

DIETA MEDITERRANEA IN VIAGGIO TRA BIOLOGICO E CONVENZIONALE

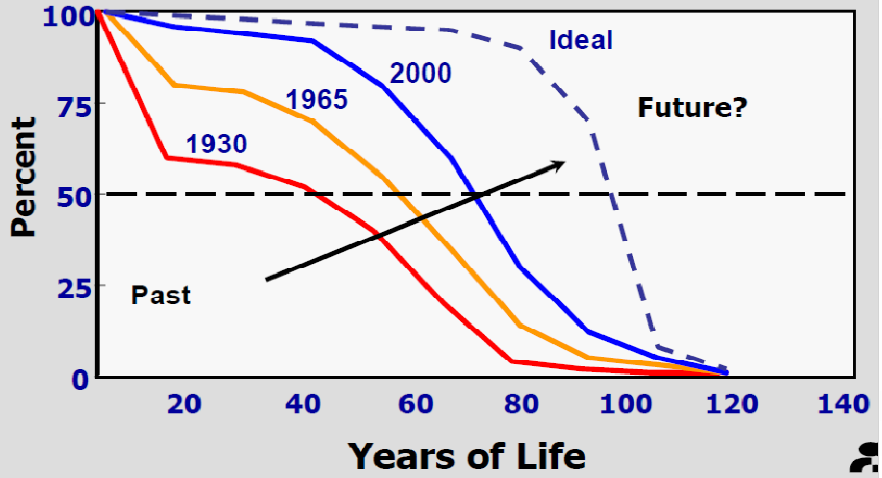
Antonino De Lorenzo e Laura Di Renzo, PhD

Università di Roma Tor Vergata

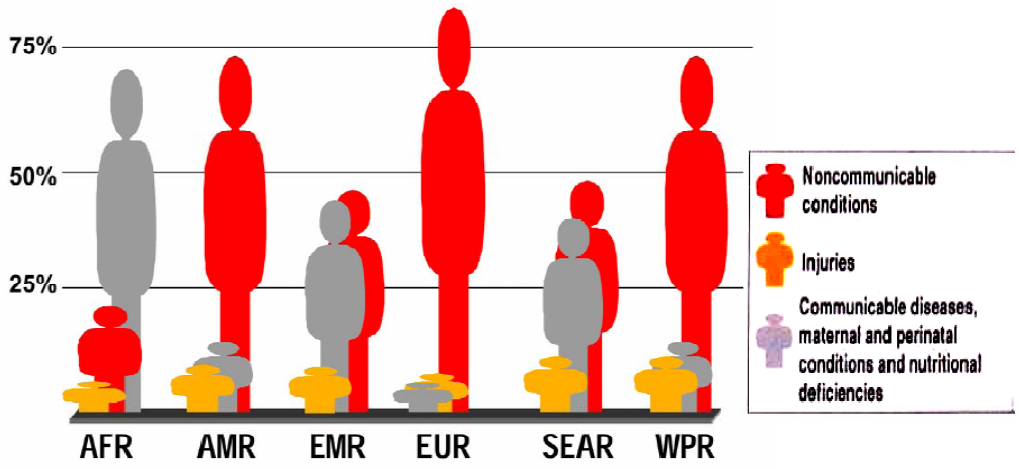
Istituto Nazionale Dieta Mediterranea e nutrigenpmica

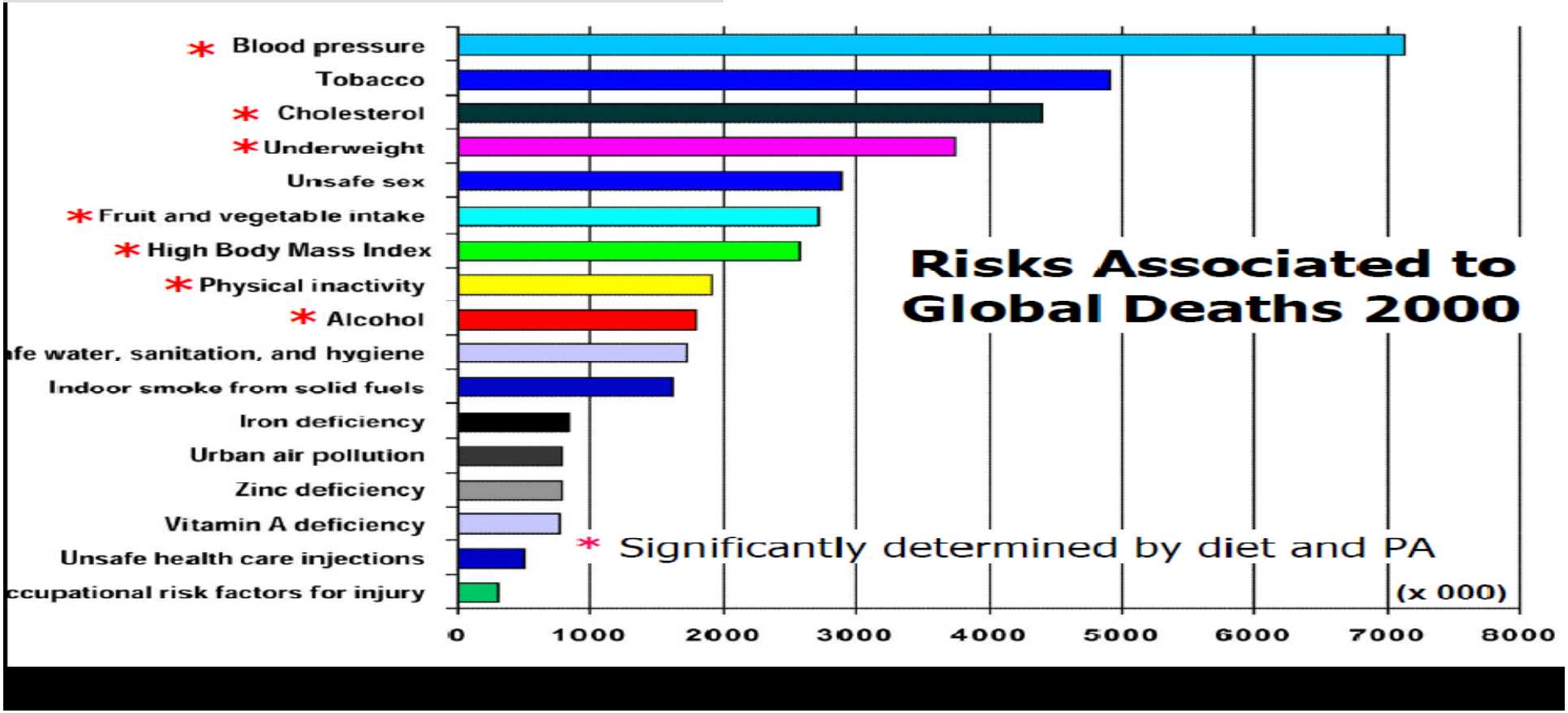
Accademia Italiana della cucina mediterranea

Improvements in Life Expectancy



Cause of Death by WHO region WHR 2002





Therapeutic Lifestyle Changes for disease prevention

Reduce	Increase
• Total fat	• PHYSICAL ACTIVITY
• Saturated Fats (C14,C16)	• Vegetables
• Trans fatty acids	• Fruits, legumes
• Refined starches	• Fibre/NSP
• Free sugars	• ω - 3 fatty acids (EPA+DHA)
• Sodium/salt	• Iron/iodine/Zinc
• Preserved meats	• Folate

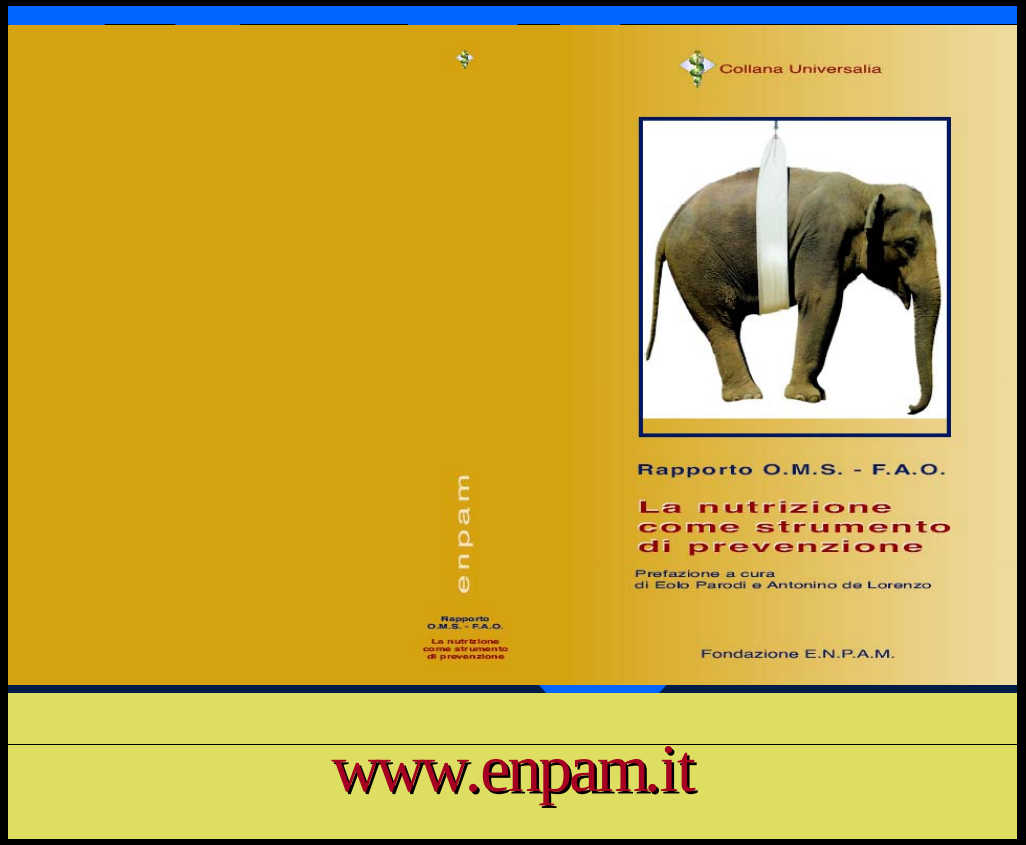
Component	*Population goals*	*Levels of evidence*
Physical activity levels (PAL)	1.75	++
BMI (kg/m^3)	21–22	++
Dietary fat as % of total energy	<30	++
Fatty acids as % of total energy		
Saturated	<10	++++
Trans	<2	++
Polyunsaturated (PUFA)		
n-6	4–8	+++
n-3	2g linoleic + 200 mg very long chain	++
Carbohydrates as % of total energy	>55	+++
Sugary food consumption occasions per day	≤4	++
Fruit and vegetables (g/d)	>400	++
Folate from food (µg/d)	>400	+++
Dietary fibre (g/d)	>25 (or 3g/MJ)	++
Sodium (expressed as sodium chloride) (g/d)	<6	+++
Iodine (µg/d)	150 (infants 50; in pregnancy 200)	+++
Exclusive breastfeeding	About 6 months	+++

Source: European Commission 2000.
Notes: Levels of evidence: (++++) multiple double blind placebo controlled trials; (+++) single study of double blind analyses (breastfeeding – series of non-double blind analyses); (++) ecological analyses compatible with non-double blind intervention and physiological studies; (+) integration of multiple levels of evidence by expert groups.



European dietary guidelines based on existing evidence on health promotion programmes for the prevention of chronic diseases in Europe (European Commission 2000).

L’impegno per la promozione di salute



APPROCCIO PAN

PREFERENZA
ACCETTAZIONE
NECESSITA’


Welcome to
DARK SIDE
©URUSHIDA

Le moderne piante alimentari sono impoverite di fitonutrienti.

La selezione agricola ha ridotto il contenuto di fitocomponreti nelle piante. Le piante edibili moderne sono infatti selezionate in funzione di fattori quali gusto e resa, e la loro gradevolezza è stata aumentata **riducendo la naturale produzione di difese naturali e sostituendole con pesticidi.**

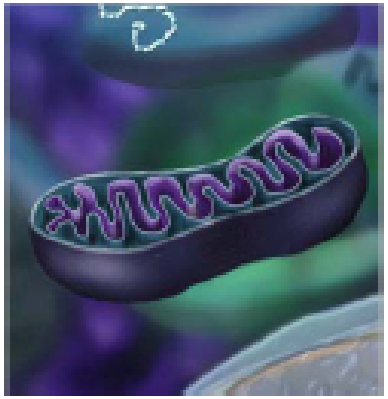






RAZIONALE…

L'ipotesi di Ames : la carenza di micronutrienti porta all'insorgenza di malattie croniche degenerative



La carenza di micronutrienti porta uno squilibrio metabolico cronico e decadimento dei mitocondri, con eccesso di ossidanti ed invecchiamento cellulare.

La selezione naturale favorisce la **sopravvivenza a breve termine** alle spese della **salute a lungo termine**, ed un meccanismo di selezione viene attivato per favorire la **produzione di DNA** alle spese della **riparazione del DNA**, eritrociti sopra leucociti, cuore sopra fegato.



Questa risposta selettiva accelera il corso di malattie croniche degenerative quali tumori, invecchiamento precoce e naturale decadimento.

Ames, B.M. *PNAS* **2006**, *103*, 17589-17594

indena

HOME AND INDUSTRIAL PROCESSING METHOD

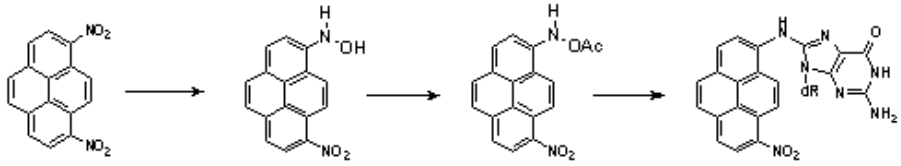


US FDA estimates of intake

Acrylamide Intake of Population (ages 2 and older)

Mean intake =0.37 µg/kg body weight/day

Exponent



SHORT COMMUNICATION

Advanced Glycation End Products and Nutrition

M. KRAJČOVIČOVÁ-KUDLÁČKOVÁ, K. ŠEBEKOVÁ, R. SCHINZEL[1], J. KLVANOVÁ

Institute of Preventive and Clinical Medicine, Bratislava, Slovak Republic and [1]Institute of Physiological Chemistry, University of Würzburg, Würzburg, Germany

Received June 27, 2001
Accepted September 26, 2001

Summary

Advanced glycation end products (AGEs) may play an important adverse role in process of atherosclerosis, diabetes, aging and chronic renal failure. Levels of N^{ε}-carboxymethyllysine and fluorescent AGE values were estimated in two nutritional population groups – alternative group (vegetarians - plant food, milk products, eggs) and traditional group (omnivorous subjects). Vegetarians have a significantly higher carboxymethyllysine content in plasma and fluorescent AGE values. Intake of proteins, lysine and monosaccharides as well as culinary treatment, consumption of food AGEs (mainly from technologically processed products) and the routes of Maillard reaction in organism are the substantial sources of plasma AGEs. Vegetarians consume less proteins and saccharides. Lysine intake is significantly reduced (low content in plant proteins). Subjects on alternative nutrition do not use high temperature for culinary treatment and consume low amount of technologically processed food. Fructation induced AGE fluorescence is greater as compared with that induced by glucose. It is due to higher participation of a more reactive acyclic form of fructose. Intake of vegetables and fruit with predominance of fructose is significantly higher in vegetarians. Comparison of nutrition and plasma AGEs in vegetarian and omnivorous groups shows that the higher intake of fructose in alternative nutrition of healthy subjects may cause an increase of AGE levels.

