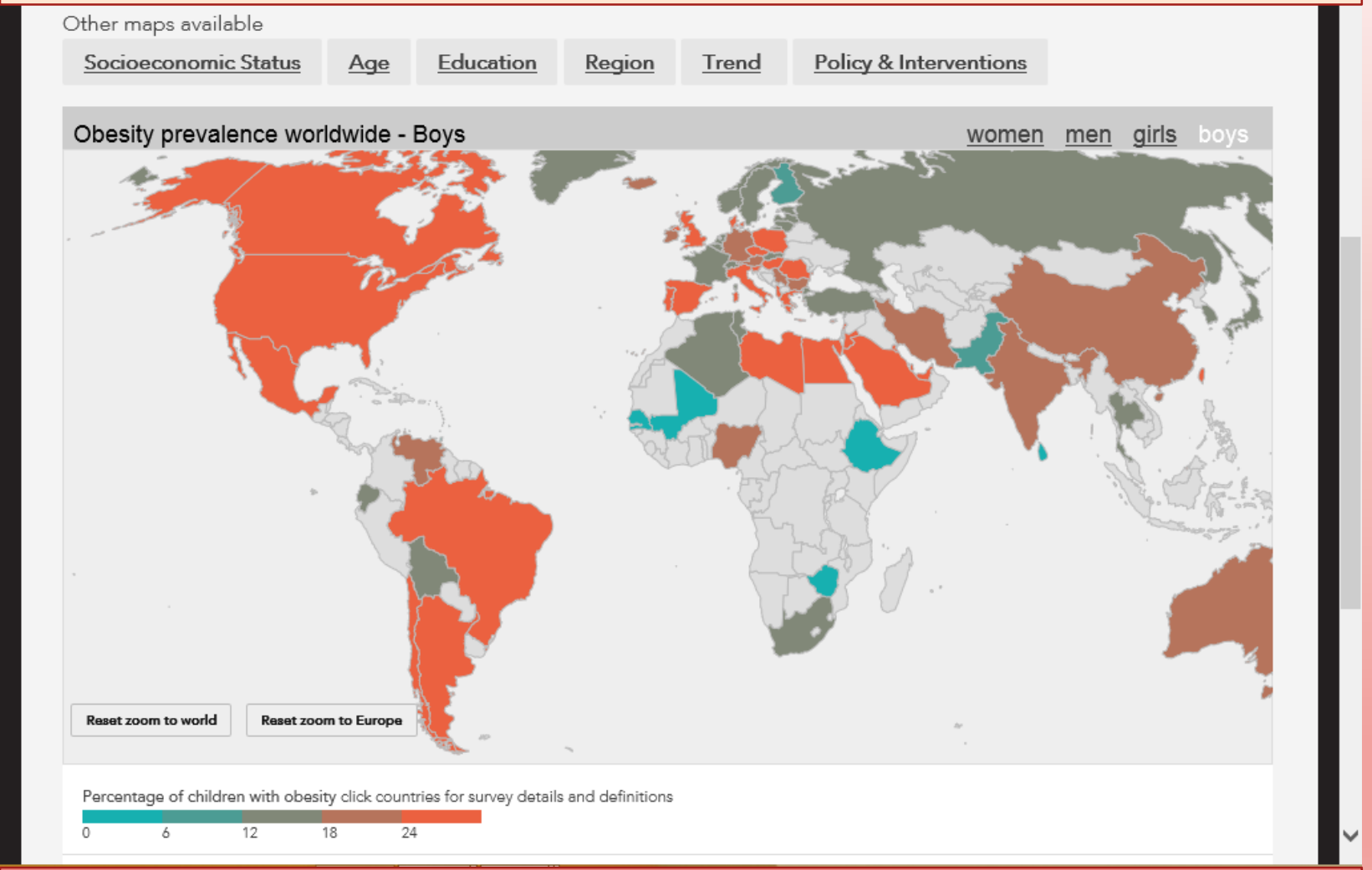
L'IMPORTANZA DEL MONDO DEI GIOVANI: DALL'INFANZIAALL'ADOLESCENZA.
Un confronto tra due realtà: Italia e Argentina.
El Bolson, Rio Negro, Argentina
27 – 29 aprile 2016

Obesità in età evolutiva
G. Farello – Clinica Pediatrica
Università dell'Aquila



ARGENTINA OBESITY INFORMATION

THIS SURVEY IN ARGENTINA WAS CONDUCTED DURING 2005. THE SURVEY FOUND THAT:

21.6 PERCENT OF BOYS (AGED 10-10) WERE OVERWEIGHT

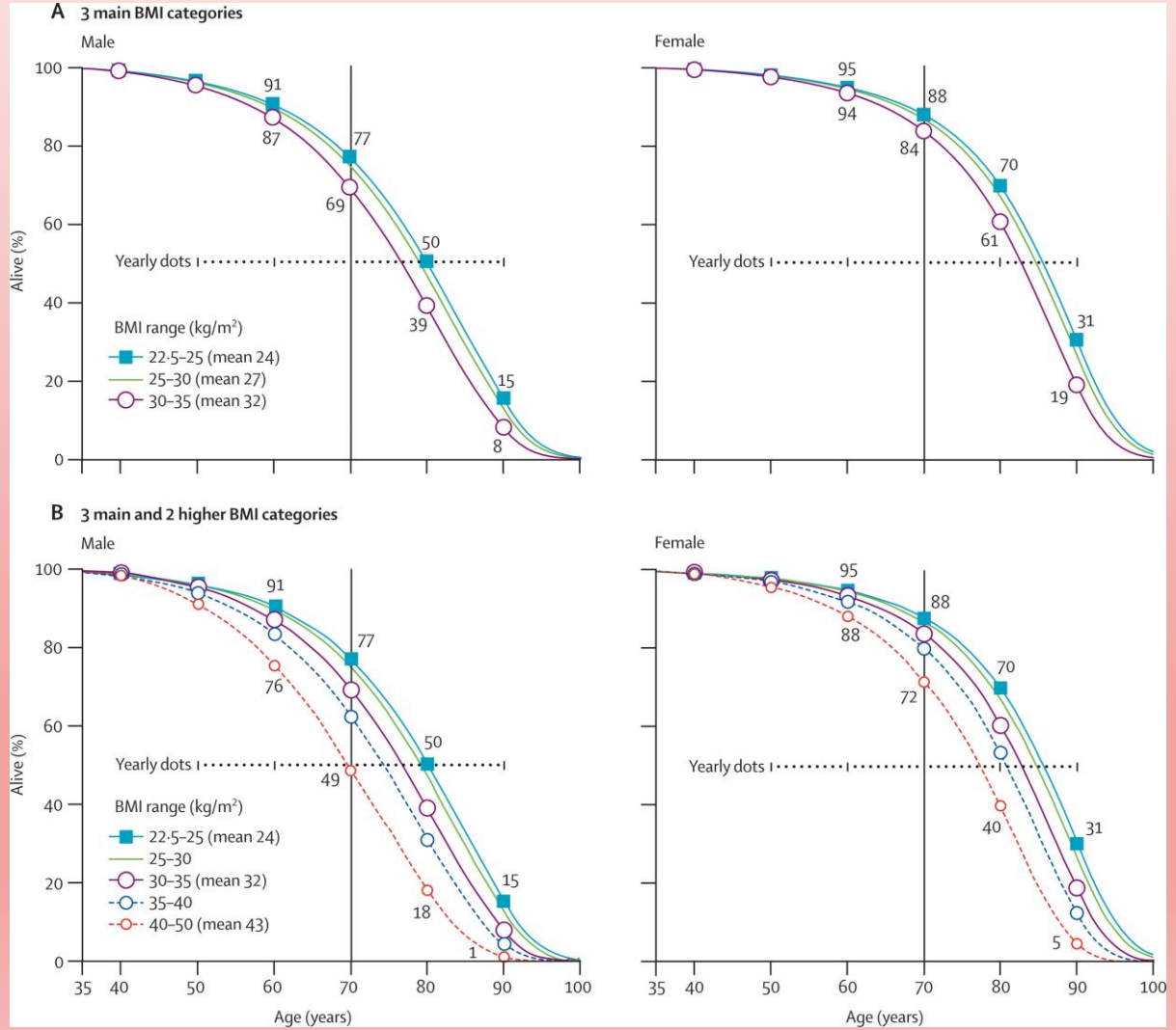
10.5 PERCENT OF BOYS (AGED 10-10) WERE OBESE

22.5 PERCENT OF GIRLS (AGED 10-10) WERE OVERWEIGHT

5 PERCENT OF GIRLS (AGED 10-10) WERE OBESE

REFERENCE
WORLD OBESITY MADE THE ABOVE CONCLUSIONS BASED ON DATA FROM THE SURVEY. SO PLEASE QUOTE WORLD OBESITY WHEN CITING THIS INFORMATION. REFERENCES FOR THE SURVEY ITSELF ARE HERE: KOVALSKYS I, RAUSCH HERSCOVICI C, DE GREGORIO MJ. NUTRITIONAL STATUS OF SCHOOL-AGED CHILDREN OF BUENOS AIRES, ARGENTINA: DATA USING THREE REFERENCES.J PUBLIC HEALTH (OXF). 2011 SEP;33(3):403-11. DOI: 10.1093/PUBMED/FDQ079. EPUB 2010 OCT

La obesidad acorta la vida



Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies.

