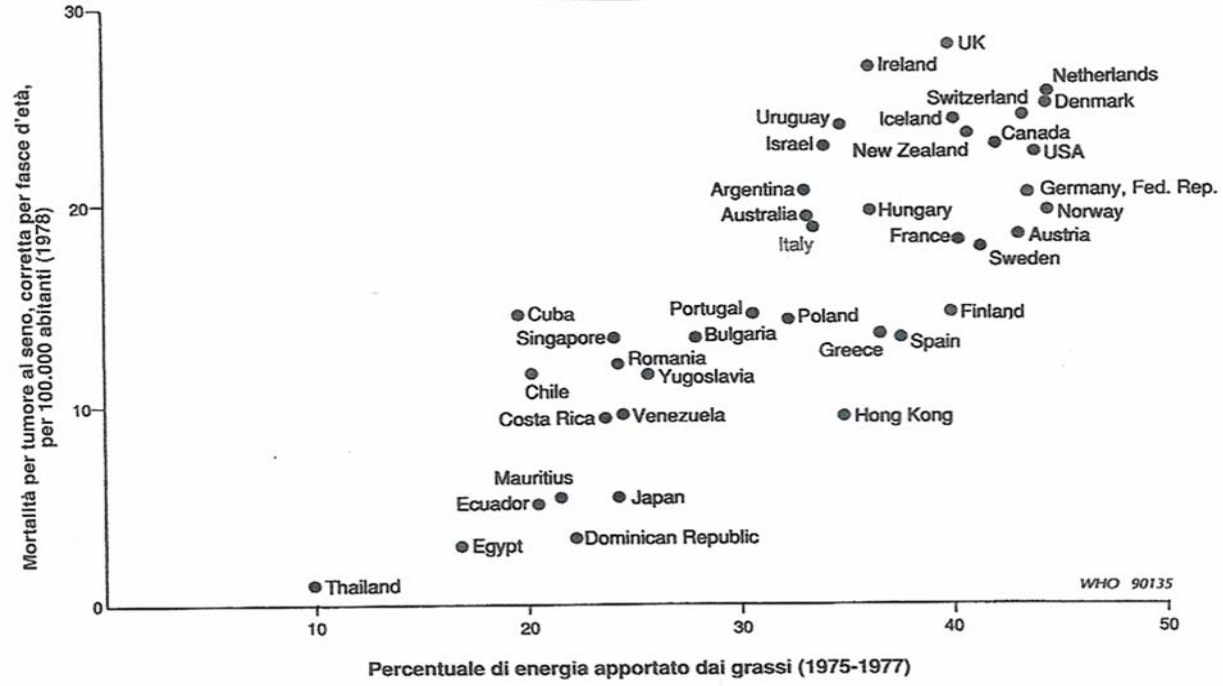
CONVEGNO: *Alimentazione e Salute*: un approccio multidisciplinare
09 maggio 2008

STILI DI VITA ALIMENTAZIONE OBESITA' E SALUTE

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

- From Farm to ForkMalattie cardiovascolari e ischemiche
- Obesità
- 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.*

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.

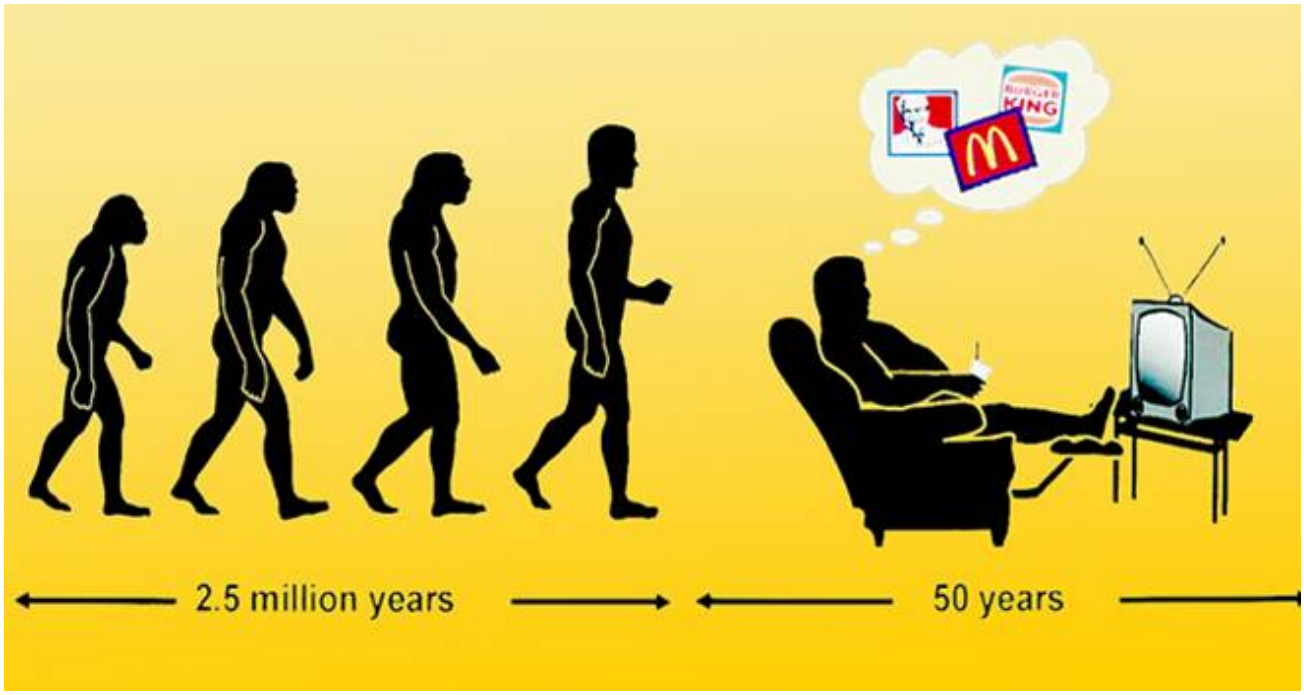
The heaviest members of this cohort (body-mass index of at least 40) had death rates from all cancers combined that were 52 percent higher (for men) and 62 percent higher (for women) than the rates in men and women of normal weight.

