Uloga lečenja dislipidemija u smanjenju kardiovaskularnog rizika

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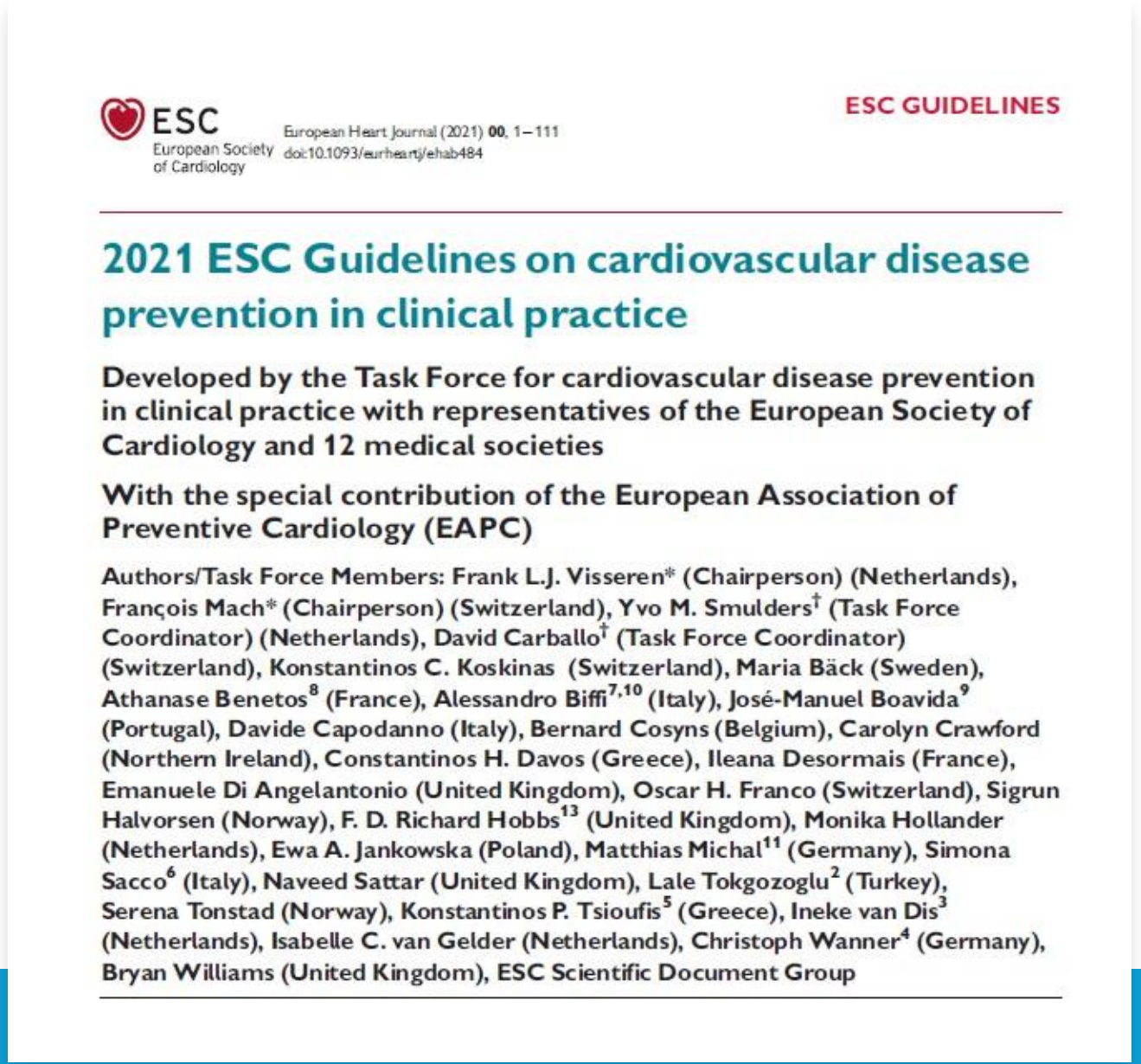
KVB su vodeći uzrok smrti u svetu -
odgovorne su za
~18.6 milliona smrti godišnje

U 2030. očekuje se 22,2 miliona smrti zbog KV bolesti

Roth GA et al. J Am Coll Cardiol 2020;76:2982-302
Virani SS et al. Circulation 2020;141:e 139-e596

- Personalizovana prevencija
- Starosnoj dobi prilagodjeni ciljevi
- Osavremenjen princip stratifikacije rizika
- Potvrda definisanih ciljeva
- Obaveznost podele ciljeva sa pacijentom



ESC European Society of Cardiology

European Heart Journal (2021) 00, 1–111
doi:10.1093/eurheartj/ehab484

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Developed by the Task Force for cardiovascular disease prevention in clinical practice with representatives of the European Society of Cardiology and 12 medical societies

With the special contribution of the European Association of Preventive Cardiology (EAPC)

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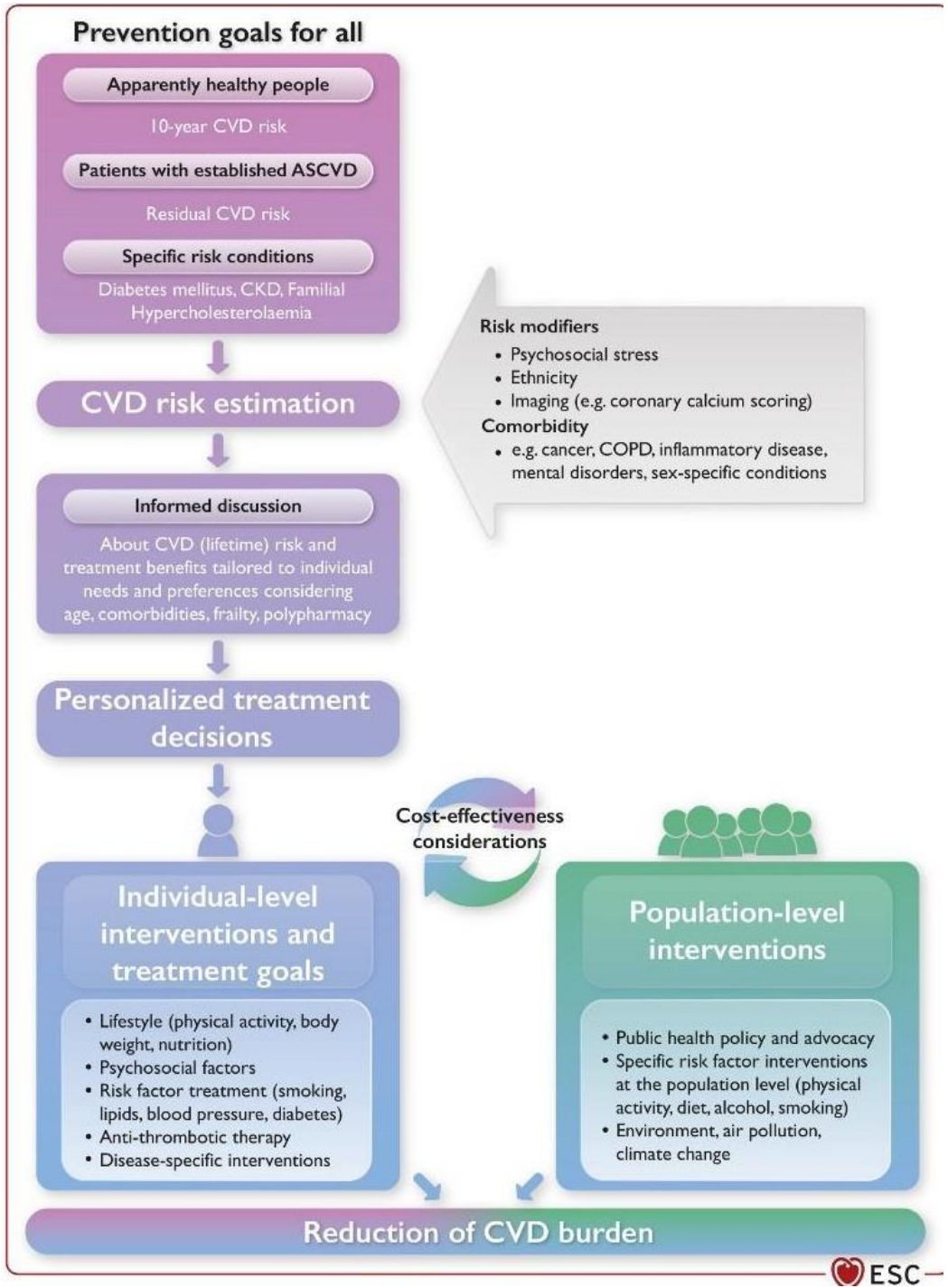
Prevencija KVB

- ✓ Naizgled zdrave osobe
- ✓ Pacijenti sa dokazanom ASKVB
- ✓ Osobe sa specifičnim rizikom (DM,FH,HBB)



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European Heart Journal (2021)doi:10.1093/eurheartj/ehab484

Naizgled zdrave osobe

Osobe bez

- ✓ Dokazane ASKVB (dogadjaja ili aka)
- ✓ Hronične bubrežne bolesti
- ✓ Dijabetesa
- ✓ Familijarne hiperholesterolemije

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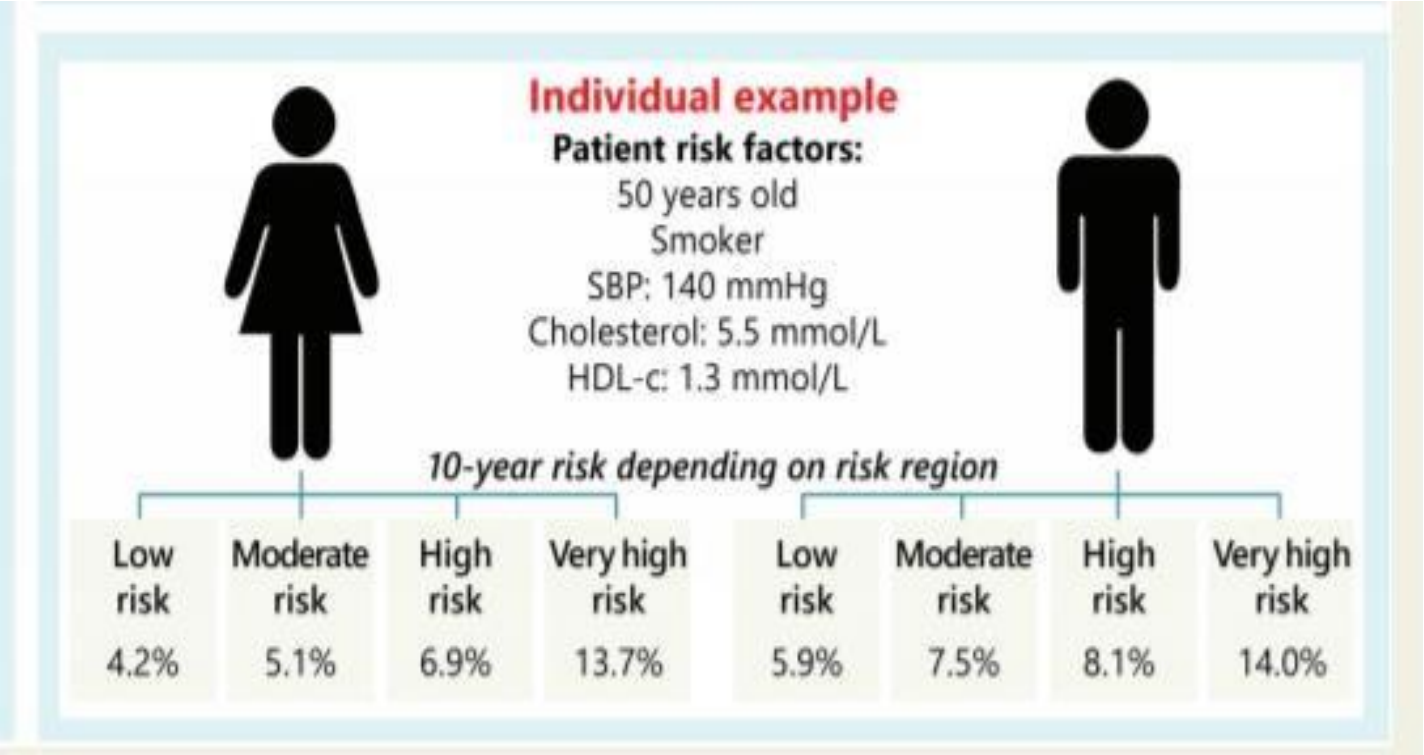
KV rizik svakog pojedinca zavisi od:

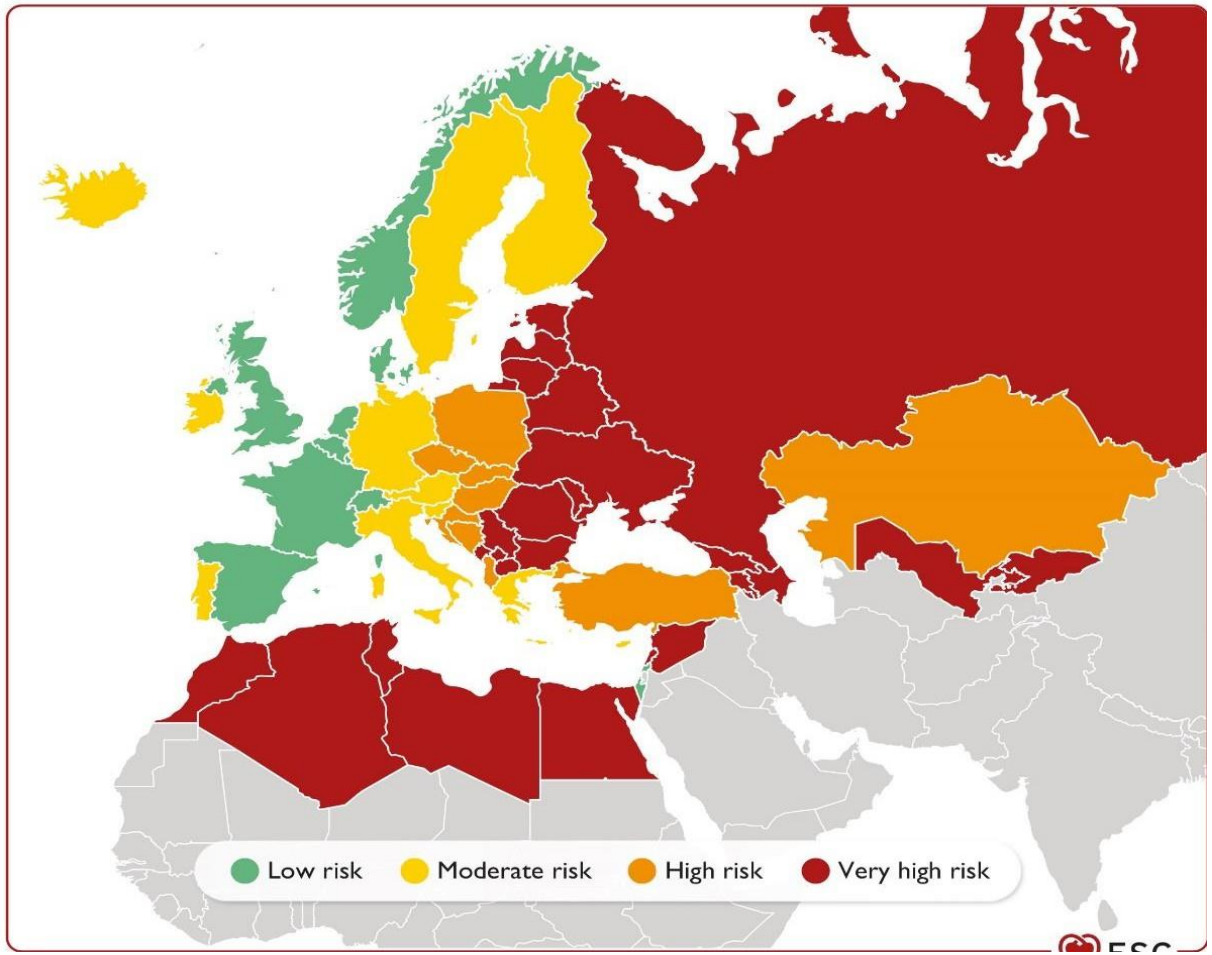
- prisustva individualnih faktora rizika (pušenje, hipertenzija, dislipidemije...)

- mortaliteta od KV bolesti u populaciji



SCORE2 working group and ESC Cardiovascular risk collaboration.
Eur Heart J 2021

WHO - regioni prema KV riziku



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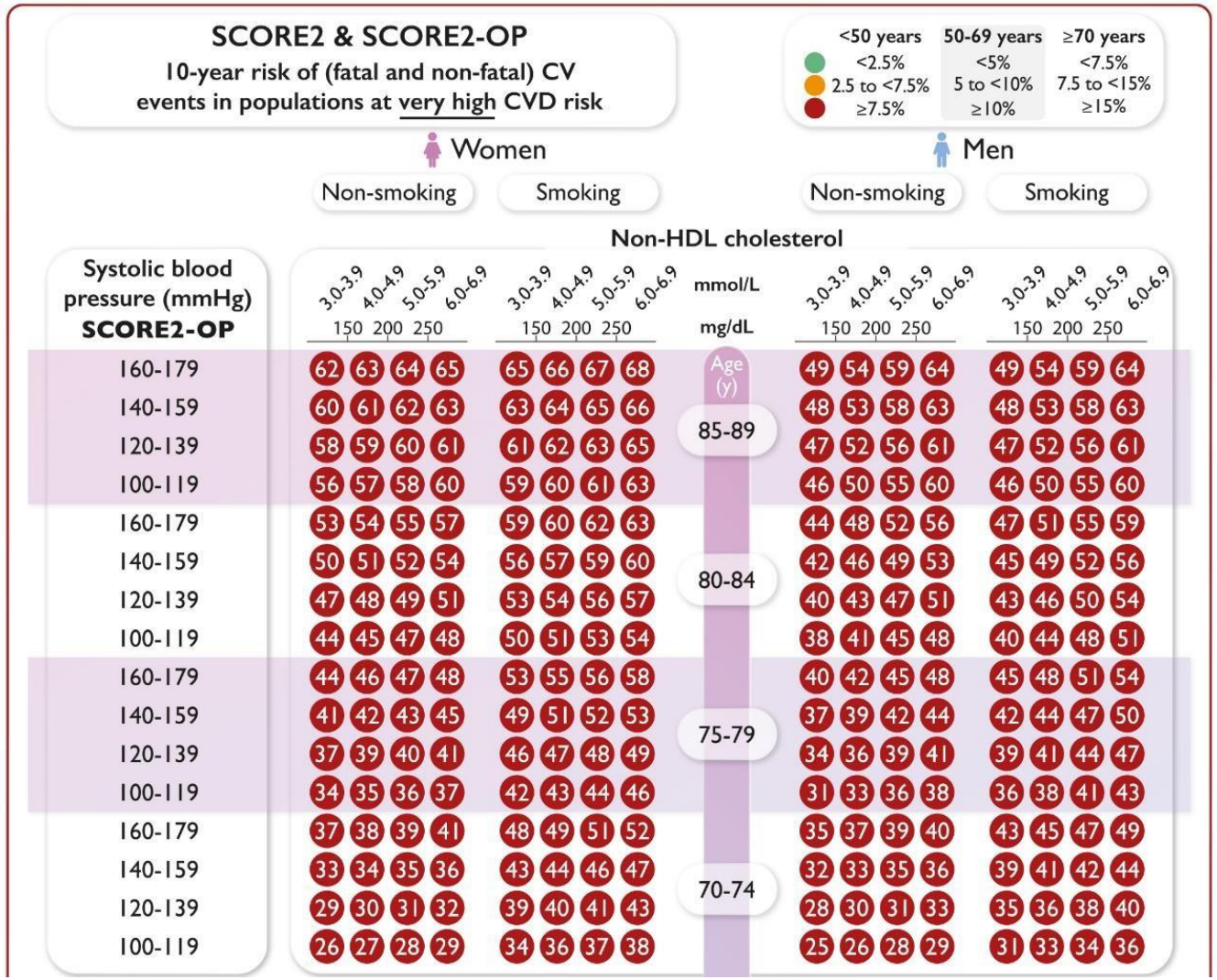
SCORE2 i SCORE2-OP tablice
za procenu rizika od fatalne i nefatalne ASKVB



