



APPROCCIO FARMACOLOGICO E DIETETICO IN RELAZIONE AL RISCHIO CARDIOVASCOLARE

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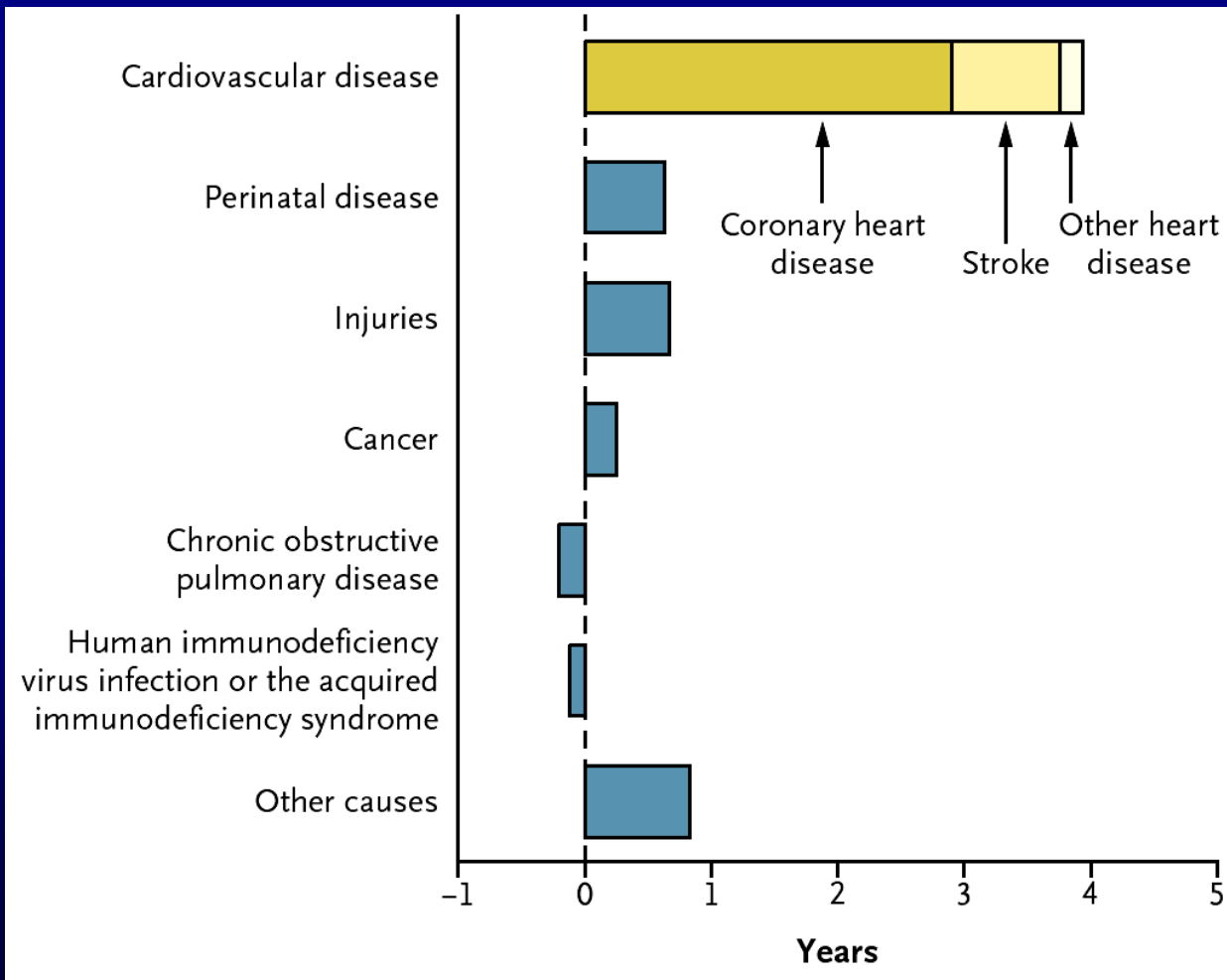
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Baveno (VB), 8-10 Novembre 2007

Clinical Research to Clinical Practice Lost in Translation?

MODIFICAZIONI DELL'ASPETTATIVA DI VITA DAL 1970 AL 2000



Negli USA, l'aspettativa di vita è aumentata di 6 anni: la vita si è allungata di 3.9 anni per la riduzione della mortalità per cause cardiovascolari

Lenfant, NEJM, 349:868, 2003

Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980–2000

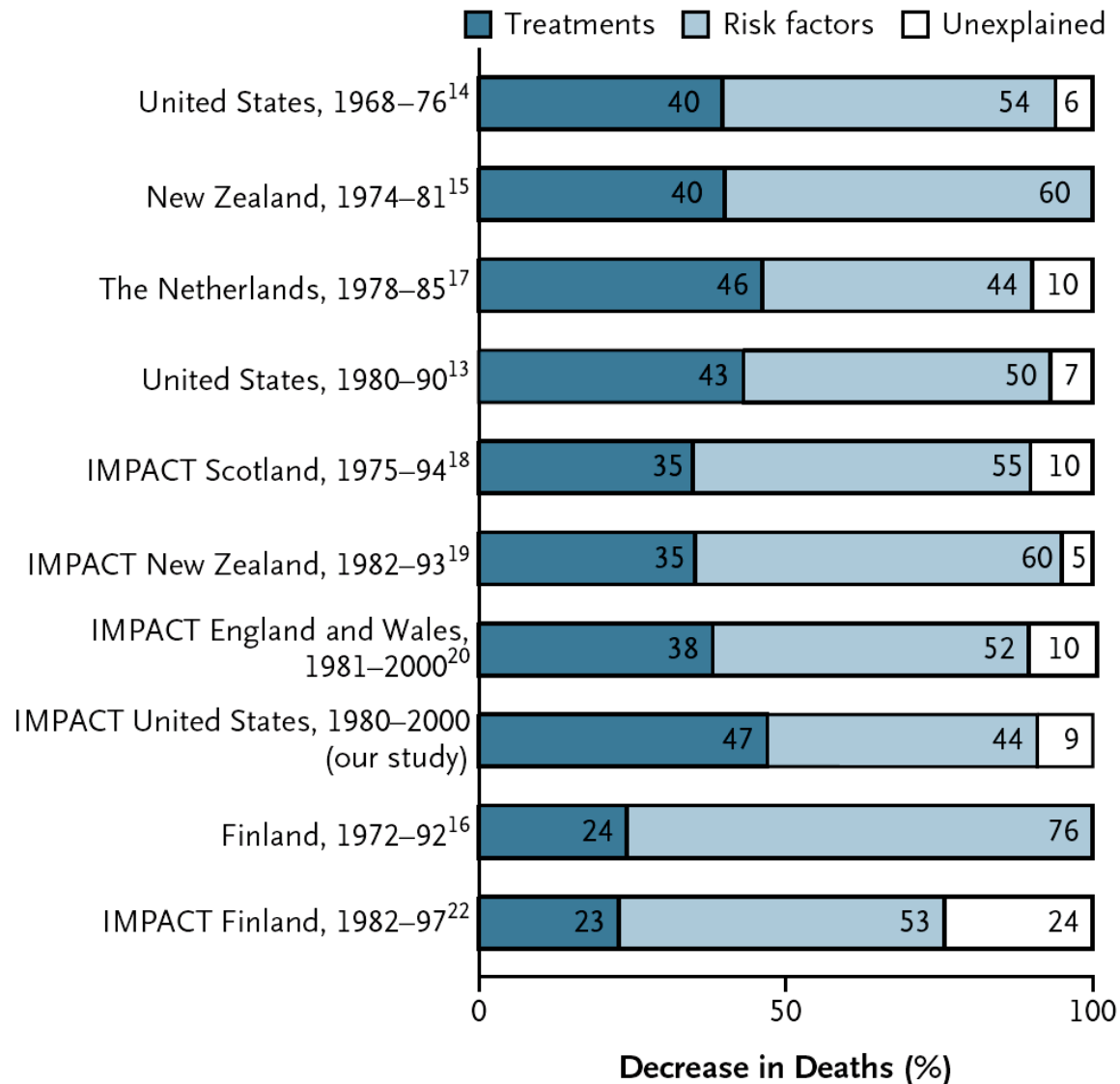
Dal 1980 al 2000 la mortalità per malattia coronarica, aggiustata per età, si è ridotta da 542.9 a 266.8 decessi per 100.000 uomini e da 263.3 a 134.4 decessi per 100.000 donne

Tale riduzione è associata ad un significativo decremento di alcuni dei maggiori fattori di rischio cardiovascolare, quali il *fumo*, gli elevati valori di *pressione arteriosa* e le elevate concentrazioni di *colesterolo* plasmatico.

Per contro, la prevalenza della *obesità* e del *diabete mellito* sono aumentate in maniera allarmante.

Contemporaneamente abbiamo assistito ad una rivoluzione nel trattamento della cardiopatia ischemica, con la utilizzazione di trombolisi, angioplastica, bypass, ACE-inibitori, sartanici e statine.

PERCENTUALE DEL DECREMENTO DELLA MORTALITA' PER MALATTIA CORONARICA ATTRIBUITA A TRATTAMENTO FARMACOLOGICO O A MODIFICAZIONI DEI FATTORI DI RISCHIO



Ford et al, NEJM,
356: 2388–98, 2007

ATP - III

JAMA, May 16, 2001
Vol 285: 2486-2496

ATP - III

Circulation 2004;
Vol 110: 227-239

Table 4. Three Categories of Risk That Modify LDL Cholesterol Goals

Risk Category	LDL Goal (mg/dL)	New LDL Goal (mg/dL)
CHD and CHD risk equivalents	<100	<70
Multiple (2+) risk factors*	<130	<100
0-1 risk factor	<160	<160

*Risk factors that modify the low-density lipoprotein (LDL) goal are listed in Table 3. CHD indicates coronary heart disease.

