

Obès metabòlicament sa, mite o realitat ?

Jornada de recerca ICS

03.06.2016

Silvia Pellitero



OBESITAT METABÒLICAMENT SANA, MITE O REALITAT?

- Heterogeneïtat
- Risc cardiovascular:

....”PARADOXA OBESITAT”

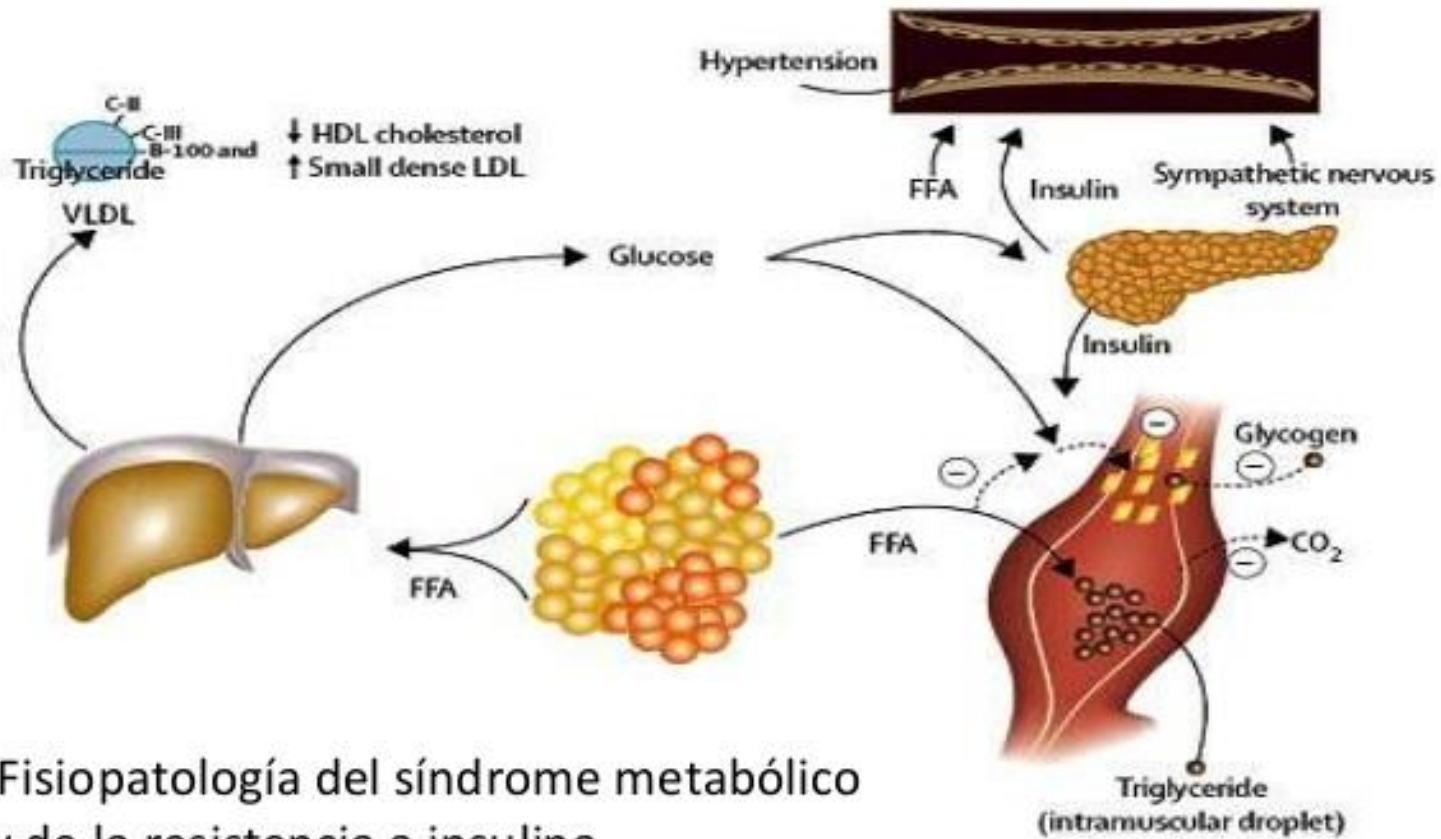
... “OBESITAT METABÒLICAMENT SANA”

❖ DEFINICIÓ OBESITAT A REVISAR

PATOGENIA



SÍNDROME METABÓLICO



Fisiopatología del síndrome metabólico y de la resistencia a insulina

Obesity paradox: can obesity be a friend?

Yesterday's enemy is today's friend

Obesitat, factors risc

A. Increases in insulin resistance

- 1) Glucose intolerance
- 2) Metabolic syndrome
- 3) Type 2 diabetes mellitus

B. Hypertension

C. D.

- 1)
- 2)
- 3)
- 4)
- 5)
- 6)

- 7) Decreased HDL cholesterol
- 8) Decreased apolipoprotein-A1

D. Abnormal left ventricular geometry

- 1) Concentric remodeling
- 2) Left ventricular hypertrophy

E. Endothelial dysfunction

F. Increased systemic inflammation and prothrombotic state

G. Systolic and diastolic dysfunction

H. Heart failure

I. Coronary heart disease

J. Atrial fibrillation

K. Obstructive sleep apnea/sleep-disordered breathing

L. Albuminuria

M. Osteoarthritis

N. Cancers

Paradoxa obesitat

Cardiovascular

A. Hypertension

The art of simplicity is a puzzle of complexity.

—Doug Horton (1891–1968)

E. Echocardiography referrals

Noncardiovascular

A. Elderly

B. End-stage renal disease and dialysis

C. Advanced cancers

D. Chronic obstructive lung disease

E. Rheumatoid arthritis

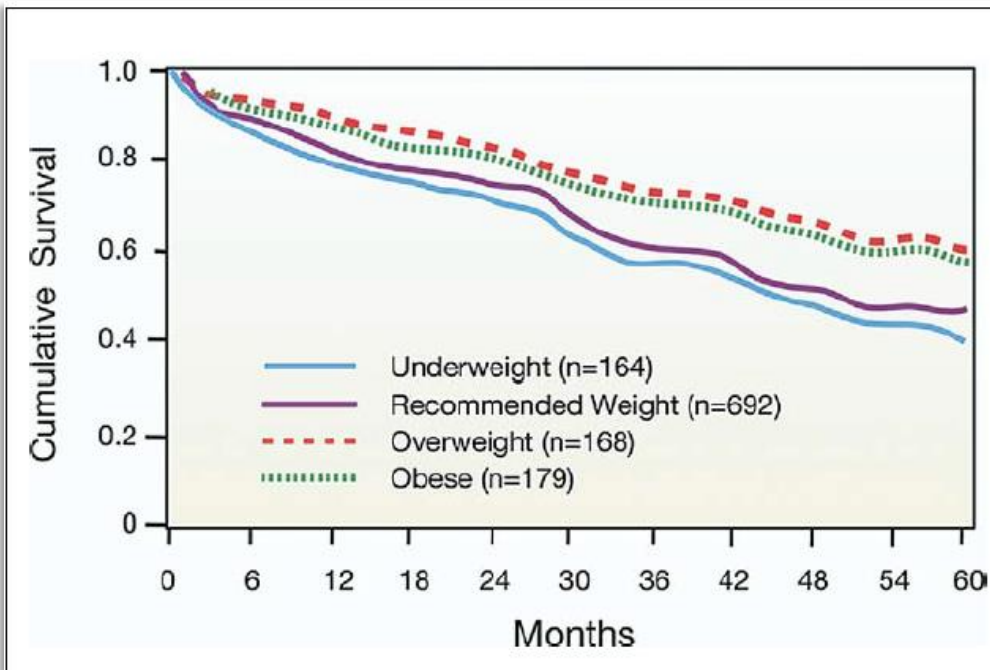
F. Human immunodeficiency virus/acquired immune deficiency syndrome

*Conditions in which obesity has been associated with a more favorable prognosis compared with that in nonobese patients.