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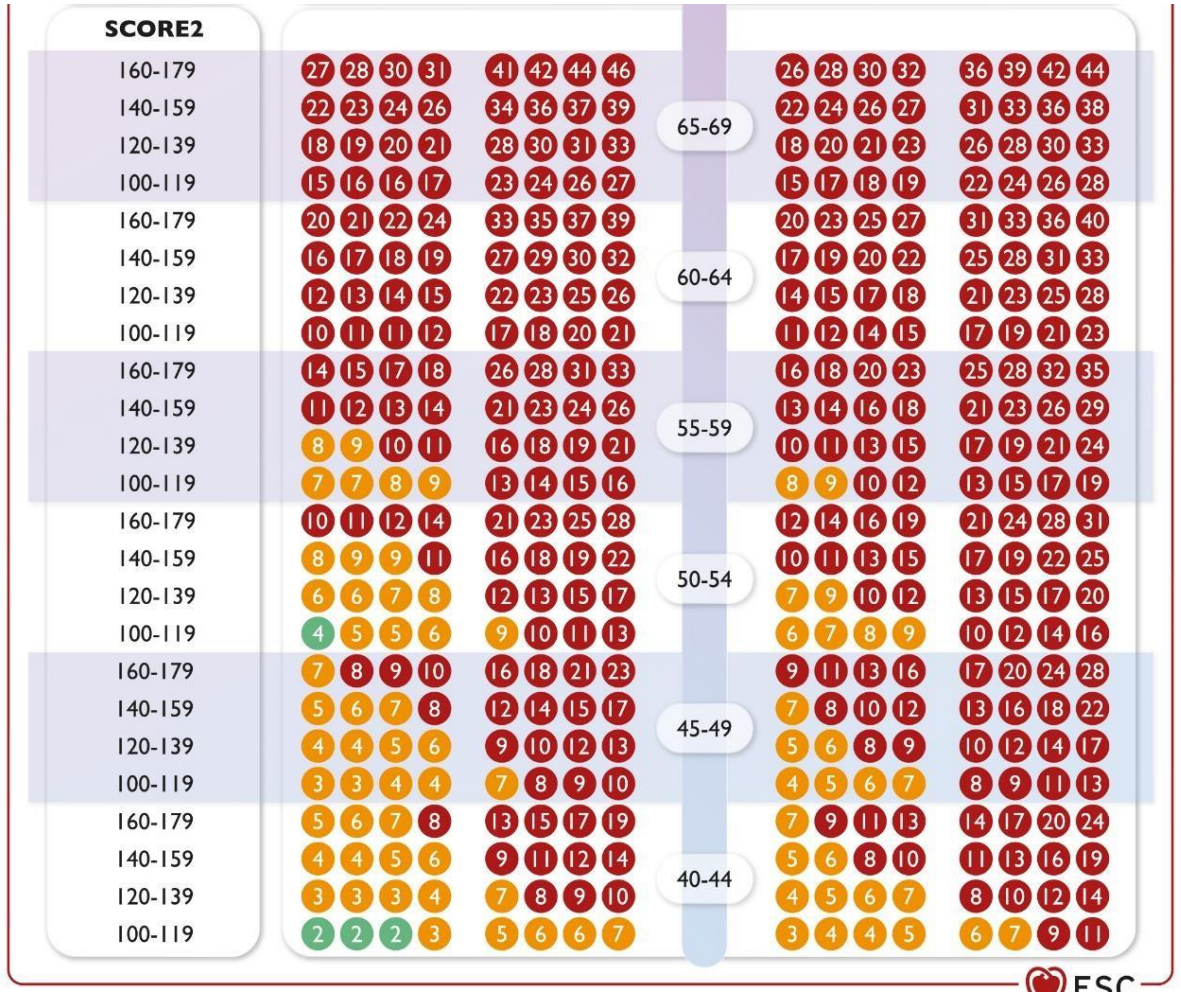

SCORE2																
160-179	27	28	30	31	41	42	44	46	65-69	26	28	30	32	36	39	42	44
140-159	22	23	24	26	34	36	37	39		22	24	26	27	31	33	36	38
120-139	18	19	20	21	28	30	31	33		18	20	21	23	26	28	30	33
100-119	15	16	16	17	23	24	26	27		15	17	18	19	22	24	26	28
160-179	20	21	22	24	33	35	37	39	60-64	20	23	25	27	31	33	36	40
140-159	16	17	18	19	27	29	30	32		17	19	20	22	25	28	31	33
120-139	12	13	14	15	22	23	25	26		14	15	17	18	21	23	25	28
100-119	10	11	11	12	17	18	20	21		11	12	14	15	17	19	21	23
160-179	14	15	17	18	26	28	31	33	55-59	16	18	20	23	25	28	32	35
140-159	11	12	13	14	21	23	24	26		13	14	16	18	21	23	26	29
120-139	8	9	10	11	16	18	19	21		10	11	13	15	17	19	21	24
100-119	7	7	8	9	13	14	15	16		8	9	10	12	13	15	17	19
160-179	10	11	12	14	21	23	25	28	50-54	12	14	16	19	21	24	28	31
140-159	8	9	9	11	16	18	19	22		10	11	13	15	17	19	22	25
120-139	6	6	7	8	12	13	15	17		7	9	10	12	13	15	17	20
100-119	4	5	5	6	9	10	11	13		6	7	8	9	10	12	14	16
160-179	7	8	9	10	16	18	21	23	45-49	9	11	13	16	17	20	24	28
140-159	5	6	7	8	12	14	15	17		7	8	10	12	13	16	18	22
120-139	4	4	5	6	9	10	12	13		5	6	8	9	10	12	14	17
100-119	3	3	4	4	7	8	9	10		4	5	6	7	8	9	11	13
160-179	5	6	7	8	13	15	17	19	40-44	7	9	11	13	14	17	20	24
140-159	4	4	5	6	9	11	12	14		5	6	8	10	11	13	16	19
120-139	3	3	3	4	7	8	9	10		4	5	6	7	8	10	12	14
100-119	2	2	2	3	5	6	6	7		3	4	4	5	6	7	9	11

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Kategorije pacijenata prema visini rizika

CKD without diabetes or ASCVD	Moderate CKD (eGFR 30–44 mL/min/1.73 m^2 and ACR <30 mg/g **or** eGFR 45–59 mL/min/1.73 m^2 and ACR 30 mg/g –300 mg/g **or** eGFR ≥60 mL/min/1.73 m^2 and ACR >300 mg/g)	**High-risk**	N/A
	Severe CKD (eGFR <30 mL/min/1.73 m^2 **or** eGFR 30–44 mL/min/1.73 m^2 and ACR >30 mg/g)	**Very high-risk**	N/A
Familial Hypercholesterolemia			
Associated with markedly elevated cholesterol levels	N/A	**High-risk**	N/A
Patients with type 2 diabetes mellitus			
Patients with type 1 DM above 40 years of age may also be classified according to these criteria	Patients with well controlled short-standing DM (e.g. <10 years), no evidence of TOD and no additional ASCVD risk factors	**Moderate-risk**	N/A
	Patients with DM without ASCVD and/or severe TOD, and not fulfilling the moderate risk criteria.	**High-risk**	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the ADVANCE risk score or DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model).

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice
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Kategorije pacijenata prema visini rizika

Patient category	Subgroups	Risk categories	CVD risk and therapy benefit estimation
Patients with type 2 diabetes mellitus (continued)			
	Patients with DM with established ASCVD and/or severe TOD: • eGFR <45 mL/min/1.73 m² irrespective of albuminuria • eGFR 45-59 mL/min/1.73 m² and microalbuminuria (ACR 30 mg/g – 300 mg/g) • Proteinuria (ACR >300 mg/g) • Presence of microvascular disease in at least 3 different sites (e.g. microalbuminuria plus retinopathy plus neuropathy)	**Very high-risk**	Residual 10-year CVD risk estimation after general prevention goals (e.g. with the SMART risk score for established CVD or with the ADVANCE risk score or with the DIAL model). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. DIAL model).
Patients with established ASCVD			
Documented ASCVD, clinical or unequivocal on imaging. Documented clinical ASCVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented ASCVD on imaging includes plaque on coronary angiography or carotid ultrasound or on CTA. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery.	N/A	**Very high-risk**	Residual CVD risk estimation after general prevention goals (e.g. 10-year risk with the SMART risk score for patients with established CVD or 1- or 2-year risk with EUROASPIRE risk score for patients with CHD). Consider lifetime CVD risk and benefit estimation of risk factor treatment (e.g. SMART-REACH model; or DIAL model if diabetes).

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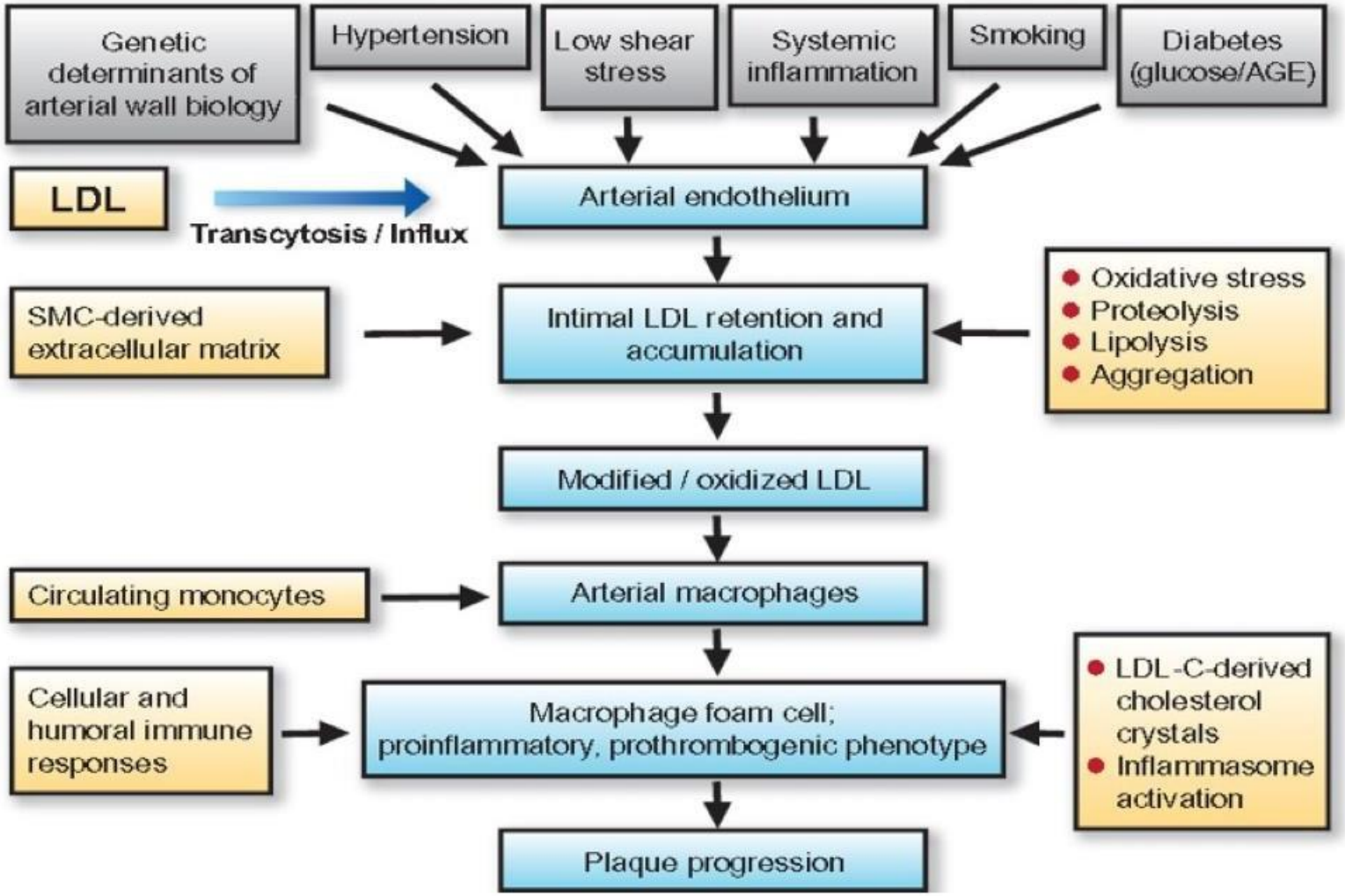
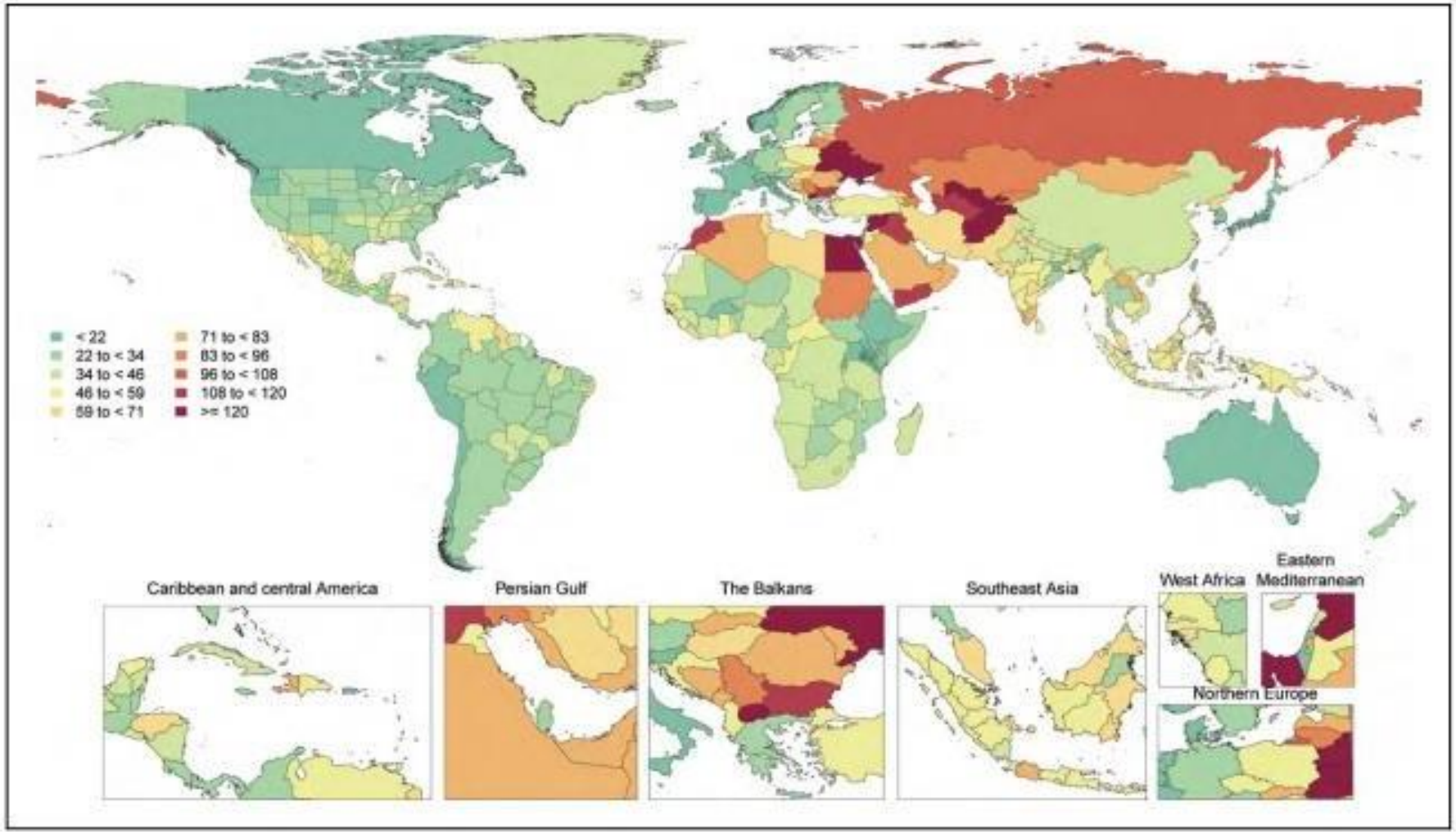
Faktori rizika u nastanku kardiovaskularnih bolesti



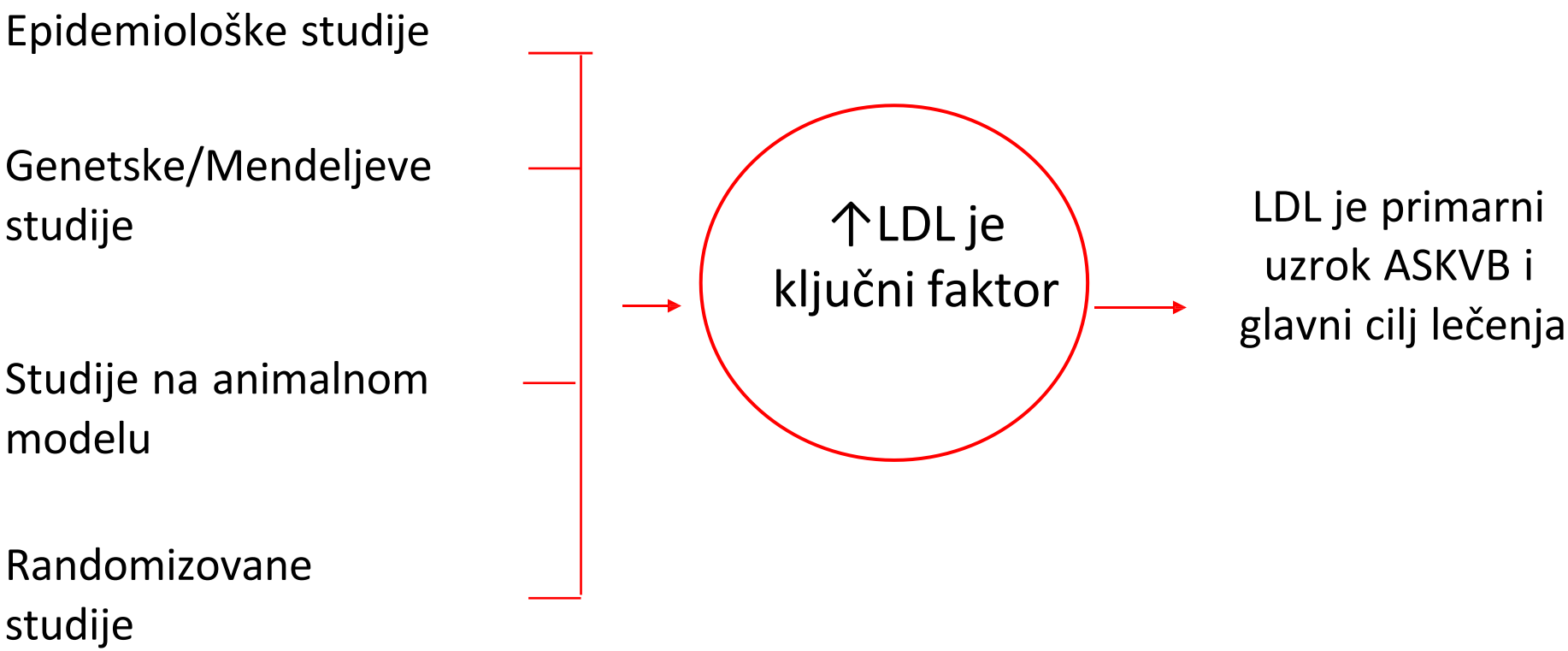
Boren J et al. Eur Heart J 2020;41:2313-2330

Uticaj visine LDL-a na kardiovaskularni mortalitet



Circulation. 2024;149:e347–e913. DOI: 10.1161/CIR.0000000000001209

Povećanje nivoa LDL-a - ključni faktor rizika za nastanak ASKVB



Ference BA et al Eur Heart J 2017;38:2459-2472 Grundy SM et al.Circulation 2019:139e1082-e1143

Osnovne poruke iz Vodiča za dislipidemije 2019.