Lancet. 2009 Mar 28;373(9669):1083-96

Thirty-year persistence of obesity after presentation to a pediatric obesity clinic

Iughetti L. et Al.
Annals of Human Biology, July–August 2008; 35(4): 439–448

Conclusion
The study reinforces the notion that obesity should be prevented at an early age and shows that adolescents with severe obesity and low educational degree are at greater risk of becoming obese adults.

- **9% of the women were underweight**
- **40% normal weigh**
- **34% overweigh**
- **16% obese**

Definición de la Obesidad

Condición caracterizada por exceso de peso corporal a la acumulación de tejido adiposo, en una medida que afecta negativamente a su salud

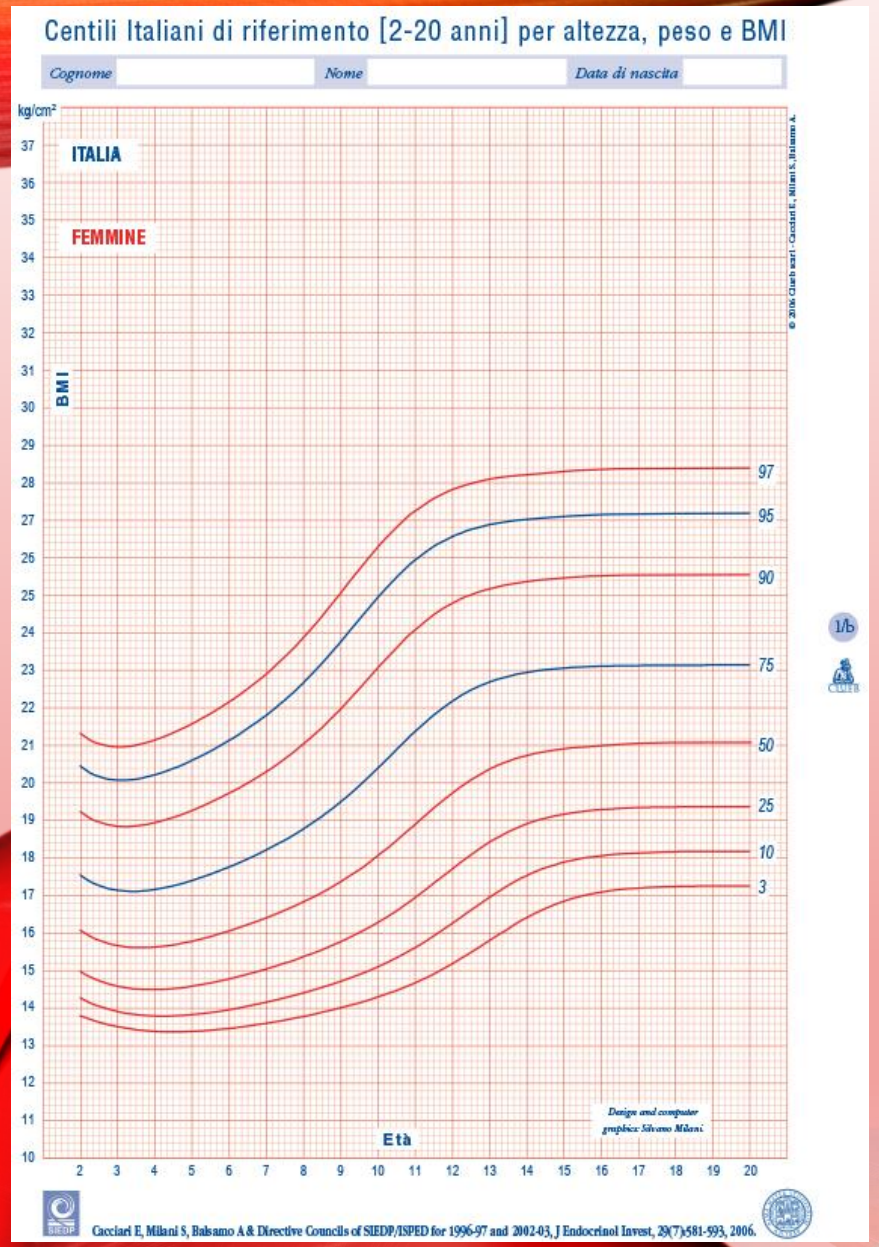
In età adulta

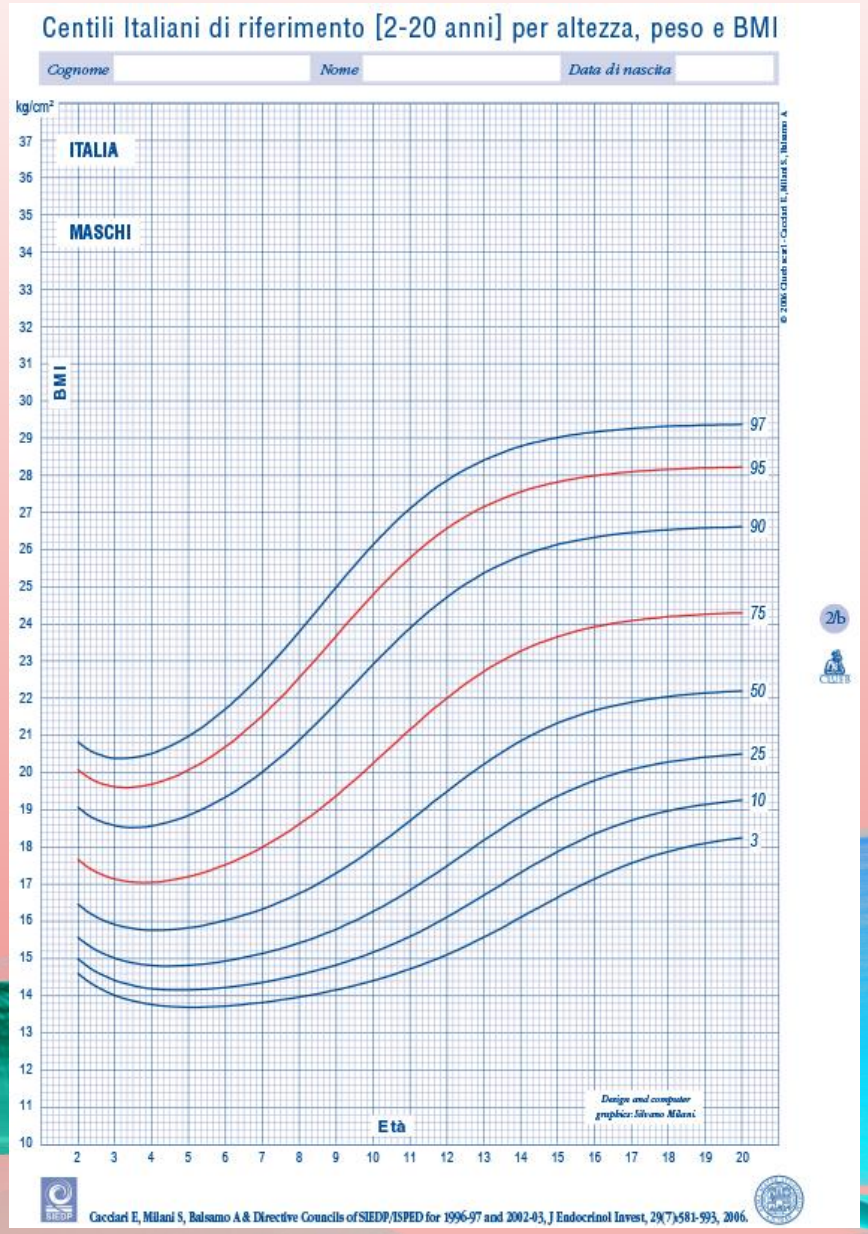
BMI	Classificazione del peso
<18,5	sottopeso
18.5-24.9	normopeso
25.0-29.9	sovrappeso
30.0-34.9	obesità di classe I
35.0-39.9	obesità di classe II
≥40.0	obesità di classe III

