



# Effetti vascolari dei nutraceutici ad azione ipocolesterolemizzante



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*Dip. di Scienze mediche e chirurgiche*

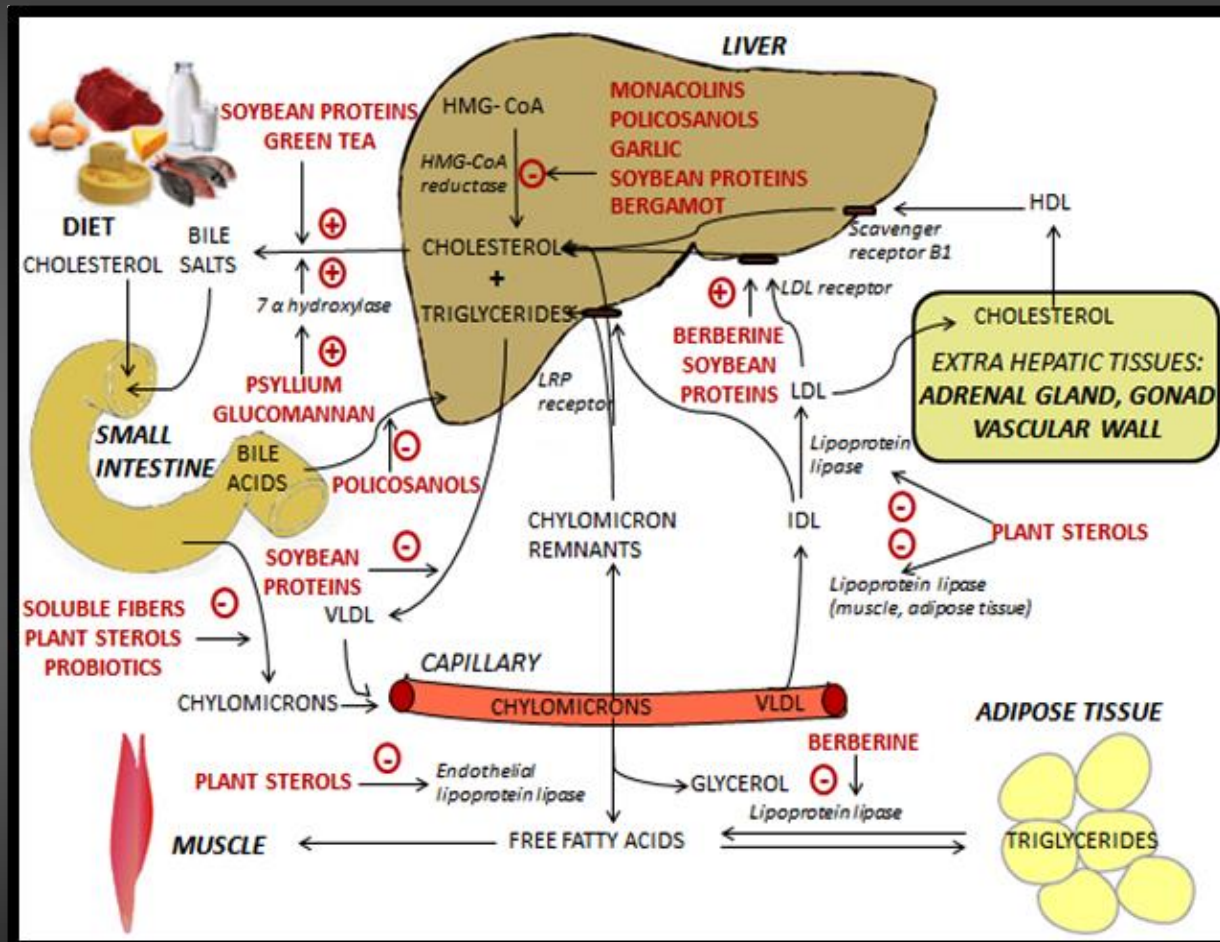
*Alma Mater Studiorum Università di Bologna*

*Presidente Soc. Italiana Nutraceutica (SINut)*

# Cosa non dobbiamo più dimostrare

- Che ridurre la colesterolemia LDL fa bene (quasi) a tutti!
- Che conosciamo la farmacodinamica e farmacocinetica dei nutraceutici ipolipemizzanti più efficaci
- Che i nutraceutici ipolipemizzanti più utilizzati sono in grado di migliorare efficacemente il metabolismo lipidico nell'uomo

# Lipid-lowering nutraceuticals: sites of action

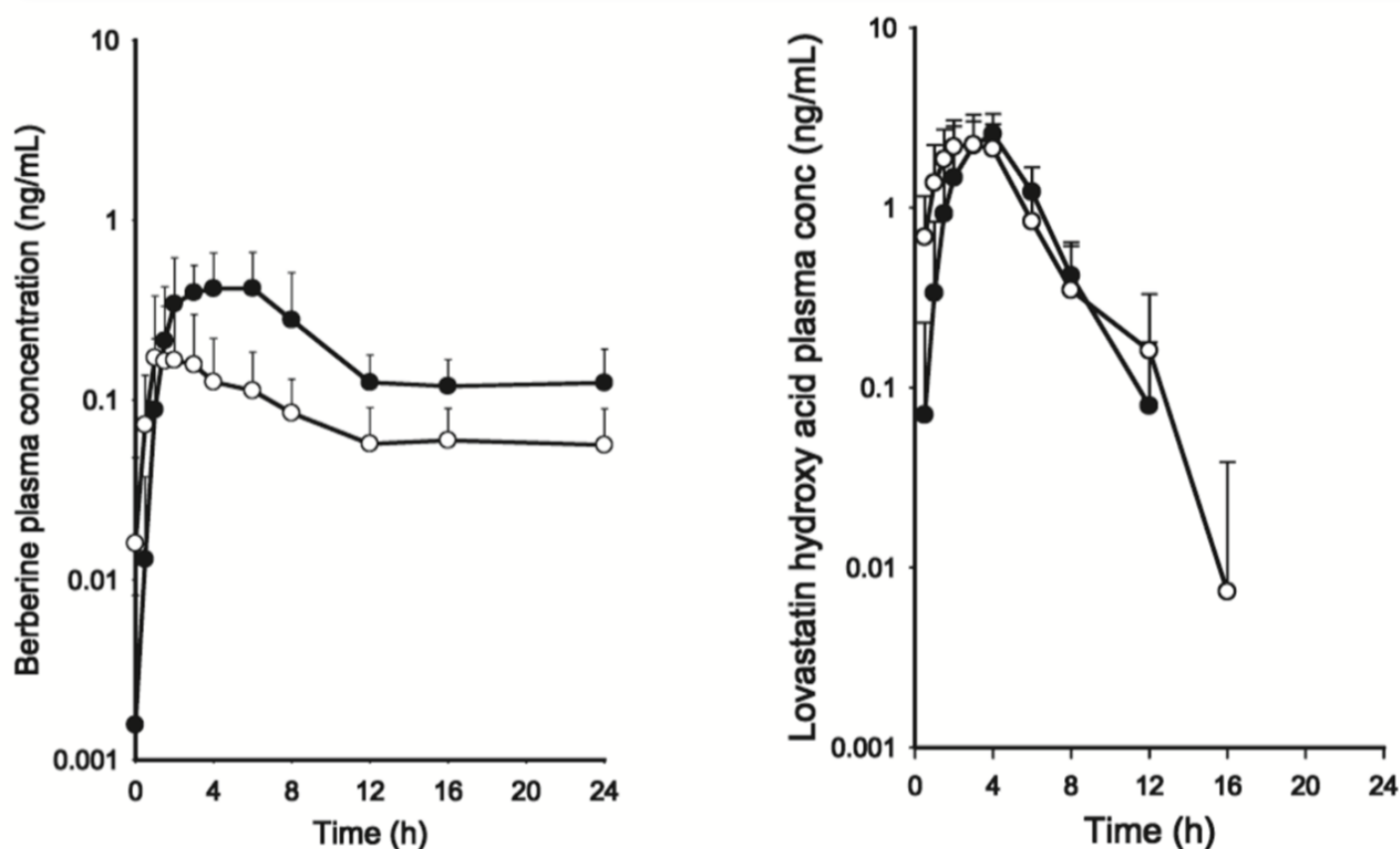


Cicero AFG, Colletti A. In: Combined therapy in dyslipidemia. Springer-Verlag. 2015