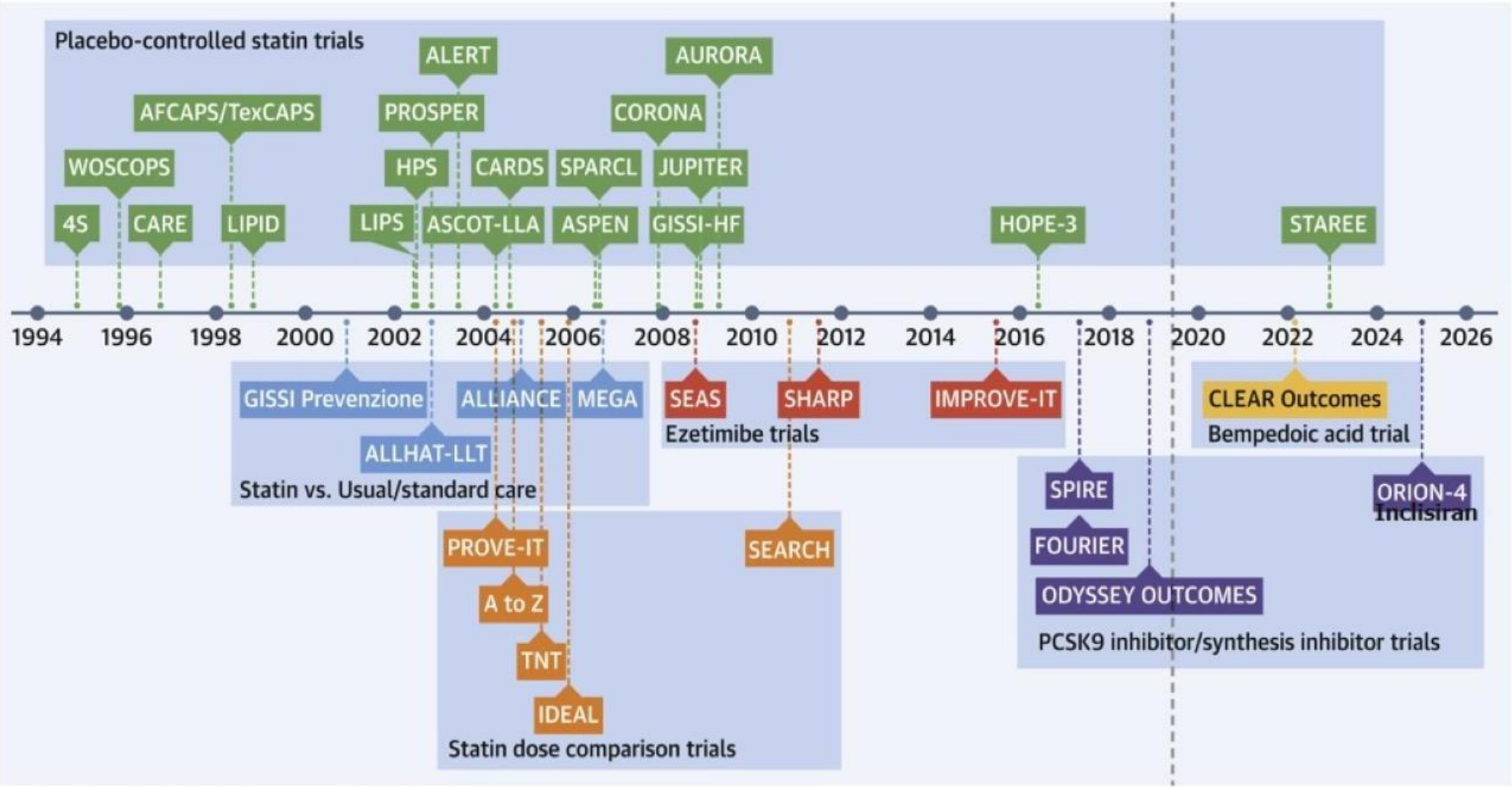
Produženo izlaganje povećanju LDL-a povećava KV rizik
Dugoročno povišen nivo LDL-a je značajno lošiji od ograničenog povećanja
Npr. pacijenti sa FH izloženi dugotrajnom povećanju nivoa LDL-a su pod značajno većim KV rizikom

Fokusiranje na globalnom/ukupnom KV riziku
Nivo LDL-a je važan ali to je samo broj
Važna je procena KV rizika (LDL+komorbiditeti+ faktori rizika)

Što niže je bolje: redukcija LDL-a na 1,4mmol/l je efikasna i sigurna

Mach F et al. Eur Heart J 2020;41:111-188

…..dokazi



J Am Coll Cardiol 2020;75:1945-1955

Dokazi o prednosti redukcije LDL na nivo niži od 1,4mmol/l

Source of evidence	Mean reduction in LDL cholesterol; mmol/L [mg/dL]	Outcome	RR (95% CI)
CTT meta-analysis[1] (high-intensity vs standard statin; subgroup <2.0 mmol/L)	1.71 [66] vs 1.32 [50]	MI, CHD death, stroke, coronary revasc.	0.71 (0.56-0.91) [per mmol/L]
IMPROVE-IT[2] (eze plus statin vs statin)	1.55 [70] vs 1.40 [54]	CV death, MI, stroke, UA, coronary revasc	0.94 (0.89-0.99)
FOURIER[3] (evolocumab plus high-dose statin ± eze vs high-dose statin ± eze)	2.37 [92] vs 0.78 [30]	CV death, MI, stroke, UA, coronary revasc	0.85 (0.79-0.92)
ODYSSEYOUTCOMES[4] (alirocumab plus high-dose statin ± eze vs high-dose statin ± eze)	2.37 [92] vs 1.37 [53]	MI, CHD death, stroke, UA	0.85 (0.78-0.93)

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. European Heart Journal 2019

Osnovne poruke iz Vodiča o ciljnim vrednostima LDL-a

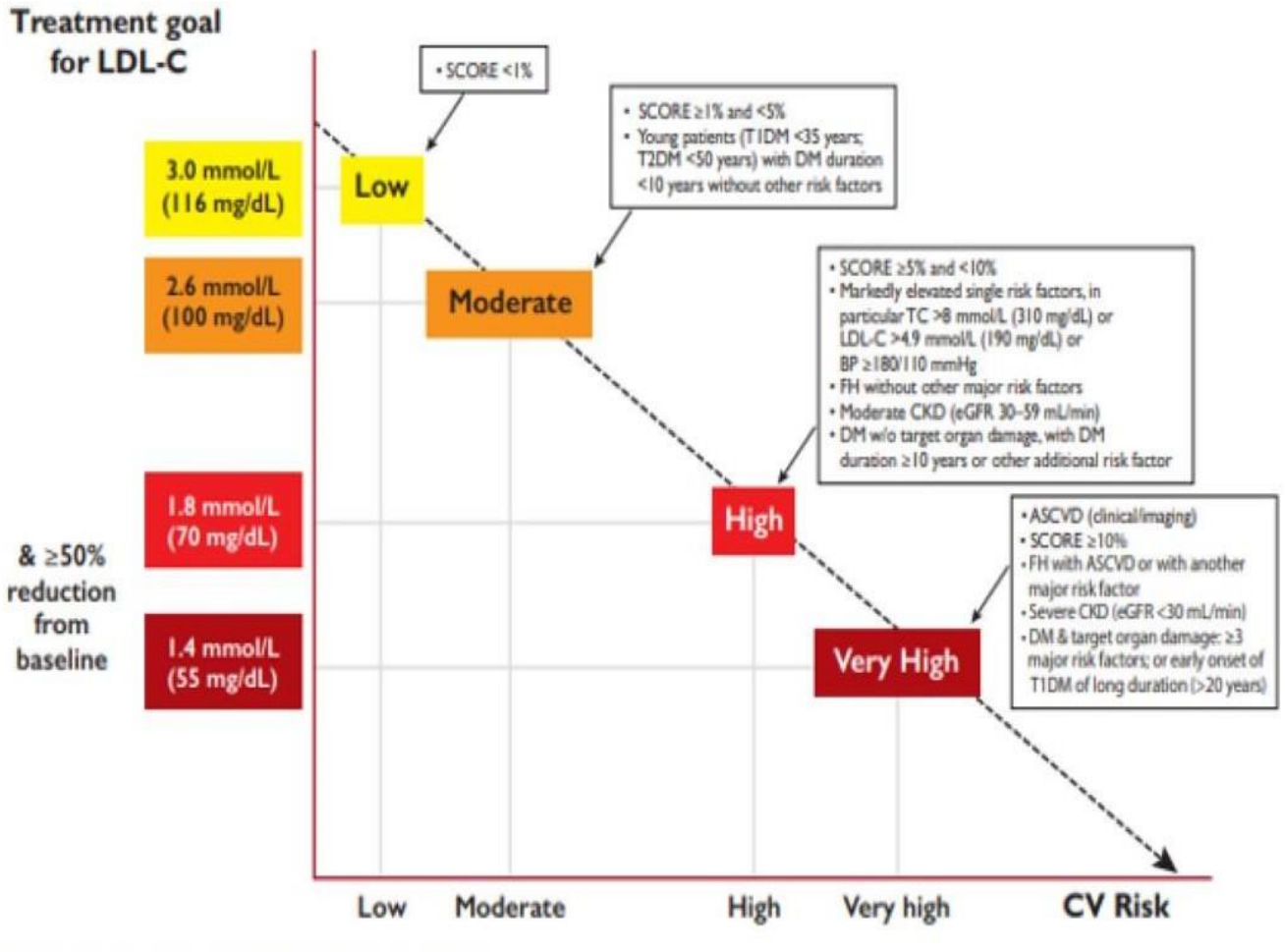
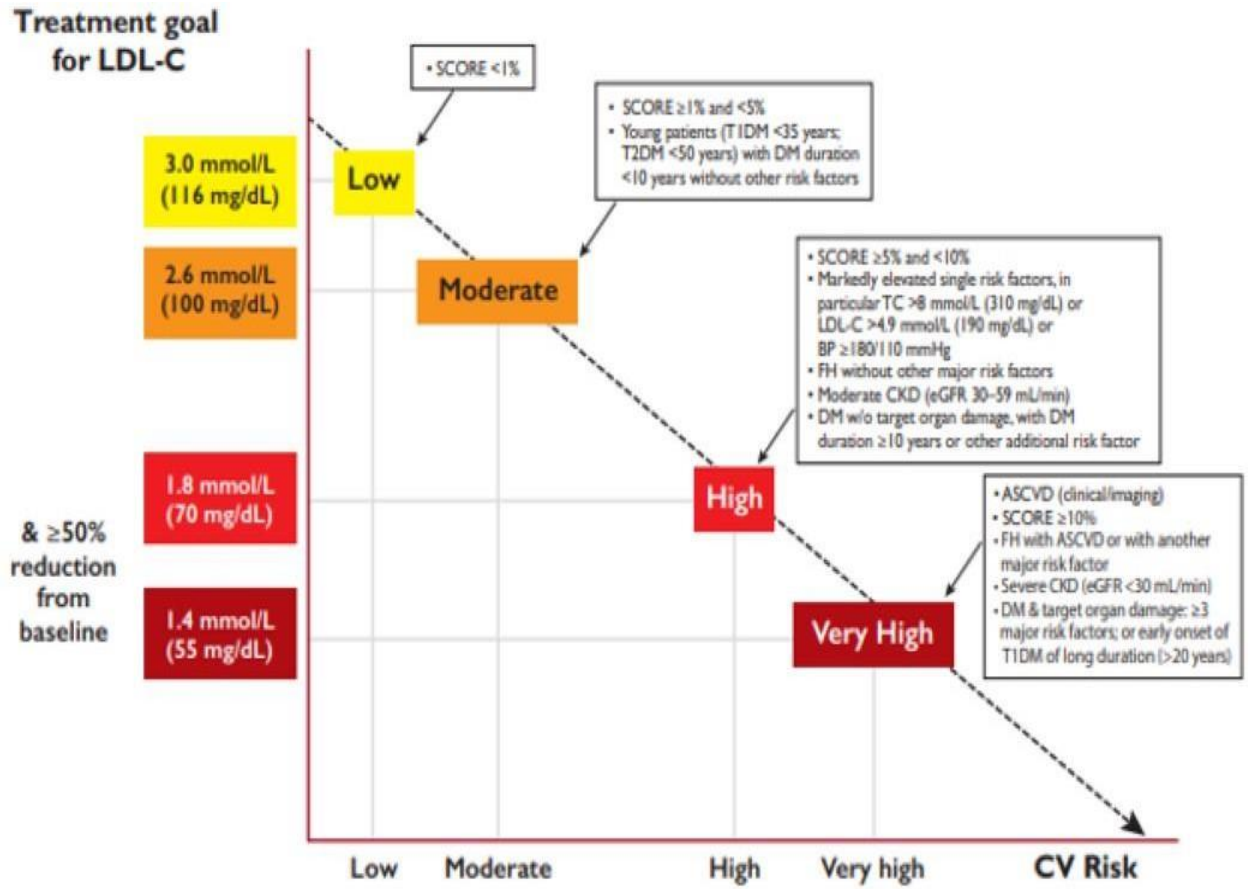


Table 4 Cardiovascular risk categories

Very-high-risk	People with any of the following: Documented ASCVD, either clinical or unequivocal on imaging. Documented ASCVD includes previous ACS (MI or unstable angina), stable angina, coronary revascularization (PCI, CABG, and other arterial revascularization procedures), stroke and TIA, and peripheral arterial disease. Unequivocally documented ASCVD on imaging includes those findings that are known to be predictive of clinical events, such as significant plaque on coronary angiography or CT scan (multivessel coronary disease with two major epicardial arteries having >50% stenosis), or on carotid ultrasound. DM with target organ damage,* or at least three major risk factors, or early onset of T1DM of long duration (>20 years). Severe CKD (eGFR <30 mL/min/1.73 m^2). A calculated SCORE ≥10% for 10-year risk of fatal CVD. FH with ASCVD or with another major risk factor.
High-risk	People with: Markedly elevated single risk factors, in particular TC >8 mmol/L (>310 mg/dL), LDL-C >4.9 mmol/L (>190 mg/dL), or BP ≥180/110 mmHg. Patients with FH without other major risk factors. Patients with DM without target organ damage,* with DM duration ≥10 years or another additional risk factor. Moderate CKD (eGFR 30–59 mL/min/1.73 m^2). A calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.
Moderate-risk	Young patients (T1DM <35 years; T2DM <50 years) with DM duration <10 years, without other risk factors. Calculated SCORE ≥1% and <5% for 10-year risk of fatal CVD.
Low-risk	Calculated SCORE <1% for 10-year risk of fatal CVD.

Mach F et al. Eur Heart J 2020;41:111-188

Osnovne poruke iz Vodiča o ciljnim vrednostima LDL-a



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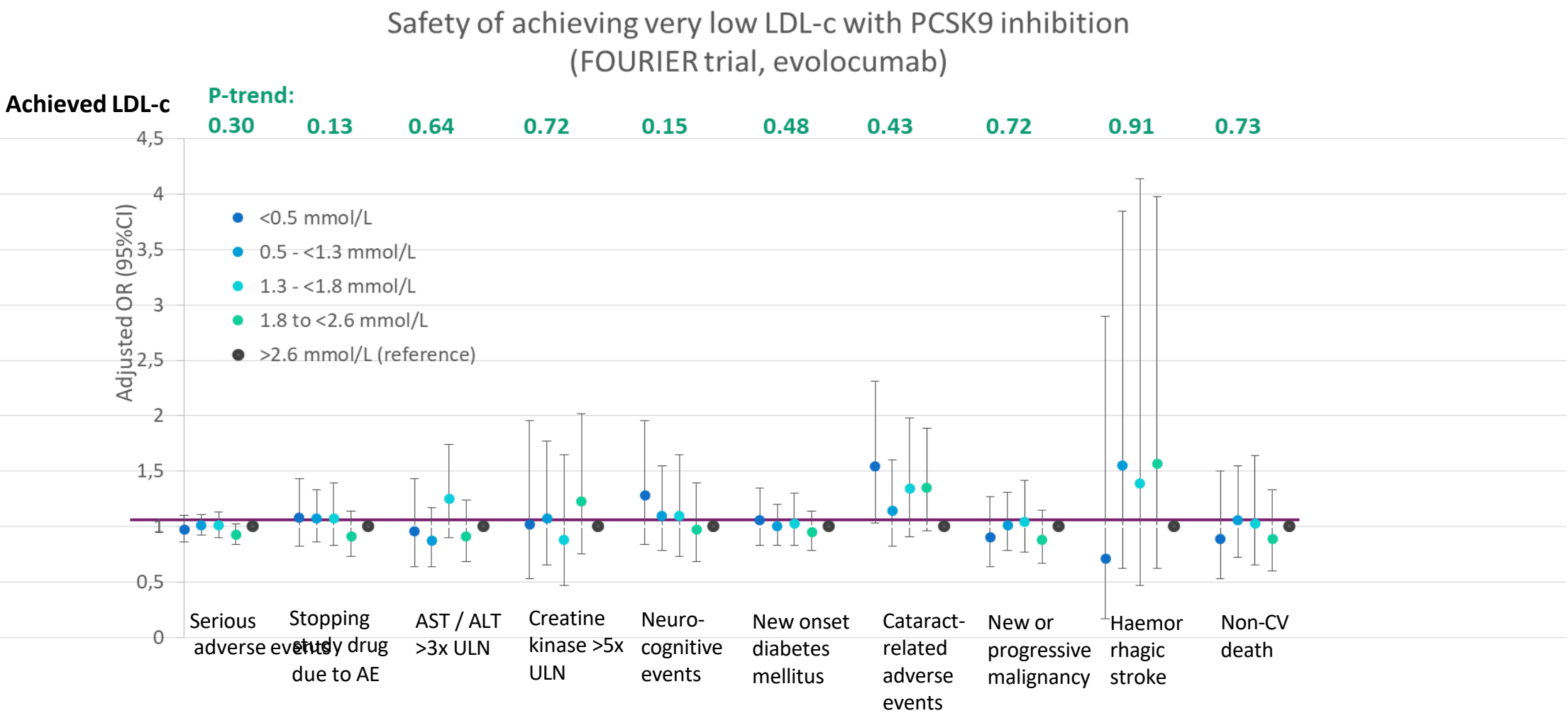
For patients with ASCVD who experience a second vascular event within 2 years (not necessarily of the same type as the first event) while taking maximally tolerated statin-based therapy, an LDL-C goal of <1.0 mmol/L (<40 mg/dL) may be considered.[119,120]	IIb	B

Mach F et al. Eur Heart J 2020;41:111-188

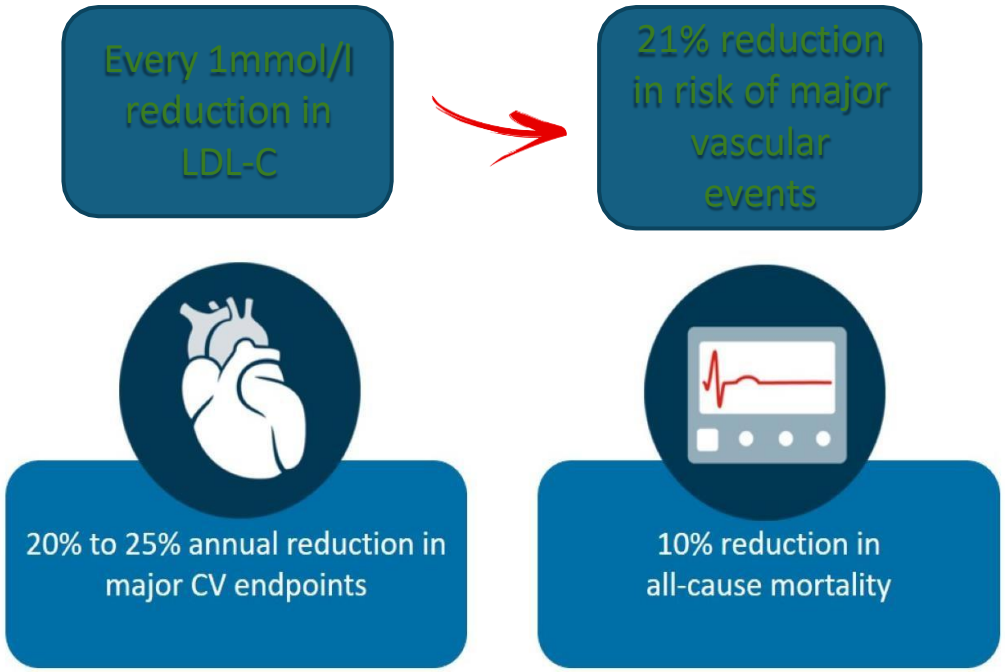
Neželjeni efekti nisu posledica niskih vrednosti LDL-a



Giuliano RP et al., Lancet. 2017;390(10106):1962-1971

Statini su osnov terapije!!

Cholesterol Treatment Trialilts Meta-Analysis - 27 randomizovanih studija (n~175000)

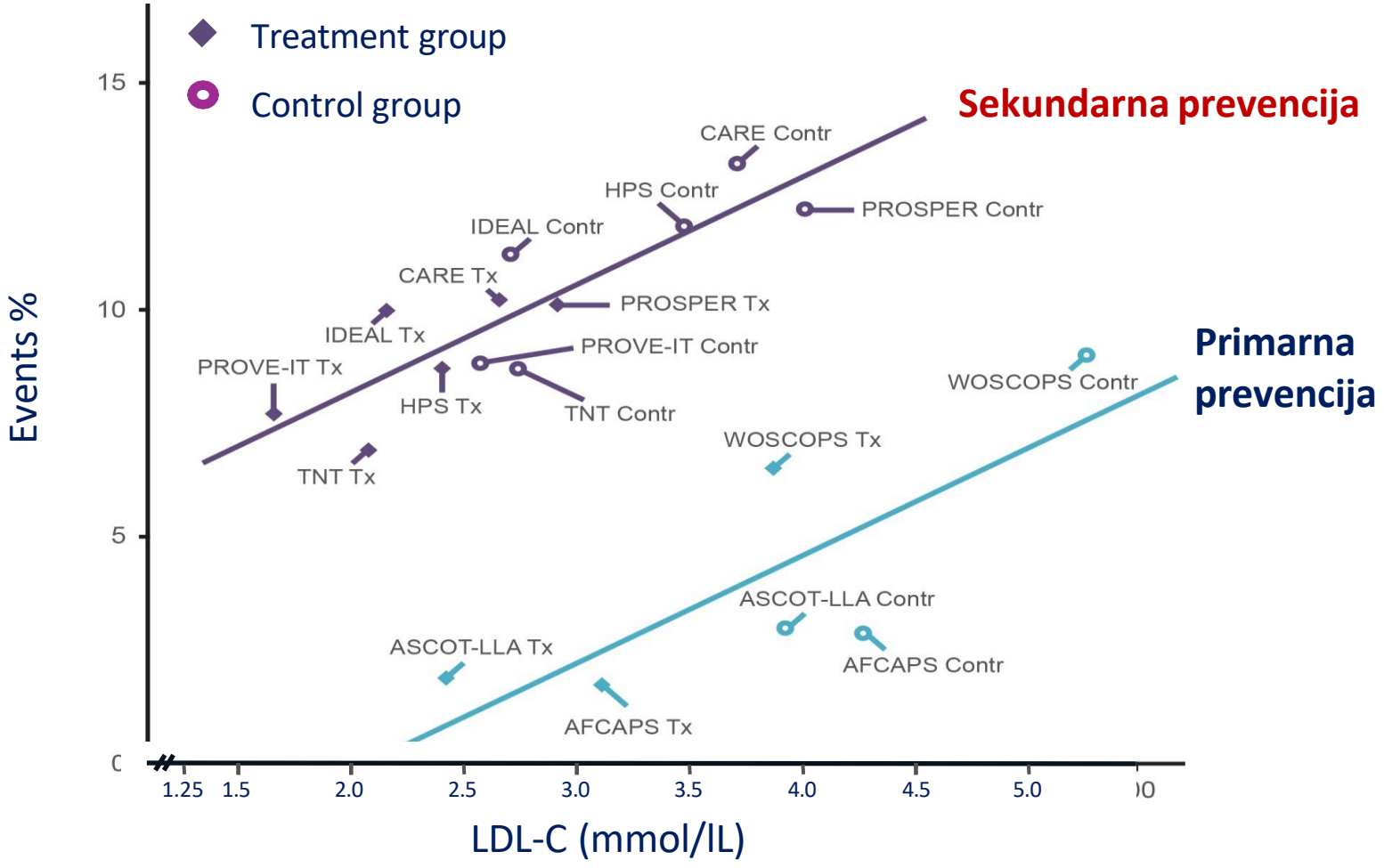


Rate ratio 0,79(95%CI 0.77, 0,81) regardless
of age, sex, baseline LDL-C prior vascular disese and all-cause mortality
Mayor vascular events included:

- Major coronary events (non-fatal MI, coronary death
- Stroke
- Coronaty revascularisation

CTT Colaboration.Lancet 2010;376:1670-1681
Sabatine MS et al.JAMA Cardiol 2018;3:823-828

Farmakološka redukcija nivoa LDL-a je povezana sa redukcijom KV dogadjaja



Besseling et al. Drugs 2013;73:293–301.

