University of Milan, Italy

Università degli Studi di Milano

Department of Biotechnology and Traslational Medicine

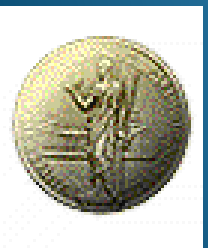
CENTER FOR STUDY AND RESEARCH ON OBESITY

NUTRIZIONE E BENESSERE

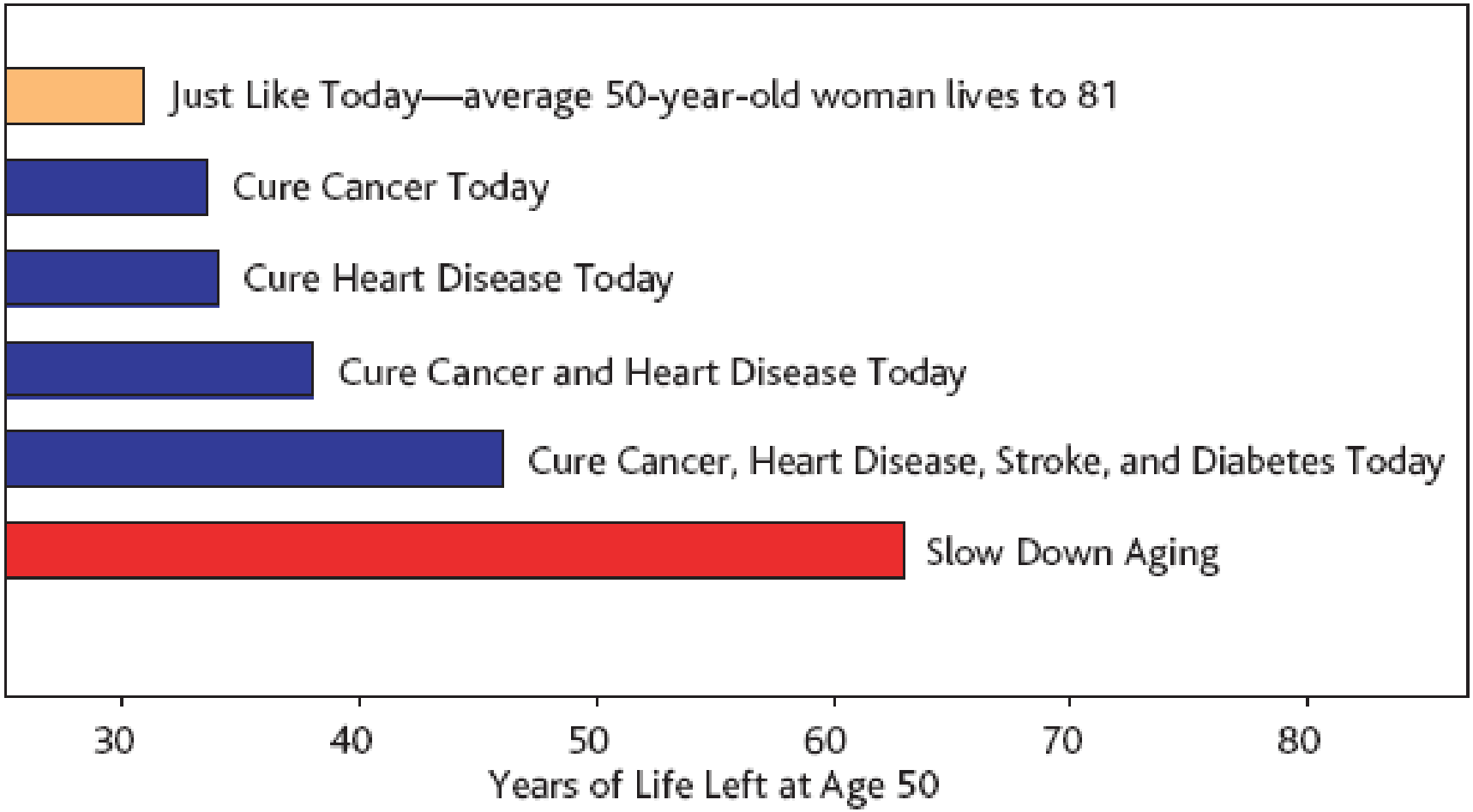
Michele O. Carruba

DETERMINANTS OF HEALTHY AGEING

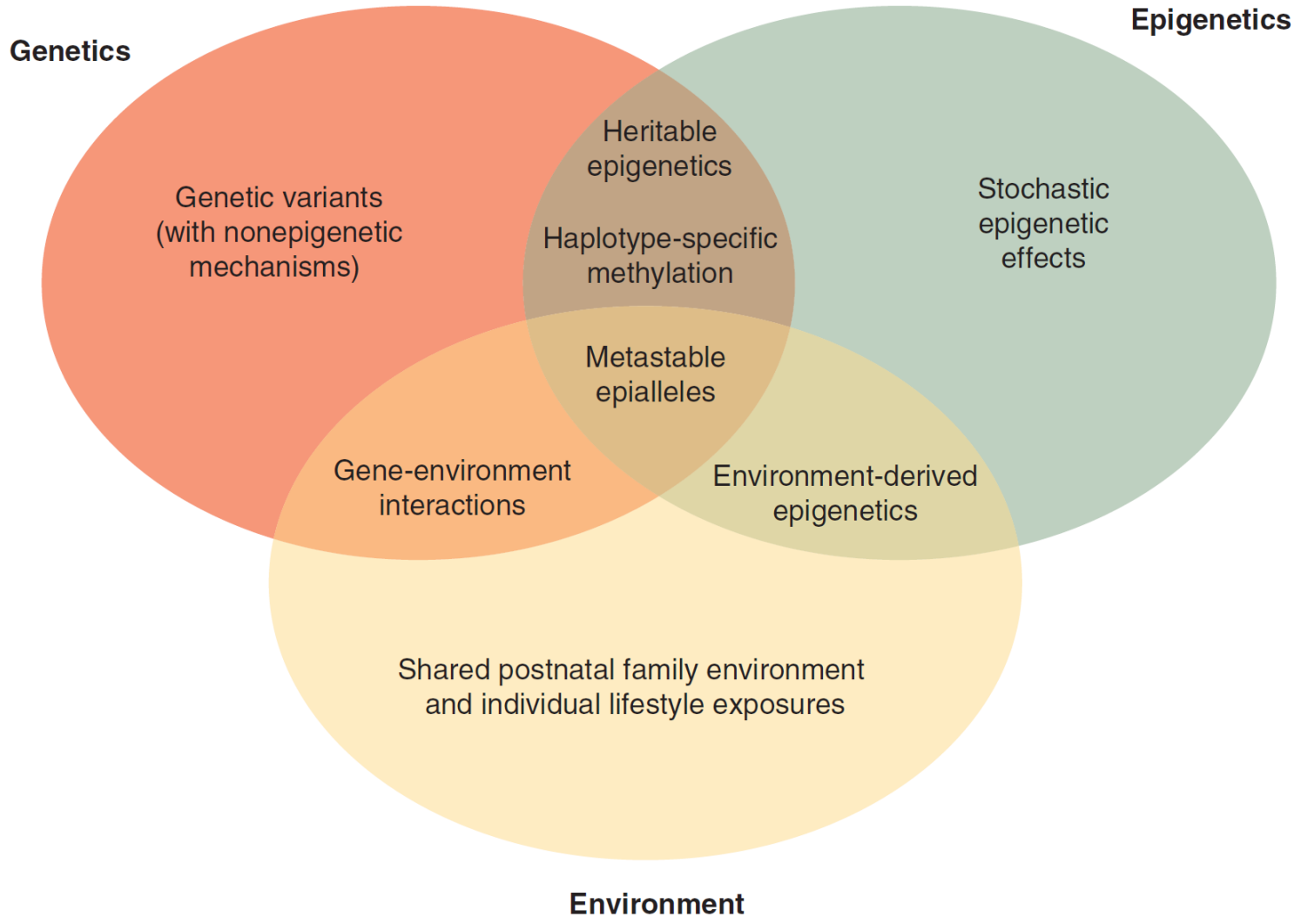
- Medical care 10 %
- Social conditions 15 %
- Genetics 25 %
- Life styles 50 %



Research on Aging: Biggest Bang for the Buck?



The complex relationship among genetics, epigenetics, and the environment in the susceptibility to obesity and type 2 diabetes

