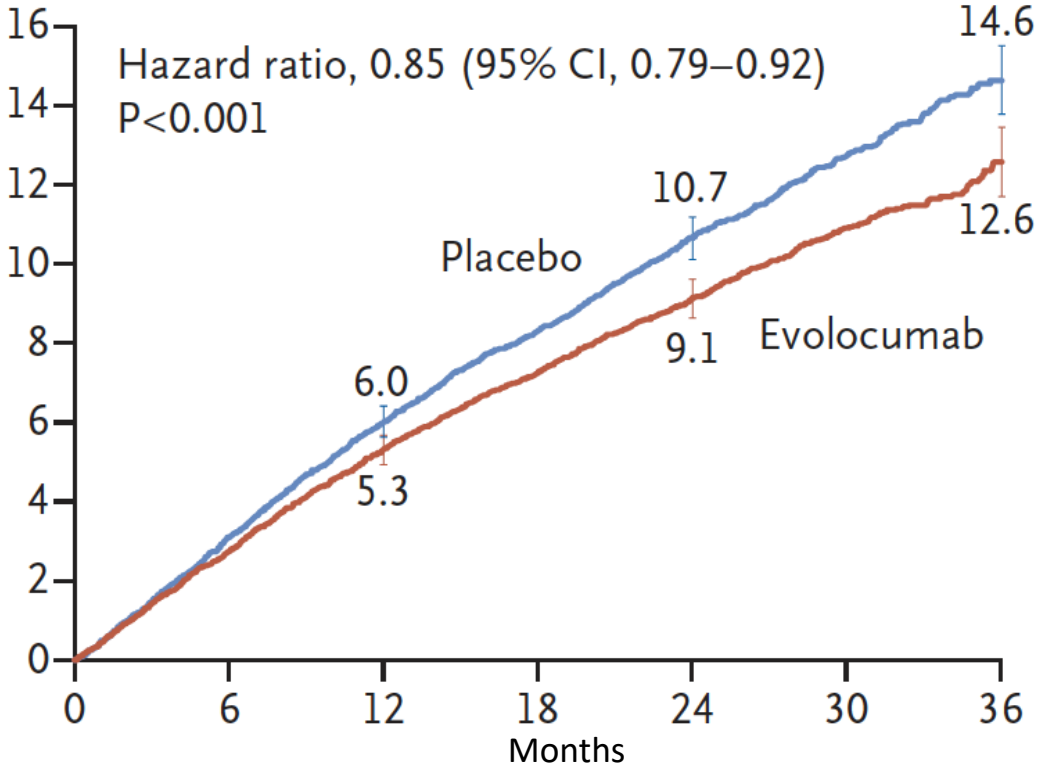


PCSK9 Inhibitors and Cardiovascular Outcomes

Evolocumab

Sabatine M et al. *N Engl J Med* 2017;376:1713-22.

Composite of CV death, MI, stroke, hospitalization for UA, or coronary revascularization

