



"Sindrome Metabolica"

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Dysmetabolic syndrome X

ICD-10

ICD-9277.7

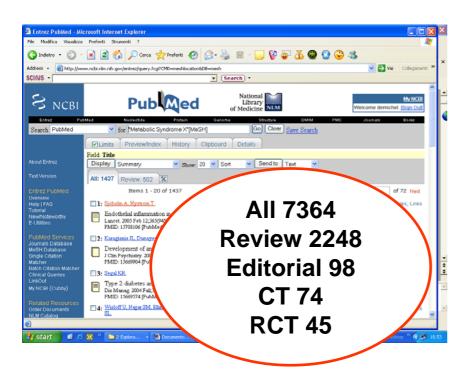
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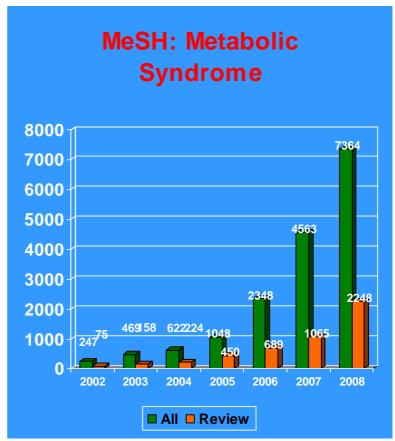
Metabolic syndrome is a combination of medical disorders that affect a large number of people in a clustered fashion.

In some studies, the prevalence in the USA is calculated as being up to 25% of the population, the end result of which is to increase one's risk for cardiovascular disease and diabetes.

Quanto si è parlato della sindrome metabolica?

Metabolic syndrome: termine MeSH introdotto nel 2002





Sindrome Metabolica: un concetto che ha più di 80 anni.....

- **1920:** Kylin descrive un quadro che comprende ipertensione, iperglicemia e gotta
- **1947:** J. Vague osserva come l'obesità "androide" si accompagni alle alterazioni metaboliche che si associano al diabete e alle malattie cardiovascolari
- 1966: Camus "trisindrome metabolica"
- 1988: Reaven introduce il concetto di "Sindrome X" (l'associazione di <u>insulino-resistenza, iperinsulinemia, stati prediabetici o DM2 conclamato</u>, dislipidemia, ipertensione, obesità centrale, iperuricemia)
- **1988-1998:** altri sinonimi (**BIG 4**, **Deadly Quartet**, Plurimetabolic Syndrome ecc.)
- **1998:** WHO decide di utilizzare il termine di "Sindrome metabolica"

Definizione

Definitions of insulin resistance

Broad definition

Insulin resistance is a clinical state in which a normal or raised insulin level produces an impaired biological response. As insulin has a number of physiological actions—including a central role in acute metabolic actions and growth and development—insulin resistance could mean impairment in any of these actions

Specific definition in relation to metabolic syndrome

Insulin resistance, when used to identify those at risk of type 2 diabetes and as a component of the metabolic syndrome, usually refers to resistance to insulin's ability to stimulate glucose uptake in insulin sensitive peripheral tissues and its ability to suppress hepatic glucose production, promote glucose storage, inhibit ketogenesis, and suppress lipolysis

Sindrome Metabolica

Due eventi hanno focalizzato l'attenzione della comunità medica sulla sindrome metabolica:

- 1. L'inclusione della sindrome nelle linee guida NCEP-ATP III (2001)
- 2. La creazione di un codice diagnostico ICD 9 (277.7) che permette un rimborso per il trattamento della sindrome



Independently raises cardiovascular risk and should be picked up in primary care

Metabolic syndrome is characterised by:

- •Hyperinsulinaemia
- Low glucose tolerance
- Dyslipidaemia
- •Hypertension
- Obesity



Independently raises cardiovascular risk and should be picked up in primary care

This cluster of factors has been recognised for many years, but the syndrome was not formally labelled until Reaven did so in 1988 and suggested that insulin resistance was its central characteristic.



Independently raises cardiovascular risk and should be picked up in primary care

It is becoming increasingly clear that a proinflammatory state is a common feature of the syndrome and of atheromatous disease.

A recent randomised controlled trial showed that insulin resistance and measurements of C reactive protein were significantly lower at two year follow-up in patients with metabolic syndrome who had been allocated to a Mediterranean diet than in those who continued their normal diets.



Independently raises cardiovascular risk and should be picked up in primary care

Although large intervention studies have shown that intensive modification of lifestyle delays the onset of diabetes in patients with impaired glucose tolerance, no similar trials have aimed at reducing all the cardiovascular disease risk factors among people with metabolic syndrome.

Independently raises cardiovascular risk and should be picked up in primary care

People meeting three of the following criteria qualify as having the metabolic syndrome:

raised blood pressure (> 130/85 mm Hg),

- a low serum concentration of HDL cholesterol (< 1.04 mmol/l in men and < 1.29 mmol/l in women),
- a high serum triglyceride concentration (> 1.69 mmol/l),
- a high fasting plasma glucose concentration (> 6.1 mmol/l), and abdominal obesity (waist circumference > 102 cm in
- men and > 88 cm in women).

A new definition, proposed recently by the International Diabetes Federation, has central obesity as an essential criterion, with a range of cut-offs for waist circumference for people from different ethnic groups.

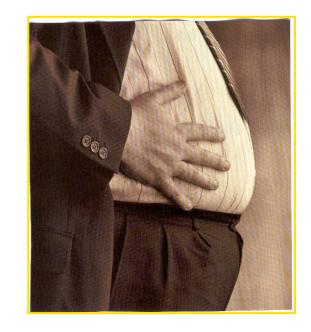
COSA DOVREBBE ESSERE LA SINDROME METABOLICA

Un semplice e precoce strumento predittivo per il clinico

✓ Aumentata mortalità totale



- ✓ Rischio e mortalità CV superiore alla somma dei fattori di rischio
- ✓ Rischio elevato di sviluppo di diabete tipo 2 (se non presente)



Definitions for metabolic syndrome

Target organ damage

	US national cholesterol education programme, adult treatment panel III*		
Definition	Three or more of the following criteria		
Impaired glucose metabolism	Fasting plasma glucose ≥6.1 mmol/l		
Hypertension	Blood pressure ≥130/85 mm Hg or treatment		
Dyslipidaemia	Triglycerides ≥1.7 mmol/l HDL cholesterol <1.04 mmol/l		
Central obesity	NCEP _{WAIST} definition: waist circumference >102 cm (age 70) NCEP _{BMI} definition: BMI>29.4 kg/m ² (ages 50 and 70)		

^{*}Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Final report. Circulation 2002;106:3143-421.

Definitions for metabolic syndrome

World Health Organization†

Presence of impaired glucose metabolism and two or more other criteria

- Glucose intolerance, impaired fasting glucose or diabetes mellitus, or insulin resistance (WHO_{CLAMP} definition: lowest fourth of clamp insulin sensitivity, age 70; WHO_{HOMA} definition: highest fourth of homeostasis model assessment-insulin resistance, age 50 and 70)
- Blood pressure ≥140/90 mm Hg or treatment
- Triglycerides ≥1.7 mmol/l or high density lipoprotein cholesterol <0.91 mmol/l</p>
- Waist to hip ratio >0.9 (WHO_{CLAMP} definition, age 70) or BMI >30 kg/m²
- Microalbuminuria: urinary albumin excretion rate ≥20 μg/min (WHO_{CLAMP} definition, age 70)

†World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications: report of a WHO consultation. Geneva, WHO, 1999. Part 1: Diagnosis and classification of diabetes mellitus.

Summary definitions of metabolic syndrome

World Health Organization*

 Insulin resistance plus at least two of the following: raised blood pressure, dyslipidaemia, obesity, microalbuminuria

American Treatment Panel III†

At least three of the following:

- High fasting glucose
- Raised blood pressure
- Raised plasma triglycerides
- Low HDL (high density lipoprotein) cholesterol
- Obesity (large waist circumference)

International Diabetes Federation‡

 Obesity (large waist) plus at least two of the following: raised triglycerides, reduced HDL cholesterol, raised blood pressure, raised fasting plasma glucose

Classification of Metabolic Syndrome

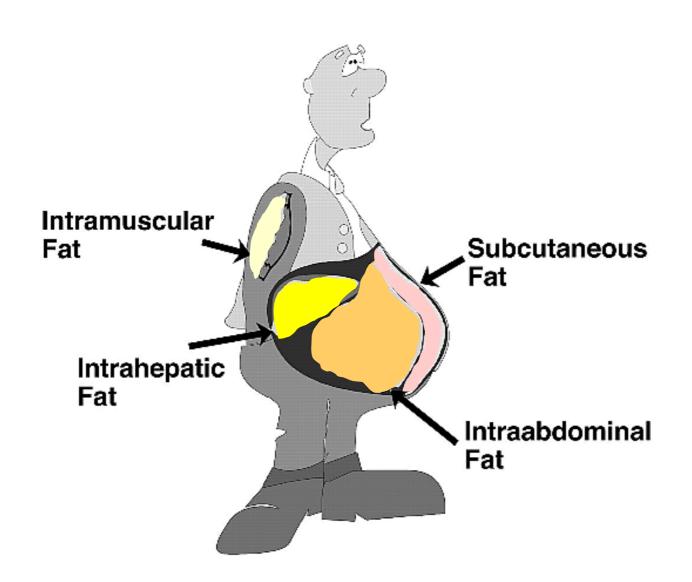
	WHO	ATP III	IDF
Insulin resistance	yes	none	none
Waist circumference male Waist circumference fem	2 /0 CIII	≥ 102 cm ≥ 88 cm	≥ 94 cm ≥ 80 cm
Blood pressure	≥ 140/90 mmHg	≥ 130/85 mmHg	≥ 130/85 mmHg
Blood glucose	≥ 110 mg/dl	≥ 110 mg/dl	≥ 100 mg/dl
Plasma triglycerides	≥ 150 mg/dl	≥ 150 mg/dl	≥ 150 mg/dl
HDL cholesterol male HDL cholesterol female	< 35 mg/dl < 39 mg/dl	< 40 mg/dl < 50 mg/dl	< 40 mg/dl < 50 mg/dl
Albuminuria	> 20 μg/min	NA	NA

Prevalenza

Prevalenza della sindrome metabolica a seconda della definizione di base della sindrome

	ATP III	WHO	Accordo
Totale	23.9	25.1	86.2
Uomini	24.2	27.9	86.1
Donne	23.5	22.6	86.3
Bianchi	25.1	27.6	86.4
Afro-A	16.5	24.9	78.0
Messicani-A	32.0	38.1	84.2

Popolazione Third National Health and Nutrition Examination Survey 1988-2004: età > 20 anni

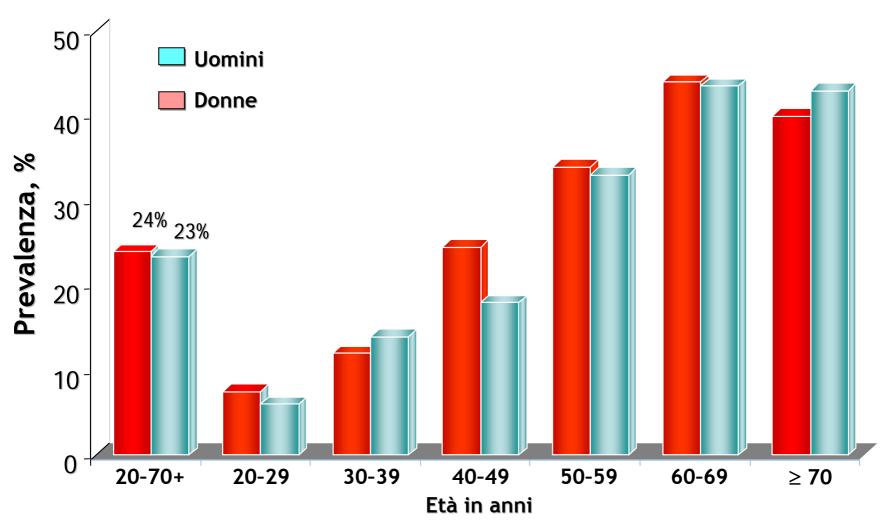


OBESITA' VISCERALE

- Misurazione della circonferenza vita
- BMI
- Rapporto vita/fianchi
 (Un rapporto vita/fianchi >0.9nell'uomo o >0.85 nella donna è
 fortemente correlato all'obesità addominale e all'insulino-resistenza).
- Alcuni suggeriscono oggi il diametro anteroposteriore (sagittale) quale miglior indicatore clinico del grasso viscerale
- STRUMENTALE: RM, DEXA

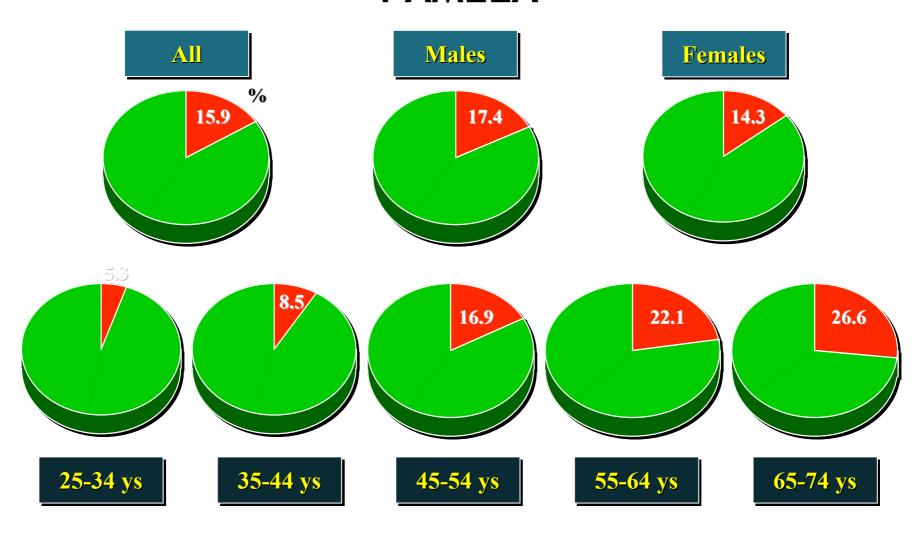
Prevalenza della sindrome metabolica secondo il NCEP nello studio NHANES III

8814 adulti USA ≥ 20 anni



Ford ES et al. JAMA 2002;287:356-359.