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

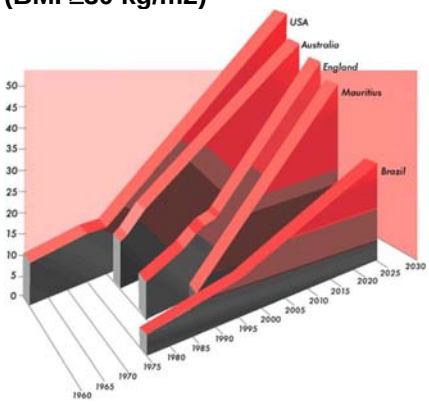
L'evoluzione della specie



Sovrappeso/Obesità - l'epidemia *mondiale*

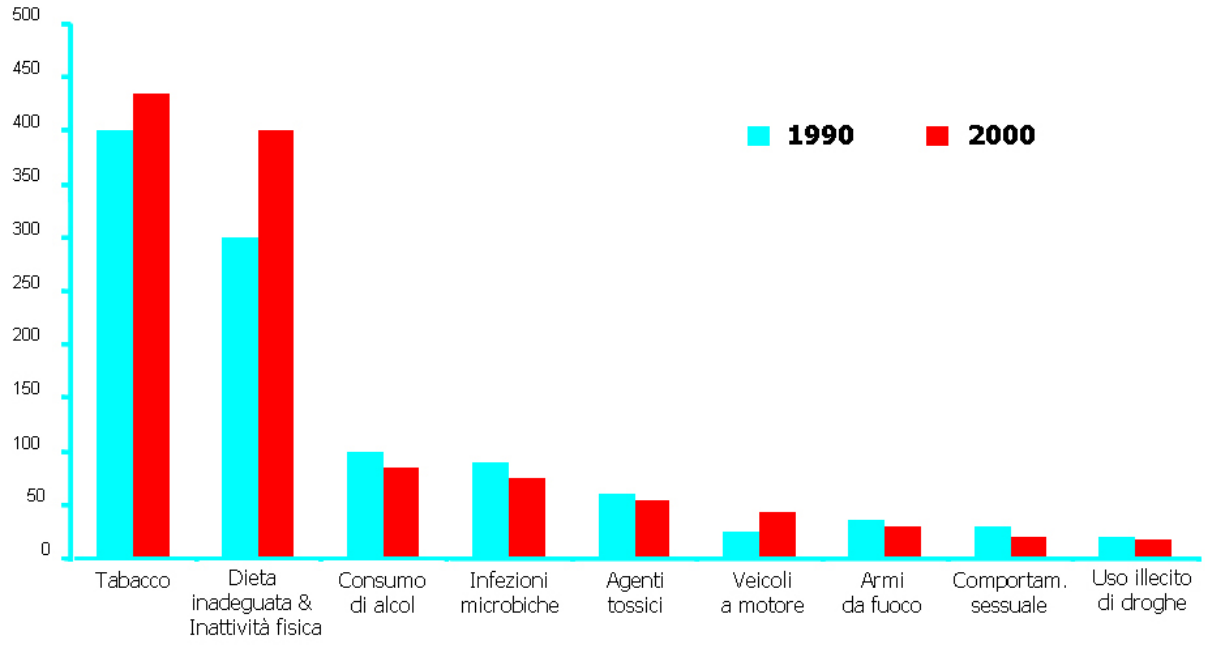
- >1 miliardo di adulti nel mondo erano in sovrappeso
- (BMI >25 kg/m2) nel 20021
- Almeno 300 milioni sono obesi (BMI >30 kg/m2)[2]
- Ragioni dell'incremento della prevalenza: (vd. nota 2)
  - Abbondanza di cibo
  - Livelli più bassi di attività fisica

% di Popolazione obesa (BMI ≥30 kg/m2)[1]



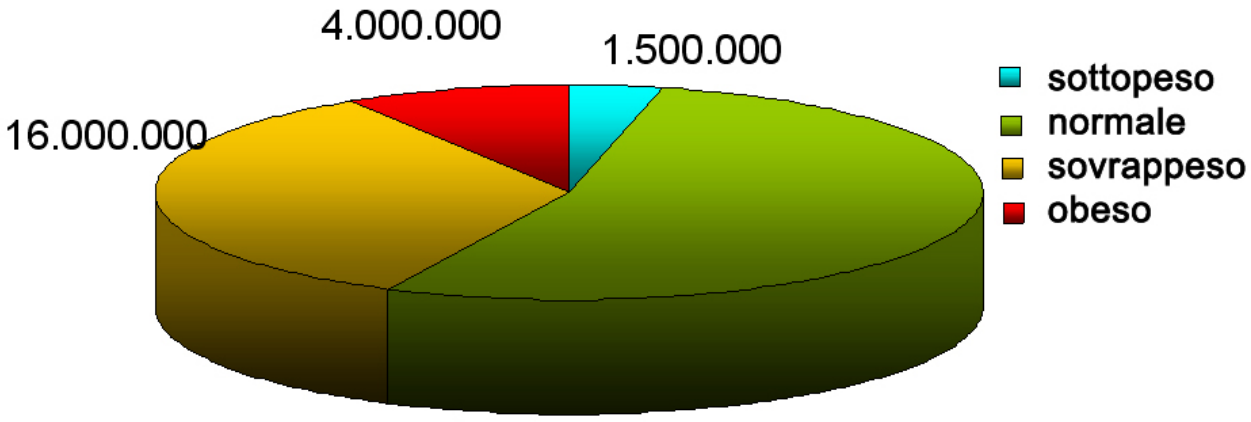
[1] International Obesity Task Force. Available at: http://www.iotf.org. Accessed November 13, 2003.
[2] World Health Organization. Global strategy on diet, physical activity and health, 2003. Available at: http://www.who.int/hpr/NPH/docs/gs_obesity.pdf. Accessed November 11, 2003.

Cause di morte negli U.S.A.