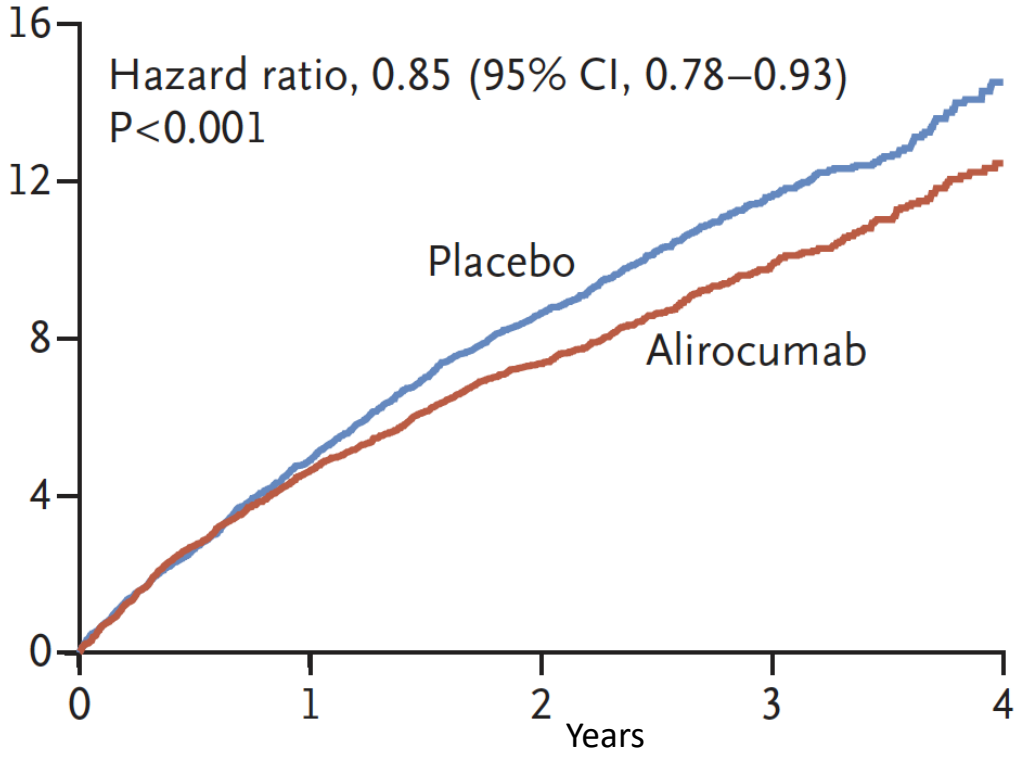


N=27,564 patients with atherosclerosis

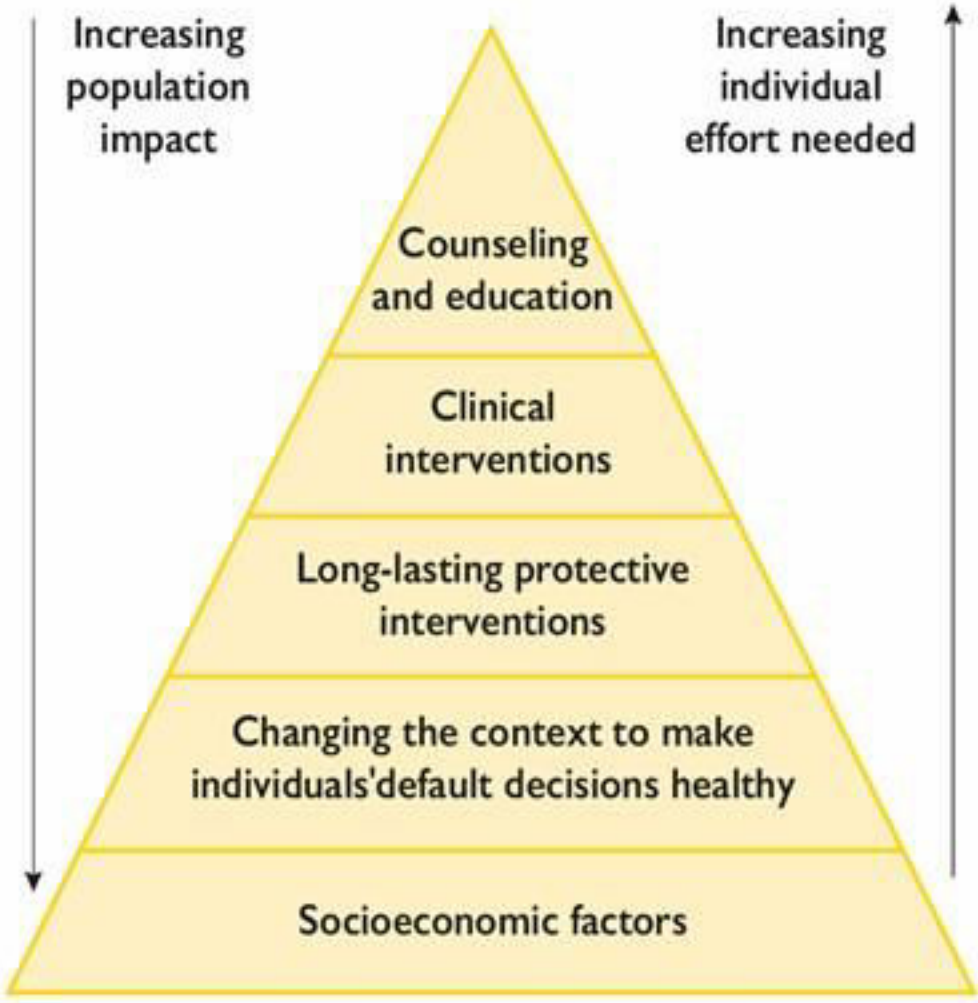
Alirocumab

Schwartz GG et al. *N Engl J Med* 2018;379:2097-107

Coronary death, MI, stroke, or UA requiring hospitalization

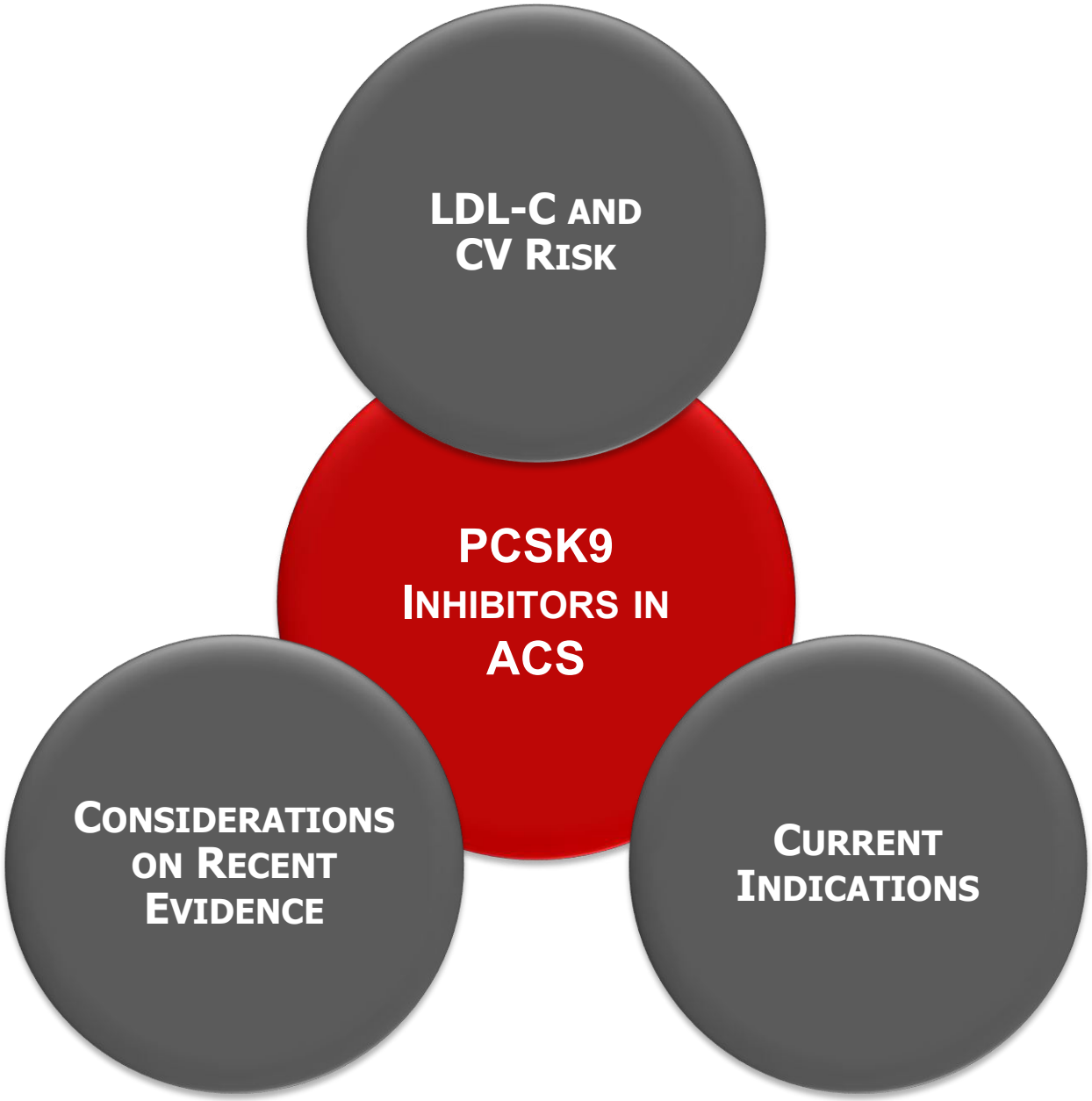


N=18,924 patients with a recent ACS



Health impact pyramid

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)


LDL-C and CV Risk
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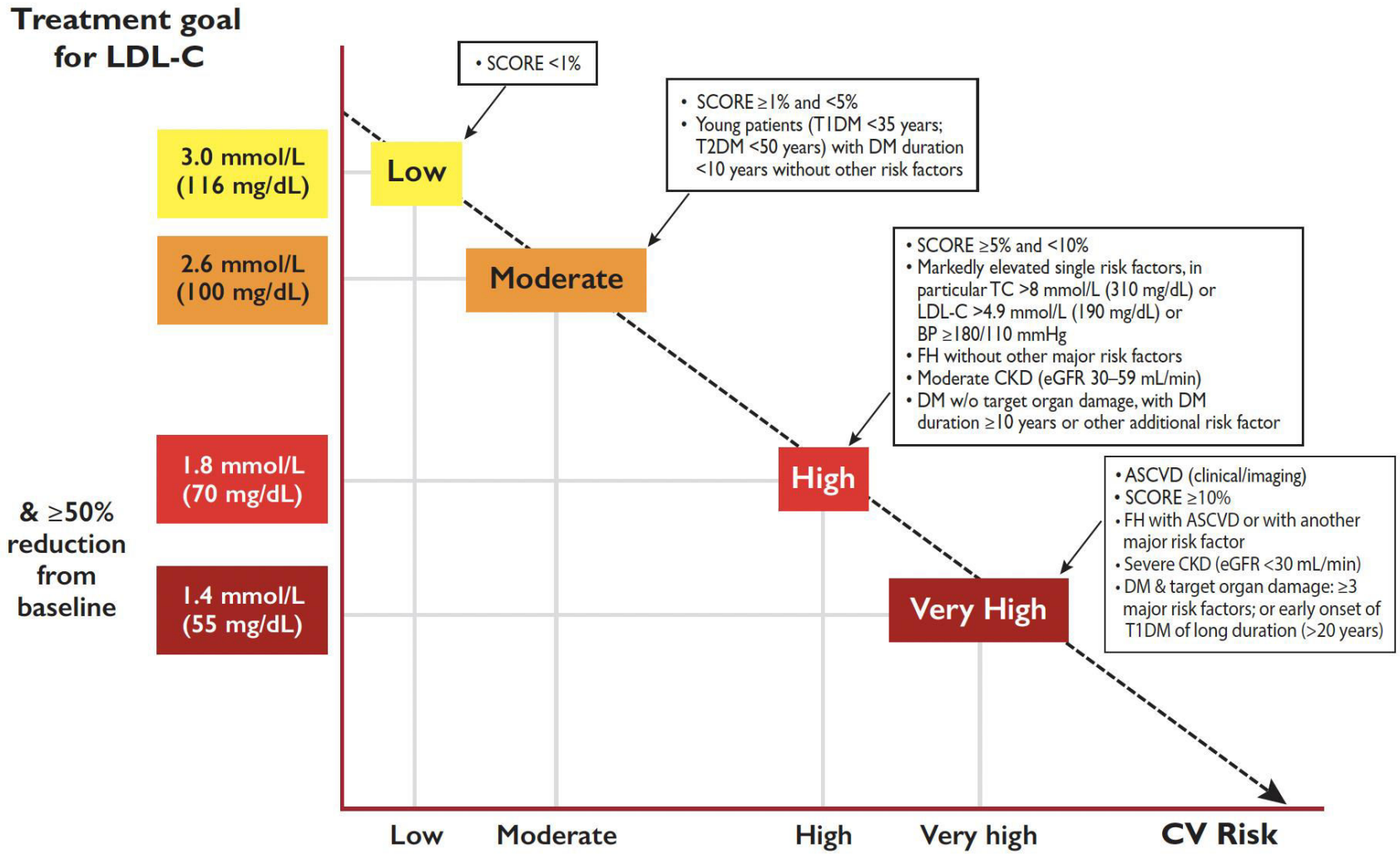
LDL-C Treatment Goals According to CV Risk

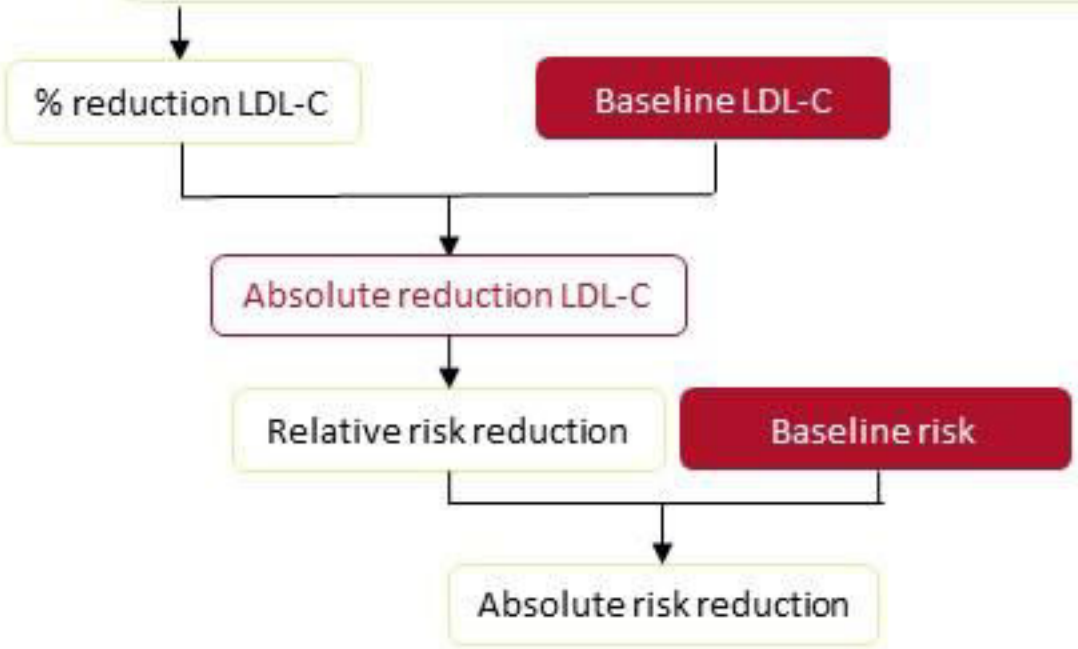


2019 ESC/EAS Guidelines for the management of dyslipidaemias

Expected clinical benefit of low-density lipoprotein cholesterol lowering therapies

Intensity of lipid lowering treatment

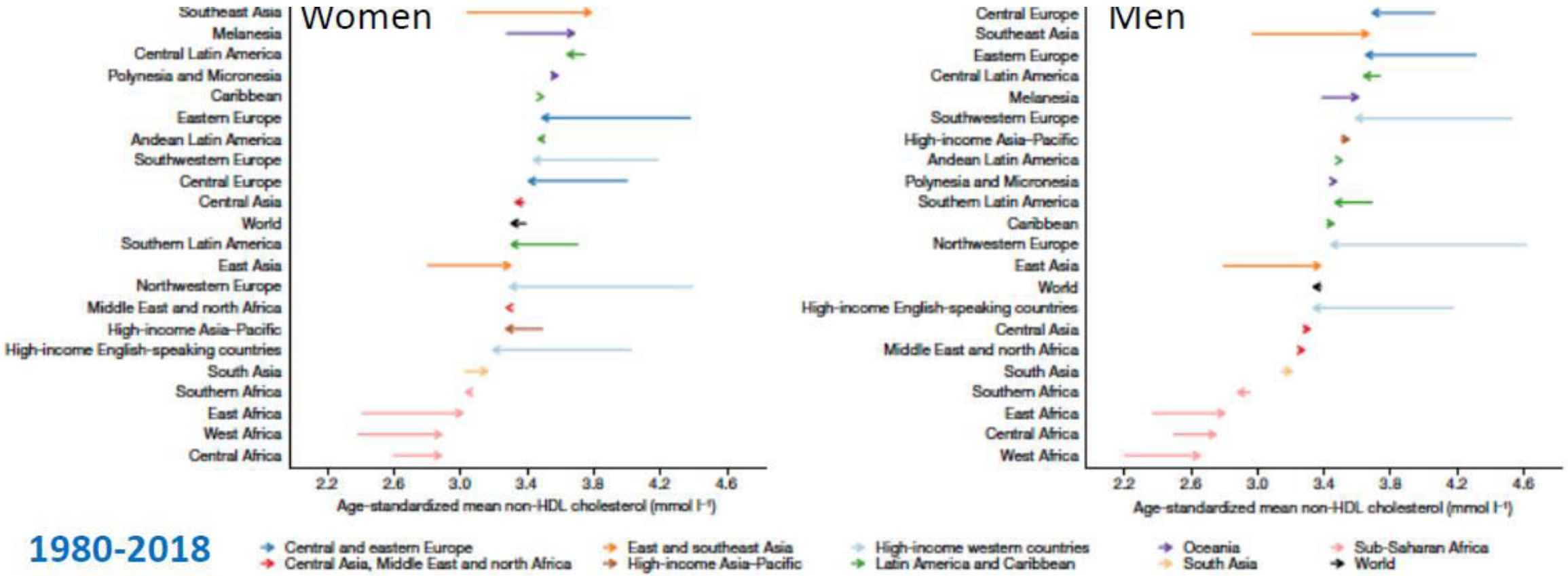
Treatment	Average LDL-C reduction
Moderate intensity statin	≈ 30%
High intensity statin	≈ 50%
High intensity statin plus ezetimibe	≈ 65%
PCSK9 inhibitor	≈ 60%
PCSK9 inhibitor plus high intensity statin	≈ 75%
PCSK9 inhibitor plus high intensity statin plus ezetimibe	≈ 85%