Prevalence of the Metabolic Syndrome in PAMELA



Rate of WHO defined MS in eight European countries for non-diabetic man aged 40-55

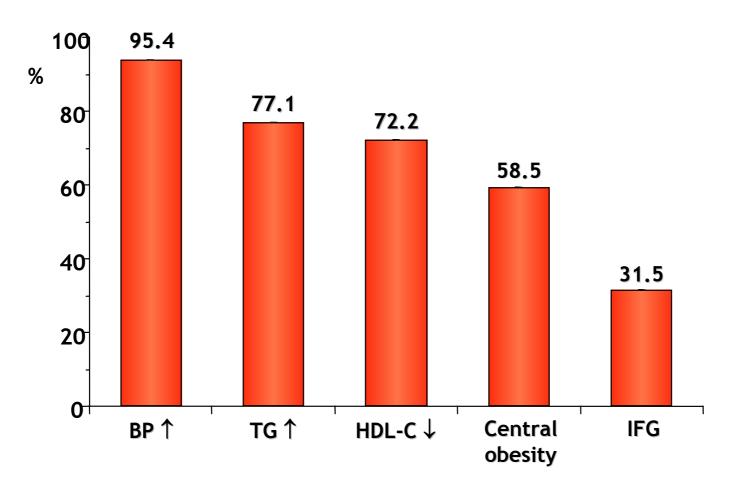
Men 40-55 ys	Sample (nr.)	Prevalence (%)
Goodlinge, UK	210	7
Barilla, Italy	230	12
MORGEN, Netherlands	270	19
D.E.S.I.R., France	1033	21
VIVA, Spain	459	21
Malmoe, Sweden	679	27
Ely, UK	234	36
Overall	3250	20

MS prevalence

- Highest prevalence in older persons
- Prevalence increases with age
- •Frequency rises rapidly in middle age
- Frequency parallels with some lagtime the development obesity in the population

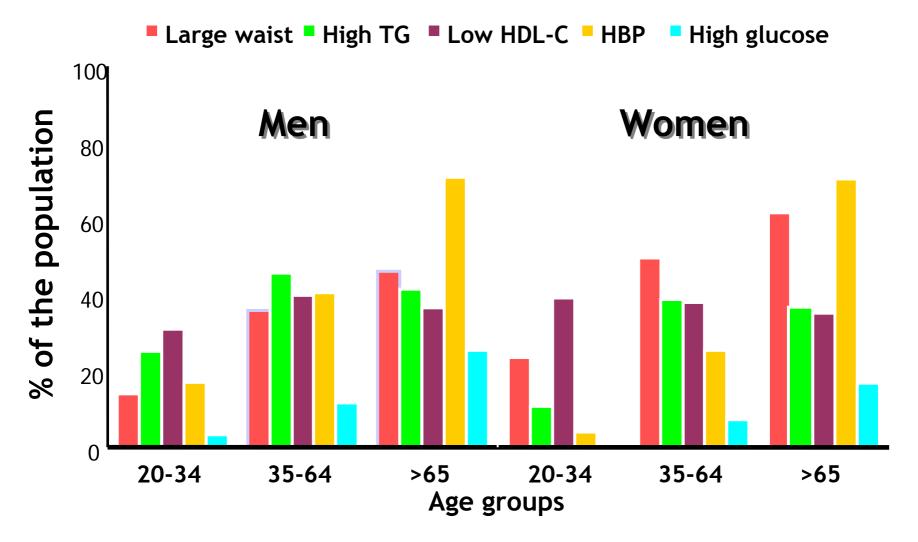
1/3 of overweight - obese subject manifest MS in USA

Prevalence of Various Components of the Metabolic Syndrome in the PAMELA Population



Mancia G et al., 2005

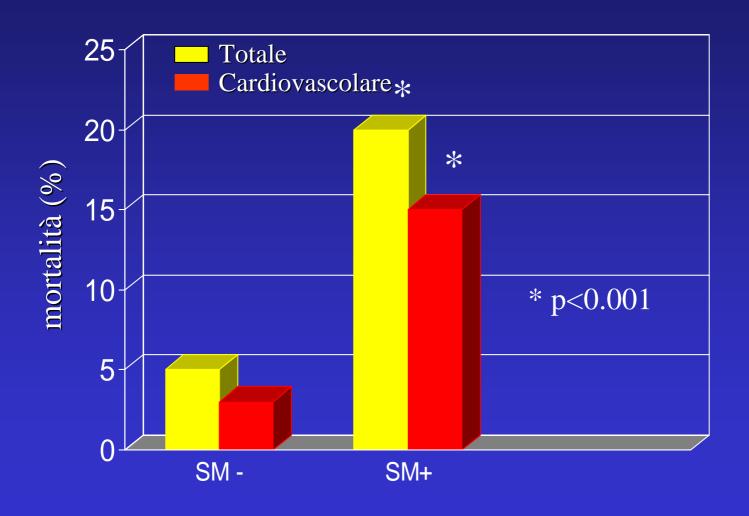
Prevalence of each metabolic syndrome component in the NHANES III population



Park T-W et al, Arch Intern Med 2003

Sindrome Metabolica e Mortalità

Mortalità cardiovascolare e totale nella SM



Isomaa et al. Diabetes Care 24:683. 2001

Impact of the Metabolic Syndrome on Mortality From Coronary Heart Disease, Cardiovascular Disease, and All Causes in United States Adults

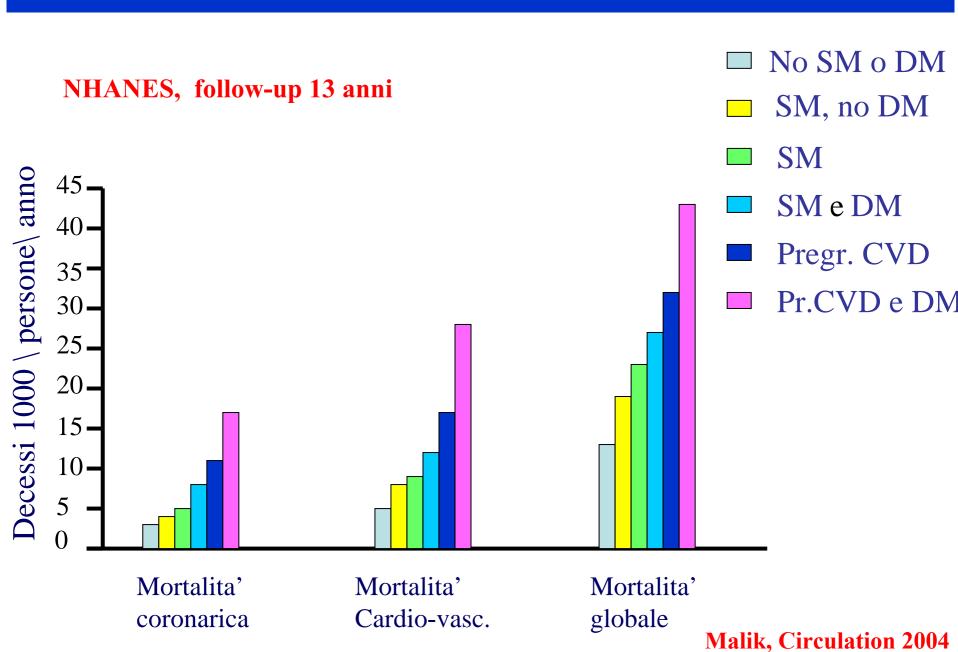
Shaista Malik, MD, MPH; Nathan D. Wong, PhD, MPH; Stanley S. Franklin, MD; Tripthi V. Kamath, PhD; Gilbert J. L'Italien, PhD; Jose R. Pio, BS; G. Rhys Williams, ScD

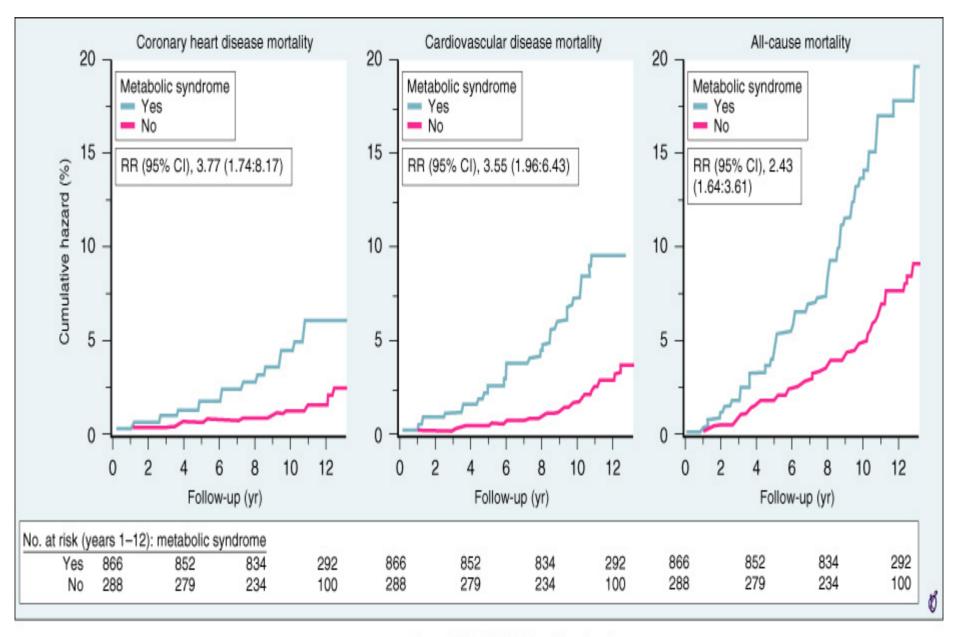
TABLE 3. Multivariable Cox Proportional-Hazards Regression Relating Each Disease/Condition Compared With Neither Condition to CHD, CVD, and Overall Mortality in US Adults

		CHD Mortality		CVD Mortality			Overall Mortality			
Condition	n	HR	95% CI	Р	HR	95% Cl	Р	HR	95% Cl	Р
No MetS, diabetes, or CVD	2878	1.0			1.0			1.0		
MetS (all)	1698	2.02	1.42-2.89	0.0001	1.82	1.40–2.37	< 0.0001	1.40	1.19–1.66	0.0001
MetS (no diabetes)*	1178	1.65	1.10-2.47	0.02	1.56	1.15–2.12	0.005	1.17	0.96-1.42	0.11
Diabetes*	520	2.87	1.84-4.47	< 0.0001	2.42	1.75–3.35	< 0.0001	1.97	1.59–2.43	< 0.0001
Pre-existing CVD (all)	1679	4.19	3.04–5.79	< 0.0001	3.14	2.49-3.96	< 0.0001	1.87	1.60–2.17	< 0.0001
Pre-existing CVD (no diabetes)*	1398	3.89	2.79–5.43	< 0.0001	2.83	2.23–3.61	< 0.0001	1.74	1.48–2.03	< 0.0001
Diabetes and CVD*	281	6.45	4.24–9.79	< 0.0001	5.26	3.82–7.23	< 0.0001	2.80	2.21-3.54	< 0.0001

n Indicates unweighted sample sizes. HRs and 95% CIs are weighted to US population and adjusted for gender, age, smoking, physical activity, and total cholesterol. *Categories represented in lieu of MetS (all) and pre-existing CVD (all) in a separate regression model.

Sindrome Metabolica e Mortalità Cardiovascolare







Elsevier Inc.