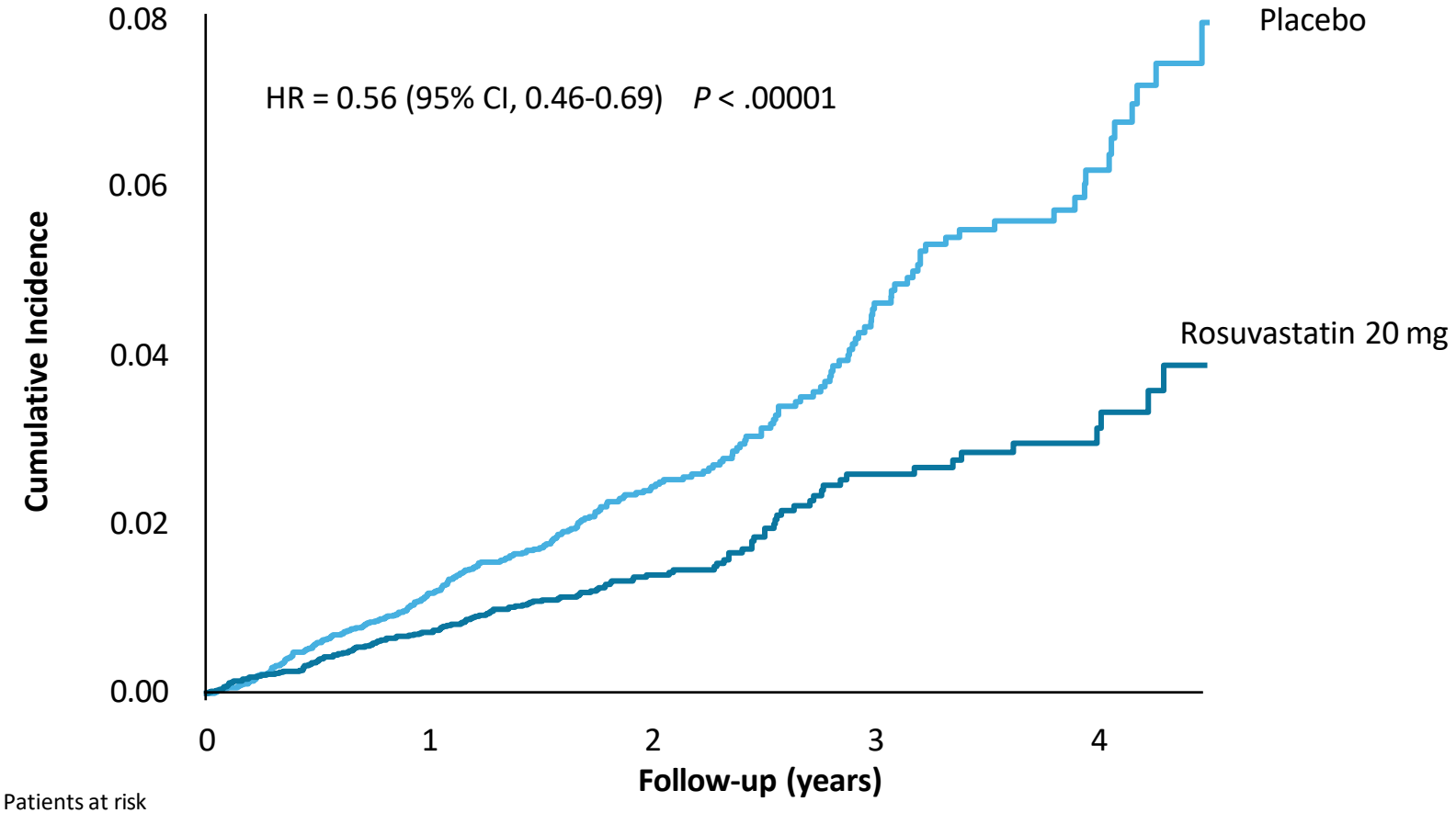
Intenzitet statinske terapije

	High Intensity	Moderate Intensity	Low Intensity
LDL-C* Lowering	≥ 50%	30% to 49%	< 30%
	Atorvastatin (40 mg) 80 mg Rosuvastatin 20 mg (40 mg)	Atorvastatin 10 mg (20 mg) Rosuvastatin (5 mg) 10 mg Simvastatin 20-40 mg	Simvastatin 10 mg
		Pravastatin 40 mg (80 mg) Lovastatin 40 mg (80 mg) Fluvastatin XL 80 mg Fluvastatin 40 mg twice daily Pitavastatin 1-4 mg	Pravastatin 10-20 mg Lovastatin 20 mg Fluvastatin 20-40 mg

Mach F et al. Eur Heart J 2020;41:11-188; Grundy SM et al J Am Coll Cardiol 2019;73:e285-e350

JUPITER studija

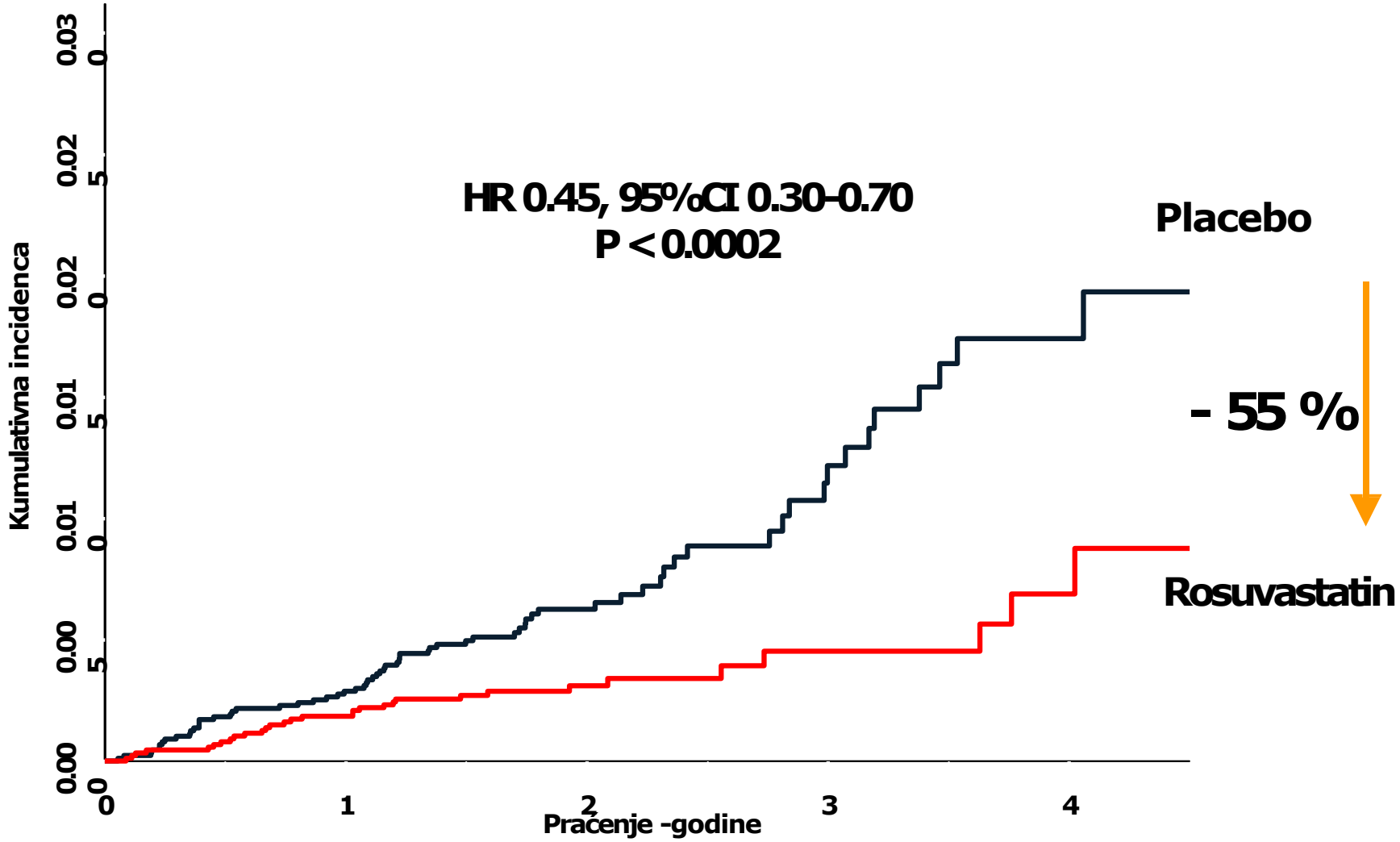
Vreme pojave KV smrti, nefatalnih moždanih udara, nefatalnih infarkta miokarda, nestabilne angine pektoris ili potrebe za revaskularizacijom



Patients at risk										
Rosuvastatin	8901	8631	8412	6540	3893	1958	1353	983	538	157
Placebo	8901	8621	8353	6508	3872	1963	1333	955	534	174

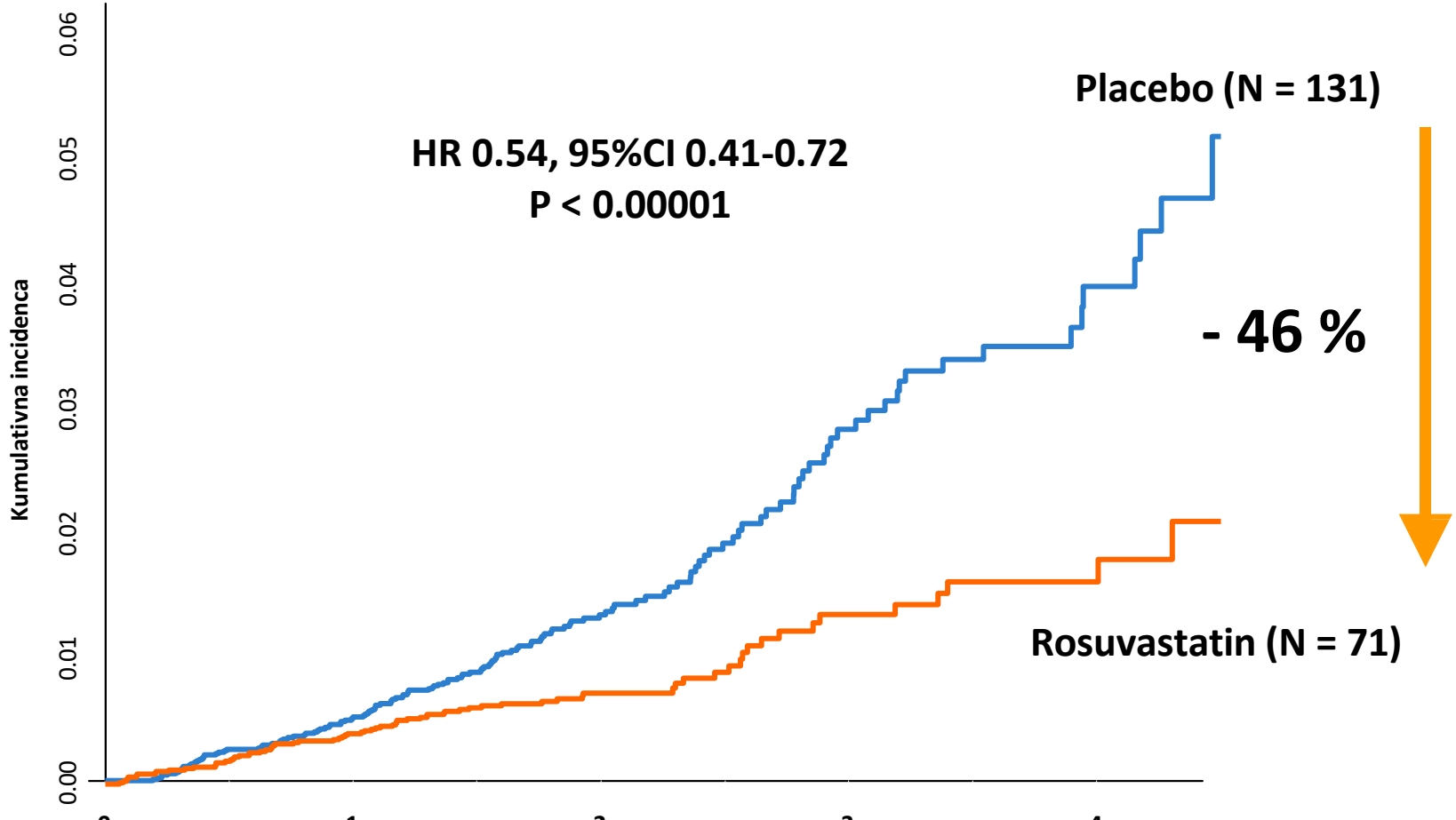
Ridker P et al. *N Eng J Med*. 2008;359:2195-2207.

JUPITER
Fatalni i nefatalni infarkti miokarda



Ridker P et al. *N Eng J Med*. 2008;359:2195-2207.

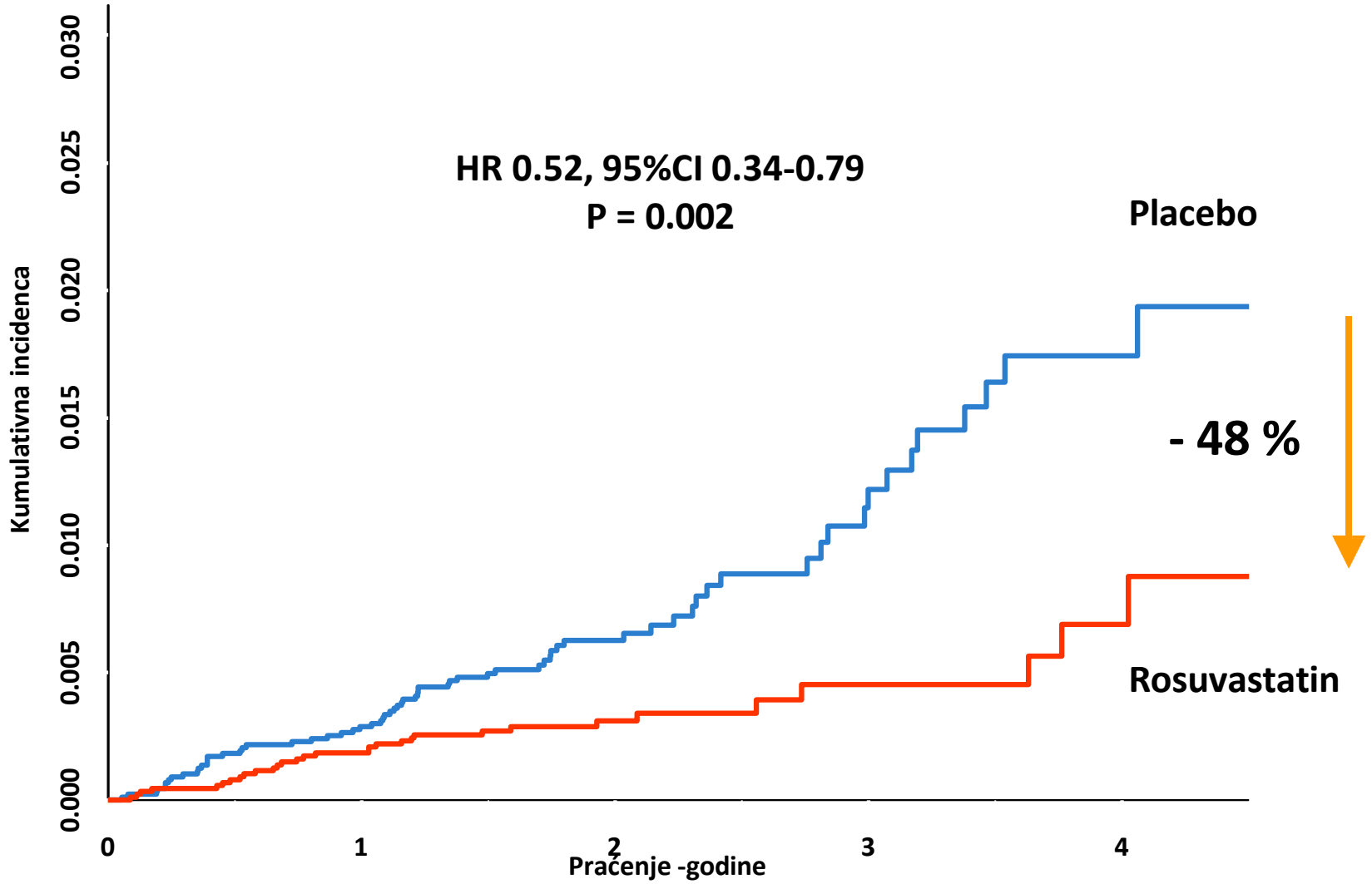
JUPITER
Hirurška revaskularizacija/angioplastika



Number at Risk										
Rosuvastatin	8,901	8,640	8,426	6,550	3,905	1,966	1,359	989	547	158
Placebo	8,901	8,641	8,390	6,542	3,895	1,977	1,346	963	538	176

Ridker P et al. *N Eng J Med*. 2008;359:2195-2207.

JUPITER
Fatalni i nefatalni moždani udari



Ridker P et al. *N Eng J Med*. 2008;359:2195-2207.