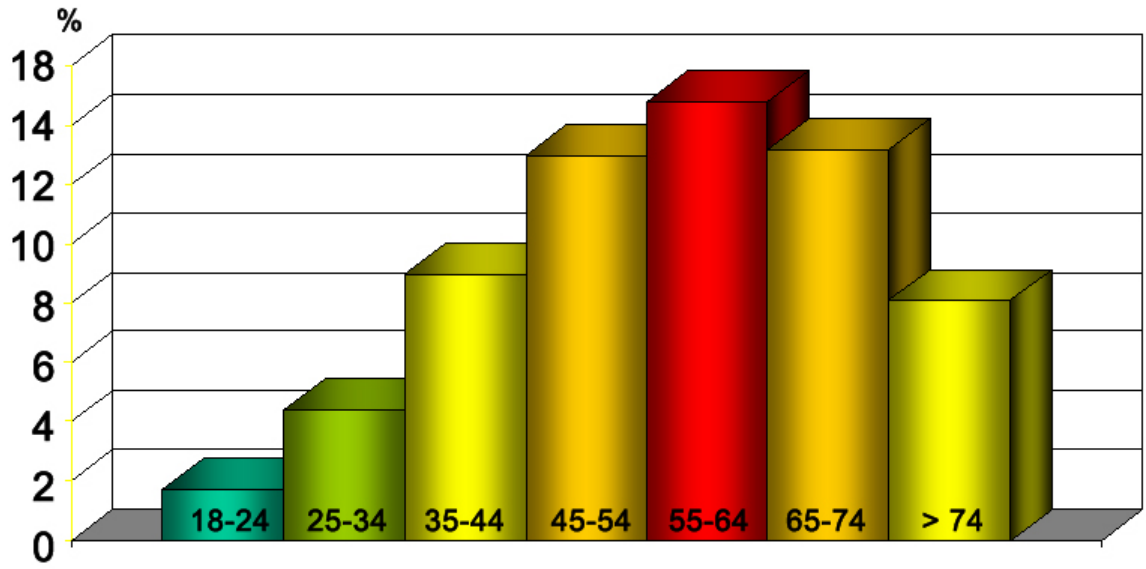
Adapted from Mokdad et al. *JAMA* 2004; 291: 1238-1245

Distribuzione della popolazione italiana nelle varie condizioni di peso



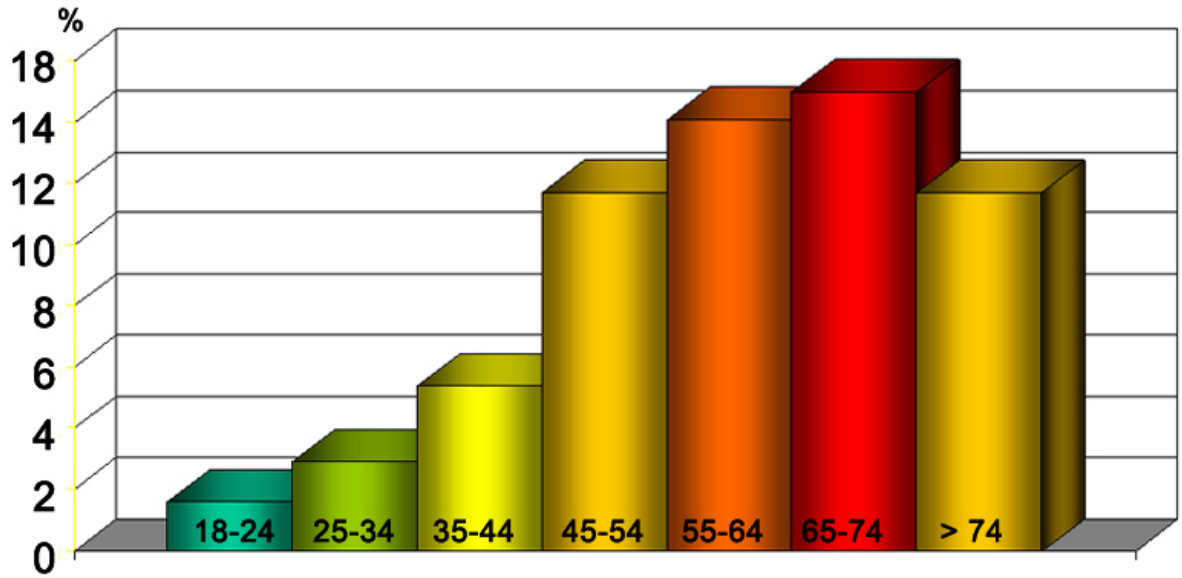
Fonte: ISTAT, 4° Rapporto sull'Obesità in Italia. Istituto Auxologico Italiano, 2002

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



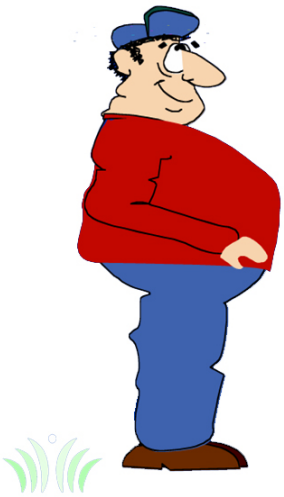
Fonte: ISTAT, 4° Rapporto sull’Obesità in Italia. Istituto Auxologico Italiano, 2002