Metabolic Syndrome and risk of CHD

TABLE 3. Metabolic Syndrome and Age-Adjusted Risk for Outcomes for Framingham Offspring at 8-Year Follow-Up

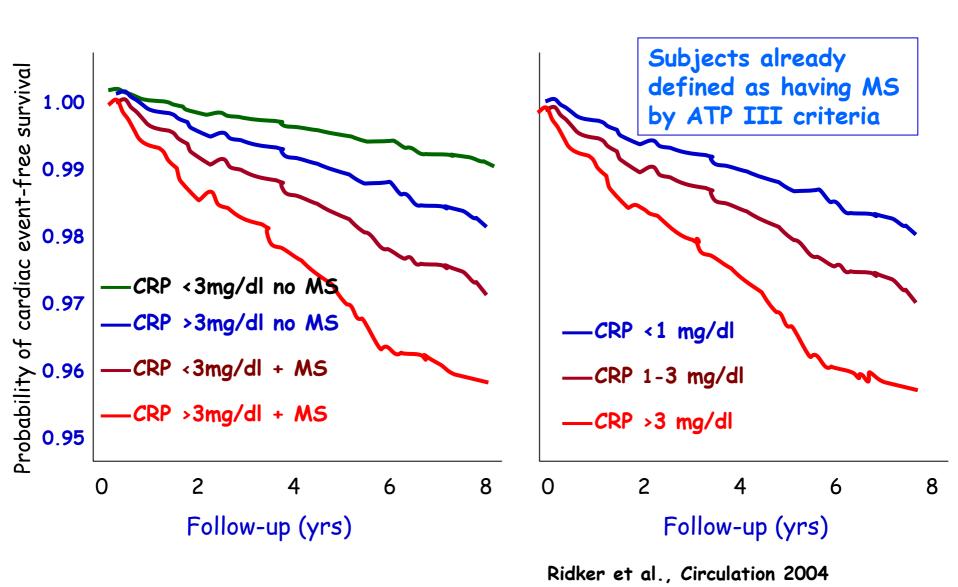
Event	No. of Metabolic Syndrome Risk Factors	Men, RR (95% CI)	Women, RR (95% CI)
CVD	0	Referent	Referent
	1 or 2	1.48 (0.69-3.16)	3.39 (1.31-8.81)
	≥3	3.99 (1.89-8.41)	5.95 (2.20–16.11)
Hard CHD	0	Referent	Referent
	1 or 2	0.98 (0.36-2.67)	3.77 (0.45-31.28)
	≥3	2.55 (0.96-6.79)	7.21 (0.81–64.37)
Total CHD	0	Referent	Referent
	1 or 2	1.24 (0.54-2.83)	3.29 (0.95-11.34)
	≥3	3.01 (1.33-6.83)	3.96 (1.02–15.38)
T2DM	0	Referent	Referent
	1 or 2	4.16 (0.98–17.64)	6.10 (1.85–20.10)
	≥3	23.83 (5.80–98.01)	29.69 (9.10–96.85)

MS accounts for up to 1/3 of CVD in men, and 1/2 of new T2DM over 8 years of follow-up

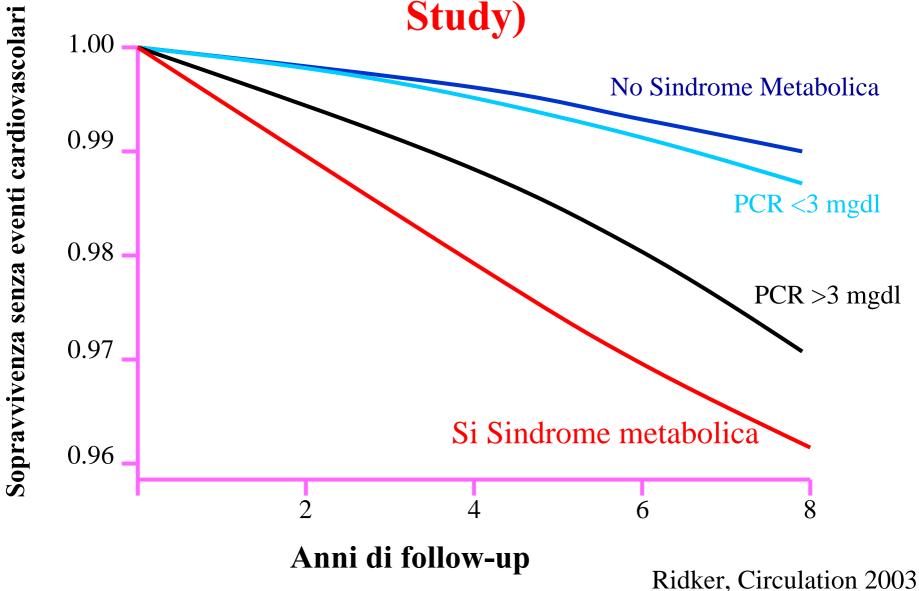
RELATIVE RISK OF FUTURE CARDIOVASCULAR EVENTS ACCORDING TO CRP LEVELS AND TO THE PRESENCE OR ABSENCE OF METABOLIC SYNDROME (MS) IN HEALTHY WOMEN

	ALL CARDIO	CORONARY EVENTS		
		LDL	LDL	
	TOTAL COHORT	<160 mg/dL	>160 mg/dL	TOTAL COHORT
	(n=14719)	(n=12453)	(n=8500)	(n=14719)
CRP<3 mg/L no MS	1.0	1.0	1.0	1.0
CRP>3 mg/L no MS	1.5	1.3	1.2	1.6
	(1.0-2.2)	(0.8-2.2)	(0.6-2.3)	(0.9-2.7)
CRP<3 mg/L + MS	2.3	2.2	2.5	3.1
	(1.6-3.3)	(1.4-3.5)	(1.4-4.4)	(2.0-4.9)
CRP>3 mg/L +(MS)	4.0	4.4	4.4	5.5
	(3.0-5.4)	(3.1-6.3)	(2.8-7.1)	(3.8-8.0)

CARDIOVASCULAR EVENT-FREE SURVIVAL ACCORDING TO CRP LEVELS AND TO THE PRESENCE OR ABSENCE OF METABOLIC SYNDROME (MS) IN HEALTHY WOMEN



PCR e Sindrome metabolica : effetto sul rischio cardiovascolare. 14716 donne (Women's Health Study)



La Sindrome Metabolica: esiste ancora?

The Metabolic Syndrome: Requiescat in Pace

Gerald M. Reaven

It is essential to emphasize at this point that insulin resistance is not a disease, but a description of a physiologic state that greatly increases the chances of an individual developing several closely related abnormalities and associated clinical syndromes. Insulin resistance does not necessarily lead to the clinical syndromes listed in Table 2, and to various degrees, the syndromes can all occur in the absence of insulin resistance. The primary

The Metabolic Syndrome: Requiescat in Pace

GERALD M. REAVEN

In conclusion, it appears that making the diagnosis of the metabolic syndrome does not bring with it much in the way of pathophysiologic understanding or clinical utility, and deciding that individuals do not have it because they fail to satisfy three of five arbitrarily chosen criteria may withhold relevant therapeutic intervention. Does the ATP III concept of the metabolic syndrome have any redeeming virtues? That is a question that only the reader can answer.

The Metabolic Syndrome: Time for a Critical Appraisal

Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes

RICHARD KAHN, PHD¹ JOHN BUSE, MD, PHD² ELE FERRANNINI, MD³ MICHAEL STERN, MD⁴

The Metabolic Syndrome: Time for a Critical Appraisal

Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes

Table 3—Summary of concerns regarding the metabolic syndrome



- 1) Criteria are ambiguous or incomplete.
 Rationale for thresholds are ill defined.
- Value of including diabetes in the definition is questionable.
- Insulin resistance as the unifying etiology is uncertain.
- No clear basis for including/excluding other CVD risk factors.
- CVD risk value is variable and dependent on the specific risk factors present.
- 6) The CVD risk associated with the "syndrome" appears to be no greater than the sum of its parts.



 Treatment of the syndrome is no different than the treatment for each of its components.



The medical value of diagnosing the syndrome is unclear.

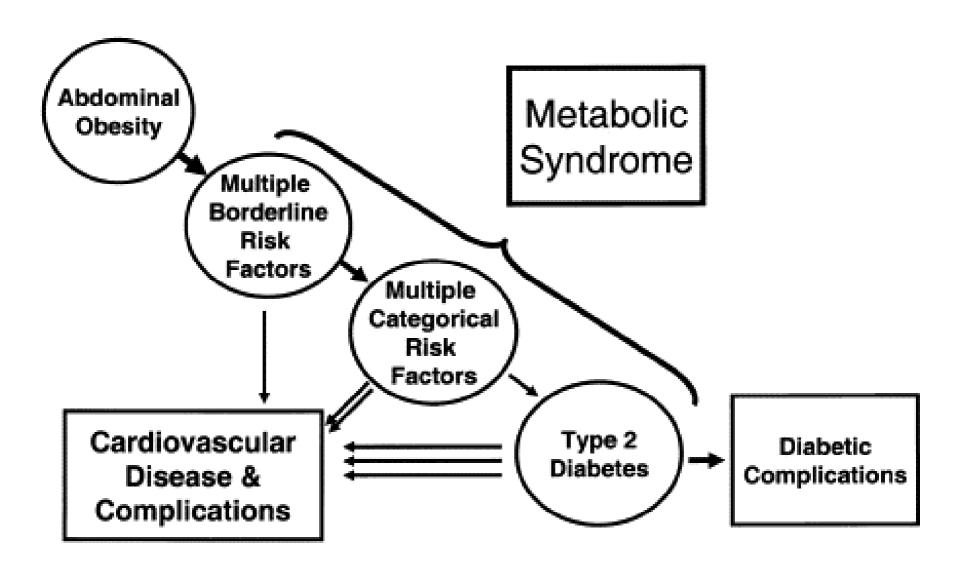
STATE-OF-THE-ART PAPER

Metabolic Syndrome: Connecting and Reconciling Cardiovascular and Diabetes Worlds

Scott M. Grundy, MD, PHD

Dallas, Texas

Progression and outcomes of the metabolic syndrome.

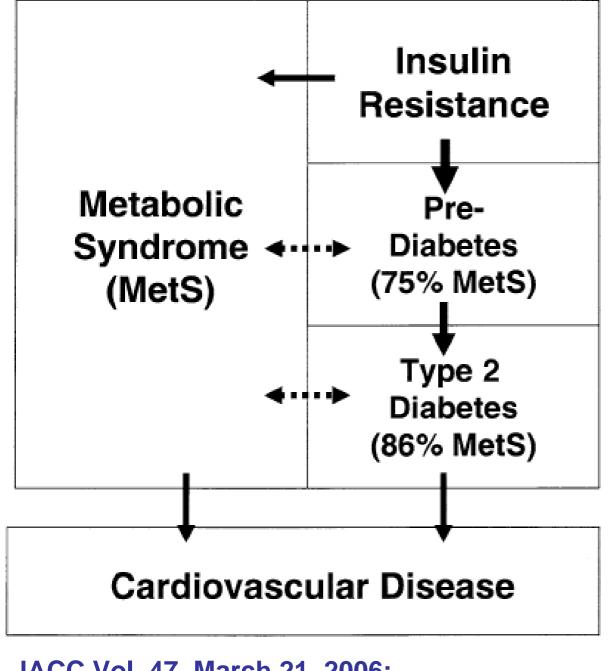


JACC Vol. 47, March 21, 2006:

Table 1. Diagnostic Criteria for Metabolic Syndrome

Measure (Any 3 of the 5 Criteria Below Constitute a Diagnosis of Metabolic Syndrome)	Categorical Cut Points
Elevated waist circumference*† Elevated triglycerides	≥102 cm (≥40 inches) in men ≥88 cm (≥35 inches) in women ≥150 mg/dl (1.7 mmol/l)
Reduced HDL-C	or drug treatment for elevated triglycerides‡ <40 mg/dl (0.9 mmol/l) in men <50 mg/dl (1.1 mmol/l) in women
Elevated blood pressure	or drug treatment for reduced HDL-C‡ ≥130 mm Hg systolic blood pressure or
Elevated fasting glucose	≥85 mm Hg diastolic blood pressure or drug treatment for hypertension ≥100 mg/dl
ol. 47, March 21, 2006:	or drug treatment for elevated glucose

JACC Vol. 47, March 21, 2006: drug treatment for elevated glucose



Interrelations and overlap of metabolic syndrome with insulin resistance, prediabetes, and type 2 diabetes. **According to the** insulin resistance hypothesis, the metabolic syndrome is caused predominantly by insulin resistance.

JACC Vol. 47, March 21, 2006:

ABC of obesity Obesity and vascular disease

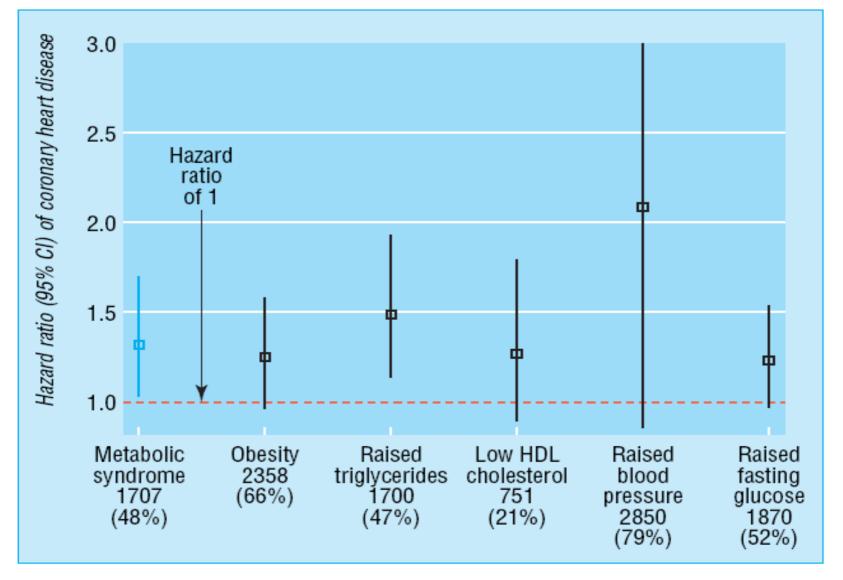
Debbie A Lawlor, Mike Lean, Naveed Sattar

Previous articles in this series have discussed the relation of overweight and obesity with coronary heart disease (CHD) and individual cardiovascular disease risk factors—such as diabetes, raised blood pressure, and dyslipidaemia. This article examines the wider impact of obesity on vascular disease: the effect on cardiovascular disease of obesity as primary cause of the metabolic syndrome and of obesity as a risk factor for heart failure, stroke, other vascular conditions, and cognitive decline.

