

Nutraceutici, riduzione del colesterolo e salute vascolare



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Dip. di Scienze Mediche e Chirurgiche

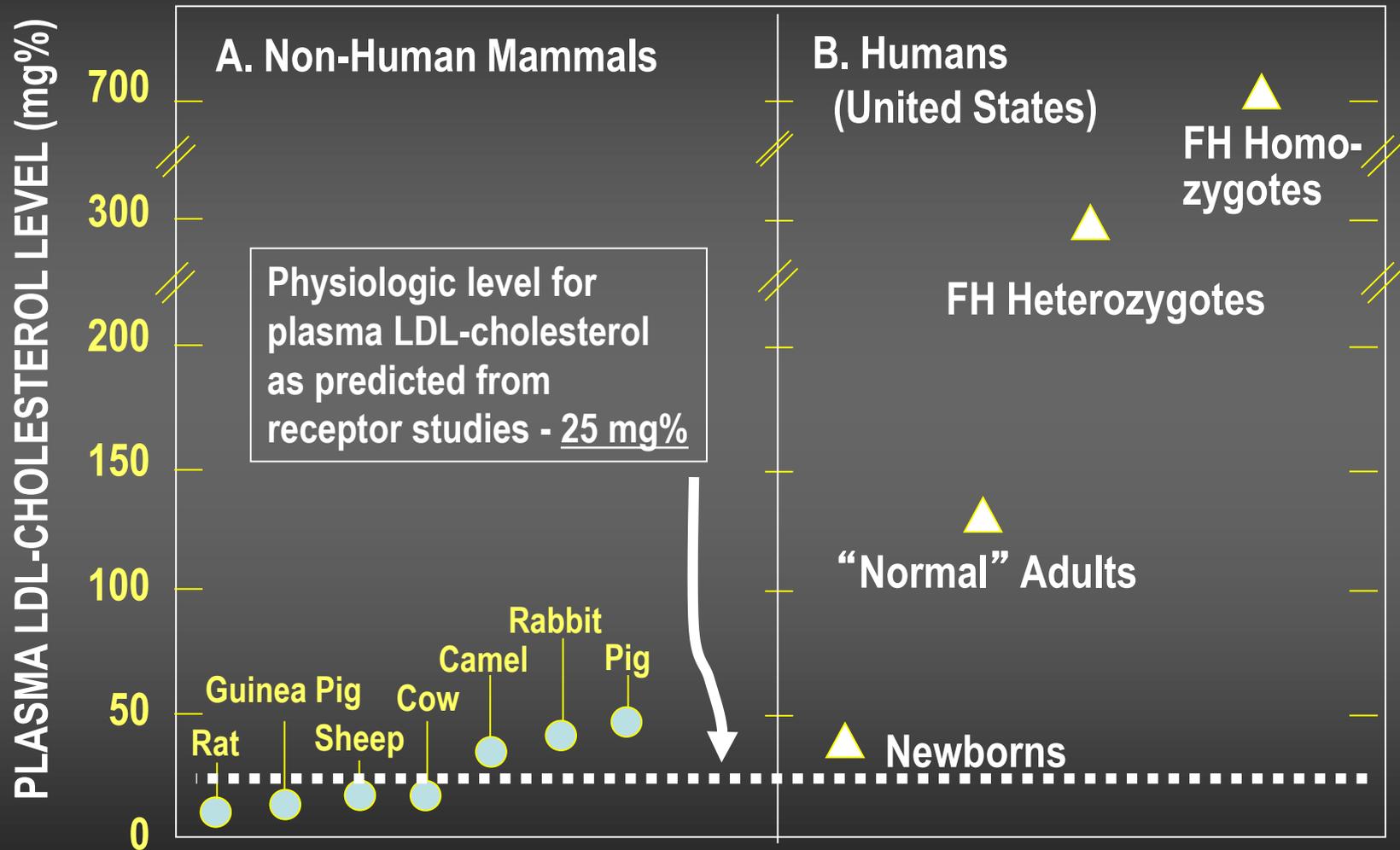
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I 5 perché

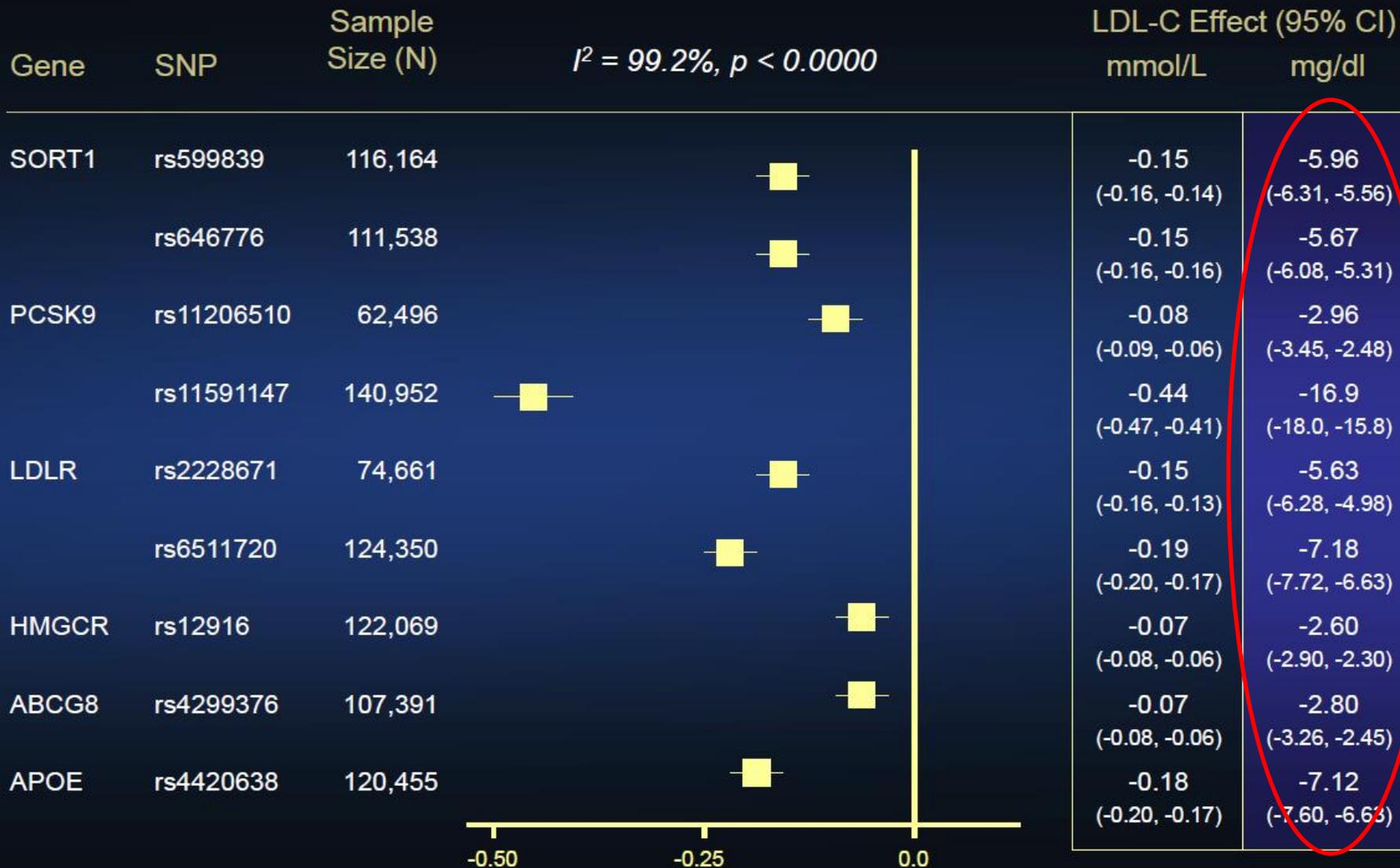
- 1) Perché l'ipercolesterolemia è altamente prevalente!
- 2) Perché la dieta e l'attività fisica hanno impatto limitato sul controllo della colesterolemia
- 3) Perché lo suggeriscono le linee guida
- 4) Perché i pazienti li assumono nel tempo
- 5) Perché (alcuni) funzionano !

LDL-C LEVELS IN HUMANS AND NON-HUMAN MAMMALS



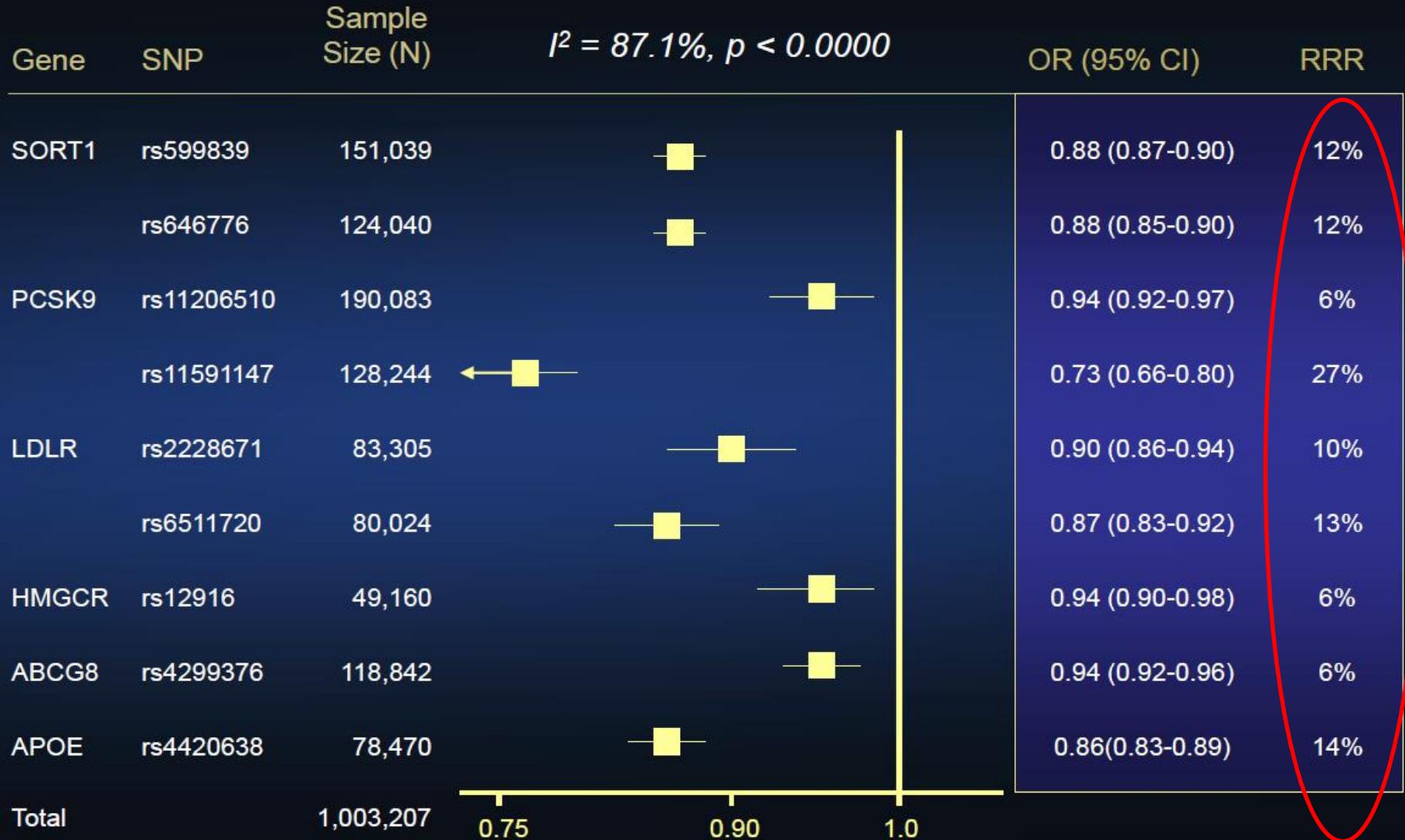
Associations with LDL-C

Ference BA et al.
JACC 2012;
60(25):2631-9.