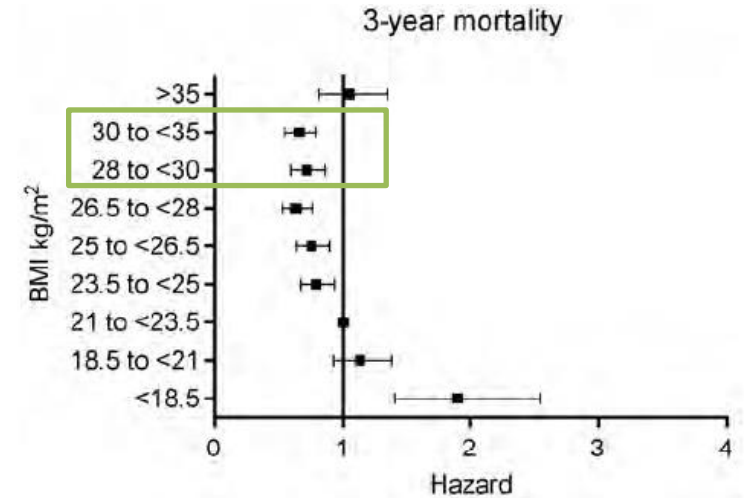
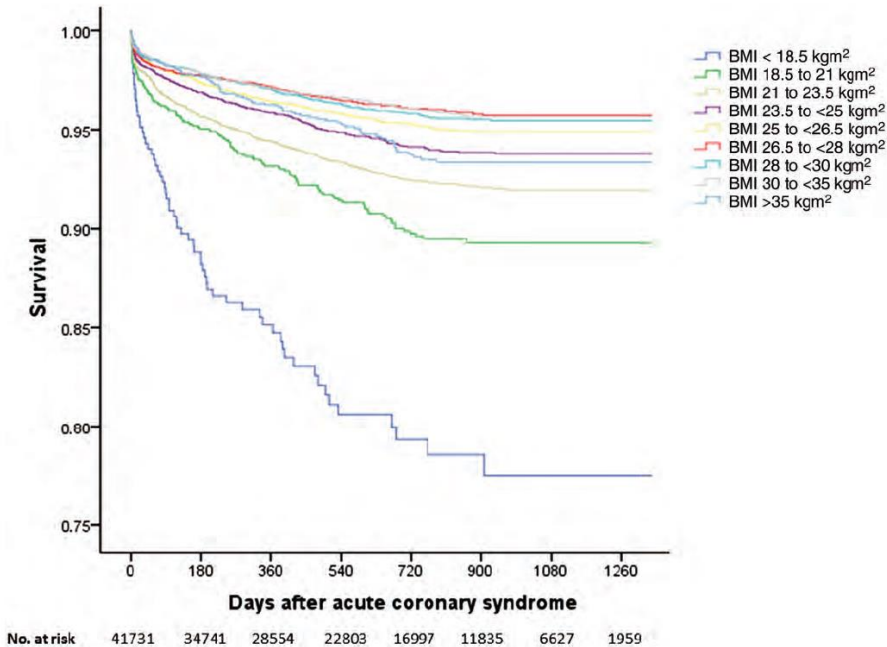
Obesity and Cardiovascular Disease

Risk Factor, Paradox, and Impact of Weight Loss



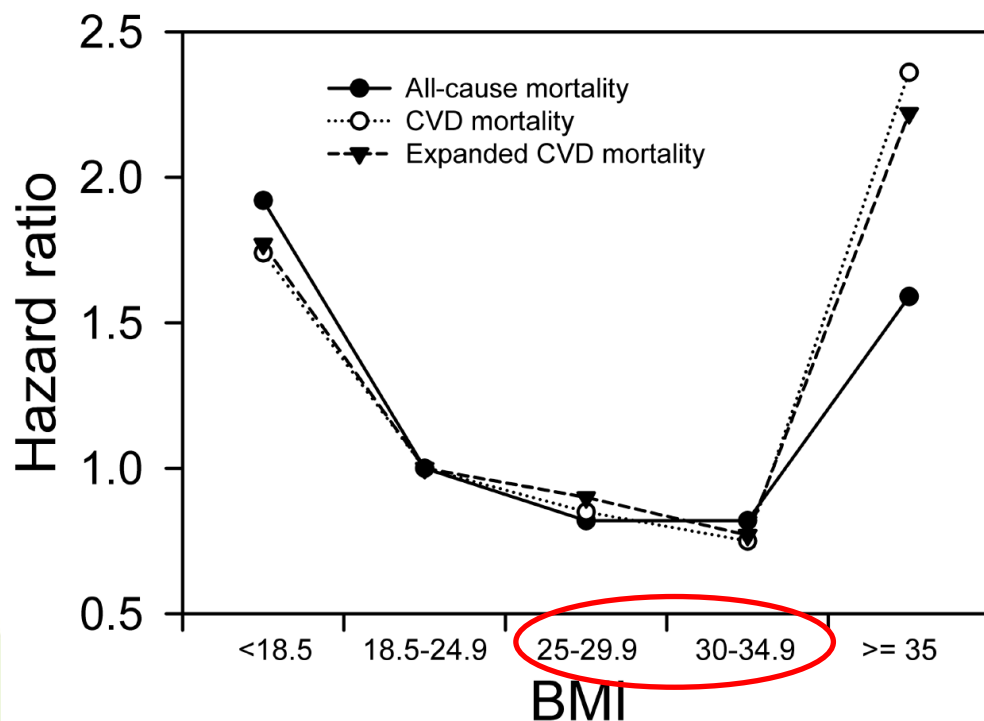
Risc de mortalitat
1200 pacients; Insuficiència
cardíaca mod-sev
64 anys
5 anys

Evidence for obesity paradox in patients with acute coronary syndromes: a report from the Swedish Coronary Angiography and Angioplasty Registry



n= 64.436 patients SCA
 edat >60 anys
 Seguiment 3 anys

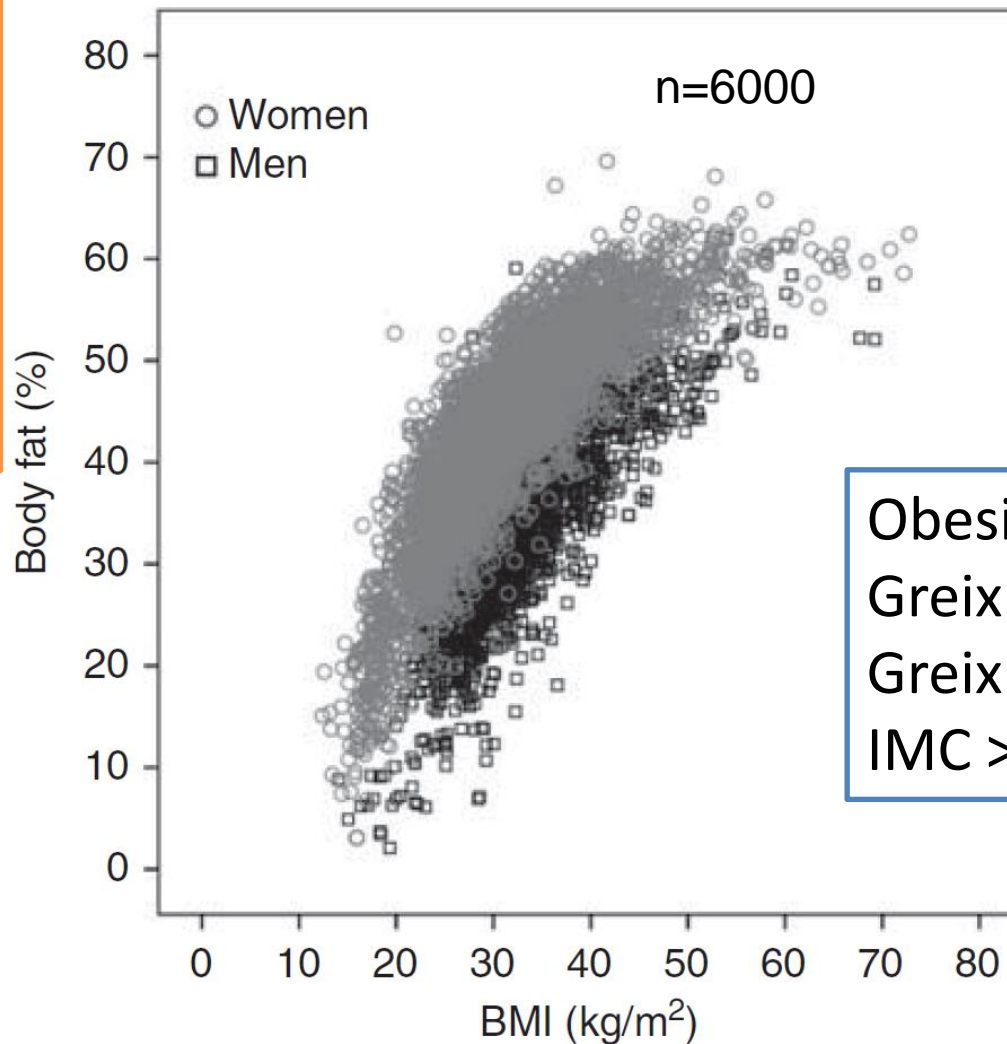
Association of Body Mass Index with All-Cause and Cardiovascular Disease Mortality in the Elderly



77.541 patients
edat >60 anys
5 anys evolució

Yu et al. Plos one 2014:9;

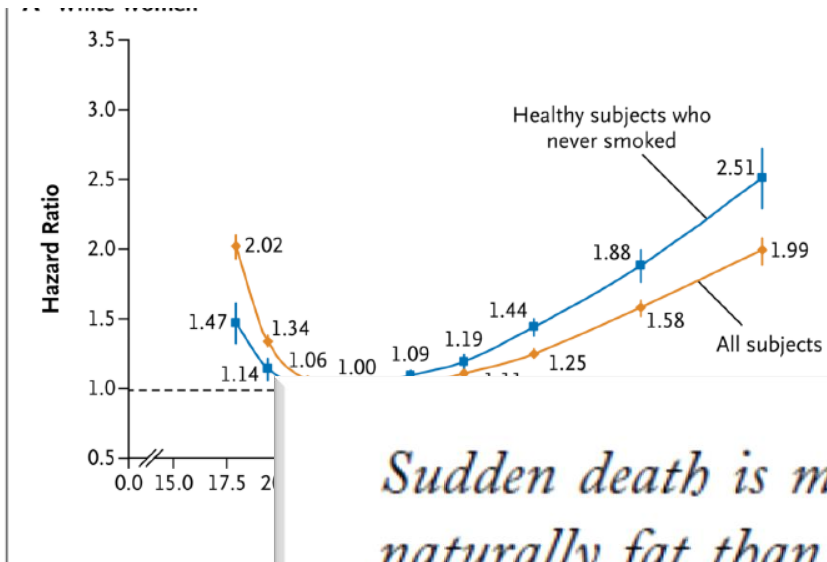
29% amb
IMC normal
tenen
augment
del greix
corporal