# Evidence/Efficacy

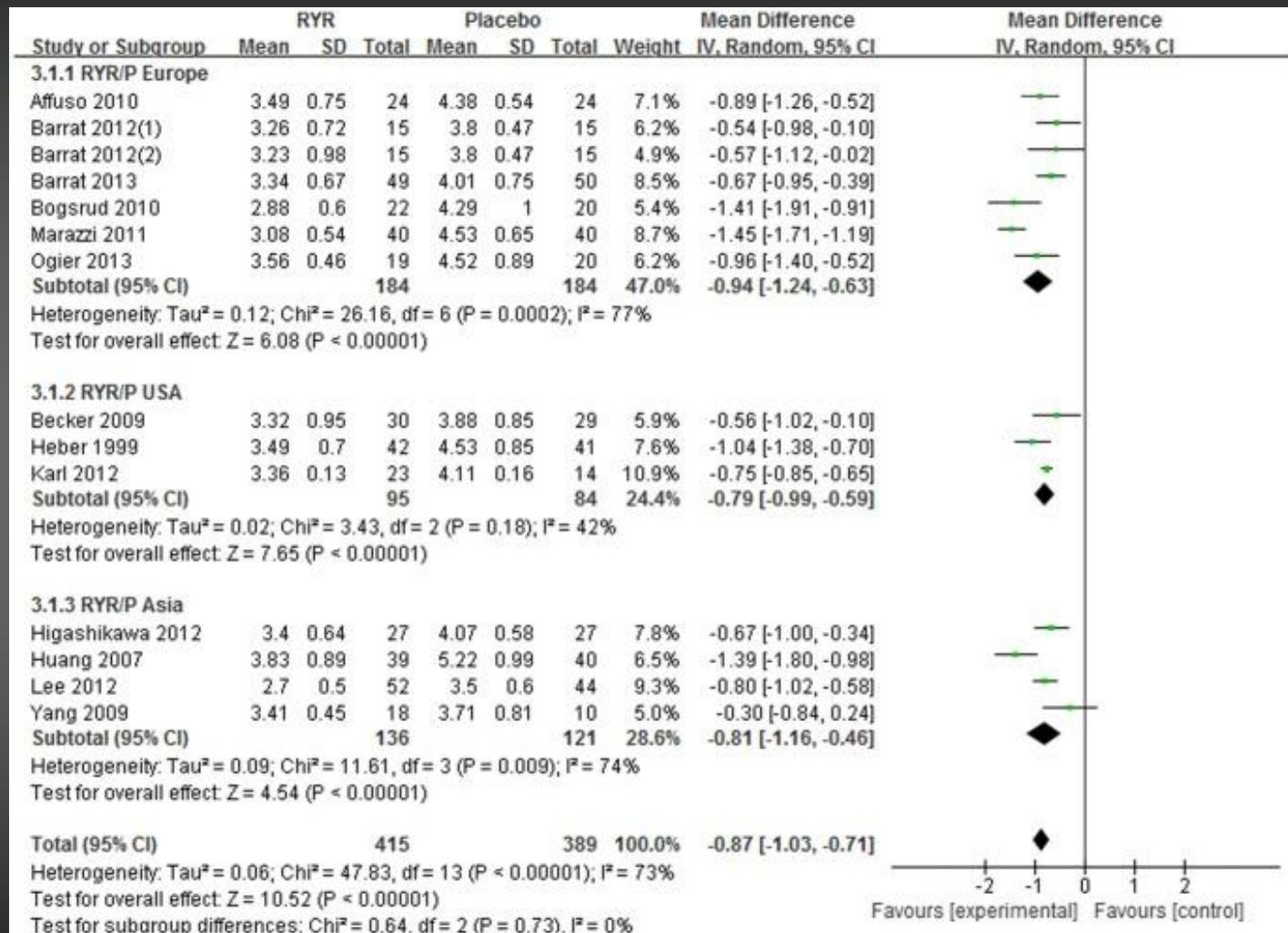
|                  | Clinical evidence | Clinical efficacy |
|------------------|-------------------|-------------------|
| Red Yeast Rice   | +++               | +++               |
| Berberine        | ++                | ++                |
| Soluble Fibers   | +++               | +              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

# Effect of Food on the Oral Bioavailability of Berberine and Monacolin Administered in Combination in Healthy Male Volunteers



**Fig. 1** Mean ( $\pm$ SD) plasma concentration-time profile of berberine and lovastatin hydroxy acid in fed condition (●) and fasted condition (○) in healthy subjects.

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



EFFECTS ON LDL-C

PLoS One. 2014; 9(6): e98611.

# Berberine is a novel cholesterol-lowering drug working through a unique mechanism distinct from statins

Weijia Kong<sup>1,5</sup>, Jing Wei<sup>2,5</sup>, Parveen Abidi<sup>3,5</sup>, Meihong Lin<sup>3</sup>, Satoru Inaba<sup>3</sup>, Cong Li<sup>3</sup>, Yanling Wang<sup>4</sup>, Zizheng Wang<sup>2</sup>, Shuyi Si<sup>1</sup>, Huaining Pan<sup>2</sup>, Shukui Wang<sup>2</sup>, Jingdan Wu<sup>2</sup>, Yue Wang<sup>4</sup>, Zhuorong Li<sup>1</sup>, Jingwen Liu<sup>3</sup> & Jian-Dong Jiang<sup>1,4</sup>

Endocrine Care

## Treatment of Type 2 Diabetes and Dyslipidemia with the Natural Plant Alkaloid Berberine

Yifei Zhang,\* Xiaoying Li,\* Dajin Zou, Wei Liu, Jialin Yang, Na Zhu, Li Huo, Peihong Wu, Guoguang Ren, and Guang Ning

Journal of Ethnopharmacology 161 (2015) 69–81



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Journal of Ethnopharmacology

journal homepage: [www.elsevier.com/locate/jep](http://www.elsevier.com/locate/jep)

Review

Meta-analysis of the effect and safety of berberine in the treatment of type 2 diabetes mellitus, hyperlipemia and hypertension

Original Papers 437

## The Effects of Berberine on Blood Lipids: A Systemic Review and Meta-Analysis of Randomized Controlled Trials

Authors Hui Dong<sup>1\*</sup>, Yan Zhao<sup>2</sup>, Li Zhao<sup>1\*</sup>, Fuer Lu<sup>1</sup>

Affiliations

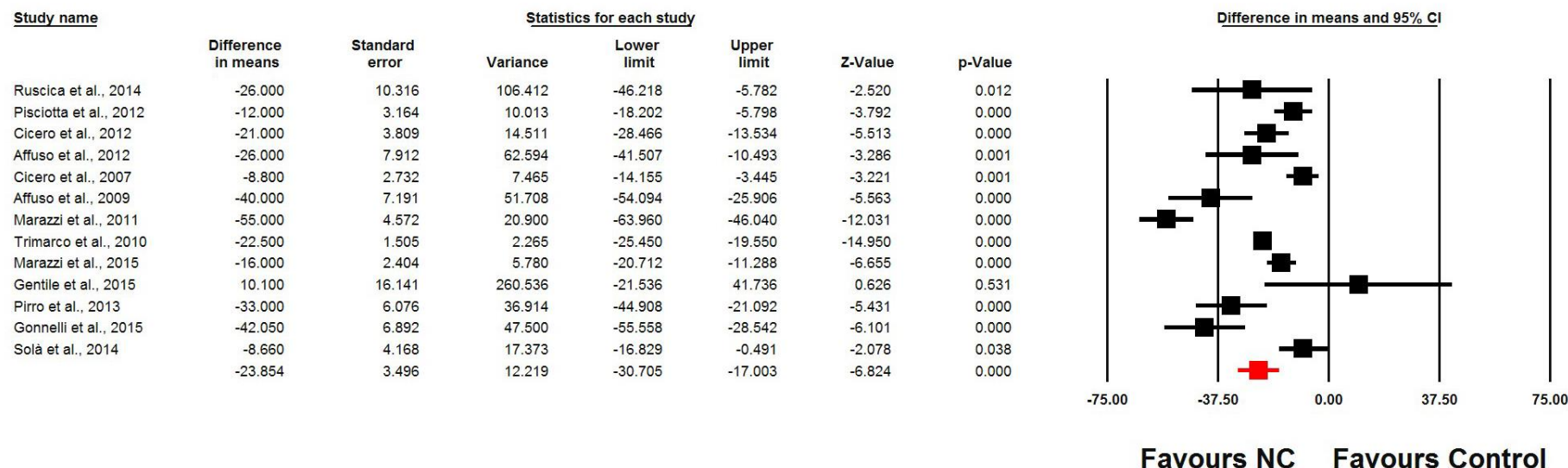
<sup>1</sup> Institute of Integrated Traditional Chinese and Western Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, P. R. China  
<sup>2</sup> Department of Integrated Traditional Chinese and Western Medicine, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, P. R. China





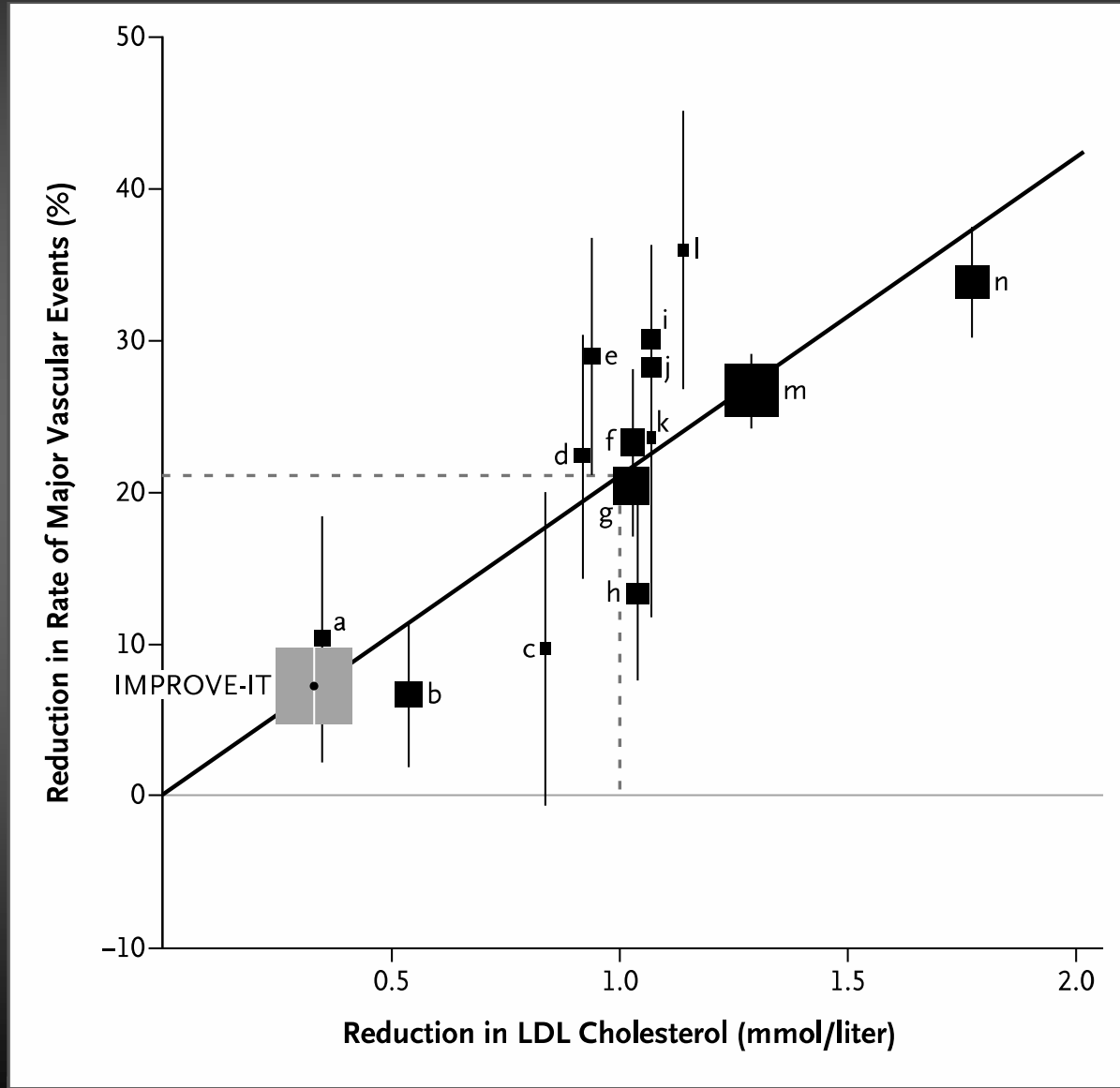
# Low-dosed red yeast-rice – berberine association: a meta-analysis of RCTs