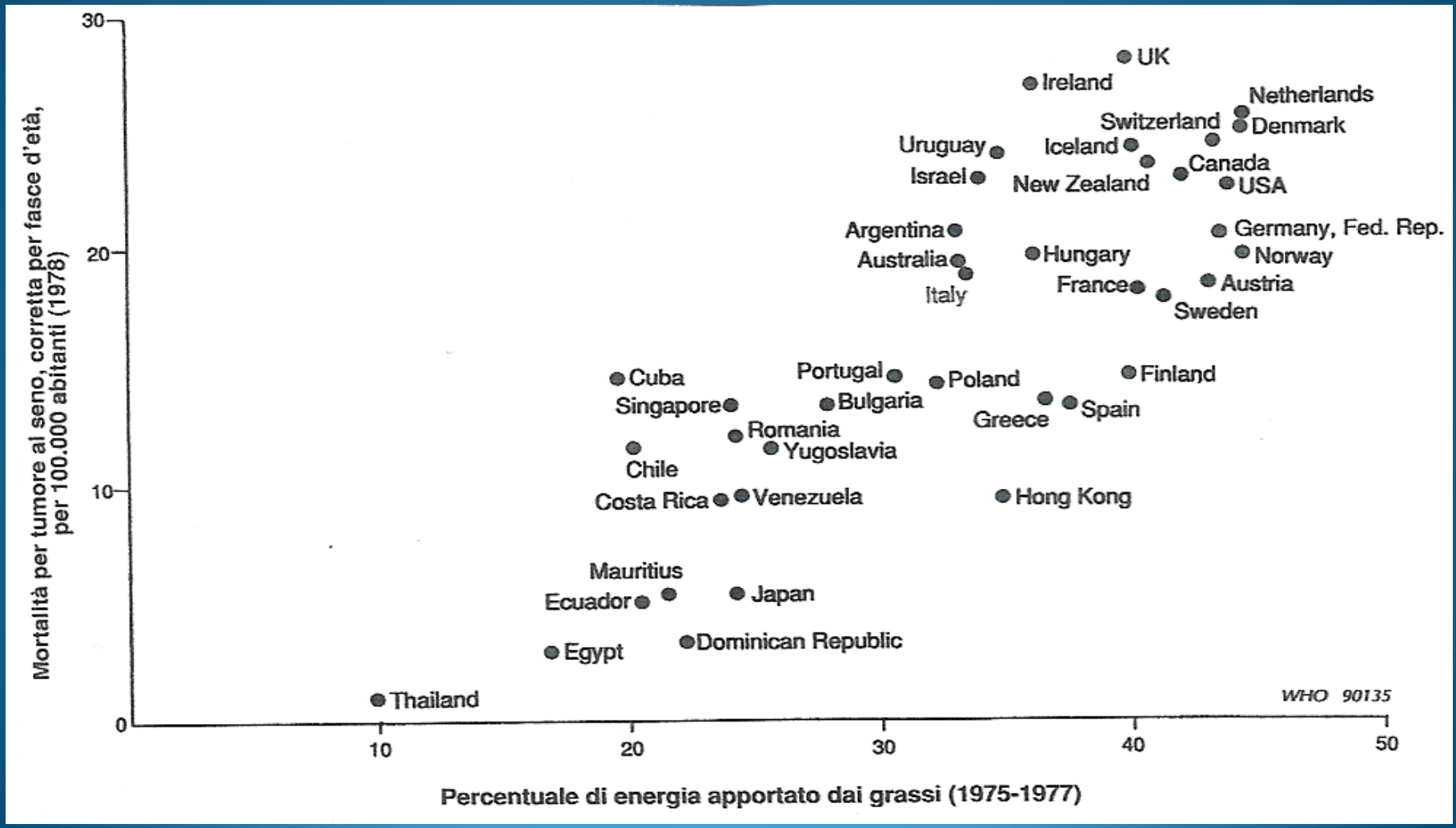


Drong et al., Clin Pharmacol & Ther 92: 707-715, 2012

Principali patologie croniche non comunicabili legate a cattiva alimentazione e a scorretti stili di vita

- Obesità
- Malattie cardiovascolari e ischemiche
- Disturbi del Comportamento Alimentare
- Diabete
- Tumori
- Osteoporosi
- Cirrosi ed altre patologie legate all'abuso di alcool
- Gozzo
- Anemie nutrizionali (ferro, folati vit. B12)
- Carie dentale
- Ipercolesterolemia familiare

Correlazione tra consumo di grassi alimentari e tassi di mortalità per tumore al seno

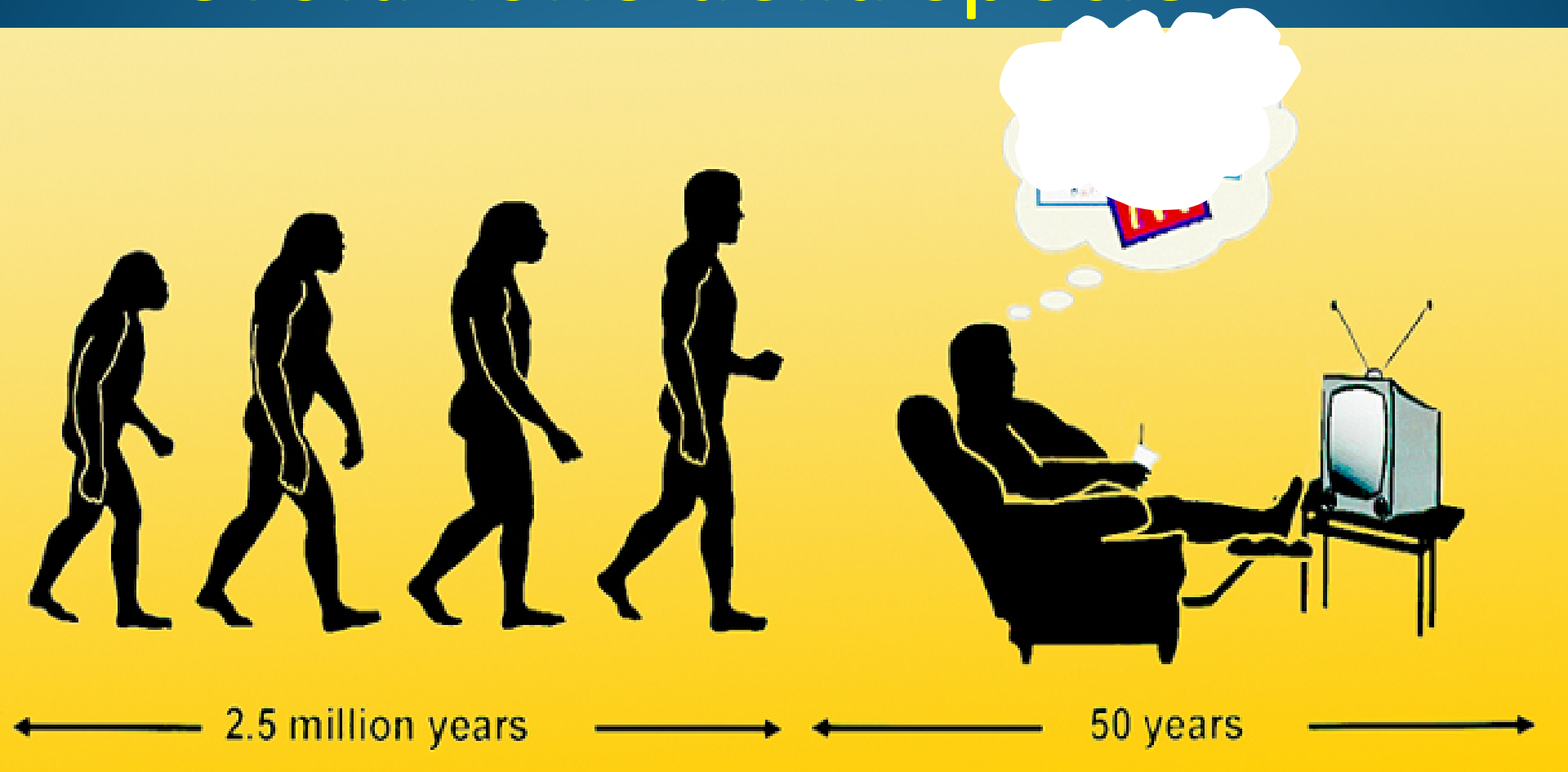


Correlazioni tra componenti selezionate della dieta e tumori

Sede del tumore	Grassi	Peso corporeo	Fibre	Frutta e ortaggi	Alcol	Cibi affumicati conservati sotto sale o salamoia
Polmoni				–		
Seno	+	+			+ / –	
Colon	+ +		–	–		
Prostata	+ +					
Vescica				–		
Retto	+			–	+	
Endometrio		+ +				
Cavità orale				–	+[b]	
Stomaco				–		+ +
Cervice				–		
Esofago				–	+ +[b]	+

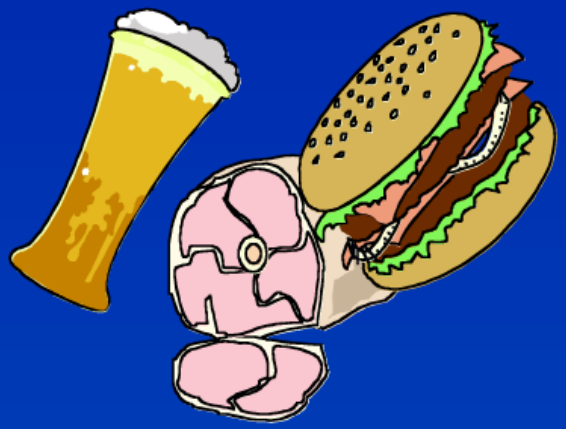
+ = Correlazione positiva: apporto aumentato e incidenza maggiore.
– = Correlazione negativa: apporto aumentato e incidenza inferiore.
[a] *Tratto e approfondito dalla nota bibliografica 44.*
[b] *Sinergia con il fumo.*