Prevalenza dell’obesità (IMC>30) in funzione dell’età nelle DONNE



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

L’obesità viene valutata mediante l’Indice di Massa Corporea

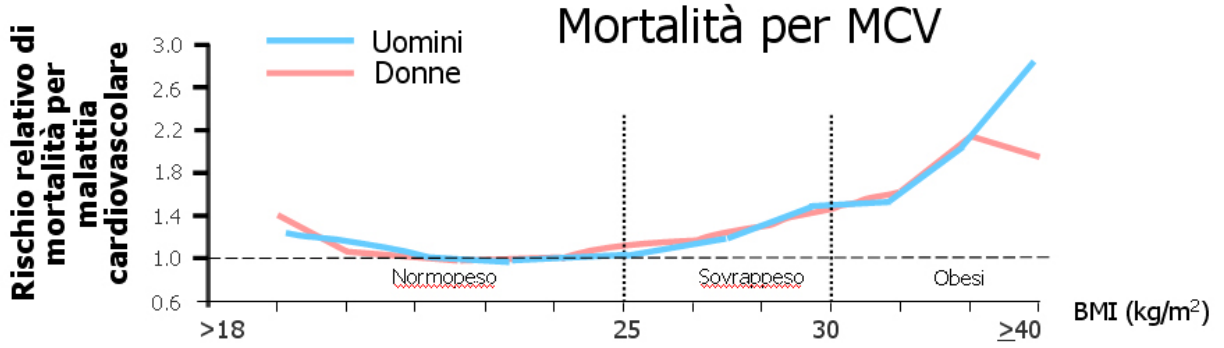


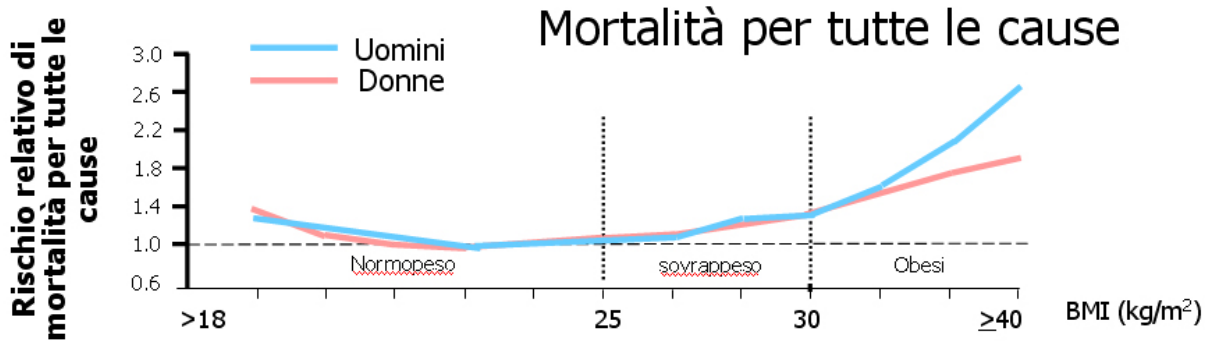
$$BMI = \frac{\text{Peso (kg)}}{\text{Altezza (m}^2\text{)}}$$

Classificazione	BMI (kg/m²)	Rischio di comorbilità
Normopeso	18,5 - 24,9	Nella media
Sovrappeso	25,0 - 29,9	Aumentato
Obesità classe I	30,0 - 34,9	Moderato
Obesità classe II	35,0 - 39,9	Elevato
Obesità classe III	≥ 40,0	Molto elevato

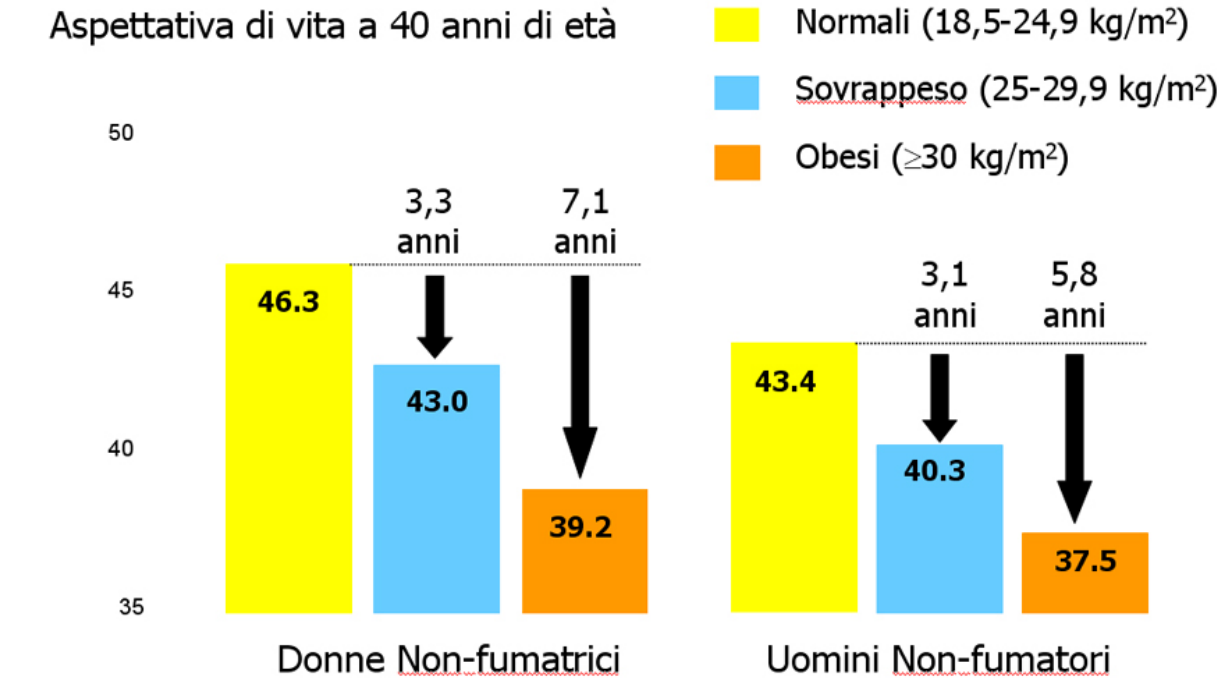
World Health Organization, 1998

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





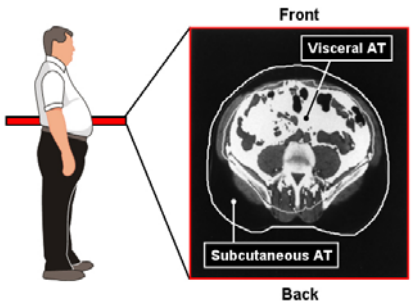
Aspettativa di vita a 40 anni: impatto dell'eccesso di peso corporeo



