PRESENT
AND FUTURE
APPROACHES TO
THE CONTROL OF
DYSLIPIDAEMIAS

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Società Italiana di Terapia Clinica e Sperimentale

LIPID LOWERING THERAPIES

Statins

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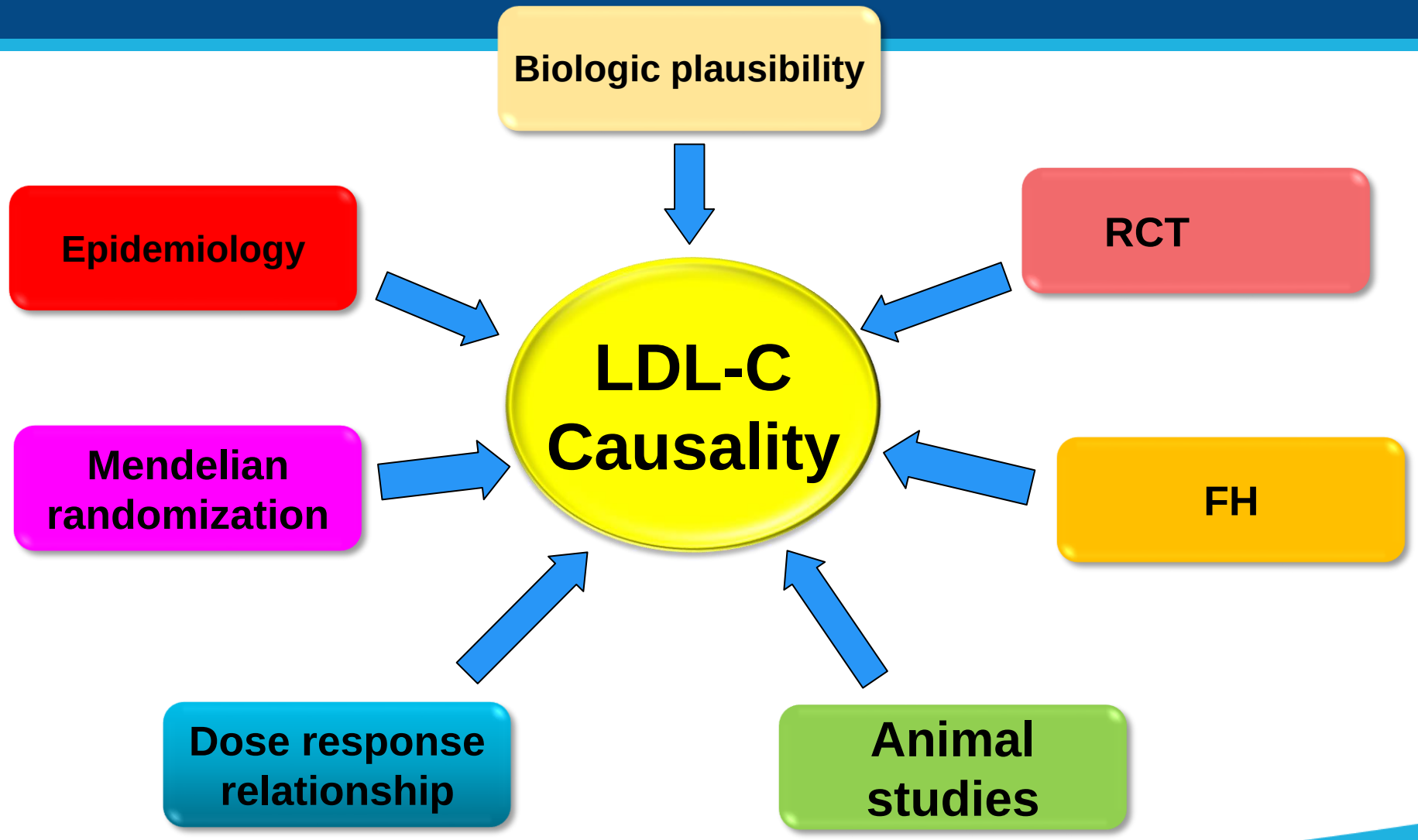
President, European Atheroscleoris Society

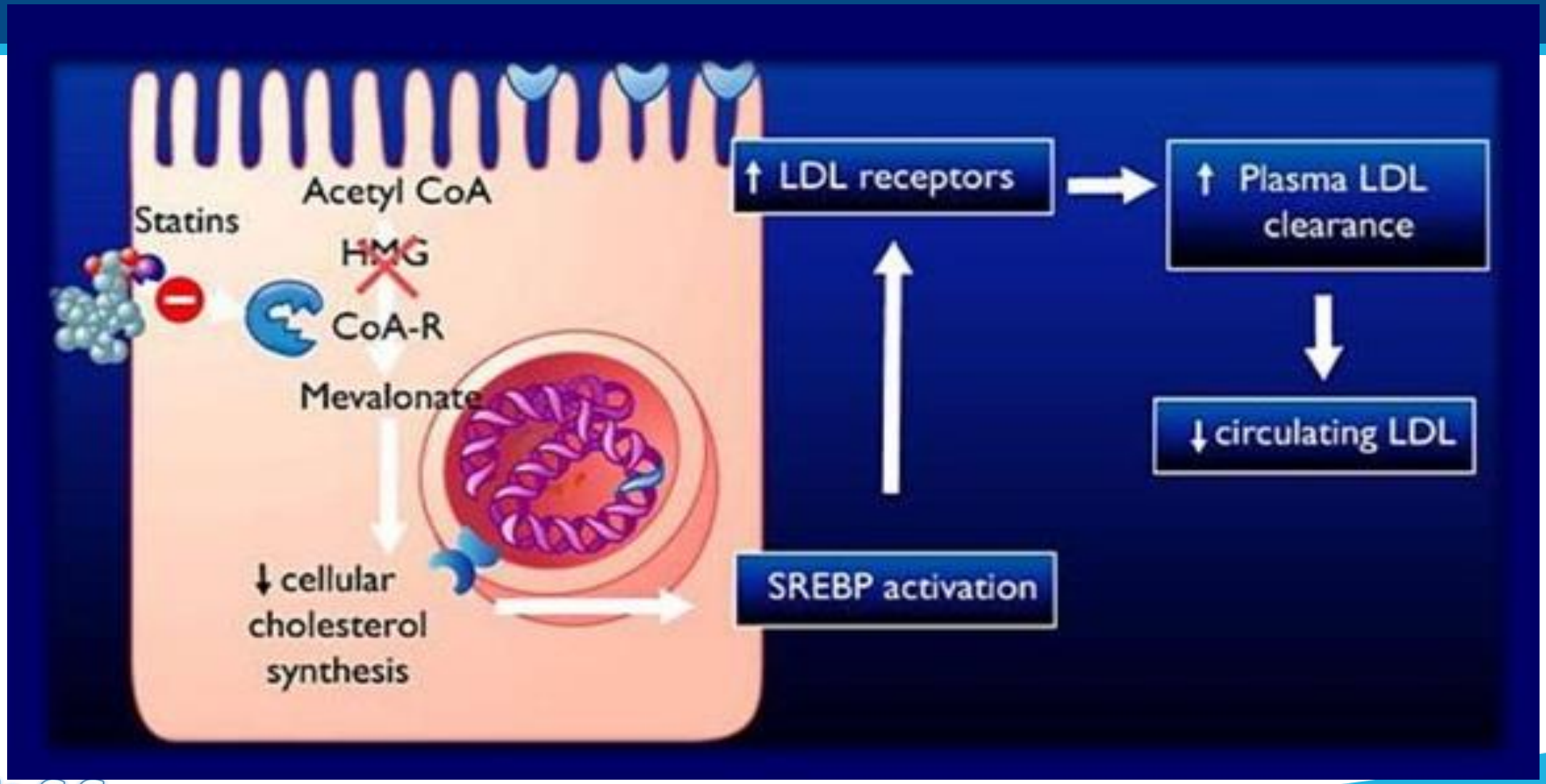
Disclosure of potential conflicts of interest

Lale Tokgözoğlu - Hacettepe University Hospitals, Ankara, Turkey

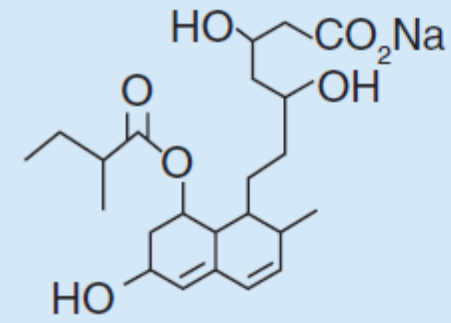
EMPLOYEMENT	None
RESEARCH GRANT / RESEARCH SUPPORT	Amgen
SPEAKER BUREAU	None
HONORARIA	Abbott,Actelion,Astra,Amgen,Bayer,Daiichi-Sankyo MSD,Mylan,Novartis, Novo Nordisk, Pfizer,Recordati, Sanofi,Sanovel,Servier
EXPERT WITNESS	None
OWNERSHIP INTEREST	None
CONSULTANT/ ADVISORY BOARD	Abbott, Bayer, Daiichi-Sankyo, Mylan, Novartis, Sanofi
OTHER	None


Biologic plausibility
Epidemiology
RCT
LDL-C Causality
Mendelian randomization
FH
Dose response relationship
Animal studies

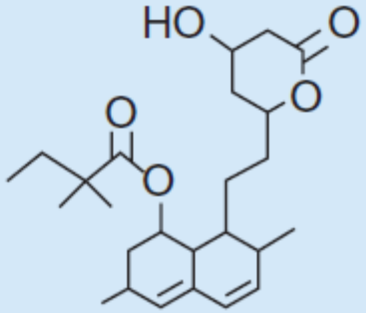
Statin action:



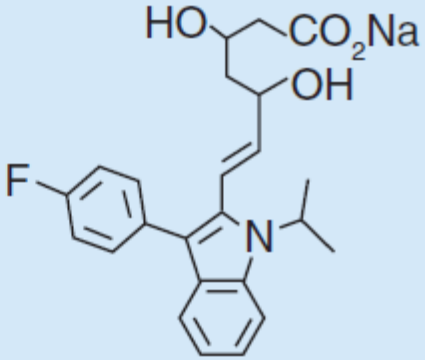
Statins: Differences in structure



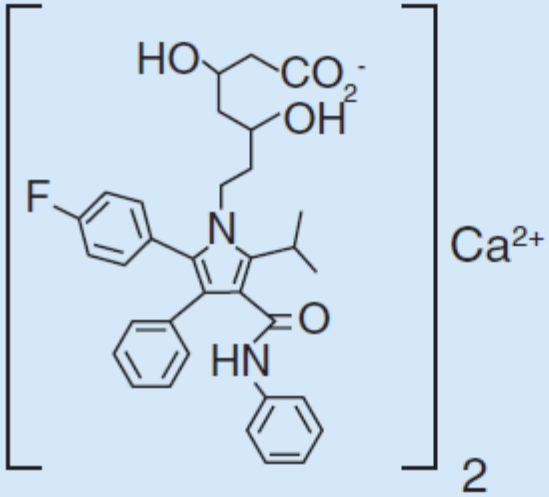
Pravastatin



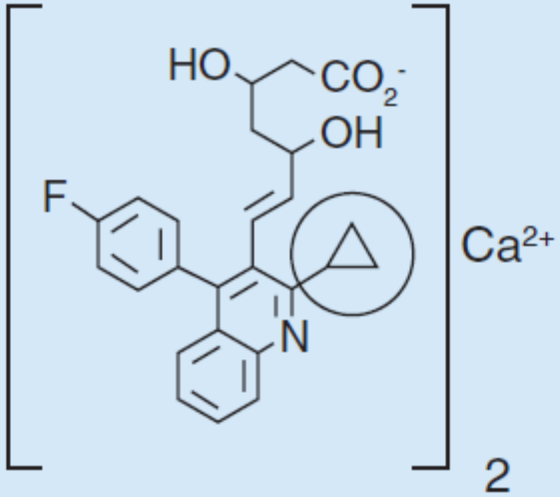
Simvastatin



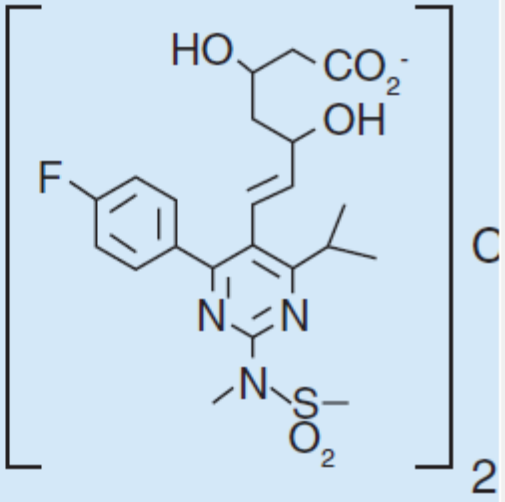
Fluvastatin



Atorvastatin



Pitavastatin



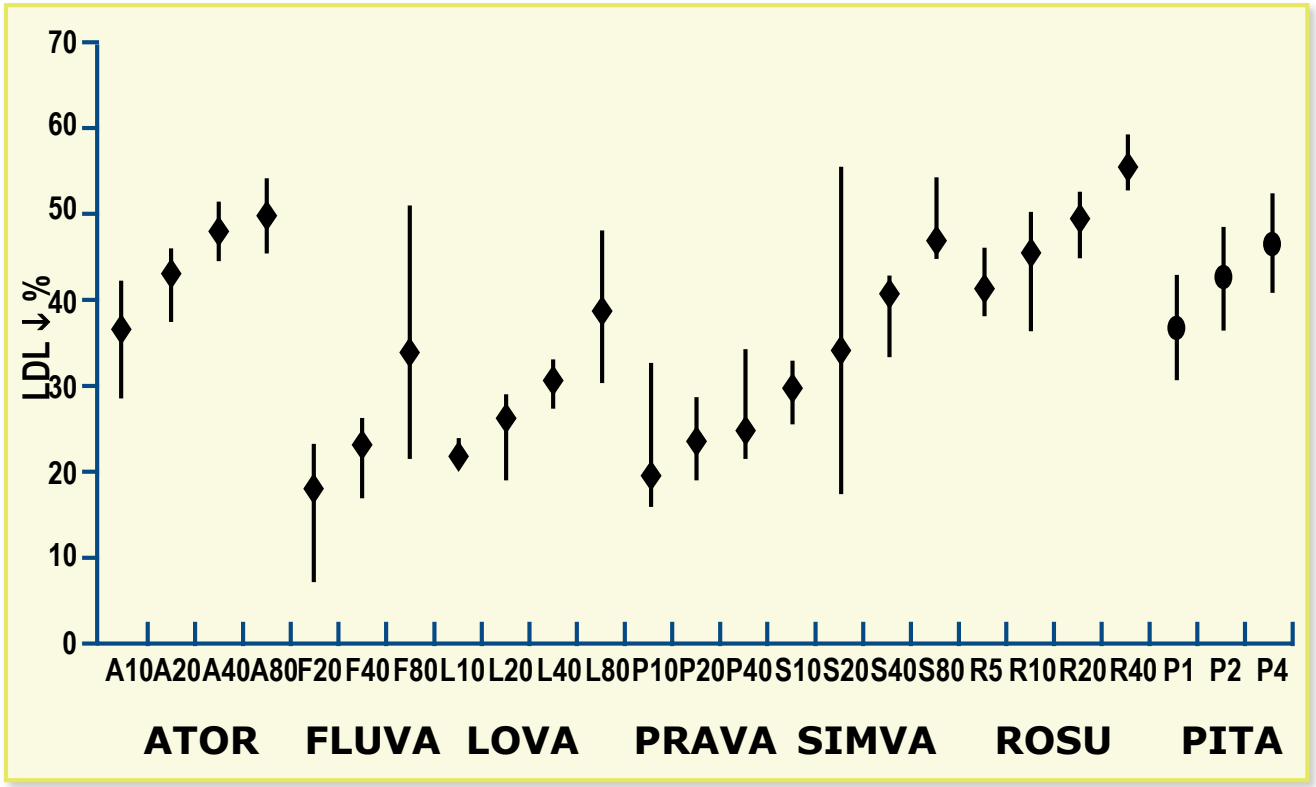
Rosuvastatin

Statin Pharmacokinetics:

	Bio-Availability	Half-Life, h	CYP450 Metabolism	Solubility
Lovastatin	< 5%	2 to 3	3A4	Lipophilic
Simvastatin	< 5%	2	3A4	Lipophilic
Pravastatin	17%	1.5 to 2	none	Hydrophilic
Fluvastatin	24%	1	2C9	Hydrophilic
Atorvastatin	12%	14	3A4	Lipophilic
Rosuvastatin	20%	20	2C9	Hydrophilic
Pitavastatin	43% to 51%	12	2C9, 2C8	Slightly Hydrophilic

Courtesy of Joyce L. Ross, MSN, CRNP, CLS, FNLA
Chapter 5 - Pharmacology of Lipid-Lowering Medications. Pharmacist's Guide to Lipid Management, 2nd edition, 2014.