Obesitat definida per
Greix > 30% homes
Greix > 25% dones
IMC >30 kg/m²

Gómez-Ambrosi et al. Int J Obes 2011

Body-Mass Index and Mortality among 1.46 Million White Adults

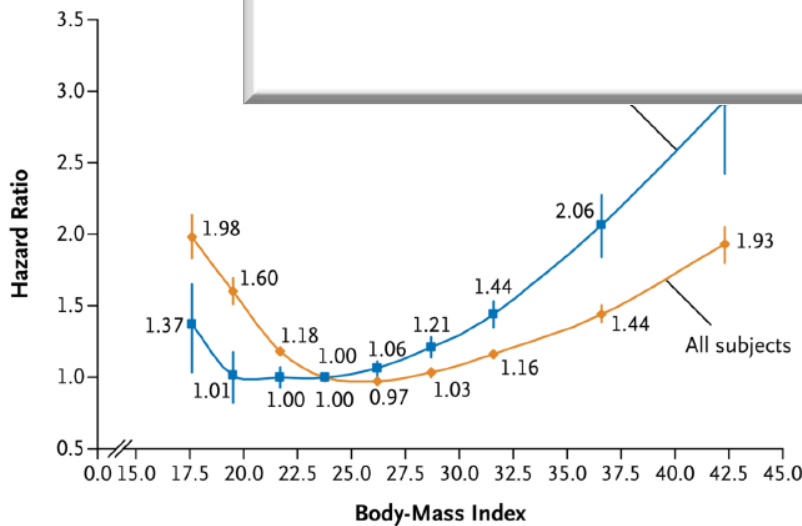


Seguiment 10 anys,
Blancs no hispànics
edat 58 anys
13% fumadors actius

Sudden death is more common in those who are naturally fat than in the lean.

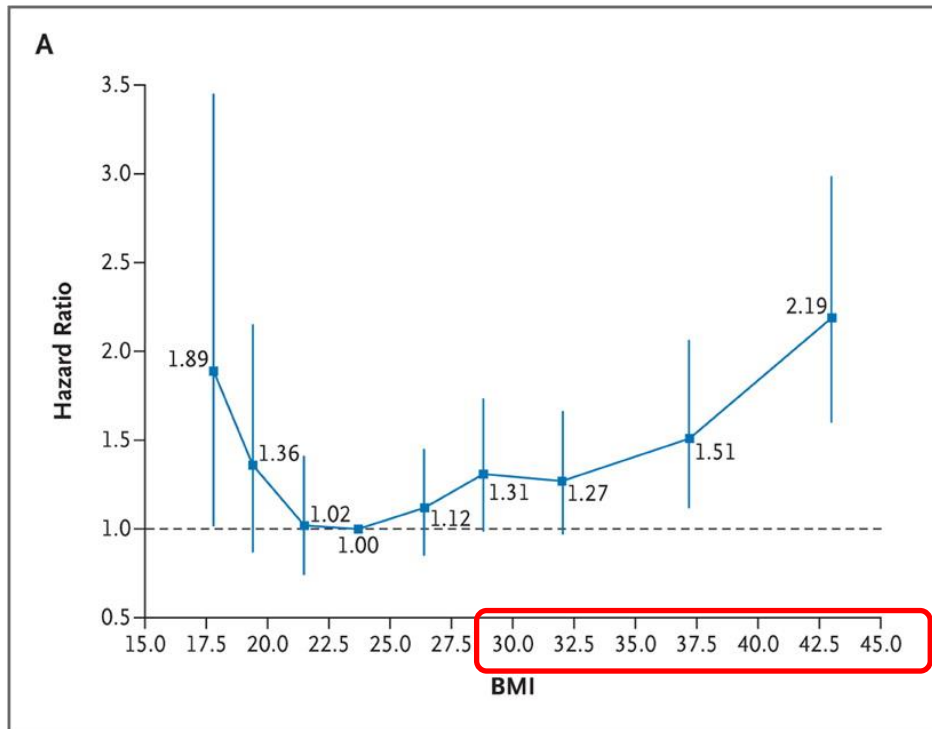
—Hippocrates

B White Men



Berrington de Gonzalez et al. N Engl J Med
2010;363(23):2211-9

General and Abdominal Obesity and Risk of Death among Black Women

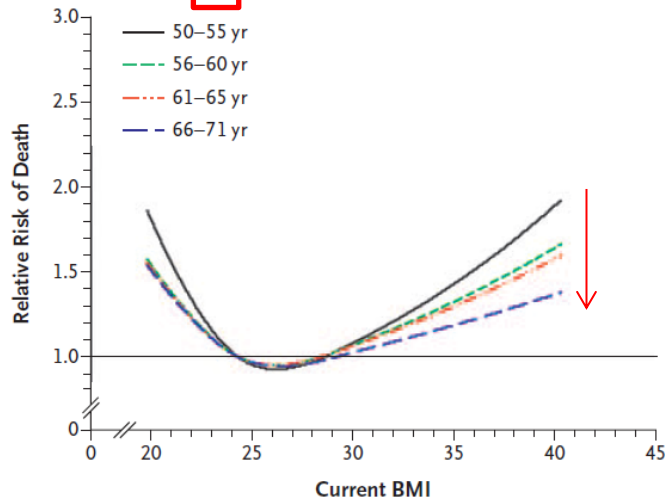


n= 51.695
Black Women Health Study
1995-2008

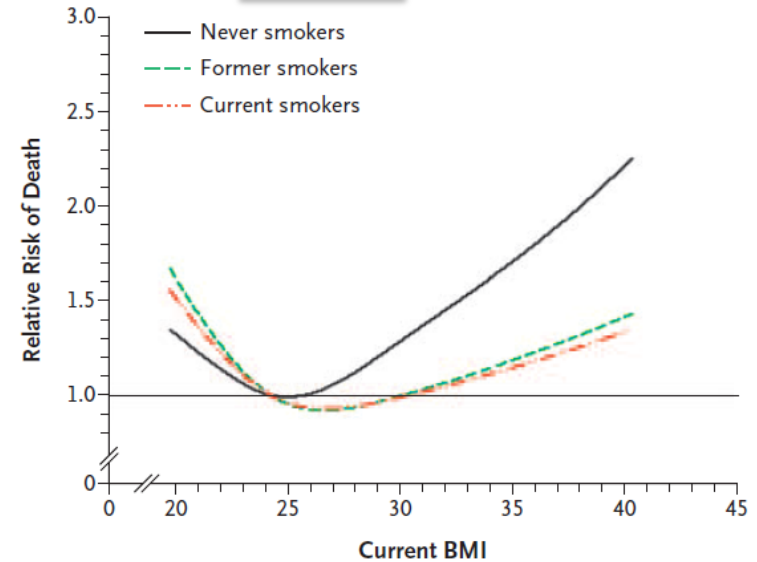
Overweight, Obesity, and Mortality in a Large Prospective Cohort of Persons 50 to 71 Years Old

Paradoxa obesitat, NO!

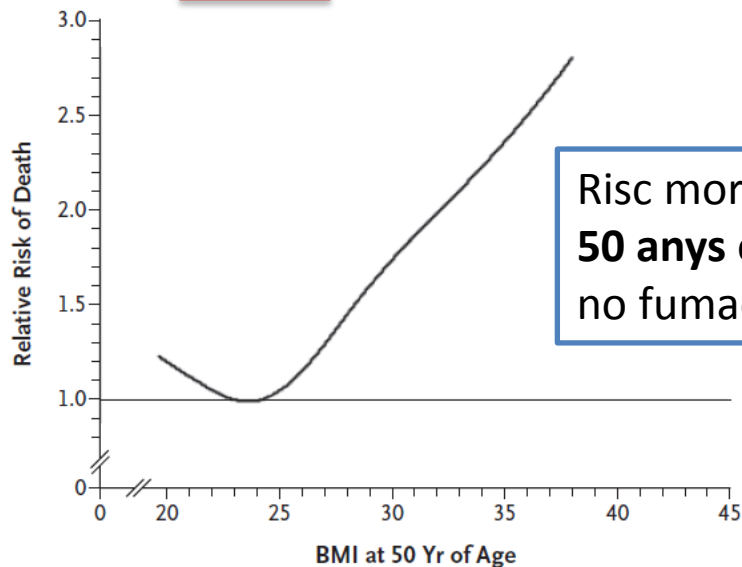
B Men According to **Age** (N=313,047; 42,173 deaths)



C Men According to **Smoking Status** (N=302,327; 40,541 deaths)



D Men Who Had **Never Smoked** (N=54,925; 4079 deaths)

