Dyslipidemia and Rosuvastatin

- An Insight

Introduction

- CVD represents a considerable economic burden to society, and this necessitates an effective approach to CVD prevention.

- More than half of the reduction in CV mortality in the last three decades has been attributed to:

  - population-level changes in CV risk factors
  - reductions in cholesterol, blood pressure levels and smoking

Carter HE et al. Open Heart. 2019 Feb 16;6(1):e000939
2016 ESC/EAS Guidelines Catapano AL et al. Atherosclerosis. 2016 Sep 1. pii: S0021-9150(16)31267-9

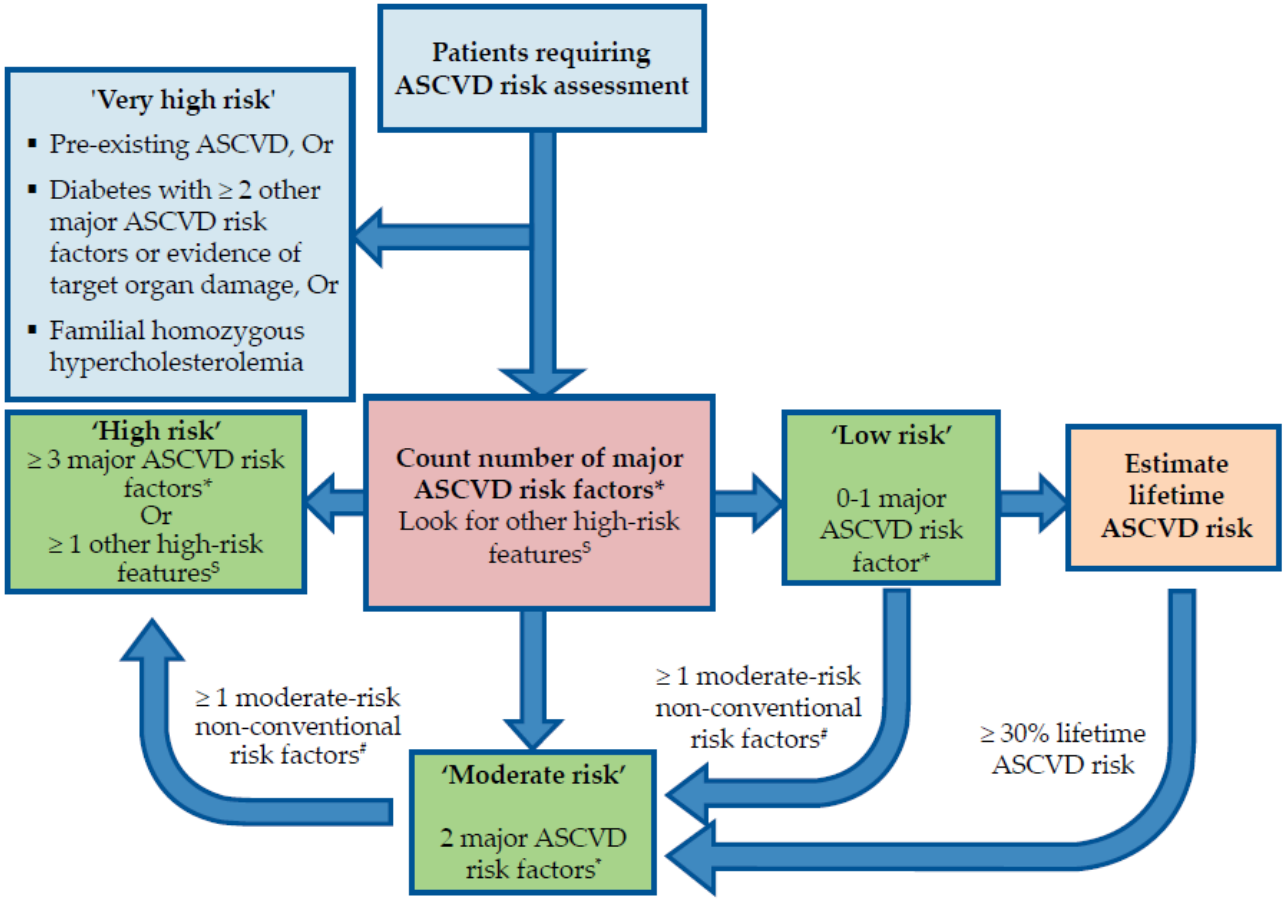
ASCVD risk categories

Risk category	Conventional risk markers	Non-conventional risk markers (optional)
Very high risk	• Pre-existing ASCVD • Diabetes with- - evidence of end organ damage - ≥2 other major ASCVD risk factors • Familial homozygous hypercholesterolemia	• None
High risk: (>15% risk of ASCVD death, MI or stroke over a period of 10 years)	• ≥3 major ASCVD risk factors.* • Diabetes with 0-1 other major ASCVD risk factors and no evidence of end organ damage • CKD stage 3B or 4 • Familial hypercholesterolemia (other than familial homozygous hypercholesterolemia) • Extreme of a single risk factor - e.g. LDL-C >190 mg/dL, strong family history of premature ASCVD, heavy smoker	• CAC score ≥300 Agatston units • Non-stenotic carotid plaque • Lp(a) ≥50 mg/dL
Moderate risk: (5-15% risk of ASCVD death, MI or stroke over a period of 10 years)	• 2 major ASCVD risk factors.*	• CAC score 100-299 Agatston units • Increased carotid intima media thickness (CIMT) or aortic pulse wave velocity (PWV) • Lp(a) 20-49 mg/dL • Metabolic syndrome
Low risk*: (<5% risk of ASCVD death, MI or stroke over a period of 10 years)	0-1 major ASCVD risk factors	None

*Estimation of lifetime ASCVD risk should be performed in these individuals and if the estimated risk is ≥30%, the person should be categorized as being at 'moderate risk'.

Iyengar SS et al. J Clin Prev Cardiol 2016;5:51-61

Atherosclerotic cardio vascular disease (ASCVD)



***Major ASCVD risk factors**

1. Age ≥ 45 years in males and ≥ 55 years in females
2. Family history of premature ASCVD
3. Current cigarette smoking or tobacco use
4. High blood pressure
5. Low HDL-C

§Other high-risk features

1. Diabetes with 0-1 other major ASCVD risk factors and no evidence of target organ damage
2. CKD stage 3B or 4
3. Familial hypercholesterolemia (other than familial homozygous hypercholesterolemia)
4. Extreme of single risk factor
5. Coronary calcium score ≥ 300
6. Non-stenotic carotid plaque
7. Lipoprotein (a) ≥ 50 mg/dL

#Moderate-risk non-conventional risk factors

1. Coronary calcium score 100-299
2. Increased carotid IMT or aortic pulse wave velocity
3. Lipoprotein (a) 20-49 mg/dL
4. Metabolic syndrome

Iyengar SS et al. J Clin Prev Cardiol 2016;5:51-61

Treatment goals and statin initiation thresholds according to ASCVD risk categories

Risk category	Treatment goal		Consider drug therapy	
	LDL-C (mg/dL)	Non-HDL-C (mg/dL)	LDL-C (mg/dL)	Non-HDL- C (mg/dL)
Very high risk	< 50	< 80	≥ 50 (preferably in all)	≥ 80 (preferably in all)
Highrisk	< 70	< 100	≥ 70 (preferably in all)	≥ 100 (preferably in all)
Moderate risk	<100	<130	≥ 100	≥ 130
Low risk	<100	<130	≥ 130*	≥ 160*

*After an initial adequate non-pharmacological intervention for at least 3 months

Iyengar SS et al. J Clin Prev Cardiol 2016;5:51-61

Relationship Between Changes in **LDL-C** and **HDL-C** Levels and CHD Risk

1% decrease in LDL-C reduces CHD risk by 1%

1% increase in HDL-C reduces CHD risk by 3%

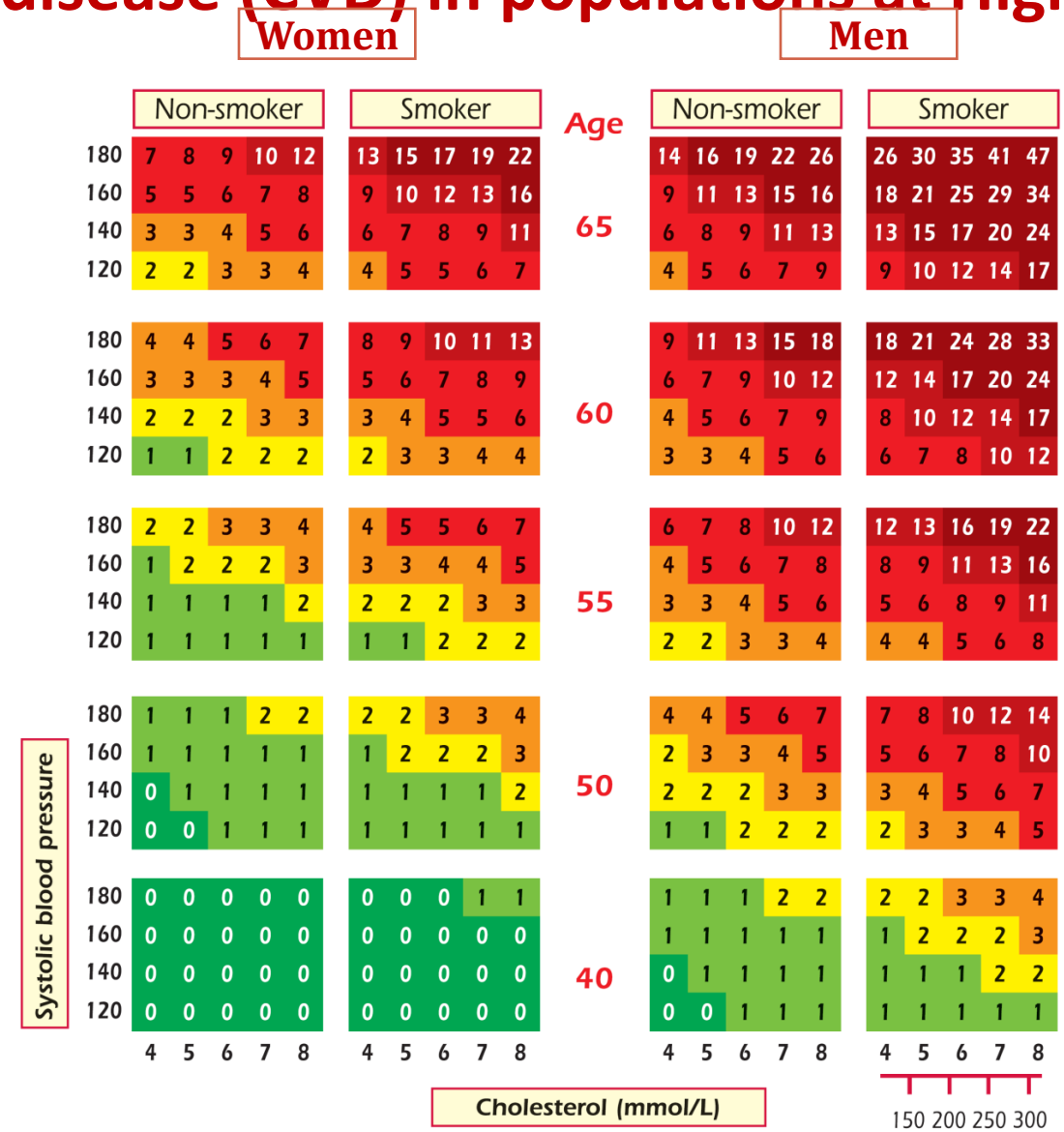
Third Report of the NCEP Expert Panel. NIH Publication No. 01-3670 2001.
http://hin.nhlbi.nih.gov/ncep_slds/menu.htm

Relative risk for acute MI in different ethnic groups, various lipid measures -INTERHEART study

	South Asians	European	Chinese	Latin American	Overall
Total cholesterol	1.23 (1.14-1.31)	1.08 (1.02-1.15)	1.16 (1.09-1.23)	1.05 (0.97-1.14)	1.16 (1.13-1.19)
HDL-C	0.97 (0.90-1.05)	0.78 (0.73-0.83)	0.83 (0.78-0.88)	1.03 (0.94-1.13)	0.85 (0.83-0.88)
Non-HDL-C	1.23 (1.15-1.31)	1.17 (1.10-1.24)	1.24 (1.18-1.31)	1.04 (0.96-1.28)	1.21 (1.17-1.24)
Apo A-I	0.72 (0.66-0.78)	0.70 (0.66-0.75)	0.67 (0.63-0.71)	0.67 (0.61-0.74)	0.67 (0.65-0.70)
Apo B	1.38 (1.29-1.48)	1.24 (1.16-1.32)	1.28 (1.20-1.36)	1.18 (1.09-1.28)	1.32 (1.28-1.36)
Total cholesterol: HDL-C ratio	1.10 (1.04-1.17)	1.31 (1.21-1.42)	1.34 (1.24-1.45)	0.97 (0.90-1.05)	1.17 (1.13-1.20)
Apo B: Apo A-Iratio	1.53 (1.42-1.64)	1.47 (1.37-1.59)	1.77 (1.63-1.92)	1.27 (1.17-1.38)	1.59 (1.52-1.64)

