



**Превенция на СС риск при
пациенти със Захарен
Диабет:
Лечение на дислипидемията**

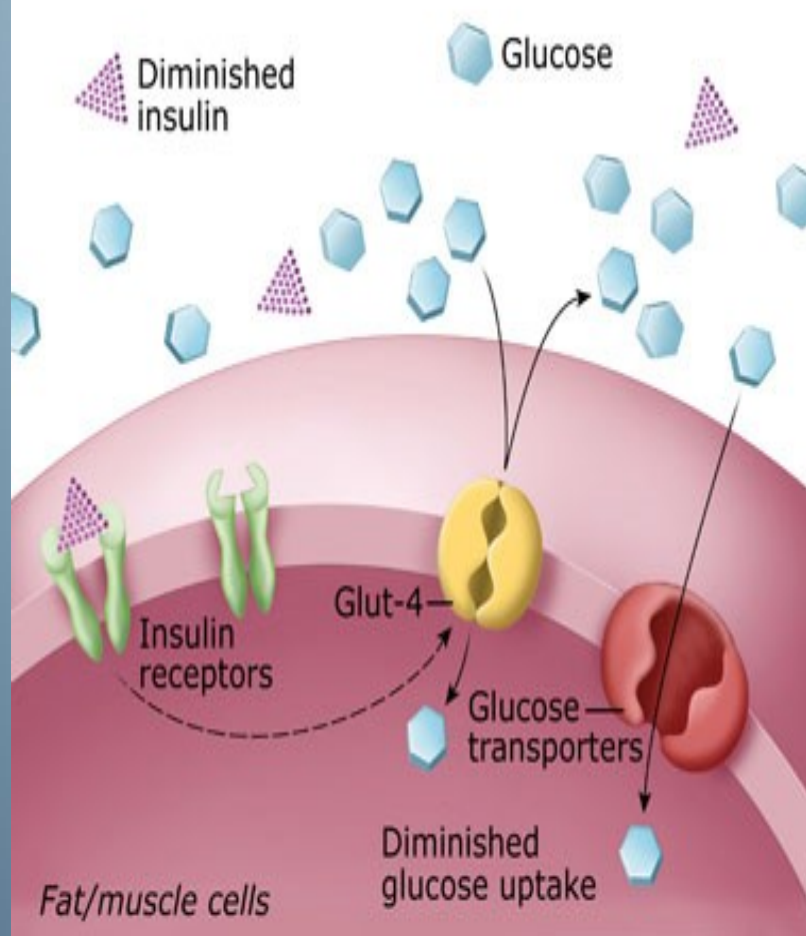
*Проф. Д-р А.Гудев, FESC, FACC
УМБАЛ “Царица Йоанна –
ИСУЛ”*

- **Захарен Диабет: Патогенеза и Дефиниция**
- **Епидемиология**
- **Захарен диабет и съдови усложнения**
- **Дислипидемия при ЗД**
- **Терапевтични стратегии при ЗД: контрол на дислипидемията:**

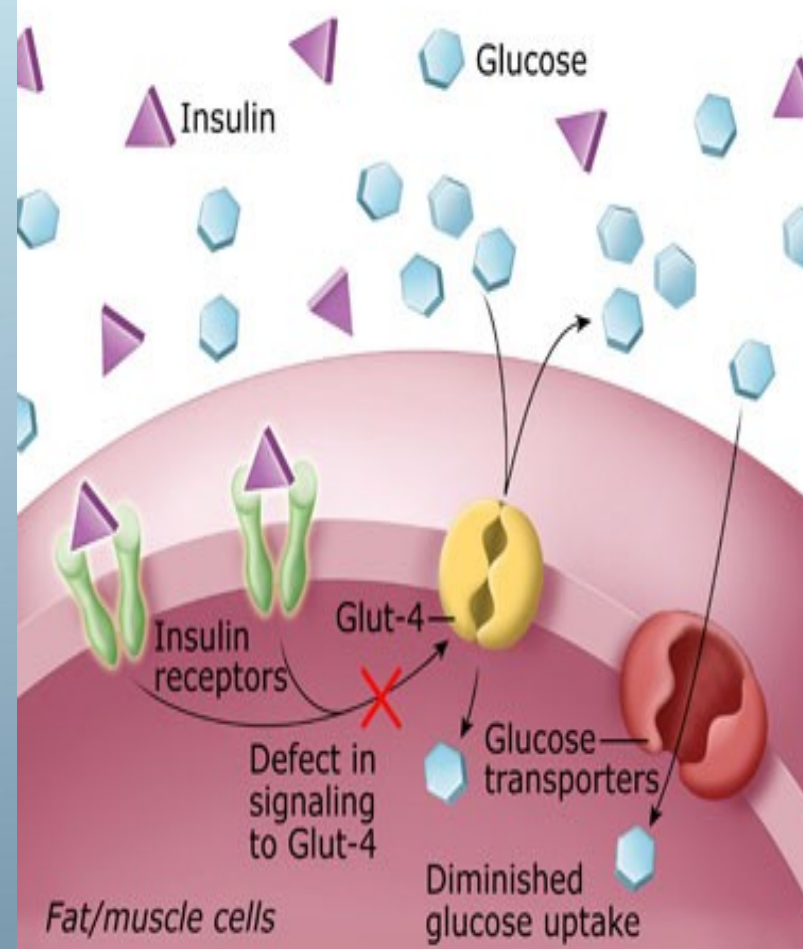
Статини и сърдечно-съдови усложнения
Ефективност на терапията със статини при пациенти със ЗД
Риск от възникване на ЗД при терапия със статини
Интензивност на терапията
Препоръки за терапевтично поведение

Патогенеза на ЗД

Type 1 Diabetes: Insufficient Insulin



Type 2 Diabetes: Insulin Resistance

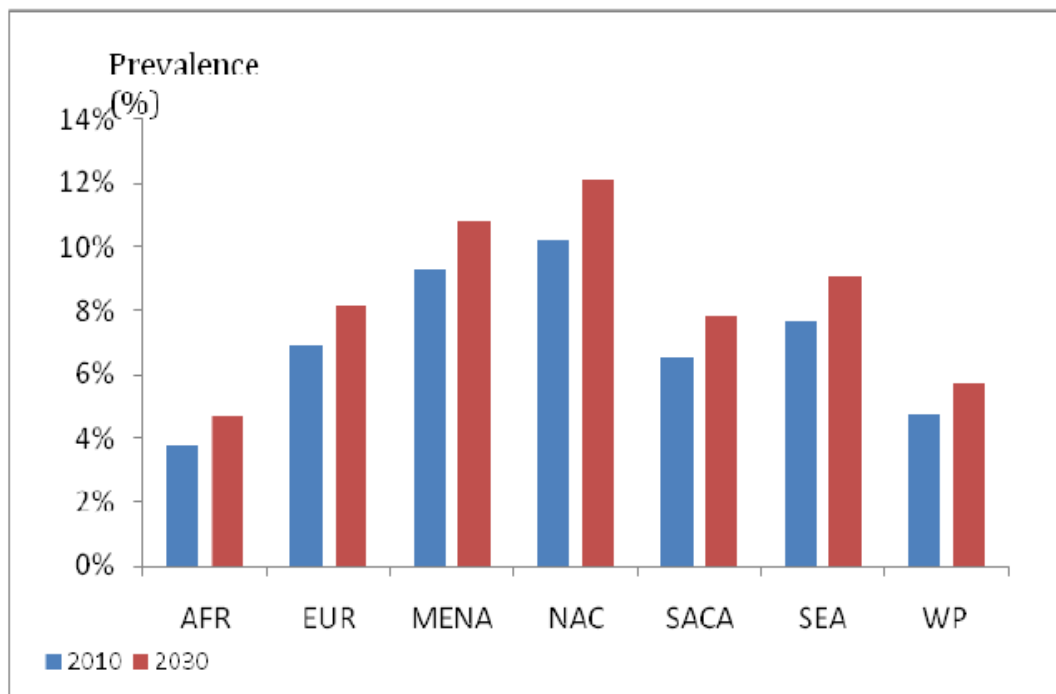


Diagnostic criteria

Diagnose/ measurement	WHO 2006 / WHO 2011	ADA 2013
Diabetes		
HbA _{1c}	Can be used If measured $\geq 6.5\%$ (48 mmol/mol)	Recommended $\geq 6.5\%$ (48 mmol/mol)
FPG	Recommended ≥ 7.0 mmol/L (≥ 126 mg/dL) or	≥ 7.0 mmol/L (≥ 126 mg/dL) or
2hPG	≥ 11.1 mmol/L (≥ 200 mg/dL)	≥ 11.1 mmol/L (≥ 200 mg/dL)
IGT		
FPG	≥ 7.0 mmol/L (≥ 126 mg/dL)	≥ 7.0 mmol/L (≥ 126 mg/dL)
2hPG	≥ 7.8 - <11.1 mmol/L (≥ 140 - <200 mg/dL)	Not required If measured 7.8-11.0 mmol/L (140-198 mg/dL)
IFG		
FPG	6.1–6.9 mmol/L (110–125 mg/dL) If measured	5.6-6.9 mmol/L (100-125 mg/dL) –
2hPG	<7.8 mmol/L (<140 mg/dL)	

FPG = fasting plasma glucose; IGT = impaired glucose tolerance; IFG = impaired fasting glucose;
2hPG = 2-h post-load plasma glucose.