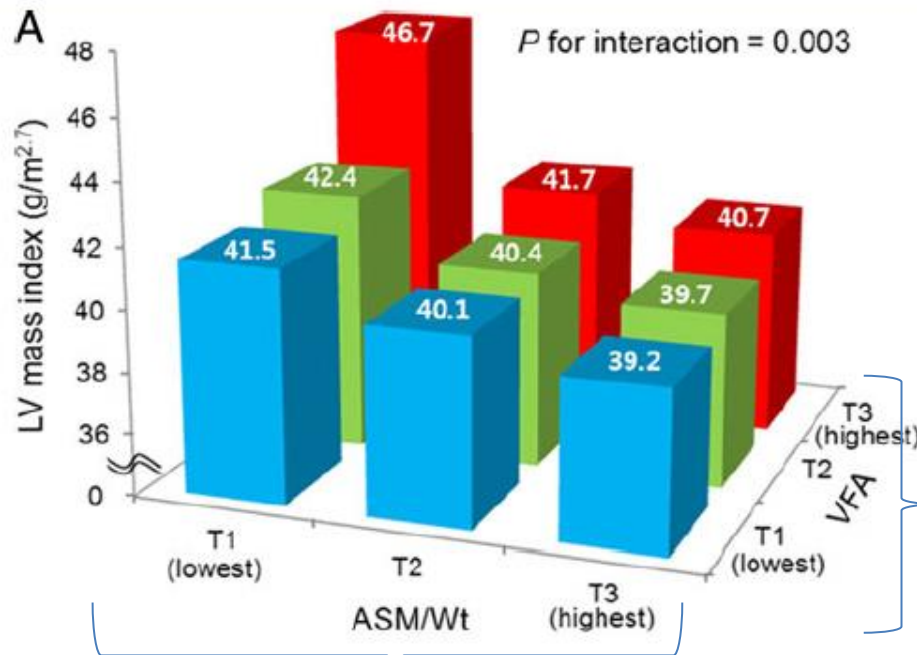


n= 61.317;
seguiment 10 anys

"PARADOXA OBESITAT" →
Composició corporal

Controversies in cardiovascular medicine

Obesity and cardiovascular disease: friend or foe?



N= 1941

Composició corporal i
funció cardíaca (índex massa VE)

Tercil menor múscul i més greix
visceral → més disfx Diastòlica del VE

“Obesity paradox”: conclusions

- **Obesitat no es pot considerar una entitat benigna**
 - **distribució greix (sc, visceral, ectòpic),**
 - **composició corporal**
 - **activitat física**
 - *** edat avançada**

Are Metabolically Healthy Overweight and Obesity Benign Conditions?

A Systematic Review and Meta-analysis

Caroline K. Kramer, MD, PhD; Bernard Zinman, CM, MD; and Paul DeFronzo, MD



European Heart Journal
doi:10.1093/eurheartj/ehv509

REVIEW

Metabolic and
Healthy Obesity

Controversies in
Obesity a
Seong Hwan Kii



Nutrition 32 (2016) 14–20

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrn.com



Mi Hae Seo¹, Eun-Jung Rhee²
<http://www.biomedcentral.com/1471-2458/14/>

Review
Metabolically healthy obese individuals: Key protective factors
Carolina G. Gonçalves M.D., Ph.D.^a, Michael J. Glade Ph.D.^b



Review	M Blüher	Metabolically healthy obesity	171:6	R20	Open Access
---------------	----------	-------------------------------	-------	-----	--------------------

MECHANISMS IN ENDOCRINOLOGY

Are metabolically healthy obese individuals really healthy?

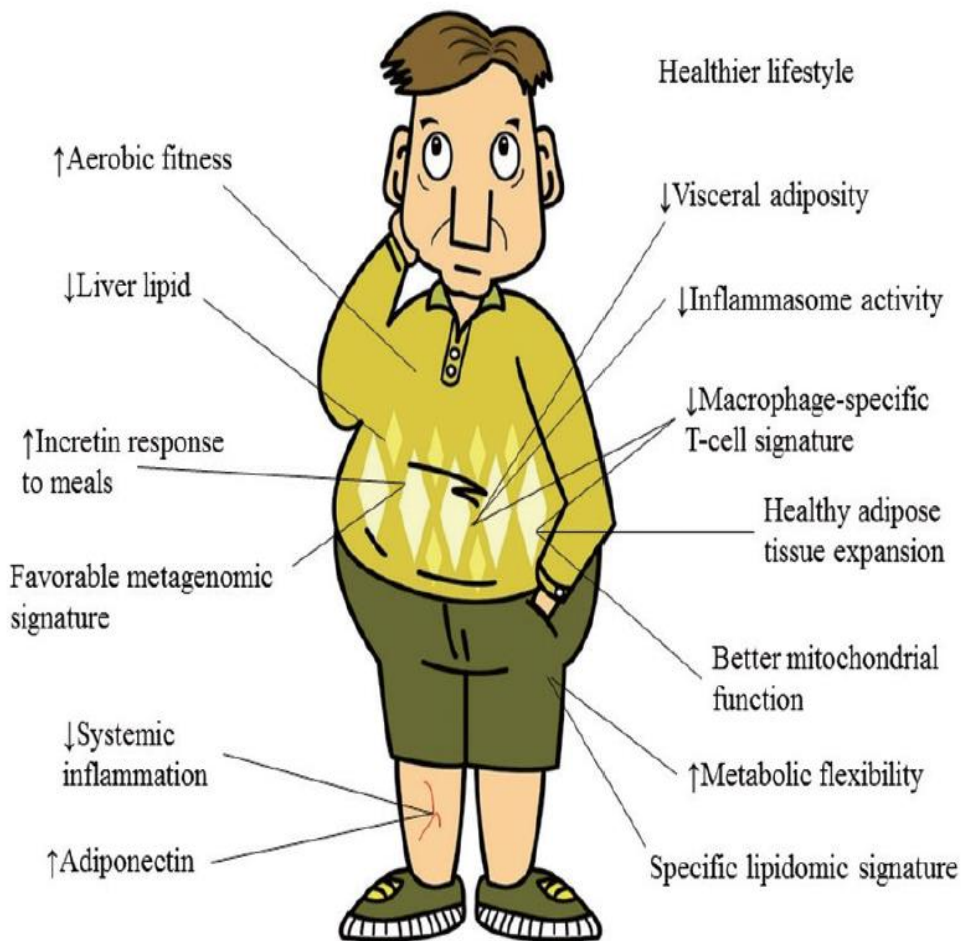
Matthias Blüher

Matthew J Budoff^{1,3,4,10*} and Khurram Nasir^{1,3,4,10*}

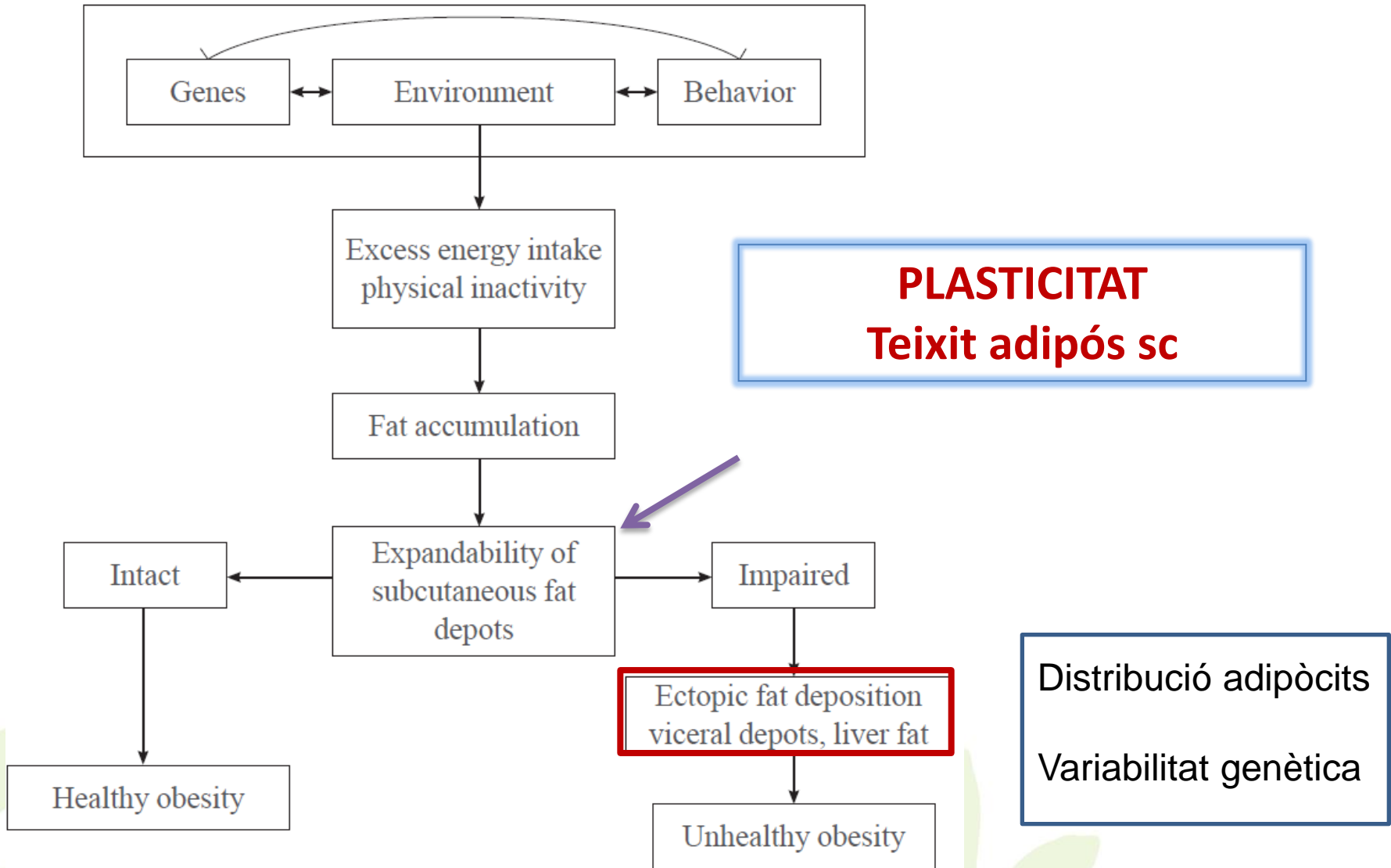
Correspondence should be addressed to M Blüher
Correspondence should be addressed to ribeth Rouseff²,
to M Blüher tein⁸,