Associations with CHD

Ference BA et al.
JACC 2012;
60(25):2631-9.



Comparative Clinical Benefit

Ference BA et al.
JACC 2012;
60(25):2631-9

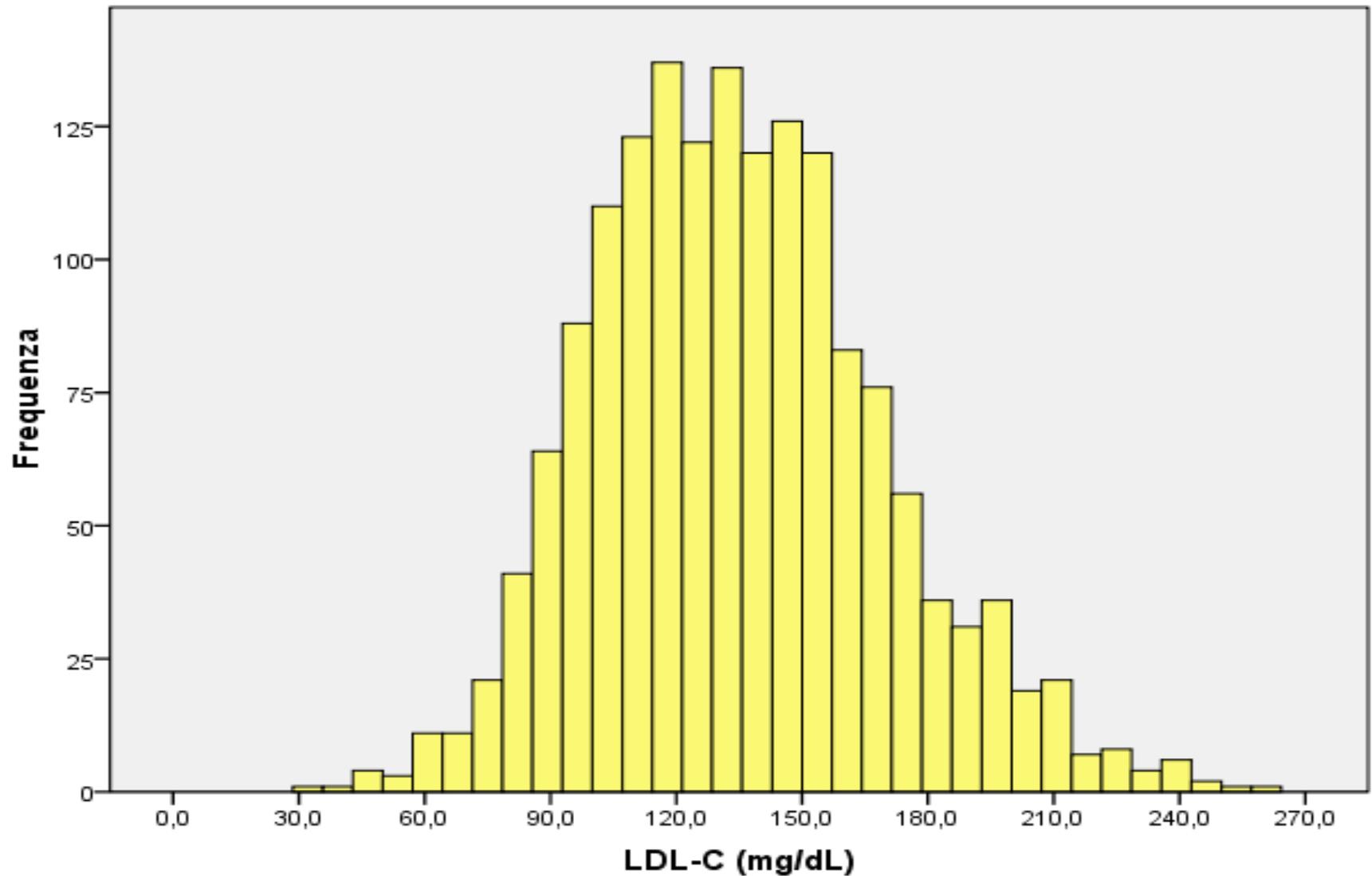
Timing of LDL-C Lowering	Source of Point Estimate	Size (N)	Adjusted per 38.7 mg/dl (1 mmol/L) Lower LDL-C		
			OR _{CHD} (95% CI)	RRR (95% CI)	p (difference)
Early in life	mRCT	326,443	0.46 (0.41-0.52)	54% (48-59)	p = 8.4x10 ⁻¹⁹
Later in life	Meta-Analysis of Statin trials	169,138	0.76 (0.74-0.78)	24% (22-26)	

Early in life: **38.7 mg/dl (1 mmol/L)** lower LDL-C → **~ 55% RRR** (OR: 0.46)

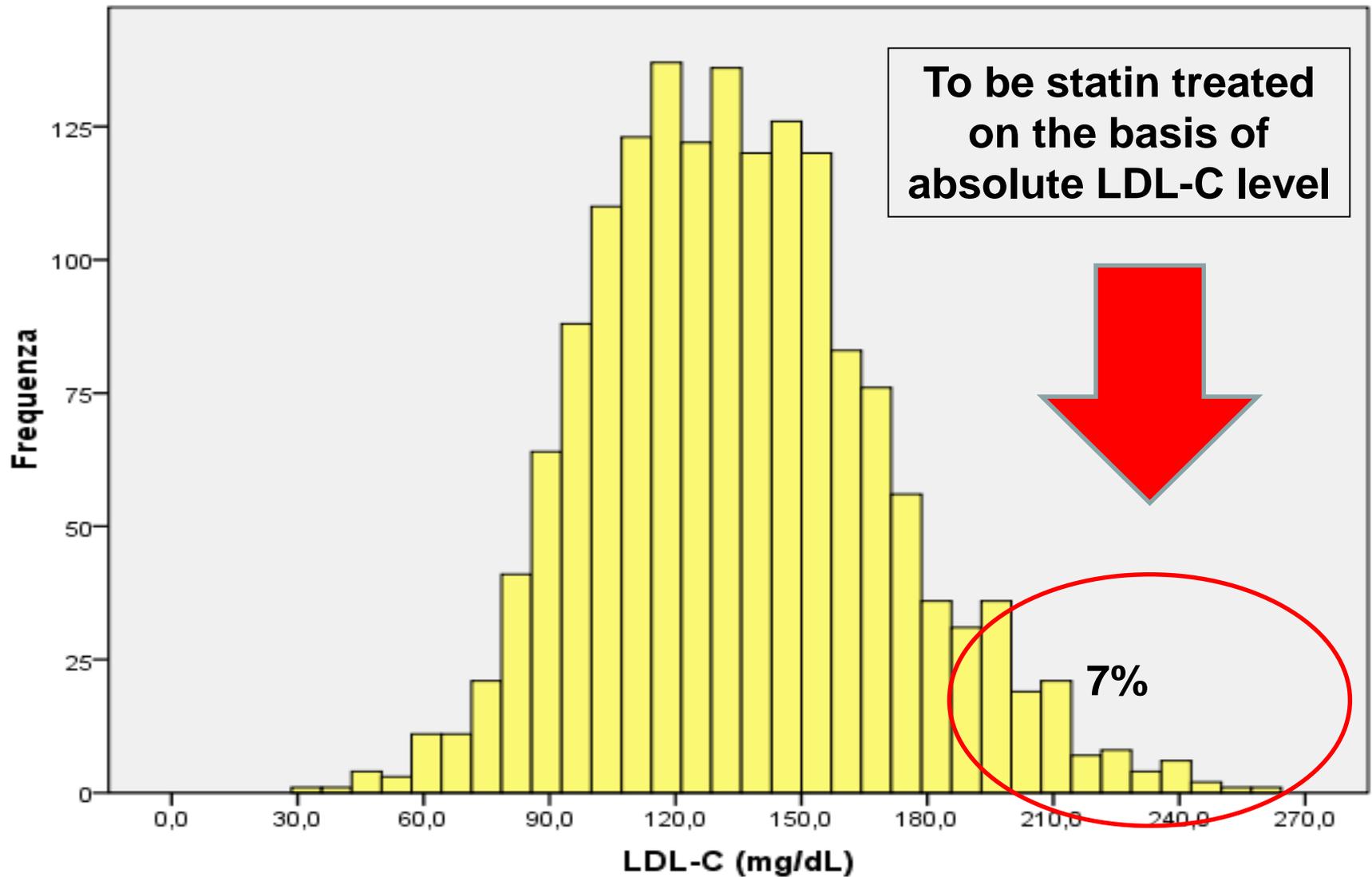
Later in life: **116 mg/dl (3 mmol/L)** lower LDL-C → **~ 55% RRR** (OR: 0.44 = 0.76*0.76*0.76)

- Prolonged exposure to lower LDL-C beginning early in life associated with *3-fold greater clinical benefit* for each unit lower LDL than treatment with a statin started later in life
 - May explain much of residual risk of coronary events experienced by persons being treated with a statin started later in life

