Επιπλοκές της παχυσαρκίας στο καρδιαγγειακό σύστημα

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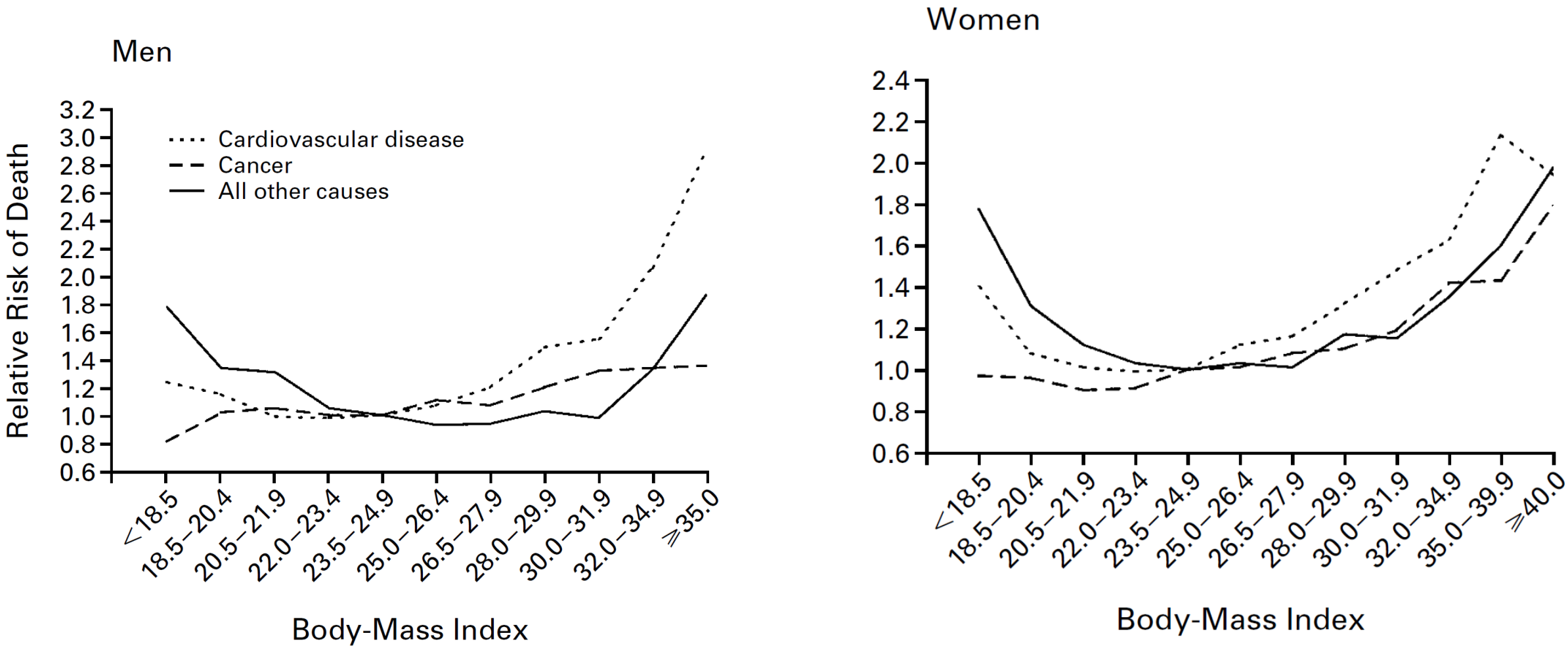
Γ. Ν. Ηρακλείου «Βενιζέλειο Πανάνειο»

«..ο αιφνίδιος θάνατος είναι πιο συνηθισμένος στα παχύσαρκα άτομα απ' ότι στα αδύνατα..»

Ιπποκράτης

(460-377πΧ)

BODY-MASS INDEX AND MORTALITY IN A PROSPECTIVE COHORT OF U.S. ADULTS

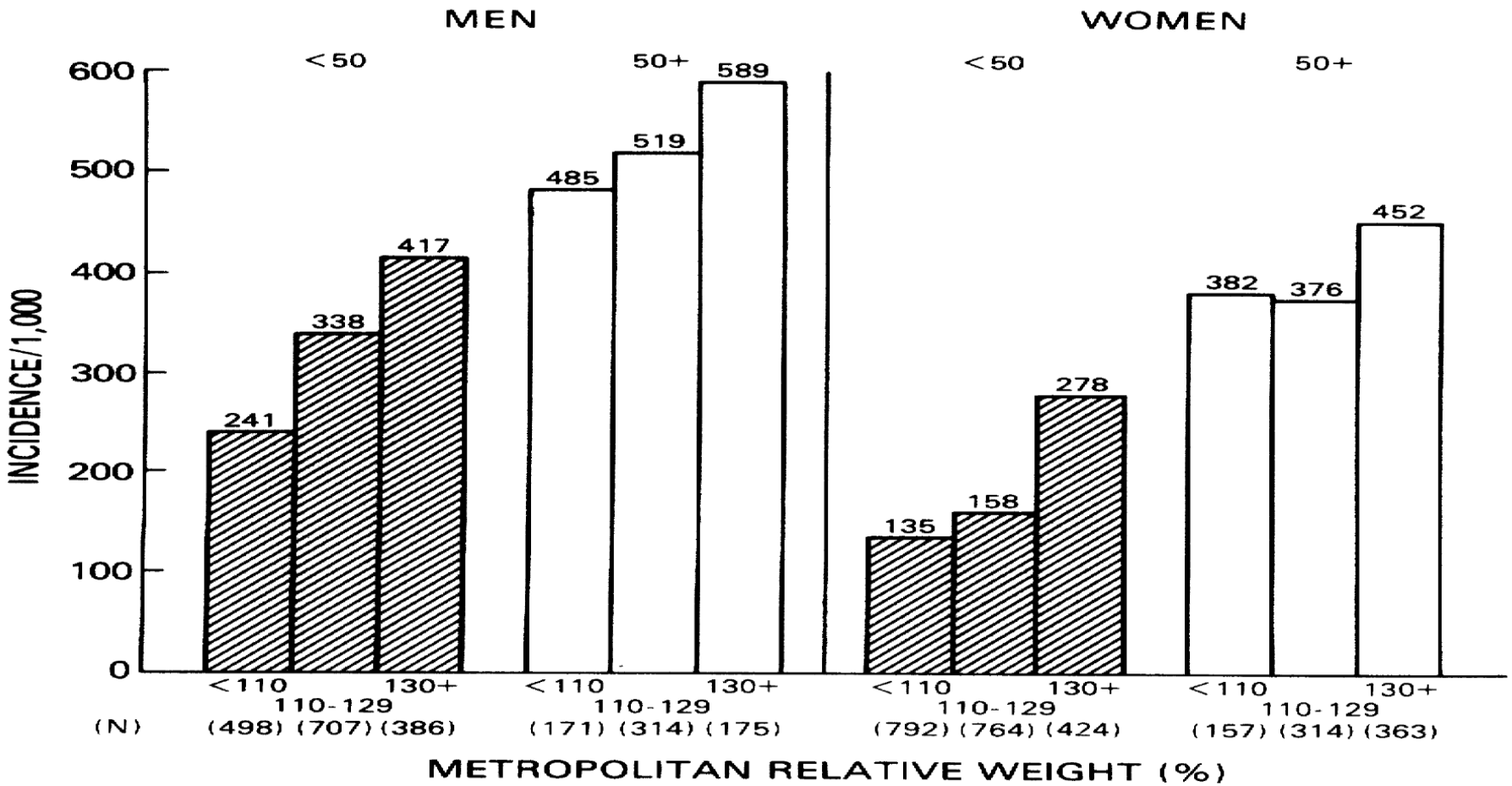


N Engl J Med 1999;341:1097-105

457,785 men and 588,369 women, 14 years follow-up

Obesity as an Independent Risk Factor for Cardiovascular Disease: A 26-year Follow-up of Participants in the Framingham Heart Study

HELEN B. HUBERT, M.P.H., PH.D., MANNING FEINLEIB, M.D., DR.P.H., PATRICIA M. MCNAMARA, AND WILLIAM P. CASTELLI, M.D.



Circulation 67, No. 5, 1983.

5209 men and women of the original Framingham cohort.
26 years follow up

Obese years and CVD risk

Table 4 Risk of cardiovascular disease according to categories of obese-years

	HR (95% CI)		
	Total population*	Males	Females
Model 3			
0 obese-years	1	1	1
1–25 obese-years	1.31 (1.15 to 1.48)	1.22 (1.02 to 1.45)	1.37 (1.14 to 1.65)
25–50 obese-years	1.37 (1.14 to 1.65)	1.39 (1.05 to 1.83)	1.36 (1.05 to 1.76)
50–75 obese-years	1.62 (1.32 to 1.99)	1.89 (1.42 to 2.51)	1.44 (1.08 to 1.94)
≥75 obese-years	1.80 (1.54 to 2.10)	1.81 (1.39 to 2.36)	1.74 (1.44 to 2.10)
Dose-response p value	0.001	0.001	0.001

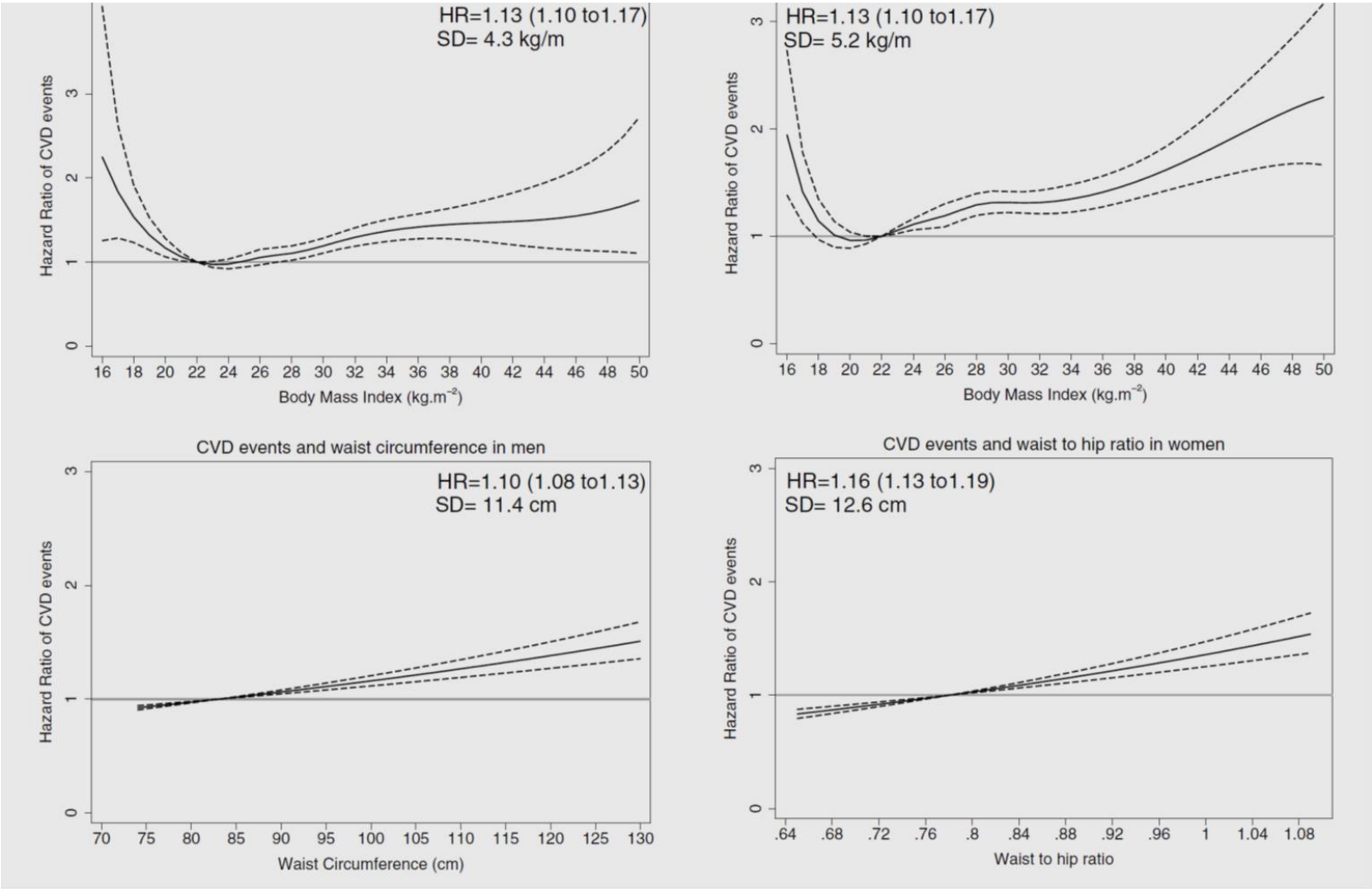
aged 28–62 years at the time of enrolment attended biennial examinations for **approximately 50 years** beginning from 1948. For the purpose of this study, only participants who were **free from CVD** (any type), **cancer and type-2 diabetes at baseline** were included in the analysis (n=5036)

Eaxample: BMI 32 for 3 years= 3X3 obese years

cohort in Framingham

Abdullah A, et al. BMJ Open 2014;4:e005629

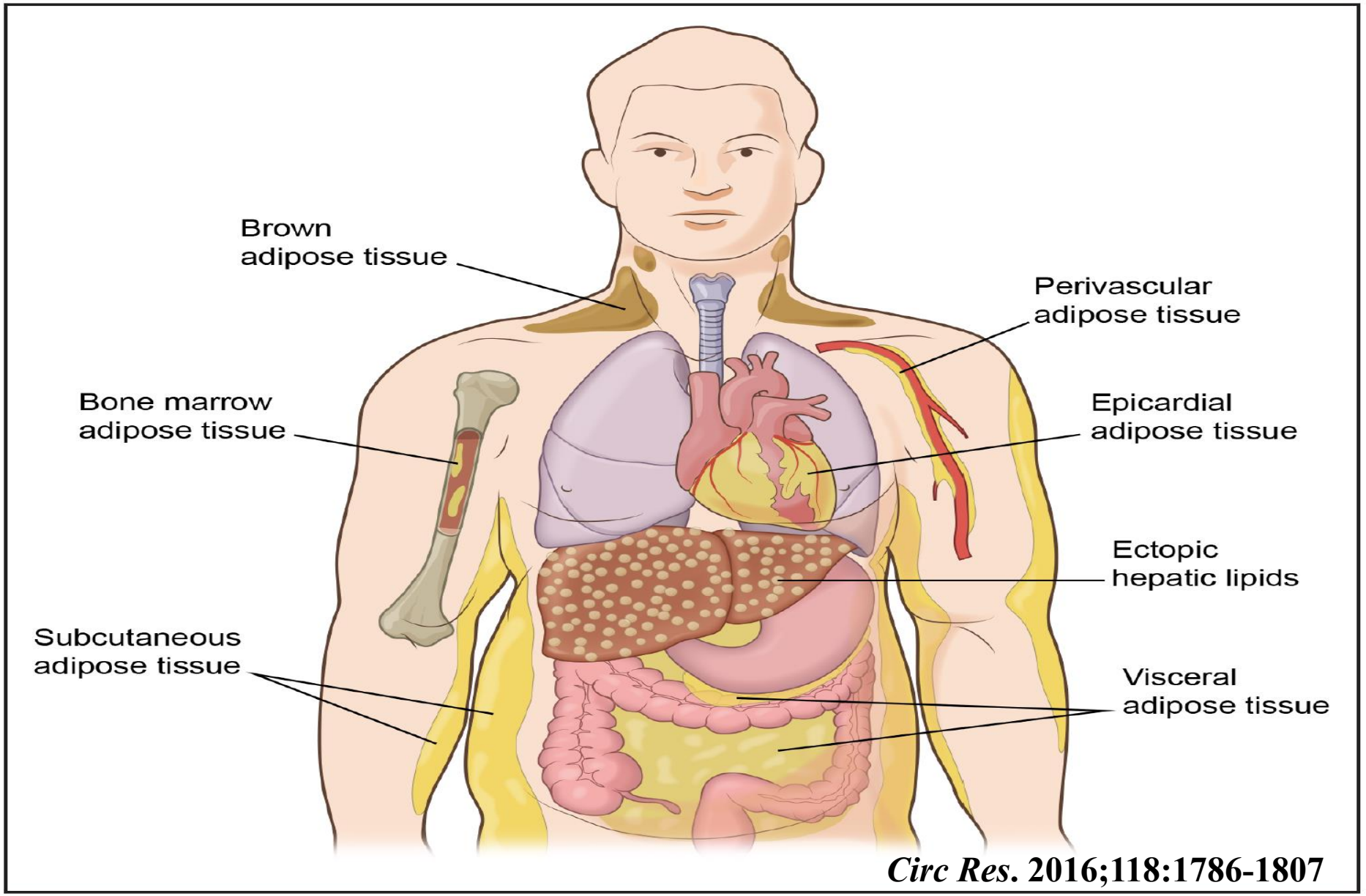
The impact of confounding on the associations of different adiposity measures with the incidence of cardiovascular disease: a cohort study of 296 535 adults of white European descent