In età pediatrica

Percentile del BMI	Classificazione del peso
85-95°C	sovrappeso
95-97°C	obesità moderata
>97°C	obesità grave

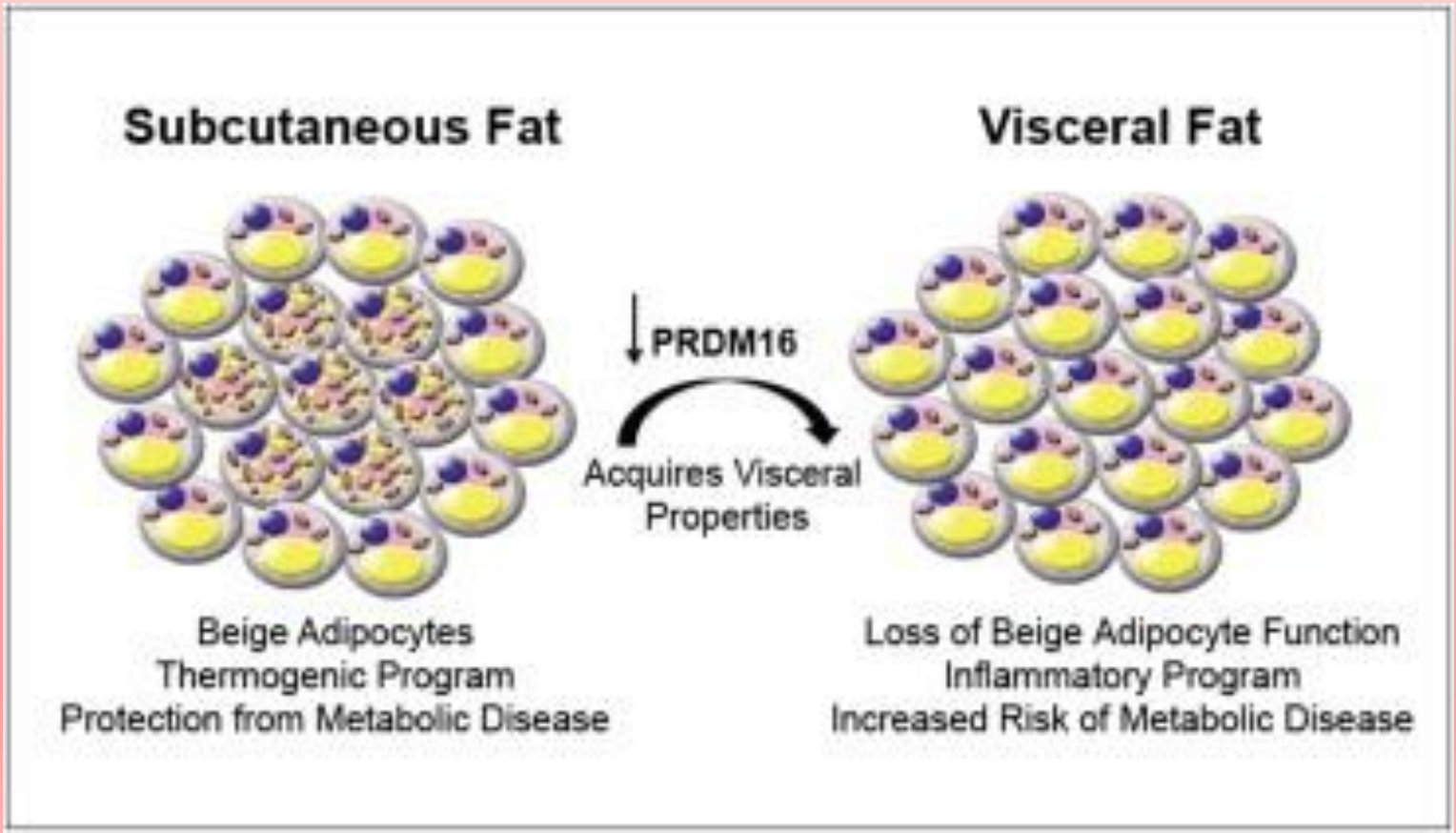
Tabelle di riferimento
Cacciari et al., 2006


Centili Italiani di riferimento [2-20 anni] per altezza, peso e BMI
Cognome
Nome
Data di nascita
kg/cm²
ITALIA
FEMMINE
BMI
97
95
90
75
50
25
10
3
Età
Design and computer graphics: Silvano Milani
1/b
Cacciari E, Milani S, Balsamo A & Directive Councils of SIEDP/ISPED for 1996-97 and 2002-03, J Endocrinol Invest, 29(7):581-593, 2006.


Centili Italiani di riferimento [2-20 anni] per altezza, peso e BMI
Cognome
Nome
Data di nascita
kg/cm²
ITALIA
MASCHI
BMI
97
95
90
75
50
25
10
3
Età
Design and computer graphics: Silvano Milani
2/b
Cacciari E, Milani S, Balsamo A & Directive Councils of SIEDP/ISPED for 1996-97 and 2002-03, J Endocrinol Invest, 29(7):581-593, 2006.

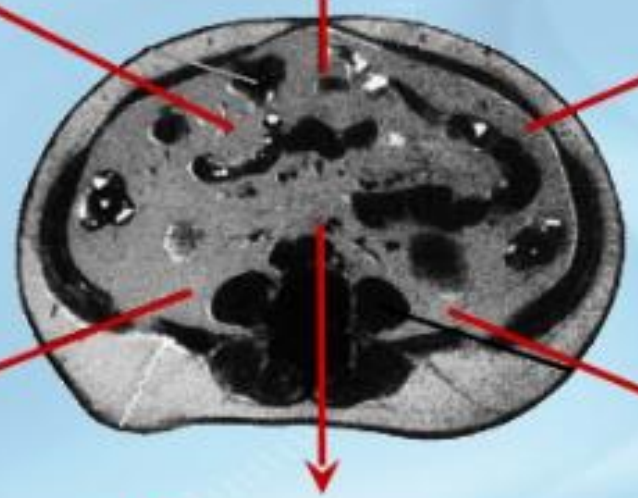
¿Obesidad todos son iguales?

Presse Med. 1947 May 24;55(30):339.
La différenciation sexuelle; facteur déterminant des formes de l'obésité.
VAGUE J.