LDL-C = low-density lipoprotein cholesterol;
PCSK9 = proprotein convertase subtilisin/kexin type 9.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

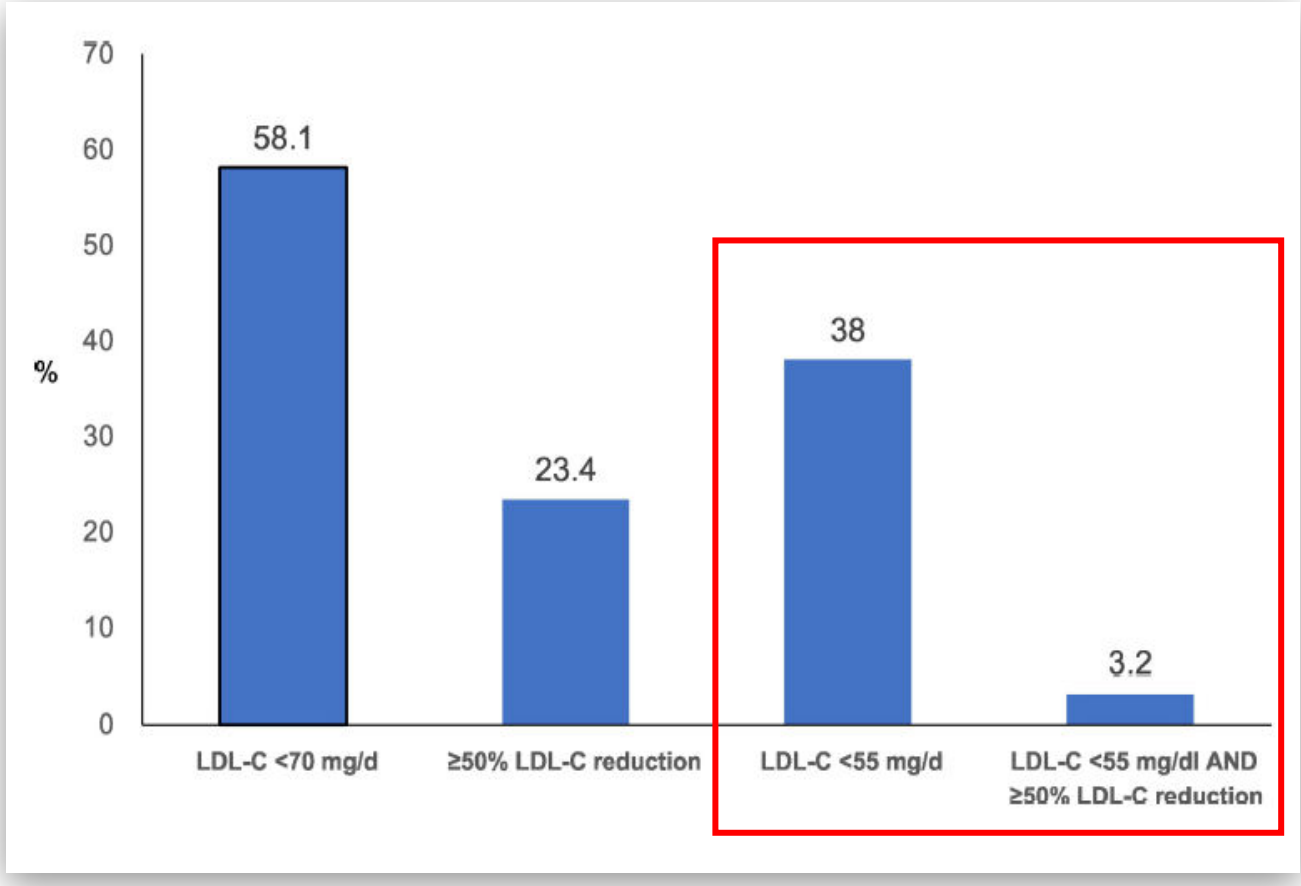
Global Cholesterol Levels Over The Past 4 Decades



Nature 2020

ITALIAN EXPERIENCE: START REGISTRY

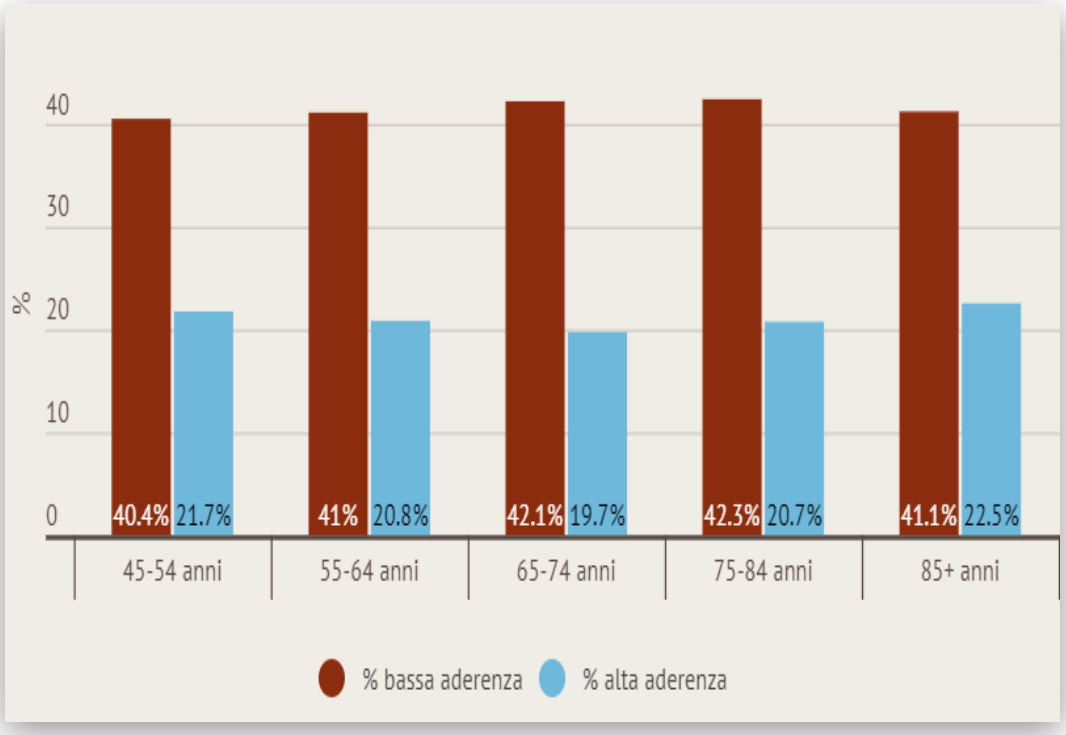
Suboptimal LDL-C Control (N=5053 Patients with ASCVD)



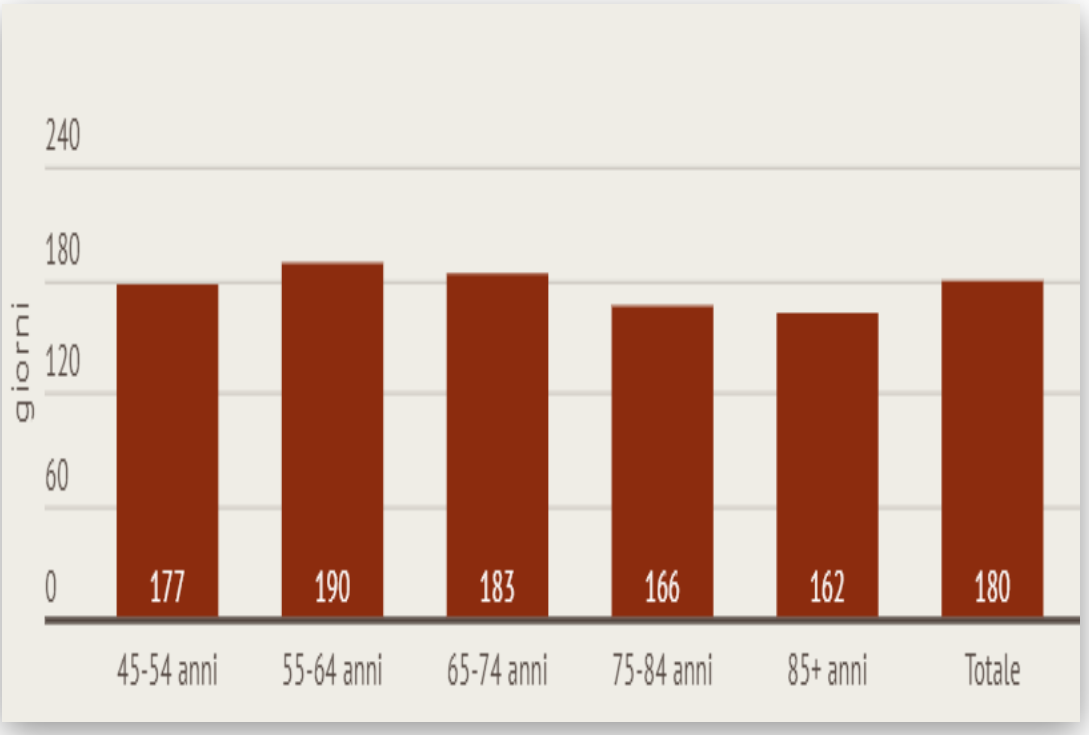
Int J Cardiol. 2020 May 26:S0167-5273(20)31949-5