Iyengar SS et al. J Clin Prev Cardiol 2016;5:51-61

SCORE chart: 10 year risk of fatal cardiovascular disease (CVD) in populations at High CVD risk

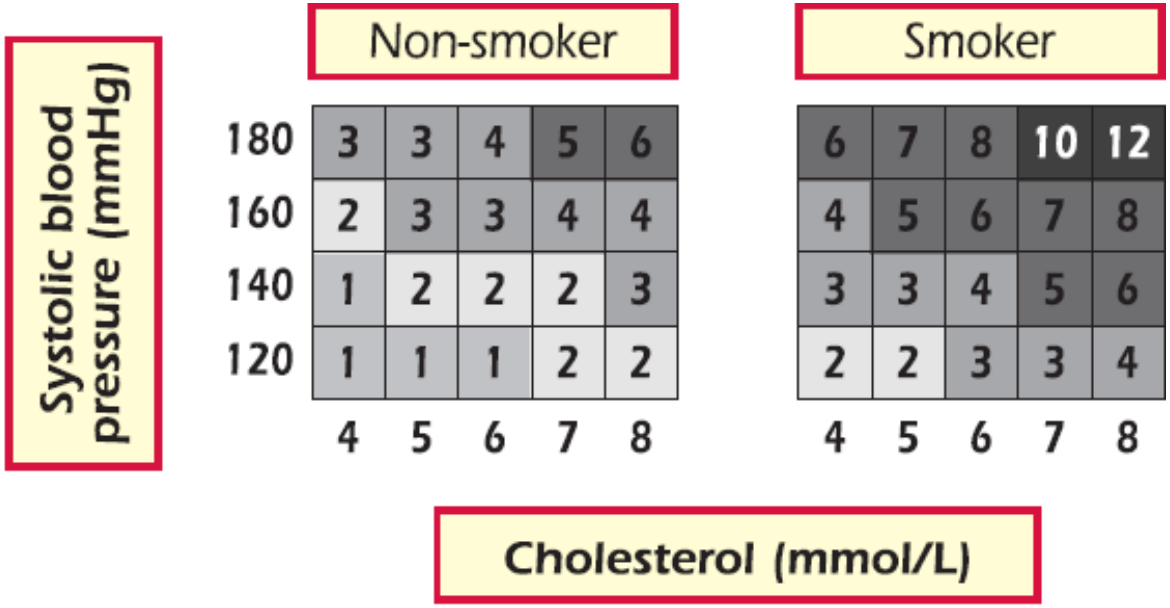


2016 ESC/EAS Guidelines Catapano AL et al. Atherosclerosis. 2016 Sep 1. pii: S0021-9150(16)31267-9

Relative risk chart

Chart may be used to show younger people at low absolute risk that, relative to others in their age group, their risk may be many times higher than necessary.

Help to motivate decisions about avoidance of smoking, healthy nutrition and exercise, as well as flagging those who may become candidates for medication



Please note that this chart shows RELATIVE not absolute risk. Risks are RELATIVE to 1 in the bottom left. Thus a person in the top right hand box has a risk that is 12 times higher than a person in the bottom left.

Levels of Risk Associated with Smoking, Hypertension and Hypercholesterolaemia

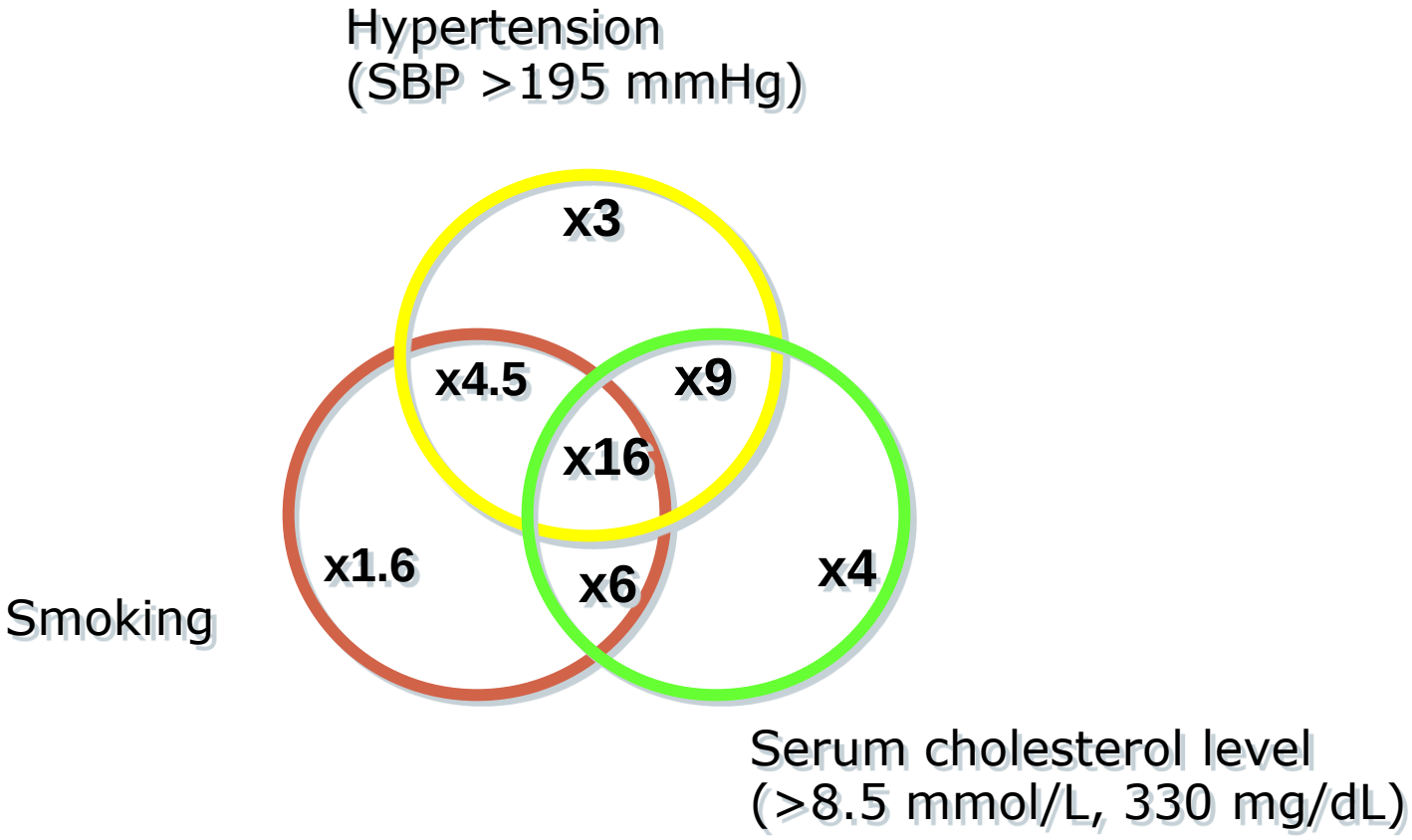


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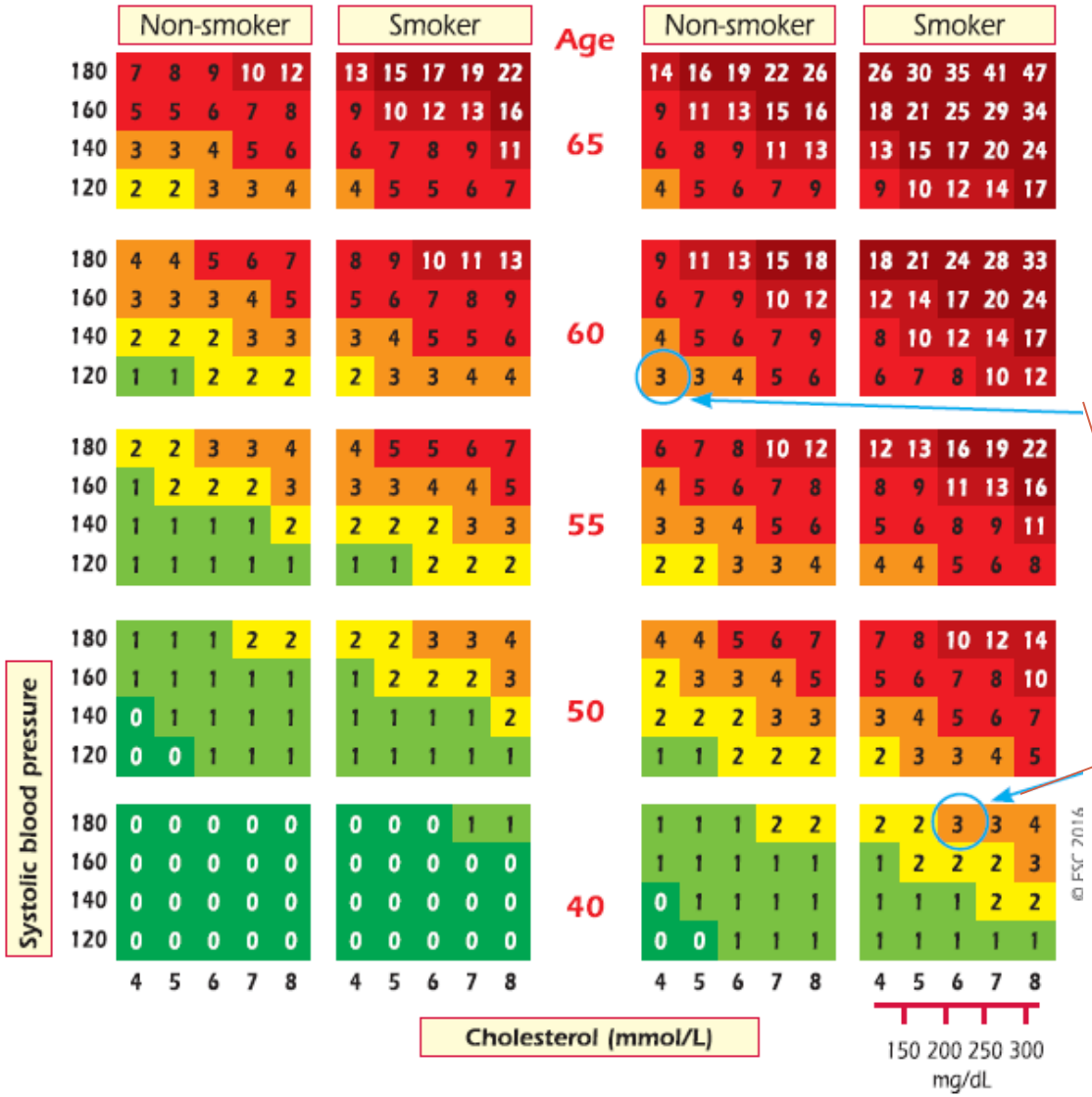
Illustration of the risk age concept.



SCORE

- 15% and over
- 10%-14%
- 5%-9%
- 3%-4%
- 2%
- 1%
- < 1%

10-year risk of fatal CVD in populations at **High CVD risk**

The risk of this 40 yr old male smoker with risk factors is same (3%) as that of a 60- yr old man with ideal risk factor levels

There fore, HIS RISK AGE IS 60 years

2016 ESC/EAS Guidelines Catapano AL et al. Atherosclerosis. 2016 Sep 1. pii: S0021-9150(16)31267-9

Factors modifying SCORE risks

- Social deprivation –the origin of many of the causes of CVD.
- Obesity and central obesity
- Physical inactivity.
- Psychosocial stress including vital exhaustion.
- Family history of premature CVD (men: <55 y; women:<60 y).
- Major psychiatric disorders.
- Left ventricular hypertrophy.
- Chronic kidney disease.
- Obstructive sleep apnoea syndrome.