followed up for an average of 5 years

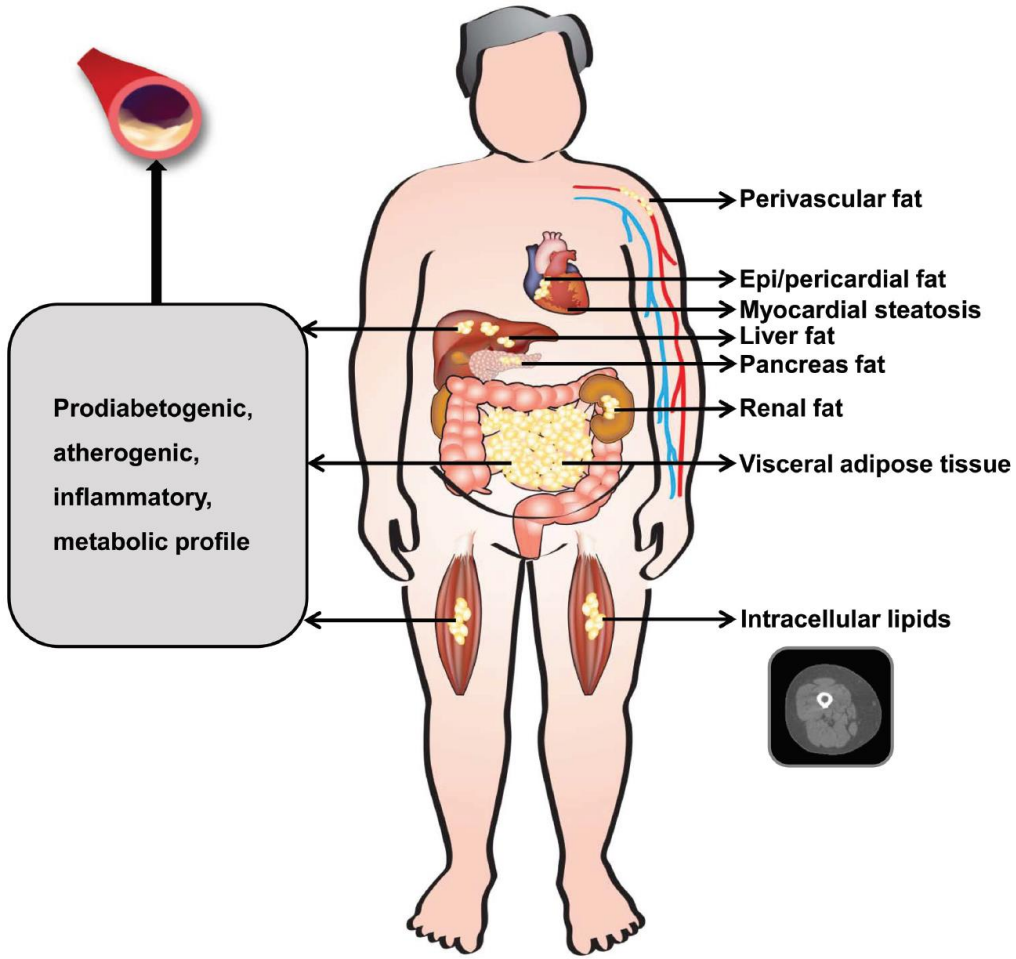
European Heart Journal (2018) 00, 1–8

Αύξηση όγκου λιπώδους ιστού-έκτοπου λίπους



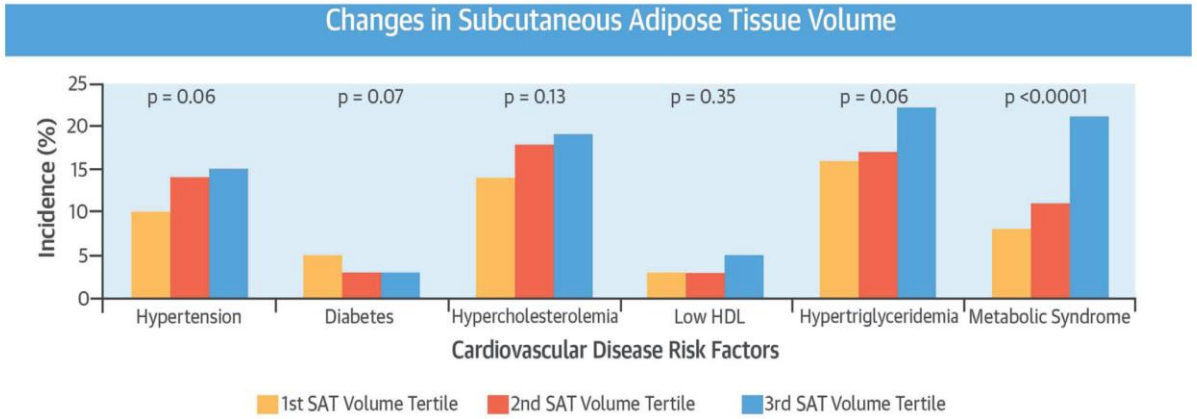
Circ Res. 2016;118:1786-1807

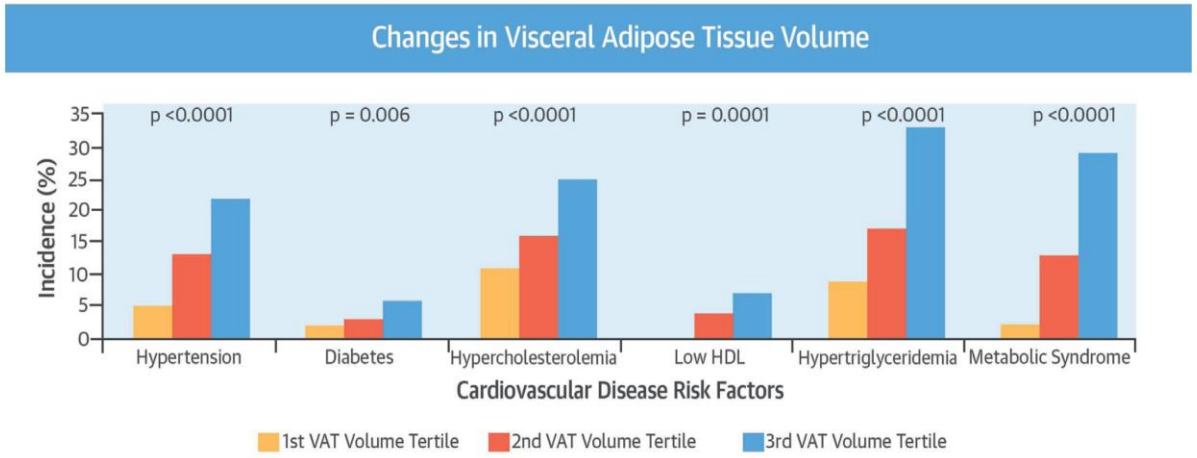
Νοσογόνο λίπος



Ectopic fat depots with systemic effects:
- Liver fat
- Visceral adipose tissue
- Intracellular lipids
- Pancreas fat

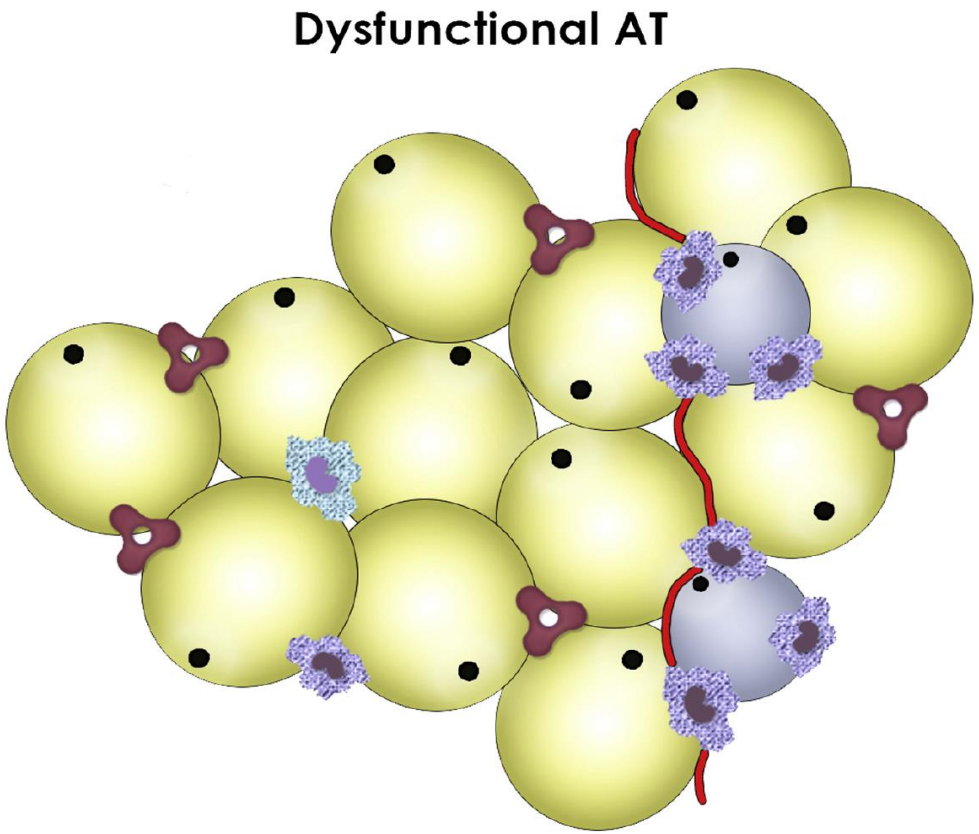
Ectopic fat depots with local effects:
- Perivascular fat
- Epi/pericardial fat
- Renal fat
- Etc.



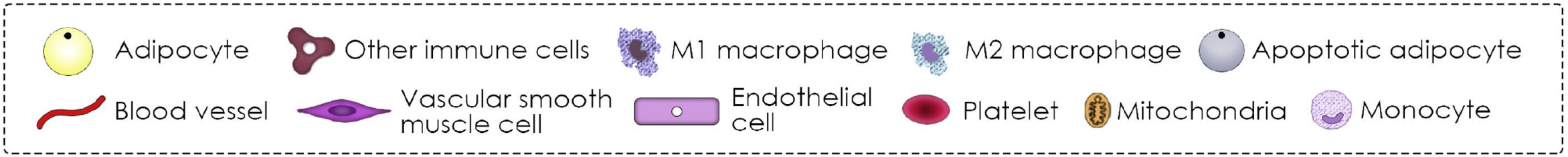


Lee, J.J. et al. J Am Coll Cardiol. 2016;68(14):1509-21.

Adisopathy-Λιποπαθεια

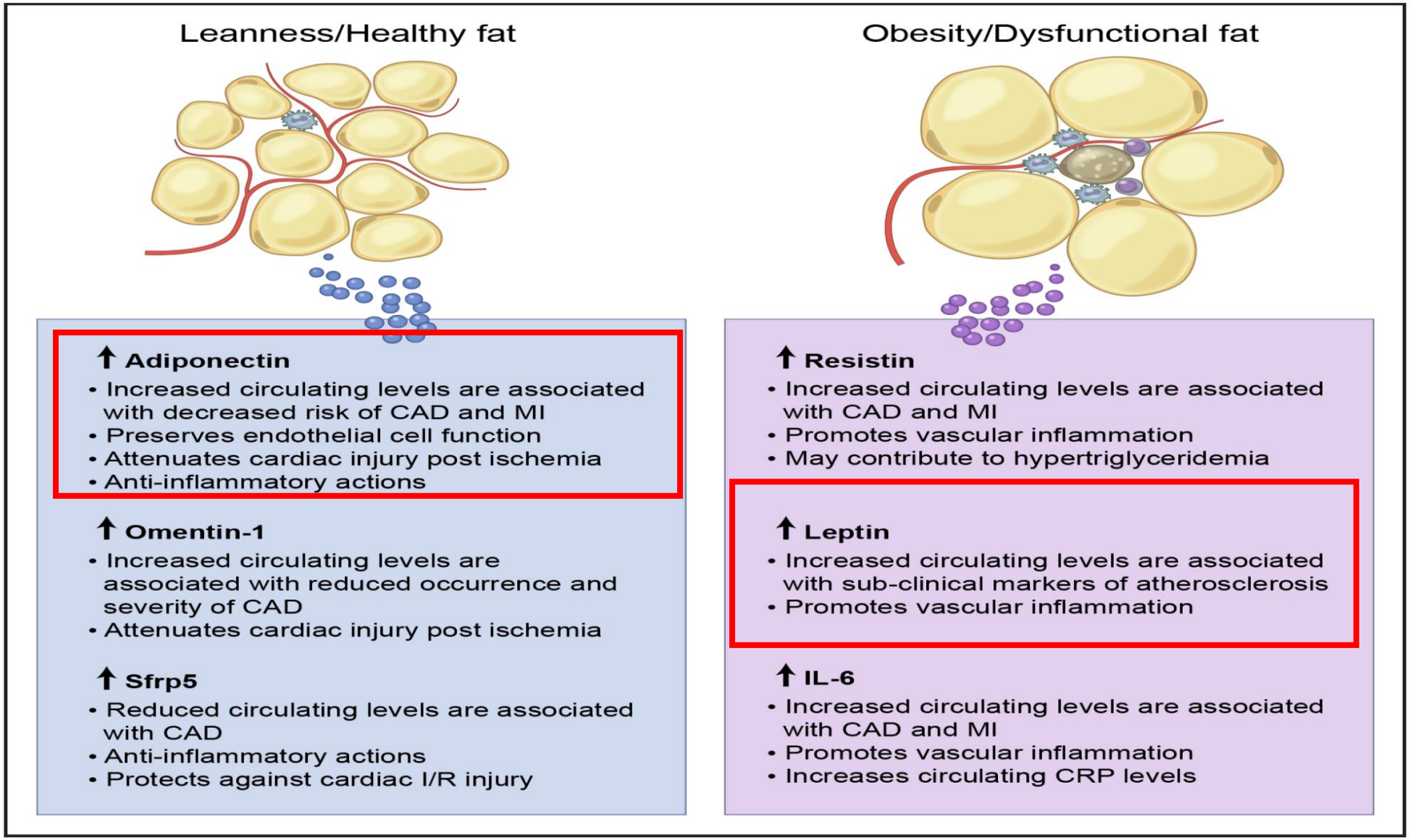


- Adipocyte hypertrophy
- ↓ vascularization
- Hypoxia
- Ischemic necrosis
- Macrophage activation
- Adipokine dysregulation
  (pro-inflammatory >>> anti-inflammatory)
- Impaired adipogenesis and expandability



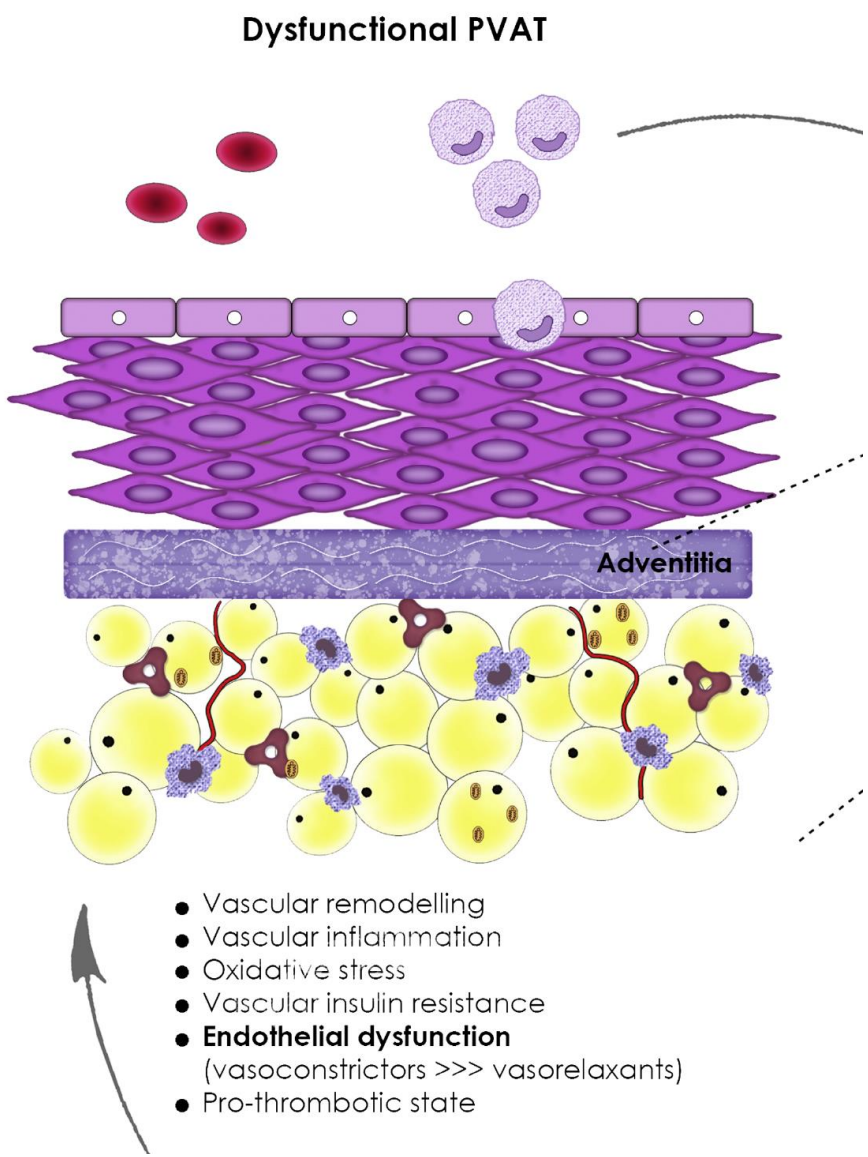
https://doi.org/10.1016/j.metabol.2018.10.011