HOPE-3 studija: redukcija nivoa holesterola kod pacijenata sa intermedijarnim rizikom bez kardiovaskularne bolesti

N=12705

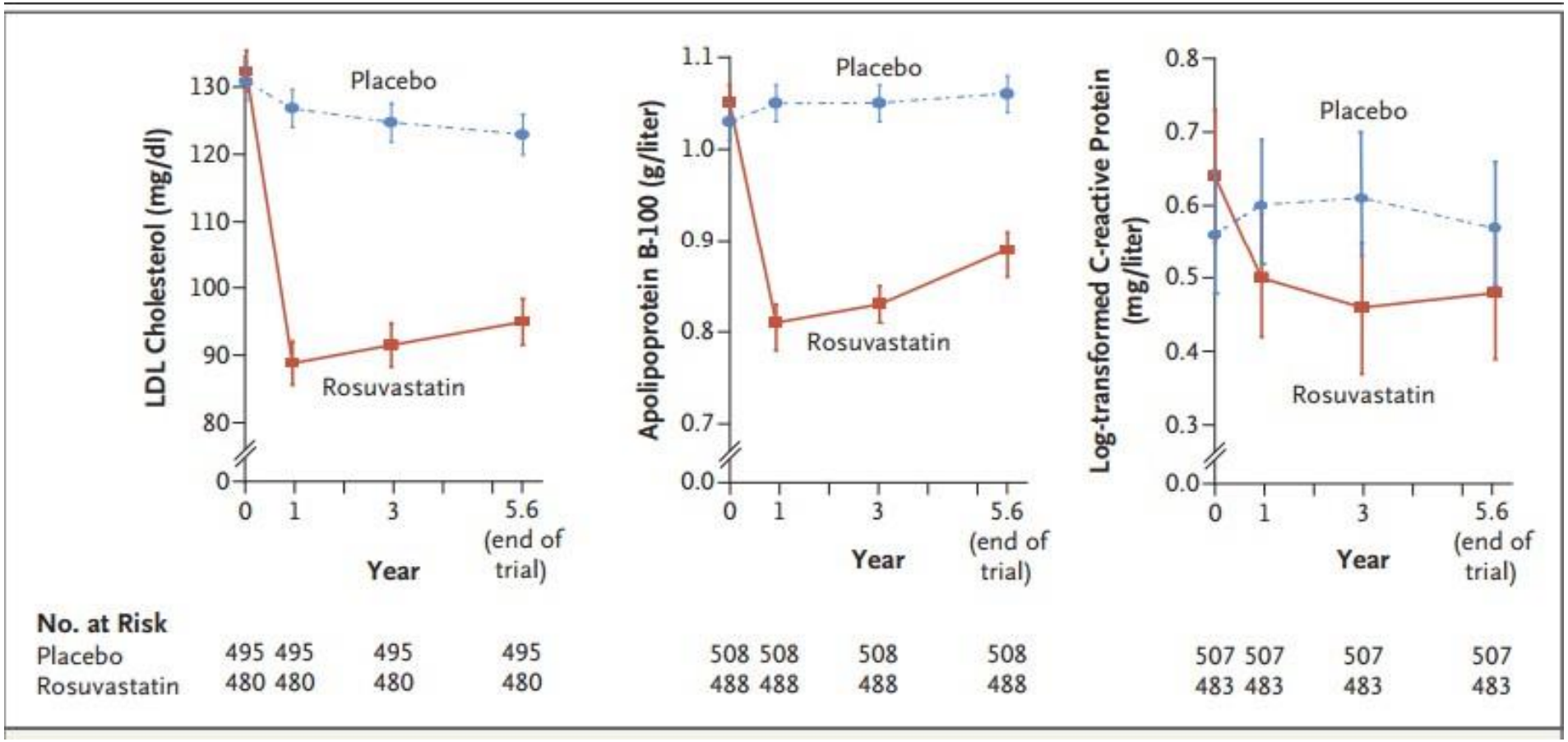
Rosuvastatin 10 mg	Placebo
N=6361	N=6344

Faktori rizika:

- Povećan odnos kuk/struk
- Nizak nivo HDL
- Pušenje
- Poremećaj metabolizma šećera
- Poremećena bubrežna funkcija
- Poroična istorija rane koronarne bolesti

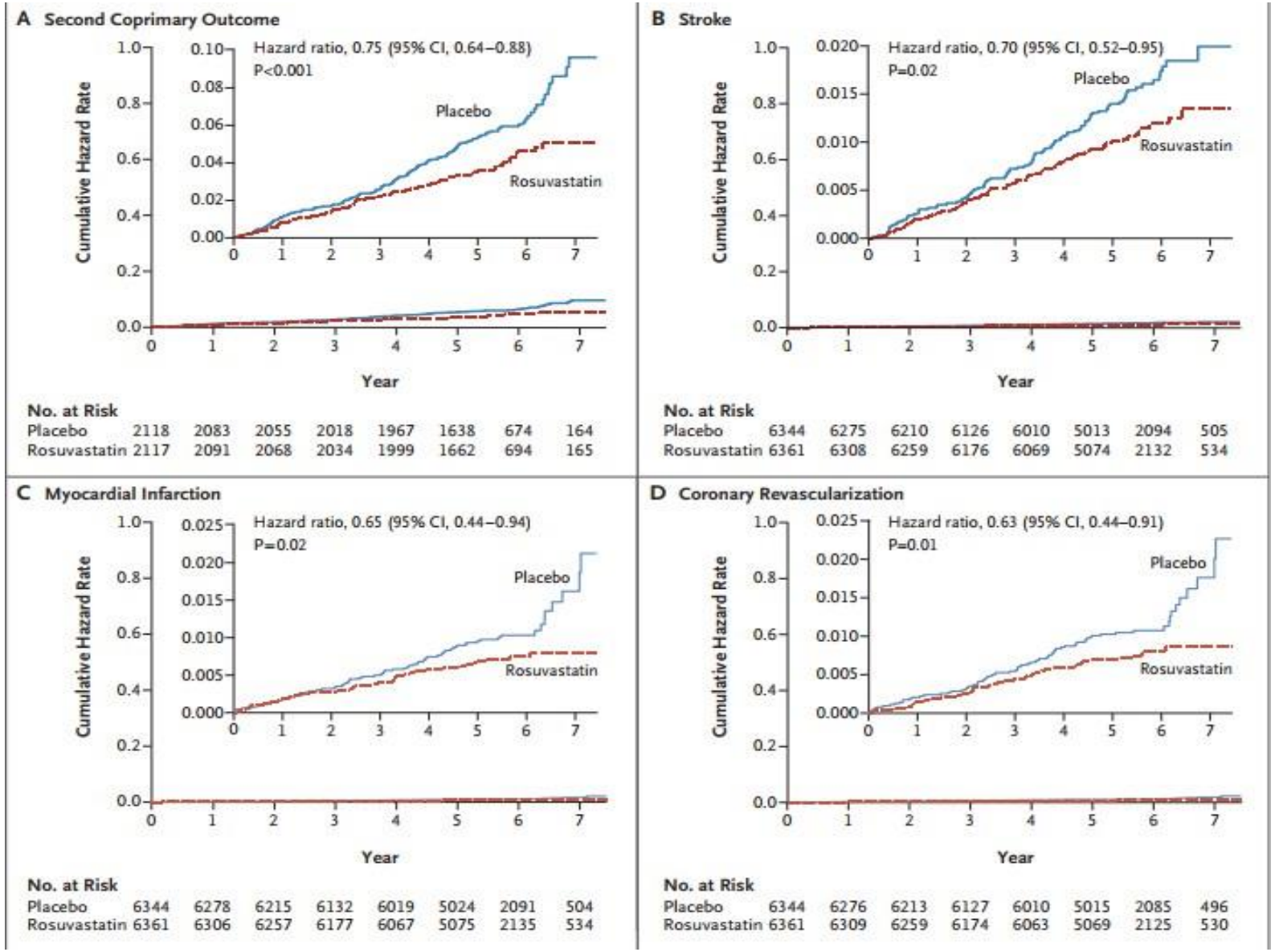
N Engl J Med 2016;374:2021-31

HOPE – 3 studija



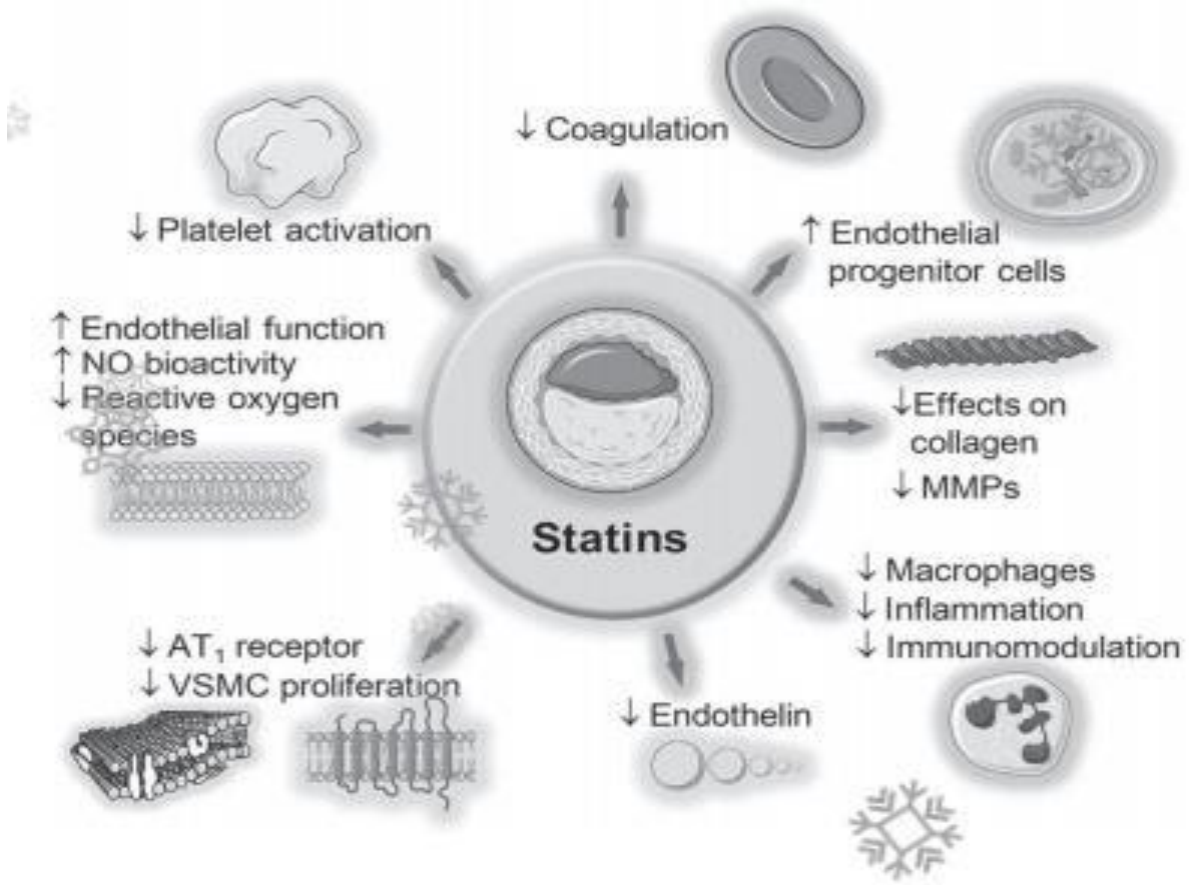
N Engl J Med 2016;374:2021-31

HOPE-3 rezultati



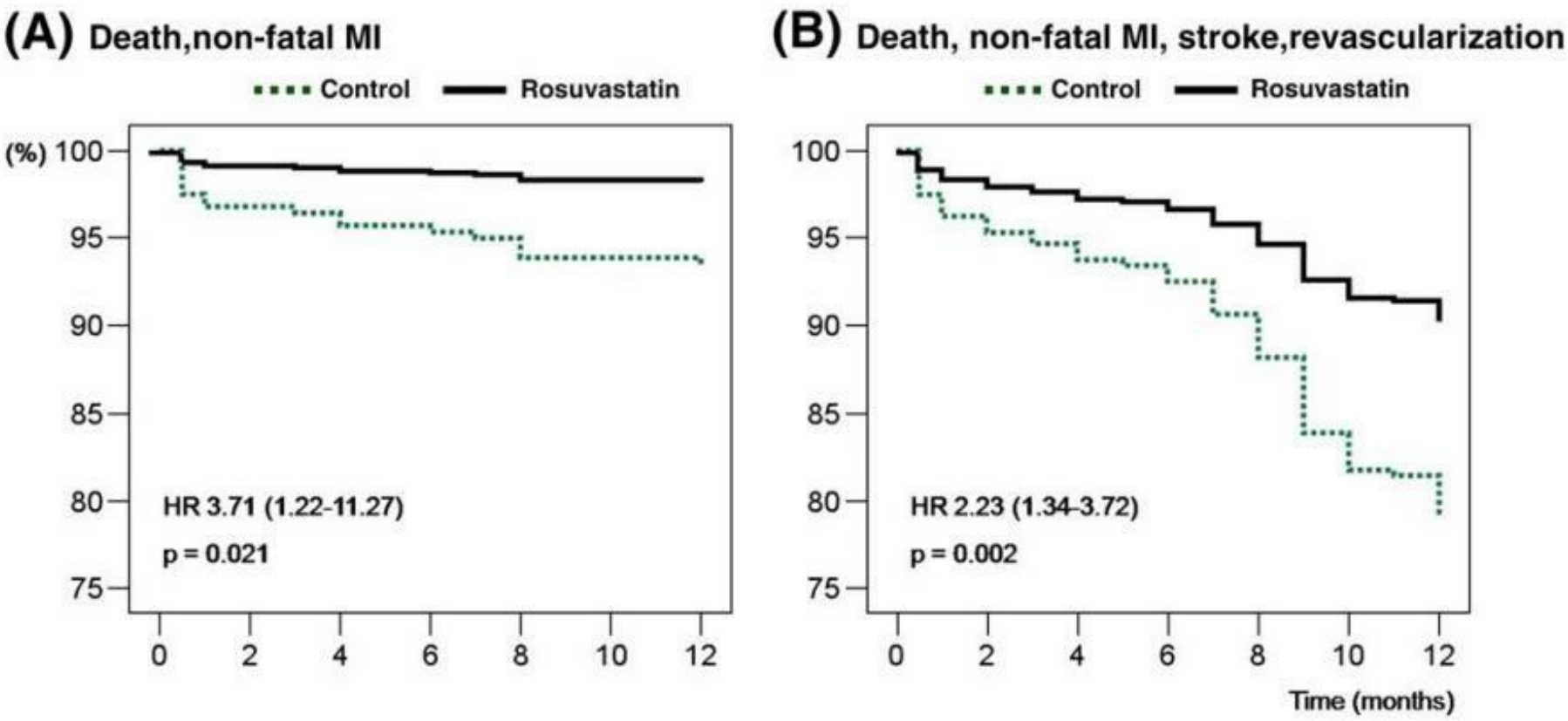
N Engl J Med 2016;374:2021-31

Uloga statina u akutnom koronarnom dogadjaju



Angeli F et al. Ther Advance Cardiovasc Therapeutics 2012 6(4) 163-174

Rosuvastatin pre PCI u AKS



Yun KH et al. Int J Cardiol. 2011;146:68-72.

Rosuvastatin uticaj na smanjenje periproceduralnog miokardnog oštećenja

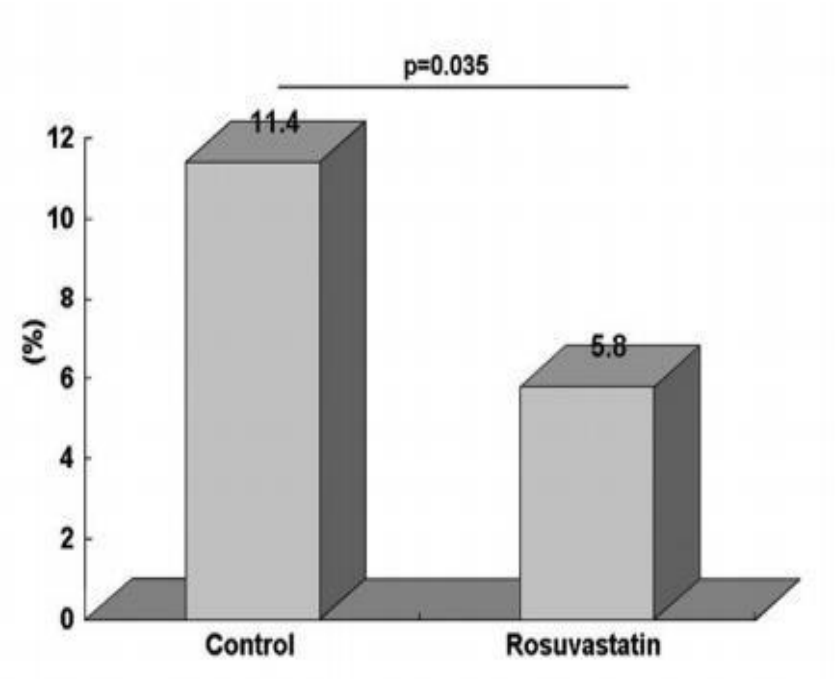


Fig. 2. Incidence of periprocedural myocardial injury, defined by post-procedural increase of creatine kinase-MB > 2 times above the upper limit of normal, in the control group and high dose rosuvastatin loading group.

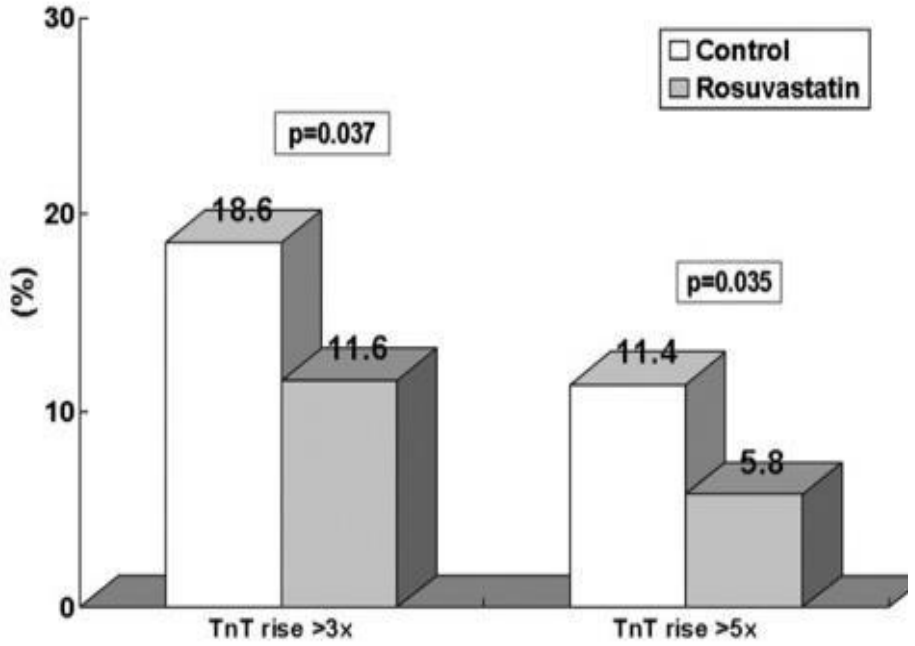
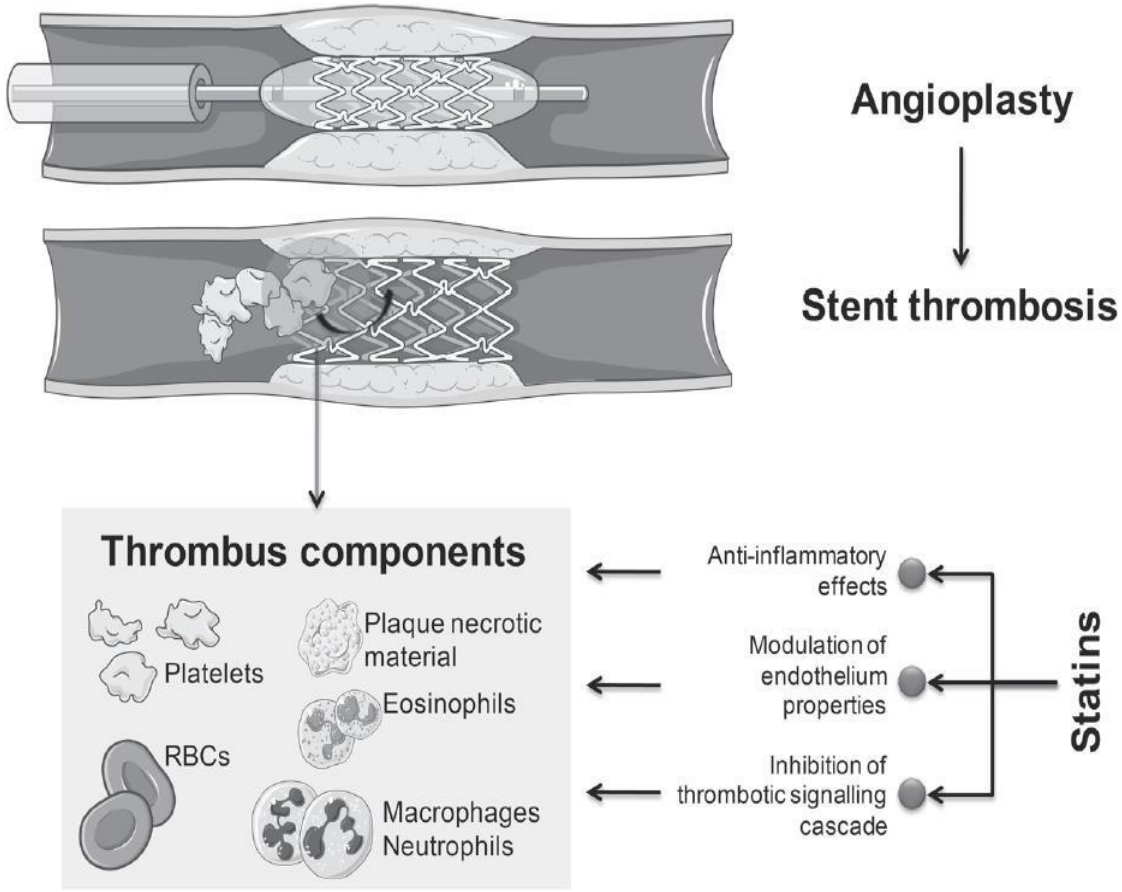


Fig. 3. Incidence of troponin T (TnT) elevation in control group a rosuvastatin loading group.

Yun KH et al. Int J Cardiol. 2009;137:246=51

Dobit od statinske terapije u PCI



Angeli F et al. Ther Advance Cardiovasc Therapeutics 2012 6(4) 163-174

Effect of a Single High Loading Dose of Rosuvastatin on Percutaneous Coronary Intervention for Acute Coronary Syndromes

Journal of Cardiovascular Pharmacology and Therapeutics
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DOI: 10.1177/1074248412474346
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Table 3. Procedural Complications.

Variable	Rosuvastatin (n = 62)	Control (n = 63)	*P* Value
Failed PCI (%)	0 (0)	0 (0)	
Slow or no flow (%)	4 (6.5)	6 (9.5)	
Distal embolization (%)	1 (1.6)	0 (0)	
Major dissection (%)	2 (3.2)	1 (1.6)	
Side branch occlusion (%)	1 (1.6)	2 (3.2)	
Any of the above (%)	8 (13.0)	9 (14.3)	.82

Abbreviation: PCI, percutaneous coronary intervention.

Table 4. The Incidence of Primary End Points at 1 Month in the 2 Groups.

Variable	Rosuvastatin (n = 62)	Control (n = 63)
Cardiac death (%)	0 (0)	0 (0)
Myocardial infarction (%)	5 (8.1)	14 (22.2)[a]
Target-vessel revascularization (%)	0 (0)	0 (0)
Total MACEs (%)	5 (8.1)	14 (22.2)[a]

Abbreviation: MACEs, major adverse cardiac events.
[a]The rate compared with the rosuvastatin group was significantly different ($P < .01$).