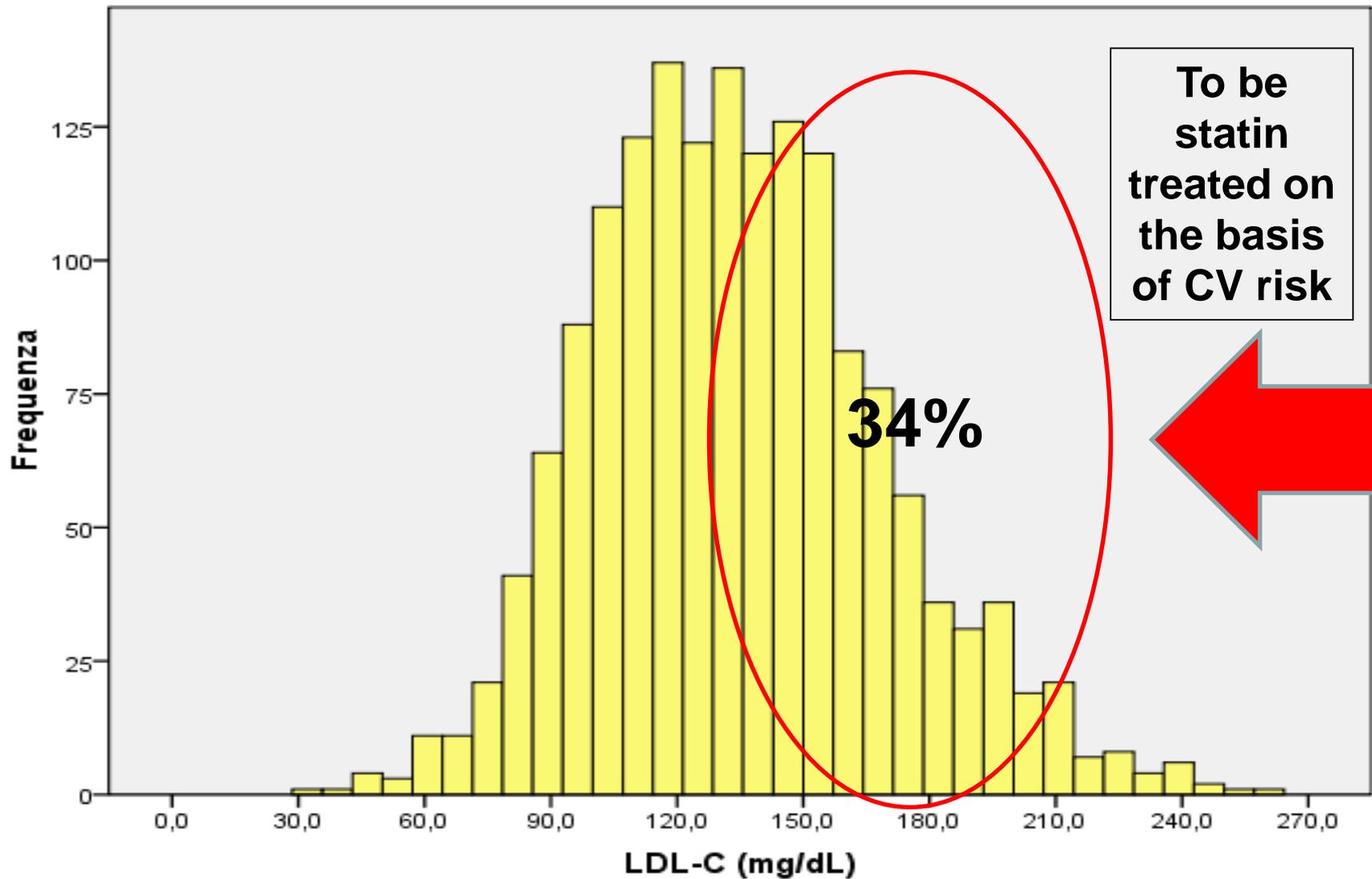
Data from 1624 non-statin treated Brisighella volunteers



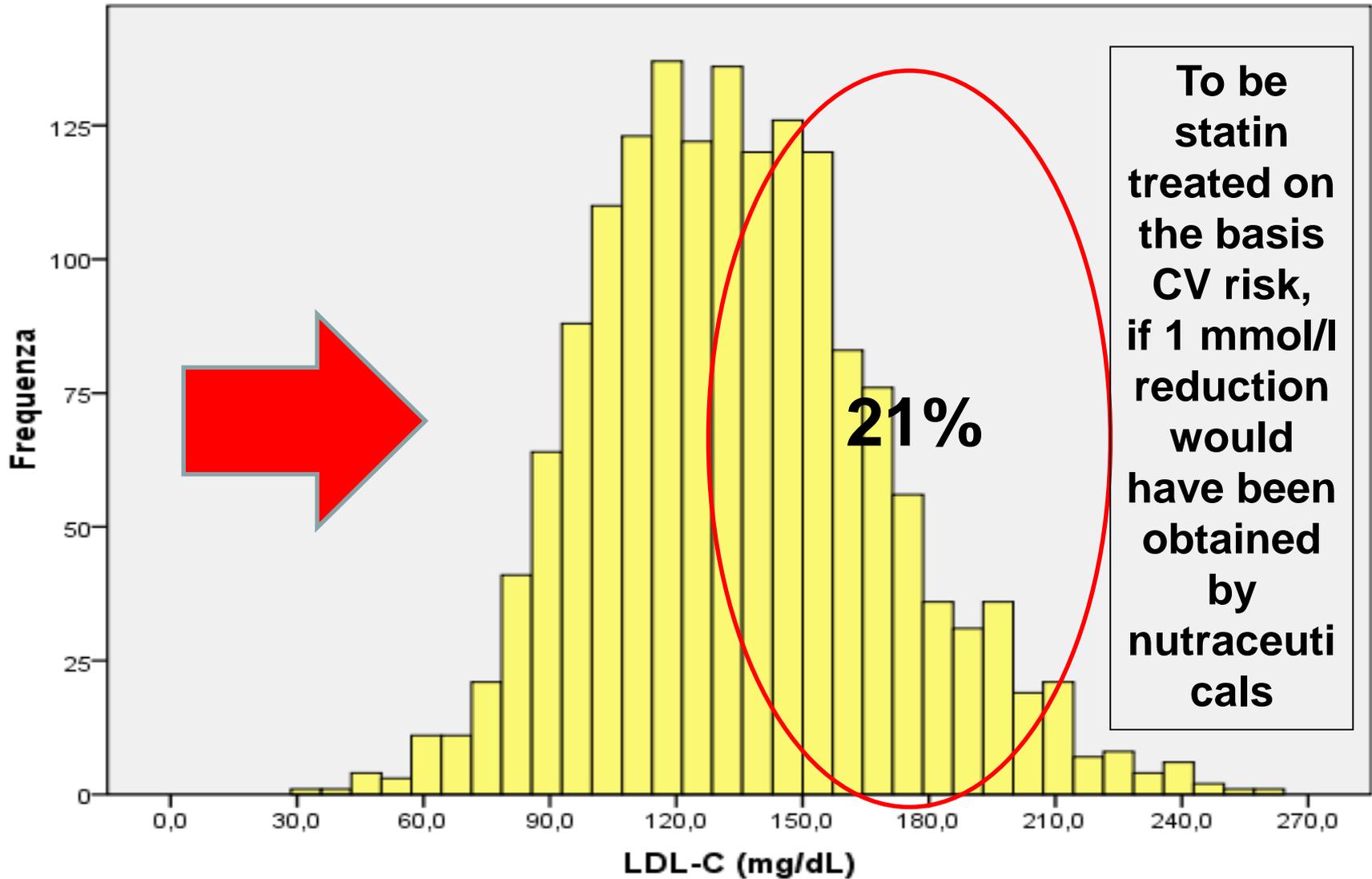
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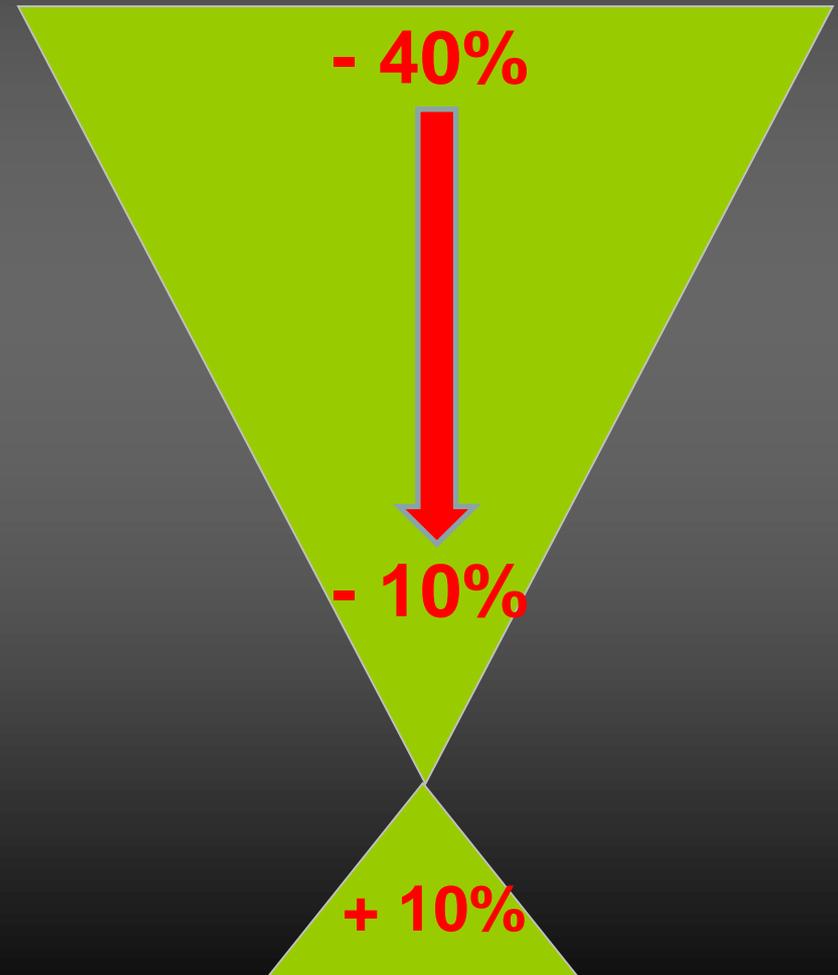


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Relative efficacy of life-style change in improving different CV risk factors

- Triglyceridemia
- Glycemia
- Blood Pressure
- Microinflammation
- LDL-C
- Lp(a)
- HDL-C



Is diet efficacious?