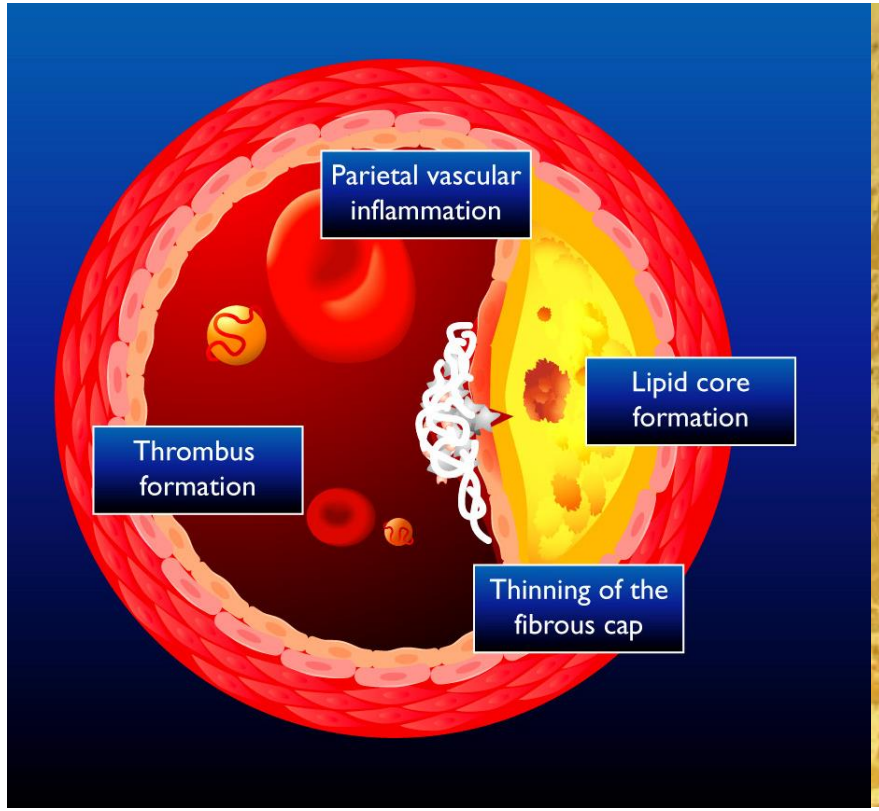
Statin Potency

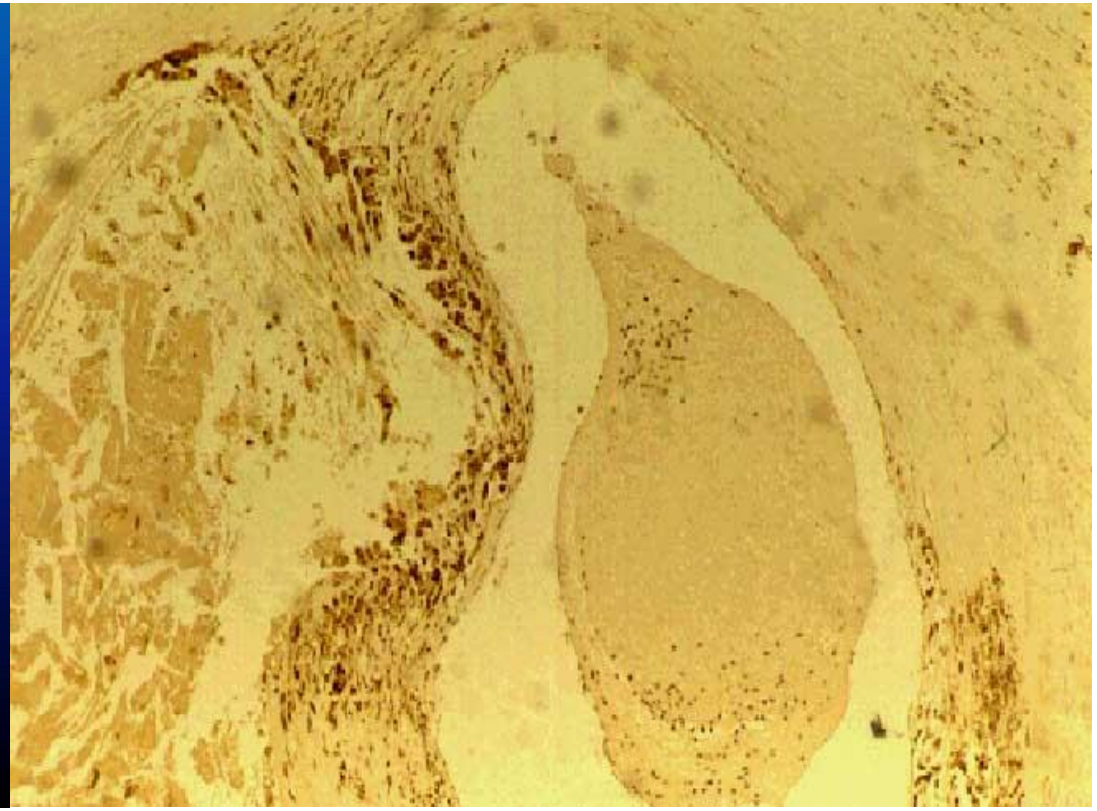


High Intensity	Moderate Intensity	Low Intensity
>= %50 reduction in LDL	**%30 - %50 reduction in LDL**	**<%30 reduction in LDL**
Atorvastatin (40↑) – 80 mg **Rosuvastatin 20** (40) **mg**	**Atorvastatin 10** (20) **mg** **Rosuvastatin** (5) **10 mg** **Simvastatin 20 – 40 mg ↑↓** **Pravastatin 40** (80) **mg** **Lovastatin 40 mg** Fluvastatin XL 80 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

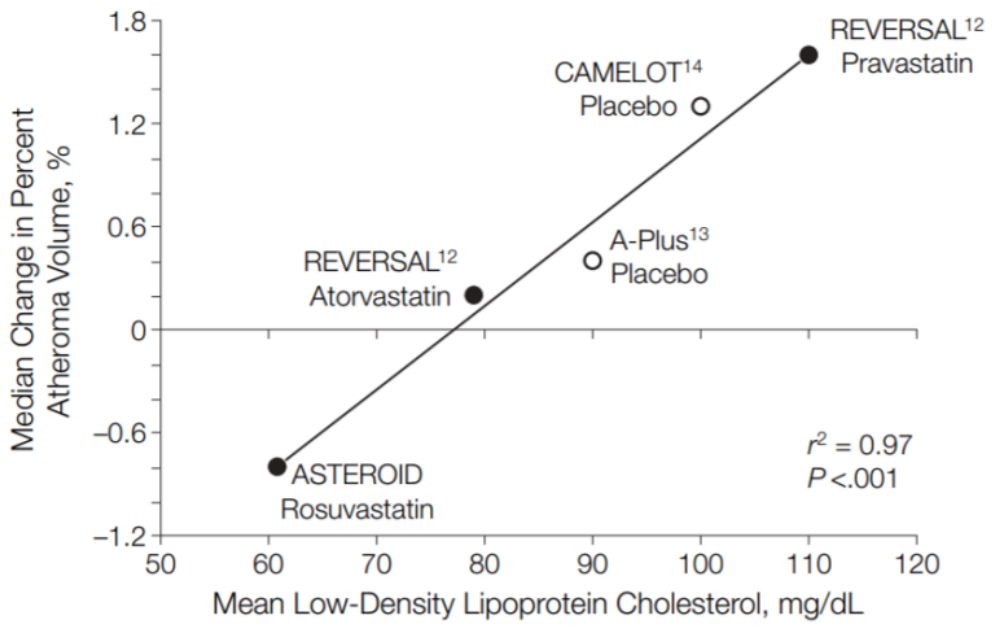
Most ACS Results from Rupture of Vulnerable Plaques:

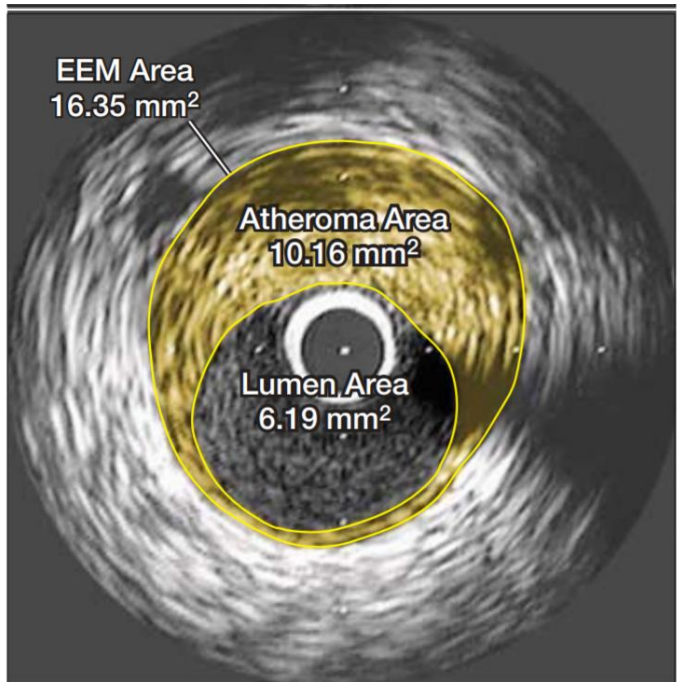
Big lipid core, thin fibrous cap, inflammation and neovascularisation

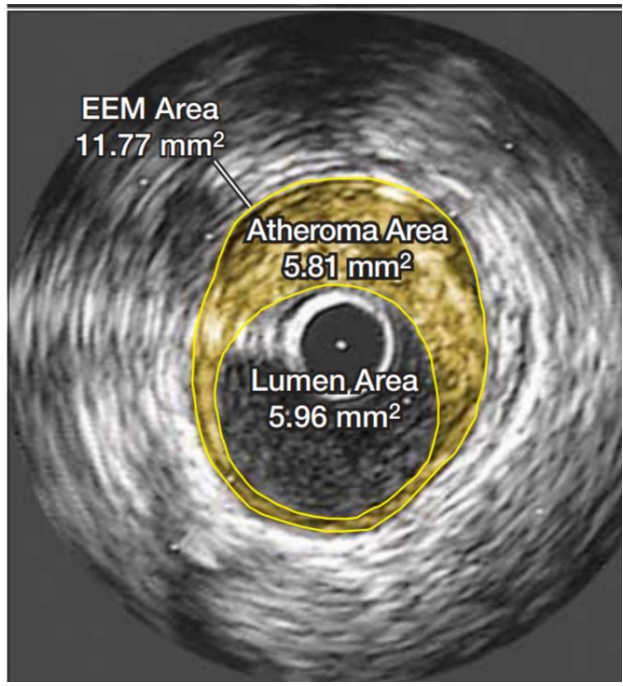




Relation between LDL and PAV:







JAMA 2006;295: 1556

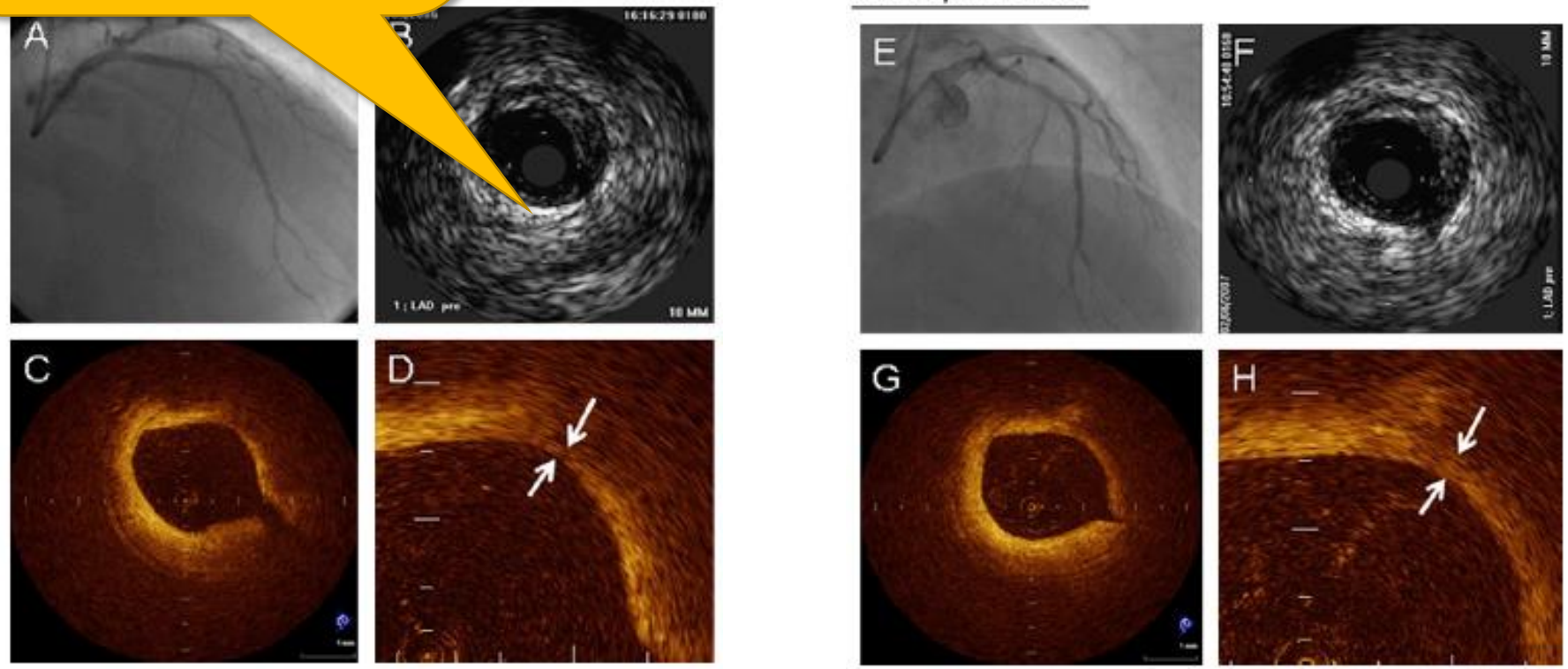
Fibrous cap thickens in 9 months

Effect of statin therapy on coronary fibrous-cap thickness in patients with acute coronary syndrome: Assessment by optical coherence tomography study

Shigeho Takarada, Toshio Imanishi, Takashi Kubo, Takashi Tanimoto, Hironori Kitabata, Nobuo Nakamura, Atsushi Tanaka, Masato Mizukoshi, Takashi Akasaka*

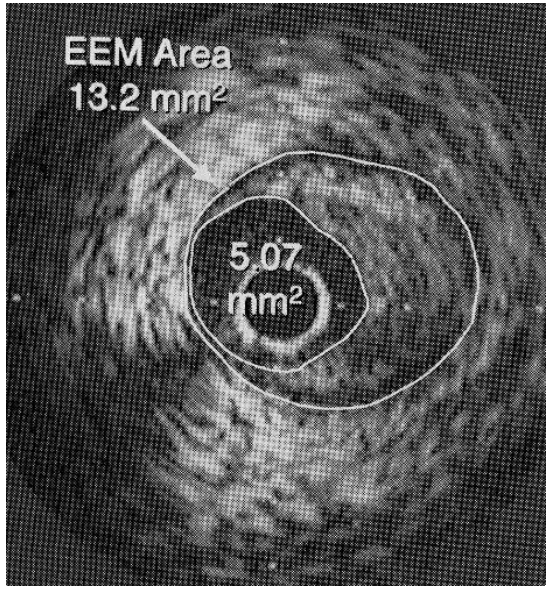
Department of Cardiovascular Medicine, Wakayama Medical University, Wakayama, Japan

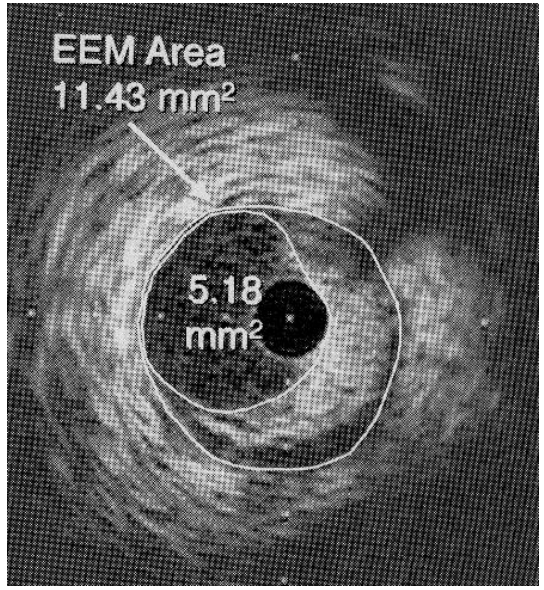
follow-up in 9 month

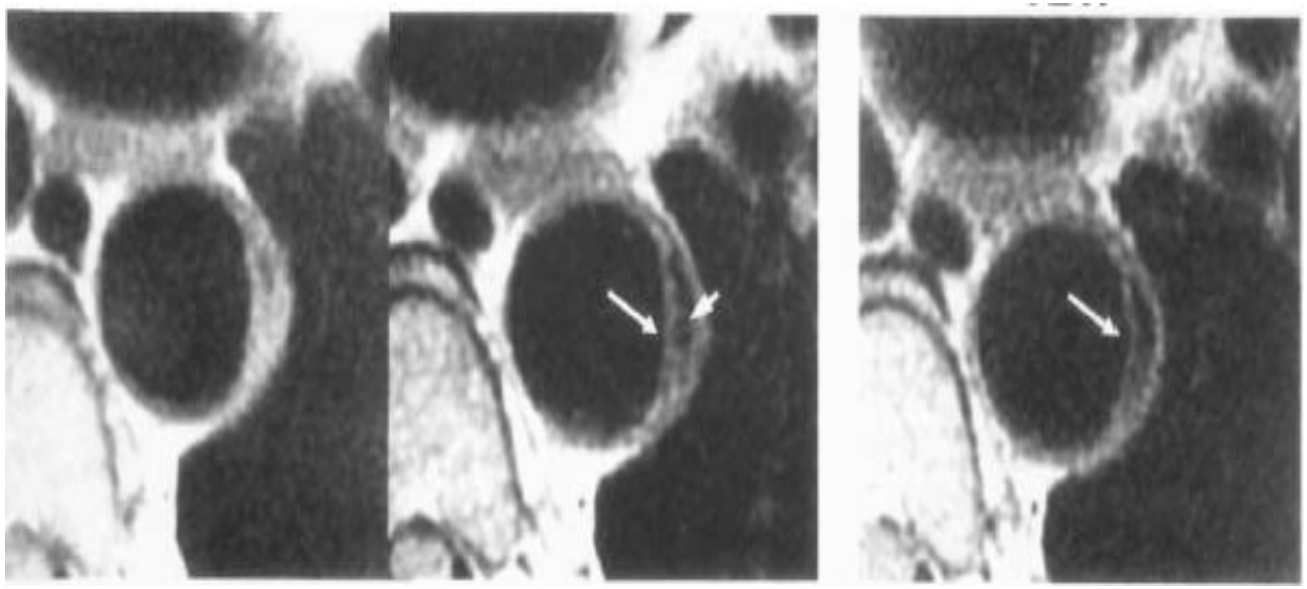


Atherosclerosis 202 (2009) 491–497

Statins Cause Plaque Regression and Stabilisation:







Atheroma Area = 8.13 mm²

Atheroma Area = 6.31 mm²

JAMA 2007;297:499
JAMA 2006;295:1556

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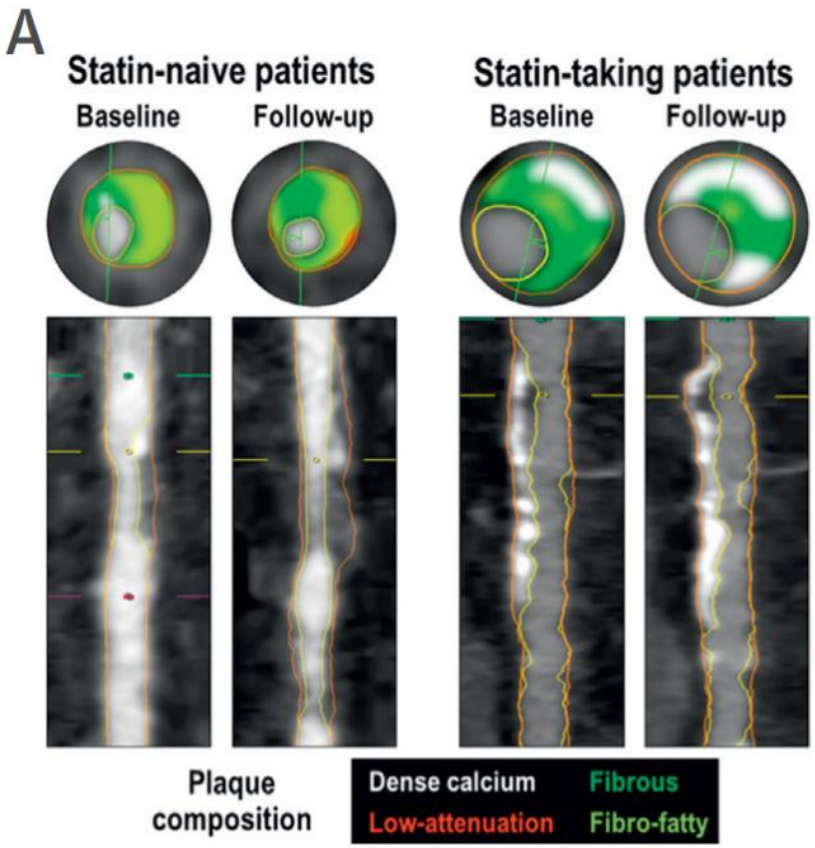
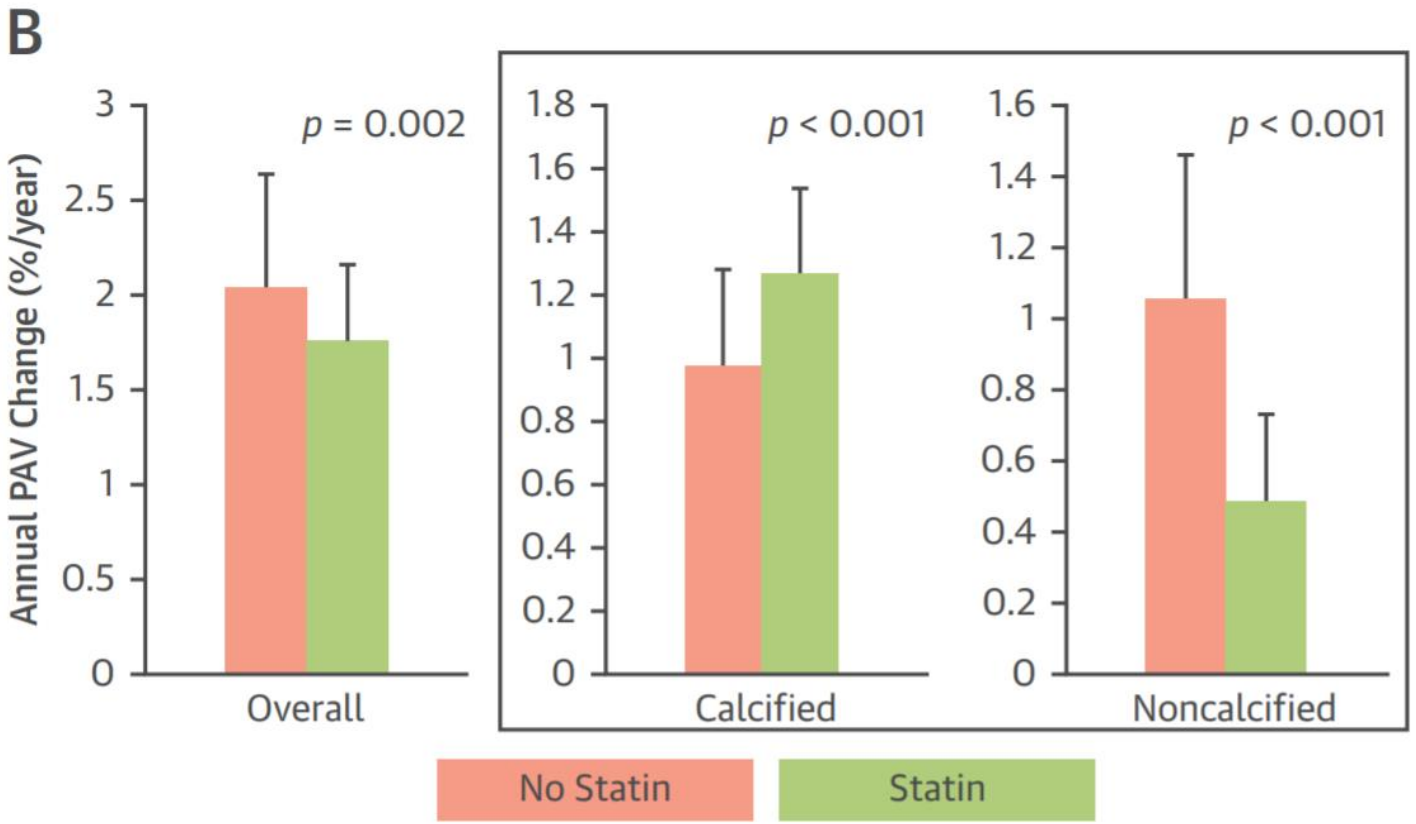
Statins Decrease Atheroma Volume and Increase Calcification: PARADIGM Study

n=1255 CT at least 2 years apart





JACC: Cardiovascular Imaging 11, 2018, 1475-1484

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Clinical Outcome Studies With Statins

1994

4S
WOSCOPS
CARE
AFCAPS/TexCAPS
LIPID

Decrease in mortality and morbidity compared to placebo

MIRACL
HPS
PROSPER
ALL-HAT LLT*
ASCOT-LLA
PROVE IT
ALLIANCE
CARDS
A to Z, 4 D*

Effective in different risk groups, ACS and active comparisons

TNT
IDEAL

More intensive LDL lowering

SPARCL
MEGA
JUPITER

2019

Other populations: Stroke, lower risk groups

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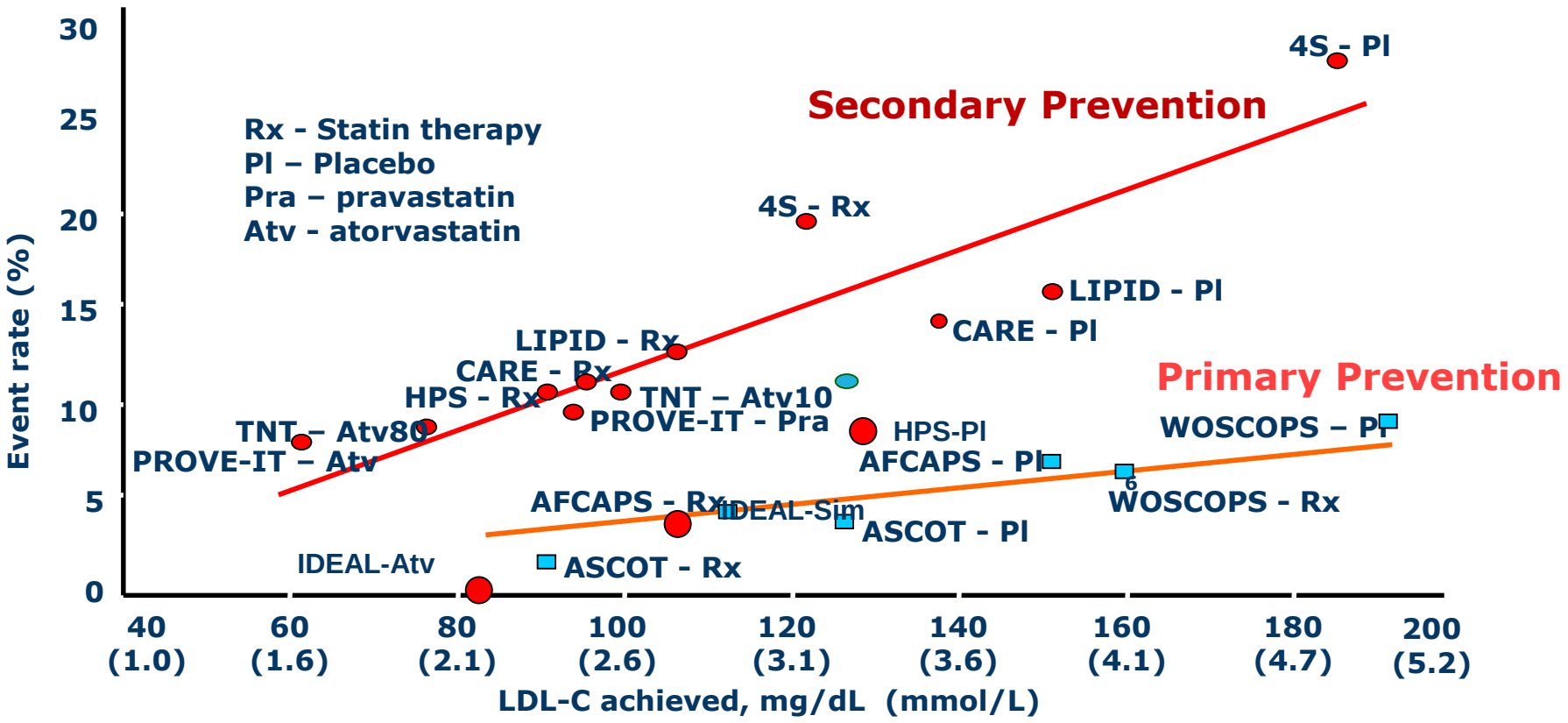
Relationship between LDL-C and CVD



Adapted from Rosenson RS. *Exp Opin Emerg Drugs.* 2004;9:269-279.
LaRosa JC et al. *N Engl J Med.* 2005;352:1425-1435.

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Key Lessons From Statin Trials (>160,000 pts)

Lowering LDL Reduces CV Events

	More statin	Less statin	Relative risk (CI)
Nonfatal MI	3485 (1.0)	4593 (1.3)	0.73 (0.69 - 0.78)
CHD death	1887 (0.5)	2281 (0.6)	0.80 (0.74 - 0.87)
Any major coronary event	5105 (1.4)	6512 (1.9)	0.76 (0.73 - 0.78)
CABG			0.75 (0.69 - 0.82)
PTCA			0.72 (0.65 - 0.80)
Unspecified			0.76 (0.70 - 0.82)
Any coronary rev			0.75 (0.72 - 0.78)
Ischaemic stroke			0.79 (0.72 - 0.87)
Haemorrhagic st			1.12 (0.88 - 1.43)
Unknown stroke			0.88 (0.76 - 1.01)
Any stroke	2302 (0.6)	2680 (0.8)	0.84 (0.79 - 0.89)
Any major vascular event	10973 (3.2)	13350 (4.0)	0.78 (0.76 - 0.80)

LDL-C reduction by 2 mmol/L would reduce the MVE risk by 45%

99% or 95% CI

0.4 0.6 0.8 1 1.2 1.4

Statin/more statin better

Control/less statin better

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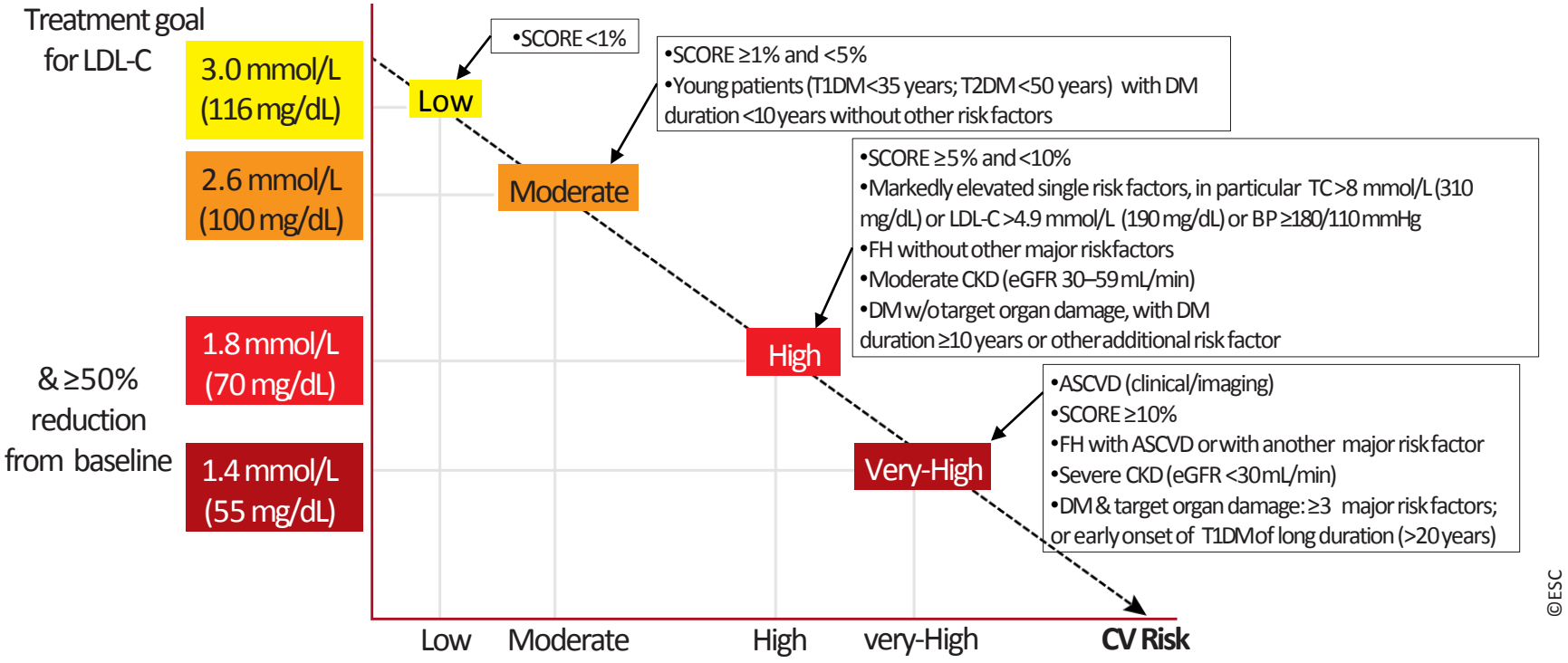
Lancet 2010;376-1670-81

Treatment Goals for Low-Density Lipoprotein Cholesterol (LDL-C) Across Categories of Total Cardiovascular Disease Risk



Recommendations for Pharmacological Low-Density Lipoprotein Cholesterol Lowering (1)

Recommendations	Class	Level
It is recommended to prescribe a high-intensity statin up to the highest tolerated dose to reach the goals[c] set for the specific level of risk.	I	A
If the goals[c] are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.	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 statin and ezetimibe, a combination with a PCSK9 inhibitor may be considered.	IIb	C

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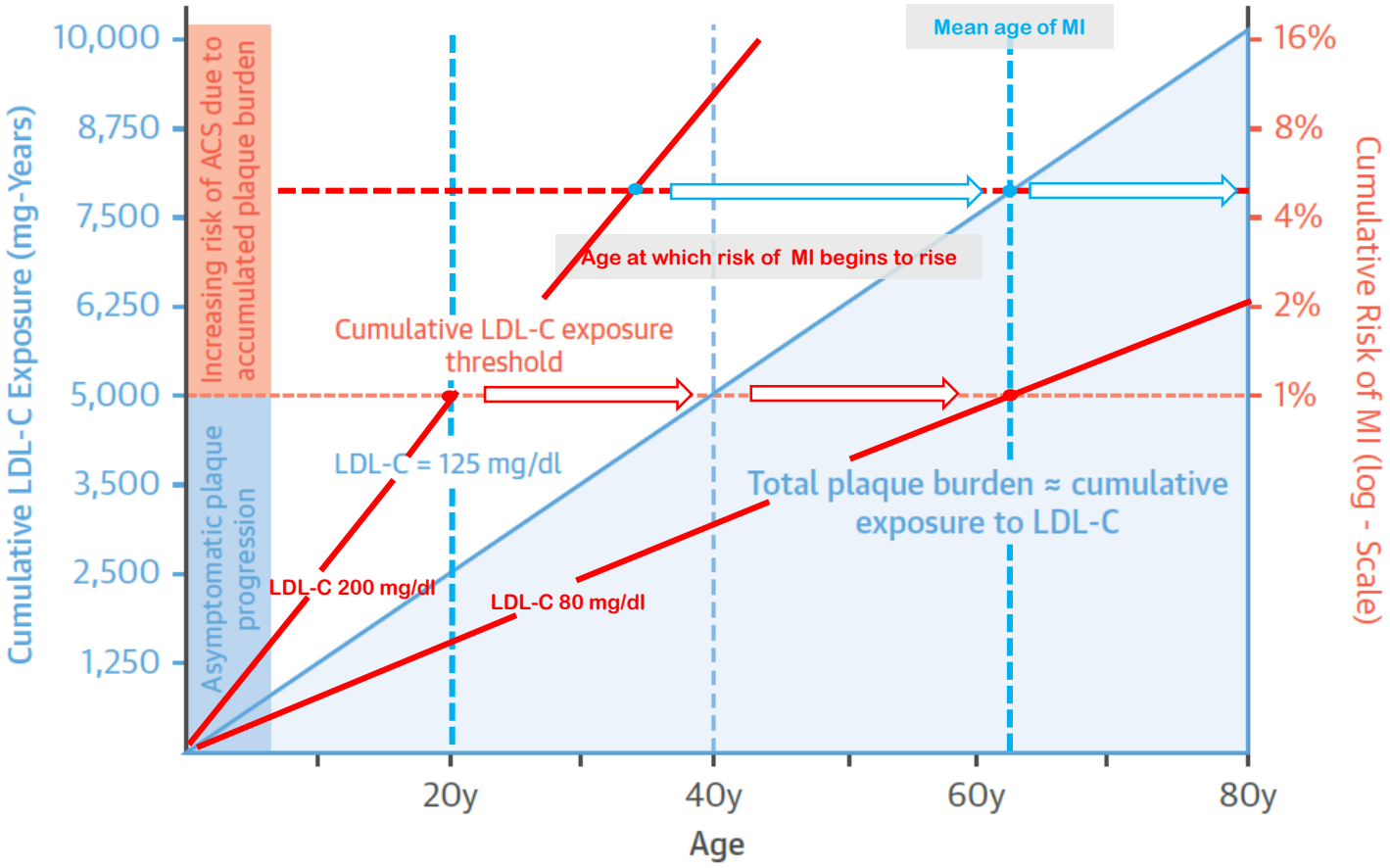
[c] For definitions see Full Text.

