

# “Studi clinico-nutrizionali”

Roberto Volpe, MD, AMS, PhD



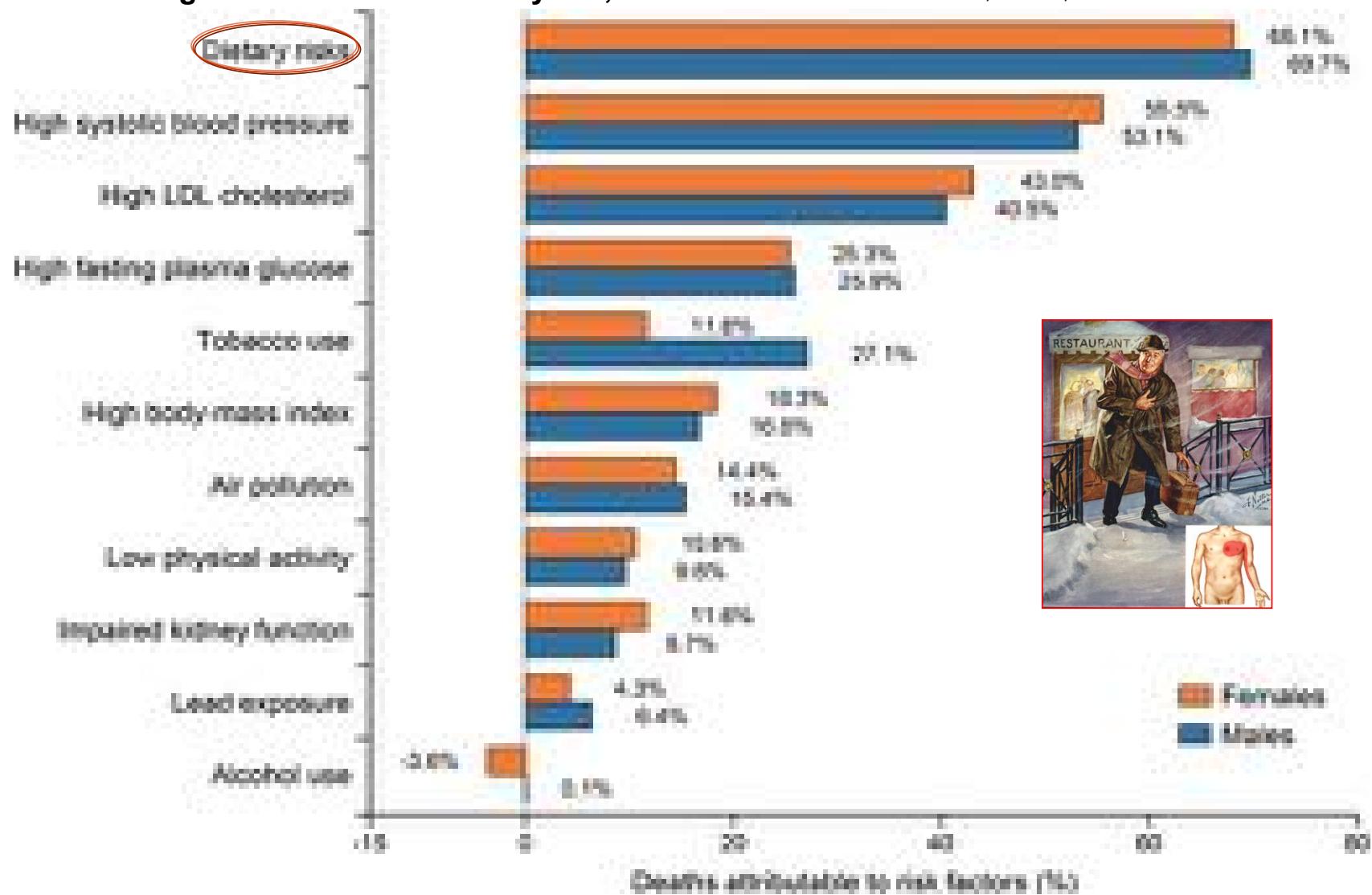
# **Principali cause dei tumori**

(Anand, 2008)