L’evoluzione della specie



IL BILANCIO ENERGETICO

Introduzione di Energia



Dispendio di Energia

Fattori di controllo

Predisposizione genetica
Alimentazione

Esercizio fisico
Metabolismo Basale
Termogenesi

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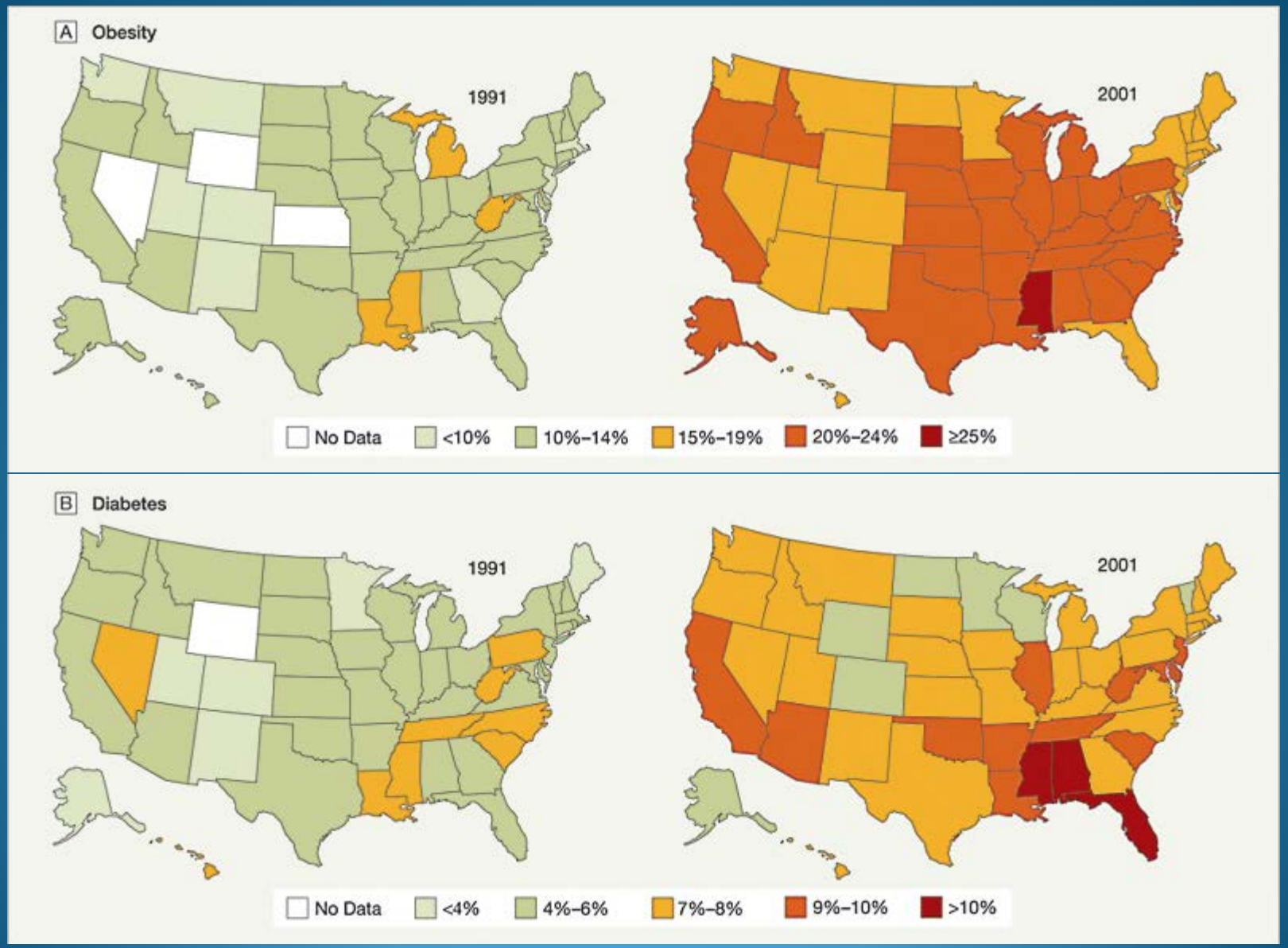
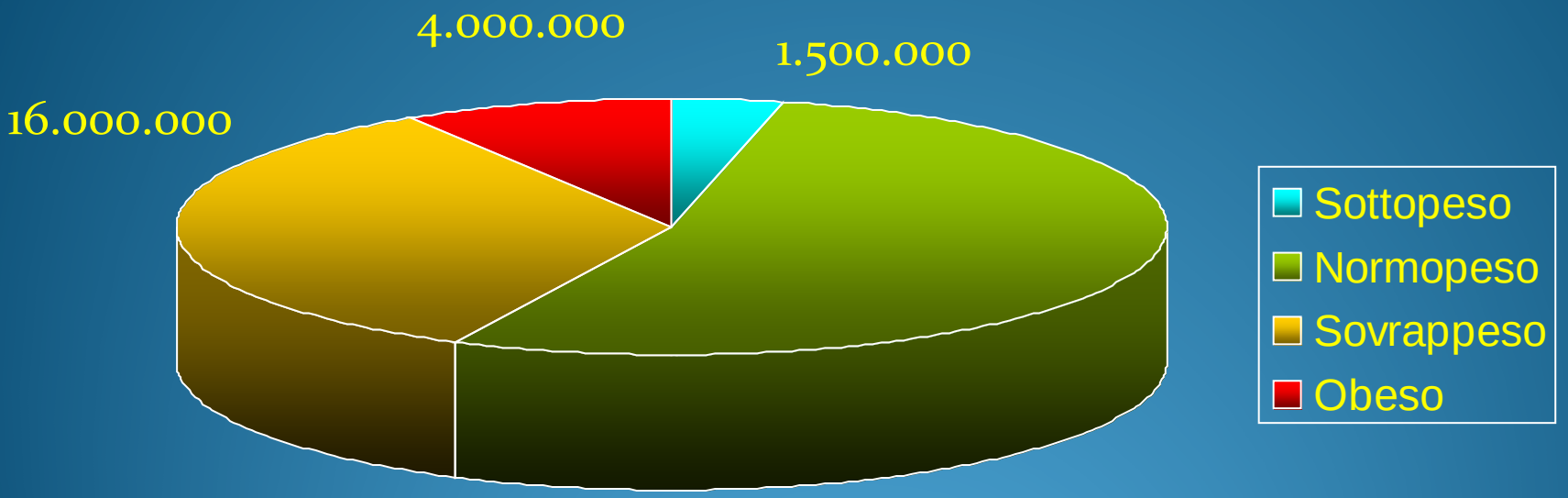
Prof. **Michele Carruba**

Prevalence of Obesity and Diagnosed Diabetes Among US Adults, 1991 and 2001



DISTRIBUZIONE DELLA POPOLAZIONE ITALIANA NELLE VARIE CONDIZIONI DI PESO



Fonte: ISTAT, 4° Rapporto sull'Obesità in Italia. Istituto Auxologico Italiano, 2002

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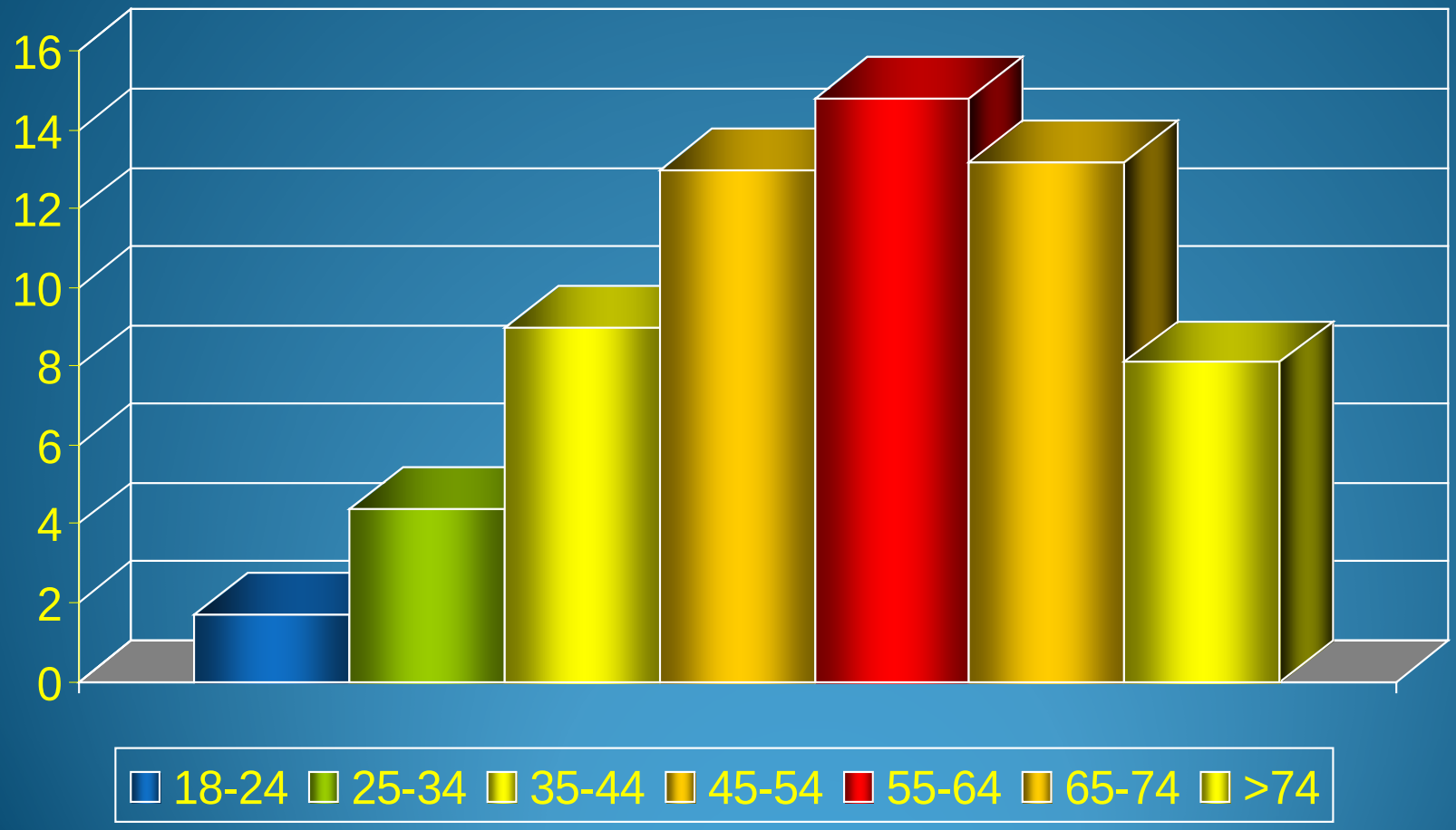
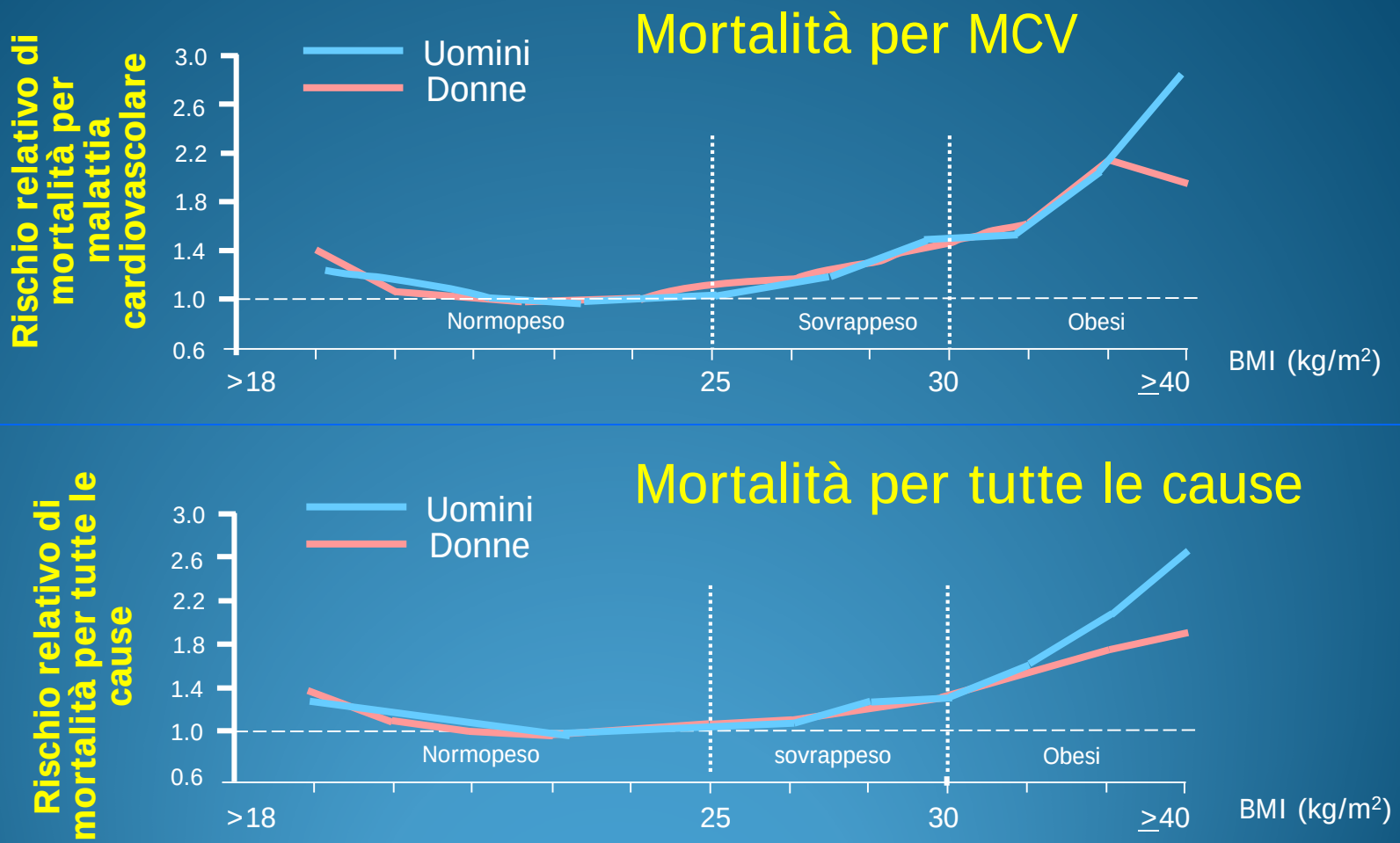
Prevalenza dell'obesità (IMC>30) in funzione dell'età negli UOMINI