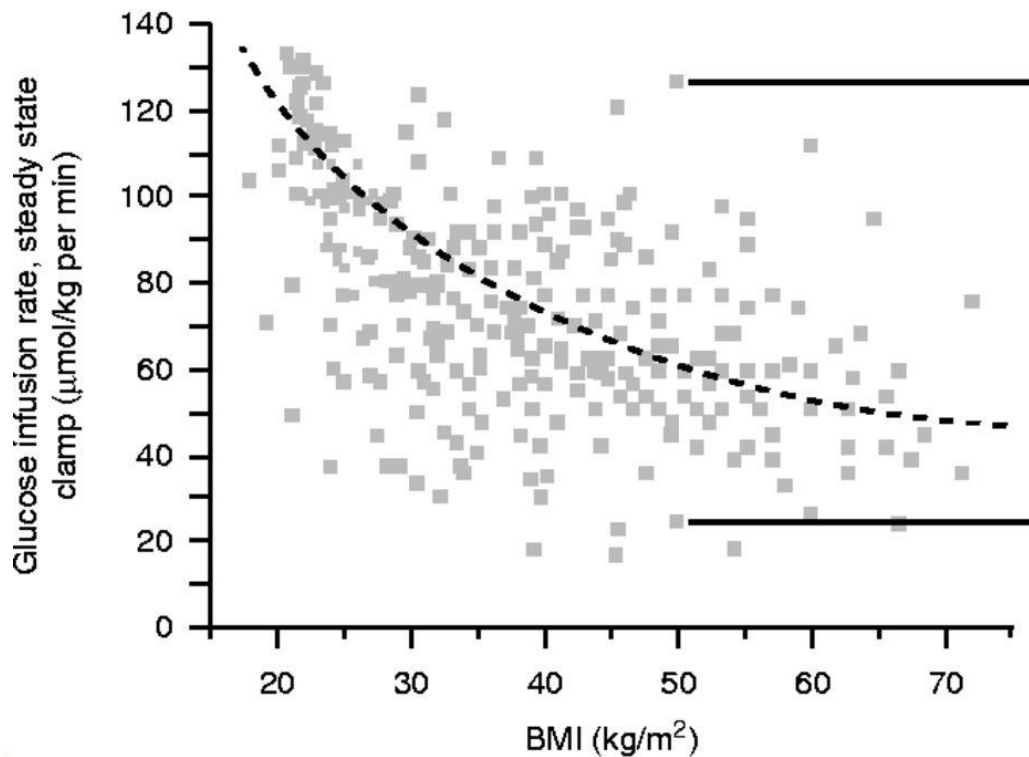


METABOLIC HEALTHY OBESITY- MHO-



- 10-30% obesitat són MHO
- **arbitrarietat** de criteris diagnòstics





BMI: 50.0kg/m²
 FPG: 5.1 mmol/l
 HbA1c: 5.4%
 HDL: 1.27 mmol/l
 TG: 1.51 mmol/l
 BP: 129/78 mmHg



BMI: 50.0kg/m²
 FPG: 5.8 mmol/l
 HbA1c: 5.9%
 HDL: 0.83 mmol/l
 TG: 1.96 mmol/l
 BP: 136/84 mmHg

Matthias Blüher Eur J Endocrinol 2014;171:R209-R219

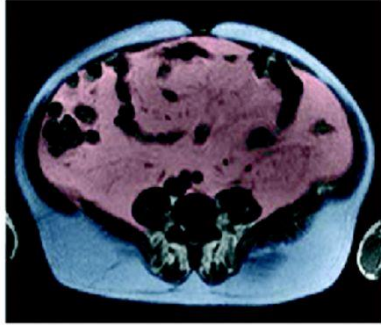
The Metabolically Healthy but Obese Individual Presents a Favorable Inflammation Profile

44 dones postmenopàusiques
Estudi de SI (clamp) i
composició corporal

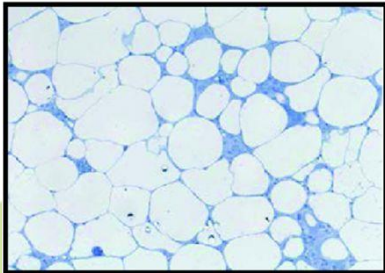
Variables	MHO (n = 22)	At risk (n = 22)
SAT area (L4/L5, cm ²)	490.9 ± 128	512.9 ± 122
Superficial SAT area (cm ²)	250.1 ± 79.8	257.1 ± 68.0
Deep SAT area (cm ²) (n = 22, 21)	239.9 ± 56.8	257.4 ± 66.6
Abdominal fat (cm ²)	670.8 ± 149	740.0 ± 161
Visceral fat content (cm ²)	179.9 ± 53.9 ^a	227.0 ± 64.6
Muscle attenuation	49.6 ± 3.7	54.7 ± 29.9

Obesity

Metabolically high risk



↑ Visceral fat
 ↑ Visceral/subcutaneous fat ratio
 ↑ Liver fat
 ↑ Skeletal muscle fat

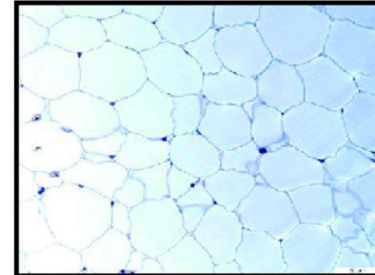


↑ Adipocyte size
 ↑ AT macrophages

Metabo Millor perfil metabòlic



↓ Visceral fat: normal
 ↓ Visceral/subcutaneous fat ratio
 ↓ Liver fat
 ↓ Skeletal muscle fat



Metabolically Healthy Obesity and Risk of All-Cause and Cardiovascular Disease Mortality

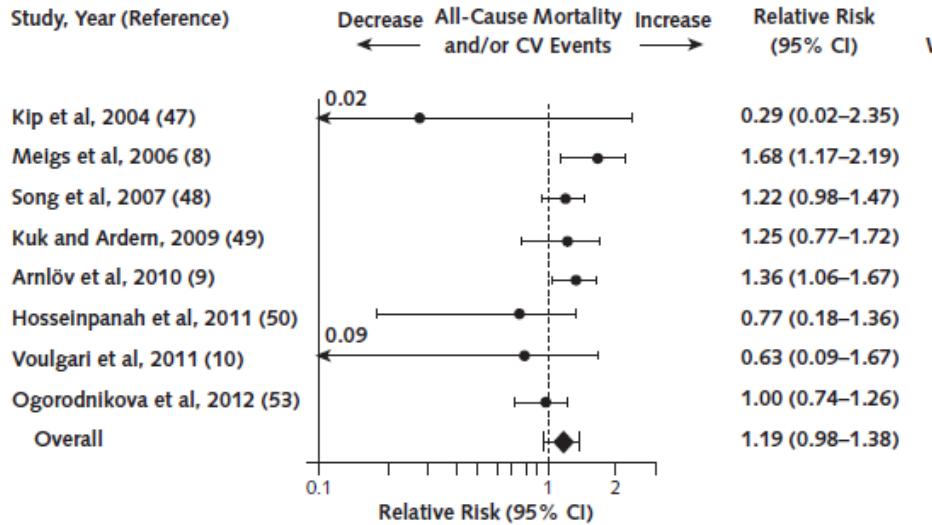
n= 22.203; edad 54 anys
 Seguiment 7±3 anys
 1868 morts, 604 events

Fully adjusted HR (95% CI)^a

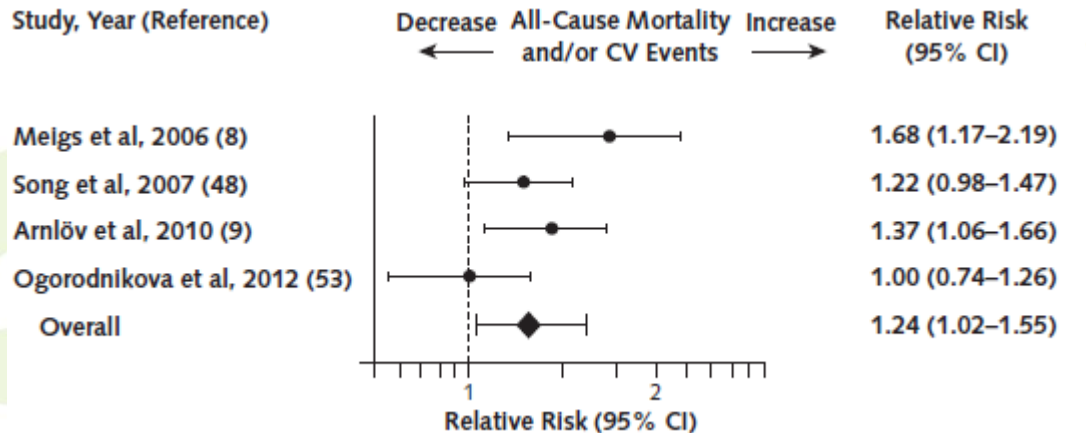
MHNO 1.00
 MUHNO 1.59 (1.42–1.77)
 MHO 0.91 (0.64–1.29)
 MUHO 1.79 (1.47–2.17)
 <0.001