IL SALVAGENTE
Diffusione: n.d. Lettori: n.d. da pag. 18

IN MEZZO SECOLO GLI ALIMENTI AVREBBERO PERSO BUONA PARTE DI MINERALI, VIT AMINE E PROTEINE

Più grassi e rachitici. Nel piatto le contraddizioni dei cibi moderni

È UNA DELLE TESI DI "CIBI KILLER" IL NUOVO LIBRO DI WILLIAM REYMOND, GIÀ AUTORE DI "TOXIC". LA COLPA? DI AGRICOLTURA E ALLEVAMENTI INTENSIVI. E DELL'USO MASSICCIO DI PESTICIDI E FERTILIZZANTI.

• Barbara Cataldi

Negli ospedali pediatrici della più ricca città del più ricco Stato del più ricco paese del mondo può capitare di incontrare bambini **in sovrappeso** che soffrono di **rachitismo**, una malattia legata alla malnutrizione e debellata da tempo nelle società occidentali. Morbo del passato che torna a manifestarsi con la deformazione della struttura ossea. L'anomalia, registrata negli ultimi anni presso il Children's Hospital di Oakland, **in California**, è stata a lungo studiata dalla direttrice del reparto di endocrinologia, Suruchi Batia, e ha condotto la specialista a una conclusione stupefacente: i piccoli pazienti sono cresciuti mangiando cibo pieno di calorie, ma **poverissimo** di nutrienti.

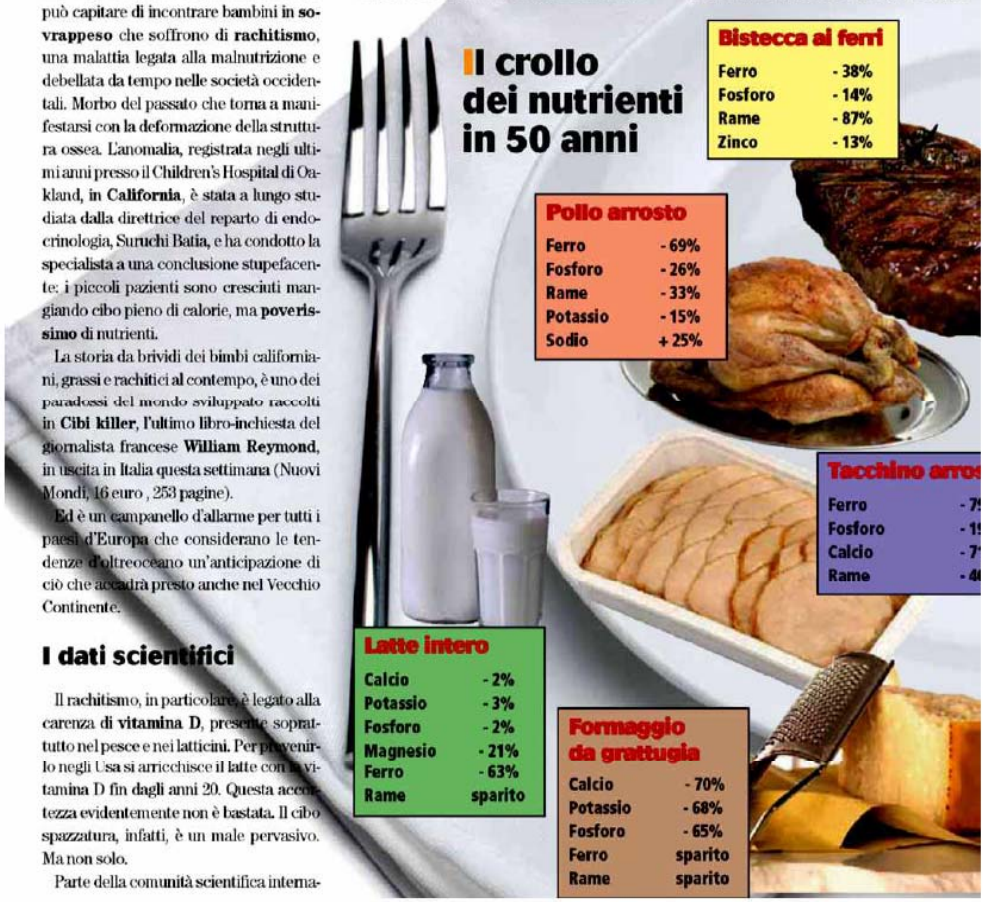
La storia da brividi dei bimbi californiani, grassi e rachitici al contempo, è uno dei paradossi del mondo sviluppato raccolti in **Cibi killer**, l'ultimo libro-inchiesta del giornalista francese **William Reymond**, in uscita in Italia questa settimana (Nuovi Mondi, 16 euro , 253 pagine).

Ed è un campanello d'allarme per tutti i paesi d'Europa che considerano le tendenze d'oltreoceano un'anticipazione di ciò che accadrà presto anche nel Vecchio Continente.

I dati scientifici

Il rachitismo, in particolare, è legato alla carenza di **vitamina D**, presente soprattutto nel pesce e nei latticini. Per prevenirlo negli Usa si arricchisce il latte con la vitamina D fin dagli anni 20. Questa accortezza evidentemente non è bastata. Il cibo spazzatura, infatti, è un male pervasivo. Ma non solo.

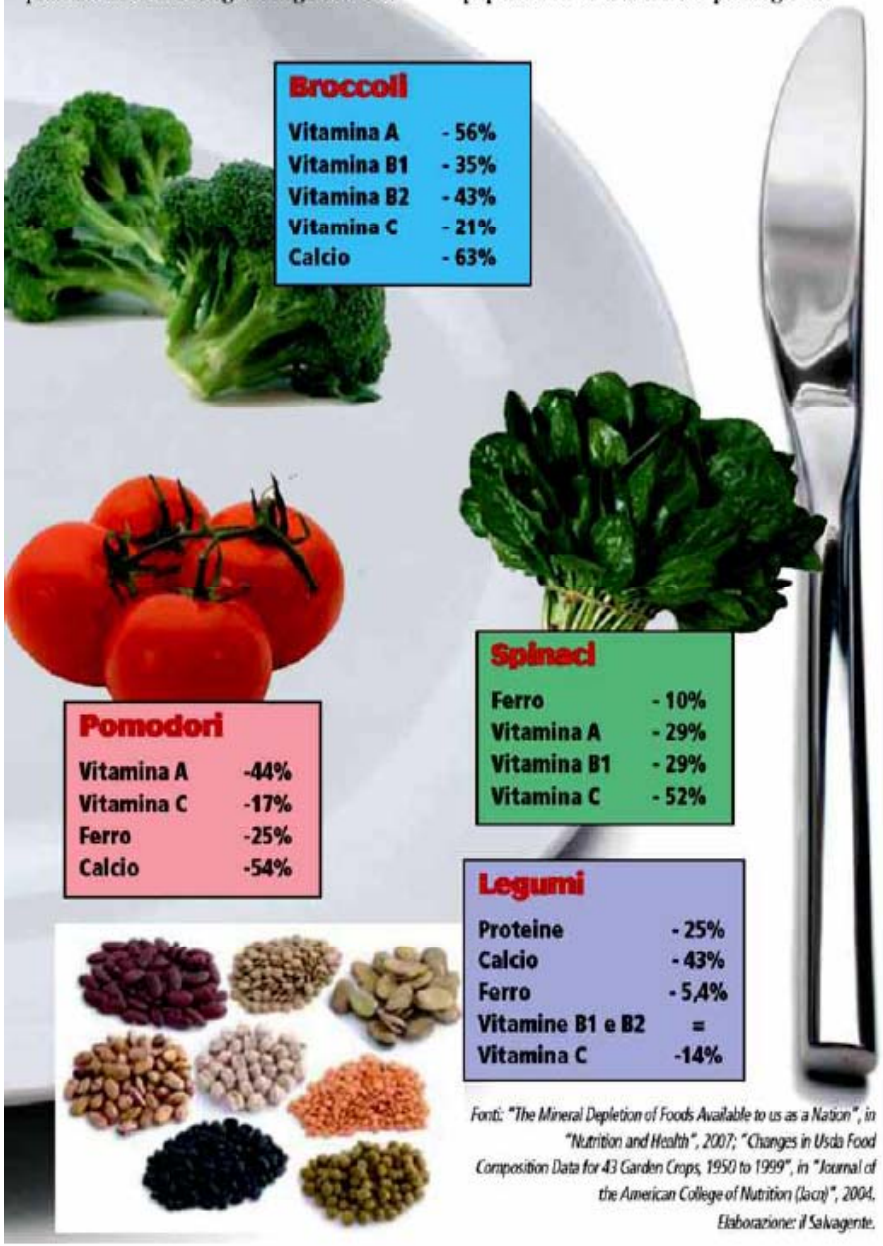
Parte della comunità scientifica internazionale è convinta che gli alimenti che mangiamo, con il passare del tempo, hanno **perso** molti dei **nutrienti** che contenevano. E questo non solo perché la trasformazione industriale li impoverisce dal punto di vista nutritivo caricandoli di calorie, con l'aggiunta di grassi, zuccheri e sale, per renderli più appetibili. Ma anche perché l'**agricoltura massiva**, l'abuso di **pesticidi** e **fertilizzanti** chimici, gli **allevamenti intensivi** e la selezione praticata dall'uomo per aumentare la resa delle coltivazioni hanno impoverito il suolo e modificato le stesse materie prime. Per assumere gli stessi nutrienti di 50-60 anni fa, insomma, bisognerebbe mangiare di più



una ricerca sul tema pubblicata circa 15 anni fa sul "British Food Journal".

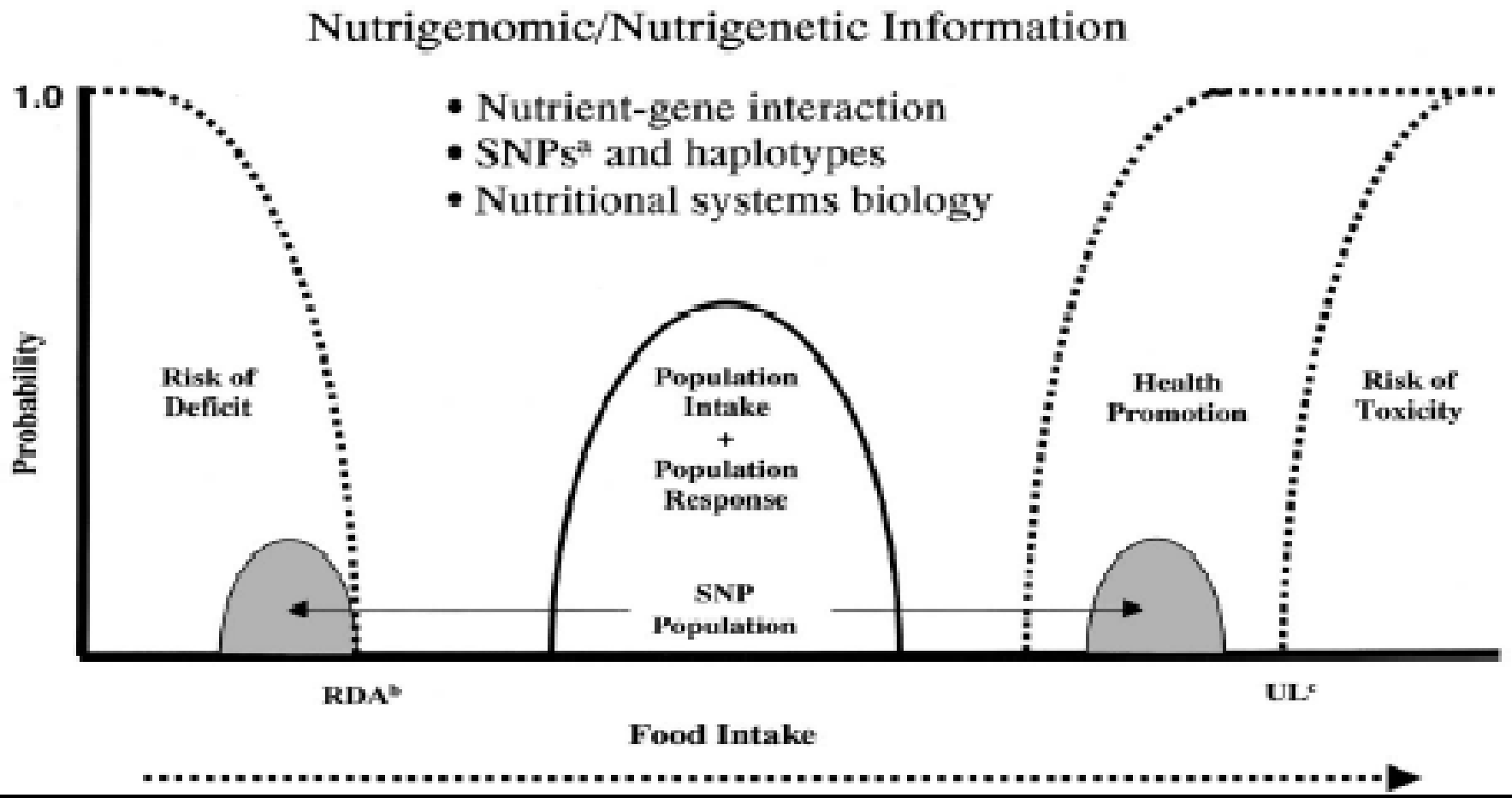
Da allora gli studi si sono moltiplicati, soprattutto in Gran Bretagna e negli Usa. Uno

Secondo Thomas la radicale diminuzione dei micronutrienti dagli alimenti essenziali ha un legame con l'insorgenza nella popolazione di una serie di patologie fisi-