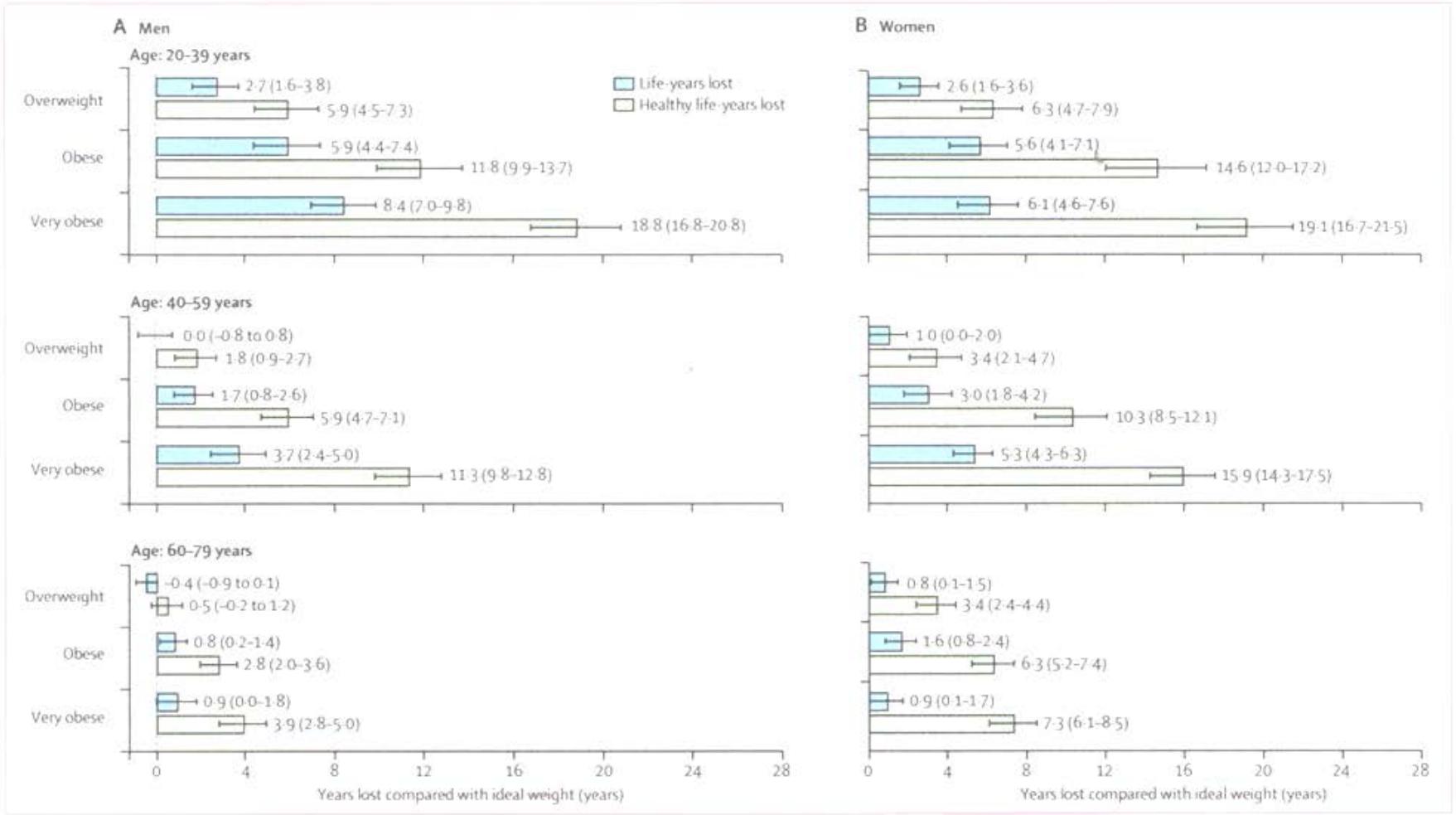
Fonte: ISTAT, 4° Rapporto sull'Obesità in Italia. Istituto Auxologico Italiano, 2002

Sovrappeso e obesità aumentano il rischio di MCV e di mortalità per tutte le cause

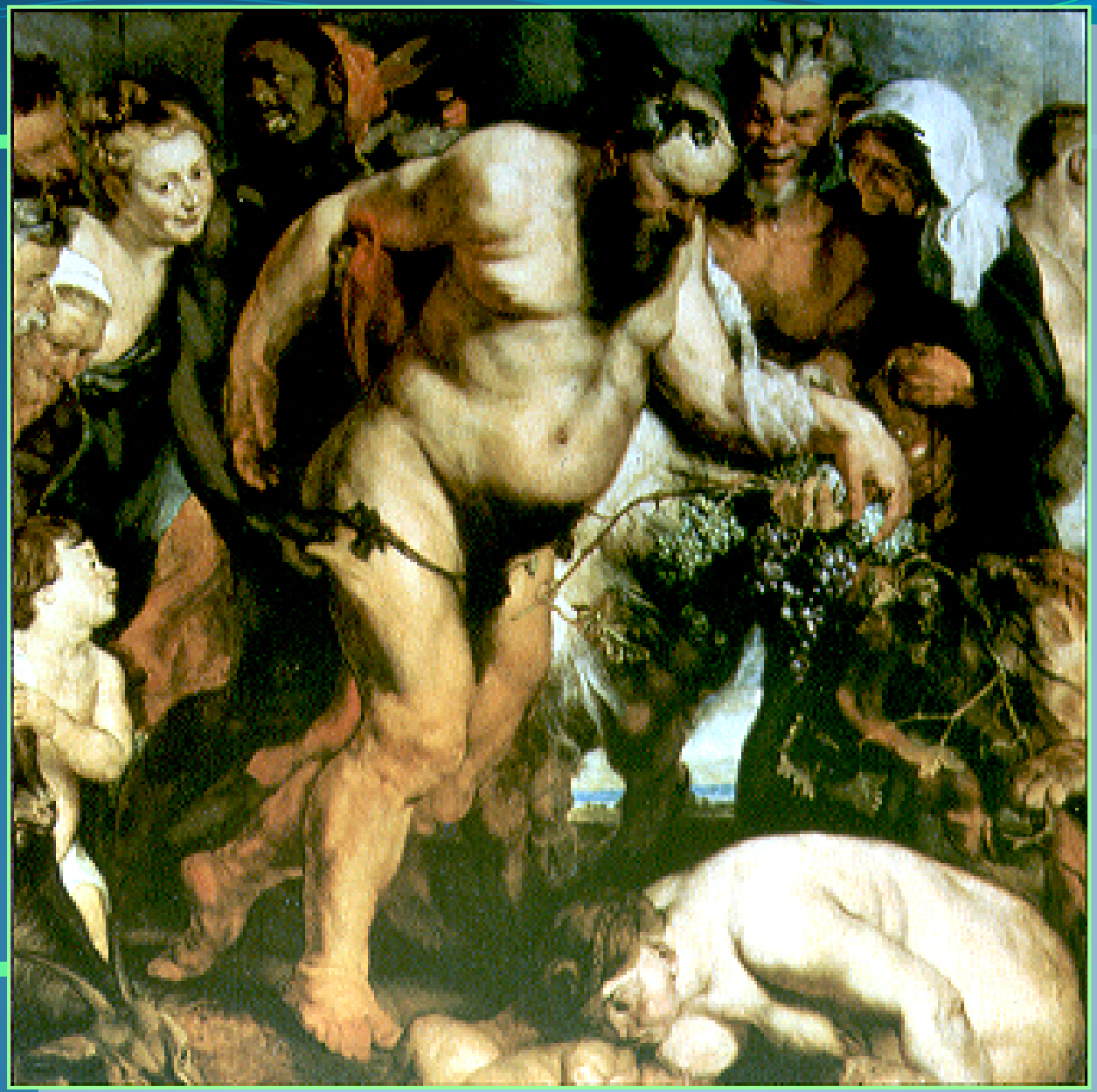


Dati relativi a 1 milione di uomini e donne seguiti per 16 anni con età media di 57 anni che non hanno mai fumato e non avevano una storia di malattia all'arruolamento.