- Diet combined with aerobic exercise, but not diet or exercise alone, may reduce non-HDL-C among adults in some settings

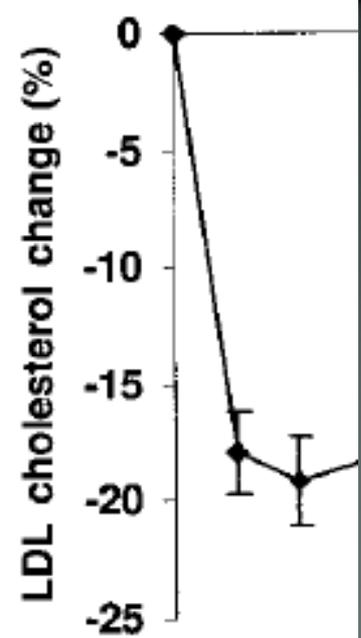
(Cholesterol. 2012;2012:840935)

- A small but potentially important reduction in CV risk on modification of dietary fat, but not reduction of total fat, in longer trials. Lifestyle advice to all those at risk of CV disease and to lower risk population groups, should continue to include permanent reduction of dietary saturated fat and partial replacement by unsaturates. The ideal type of unsaturated fat is unclear

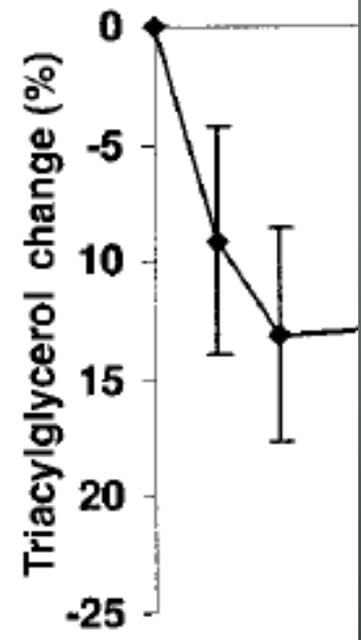
(Cochrane Database Syst Rev. 2012;5:CD002137)

Short-term Jenkins Diet

- 20%



- 15%

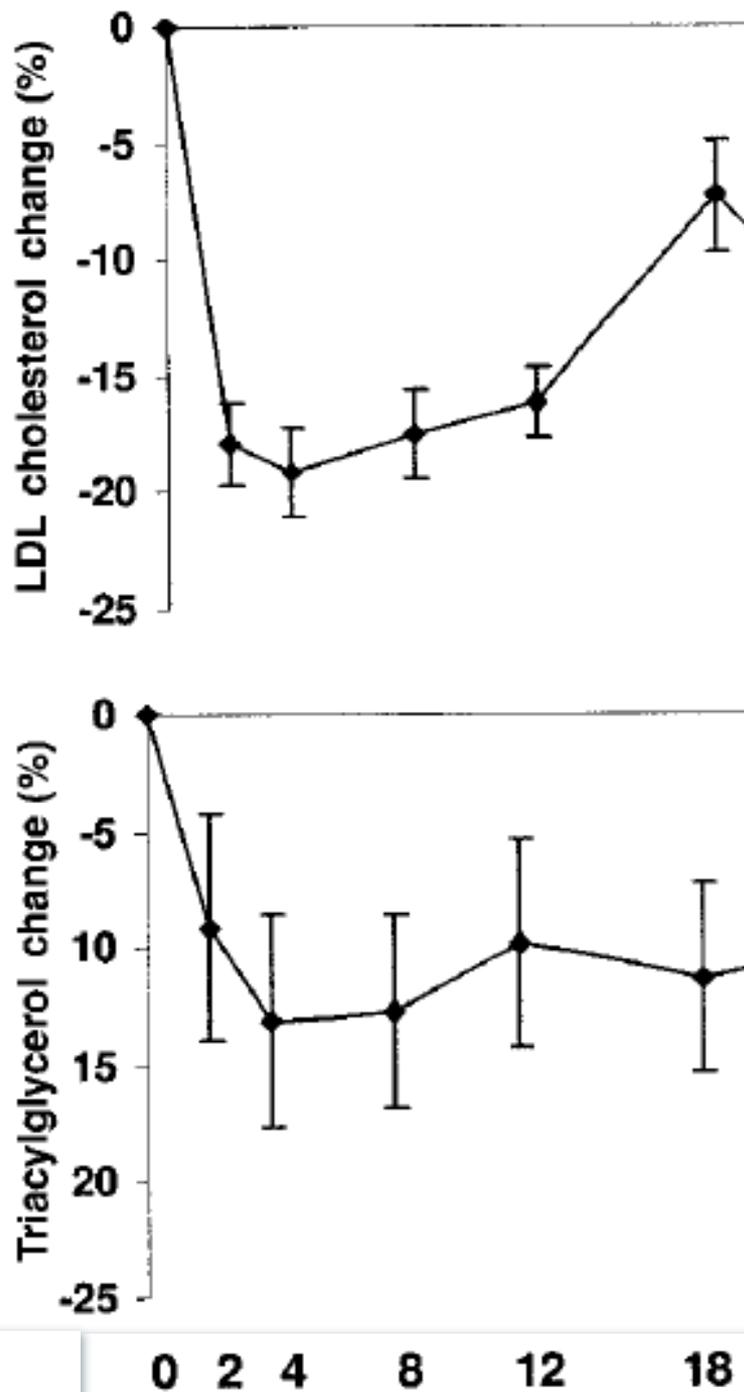


*Jenkins DJA et al. Am J
Clin Nutr 2006;83:582–91.*



Middle-term Jenkins diet

*Jenkins DJA et al.
Am J Clin Nutr
2006;83:582–91.*



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NCEP ATP III 2001:

role of nutraceuticals and functional foods in dyslipidemia management

- Life-style improvement (TLS)
- Life-style + Functional foods/Nutraceuticals
- Life-style improvement (TL + Drugs)
- Life-style + Drugs + Functional foods/Nutraceuticals

ESC/EAS Guidelines for the management of dyslipidaemias

- Life-style improvement (TLS)
- Life-style + Functional foods/Nutraceuticals
- Life-style improvement (TL + Drugs)
- Life-style + Drugs + Functional foods/Nutraceuticals

Ethical prescription of cholesterol-lowering nutraceuticals

- «Resistance» to the therapeutic life-style changes
- Psychological need of quick results (as a support to the diet)
- Low level of added global CVD risk
- “Resistance” to conventional treatments
- “Intolerance” to conventional treatments
- Need to improve the efficacy of conventional treatments without increasing dosages or number of administrations
- Scarse confidence and/or fear against conventional therapies

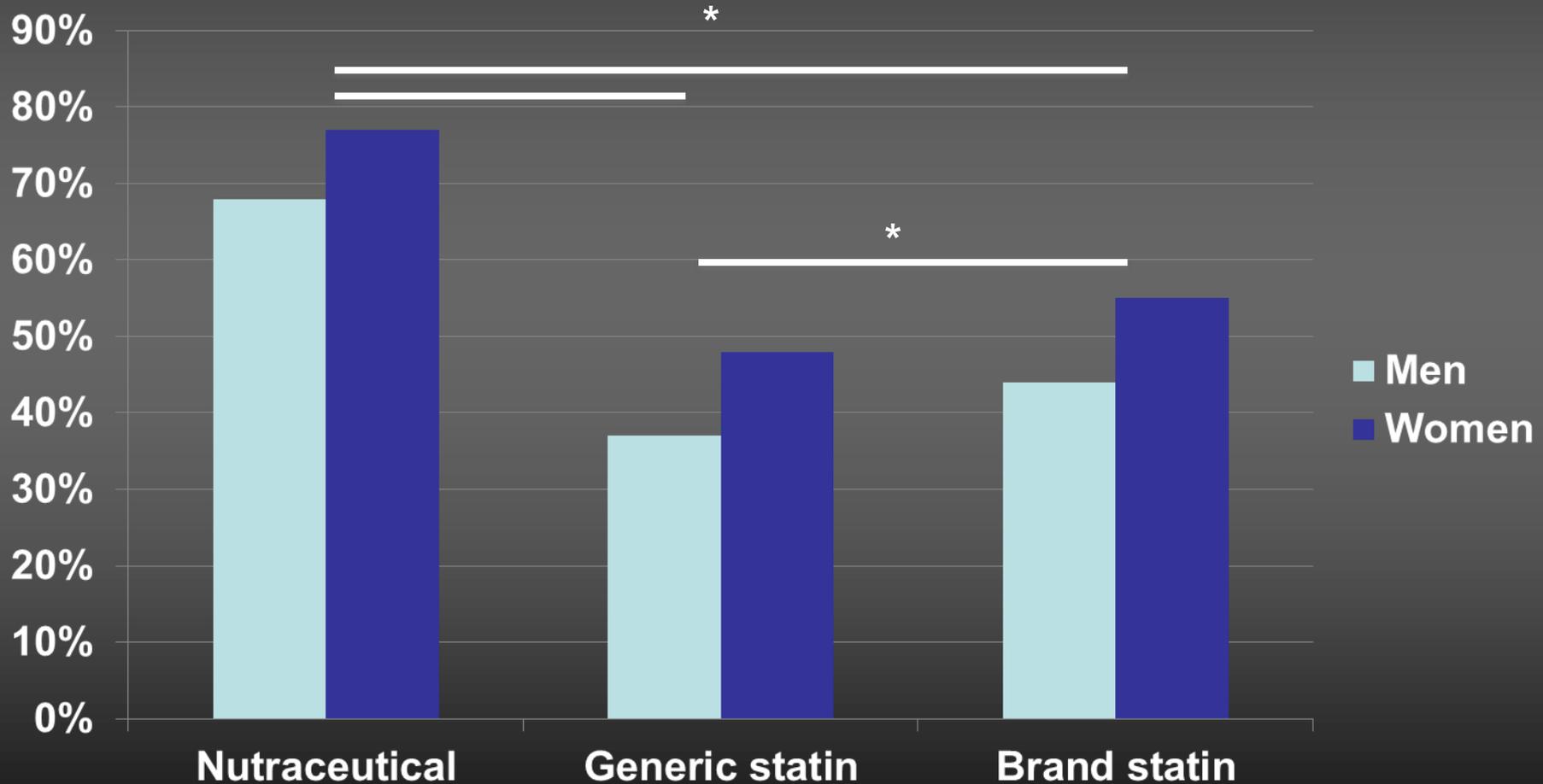
Ethical prescription of cholesterol-lowering nutraceuticals

All those patients with LDL-C above the desired one and for which a statin treatment is not advisable