Visceral Fat Accumulation is an Important Determinant of Metabolic and Cardiovascular Disease

Clip slide



Type 2 Diabetes Dyslipidemia

Fujioka S et al.
Metabolism 1987; 36: 54-9

Insulin Resistance

Yamashita S et al.
Diabetes Care 1996; 19: 287-91

Left Ventricular Dysfunction

Nakajima T et al.
Am J Cardiol 1989; 64: 369-73

Hypertension

Kanai H et al.
Hypertension 1990; 16: 484-90
Kanai H et al.
Hypertension 1996; 27: 125-9

Sleep Apnea Syndrome

Shinohara E et al.
J Intern Med 1997; 241: 11-8

Coronary Artery Disease

Nakamura T et al. Int J Obes Relat Metab Disord 1997; 21: 580-6
Nakamura T et al. Atherosclerosis 1994; 107: 239-46

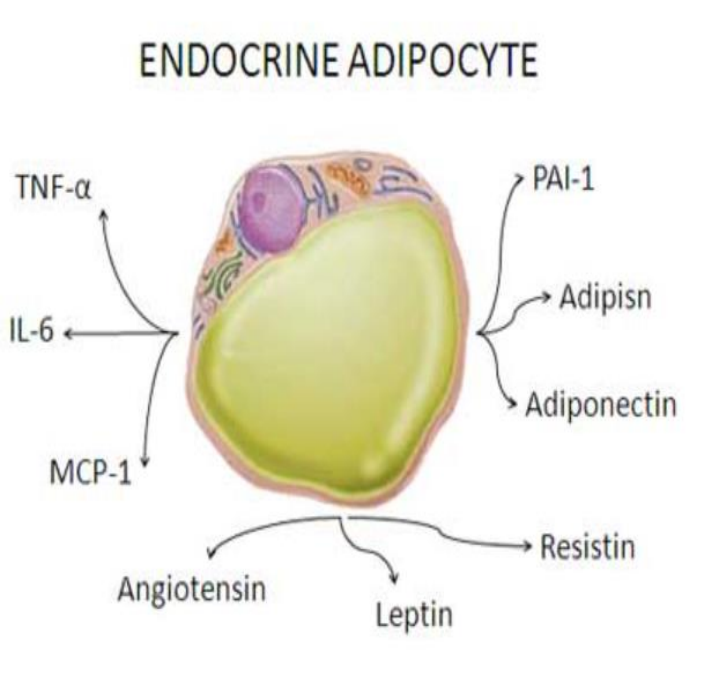
Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

ANALISI COMPARATIVA DEI METODI DI VALUTAZIONE DELL'ADIPOSITÀ VISCERALE

Metodi	Disponibilità	Specificità	Accuratezza	Riproducibilità	Esposizione a radiazioni
Antropometria	Il più accessibile	Bassa	Bassa	Molto variabile	No
BIA	Accessibilità buona	Bassa	Media	Coefficiente di variabilità 4–9.8%	No
ADP	Accessibilità scarsa	Media	Alta	Coefficiente di variabilità adulti, 1.7–4.5%; ragazzi 25% ragazze 44%	No
Ultrasuoni	Accessibilità buona	Media	Alta	Coefficiente di variabilità varia da <2% a 4.5–7.9%	No
DXA	Accessibilità scarsa	Bassa	Alta	Coefficiente di variabilità varia da <1% a 4%	Dose effettiva per scansione 0.003–0.06 mSv
CT	Accessibilità scarsa	Molto alta	Molto alta	Coefficiente di variabilità 1.2–4.3%	Dose effettiva per scansione 6.0–10.0 mSv per TAC addominale multistrato con il protocollo di routine
MRI	Molto meno disponibile degli altri metodi	Molto alta	Molto alta	Coefficiente di variabilità 2.1–6.5%	No

ADP = air displacement plethysmography; BIA = bioelectrical impedance analysis; DXA = dual energy X-ray absorptiometry

Modificata da: A Shuster, Br J Radiol. 2012 January; 85(1009): 1–10



Adiponectin is found more in the subcutaneous adipose deposits than in the visceral deposits.

Insulin sensitivity increases adiponectin activity whereas insulin resistance decreases activity.

In the vasculature, adiponectin acts through the insulin receptor to increase nitric oxide (NO); which increases the anti-atherogenic activities of the endothelium.

The primary function of leptin is to increase satiety and energy expenditure through action on the hypothalamus.

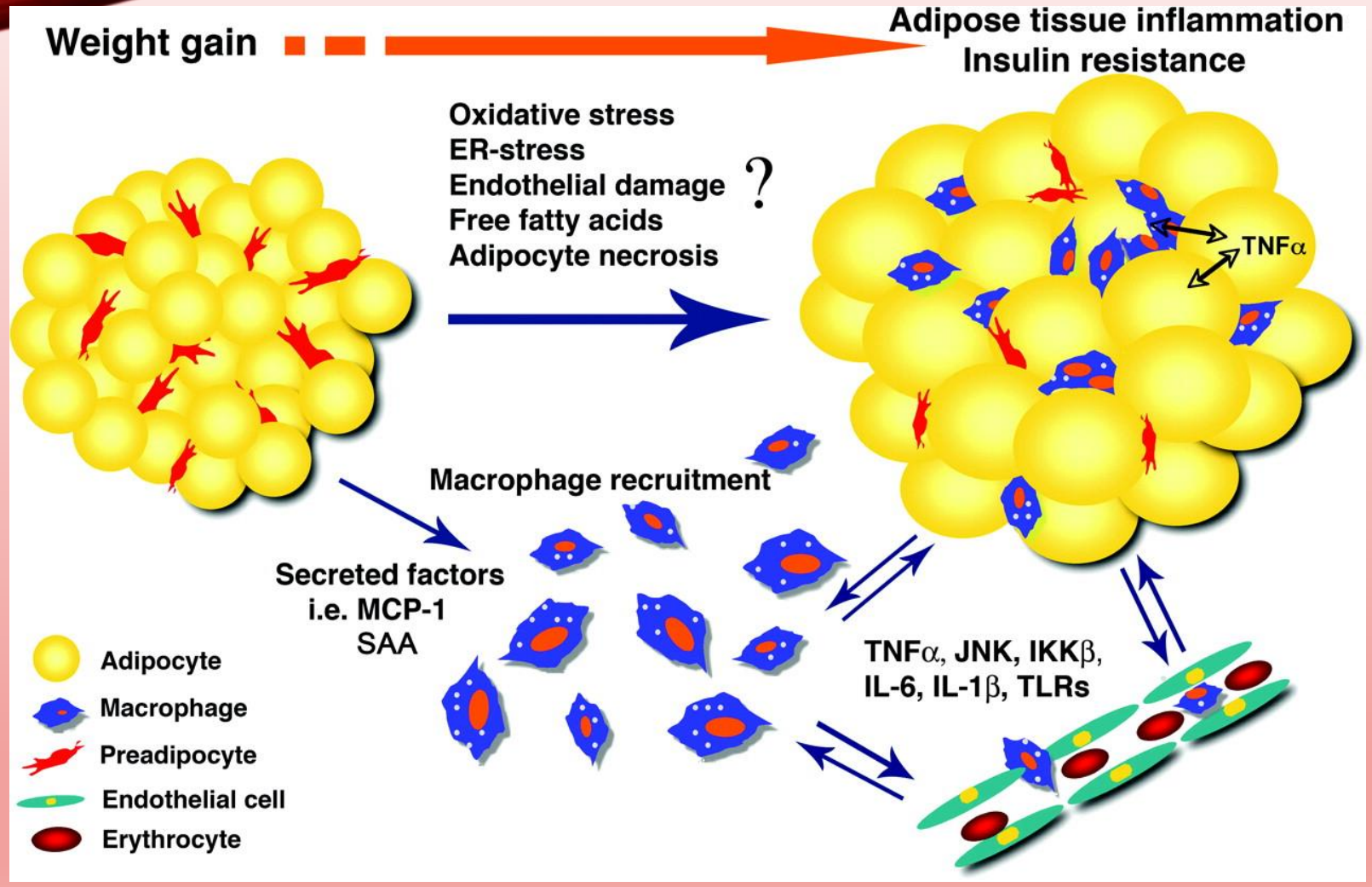
In the muscle, leptin action increases glucose uptake and glucose metabolism. In the liver, leptin increases glucose production.

The primary action of TNF alpha is to increase insulin resistance in liver, muscle and adipose tissue.

IL-6 primary function is to increase insulin resistance at the insulin receptor or insulin signaling pathway in hepatic, muscle and adipose tissue.

Resistin is 15 times greater in the visceral adipose deposits than in the subcutaneous deposits.

The primary function of resistin is an increase in insulin resistance.



Birgit Gustafson et al. Arterioscler Thromb Vasc Biol. 2007;27:2276-2283

The IDF definition of the at risk group and metabolic syndrome in children and adolescents

Curr Opin Lipidol. 2010 Feb;21(1):38-43. doi: 10.1097/MOL.0b013e3283346ccc.

The distinction of metabolically 'healthy' from 'unhealthy' obese individuals.

Blüher M[1].