2016 ESC/EAS Guidelines Catapano AL et al. Atherosclerosis. 2016 Sep 1. pii: S0021-9150(16)31267-9

Key Studies on Statins

Pharmacokinetics of statins

Parameter	Rosuvastatin	Atorvastatin	Simvastatin	Pravastatin	Fluvastatin	Pitavastatin	Lovastatin
T_{max} (h)	3	2–3	1.3–2.4	0.9–1.6	0.4–2.1	0.6–0.8	2–4
Bioavailability	20	12	5	18	24	80	5
Lipophilicity	No	Yes	Yes	No	Yes	Yes	Yes
Protein binding	88	80–90	94–98	43–55	>98	96	95
Metabolism	Minimal CYP2C9 CYP2C19 Biliary excretion	CYP3A4	CYP3A4	Sulfation Biliary & urine excretion	CYP2C9	Minimal CYP2C8 CYP2C9	CYP3A4
Metabolites	Active (minor)	Active	Active	Inactive	Inactive	Active (minor)	Active
$T^1/_2$ (h)	19	15	2–3	1.3–2.8	1.2	10–11	2.9
Urinary excretion	10	2	13	20	6	NA	10
Faecal excretion	90	70	58	71	90	90	83

Note: Data from Soran et al.[34]
Abbreviations: T_{max}, time to peak plasma concentration; $T^1/_2$ (h), half life.

Luvai, et al. Clin Med Insights Cardiol. 2012; 6: 17–33

Trial Data

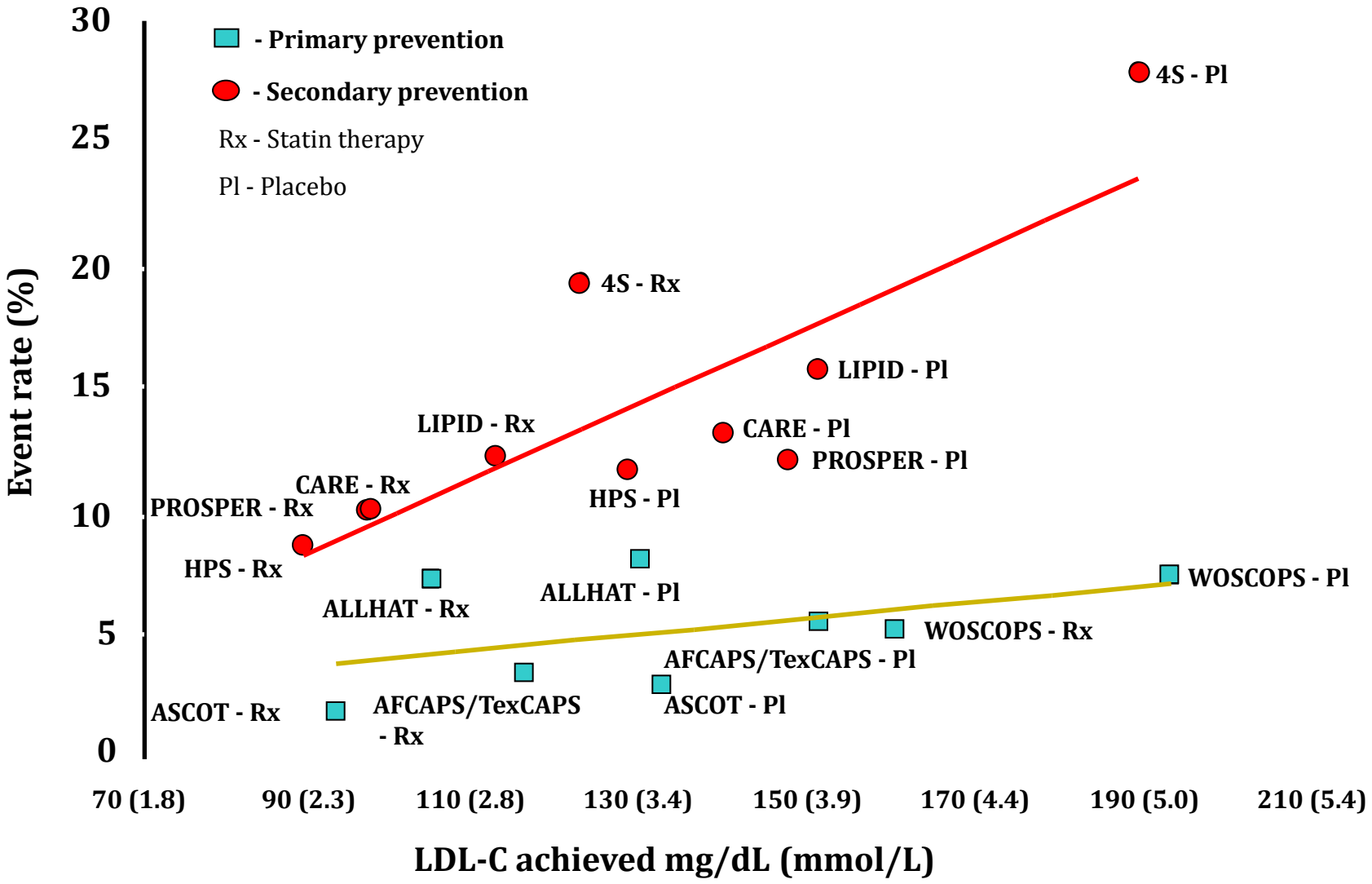
Statin vs. Control

- SSSS
- HPS
- ALLIANCE
- CARDS
- JUPITER
- ASCOT-LLA
- Post-CABG
- WOSCOPS
- PROSPER
- CARE
- LIPID
- ASPEN
- AURORA
- AFCAPS/ TexCAPS
- LIPS
- GISSI-HF
- 4D
- ALERT
- MEGA
- ALLHAT-LLT
- GISSI-P

More vs. Less Statin

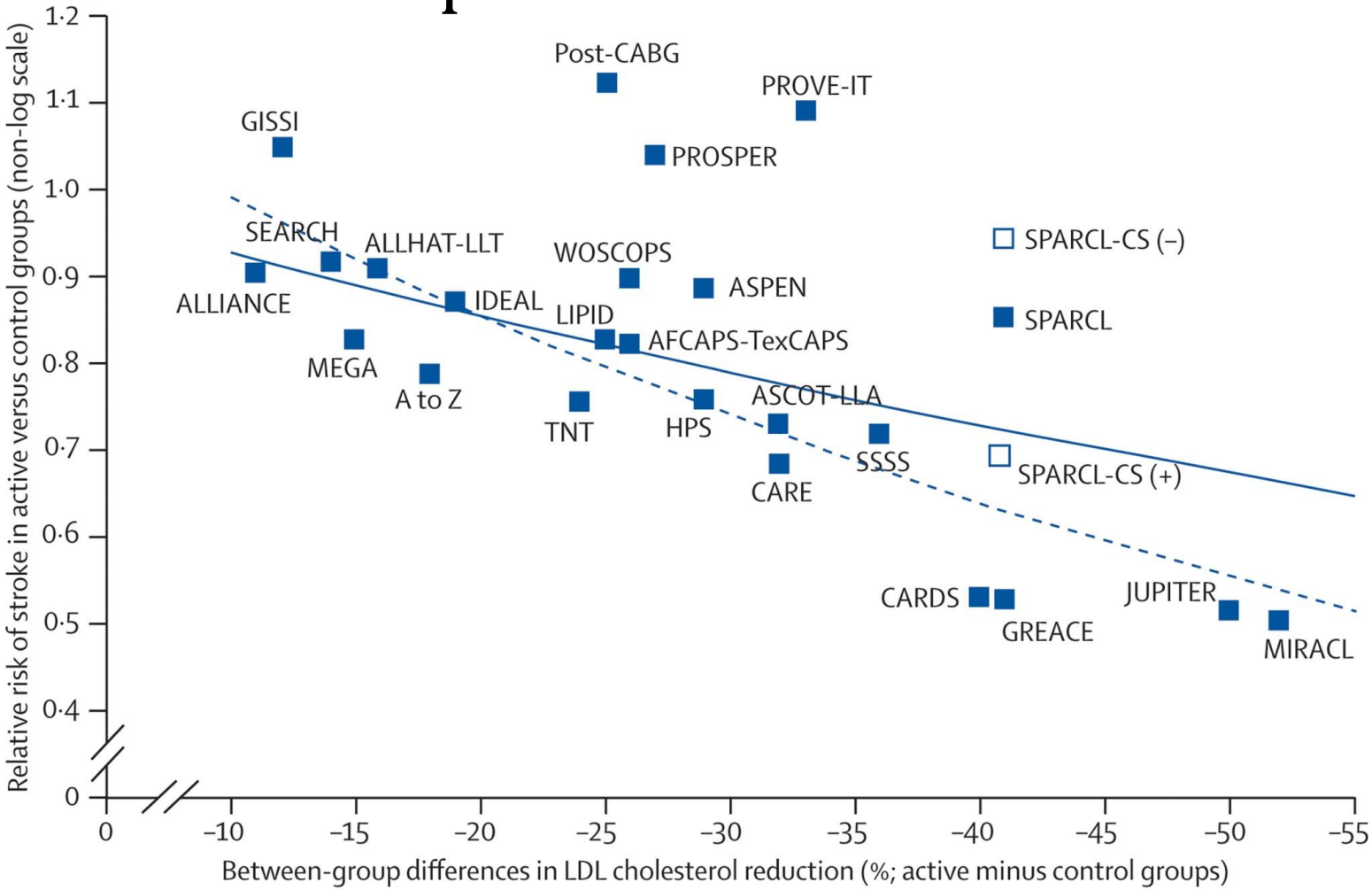
- PROVE-IT
- TNT
- IDEAL
- SEARCH
- A to Z

Relationship between LDL-C and CV Event Rate



Jones PH et al. *Am J Cardiol* 2003;92:152–160

Relationship between LDL-C and Stroke

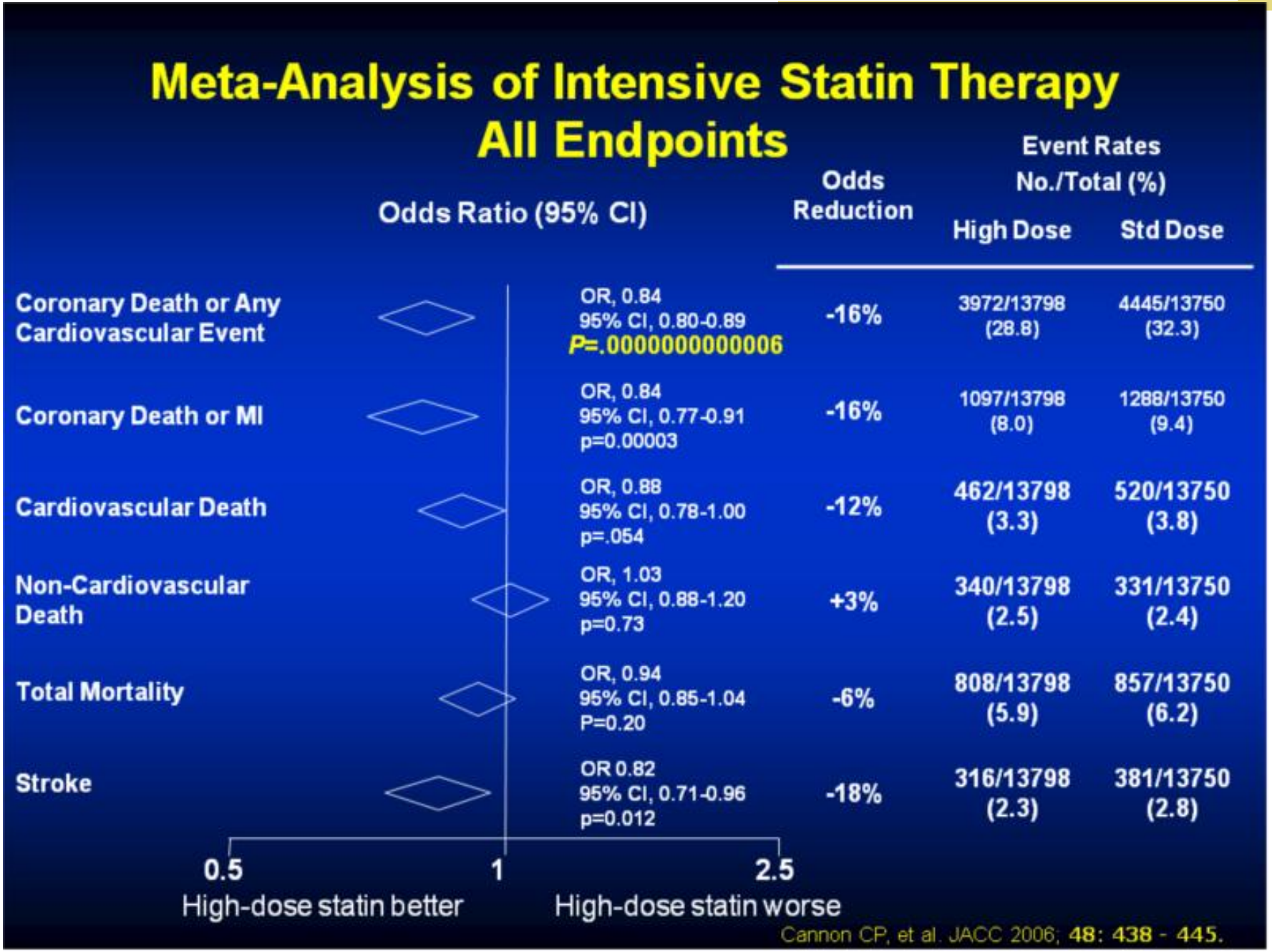


Estimates of relative risk reduction

- 10% LDL reduction: relative risk reduction 7·5% (2·3–12·5) overall
  relative risk reduction 13·5% (7·7–18·8) for primary prevention of stroke
- 1 mmol/L (39 mg/dL) LDL reduction: relative risk reduction 21·1% (6·3–33·5) overall
  relative risk reduction 35·9% (21·7–47·6) for primary prevention of stroke