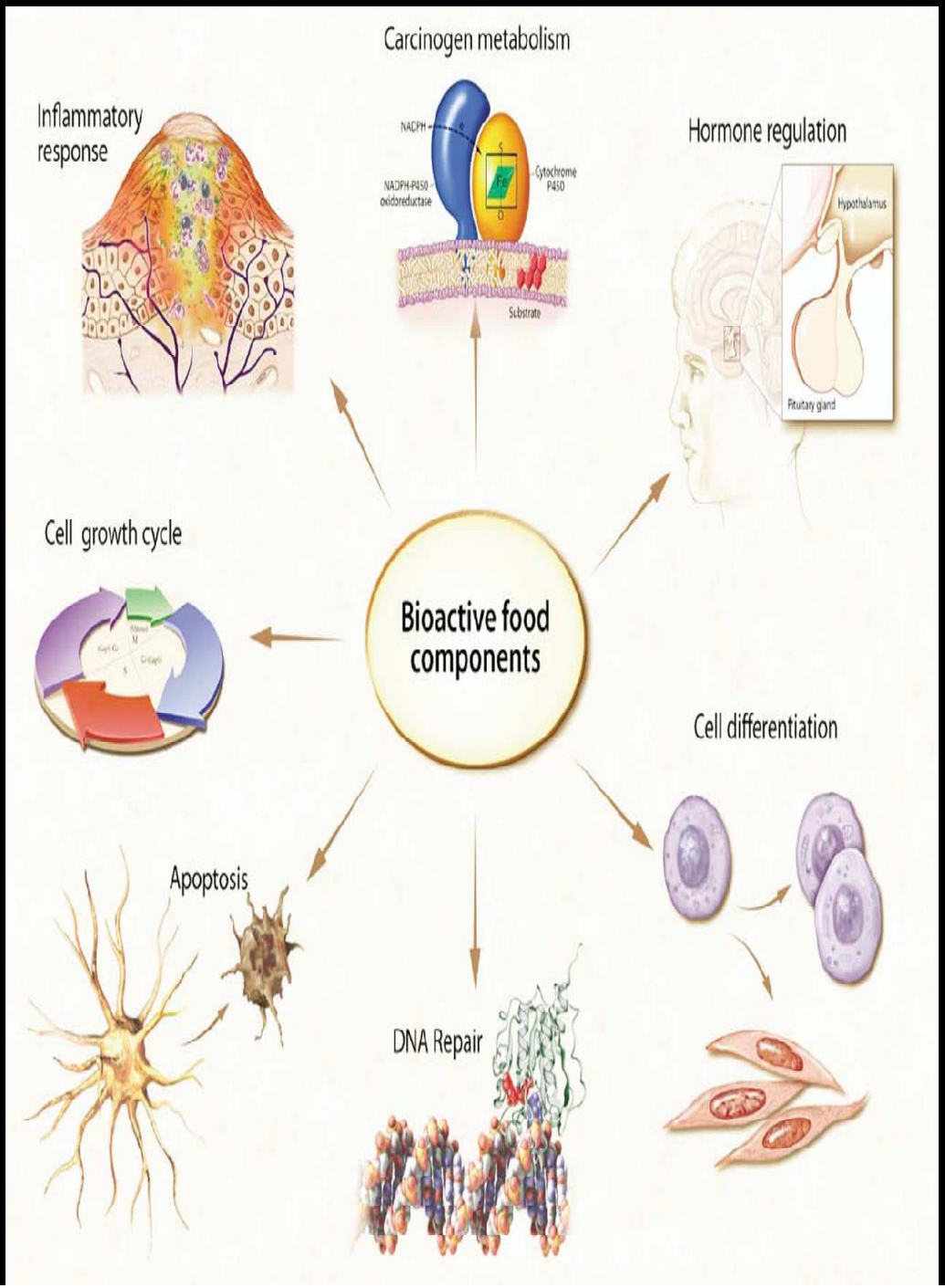


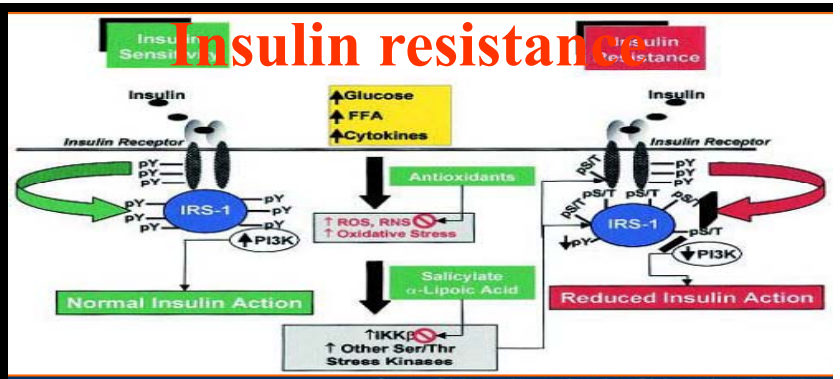
Fonti: "The Mineral Depletion of Foods Available to us as a Nation", in "Nutrition and Health", 2007; "Changes in Usda Food Composition Data for 43 Garden Crops, 1950 to 1999", in "Journal of the American College of Nutrition (Jacn)", 2004. Elaborazione: il Salvagente.

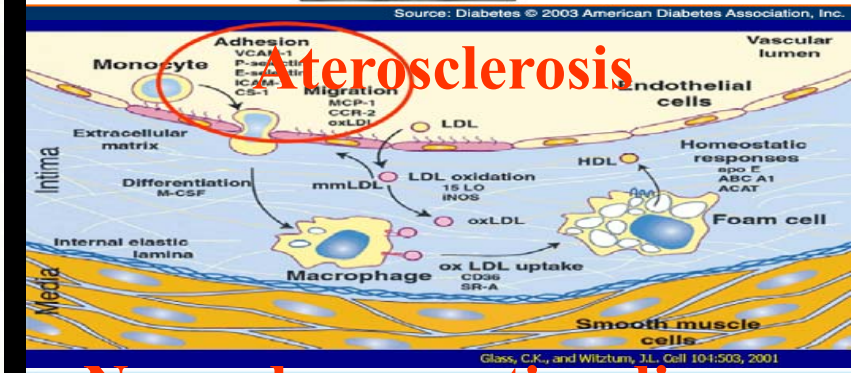
Nutrigenetics and Nutrigenomics

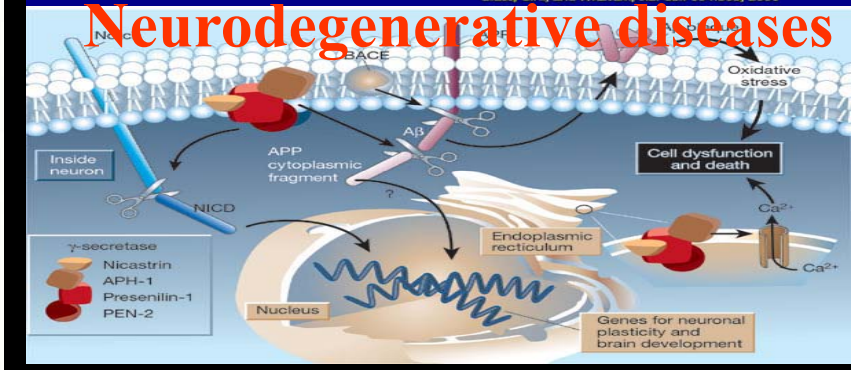


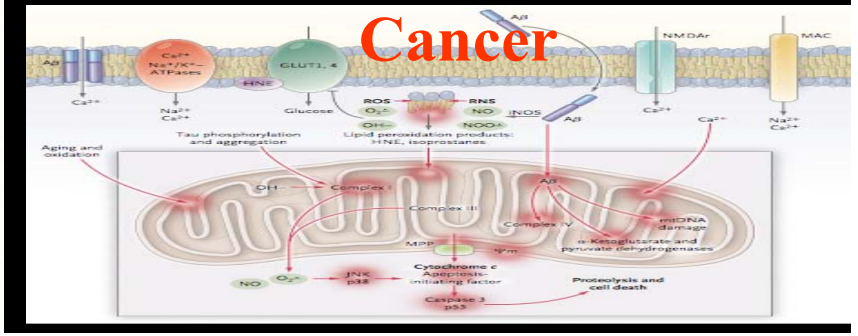
RDA=recommended dietary allowance; UL=Upper limits


Carcinogen metabolism
Inflammatory response
Hormone regulation
Cell growth cycle
Bioactive food components
Cell differentiation
Apoptosis
DNA Repair
NADPH
NADPH-P450 oxidoreductase
Cytochrome P450
Substrate
Hypothalamus
Pituitary gland


Insulin resistance
Insulin
Insulin Receptor
IRS-1
PI3K
Glucose
FFA
Cytokines
Antioxidants
↑ ROS, RNS
↑ Oxidative Stress
Salicylate
α-Lipoic Acid
↑IKKβ
↑ Other Ser/Thr Stress Kinases
Normal Insulin Action
Reduced Insulin Action


Source: Diabetes © 2003 American Diabetes Association, Inc.
Atherosclerosis
Monocyte
Adhesion
Migration
MCP-1
CCR-2
oxLDL
Vascular lumen
Endothelial cells
Extracellular matrix
LDL
Intima
Differentiation
M-CSF
mmLDL
LDL oxidation
15 LO
iNOS
HDL
Homeostatic responses
apo E
ABC A1
ACAT
oxLDL
Foam cell
Internal elastic lamina
Macrophage
ox LDL uptake
CD36
SR-A
Media
Smooth muscle cells
Glass, C.K., and Witztum, J.L. Cell 104:503, 2001


Neurodegenerative diseases
BACE
Oxidative stress
Aβ
Inside neuron
APP cytoplasmic fragment
Cell dysfunction and death
NICD
γ-secretase
Nicastrin
APH-1
Presenilin-1
PEN-2
Endoplasmic recticulum
Ca2+
Nucleus
Genes for neuronal plasticity and brain development


Cancer
Aβ
NMDAr
MAC
GLUT1, 4
HNE
Glucose
ROS
RNS
NO
iNOS
Tau phosphorylation and aggregation
Lipid peroxidation products: HNE, isoprostanes
Aging and oxidation
Complex I
Complex III
Complex IV
MPP
mtDNA damage
α-Ketoglutarate and pyruvate dehydrogenases
Cytochrome c
Apoptosis-initiating factor
JNK
p38
Caspase 3
p53
Proteolysis and cell death

NEWS

Criteri di una dieta salutare

È auspicabile un cambiamento nel modo di pensare per sviluppare strategie attive che pongano la nutrizione, in particolare mediterranea e biologica, in prima linea nelle politiche e nei programmi di sanità pubblica.

É provato dall'evidenza scientifica e si sta radicando nella percezione dei consumatori che un'alimentazione sana è necessaria per mantenere e raggiungere lo stato di salute. Come deve essere quali/quantitativamente questo tipo di alimentazione?

C'è una prova scientifica per definire i criteri di qualità e sicurezza di un'alimentazione ideale? L'idonea combinazione degli alimenti secondo l'Indice di Adeguatezza Mediterranea (IAM: rapporto tra % energia totale da pane, cereali, legumi, patate, vegetali, frutta, pesce, vino rossa, olio d'oliva/latte, formaggio, carne, uova, grassi animali, bevande dolci, dolci e zuccheri), gli Indici di Qualità Nutrizionale (colesterolo saturo, indice glicemico, rapporto tra protidi vegetali/animali, grassi mono-polinsaturi, saturi) e la misura della capacità antiossidante, permette di prevenire le inadeguatezze nutrizionali per eccesso o difetto.

Fondamentale è il consumo di prodotti freschi, del territorio, tradizionali e biologici, in accordo con il regime alimentare della Dieta Mediterranea italiana di riferimento (DM): la dieta di Nicotera, il cui ruolo preventivo sulle malattie cronico degenerative evidenziato nel '57 dallo Studio Cooperativo Internazionale di Epidemiologia della Cardiopatia Coronarica, è stato confermato dagli



LAURA DI RENZO
Ricercatore e docente Università degli studi di Roma Tor Vergata.

studi del Prof. A. Fidanza e dal Prof. A. De Lorenzo. Se nel '57 lo IAM a Nicotera raggiungeva il valore di 9 oggi arriva a 2.1 e se l'alimentazione non è mediterranea scende al di sotto di 2.

Un particolare interesse riveste la presenza nella dieta degli antiossidanti e la valutazione nell'uomo dei loro effetti. La capacità antiossidante spiega gran parte dell'azione protettiva della dieta per meccanismo anti-radicali liberi.

I risultati delle nostre ricerche condotte all'Università Tor Vergata per il Progetto "Sostenibilità dell'agricoltura biologica" del MIPAAF dimostra che la DM biologica, induce un cambiamento della composizione corporea ed un aumento della capacità totale antiossidante plasmatica e della quantità di acido folico e vitamina B12, contro gli effetti dei radicali liberi e dei processi infiammatori.

In definitiva la dieta mediterranea biologica garantisce un'efficace azione per la prevenzione di patologie cronico-degenerative, fondamentale per la longevità e qualità della vita.

PILLOLE



La nuova rivoluzione copernicana: la nutrizione molecolare

- Il Progetto Genoma Umano ha condotto la nutrizione umana in una nuova era di ricerca ed applicazione clinica: la genomica nutrizionale (nutrigenetica e nutrigenomica)
- In base al profilo genetico e fenotipico di ciascuno, è oggi possibile predisporre un piano dietetico mediterraneo personalizzato che soddisfa le preferenze sensoriali, le necessità nutrizionali e fisiologiche, e le scelte del consumatore, secondo il nuovo approccio PAN (Preferenza Approvazione Necessità).

Sole 24 ore giugno 2010

…una dieta "che si rispetti"…
…come quella mediterranea….
…deve avere queste proprietà:

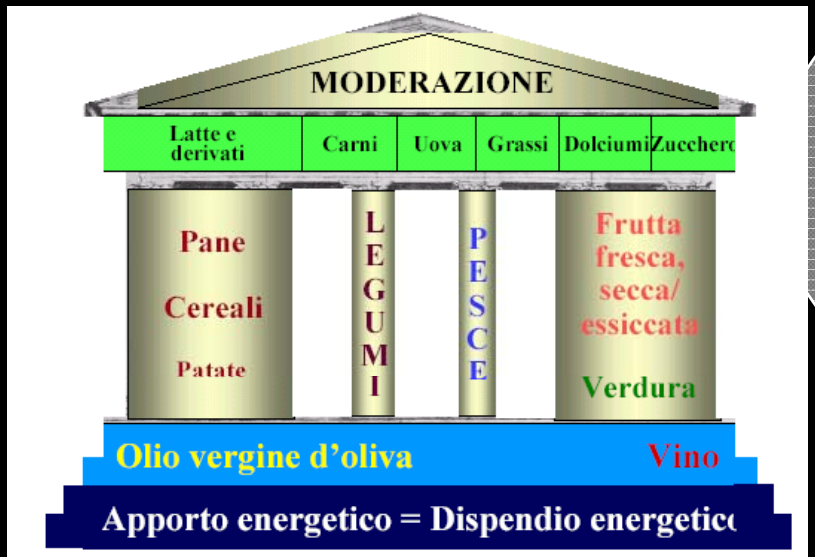
EQUILIBRATA

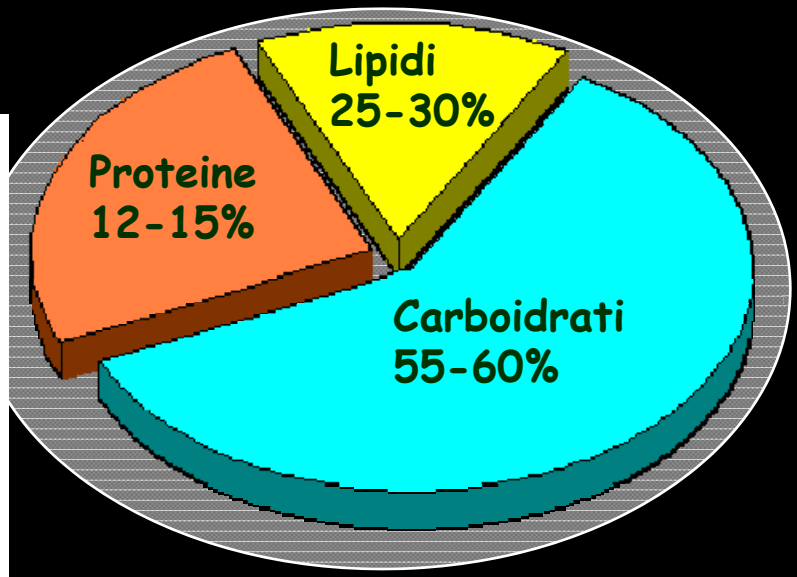
BILANCIATA

ADEGUATA

OTTIMALE

Il fabbisogno energetico giornaliero deve corrispondere a:





Indice di Adeguatezza Mediterraneo (IAM):

$$IAM = \frac{\%\ \text{energia da CARBOIDRATI (gr. 1)+PROTETTIVI (gr. 2)}}{\%\ \text{energia da DERIVATI ANIMALI (gr. 3)+DOLCI (gr. 4)}}$$

Carboidrati (gruppo1): ***pane, cereali, legumi, patate***

Protettivi (gruppo 2): ***vegetali, frutta, pesce, vino rosso, olio d'oliva***

(Gruppi di alimenti appartenenti alla dieta mediterranea)

Derivati animali (gruppo 3): ***latte, formaggio, carne, uova, grassi animali e margarina***

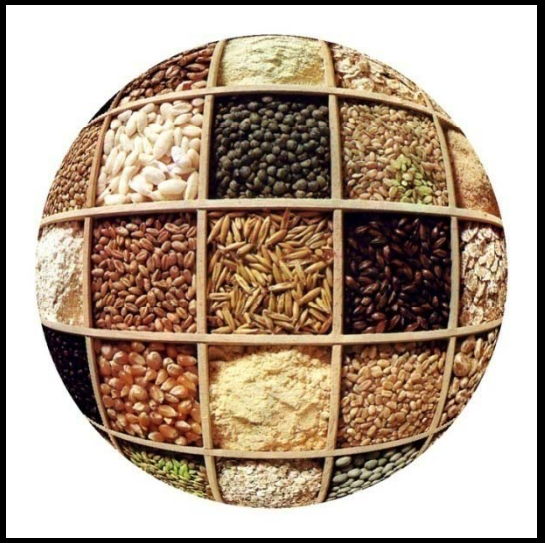
Dolci (gruppo 4): ***bevande dolci, biscotti/torte, zucchero***

(Gruppi di alimenti non appartenenti alla dieta mediterranea)

Alberti et all. Eur J Clin Nutr 1999

Healthy Eating Index

- Aterogenicity Index (AI)
- Cholesterol satured fat index (CSI)
- Trombogenecity Index (TI)
- Mediterranean Adeguacy Index (MAI)



- **Macronutrient percentage** (%Fats; % Carbohydrates , %proteins, %fiber)

Glicemic Index

- **Micronutrient** (%vitams, %minerals)

Use of quality control indexes in Moderately Mediterranean Diets for treatment of obesity

Nicotera DIET

1500 kcal MHD

Meat (130 g), or fish (170 g) or cheese (70 g) portion.