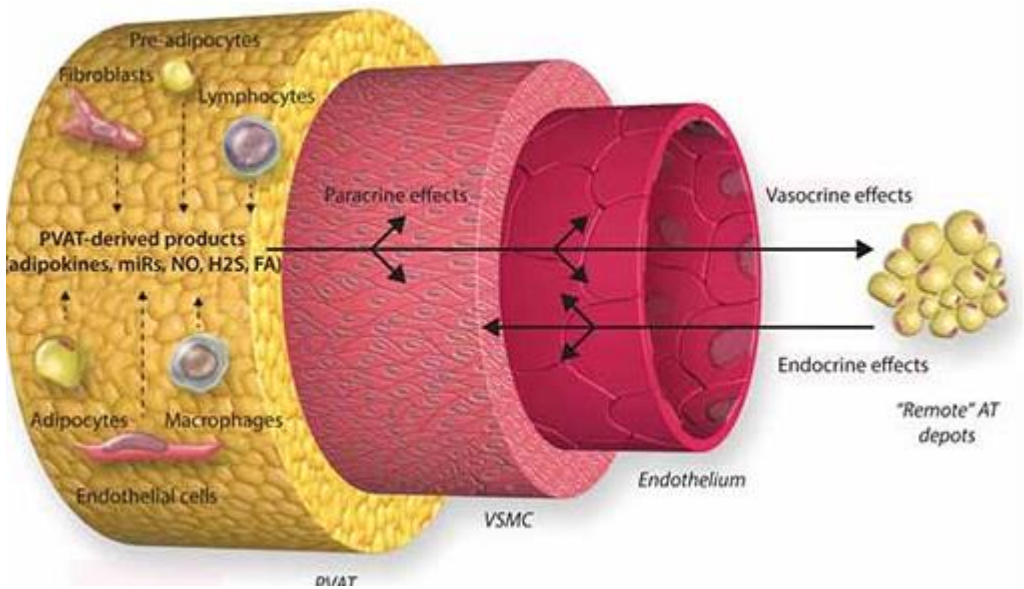
Adipokines and CVD

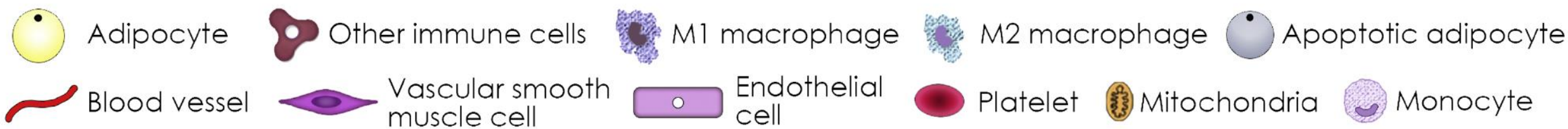


Circ Res. 2016;118:1786-1807

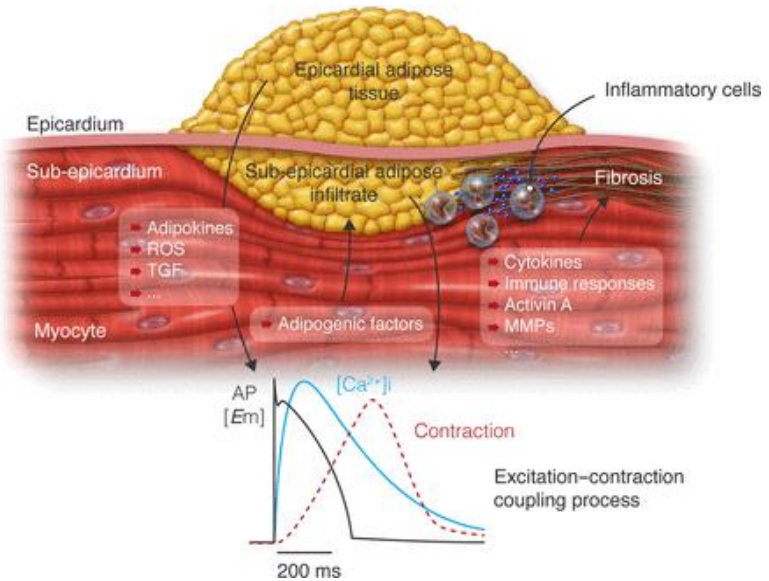
Perivascular Fat

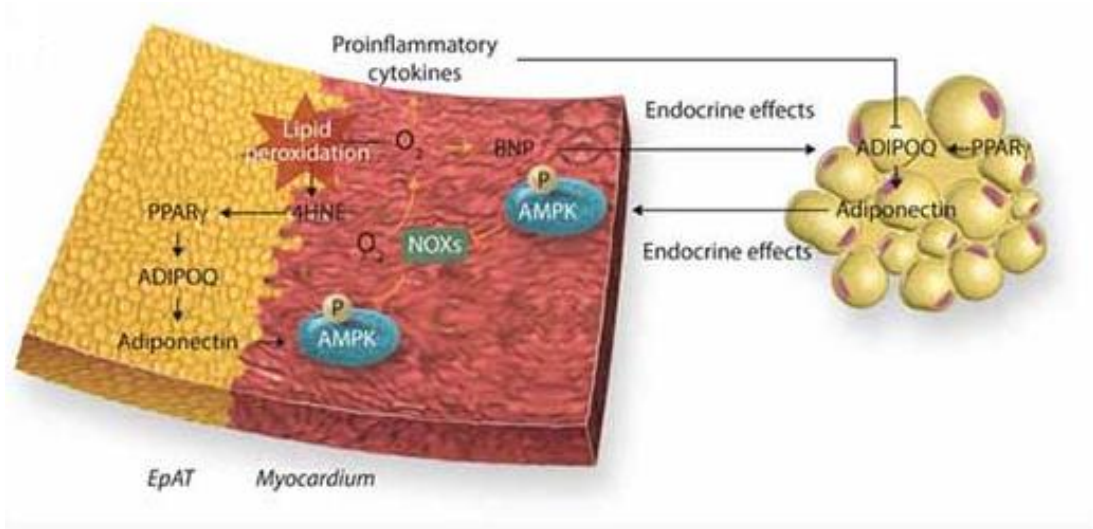


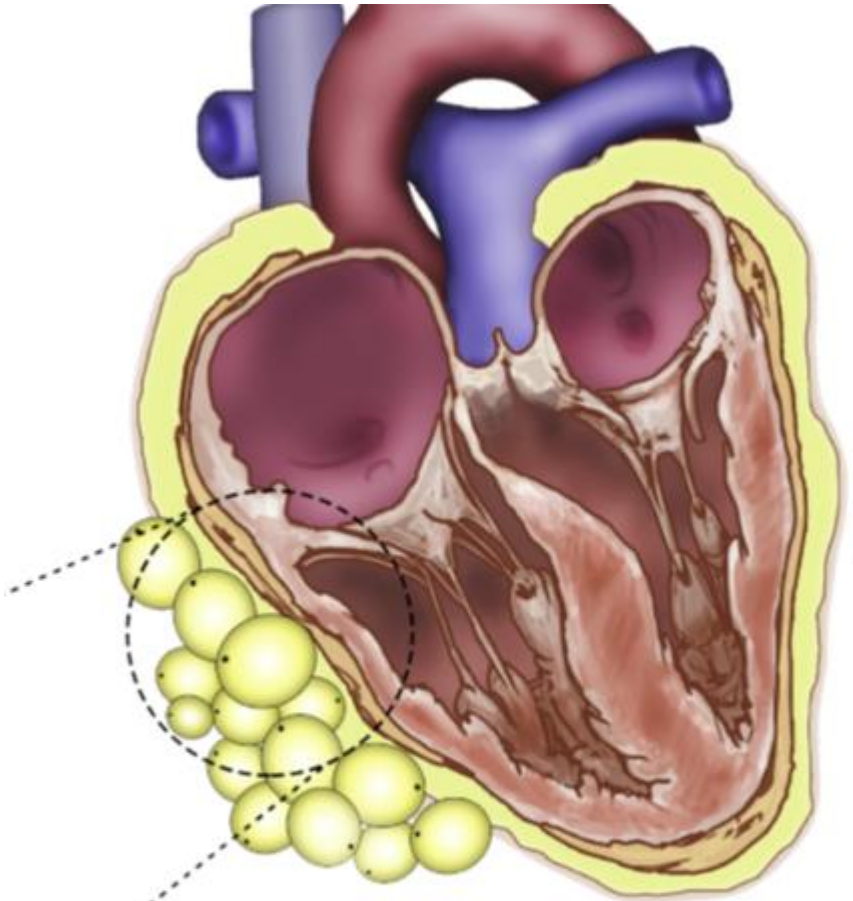




Epicardial Fat

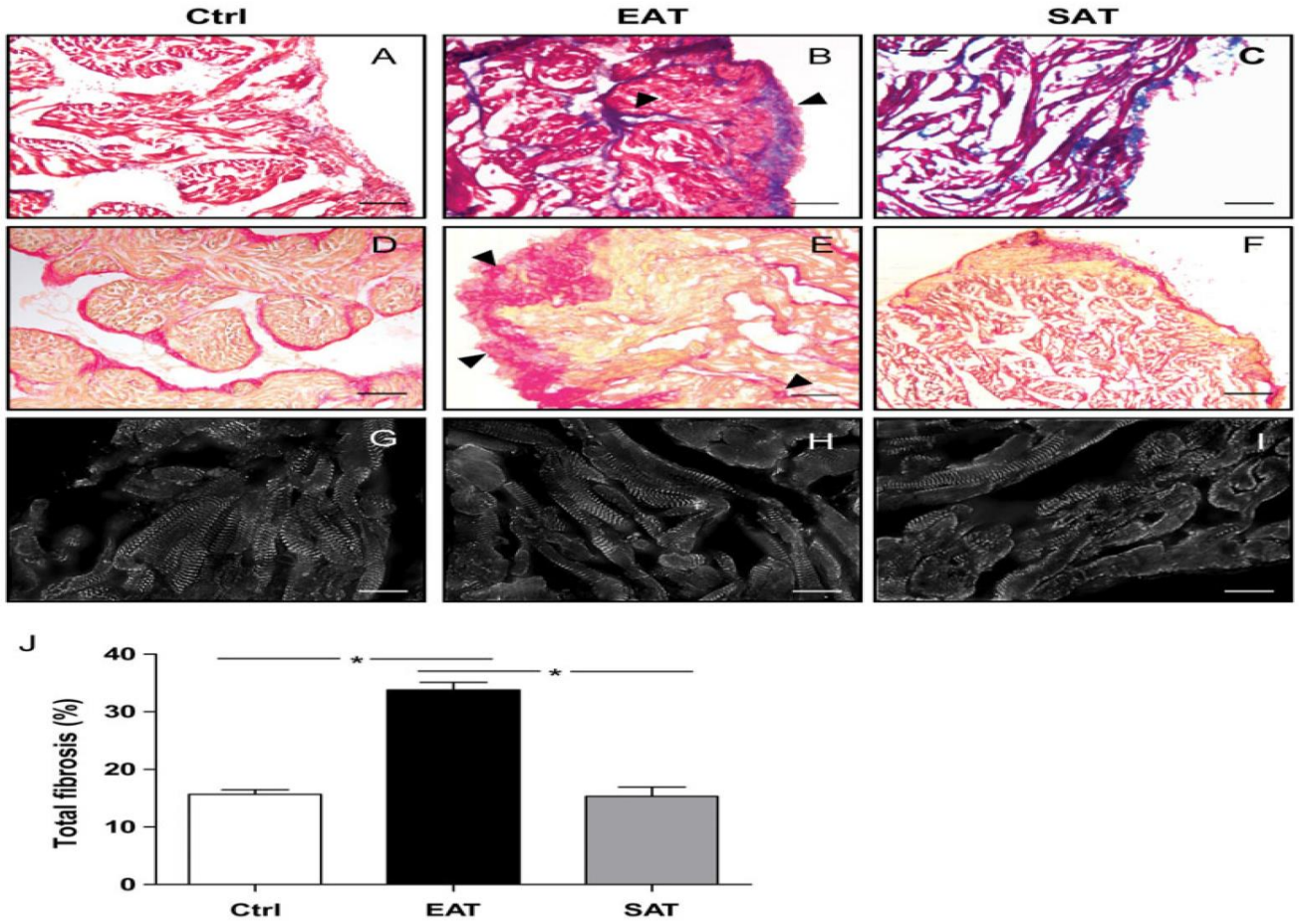






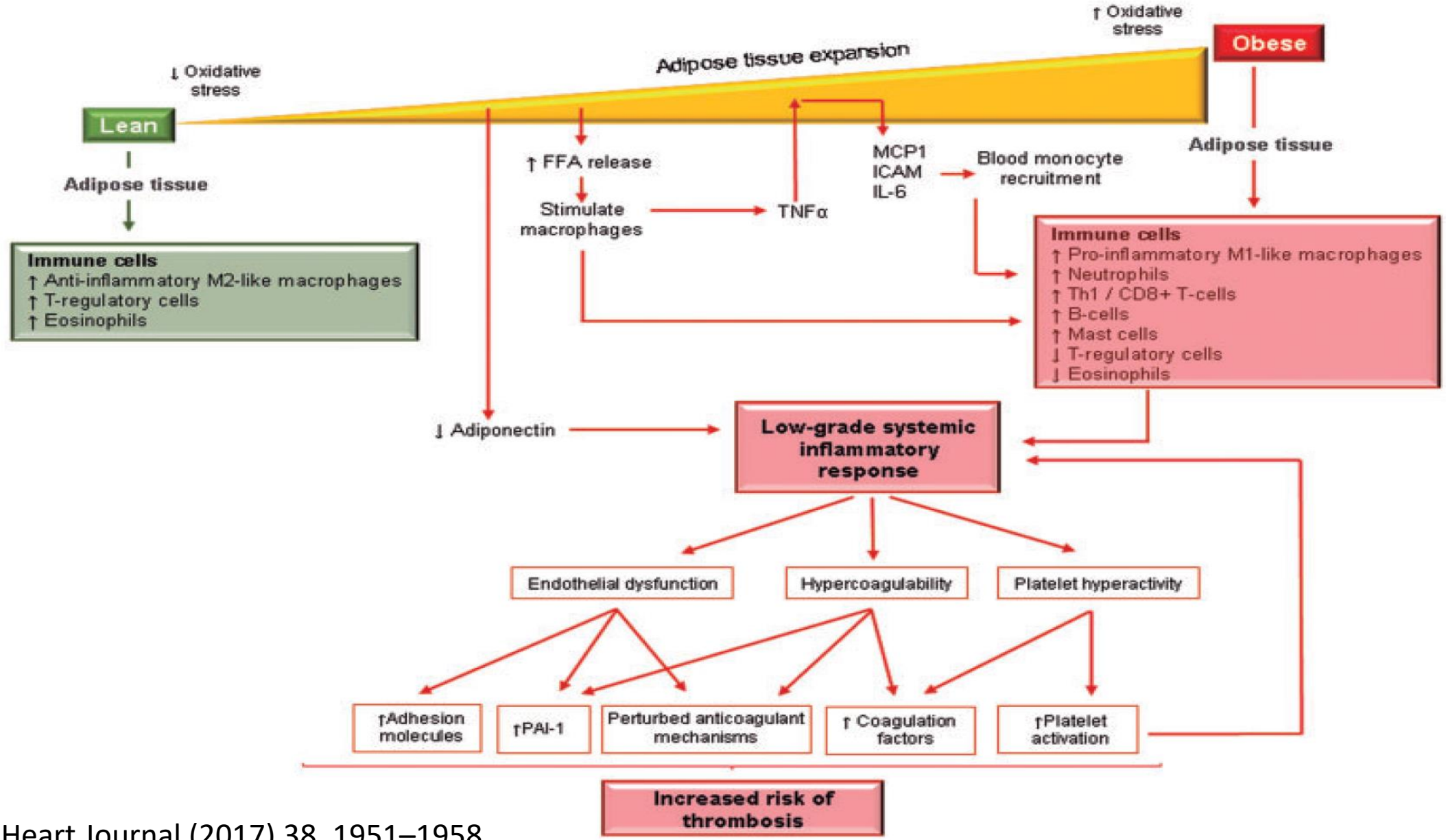
- Cardiomyocyte hypertrophy
- Steatosis
- Fibrosis
- Lipotoxicity
- LV remodelling + diastolic dysfunction

Fibrosis and Epicardial Adipose Tissue



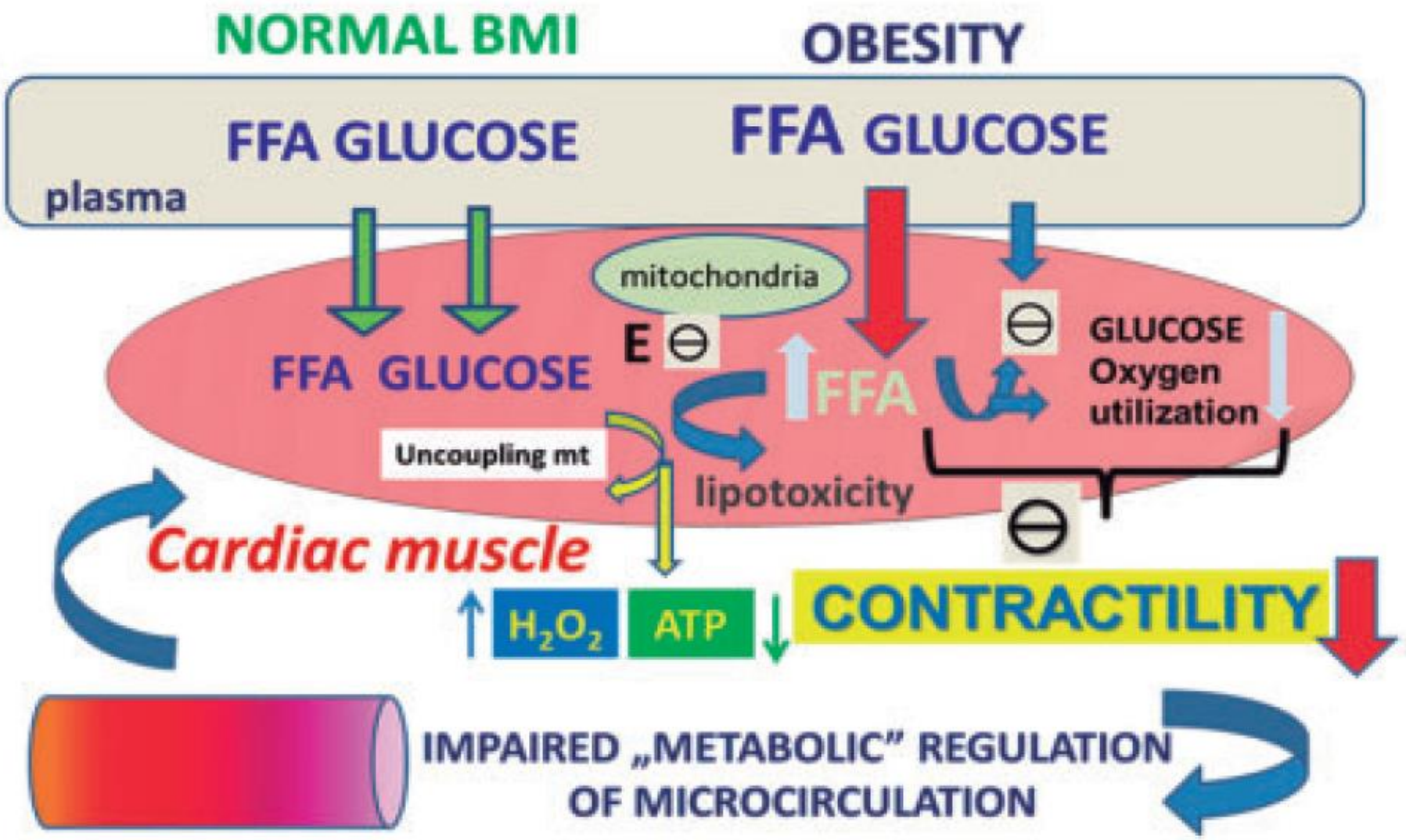
European Heart Journal (2015) 36, 795–805

Obesity, inflammation and thrombosis



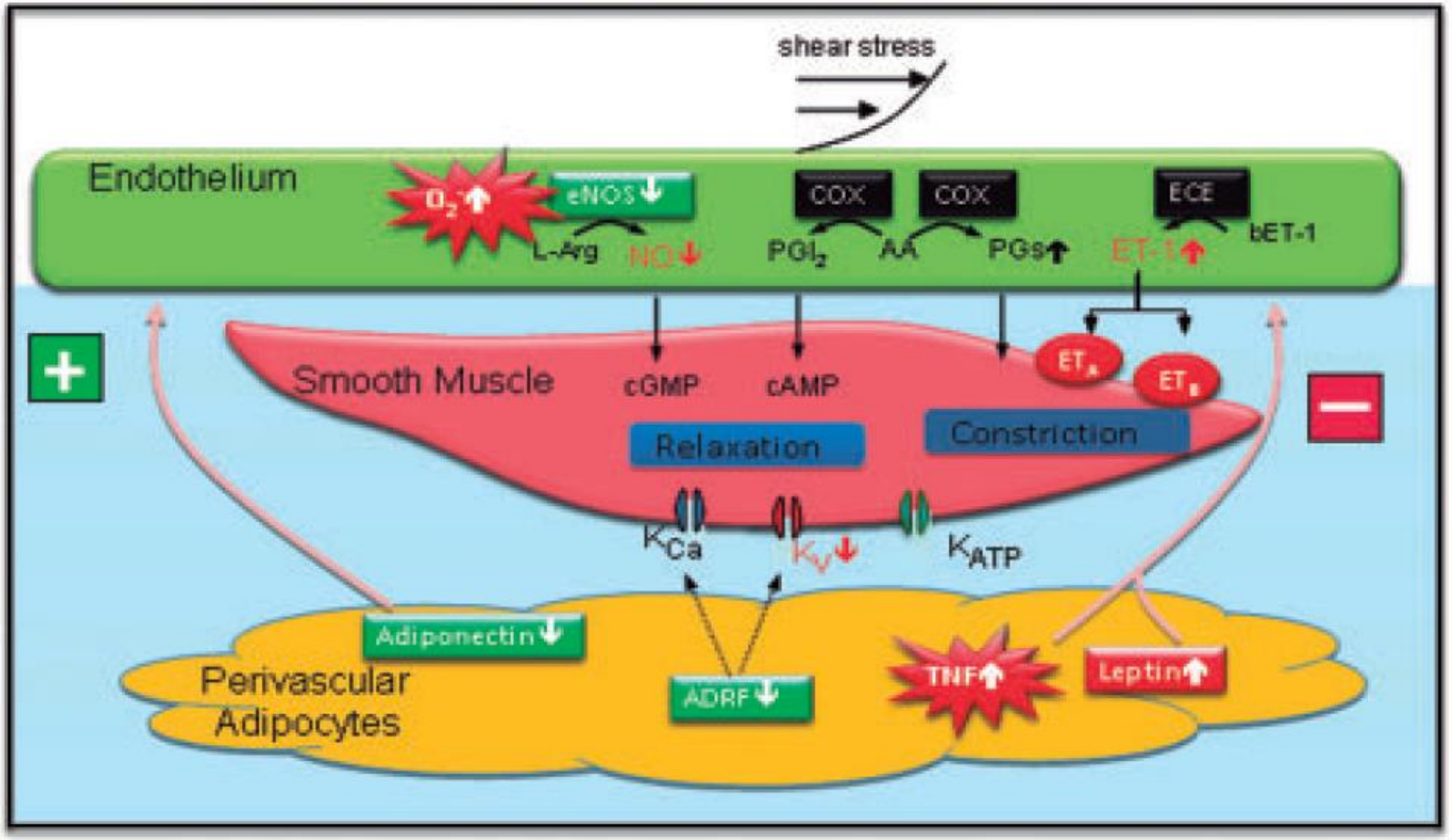
European Heart Journal (2017) 38, 1951–1958