## LDL-cholesterol



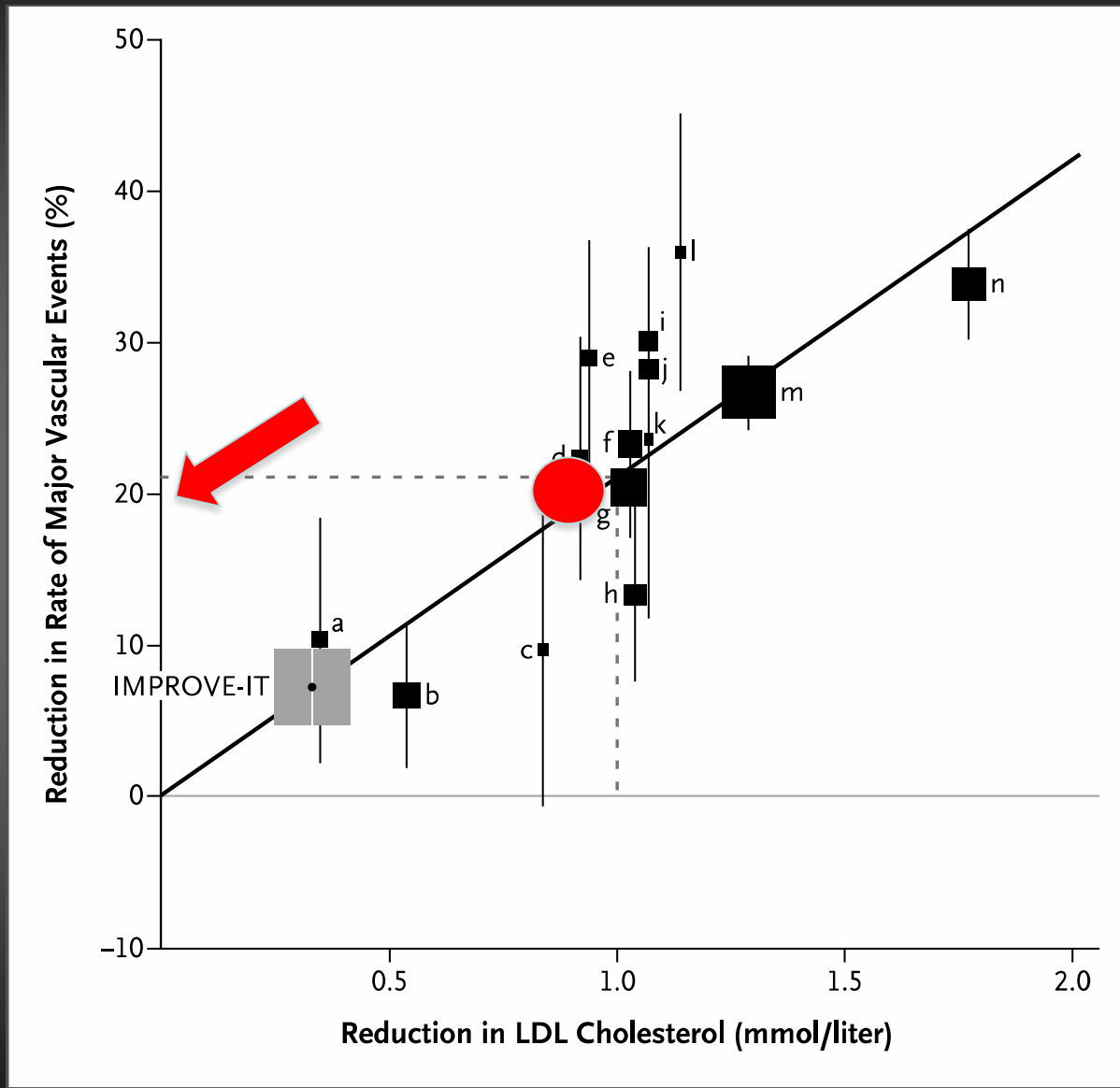


# Plot of the IMPROVE-IT Trial Data and Statin Trials for Change in LDL-C vs Clinical Benefit



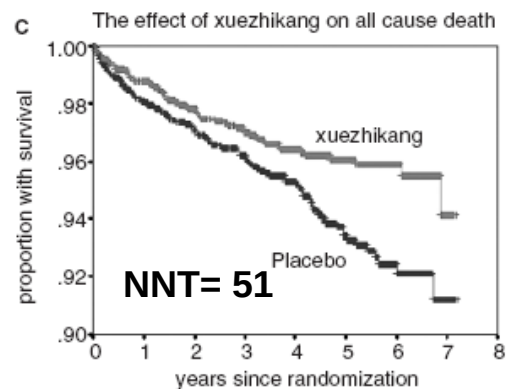
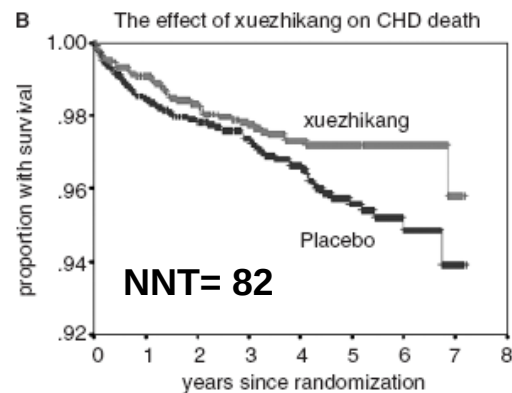
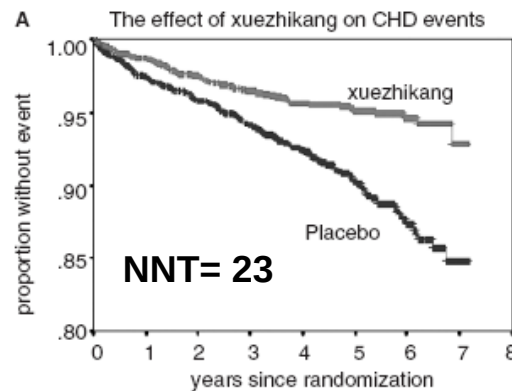
Cannon CP  
et al. NEJM  
2015;  
DOI:  
10.1056/NEJ  
Moa141048  
9

# LDL-reduction by CV risk reduction

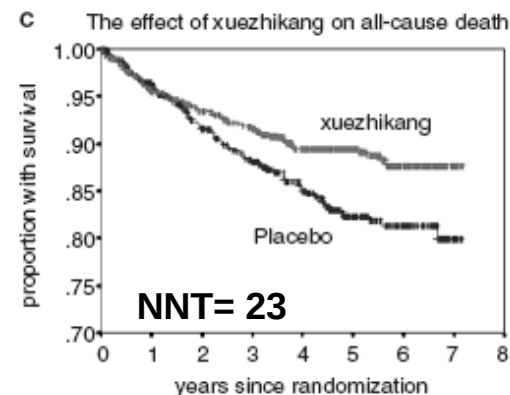
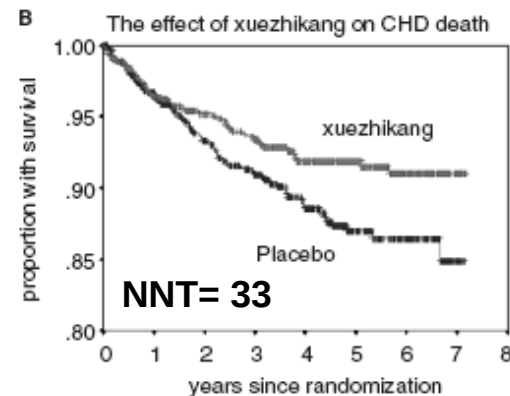
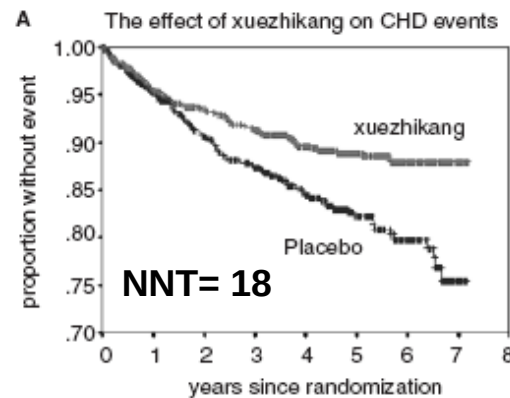


# China Coronary Secondary Prevention Study

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.