Variable	Metabolically healthy nonobese (n = 12,716)	Metabolically unhealthy nonobese (n = 4,201)	Metabolically healthy obese (n = 1,160)	Metabolically unhealthy obese (n = 4,128)
Age (yr)	51.9 ± 12.4	59.3 ± 12.5	51.3 ± 11.5 ^a	56.3 ± 12.3
Men (%)	45.4	47.2	52.6	40.4
Highest socioeconomic group (III) (%)	42.5	36.9	38.9 ^a	32.8
Current smokers (%)	25.6	28.7	16.7 ^b	19.7
Physical activity (% at least three times per week MVPA)	35.1	21.0	28.9 ^a	19.3
HDL cholesterol (mmol/liter)	1.6 ± 0.4	1.3 ± 0.4	1.5 ± 0.3 ^b	1.3 ± 0.4
BMI (kg/m ²)	24.8 ± 2.6	26.7 ± 2.3	32.2 ± 2.7 ^b	34.2 ± 3.8
Waist (cm)	84.5 ± 9.6	93.1 ± 9.5	99.5 ± 10.1 ^b	106.1 ± 10.4
Diabetes (%)	0.5	7.0	0.3 ^a	6.5
Systolic BP (mm Hg)	129.2 ± 17.5	142.8 ± 17.5	131.9 ± 15.5 ^b	141.6 ± 20.6
Hypertension risk (%)	18.6	71.2	10.9 ^b	64.8
CRP (mg/liter)	2.0 ± 4.5	6.2 ± 8.6	2.1 ± 3.1 ^a	6.1 ± 7.0
Inflammation (CRP ≥ 3 mg/liter) (%)	12.5	65.5	8.8 ^a	67.5

Are Metabolically Healthy Overweight and Obesity Benign Conditions?

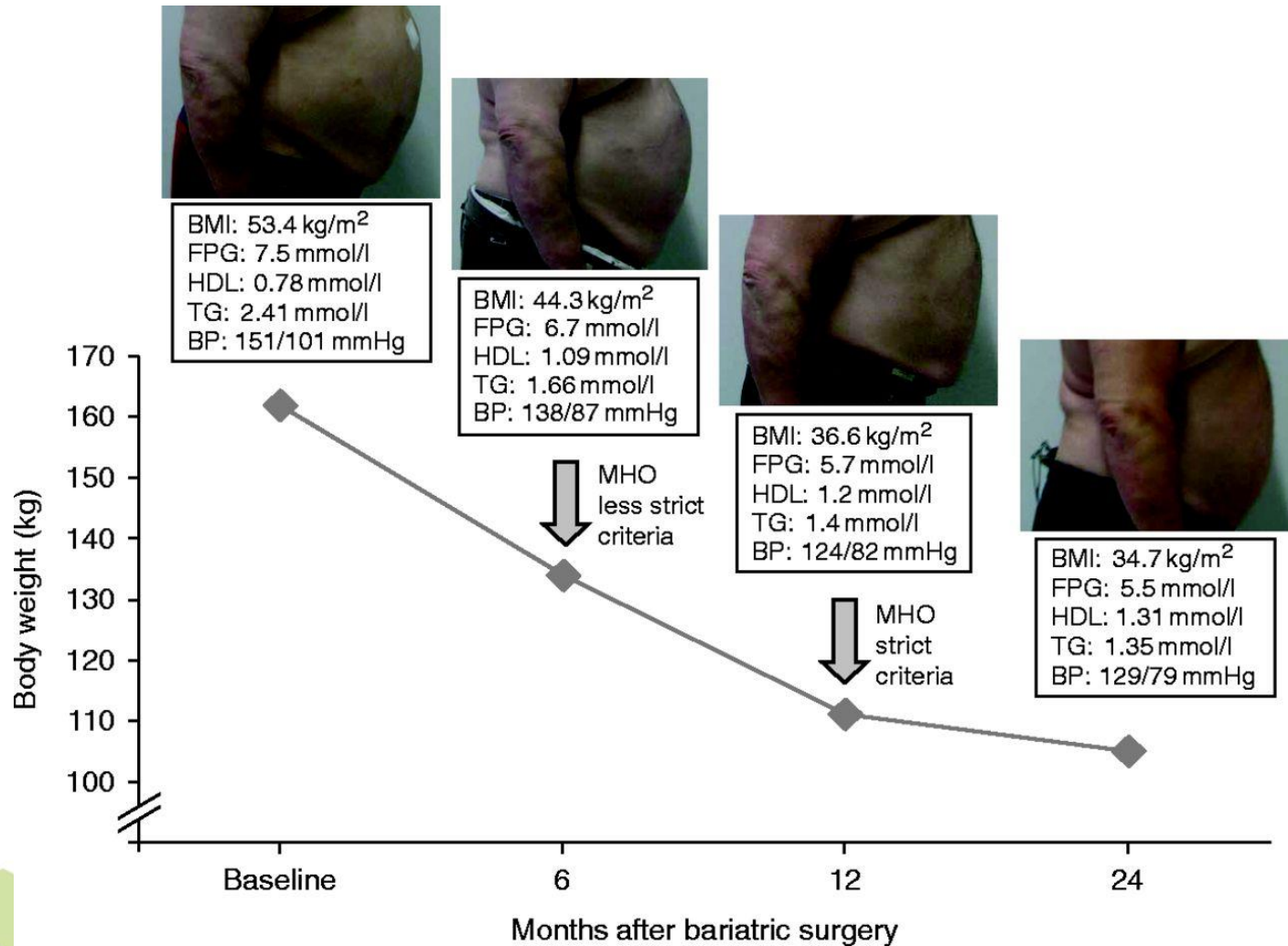


MHO globalment



**MHO: estudis a >10 a
RR 1.24**

Figure 2 The obesity phenotype changes upon weight loss after Roux-en-Y gastric bypass surgery.



Impact of Body Mass Index and the Metabolic Syndrome on the Risk of Cardiovascular Disease and Death in Middle-Aged Men

- 1758 homes no DM; 50 anys edat
- **seguiment 30 anys**, 845 morts

Deaths and Major Cardiovascular Events in Groups With Different Combinations of BMI and MetS

	Normal Weight Without MetS	Normal Weight With MetS	Overweight Without MetS	Overweight With MetS	Obese Without MetS	Obese With MetS
Total death						
No. of events/No. at risk	391/891	34/64	276/582	76/125	18/30	50/66
Multivariable hazard ratio	Referent	1.28 (0.90–1.82)	1.21 (1.03–1.40)*	1.53 (1.19–1.96)‡	1.65 (1.03–2.66)*	2.43 (1.81–3.27)‡
Cardiovascular death						
No. of events/No. at risk	155/891	20/64	133/582	46/125	5/30	27/66
Multivariable hazard ratio	Referent	1.77 (1.11–2.83)*	1.44 (1.14–1.83)‡	2.19 (1.57–3.06)‡	1.20 (0.49–2.93)	3.20 (2.12–4.82)‡
Major cardiovascular events						
No. of events/No. at risk	287/891	30/64	250/582	62/125	14/30	38/66
Multivariable hazard ratio	Referent	1.63 (1.11–2.37)*	1.52 (1.28–1.80)‡	1.74 (1.32–2.30)‡	1.95 (1.14–3.34)†	2.55 (1.82–3.58)‡

Multivariable model adjusted for age, smoking status, and LDL cholesterol.

* $P < 0.05$, † $P < 0.01$, ‡ $P < 0.001$.