Jones PH et al. *Am J Cardiol* 2003;92:152–160c

Meta-Analysis of Intensive Statin Therapy
All Endpoints



Cannon CP, et al. JACC 2006; **48: 438 - 445.**

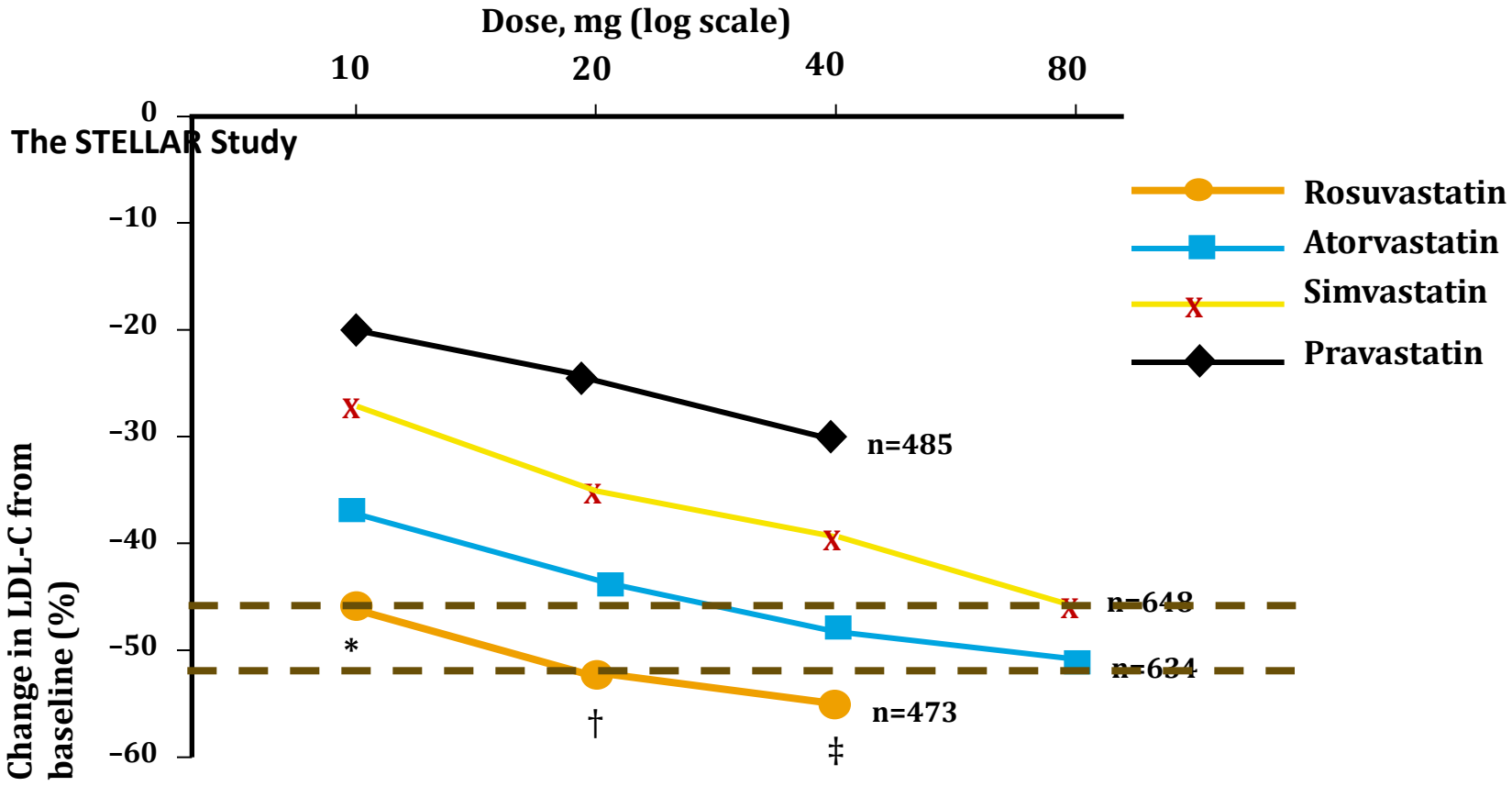
High Intensity (Lowers LDL-C by ≥ 50%)	**Moderate-Intensity** (Lowers LDL-C by 30-50%)	**Low-Intensity** (Lowers LDL-C by < 30%)
Atorvastatin 40-80 mg Rosuvastatin 20-*40* mg	Atorvastatin 10-*20* mg Rosuvastatin *5*-10 mg Simvastatin 20-40 mg Pravastatin 40-*80* mg Lovastatin 40 mg Fluvastatin 40 mg BID *Pitavastatin 2-4 mg*	*Simvastatin 10 mg* Pravastatin 10-20 mg Lovastatin 20 mg *Fluvastatin 20-40 mg* *Pitavastatin 1 mg*

Statins and doses listed in italics are approved for use but have not been studied in randomized controlled trials. Adapted from Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline.

Trial, year	Imaging modality	No. of patients	Duration	LDL-C achieved (mg/dL)	LDL-C/ HDL-C ratio	Primary endpoints
REVERSAL,[141] 2004	IVUS	502	1.6 years	Atorvastatin 79; Pravastatin 110	Atorvastatin 1.9; Pravastatin 2.5	Intensive lipid lowering reduced progression of coronary atherosclerosis as compared to less intensive therapy.
ASTEROID,[139] 2006	IVUS	507	2 years	Rosuvastatin 60.8; Placebo 130	Rosuvastatin 1.3; Placebo 3.2	There was significant reduction in all three pre-specified IVUS measures of disease burden (change in percent atheroma volume, change in atheroma volume in the 10-mm sub-segment with greatest disease severity at base line and change in normalized total atheroma volume for the entire coronary artery).
METEOR,[142] 2007	Carotid ultrasound	984	2 years	Rosuvastatin 78; Placebo 152	Rosuvastatin 1.5; Placebo 3.1	After two years, treatment with rosuvastatin was associated with statistically significant reduction in the rate of progression of CIMT in overall carotid segments, while the placebo group experience progression.
ORION,[143] 2008	MRI	43	2 years	Rosuvastatin 5 mg 96; Rosuvastatin 40 mg 57.7	Not available	Subjects whose wall volume regressed (n=16) had an on-treatment mean LDL-C of 69 mg/dL (-56%), whereas subjects whose wall volume progressed (n=19) had an LDL-C of 84 mg/dL (-45%).
SATURN,[144] 2011	IVUS	1039	104 weeks	Rosuvastatin 62.6; Atorvastatin 70.2	Rosuvastatin 1.3; Atorvastatin 1.5	For the primary IVUS endpoint, the extent of regression was similar for both the regimens (P=0.17). However, for the secondary IVUS endpoint, a greater degree of regression was observed with rosuvastatin compared with atorvastatin (P=0.01).
YELLOW,[145] 2013	NIRS IVUS	87	6-8 weeks	Rosuvastatin 58.4; Simvastatin 81.9	Rosuvastatin 1.5; Simvastatin 2.3	Aggressive lipid lowering therapy resulted in significant reduction in the lipid component of coronary atherosclerotic plaques as detected by NIRS in a short time frame (6-8 weeks).
PRECISE-IVUS,[146] 2015	IVUS	202	9-12 mths	Atorvastatin with ezetimibe 63.2; Atorvastatin alone 73.3		The absolute change in percent atheroma volume of a select target segment of a coronary artery from baseline to follow-up (the primary efficacy outcome) was greater with the dual lipid lowering strategy than with atorvastatin alone.

Rosuvastatin and Dyslipidemia

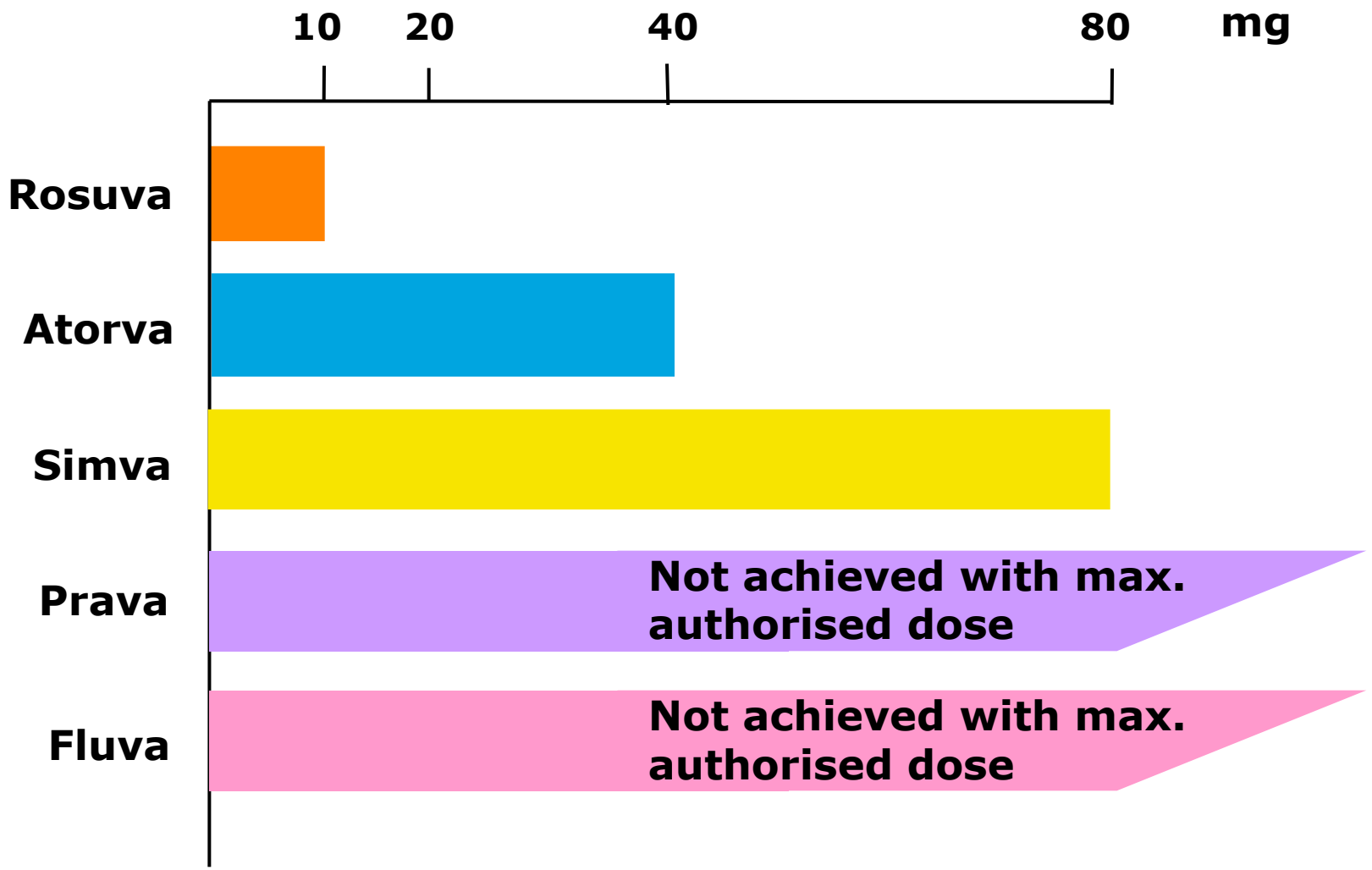
Rosuvastatin versus Comparators: LDL-C Efficacy Across the Dose Range