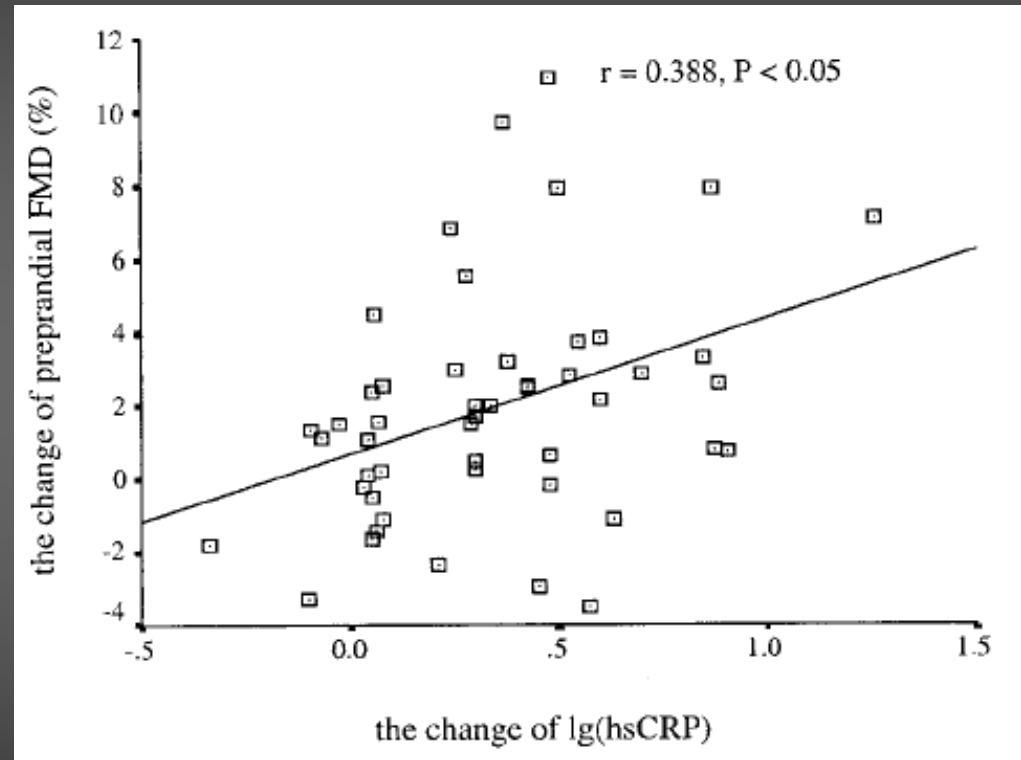
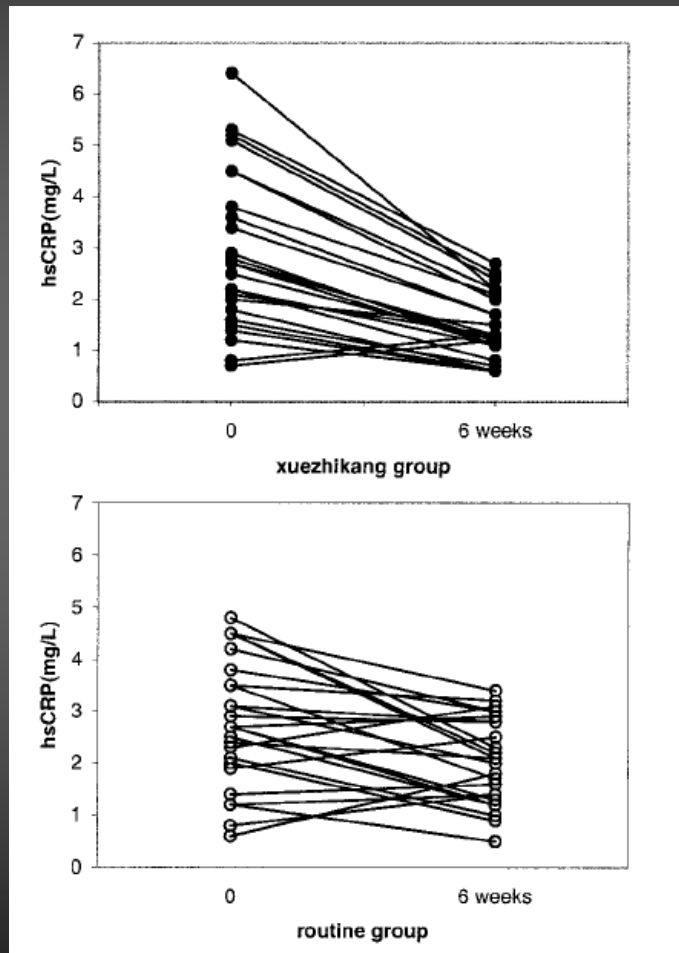
# **ESC/EAS Guidelines for the management of dyslipidaemias**

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

**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 ???**

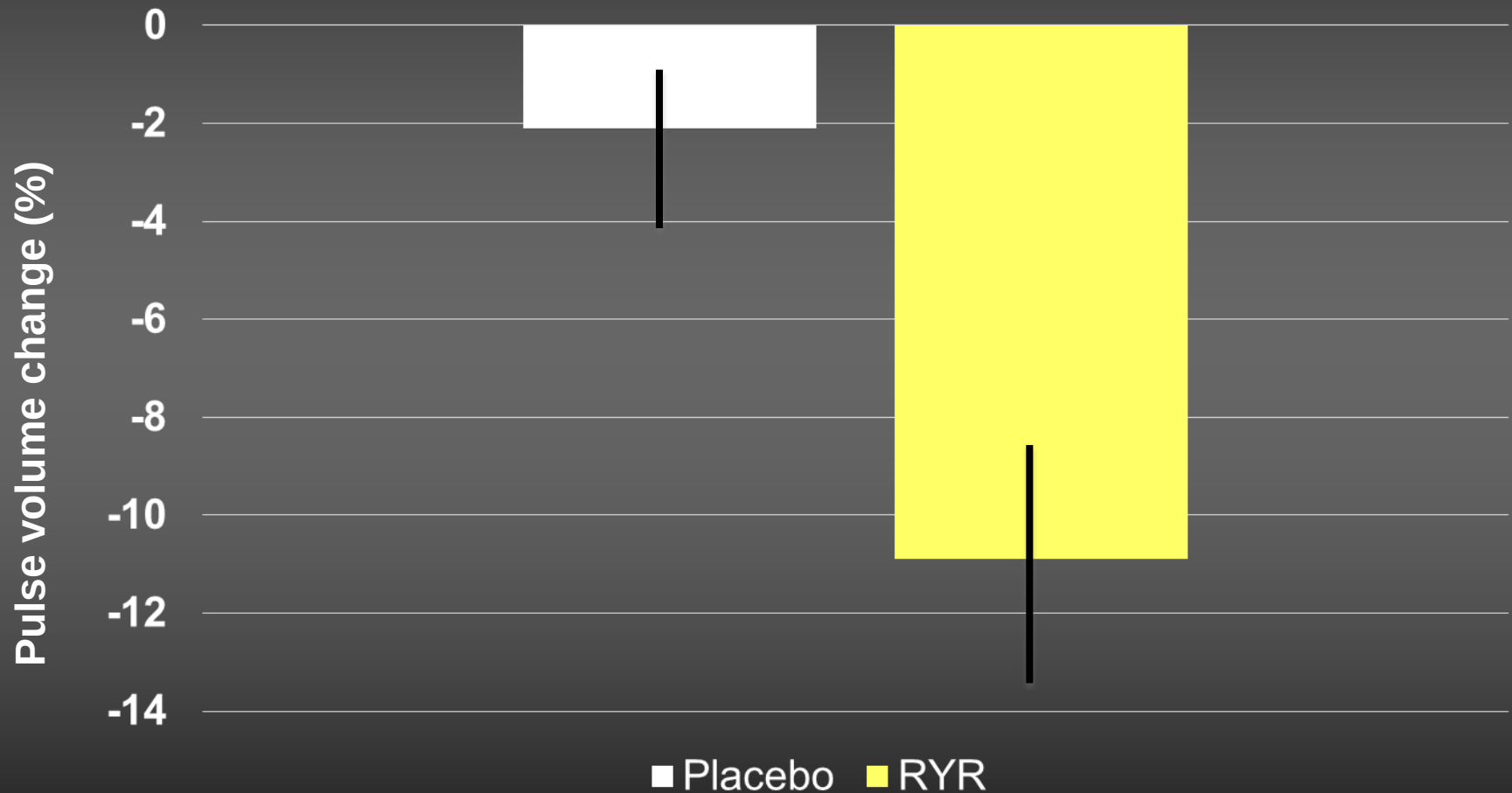
# Highly dosed RYR, hsCRP and FMD in patients with CAD