Figure 3 Prevalence of diabetes* (20- 79 age group) by region, 2010 and 2030



*Comparative prevalence

Top 10 countries for number of people with diabetes (20-79 years), 2013

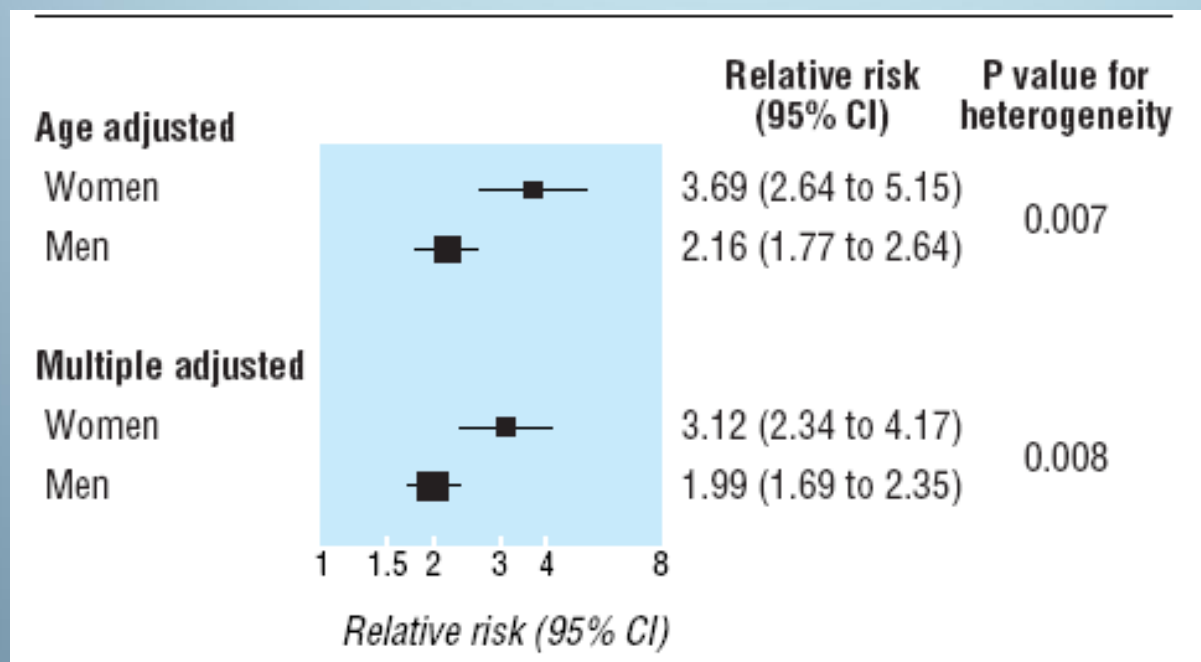
Country/territory	Number
China	98.4 million
India	65.1 million
United States of America	24.4 million
Brazil	11.9 million
Russian Federation	10.9 million
Mexico	8.7 million
Indonesia	8.5 million
Germany	7.6 million
Egypt	7.5 million
Japan	7.2 million

International Diabetes Federation 2011. Global Burden: Prevalence and Projections, 2011 and 2030.

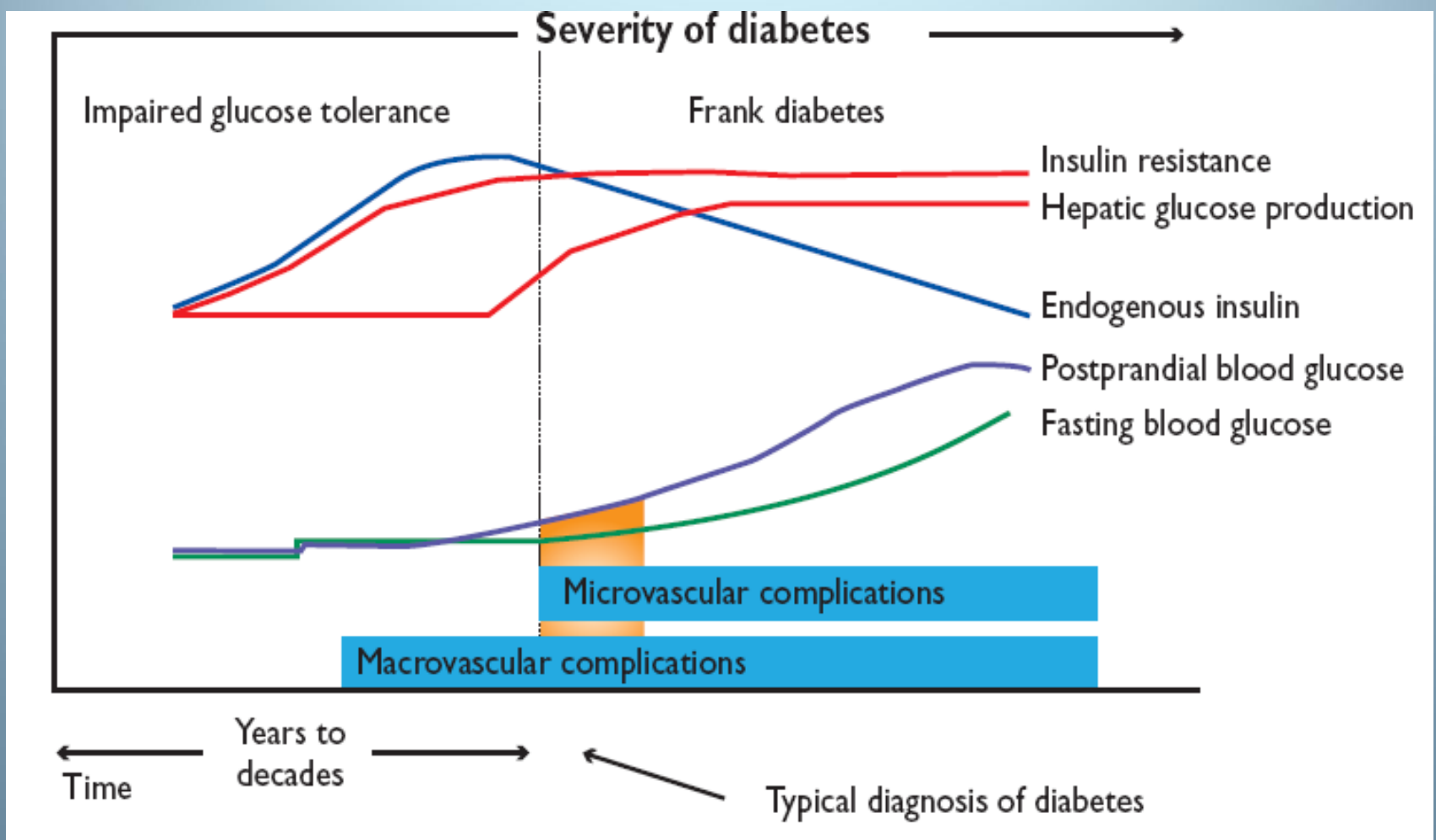
Available from <http://www.diabetesatlas.org/content/>

Excess risk of fatal coronary heart disease associated with diabetes in men and women: meta-analysis of 37 prospective cohort studies

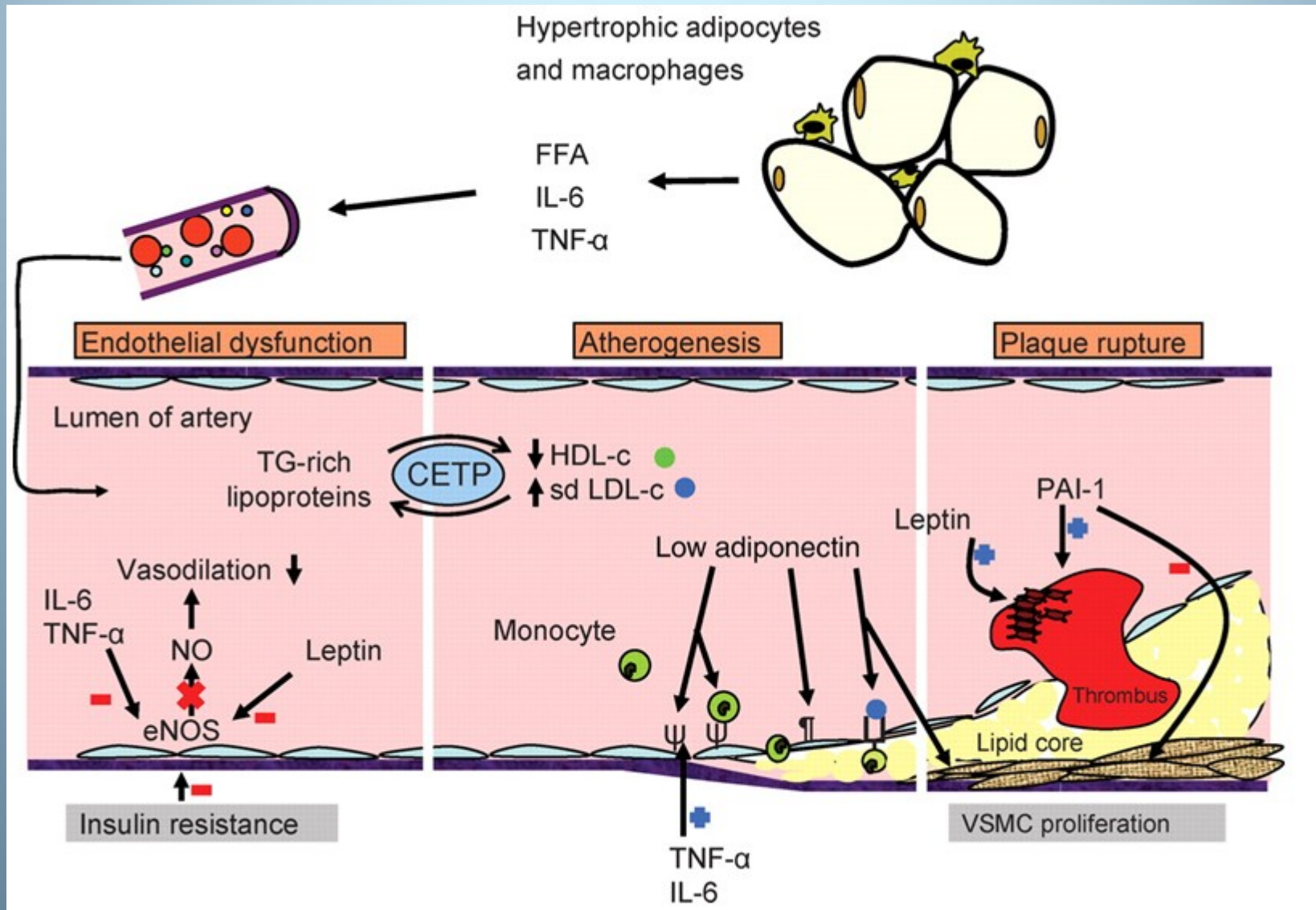
Rachel Huxley, Federica Barzi, Mark Woodward



Overall summary estimates of relative risks and 95% confidence intervals for fatal coronary heart disease in men and women with and without diabetes in 22 studies that reported both age and multiple adjusted coefficients



Glycaemic continuum and cardiovascular disease.