Weekly frequency:
animal foods was 4 times for fish, 2 for meat and 2 for cheese.

Daily intake of carbohydrates derived mainly from pasta (80 g), bread (100 g) and fresh legumes (60 g, 3 times/week).
Daily intake for fruit was 500 ± 50g and for vegetables 250 ± 50g.

Extravirgin olive oil was taken daily in a amount of 20 ± 5g.
Fibers intake (27-30 g/day) and of the main micronutrients covered the Italian Recommended Daily Allowances

A. De Lorenzo et al, Diab Nutr Met 2001; Diabetes Care 2001 and Chest 2001

Use of quality control indexes in Moderately hypocaloric Mediterranean Diets for treatment of obesity

Table 1: Antropometric and body composition parameters before and after MHD.

	bseline	2-mounths MHD	statistial significance
Weight, Kg	84.70 ± 9.56	78.1 ± 10.53	p<0.0001
BMI , Kg/m2	33.05 ± 2.61	31.18 ± 2.74	p<0.0001
Waist, mm	104.19 ± 7.6	99.85 ± 9.4	p<0.0001
Hip, mm	116.63 ± 7.95	110.50 ± 7.01	p<0.0001
WHR	0.92 ± 0.08	0.88 ± 0.07	p<0.001
FMTOT, Kg	39.619 ± 6360	37.010 ± 12899	p<0.0001
FMLEG, Kg	10.472 ± 3519	9.081± 3439	p<0.0001
FMTRN, Kg	18.214 ± 2955	17.540 ± 6505	p<0.0001
LBMTOT, Kg	40.847± 5061	40.155 ± 4837	NS
LBMLEG, Kg	17.149 ± 5175	16.653 ± 5135	NS
LBMTRN, Kg	20.253 ± 2309	19.213 ± 2257	NS
BMD, g/cm2	1.2364 ± 0.122	1.2431 ± 0.123	NS
BMC, Kg	2.362 ± 331	2.340 ± 335	NS
FATABD, Kg	3.927± 643	2.447 ± 615	p<0.0001
LEANABD, Kg	3.945 ± 605	3.858 ± 596	NS
RMR kcal	1531 ±152	1497 ±123	NS

Values are expressed as mean ± SD
Statistical analysis was performed using un-paired *student's t-test.*

A. De Lorenzo et all; Diab Nutr Met 14(3); 121-5; 20

Table 2: Plasma chemistry and metabolic parameters before and after MHD

	bseline	2-mounths MHD	statistial significance
Albumin (g/100 ml)	4.15 ± 0.14	4.02 ± 0.39	NS
Fasting glucose (mmol/L)	5.05± 0.45	4.98 ± 0.43	NS
Fasting insulin (mU/ml)	11.48 ± 6.77	8.07 ± 4.17	p<0.01
AUC glucose	29.50± 6.24	28.07 ± 5.29	NS
AUC insulin	263.2 ± 118.7	208.7 ± 82.6	p<0.005
Fibrinogen (mg/100 ml)	359 ± 78	324± 87	p<0.0001
Total cholesterol	5.40 ± 1.04	4.97 ± 0.92	p<0.05
HDL cholesterol (mmol/L)	1.30 ± 0.30	1.33 ± 0.33	NS
LDL cholesterol (mmol/L)	3.36 ± 1.07	2.90 ± 0.74	p<0.005
Triglycerides (mmol/L)	1.70 ± 1.00	1.46 ± 0.66	NS
Uric acid (mmol/L)	0.30 ± 0.06	0.28 ± 0.05	p<0.01

Values are expressed as mean ± SD
Statistical analysis was performed using un-paired *student's t-test.*

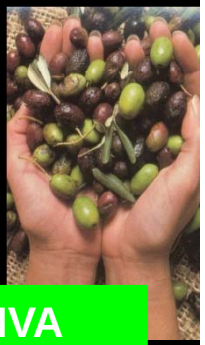
A. De Lorenzo et all; Diab Nutr Met 2001



AJCN. First published ahead of print September 1, 2010 as doi: 10.3945/ajcn.2010.29673.

Accruing evidence about benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis[1,2]

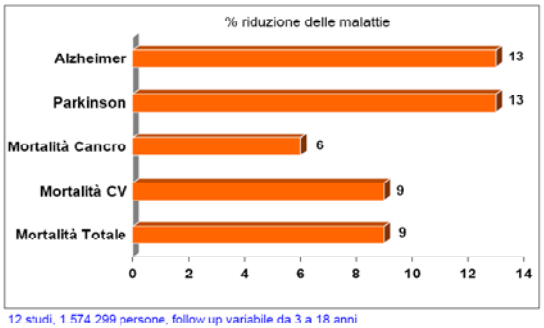
Francesco Sofi, Rosanna Abbate, Gian Franco Gensini, and Alessandro Casini



VINO
polifenoli e resveratrolo

OLIO D'OLIVA
acidi grassi monoinsaturi

L'ADERENZA ALLA DIETA MEDITERRANEA SI ASSOCIA AD UN SIGNIFICATIVO MIGLIORAMENTO DELLA SALUTE



Neutralizzazione
di radicali liberi

Prevenzione
della formazione di radicali liberi





FRUTTA, VERDURA, LEGUMI
Vitamine antiossidanti, fibra, licopene, flavonoidi

PANE INTEGRALE E PASTA:
minore iperglicemia post-prandiale, con minore ossidazione di zuccheri e iperinsulinemia

Mediterranean food pattern and the primary prevention of chronic disease: recent developments

Miguel Angel Martinez-Gonzalez, Maira Bes-Rastrollo, Lluis Serra-Majem, Denis Lairon, Ramón Estruch, and Antonia Trichopoulou

Recent evidence supports the cardioprotective role of a Mediterranean food pattern. The major findings of the Greek and EPIC-Elderly cohort, the SUN study, the Medi-RIVAGE and the PREDIMED trials are reviewed. Definitive answers will come from ongoing primary prevention trials that assess clinical events as outcomes.

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Table 1 **Adjusted hazard ratios (HRs) for total mortality associated with a two-point increment in the Mediterranean-diet score in the EPIC study.**

Study population	No. of deaths/no. of participants	HR* (95% CI)
Greek EPIC	275/22,043	0.75 (0.65–0.87)
European EPIC-elderly (≥60 years)	4,047/74,607	0.92 (0.88–0.97)

* Greek EPIC data adjusted for age, gender, waist-to-hip ratio, energy-expenditure score, years of education, smoking status, body mass index, consumption of potatoes, consumption of eggs, and total energy intake. European EPIC-Elderly data adjusted for age, gender, diabetes mellitus at baseline, waist-to-hip ratio, body mass index, educational achievement, smoking status, physical activity at work, physical activity at leisure, consumption of potatoes, consumption of eggs, consumption of sugar and confectionery, and total energy intake.

Table 3 **Mean relative changes in cardiovascular disease (CVD) risk factors in the Medi-RIVAGE study by treatment group at 3 months of follow-up.**

CVD risk factor	Mediterranean group ($n = 88$)	Low-fat group ($n = 81$)	*P* value
Body mass index	−5.2%	−4.2%	<0.05
Total cholesterol	−7.4%	−4.4%	<0.05
LDL cholesterol	−9.9%	−5.4%	<0.05
HDL cholesterol	+1.5%	+0.03%	ns
Triglycerides	−13.0%	−7.9%	<0.05
Glucose	−3.0%	−3.5%	<0.05
Insulin	−21.3%	−17.5%	<0.05

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; ns, nonsignificant differences ($P > 0.05$).

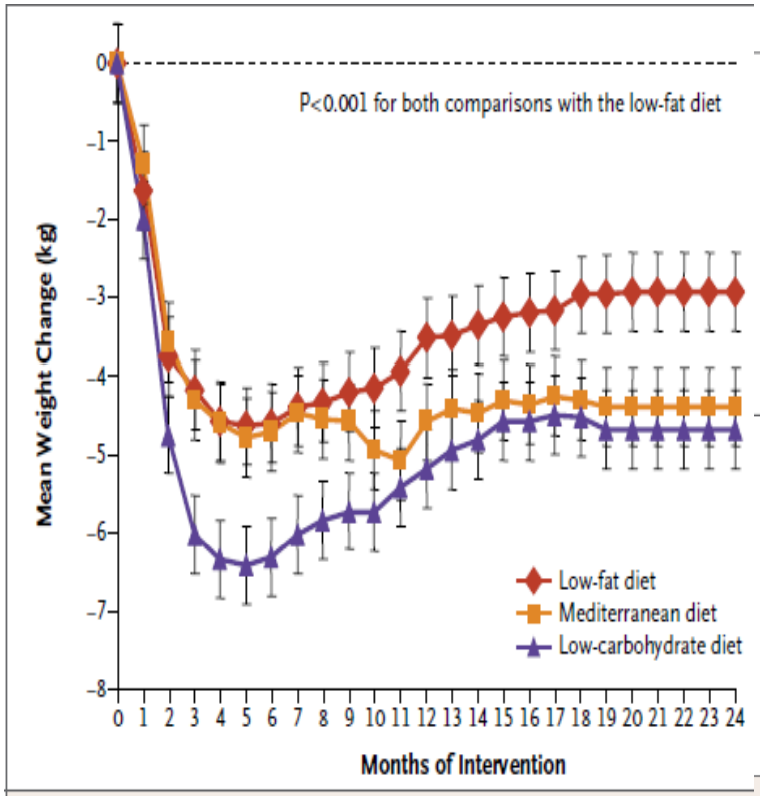


Figure 2. Weight Changes during 2 Years According to Diet Group.

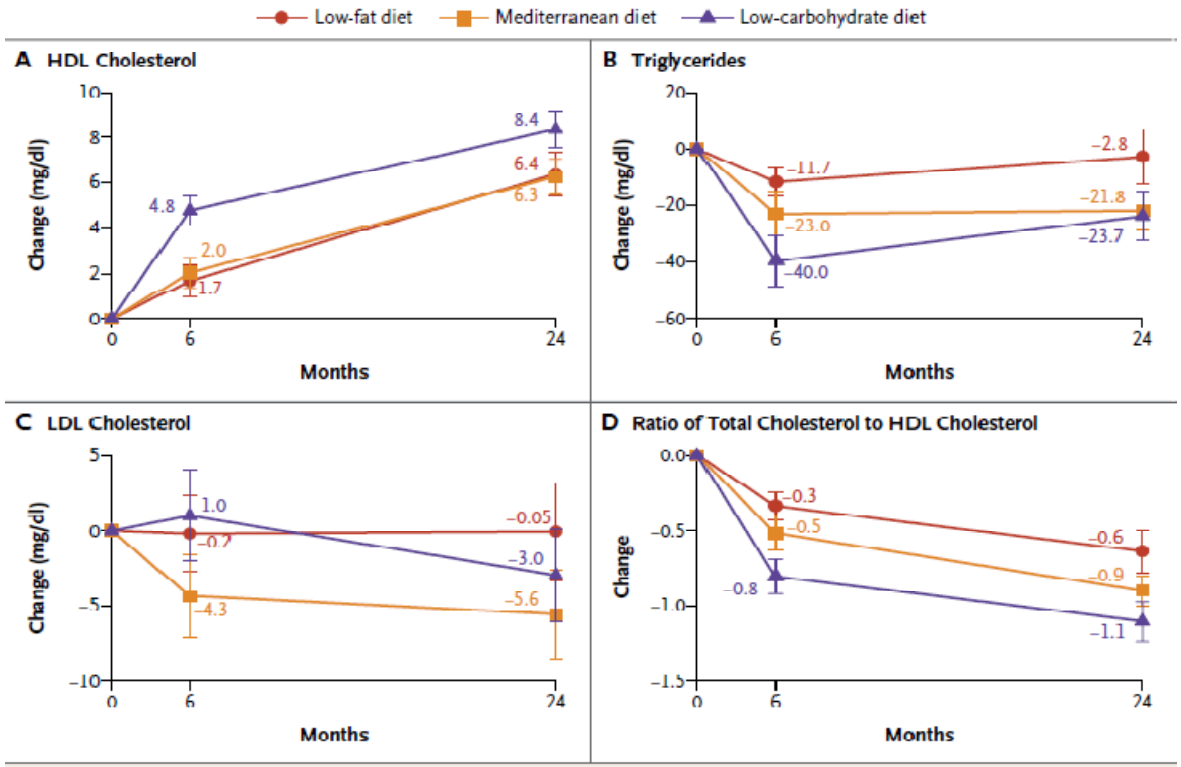


Figure 3. Changes in Cholesterol and Triglyceride Biomarkers According to Diet Group during the Maximum Weight-Loss Phase (1 to 6 Months) and the Weight-Loss Maintenance Phase (7 to 24 Months) of the 2-Year Intervention.