Adherence To Statins Over Time

Adherence to Statins

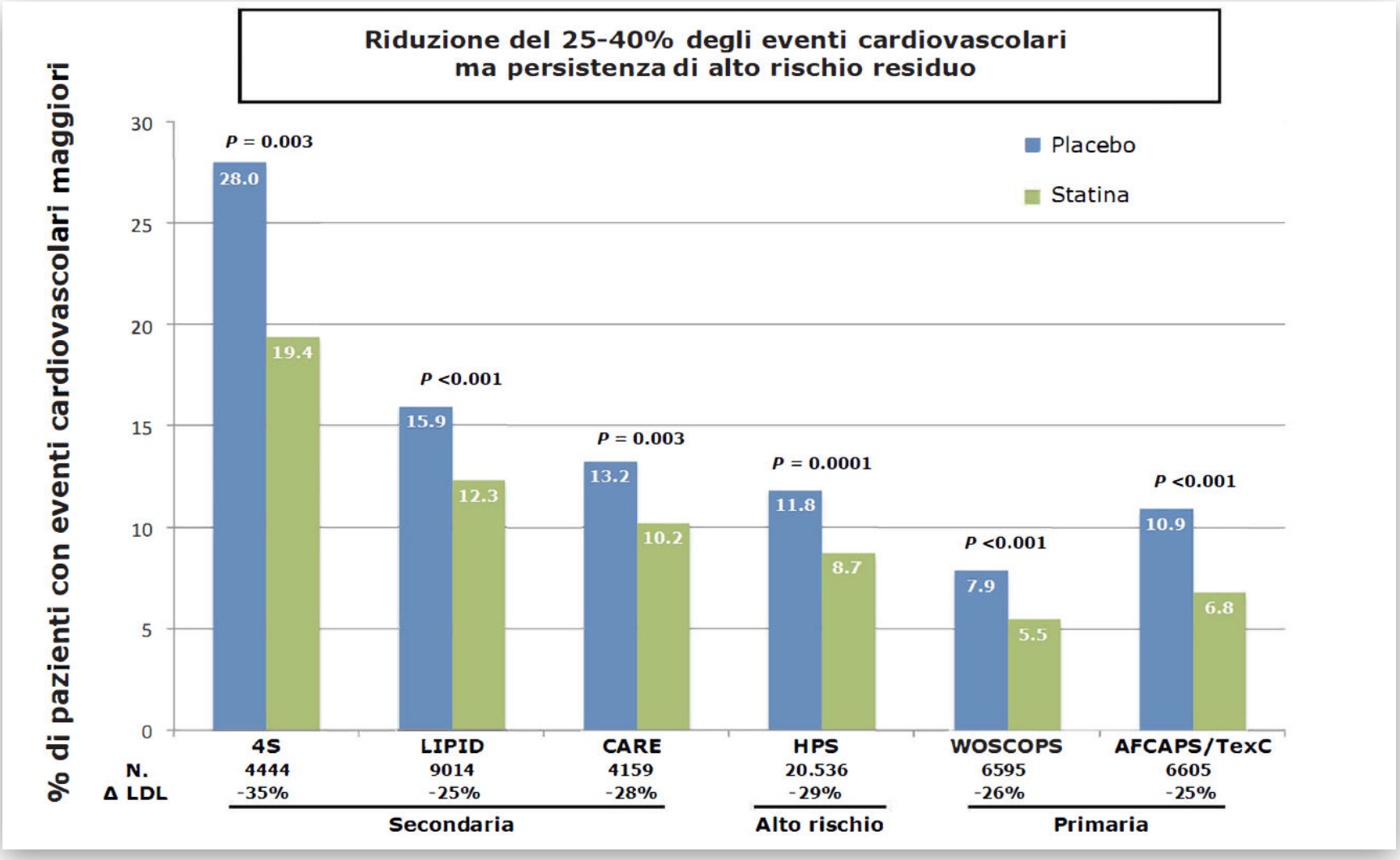


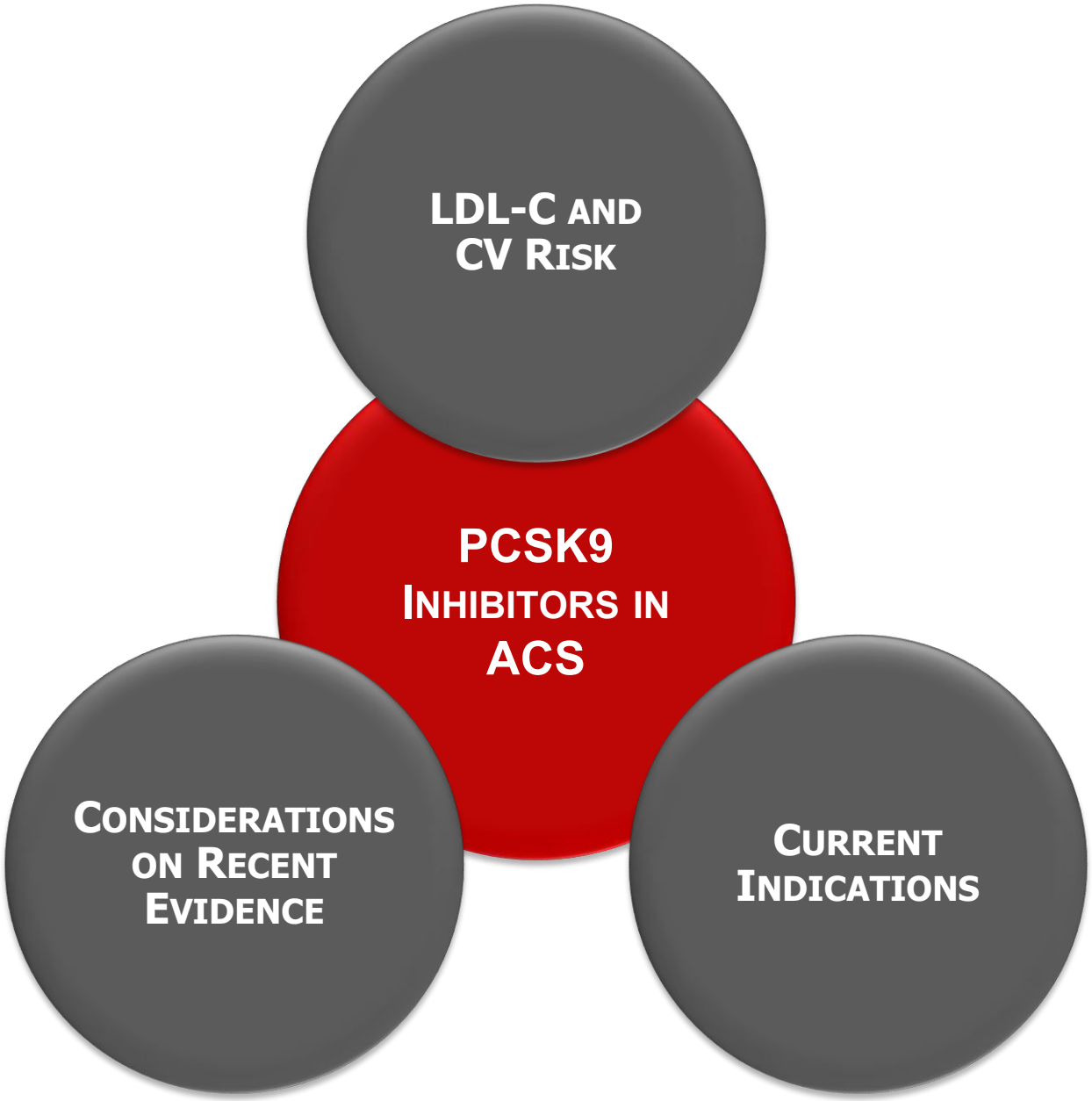
Median Days to Discontinuation



Fonte: AIFA - "L'uso dei farmaci in Italia. Rapporto Nazionale Anno 2019"

Residual Risk Despite Statin Therapy




LDL-C and CV Risk
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Treatment targets and goals for cardiovascular disease prevention (2)

EAS ESC European Society of Cardiology

LDL-C	**Very-high-risk in primary or secondary prevention** A therapeutic regimen that achieves at least a 50% LDL-C reduction from baseline[b] and an LDL-C goal of <1.4 mmol/L (<55 mg/dL). No current statin use: this is likely to require high-intensity LDL-lowering therapy. Current LDL-lowering treatment: an increased treatment intensity is required. **High risk:** A therapeutic regimen that achieves at least a 50% LDL-C reduction from baseline[b] and an LDL-C goal of <1.8 mmol/L (<70 mg/dL).

[b]The term 'baseline' refers to the LDL-C level in a person not taking any lipid lowering medication, or to the extrapolated baseline value for those who are on current treatment.

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Intervention Strategies According to Total CV Risk and LDL-C Levels

	Total CV risk (SCORE) %	Untreated LDL-C levels					
		<1.4 mmol/L (55 mg/dL)	1.4 to <1.8 mmol/L (55 to <70 mg/dL)	1.8 to <2.6 mmol/L (70 to <100 mg/dL)	2.6 to <3.0 mmol/L (100 to <116 mg/dL)	3.0 to <4.9 mmol/L (116 to <190 mg/dL)	≥4.9 mmol/L (≥190 mg/dL)
Secondary prevention	Very-high-risk	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	IIa/A	I/A	I/A	I/A	I/A	I/A

2019 ESC/EAS Guidelines for the management of dyslipidaemias

Recommendations for lipid-lowering therapy in very-high-risk patients with acute coronary syndromes (1)

Recommendations	Class	Level
In all ACS patients without any contra-indication or definite history of intolerance, it is recommended to initiate or continue high dose statin as early as possible, regardless of initial LDL-C values.	I	A
Lipid levels should be re-evaluated 4–6 weeks after ACS to determine whether a reduction of at least 50% from baseline and goal levels of LDL-C <1.4 mmol/L (<55 mg/dL) have been achieved. Safety issues need to be assessed at this time and statin treatment doses adapted accordingly.	IIa	C
If the LDL-C goal is not achieved after 4–6 weeks with the maximally tolerated statin dose, combination with ezetimibe is recommended.	I	B