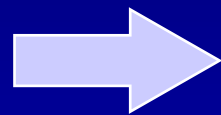
NCEP ATP - III

JAMA, May 16, 2001 - Vol 285: 2486-2496

GLI EQUIVALENTI DI RISCHIO CHD (*CHD risk equivalents*)

- 1) ALTRE FORME DI ATEROSCLEROSI:
 - ARTERIOPATIA PERIFERICA
 - ANEURISMA DELL'AORTA ADDOMINALE
 - PLACCHE CAROTIDEE
- 2) DIABETE
- 3) PIU' FATTORI DI RISCHIO CHE DETERMINANO UN RISCHIO GLOBALE >20% A 10 ANNI

LA TERAPIA CON STATINE



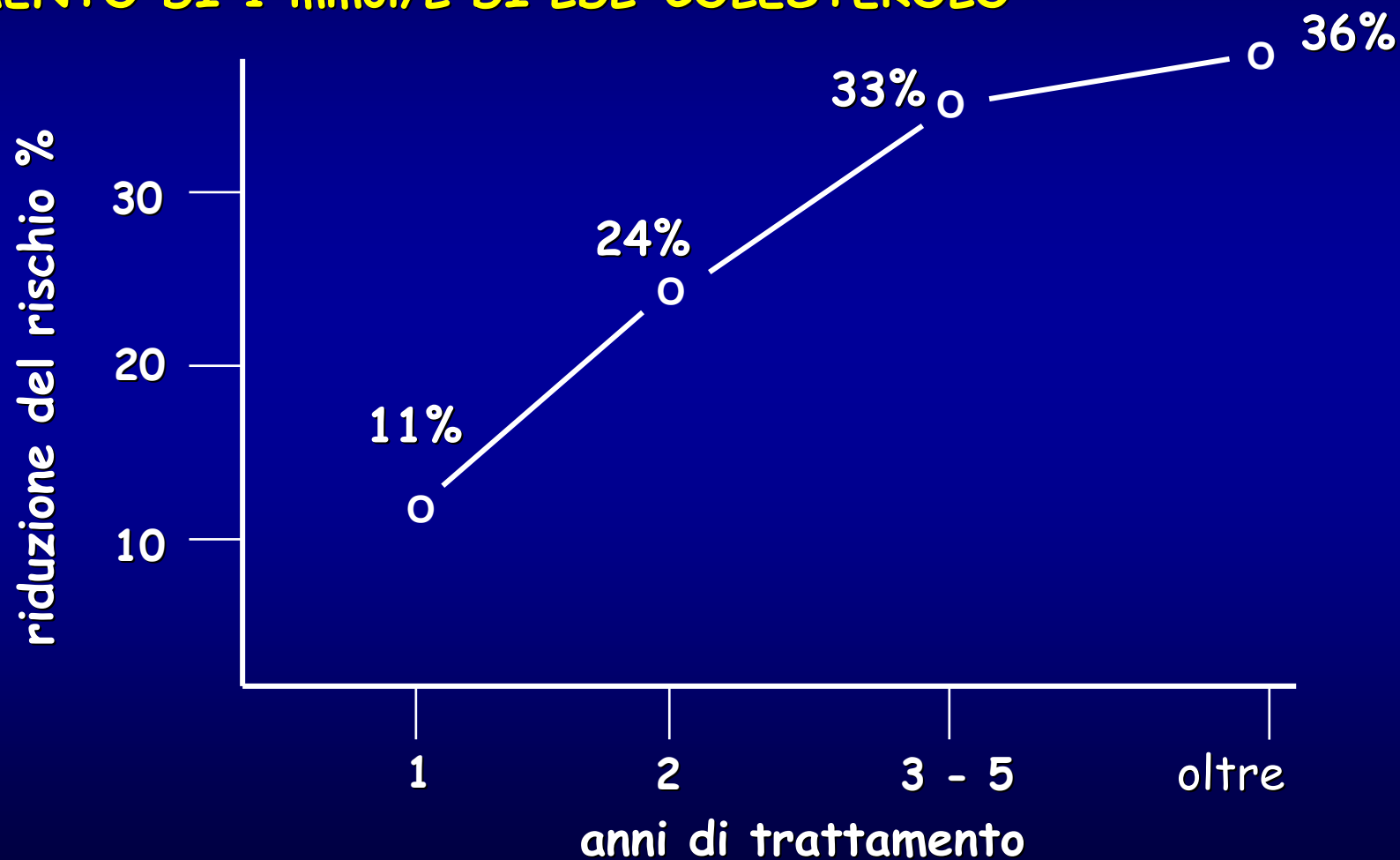
Durata

Aggressività

Tempestività

Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis

RIDUZIONE DEL RISCHIO DI IHD PER IL DECREMENTO DI 1 mmol/L DI LDL-COLESTEROLO

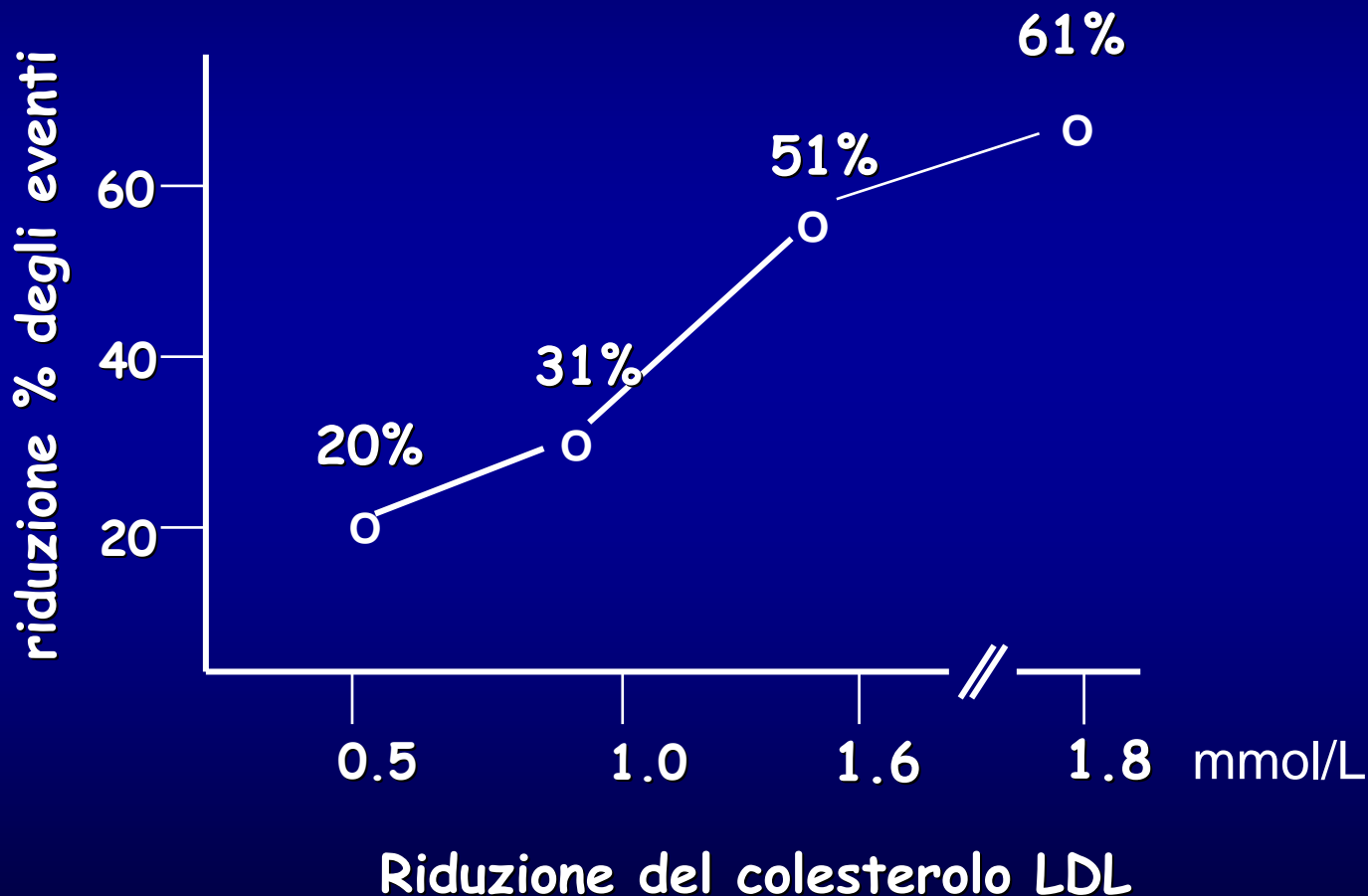


Law et al, BMJ, 326: 1423-7, 2003

Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis

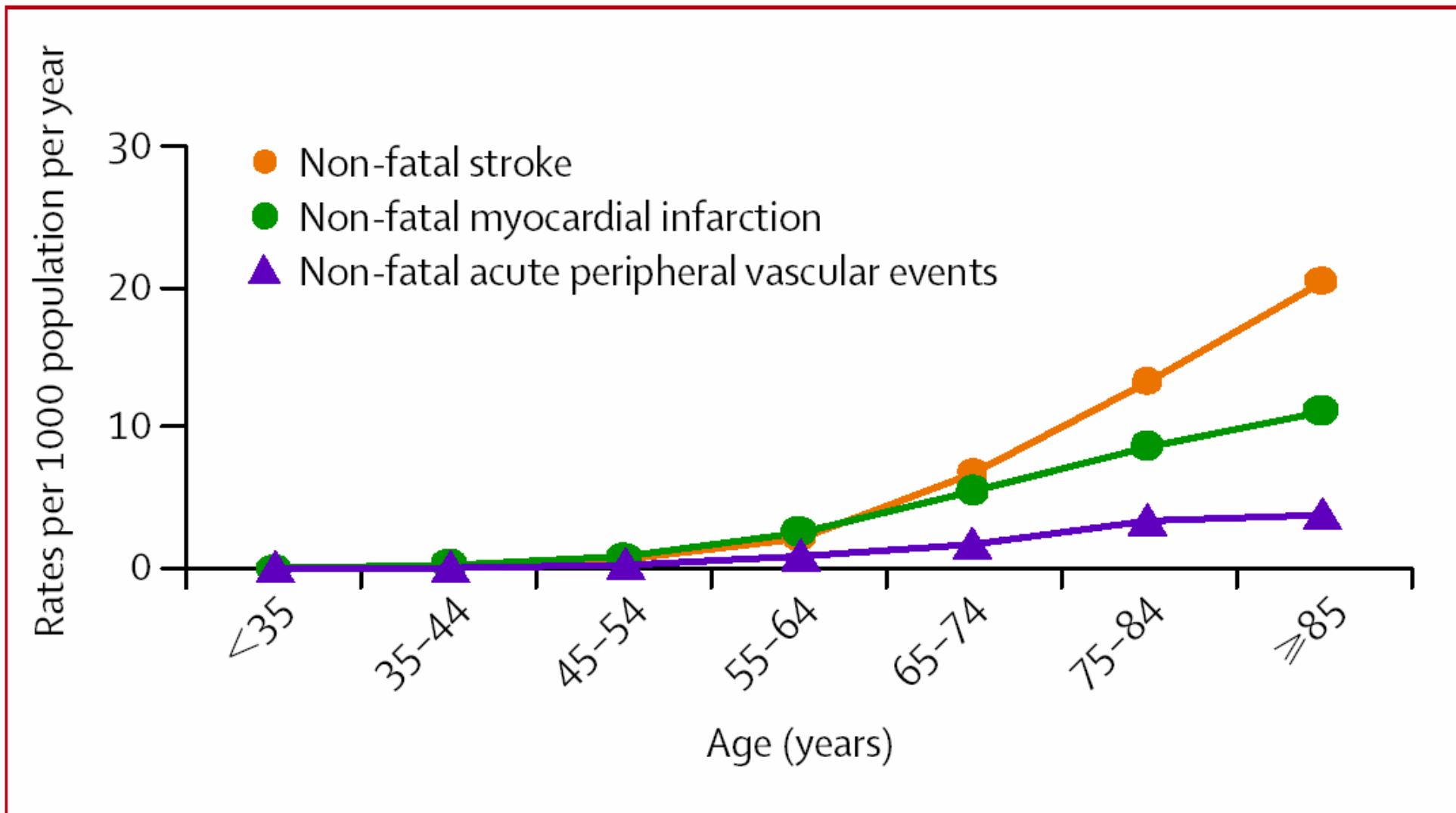
Riduzione dello "stroke rate" in 58 trials:
• 1 mmol di riduzione di LDL-colesterolo: - 10% stroke
• 1.8 mmol riduzione di LDL-colesterolo: - 17% stroke