*Circulation.* 2004;110:915-920

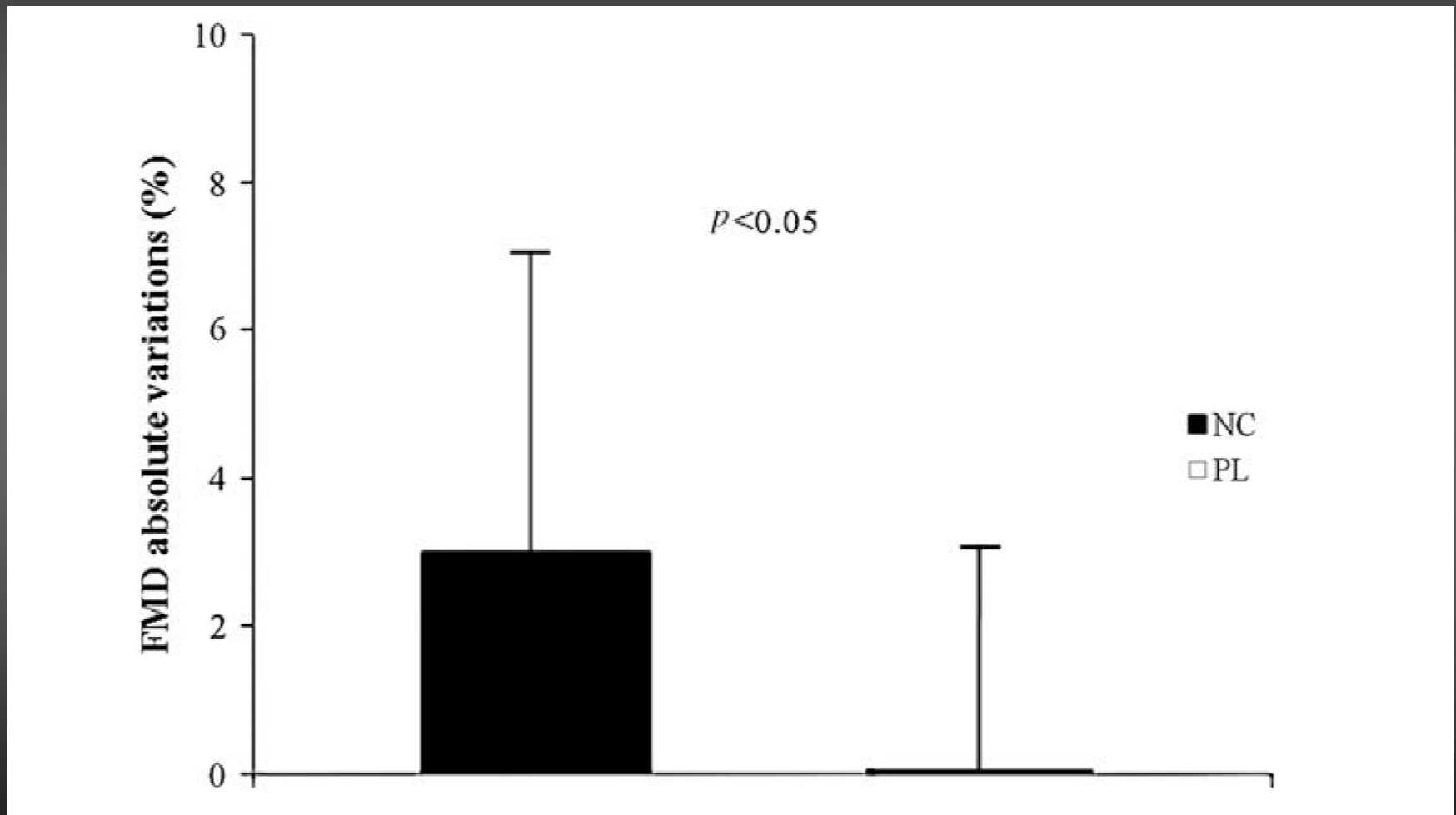


# 10 mg monacolins and endothelial reactivity improvement in mildly hypercholesterolemic subjects

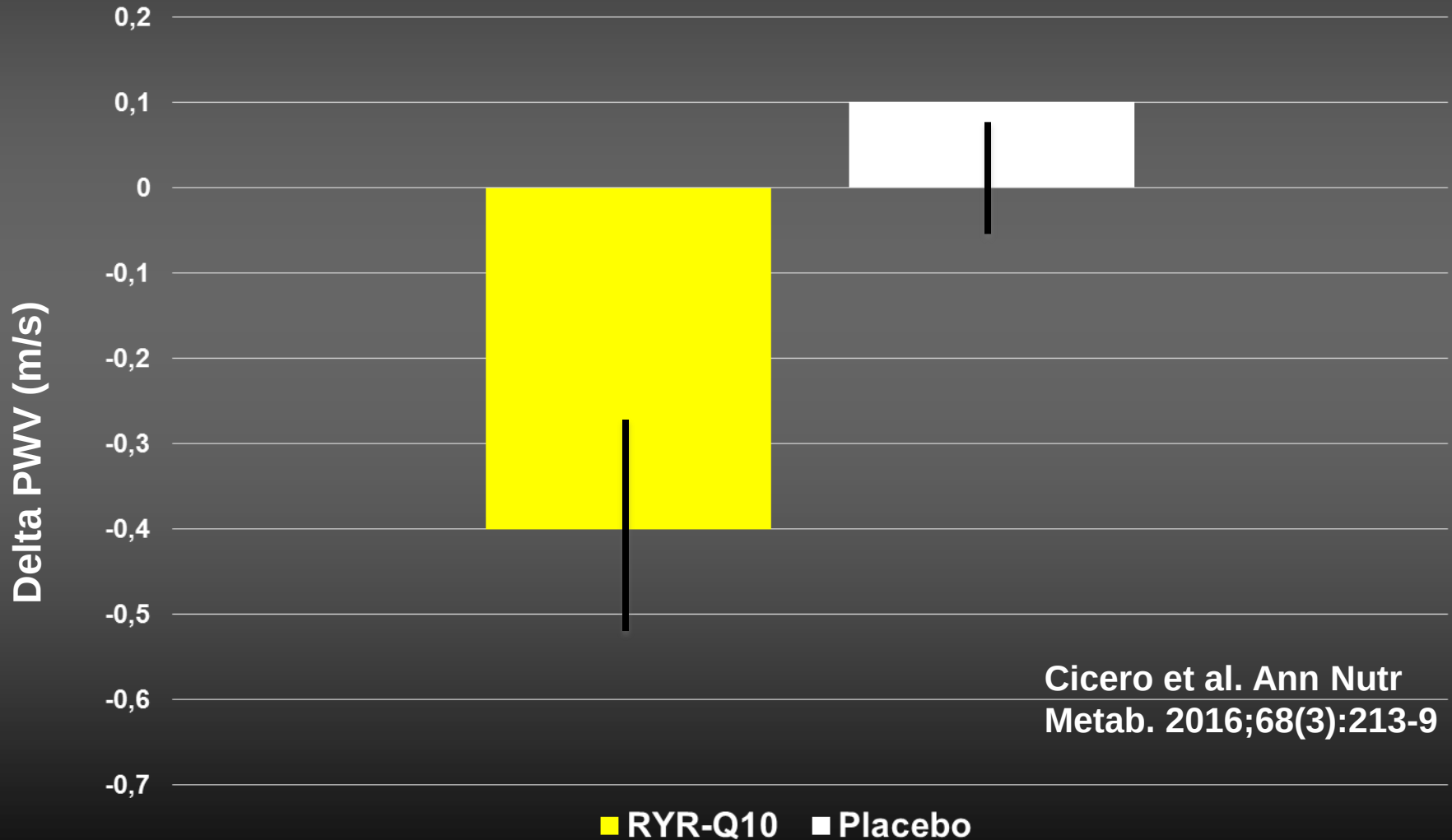


Cicero et al. *J Biol Reg Hom Agents* 2016 (In press); *Ann Nutr Metab.* 2016;68(3):213-9 ; *Ther Clin Risk Manag.* 2016 Feb 23;12:281-6.

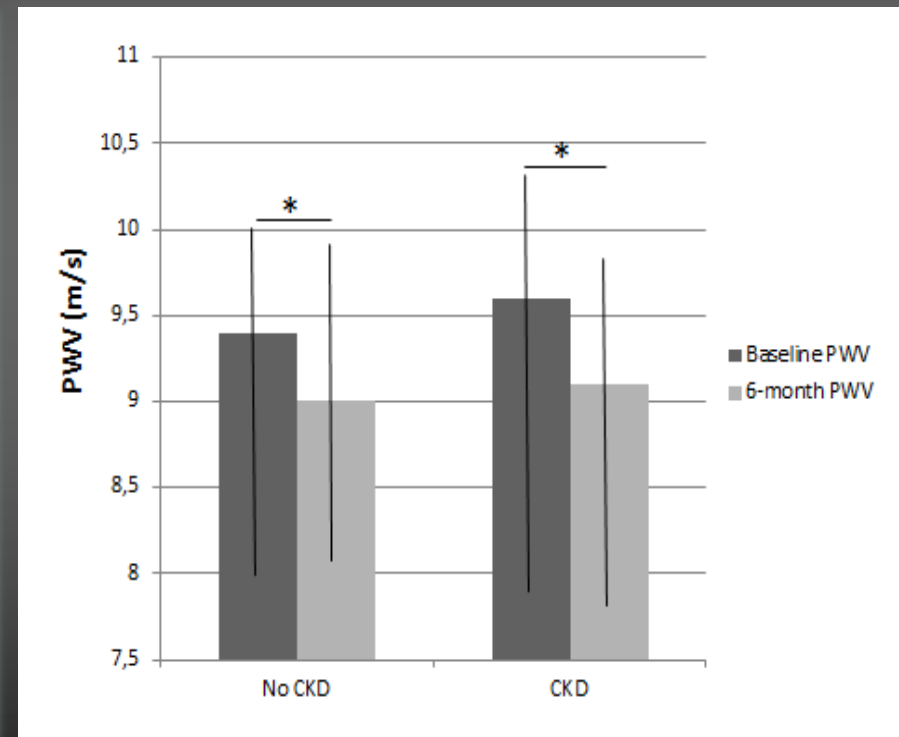
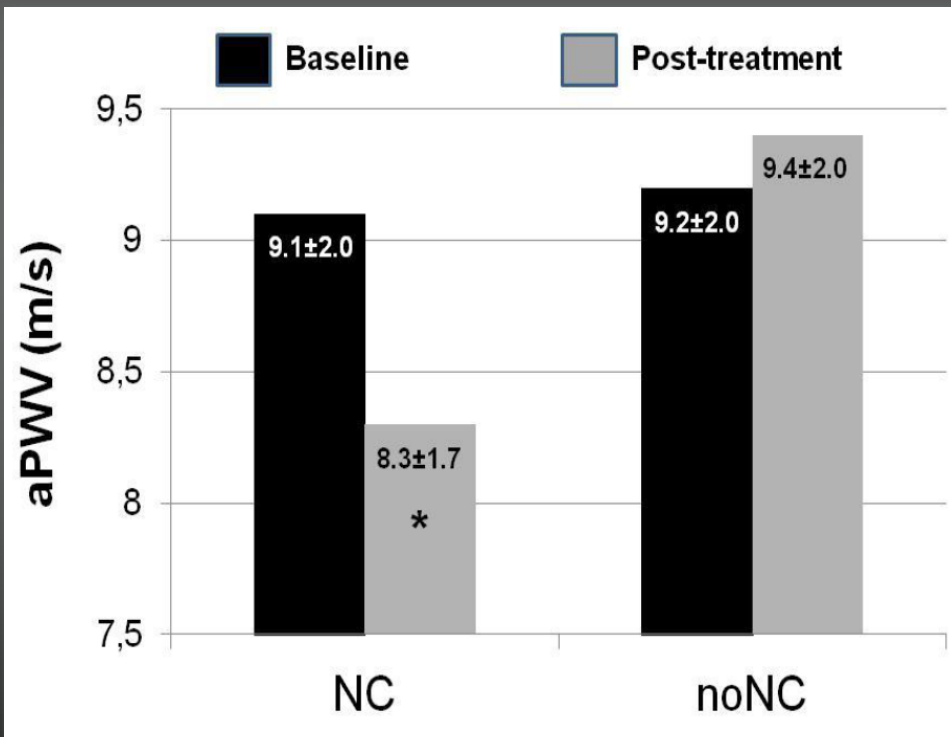
# Low-dosed red yeast-rice – berberine association effect on FMD