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

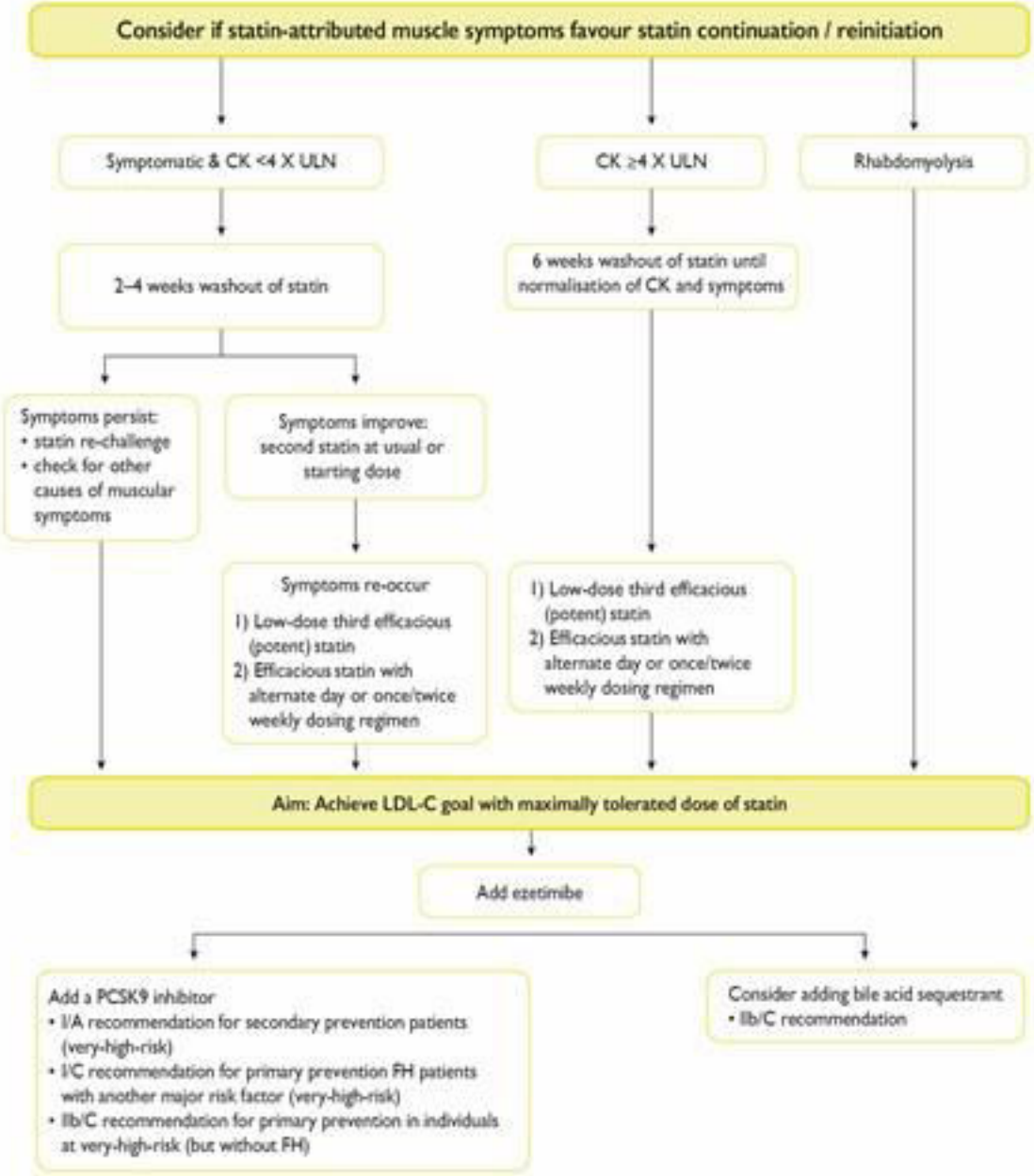
Recommendations for lipid-lowering therapy in very-high-risk patients with acute coronary syndromes (2)

EAS ESC European Society of Cardiology

Recommendations	Class	Level
If the LDL-C goal is not achieved after 4–6 weeks despite maximal tolerated statin therapy and ezetimibe, adding a PCSK9 inhibitor is recommended.	I	B
In patients with confirmed statin intolerance or in patients in whom a statin is contra-indicated, ezetimibe should be considered.	IIa	C
For patients who present with an ACS and whose LDL-C levels are not at goal despite already taking a maximally tolerated statin dose and ezetimibe, adding a PCSK9 inhibitor early after the event (if possible, during hospitalization for the ACS event) should be considered.	IIa	C

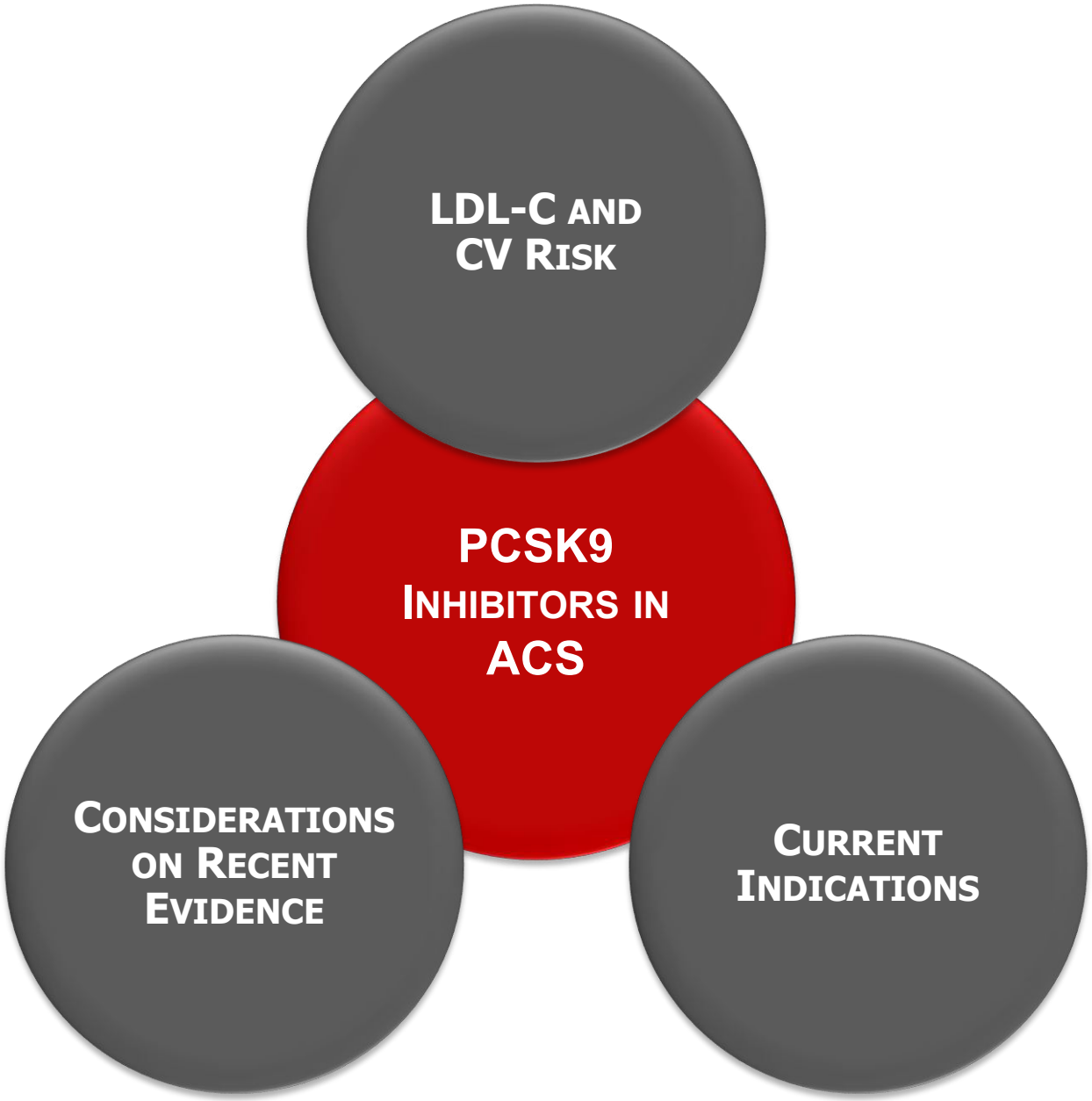
2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Algorithm for treatment of muscular symptoms during statin treatment