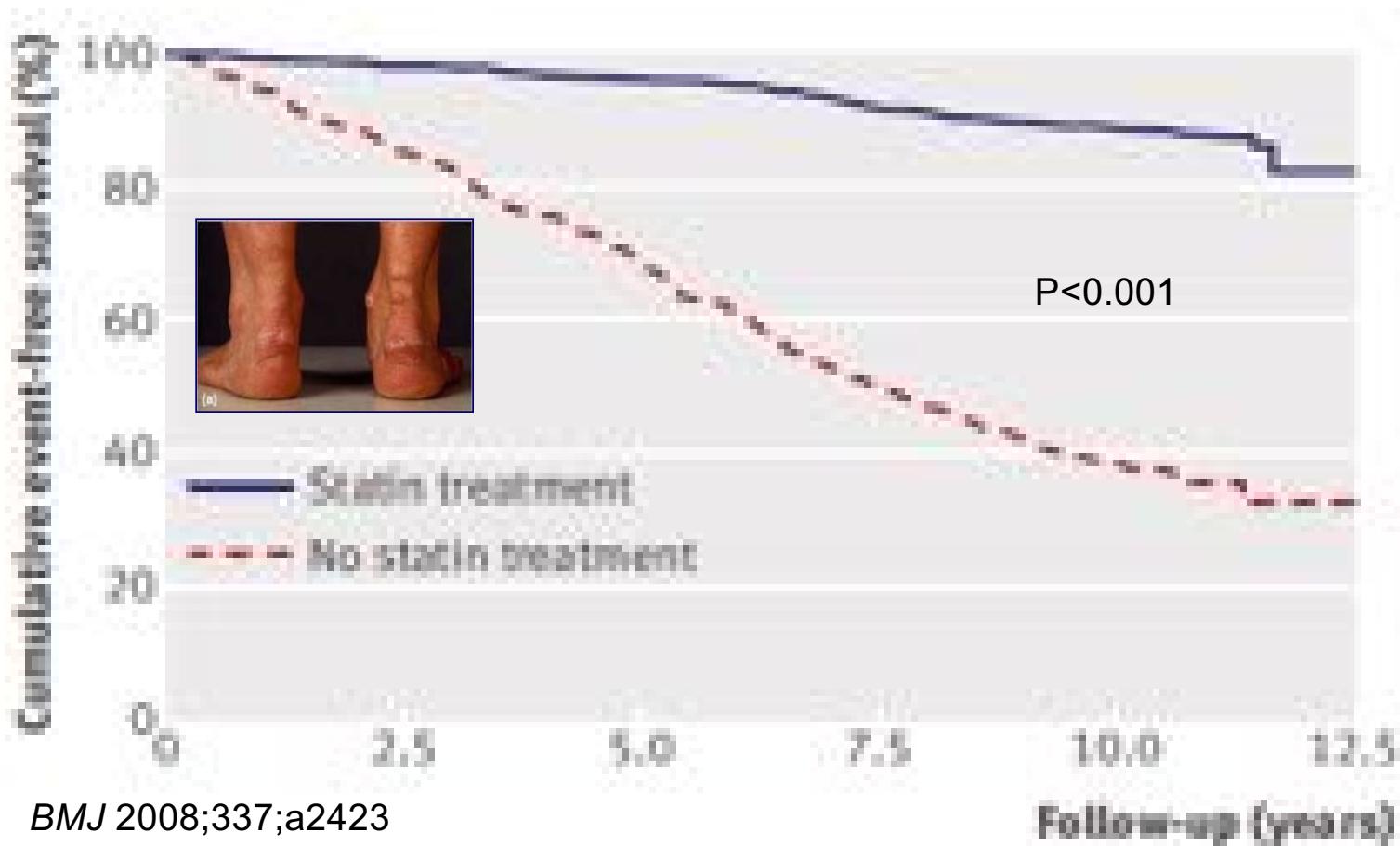
%

<b>Alimentazione /obesità</b>	<b>30-35</b>
<b>Fumo</b>	<b>25-30</b>
<b>Infezioni</b>	<b>15-20</b>
<b>Fattori geofisici (radiazioni)</b>	<b>&lt;10</b>
<b>Genetica</b>	<b>5-10</b>
<b>Inattività fisica</b>	
<b>Inquinamento ambientale</b>	