RECENT FINDINGS: The majority of individuals with obesity develop insulin resistance, type 2 diabetes, dyslipidemia, gout, hypertension and cardiov 25% of obese individuals are metabolically healthy mo Recent studies suggest that inflammation of visceral a adipose tissue dysfunction mediate insulin resistance i fat mass. This suggests that mechanisms beyond a po and adipokine release determine the pathological meta

SUMMARY: Recommendations for obesity treatment s from 'unhealthy' obese phenotype to identify early the losing weight. In addition, novel antiobesity treatment s are needed.

Diabetes Care. 2014 May;37(5):1462-8. doi: 10.2337/dc13-1697. Epub 2014 Feb 26.

Predictors of metabolically healthy obesity in children.

Prince RL[1], Kuk JL, Ambler KA, Dhaliwal J, Ball GD.

Author information

Abstract

OBJECTIVE: To determine the prevalence of metabolically healthy obesity (MHO) in children and examine the demographic, adiposity, and lifestyle predictors of MHO status.

RESEARCH DESIGN AND METHODS: This cross-sectional study included 8-17 year olds with a BMI ≥85th percentile who were enrolled in a multidisciplinary pediatric weight management clinic from 2005-2010. Demographic, anthropometric, lifestyle, and cardiometabolic data were retrieved by retrospective medical record review. Participants were dichotomized as either MHO or metabolically unhealthy obese (MUO) according to two separate classification systems based on: 1) insulin resistance (IR) and 2) cardiometabolic risk (CR) factors (blood pressure, serum lipids, and glucose). Multivariable logistic regression was used to determine predictors of MHO using odds ratios (ORs) with 95% CIs.

RESULTS: The prevalence of MHO-IR was 31.5% (n = 57 of 181) and MHO-CR was 21.5% (n = 39 of 181). Waist circumference (OR 0.33 [95% CI 0.18-0.59]; P = 0.0002) and dietary fat intake (OR 0.56 [95% CI 0.31-0.95]; P = 0.04) were independent predictors of MHO-IR; moderate-to-vigorous physical activity (OR 1.80 [95% CI 1.24-2.62]; P = 0.002) was the strongest independent predictor of

Eur J Pediatr. 2015 Dec;174(12):1649-55. doi: 10.1007/s00431-015-2587-4. Epub 2015 Jul 5.

Preserved insulin sensitivity predicts metabolically healthy obese phenotype in children and adolescents.

Vukovic R[1], Milenkovic T[2], Mitrovic K[3], Todorovic S[4], Plavsic L[5], Vukovic A[6], Zdravkovic D[7,8].

Eur J Pediatr (2015) 174:1649–1655

Table 3 Glucose regulation and insulin secretion in MHO and MUO subjects during oral glucose tolerance test

	MHO (n=53)	MUO (n=96)	p value
Glucose 0 min (mmol/l)	4.70±0.37	4.73±0.64	0.413
Glucose 60 min (mmol/l)	7.04±1.48	7.62±1.89	0.072
Glucose 120 min (mmol/l)	6.06±1.10	6.41±1.66	0.307
Glucose 180 min (mmol/l)	5.59±7.54	4.60±1.34	0.515
$Glucose_{AUC}$ (mmol/l/h)	18.2±4.4	18.6±3.7	0.598
Insulin 0 min (μIU/ml)	15.1±11.5	27.1±20.6	<0.001
Insulin 60 min (μIU/ml)	112.6±85.8	161.4±105.0	0.001
Insulin 120 min (μIU/ml)	95.5±90.1	152.9±142.7	0.001
Insulin 180 min (μIU/ml)	43.8±60.2	61.5±60.1	0.002
$Insulin_{AUC}$ (μIU/ml/h)	237.6±191.3	362.9±247.7	0.002

Values are presented as means±SD, to convert glucose to conventional units (mg/dl) divide by 0.0555

$Glucose_{AUC}$ area under the glucose curve, *$Insulin_{AUC}$* area under the insulin curve

What is New:

- Insulin resistance was found to be the only significant laboratory predictor of MUO when adjusted for gender, puberty, and the degree of abdominal obesity.
- Besides basal insulin resistance, MUO children were found to have a significantly higher insulin secretion throughout OGTT in order to maintain glucose homeostasis.

La flora intestinale:

Gram positivi : Firmicutes Lactobacillus
Mycoplasma
Bacillus
Clostridium
Actinobacteria

Gram negativi: Bacteroides

Nel topo privo del gene per la leptina si ha una diminuzione del 50% dei *bacteroides* ed un proporzionale aumento dei *firmicutes*

Studi su animali da esperimento alimentati con diete ricche di zuccheri e di grassi hanno dimostrato un'alterazione della flora batterica :

- > firmicutes
- < bacteroides

Tale alterazione risultava reversibile lì dove si ripristinava una dieta con corretto apporto di zuccheri e di grassi.

A dimostrazione che l'alterazione della flora batterica è causa e non conseguenza dell'obesità si è proceduto a "trapiantare" la flora batterica di topi obesi e topi magri in topi "germ-free" Dopo 2 settimane i topi che avevano ricevuto la flora batterica "obesogena" estraevano maggior quantitativo calorico dalla dieta aumentando la loro massa grassa rispetto al gruppo di controllo.