Is There Any Debate About When to Use Statins ?

- **Primary prevention with high LDL-C**
- **Primary prevention with low CV risk**
- **Elderly over 75 years**

Effect of Cumulative Exposure to LDL on Plaque Burden and CV Risk:



JACC 2018;72: 1141

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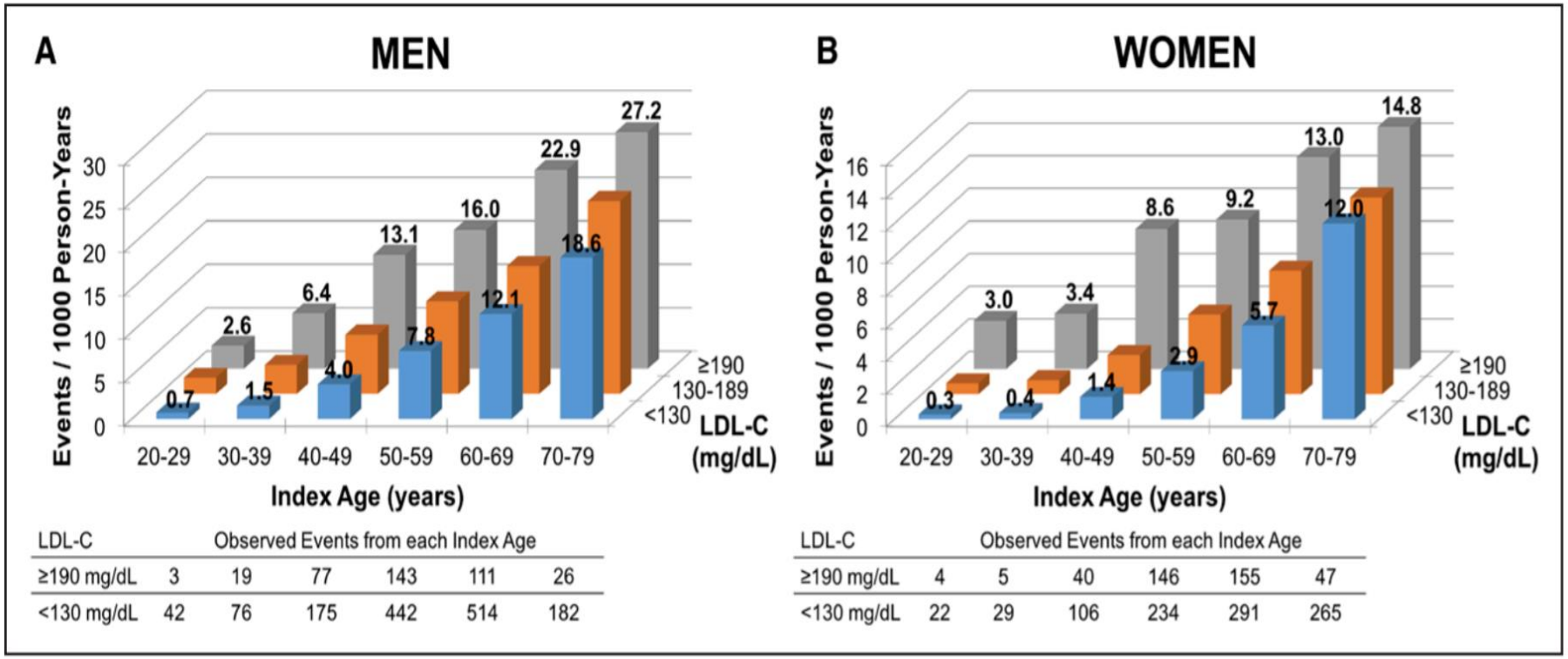
- **Exposure to lower LDL-C levels from a young age produce larger risk reductions given thereduced lifetime cumulative exposure to LDL-C**
- **Earlier LDL-C reduction more beneficial**

LDL Over 190 mg/dL Leads to 5 Fold 30 Year Risk of CAD



LDL-C	Observed Events from each Index Age					
≥190 mg/dL	3	19	77	143	111	26
<130 mg/dL	42	76	175	442	514	182

LDL-C	Observed Events from each Index Age					
≥190 mg/dL	4	5	40	146	155	47
<130 mg/dL	22	29	106	234	291	265

Circulation. 2016;134:9-19.

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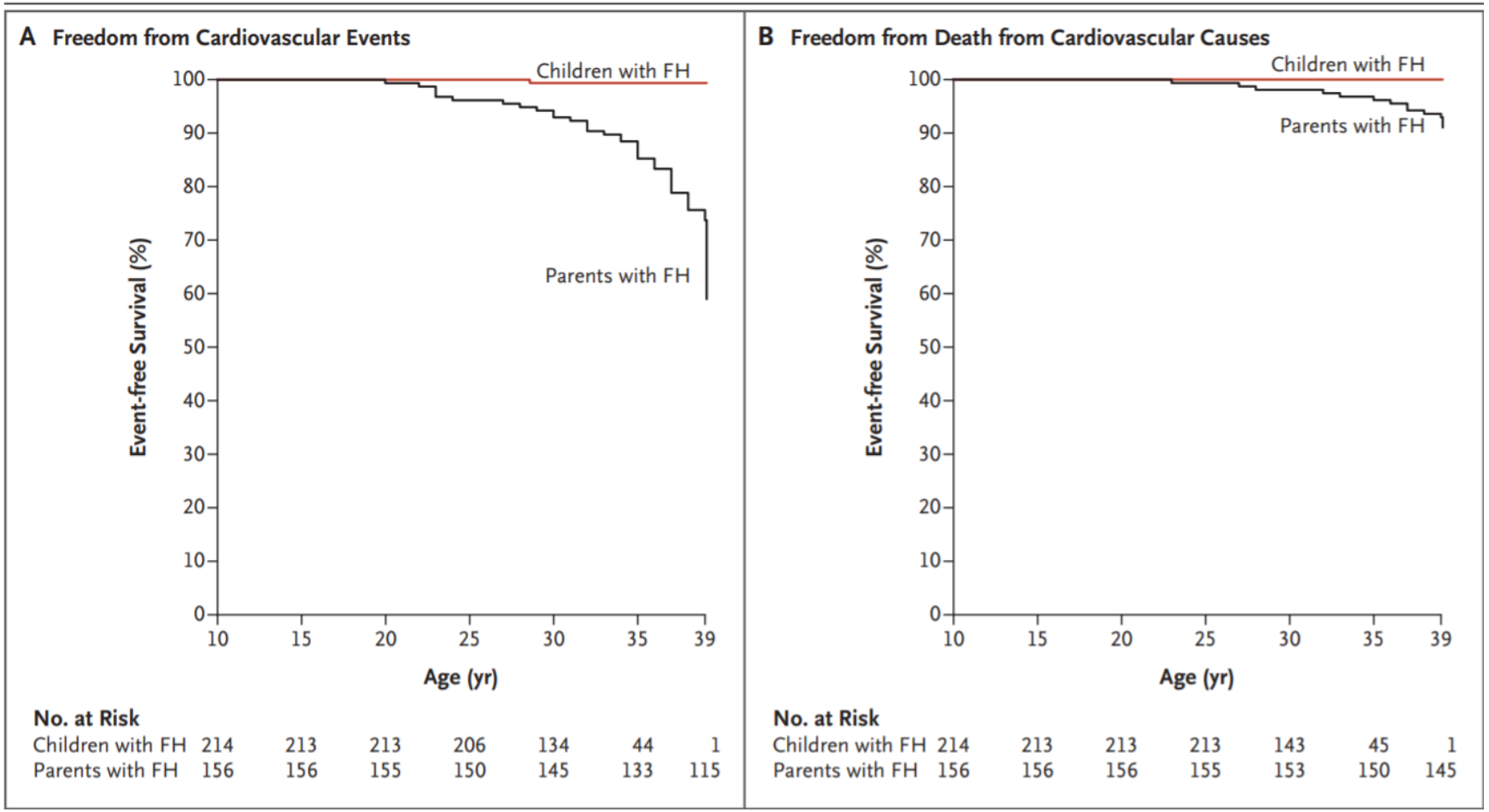
20 year Follow-up of Children With FH:



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NEJM 381;16 nejm.org October 17, 2019

Intervention Strategies as a Function of Total Cardiovascular Risk and Untreated Low-Density Lipoprotein Cholesterol 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)
Primary Prevention	<1 low-risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	I/C	I/C	IIa/A	IIa/A
	≥1 to <5, or moderate risk	Lifestyle advice	Lifestyle advice	Lifestyle advice	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention, consider adding drug if uncontrolled	Lifestyle intervention and concomitant drug intervention
	Class[a]/Level[b]	I/C	I/C	IIa/A	IIa/A	IIa/A	IIa/A
	≥5 to <10, or high- risk	Lifestyle advice	Lifestyle advice	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
	Class[a]/Level[b]	IIa/A	IIa/A	IIa/A	I/A	I/A	I/A
	≥10, or at very-high risk due to a risk condition	Lifestyle advice	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
	Class[a]/Level[b]	IIa/B	IIa/A	I/A	I/A	I/A	I/A
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

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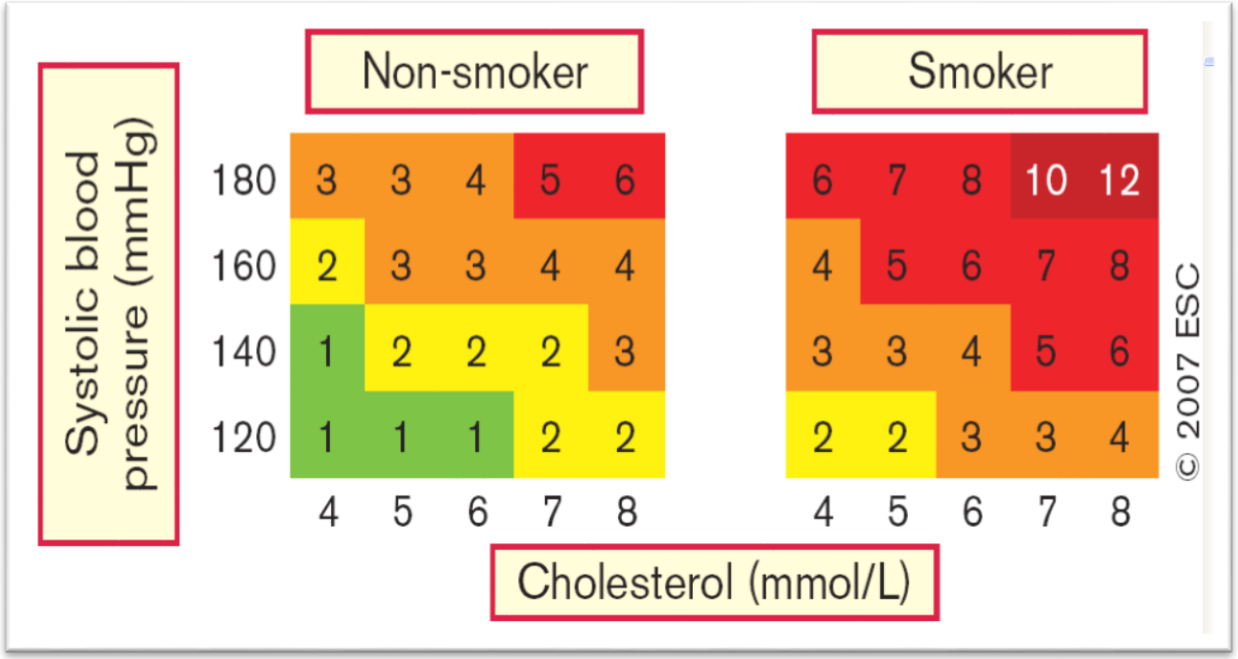
What About Subjects With Low Risk ?

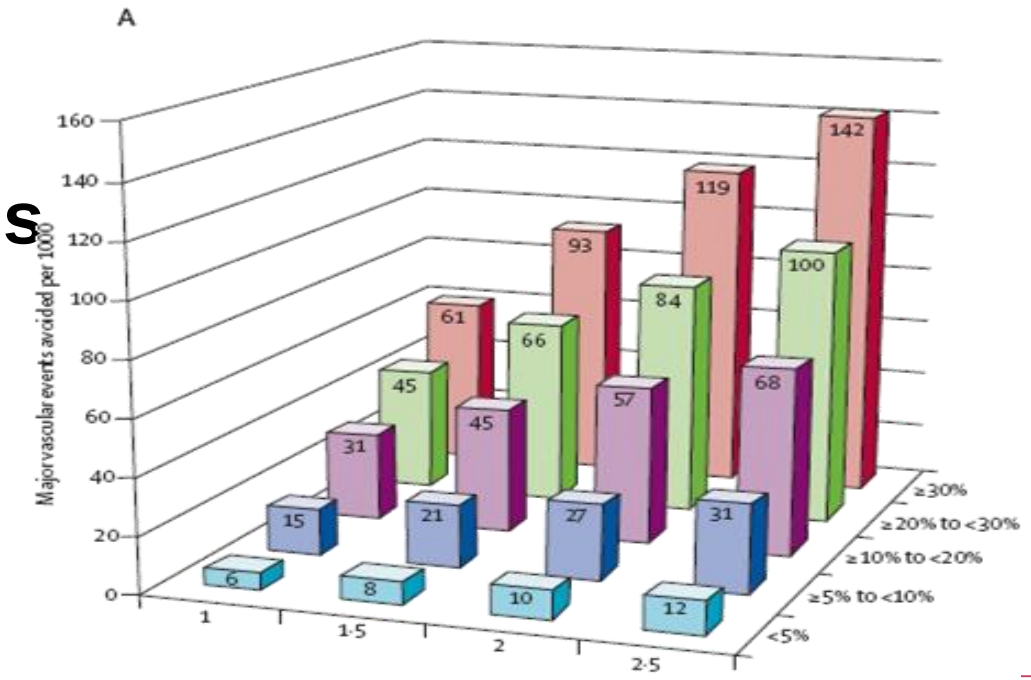
A low absolute 10 year risk in a younger person may conceal a high relative risk:

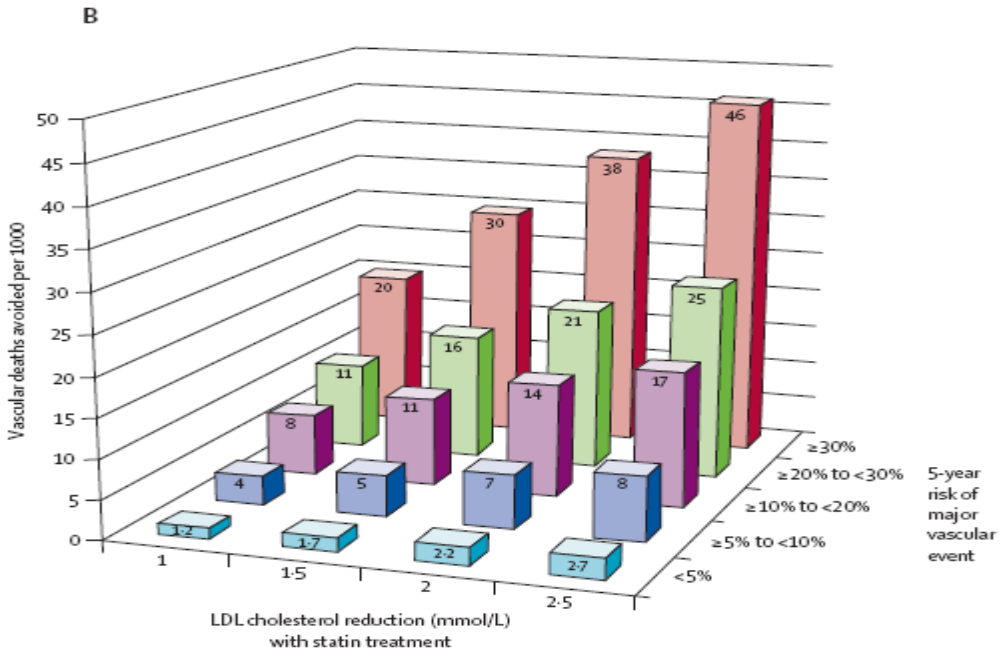
- **Use relative risk chart**
- **Risk age**
- **Calculate lifetime risk ?**



Low Risk Patients Benefit From Statins:

AFCAPS/TexCAPS
JUPITER
HOPE-3
CTT analysis





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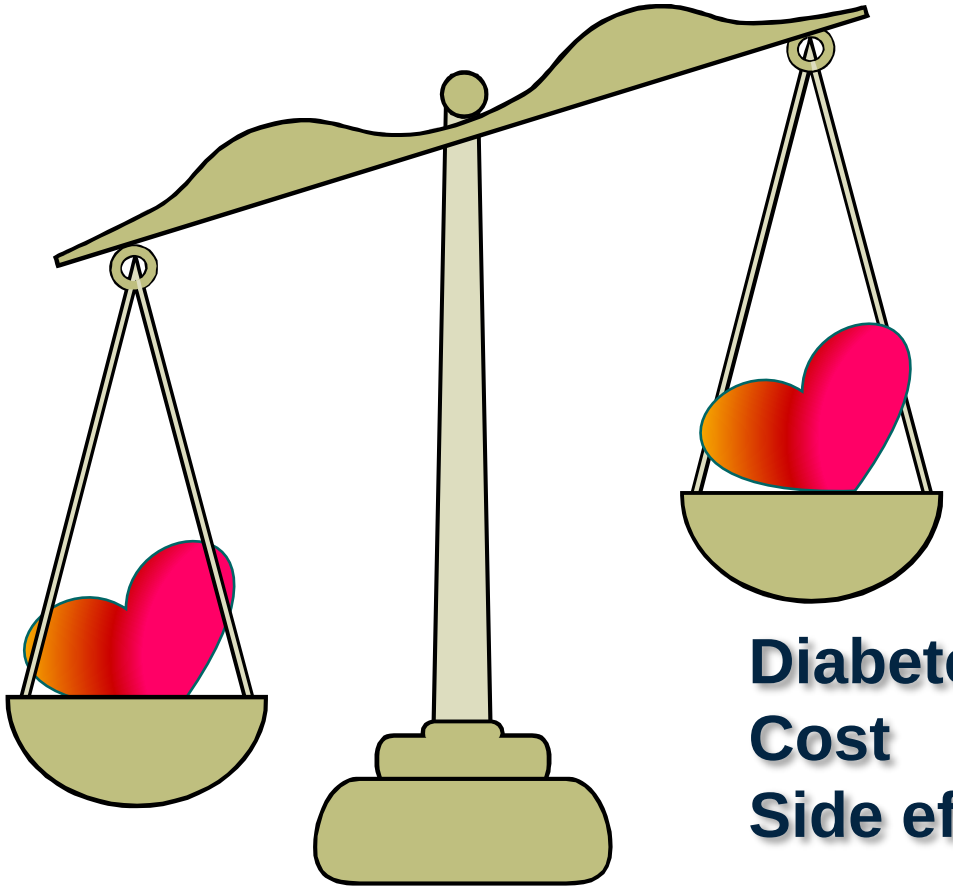
Lancet 2012

Prolonged Use of Statins in Low Risk:



CV benefits

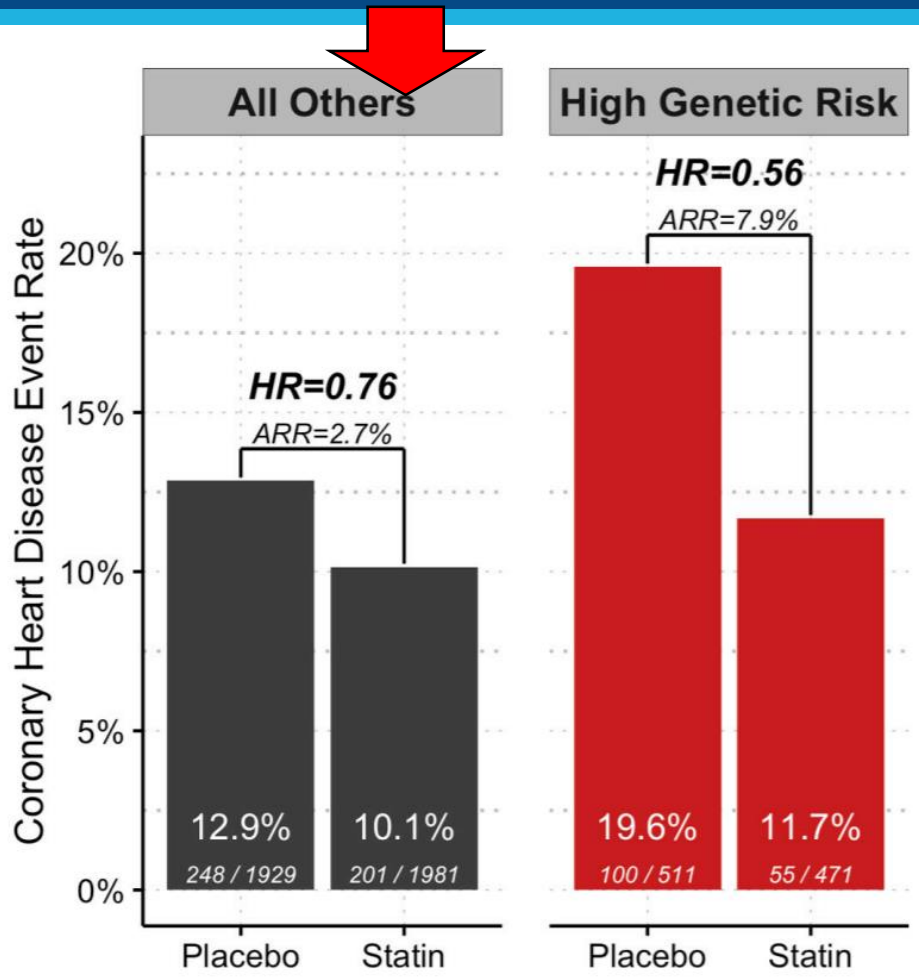
Diabetes risk
Cost
Side effects

What Other Parameter Can Help Us Decide in Seemingly Low Short Term Risk Patients?

- Genetics
- Biomarkers
- Imaging

Polygenic scores identify who will benefit most from statin despite similar LDL lowering:

RRR with statin 46 % at high risk, 26 % in others



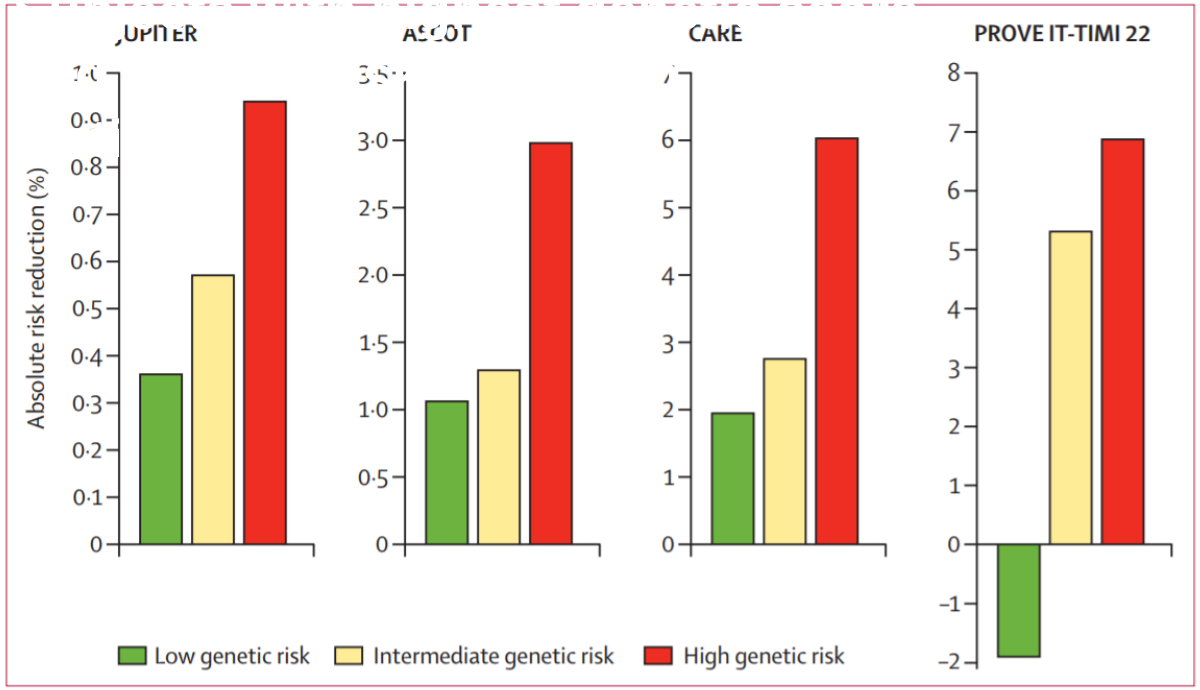


Figure 3: Absolute risk reductions of coronary heart disease events with statin therapy across genetic risk score categories

Mega et al Lancet (2015) 385:2264-71

Natarajan et al Circulation (2017) 135:2091-101

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Can We Improve Risk Prediction by Adding More Parameters-Biomarkers ?

Inflamation:
hs CRP
GDF-15
Fibrinogen

Plaque instability:
PAPP-A
MPO
MMPs

Neurohormonal activation:
Copeptin
MR-proADM

Platelet activation/thrombosis:
Lp-PLA_2
S-PLA_2
S CD40L
PAI-1
D-Dimer

Myocardial stress:
NT-proBNP
NT-proANP
ST 2
ET-1
Gal-3
NRG-1

Micro RNAs

Myocardial necrosis:
hs-Tn
H-FABP

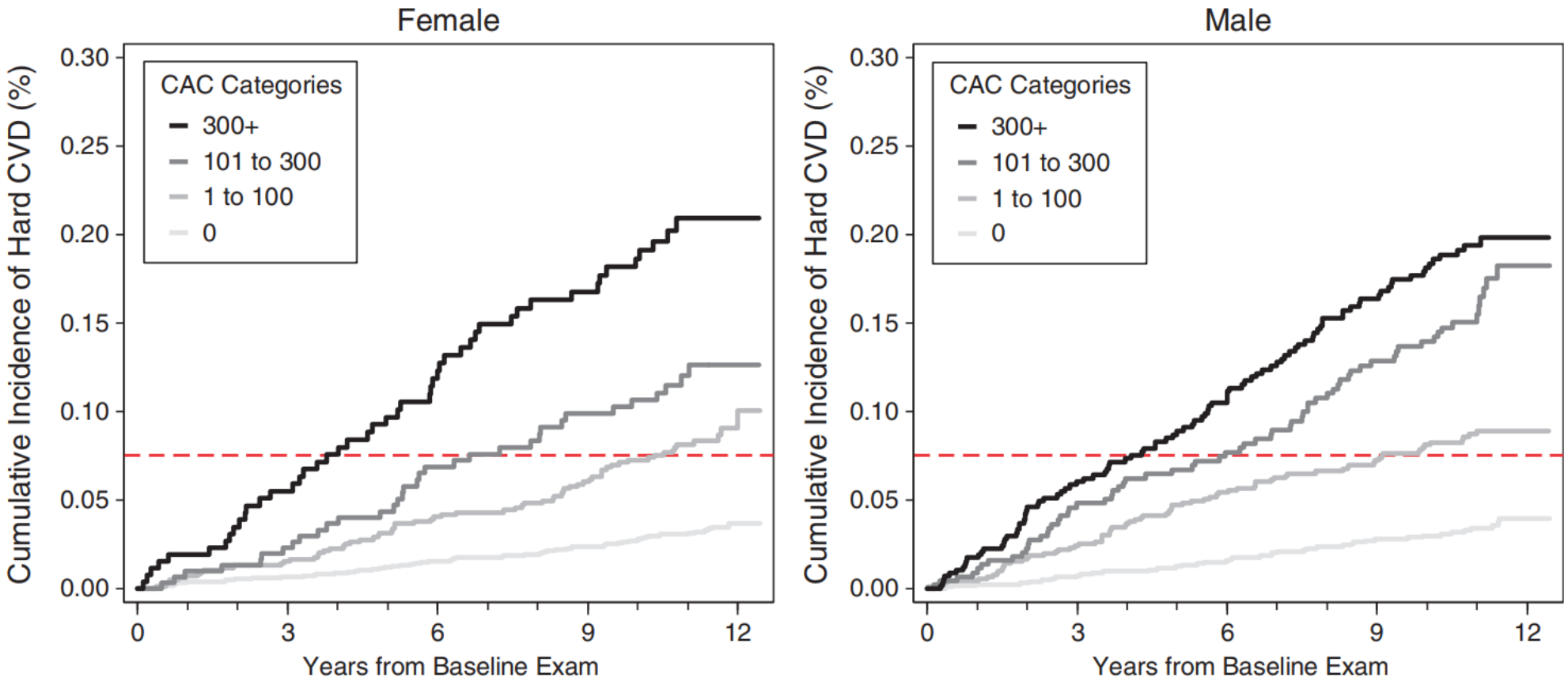
Lipidomics:
TAG
CE
PE

Proteomics:
Brached chain amino acids

Metabolomics:
Quartose IR

Ten-year Association of Coronary Artery Calcium with ASCVD Events: MESA CAC a risk modifier !

(n=6814, age 45-84)



N=6,783. Red dashed line shows 7.5% risk.

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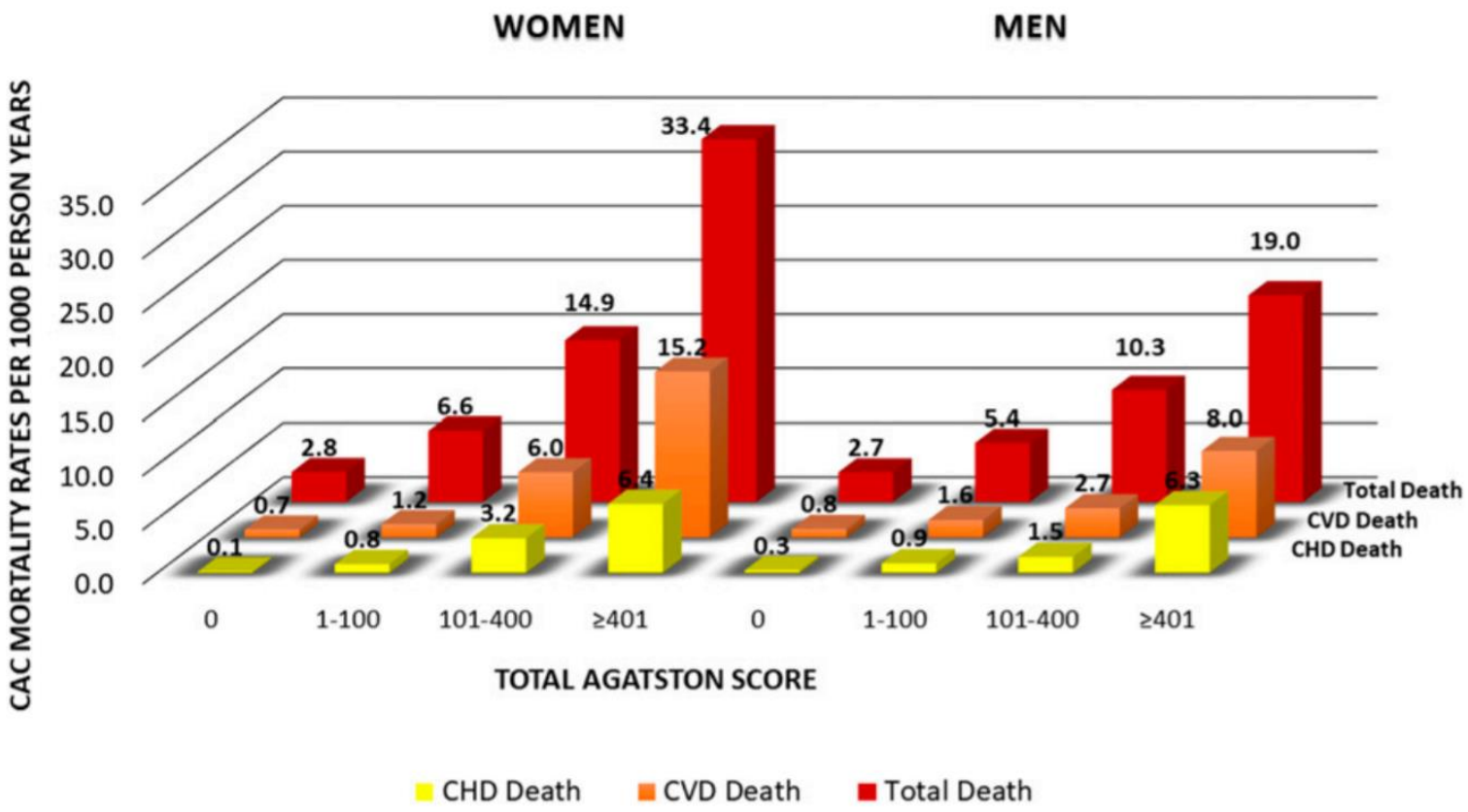
European Heart Journal (2018) 39, 2401

CAC Predicts Mortality Better in Women:



Diabetes Care August 17, 2020

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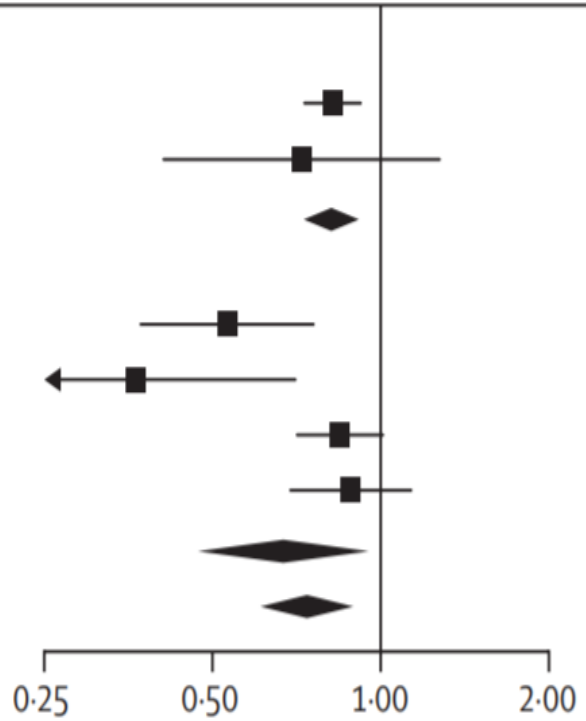
Effect of LLT on Risk of MACE in Elderly:

	Events (% per year)		Weight (%)	RR (95% CI) per 1 mmol/L reduction in LDL cholesterol
	Experimental group	Control group		
Statin				
CTTC[5]	802 (4·1%)	893 (4·7%)	96·0	0·82 (0·73–0·92)
Treat Stroke to Target[14]	32 (2·9%)	42 (3·6%)	4·0	0·72 (0·41–1·28)
Random effects model for statin (p=0·0005)				0·82 (0·73–0·91)
Non-statin				
IMPROVE–IT[11]	454 (5·5%)	563 (6·6%)	25·0	0·53 (0·36–0·74)
EWTOPIA 75[12]	89 (1·3%)	133 (1·9%)	15·4	0·36 (0·18–0·69)
FOURIER[15]	128 (4·5%)	155 (5·7%)	30·9	0·85 (0·71–1·01)
ODYSSEY OUTCOMES[13]	105 (7·6%)	123 (8·5%)	28·7	0·88 (0·69–1·13)
Random effects model for non-statin (p=0·0256)				0·67 (0·47–0·95)
Random effects model for all studies (p=0·0019)				0·74 (0·61–0·89)



Lancet Vol 396 November 21, 2020

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Effect of LLT on Risk of MACE in Elderly vs Young

	Events (% per year)		RR (95% CI) per 1 mmol/L reduction in LDL cholesterol
	Experimental group	Control group	
Older patients			
Statin treatment	834 (4·1)	935 (4·7)	0·82 (0·73–0·91)
Non-statin treatment	776 (5·1)	974 (6·1)	0·67 (0·47–0·95)
Random effects model for older patients (p=0·0019)			0·74 (0·61–0·89)
Younger patients			
Statin treatment	9805 (2·9)	12 161 (3·6)	0·77 (0·75–0·79)
Non-statin treatment	4525 (4·5)	4933 (5·2)	0·90 (0·86–0·94)
Random effects model for younger patients (p=0·0001)			0·85 (0·78–0·92)

Lancet Vol 396 November 21, 2020

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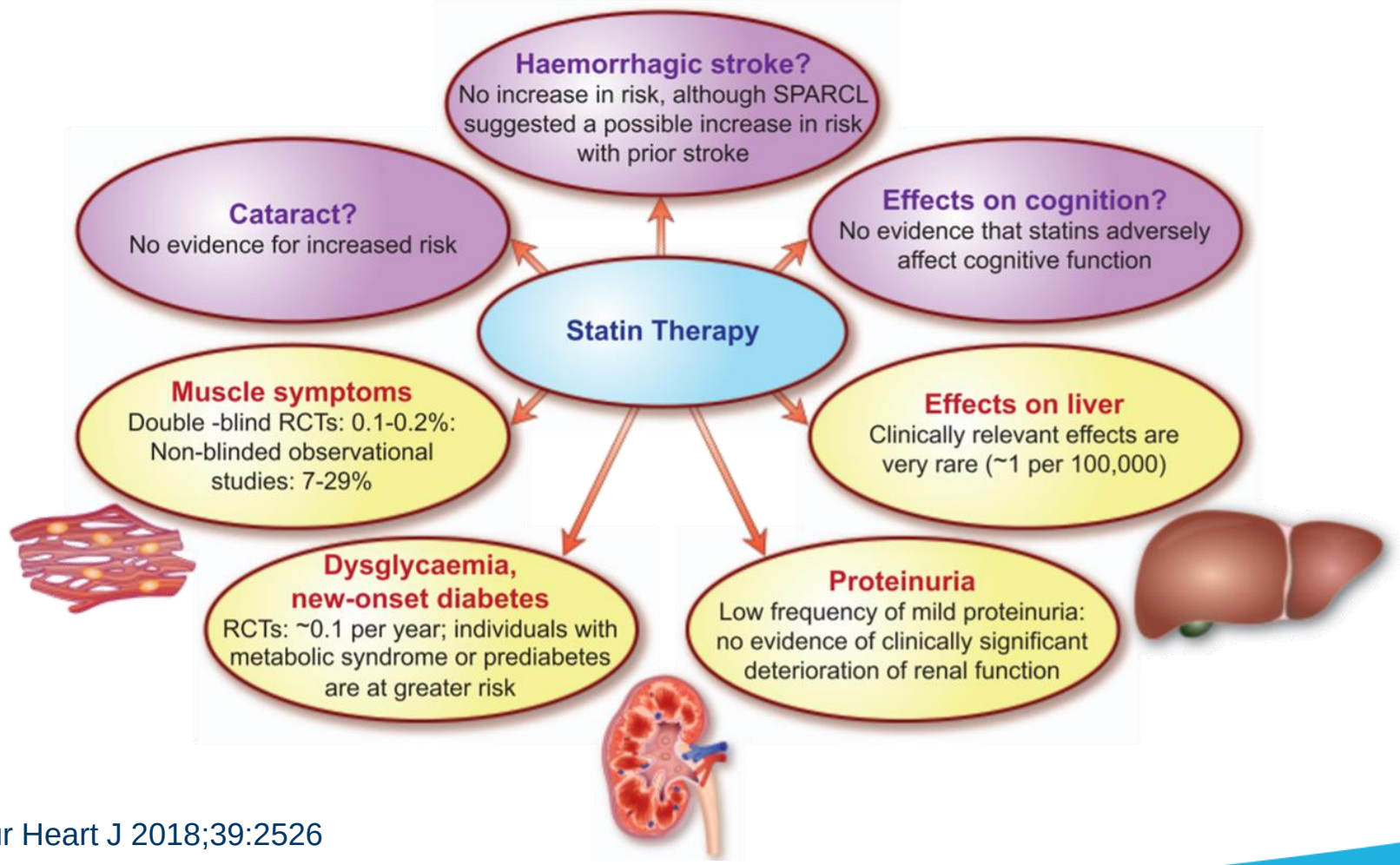
The Established Cardiovascular Benefits of Statins Outweigh the Risk of Adverse Effects:



Eur Heart J 2018;39:2526

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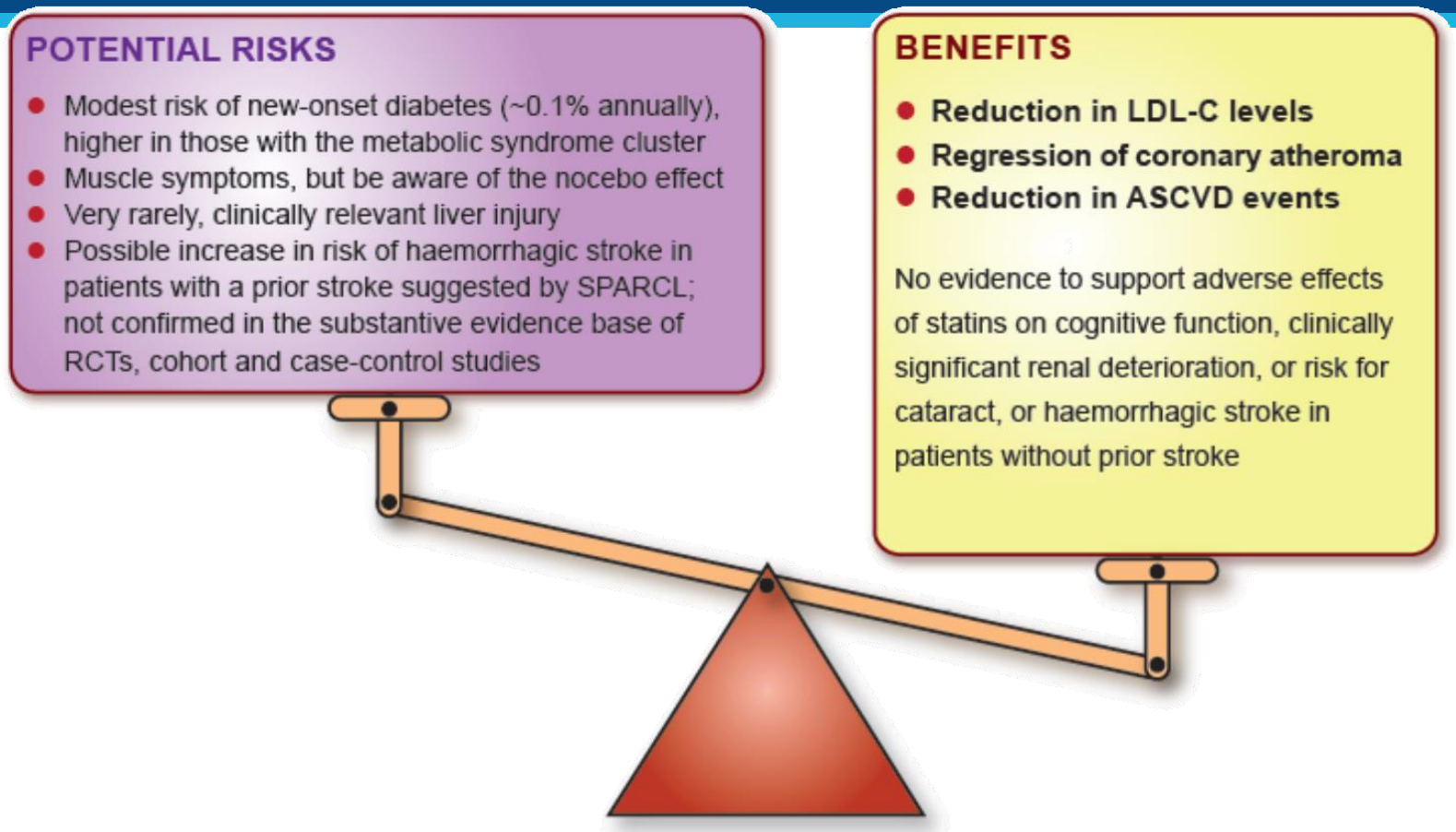
STATINS:
Highly Favourable Benefit vs. Risk Ratio



the established cardiovascular benefits of statin therapy far outweigh the risk of any such adverse effects

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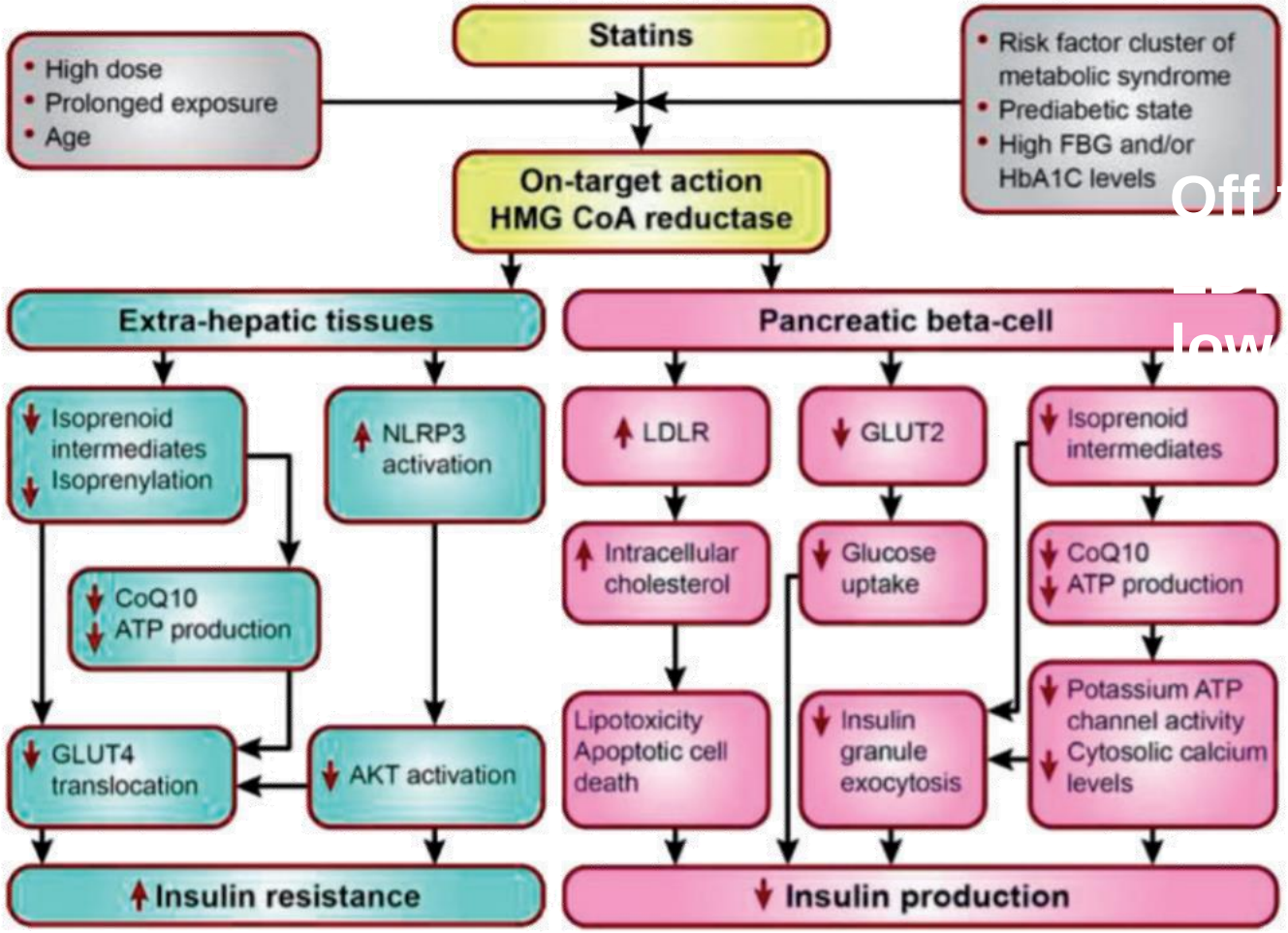
Highest Risk of Adverse Events:

- Elderly sp after age 80
- Female
- Low BMI
- Hypothyroid
- Renal-hepatic impairment
- Recent surgery
- Polypharmacy
- Vit D deficient-for myalgia

Common Drug Interactions:

- Macrolide antibiotics
- Fibrates
- Cyclosporine
- Amiodarone
- Verapamil
- Antifungals
- HIV protease inhibitors
- CYP450 metabolism may be important

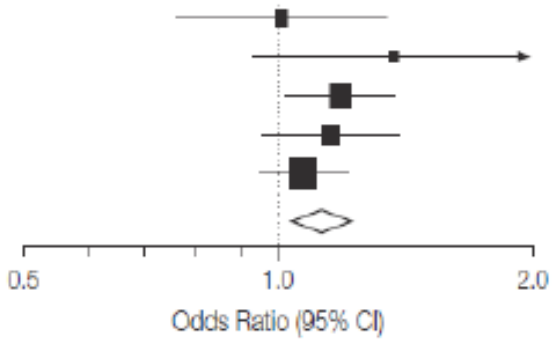
Why do Statins Affect DM ?

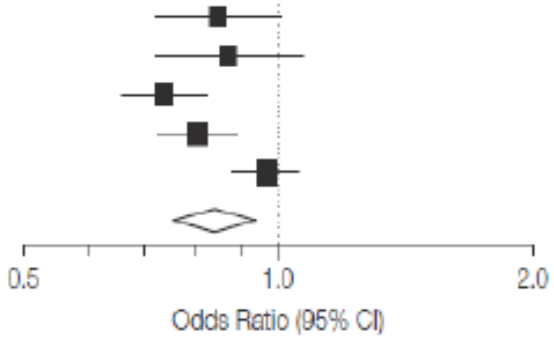


European Heart Journal (2018) 39, 2526

Statins, Dysglycemia and CV Risk:

	Cases/Total, No. (%)		
	Intensive Dose	Moderate Dose	OR (95% CI)
Incident Diabetes			
PROVE IT–TIMI 22,[18] 2004	101/1707 (5.9)	99/1688 (5.9)	1.01 (0.76-1.34)
A to Z,[17] 2004	65/1768 (3.7)	47/1736 (2.7)	1.37 (0.94-2.01)
TNT,[15] 2005	418/3798 (11.0)	358/3797 (9.4)	1.19 (1.02-1.38)
IDEAL,[16] 2005	240/3737 (6.4)	209/3724 (5.6)	1.15 (0.95-1.40)
SEARCH,[5] 2010	625/5398 (11.6)	587/5399 (10.9)	1.07 (0.95-1.21)
Pooled odds ratio	1449/16 408 (8.8)	1300/16 344 (8.0)	1.12 (1.04-1.22)
Heterogeneity: $I^2=0\%$; $P=.60$			
Incident CVD			
PROVE IT–TIMI 22,[18] 2004	315/1707 (18.4)	355/1688 (21.0)	0.85 (0.72-1.01)
A to Z,[17] 2004	212/1768 (12.0)	234/1736 (13.5)	0.87 (0.72-1.07)
TNT,[15] 2005	647/3798 (17.0)	830/3797 (21.9)	0.73 (0.65-0.82)
IDEAL,[16] 2005	776/3737 (20.8)	917/3724 (24.6)	0.80 (0.72-0.89)
SEARCH,[5] 2010	1184/5398 (21.9)	1214/5399 (22.5)	0.97 (0.88-1.06)
Pooled odds ratio	3134/16 408 (19.1)	3550/16 344 (21.7)	0.84 (0.75-0.94)
Heterogeneity: $I^2=74\%$; $P=.004$			





JAMA 2011;305:2556

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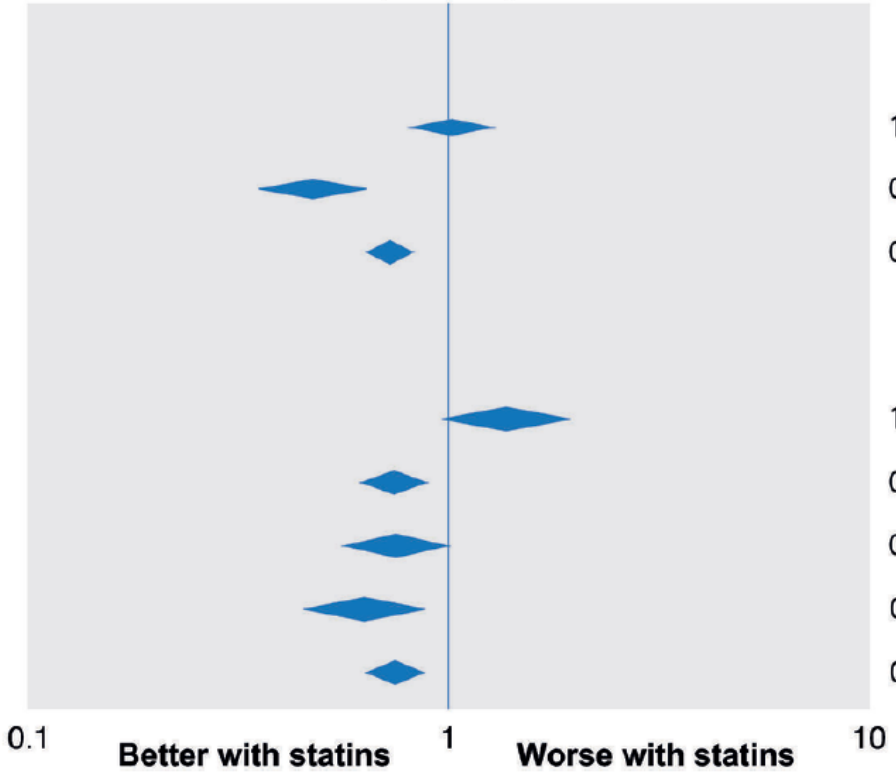
Statins and Diabetes:

- New onset DM seen in 1 case per 1000 patients per year of exposure while 5 CVD events prevented
- Higher dose of statins, elderly, patients with hypertension,multiple risk factors, obesity and metabolic syndrome
- Prava and pitava neutral on glycemic parameters
- DM diagnosed as HbA1c over 6.5 without symptoms, relevance for outcome?