**Percentage contributions of major risk factors to ischaemic heart disease age-standardized deaths by sex, 2017.** GBD 2017 Diet Collaborators, Lancet, 2019



## Kaplan-Meier curve estimates of cumulative coronary heart disease-free survival among patients with familial hypercholesterolaemia according to statin treatment



## **Statins therapy: cost-benefit analyses in relation to the coronary heart disease risk at 10 years**

(Lipid Management in Adults 2009, [www.icsi.org](http://www.icsi.org))

% CHD risk at 10 years	NNT to prevent 1 event in 5 years
35	9,5
30	11
25	13
20	17
15	19
10 (mild)	33
5 (low)	67

## ESC/EAS Guidelines for the management of dyslipidaemias

The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS)

Developed with the special contribution of: European Association for Cardiovascular Prevention & Rehabilitation<sup>†</sup>

cessation may also contribute to HDL-C elevation.<sup>149</sup>

### 6.4 Dietary supplements and functional foods active on plasma lipid values

Innovative nutritional strategies to improve dyslipidaemias have been developed. They are based either on changing some 'unhealthy' dietary components or on encouraging the consumption of specifically targeted 'healthy' functional foods and/or dietary supplements. These so-called 'supplements' can be used either as alternatives or in addition to lipid-lowering drugs.<sup>150</sup>

Nutritional evaluation of functional foods includes not only the search for the clinical evidence of beneficial effects relevant to improved health or reduction of disease risk, but also the demonstration of good tolerability and the absence of major undesirable effects. The substantiation of health claims relevant for each food should be based on results from intervention studies in humans that are consistent with the proposed claims.<sup>151</sup>

Overall, the available evidence on functional foods so far identified in this field is lacking; the major gap is the absence of detailed intervention trials of sufficient duration to be relevant for the natural history of dyslipidaemias and CVD.

#### Phytosterols

The principal phytosterols are cholesterol, campesterol, and sitosterol, and they occur naturally in vegetable oils and in smaller amounts in vegetables, fresh fruits, chestnuts, grains, and legumes. The dietary intake of plant sterols ranges between an average of 250 mg/day in Northern Europe to ~300 mg/day in Mediterranean countries. Phytosterols compete with cholesterol for intestinal absorption, thus modulating TC levels.

#### n-3 unsaturated fatty acids

Supplementation with n-3 fatty acids (rich in long chain n-3 fatty acids) can reduce TG levels by 25–30% in both normolipidaemic and hyperlipidaemic individuals. n-3 docosanoic acid (a medium chain n-3 fatty acid present in chia seeds, some vegetables, and some seed oils) is less effective on TG levels. Long chain n-3 PUFAa also reduce the post-prandial lipoprotein response. Long chain n-3 PUFAa, at doses of ~3 g/day given as supplements, may increase HDL-C by ~5% in severely hypertriglyceridaemic patients.<sup>152</sup> However, a low dose supplementation of a margarine with n-3 PUFAa (400 mg/day) or n-3 docosanoic acid (3 g/day) did not significantly reduce TG levels in an RCT involving 482 post-MI patients; neither did the supplementation reduce the rate of major CV events.<sup>153</sup>

#### Polygonol and red yeast rice

Polygonol is a natural mixture of long chain aliphatic alcohols extracted primarily from sugar cane wax.<sup>154</sup> Studies show that polygonol from sugar cane, rice, or wheat germ has no significant effect on LDL-C, HDL-C, TG, apo B, Lp(a), homocysteine, hs-CRP, fibrinogen, or blood coagulation factors.<sup>155</sup>

Red yeast rice (RYR) is a source of fermented pigment used in China as a food colourant and flavour enhancer for centuries. Possible bioactive effects of RYR are related to a statin-like mechanism (inhibition of hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase). Different commercial preparations of RYR have different concentrations of monacolin, the bioactive ingredient, and lower TC and LDL-C,<sup>156</sup> but the long term safety of the regular consumption of these products is not fully documented. In one RCT from China in patients with CAD, a partially purified extract of RYR reduced recurrent events by 45%.<sup>157</sup>