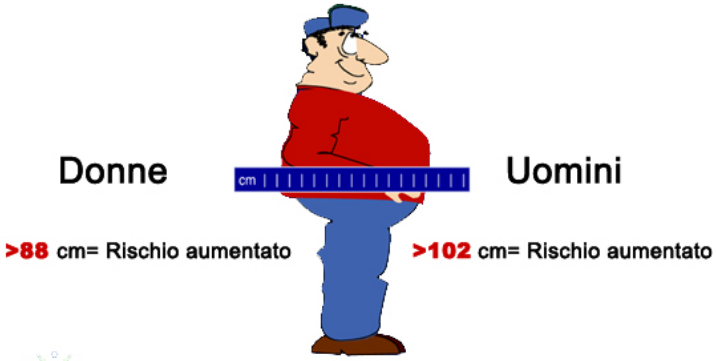
Peeters et al. *Ann Intern Med* 2003; 138: 24-32

Un parametro fondamentale: la circonferenza addominale

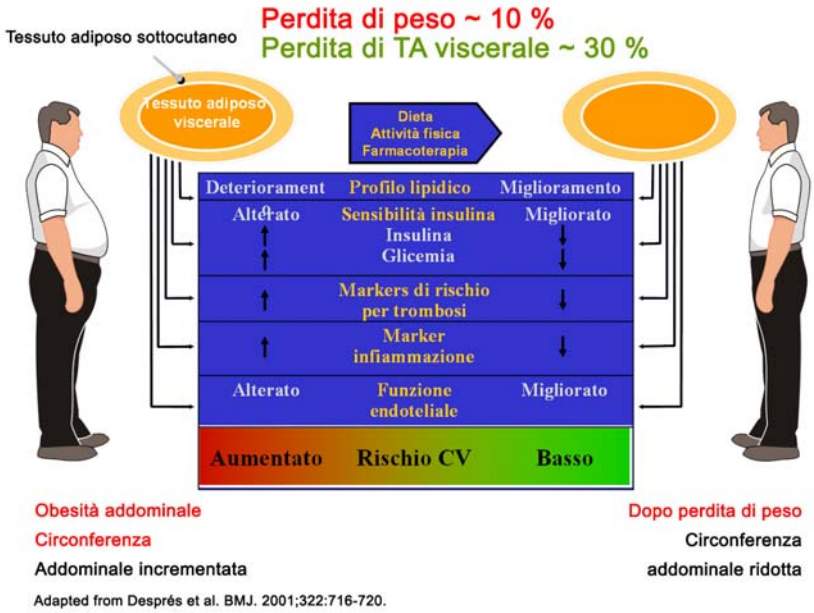
Intra-Abdominal (Visceral) Fat The dangerous inner fat!



La circonferenza vita è un indicatore del tessuto adipose viscerale



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

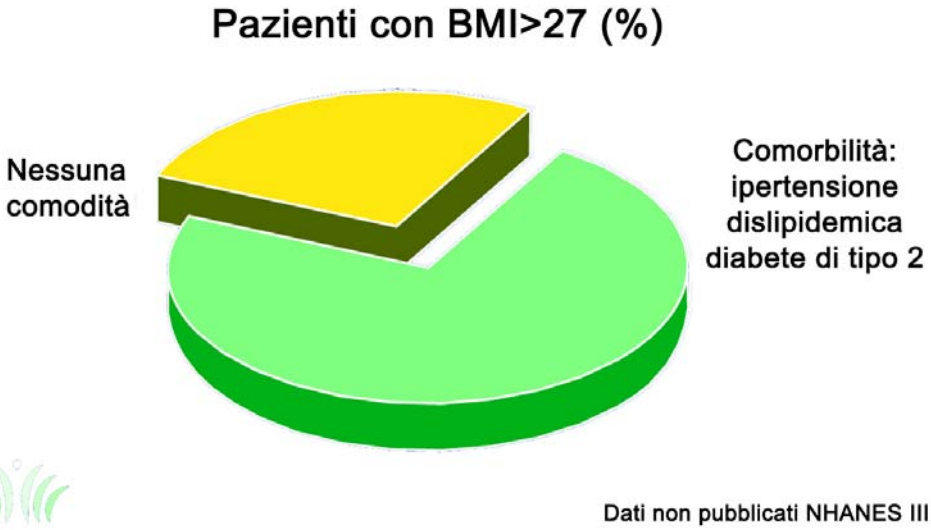


Obesità addominale
Circonferenza
Addominale incrementata

Dopo perdita di peso
Circonferenza
addominale ridotta

Adapted from Després et al. BMJ. 2001;322:716-720.

BMI e comorbità



Dati non pubblicati NHANES III

Sindrome metabolica

Reaven GM Annu Rev.Med 1993; 44 121-31

Studio SPESA: composizione dei costi sanitari dell'Obesità Tot 22,8 mld Euro/anno

Voce di costo	Percentuale
Ospedalizzazioni	64%
Diagnostica	12%
Farmaci	7%
Visite	6%
Altro	11%