RIDUZIONE DEL RISCHIO DI IHD PER IL DECREMENTO DI LDL-COLESTEROLO



Law et al, BMJ, 326: 1423-7, 2003

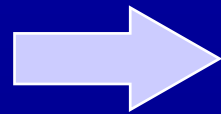
PREVALENZA DEGLI EVENTI NON FATALI



Rothwell et al, Lancet, 326: 1423-7, 2005

LA TERAPIA CON STATINE

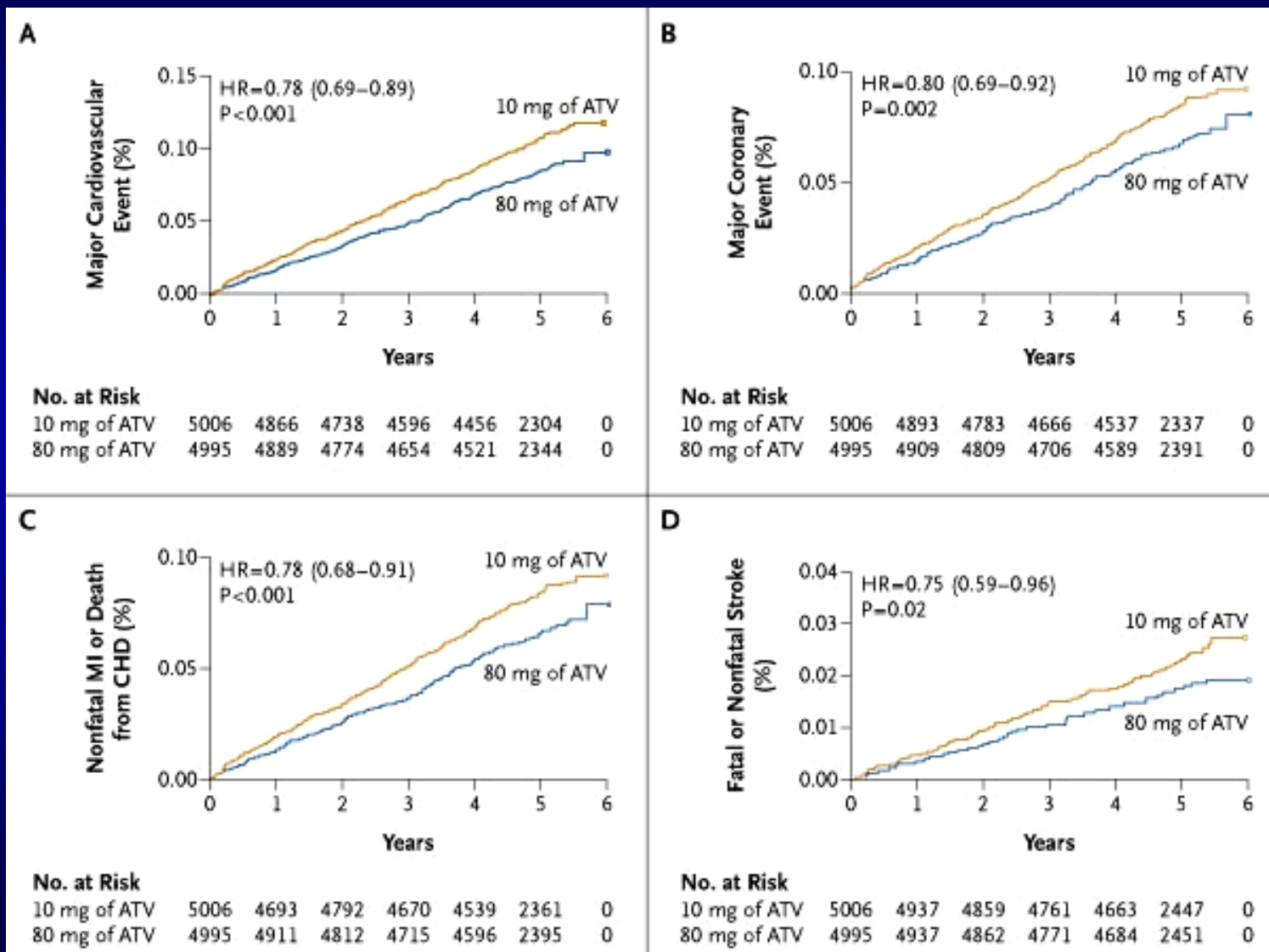
Durata



Aggressività

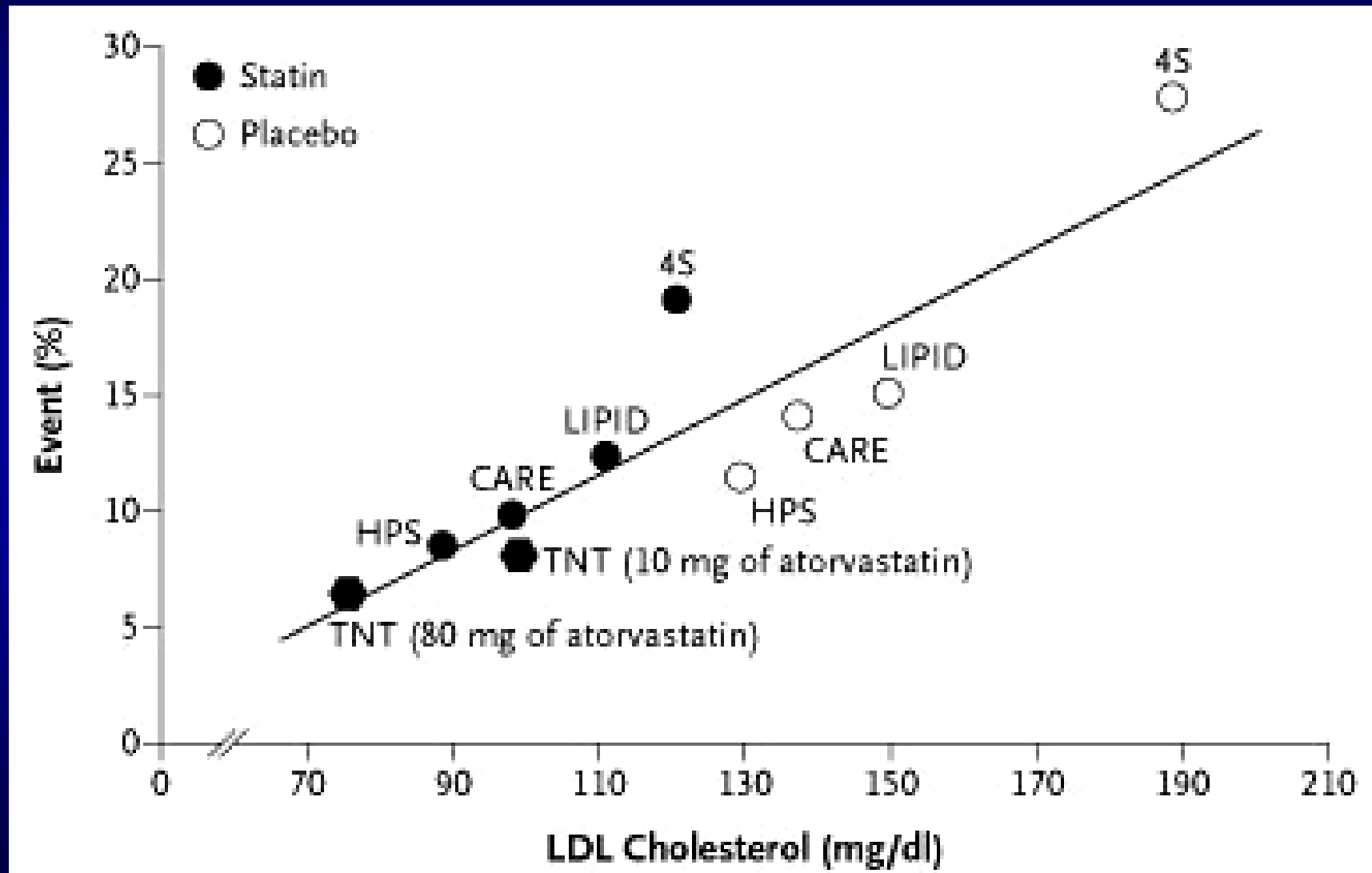
Tempestività

Intensive Lipid Lowering with Atorvastatin in Patients with Stable Coronary Disease