LDL particle count vs. cholesterol content

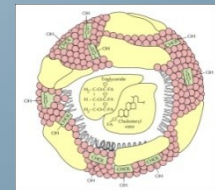
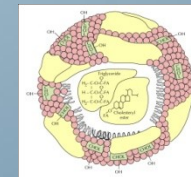
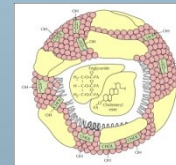
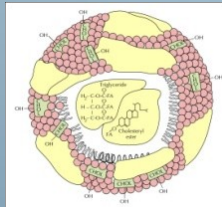
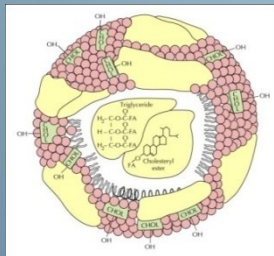
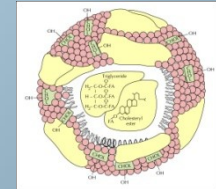
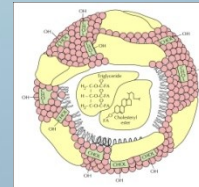
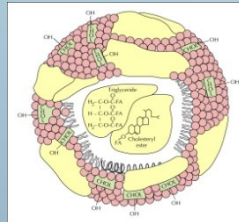
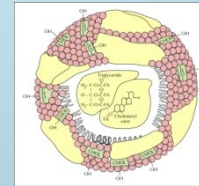
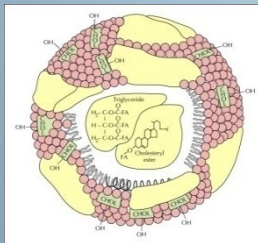
To carry the same amount of cholesterol, a larger number of particles are needed if they are smaller

Large, buoyant: 30-35 nm

Small, dense: 25-30 nm

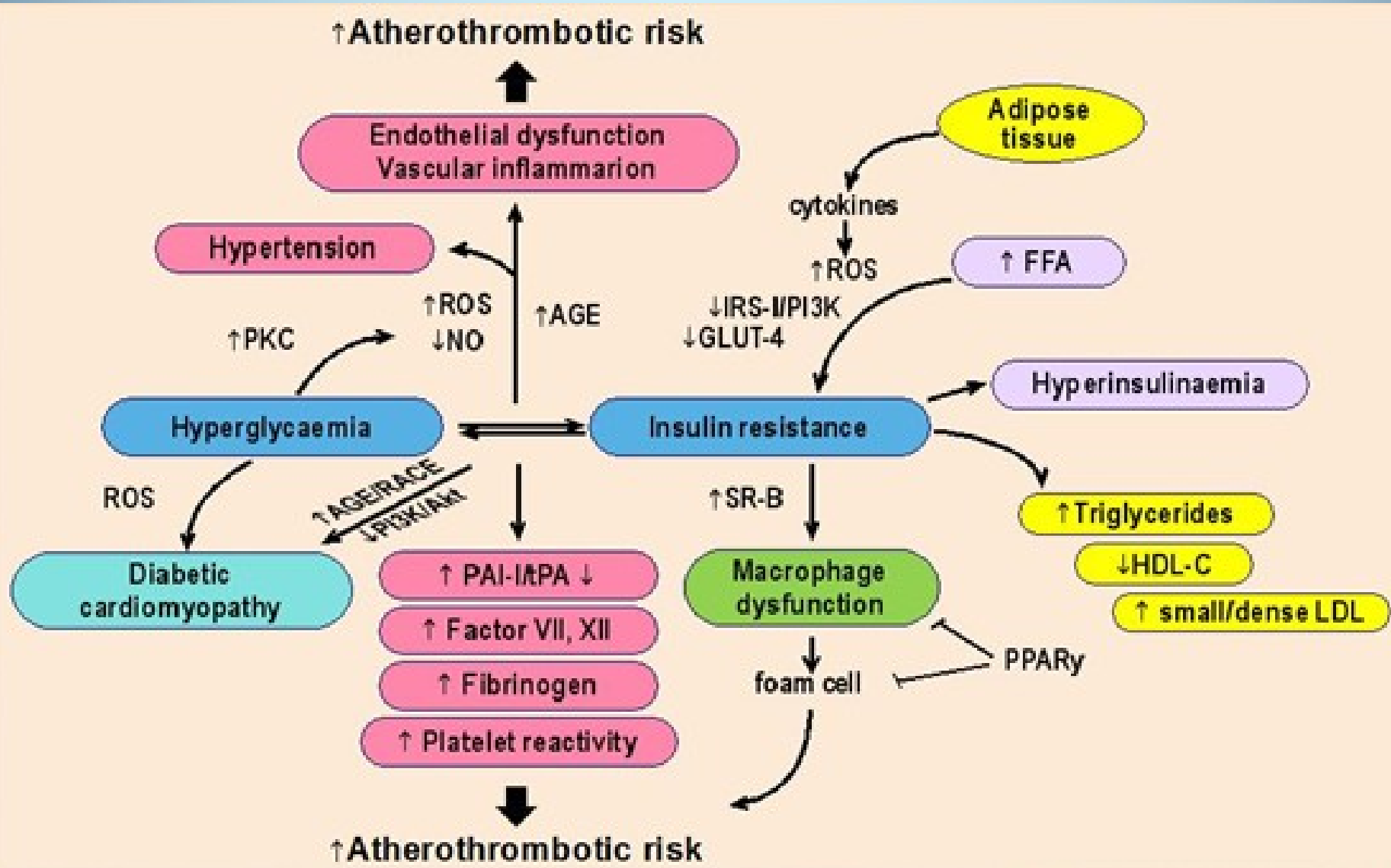
LDLc=115 mg/dl

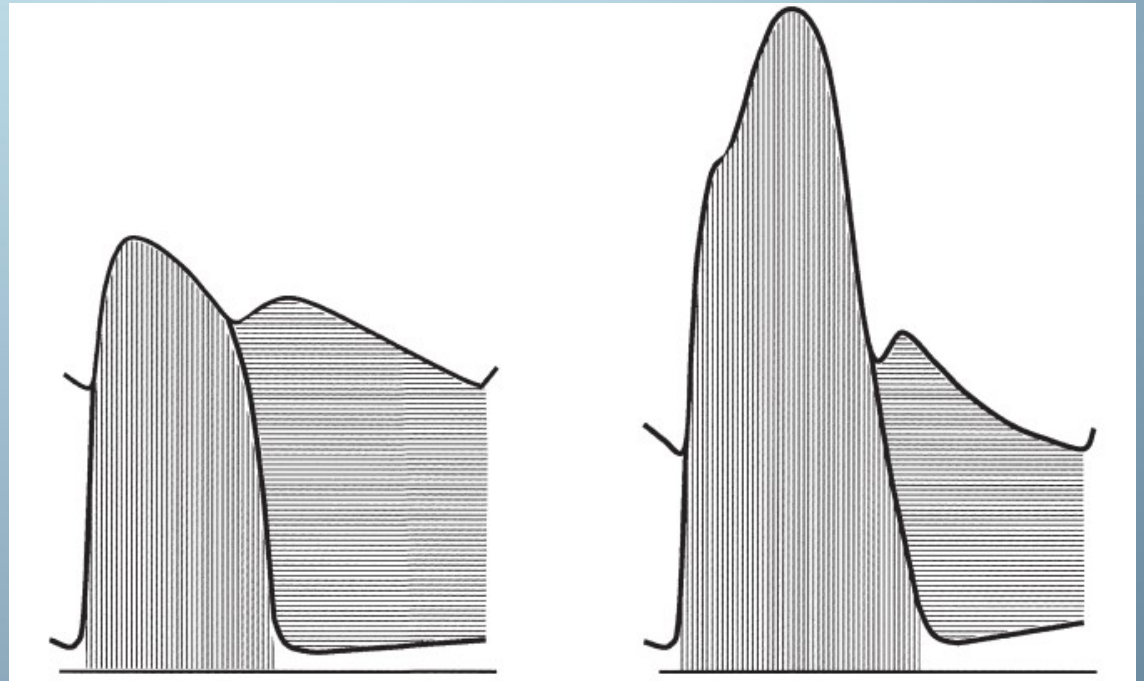
LDLc=115 mg/dl



apoB is a measure of number of atherogenic lipoproteins (essentially VLDL, IDL, LDL). Non-HDL is measure of cholesterol carried in these same particles