Elaborazioni: Centro di Farmacoeconomia

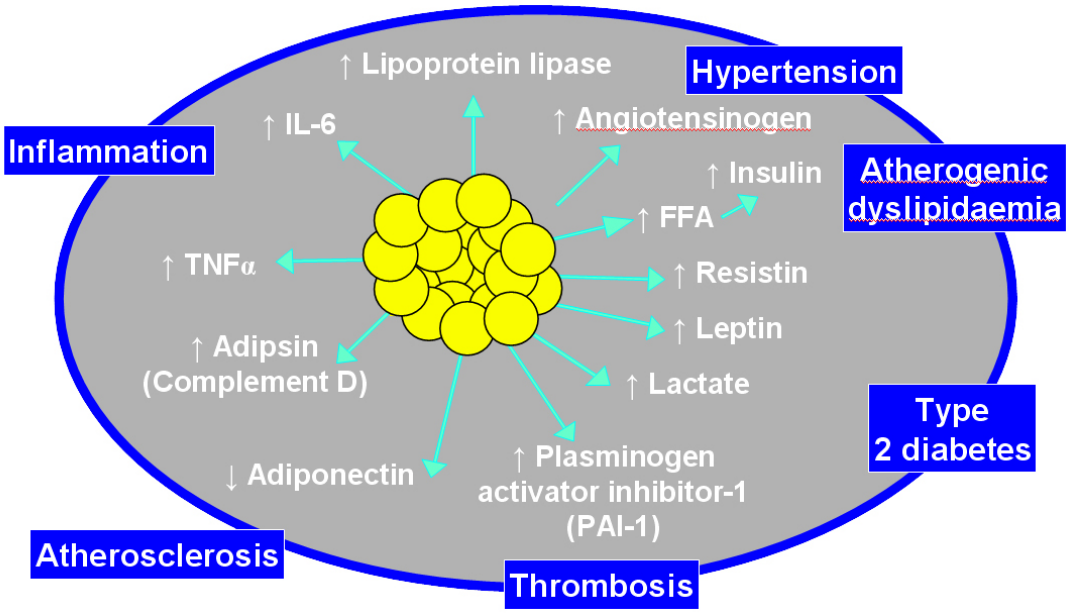
Impatto economico annuo dell'obesità

BMI	Costo	% pop	Totale
25 - 30	**878**	**35**	**16 mld**
30 - 40	**1653**	**9**	**6 mld**
40 o più	**2220**	**1**	**1 mld**

TOTALE **23 mld**

Elaborazioni: Centro di Farmacoeconomia

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 Invesigation

Mitochondrial Biogenesis in Mammals: The Role of Endogenous Nitric Oxide

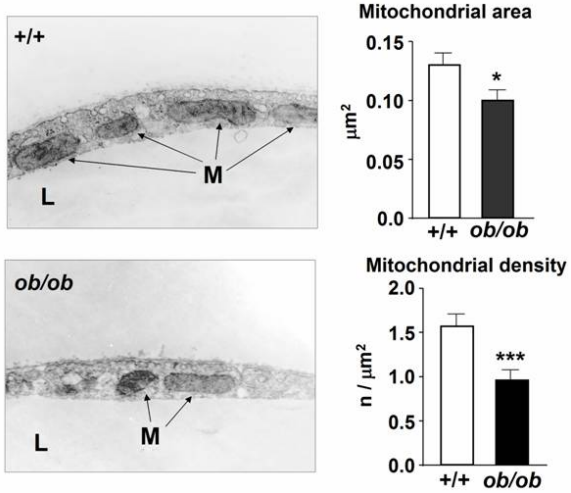
Enzo Nisoli,[1,2*†] Emilio Clementi,[3,4*] Clara Paolucci,[3] Valeria Cozzi,[1] Cristina Tonello,[1] Clara Sciorati,[3] Renata Bracale,[1] Alessandra Valerio,[5] Maura Francolini,[6] Salvador Moncada,[7] Michele O. Carruba[1,2]

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.

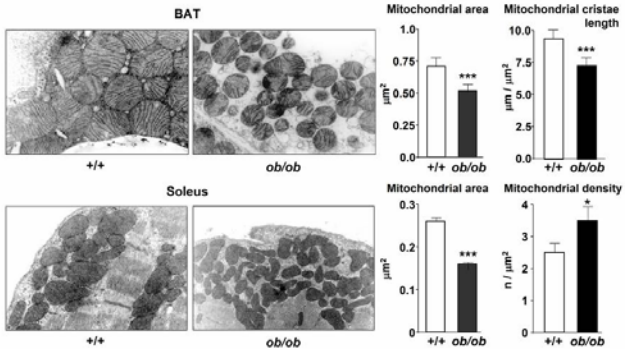
Science 299: 896-899, 2003

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

Nisoli Fig. 3



Supplemental Fig. 4



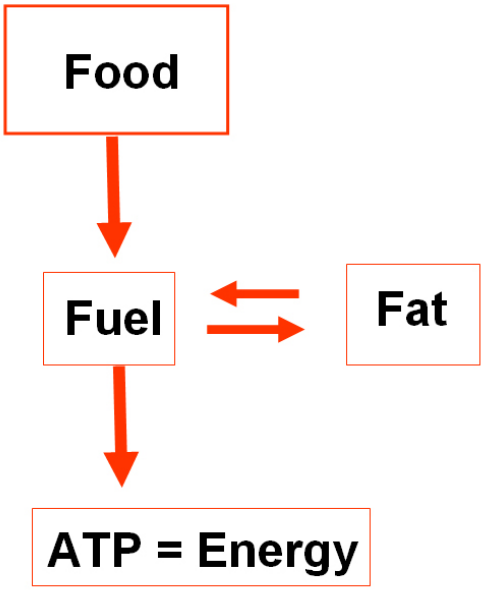
Valerio et al., J. Clin. Invest., Oct. 2006

Visceral fat depot in eNOS-/- *vs.* wild-type mice

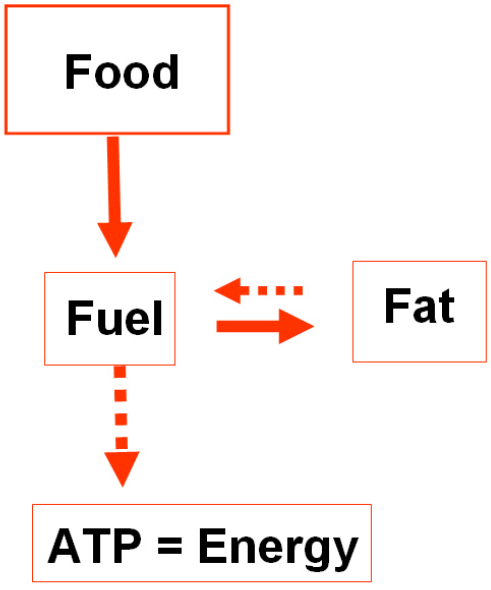
wt

eNOS-/-

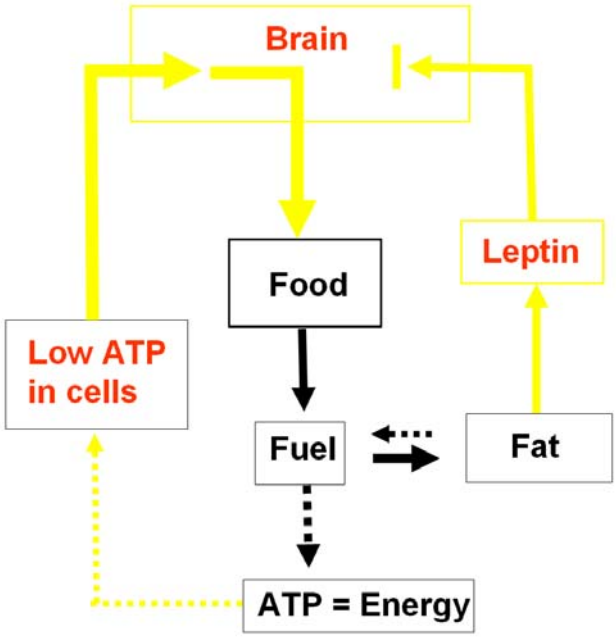
Decreased energy levels can cause and sustain obesity