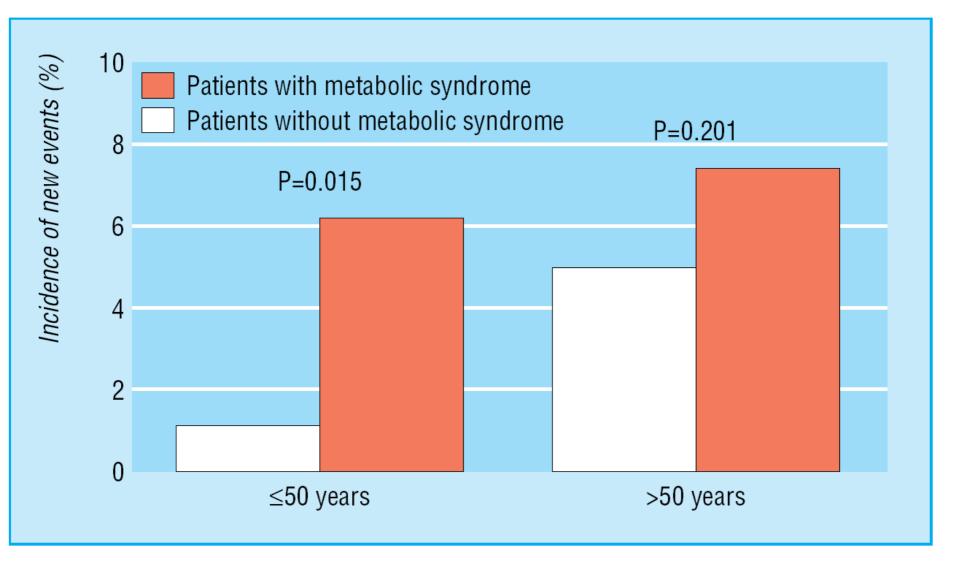
This is the eighth article in the series



BMJ VOLUME 333 18 NOVEMBER 2006 bmj.com



Age adjusted hazard ratio of coronary heart disease associated with International Diabetes Federation's definition of metabolic syndrome and each component of this definition among 3589 British women aged 60-79 years. Data from Lawlor et al (*Diabetologia* 2006 doi: 10.1007/s00125-005-0040-3)

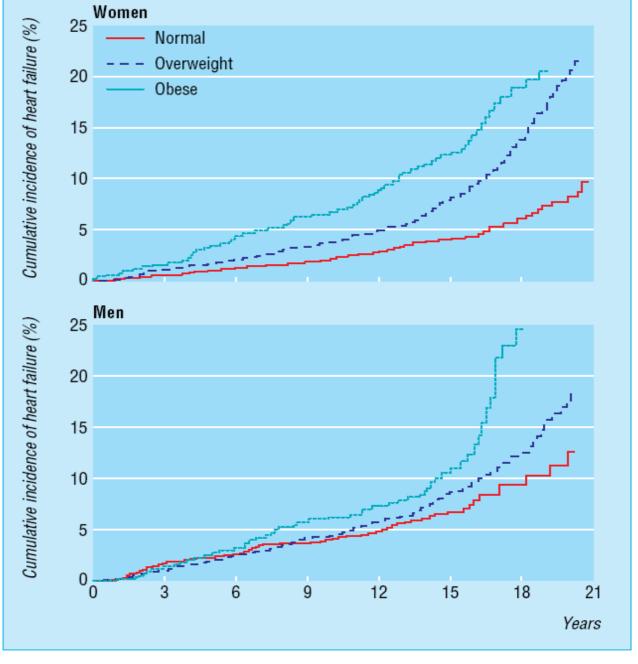


Age stratified incidence of new cardiovascular events (myocardial infarction, revascularisation, cardiac death) in patients with or without metabolic syndrome (according to modified criteria of American Treatment Panel III). Adapted from Reinhard et al (Am J Cardiol 2006;97:964-7)

BMJ VOLUME 333 18 NOVEMBER 2006

CHF

BMJ VOLUME 333 18 NOVEMBER 2006



Cumulative incidence of heart failure by weight category (based on body mass index) at baseline examination in Framingham study. Adapted from Kenchajah et al (see Further Reading box)

Terapia

Trattamento della Sindrome metabolica?

- La riduzione dell'apporto calorico e l'incremento dell'esercizio fisico sono essenziali per il trattamento di tutte le componenti della sindrome metabolica
- La presenza di più fattori di rischio rende necessario un trattamento più aggressivo di ciascuno di essi
- La scelta della terapia farmacologica per ciascun fattore di rischio richiede attenta considerazione agli effetti sui fattori di rischio associati

Come possiamo intervenire?

Modificazioni

dello stile di vita

(riduzione del

peso e aumento dell' esercizio fisico)

Ottimo effetto su tolleranza glicidica e TG

Discreto effetto sulla PA

Modesto effetto su LDL (-15%)





To prevent the slippery slope of the MS towards diabetes and CHD ...

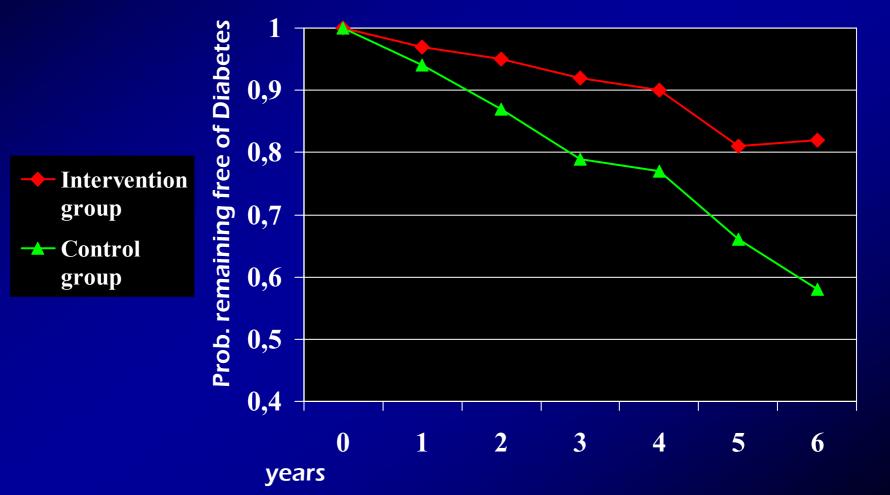
Modest weight loss	5-7%
Modest increase in physical activity	150 min/week

Absolute risk reduction of diabetes of 14,5% over 3 years

JAMC 2004; 170 (9): 1390

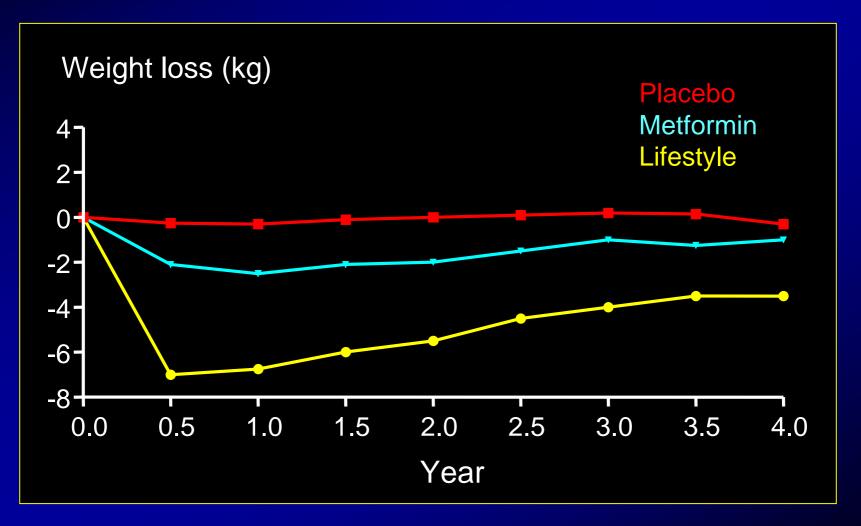
Prevention of Type 2 Diabetes Mellitus by changes in lifestyle among subjects with impaired glucose tolerance

RCT, 523 patients with IGT,BMI>25 kg/m2;follow-up 3.2 years



Tuomilehto et al., N Engl J Med 2001;344:1343

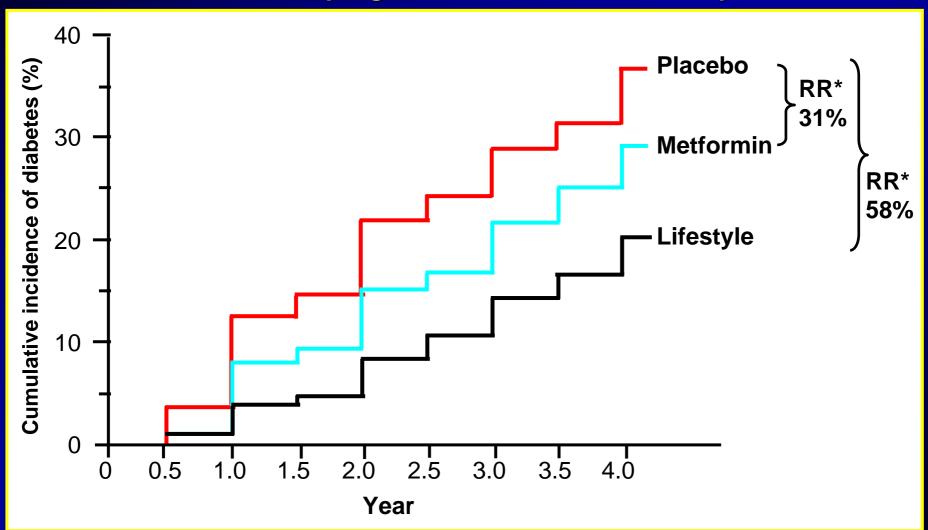
Diabetes Prevention Program





Diabetes Prevention Program

*Riduzione del rischio di progressione a diabete versus placebo



Validation of a Counseling Strategy to Promote the Adoption and the Maintenance of Physical Activity by Type 2 Diabetic Subjects Diabetes Care Diabetes Care 2003

CHIARA DI LORETO, MD CARMINE FANELLI, MD Paola Lucidi, md GIUSEPPE MURDOLO, MD ARIANNA DE CICCO, MD

BMI (kg/m²)

HbA_{1c} (%)

Natascia Parlanti, md FAUSTO SANTEUSANIO, MD PAOLO BRUNETTI, MD Pierpaolo De Feo, md

Table 3—Effects of the 2-year intervention on levels of physical activity (energy expenditure through voluntary physical activity, METs × h/week), caloric intake, BMI, and HbA_{1c} compared with the usual care (control group)

	Intervention group		Control group			
	2 years	Δ versus basal	2 years	Δ versus basal	P*	
Percent of patients > 10 METs × h/week	69	+66.2	18	+14.2	< 0.001	
METa × h/woolz	271 + 20	±26 ± 2.0	4.1 + 0.9	$\pm 2.2 \pm 0.7$	<0.001	

	IIIterver	ition group	Conti		
	2 years	Δ versus basal	2 years	Δ versus basal	P*
Percent of patients $>$ 10 METs \times h/week	69	+66.2	18	+14.2	< 0.001
METs × h/week	27.1 ± 2.0	$+26 \pm 2.0$	4.1 ± 0.8	$+3.2 \pm 0.7$	< 0.001
Diet prescription (kcal/day)	1.677 ± 36	$+142 \pm 10$	1.485 ± 31	-25 ± 4	< 0.01

 -0.4 ± 0.1

 -0.6 ± 0.05

 30.4 ± 0.3

 7.6 ± 0.1

 $+0.6 \pm 0.1$

 -0.1 ± 0.04

< 0.01

< 0.001

 28.9 ± 0.2

 7.0 ± 0.1

The Finnish Diabetes Prevention Study (DPS)

Lifestyle intervention and 3-year results on diet and physical activity

Jaana Lindström, msc¹ Anne Louheranta, phd² Marjo Mannelin, msc³ Merja Rastas, msc⁴ Virpi Salminen, msc⁵

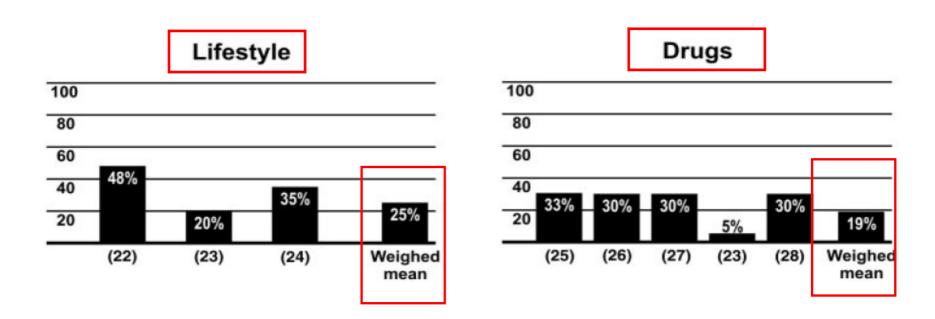
JOHAN ERIKSSON, MD, PHD¹
MATTI UUSITUPA, MD, PHD²
JAAKKO TUOMILEHTO, MD, PHD^{1,6}
FOR THE FINNISH DIABETES PREVENTION
STUDY GROUP

Table 2—Changes in physical activity and nutrient intakes from baseline to years 1 and 3

	From	baseline to year 1		From		
Leisure Time Intervention Physical Activity group Control group		P*	Intervention group	Control group	P*	
n	256	250		231	203	
Total LTPA (min/week)	16 (-126 to 115)	21 (-133 to 138)	0.9045	50 (-126 to 115)	23 (-1 4 2 to 171)	0.2415
Moderate-to-vigorous LTPA (min/week)	49 (-41 to 140)	14 (-47 to 90)	0.0073	61 (-33 to 168)	6 (-91 to 10 1)	0.0057

Are there specific treatments for the metabolic syndrome? 1-3

Dario Giugliano, Antonio Ceriello, and Katherine Esposito

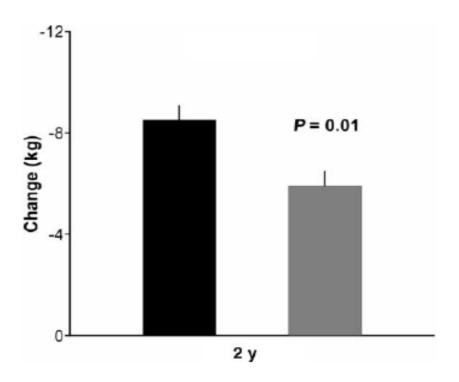


Percentage resolution of metabolic syndrome

according to therapeutic strategies

Are there specific treatments for the metabolic syndrome? 1-3

Dario Giugliano, Antonio Ceriello, and Katherine Esposito



Mean changes in body weight at the 2-year follow-up in 115 women consuming a **Mediterranean-style diet**