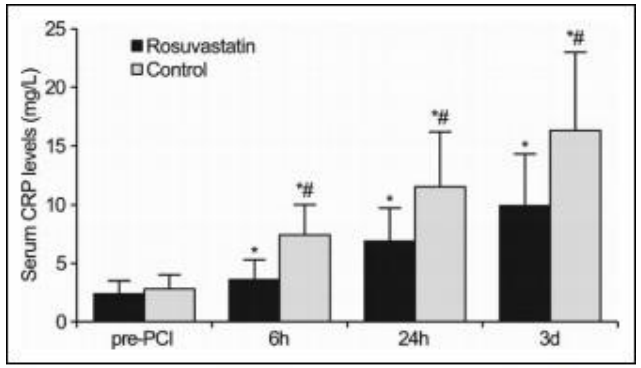


Figure 2. Changes in hs-CRP levels in the 2 groups. *$P < .01$ versus pre-PCI; #$P < .01$ versus the rosuvastatin group. hs-CRP indicates high-sensitivity C-reactive protein.

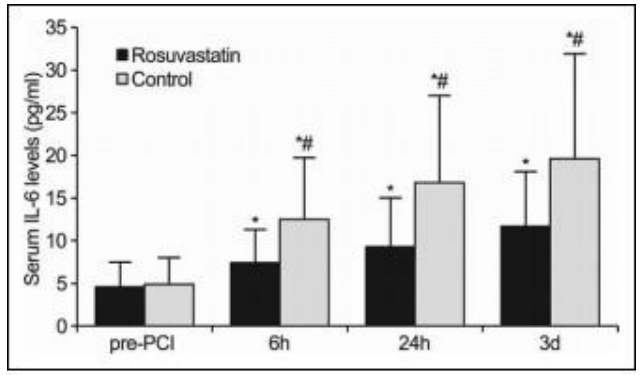


Figure 3. Changes in IL-6 levels in the 2 groups. *$P < .01$ versus pre-PCI; #$P < .01$ versus the rosuvastatin group. IL-6 indicates interleukin 6.

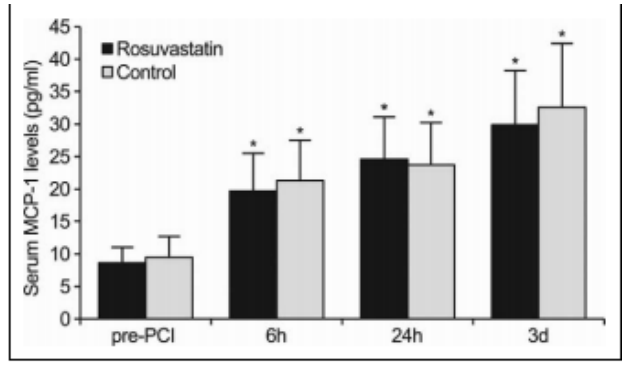


Figure 4. Changes in MCP-1 levels in the 2 groups. *$P < .01$ versus pre-PCI. No significant difference was detected between the levels in the rosuvastatin and control groups at 6 hours, 24 hours, and 3 days after PCI. MCP-1, indicates monocyte chemotactic protein; PCI, aneous coronary intervention.

Table 5. The Proportion of Patients With Cardiac Markers Elevated Above the ULN.

Variable	Pre-PCI	6 h	24 h	3 d
Elevated CK-MB in rosuvastatin group (%)	3 (4.8)	10 (16.1)[a,b]	12 (19.4)[a,b]	8 (12.9)[b]
Elevated CK-MB in control group (%)	4 (6.3)	20 (31.7)[a]	22 (34.9)[a]	19 (30.1)[a]
Elevated cTnI in rosuvastatin group (%)	9 (14.5)	19 (30.6)[a,b]	21 (33.9)[a,b]	17 (27.4)
Elevated cTnI in control group (%)	11 (17.5)	31 (49.2)[a]	33 (52.3)[a]	25 (39.7)[a]

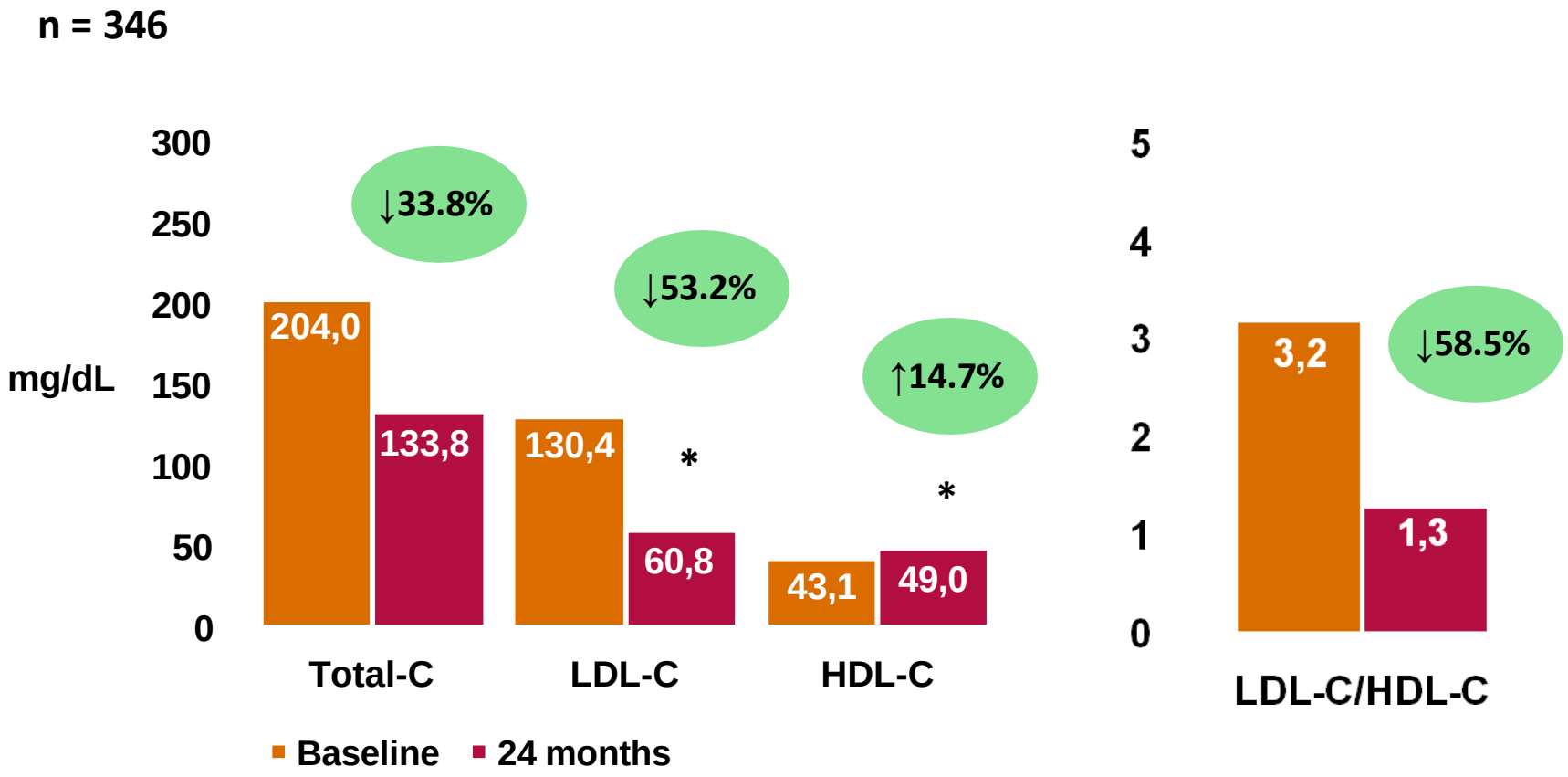
Abbreviations: CK-MB, creatine kinase MB; cTnI, cardiac troponin I; ULN, upper limit of normal.
[a]The rate compared with pre-PCI rate was significantly different ($P < .05$).
[b]The rate compared with the rate in the control group was significantly different ($P < .05$).

Nivo LDL-a i stabilnost plaka

	LDL-C <50 mg/dL (<1.3 mmol/L) (87 plaques)	LDL-C 50–70 mg/dL (1.3–1.8 mmol/L) (81 plaques)	LDL-C 70–100 mg/dL (1.8–2.6 mmol/L) (117 plaques)	LDL-C >100 mg/dL (>2.6 mmol/L) (130 plaques)	P
Plaque microstructures in lipid plaques (n=293)					
Fibrous cap thickness (µm)	139.9 ± 93.9	103.1 ± 66.4	92.5 ± 48.5	92.1 ± 47.8	0.001
Plaque rupture, n (%)	1/42 (2.3)	2/46 (4.3)	7/91 (7.6)	12/114 (10.5)	0.17
Thrombus, n (%)	0/42 (0.0)	1/46 (2.1)	2/91 (2.1)	3/114 (2.6)	0.18

Kataoka et al. Atherosclerosis 2015;242:490-495

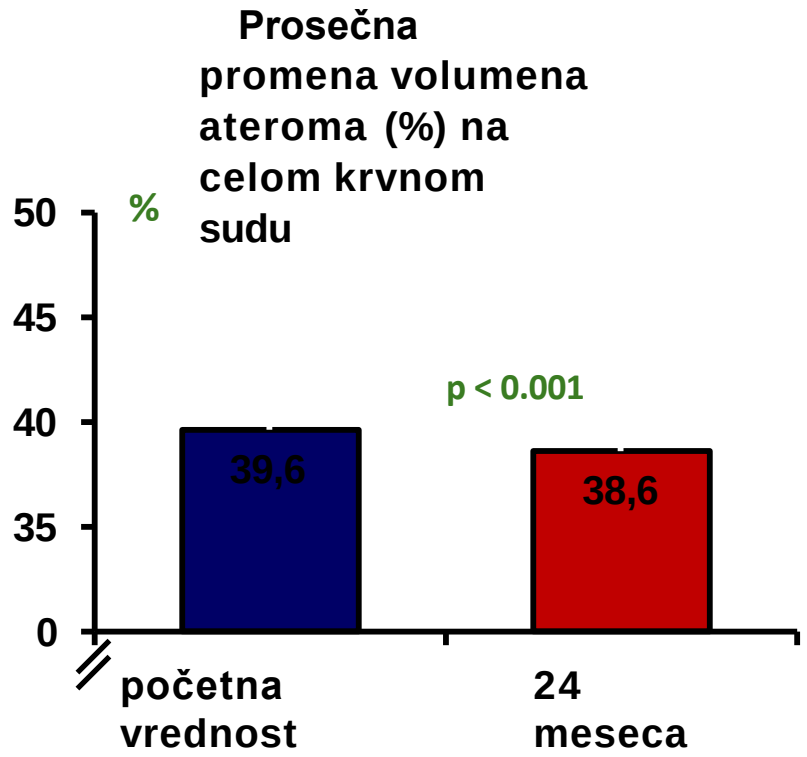
ASTEROID: efikasnost rosuvastatina u redukciji nivoa LDL

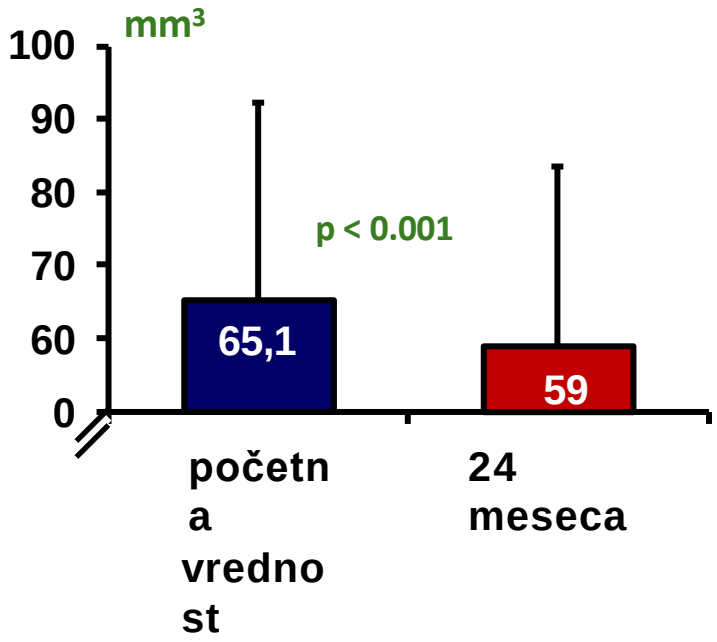


*P < 0.001 vs baseline

Nissen SE et al. JAMA. 2006;295:1556-65.

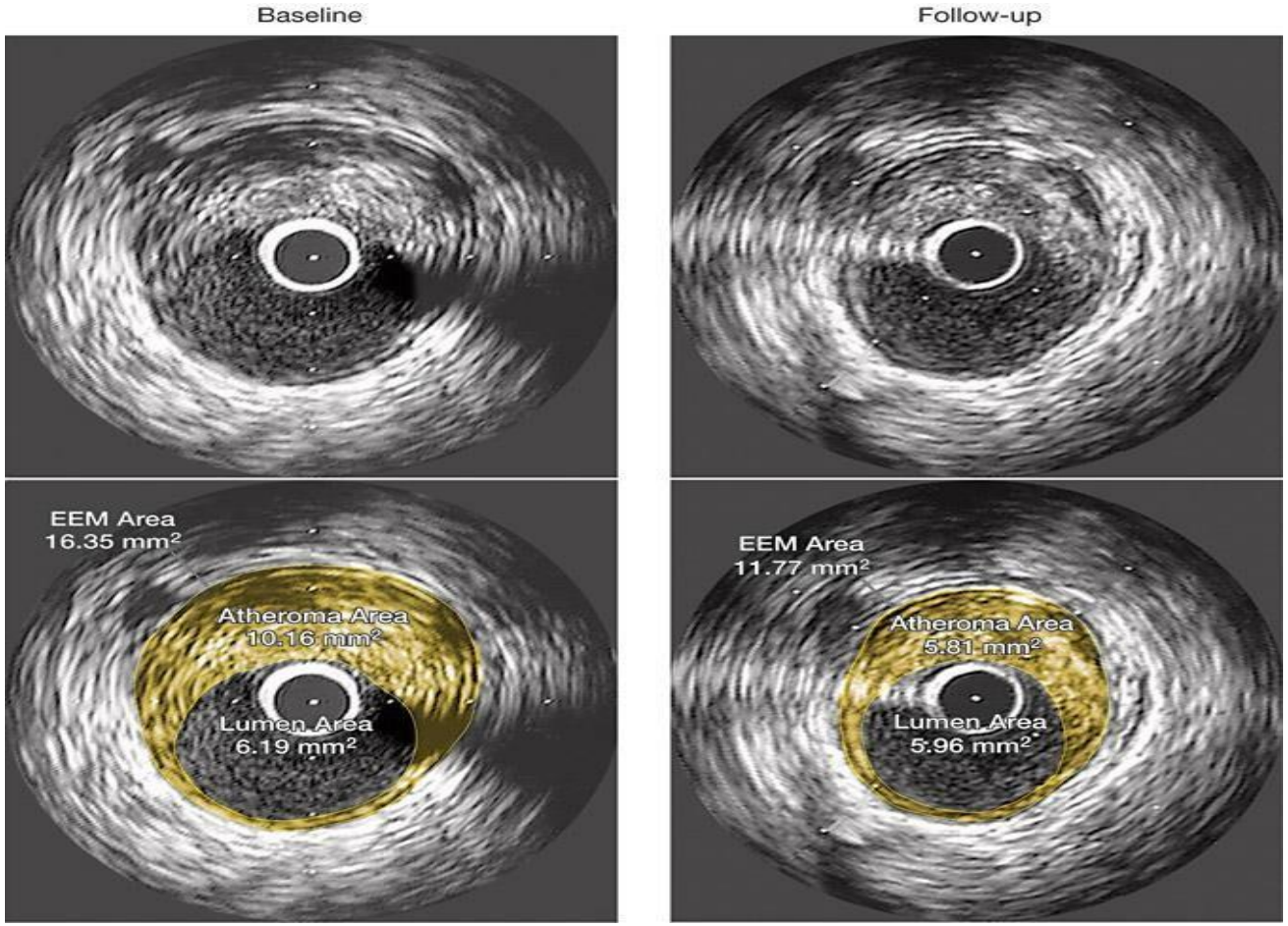
ASTEROID
Uticaj na aterosklerozu





Nissen SE et al. JAMA. 2006;295:1556-65.

Terapija rosuvastatninom usporava progresiju ateroskleroze



Donje dve slike ilustruju iste preseke sa merenjem ateroma.

Površina ateroma se smanjila sa **10.16 mm² na 5.81 mm².**

Crouse JR, Raichlen JS, et al. The METEOR Trial. JAMA 2007; 297: 1344–53.
Nissen SE, Nicholls SJ, et al. The ASTEROID Trial. JAMA 2006; 295 (13): 1556-65

Effect of Rosuvastatin on Coronary Atheroma in Stable Coronary Artery Disease

—— Multicenter Coronary Atherosclerosis Study Measuring Effects of Rosuvastatin Using Intravascular Ultrasound in Japanese Subjects (COSMOS) ——

Tadateru Takayama, MD; Takafumi Hiro, MD; Masakazu Yamagishi, MD*; Hiroyuki Daida, MD**; Atsushi Hirayama, MD; Satoshi Saito, MD†; Tetsu Yamaguchi, MD††; Masunori Matsuzaki, MD‡ for the COSMOS Investigators

Table 2. Baseline and Follow-up Laboratory Results (n=126)

	Baseline		Follow-up		% change	P value*
	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)		
Lipids (mg/dl)						
TC	213.6±34.7	210.0 (188.0, 236.0)	157.8±24.1	157.0 (142.0, 170.0)	−24.7±14.2	<0.0001
TG	147.8±85.7	128.5 (96.0, 160.0)	130.3±64.6	114.0 (85.0, 165.0)	−4.8±38.4	0.1639
HDL-C	47.1±10.8	45.0 (40.0, 53.0)	55.2±11.7	55.5 (47.0, 61.0)	19.8±22.9	<0.0001
LDL-C	140.2±31.5	138.5 (118.0, 155.0)	82.9±18.7	78.5 (70.0, 91.0)	−38.6±16.9	<0.0001
VLDL-C	25.8±16.7	23.2 (15.6, 30.6)	21.8±12.4	19.3 (13.4, 28.0)	2.9±67.5	0.6264
Non-HDL-C	166.5±33.5	163.5 (145.0, 186.0)	102.5±21.5	98.0 (88.0, 114.0)	−36.7±15.0	<0.0001
ApoA-1	123.9±22.0	121.5 (110.0, 136.0)	143.3±24.1	141.0 (130.0, 157.0)	17.0±17.5	<0.0001
ApoA-2	26.8±5.3	26.2 (23.3, 29.2)	29.0±4.1	28.8 (26.3, 31.3)	10.9±17.6	<0.0001
ApoB	115.4±23.0	113.5 (99.0, 128.0)	77.2±15.0	74.0 (68.0, 86.0)	−31.3±16.1	<0.0001
Lp(a)	30.0±34.5	19.0 (8.0, 34.0)	31.0±41.7	15.0 (6.5, 36.0)	−1.7±38.4	0.6185
sdLDL	0.36±0.04	0.36 (0.34, 0.37)	0.35±0.03	0.35 (0.33, 0.36)	−2.4±11.0	0.003
ApoB/A-I ratio	0.96±0.28	0.92 (0.77, 1.12)	0.55±0.13	0.53 (0.47, 0.61)	−40.2±16.0	<0.0001
Non-HDL-C/HDL-C ratio	3.72±1.14	3.57 (2.93, 4.37)	1.94±0.57	1.84 (1.54, 2.15)	−47.33±15.82	<0.0001
LDL-C/HDL-C ratio	3.12±0.95	3.03 (2.46, 3.66)	1.56±0.45	1.47 (1.27, 1.78)	−47.54±15.09	<0.0001
HbA_{1c} (%)†	5.92±0.98	5.60 (5.30, 6.50)	6.25±1.00	6.00 (5.50, 7.00)	1.15±9.94	0.3205
hs-CRP (ng/ml)	3,362±7,823	911 (353, 3,210)	933±1,549	484 (260, 995)	18.1±291.3	0.4868

	Baseline		Follow-up		Percent change (%)		95%CI	P value*
	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)	Mean±SD	Median (IQR)		
Volume, mm^3								
Plaque	72.1±38.1	63.2 (41.9, 101.4)	66.8±34.0	60.3 (40.7, 91.5)	−5.1±14.1	−6.5 (−15.5, 4.5)	−7.6, −2.6	<0.0001
Lumen	78.3±40.2	69.9 (47.4, 105.8)	81.6±39.3	73.5 (52.9, 110.4)	7.3±15.6	5.9 (−1.7, 16.2)	4.5, 10.0	<0.0001
Vessel	150.4±72.4	136.0 (93.4, 204.4)	148.5±67.4	133.0 (98.9, 207.6)	0.8±11.7	−1.0 (−7.3, 8.6)	−1.3, 2.8	0.4673
Area, mm^2								
Plaque	8.9±3.6	8.8 (6.4, 10.8)	6.9±3.1	6.8 (4.6, 8.6)	−21.9±20.0	−23.4 (−34.2, −8.3)	−25.4, −18.3	<0.0001
Lumen	6.1±2.7	5.8 (3.7, 7.8)	7.1±3.1	6.5 (4.7, 9.1)	20.7±28.5	17.8 (0.8, 35.5)	15.7, 25.7	<0.0001
Vessel	15.0±5.4	14.7 (12.0, 18.3)	14.0±5.1	14.3 (10.1, 17.0)	−5.8±14.6	−6.4 (−15.4, 2.5)	−8.4, −3.3	<0.0001