Healthy subject



Obese subject



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

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

Quindi? Stile di vita!
Abitudini alimentari e Attività fisica

Adherence to a Mediterranean Diet and Survival in a Greek Population

Antonia Trichopoulou, M.D., Tina Costacou, Ph.D., Christina Bamia, Ph.D., and Dimitrios Trichopoulos, M.D.

We conducted a population-based, prospective investigation involving 22,043 adults in Greece who completed an extensive, validated, food-frequency questionnaire at base line.

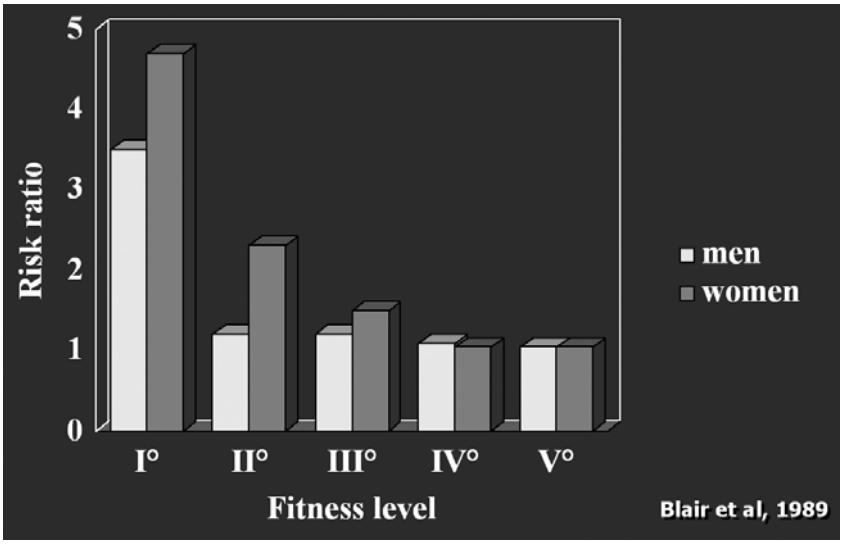
During a median of 44 months of follow-up, there were 275 deaths. A higher degree of adherence to the Mediterranean diet was associated with a reduction in total mortality.

An inverse association with greater adherence to this diet was evident for both death due to coronary heart disease and death due to cancer.

Conclusions. Greater adherence to the traditional Mediterranean diet is associated with a significant reduction in total mortality.

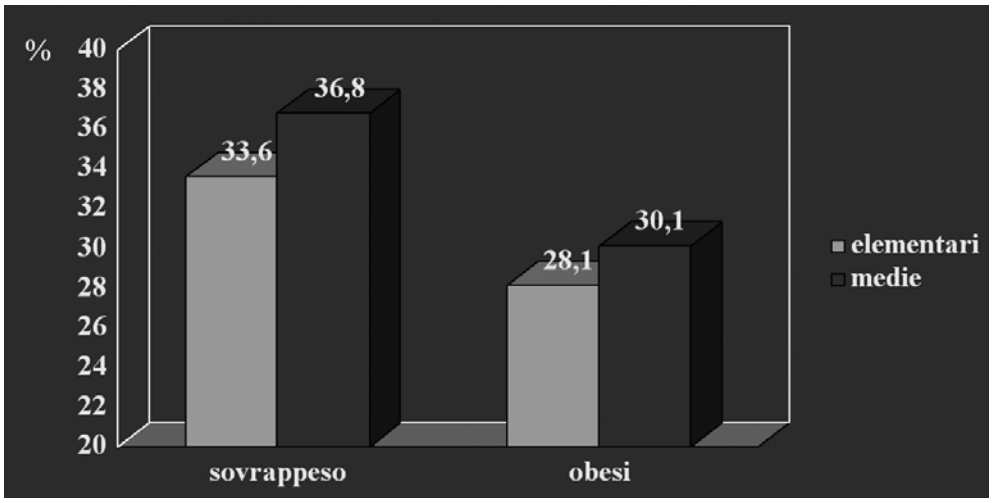
The New England Journal of Medicine, 348: 2599-2608, 2003