*p<0.002 vs atorvastatin 10 mg; simvastatin 10, 20, 40 mg; pravastatin 10, 20, 40 mg
†p<0.002 vs atorvastatin 20, 40 mg; simvastatin 20, 40, 80 mg; pravastatin 20, 40 mg
‡p<0.002 vs atorvastatin 40 mg; simvastatin 40, 80 mg; pravastatin 40 mg

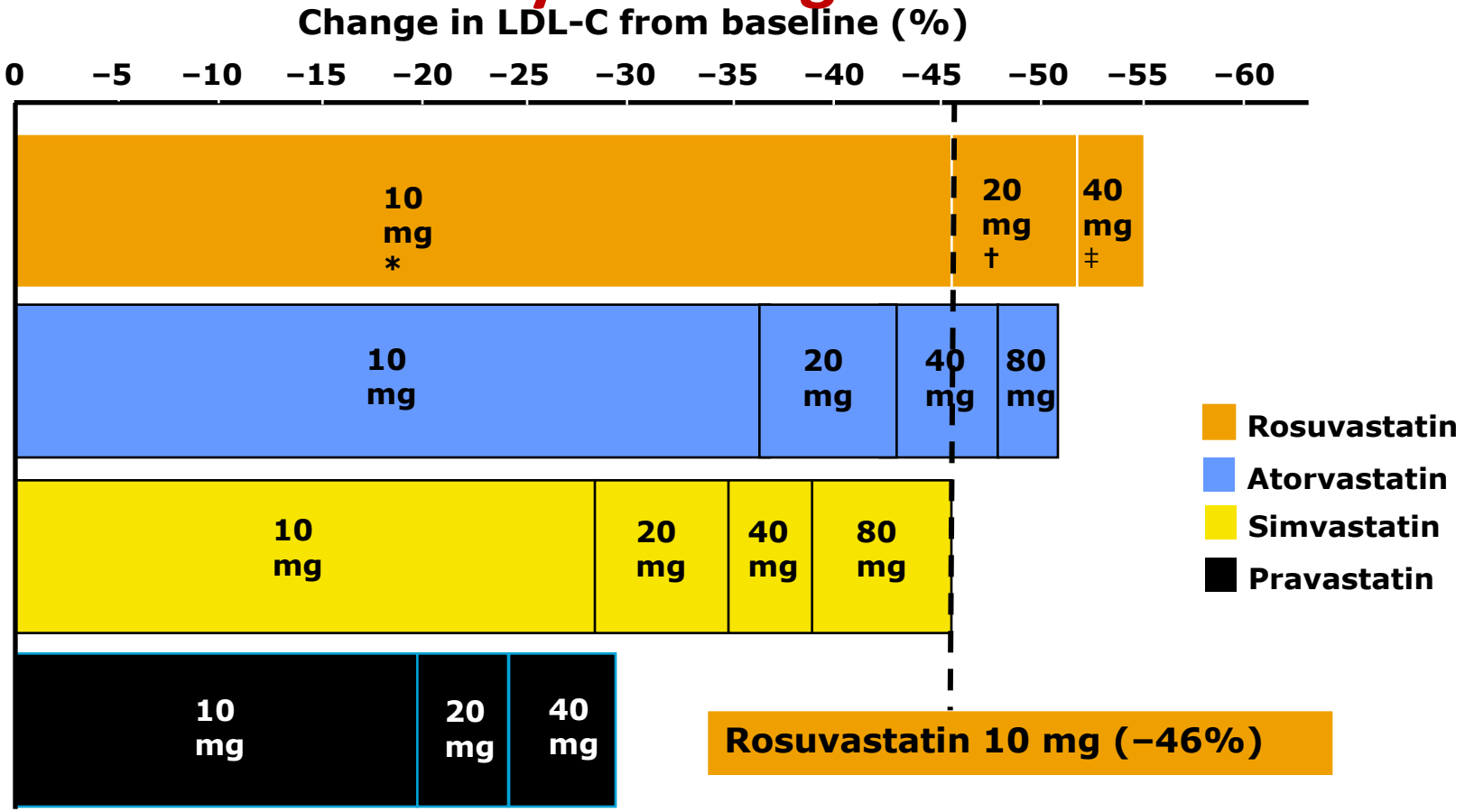
Jones PH et al. *Am J Cardiol* 2003;92:152–160c

Statin Dose Required to Achieve 45–50% LDL-C Reduction



Jones PH et al. *Am J Cardiol* 2003;92:152–160c

Rosuvastatin versus Comparators: LDL-C efficacy at 10mg Dose

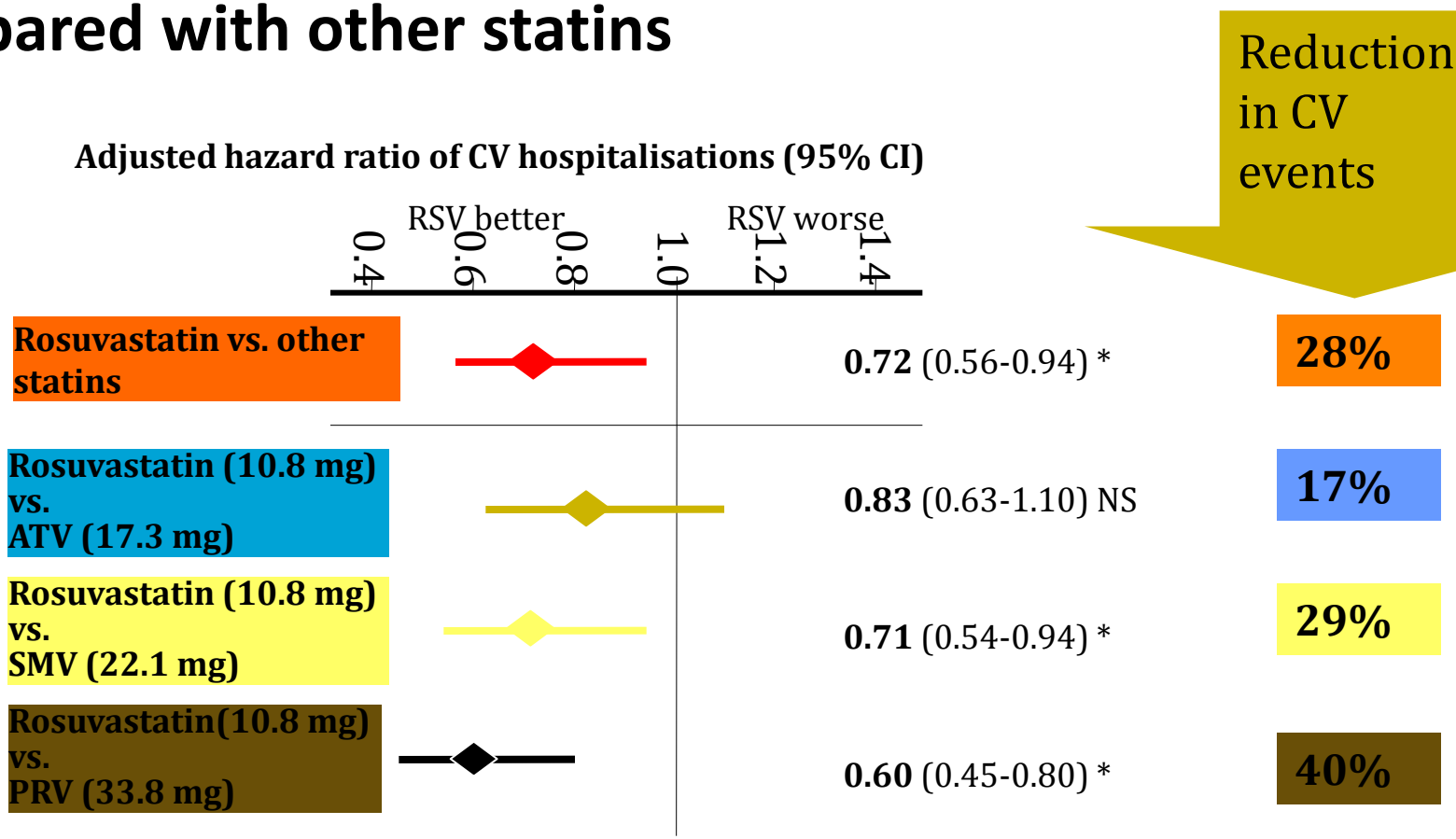


*p<0.002 vs atorvastatin 10 mg; simvastatin 10, 20, 40 mg; pravastatin 10, 20, 40 mg
†p<0.002 vs atorvastatin 20, 40 mg; simvastatin 20, 40, 80 mg; pravastatin 20, 40 mg
‡p<0.002 vs atorvastatin 40 mg; simvastatin 40, 80 mg; pravastatin 40 mg

Jones PH et al. *Am J Cardiol* 2003;92:152–160

Primary Outcome

Rates of CV events were 28% lower on Rosuvastatin compared with other statins

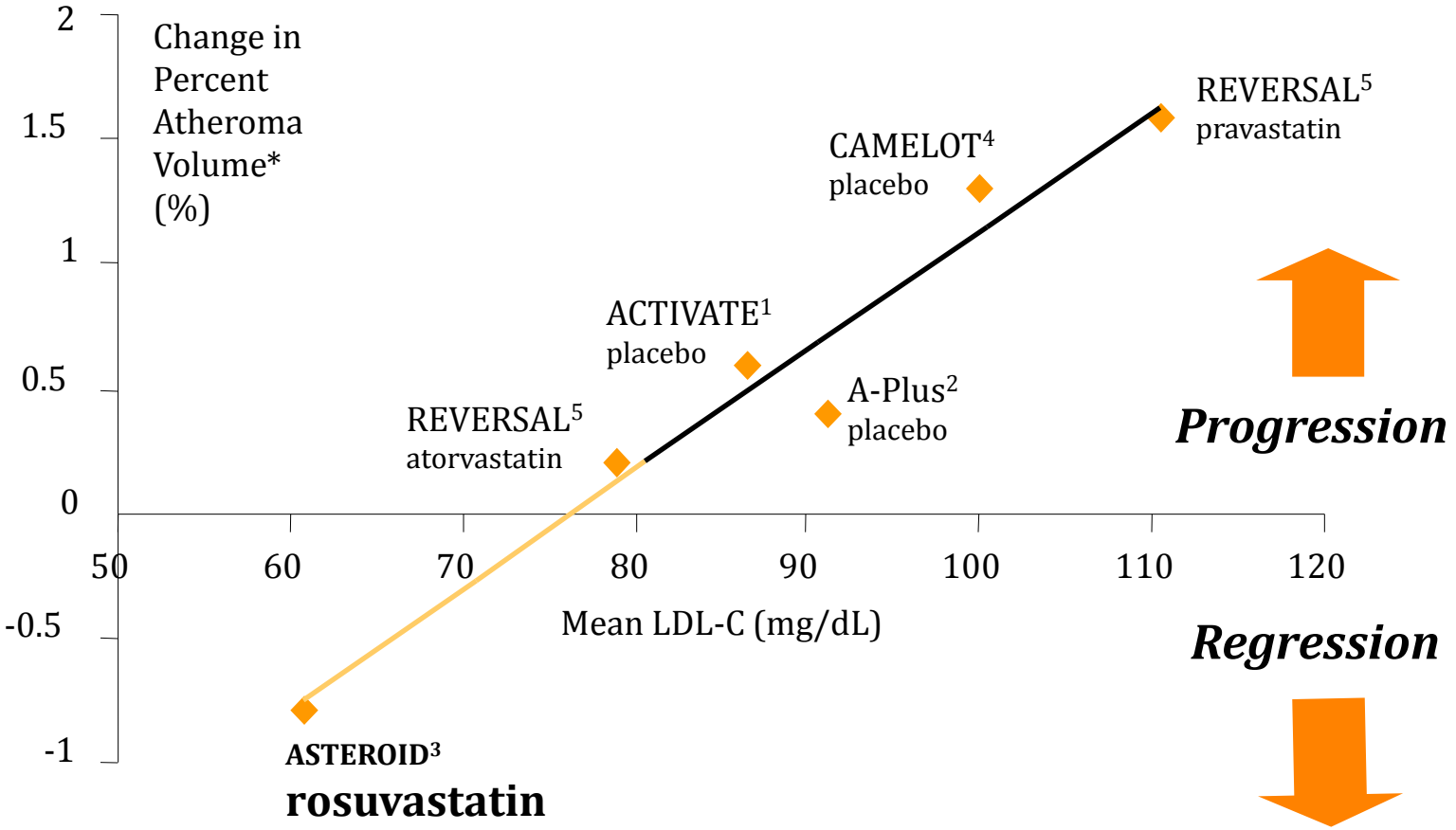


* A 95% CI that does not exceed 1 indicates a statistically significant hazard ratio