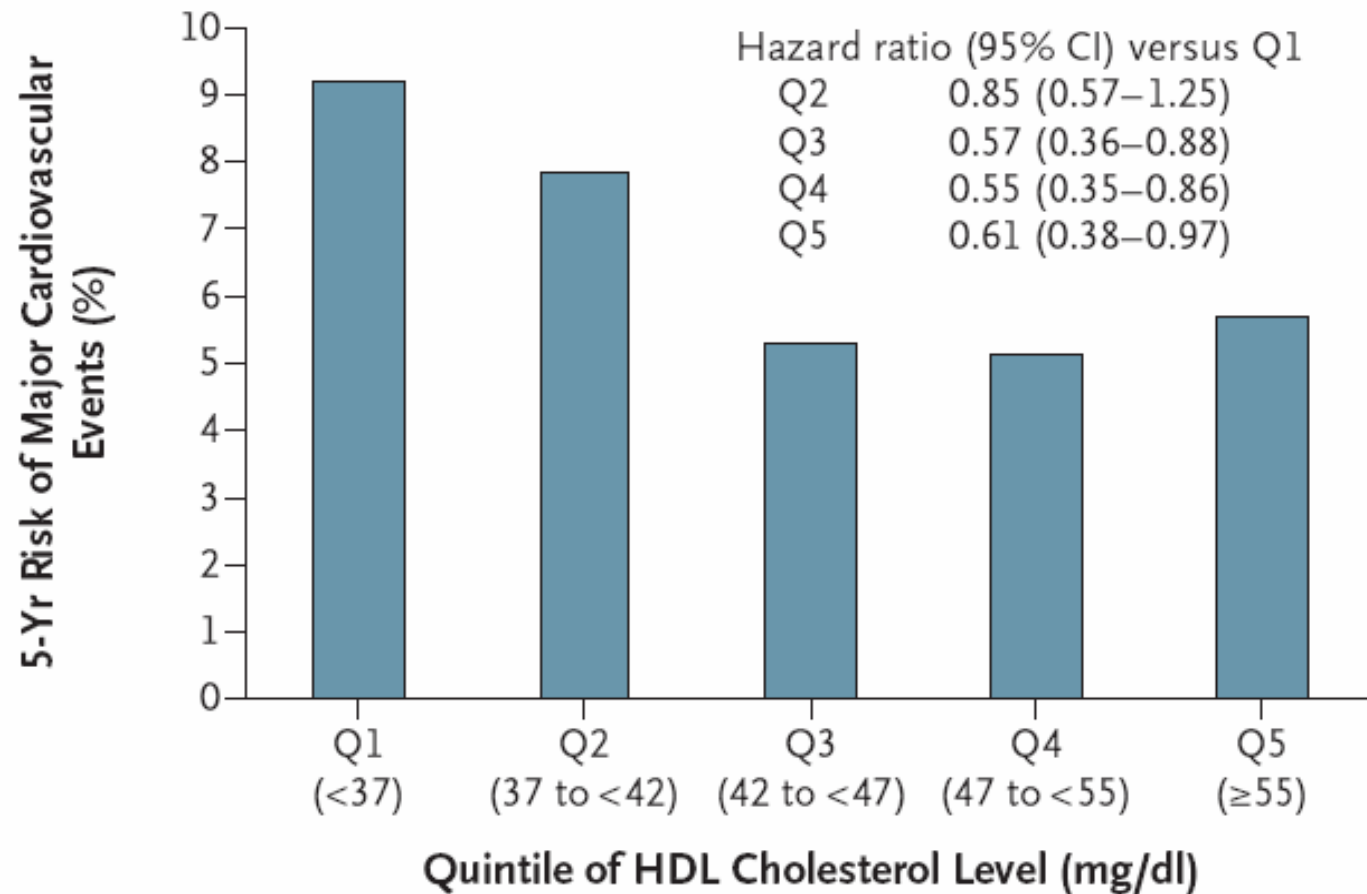
LaRosa et al, NEJM, 352: 1425-35, 2005

Intensive Lipid Lowering with Atorvastatin in Patients with Stable Coronary Disease



HDL Cholesterol, Very Low Levels of LDL Cholesterol, and Cardiovascular Events

Pazienti con LDL-CH < 70 mg/dL

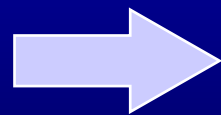


Barter et al, NEJM, 357: 1301-10, 2007

LA TERAPIA CON STATINE

Durata

Aggressività

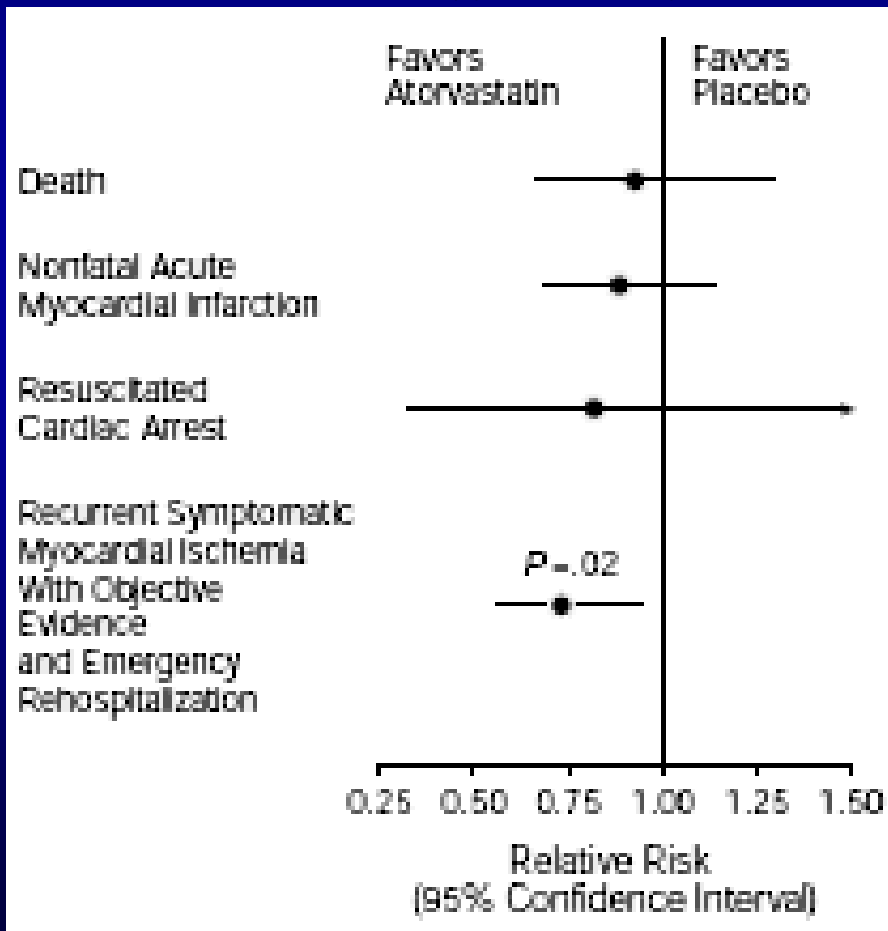


Tempestività

Effects of Atorvastatin on Early Recurrent Ischemic Events in Acute Coronary Syndromes

The MIRACL Study: A Randomized Controlled Trial

Risk Ratio Plot



Atorvastatin 80 mg versus placebo

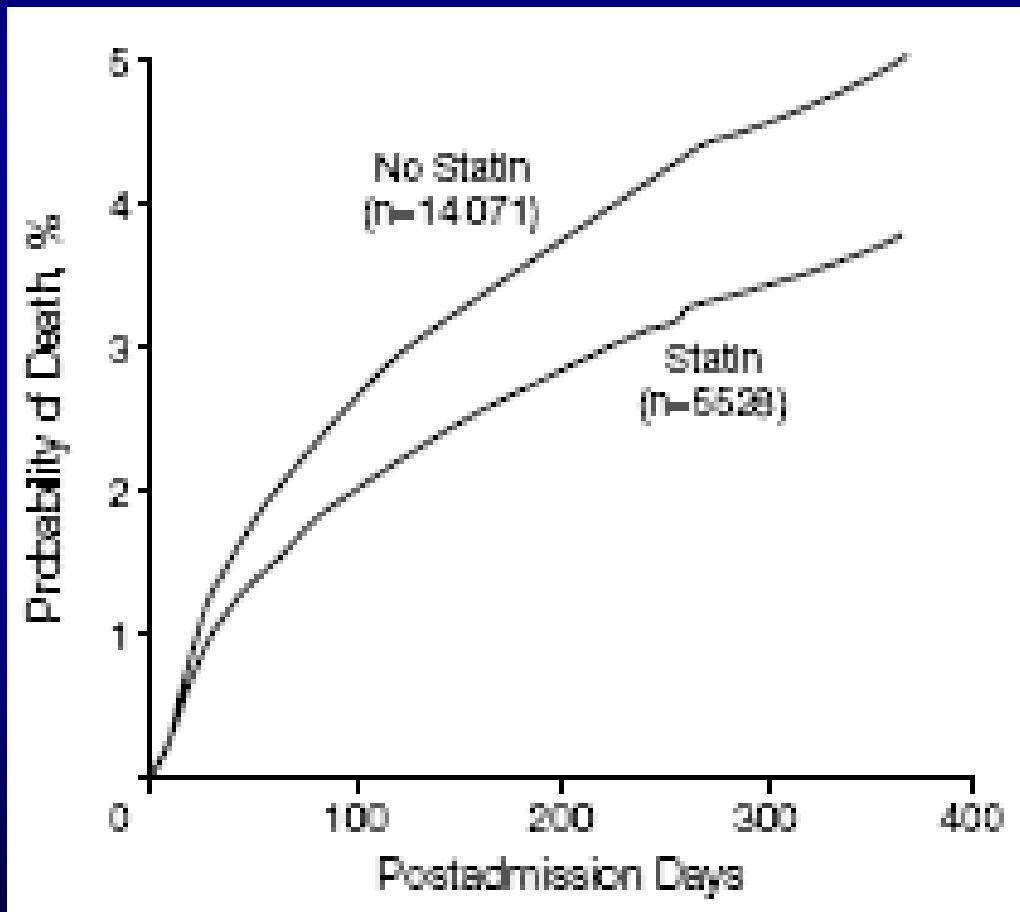
Razionale

- Somministrazione precoce di atorvastatina (24-96 ore dopo IMA)
- Durata dello studio: 16 settimane
- No. pazienti : 3086
- End points primari combinati: morte, M.I. non fatale, arresto cardiaco con resuscitazione, episodi ischemici recidivanti