Circ J 2009; 73: 2110–2117

Effect of Rosuvastatin on Coronary Atheroma in Stable Coronary Artery Disease

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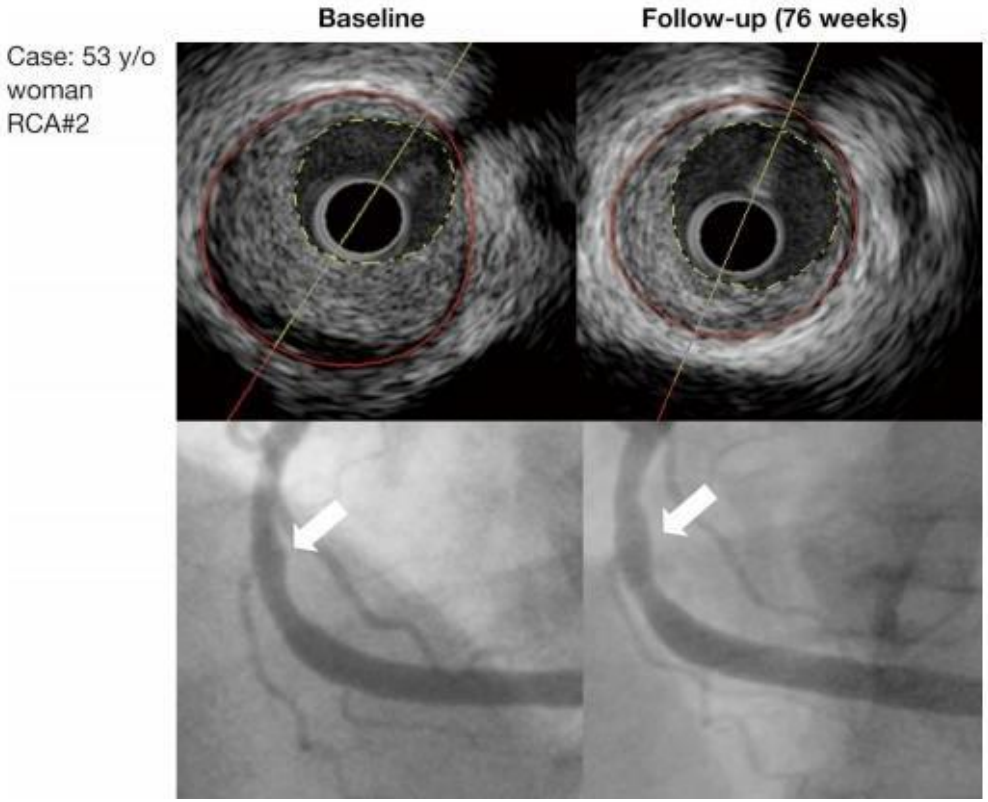
Tadateru Takayama, MD; Takafumi Hiro, MD; Masakazu Yamagishi, MD*; Hiroyuki Daida, MD**; Atsushi Hirayama, MD; Satoshi Saito, MD†; Tetsu Yamaguchi, MD††; Masunori Matsuzaki, MD‡ for the COSMOS Investigators



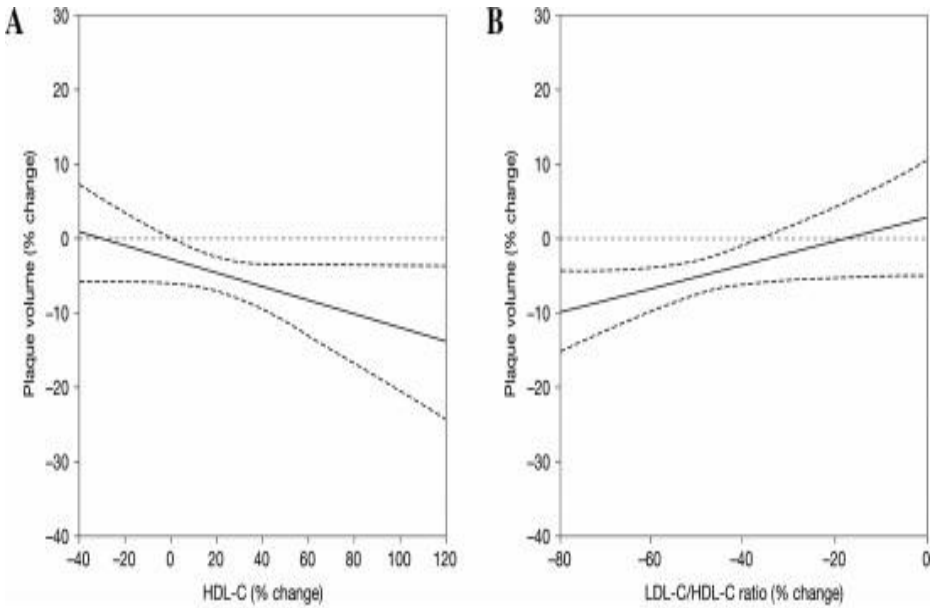


Figure 3. Correlation between change in (**A**) HDL-C and (**B**) LDL-C/HDL-C ratio and change of plaque volume. Relationship between change in HDL-C level or LDL-C/HDL-C ratio and change in plaque volume (Solid line). Upper and lower limits for 95% confidence interval of mean values (Dotted lines). HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

Circ J 2009; 73: 2110–2117

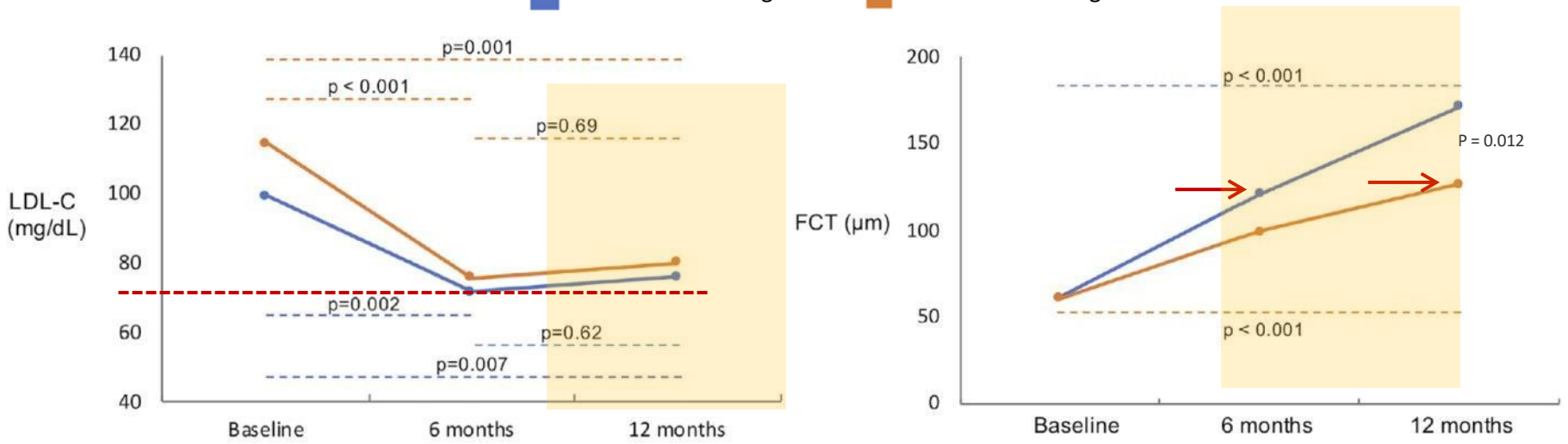
Nastavak stabilizacije plaka i nakon 6 meseci, u odsustvu sniženja vrednosti LDL-C

brža stabilizacija plaka i regresija volumena plaka sa rosuvastatinom u odnosu na atorvastatin

Posle 6 meseci nastavila se stabilizacija plaka, i u odsustvu sniženja LDL-C

43 Asian patients with de novo CAD undergoing PCI

Rosuvastatin 10mg vs Atorvastatin 20mg



FCT – fibrous cap thickness

Thondapu V et al. *Am J Cardiol*. 2019;123:1565-1571

Early High-Dose Rosuvastatin for Contrast-Induced Nephropathy Prevention in Acute Coronary Syndrome

Results From the PRATO-ACS Study (Protective Effect of Rosuvastatin and Antiplatelet Therapy On Contrast-Induced Acute Kidney Injury and Myocardial Damage in Patients With Acute Coronary Syndrome)

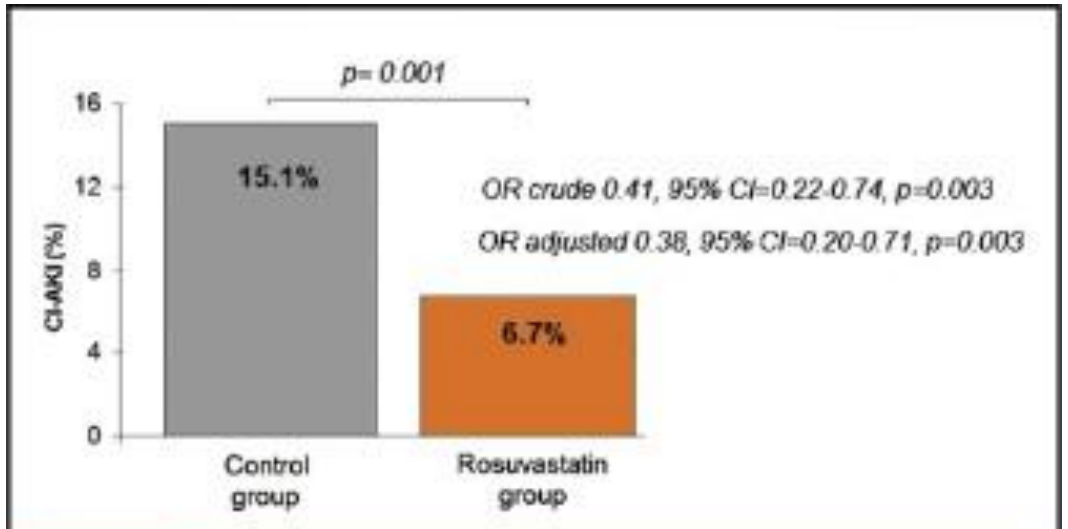


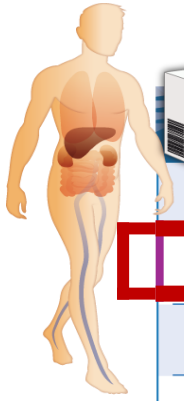
Figure 2 Incidence of Contrast-Induced Acute Renal Injury

Table 2 Cumulative Incidence of Primary and Additional Endpoints by Treatment Group*

Endpoint	Statin	Control	ORc (95% CI)	p Value	ORadj (95% CI)	p Value
Primary CI-AKI endpoint						
Creatinine >0.5 mg/dl or >25% within 72 h	17 (6.7)	38 (15.1)	0.41 (0.22–0.74)	0.003	0.38 (0.20–0.71)	0.003
Additional endpoints (different CI-AKI criteria)						
Creatinine >0.5 mg/dl or >25% within 48 h	16 (6.3)	30 (11.9)	0.50 (0.27–0.95)	0.033	0.48 (0.25–0.91)	0.025
Creatinine >0.3 mg/dl within 48 h	9 (3.6)	22 (8.7)	0.39 (0.17–0.86)	0.02	0.35 (0.15–0.83)	0.017
Creatinine >0.3 mg/dl within 72 h	11 (4.4)	27 (10.7)	0.38 (0.18–0.78)	0.009	0.36 (0.17–0.77)	0.009
Creatinine >0.5 mg/dl within 72 h	6 (2.4)	15 (5.9)	0.38 (0.15–1.01)	0.052	0.43 (0.15–1.23)	0.115
eGFR <25% within 72 h	14 (5.6)	29 (11.5)	0.45 (0.24–0.86)	0.015	0.44 (0.23–0.86)	0.016

Am Coll Cardiol 2014;63:71–9

Hidrofilnost rosuvastatina ga čini drugačijim statinom



	Solubility	Optimal time of dosing	Bioavailability	Effect of food on bioavailability	Elimination half-life	CYP450 metabolism
Atorvastatin	Lipophilic	Any time of day	12%	↘	11- 30 h	✓ (3A4)
Rosuvastatin	Hydrophilic	Any time of day	20%	No effect	20 h	Limited
Fluvastatin	Lipophilic	Bedtime	24%	↘	2.5 - 3 h	✓ (2C9)
Lovastatin	Lipophilic	With meals morning and evening	5%	↗	0.5 - 2.3 h	✓ (3A4)
Pravastatin	Hydrophilic	Bedtime	18%	↘	0.8 - 3 h	X
Simvastatin	Lipophilic	Evening	5%	No effect	1.9 - 3 h	✓ (3A4)

Rastvorljivi u mastima

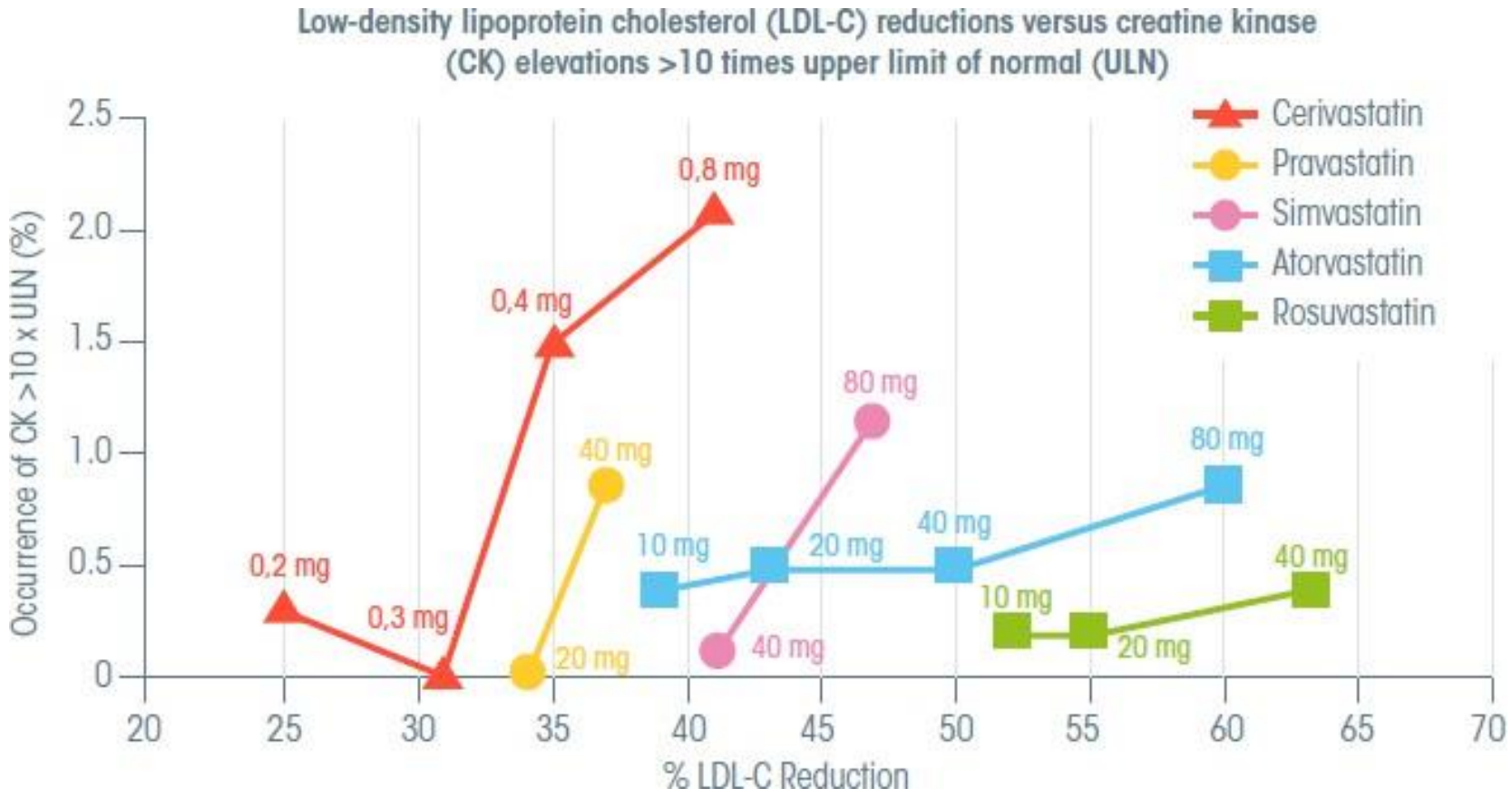
Metabolizam u jetri
preko citohroma P450 (CYP450)

Rastvorljivi u vodi

Ne metabolišu se
preko citohroma P450 (CYP450)
-manje neželjenih reakcija
-manje interakcija sa drugim lekovima

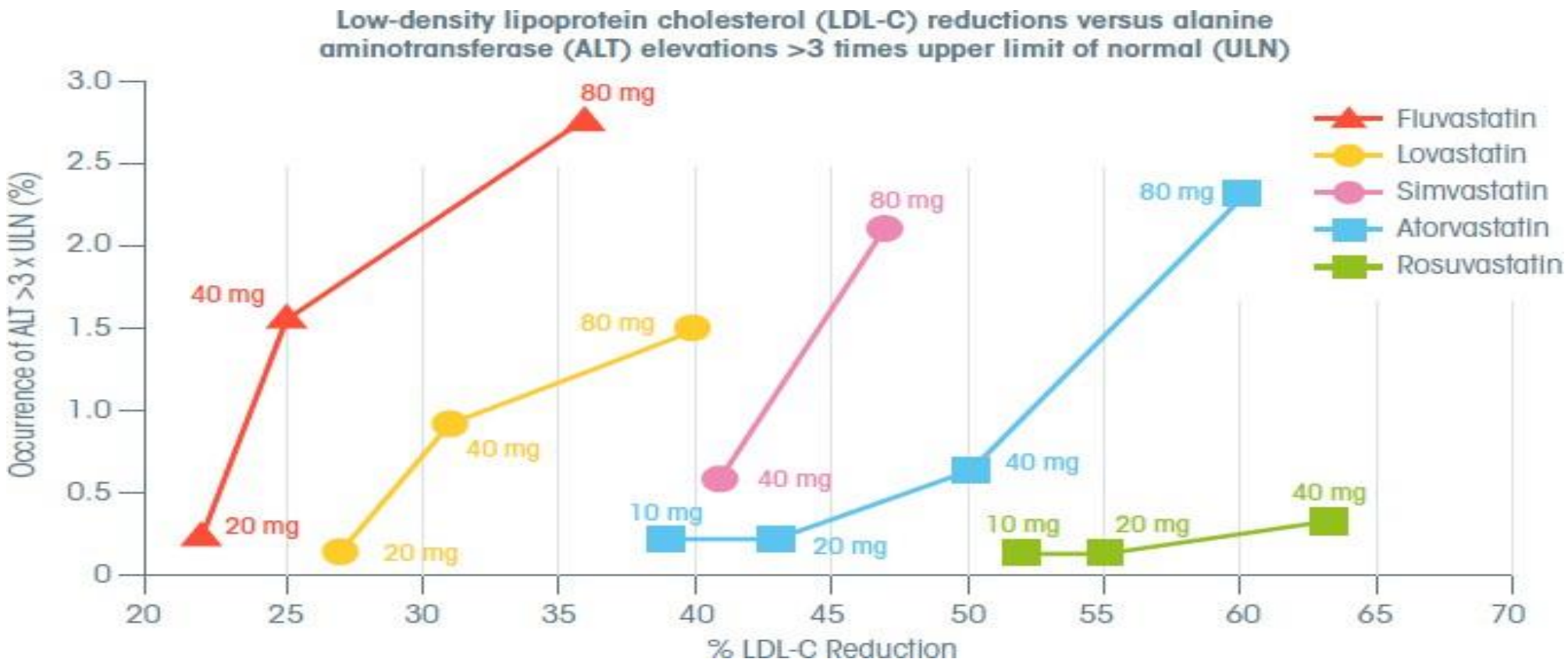
White CM. J Clin Pharmacol. 2002 Sep;42(9):963-70.

Bezbednosni profil rosuvastatina -dejstvo na mišiće-



Adapted from Brewer HB Jr. Benefit-risk assessment of Rosuvastatin 10 to 40 milligrams. *Am J Cardiol*. 2003;92(4B):23K-29K.

Bezbednosni profil rosuvastatina -dejstvo na jetru-



Adapted from Brewer HB Jr. Benefit-risk assessment of Rosuvastatin 10 to 40 milligrams. *Am J Cardiol*. 2003;92(4B):23K-29K.