Obesity and cardiometabolic dysfunction



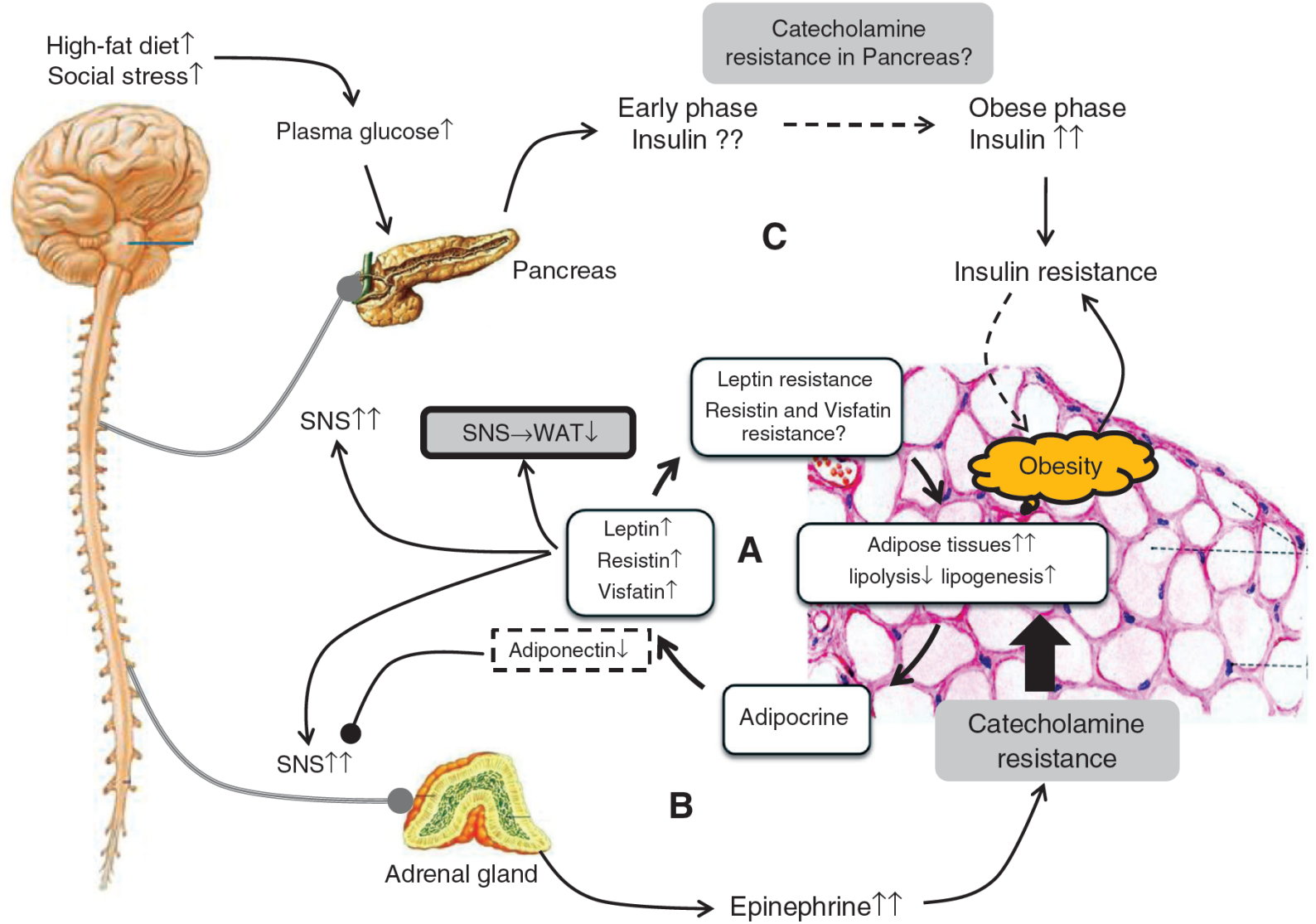
European Heart Journal (2017) 38, 1951–1958

Obesity and vascular tone



European Heart Journal (2017) 38, 1951–1958

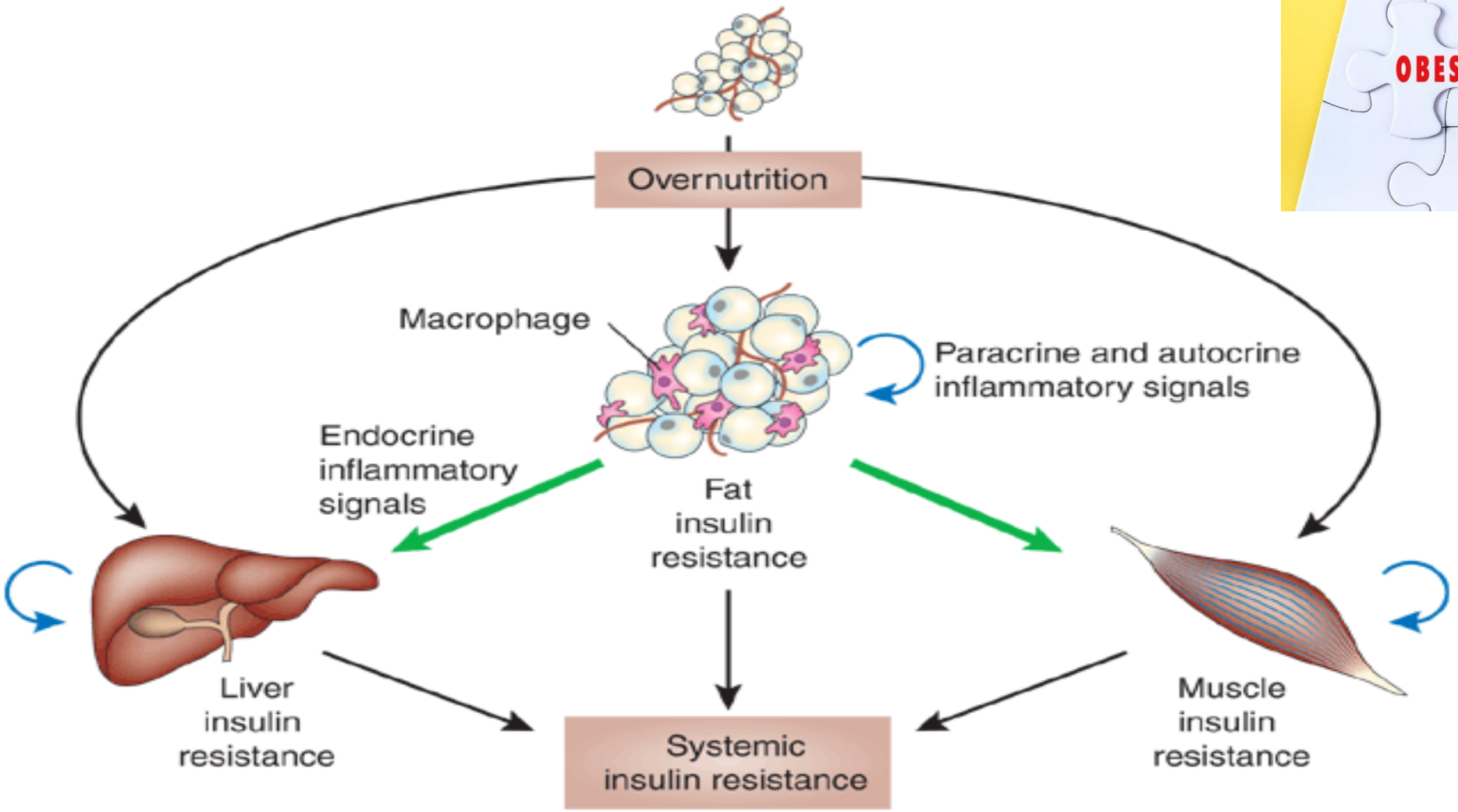
Obesity and sympathetic nervous system



J Pediatr Endocrinol Metab 2015 DOI: 10.1515/jpem-2015-0182

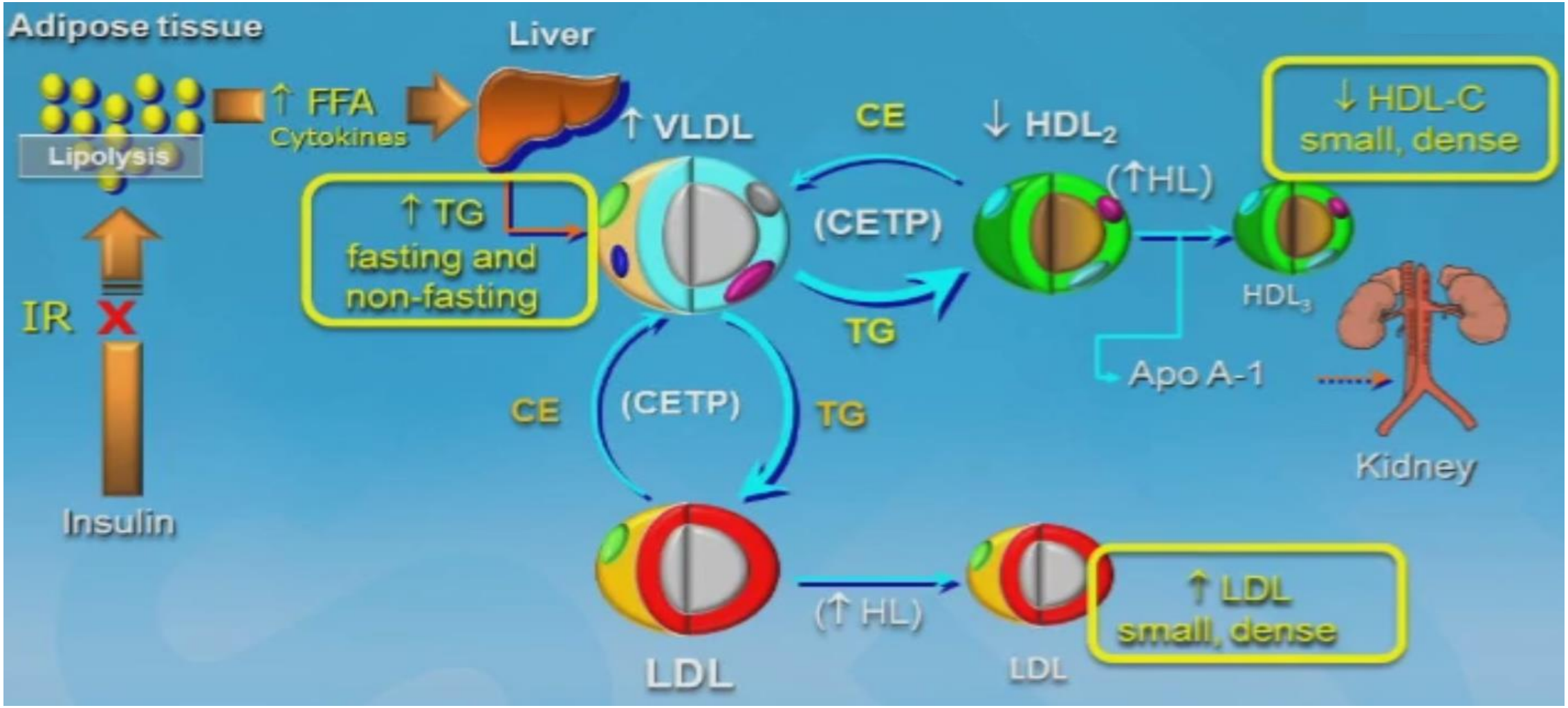
Obesity Insulin Resistance and Type 2 Diabetes

Diabesity



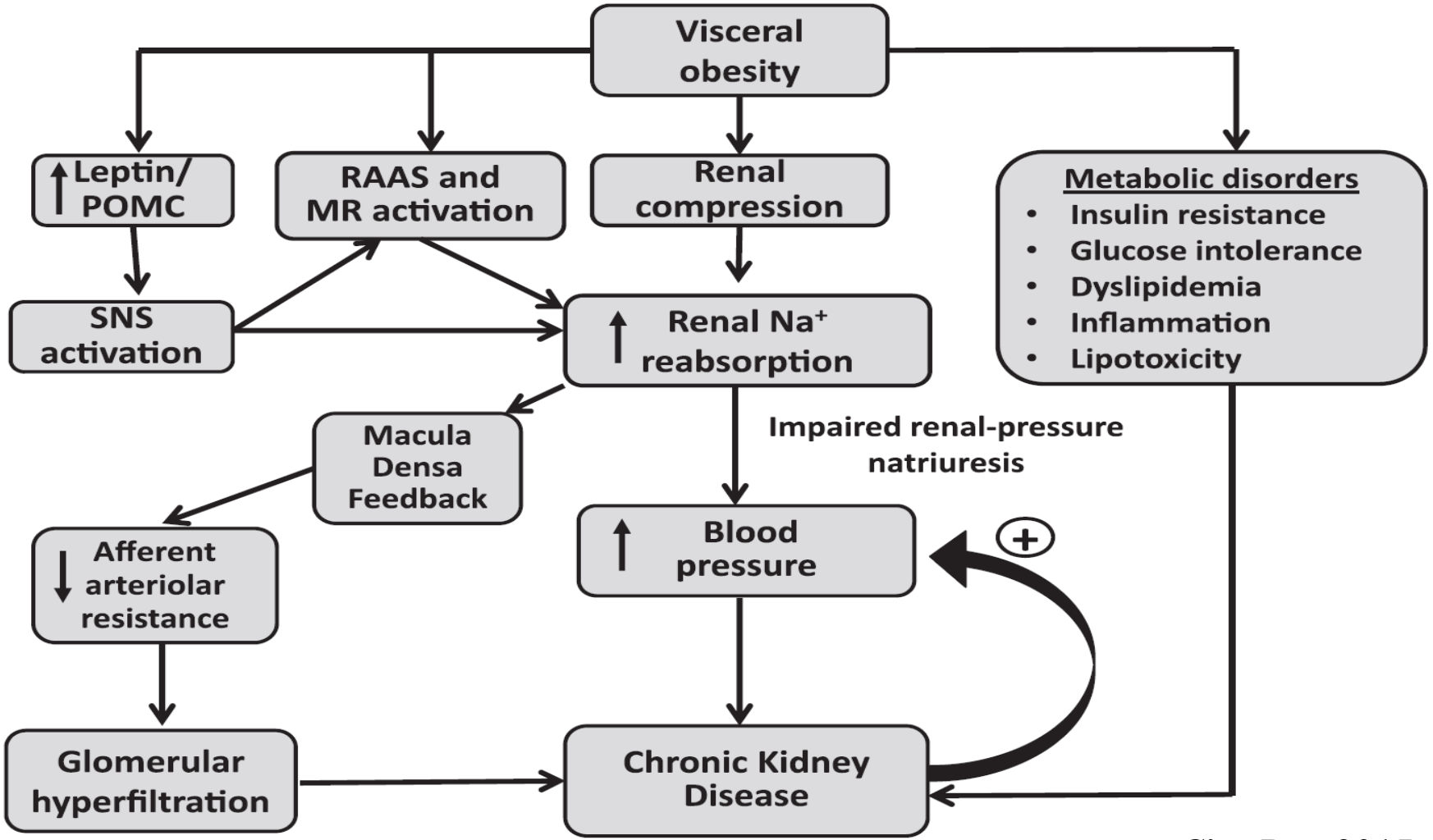
Nature Medicine **volume12**, pages41–42 (2006)

Obesity and dyslipidemia



Austin et al Circulation 1990

Obesity-Induced Hypertension



Circ Res. 2015;116:991-1006

BMI and Hypertension

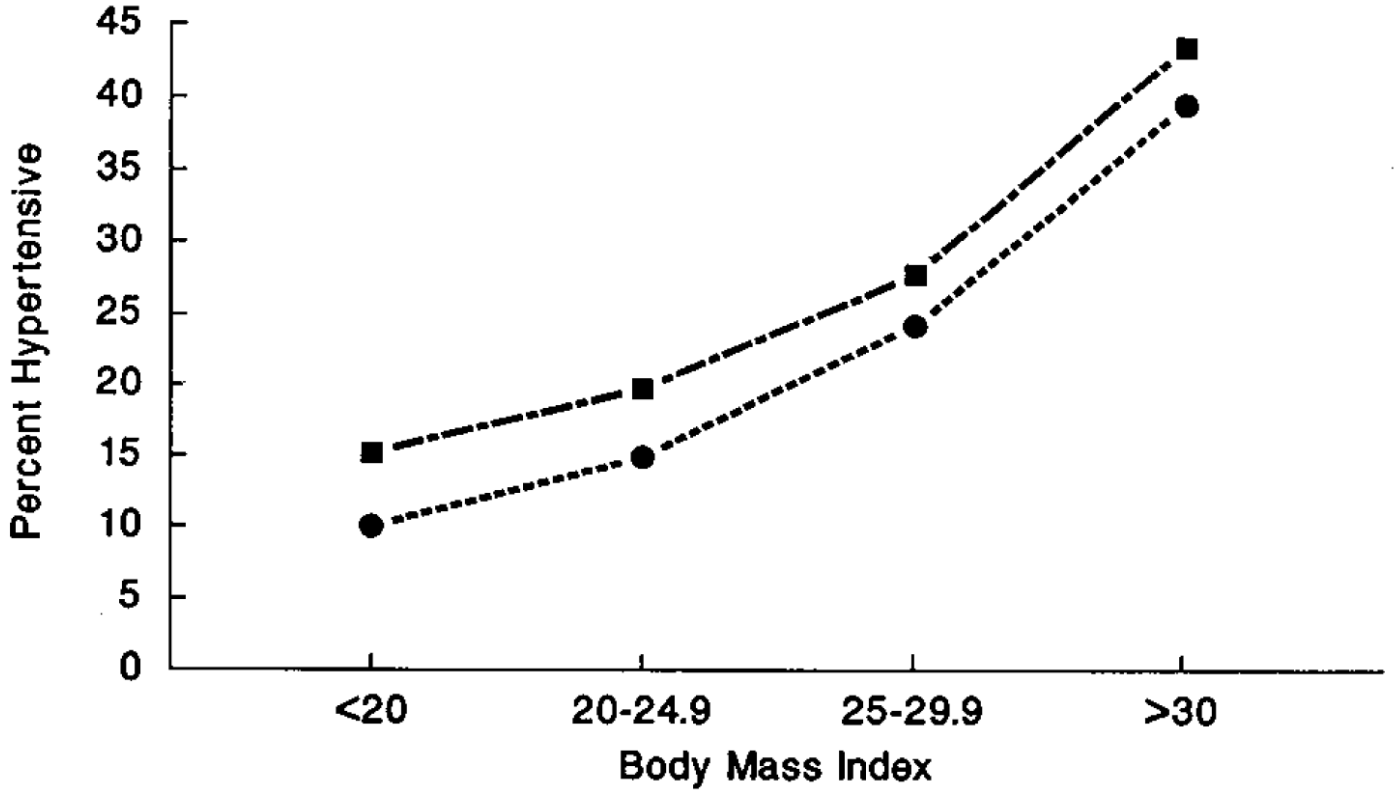
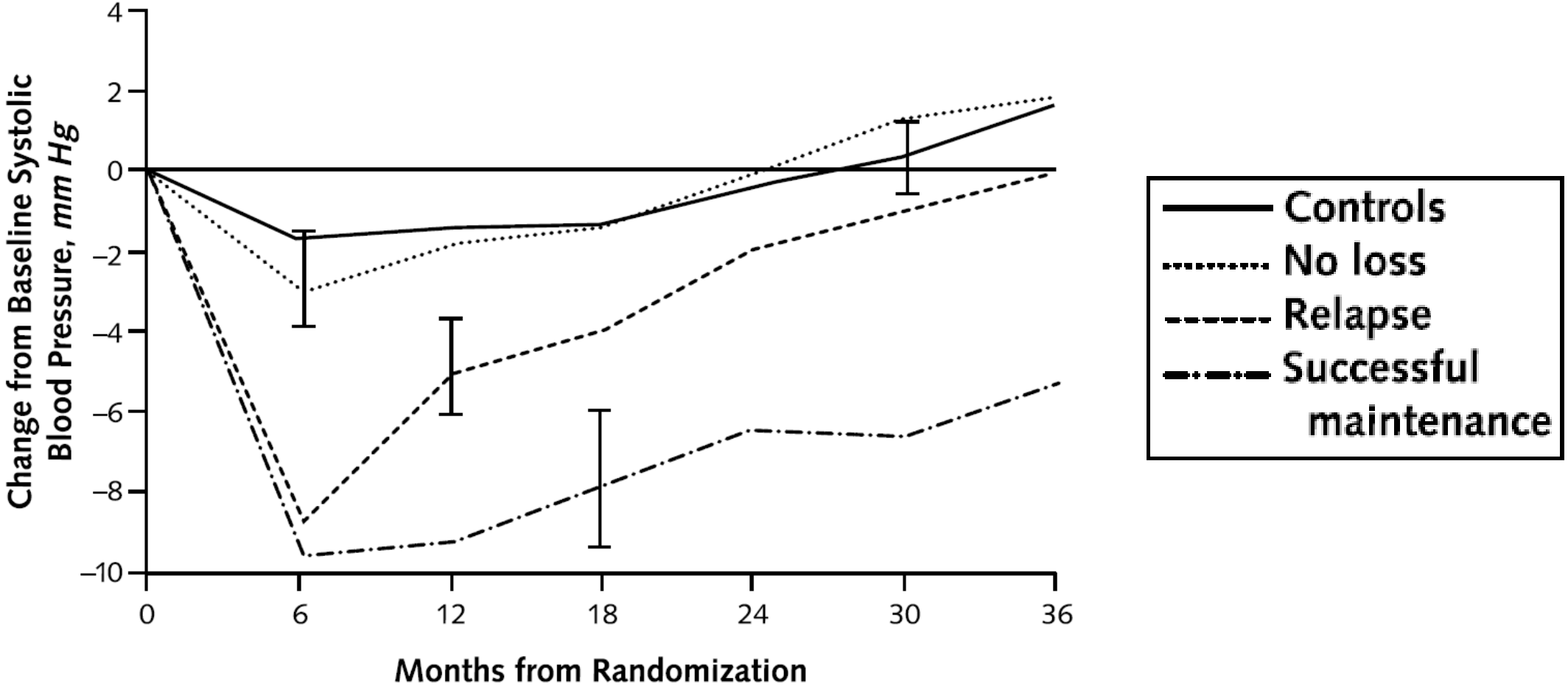


Fig. 7. Percentage of subjects hypertensive by each body mass index category (kg/m^2): ■, males; ●, females.