LDLc measures cholesterol carried in LDL and IDL



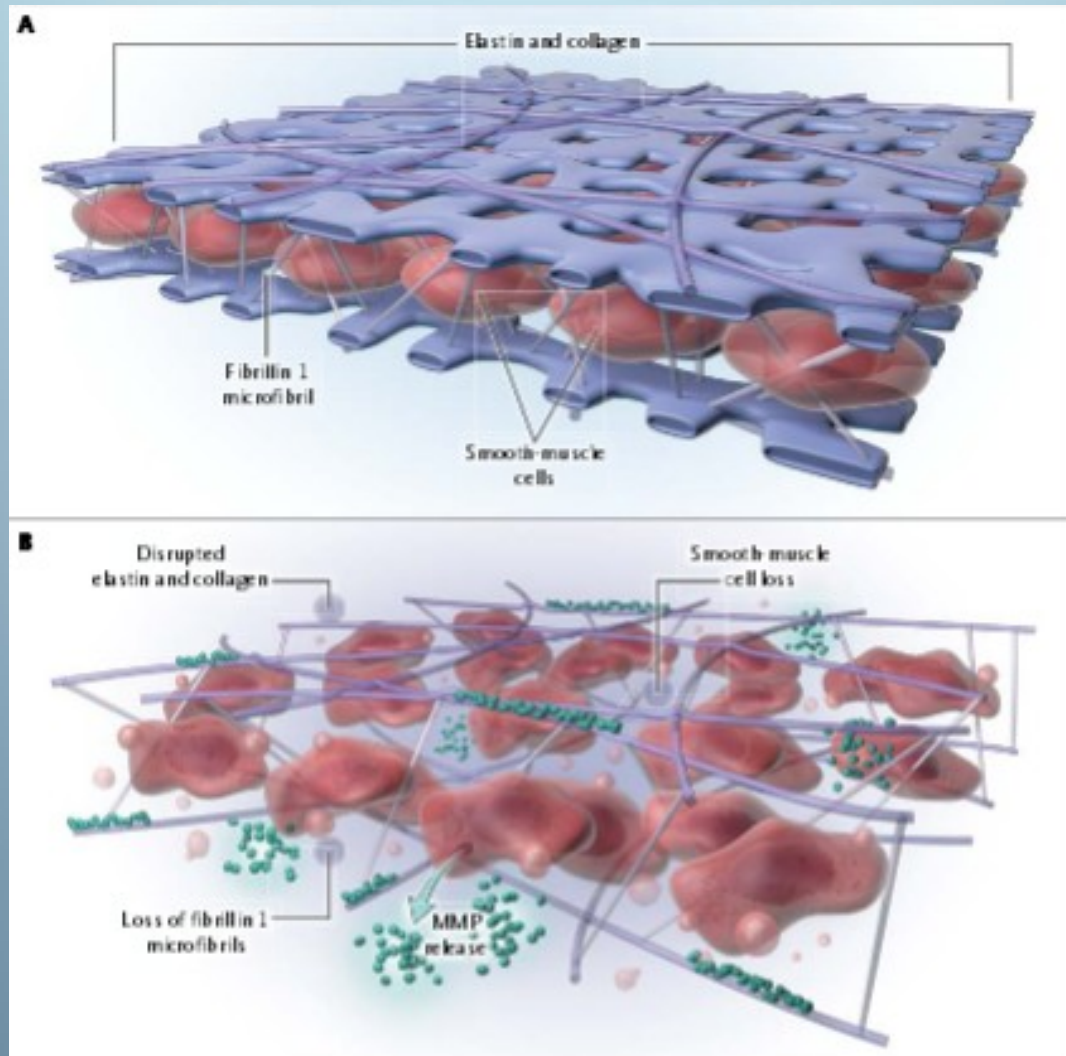


M. O'Rourke et al. J. Am. Coll. Cardiol. 2007;50;1-13

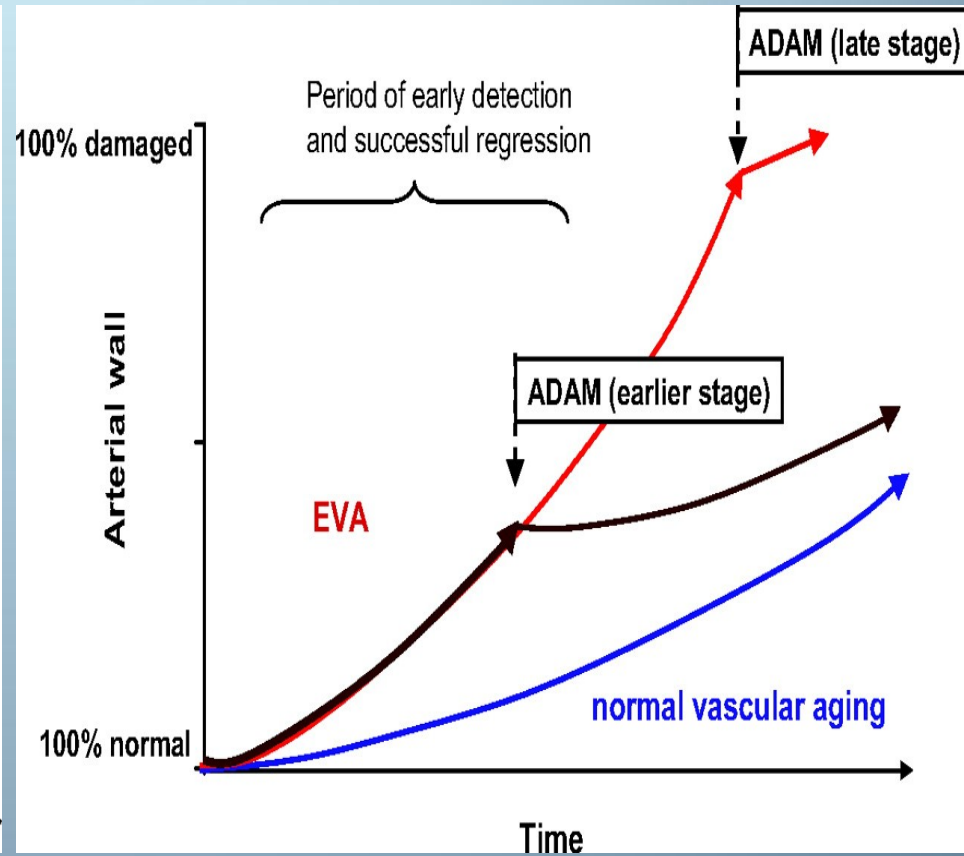
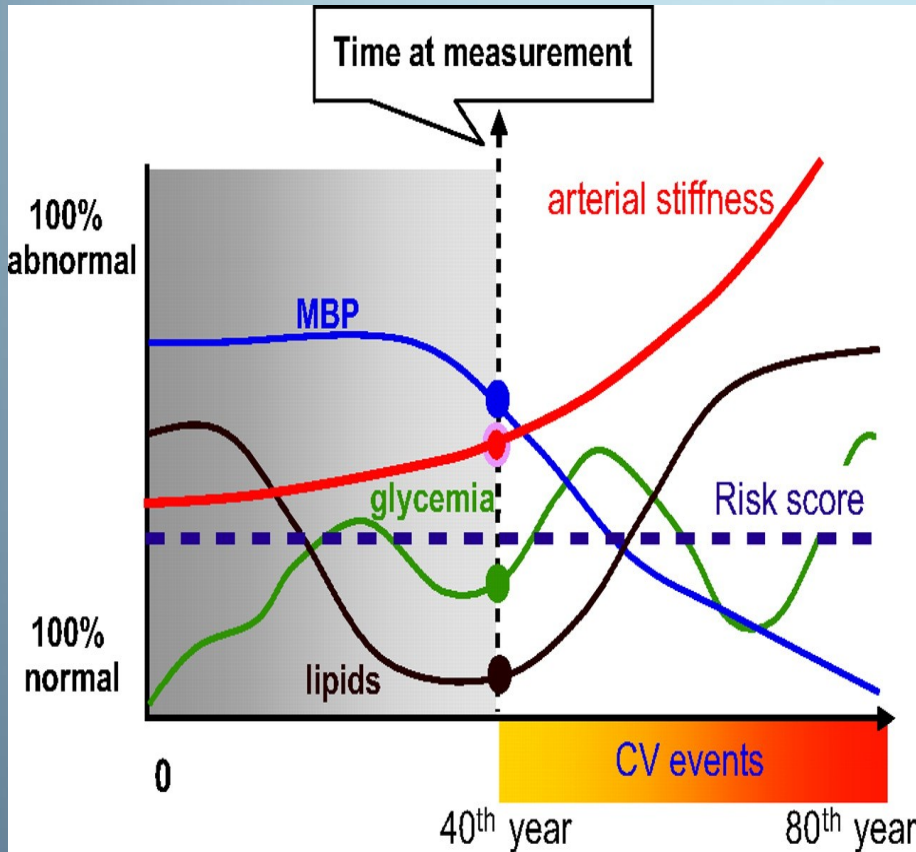
Aortic Dilatation in Patients with Bicuspid Aortic Valve

Subodh Verma, M.D., Ph.D., and Samuel C. Siu, M.D.

The NEW ENGLAND JOURNAL of MEDICINE



Ранно съдово стареене ...