## **2016 European Guidelines on cardiovascular disease prevention in clinical practice**

**The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)**

**Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR)**

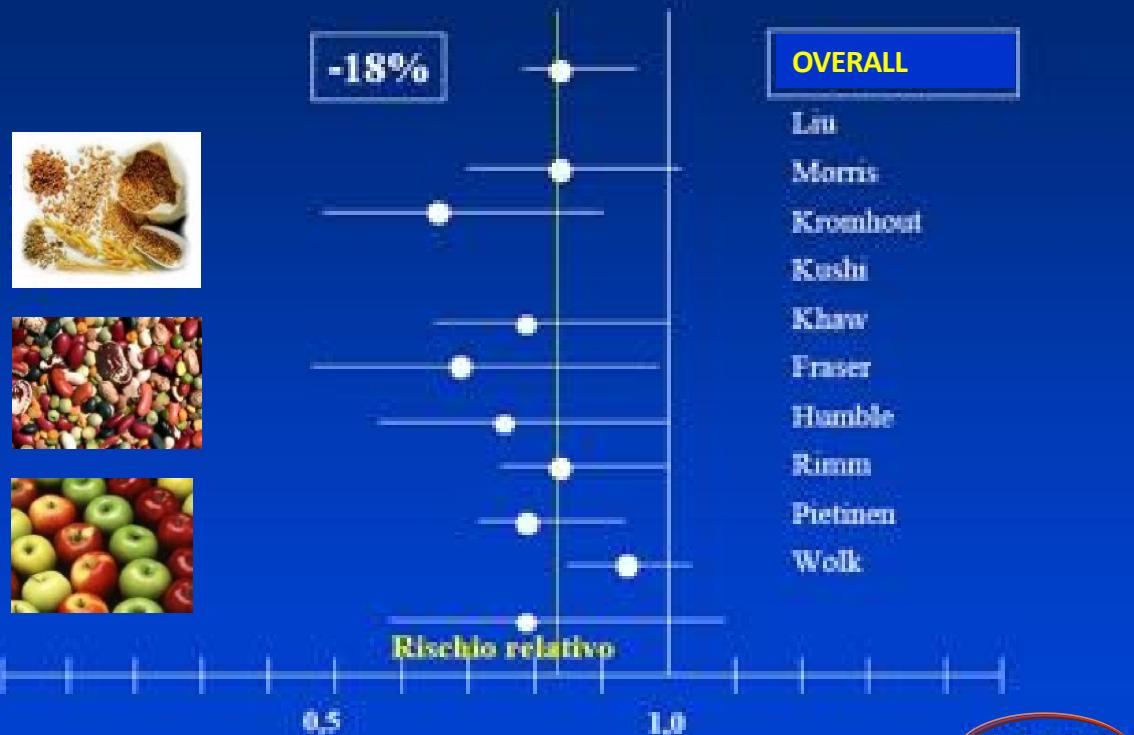
**-Life-style**

**-Fibres (whole grains, legumes, vegetables, fruit), EVOO as functional food**

**-Nutraceuticals (phytosterols, red yeast rice, omega-3)**

**-Drugs**

# Fibres and CVD



## 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias

The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)

closely on HDL-C, but special attention should be paid in order to prevent weight gain in people who stop smoking.<sup>14</sup>

### 5.5 Dietary supplements and functional foods for the treatment of dyslipidaemias

Innovative nutritional strategies to improve dyslipidaemias have been developed. They are based on either changing some 'key' dietary components or encouraging the consumption of specifically targeted 'healthy' functional foods and/or dietary supplements. These so-called nutraceuticals can be used either as alternatives or in addition to lipid-lowering drugs.<sup>145</sup> Nutritional evaluation of functional foods includes not only the search for clinical evidence of beneficial effects relevant to improved health or reduction of disease risk, but also the demonstration of good tolerability and the absence of major undesirable effects. The substantiation of health claims relevant for each food should be based on results from intervention studies in humans that are consistent with the proposed claims. Overall, the available evidence on functional foods so far identified in this field is incomplete; the major gap is the absence of double-blind intervention trials of sufficient duration to be relevant for the natural history of dyslipidaemias and CVD.

#### 5.5.1 Phytonutrients

The principal phytonutrients are sterols, carotenoids and flavonoids; they occur naturally in vegetable oils and in smaller amounts in vegetables, fresh fruits, cereals, grains and legumes. The dietary intake of plant sterols ranges between an average of 250 mg/day in Northern Europe to ~500 mg/day in Mediterranean countries. Phytonutrients compete with cholesterol for intestinal absorption, thereby modulating TC levels.