Journal of Hypertension 1994, **12**:1433–1437

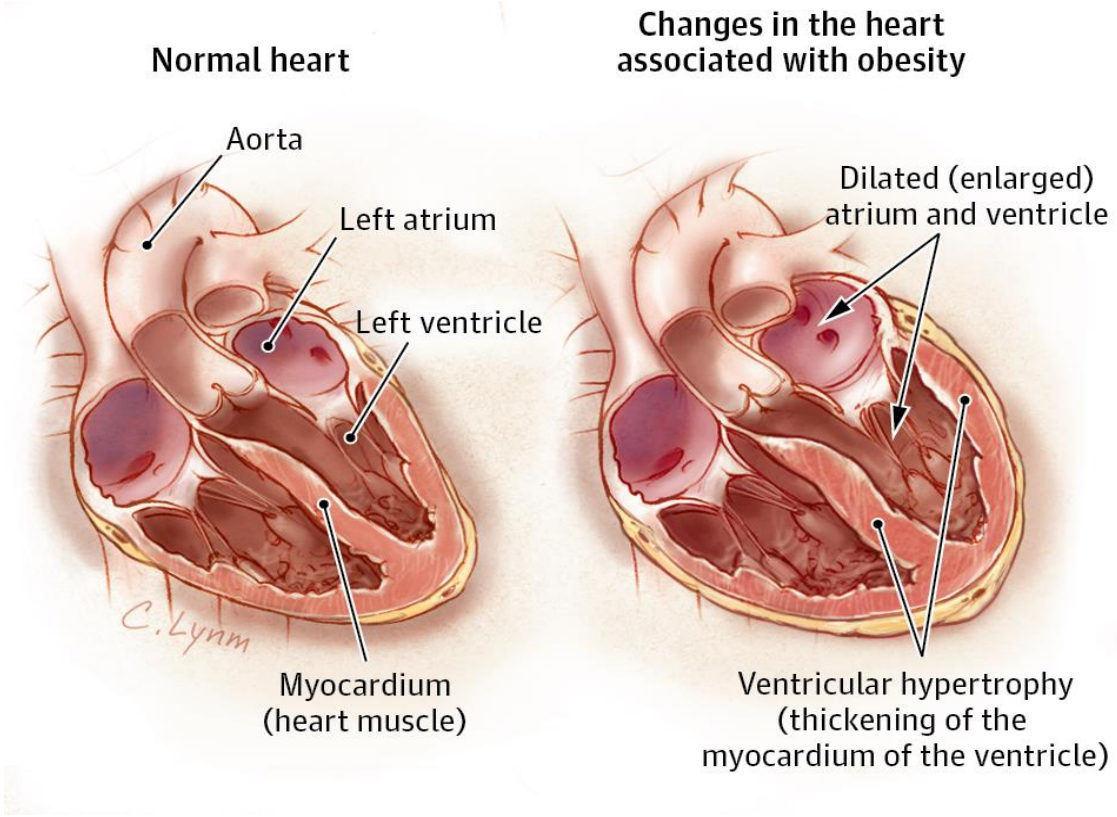
Weight loss and Hypertension



Ann Intern Med. 2001;134:1-11.

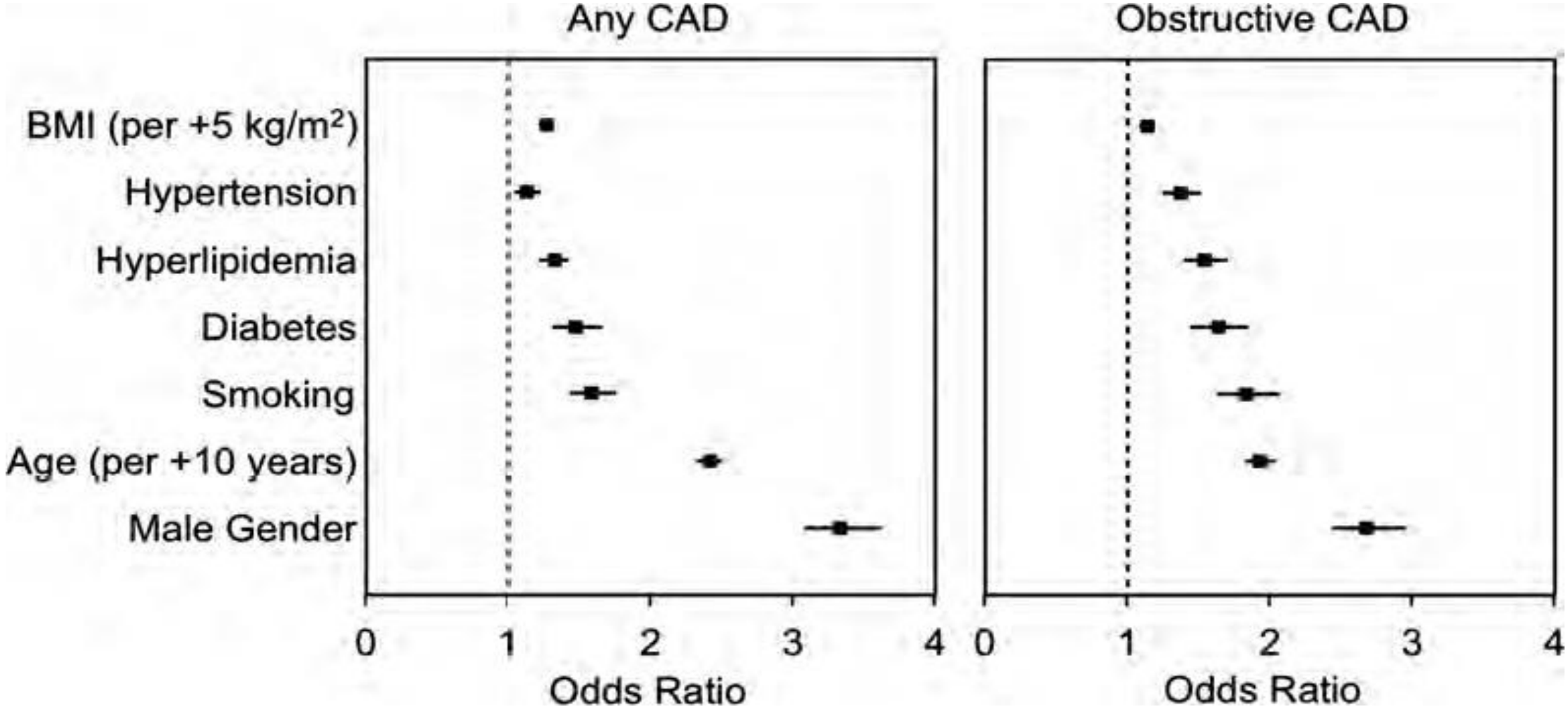
Hemodynamic and cardiac adaptations

- Αύξηση ενδοαγγειακού όγκου
- Αύξηση όγκου παλμού
- Αύξηση καρδιακής συχνότητας
- Αύξησης καρδιακής παροχής
- Αύξηση αρτηριακής πίεσης
- Αύξηση Συστολικής πίεσης πνευμονικής
- Αύξησης πίεσης πλήρωσης αριστερής-δεξιάς κοιλίας
- Διάταση αριστερού κόλπου
- Υπερτροφία Αριστερής κοιλίας (έκκεντρη –συγκεντρική)
- Διάταση αριστερής κοιλίας



Obesity and Coronary Artery Disease

[odds ratio (OR) 1.25 per +5 kg/m2, 95% confidence interval (CI): 1.20–1.30, P , 0.001]



prospective 13 874 patients without known CAD
follow-up was 2.4+1.2 years

European Heart Journal – Cardiovascular Imaging (2013) 14, 456–463

Obesity and Myocardial Infarction

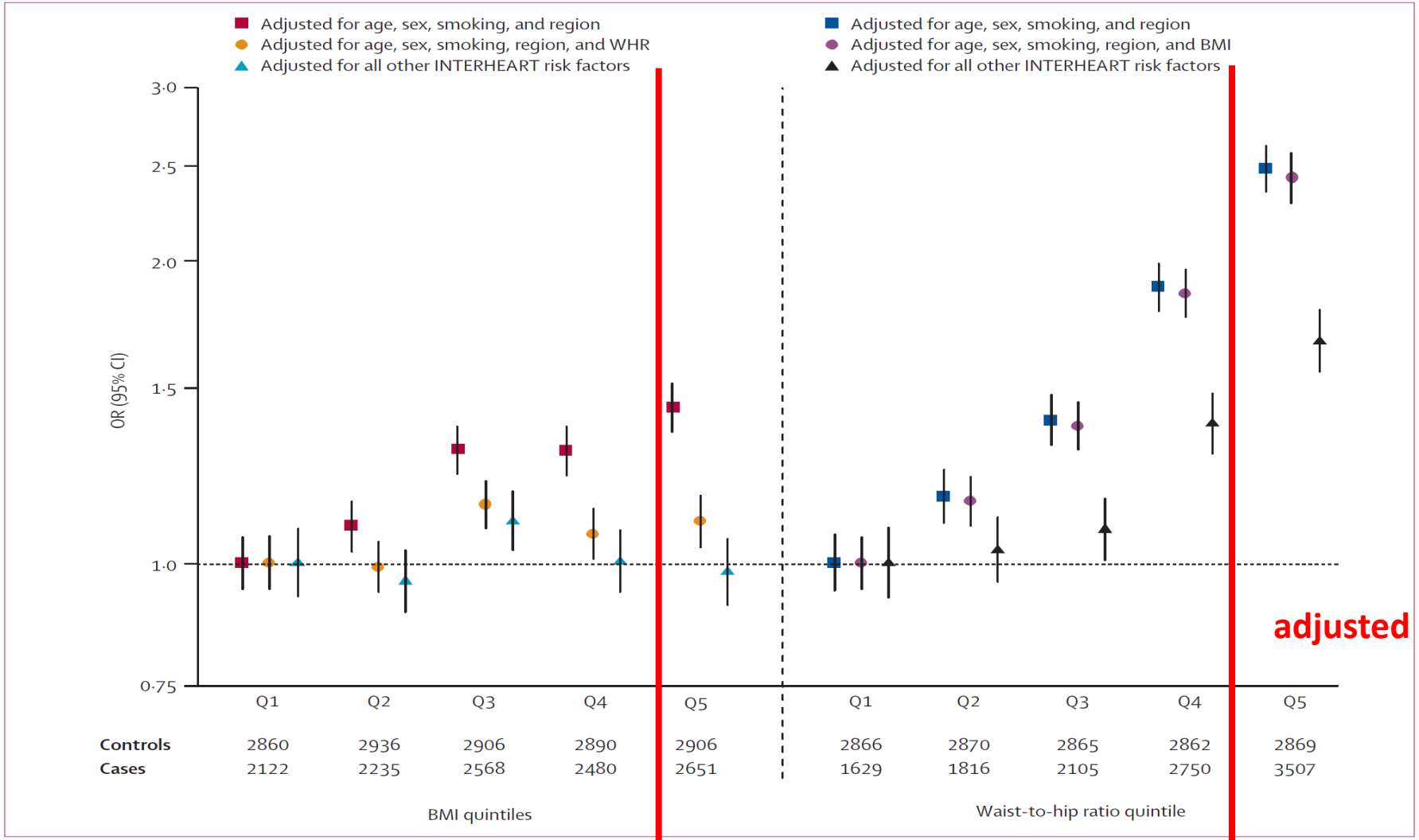


Figure 3: Association of BMI and waist-to-hip ratio with myocardial infarction risk

adjusted OR 1·77; 1·59–1·97

Lancet 2005; 366: 1640–49

>28 BMI

>98cm 28 waist

Obesity and Fatal CAD

Table 2 Association of BMI category with CHD events

BMI (kg/m^2)	18.5–22.4 N=721 HR (95% CI)	22.5–24.9 N=1804 HR (95% CI)	25.0–27.4 N=1938 referent	27.5–29.9 N=1038 HR (95% CI)	30.0–39.9 N=581 HR (95% CI)
CHD events					
Events, n (%)	**136 (18.9)**	**351 (19.5)**	**381 (19.7)**	**232 (22.4)**	**141 (24.3)**
Model 1	0.97 (0.79 to 1.18)	1.00 (0.87 to 1.15)	1.0	1.18 (1.00 to 1.39)	1.29 (1.07 to 1.57)
Model 2	1.06 (0.87 to 1.30)	1.04 (0.89 to 1.20)	1.0	1.08 (0.92 to 1.27)	1.14 (0.94 to 1.39)
Non-fatal CHD					
Events, n (%)	**110 (15.3)**	**293 (16.2)**	**324 (16.7)**	**188 (18.1)**	**112 (19.3)**
Model 1	0.93 (0.75 to 1.15)	0.98 (0.84 to 1.15)	1.0	1.13 (0.94 to 1.35)	1.21 (0.97 to 1.50)
Model 2	1.04 (0.84 to 1.30)	1.03 (0.88 to 1.21)	1.0	1.03 (0.86 to 1.23)	1.06 (0.86 to 1.32)
Fatal CHD					
Events, n (%)	**26 (3.6)**	**58 (3.2)**	**57 (2.9)**	**44 (4.2)**	**29 (5.0)**
Model 1	1.20 (0.76 to 1.91)	1.10 (0.77 to 1.59)	1.0	1.47 (0.99 to 2.18)	1.75 (1.12 to 2.74)
Model 2	1.18 (0.74 to 1.90)	1.08 (0.74 to 1.56)	1.0	1.37 (0.92 to 2.04)	1.60 (1.02 to 2.53)

Model 1: adjusted for randomised treatment and age.
Model 2: adjusted for smoking, BP, hypertension, cholesterol (HDL and LDL), triglycerides, nitrates use, history of angina, social deprivation score (DEPCAT), various drugs (aspirin, ACE inhibitors, β blockers, calcium channel blockers, diuretics, other).
BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; DEPCAT, deprivation category; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

W0SCOPS: 6082 men (mean age 55 years) with hypercholesterolaemia, but no history of diabetes or CVD, 14.7 years of follow-up.

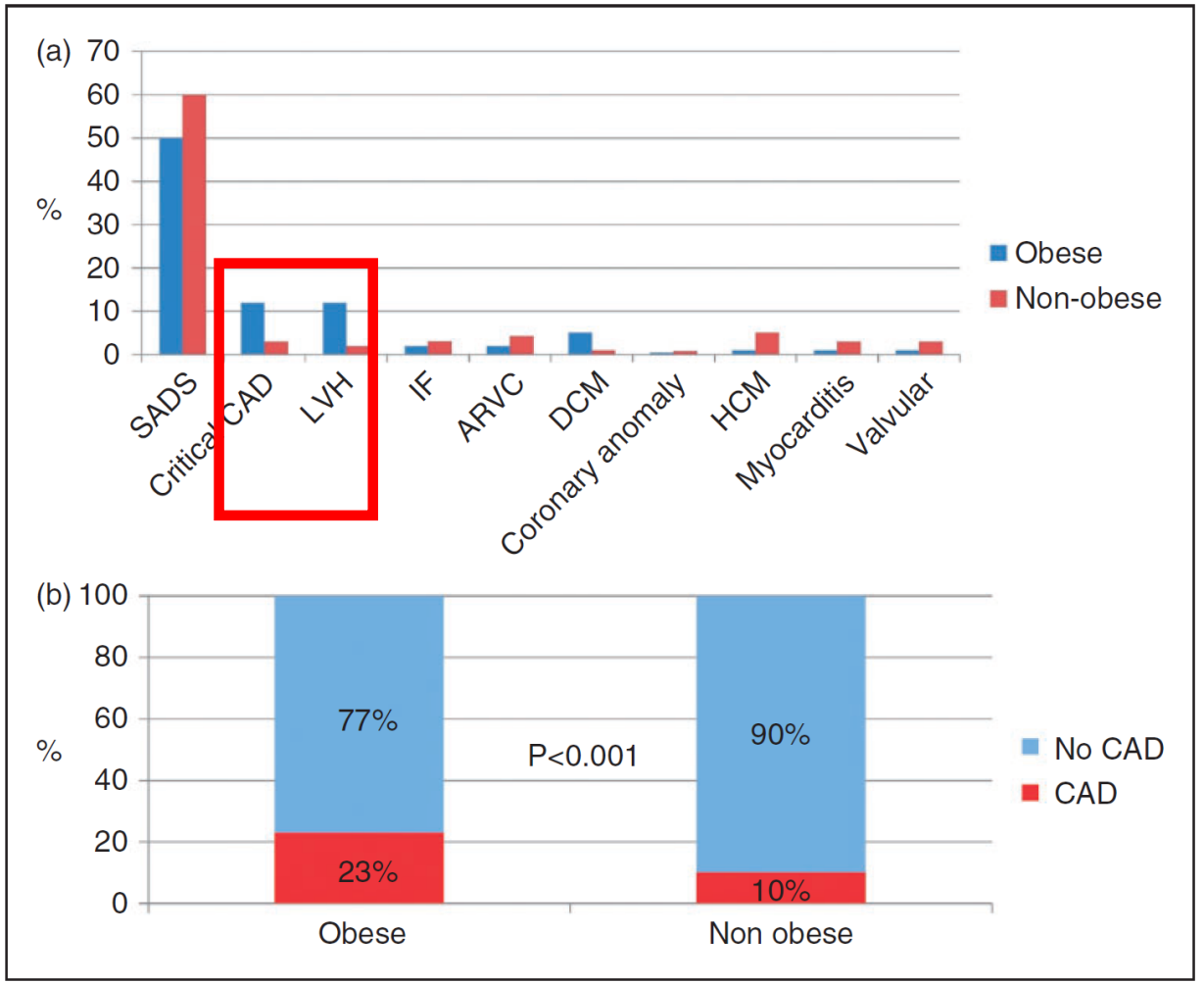
Heart 2011;97:564e568. doi:10.1136/hrt.2010.211201

Obesity and Sudden Cardiac Death

Table 2. Demographic and clinical data of obese and non-obese SCD patients.