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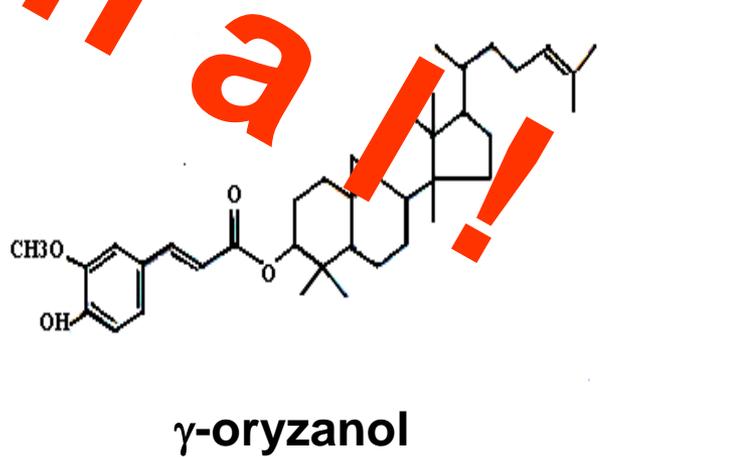
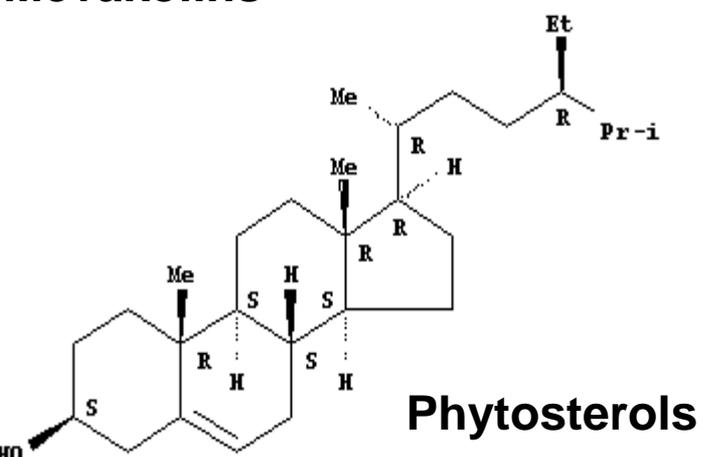
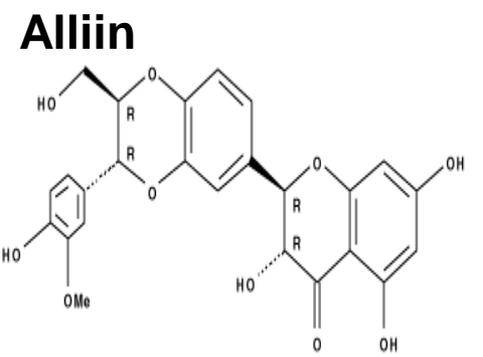
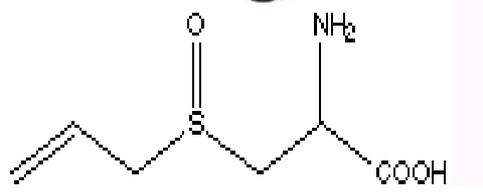
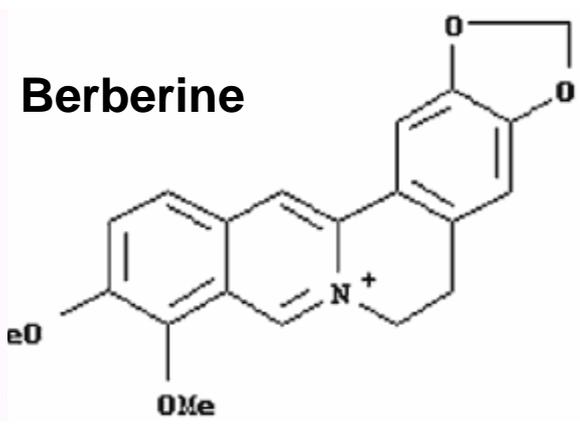
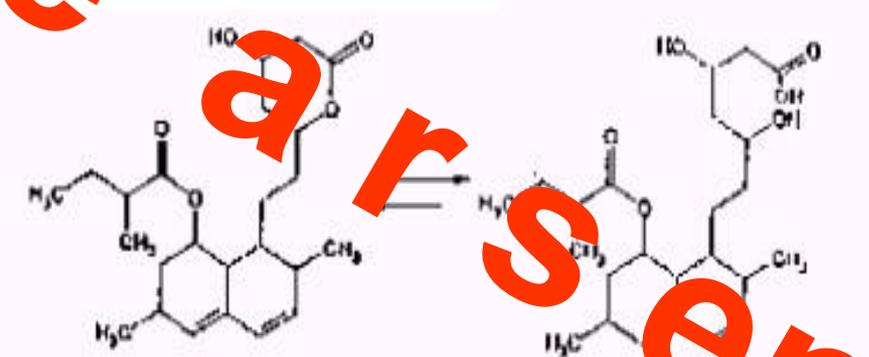
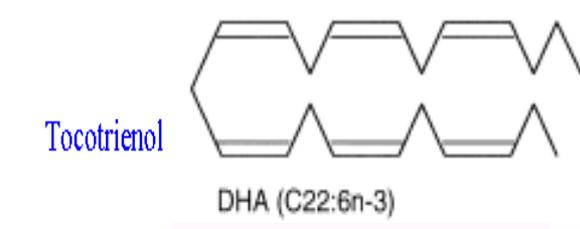
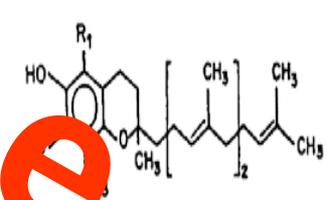
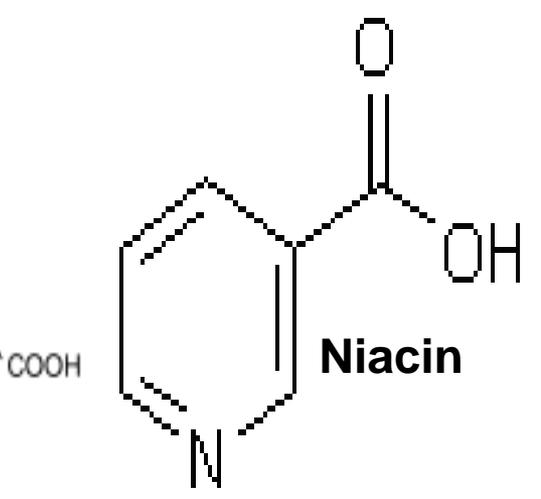
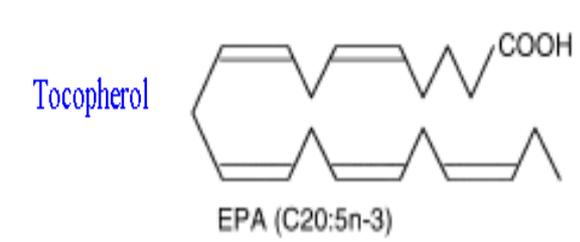
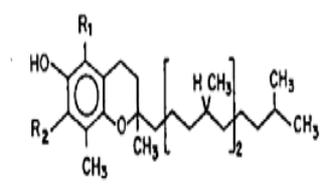
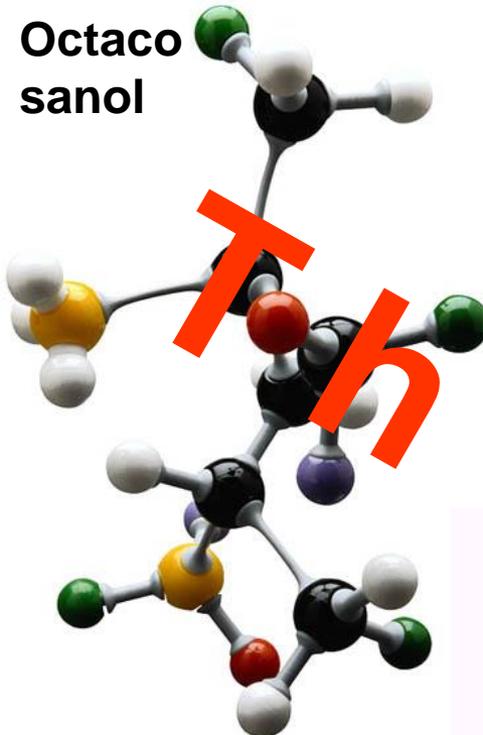
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2-years persistence in paid LDL-lowering treatment



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The arsenal!

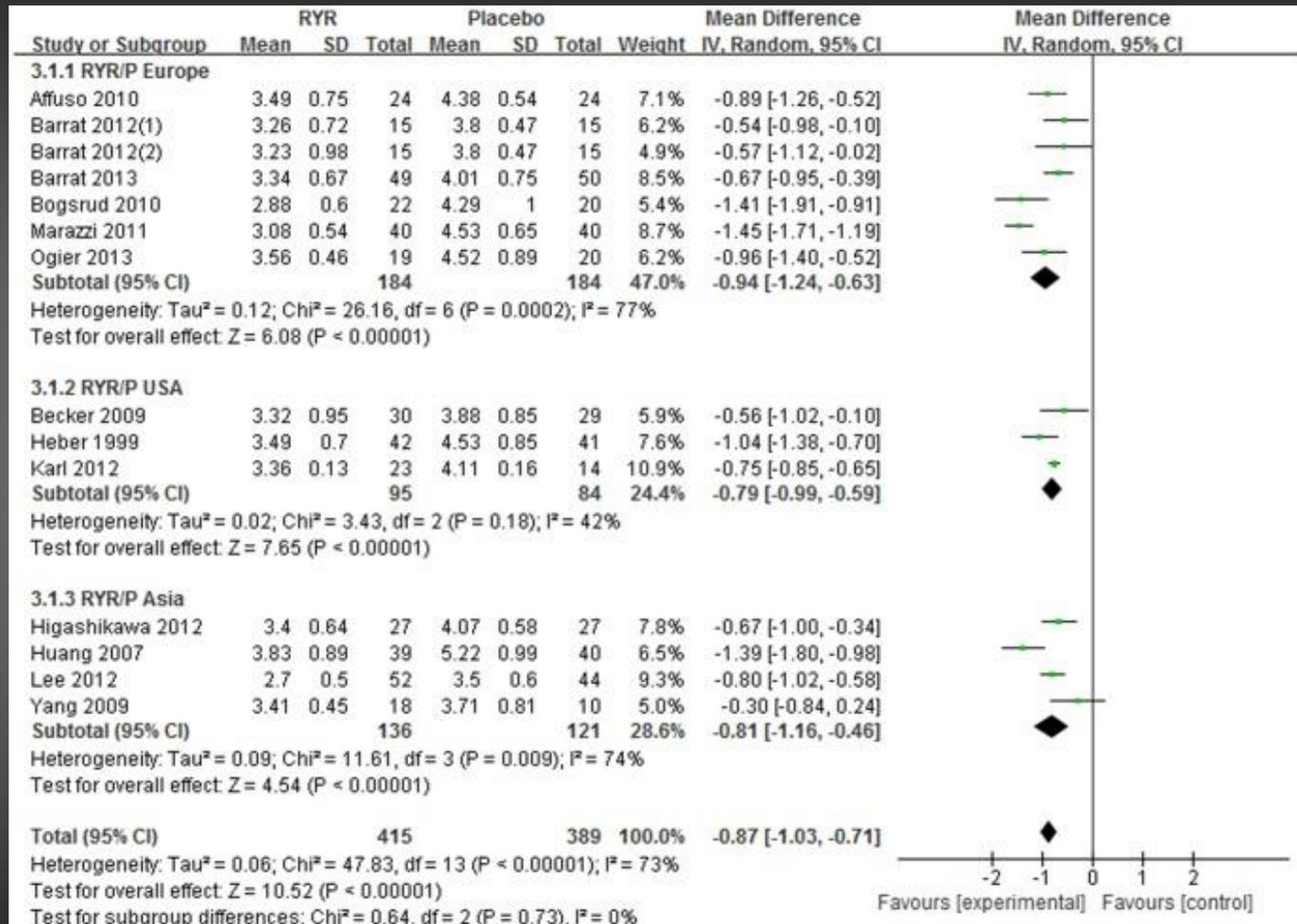
Active principles with lipid-lowering activity