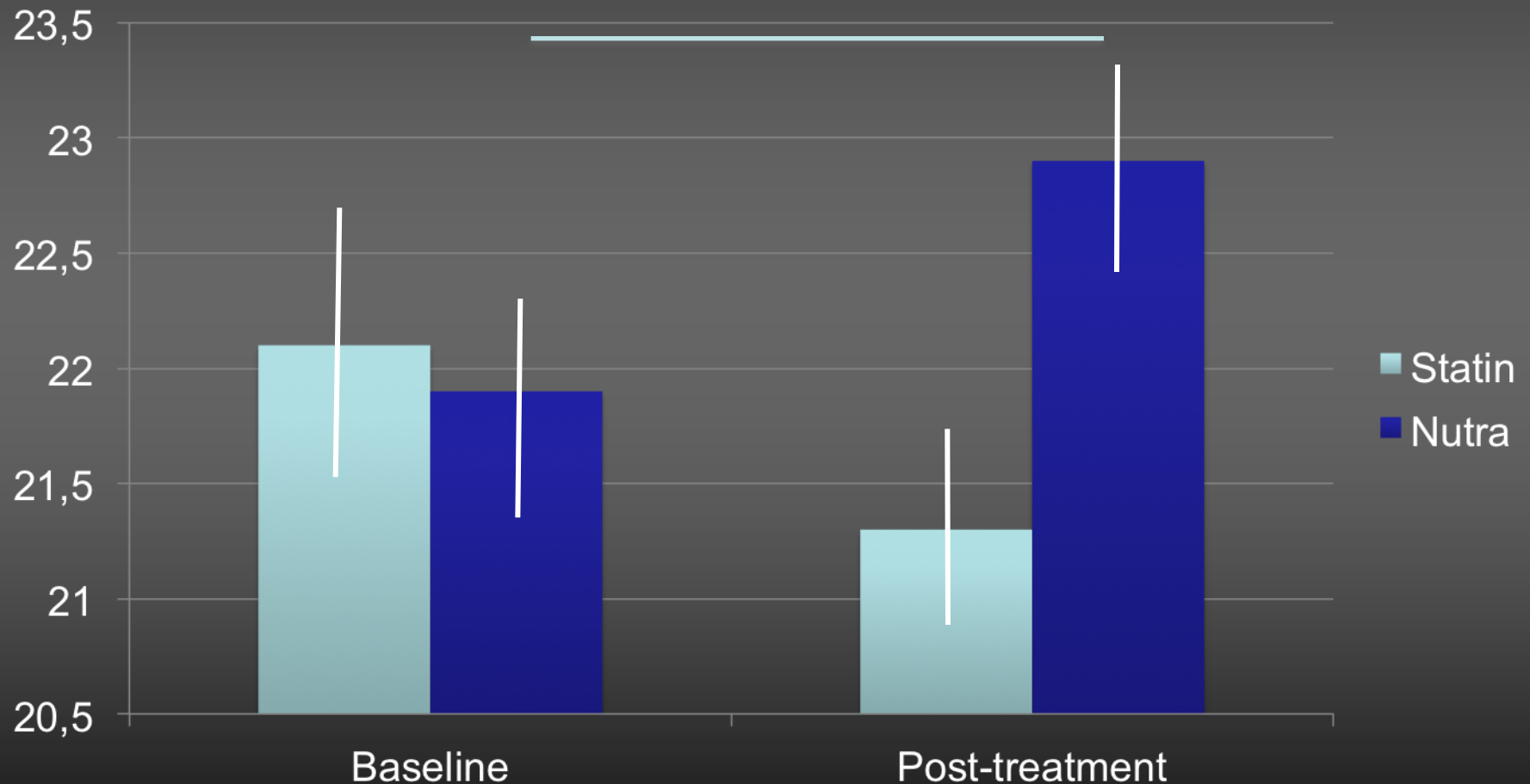
# RYR-CoQ10 middle-term effect on PWV



# Low-dosed red yeast-rice – berberine association effect on PWV



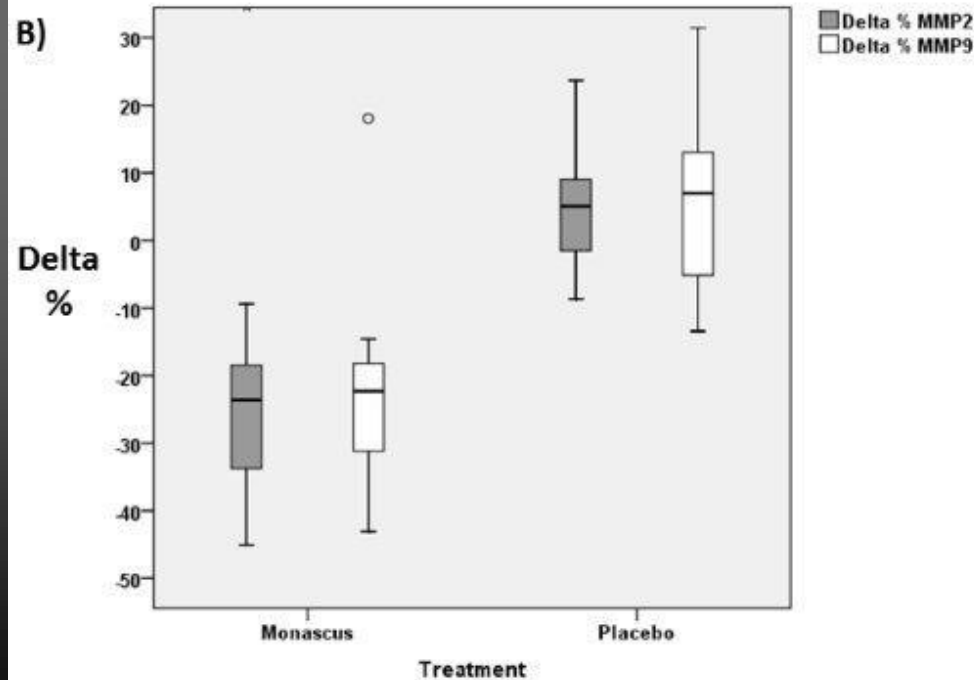
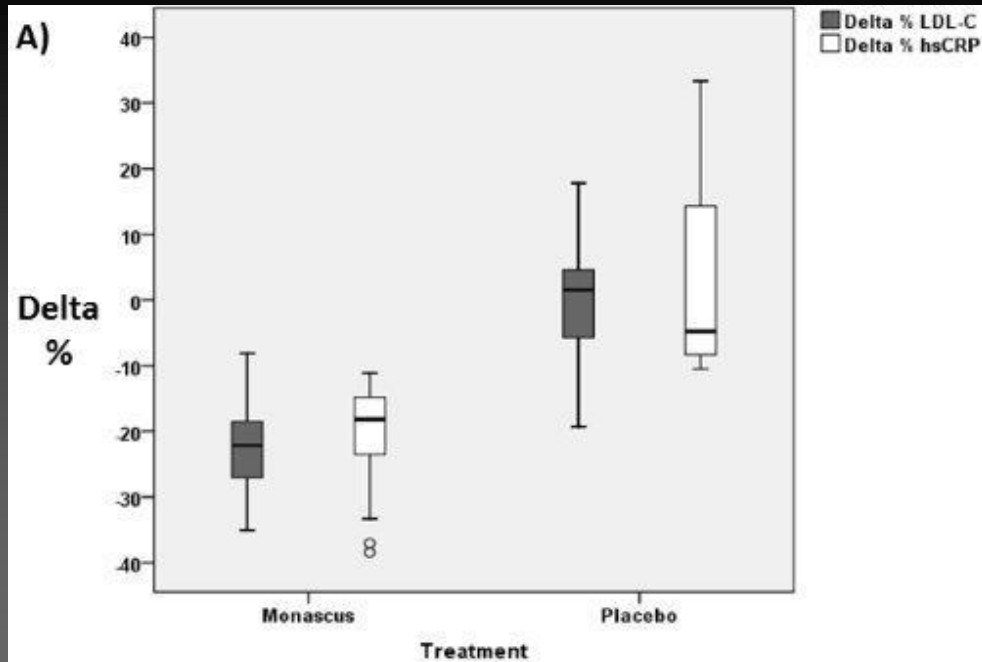
# IIEF-5 Score in patients previously reporting sexual performance worsening during statin-treatment