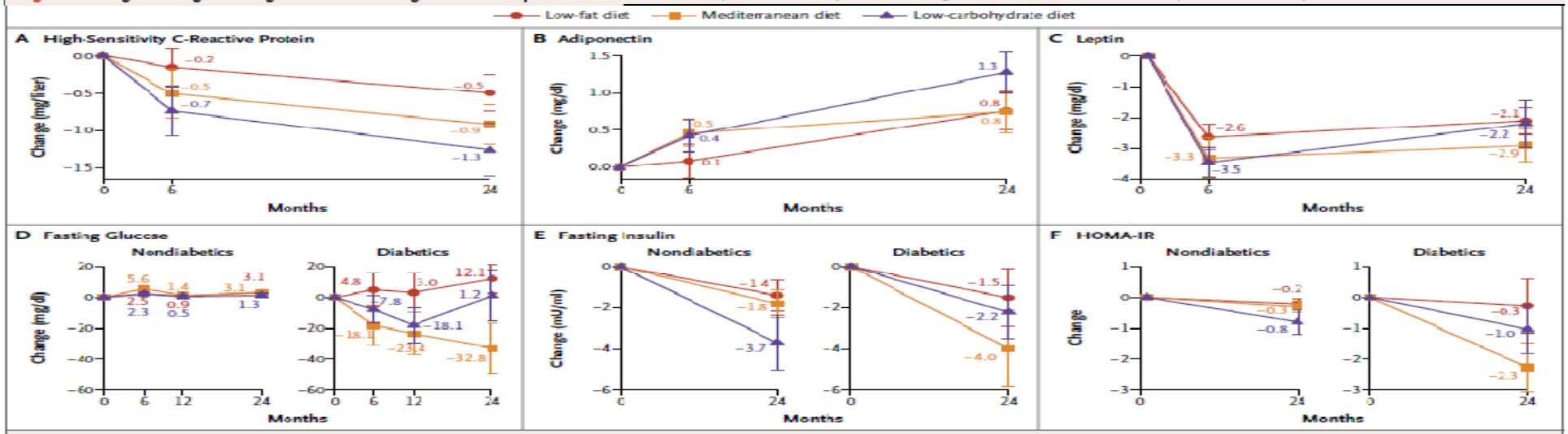


Figure 4. Changes in Biomarkers According to Diet Group and Presence or Absence of Type 2 Diabetes.

Iris Shai,et al. Weight Loss with a Low-Carbohydrate, Mediterranean, or Low-Fat Diet. N Engl J Med 2008;359:229-

Effect of a Mediterranean-Style Diet on Endothelial Dysfunction and Markers of Vascular Inflammation in the Metabolic Syndrome

A Randomized Trial

Katherine Esposito, MD
Raffaele Marfella, MD, PhD
Miryam Ciotola, MD
Carmen Di Palo, MD
Francesco Giugliano, MD
Giovanni Giugliano, MD
Massimo D'Armiento, MD
Francesco D'Andrea, MD
Dario Giugliano, MD, PhD

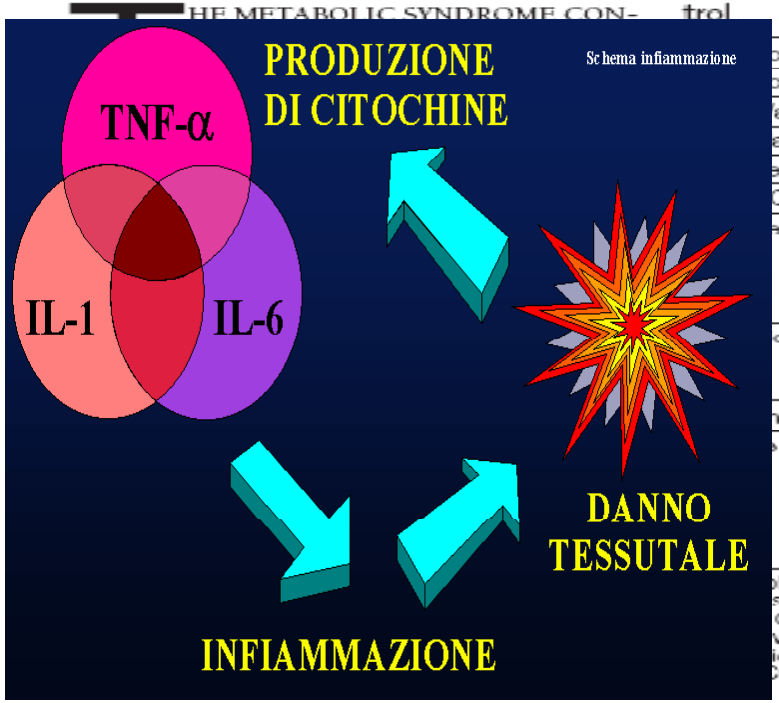
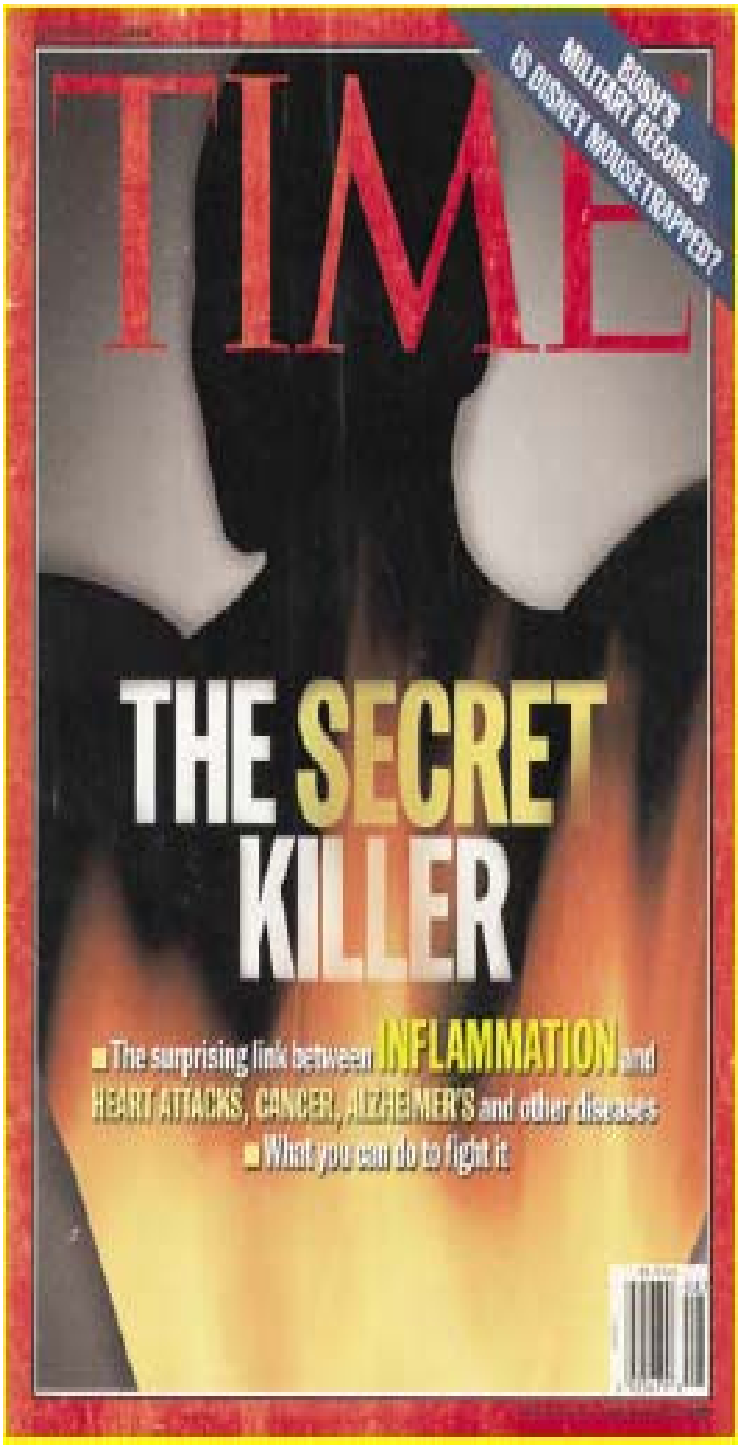


Table 1. Characteristics of the Study Participants

Characteristics	Mean (SD) Intervention Diet (n = 90)	Mean (SD) Control Diet (n = 90)	*P* Value
Sex, No. (%) Men	49 (54)	50 (56)	.70
Age, y	44.3 (6.4)	43.5 (5.9)	.56
No. of components of the metabolic syndrome, No. (%)			
3	74 (82)	76 (84)	.34
4	18 (20)	16 (18)	
5	8 (9)	8 (9)	
ody weight, kg	78 (8)	77 (8)	.36
ody mass index*	27.9 (3.4)	28.1 (3.2)	.55
aist circumference, cm	92 (9)	93 (10)	.62
asma glucose, mg/dL	113 (10)	114 (10)	.43
erum insulin, µU/mL	15 (6)	16 (7)	.15
OMA score	3.7 (0.7)	3.8 (0.7)	.18
erum lipids, mg/dl			
Total cholesterol	199 (34)	193 (32)	.18
HDL-C	41 (9)	42 (9)	.35
Triglycerides	168 (57)	172 (54)	.24
ood pressure, mm Hg			
Systolic	134 (9)	136 (10)	.11
Diastolic	85 (6)	86 (7)	.21
ndothelial function score	6.0 (1.2)	5.9 (1.1)	.13
CRP and cytokines, median (IQR)			
hs-CRP, mg/L	2.8 (0.7-5.4)	2.9 (0.5-5.7)	.25
IL-6, pg/mL	2.1 (0.5-4.8)	1.9 (0.5-4.7)	.14
IL-7, pg/mL	2.4 (0.6-5.9)	2.6 (0.7-6.0)	.12
IL-18, pg/mL	167 (102-232)	175 (104-236)	.10

bbreviations: HDL-C, high-density lipoprotein cholesterol; HOMA, homeostatic model assessment; hs-CRP, high-sensitivity C-reactive protein; IL, interleukin; IQR, interquartile range.
conversion factors: To convert glucose to mmol/L, multiply values by 0.0555; to convert insulin to pmol/L, multiply values by 7.715; to convert total cholesterol and HDL-C to mmol/L, multiply values by 0.0259; to convert triglycerides to mmol/L, multiply values by 0.0113.
Calculated as weight in kilograms divided by the square of height in meters.



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Journal of Nutritional Biochemistry 19 (2008) 491–504
Journal of Nutritional Biochemistry

REVIEWS: CURRENT TOPICS

Oxidative stress-induced risk factors associated with the metabolic syndrome: a unifying hypothesis☆

Ignazio Grattagliano*, Vincenzo O. Palmieri, Piero Portincasa, Antonio Moschetta, Giuseppe Palasciano

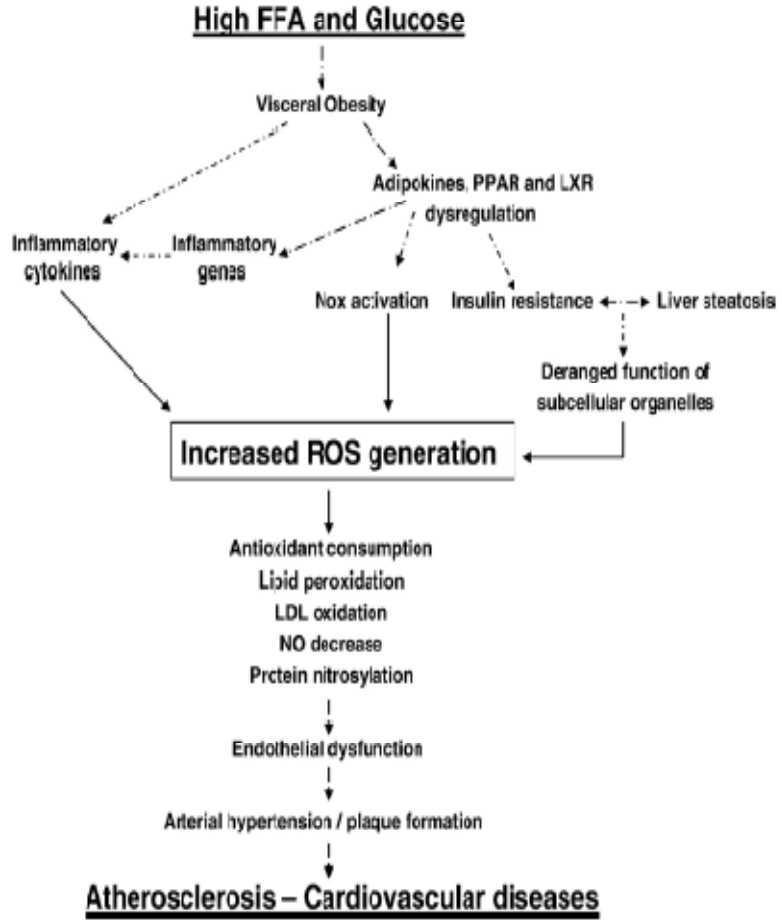


Fig. 4. Conceptual view of increased ROS generation and consequent oxidative stress as a "second-level" event causing metabolic syndrome-associated cardiovascular risk factor manifestation. LXR=liver X receptor.

Public Health Nutrition: 9(8A), 1136–1140 DOI: 10.1017/S1368980007668530

Importance of functional foods in the Mediterranean diet

RM Ortega*
Departamento de Nutrición, Facultad de Farmacia, Universidad Complutense, 28040-Madrid (Spain)

Submitted 18 April 2006: Accepted 26 November 2006





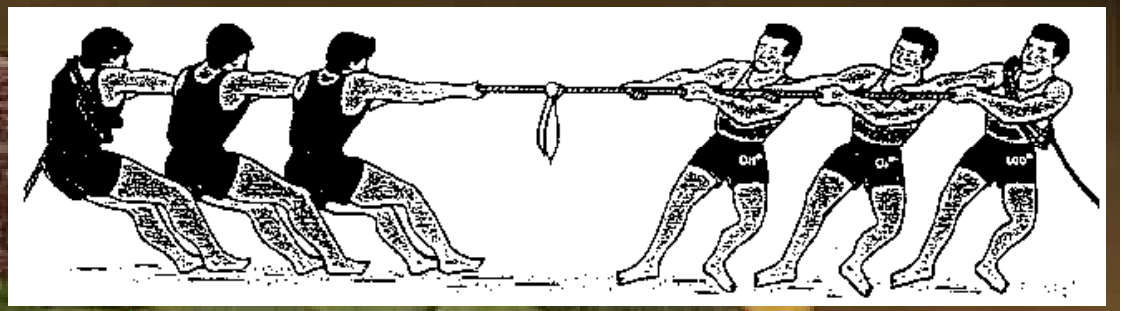




(Foto Bonavia)







Protezione dalle malattie ← **Antiossidanti** | **Radicali liberi** → **Danno cellulare (invecchiamento e malattie)**

Adherence to the Mediterranean diet is associated with total antioxidant capacity in healthy adults: the ATTICA study[1–3]

Christos Pitsavos, Demosthenes B Panagiotakos, Natalia Tzima, Christina Chrysohoou, Manolis Economou, Antonis Zampelas, and Christodoulos Stefanadis

TABLE 2
Frequency consumption of several food groups, according to Mediterranean diet score[1]