- 1284 in vitro
- 238 in vivo
- 52 in humans
- 13 confirmed in repeated RCTs
- 96 dietary supplements registered in the Italian market
- 12 supported by «a kind» of clinical test
- 4 supported by published RCTs

Evidence/Efficacy

	Clinical evidence	Clinical efficacy
Red Yeast Rice	+++	+++
Berberine	++	++
Soluble Fibers	+++	+
Phytosterols	+++	+
Garlic	++	+
Policosanols	++	+/-
Vegetal proteins	++	+
Tocotrienols	+	+
Panthenine	+	+
Probiotics	+	+

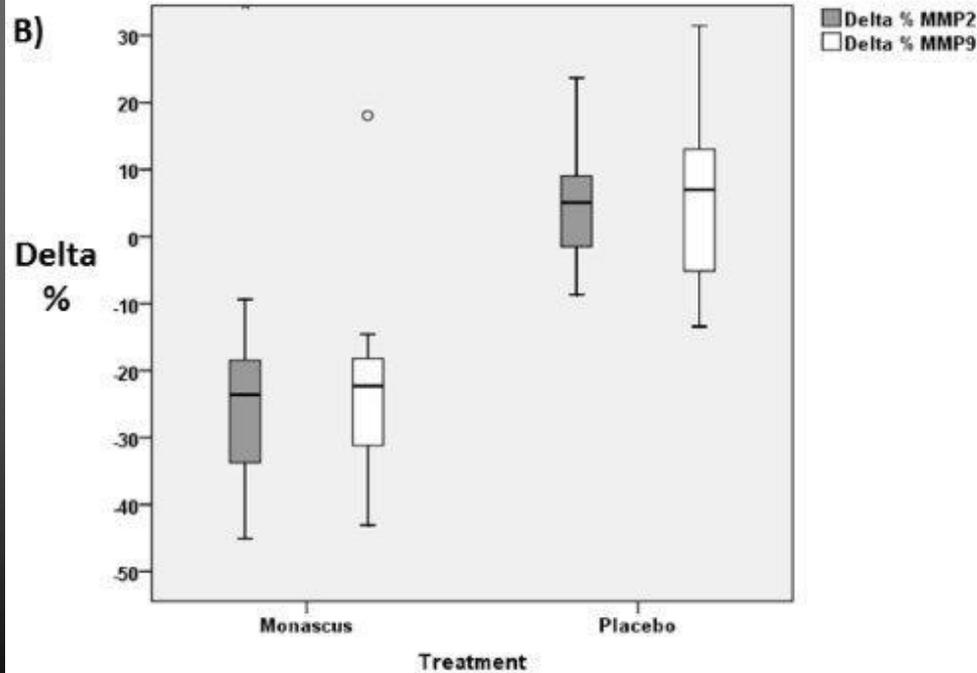
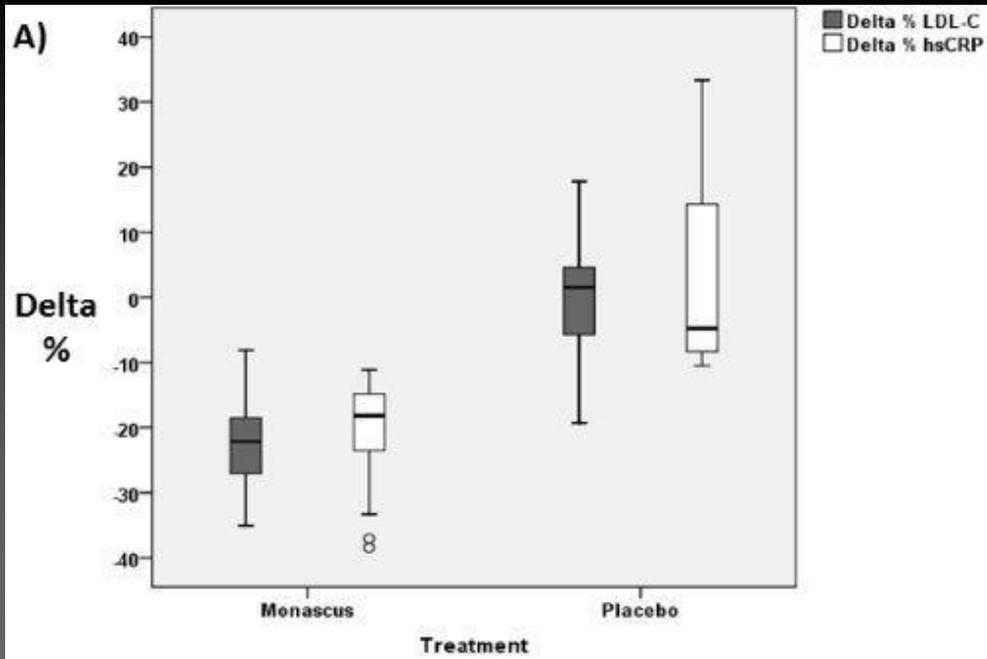
A Meta-Analysis of Red Yeast Rice: An Effective and Relatively Safe Alternative Approach for Dyslipidemia



The efficacy of a nutraceutical emerges when its pharmacological power overwhelms the spontaneous variance of the studied parameters.

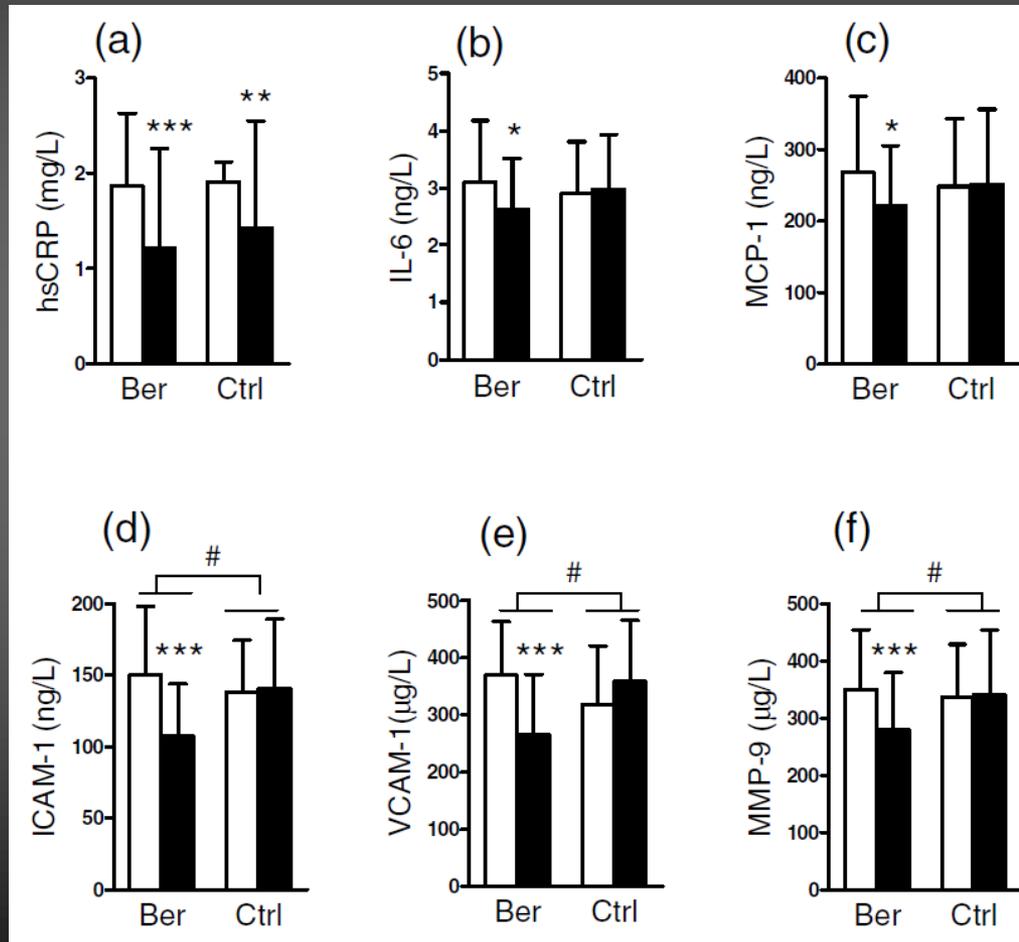
Do exist clinical evidence of nutraceutical efficacy on «intermediate/hard» outcomes ???