Calle et al. *N Engl J Med.* 1999;341:1097-1105

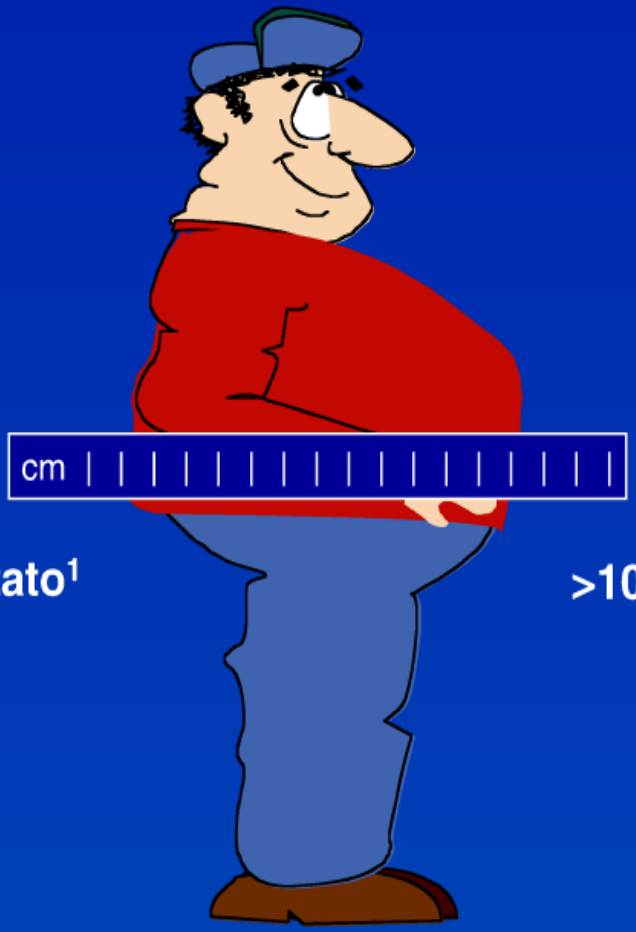


Grover SA, et al. Lancet Diabetes Endocrinol. 2015 Feb ;3(2):114-22.



Un parametro fondamentale: la circonferenza addominale

La circonferenza vita è un indicatore del tessuto adiposo viscerale



Donne

>88 cm = Rischio aumentato[1]

Uomini

>102 cm = Rischio aumentato[1]

[1]Lean MEJ, et al. Lancet;1998:351:853–6

Rischio Relativo di Problemi di Salute Associati all'Obesità

RR >3 volte	RR tra 2-3 volte	RR tra 1-2 volte
Diabete di tipo 2	Pat. cardiovascolari	Alterazioni dell'asse HPG
Problemi cistifellea	Ipertensione	Cancro
Dislipidemie	Osteoartriti	Problemi lombosacrali
Apnee notturne	Gotta	Difetti alla nascita

Adapted from WHO Report, Geneva 1998

Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults

Eugenia E. Calle, Ph.D., Carmen Rodriguez, M.D., M.P.H., Kimberly Walker-Thurmond, B.A., and Michael J. Thun, M.D.

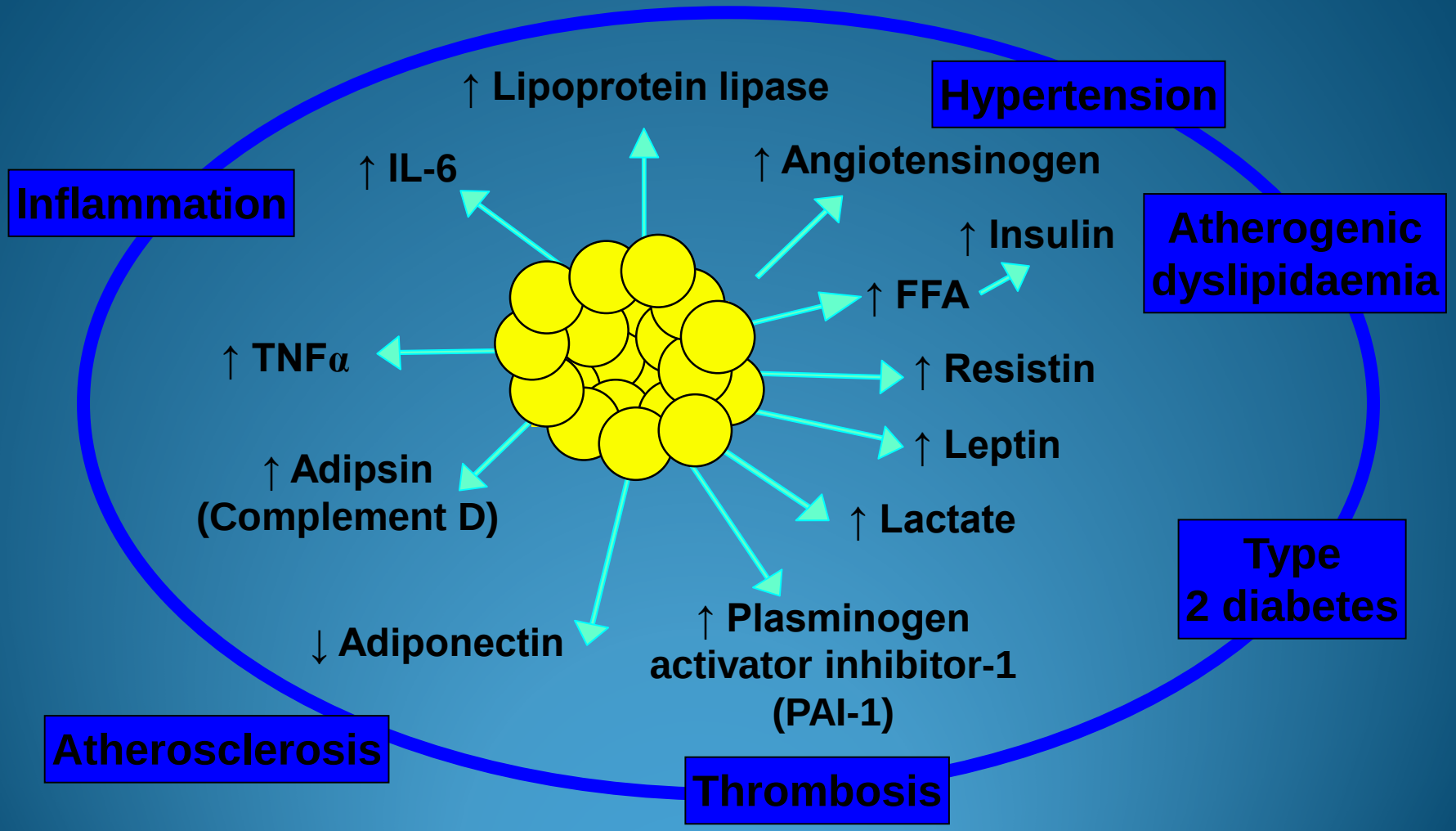
The heaviest members of this cohort (body-mass index of at least 40) had death rates from all cancers combined that were 52 percent higher (for men) and 62 percent higher (for women) than the rates in men and women of normal weight.

In both men and women, body-mass index was also significantly associated with higher rates of death due to cancer of the esophagus, colon and rectum, liver, gallbladder, pancreas, and kidney; the same was true for death due to non-Hodgkin's lymphoma and multiple myeloma. Significant trends of increasing risk with higher body-mass-index values were observed for death from cancers of the stomach and prostate in men and for death from cancers of the breast, uterus, cervix, and ovary in women.

Conclusions. Increased body weight was associated with increased death rates for all cancers combined and for cancers at multiple specific sites.

The New England Journal of Medicine, 348: 1625-1638, 2003

Adverse cardiometabolic effects of products of adipocytes



Lyon 2003; Trayhurn et al 2004; Eckel et al 2005

TNF-α downregulates eNOS expression and mitochondrial biogenesis in fat and muscle of obese rodents

Alessandra Valerio,[1] Annalisa Cardile,[1,2] Valeria Cozzi,[1,2] Renata Bracale,[1,2,3] Laura Tedesco,[1,2,4] Addolorata Pisconti,[2,5] Letizia Palomba,[6] Orazio Cantoni,[6] Emilio Clementi,[2,5,7] Salvador Moncada,[8] Michele O. Carruba,[1,4] and Enzo Nisoli[1,4]

[1]Integrated Laboratories Network, Center for Study and Research on Obesity, Department of Pharmacology, School of Medicine, University of Milan, Milan, Italy. [2]Department of Preclinical Sciences, University of Milan, Milan, Italy. [3]CEINGE Biotecnologie Avanzate, Naples, Italy. [4]Istituto Auxologico Italiano, Milan, Italy. [5]Stem Cell Research Institute, San Raffaele Scientific Institute, Milan, Italy. [6]Istituto di Farmacologia e Farmacognosia, University of Urbino "Carlo Bo," Urbino, Italy. [7]Eugenio Medea Scientific Institute, Lecco, Italy. [8]Wolfson Institute for Biomedical Research, University College London, London, United Kingdom.