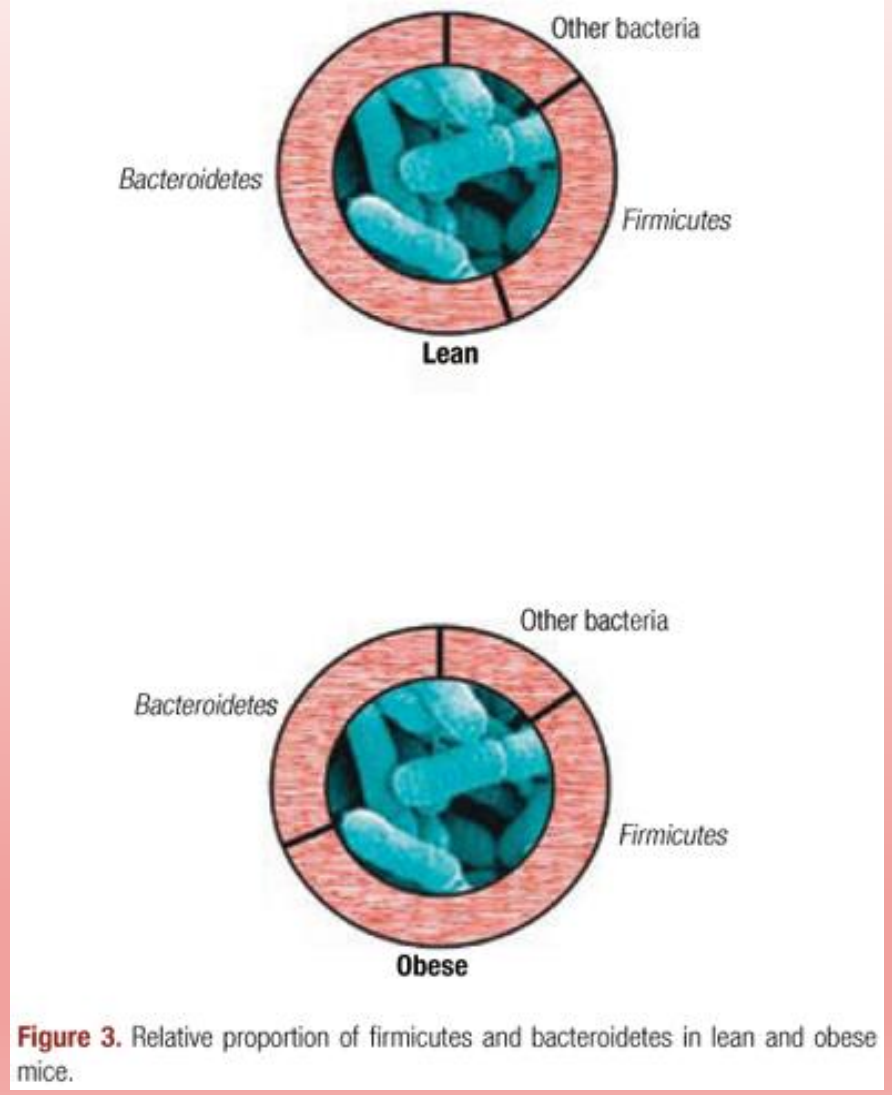
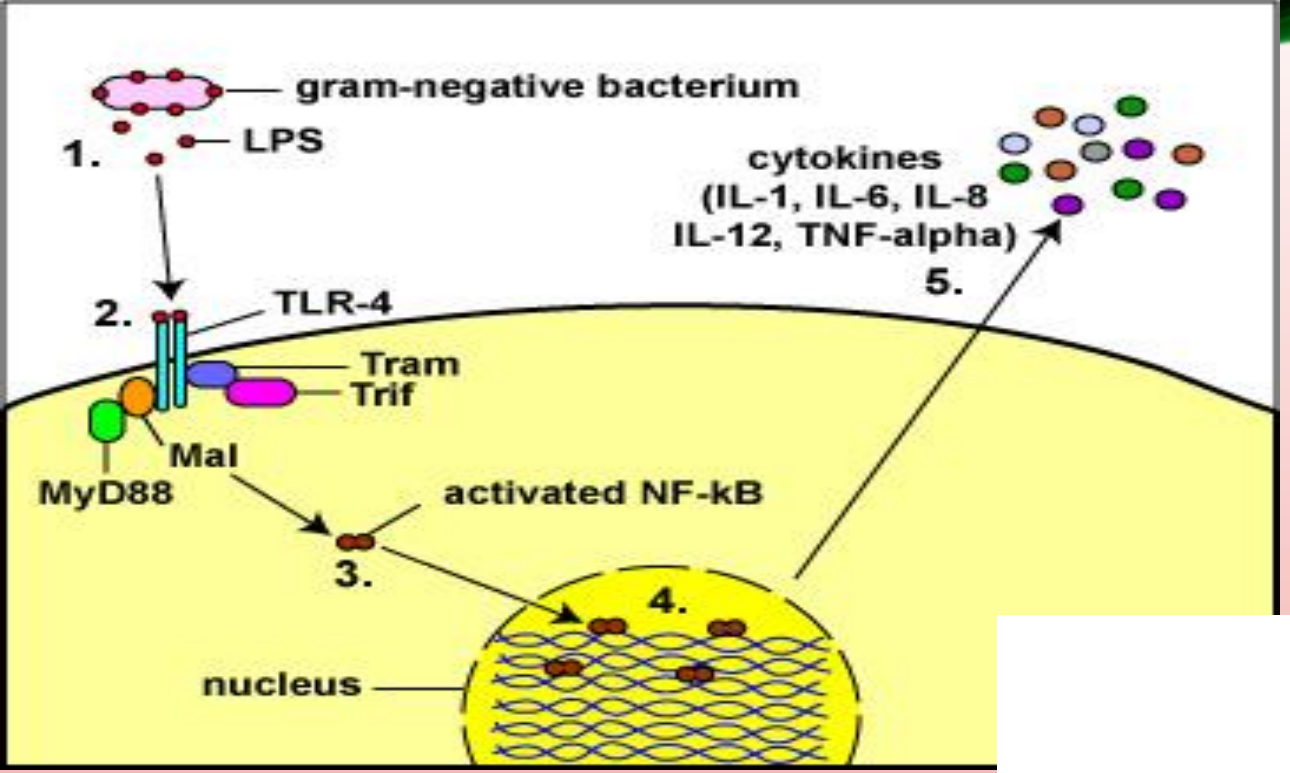


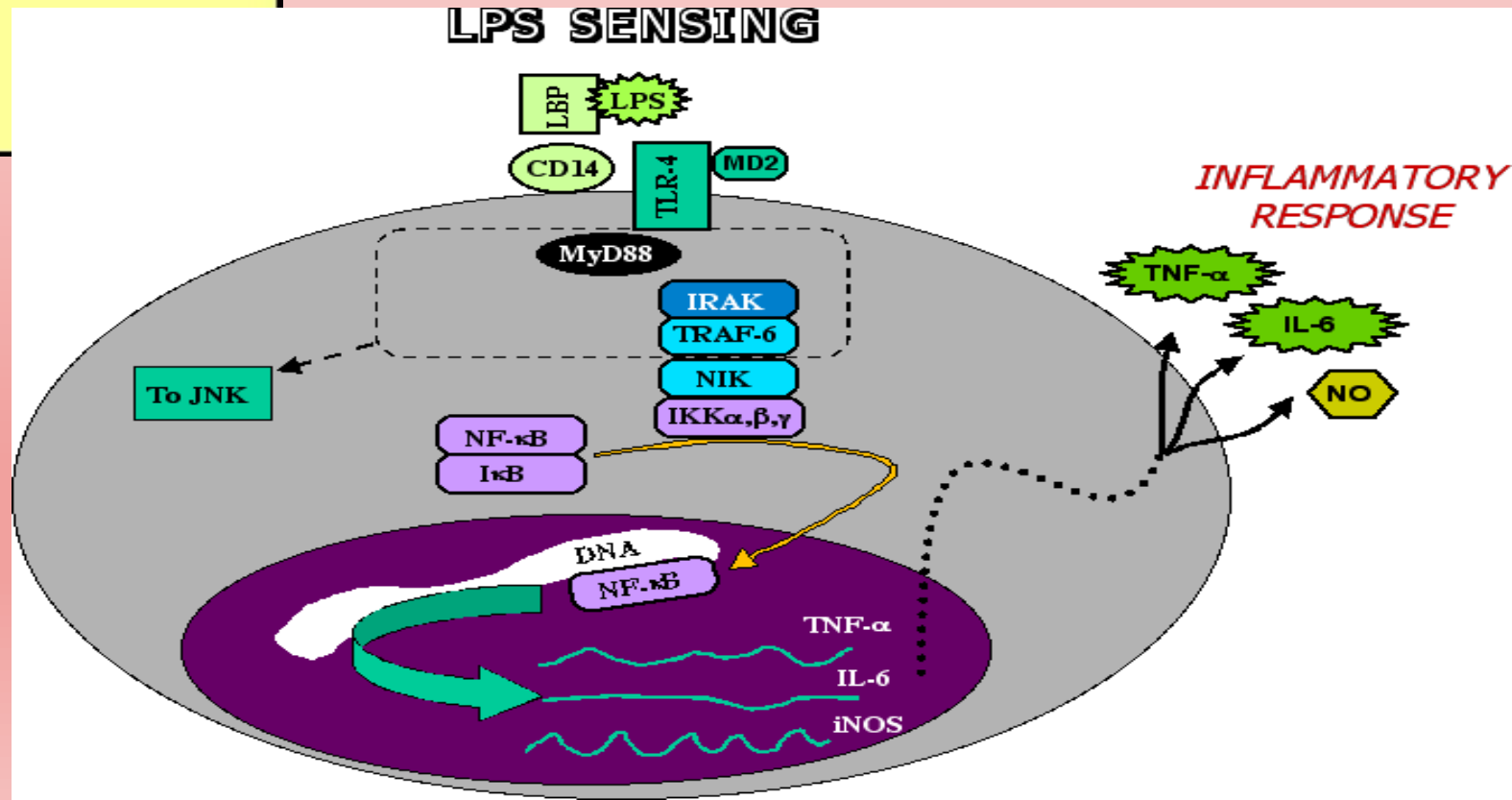
Figure 3. Relative proportion of firmicutes and bacteroidetes in lean and obese mice.

Meccanismi di connessione tra flora batterica, obesità, IR e T2D

1) Aumento dell'estrazione dalla dieta di un maggior quatitativo calorico in base ad una data flora batterica
2) Istaurazione de un "endotossemia cronica di basso grado"
3) Rimodulazione della secrezione di peptidi intestinali.