Schwartz et al, JAMA, 285: 1711-8, 2001

Early Statin Treatment Following Acute Myocardial Infarction and 1-Year Survival

Adjusted Probability of Mortality by Statin Treatment



Studio di Coorte Prospettico

Esaminate 58 U. C. Svedesi

5528 pazienti hanno ricevuto statine

14071 pazienti non hanno ricevuto statine

Le statine sono state somministrate prima della dimissione

Rischio Relative con statine: 0.75%

Stenestrand et al, JAMA, 285: 430-6, 2001

Atorvastatin Pretreatment Improves Outcomes in Patients With Acute Coronary Syndromes Undergoing Early Percutaneous Coronary Intervention

Results of the ARMYDA-ACS Randomized Trial

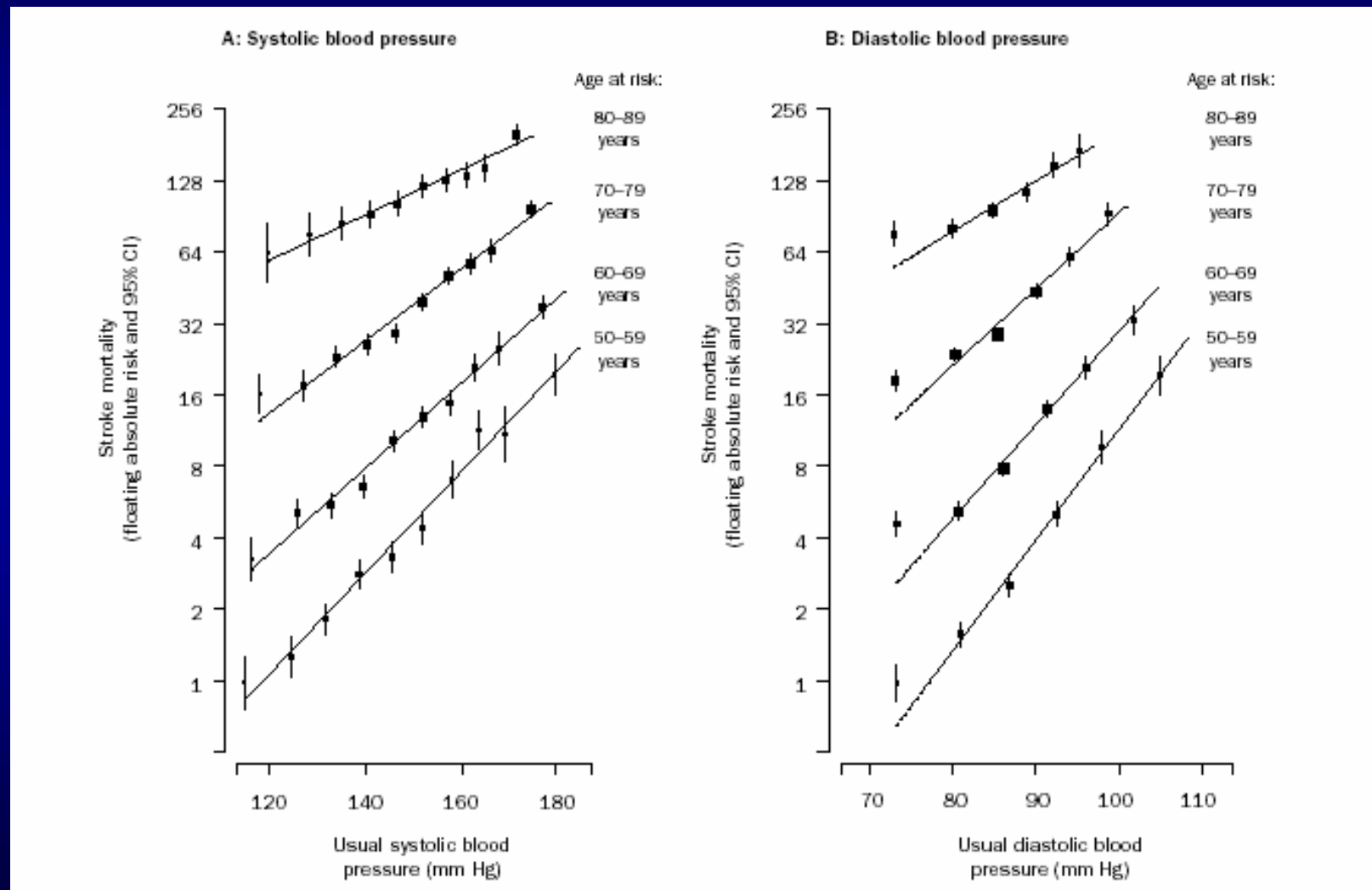
SCOPO DELLO STUDIO:

In pazienti con sindrome coronarica acuta non-ST (MI o angina), sottoposti ad angioplastica: valutare l'effetto del pre-trattamento con atorvastatina: 80 mg (12 ore prima) + 40 mg (2 ore prima) sugli outcome a 30 giorni dalla PCI

	Atorvastatin (n = 86)	Placebo (n = 85)	p Value
Death	—	—	
Myocardial infarction	4 (5)	13 (15)	0.04
Target vessel revascularization	—	1 (2)	1
Total MACE	4 (5)	14 (17)	0.01

Patti et al, JACC, 49: 1272-8, 2007

Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies



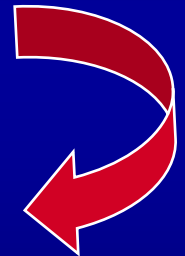
Lancet, 360: 1903-1913, 2002

Blood Pressure and Stroke

An Overview of Published Reviews

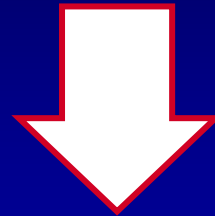
Meta-analisi di 40 studi prospettici di coorte
188.000 partecipanti, 6800 strokes

10 mmHg di riduzione di pressione sistolica
30% riduzione del RR di stroke (60-80 anni)



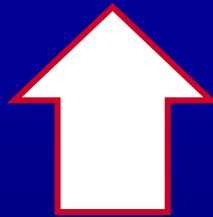
Tale riduzione del RR è lineare sino a valori di
115/75

Terapia anti-ipertensiva



INFARTO MIOCARDICO

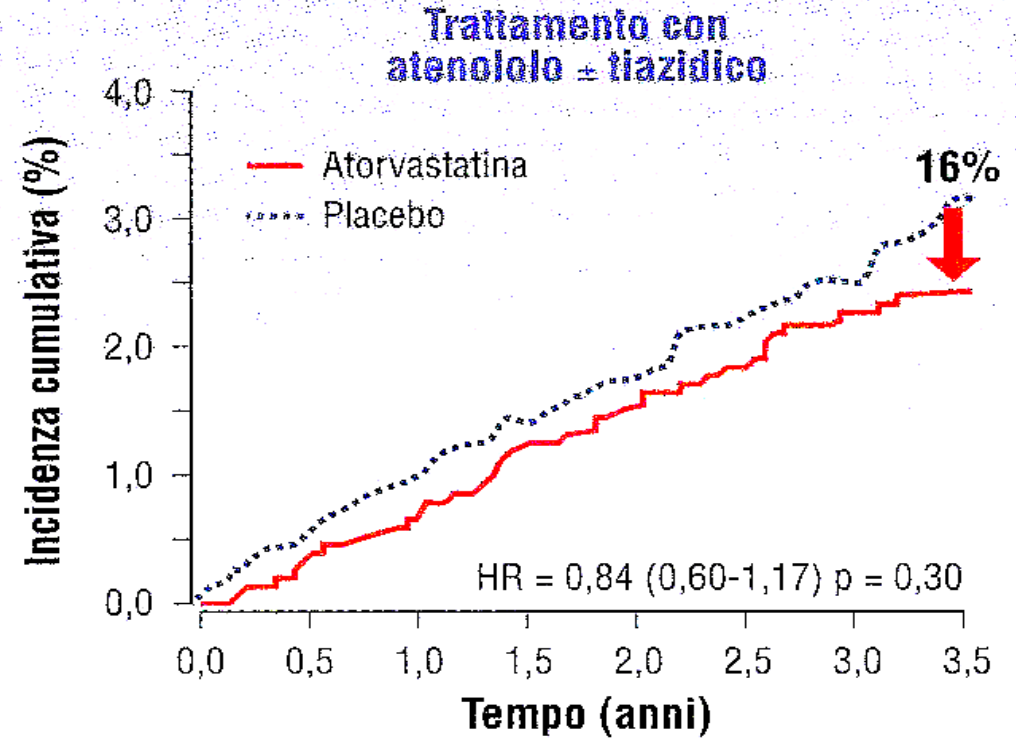
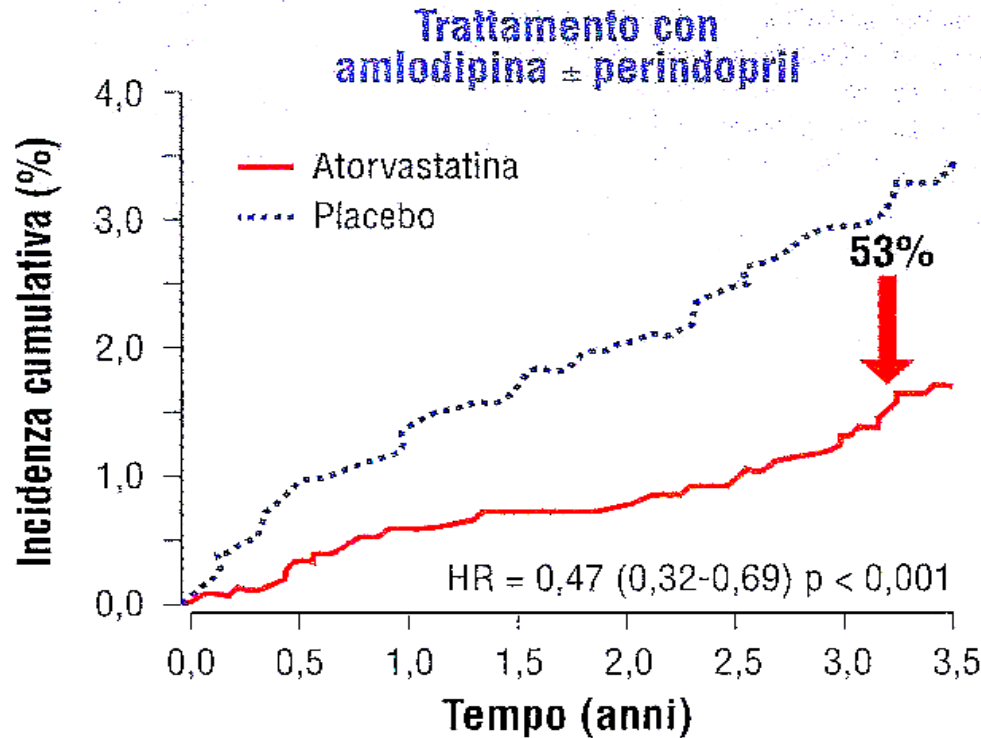
STROKE