Cicero AFG - Unibo 2007

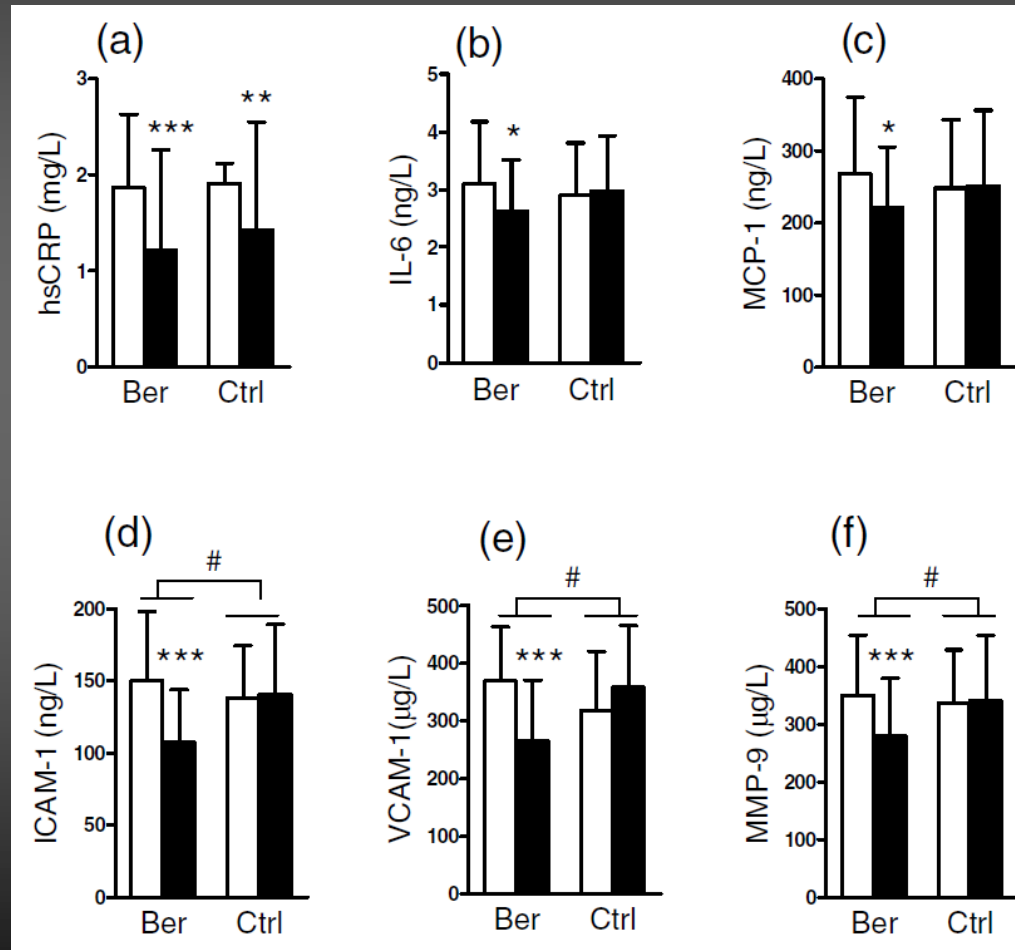
*Cicero AFG et al. Nutrafoods 2015*

# 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.

# Low-dosed red yeast-rice – berberine association effect on LDL size

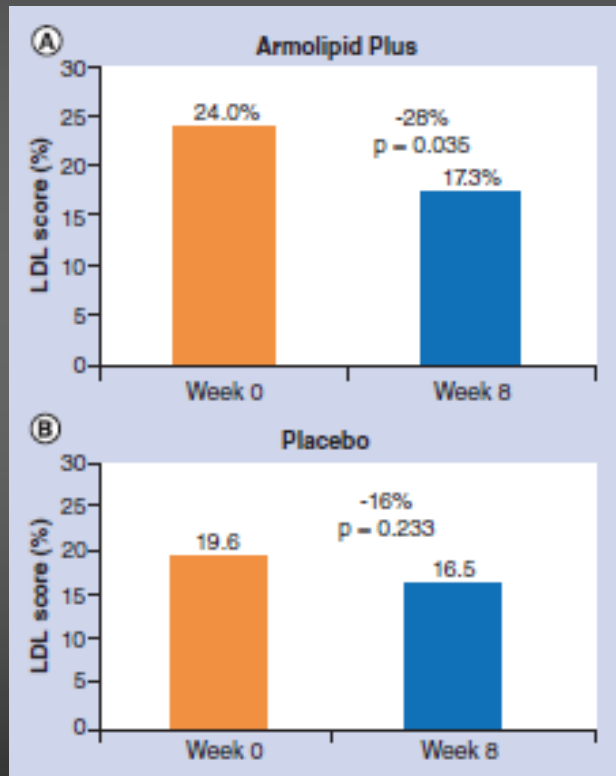


Figure 1. Modifications of LDL score. (A) Armolipid Plus group (n = 14) and (B) placebo group (n = 15). Values are expressed as mean  $\pm$  standard deviation.

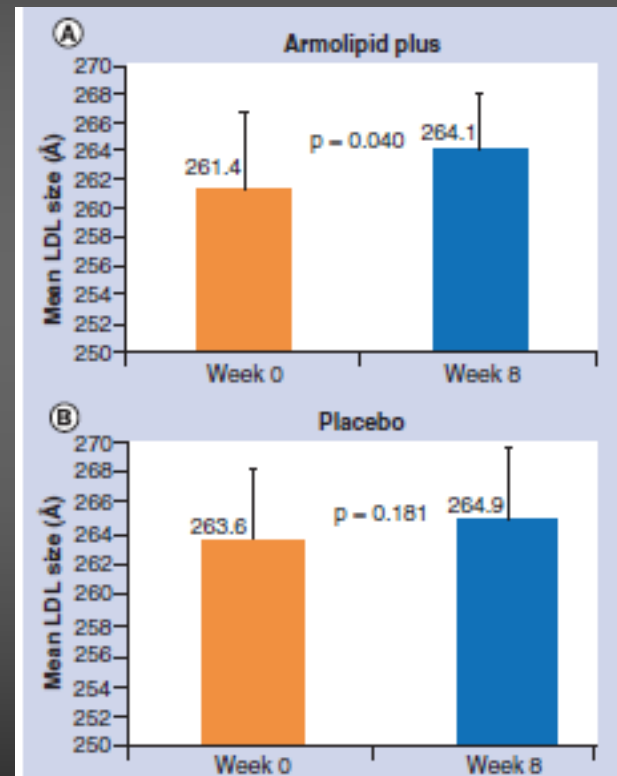
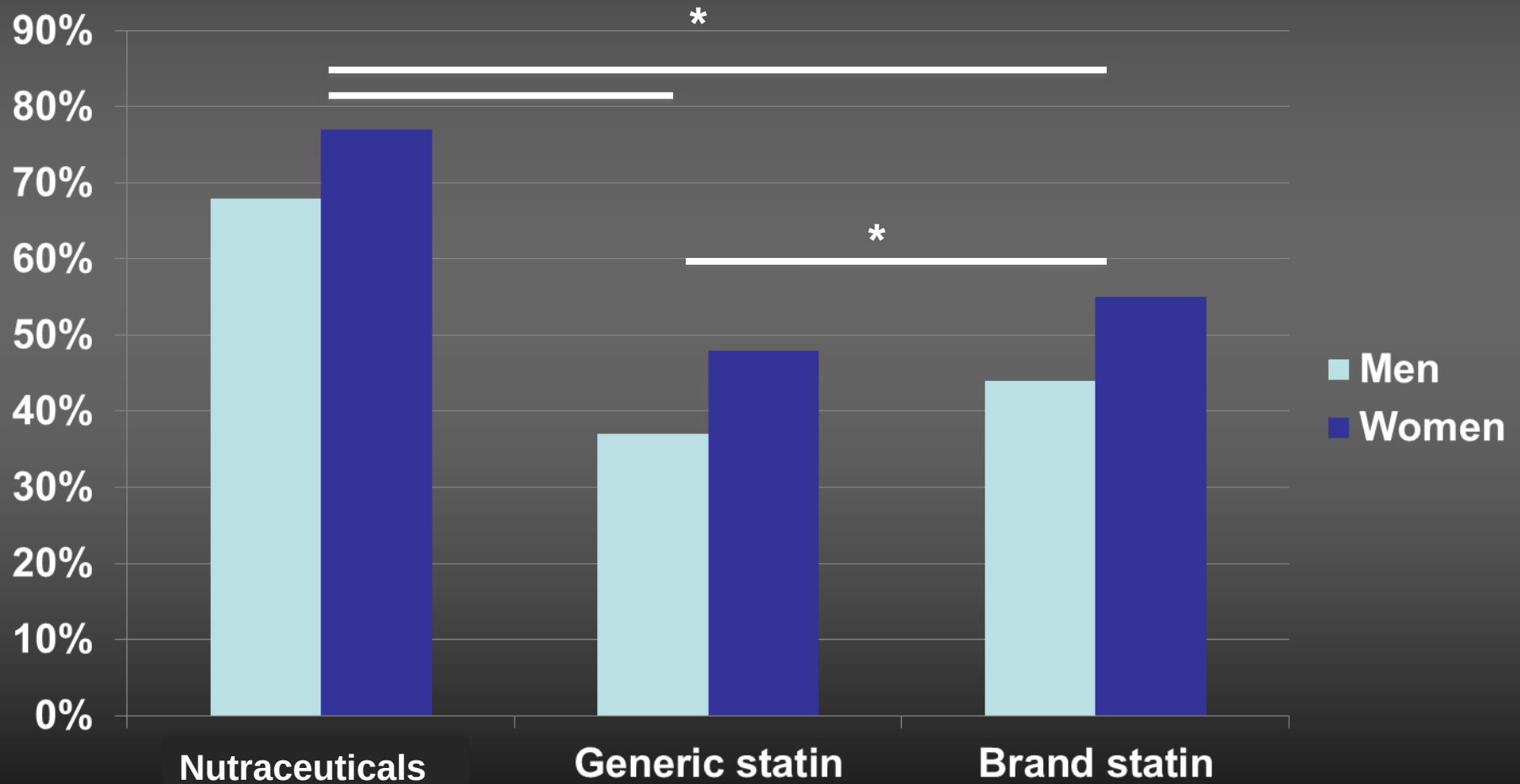


Figure 2. Modifications of mean LDL size. (A) Armolipid Plus group (n = 14) and (B) placebo group (n = 15).