Livello di attività fisica e rischio di mortalità

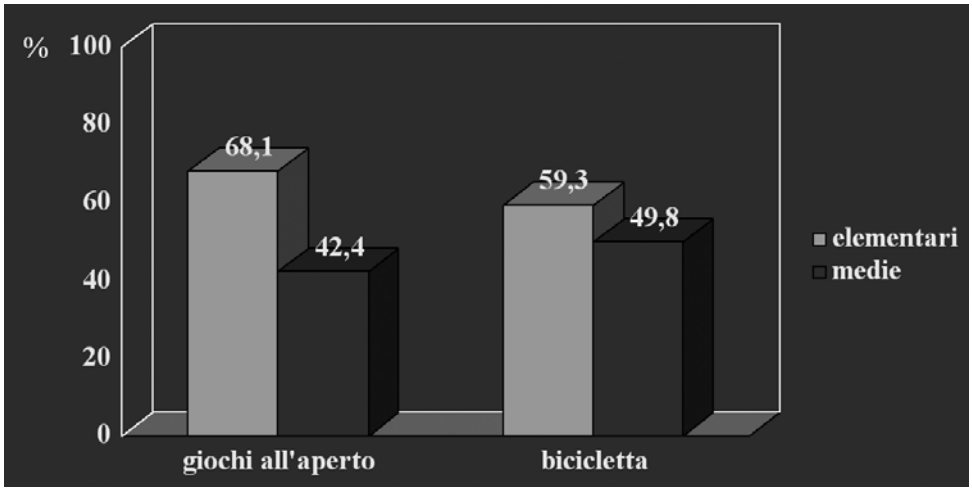


CAMPAGNA STAMPA sulla CORRETTA ALIMENTAZIONE IMMAGINI

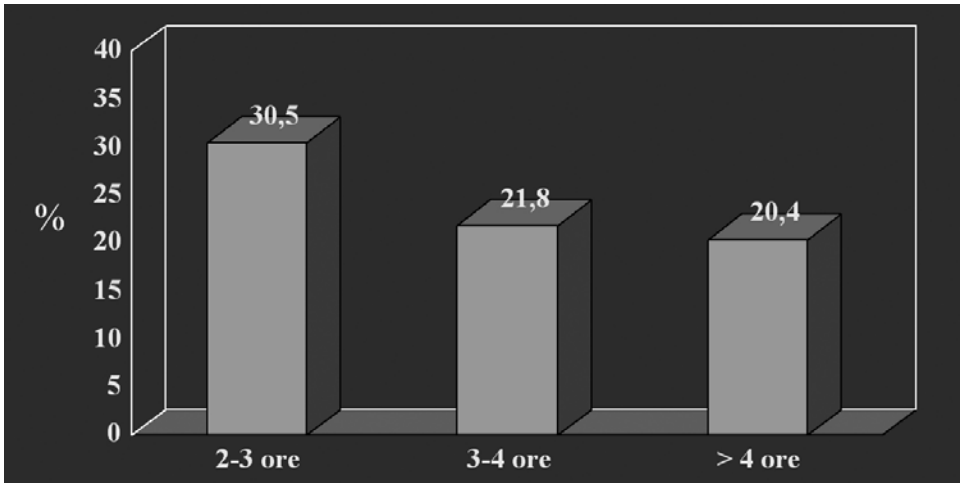
Prevalenza di sovrappeso e obesità in 1280 ragazzi di Legnago (2001,Vr)



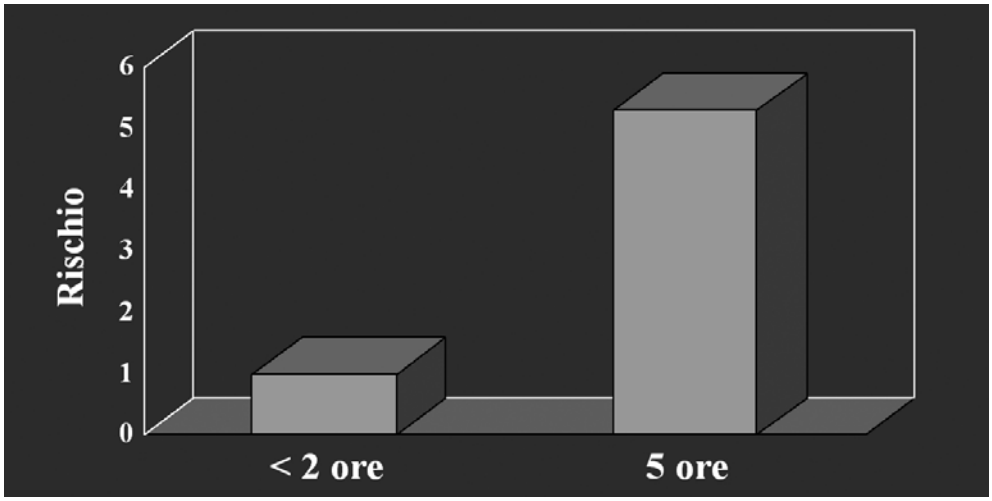
L'attività fisica in 1280 ragazzi di Legnago *(2001,Vr)*



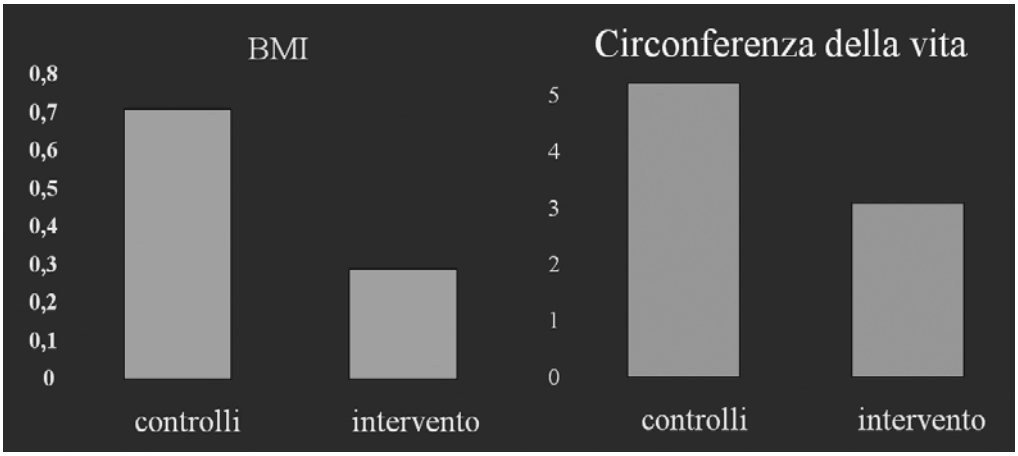
Tempo passato quotidianamente alla TV da ragazzi 6-14 anni *ISTAT, 2001*



Tempo quotidiano dedicato alla TV e rischio di obesità in bambini di 6-10 anni
Dati pareggiati per livello socioeconomico



Effetto della riduzione del tempo dedicato alla Tv sull'aumento del BMI e della Circonferenza della vita in studenti di 3° e 4° elementare



Robinson 1999

Michele O. Carruba
University of Milan, Italy
Department of Pharmacology, Chemotherapy and Medical Toxicology
CENTER FOR STUDY AND RESEARCH ON OBESITY