Phytosterols have been added to spreads and vegetable oils (functional margarine, butter and cooking oils), as well as yogurt and other foods; however, food matrices do not significantly influence the cholesterol-lowering efficacy of phytosterols at equivalent doses.<sup>146</sup> The daily consumption of 2 g of phytosterols can effectively lower TC and LDL-C by 7–10% in humans (with a certain degree of heterogeneity among individuals), while it has little or no effect on HDL-C and TG levels.<sup>147</sup> Although the effect of plant sterol consumption on TC levels has been clearly shown, no studies have been performed yet on the subsequent effect on CVD. However, the meta-analysis of Robinson et al.<sup>148</sup> indicates that LDL-C reduction translates into CV benefits, independent of the mechanism involved. Long-term surveillance is also needed to guarantee the safety of the regular use of phytosterol-enriched products. The

#### 5.5.2 Monacolin and red yeast rice

Red yeast rice (RYR) is a source of fermented pigment that has been used in China as a food colourant and flavour-enhancer for centuries. Hypocholesterolaemic effects of RYR are related to a statin-like mechanism: inhibition of hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase, of monacolin, which represent the active ingredient. Different commercial preparations of RYR have different concentrations of monacolin, and lower TC and LDL-C to a variable extent,<sup>149</sup> but the long-term safety of the regular consumption of these products is not fully documented. However, side effects similar to those observed with statins have been reported in some people using them extraproctically; furthermore, their quality may vary widely.

In one RCT from China in patients with CAD, a partially purified extract of RYR reduced recurrent events by 45%.<sup>149</sup> No other trial has been performed to confirm this finding. A clinically-relevant hypocholesterolaemic effect (up to a 20% reduction) is observed with RYR preparations providing a daily dose of ~2.5–10 mg monacolin K.<sup>149</sup> Nutraceuticals containing purified RYR may be considered in people with elevated plasma cholesterol concentrations who do not qualify for treatment with statins in view of their global CV risk.

#### 5.5.3 Dietary fibre

Available evidence consistently demonstrates a TC- and LDL-C-lowering effect of water-soluble fibre from oat and barley beta-glucan foods enriched with these fibres are well tolerated, effective and recommended for LDL-C lowering at a daily dose of at least 3 g/day.<sup>150</sup>

#### 5.5.4 Soy protein

Soy protein has been indicated as being able to induce a modest LDL-C-lowering effect when replacing animal protein foods.<sup>151</sup> However, this was not confirmed when changes in other dietary components were taken into account.

#### 5.5.5 Policosanol and berberine

Policosanol is a natural mixture of long chain aliphatic alcohols extracted primarily from sugarcane wax.<sup>152</sup> Studies show that policosanol from sugarcane, rice or wheat germ has no significant effect on LDL-C, HDL-C, TGs, apol., Lp(a), homocysteine, hs-CRP, fibrinogen or blood coagulation factors.<sup>153</sup>

As for berberine, a recent metaanalysis has evaluated its effects on plasma lipids in humans; six trials were available for this purpose: the berberine group contained 229 patients and the control group contained 203 patients.<sup>154</sup> The studies, showing a statistically

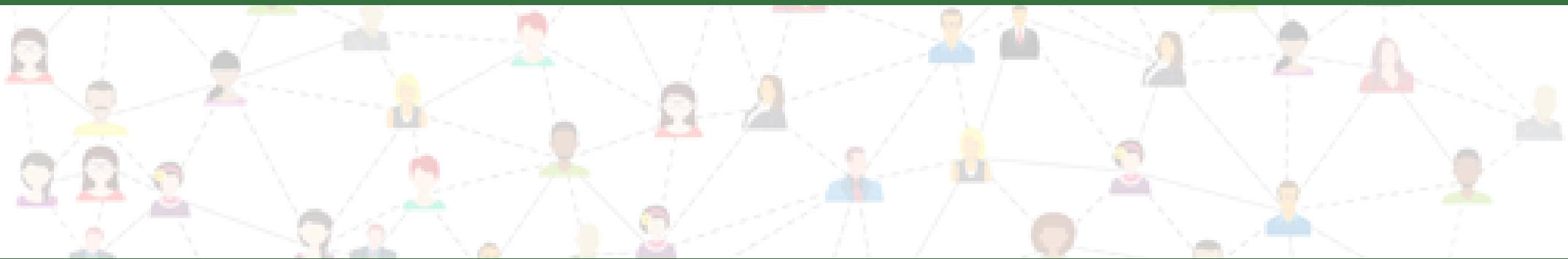
## **Cardio-metabolic risk factors. Non-pharmacological treatment could be considered an option in**