All-cause Mortality Risk of Metabolically Healthy Abdominal Obese Individuals: The EPIC-MORGEN Study

- Cohort prospectiva 1993-1997
 - 22.654 p; 20-59 anys; seguiment **13,4 anys**
 - **4% MHO**

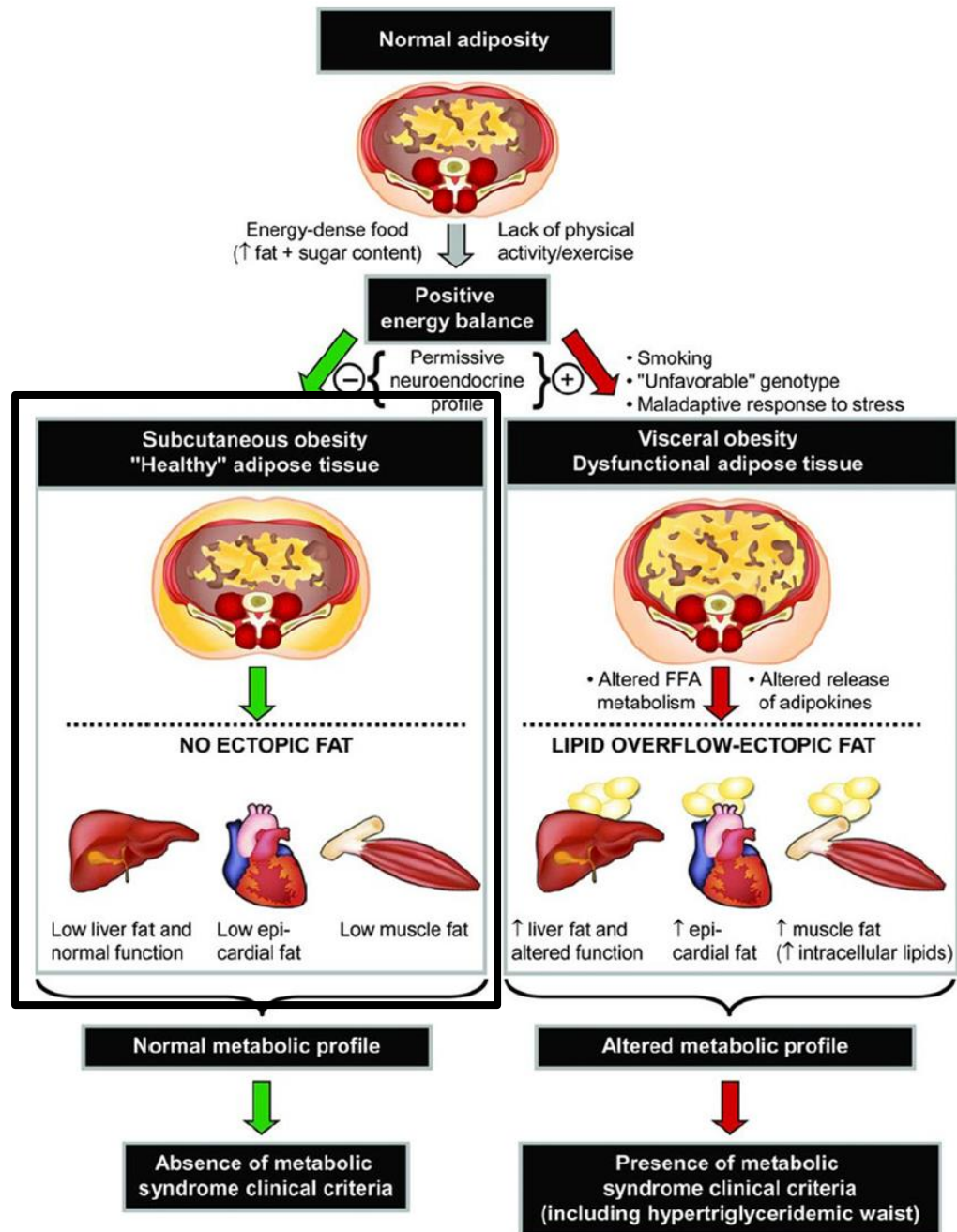
	<i>N</i> = 19,680; <i>n</i> deaths/ <i>n</i>	Age- and sex-adjusted I; HR (95% CI)	<i>N</i> = 16,199; <i>n</i> deaths/ <i>n</i>	Age- and sex- adjusted II; HR (95% CI) ^a	Multivariate adjusted HR (95% CI) ^{a,b}
Waist-defined					
Metabolically healthy non abdominal obese (MHNAO)	153/7,439	1.0	119/6,182	1.0	1.0
Metabolically unhealthy non abdominal obese (MUNAO)	338/7,837	1.31 (1.08-1.59)	249/6,360	1.29 (1.03-1.61)	1.21 (0.97-1.51)
Metabolically healthy abdominal obese (MHAO)	39/864	1.43 (1.00-2.04)	35/737	1.59 (1.09-2.33)	1.63 (1.11-2.38)
Metabolically unhealthy abdominal obese (MUAO)	308/3,540	1.99 (1.62-2.43)	232/2,920	1.90 (1.51-2.39)	1.81 (1.43-2.30)

Body Composition Determinants of Metabolic Phenotypes of Obesity in Nonobese and Obese Postmenopausal Women

Indices of body composition	MHNO (N = 22)	MONO (N = 38)	MHO (N = 22)	MUHO (N = 68)
Overall adiposity				
Total FM (kg)	20.7 ± 3.9	22.3 ± 3.7	32.8 ± 6.8 ^{a,b}	36.1 ± 8.8 ^{c,d}
FM (%)	35 ± 4	35.9 ± 4	41.5 ± 4 ^{a,b}	43.2 ± 4.1 ^{c,d}
FMI (kg/m ²)	8.3 ± 1.6	8.8 ± 1.3	13 ± 2.5 ^{a,b}	14.5 ± 3.4 ^{c,d}
Central fat distribution				
TrFM (kg)	8 ± 2.1	9.8 ± 2.2	15.1 ± 3.7 ^{a,b}	17.4 ± 4.8 ^{c,d}
AFM (kg)	1.5 ± 0.4	2 ± 0.6	3.2 ± 0.9 ^{a,b}	4 ± 1.2 ^{c,d,e}
TFM (kg)	3.1 ± 1	4.3 ± 1.3 ^f	6.4 ± 1.8 ^{a,b}	7.9 ± 2.4 ^{c,d,e}
TrFM/LFM ratio	0.85 ± 0.2	1.14 ± 0.3 ^f	1.19 ± 0.2 ^a	1.37 ± 0.4 ^{c,d,e}
AFM/GFM ratio	0.16 ± 0.03	0.2 ± 0.05 ^f	0.22 ± 0.04 ^a	0.26 ± 0.05 ^{c,d,e}
Peripheral fat distribution				
ArFM (kg)	2.6 ± 0.6	2.8 ± 0.6	3.8 ± 0.7 ^{a,b}	4.4 ± 1.2 ^{c,d,e}
LrFM (kg)	9.4 ± 1.6	8.8 ± 1.7	13 ± 3.3 ^{a,b}	13.2 ± 3.8 ^{c,d}
GFM (kg)	9.9 ± 1.8	9.9 ± 1.7	15 ± 3.9 ^{a,b}	15.5 ± 4.2 ^{c,d}
Lean body mass				
LBM (kg)	36.2 ± 3	37.7 ± 4	43.8 ± 5.9 ^{a,b}	44.5 ± 5.2 ^{c,d}
LBMI (kg/m ²)	21.1 ± 0.9	21.9 ± 0.8	27.4 ± 1.0 ^{a,b}	27.8 ± 1.7 ^{c,d}
TrLM (kg)	17.9 ± 1.7	18.6 ± 1.9	21.7 ± 2.9 ^a	21.9 ± 2.7 ^{c,d}
AppLM (kg)	15 ± 1.3	15.7 ± 2.1	18.4 ± 3 ^{a,b}	18.9 ± 2.6 ^{c,d}

Conclusió:

• fenotip metabòlic s'associa a una ratio adipositat central / perifèrica en dones postmenopàusiques.

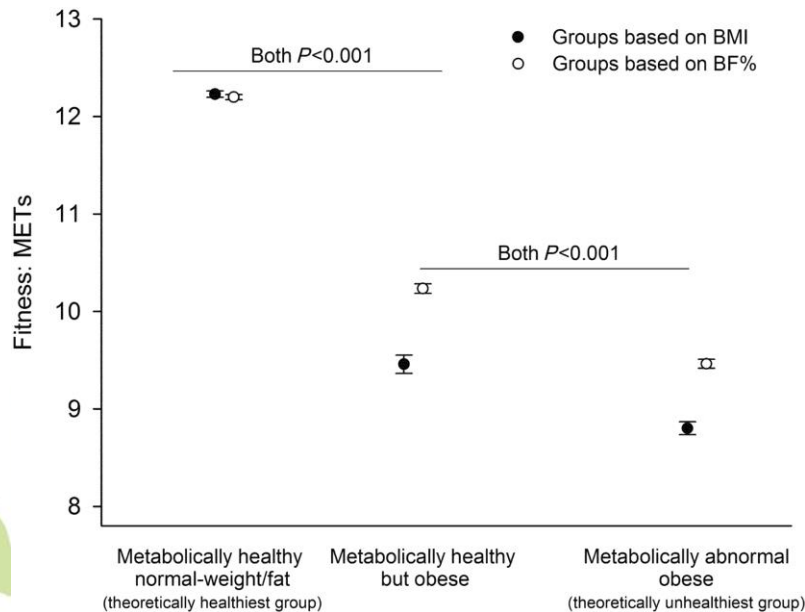


The intriguing metabolically healthy but obese phenotype: cardiovascular prognosis and role of fitness

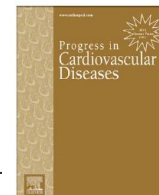
- Aerobic Center Longitudinal Study
 - 43265 individuals 14 anys seguiment