	Tertile of diet score						
	Men (n = 1514)			Women (n = 1528)			
Food groups	1st (0–20) (n = 504)	2nd (21–35) (n = 505)	3rd (36–55) (n = 505)	1st (0–20) (n = 509)	2nd (21–35) (n = 509)	3rd (36–55) (n = 510)	P^2
Red meat and red meat products (servings/wk)	3.0 ± 1.1[3]	1.6 ± 1.9[4]	1.1 ± 1.8[4]	2.5 ± 1.1	1.7 ± 1.2[4]	0.9 ± 1.1[4]	0.02
Poultry (servings/wk)	1.7 ± 1.1	1.4 ± 0.6	0.8 ± 0.9	1.3 ± 0.5	1.3 ± 0.7	1.0 ± 0.4	0.44
Sweets (servings/wk)	1.0 ± 1.4	1.1 ± 1.3	1.2 ± 1.2	1.1 ± 1.9	1.2 ± 1.6	1.3 ± 1.9	0.33
Fish (servings/wk)	1.0 ± 1.1	1.3 ± 2.1	1.6 ± 2.2	1.0 ± 1.3	1.3 ± 2.0	1.9 ± 1.4	0.87
Dairy products, low-fat (servings/wk)	4.1 ± 2.2	5.9 ± 2.2	6.2 ± 2.4[5]	5.0 ± 1.3	6.2 ± 1.1[4]	6.9 ± 2.1[5]	0.001
Fruit (servings/wk)	5.0 ± 3.1	5.3 ± 2.9	7.1 ± 2.2[5]	5.0 ± 3.2	5.7 ± 2.1[4]	7.0 ± 2.1[5]	0.03
Vegetables (servings/wk)	1.4 ± 1.4	1.9 ± 1.2[4]	2.4 ± 1.5[5]	1.2 ± 1.1	2.3 ± 1.2[4]	3.1 ± 1.2[4]	0.01
Legumes (servings/wk)	1.3 ± 1.1	1.8 ± 1.2[4]	2.1 ± 1.1[4]	0.9 ± 1.5	1.3 ± 1.4	1.7 ± 0.7[4]	0.03
Potatoes (servings/wk)	1.7 ± 1.4	1.9 ± 1.6[4]	2.1 ± 1.3[4]	1.9 ± 1.5	2.7 ± 1.4[4]	2.9 ± 1.1[4]	0.03
Nonrefined cereals (servings/wk)	1.2 ± 1.5	1.8 ± 1.3	2.4 ± 1.4	1.2 ± 1.4	1.7 ± 1.5	2.2 ± 1.2	0.12
Alcoholic beverages (mL/d)	160 ± 44	115 ± 35[4]	95 ± 25[5]	85 ± 30	80 ± 25[4]	75 ± 45[5]	0.001
Daily use of olive oil (%)	77	86	91	79	88	95	0.001

[1] No significant interactions were observed between tertile of diet score and sex.
[2] Derived from ANOVA. Reflect the association between food consumption and tertiles of diet score, after adjustment for sex.
[3] $\bar{x}$ ± SD (all such values).

ACIDI GRASSI POLI-INSATURI





(Foto Bonavia)

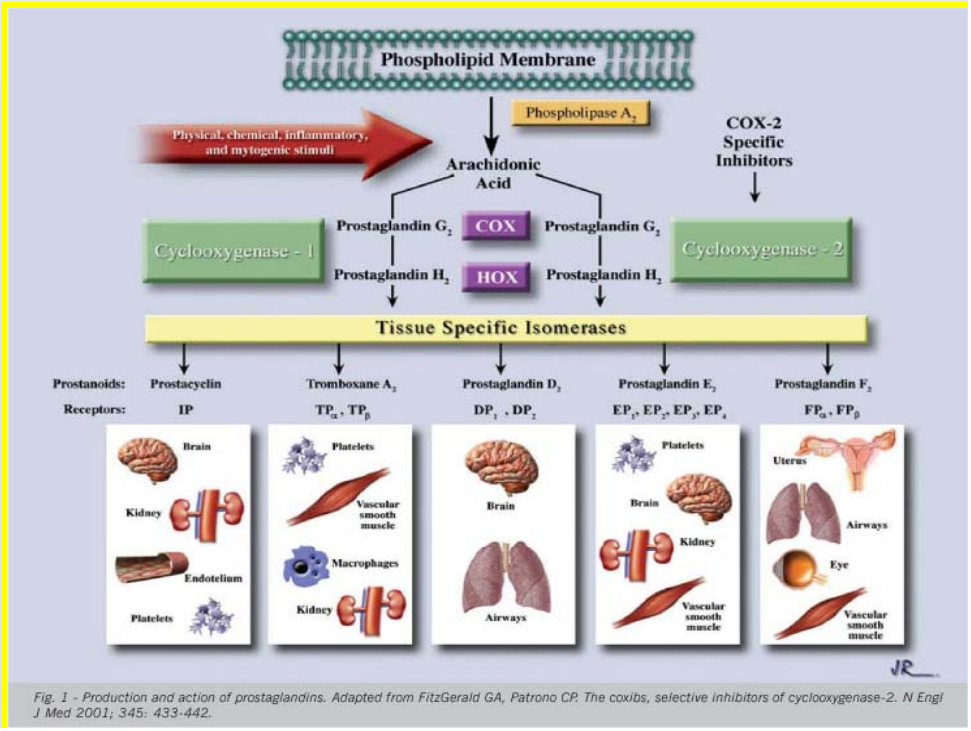


Fig. 1 - Production and action of prostaglandins. Adapted from FitzGerald GA, Patrono CP. The coxibs, selective inhibitors of cyclooxygenase-2. N Engl J Med 2001; 345: 433-442.

Walnut: Brain Food (organ-specific)

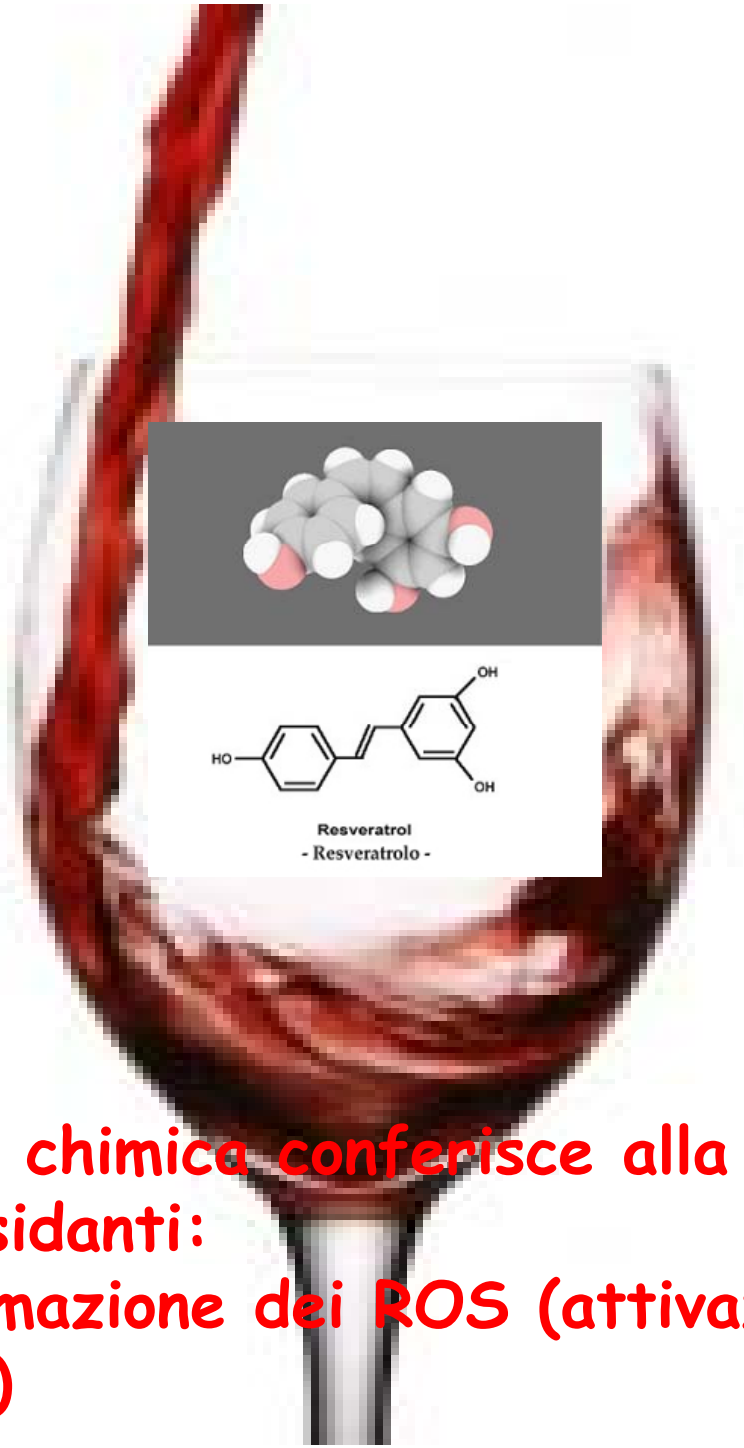


Rich in Omega-3 PUFAS

Walnut extract inhibit the fibrillization of amyloid beta-protein, and also defibrillizes its preformed fibrils.

(Chauhan N et al., Curr Alzheimer Res 2004 1:183-8)

(Foto Bonavia)



La sua struttura chimica conferisce alla molecola proprietà antiossidanti:
contrasta la formazione dei ROS (attivazione catalasi ad opera SIRT1)

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Journal of Nutritional Biochemistry 17 (2006) 429–445
Journal of Nutritional Biochemistry

REVIEWS: CURRENT TOPICS

The role of virgin olive oil components in the modulation of endothelial function

Javier S. Perona, Rosana Cabello-Moruno, Valentina Ruiz-Gutierrez*
Nutrition and Lipid Metabolism Group, Instituto de la Grasa (CSIC), Seville 41012, Spain
Received 30 September 2005; received in revised form 27 October 2005; accepted 1 November 2005

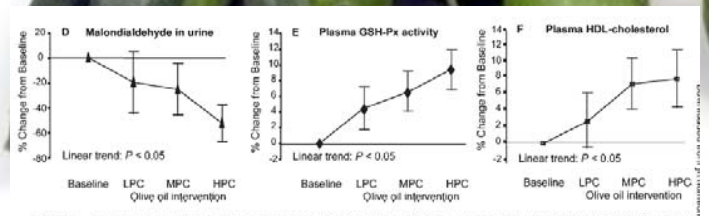


FIGURE 1 The percentage change in plasma oxidized LDL (*A*), 8-oxo-dG in mtDNA (*B*), and urine (*C*), malondialdehyde in urine (*D*), plasma GSH-Px activity (*E*), and serum HDL-C (*F*) in men after 4 d of sustained consumption of olive oil with low (LPC), moderate (MPC), and high (HPC) phenolic content. Values are means ± SEM, $n = 12$.

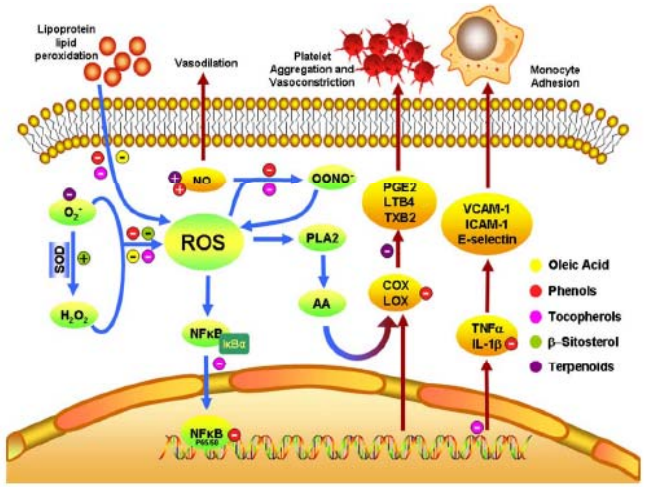


Fig. 1. Proposed model for the action mechanisms of oleic acid and minor compounds from olive oil based on the literature gathered for the present review. Despite the number of studies contributing to this model, several gaps that should be filled with further investigation are still present. The main mechanism by which the components of olive oil influence endothelial activation involves inhibition and/or scavenging of ROS. Oleic acid and β-sitosterol may reduce intracellular ROS by creating a less-oxidant environment through inhibition of intracellular ROS production. β-Sitosterol may also enhance SOD activity, hence decreasing O_2^- levels. This reduction has also been observed for the terpenoid oleanolic acid, although the mechanism is not presently known. Tocopherols and phenolic compounds are potent antioxidants that may help reduce lipid peroxidation and scavenge intracellular ROS and free NO, reducing the formation of $OONO^-$. ROS can activate the NFκB, which is then translocated into the nucleus, where it binds to recognition sequences in DNA to induce gene expression. This mobilization of NFκB is blocked by α-tocopheryl succinate but not by α-tocopherol. In contrast, phenolic compounds have been proposed to act blocking the formation of NFκB/DNA binding complexes. NFκB modulates the expression of cytokines, LOX and COX, thereby affecting the levels of adhesion molecules and eicosanoids. However, some of the minor compounds of olive oil may act directly on these enzymes and cytokines. LOX and COX activities are inhibited at different points by phenolics and triterpenoids whereas IL-1β expression is inhibited by phenolics and tocopherols, contributing to protect the endothelium against vasoconstriction, platelet aggregation and monocyte adhesion. Vasodilation is also suggested to be enhanced by oleuropein and oleanolic acid through an increase in the production of NO.

Mol. Nutr. Food Res. 2010, *54*, 1–8 DOI 10.1002/mnfr.200900257

RESEARCH ARTICLE

A Mediterranean diet rich in virgin olive oil may reverse the effects of the -174G/C IL6 gene variant on 3-year body weight change

Cristina Razquin[1], J. Alfredo Martinez[1], Miguel A. Martinez-Gonzalez[2], Joaquin Fernández-Crehuet[4], José Manuel Santos[4] and Amelia Marti[1]

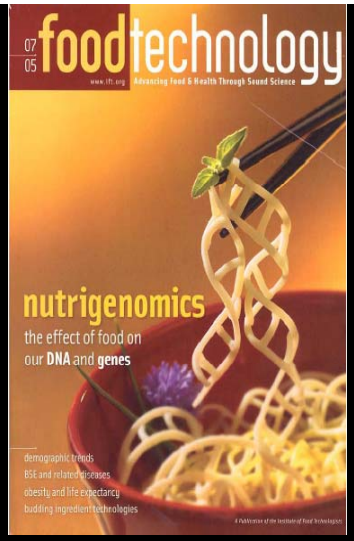


Table 2. Baseline characteristics according to the genotype for the -174G/C polymorphism of IL6 gene

	GG+GC ($n = 622$)	CC ($n = 115$)
Sex (% Female)	55	54
Age (years)	67.7±6.3	68.3±7.4
Waist/height	0.6±0.1	0.6±0.1
Waist circumference (cm)	95.1±10.1	97.1±11.4
Weight (kg)	74.6±11.3[a)]	77.2±11.4
BMI (kg/m^2)	29.1±3.2[b)]	29.8±3.5
Systolic blood pressure (mm Hg)	155.0±21.2	155.5±20.5
Diastolic blood pressure (mm Hg)	86.4±10.4	86.2±11.4
Diabetes (%)	65	65
Smoking habit (% Current smokers)	15	18

a) The differences between GG+GC and CC subjects were statistically significant ($p = 0.024$).
b) The differences between GG+GC and CC subjects were statistically significant ($p = 0.020$).