Terapia con statine

STUDIO ASCOT-LLA

Endpoint Primario (IM non fatale e CHD fatale)

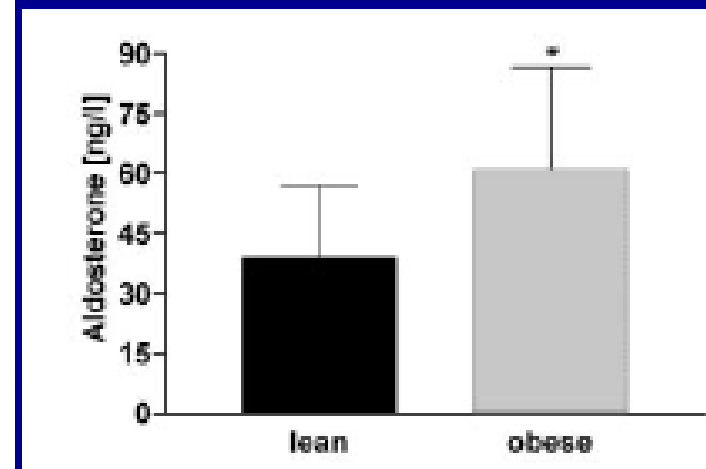
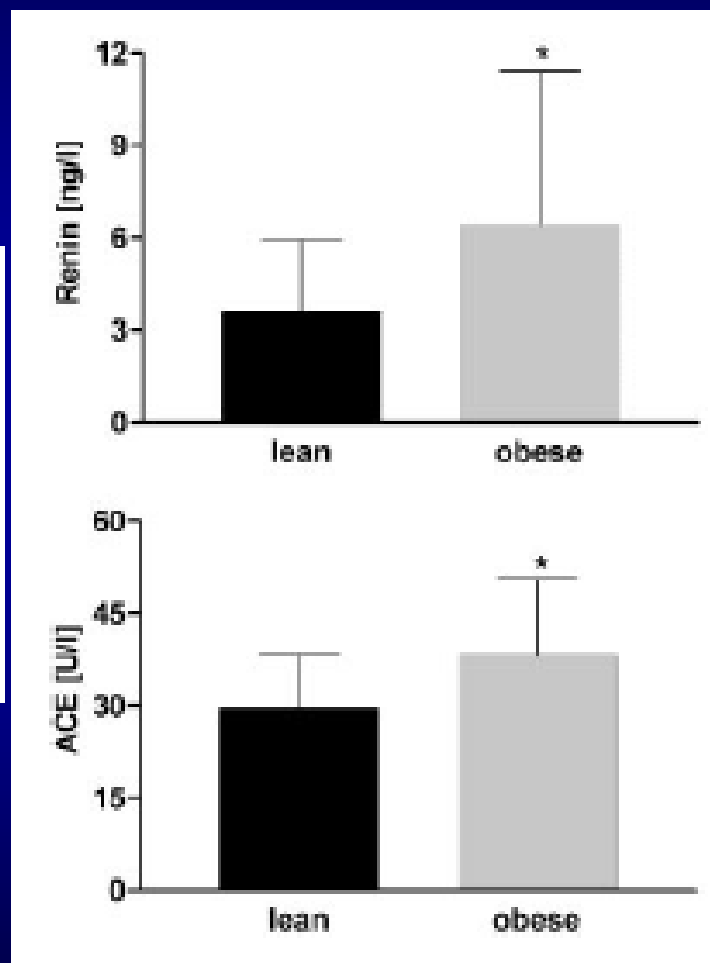
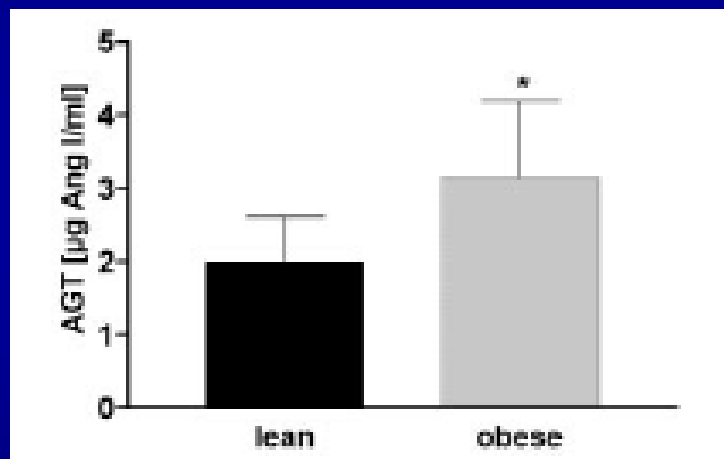


Effetto sinergico della statina con il Ca-antagonista sul doppio strato lipidico delle membrane delle cellule muscolari lisce.

La statina indurrebbe il recupero della funzionalità dei canali del calcio di tipo L, persa durante l'attivazione pro-infiammatoria delle SMC

Sever PS et al, Lancet, 361: 1149-58, 2003

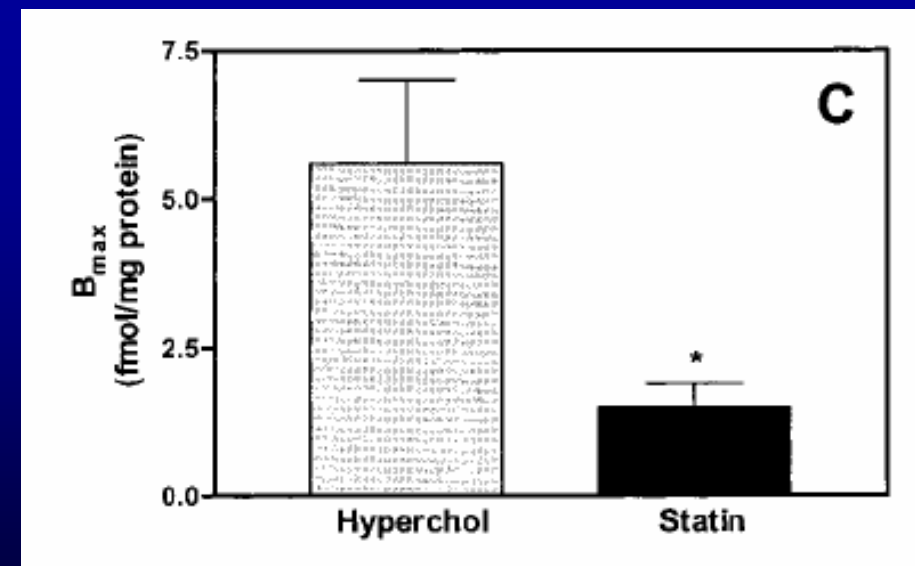
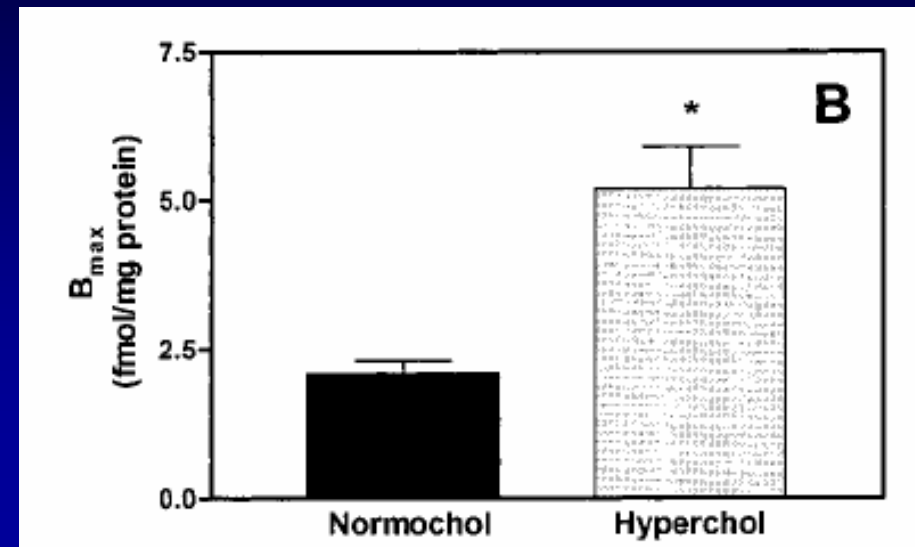
Renin-Angiotensin-Aldosterone System