Hazard ratios of CV were adjused for age, gender, nitrates, classic antihypertensives and diabetes

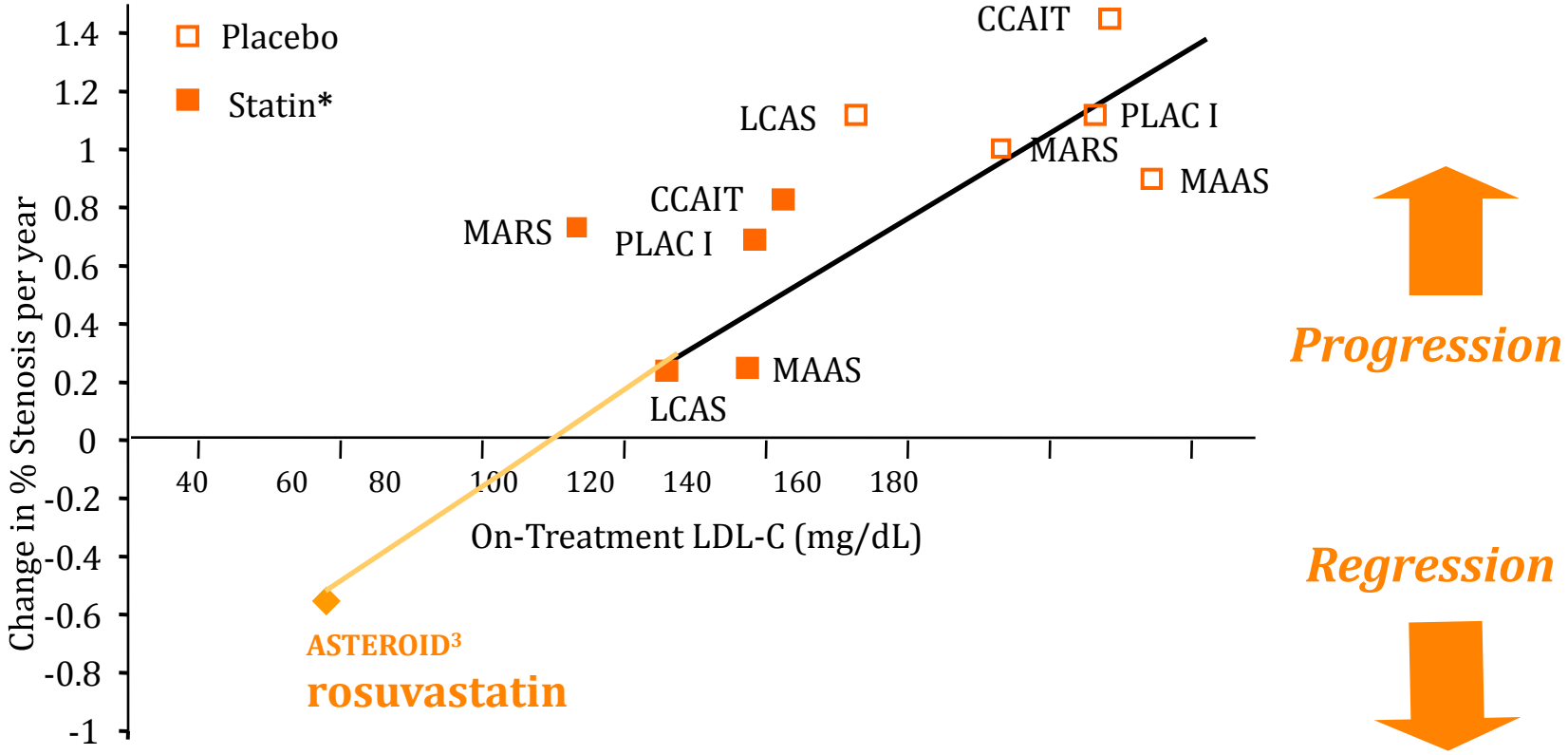
Heintjes EM et al. Curr Med Res Opin. 2008;24:2241–2250

The relationship between mean LDL-C and change in percent atheroma volume (PAV) in IVUS studies†



1 Nissen S et al. N Engl J Med 2006;354:1253-1263. **2** Tardif J et al. Circulation 2004;110:3372-3377.
3 Nissen S et al. JAMA 2006;295 (13):1556-1565 **4** Nissen S et al. JAMA 2004;292: 2217–2225.
5 Nissen S et al. JAMA 2004; 291:1071–1080

Change in Percent Diameter Stenosis vs On-Treatment LDL-C in QCA Trials

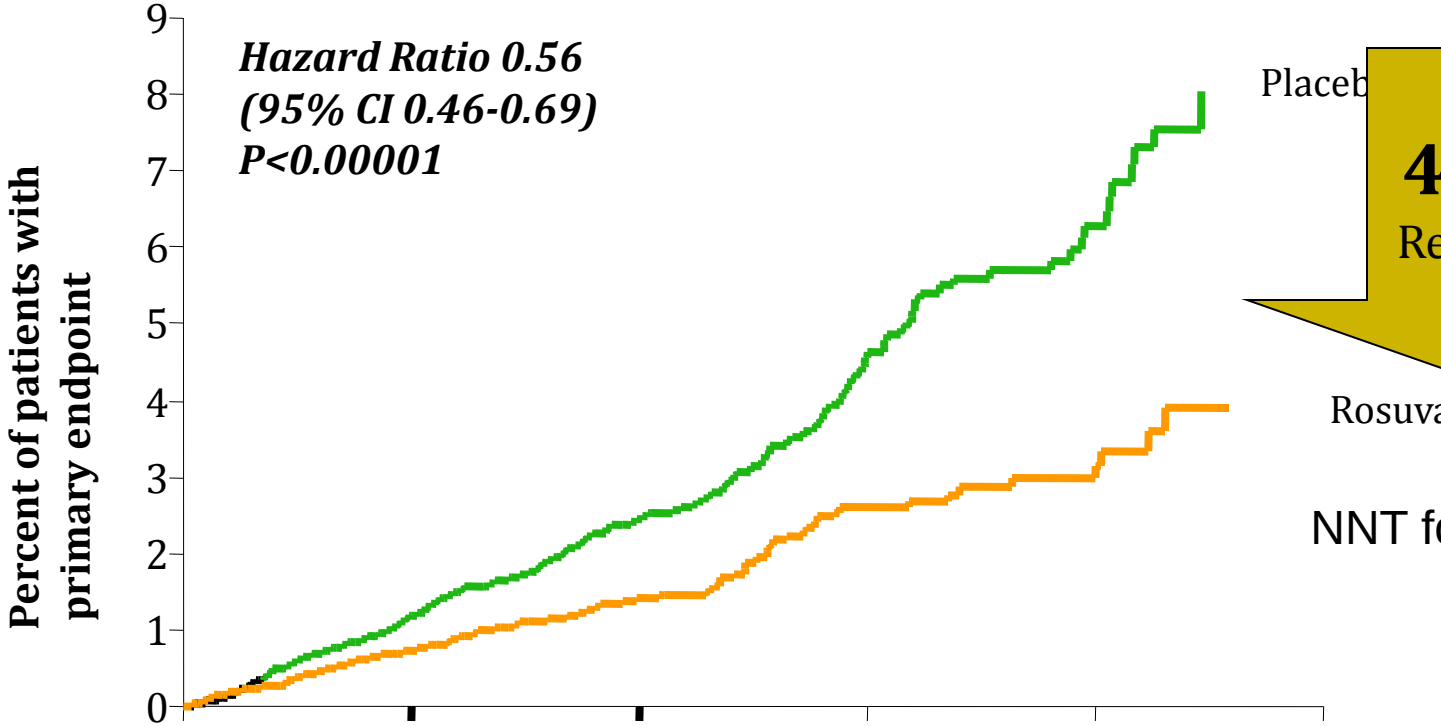


* **ASTEROID** - rosuvastatin; **MAAS** - simvastatin; **CCAIT** - lovastatin; **MARS** – lovastatin; **LCAS** - fluvastatin; **PLAC I** - pravastatin

Nissen S *et al.* JAMA 2006;295 (13):1556-1565;
Ballantyne C *et al.* Circulation 2008 DOI: 10.1161/CIRCULATIONAHA.108.773747.

JUPITER - Primary Endpoint

Time to first occurrence of a CV death, non-fatal stroke, non-fatal MI, unstable angina or arterial revascularization

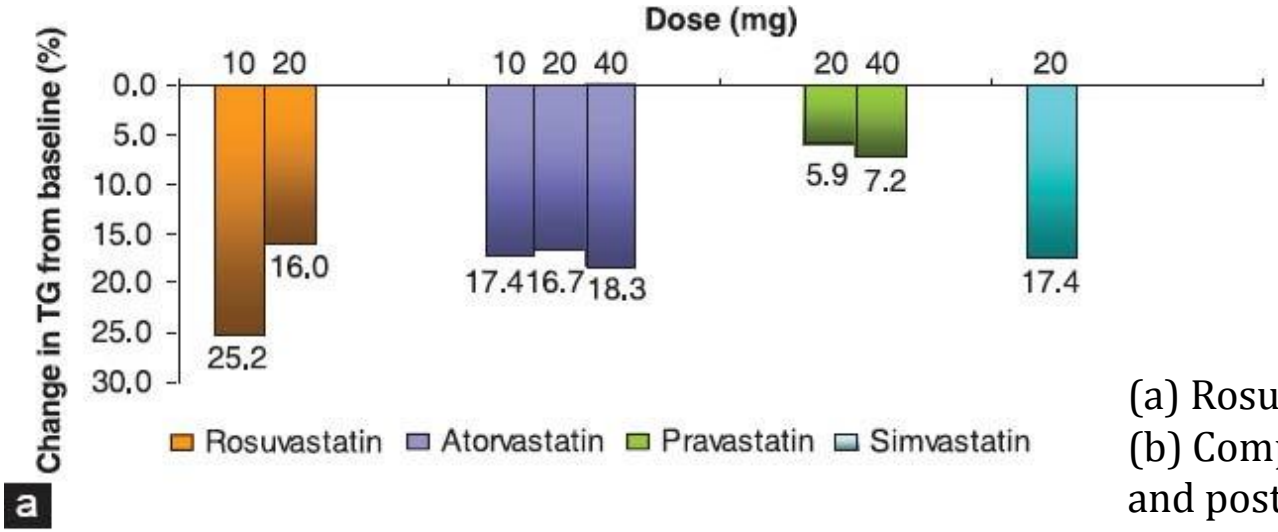


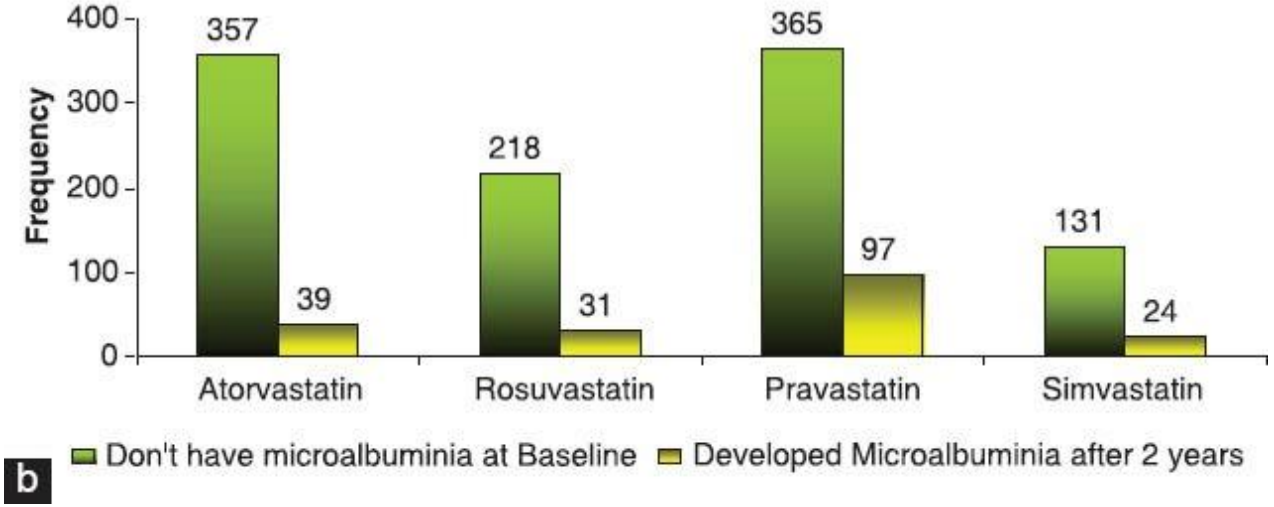
NNT for 2y = 95
5y* = 25

Number at risk

RSV	8901	8412	3893	1353	538	157
Placebo	8901	8353	3872	1333	531	174

Comparison of various statins





(a) Rosuvastatin versus other statins, (b) Comparison of patients with pre- and posttreatment microalbuminuria at the end of 2 years

Bener A et al. Indian J Pharmacol. 2014 Jan-Feb; 46(1): 88–93

New evidence from ASCOT-LLA

- The data suggests that there is *no evidence for increased AEs associated with the use of statins.*

- The reported excess of muscle-related AEs, in observational studies, is possibly due to confounding by knowledge of the use of statins among patients and physicians alike, and compounded by the widespread adverse media publicity – The "Nocebo" effect.