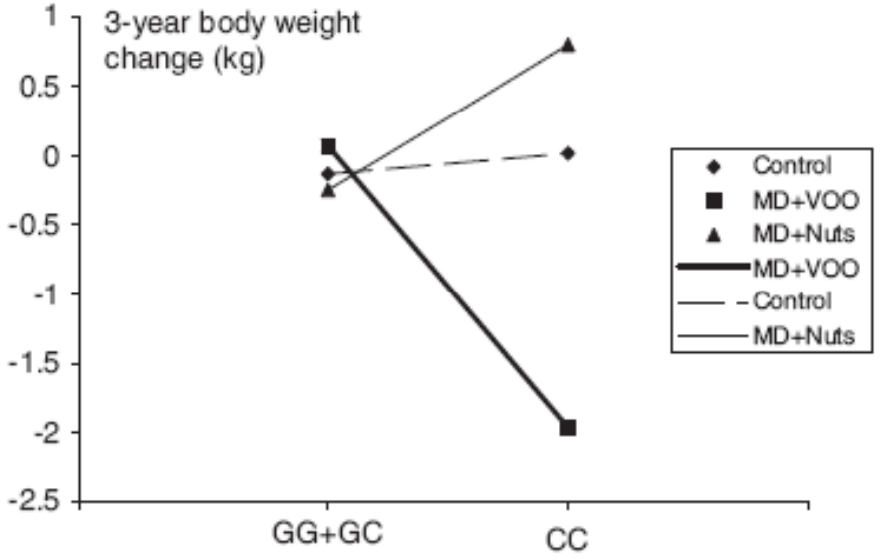
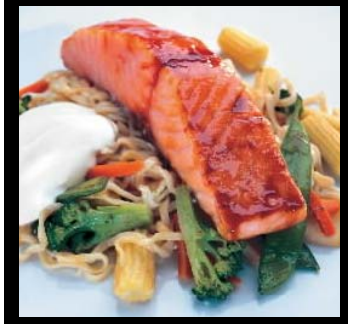


Figure 3. Interaction plots showing the effects of the interaction between the nutritional group and the genotype for the -174G/C polymorphism of IL6 gene on 3-year body weight changes. The model was adjusted for age, sex, baseline BMI, and diabetes.

Components are “complex mixtures” - act synergistically







Dietary Component	% Reduction *
➢ Wine (150 ml/day)	32%
➢ Fish (114 g 4x/week)	14%
➢ Dark Chocolate (100 g/day)	21%
➢ Fruits and Vegetables (400 g/day)	21%
➢ Garlic (2.7 g/day)	25%
➢ Almonds (68 g/day)	12%

* decreased risk of CVD







Franco et al. BMJ 329:1447-1450, 2004

BIOLOGICO VS CONVENZIONALE



(Foto Bonavia)



2007



American Journal of Clinical Nutrition, 2009



QN, 2006

Am J Clin Nutr. 2010 Jul;92(1):203-10. Epub 2010 May 12.

Nutrition-related health effects of organic foods: a systematic review.

Dangour AD, Lock K, Hayter A, Aikenhead A, Allen E, Uauy R.

AJCN. First published ahead of print July 29, 2009 as doi: 10.3945/ajcn.2009.28041.

Nutritional quality of organic foods: a systematic review[1–4]

Alan D Dangour, Sakhi K Dodhia, Arabella Hayter, Elizabeth Allen, Karen Lock, and Ricardo Uauy

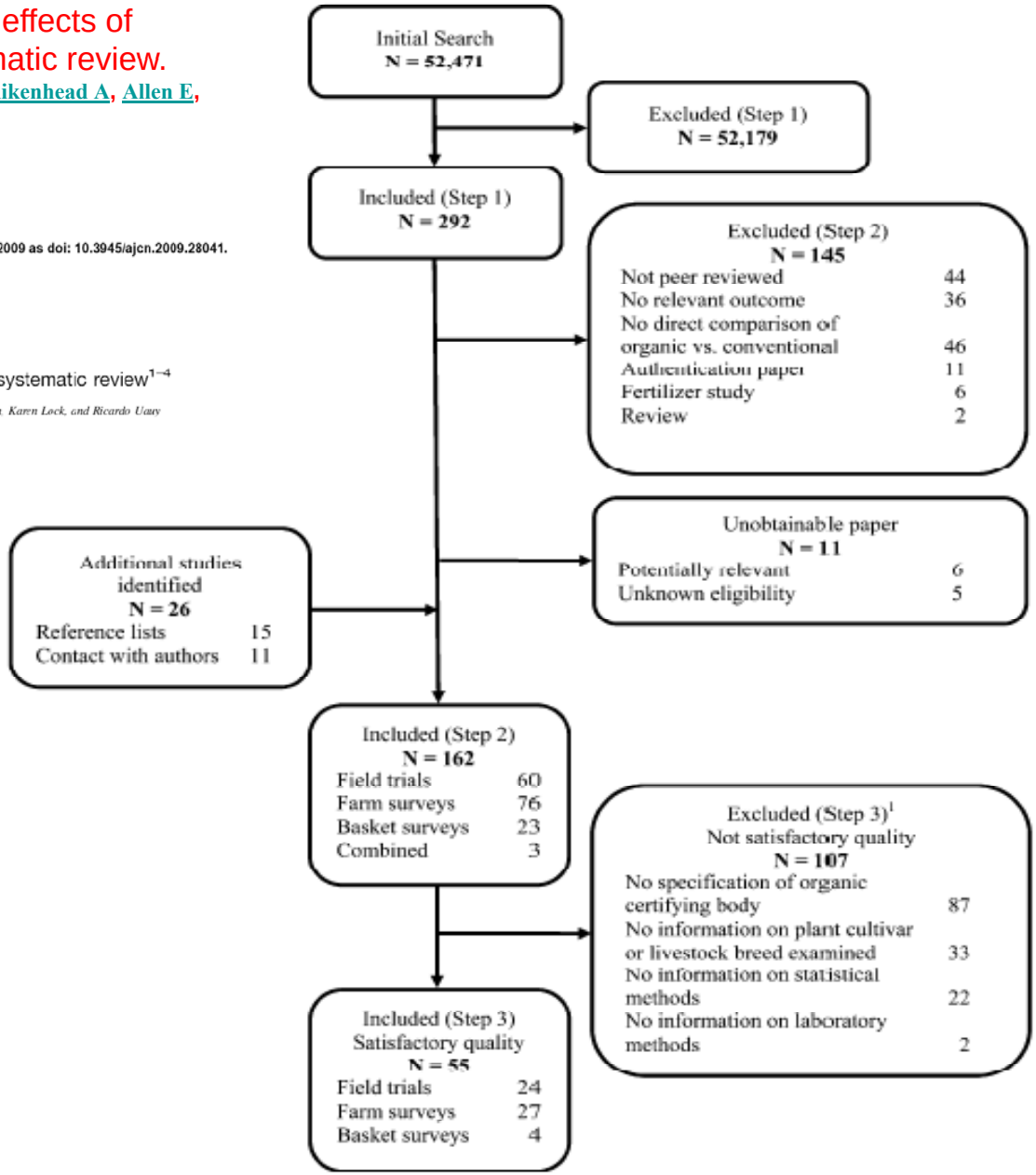


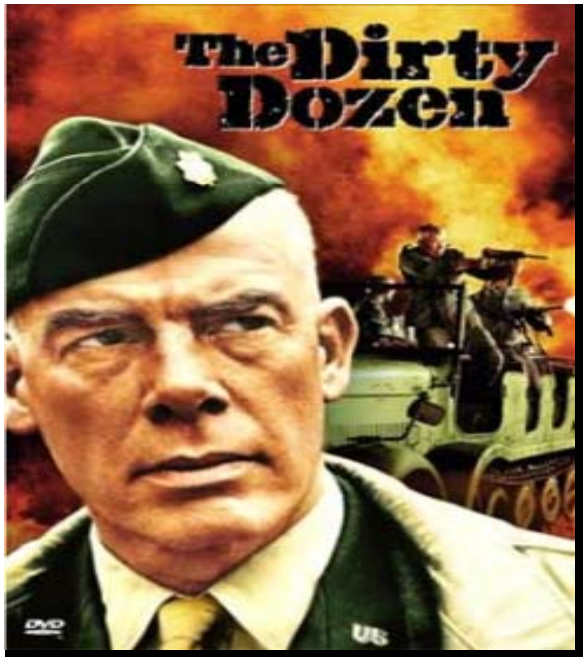
FIGURE 1. Study selection process for systematic review of the nutrient content of organic foodstuffs. [1]Reasons for exclusion at step 3 were not mutually exclusive.

SABio
Nutrire per prevenire
Quali nuovi indicatori di rischio nutrizionale

RUOLO DELLA DIETA MEDITERRANEA BIOLOGICA SULLO STATO DI SALUTE

di Antonino De Lorenzo
e
Laura Di Renzo

UNIVERSITA' DEGLI STUDI DI ROMA
TorVergata
Università





	MELE		VERDURA	
	biologico	convenz	biologico	convenz
FITOFARMACI GC-MS (A) mg/Kg				
ACRINATRINA	< 0,01	< 0,01	< 0,01	< 0,01
BOSCALID	< 0,01	**0,044§**	< 0,01	< 0,01
BROMACIL	< 0,01	< 0,01	< 0,01	< 0,01
CLORPIRIFOS-ETILE	< 0,01	**0,02§**	< 0,01	**0,264§§**
CLORPIRIFOS-METILE	< 0,01	< 0,01	< 0,01	< 0,01
FITOFARMACI GC-MS (B) mg/Kg				
ETOPROFOS	< 0,01	< 0,01	< 0,01	< 0,01
ETOSSAZOLO	< 0,01	< 0,01	< 0,01	< 0,01
ATRIDIAZOLO	< 0,01	< 0,01	< 0,01	< 0,01
FENAMIFOS	< 0,01	< 0,01	< 0,01	< 0,01
FITOFARMACI GC-MS (C) mg/Kg				
PICOXISTROBIN	< 0,01	< 0,01	< 0,01	< 0,01
PIPERONIL BUTOSSIDO	< 0,01	< 0,01	< 0,01	< 0,01
PIRAZOFOS	< 0,01	< 0,01	< 0,01	< 0,01

Livelli micotossine nei cereali
BIO vs CONV



	PANE		PASTA		FARINA	
	biologico	convenz	biologico	convenz	biologico	convenz
OCRATOSSINA A µg/kg	< 0,5	< 0,5	< 0,5	< 0,5	< 0,5	< 0,5
AFLATOSSINE µg/kg						
B1	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3
B2	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3
G1	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3
G2	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3
B1+B2+G1+G2	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3	< 0,3
ZEARALENONE µg/kg	< 15	< 15	< 15	< 15	< 15	< 15

< equivale ad inferiore al LOQ (limite di quantificazione/determi



Table 2. Rumenic acid, other conjugated linoleic acids, *trans*-vaccenic acid and other relevant fatty acid classes in breast milk (as weight percentage (wt%) of total milk fat) by origin of meat and dairy (*n* 312)†

(Mean values and standard deviations)

	Conventional (*n* 186)		> 50 % organic meat and dairy (*n* 33)		> 90 % organic meat and dairy (*n* 37)		Other (*n* 57)	
Fatty acids	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Rumenic acid (*cis*9,*trans*11-C18 : 2)	0·25	0·07	0·29*	0·10	0·34***	0·10	0·27	0·11
Other conjugated linoleic acids	0·07	0·03	0·06*	0·03	0·07	0·03	0·07	0·03
trans-Vaccenic acid (*trans*11-C18 : 1)	0·48	0·21	0·54	0·26	0·59***	0·16	0·53*	0·16
LA (C18 : 2*n*-6)	13·73	3·19	13·81	4·28	14·90	4·40	13·06	2·87
Sum of LA derivatives‡	1·33	0·23	1·29	0·19	1·36	0·25	1·30	0·23
LA + LA derivatives	15·06	3·26	15·10	4·28	16·26	4·48	14·37	2·90
α-Linolenic acid (C18 : 3*n*-3)	1·05	0·38	0·89*	0·41	0·82***	0·28	0·93*	0·27
Sum of ALA derivatives§	0·79	0·32	0·77	0·22	0·79	0·43	0·81	0·44
ALA + ALA derivatives	1·84	0·56	1·65*	0·47	1·61*	0·61	1·74	0·48
Total PUFA	18·45	3·53	18·27	4·36	19·51	4·67	17·66	2·95
Total MUFA	40·84	3·08	39·48	4·12	38·57***	3·20	40·28	3·97
Total SFA	40·71	4·33	42·25	5·82	41·91	5·36	42·07	4·75

ALA, α-linolenic acid; LA, linoleic acid

Mean values were significantly different from those of the conventional group (Student's *t* test): *$P<0·05$; **$P<0·01$; ***$P<0·001$.

† For details of procedures, see pp. 736–737.

‡ Sum of LA derivatives includes: C18 : 3*n*-6, C20 : 3*n*-6, C20 : 4*n*-6, C22 : 4*n*-6 and C22 : 5*n*-6.

§ Sum of ALA derivatives includes: C18 : 4*n*-3, C20 : 4*n*-3, C22 : 4*n*-3, C22 : 5*n*-3 and C22 : 6*n*-3.

RUOLO DELLA DIETA MEDITERRANEA BIOLOGICA SULLO STATO DI SALUTE

di

Antonino De Lorenzo

Laura Di Renzo

Tabella 6.1 - Indici di qualità nutrizionale (INQ) giornalieri

	Indici di qualità Nutrizionali (INQ)					
	Giorno 1	Giorno 2	Giorno 3	Giorno 4	Giorno 5	Giorno 6
Glucidi	0,96	0,93	1,01	0,93	0,93	0,95
Lipidi	0,97	1,04	0,93	1	1,08	1,04
Protidi	1,3	1,27	1,14	1,33	1,16	1,16

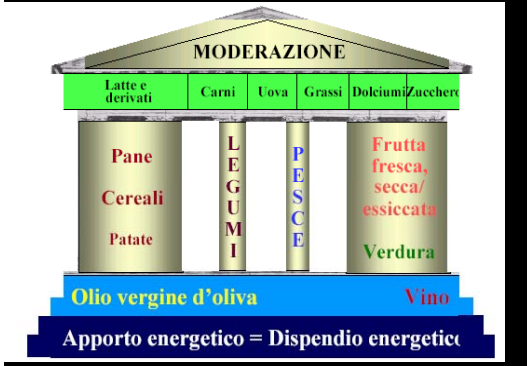


Tabella 7.9 - Valori NAE (escrezione acida globale), PRAL (carico renale giornaliero), CSI (indice di qualità lipidica), TI (indice di trombogenicità), AI (indice di aterogenicità)

	NAE	PRAL	CSI	TI	AI
Giorno 1	36,21	-9,99	19,95	0,53	0,25
Giorno 2	62,56	16,36	26,62	1,43	0,82
Giorno 3	30,8	-15,4	28,63	0,7	0,32
Giorno 4	31,9	-14,2	17,78	0,61	0,29
Giorno 5	41,08	-5,12	30,1	1,32	0,8
Giorno 6	25,8	-20,4	26,63	0,67	0,3
Giorno 7	39,82	-6,38	21,62	0,65	0,32
Giorno 8	44,38	-1,82	20,17	0,85	0,42



Documento di Ricerca SABIO, INEA 2009

European Review for Medical and Pharmacological Sciences 2007; 11: 185-192

Is antioxidant plasma status in humans a consequence of the antioxidant food content influence?

L. DI RENZO[1,2], D. DI PIERRO[3], M. BIGIONI[1], V. SODI[1], F. GALVANO[4], R. CIANCI[1,5], L. LA FAUCI[4], A. DE LORENZO[1]

[1]Department of Neuroscience, Division of Human Nutrition, University of Tor Vergata, Rome (Italy)
[2]I.N.Di.M., National Istitute for Mediterranean Diet and Nutrigenomic, Reggio Calabria (Italy)

Table I. Antioxidant capacity in conventional and organic produts.