	Obese ($n=212$)	Non-obese ($n=821$)	P value
Age (years)	23 ± 8	27 ± 6	<0.001
Men, *n* (%)	137 (65)	575 (70)	0.19
Caucasian, *n* (%)	194 (91)	749 (91)	0.89
BSA (m^2)	2.3 ± 0.3	1.8 ± 0.4	<0.001
Family history of SD,[a] *n* (%)	21 (9)	70 (8)	0.74
Heart weight (g)	450 ± 141	361 ± 129	<0.001
LV fibrosis, *n* (%)	42 (20)	131 (16)	0.19

BSA: body surface area; LV: left ventricular; SD: sudden death.
[a]Sudden death in a family member of less than 50 years of age.



European Journal of Preventive Cardiology 2018

3684 consecutive cases, <35y

Obesity and Stroke

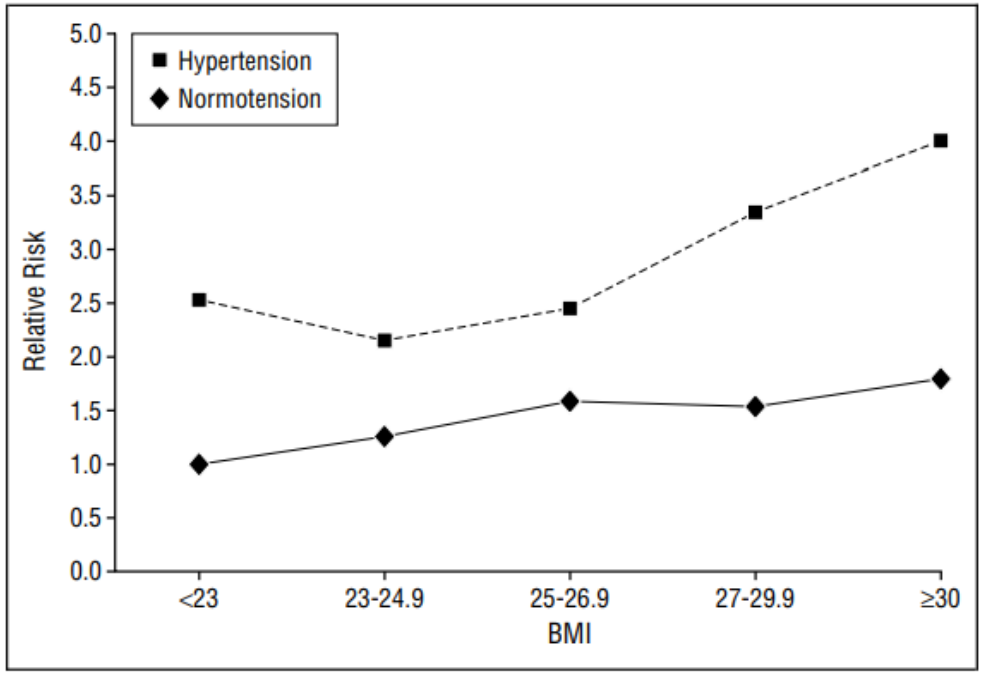


Figure 1. Age-adjusted relative risk for ischemic stroke according to body mass index (BMI) categories (calculated as self-reported weight in kilograms divided by the square of the height in meters), and hypertension status. Reference (relative risk=1.0): normotensive with a BMI less than 23 (*P* for trend: hypertension, *P*=.02; normotension, *P*=.001).

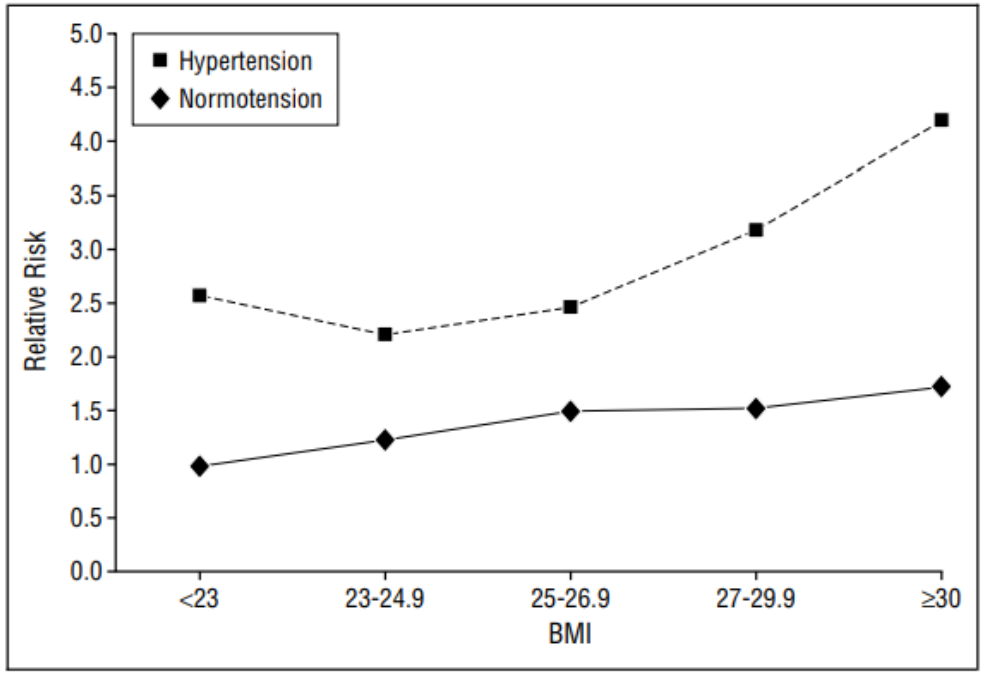
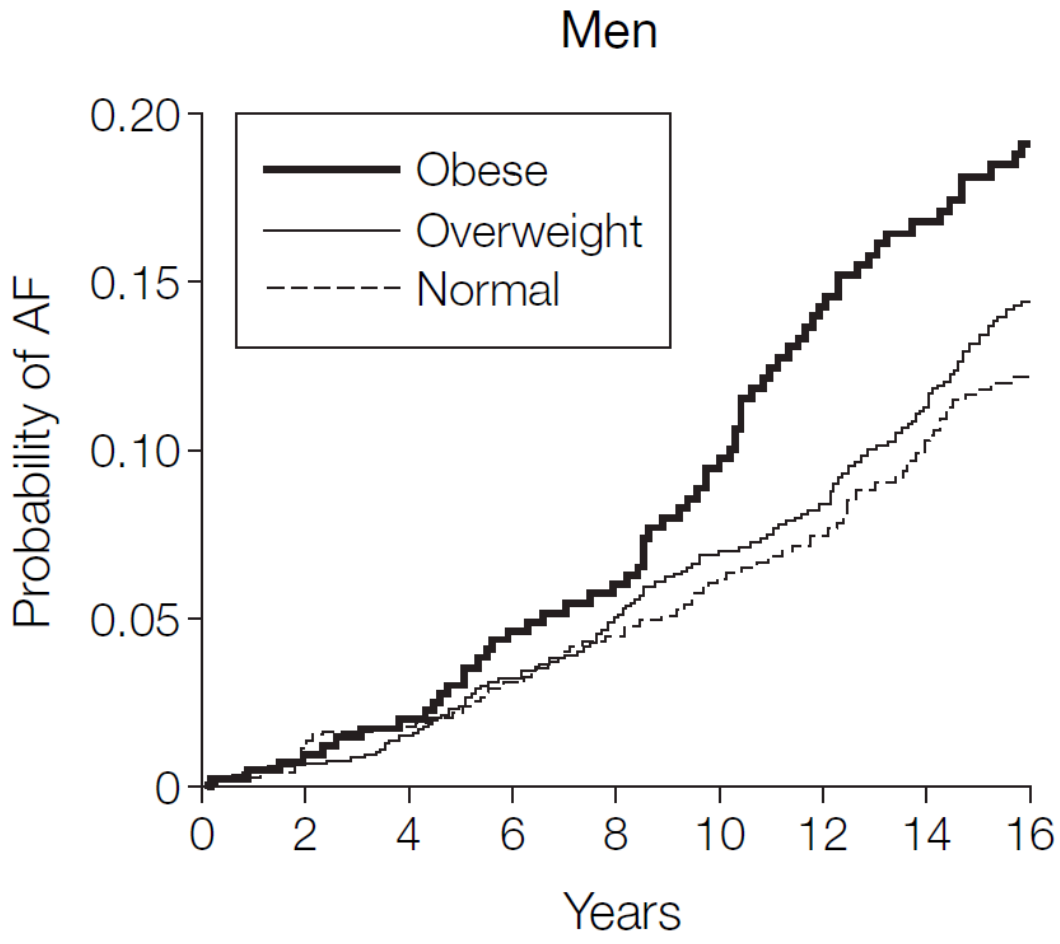


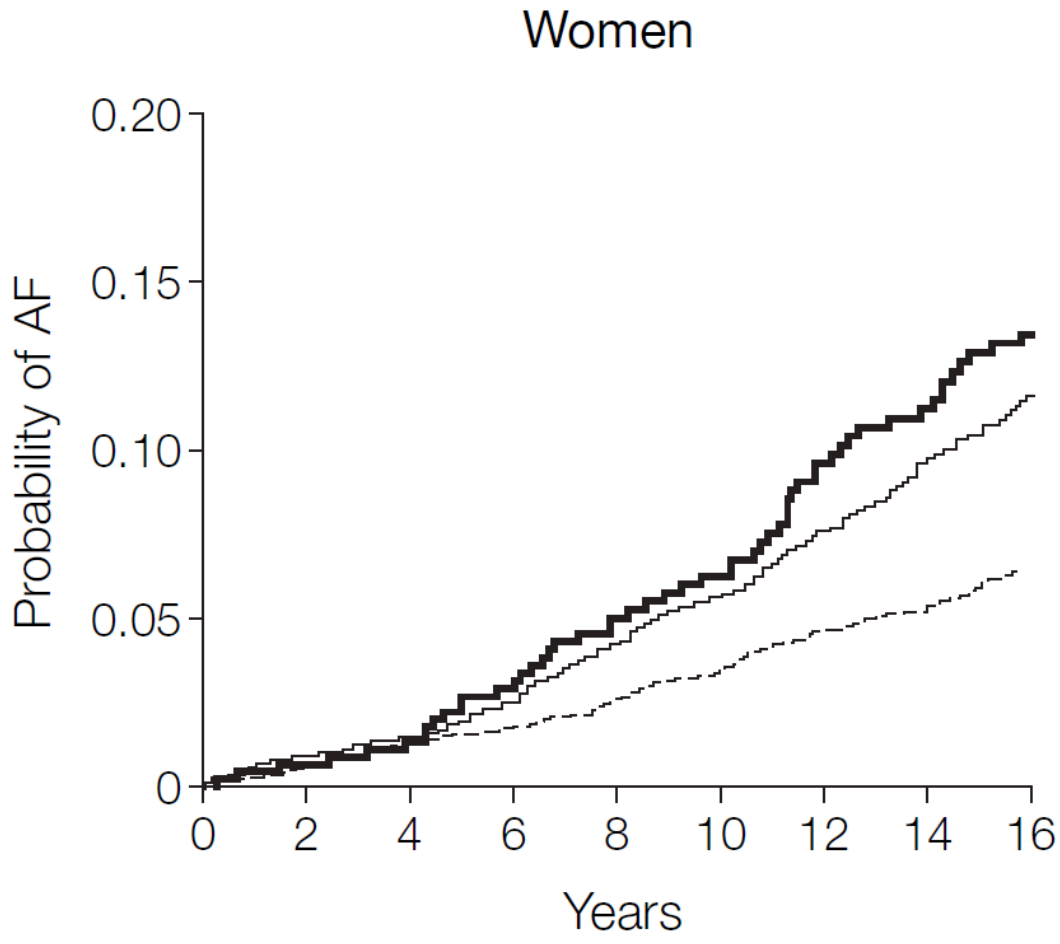
Figure 2. Age-adjusted relative risk for hemorrhagic stroke according to body mass index (BMI) (for calculation of BMI, see legend to Figure 1) categories and hypertension status. Reference (relative risk=1.0): normotensive with a BMI less than 23 (*P* for trend: hypertension, *P*=.34; normotension, *P*=.20).

Arch Intern Med. 2002;162(22):2557-2562.

Obesity and Atrial Fibrillation

4% increase in AF risk per 1-unit increase in BMI in men (95% CI, 1%-7%; *P*=.02) and in women (95% CI, 1%-7%; *P*=.009).