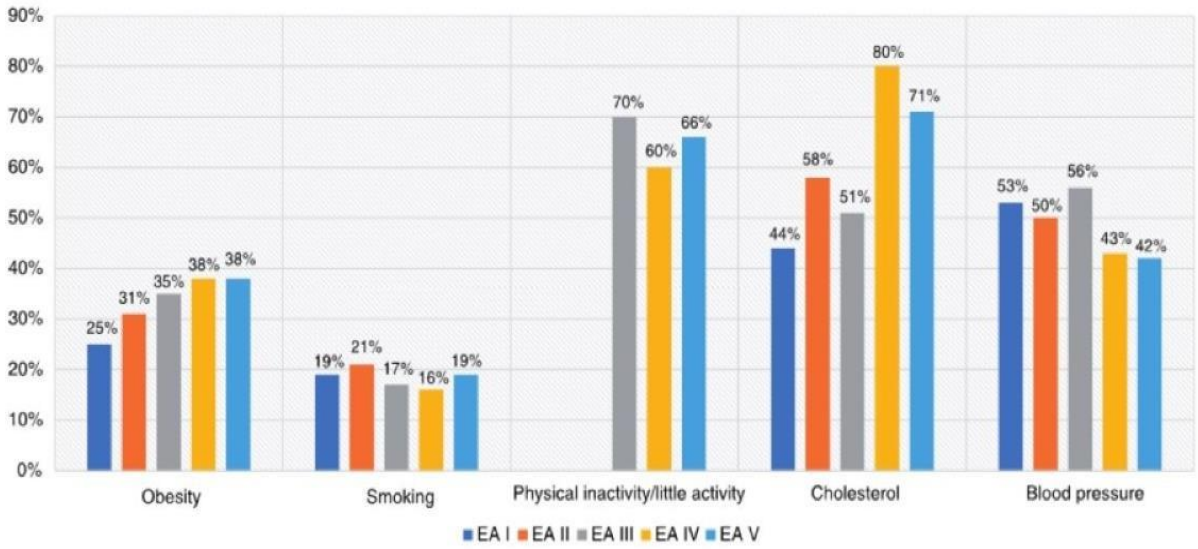
Sve je jasno….

Ali….

EUROASPIRE - slika KV prevencije u Evropi

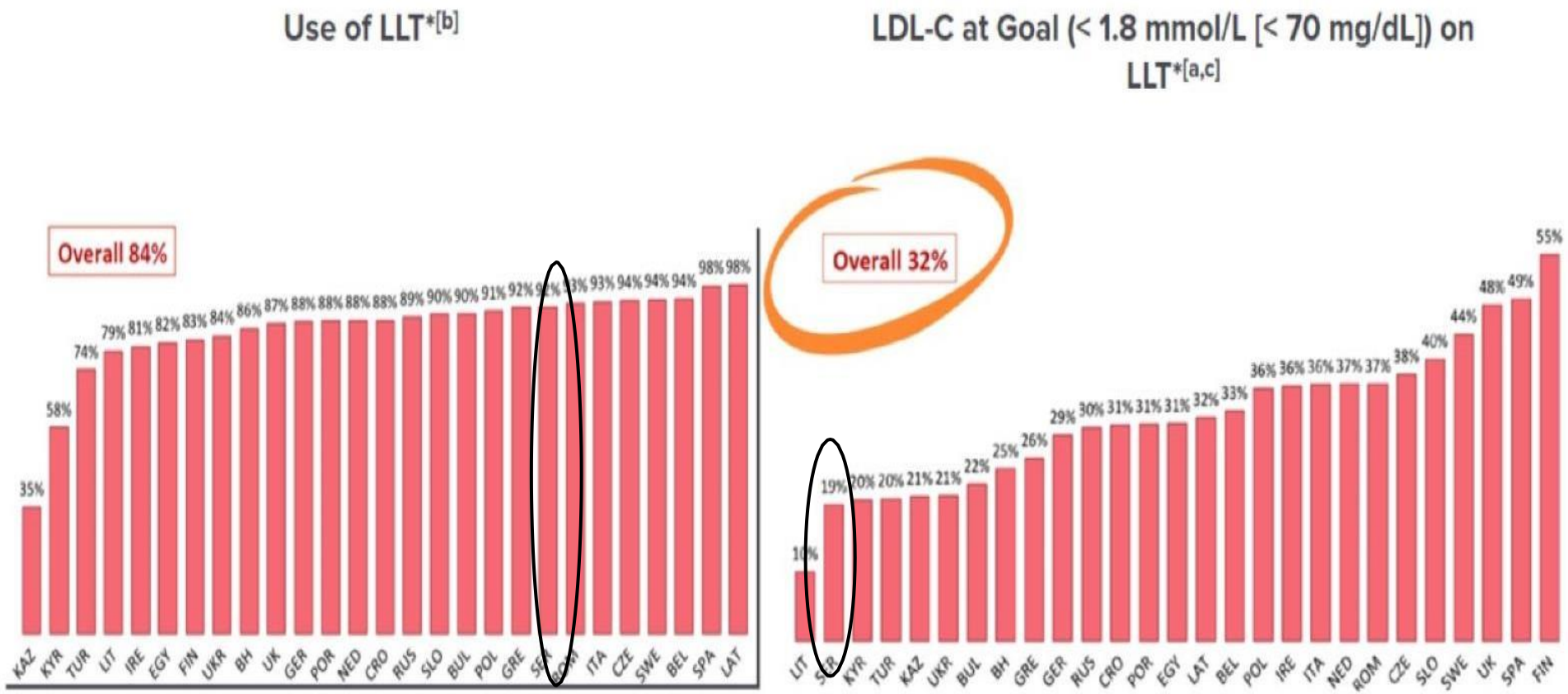
- Prvi ESC/EAS/ESH vodič objavljen 1994.
- EUROASPIRE planirana da prati preventivne mere u Evropi započeta 1995.
- Pregled demonstrira visoku prevalencu korektibilnih faktora rizika kod pacijenata sa KVB u 9 zemalja Evrope

30 god evolucije kontrole faktora za ASKVB



Eur Heart J 1997;18:1569-1582, Eur J prev Cardiol 2019;26:820-823

EUROASPIRE V – LDL-c



Eur J Prev Cardiol 2019;26:824-835

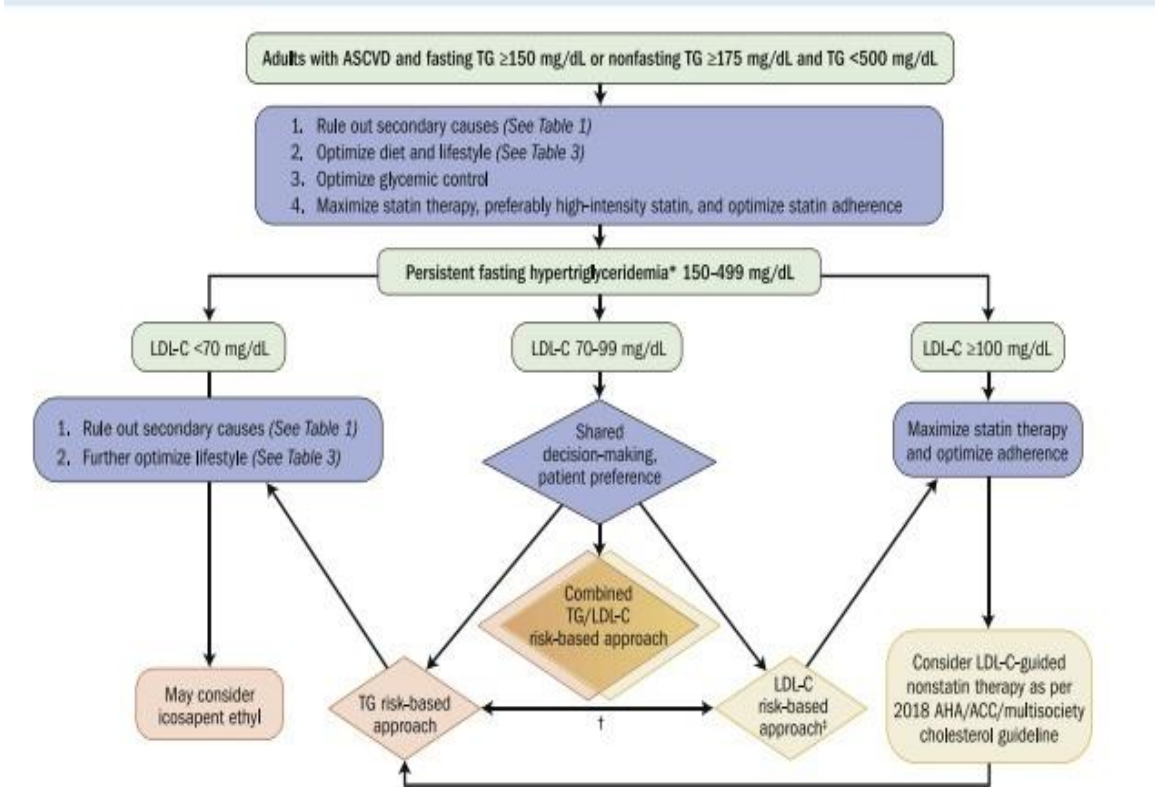
Osnovni postulati lečenja

Nema odlaganja lečenja kod otkrivene dislipidemije

Potrebno je propisati intenzivnu statinsku terapiju u dozi do postizanja ciljne vrednosti ili primeniti kombinovanu terapiju

Potrebno je lečiti i hipertrigliceridemiju

Hipertrigliceridemija kod pacijenata sa ASKVB



Varini et al. JACC 2021;78:960-993

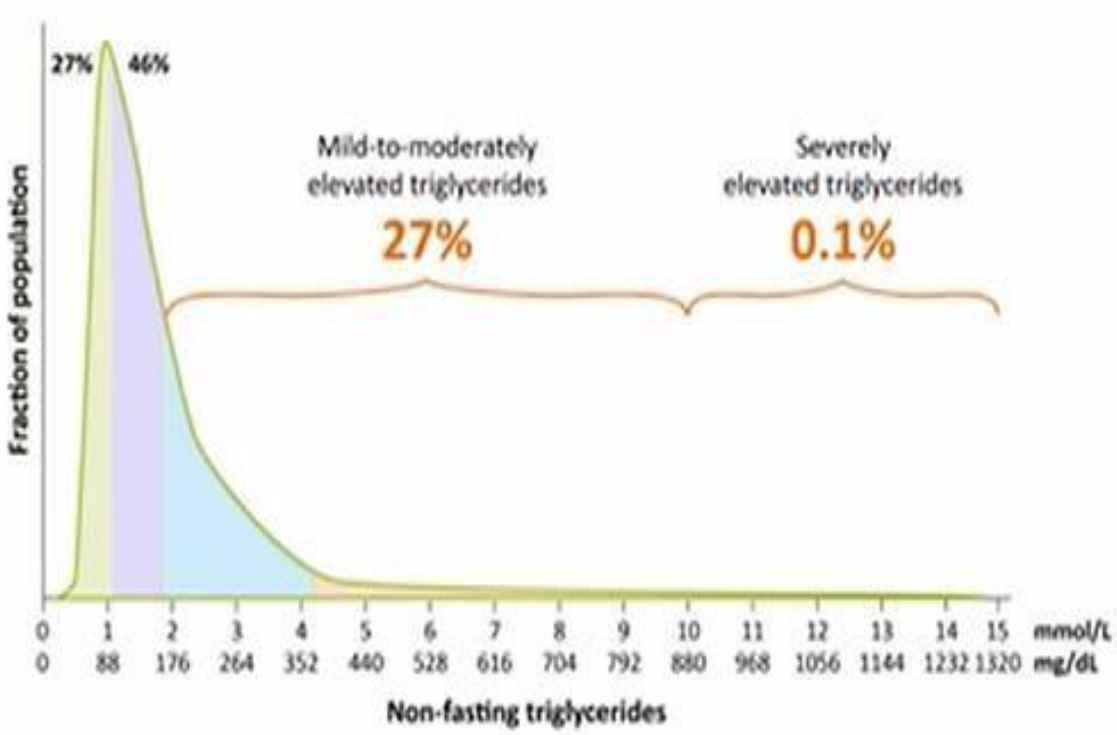
HTG
1. High risk with ↑ TG: Statin - first choice[a,b]
2. High risk or on statins with ↑ TG: consider n-3 PUFAs (icosapent ethyl 2 × 2 g/day) with statins[b]
3. High risk, at LDL-C goal, ↑ TG: consider fenofibrate or bezafibrate with statins[b]
4. Primary prevention, at LDL-C goal, ↑ TG: consider fenofibrate or bezafibrate with statins[b]

Mach F et al.Eur Hert J 2020;41:111-188

Epidemiologija hipertrigliceridemije

- Prevalenca u odrasloj populaciji je 10%
- Poslednjih decenija prevalenca blage do umerene hipertrigliceridemije koja je povezana sa gojaznošću i dijabetes melitusom je u porastu
- Teška hipertrigliceridemija koju definišemo kao povećanje TG>10mmol/l je retka sa prevalencom 0.10 to 0.20%
- Za vrlo tešku hipertrigliceridemiju je karakteristično povećanje nivoa TG> >20mmol/L (>1770mg/dL) a ona je sasvim retka sa prevalencom 0, 014%

Copenhagen General Population Study



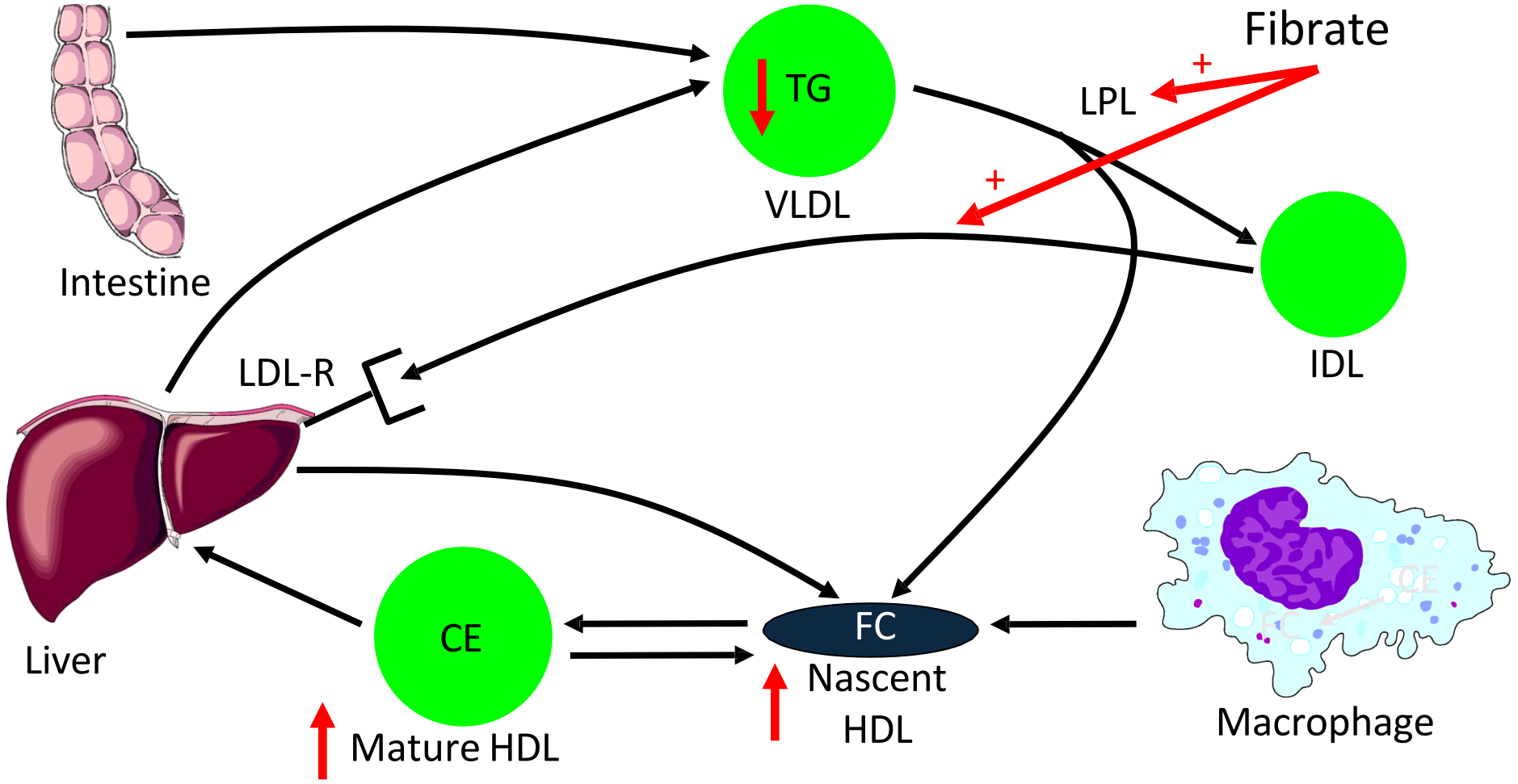
Nordestgard BG Cir Res 2016;118(4):547-63

Hipertrigliceridemija i ateroskleroza

- Trigliceridi ne indukuju aterosklerozu direktno
- Trigliceridi bivaju transportovani u lipoproteinima zajedno sa holesterolom, drugim lipidima, apoB i drugim apoproteinima
- Trigliceridima bogati lipoproteini ulaze u arterijski zid i indukuju aterosklerozu holesterolom, apoproteinima i drugim komponentama
- Trigliceridima bogati lipoproteini indukuju promene u LDL-u i metabolizmu HDL-a odnosno umanjuju protektivnu ulogu HDL a povećavaju oksidaciju LDL

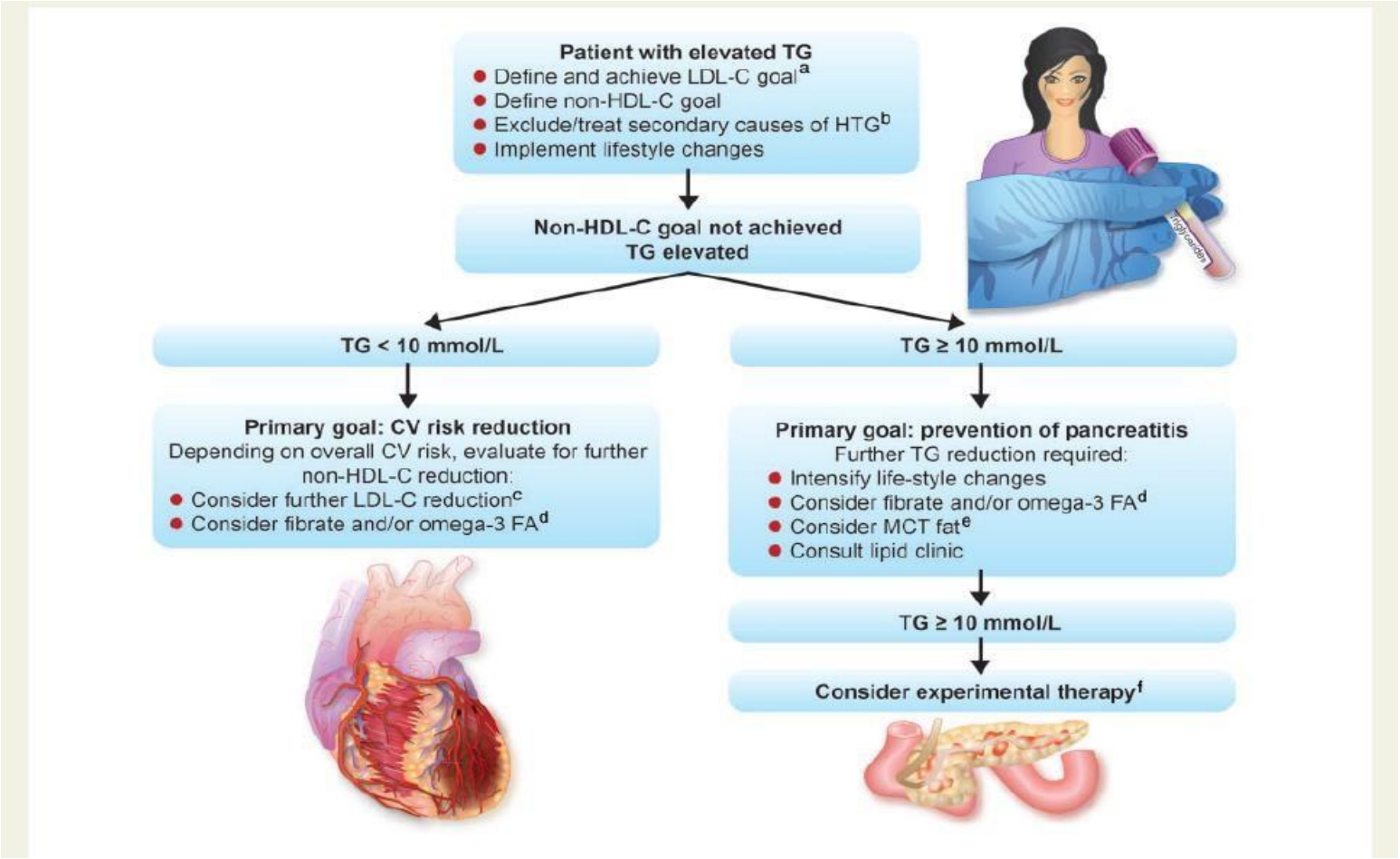
Am J Cardiol 2020;132:36−43
Lancet 2014; 384: 626–635

Fibrati – mehanizam delovanja



CE=Cholesterol ester, FC=Free cholesterol, HDL=High density lipoprotein, IDL=Intermediate density lipoprotein, LDL-R=Low density lipoprotein receptor, LPL=Lipoprotein lipase, TG=Triglyceride, VLDL=Very low density lipoprotein

Algoritam lečenja



European Heart Journal (2020) 41, 99–109

Kombinacija statina i fibrata

- Opravdanost – komplementarni metabolički efekat fibrata i statina
- Efikasnost kod primene statina i fibrata

✓Redukcija LDL-a za>40% TG>50%

✓Povećanje HDL >20%

- Posebno indikovana kod kombinovane hiperlipidemije i dijabetes melitusa tip 2 i metaboličkg sindroma

Farnier Am J Cardiovasc Drugs 2003;3:169