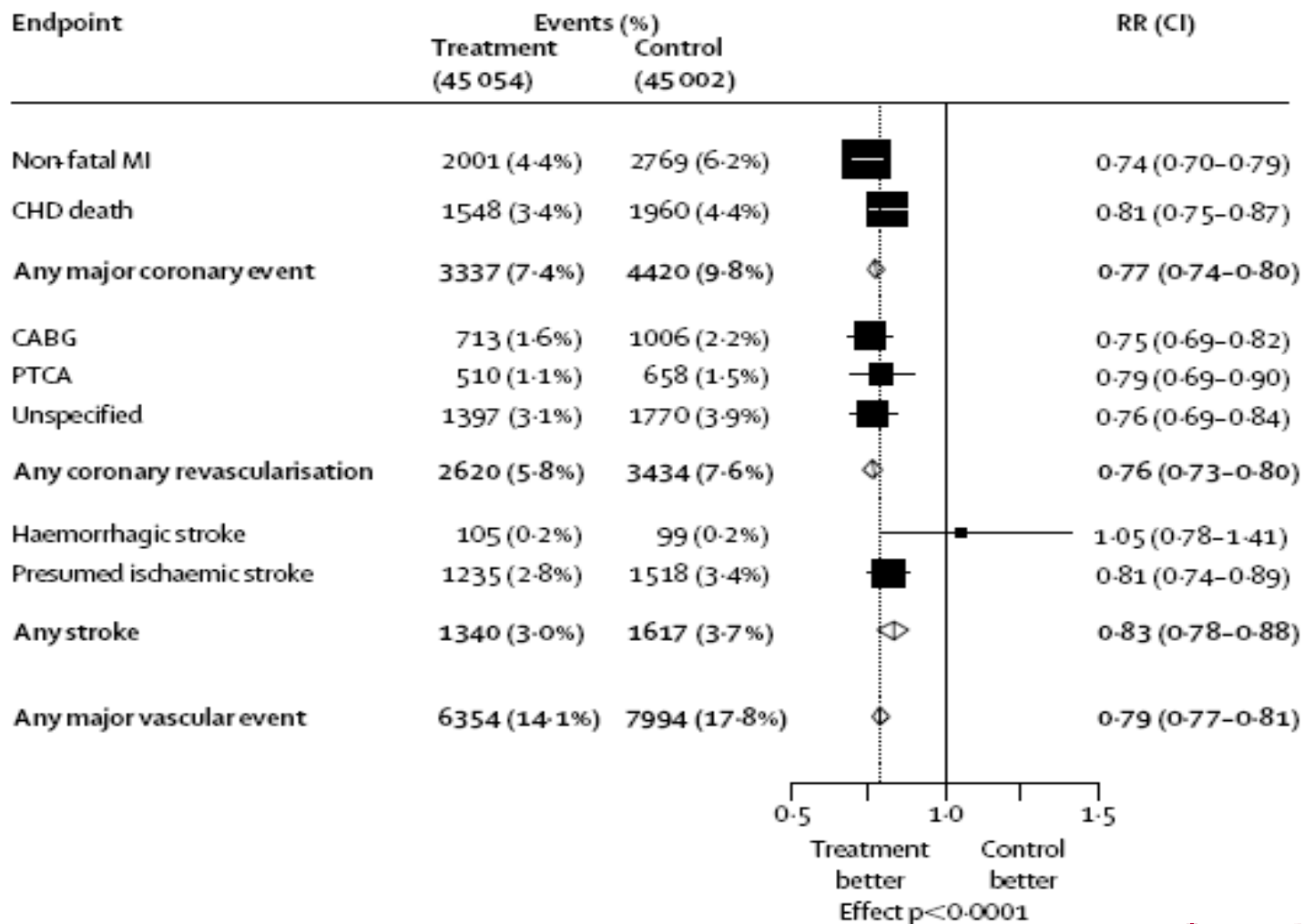
Терапевтични стратегии при пациенти със ЗД тип 2

- *Промяна в начина на живот*
- *Контрол на гликемията*
- *Контрол на артериалното налягане*
- *Контрол на дислипидемията*



Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90 056 participants in 14 randomised trials of statins

Cholesterol Treatment Trialists' (CTT) Collaborators*



Възможни съдово-протективни ефекти на статините

↓ Серумен LDL и TG
↑ Серумен HDL

↓ Прогресия на лезията
↑ Стабилност на плаката



↓ Образуване на лезии
↑ Възстановяване

- Възстановява ендотелната функция
- ↑ NO производство
- ↑ Антиоксидантен ефект
- ↓ Ендотелна пропускливост
- ↑ Миграция на ендотелни клетки

↓ Липидна
↑ Сърцевина

↓ Оксидация

↓ Възпаление

↓ Образуване на
↑ пенести клетки

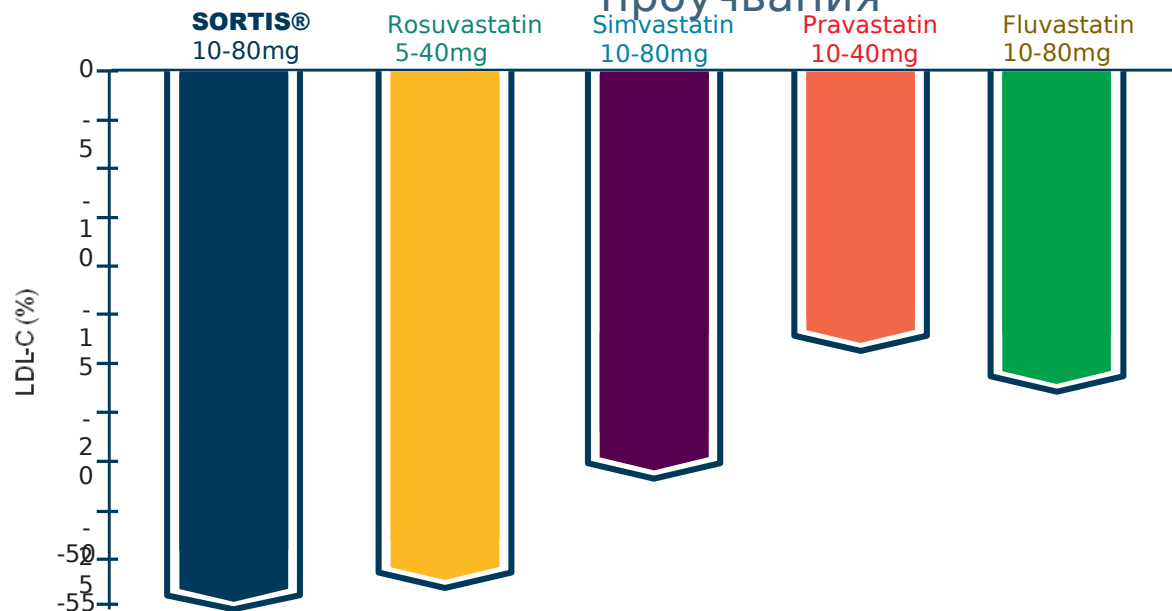
↓ Иmunна увреда

↓ С-реактивен протеин

↓ Възпалителните
↑ цитокини

SORTIS®: сигнификантна редукция на LDL-C в целия дозов диапазон¹⁵

Мета-анализ на 164 рандомизирани, плацебо-контролирани проучвания



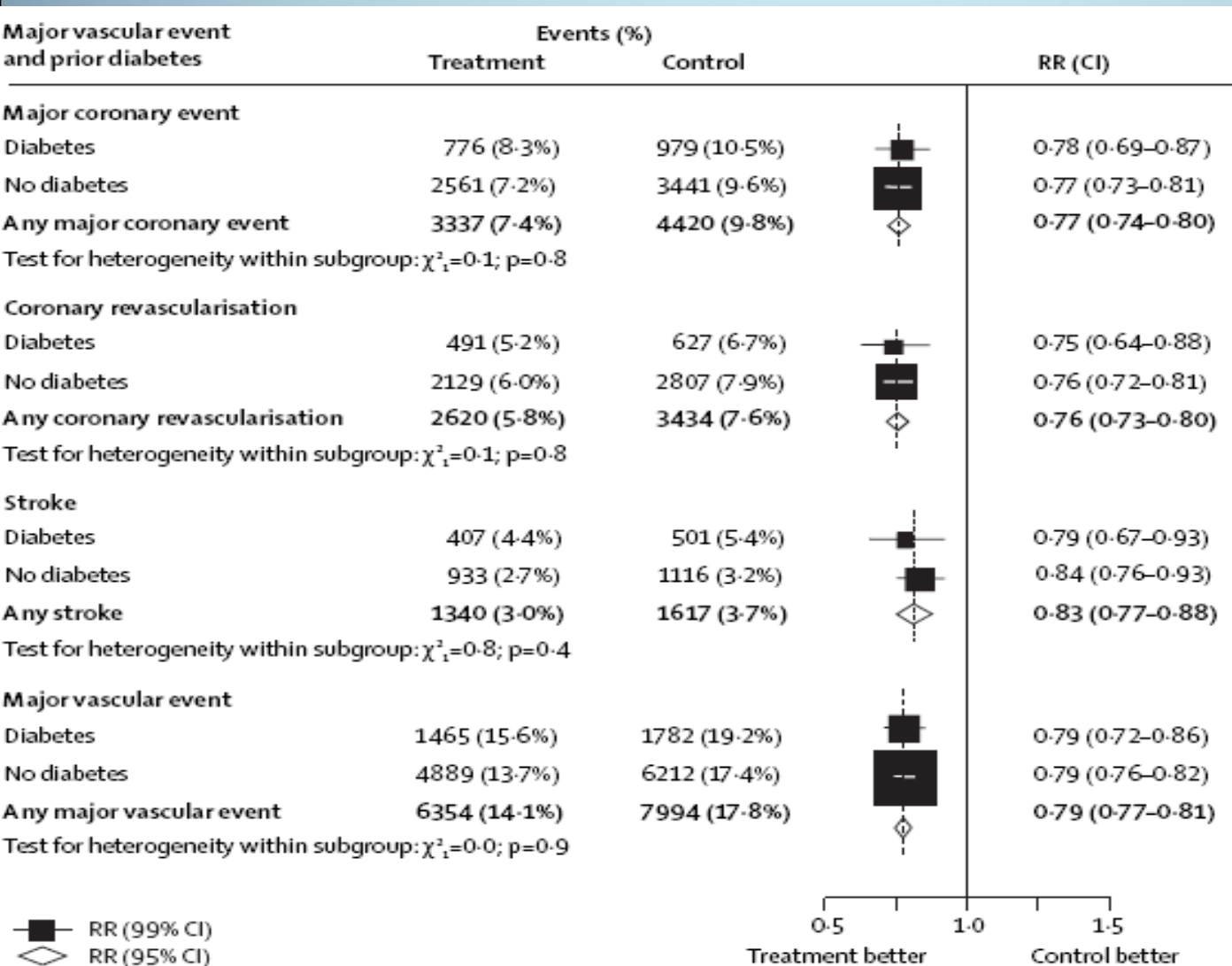
Адаптирано по Law MR et al.¹⁵

LDL - липопротеини с ниска плътност

® Търговска марка на Pfizer H.C.P. Corporation

Efficacy of cholesterol-lowering therapy in 18 686 people with **diabetes** in 14 randomised trials of statins: a meta-analysis