Effetti della stimolazione dei Recettori AT_1 da parte dell'Angiotensina II

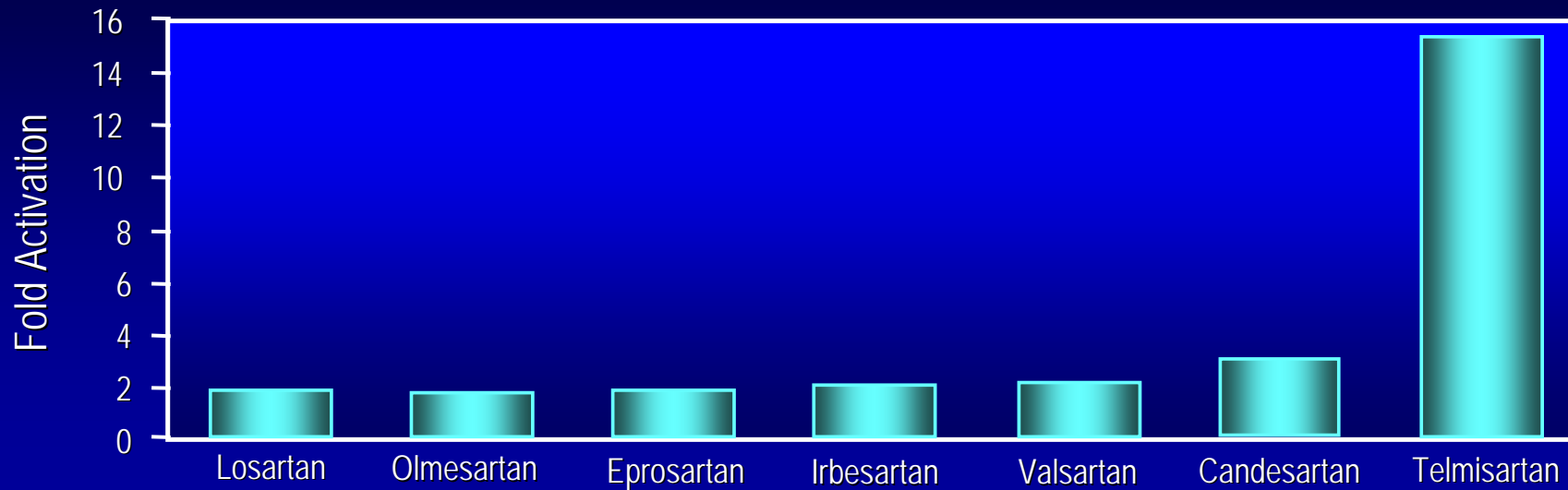
- ▲ Vasocostrizione
- ▲ Secrez. Aldosterone
- ▲ Secrez. Vasopressina
- ▲ Riassorbimento tubul. Na
- ▲ Ipertrofia cardiaca
- ▲ Proliferaz. SMC vasale
- ▲ Attività noradrenergica
- ▲ Formaz. matrice cellulare
- ▼ Flusso sanguigno renale

Statin-Sensitive Dysregulated AT_1 Receptor Function and Density in Hypercholesterolemic Men

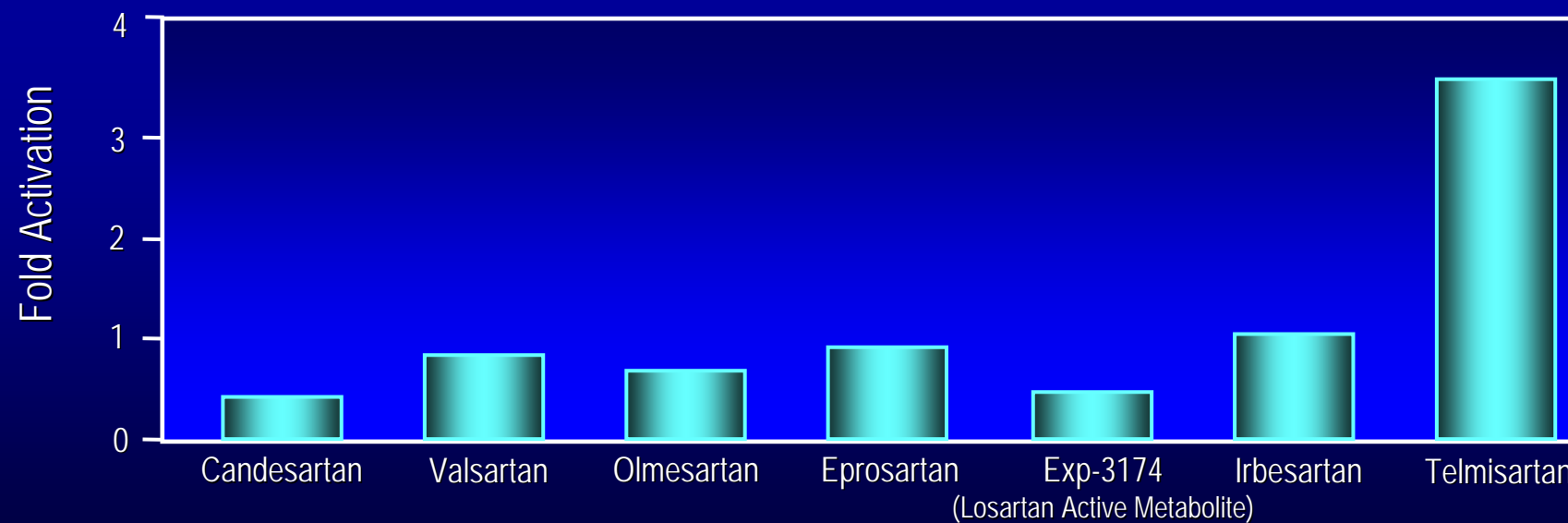


Nickening et al, *Circulation*, 100: 213, 1999

Activation of PPAR γ by Telmisartan



Activation of PPAR γ by ARBs in a cell-based transient transfectin assay



Effects of ARBs on the expression of the PEPCK gene in mature human adipocytes

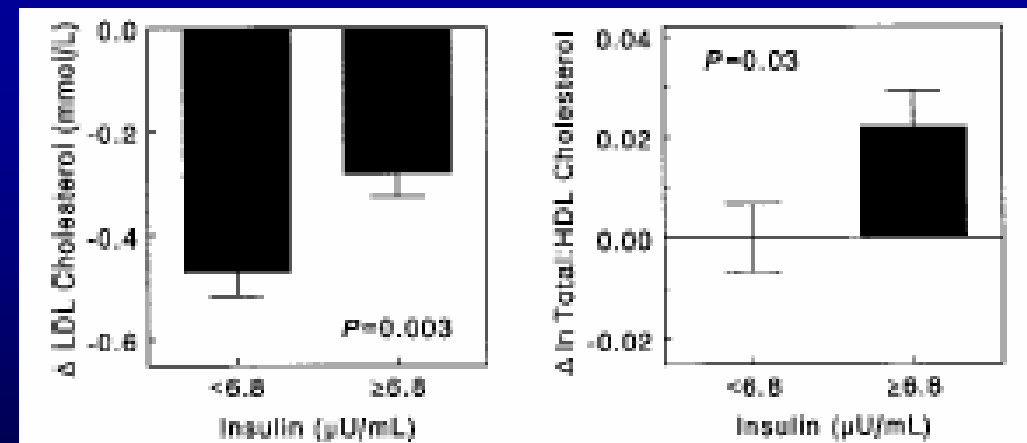
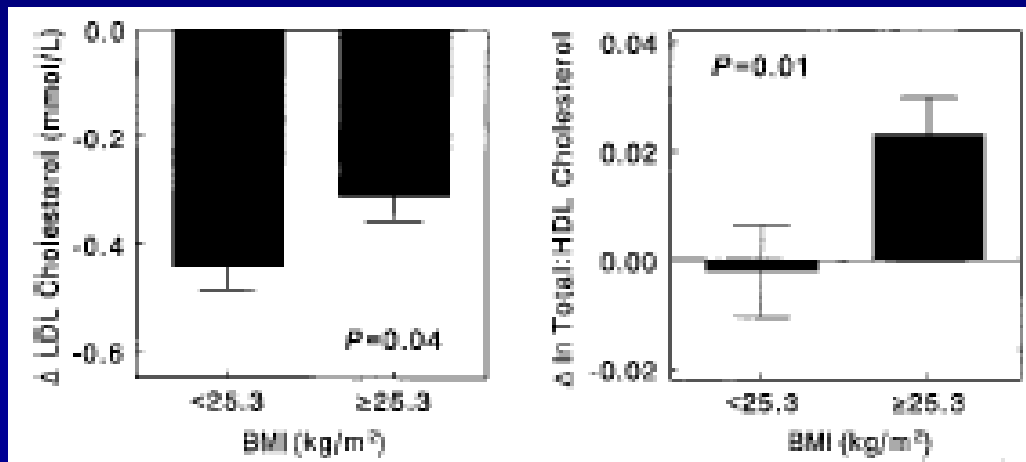
Diet and Lifestyle Recommendations Revision 2006

A Scientific Statement From the American Heart Association Nutrition Committee

TABLE 2. AHA 2006 Diet and Lifestyle Recommendations for Cardiovascular Disease Risk Reduction

-
- Balance calorie intake and physical activity to achieve or maintain a healthy body weight.
 - Consume a diet rich in vegetables and fruits.
 - Choose whole-grain, high-fiber foods.
 - Consume fish, especially oily fish, at least twice a week.
 - Limit your intake of saturated fat to <7% of energy, trans fat to <1% of energy, and cholesterol to <300 mg per day by
 - choosing lean meats and vegetable alternatives;
 - selecting fat-free (skim), 1%-fat, and low-fat dairy products; and
 - minimizing intake of partially hydrogenated fats.
 - Minimize your intake of beverages and foods with added sugars.
 - Choose and prepare foods with little or no salt.
 - If you consume alcohol, do so in moderation.
 - When you eat food that is prepared outside of the home, follow the AHA Diet and Lifestyle Recommendations.
-