4) Recenti evidenze dimostrano che batteri intestinali inducono lo stato "infiammatorio" dell'obesità attraverso l'attivazione di *lipopolissacaride (LPS)* (una componente della parete della cellula gram –) che attiva il processo infiammatorio legandosi al TLR-4 (recettore sul CD14) posto sulla superficie della cellula immune nativa.
La conferma : l'assenza di tale recettore previene l'aumento dell'IR indotta da una dieta ricca di grassi


gram-negative bacterium
1.
LPS
cytokines
(IL-1, IL-6, IL-8
IL-12, TNF-alpha)
5.
2.
TLR-4
Tram
Trif
Mal
MyD88
activated NF-kB
3.
4.
nucleus


LPS SENSING
LBP
LPS
CD14
TLR-4
MD2
MyD88
IRAK
TRAF-6
NIK
IKKα,β,γ
To JNK
NF-κB
IκB
DNA
NF-κB
TNF-α
IL-6
iNOS
INFLAMMATORY
RESPONSE
TNF-α
IL-6
NO

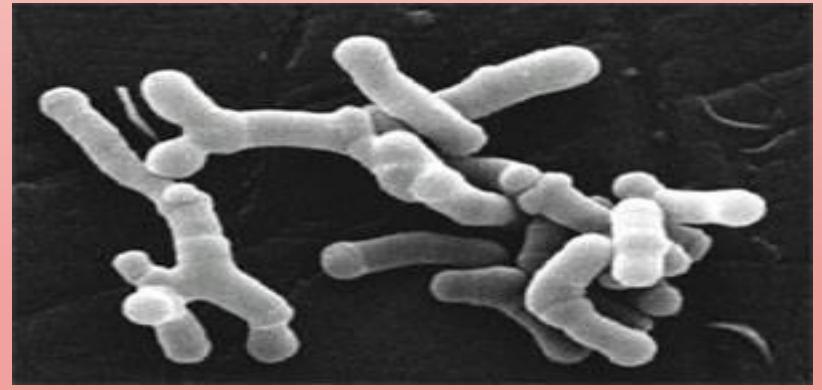
Maturazione della flora intestinale :

E' nel I anno di vita che avvengono le più sostanziali modificazioni della flora intestinale.

Bambini che hanno sviluppato obesità al 7' anno di vita avevano valori di bifidobacter ad 1 anno inferiori rispetto a bambini che non avevano sviluppato obesità.
Ciò dimostra che uno squilibrio della flora batterica nei primi anni di vita è in grado di influenzare significativamente l'insorgenza di obesità nelle età successive.

L'impatto di una terapia antibiotica orale di 5 giorni sulla flora batterica è notevole : sono necessarie 4 settimane prima che inizi la reversione verso la composizione originaria e ben 6 mesi sono necessari ad alcuni ceppi per rigenerarsi.

L'uso di antibiotici nell'infanzia è associato con una diminuzione di Bifidobacteria e Bacteroides (antiobesogeni)



BMC Med. 2016 Apr 19;14(1):57. doi: 10.1186/s12916-016-0605-7.

Antibiotics, obesity and the link to microbes - what are we doing to our children?

Turta O[1], Rautava S[2].

Author information

Abstract

BACKGROUND: Childhood obesity and overweight are among the greatest health challenges in the pediatric population. Obese individuals exhibit marked differences in the composition of the intestinal microbial community as compared to lean subjects. These changes in the gut microbiota precede the clinical manifestation of overweight. Convincing experimental data suggest a causal role for intestinal microbes in the development of obesity and associated metabolic disorders.

DISCUSSION: Exposure to antibiotics exerts a devastating impact on the intestinal microbial community. Epidemiological studies have provided evidence indicating that early or repeated childhood exposure to antibiotics is associated with increased risk of overweight later in childhood but the causal role of this exposure in obesity development is not clear. However, data from studies conducted using experimental animal models indicate that antibiotic-induced changes in the gut microbiota influence host metabolism and lead to fat accumulation. The intestinal microbiota perturbation caused by antibiotic exposure in the perinatal period appears to program the host to an obesity-prone metabolic phenotype, which persists after the antibiotics have been discontinued and the gut microbiota has recovered. These observations may have serious implications in the clinical setting, since a substantial number of human infants are subjected to antibiotic treatment through the mother during delivery or directly in the immediate neonatal period. The clinical significance of these exposures remains unknown. Prudent use of antibiotics is paramount not only to reduce the propagation of antibiotic-resistant organisms but also to minimize the potentially detrimental long-term metabolic consequences of early antibiotic exposure. Improved means of reliably detecting neonates with bacterial infection would reduce the need for empirical antibiotic exposure initiated based on nonspecific symptoms and signs or risk factors. Finally, means to support healthy microbial contact in neonates and infants requiring antibiotic treatment are needed.

KEYWORDS: Antibiotics; Gut microbiota; Infant; Neonate; Obesity; Overweight

BIOLOGICAL PREDISPOSITION TO WEIGHT GAIN

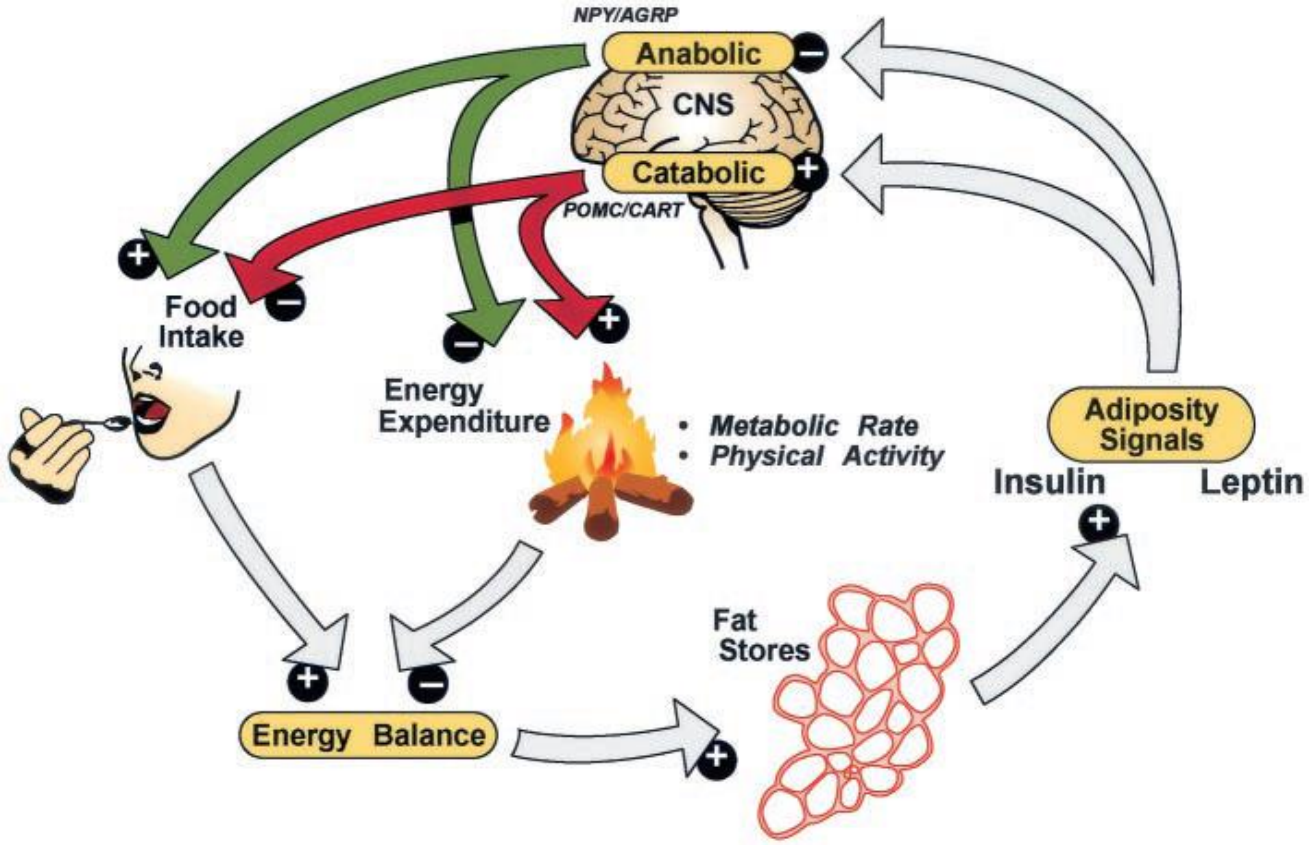
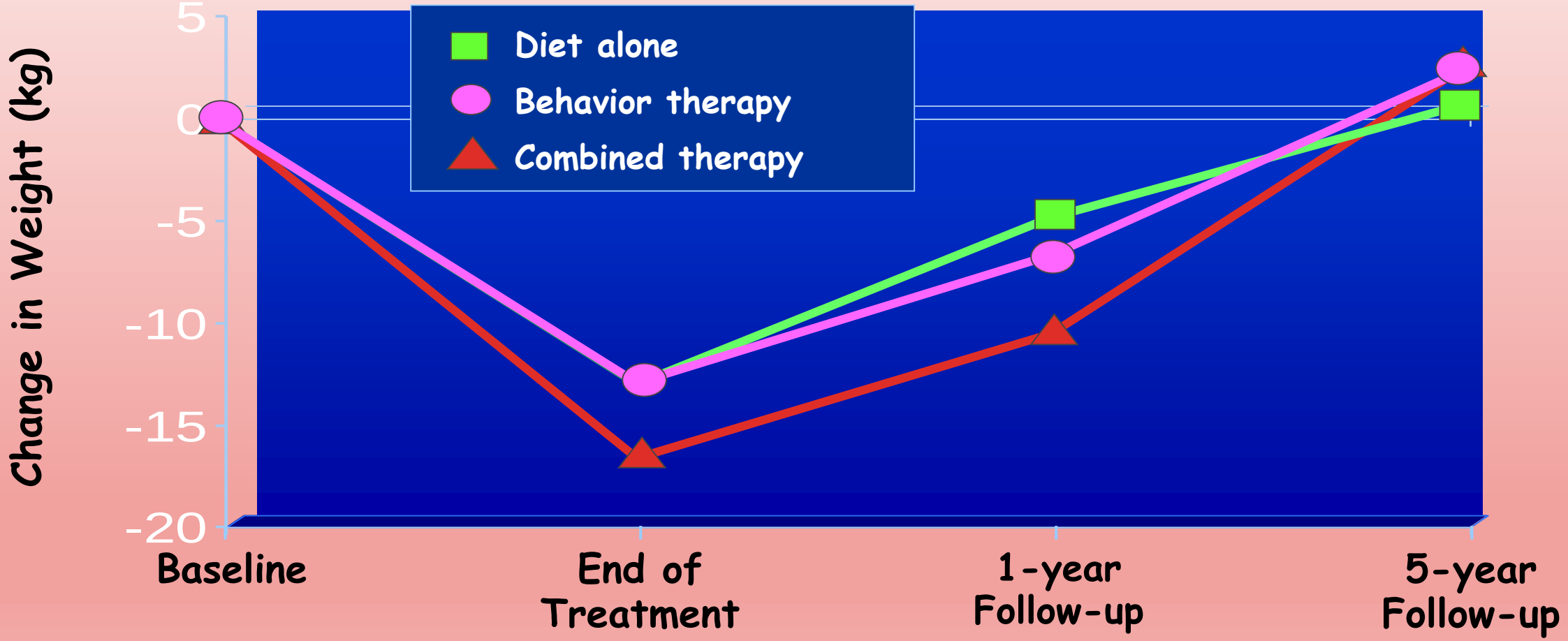