Meta-analysis on Statins in Patients With Previous Stroke:

Outcome	No of events/total		Risk ratio (95% CI)
	Statin group	Control group	
Population: Previous intracerebral haemorrhage			
Recurrent ICH (3)	319/3052	2489/20643	1.04 (0.86 to 1.25)
All-cause mortality (12)	712/4743	6840/26778	0.49 (0.36 to 0.67)
Poor functional outcome (7)	919/1753	2795/6889	0.71 (0.67 to 0.75)
Population: Previous ischaemic stroke			
ICH (11)	332/51437	258/26949	1.36 (0.96 to 1.91)
Recurent ischaemic stroke (3)	1738/40808	862/11492	0.74 (0.66 to 0.83)
Any stroke (7)	2119/41628	1167/12353	0.82 (0.67 to 0.99)
All-cause mortality (13)	1045/48338	1638/20251	0.68 (0.50 to 0.92)
Poor functional outcome (19)	2915/9726	3592/9902	0.83 (0.76 to 0.91)



J Neurol Neurosurg Psychiatry 2019;**90**:75–83.

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- **Statins clearly decreased mortality and recurrence in stroke survivors**
- **Non-significant increase in ICH**
- **Limitations:**
  Not individual data, ICH definition differed between groups

Statin Intolerance:

- **Inability to use statins for long term because of significant symptoms and/or biomarker abnormalities that can be attributed to statins**
- **Inability to tolerate at least 2 different statins, one at the lowest dose**
- **Not attributable to established predispositions: hypothyroidism, drug interaction**

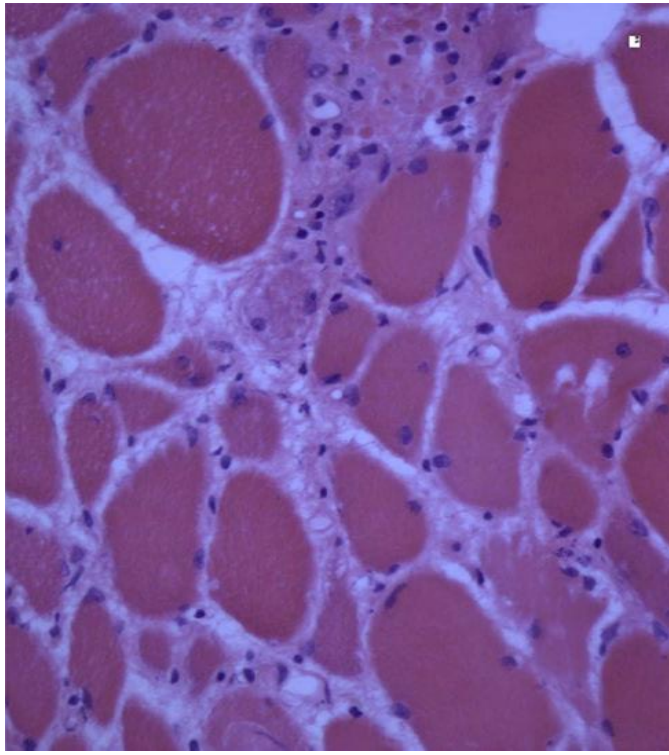
Can J Cardiol 2013;29: 1553

Diagnosis of True Intolerance is a Challenge:

- **Symptoms subjective, myalgia due to other causes common**
- **Unfounded fear of drug toxicity by patient and physician leads to overdiagnosis and use of the term ‘intolerance’ liberally**

SAMS:

- Usually symmetrical, proximal, large muscle groups
- Occurs within 4-6 wk of statin initiation
- Increasing dose, activity or interacting drug will precipitate it
- Consider risk factors:
  Age, female, low BMI, excess physical activity, alcohol, grapefruit juice, acute infections, surgery, vit D deficiency, renal or hepatic dysfuncion, myopathies, hypothyroidism



Defining SAMS:

- **There is no "gold standard" diagnostic test**

Symptoms	CK	When to consider SAMS?
Muscle symptoms	Normal	Often called myalgia; may be statin-related
Muscle symptoms	> ULN and <4 x ULN >4 <10 X ULN	Consider increased exercise; may be statin-related
Muscle symptoms	>10 X ULN	Often called myositis or 'myopathy' even in the absence of a muscle biopsy; Associated with statin or underlying muscle disease
Muscle symptoms	>40 X ULN	Rhabdomyolysis
None	> ULN and <4 X ULN	May be statin related
None	>4 X ULN	Clinical significance unknown

Stroes ES et al. Eur Heart J 2015 ;36:1012-1022

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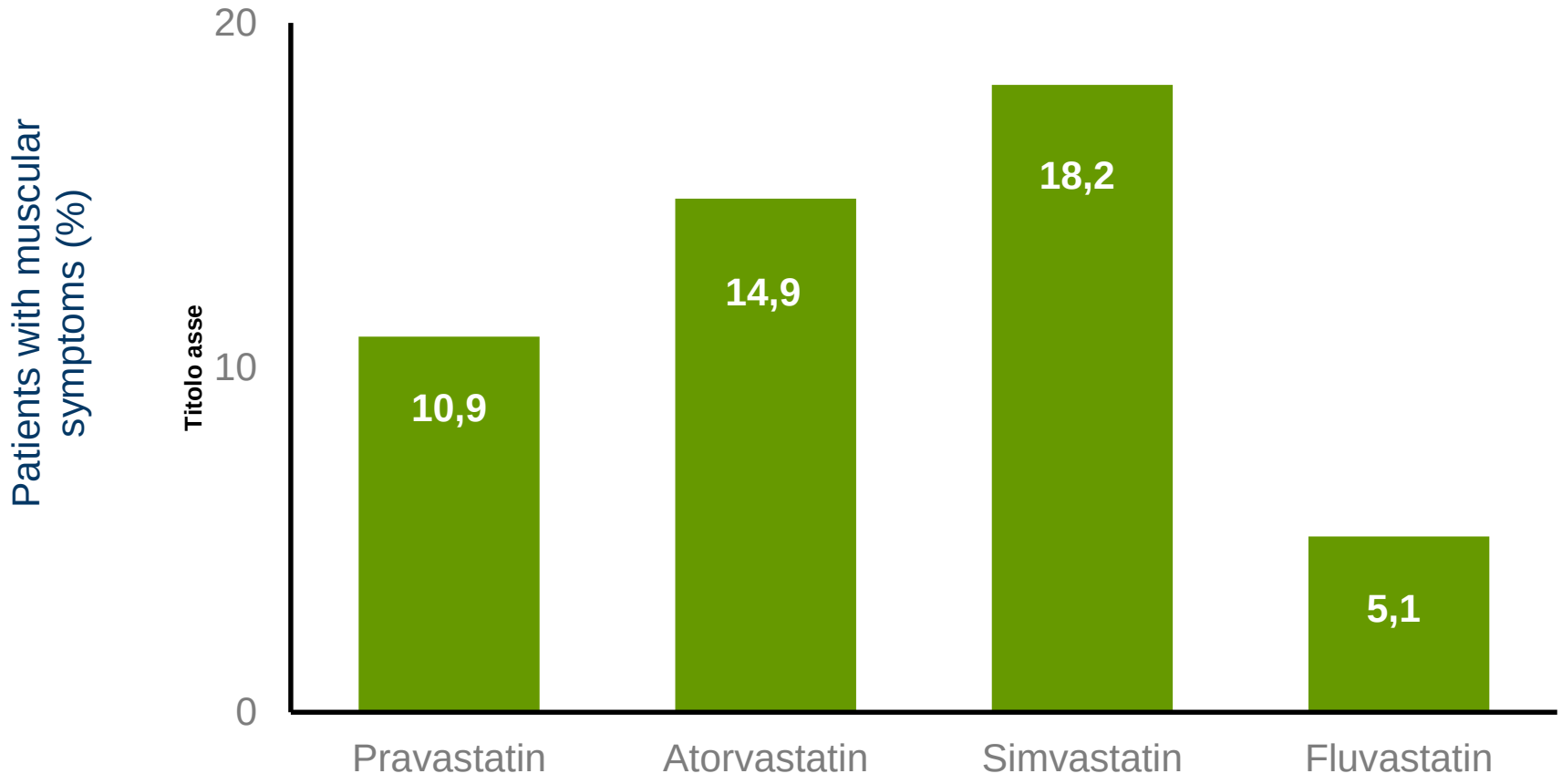
Muscle symptoms associated with statins are common in observational studies

PRIMO: 7924 patients with hyperlipidaemia receiving high-dosage statin therapy



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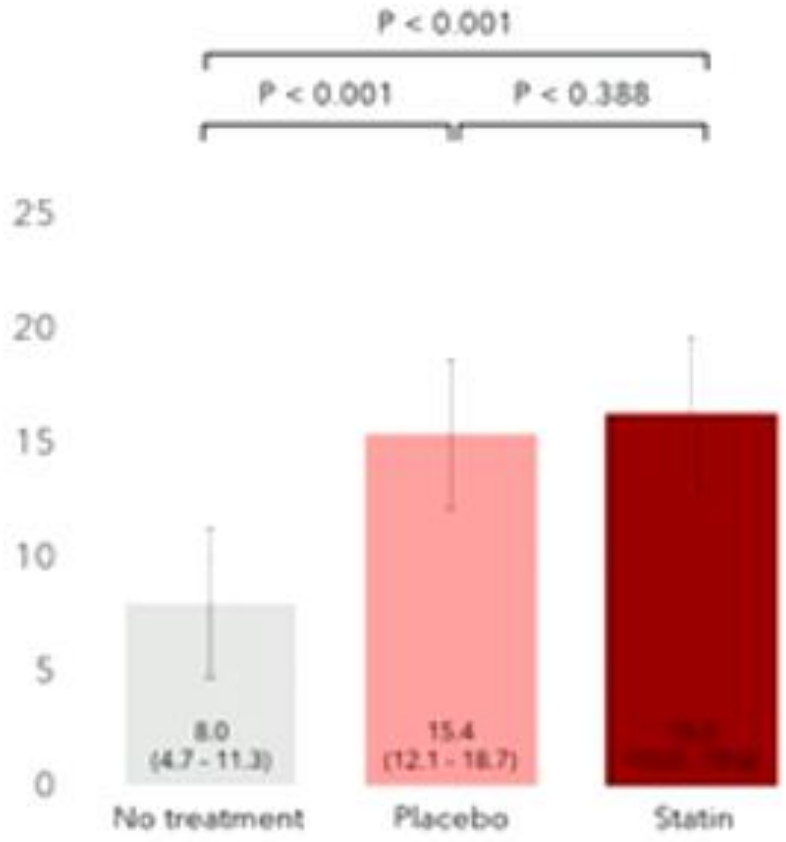
Bruckert E, et al. Cardiovasc Drugs Ther 2005;19:403–414.

N-of-1 SAMSON Study:

- 60 subjects with any adverse event on statin
- Randomized in crossover fashion to no treatment, placebo or statin for 1 month each
- Symptom score rated



N Engl J Med 2020; 383:2182-2184

Exclude other causes of muscle symptoms and interactions

TAKE TIME for patient,
inform patient about long-term risk reduction and safety

3-4 weeks break of statin

No resolution of symptoms:
Search for other cause of
muscle symptoms

Resolution of symptoms: Re-start statin
Use a different statin
Start with very low dose

Slowly increase dose, e.g. every 2 weeks,
to establish the highest tolerable statin dose

Check LDL-C

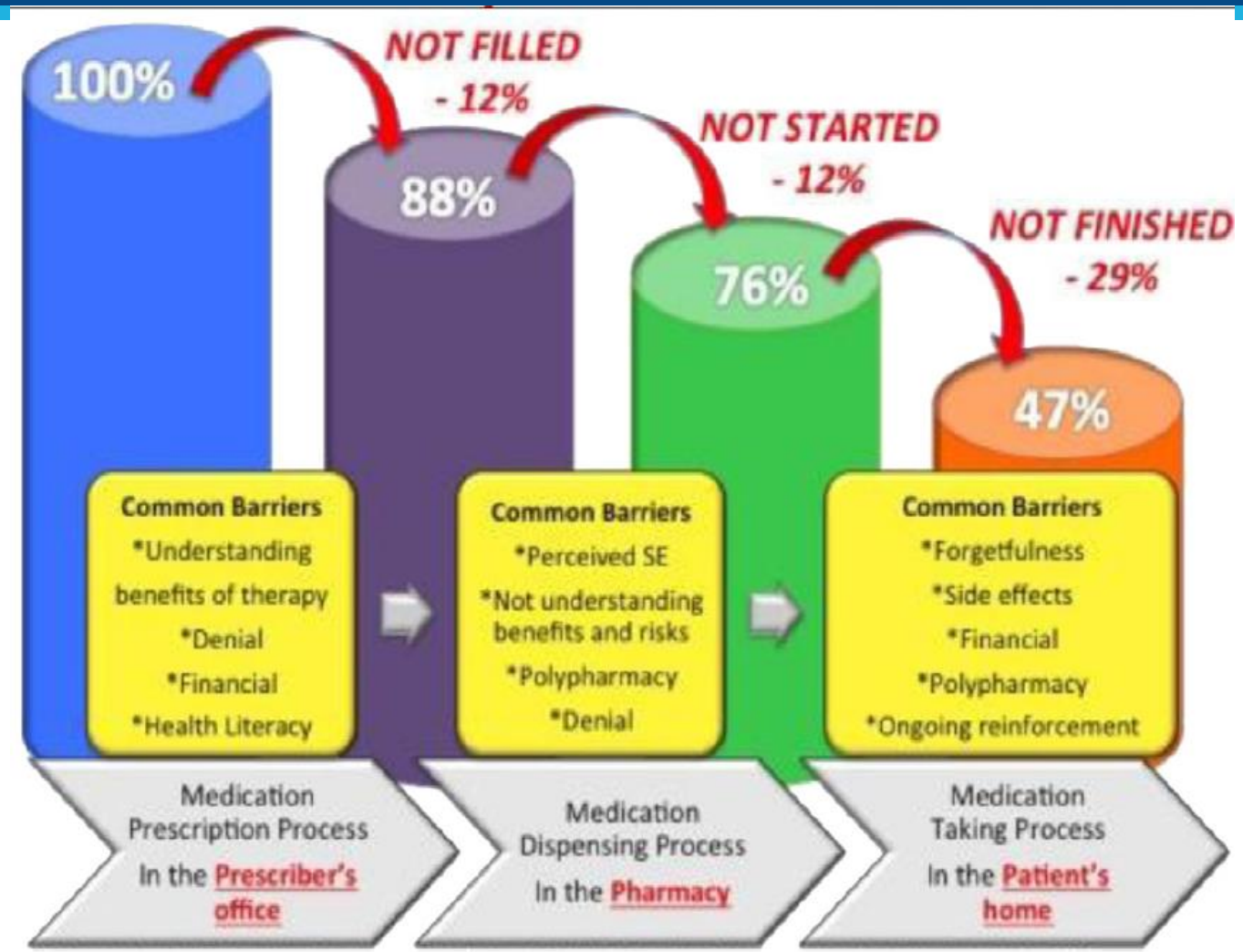
When LDL-C goals are not reached, combine the highest tolerated dose of statin with

- Ezetimibe*
- Ezetimibe + Bempedoic Acid**
- PCSK9 inhibitors*

*positive outcome data
**outcome data pending

European Heart Journal (2020) 41, 3343–3345

Statin Compliance Over Time:



Journal of Clinical Lipidology (2013) 7, 573–609

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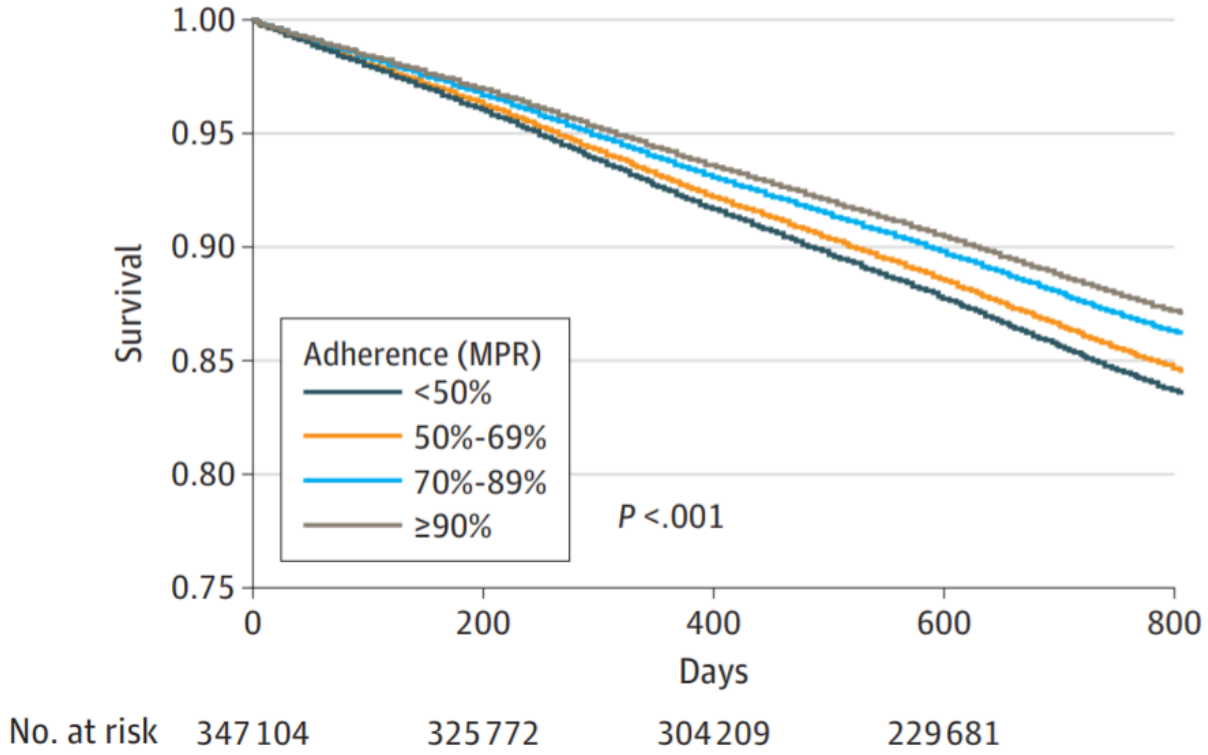
Low Statin Adherence Increases Mortality:

n=347104

Figure. Survival Curves by Statin Adherence Level as Defined by Medication Possession Ratios (MPRs)



JAMA Cardiol.doi:10.1001/jamacardio.2018.4936 Published online February 13, 2019

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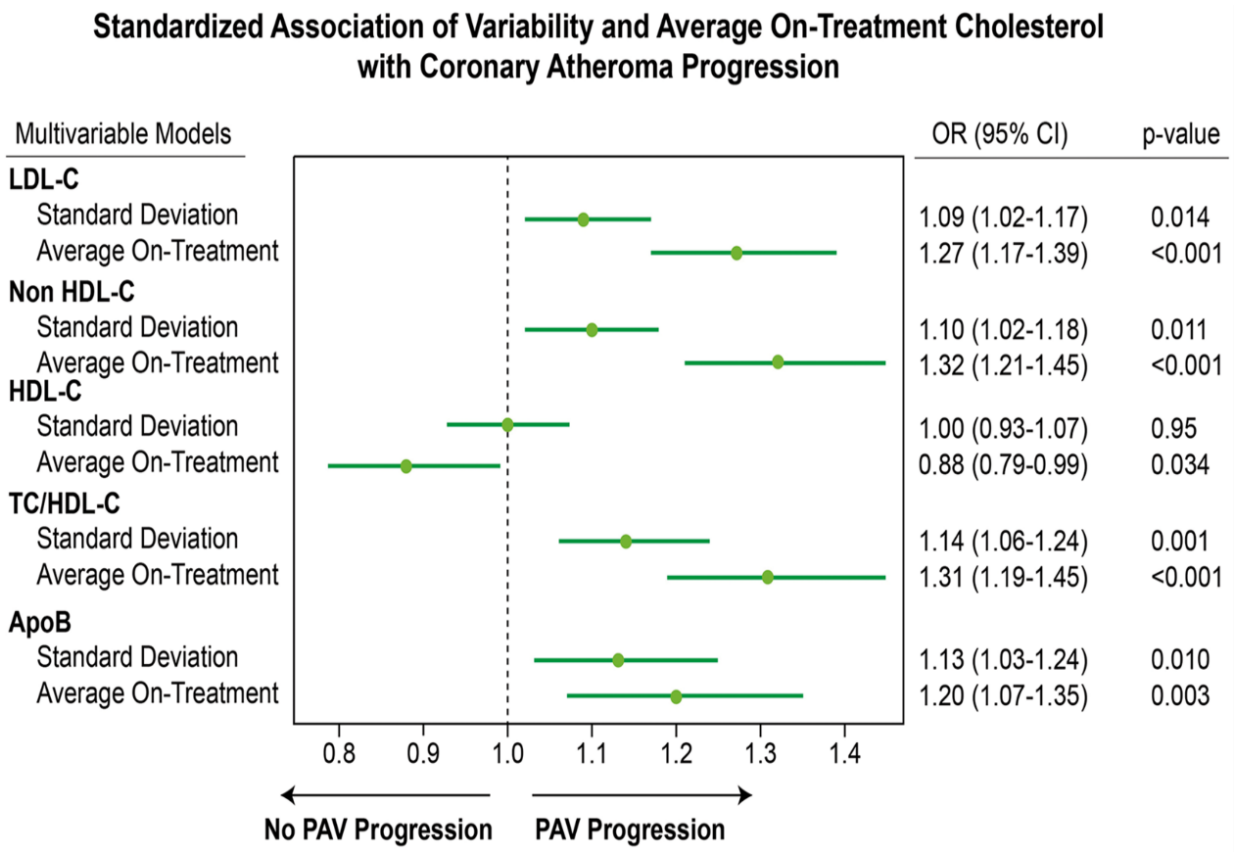
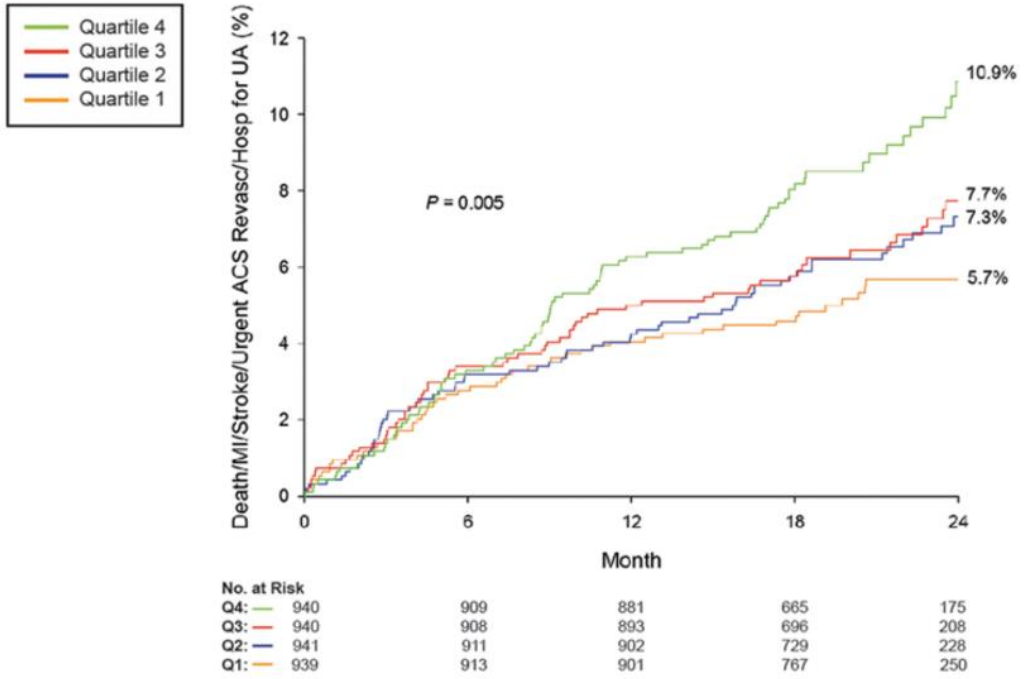
Visit-to-visit Cholesterol Variability Correlates With Coronary Atheroma Progression and Clinical Outcomes

n=4978





Achieved level more important but variability counted

Eur Heart J. 2018;39(27):2551-2558

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Can We Identify the Non-compliant Patient ?
Determinants of Nonadherence:

- Female sex
- Age less than 45, over 75
- Multiple dosing and polypharmacy
- Low socioeconomic status
- Primary prevention, asymptomatic
- Comorbidity like depression, dementia
- Low health literacy, low education level

Ann Pharmacother 2010;44:1410

USAGE Study:
Survey on 10.138 Current and Former Statin Users

Reason for stopping statin among former users:

- **Side effect 62 % (mostly myalgia)**
- **Cost 17 %**
- **Efficacy 12 %**
- **One third stopped without consulting their doctor first !**
- **Not satisfied with doctor discussion:**
  83 % of those who stopped, 65 % of those who continued !

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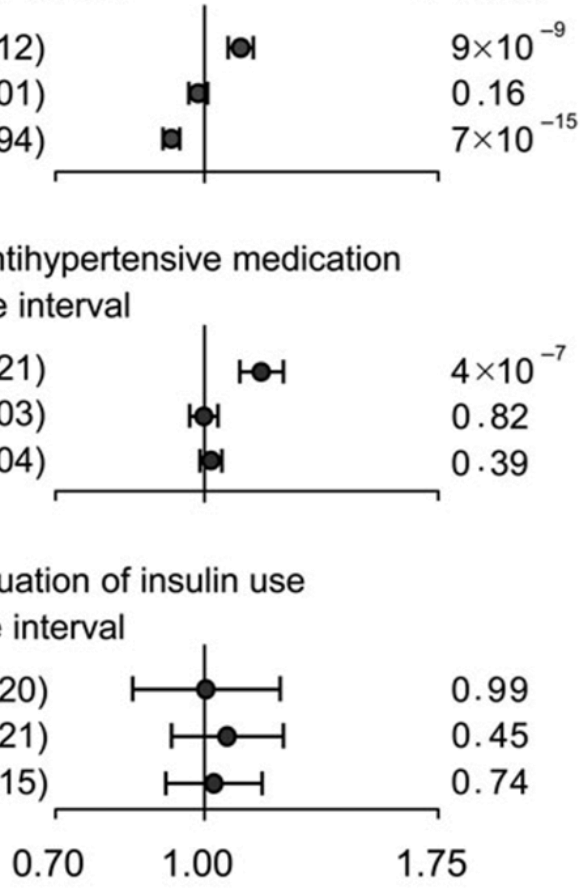
J Clin Lipidol 2012:6:208

Effects of Media on Statin Use:

Predictor	Odds ratio for early statin discontinuation with 95% confidence interval	*P*-value
Negative nationwide statin-related news story	1.09 (1.06–1.12)	9×10^{-9}
Neutral nationwide statin-related news story	0.98 (0.96–1.01)	0.16
Positive nationwide statin-related news story	0.92 (0.90–0.94)	7×10^{-15}

	Odds ratio for early discontinuation of antihypertensive medication with 95% confidence interval	
Negative nationwide statin-related news story	1.15 (1.09–1.21)	4×10^{-7}
Neutral nationwide statin-related news story	1.00 (0.96–1.03)	0.82
Positive nationwide statin-related news story	1.01 (0.98–1.04)	0.39

	Odds ratio for early discontinuation of insulin use with 95% confidence interval	
Negative nationwide statin-related news story	1.00 (0.83–1.20)	0.99
Neutral nationwide statin-related news story	1.05 (0.92–1.21)	0.45
Positive nationwide statin-related news story	1.02 (0.91–1.15)	0.74



European Heart Journal (2016) 37, 908

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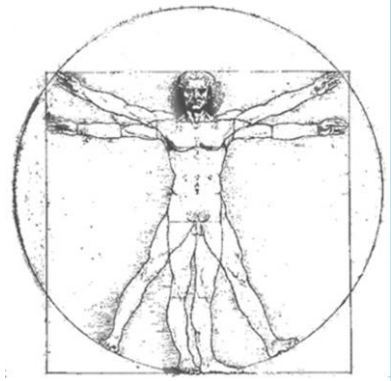
Imperial College London



The DA VINCI Study

What have we learnt from 18 European countries on lipid management

Prof KK Ray, Imperial College, London, UK
On behalf of the DA VINCI investigators and collaborators

This study was funded by Amgen (Europe) GmbH, C Desborough of Amgen UK provided medical writing assistance for this presentation

ICTU
Imperial Clinical Trials Unit

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EU Wide Cross-Sectional Observational Study of Lipid-Modifying Therapy Use in Secondary and Primary Care

Objectives

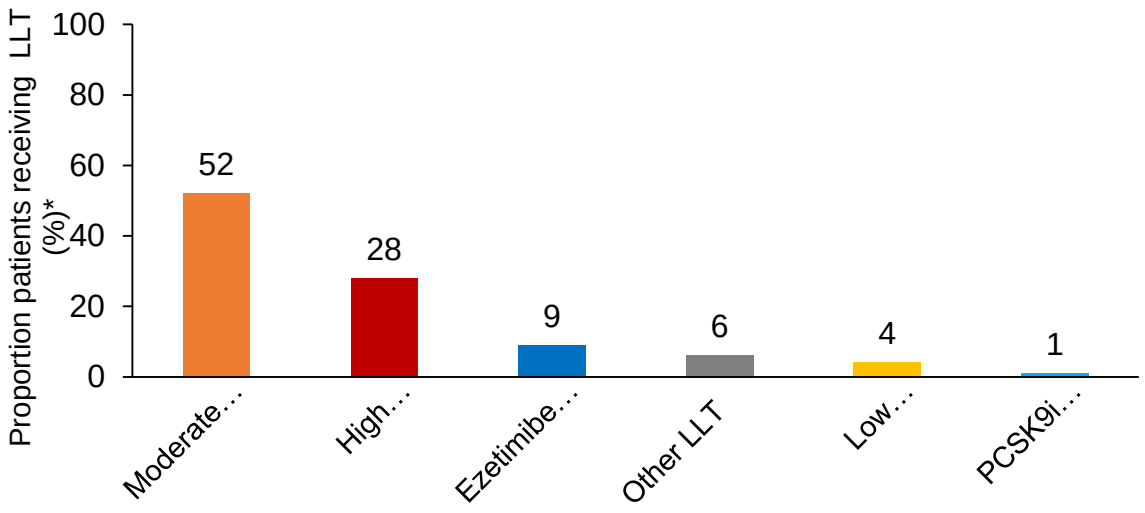
- Describe how LLT is used across a broad range of patient populations in Europe and assess how current practice impacts risk-based LDL-C goal attainment

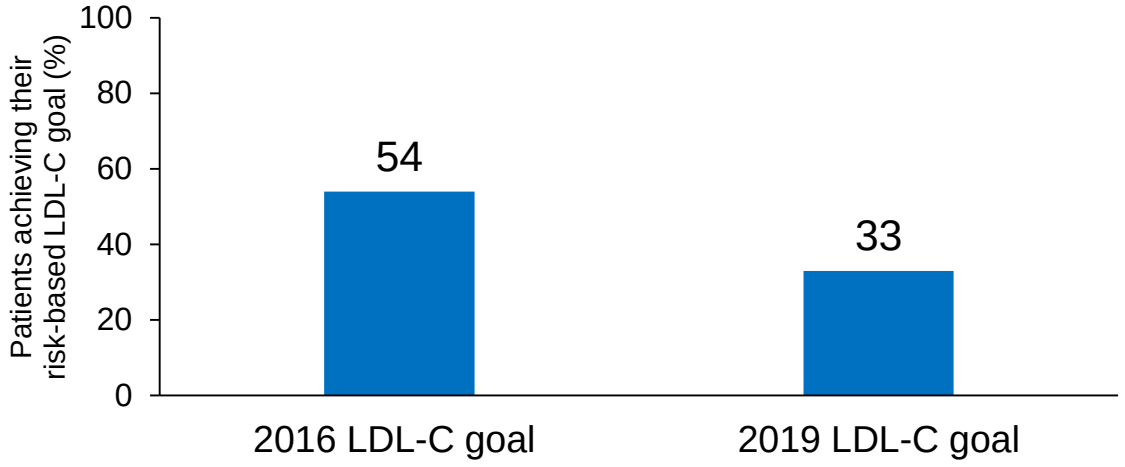
Key differences from other studies

- Additional European countries
- Both primary and secondary prevention patients
- Both primary and secondary care sites managing patients from less well-studied groups (e.g. peripheral and cerebral vascular disease)
- Assessment of LDL-C goals in 2019 ESC/EAS guidelines[1]

EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; LDL-C, low-density lipoprotein cholesterol; LLT, lipid lowering therapy. 1. Mach F, et al. *Eur Heart J* 2019; 41: 111-188

Overall LLT use & risk-based LDL-C goal attainment





- **The majority of patients were receiving moderate intensity statin monotherapy**
- **Only 28% of patients were receiving high intensity statin monotherapy**
- **Few patients (9%) were receiving ezetimibe combo**
- **A small number of patients (1%) received PCSK9i combo**

- **Approximately half of all patients did not achieve their 2016 risk-based LDL-C goal**
- **Only one-third achieved their 2019 risk-based LDL-C goal**

*Stabilised LLT at time of LDL-C measurement. combo, combination; LDL-C, low-density lipoprotein cholesterol; LLT, lipid lowering therapy; PCSK9i; proprotein convertase subtilisin/kexin type 9 inhibitor

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Conclusion:

First line

Statins

Second line

- Ezetimibe
- PCSK9
- Bempedoic acid
- EPA
- Fibrates

The benefit to risk ratio is highly favourable
Compliance is a major challenge