	Conventional		Organic		
	Median	Range	Median	Range	_%
Garlic	2572,5	70	3816,5	52	48**
Orange	900	50	1606	56	79**
Banana	205,9	16	339	38,6	65**
Carrot	116,4	27,2	166,8	58,4	43**
Beans	50,4	21,2	207,6	31,2	312**
Strawberry	846,7	37,2	921,2	41,6	9**
Lettuce	756,3	99,8	608,5	80,8	-20**
Limon	1505	54	1603	48	7**
Apple	454	81,9	610,5	47	34**
Potato	298,8	4,4	423,6	50,8	42**
Tomato Souce	205,2	19,8	213,8	58,8	4
Pear	246,4	132,2	185,3	58,4	-25**
Peas	88,2	41,8	164,8	65	87**
Tomato	280,8	72,6	475,2	98,4	69**
Celery	265,7	119,8	414,9	40,4	56**
Wine	3132	280,2	4725	164	51**
Courgettes	774	148,8	894	60,6	15**
Milk	195,8	78,4	216,6	38,6	11*

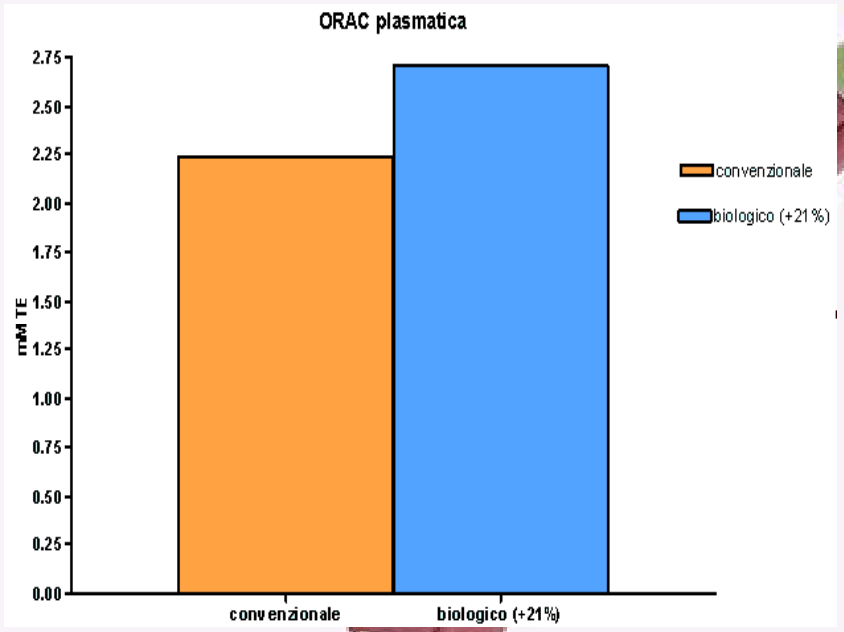
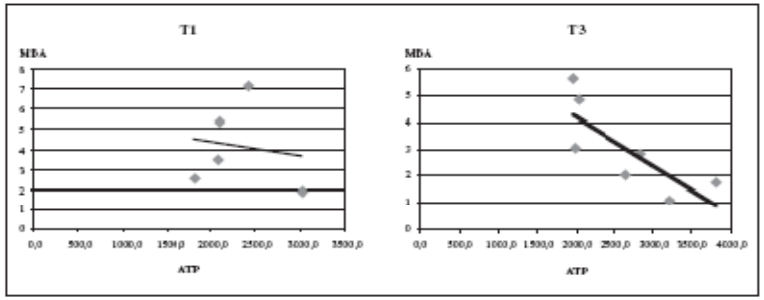


Figura 7.1 - Analisi di regressione lineare tra livelli di ATP e MDA



La diminuzione della fosforemia ematica (12%), di grande rilevanza in pazienti uremici, può essere in parte da collegare all'aumentata fosforilazione dell'AMP e ADP a beneficio di una più alta concentrazione di ATP come risulta evidente dopo i 15 gg di alimentazione biologica.



Current Pharmaceutical Design, 2010, *16*, 000-000

The effects of Italian Mediterranean Organic Diet (IMOD) on Health Status

A. De Lorenzo[1,2,*], A. Noce[3], M. Bigioni[1], V. Calabrese[4], D.G. Della Rocca[1], N. Di Daniele[5], C. Tozzo[3] and Laura Di Renzo[1,2]

[1]Department of Neuroscience, Division of Human Nutrition, University of Tor Vergata, Rome, Italy; [2]I.N.Di.M., National Institute for Mediterranean Diet and Nutrigenomic, Reggio Calabria, Italy; [3]Nephrology and Dialysis Service, University Hospital "Tor Vergata", Rome, Italy; [4]Biochemistry & Molecular Biology Section, Department of Chemistry, Faculty of Medicine, University of Catania, Catania, Italy; [5]Department of Internal Medicine, University Hospital Tor Vergata, Rome, Italy

Table 4. Laboratory Parameters in Healthy Subjects and in CKD Patients at T1 and T2

	Healthy Subjects					CKD Patients				
	T1		T2			T1		T2		
	Mean	SD	Mean	SD	*P**	Mean	SD	Mean	SD	*P**
Homocysteine(μM/L)	23.06	± 5.17	12.71	± 6.15	0.0106	22.12	± 5.17	17.81	± 5.29	0.0026
Azotemia (mg/dl)	33.20	± 11.33	30.66	± 8.51	NS	83.21	± 47.49	80.76	± 50.92	NS•
Creatinine (mg/dl)	0.88	± 0.29	0.95	± 0.18	NS	1.75	± 0.61	1.67	± 0.27	NS
Total Cholesterol (mg/dl)	167.02	± 60.55	189.66	± 36.21	NS	181.57	± 14.84	165.57	± 27.71	0.0369
HDL cholesterol (mg/dl)	33.04	± 12.30	39	± 6.86	NS	30.92	± 7.41	32.07	± 6.76	NS

	Healthy Subjects					CKD Patients				
	T1		T2			T1		T2		
	Mean	SD	Mean	SD	*P**	Mean	SD	Mean	SD	*P**
Triglycerides (mg/dl)	98.44	± 47.56	113.44	± 26.70	NS	168.71	± 54.53	156.85	± 37.88	NS
Calcium (mg/dl)	9.64	± 0.16	9.43	± 0.37	NS	9.93	± 0.57	9.33	0.44	<0.0001
Phosphorus (mg/dl)	4.64	± 0.15	3.01	± 0.13	<0,0001	4.10	± 0.88	3.54	± 0.26	0.0382
Sodium (mEq/L)	140.97	± 0.86	139.51	± 1.11	0,0141	140.85	± 1.09	140.57	± 0.85	NS
Potassium (mEq/L)	4.34	± 0.15	4.31	± 0.39	NS	4.90	± 0.34	4.67	±0.65	NS
Glucose (mg/dl)	98.91	± 24.28	92.66	± 22.02	NS	86.78	± 6.71	90.23	±8.55	NS
Vitamin B_{12} (pg/ml)	217.33	± 20.10	259.11	± 22.65	0.0019	574.92	± 247.49	516.42	±195.42	NS
Microalbuminuria (mg/L)	-	-	-	-	-	93.55	± 121.9	71.7	±100.48	0.00286
hs-CRP (mg/dl)	0.44	±0.64	0.05	±0.01	0.001	5.63	±4.82	4.51	±4.94	<0.001

LA DIFESA DELLA SALUTE

Dal 1993 il National Research Council (NRC) ha pubblicato vari rapporti secondo cui residui di antiparassitari presenti nei prodotti alimentari derivati dall'agricoltura convenzionale intensiva possono costituire la fonte principale d'esposizione a sostanze tossiche per i lattanti ed i bambini.

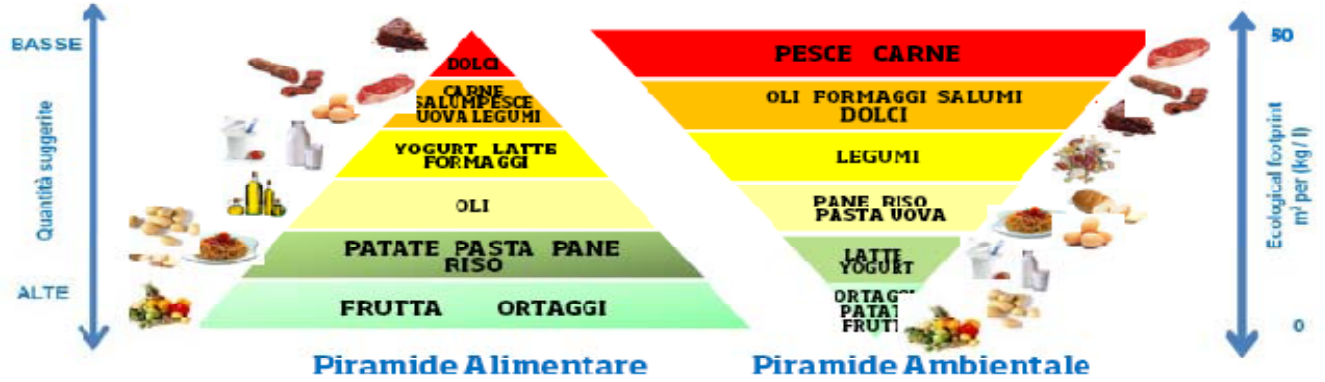


Uno studio condotto nel 2003 dal National Institute of Environmental Health Sciences (NIEHS), rileva residui di antiparassitari e diserbanti nell'urina di bambini che consumano prodotti alimentari derivati dall'agricoltura industriale, ma non in quella di bambini che consumano prodotti biologici.

Uno studio condotto nel 2008 dal NIEHS e dal National Cancer Institute (NCI) rileva un incremento del rischio del diabete dal 20% al 200% in soggetti esposti per oltre 100 giorni di vita a pesticidi, erbicidi e insetticidi autorizzati di tipo clorurato, organoclorurato o organofosfato.

AMBIENTE E SALUTE: LA PIRAMIDE AMBIENTALE (ROVESCIATA)

- **Piramide alimentare** (che suggerisce uno stile alimentare orientato alla promozione e alla conservazione della salute) e **piramide ambientale** (che indica gli alimenti a maggiore e minore impatto ambientale) sono allineate



Fonte: Elaborazione TEH-Ambrosetti su dati LCE

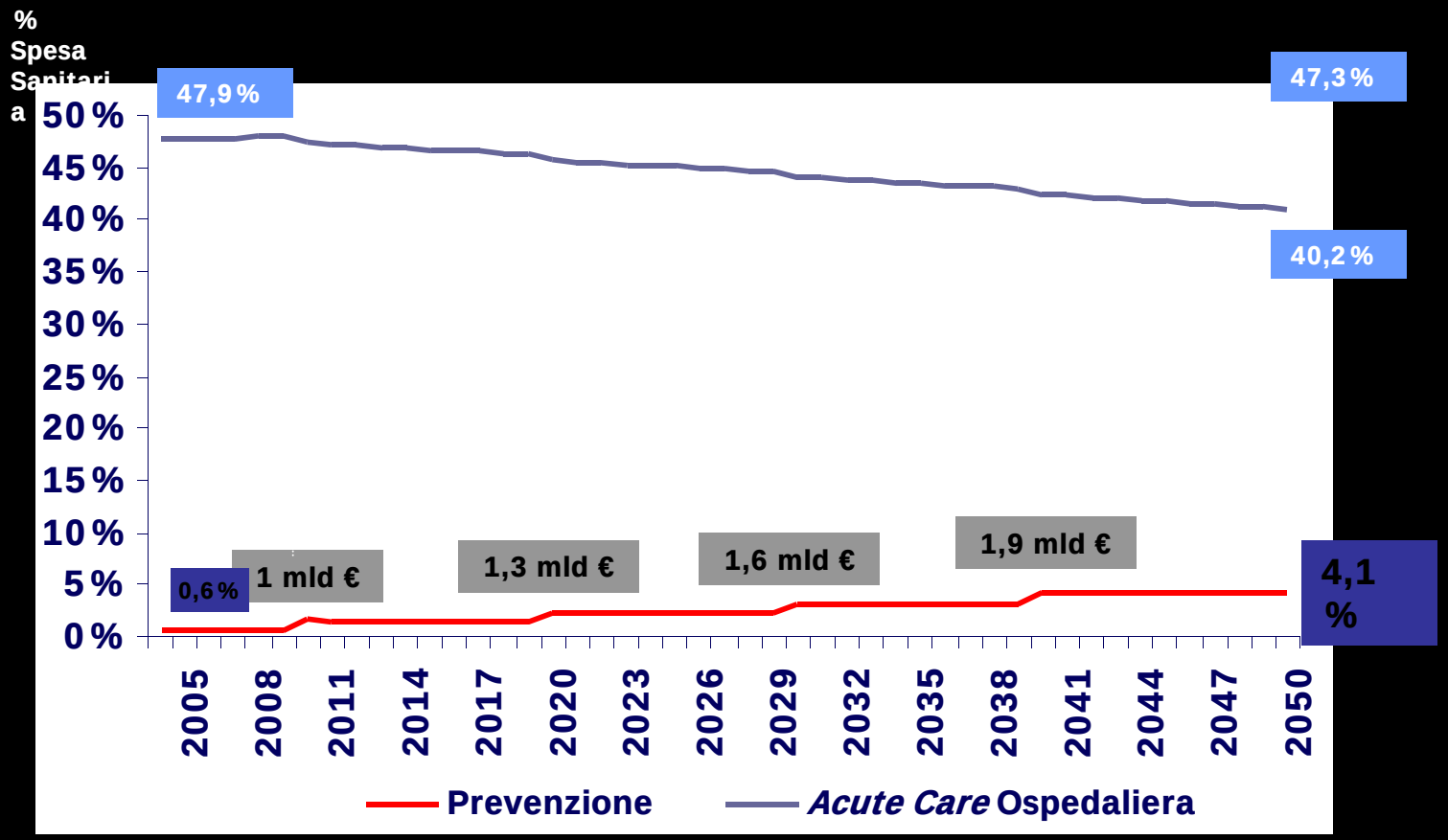
I BENEFICI DELLA DIETA MEDITERRANEA

Se la sola popolazione nord americana si convertisse alla dieta mediterranea si otterrebbe un risparmio di:

Emissioni di CO_2	**360 milioni tonnellate**
Superficie occupata	**1,6 milioni km^2**
Acqua virtuale consumata	**180 km^3**

Investimento in prevenzione e impatto sulla spesa medica in Italia

Il beneficio al 2050 di un incremento strutturale dell'1% nel rapporto spese in prevenzione su spesa sanitaria pubblica è stimato in 17,1 miliardi di euro, pari a una riduzione dello 0,6% nel rapporto spesa sanitaria pubblica su PIL



COSTO-BENEFICIO Prevenzione patologie CARDIOVASCOLARI



Treatment	Cost per life year gained (£ sterling)
Aspirin	50
Thiazide (antihypertensive)	66
Mediterranean Diet	***290***
ACE Inhibitor (antihypertensive)	5634
Simvastatin (cholesterol lowering)	8240

Source: Ebrahim S, Davey-Smith G, McCabe C, Payne N, Pickin M, Sheldon TA et al. What role for statins? A review and Economic model. Health Technol Assess 1999;3:No (19)

(Foto Bonavia)



Grazie per l’attenzione