DIETA MEDITERRANEA



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

A Randomized Trial

90 subjects following a Mediterranean diet vs. 90 following a prudent diet

	Interventi	tervention Diet (n = 90) Control Diet (n = 90)			Between-Group Comparison of Change			
	Mean ((SD)	'	Mean ((SD)	'		
Variable	2 Years	Change	<i>P</i> Value	2 Years	Change	<i>P</i> Value	Difference (95% CI)	P Value at 2 Years
Weight, kg	74 (7)	-4 (1.1)	<.001	75.8 (7)	-1.2 (0.6)	.02	-2.8 (-5.1 to -0.5)	<.001
Body mass index*	26.7 (3.1)	-1.2 (0.3)	<.001	27.7 (3.1)	-0.4 (0.4)	.06	-0.8 (-1.4 to -0.2)	.01
Waist circumference, cm	90 (8)	-2 (0.5)	.01	93 (10)	0 (0.01)	.74	-2 (-3.5 to -0.5)	.01
Plasma glucose, mg/dL	105 (9)	-8 (3)	<.001	112 (9)	-2.0 (1.5)	.21	-6 (−11 to −2)	<.001
Serum insulin, µU/mL	11 (5)	-4 (1.9)	.01	15.5 (7)	-0.5 (1.0)	.45	-3.5 (-6.1 to -1.7)	.01
HOMA score	2.5 (0.6)	-1.2 (0.5)	<.001	3.7 (0.7)	-0.1 (0.2)	.12	-1.1 (-1.9 to -0.3)	<.001
Serum lipids, mg/dL Total cholesterol	188 (29)	-11 (6)	.01	191 (30)	-2 (2)	.23	-9 (-17 to -1)	.02
HDL-C	45 (10)	+4 (2)	.01	43 (9)	+1 (1)	.08	+3 (0.8 to 5.2)	.03
Triglycerides	150 (49)	-18 (8)	.01	173 (53)	+1 (3)	.15	-19 (-32 to -6)	.001
Blood pressure, mm Hg Systolic	130 (8)	-4 (2)	<.001	135 (10)	-1 (1)	.06	−3 (−5 to −1)	.01
Diastolic	82 (5)	-3 (1)	<.001	85 (6)	-1 (1)	.05	-2 (-3.5 to -0.5)	.03
Endothelial function score	7.9 (1.3)	+1.9 (0.6)	<.001	6.1 (1.1)	+0.2 (0.2)	.09	+1.7 (1.0 to 2.4)	<.001
ns-CRP and cytokines, median (IQR) hs-CRP, mg/L	1.7 (0.4-4.9)	-1.1 (0.4)	.01	2.8 (0.5-5.5)	-0.1 (0.3)	.12	-1 (-1.7 to -0.3)	.01
IL-6, pg/mL	1.4 (0.4-3.8)	-0.7 (0.3)	.02	1.8 (0.5-4.5)	-0.1 (0.2)	.21	-0.6 (-1.1 to -0.1)	.04
IL-7, pg/mL	1.9 (0.5-5.2)	-0.5 (0.2)	.04	2.6 (0.7-6.0)	0 (0.1)	.78	-0.5 (-0.9 to -0.1)	.04
IL-18, pa/mL	148 (92-219)	-19 (9)	.03	171 (100-230)	-4 (3)	.08	-15 (-28 to -2)	.03
No. of components of the metabolic syndrome, No. (%) Adjusted for weight changes 3	31 (34)	-43		59 (66)	-17		-26 7	
4	10 (11)	-8		12 (13)	-4		-4	<.001
5	1 (1)	-7		7 (8)	-1		-6 _	
Unadjusted for weight changes								
3	24 (27)	-50		55 (61)	-21		-29	
4	6 (7)	-12		11 (12)	-5		-7	<.001
5	0	-8		6 (7)	-2		-6 <u></u>	

Giugliano et al. JAMA 2004

Adherence to Mediterranean diet and risk of developing diabetes: prospective cohort study



Table 2 | Incidence and relative risk of type 2 diabetes (confirmed cases) during follow-up according to adherence (Trichopoulou's score²²) to Mediterranean food pattern at baseline

	No in group	Unadjusted cumulative incidence of type 2 diabetes (%)	Incidence rate ratio* adjusted for age and sex (95% CI)	Multivariate adjusted incidence rate ratio (95% CI)†
Low (score 0-2)	2253	0.40	1 (reference)	1 (reference)
Moderate (score 3-6)	9604	0.23	0.41 (0.19 to 0.87)	0.40 (0.18 to 0.90)
High (score 7-9)	1523	0.13	0.17 (0.04 to 0.75)	0.17 (0.04 to 0.72)

^{*}Poisson regression model with robust standard errors.

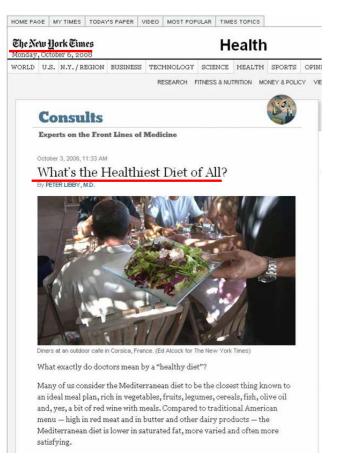
†Adjusted for sex, age, years of university education (three categories), body mass index (continuous), family history of diabetes (two categories), hypertension at baseline (two categories), physical activity (three categories), hours/week sitting down (five categories), smoking (three categories), total energy intake (continuous). P=0.04 for trend from likelihood ratio test when Trichopoulou's score was introduced as continuous variable in fully multivariate adjusted model.



RESEARCH

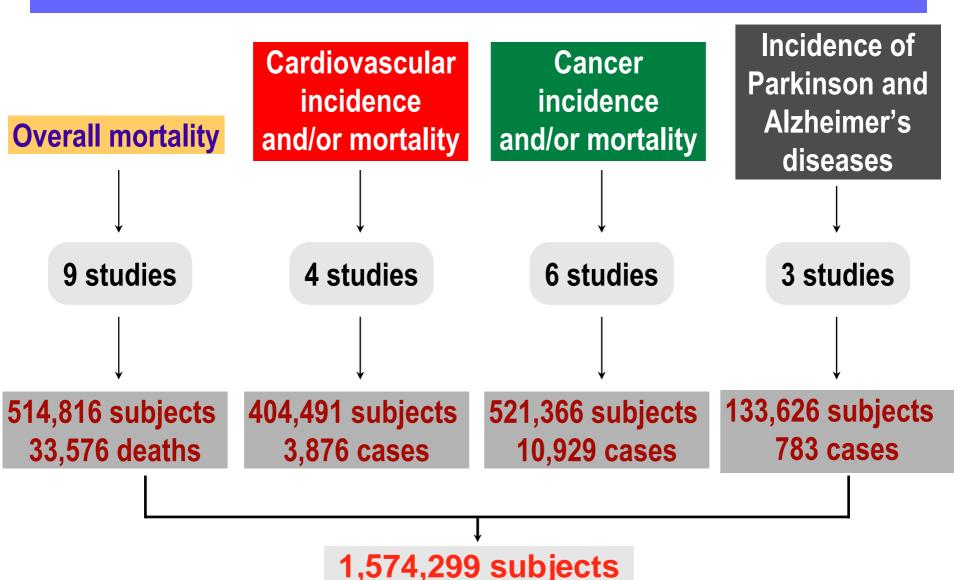
Adherence to Mediterranean diet and health status: meta-analysis

Francesco Sofi, researcher in clinical nutrition, 1.25 Francesca Cesari, researcher, 1 Rosanna Abbate, full professor of internal medicine, 1.5 Gian Franco Gensini, full professor of internal medicine, 3 Alessandro Casini, associate professor of clinical nutrition 2.4.5





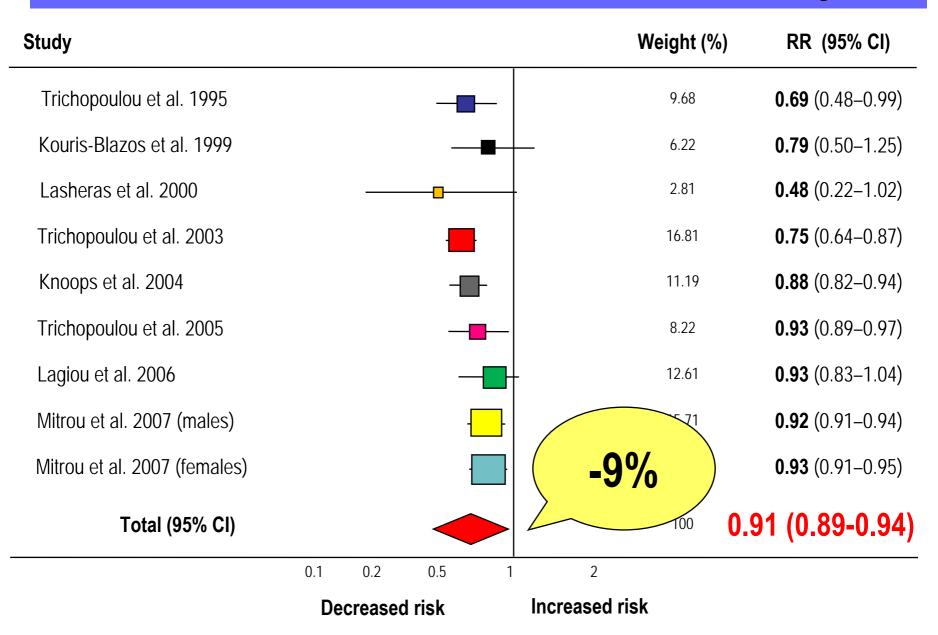
Studies included



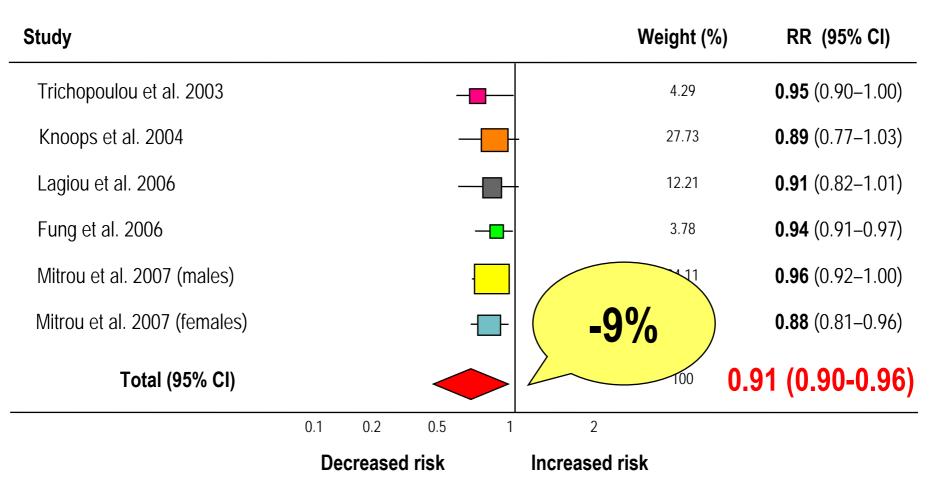
49,164 cases

Sofi et al., BMJ 20 September 2008

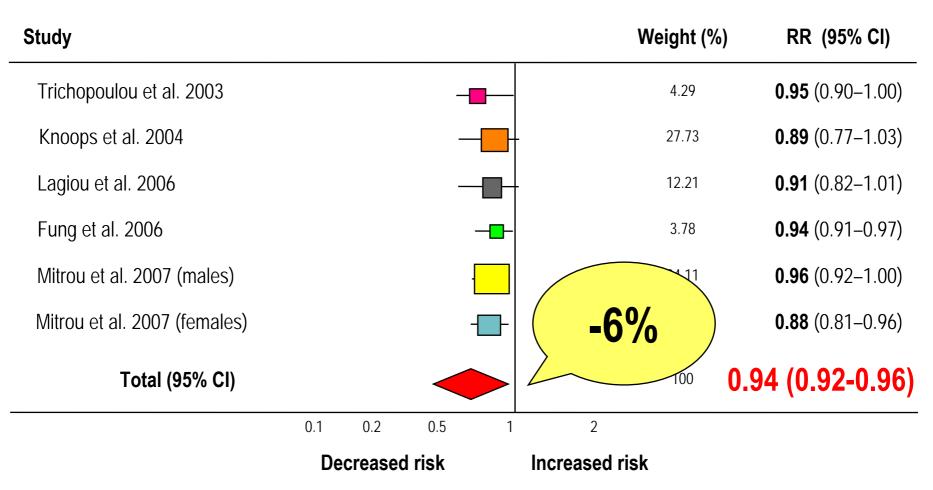
Adherence to MD and overall mortality



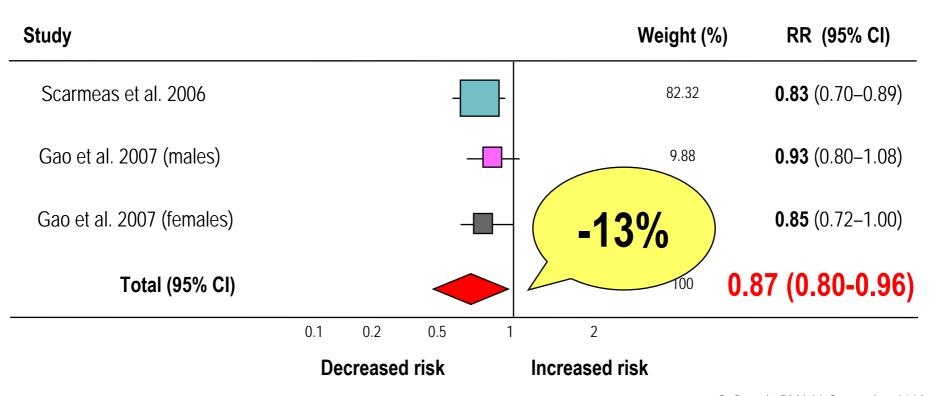
Adherence to MD and cardiovascular incidence and/or mortality