30,8% (IMC) / 46,3% (%BF) QMIH

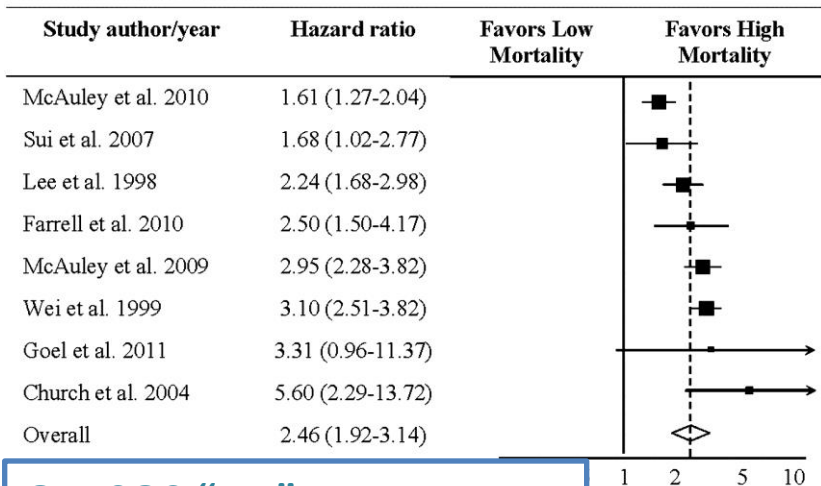
Fat and fit hypothesis



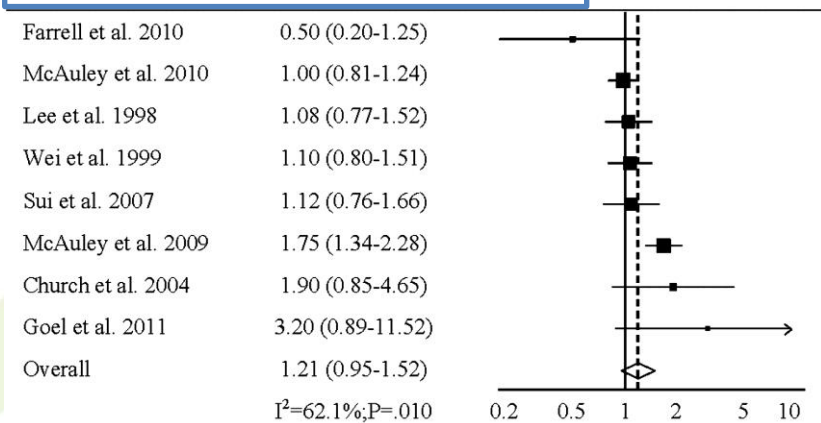
Fitness vs. Fatness on All-Cause Mortality: A Meta-Analysis



OBESOS "UNFIT"

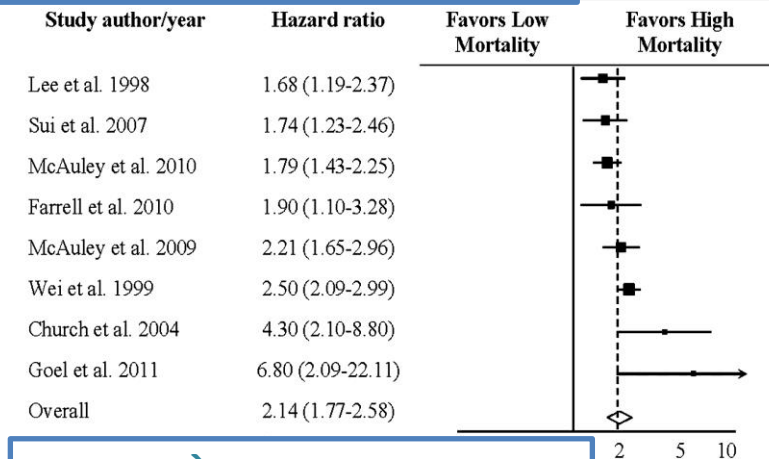


OBESOS "FIT"

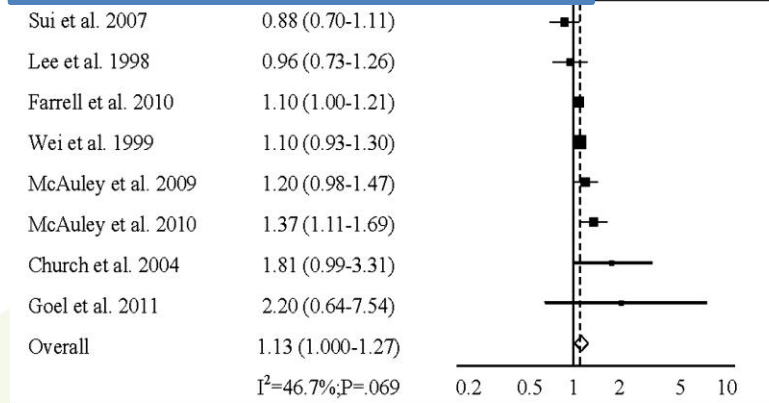


* Compared to normal weight fit individuals; CRF: Cardiorespiratory Fitness

SOBREPÈS "UNFIT"



SOBREPÈS "FIT"



* Compared to normal weight fit individuals

OBÈS METABÒLICAMENT SA?

- ÉS UN MITE, TÉ ALT RISC CARDIOVASCULAR

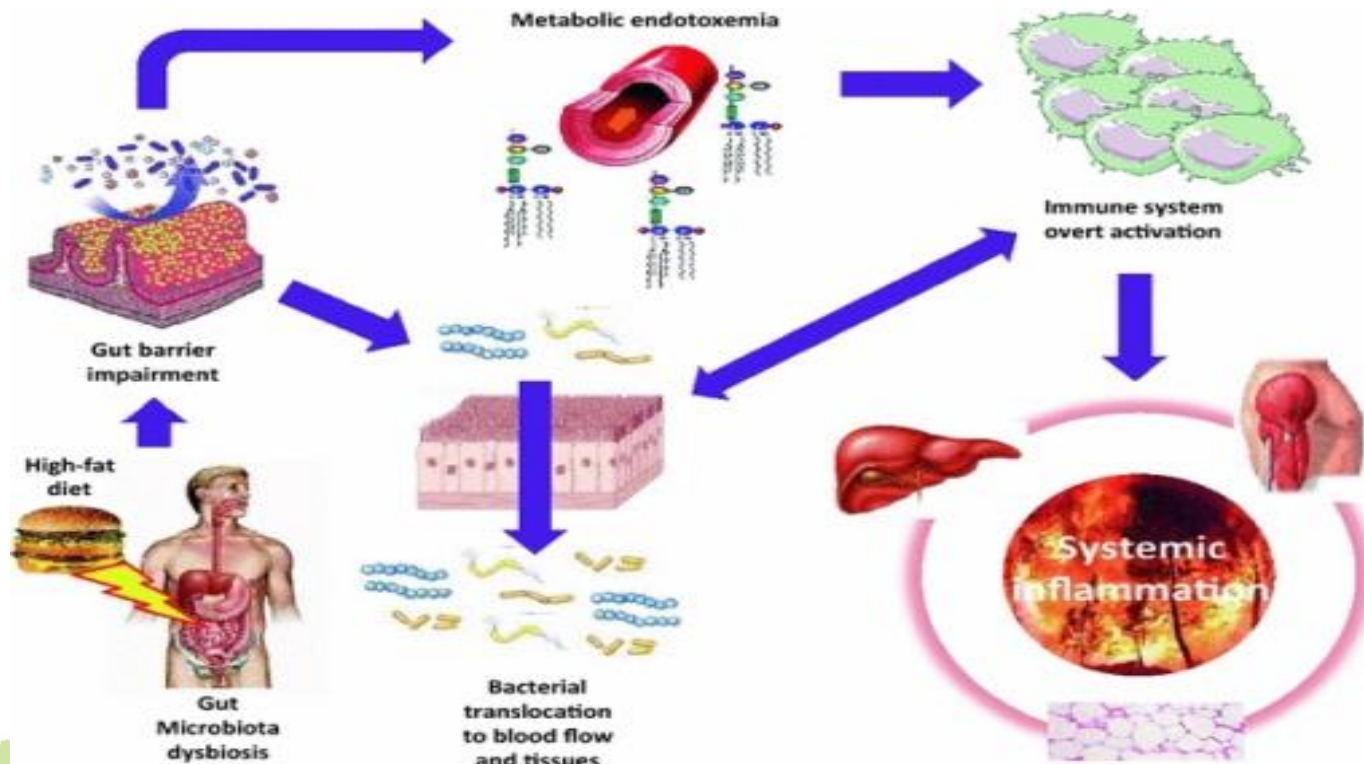
.... SI BÉ.....

➤ DISTRIBUCIÓ GREIX i MASSA MAGRA

➤ ACTIVITAT FÍSICA

😊 **Determinar la distribució tipus de greix per aproximar-nos millor al risc CV del pacient amb obesitat**

APROXIMACIÓ AL PACIENT AMB OBESITAT NO DIABÈTIC DIFERENTS GRAUS DE IR



Estudi incretines / endotoxèmia mtb pacients no DM

Proyecto FIS PI14/01997

- Estudi 3 centres
 - Secreció incretines amb la ingesta (GLP-2)
 - Microbiota intestinal
 - Endotoxèmia metabòlica
 - Composició corporal
 - Hosp JXXIII (grup no quirúrgic) (Dr. J Vendrell)
 - Hosp Bellvitge (grup quirúrgic amb DM) (Dra N. Vilarrasa)
 - Hosp GTiP (grup quirúrgic sense DM) **

Gràcies per la seva atenció