www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)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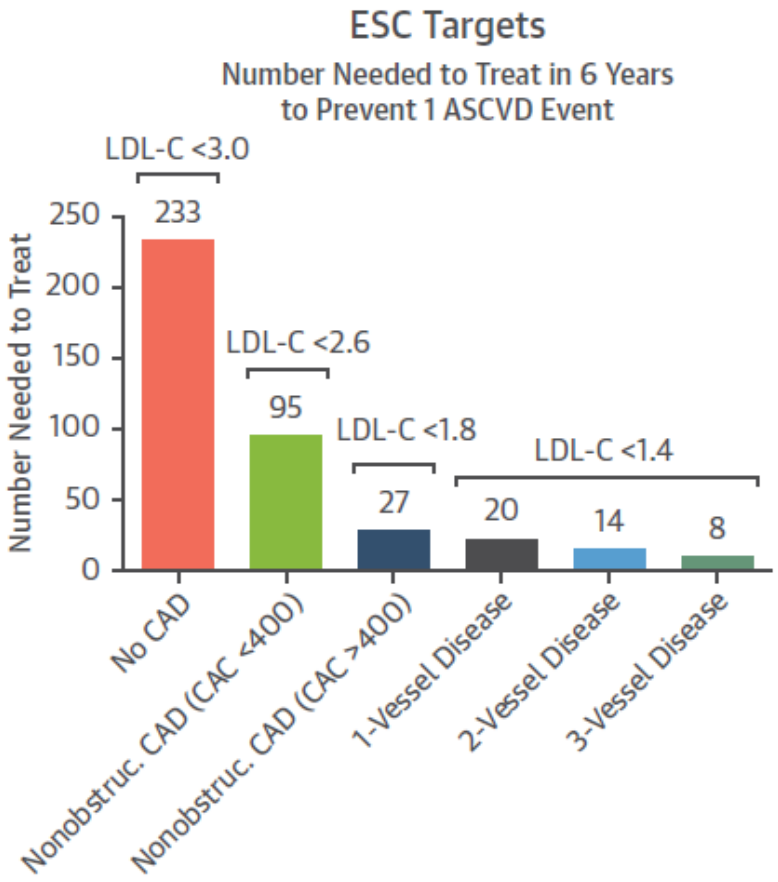
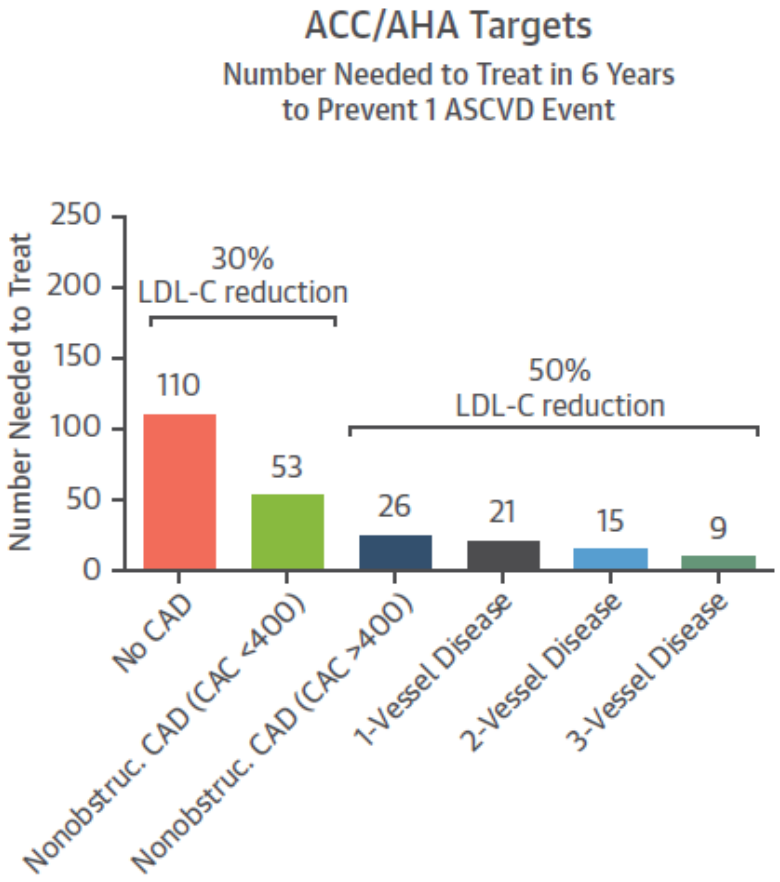
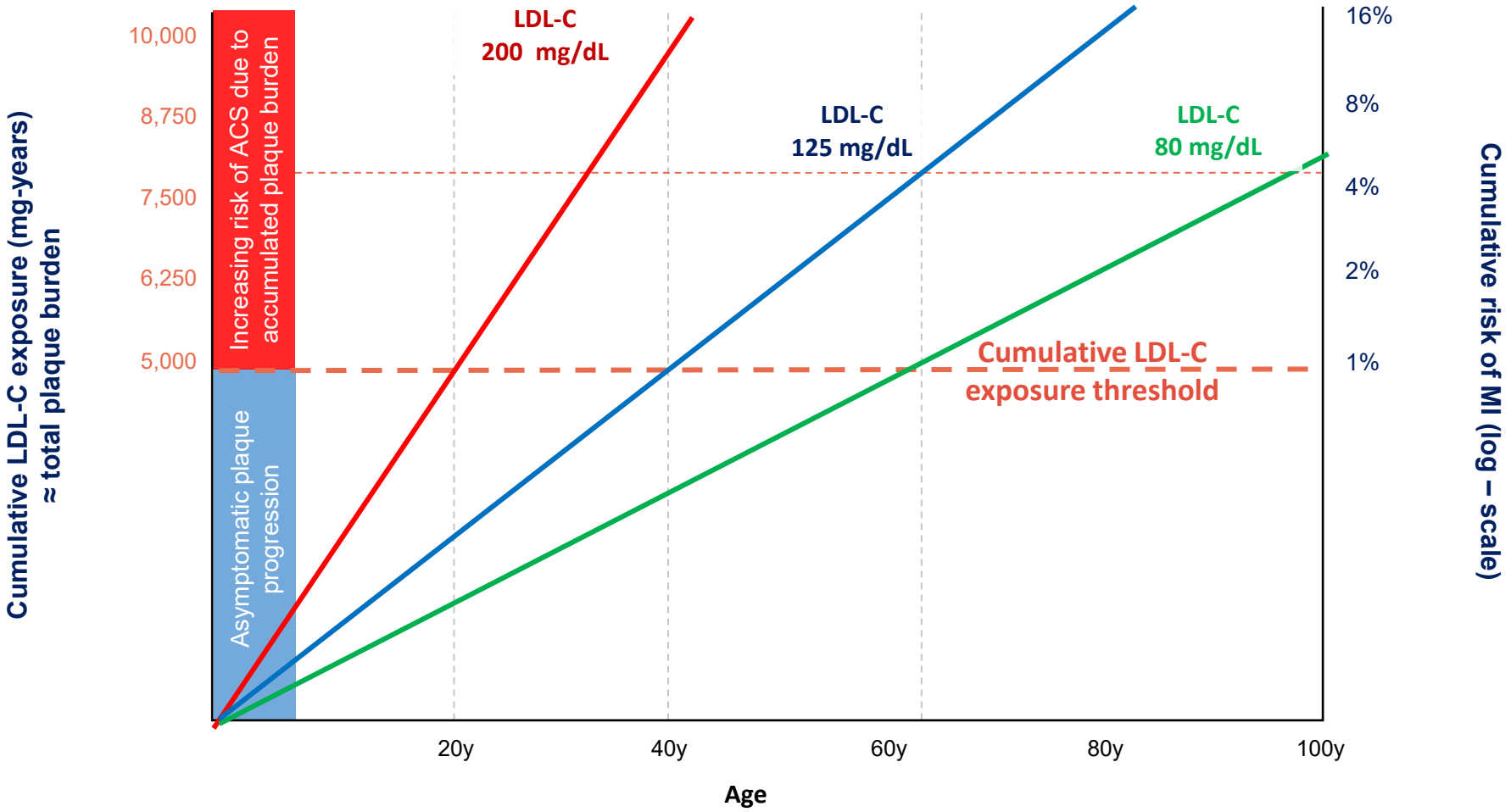
CAD Severity on CCTA And Benefits From LDL-C Reduction





Mortensen et al JACC Img 2020

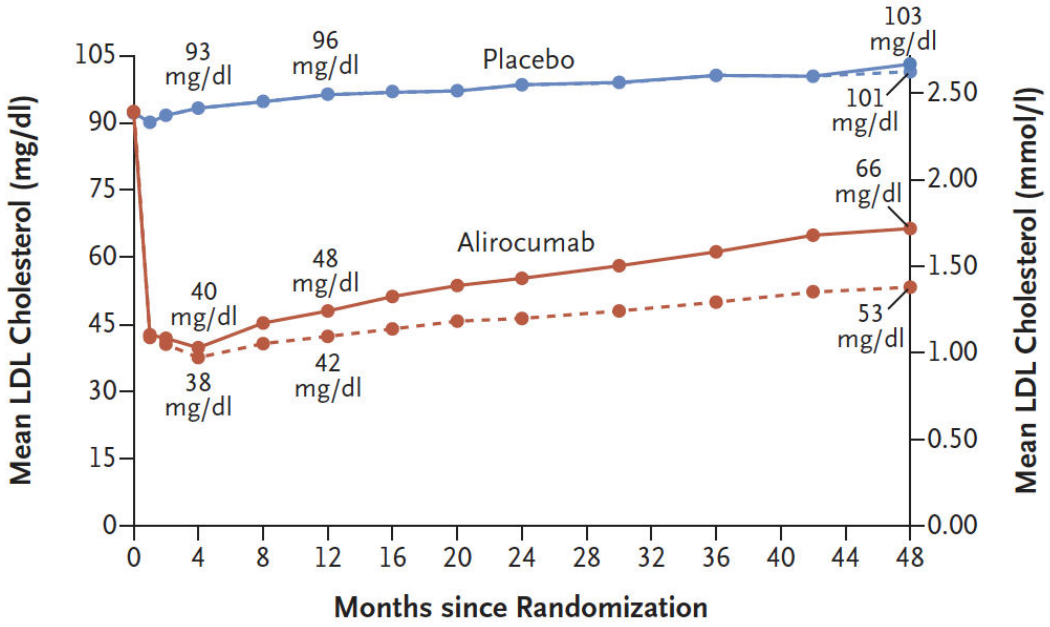
RELEVANCE OF AN ADEQUATE LDL-C CONTROL OVER TIME



. Ference BA, et al. *J Am Coll Cardiol.* 2018;72(10):1141-1156.