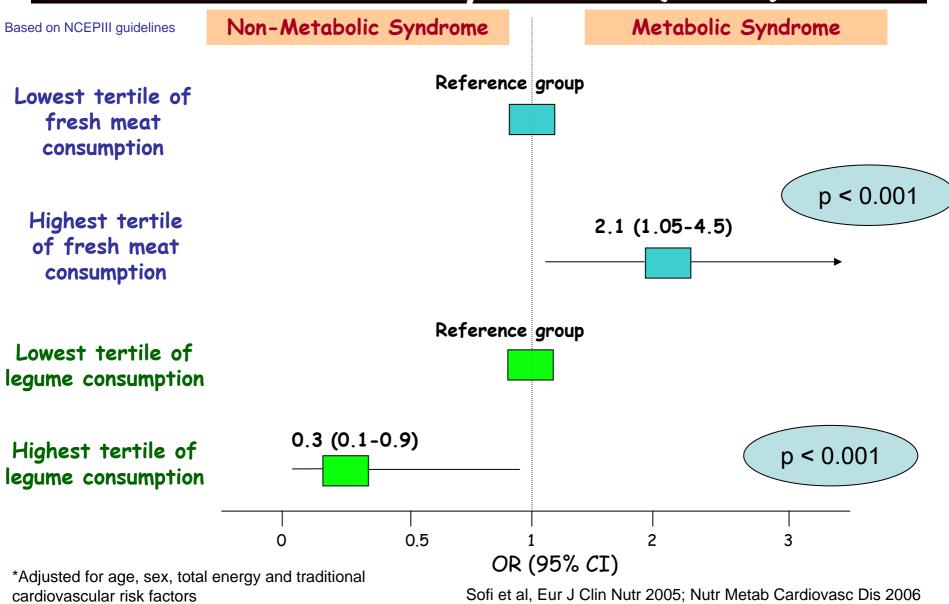
Adherence to MD and cancer incidence and/or mortality



Adherence to MD and incidence of Parkinson and Alzheimer's diseases



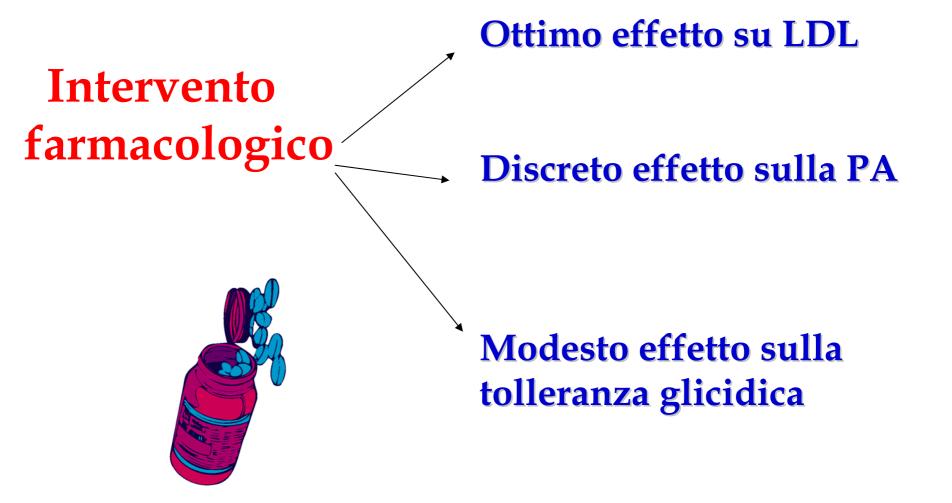
Multivariate logistic regression analysis on Metabolic Syndrome (n=54)*



Trattamento della Sindrome metabolica?

- La riduzione dell'apporto calorico e l'incremento dell'esercizio fisico sono essenziali per il trattamento di tutte le componenti della sindrome metabolica
- La presenza di più fattori di rischio rende necessario un trattamento più aggressivo di ciascuno di essi
- La scelta della terapia farmacologica per ciascun fattore di rischio richiede attenta considerazione agli effetti sui fattori di rischio associati

Come possiamo intervenire?



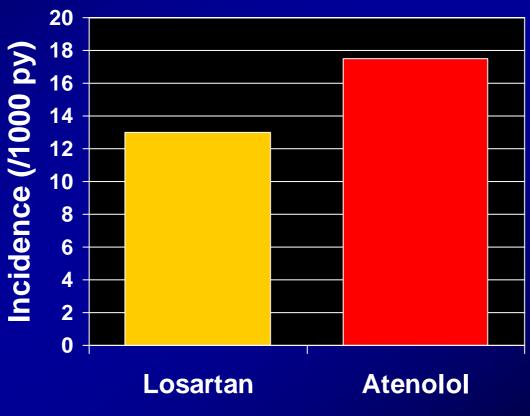
Global Guidline for type 2 Diabetes. International Diabetes Federation 2005

Trattamento della Sindrome metabolica?

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Losartan and diabetes

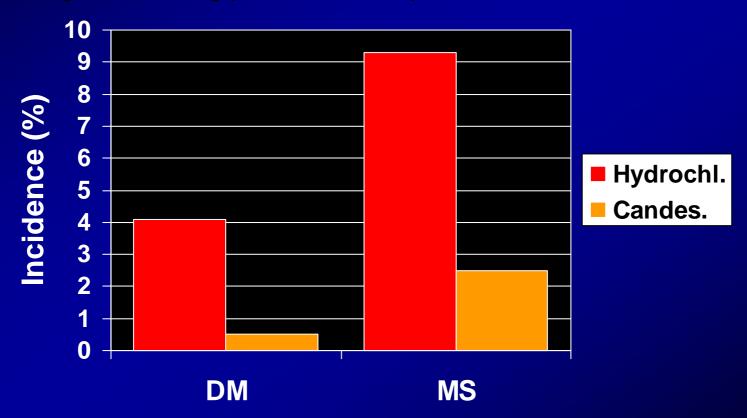
9193 patients with hypertension and LVH; losartan vs. atenolol, double-blind.



Lindholm et al., J Hypert 20:1879, 2002

ALPINE Study

RCT, PS; hydrochlorothiazide vs. candesartan, DB, 1yr. 386 hypertensive patients.



Lindholm et al., J Hypertens 21:1563, 2003

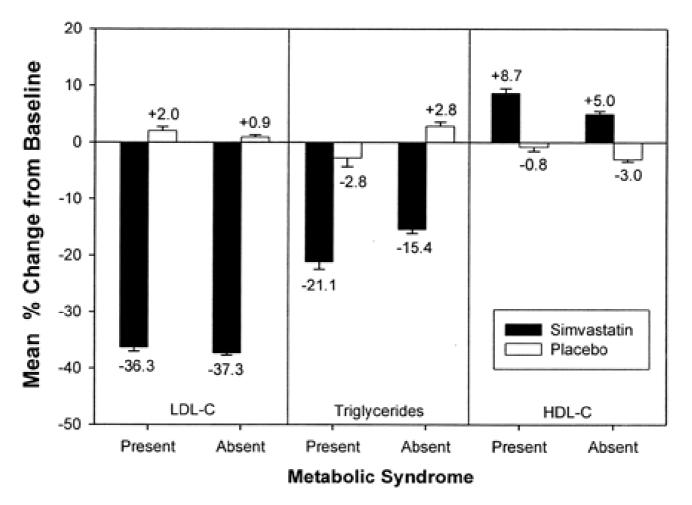
ALPINE Study

Metabolic effects of antihypertensive treatment: long live the debate

Ele Ferrannini and Michaela Kozáková

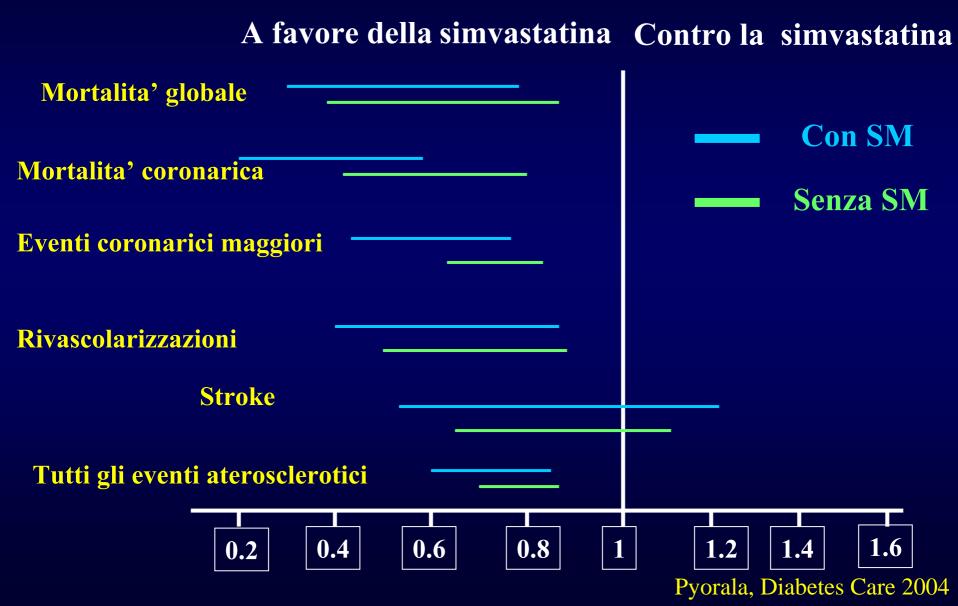
Journal of Hypertension 2003, 21:1459-1462

Change in lipid parameters in nondiabetic CHD patients with and without the metabolic syndrome after treatment with simvastatin in the 4S



Pyorala K et AL., Diabetes Care 2004

Statine nella sindrome metabolica: dati dal 4S

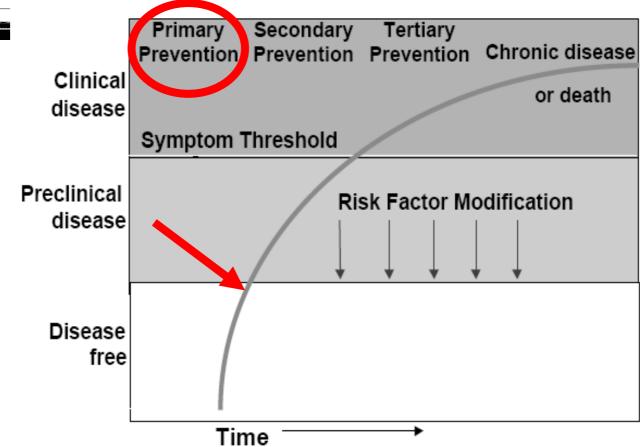


- ✓ La SM *deve essere* vista uno strumento semplice per individuare facilmente e precocemente pazienti su cui intervenire aggressivamente con interventi farmacologici e non
- ✓ E' certamente un buon predittore di sviluppo di diabete di tipo 2 e malattia CV
- ✓ L'intervento sul peso e sull'attività fisica ha ottimi effetti soprattutto sulla tolleranza glicidica
- ✓ L'intervento sul colesterolo LDL, il più precoce da attuare, è attualmente il più agevole ed efficace grazie alla presenza di statine sicure e sperimentate
- ✓ Le associazioni di statine con altri farmaci CV è sicura e vantaggiosa

Daniel F Hanley MD

The Challenge of

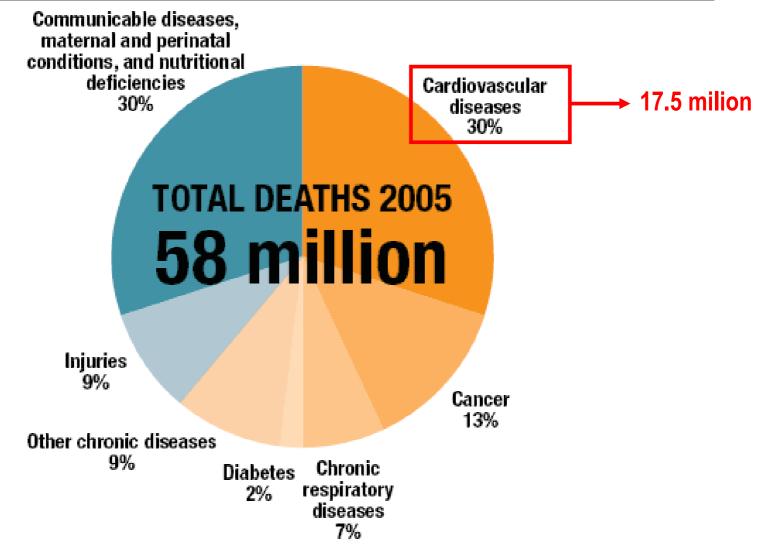
Prevention



The World Health Report 2006



Main causes of death worldwide at all ages (year: 2005)



Worlwide deaths by causes (year: 2005)