FIG. 1. Negative feedback model for regulation of body fat content. Leptin and insulin are signals that circulate in proportion to body adiposity and act in the hypothalamus to stimulate catabolic- (e.g., POMC/CART) and inhibit anabolic- (e.g., NPY/AgRP) effector pathways. These pathways have opposing effects on both energy intake and energy expenditure and, consequently, on the amount of body fuel stored as fat. Weight loss induced by caloric restriction lowers insulin and leptin levels, which in turn activates anabolic and inhibits catabolic effectors, and thereby promotes the recovery of lost weight. Modified from Schwartz et al. (9).

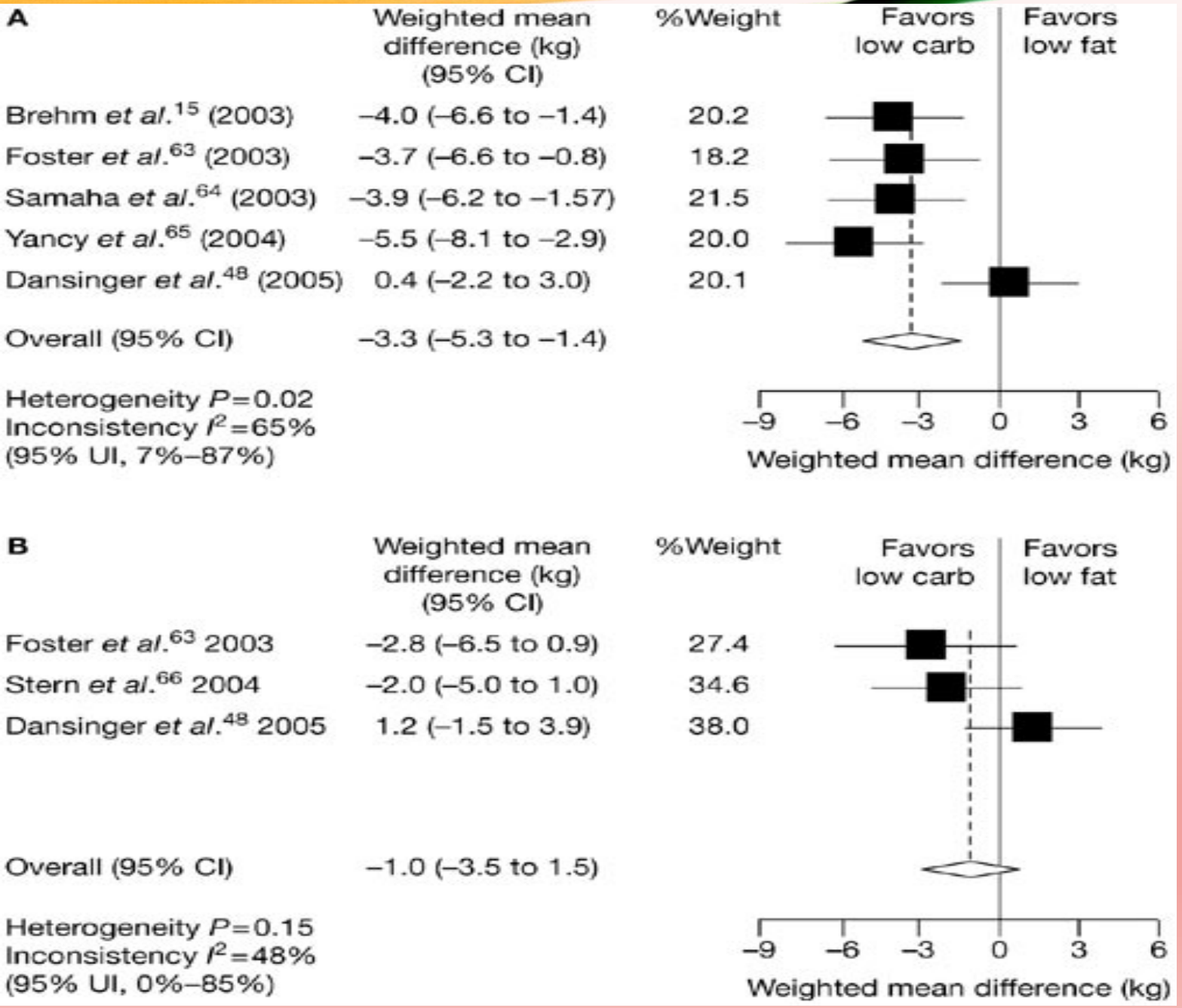
Is the Energy Homeostasis System Inherently Biased Toward Weight Gain?
Michael W. Schwartz, Stephen C. Woods, Randy J. Seeley,Gregory S. Barsh, Denis G. Baskin,and Rudolph L. Leibel
DIABETES, VOL. 52, FEBRUARY 2003

PIRAMIDE DEL TRATTAMENTO DELL'OBESITÀ

SHORT-TERM OBESITY THERAPY DOES NOT RESULT IN LONG-TERM WEIGHT LOSS



Wadden et al. *Int J Obes* 1989;13 (Suppl 2):39.



Weighted mean differences in weight loss after (A) 6 months and (B) 12 months of follow-up from a meta-analysis comparing the effects of *ad libitum* low-carbohydrate diets versus low-fat energy-restricted diets on weight loss

Malik VS and Hu FB (2007) Popular weight-loss diets: from evidence to practice
Nat Clin Pract Cardiovasc Med 4: 34–41