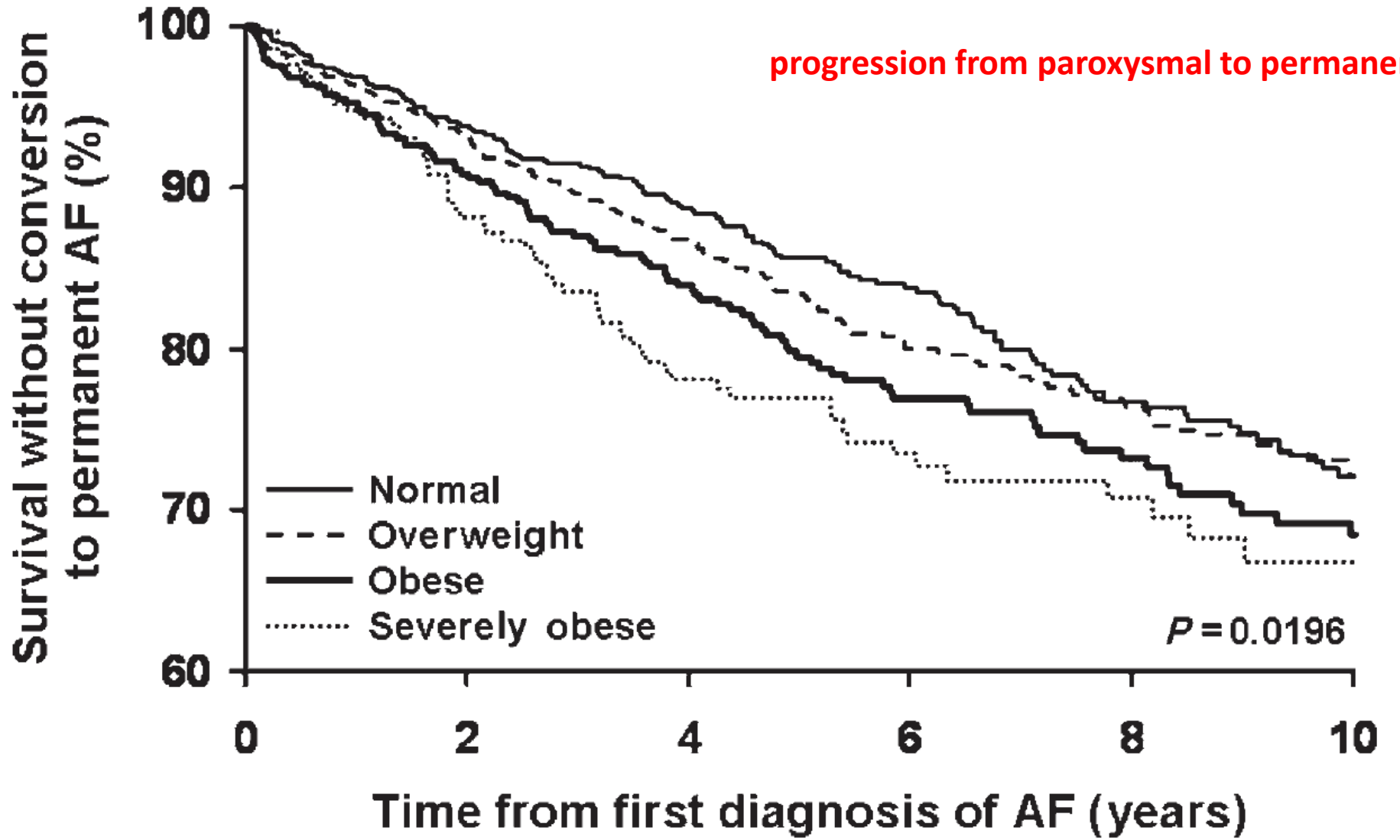


No. at Risk

JAMA. 2004;292:2471-2477

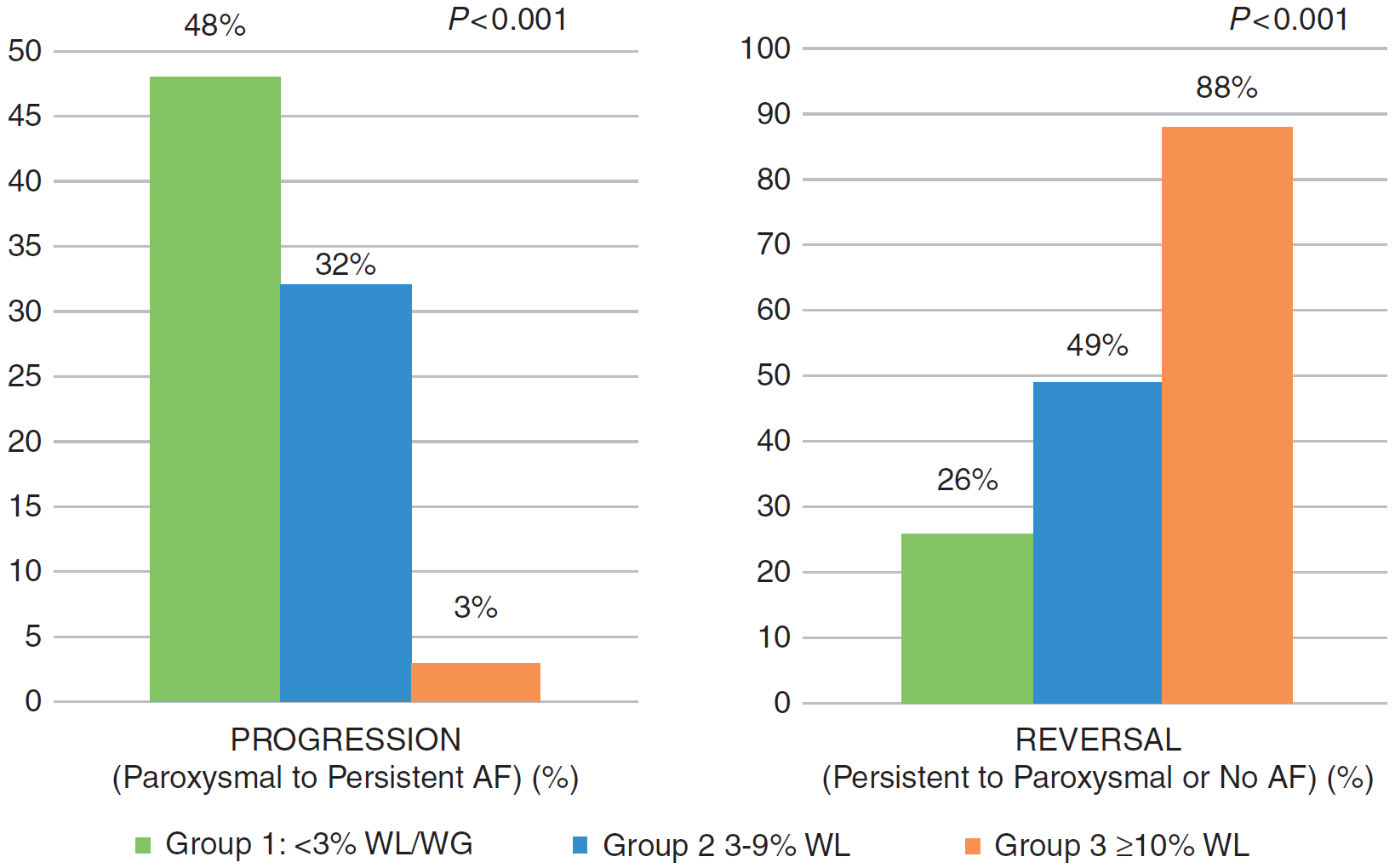
cohort in Framingham

Obesity and Atrial Fibrillation



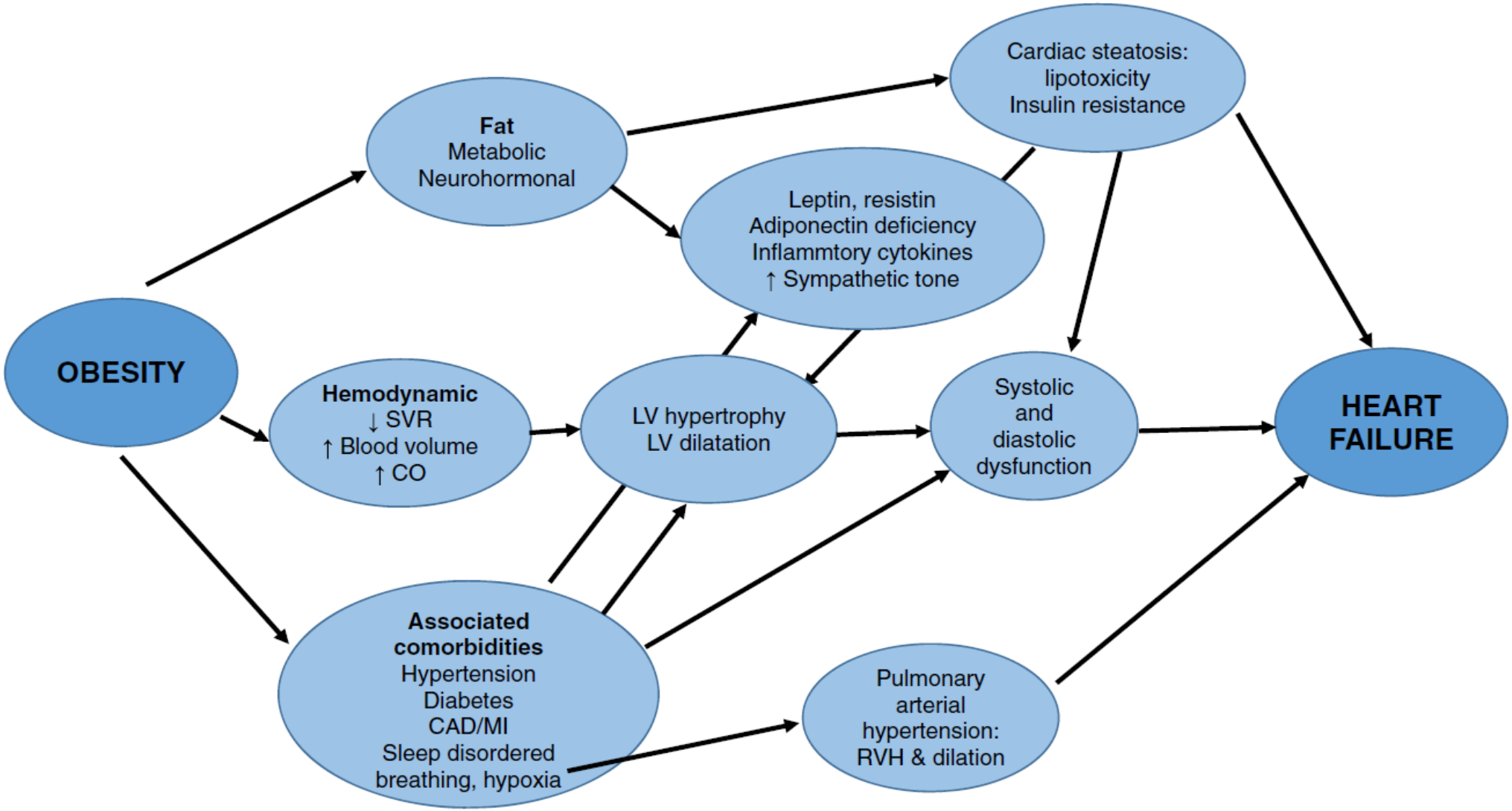
European Heart Journal (2008) 29, 2227–2233

Obesity and Atrial Fibrillation



Europace (2018) 20, 1929–1935

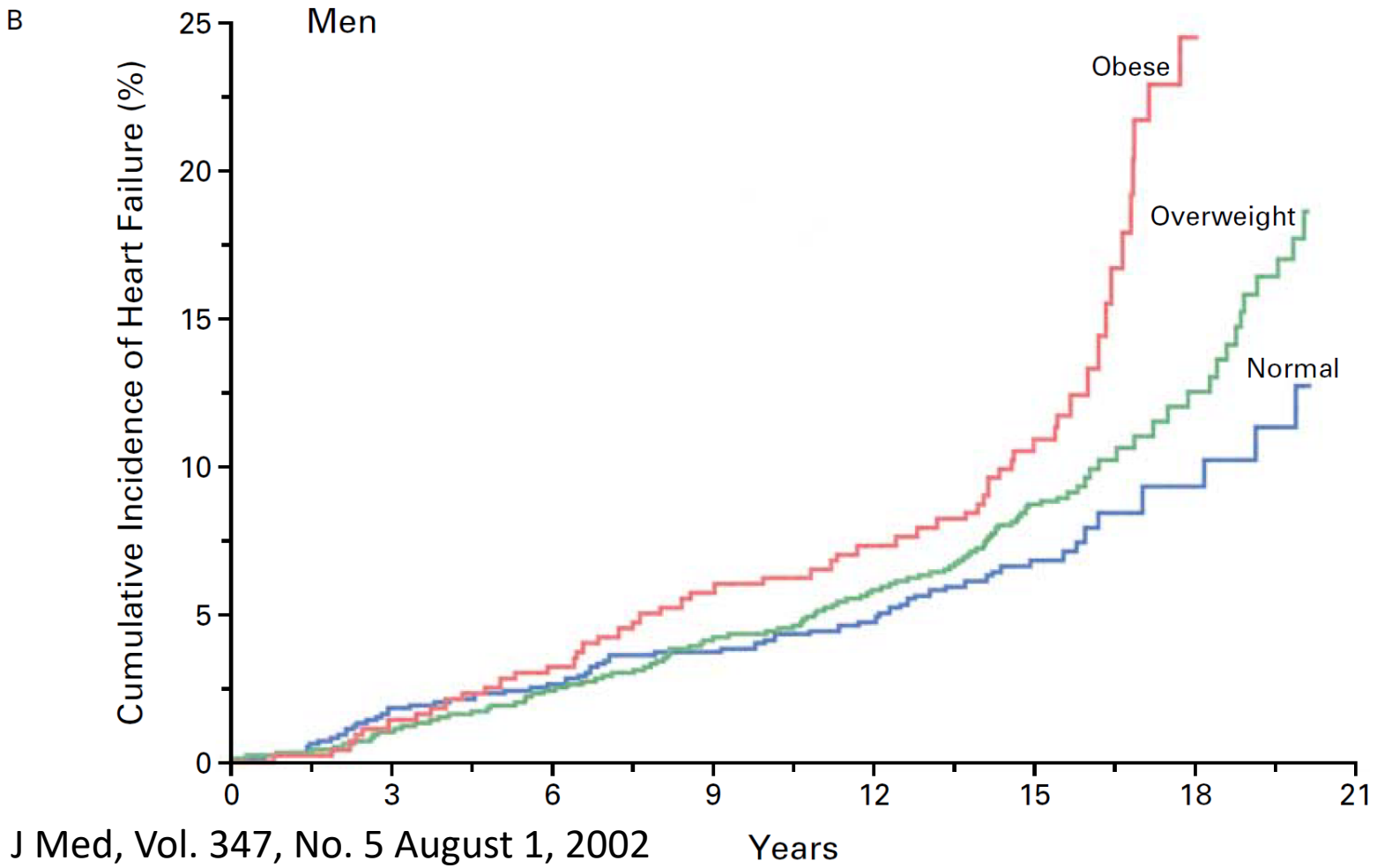
Obesity and Heart Failure



Curr Atheroscler Rep (2016) 18:21

Obesity and Heart Failure

women, the hazard ratio was 2.12 (95 percent confidence interval, 1.51 to 2.97);
men, the hazard ratio was 1.90 (95 percent confidence interval, 1.30 to 2.79).

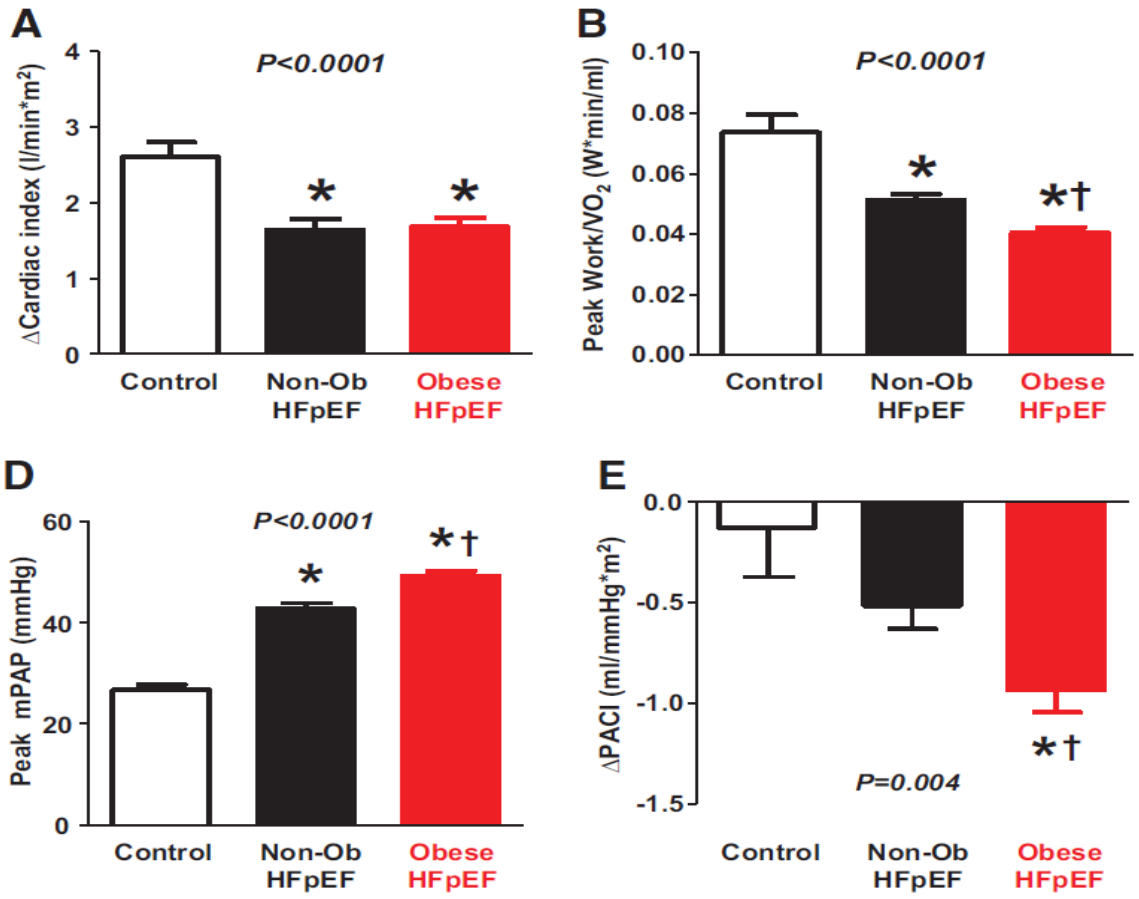


Framingham Heart Study

N Engl J Med, Vol. 347, No. 5 August 1, 2002

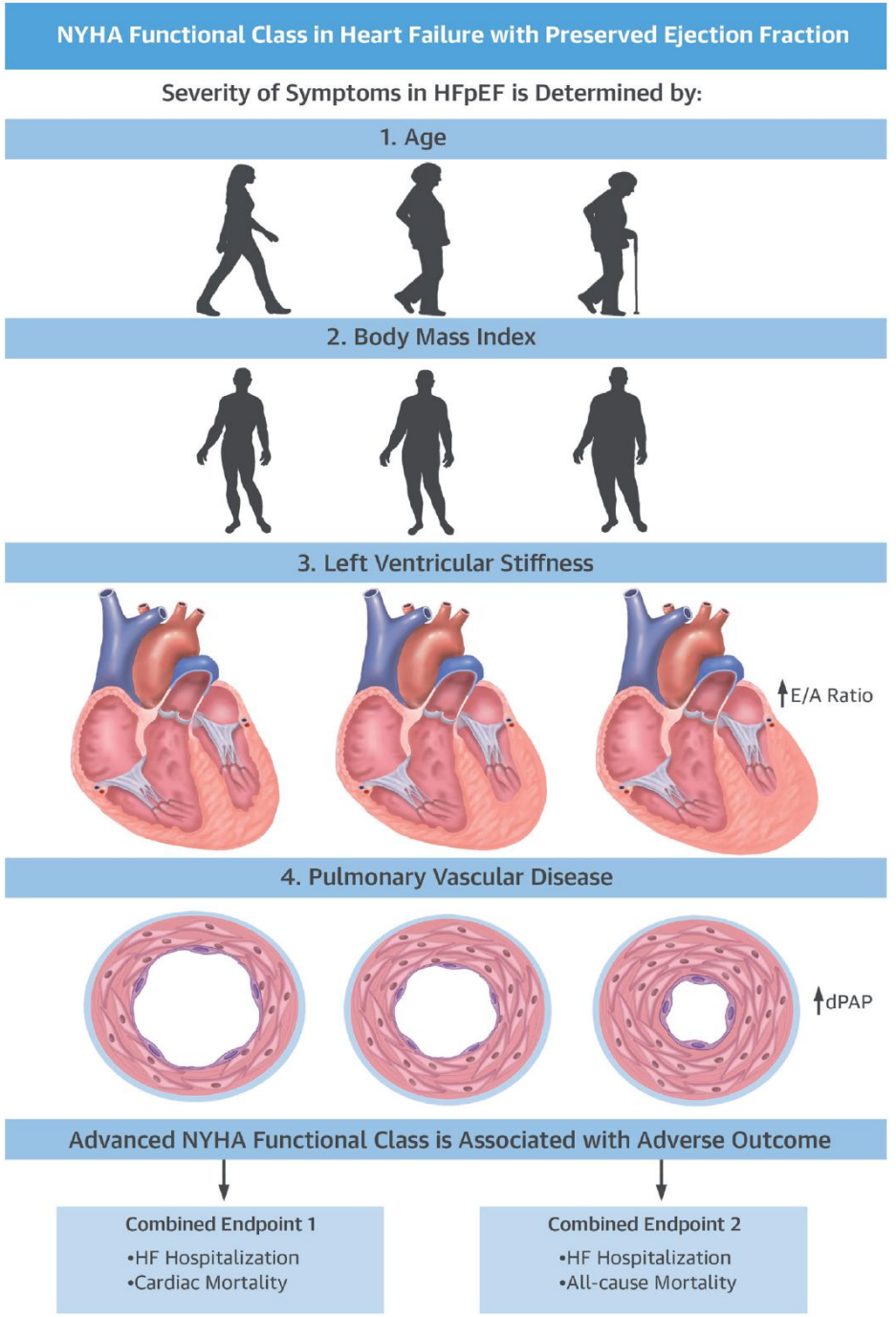
HFpEF Obesity Phenotype

	Control Subjects (n=71)	Patients With Nonobese HFpEF (n=96)	Patients With Obese HFpEF (n=99)	*P* Value
LV structure and function				
LV diastolic dimension, mm	47±5	47±5	49±5*†	0.0005
LV end-diastolic volume, mL	104±24	103±26	116±26*†	0.0006
LV end-diastolic volume index, mL/m^2	57±12	56±13	53±11	0.1
LV mass, g	151±38	166±49	205±54*†	<0.0001
LV mass index, g/m$^{2.7}$	37±9	41±12	51±13*†	<0.0001
LV mass/LVEDV, g/mL	1.5±0.3	1.6±0.4*	1.8±0.3*†	<0.0001
LVEF, %	63±4	63±6	63±6	1.0
Mitral E wave, cm/s	74±24	91±34*	89±30*	0.001
Mitral annular e', cm/s	8±2	7±2*	7±2	0.004
E/e' ratio	9 (7–11)	13 (10–17)*	12 (9–15)*	<0.0001
Longitudinal strain, %	–17±3	–15±4*	–15±4*	0.006
RV structure and function				
RV basal dimension, mm	30±6	31±6	34±7*†	0.0005
RV mid cavity dimension, mm	23±5	24±5	27±6*†	0.0003
RV longitudinal dimension, mm	61±7	61±7	66±7*†	<0.0001
RV fractional area change, %	52±7	49±9	48±9*	0.02



Circulation. 2017;136:6–19

The Elephant in the Room



Dalos, D. et al. J Am Coll Cardiol. 2016;68(2):189-99.

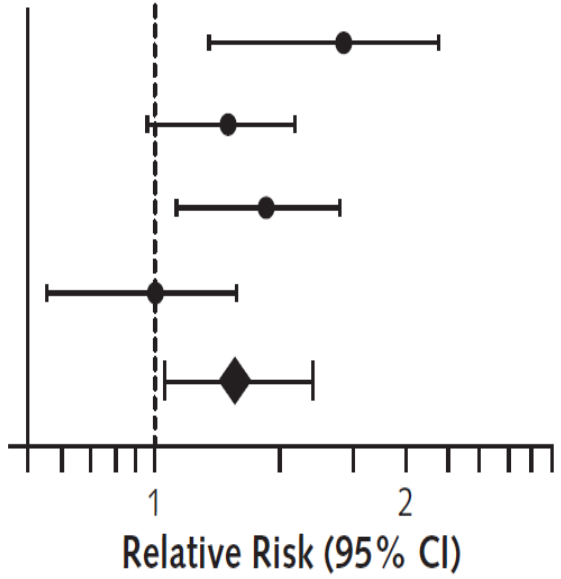
BNP "Paradox"

	Cut-point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)/Reference
BNP	100 pg/mL	90	76	79	89	76 [4]
All patients						
BNP						[6]
BMI < 25	170 pg/mL	90	70			
≥ 25 BMI < 35	110 pg/mL	90	70			
BMI ≥ 35	54 pg/mL	90	70			
Nt-proBNP						
Confirmatory (rule in) cut-points						
	450 pg/mL	97	93	76	99	94 [64]
< 50 years	900 pg/mL	90	82	83	88	85
50–75 years	1800	85	73	92	55	83
> 75 years	pg/mL					
		90	84	88	66	85
Rule in, overall						
Exclusionary (rule out) cut-point	300 pg/mL	99	60	77	98	83 [64]
All patients						

Int J Cardiol. 2014 October 20; 176(3): 611–617

Metabolic Healthy Obesity (MHO)

D.