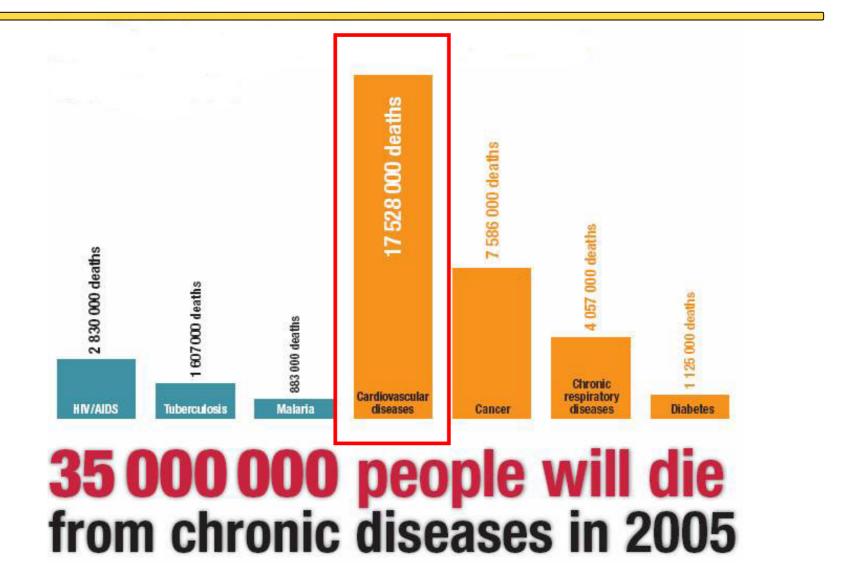


Figure 4.9 Global distribution of burden of disease attributable to 20 leading selected risk factors

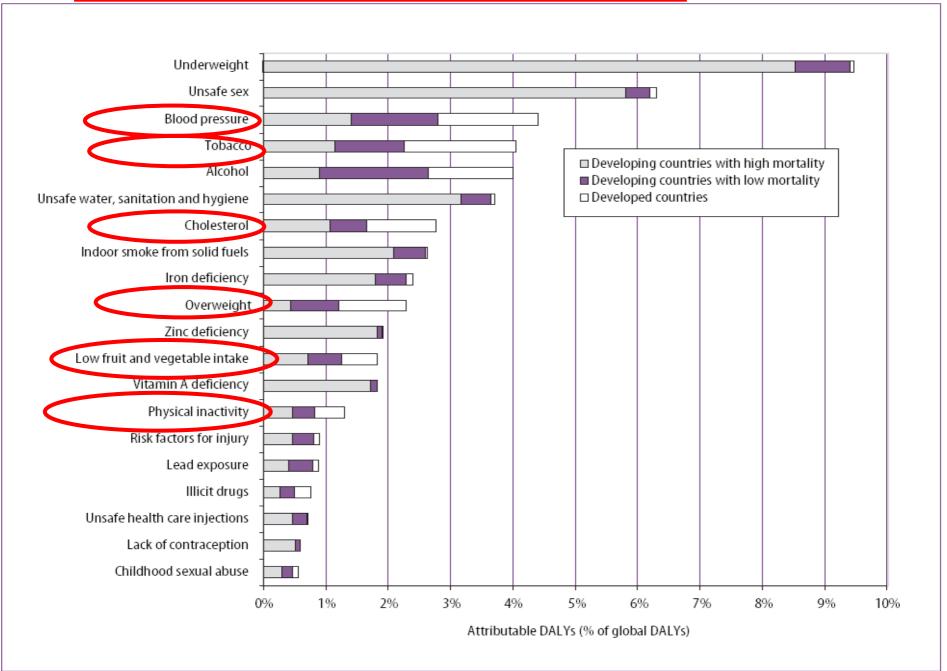


Table 4.11 Ranking of estimated attributable and avoidable burdens of 10 leading selected risk factors

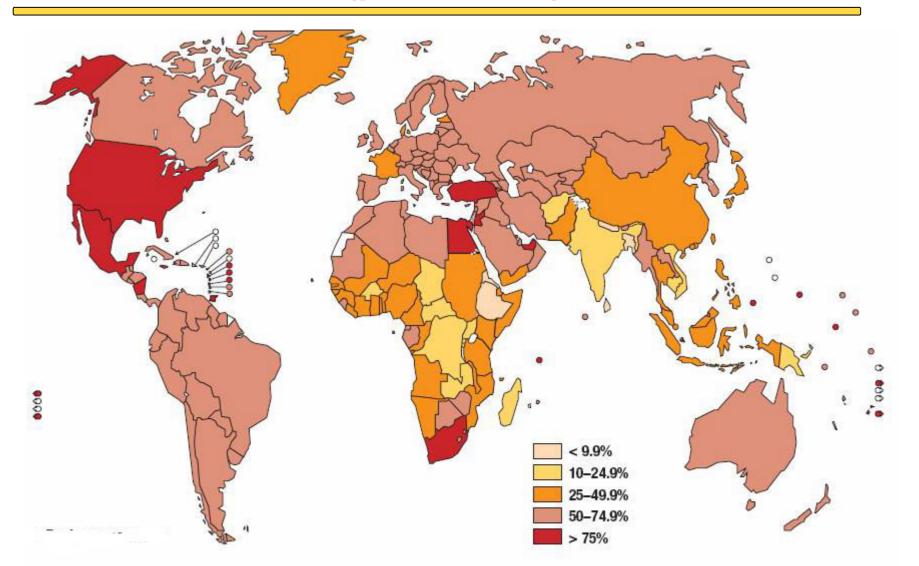
		_	Estimated attributable burden			Estimated avoidable burden after 25% distributional transition from 2001				
	Rank	2000	DALYs (millions)	000 % total	2010	in 2 DALYs (millions)	2010 % total	2020	in 20 DALYs (millions)	020 % total
	1	Underweight	138	9.5	Unsafe sex	42	3.0	Unsafe sex	71	4.8
	2	Unsafe sex	92	6.3	Blood pressure	25	1.7	Blood pressure	27	1.9
	3	Blood pressure	64	4.4	Underweight	23	1.6	Tobacco	22	1.5
	4	Tobacco	59	4.1	Tobacco	17	1.2	Cholesterol	17	1.2
Ī	5	Alcohol	58	4.0	Cholesterol	15	1.1	Underweight	16	1.1
	6	Unsafe water sanitation and hygiene	e 54	3.7	Alcohol	15	1.1	Alcohol	16	1.1
	7	Cholesterol	40	2.8	Overweight	13	0.9	Overweight	15	1.0
	8	Indoor smoke from solid fuels	39	2.6	Iron deficiency	9	0.6	Low fruit and vegetable intake	9	0.6
	9	Iron deficiency	35	2.4	Low fruit and vegetable intake	9	0.6	Iron deficiency	7	0.5
	10	Overweight	33	2.3	Unsafe water, sanitation and hygien	e 8	0.6	Physical inactivity	6	0.4
	Total	DALYs	1 455			1 417			1 459	

Table 4.11 Ranking of estimated attributable and avoidable burdens of 10 leading selected risk factors

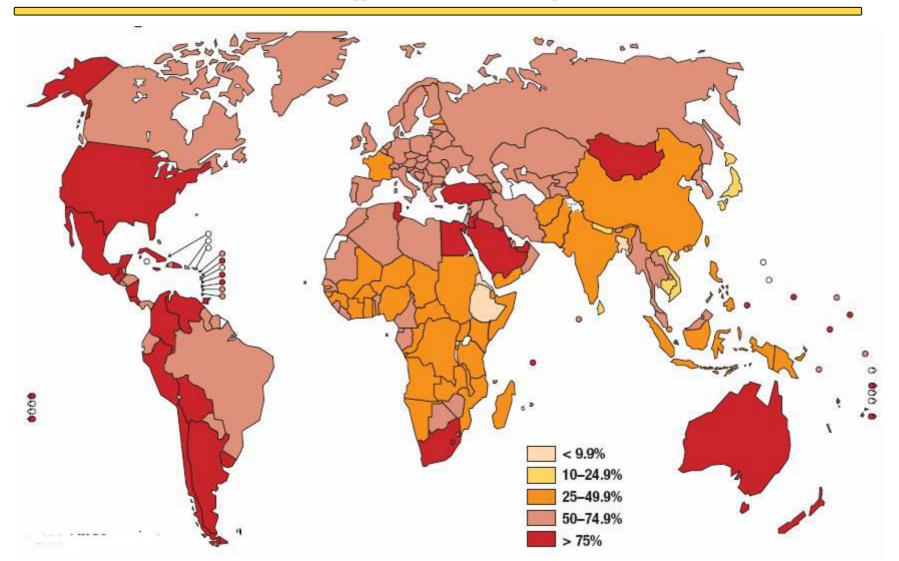
	Estimated attributable burden				Estimated avoidable burden after 25% distributional transition from 2001					
R	tank	2000	DALYs (millions)	00 % total	2010	in 2 DALYs (millions)	2010 % total	2020	in 2 DALYs (millions)	020 % total
	1	Underweight	138	9.5	Unsafe sex	42	3.0	Unsafe sex	71	4.8
	2	Unsafe sex	92	63	Blood pressure	25	1.7	Blood pressure	27	1.9
1	3	Blood pressure	64	4.4	Underweight	23	1.6	lobacco	22	1.5
	4	Tobacco	59	→	Tobacco	17	11	Cholesterol	17	1.2
	5	Alcohol	58	4.0	Cholesterol	15	1.1	Underweight	16	1.1
	6	Unsafe water sanitation and hygien	e 54	3.7	Almini	15	1.1	Alcohol	16	1.1
	7	Cholesterol	40	2.8	Overweight	13	0.9	Overweight	15	1.0
	8	Indoor smoke from solid fuels	39	2.6	Iron deficiency	9	0.6	Low fruit and vegetable intake	9	0.6
	9	Iron deficiency	35	2.4	Low fruit and vegetable intake	9	0.6	Iron deficiency	7	0.5
	10	Overweight	33	2.3	Unsafe water, sanitation and hygien	e 8	0.6	Physical inactivity	6	0.4
1	otal	DALYs	1 455			1 417			1 459	

Obesity

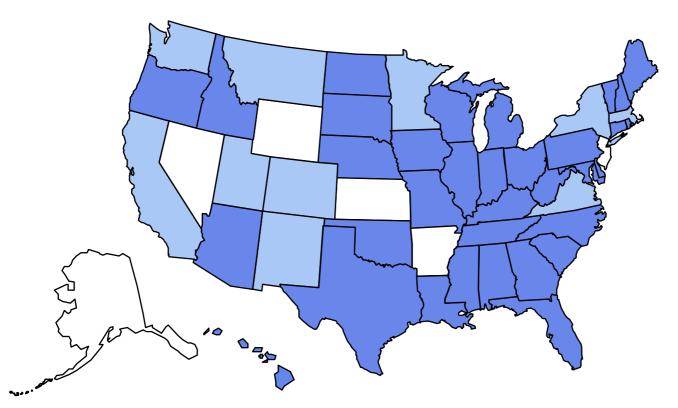
Prevalence of overweight (BMI>25 kg/m₂) (year: 2005)



Prevalence of overweight (BMI>25 kg/m₂) (year: 2015)

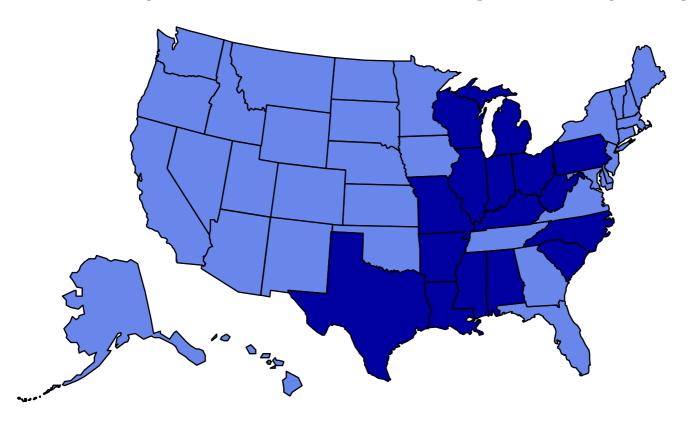


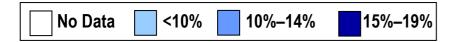
BRFSS, 1990 (*BMI ≥30, or ~ 30 lbs overweight for 5' 4" person)



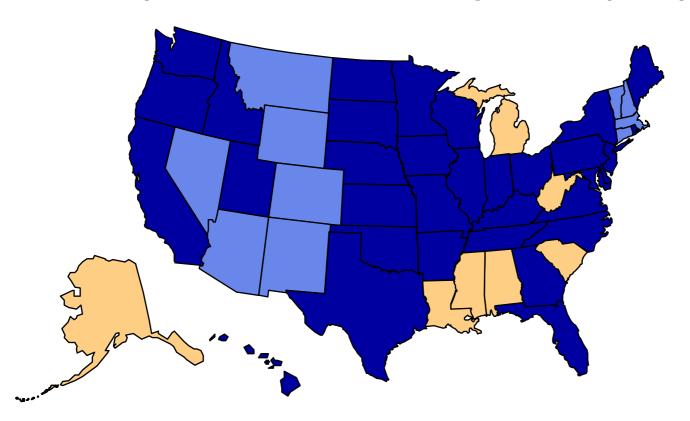


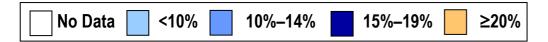
BRFSS, 1994
(*BMI ≥30, or ~ 30 lbs overweight for 5' 4" person)



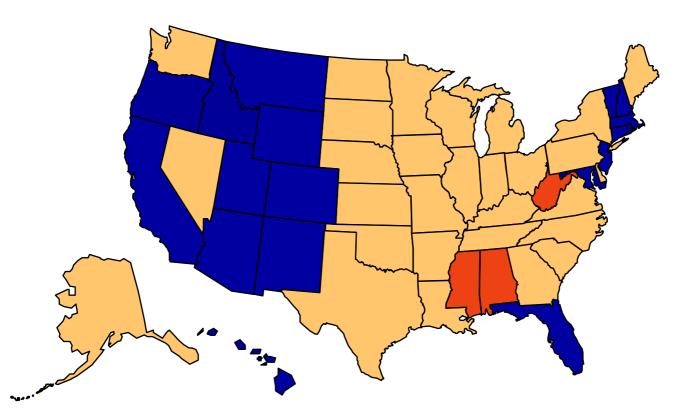


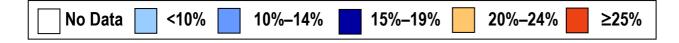
BRFSS, 1998 (*BMI ≥30, or ~ 30 lbs overweight for 5' 4" person)