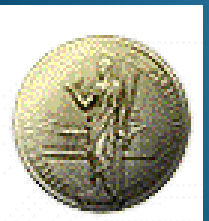
The Journal of Clinical Investigation

Mitochondrial Biogenesis in Mammals: The Role of Endogenous Nitric Oxide

Enzo Nisoli,[1,2*†] Emilio Clementi,[3,4*] Clara Paolucci,[3] Valeria Cozzi,[1] Cristina Tonello,[1] Clara Sciorati,[3] Renata Bracale,[1] Alessandra Valerio,[5] Maura Francolini,[6] Salvador Moncada,[7] Michele O. Carruba[1,2]

Nitric oxide was found to trigger mitochondrial biogenesis in cells as diverse as brown adipocytes and 3T3-L1, U937, and HeLa cells. This effect of nitric oxide was dependent on guanosine 3′,5′-monophosphate (cGMP) and was mediated by the induction of peroxisome proliferator–activated receptor γ coactivator 1α, a master regulator of mitochondrial biogenesis. Moreover, the mitochondrial biogenesis induced by exposure to cold was markedly reduced in brown adipose tissue of endothelial nitric oxide synthase null-mutant ($eNOS^{-/-}$) mice, which had a reduced metabolic rate and accelerated weight gain as compared to wild-type mice. Thus, a nitric oxide–cGMP–dependent pathway controls mitochondrial biogenesis and body energy balance.

Science 299: 896-899, 2003



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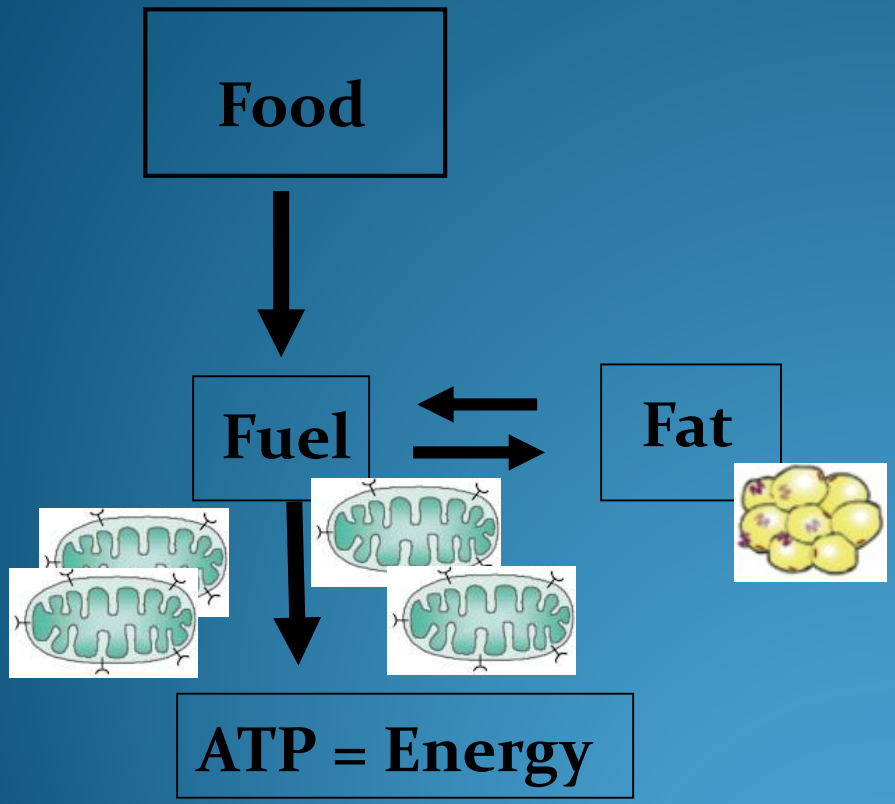
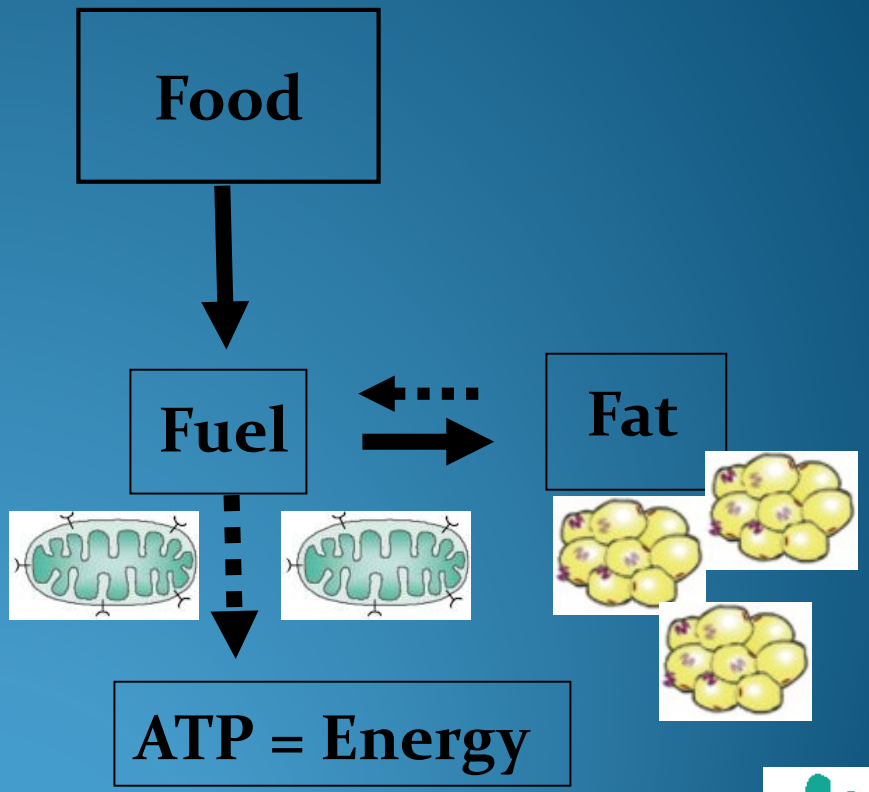
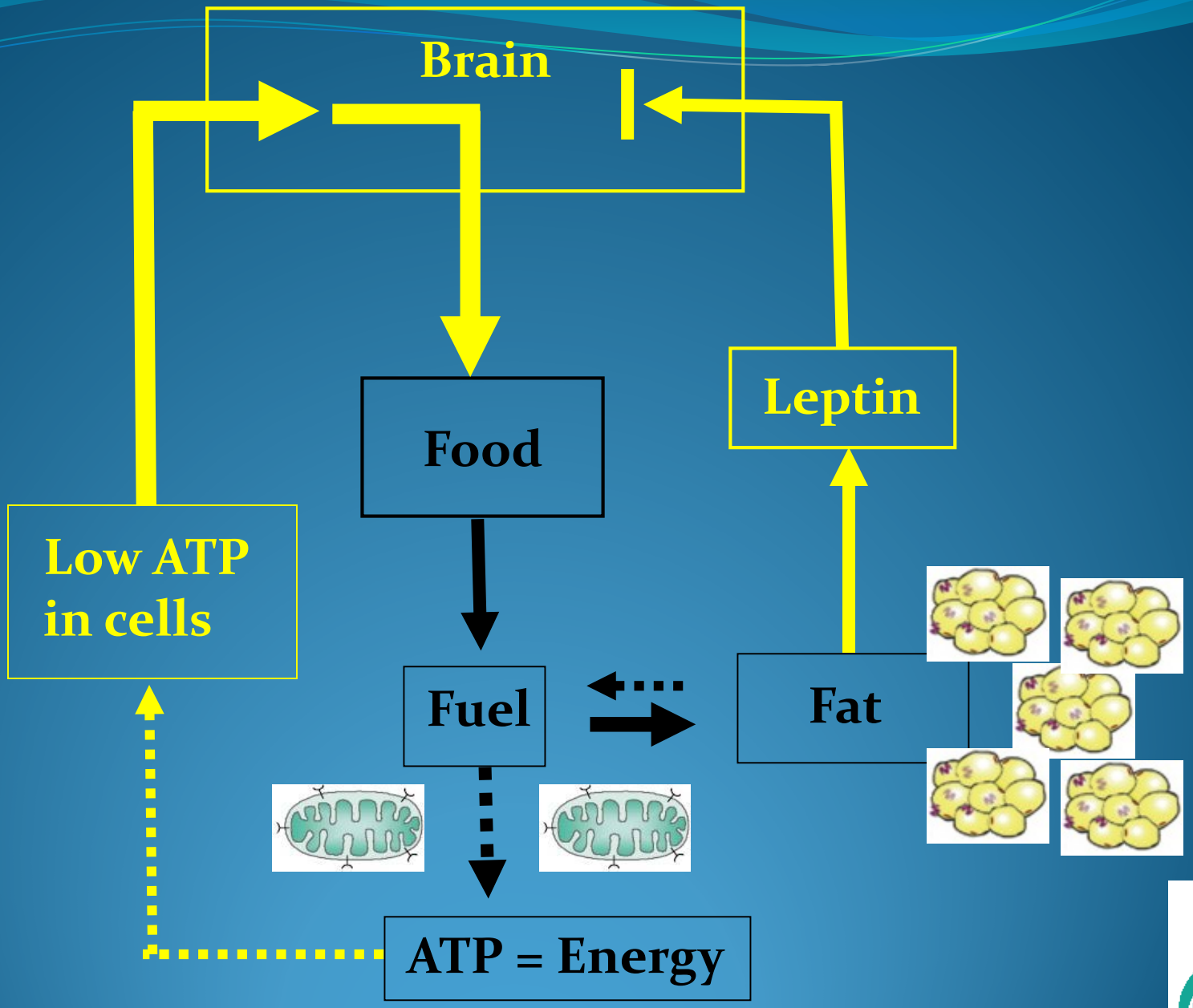
Decreased energy levels can cause and sustain obesity