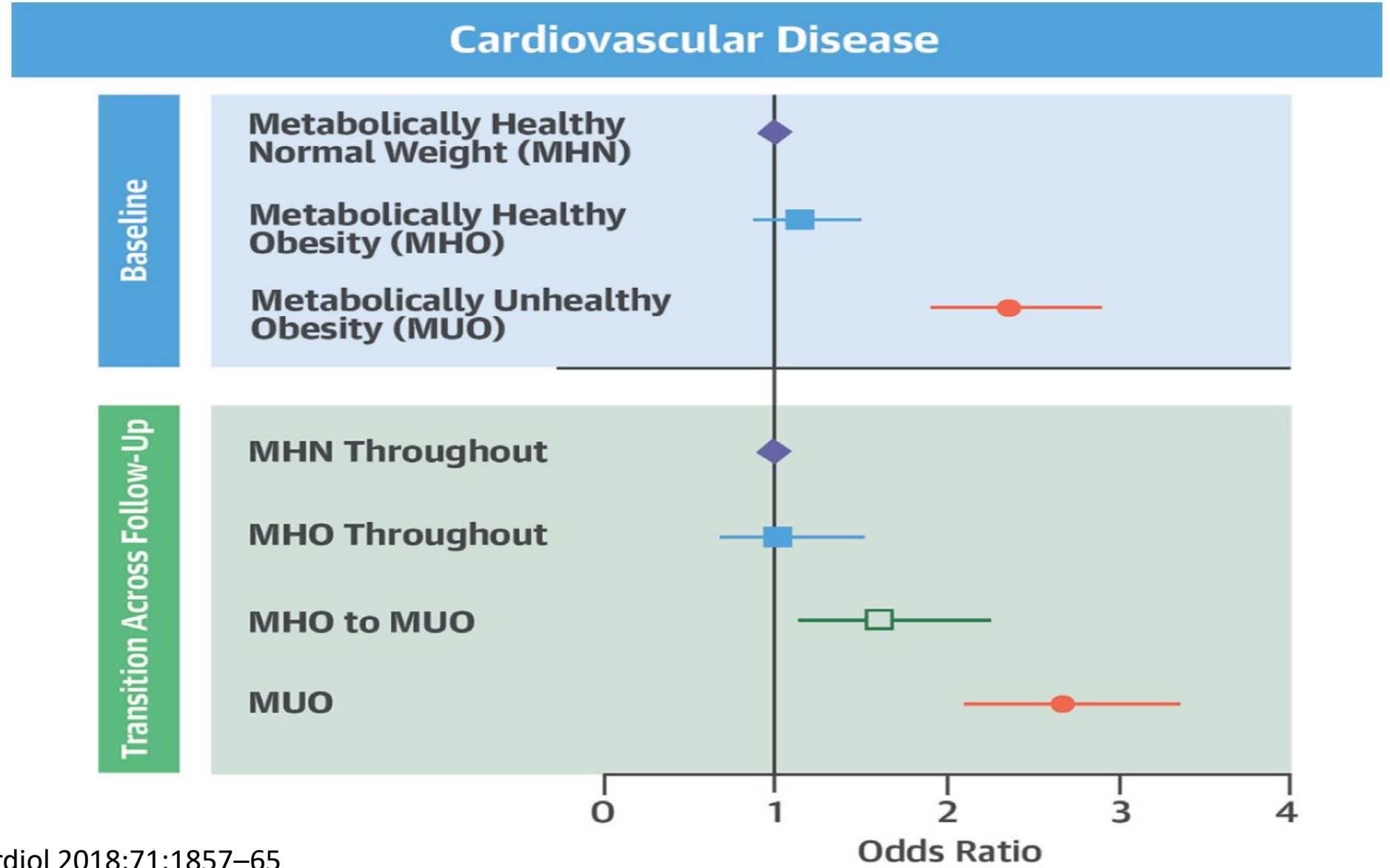
Study, Year (Reference)	Relative Risk (95% CI)	Weight, %	Metabolically Healthy Obese Events/Participants, *n/N*	Metabolically Healthy Normal Weight Events/Participants, *n/N*
Meigs et al, 2006 (8)	1.68 (1.17–2.19)	11.3	19/236	47/981
Song et al, 2007 (48)	1.22 (0.98–1.47)	32.23	77/2925	278/12 943
Arnlöv et al, 2010 (9)	1.37 (1.06–1.66)	25.49	18/30	391/891
Ogorodnikova et al, 2012 (53)	1.00 (0.74–1.26)	30.98	70/1167	242/4036
Overall	1.24 (1.02–1.55)	100.00	184/4358	958/18 851

Heterogeneity: $I^2 = 33.6\%$; $P = 0.08$

Ann Intern Med. 2013;159:758-769

Metabolically healthy obese individuals ([RR], 1.24; 95% CI, 1.02 to 1.55) compared with metabolically healthy normal-weight individuals when only studies with 10 or more years of follow-up were considered.

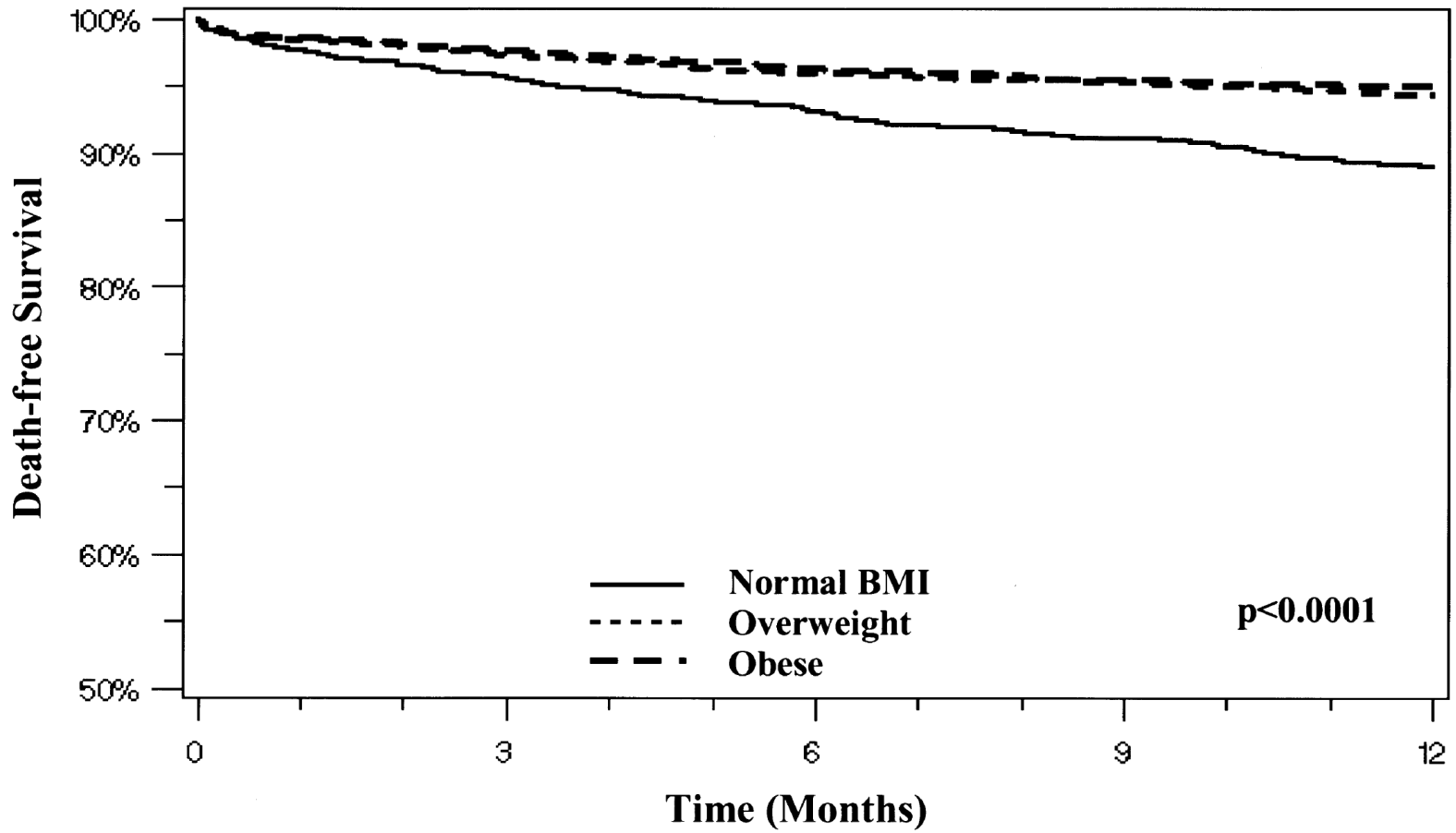
Metabolic Healthy Obesity (MHO)



J Am Coll Cardiol 2018;71:1857–65

MESA (Multi-Ethnic Study of Atherosclerosis)

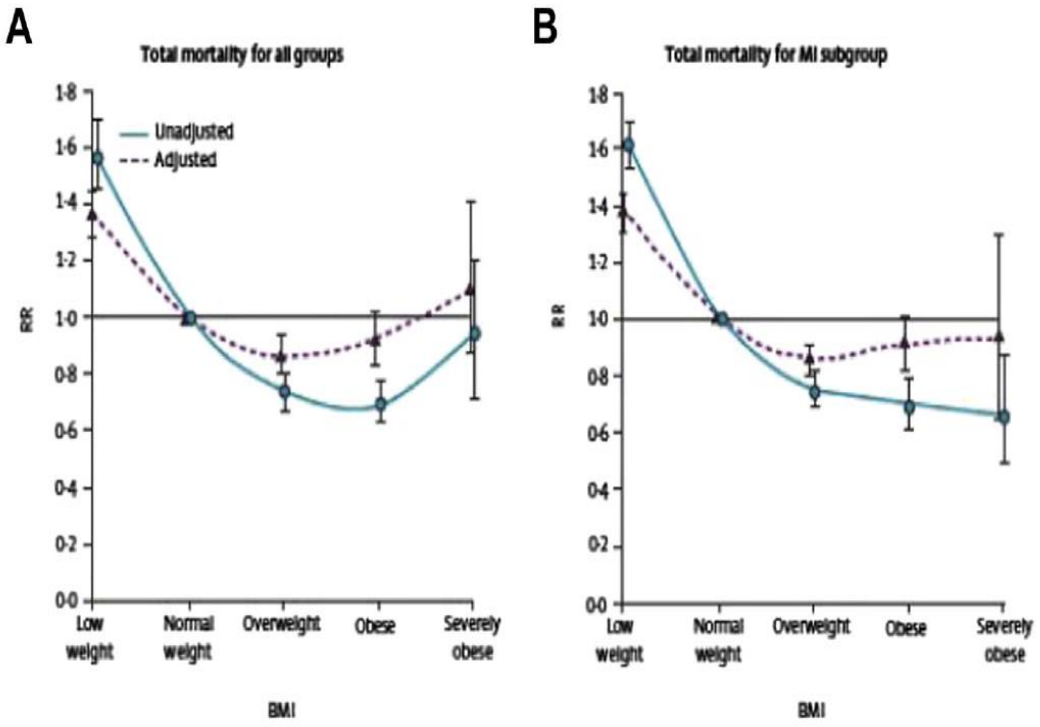
The Impact of Obesity on the Short-Term and Long-Term Outcomes After Percutaneous Coronary Intervention: The Obesity Paradox?



J Am Coll Cardiol 2002;39:578–84

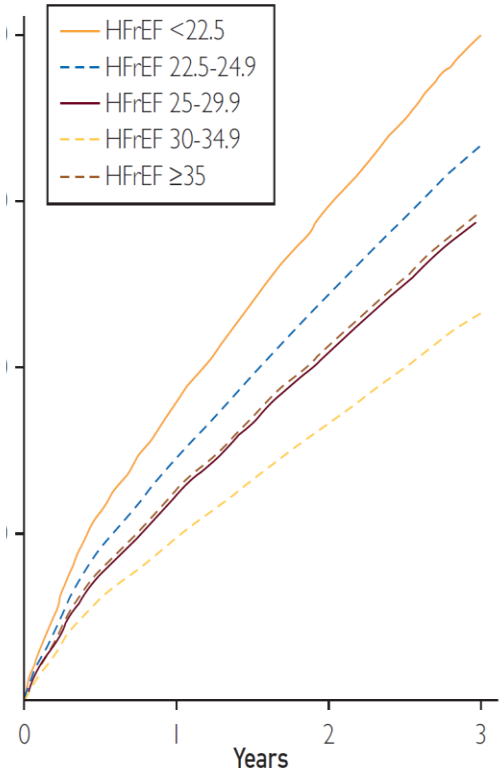
Obesity Paradox

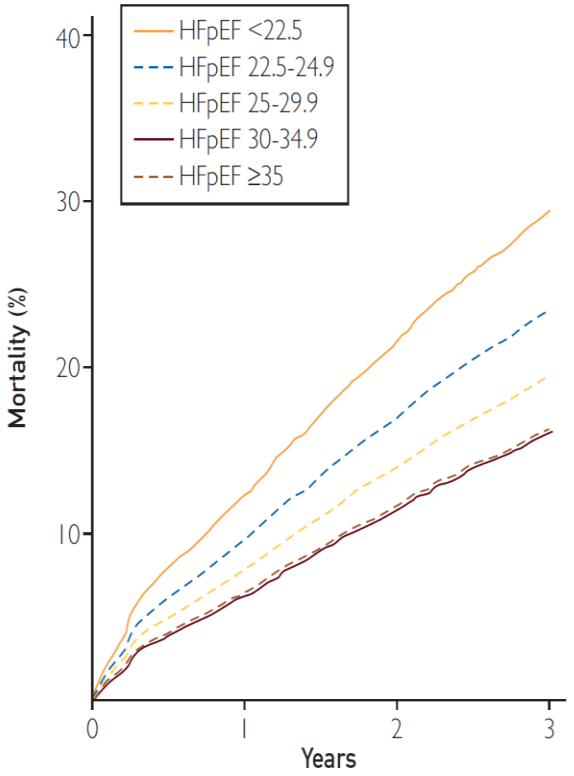
CAD



The Lancet 2006, 368 19-25

HEART FAILURE





Int J Obes (Lond). 2014;38(8):1110-1114.

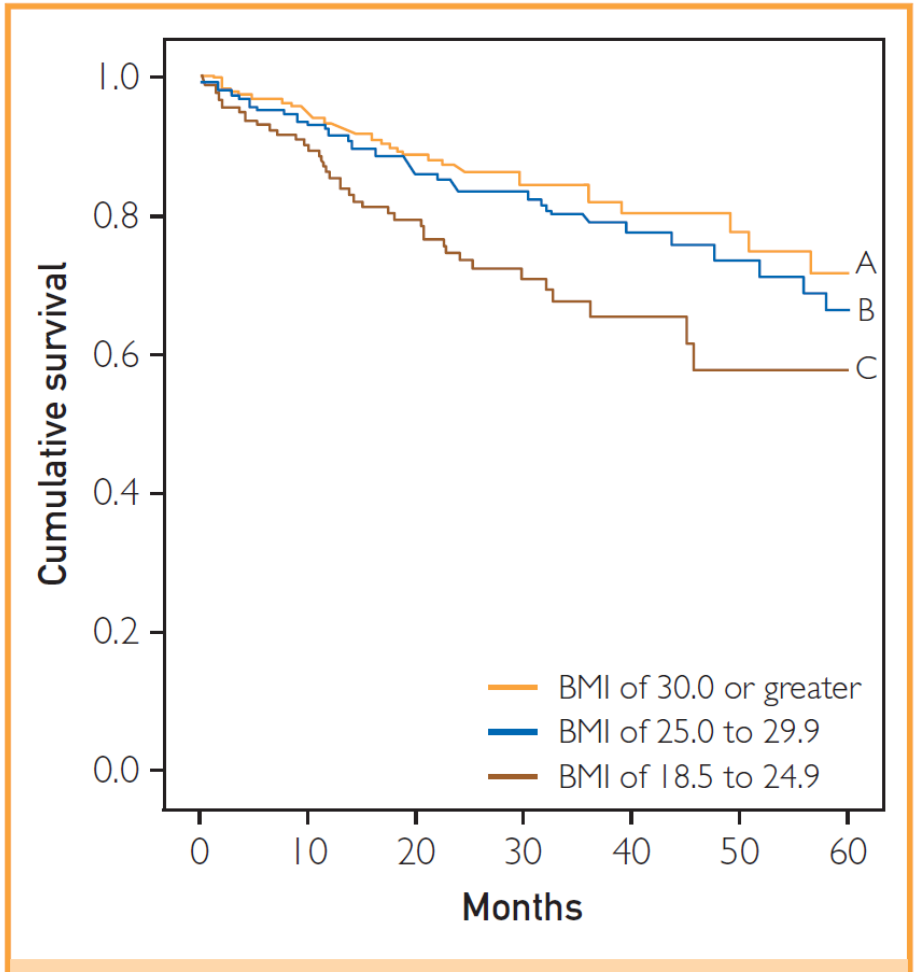
Obesity Paradox

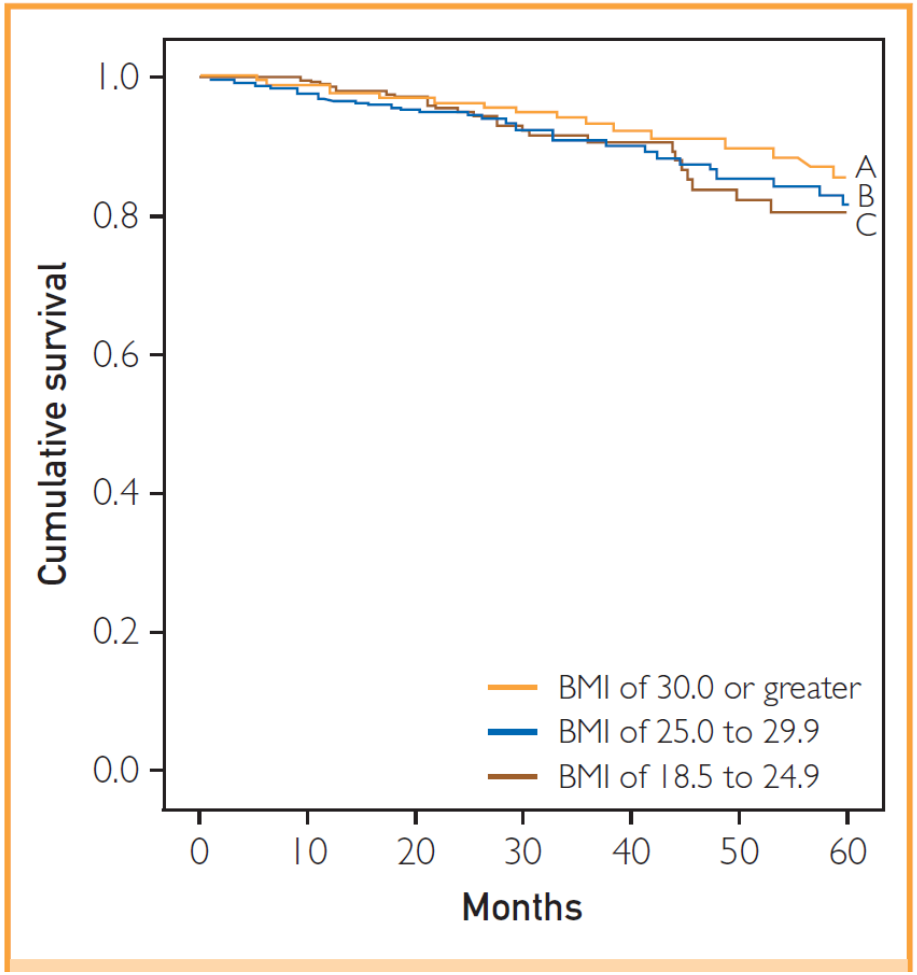
- Ανάστροφη αιτιολογική σχέση. (Reverse causality)
  - Η σχέση της παχυσαρκίας με τον κίνδυνο εμφάνισης της νόσου μπορεί να αλλάξει εφόσον υπάρχει απώλεια βάρους πριν την είσοδο στη μελέτη για να αποφευχθεί ο κίνδυνος
- Σφάλμα επίδρασης συγχυτικού παράγοντα. (Collider stratification bias)
  - Κάπνισμα, Καχεξία
- Συστηματικό σφάλμα επιλογής. (Selection bias)
  - Ενώ οι παχύσαρκοι έχουν ως αιτία εμφάνισης την παχυσαρκία, οι μη παχύσαρκοι έχουν άλλα αίτια που κάνουν την πρόγνωση δυσμενέστερη
- Συστηματικό σφάλμα μέτρησης. (Measurement bias)
  - BMI ως μέτρο της παχυσαρκίας

Obesity Paradox

- Καλύτερη μεταβολική εφεδρεία, μικρότερη καχεξία
- Μικρότερη ηλικία
- Μεγαλύτερη μυϊκή μάζα
- Μεγαλύτερη απάντηση στη θεραπεία καταστολής του άξονα RAAS
- Ανοχή μεγαλύτερων δόσεων αντιυπερτασικών φαρμάκων
- Αδρανοποίηση ενδοτοξινών λόγω των κυκλοφορούντων λιποπρωτεινών

Cardiorespiratory Fitness -Obesity Paradox-Heart Failure





Mayo Clin Proc. n March 2013;88(3):251-258

Αφροδίτη του Willendorf

Αφροδίτη της Μήλου

Καθημερινά εργαλεία