- patients at low-mild cardiovascular risk
- pre-menopausal women
- children of parents with premature cardiovascular diseases
- patients not controlled with available drugs
- patients already consuming multiple drugs
- patients intolerant to drugs

**Offer a CV prevention to those patients  
who are not classified as high-risk but that are at risk**



Consiglio Nazionale  
delle Ricerche



**Nutrheff: 34 ricercatori censiti  
nell'area “Studi clinico-nutrizionali”**

**Le sfide: alimenti funzionali, nutraceutici, disseminazione**



## EWHETA (Eat Well for a HEalthy Third Age) Project: novel foods to improve the nutrition in the elderly people

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Food and Nutrition Sciences, 2017, 8, 591-597

<http://www.scirp.org/journal/fns>

ISSN Online: 2157-9458

ISSN Print: 2157-944X

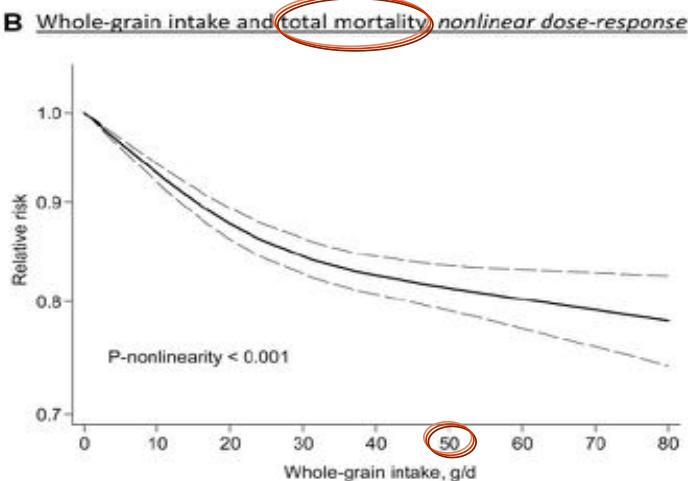
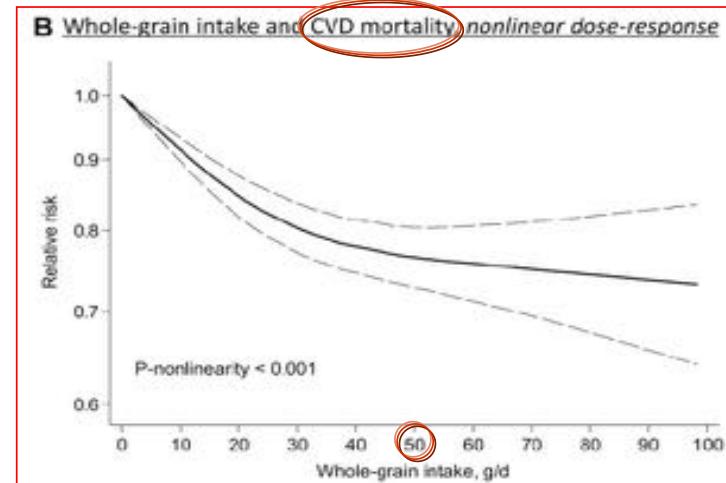
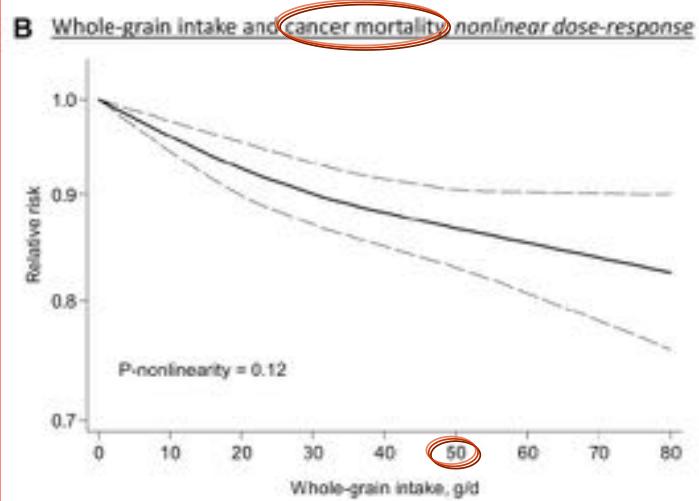
## Replacement Meal: Effectiveness of a Soluble Powder Rich in Fibers and at Low Glycemic Index in Overweight but Not in Obese Patients