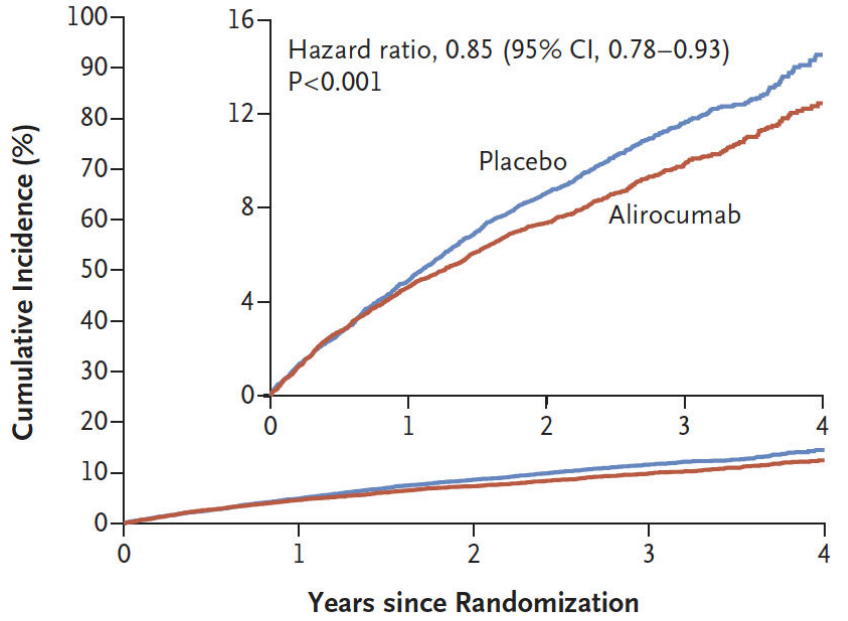
ODYSSEY OUTCOMES: ALIROCUMAB AFTER ACS

LDL-C Levels



Primary Endpoint

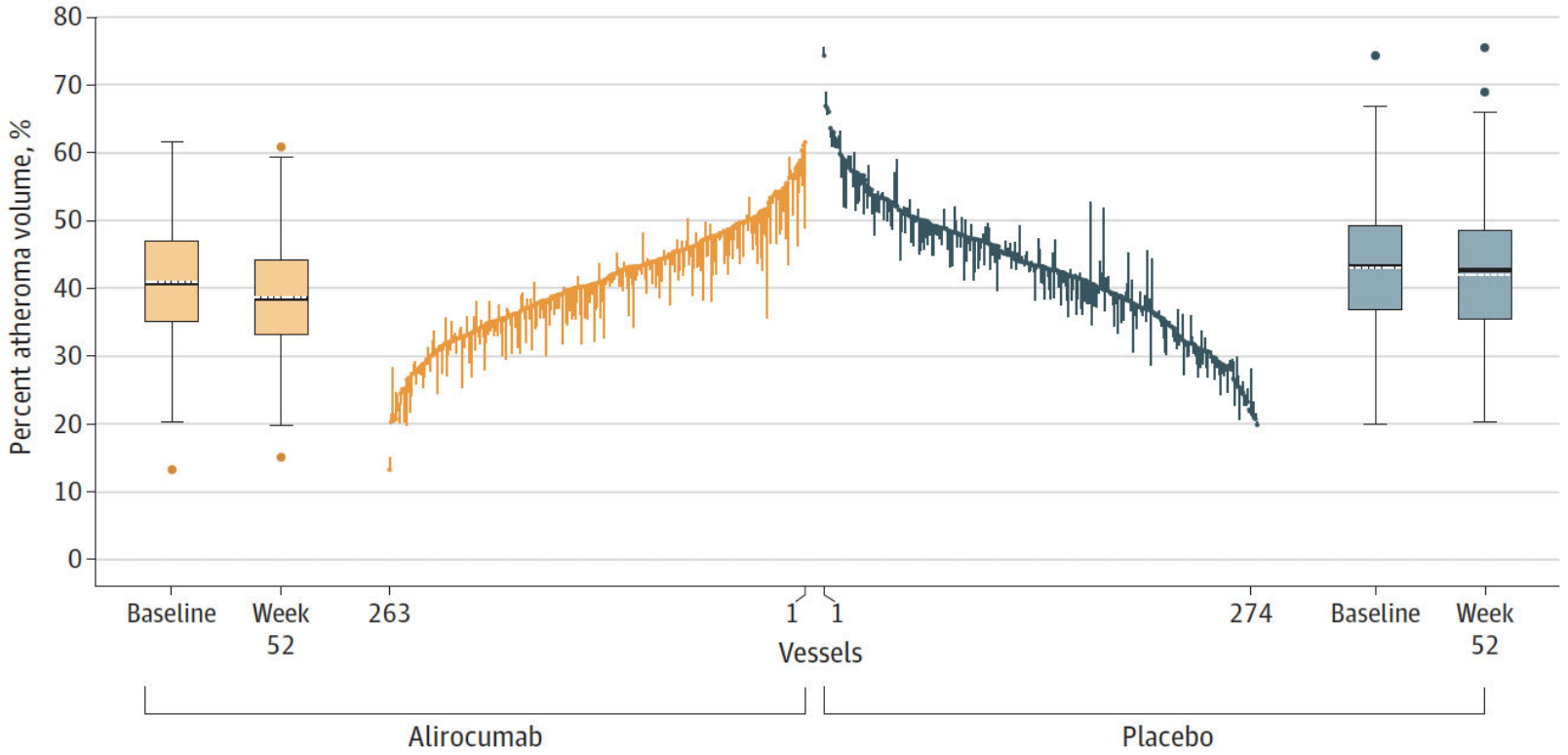
Coronary death, MI, stroke, or UA requiring hospitalization

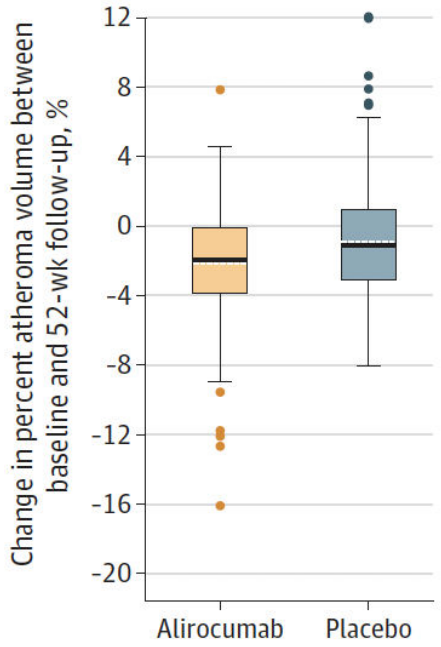


No. at Risk					
Placebo	9462	8805	8201	3471	629
Alirocumab	9462	8846	8345	3574	653