- Apparent beneficial effects on sleep disturbance, and possibly on erectile dysfunction, with the use of statins need to be confirmed in other studies.

(ASCOT-LLA)- Lipid-lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial

Statins and Combinations

The Heart Outcomes Prevention Evaluation (HOPE -3) Trial

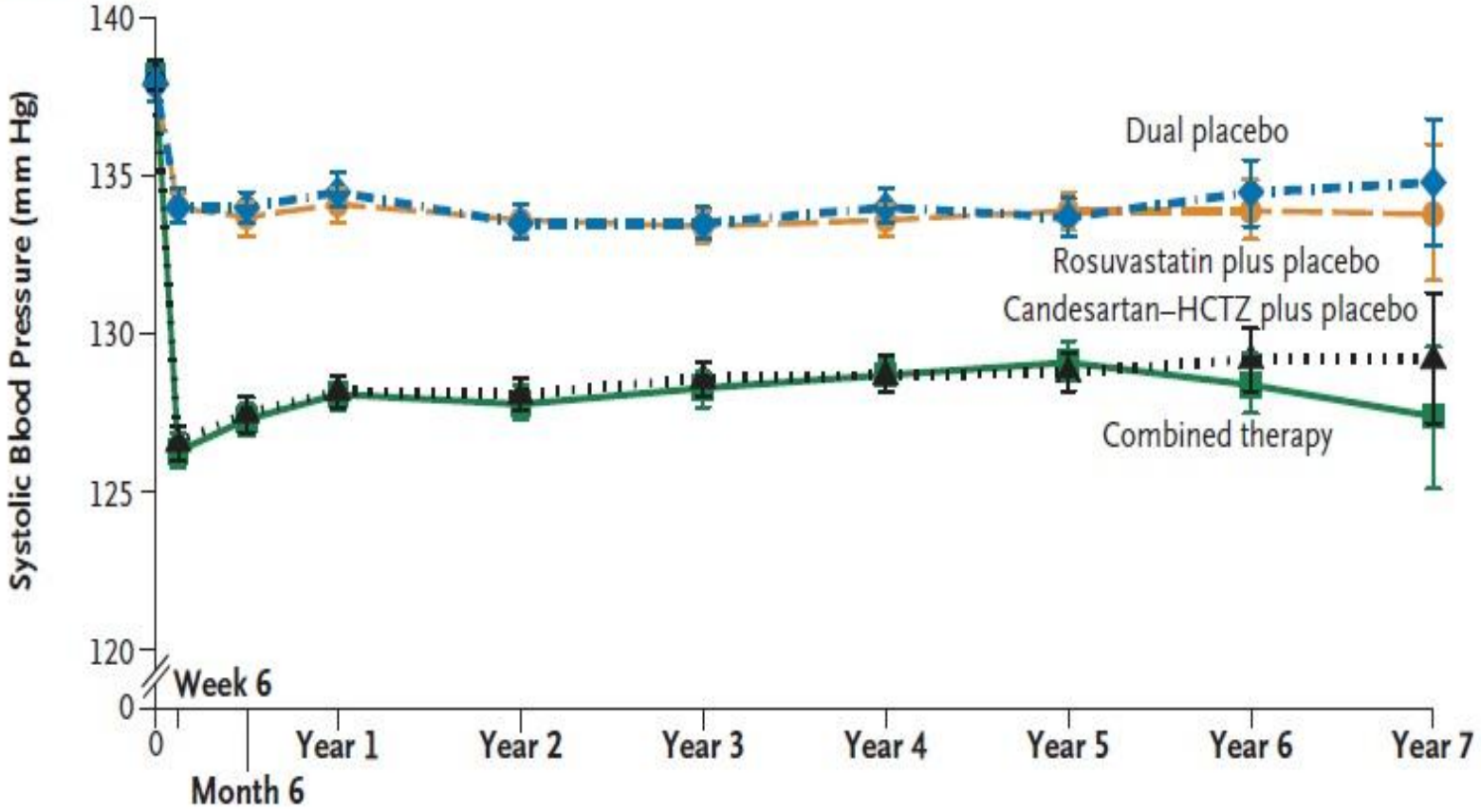
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Blood-Pressure and Cholesterol Lowering in Persons without Cardiovascular Disease

Salim Yusuf, M.B., B.S., D.Phil., Eva Lonn, M.D., Prem Pais, M.D., Jackie Bosch, Ph.D., Patricio López-Jaramillo, M.D., Ph.D., Jun Zhu, M.D., Denis Xavier, M.D., Alvaro Avezum, M.D., Ph.D., Lawrence A. Leiter, M.D., Leopoldo S. Piegas, M.D., Ph.D., Alexander Parkhomenko, M.D., Ph.D., Matyas Keltai, M.D., Ph.D., Katalin Keltai, M.D., Ph.D., Karen Sliwa, M.D., Ph.D., Irina Chazova, M.D., Ph.D., Ron J.G. Peters, M.D., Ph.D., Claes Held, M.D., Ph.D., Khalid Yusoff, M.D., Basil S. Lewis, M.D., Petr Jansky, M.D., Kamlesh Khunti, M.D., Ph.D., William D. Toff, M.D., Christopher M. Reid, Ph.D., John Varigos, B.Sc., Jose L. Accini, M.D., Robert McKelvie, M.D., Ph.D., Janice Pogue, Ph.D.,* Hyejung Jung, M.Sc., Lisheng Liu, M.D., Rafael Diaz, M.D., Antonio Dans, M.D., and Gilles Dagenais, M.D., for the HOPE-3 Investigators†

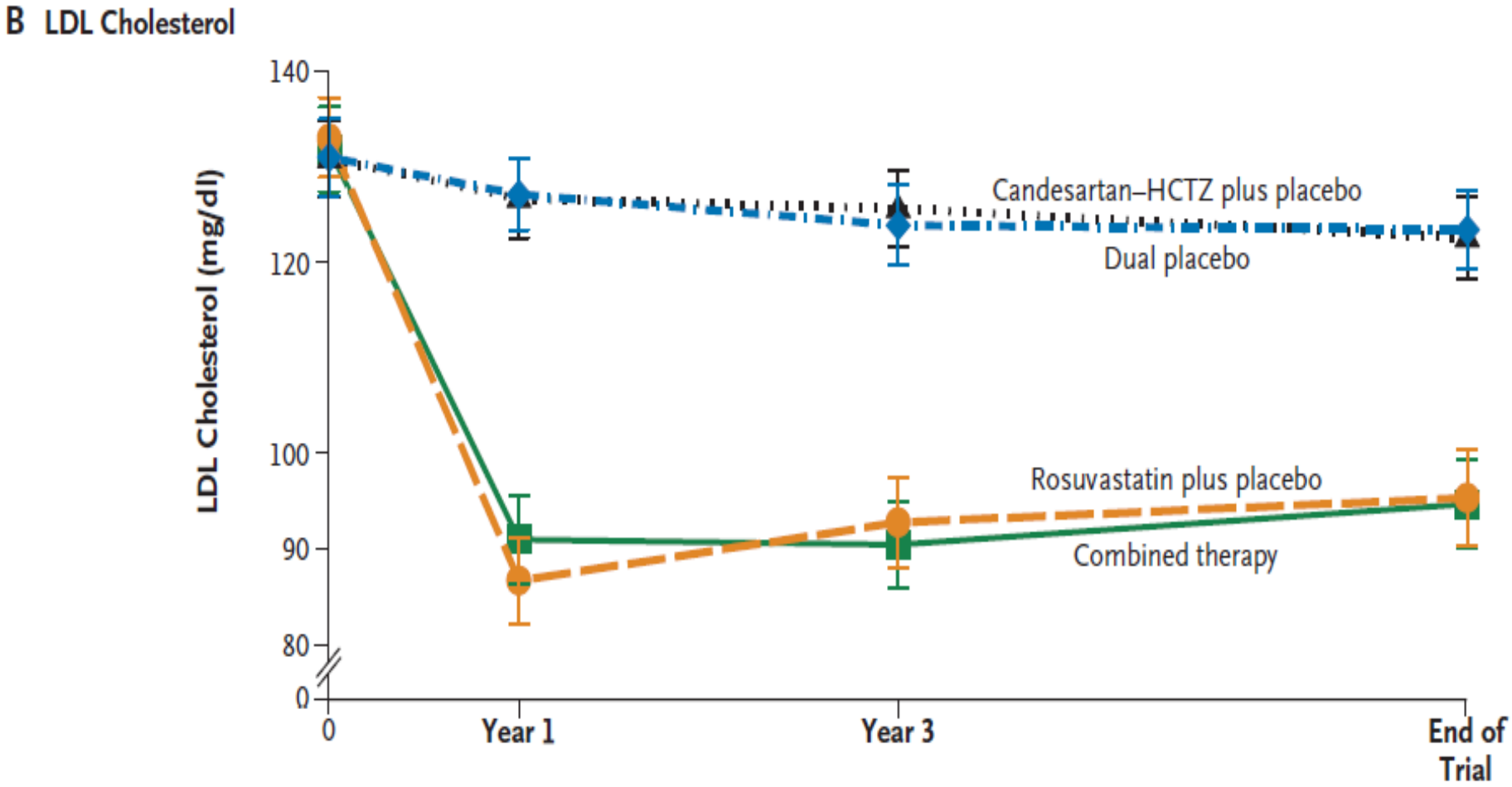
A Systolic Blood Pressure



No. at Risk

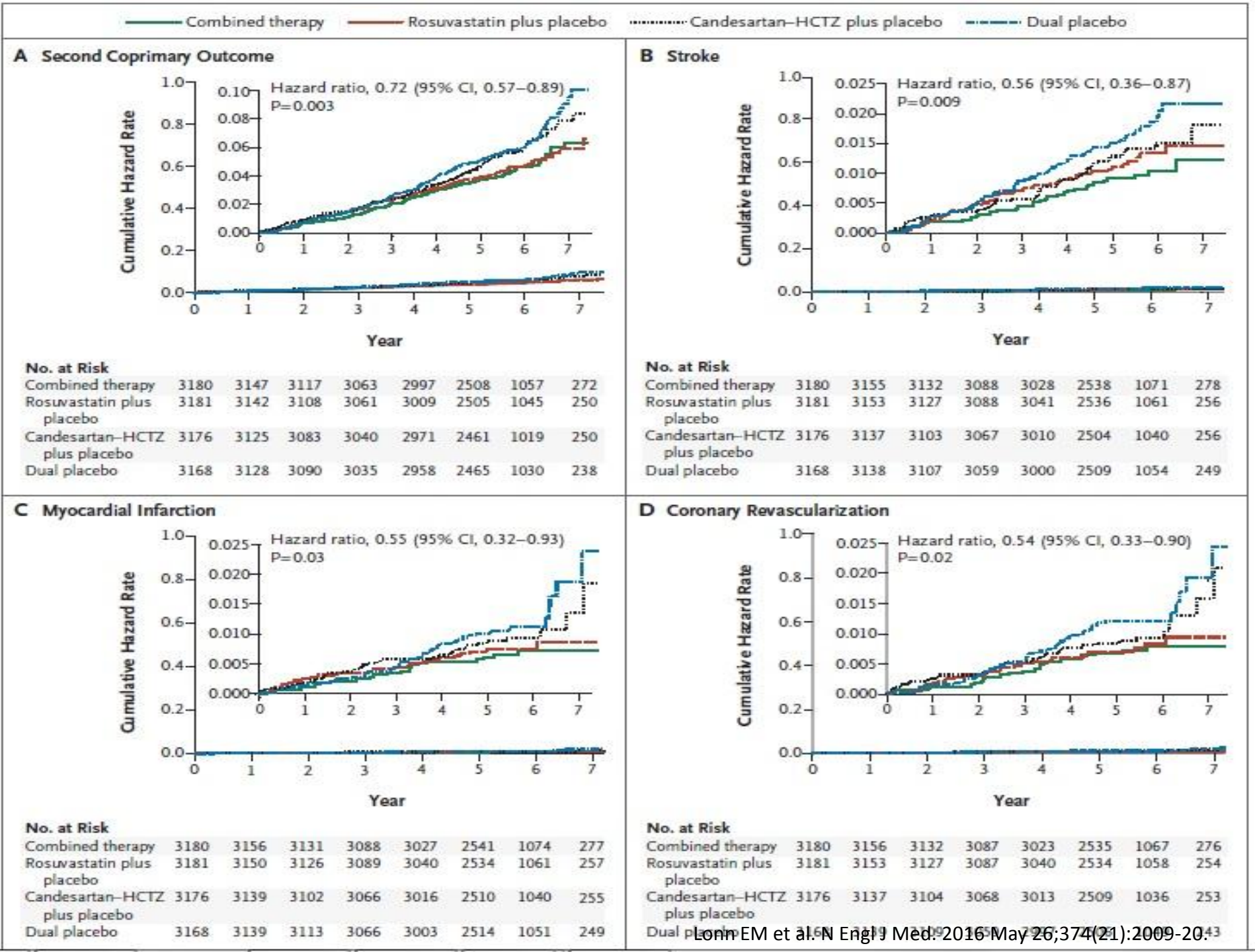
Combined therapy	3180	3091	3009	2953	2836	2718	2594	1921	731	178
Rosuvastatin plus placebo	3181	3105	3033	2957	2832	2741	2615	1929	728	167
Candesartan–HCTZ plus placebo	3176	3109	3022	2954	2831	2728	2619	1941	706	172
Dual placebo	3166	3093	3000	2922	2791	2701	2571	1893	696	167

Lonn EM et al. N Engl J Med. 2016 May 26;374(21):2009-20.