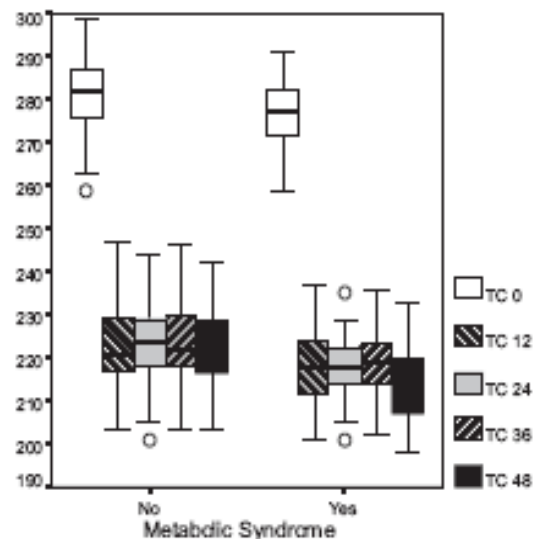
# 2-years persistence in paid LDL-lowering treatment



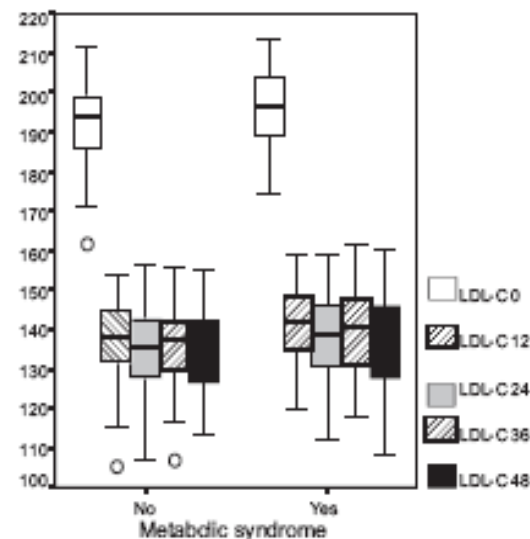
# Long-term effectiveness and safety of a combined nutraceutical based approach to reduce cholesterolemia in statin intolerant subjects with and without metabolic syndrome

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

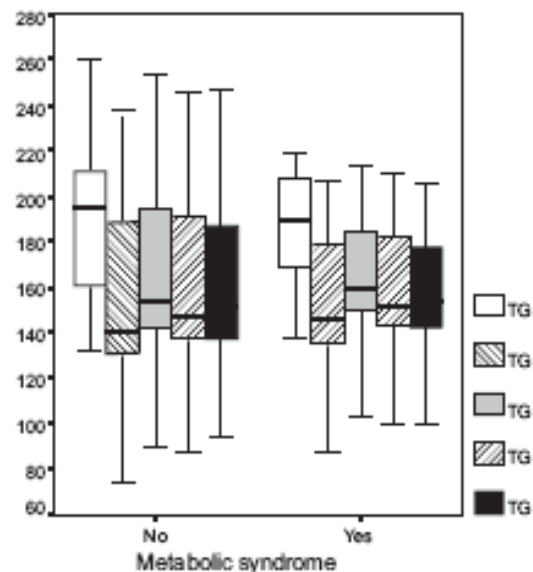
TC



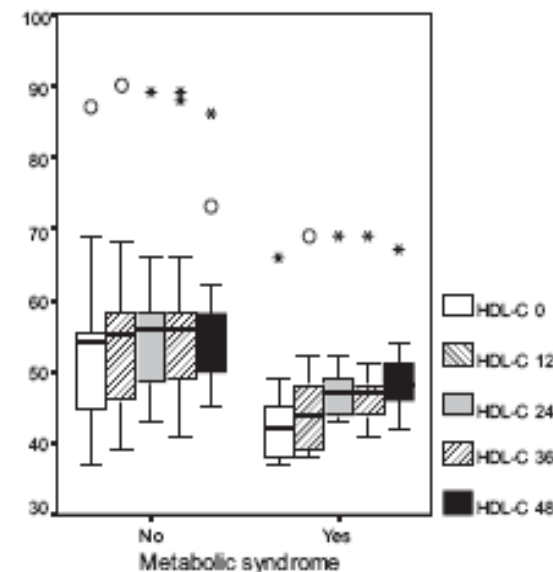
LDL-C



TG

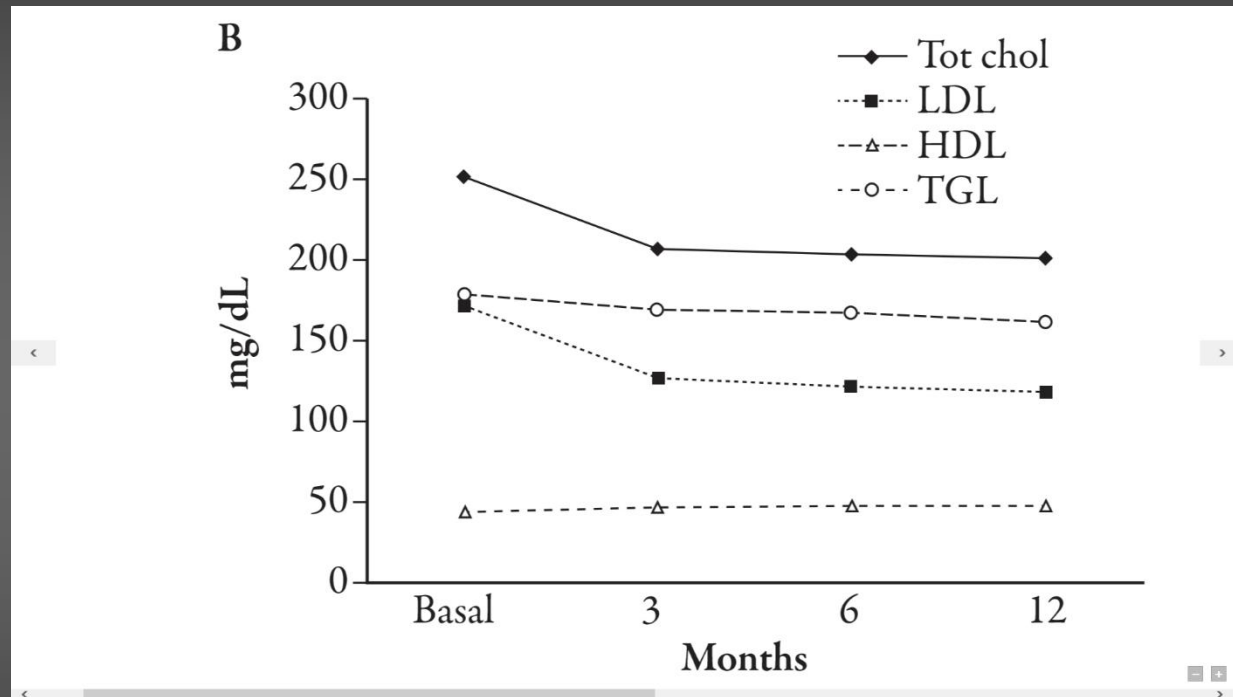


HDL-C



# RYR-berberine tolerability in elderly (>75) statin intolerant patients (N. 80): a single-blind, placebo-controlled RCT

Marazzi G et al. Adv Ther 2011;28(12):1105-13.



|            | NCP group |        | Placebo group |        |
|------------|-----------|--------|---------------|--------|
|            | Basal     | End    | Basal         | End    |
| AST (U/L)  | 23±5      | 24±5   | 22±4          | 22±4   |
| ALT (U/L)  | 25±6      | 28±5   | 26±4          | 26±4   |
| CK (mU/mL) | 113±25    | 119±18 | 116±20        | 117±25 |

# No PK interaction with common drugs

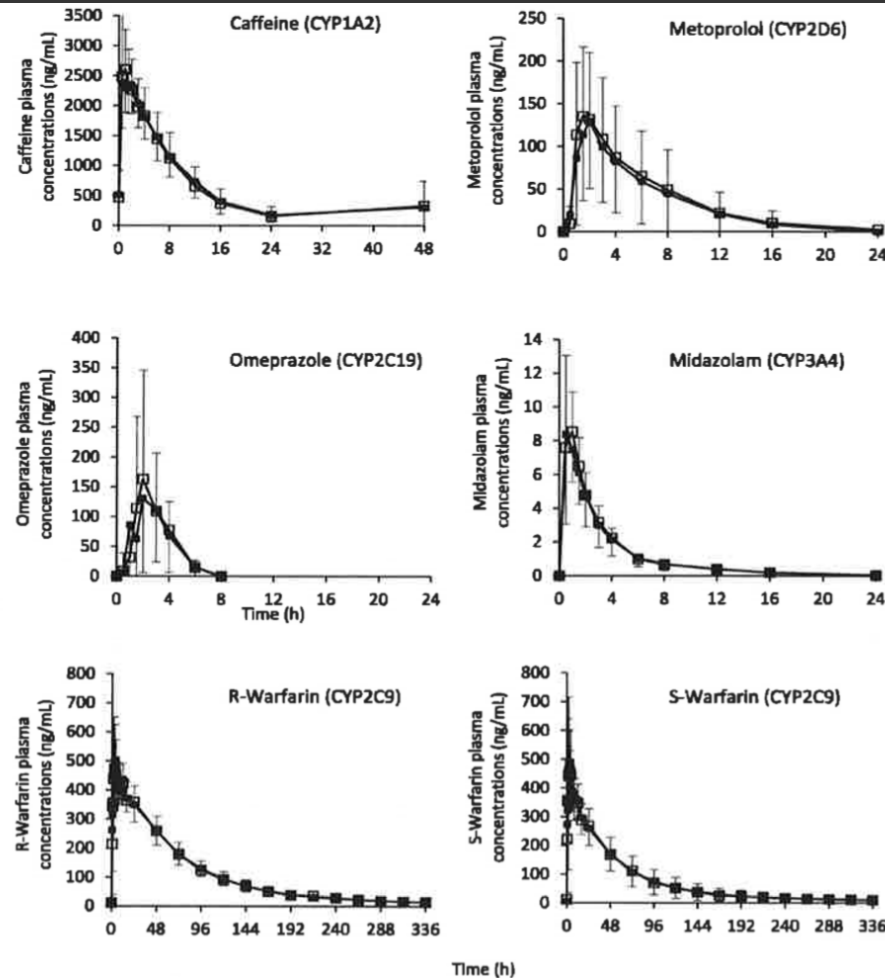


Fig. 1 Mean plasma concentrations for each probe administered as cocktail alone (reference treatment, open symbols) or with the combination of berberine and monacolin (test treatment, close symbol).

$N = 12$ , SD are shown by positive vertical bar for the reference treatment and by negative vertical bar for the test treatment.



**“Dottore ... Mi creda! lo cerco di mangiare sano... Non aggiungo mai sale al gelato, mangio solo pizza decaffeinata e la mia birra non contiene grassi!!!”**