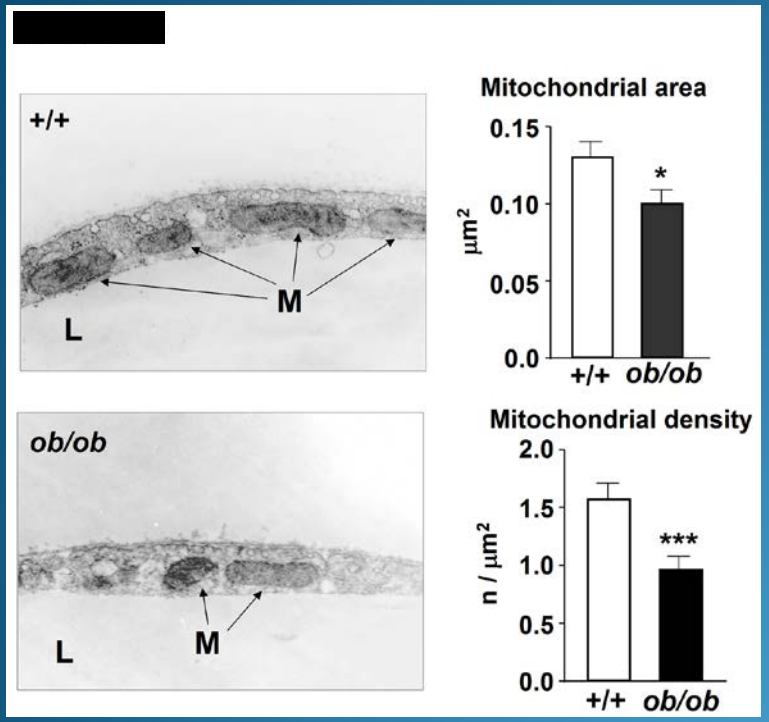


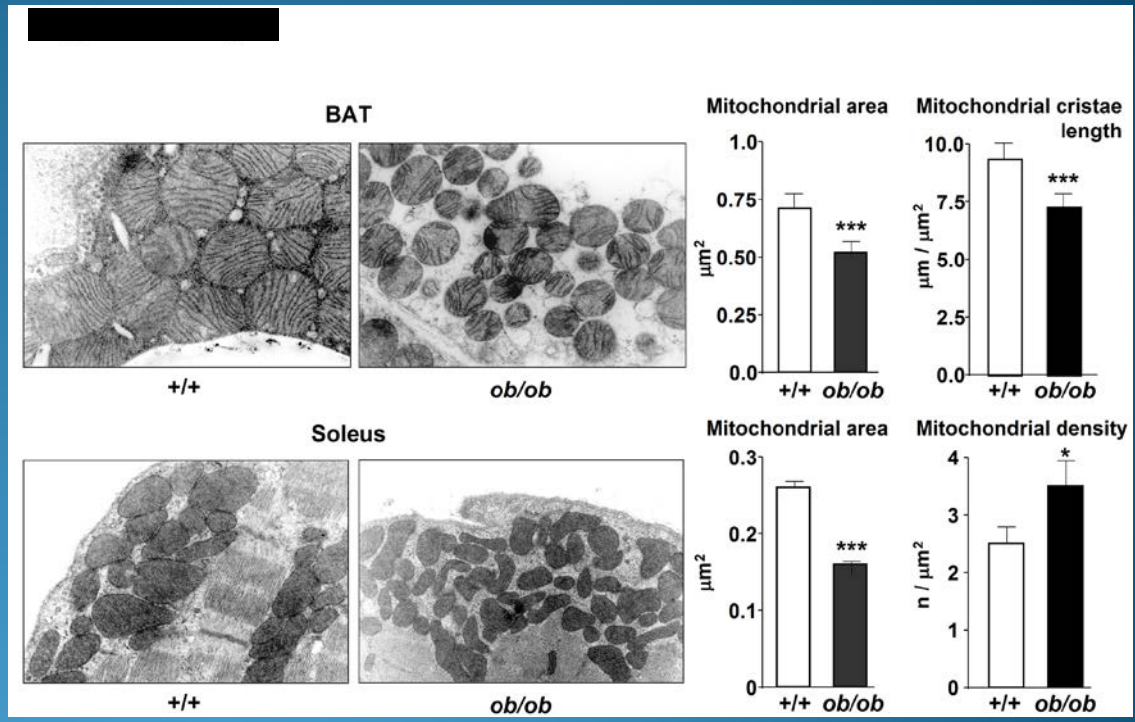
Healthy subject

Obese subject


Brain
Food
Leptin
Low ATP
in cells
Fuel
Fat
ATP = Energy

Electron microscopy analysis of WAT, BAT and muscle in *ob/ob* mice





Valerio et al., J. Clin. Invest., Oct. 2006

Calorie Restriction Promotes Mitochondrial Biogenesis by Inducing the Expression of eNOS

Enzo Nisoli,[1,2*] Cristina Tonello,[1] Annalisa Cardile,[1]
Valeria Cozzi,[1] Renata Bracale,[1] Laura Tedesco,[1]
Sestina Falcone,[1,3] Alessandra Valerio,[1] Orazio Cantoni,[4]
Emilio Clementi,[1,3,5] Salvador Moncada,[6] Michele O. Carruba[1,2]

Calorie restriction extends life span in organisms ranging from yeast to mammals. Here, we report that calorie restriction for either 3 or 12 months induced endothelial nitric oxide synthase (eNOS) expression and 3′,5′-cyclic guanosine monophosphate formation in various tissues of male mice. This was accompanied by mitochondrial biogenesis, with increased oxygen consumption and adenosine triphosphate production, and an enhanced expression of sirtuin 1. These effects were strongly attenuated in eNOS null-mutant mice. Thus, nitric oxide plays a fundamental role in the processes induced by calorie restriction and may be involved in the extension of life span in mammals.

Sience October 14, 2005

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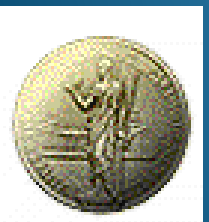
Skeletal muscle mitochondrial DNA content in exercising humans

A. Marcuello,[1] J. González-Alonso,[2] J. A. L. Calbet,[3]
R. Damsgaard,[2] M. J. López-Pérez,[1] and C. Díez-Sánchez[1]

[1]*Department of Biochemistry, Molecular and Cell Biology, University of Zaragoza, Zaragoza, Spain;*
[2]*The Copenhagen Muscle Research Centre, Rigshospitalet, University of Copenhagen, Denmark; and*
[3]*Department of Physical Education, University of Las Palmas de Gran Canaria, Canary Islands, Spain*

Several weeks of intense endurance training enhances mitochondrial biogenesis in humans.

***J Appl Physiol* 99: 1372–1377, 2005**



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Quindi? Stile di vita!

Abitudini alimentari

e

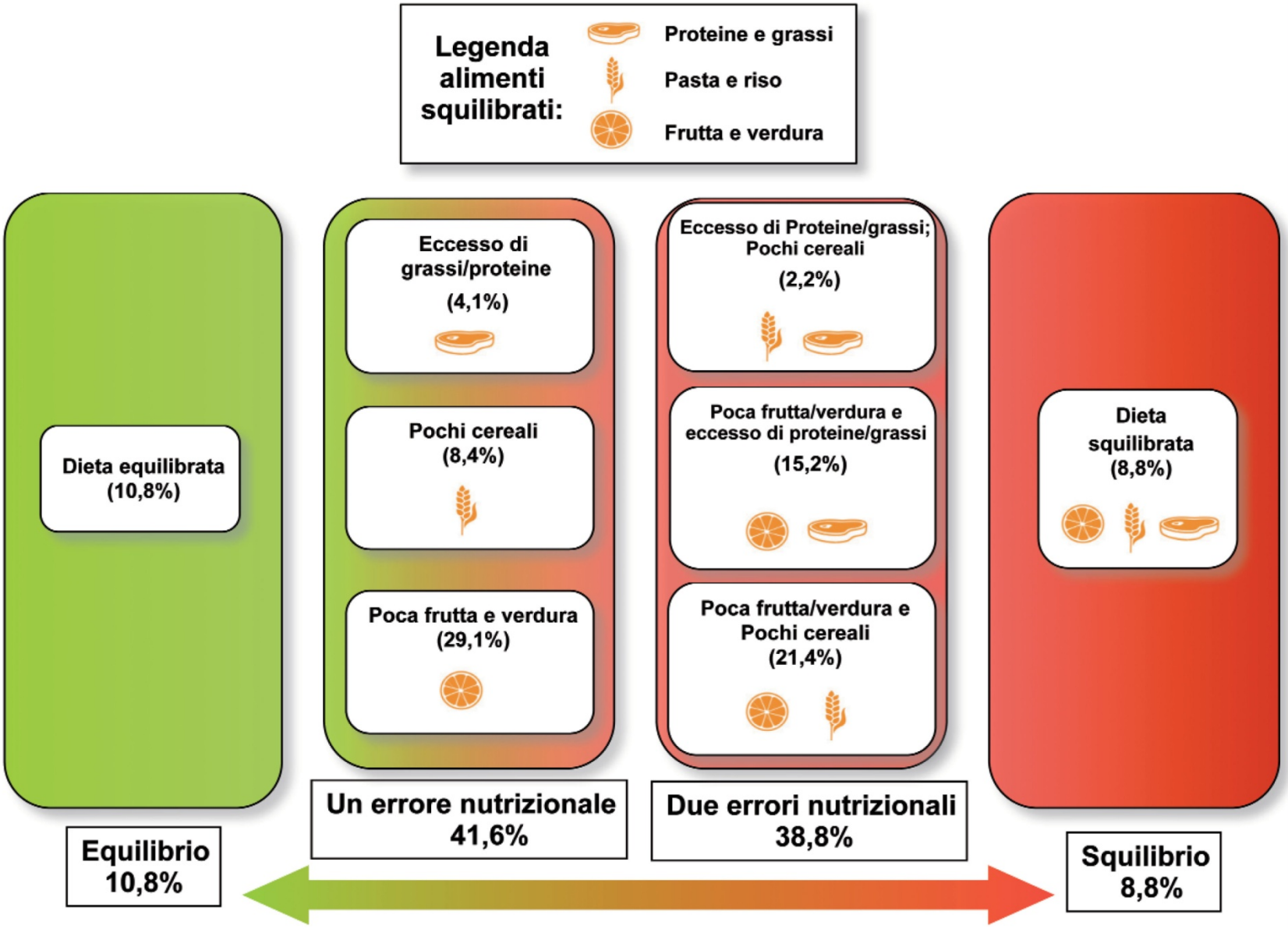
Attività fisica

Tipologie di comportamento alimentare e criteri di valutazione

TIPOLOGIA	FRUTTA E VERDURA	PASTA E RISO	PROTEINE E GRASSI
Virtuosi			
Sbilanciati proteine			
Sbilanciati cereali			
Sbilanciati frutta			
Disordinati proteine e cereali			
Disordinati proteine e frutta			
Disordinati frutta e cereali			
Globalmente disordinati			