PACMAN AMI: Alirocumab in Patients with AMI

Changes in % Atheroma Volume



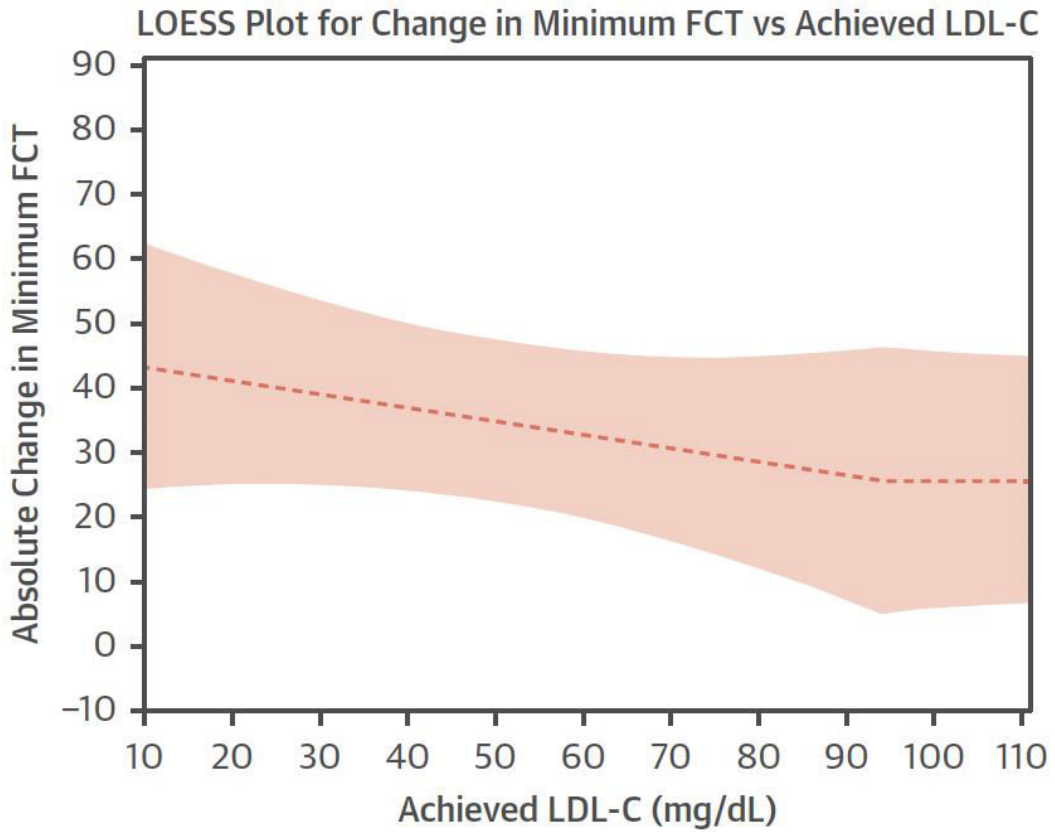


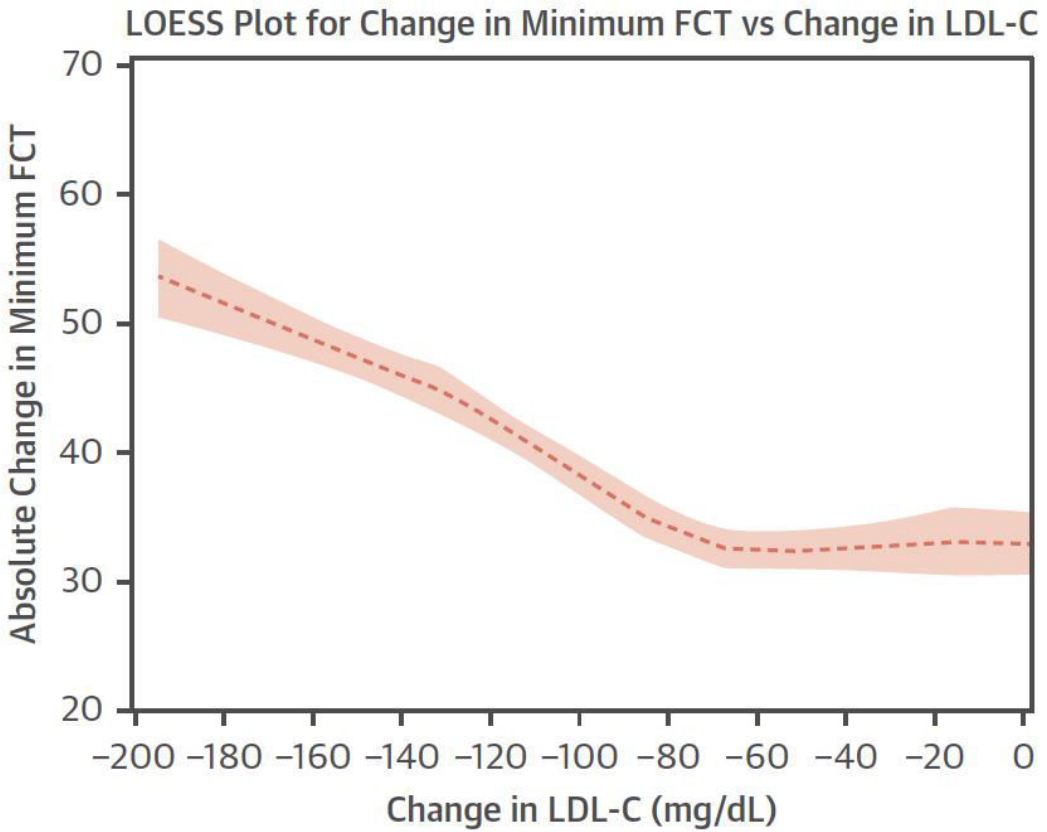
N = 300
IVUS, OCT, NIRS

Raber L et al. JAMA 2022

HUYGENS: EVOLOCUMAB IN PATIENTS WITH NSTEMI

Effects on Plaque Phenotype and Burden



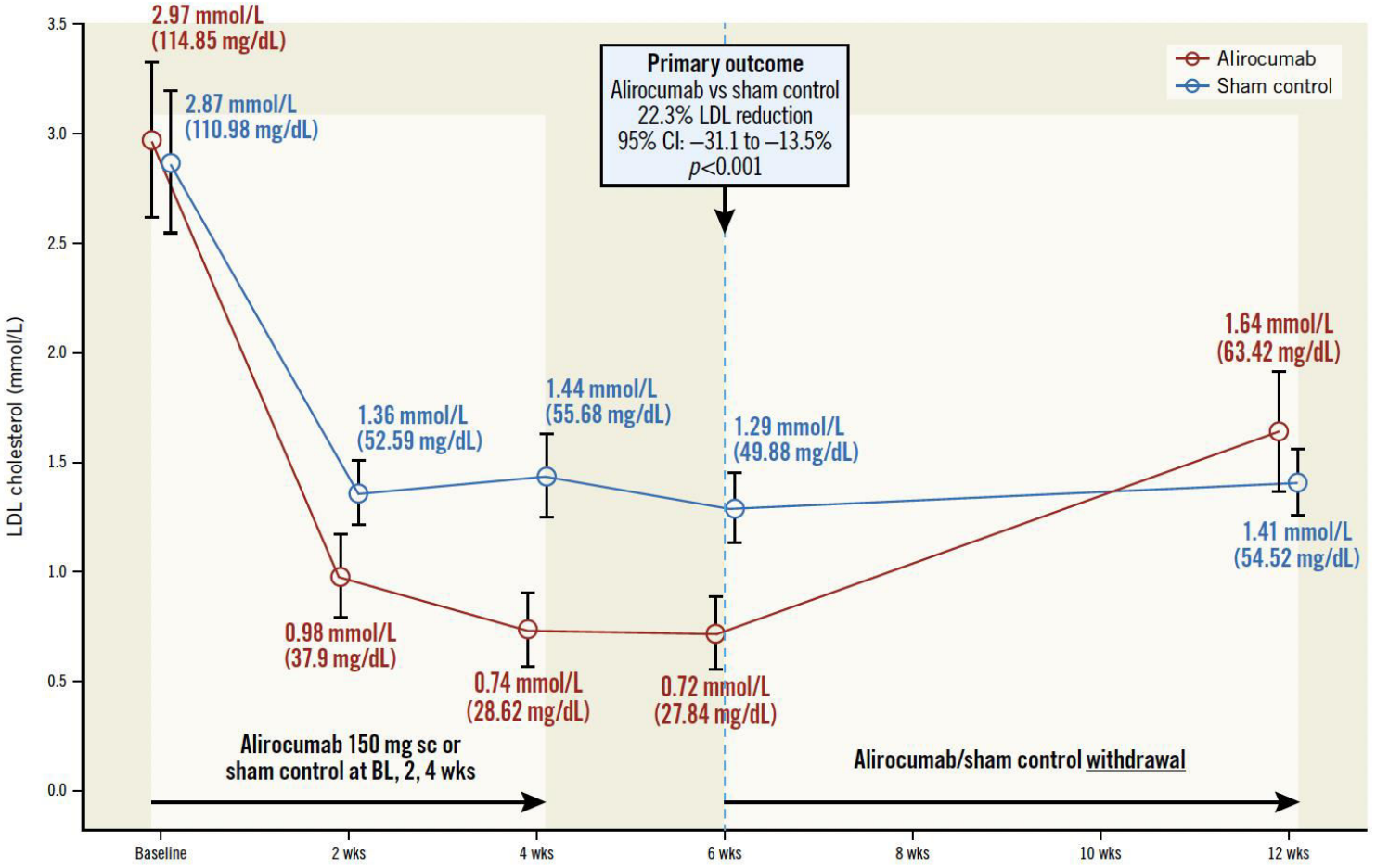


N = 164
OCT

Nicholls S et al. J Am Coll Cardiol Img 2022;15:1308–1321

EPIC STEMI: Early Alirocumab in STEMI Irrespective of LDL-C at BL

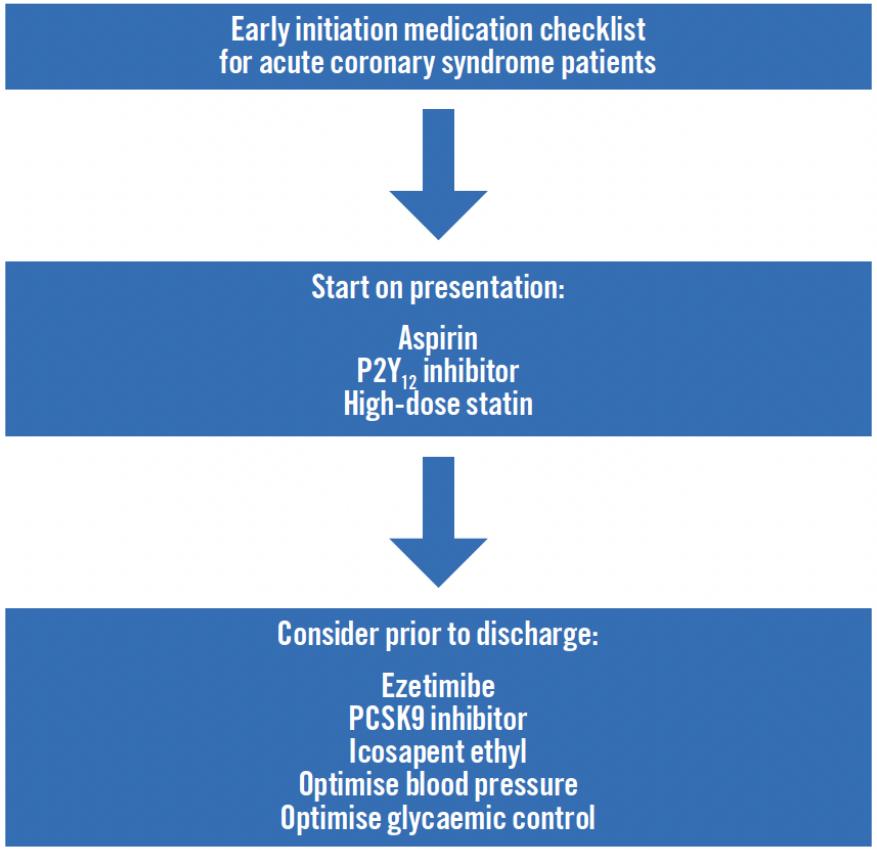
LDL-C Levels During 12 Weeks Follow-up



N = 68

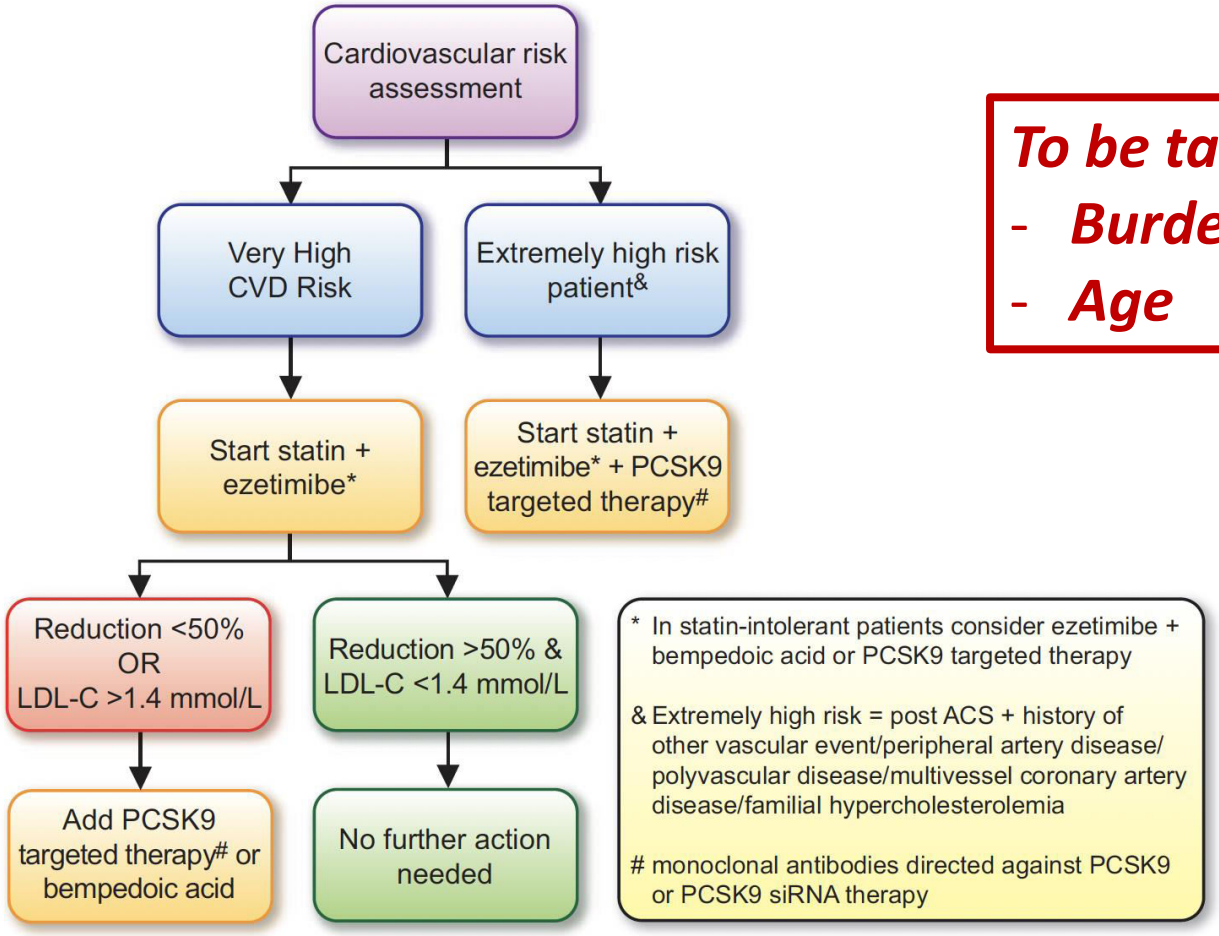
Mehta S et al. EuroIntervention 2022

Early Initiation Medication Checklist for ACS Patients



Bhatt D et al. EuroIntervention 2022;18:e865-e867

In Which Patients Should We Use PSCK9-Inhibitors?
A Stepwise Approach



To be taken into consideration:

- ***Burden of atherosclerosis***
- ***Age***

Ray KK et al. European Heart Journal 2022; **43:** 830–833

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THANKS FOR YOUR KIND ATTENTION !

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