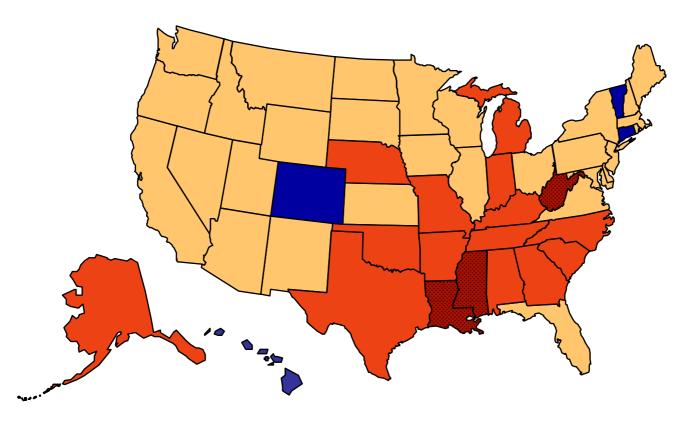


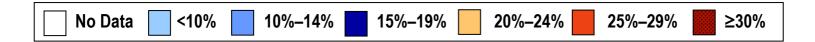
(*BMI ≥30, or ~ 30 lbs overweight for 5' 4" person)





BRFSS, 2005
(*BMI ≥30, or ~ 30 lbs overweight for 5' 4" person)





ABC of obesity

Obesity and vascular disease

Debbie A Lawlor, Mike Lean, Naveed Sattar

Conclusion

- Clear evidence exists that obesity has a wider impact on cardiovascular health beyond its effect on coronary heart disease
- Individuals who are obese in mid-life are at increased risk of heart failure and stroke in later life, and emerging evidence shows that they may also be at increased risk of dementia. For all these associations, the link between obesity and disease outcome could result from the behaviours that cause adult weight gain—namely, inactivity and high fat diets
- Further, the associations may in part be mediated by obesity related diabetes, hypertension, and dyslipidaemia, but the causal pathway still involves adult weight gain. This emphasises the importance of reversing the current obesity epidemic, not only because of its impact on premature mortality but because of the devastating effect it will have on quality of life in older age through its impact on these disease outcomes

Practical strategy for managing raised waist circumference in relation to cardiovascular disease risk

Patient characteristics	Treatment
Circumference < 80 cm in women, < 94 cm in men (low risk)	Requires no intervention (avoid weight gain and stay below these levels)
Circumference ≥80 cm in women,	Requires health promotion
≥94 cm men, and <10% risk of	and public health measures
cardiovascular disease* over next 10	for self directed treatment to
years (raised risk)	prevent further weight gain
Circumference 80-88 cm in women	Requires effective treatment
and 94-102 cm men, and > 10% risk	to lose 5-10% body weight
of cardiovascular disease* over next	and to prevent further weight
10 years (high risk)	gain
Circumference > 88 cm in women	Requires effective treatment
and > 102 cm in men irrespective of	to lose 5-10% body weight
10 year risk of cardiovascular disease*	and to prevent further weight
(high risk for other medical problems	gain
associated with obesity or intra-abdominal fat accumulation)	BMJ VOLUME 333 18 NOVEMBER 2006

Glucose, waist circumference, and triglyceride—three of the key components of the criteria for metabolic syndrome—are far stronger predictors of diabetes than of cardiovascular disease

The outlined conclusions on the associations of obesity with heart failure, stroke, and cognitive decline are based on the best available published evidence from prospective cohort studies that have used measures to minimise these sources of bias

Obesity is also associated with increased risk of atrial fibrillation, venous thromboembolism, and sudden death. Obesity is therefore associated with a broad range of fatal and non-fatal cardiovascular events

Potential weaknesses of current criteria for metabolic syndrome for predicting risk

- The current criteria have not yet been shown definitively to add to risk prediction for cardiovascular disease beyond current charts
- Arbitrary thresholds for risk factors and differing combinations of risk factors in the different definitions may lead to loss of important information about an individual's risk of cardiovascular disease
- The criteria fail to include important risk factors such as age, low density lipoprotein cholesterol, and smoking—a weakness if metabolic syndrome is used as the sole means of defining cardiovascular disease risk
- Prediction models that include additional risk factors (not just components of the metabolic syndrome) are a better means of identifying those at greatest risk

Requirements of future research

- Identify the best prediction models for cardiovascular disease and diabetes in different population groups (by pooling data from large number of individual prospective data sets in different populations)
- Evaluate the long term effect on disease risk of using these prediction models in clinical practice
- Determine the long term effect of weight maintenance and reduction programmes on cardiovascular disease risk using appropriately resourced and powered prospective trials

Dalla parte del paziente

The Metabolic Syndrome

Since cardiovascular (heart and blood vessel) disease is the leading cause of death for adults in developed countries, many medical studies focus on treating or preventing heart disease and stroke. The metabolic syndrome, a collection of unhealthy body measurements and abnormal laboratory test results, may identify persons at high risk for developing cardiovascular disease. Aggressive lifestyle modification and possible use of medications to treat the conditions that make up the metabolic syndrome may reduce a person's chances of developing heart disease or stroke. The metabolic syndrome has also been called syndrome X or insulin resistance syndrome. The February 15, 2006, issue of IAMA includes an article about the metabolic syndrome.

DEFINITION OF THE METABOLIC SYNDROME

- Abdominal (waist) circumference greater than 40 inches for men or 35 inches for women
- High blood pressure (hypertension)
- Hyperglycemia (fasting blood sugar more than 110 mg/dL)
- Elevated triglycerides (a type of fat in the bloodstream)
- Low levels of high-density lipoprotein, also known as HDL or "good cholesterol"

Having at least 3 of the above measurements means that an individual has metabolic syndrome and is at risk for developing type 2 diabetes, coronary heart disease, heart attack, or stroke.

TREATING THE METABOLIC SYNDROME

Lifestyle modifications include weight loss, regular exercise, stopping smoking, and reducing dietary fat intake. Losing just 10% of excess body weight lowers blood pressure and improves insulin resistance. Some persons may be able to treat high blood pressure and hyperglycemia by altering their lifestyle alone. In many individuals, lifestyle modification is not adequate, and medications must be used to decrease blood pressure, lower triglycerides, and increase the level of HDL.

Because these problems are often linked, treating one aspect of the metabolic syndrome may help the other issues. For example, regular exercise can help you lose weight, reduce blood pressure, and manage hyperglycemia and insulin resistance. Combining healthful eating with a regular exercise program is the cornerstone of treating the metabolic syndrome and reducing risk for heart disease, stroke, diabetes, and other medical problems.

PREVENTION

- Exercise regularly throughout your life.
- Encourage children to have daily physical activity and make healthful food choices.
- Eat a healthful, balanced diet low in saturated fats and high in nutrient-rich fruits and vegetables.
- · Do not smoke.
- Recognize that you may have a genetic (inherited) predisposition for diabetes, heart disease, and the metabolic syndrome.
- Have regular medical check-ups and initiate early treatment for high blood pressure.

Sources: National Heart, Lung, and Blood Institute; American Heart Association; National Cholesterol Education Program; American Diabetes Association

Janet M. Torpy, MD, Writer The JAMA Patient Page is a public service of JAMA. The information and recommendations appearing on this page are appreating on this page are appearing on this page are appreated in most instances, but they are not a substitute for medical diagnosis. For specific information concerning your personal medical condition, JAMA suggests that you consult you physician. This page may be photocopied noncommercially by physicians and other health care professionals to share with patients. To purchase bulk reports, call 2032/59-8724.

FOR MORE INFORMATION

- National Heart, Lung, and Blood Institute www.nhlbi.nih.gov
- American Heart Association www.americanheart.org
- American Diabetes Association www.diabetes.org

INFORM YOURSELF

To find this and previous JAMA Patient Pages, go to the Patient Page link on *JAMA*'s Web site at www.jama.com. Many are available in English and Spanish. A Patient Page or coronary artery disease was published in the November 24, 2004, issue; and one on weight gain and diabetes was published in the August 25, 2004, issue



YOUR PATIENTS





PREVENTION

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- Encourage children to have daily physical activity and make healthful food choices.
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TREATING THE METABOLIC SYNDROME

Because these problems are often linked, treating one aspect of the metabolic syndrome may help the other issues. For example, **regular exercise** can help you lose weight, reduce blood pressure, and manage hyperglycemia and insulin resistance.

Combining healthful eating with a regular exercise program is the cornerstone of treating the metabolic syndrome and reducing risk for heart disease, stroke, diabetes, and other medical problems



...per chi (Medico non è...



Perché "...per chi medico non è..."

La nascita di *Internal and Emergency Medicine* è il frutto di una lunga riflessione che ha portato anche a focalizzare l'importante ruolo educativo sul paziente che può svolgere la Società Italiana di Medicina Interna.

È così nato un inserto di quattro pagine in italiano dedicato al paziente. In ogni numero sarà trattato un argomento importante della patologia sul quale si vorrà richiamare l'attenzione del pubblico. Poiché l'inserto arriva ad oltre 2500 internisti membri della Società, l'idea è che esso sia messo a disposizione dei pazienti nelle sale di attesa degli ambulatori medici contribuendo alla diffusione delle conoscenze che il paziente ha su patologie di grande diffusione.

Research



Randomised controlled trial of four commercial weight loss programmes in the UK: initial findings from the BBC "diet trials"

Helen Truby, Sue Baic, Anne deLooy, Kenneth R Fox, M Barbara E Livingstone, Catherine M Logan, Ian A Macdonald, Linda M Morgan, Moira A Taylor, D J Millward

The BBC diet trials

Reality television and academic researchers jointly tackle the weight loss industry

Recruitment strategy

We identified potential participants via a BBC advertising campaign (television and other forms of media). Participants

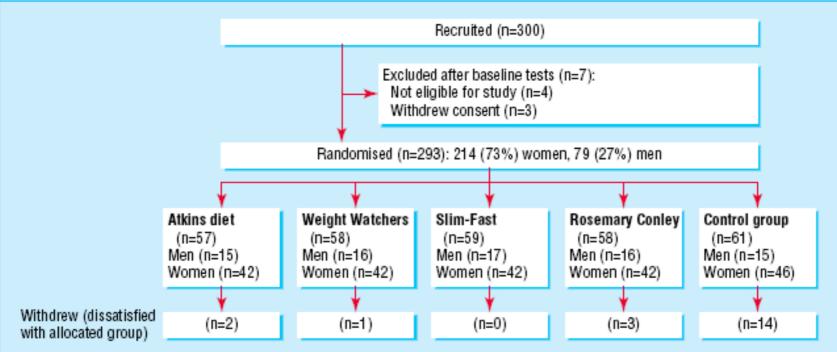
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Conclusions

Clinically useful weight loss and fat loss can be achieved in adults who are motivated to follow commercial diets for a substantial period. Given the limited resources for weight management in the NHS, healthcare practitioners should discuss with their patients programmes known to be effective.

BMJ, 23 May 2006

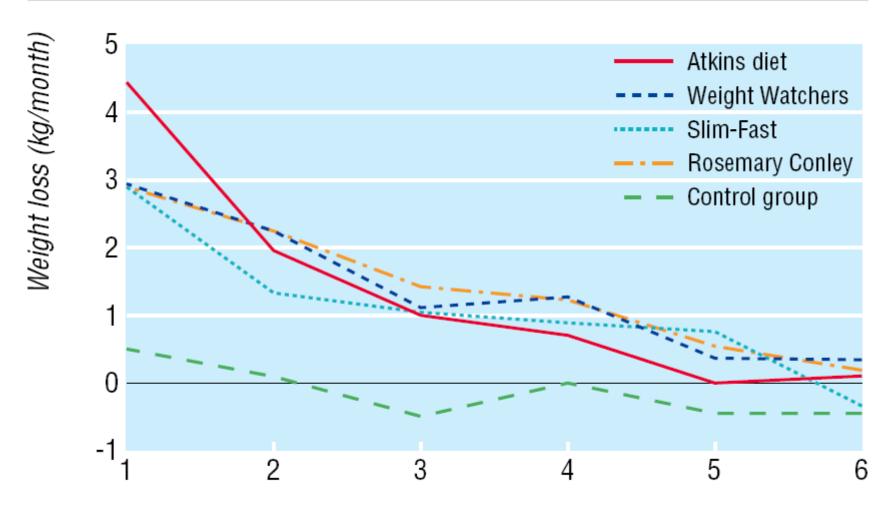


Week	Atkins diet	Weight Watchers	Slim-Fast	Rosemary Conley	Control group
4	50	56	54	52	46
8	46	52	49	46	41
12	42	48	46	43	38
16	38	49	42	40	37
20	24	35	30	30	28
24	40	47	42	41	40
Included in analysis	40	47	42	41	40
of participants who	(men 13,	(men 14,	(men 12,	(men 10,	(men 10,
completed (n=210)	women 27)	women 33)	women 30)	women 31)	women 30)
Included in	57	58	58*	58	61
intention to treat					

Follow-up measures

^{*1} excluded because of pregnancy

Weight loss during the BBC diet trials



Time (months)

BMJ, 23 May 2006

Research



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Editorials

The BBC could also greatly serve the public by presenting data on efficacy, safety, and cost in their health related programming—thereby imposing some reality on "reality television."

David Arterburn assistant investigator