Cholesterol Treatment Trialists' (CTT) Collaborators*



Reduction in Cardiovascular Events With Atorvastatin in 2,532 Patients With Type 2 Diabetes

Anglo-Scandinavian Cardiac Outcomes Trial—Lipid-Lowering Arm (ASCOT-LLA)

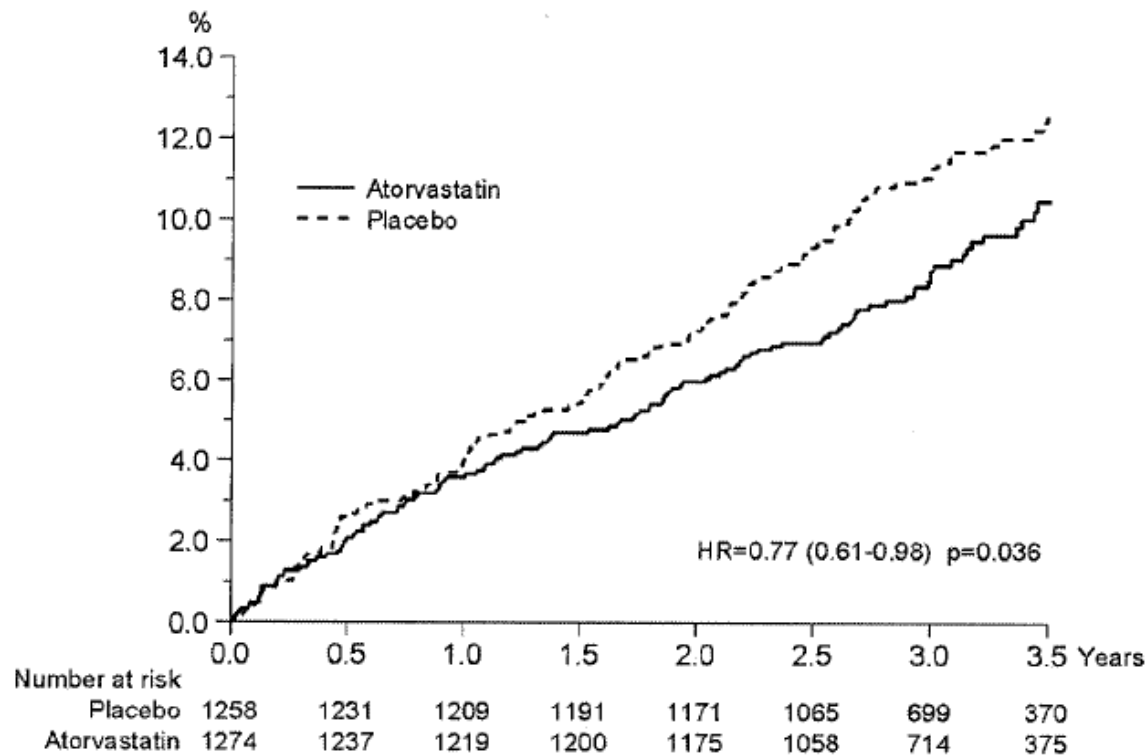
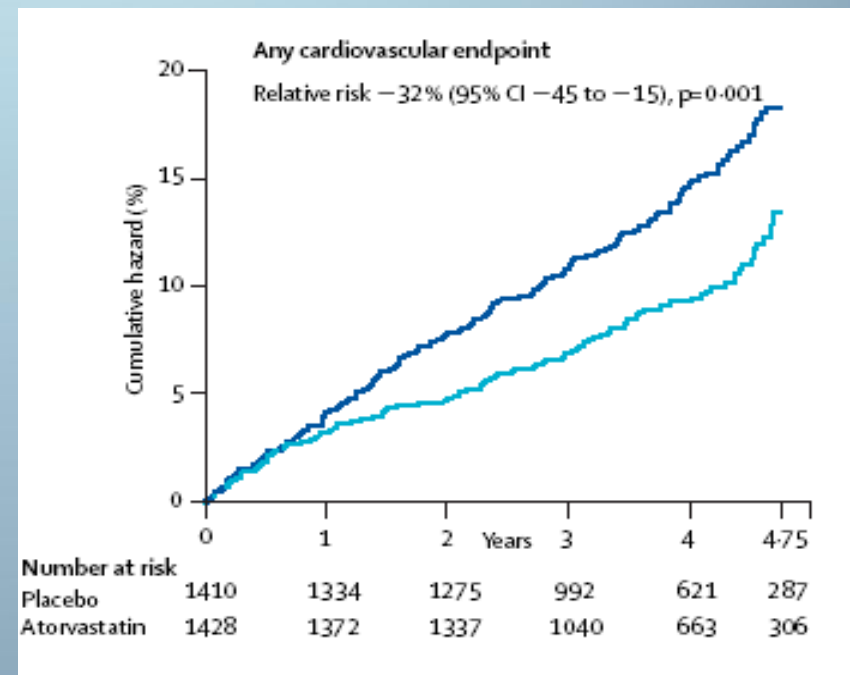
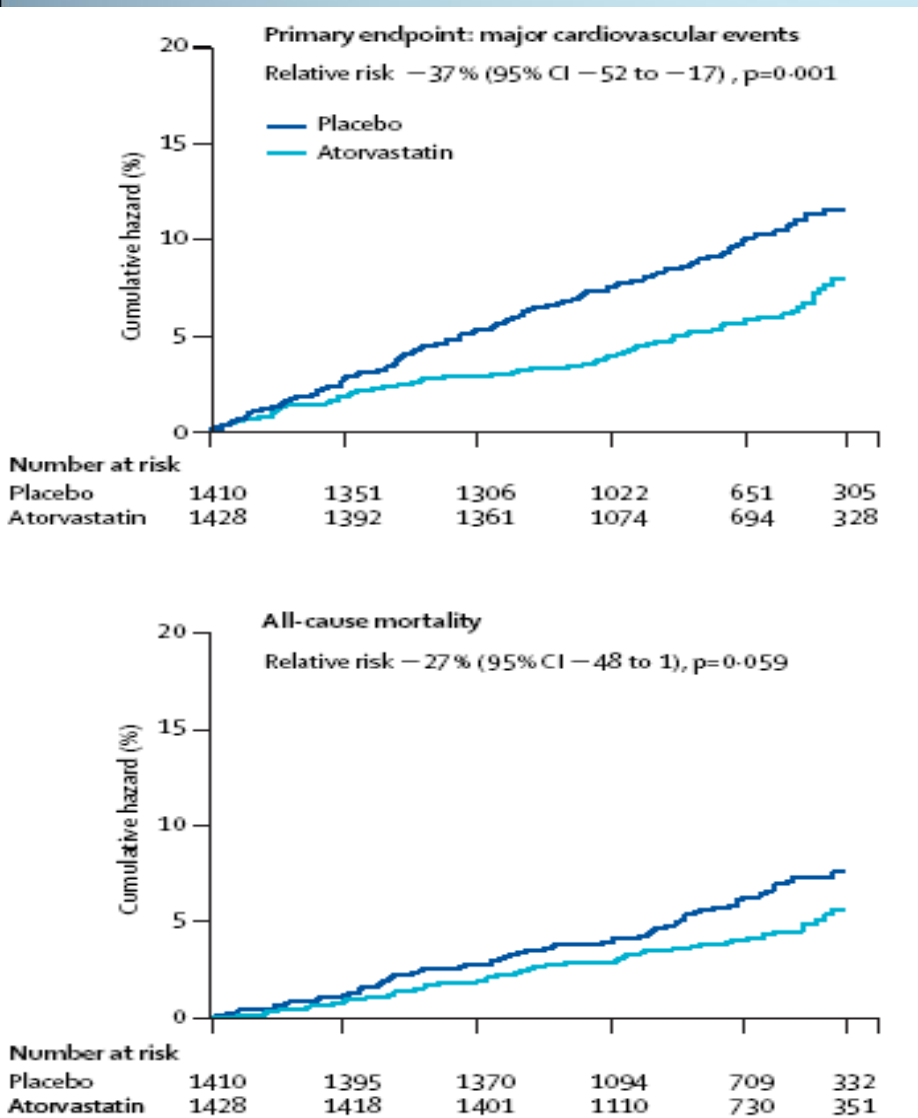


Figure 1—Cumulative incidence for total cardiovascular events and procedures among diabetic participants in ASCOT-LLA.

Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial

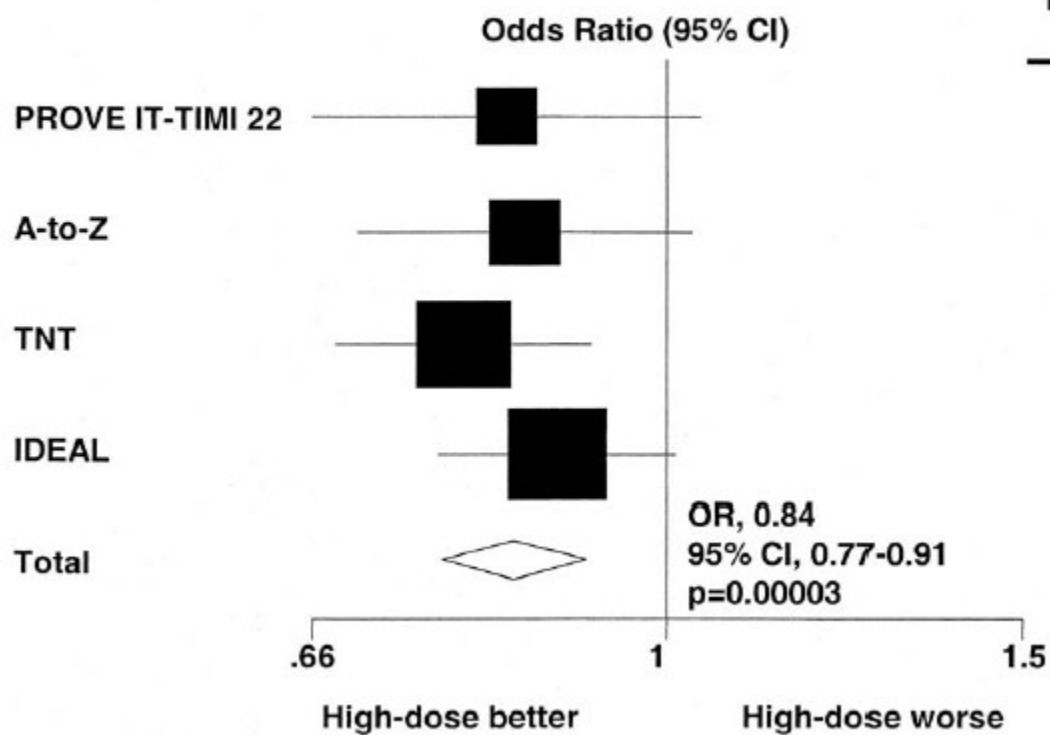


Cumulative hazard of primary endpoint, all-cause mortality, and any cardiovascular endpoint
*p for heterogeneity.

Meta-Analysis of Cardiovascular Outcomes Trials Comparing Intensive Versus Moderate Statin Therapy

Christopher P. Cannon, MD, Benjamin A. Steinberg, BA, Sabina A. Murphy, MPH,
Jessica L. Mega, MD, Eugene Braunwald, MD

Journal of the American College of Cardiology



Odds Reduction	Event Rates	
	High Dose	Std Dose
-17%	147/2099 (7.0)	172/2063 (8.3)
-15%	205/2265 (9.1)	235/2232 (10.5)
-21%	334/4995 (6.7)	418/5006 (8.3)
-12%	411/4439 (9.3)	463/4449 (10.4)
-16%	1097/13798 (8.0)	1288/13750 (9.4)

Individual trials and pooled analysis showing a highly significant 16% reduction in the risk of coronary death or myocardial infarction (p < 0.0001). CI = confidence interval; OR = odds ratio.

Effect of Lowering LDL Cholesterol Substantially Below Currently Recommended Levels in Patients With Coronary Heart Disease and Diabetes

The Treating to New Targets (TNT) study

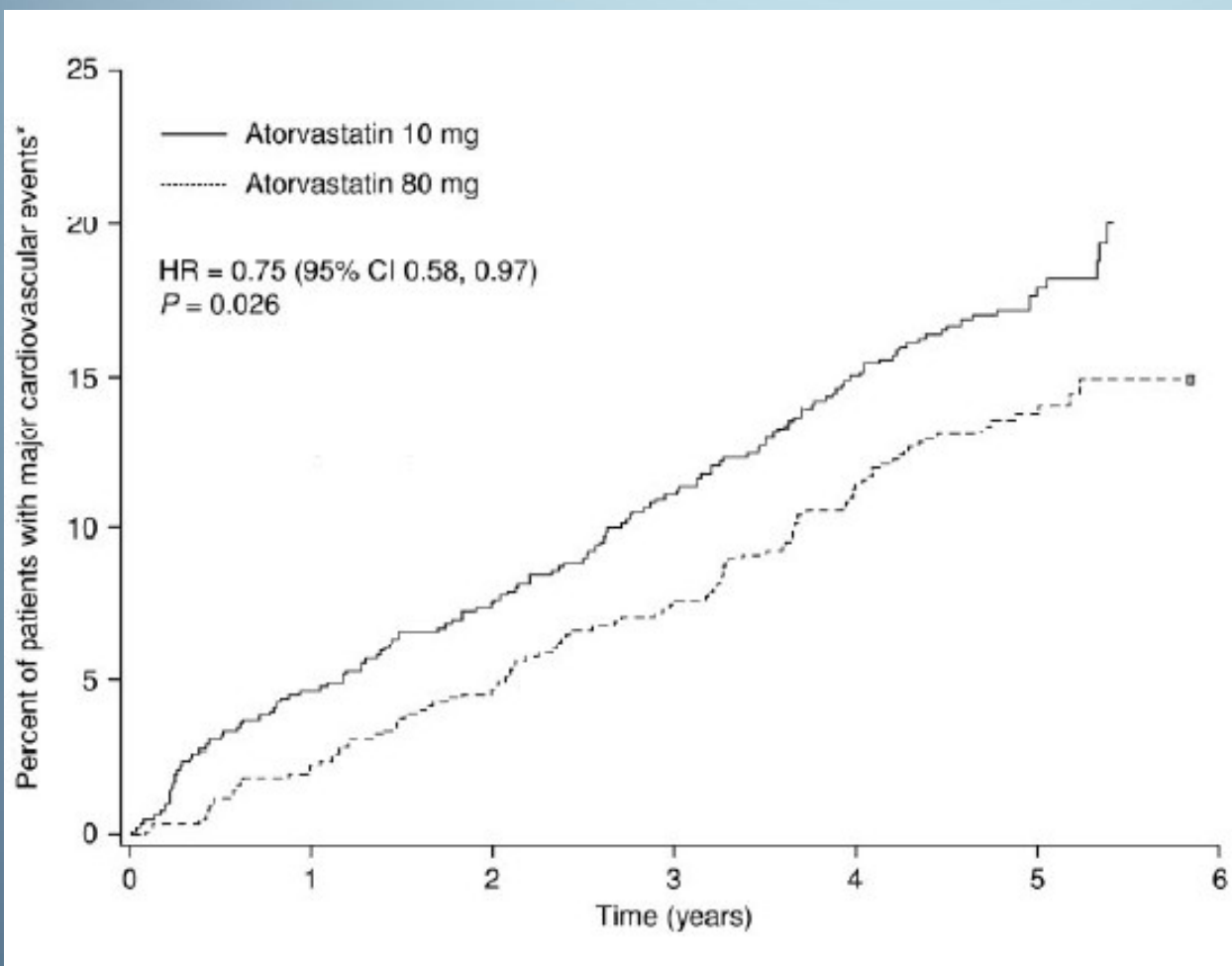
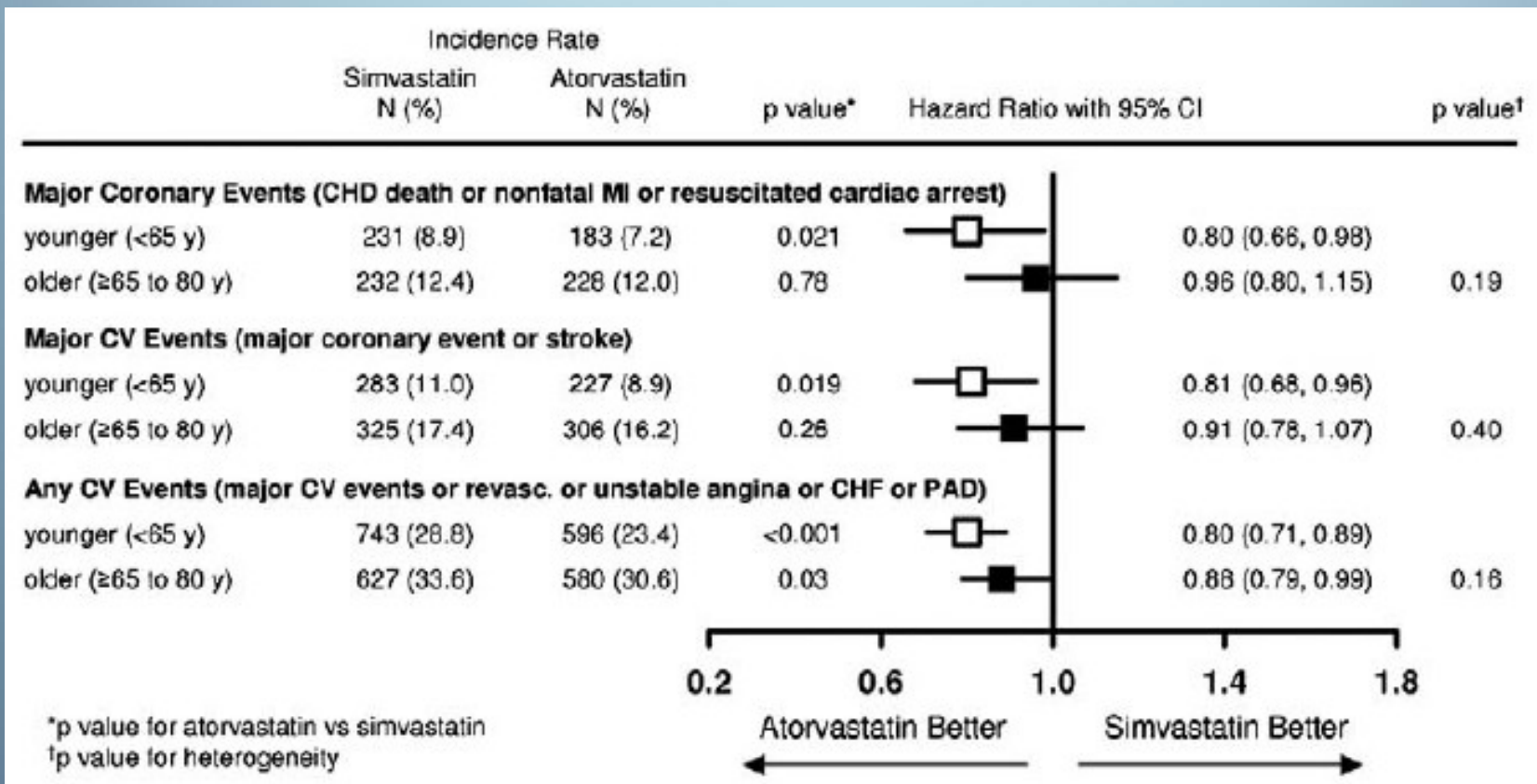


Figure 1—Kaplan-Meier estimates of the incidence of major cardiovascular events in patients with diabetes. *Composite of CHD death, nonfatal non-procedure-related myocardial infarction, resuscitated cardiac arrest, and fatal or nonfatal stroke.