Volpe Roberto<sup>1</sup>, Abdulkader Bisan<sup>2</sup>, Pacioni Fabrizio<sup>3</sup>, Reggiani Francesco<sup>4</sup>, Schiavetto Emanuela<sup>1</sup>

## A diet rich in whole grains is protective

**Whole-grain intake and cardiovascular, cancer, and total mortality (n. 104,061): a systematic review and meta-analysis of prospective studies (n. 13)**

Chen GC et al, Am J Clin Nutr 2016



Suggested by EBM: about 50 grams of whole grain per day (about 100 g of WG food)

**Quantità giornaliera di cereal integrali suggerita: 3 porzioni**  
(1 porzione = 16 g di peso secco, US 2015 Dietary Guidelines)

**1 fettina di pane** (circa 80-100 kcal)

**3-4 fette biscottate** (circa 90-120 kcal)

**2-3 cucchiai di cereali da colazione** (circa 140-210 kcal)

**80 g di pasta** (circa 280-310 kcal)

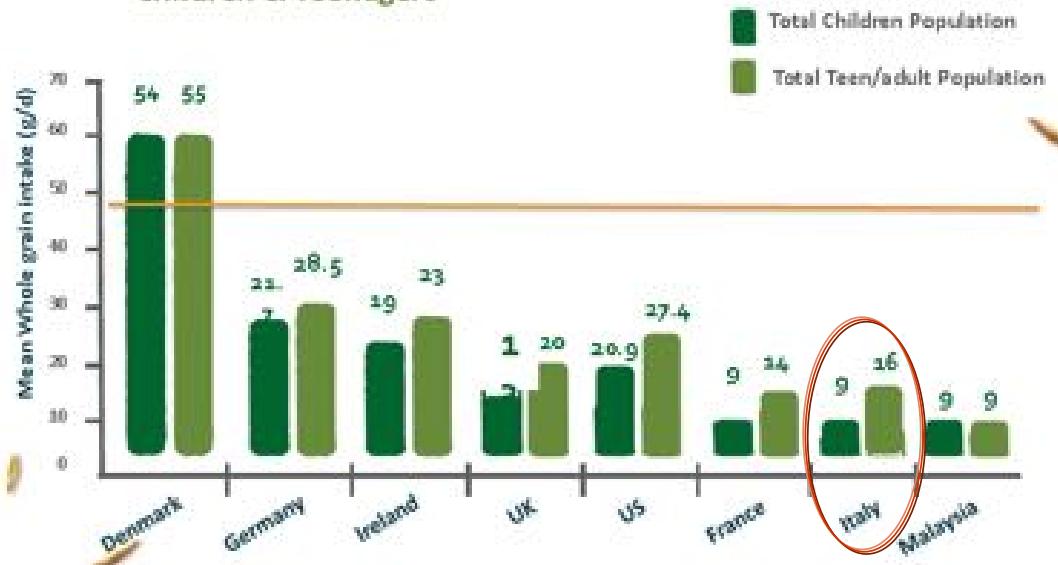
**80 g di riso** (circa 270-300 kcal)



**Unità Prevenzione e Protezione**  
Consiglio Nazionale delle Ricerche

Few people are achieving whole grain recommendations

Global overview of the Whole Grain intakes (g/d) in  
Children & Teenagers



Mann et al 2015, Devlin et al 2013, Bellisle et al 2014, Sette et al 2015 , Albertson et al 2016, AK et al 2015, Alexy et al 2010