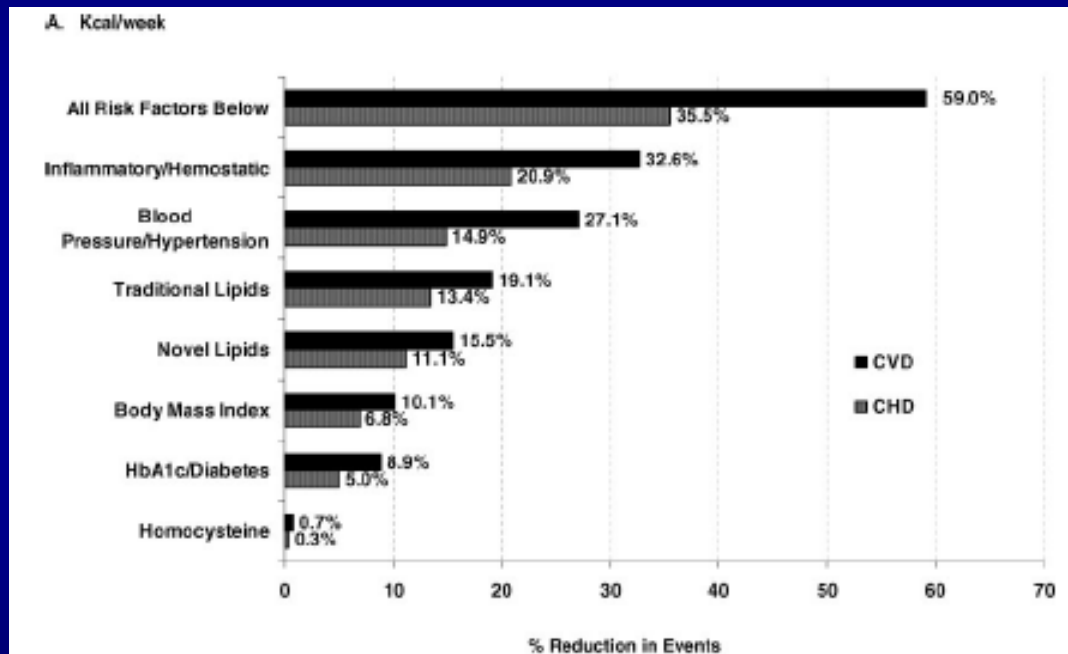
Individual variability in cardiovascular disease risk factor responses to low-fat and low-saturated-fat diets in men: body mass index, adiposity, and insulin resistance predict changes in LDL cholesterol¹⁻³



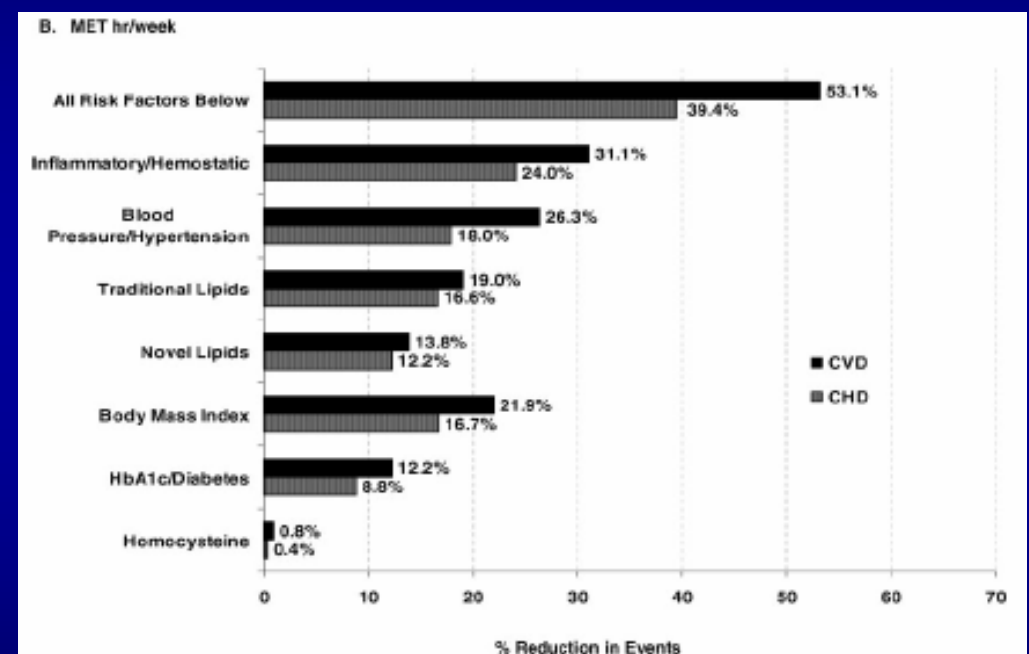
Lefevre et al, Am J Clin Nutr, 82: 957-63, 2005

Physical Activity and Reduced Risk of Cardiovascular Events

Potential Mediating Mechanisms



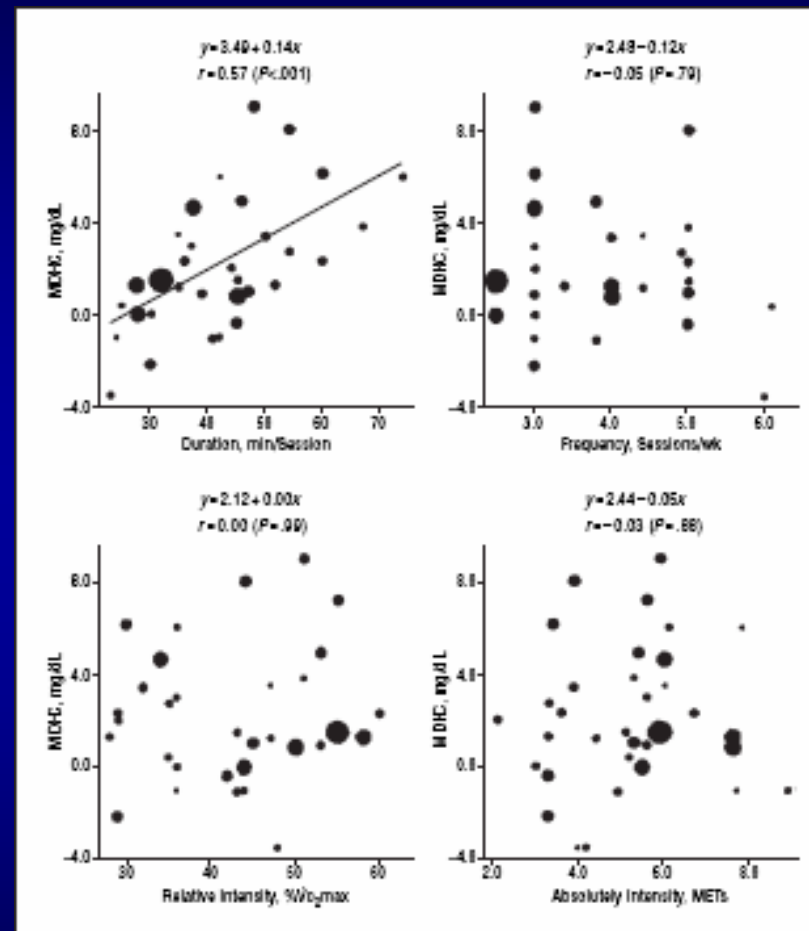
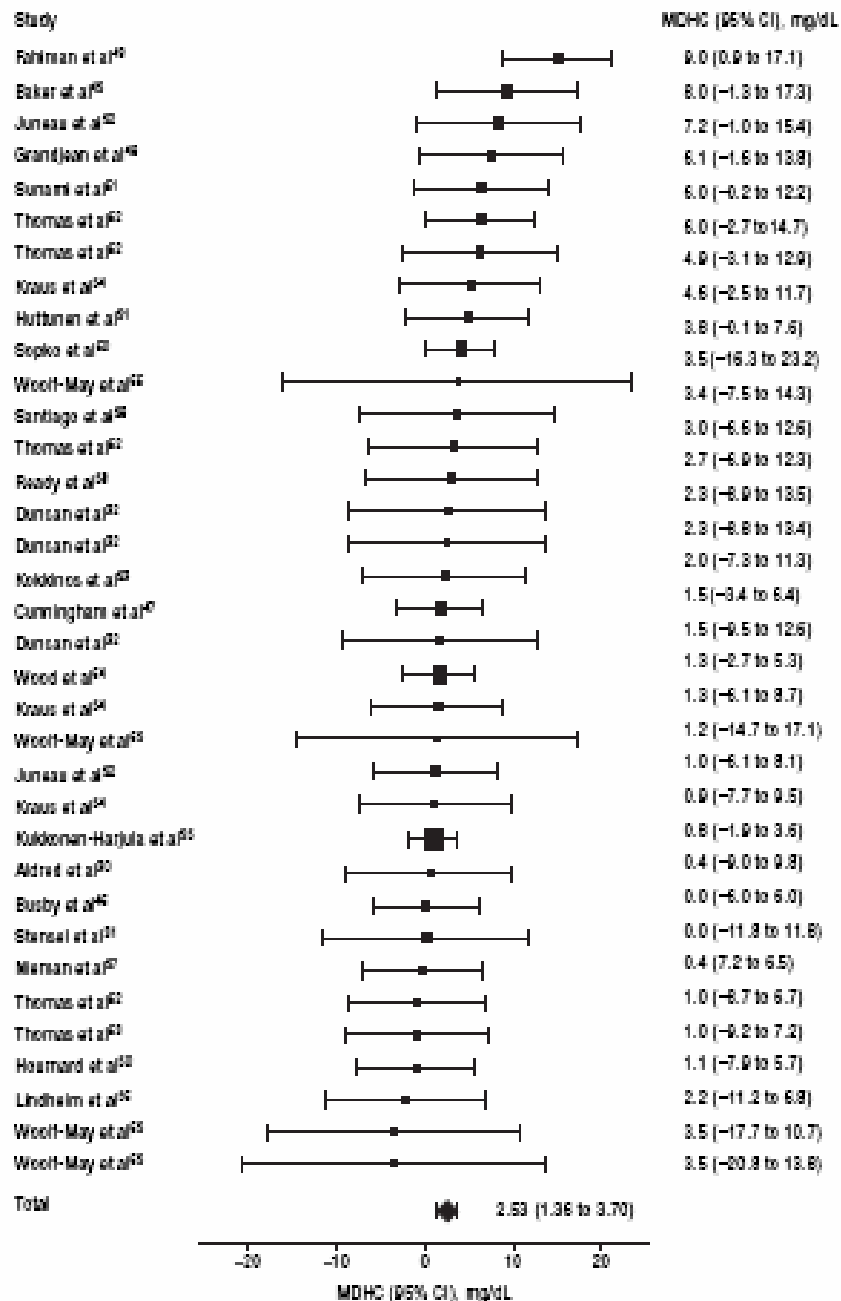
Riduzione del rischio per 1500 kcal/settimana vs il gruppo di riferimento (< 200 kcal/sett.)



Riduzione del rischio per > 20.5 MET/ora /settimana vs il gruppo di riferimento (< 2.8 MET ora/settimana)

Effect of Aerobic Exercise Training on Serum Levels of High-Density Lipoprotein Cholesterol

A Meta-analysis



I soggetti che maggiormente beneficiano dell'effetto sono quelli con i maggiori livelli di colesterolo totale e i normopeso

Kodama et al, Arch Intern Med, 167: 999, 2007