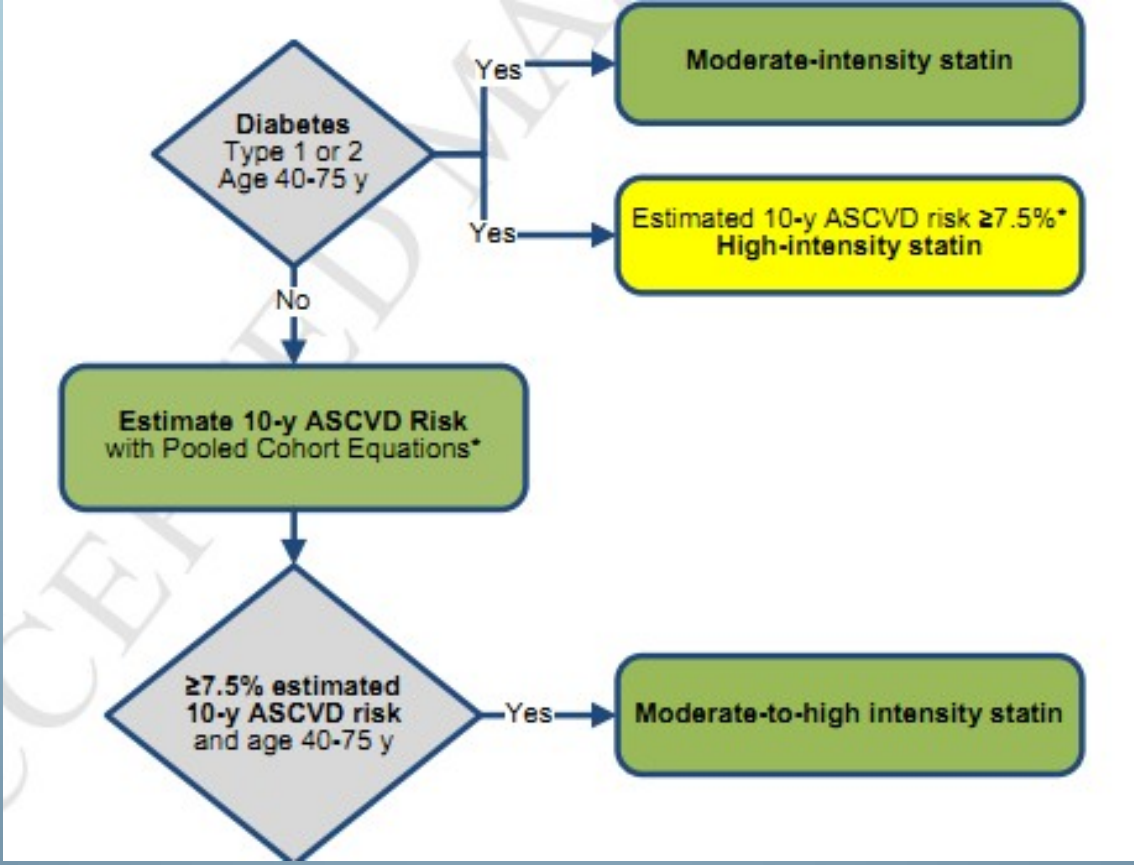
Comparison of Efficacy and Safety of Atorvastatin (80 mg) to Simvastatin (20 to 40 mg) in Patients Aged <65 Versus ≥65 Years With Coronary Heart Disease (from the Incremental DEcrease through Aggressive Lipid Lowering [IDEAL] Study)



Intensive atorvastatin therapy reduced event rates in both younger and older patients. *p values are for test of heterogeneity. CHF = congestive heart failure; CV = cardiovascular; MI = myocardial infarction; PAD = peripheral artery disease.

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines



Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials

Naveed Sattar, David Preiss, Heather M Murray, Paul Welsh, Brendan M Buckley, Anton J M de Craen, Sreenivasa Rao Kondapally Seshasai, John J McMurray, Dilys J Freeman, J Wouter Jukema, Peter W Macfarlane, Chris J Packard, David J Stott, Rudi G Westendorp, James Shepherd, Barry R Davis, Sara L Pressel, Roberto Marchioli, Rosa Maria Marfisi, Aldo P Maggioni, Luigi Tavazzi, Gianni Tognoni, John Kjekshus, Terje R Pedersen, Thomas J Cook, Antonio M Gotto, Michael B Clearfield, John R Downs, Haruo Nakamura, Yasuo Ohashi, Kyoichi Mizuno, Kausik K Ray, Ian Ford

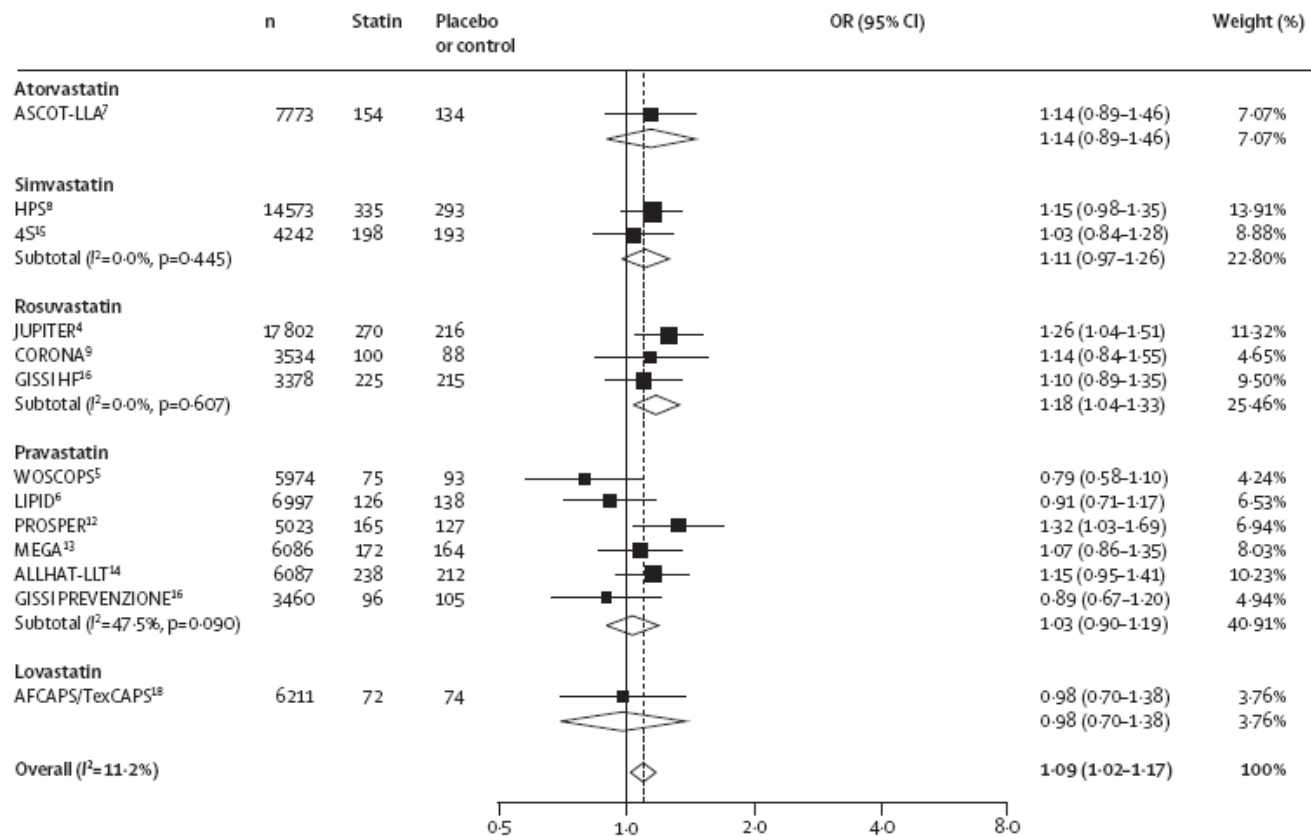


Figure 3: Association between different statins and development of diabetes

Lipid control in patients with diabetes

Recommendations	Class	Level
Statin therapy is recommended in patients with T1DM and T2DM at very high risk (i.e. if combined with documented CVD, severe CKD or with one or more CV risk factors and/or target organ damage) with an LDL-C target of <1.8 mmol/L (<70 mg/dL) or at least a ≥50% LDL-C reduction if this target goal cannot be reached.	I	A
Statin therapy is recommended in patients with T2DM at high risk (without any other CV risk factor and free of target organ damage) with an LDL-C target of <2.5 mmol/L (<100 mg/dL).	I	A
Statins may be considered in T1DM patients at high risk for cardiovascular events irrespective of the basal LDL-C concentration.	IIb	C
It may be considered to have a secondary goal of non-HDL-C <2.6 mmol/L (<100 mg/dL) in patients with DM at very high risk and of <3.3 mmol/L (<130 mg/dL) in patients at high risk.	IIb	C
Intensification of statin therapy should be considered before the introduction of combination therapy with the addition of ezetimibe.	IIa	C
The use of drugs that increase HDL-C to prevent CVD in T2DM is not recommended.	III	A