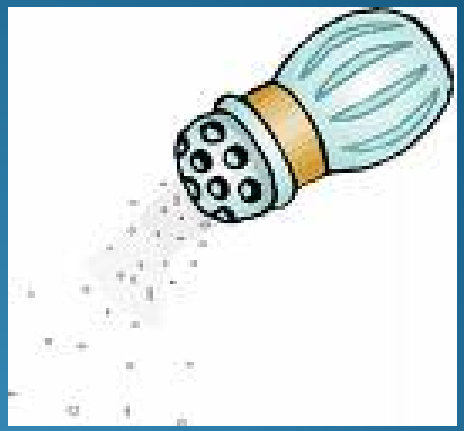
Legenda:

- Comportamento corretto
- Comportamento non corretto


Legenda alimenti squilibrati:
Proteine e grassi
Pasta e riso
Frutta e verdura
Dieta equilibrata (10,8%)
Eccesso di grassi/proteine (4,1%)
Pochi cereali (8,4%)
Poca frutta e verdura (29,1%)
Eccesso di Proteine/grassi; Pochi cereali (2,2%)
Poca frutta/verdura e eccesso di proteine/grassi (15,2%)
Poca frutta/verdura e Pochi cereali (21,4%)
Dieta squilibrata (8,8%)
Equilibrio 10,8%
Un errore nutrizionale 41,6%
Due errori nutrizionali 38,8%
Squilibrio 8,8%

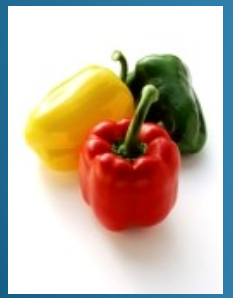
ECCESSI

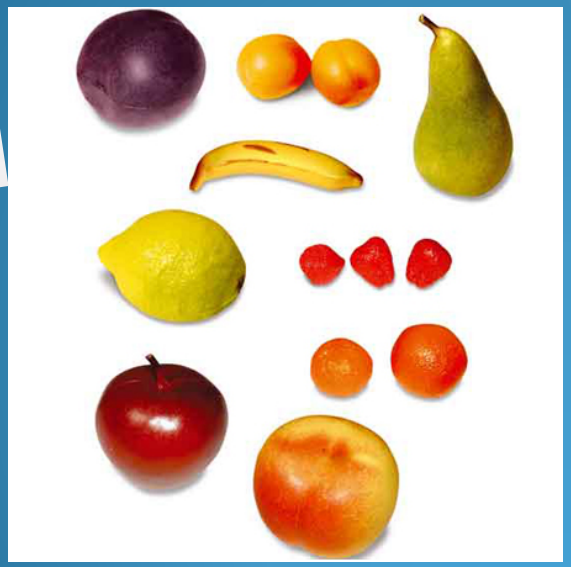
- Zuccheri semplici
- Grassi saturi
- Sale
- Proteine di origine animale
- Porzioni troppo abbondanti
- Spuntini troppo frequenti

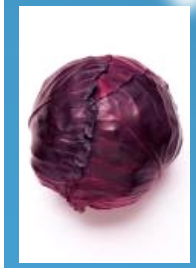


CARENZE

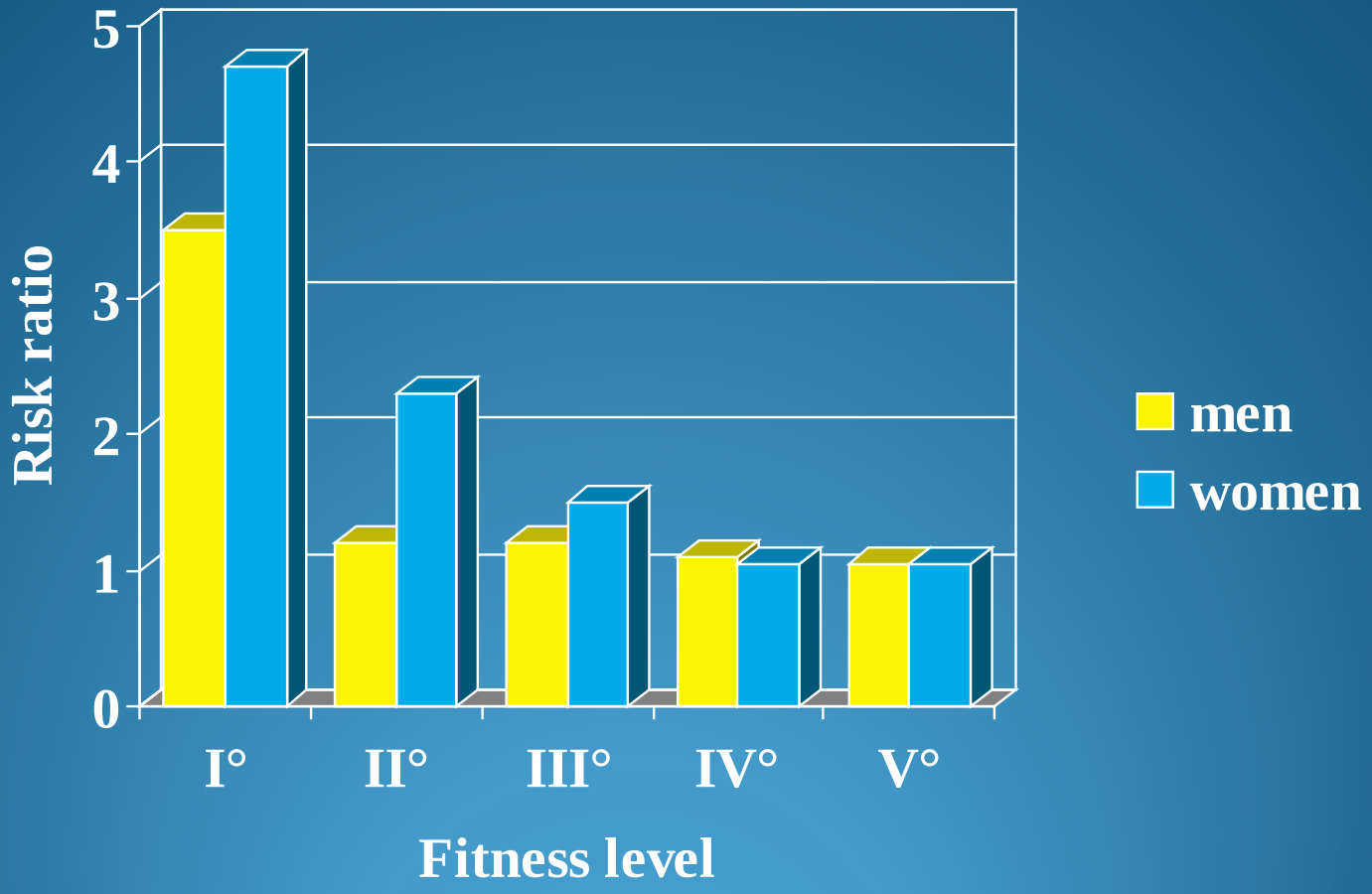
- Frutta e verdura
- Fibre
- Principi nutritivi fondamentali
- Carboidrati complessi







Livello di attività fisica e rischio di mortalità



Blair et al, 1989

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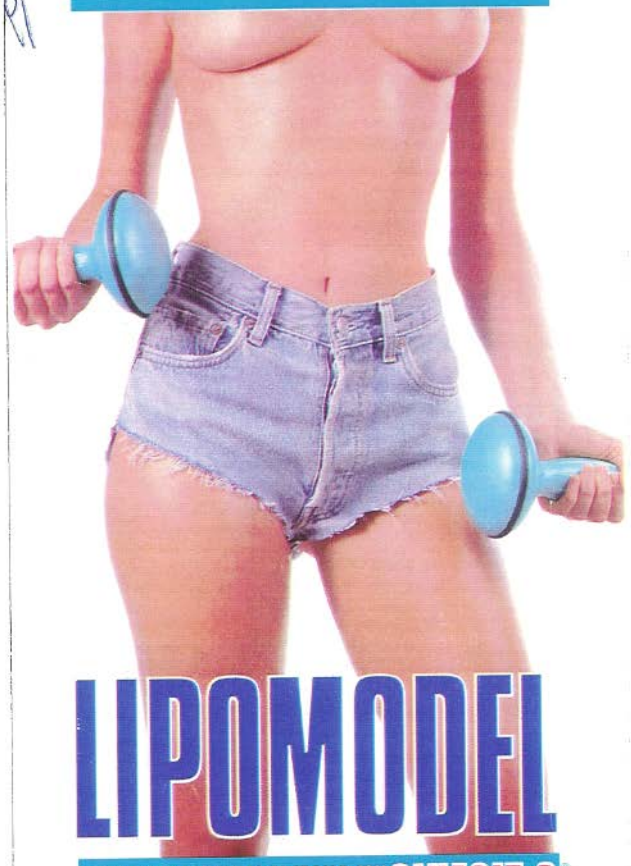
DIETA + PALESTRA =



LIPOMODEL

INTEGRATORE DIETETICO DI CROMO CON SINECIT 6®

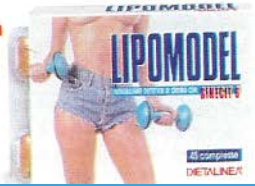
1 AZIONE DIETA

Controlla il senso dell'appetito.

Aumenta la termogenesi cellulare con riduzione della massa grassa.

2 AZIONE PALESTRA

Stimola la sintesi delle proteine, con conseguente aumento della massa magra.



DIETALINEA
Salute e bellezza del corpo

P.N. PRODOTTI NATURALI S.r.l.
Tel. 01072.02.15

Not. Min. San.