Red Yeast Rice, hsCRP and MMPs: a cross-over, RCT



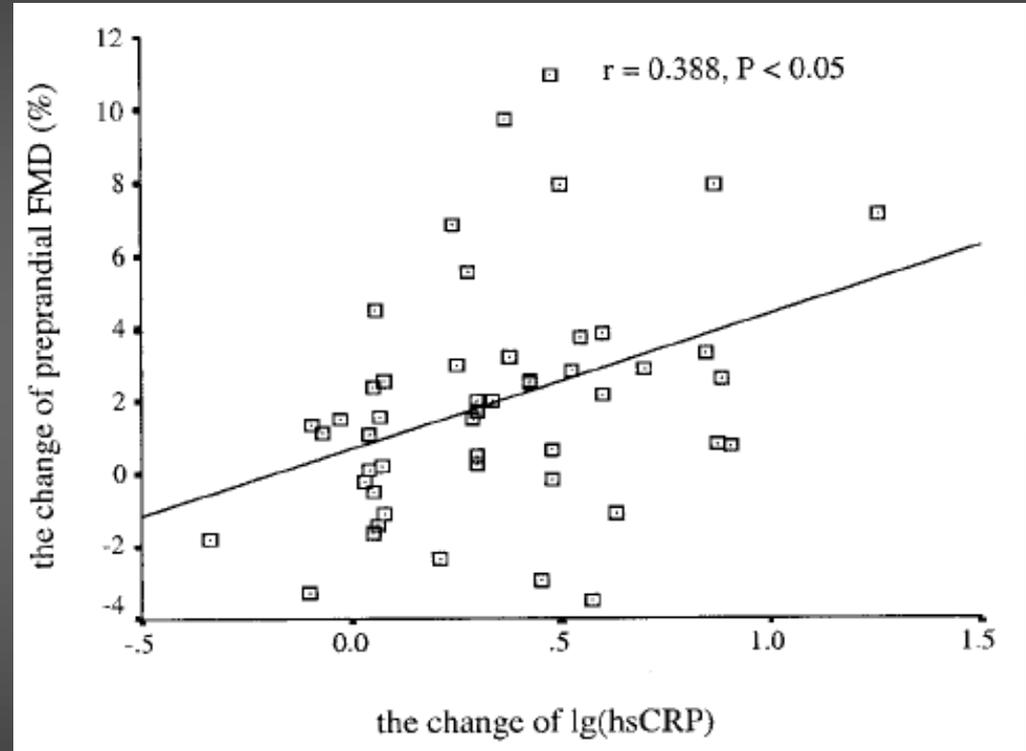
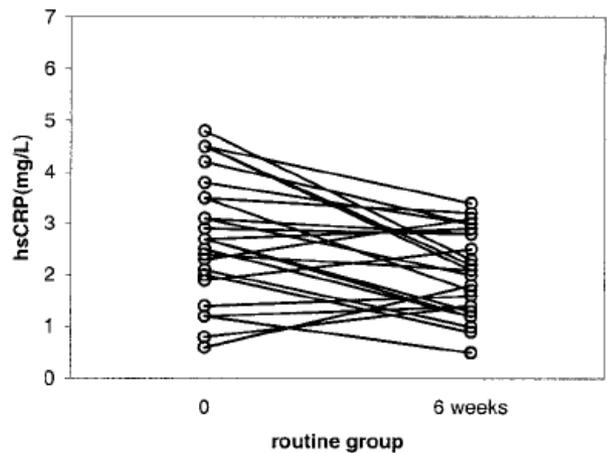
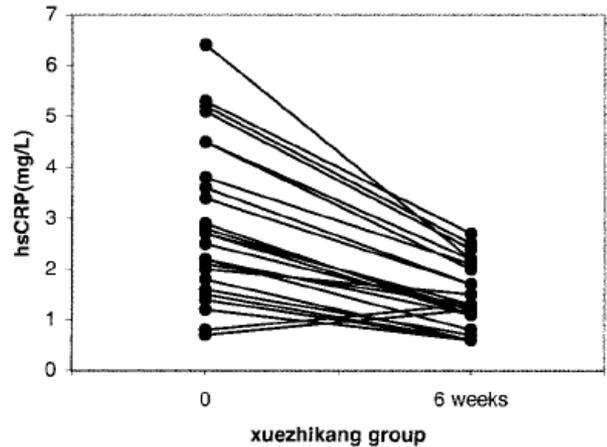
Cicero et al. 2013; Nutr Res
33(8):622-8.

Berberine ameliorates inflammation in patients with ACS following percutaneous coronary intervention



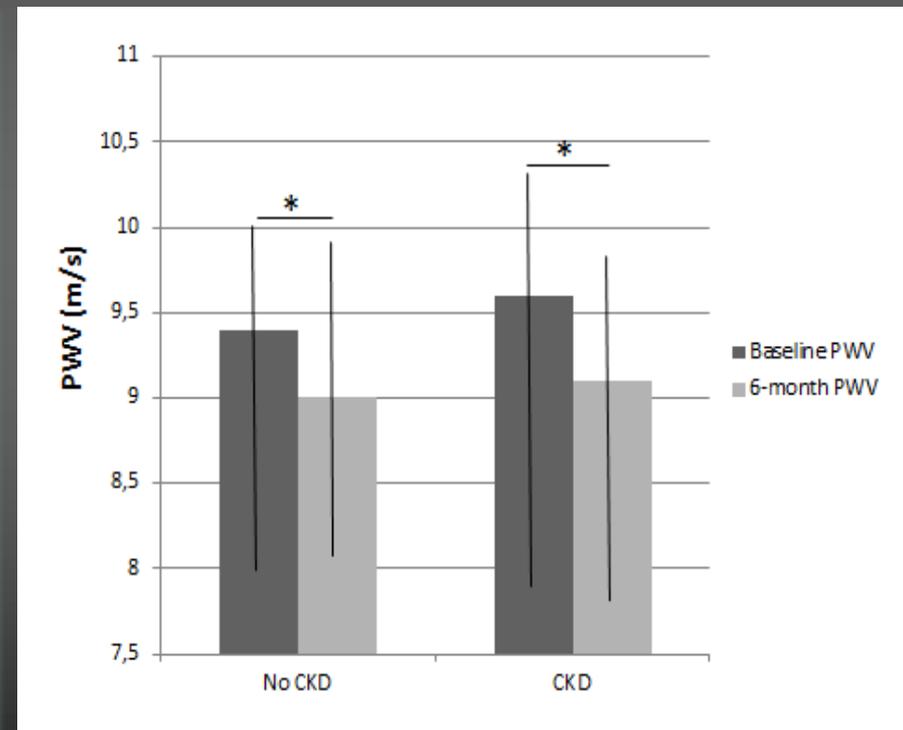
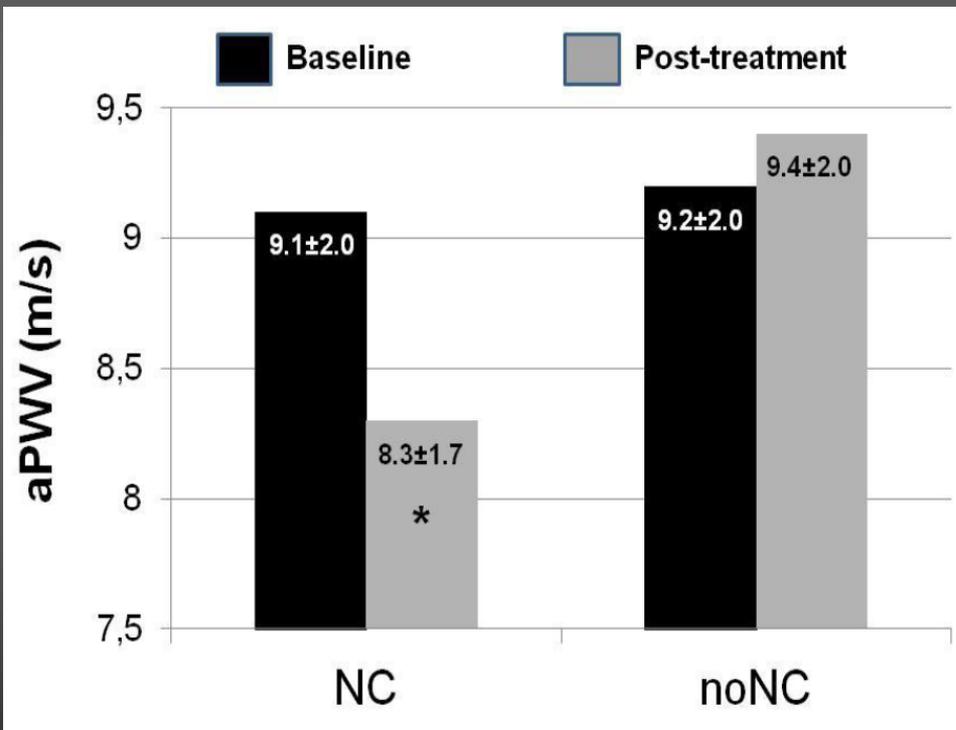
Clin Exp
Pharmacol
Physiol
2012;39(5):
406-11.

Red Yeast Rice, hsCRP and FMD in patients with CAD



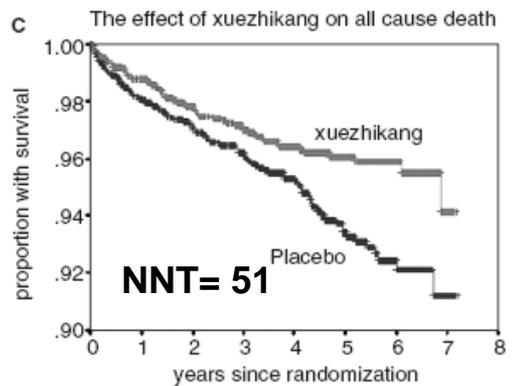
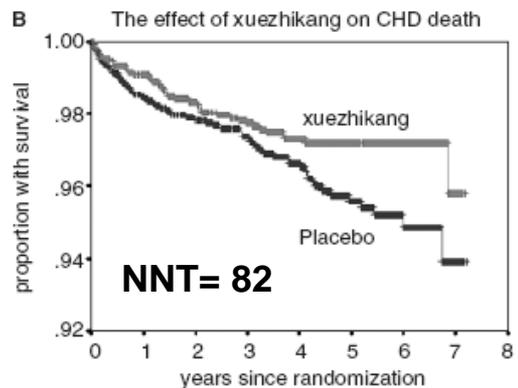
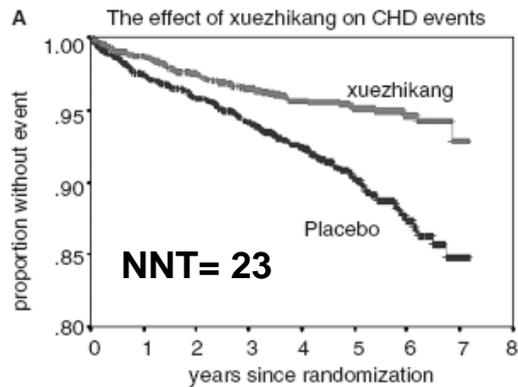
Circulation. 2004;110:915-920