No. at Risk				
Combined therapy	248	248	248	248
Rosuvastatin plus placebo	232	232	232	232
Candesartan–HCTZ plus placebo	247	247	247	247
Dual placebo	248	248	248	248

Lonn EM et al. N Engl J Med. 2016 May 26;374(21):2009-20.



Lonn EM et al. N Engl J Med. 2016 May 26;374(21):2009-20.

HOPE - 3

The combination of statin , ARB and diuretic was associated with a significantly lower rate of cardiovascular events.

Combination therapy (with a statin and anti-hypertensives) would perform best in patients with hypertension, whereas statins alone would perform best in those without elevated blood pressure.

Lonn EM et al. N Engl J Med. 2016 May 26;374(21):2009-20.

Rosuvastatin and Fenofibrate

Author	Study population	Statin dose	Fibrate dose	Duration	LDL-C[a]	TC[a]	TG[a]	HDL-C[a]	Other parameters[a]
Rosenson et al. [176]	456 patients with mixed dyslipidemia and T2DM	Rosuvastatin 5 mg	Fenofibric acid 135 mg	12 weeks	-32.8%[d]	-	-39.9%[e]	+25.5%[e]	Non-HDL-C: -41.1%[d,e], ApoB: -34.9%[d], hsCRP: -26.8%
		Rosuvastatin 10 mg	Fenofibric acid 135 mg	12 weeks	-36.8%[d]	-	-44.8%[e]	+19.6%[e]	Non-HDL-C: -43.6%[d], ApoB: -36.2%, hsCRP: -28.0%
		Rosuvastatin 20 mg	Fenofibric acid 135 mg	12 weeks	-37.0%[d]	-	-42.6%[e]	+16.4%	Non-HDL-C: -44.9%[d], ApoB: -36.2%, hsCRP: -40.7%
Jones et al. [157]	586 patients with mixed dyslipidemia and T2DM	Moderate-dose statin (rosuvastatin 20 mg, simvastatin 40 mg or atorvastatin 40 mg)	Fenofibric acid 135 mg	12 months	-32.6%[b,c]	-32.6%[b]	-43.4%[b,c]	+16.3%[c]	hsCRP: -39.3%
		Low-dose statin (rosuvastatin 10 mg, simvastatin 20 mg or atorvastatin 20 mg)	Fenofibric acid 135 mg	12 months	-34%[d]	-33.2%[d,e]	-43.9%[d,e]	+16.8%[e]	hsCRP: -25%
Gavish et al.[167]	148 patients with T2DM	Simvastatin 20 mg	Bezafibrate 400 mg	12 months	-28.9%[b,d]	-22.9%[b,d]	-41.8%[b,d,e]	+20%[b,e]	Fibrinogen: -9%[b]
Dullaart et al. [168]	14 patients with T2DM	Simvastatin 40 mg	Bezafibrate 400 mg	8 weeks	-	-26.3%[b,c,d]	-46.6%[b,c,e]	+14.7%[b]	No significant change in paraoxonase 1 activity compared with monotherapy

Agouridis AP et al. Rev Diabet Stud, 2013;10(2-3):171-190

Dual Antiplatelets For The Secondary Prevention Of Atherothrombotic Events

- The use of long term DAPT was associated with a significant decrease in composite of death, MI and stroke (5.78% vs. 6.52%; Relative Risk RR= 0.91 [0.78 -0.94]; P=0.01).
- The reduction was mainly driven by a reduction in MI, but not in death, cardiac death or stroke.
- This reduction of death, MI and stroke was mainly noticed in patients with prior MI (6.4 vs. 7.5%; RR= 0.78 [0.69 -0.90]; P=0.01).
- Long-term use of DAPT was associated with significant increase in major bleeding (1.47% vs. 0.83%; OR= 1.77 [1.49 - 2.13]; P< 0.001).

Fanari Z t al. Cardiovasc Revasc Med. 2016 Jul 20. pii: S1553-8389(16)30193-2.

Effects of rosuvastatin on platelet inhibition by clopidogrel in cardiovascular patients

- Riondino *et al.* retrospectively studied two populations of HR patients, one under aspirin alone, the other under aspirin plus rosuvastatin, before and after addition of clopidogrel.
- Light transmission platelet aggregation (LTA) was studied in response to adenosine diphosphate (ADP) (5 μM) or arachidonic acid (0.5 mM).
- The inhibitory effect of clopidogrel in reducing ADP-induced LTA was similar in the two HR groups of patients.
- No difference in ADP-induced platelet aggregation was observed in the two PCI groups of patients with either atorvastatin or rosuvastatin.
- In conclusion, rosuvastatin does not interfere with the antiplatelet effect of clopidogrel in patients with cardiovascular disease

Riondino *et al.* Journal of Thrombosis and Thrombolysis 2009August; 28(2):151–155

European Heart Journal
doi:10.1093/eurheartj/ehw272

ESC/EAS GUIDELINES

2016 ESC/EAS Guidelines for the Management of Dyslipidaemias

The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

Developed with the special contribution of the European Assocciation for Cardiovascular Prevention & Rehabilitation (EACPR)

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2016 ESC/EAS Guidelines Catapano AL et al. Atherosclerosis. 2016 Sep 1. pii: S0021-9150(16)31267-9

Intervention strategies as a function of total CV risk and LDL-C level

Total CV risk (SCORE) %	LDL-C levels				
	< 70 mg/dL < 1.8 mmol/L	70 to < 100 mg/dL 1.8 to < 2.5 mmol/L	100 to < 155 mg/dL 2.5 to < 4.0 mmol/L	155 to < 190 mg/dL 4.0 to < 4.9 mmol/L	> 190 mg/dL > 4.9 mmol/L
< 1	No lipid intervention	No lipid intervention	No lipid intervention	No lipid intervention	Lifestyle intervention, consider drug if uncontrolled
Class/Level	I/C	I/C	I/C	I/C	IIa/A
≥ 1 to < 5	No lipid intervention	No lipid intervention	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled	Lifestyle intervention, consider drug if uncontrolled
Class/Level	I/C	I/C	IIa/A	IIa/A	I/A
> 5 to < 10, or high risk	No lipid intervention	Lifestyle intervention consider drug*	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention	Lifestyle intervention and concomitant drug intervention
Class/Level	IIa/A				
≥ 10 or very high risk	Lifestyle intervention consider drug*	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/Level	IIa/A	IIa/A	I/A	I/A	I/A

2016 ESC/EAS Guidelines Catapano AL et al. Atherosclerosis. 2016 Sep 1. pii: S0021-9150(16)31267-9

Recommendations for treatment targets for LDL-C

Recommendations	Class [a]	Level[b]
In patients at VERY HIGH CV risk[d],a n LDL-C goal of <1.8 mmol/L (70 mg/dL) or a reduction of at least 50% if the baseline LDL-C[e] is between 1.8 and 3.5 mmol/L (70 and 135 mg/dL) is recommended.	I	B
In patients at HIGH CV risk[d], an LDL-C goal of <2.6 mmol/L (100 mg/dL), or a reduction of at least 50% if the baseline LDL-C[e] is between 2.6 and 5.2 mmol/L (100 and 200 mg/dL) is recommended.	I	B
In subjects at LOW or MODERATE risk[d] an LDL-C goal of <3.0 mmol/L (<115 mg/dL) should be considered.	IIa	C

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Dietary recommendations to lower LDL-C and improve overall lipoprotein profile

	To be preferred	To be used with moderation	To be chosen occasionally in limited amounts
Cereals	Whole grains	Refined bread, rice and pasta, biscuits, corn flakes	Pastries, muffins, pies, croissants
Vegetables	Raw and cooked vegetables	Potatoes	Vegetables prepared in butter or cream
Legumes	Lentils, beans, fava beans, peas, chickpeas, soybean		
Fruit	Fresh or frozen fruit	Dried fruit, jelly, jam, canned fruit, sorbets, popsicles, fruit juice	
Sweets and sweeteners	Non-caloric sweeteners	Sucrose, honey, chocolate, candies	Cakes, ice creams, fructose, soft drinks
Meat and fish	Lean and oily fish, poultry without skin	Lean cuts of beef, lamb, pork or veal, seafood, shellfish	Sausages, salami, bacon, spare ribs, hot dogs, organ meats
Dairy food and eggs	Skim milk and yogurt	Low-fat milk, low-fat cheese and other milk products, eggs	Regular cheese, cream, whole milk and yogurt
Cooking fat and dressings	Vinegar, mustard, fat-free dressings	Olive oil, non-tropical vegetable oils, soft margarines, salad dressing, mayonnaise, ketchup	Trans fats and hard margarines (better to avoid them), palm and coconut oils, butter, lard, bacon fat
Nuts/seeds		All, unsalted (except coconut)	Coconut
Cooking procedures	Grilling, boiling, steaming	Stir-frying, roasting	Frying

2016 ESC/EAS Guidelines Catapano AL et al. Atherosclerosis. 2016 Sep 1. pii: S0021-9150(16)31267-9

Management of dyslipidaemia in women

- Statin treatment is recommended for primary prevention of CAD in high risk women.
- Statins are recommended for secondary prevention in women with the same indications and targets as in men.
- Lipid-lowering drugs should not be given when pregnancy is planned, during pregnancy or during the breast feeding period.

2016 ESC/EAS Guidelines Catapano AL et al. Atherosclerosis. 2016 Sep 1. pii: S0021-9150(16)31267-9

Recommendations for treatment of dyslipidaemia in diabetes

Recommendations	Class	Level
In all patients with type I diabetes and in the presence of microalbuminuria and/or renal disease, LDL-C lowering (at least 50%) with statins as the first choice is recommended irrespective of the baseline LDL-C concentration.	I	C
In patients with type 2 diabetes and CVD or CKD, and in those without CVD who are >40 years of age with one or more other CVD risk factors or markers of target organ damage, the recommended goal for LDL-C is <1.8 mmol/L (<70 mg/dL) and the secondary goal for non-HDL-C is <2.6 mmol/L (<100 mg/dL) and for apoB is <80 mg/dL.	I	B
In all patients with type 2 diabetes and no additional risk factors and/or evidence of target organ damage, LDL-C <2.6 mmol/L (<100 mg/dL) is the primary goal. Non-HDL-C <3.4 mmol/L (<130 mg/dL) and apoB <100 mg/dL are the secondary goals.	I	B

Conclusion

- Several recent studies have shown that CVD risk reduction with lifelong low LDL-C levels is 3–5 times greater than decreasing LDL-C in middle age.
- LDL-C remains the primary target for lipid-lowering therapy and statins remain the first choice for LDL-C lowering
- Rosuvastatin is one of the most potent statins available
- Reduces circulating LDL-C levels, which enables more high-risk patients to achieve their lipid goals
- It has favorable balance of effects on atherogenic and protective lipoproteins and pleiotropic effects, including anti-inflammatory and antioxidant effects and improvement in endothelial dysfunction.
- Rosuvastatin is an appropriate therapy to reduce cardiovascular risk in patients with Dyslipidemia and co-morbid conditions.