Lipid-Lowering nutraceuticals effects on aPWV

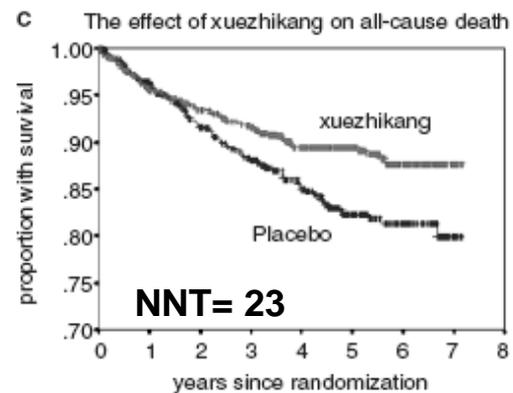
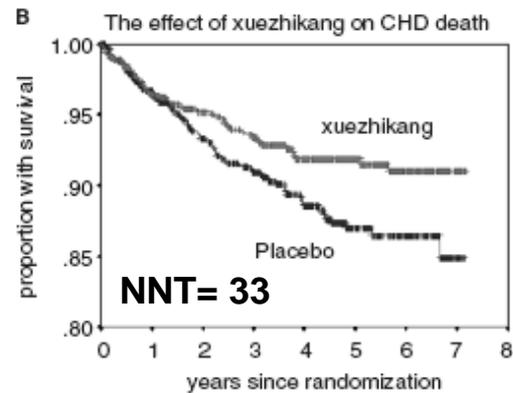
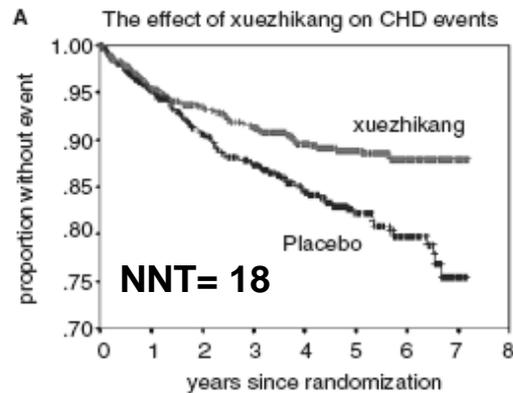


China Coronary Secondary Prevention Study

4780 patients in
secondary
prevention
1,445 aged 65 to 75
7 years follow-up



Adult patients



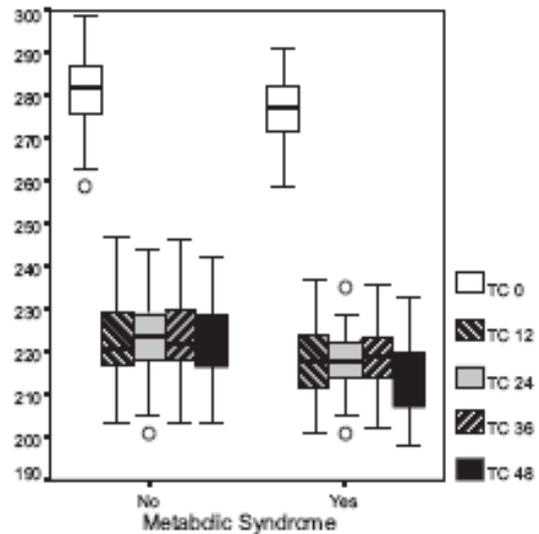
Elderly patients

Ye et al. J Am Geriatr Soc 2007;55:1015-1022.

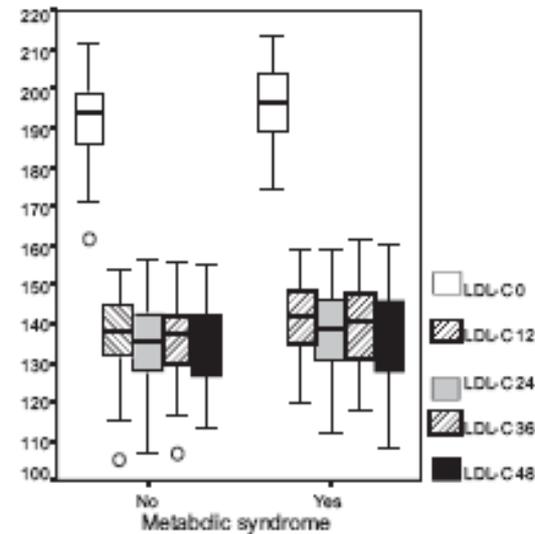
Long-term effectiveness and safety of a nutraceutical based approach to reduce cholesterolemia in statin intolerant subjects with and without metabolic syndrome

Cicero et al. Am J Cardiol. 2010;105(10):1504.

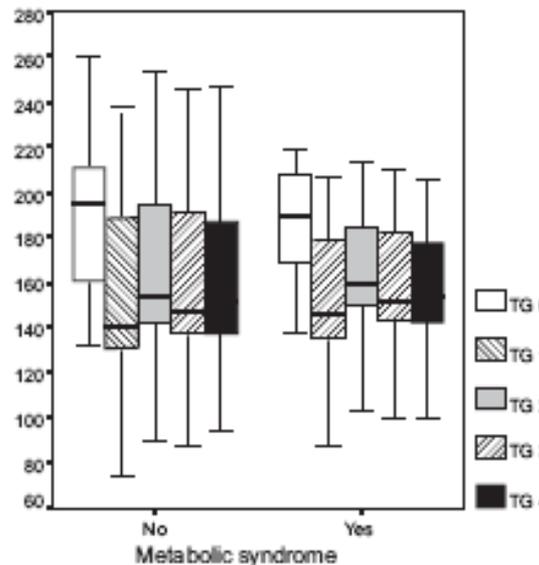
TC



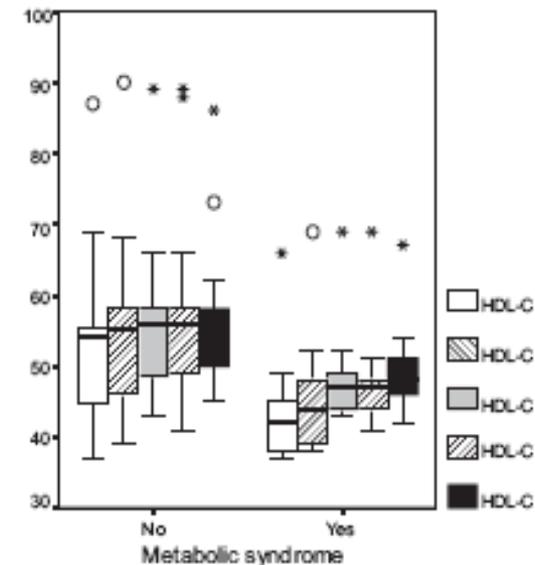
LDL-C



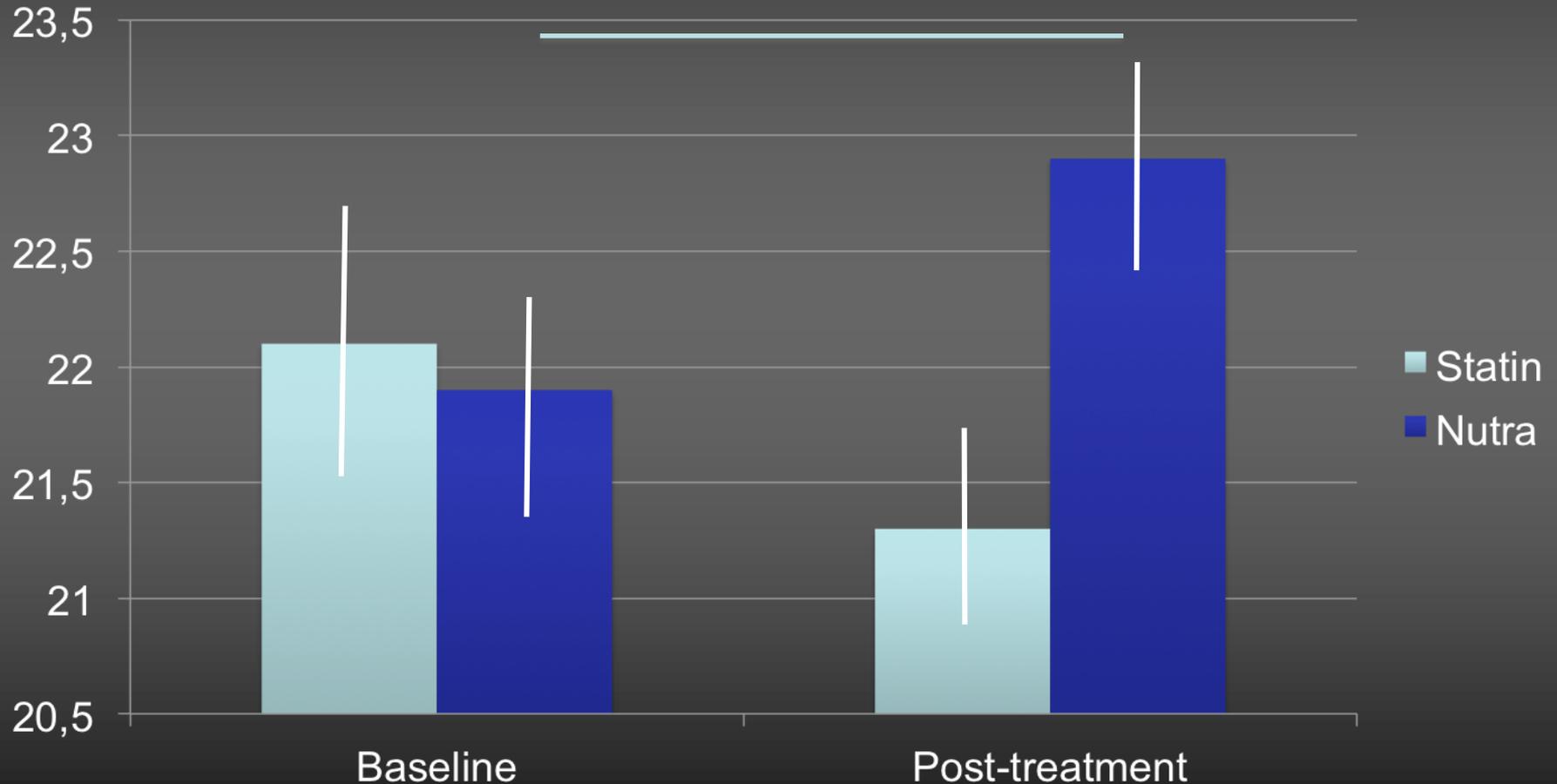
TG



HDL-C



IIEF-5 Score in patients previously reporting sexual performance worsening during statin-treatment



Cicero AFG - Unibo 2007

Cicero AFG et al. 2014; Data on file



“Dottore, io cerco di mangiare sano: non aggiungo mai sale al tiramisù, mangio solo pizza decaffeinata e la mia birra è priva di colesterolo...”