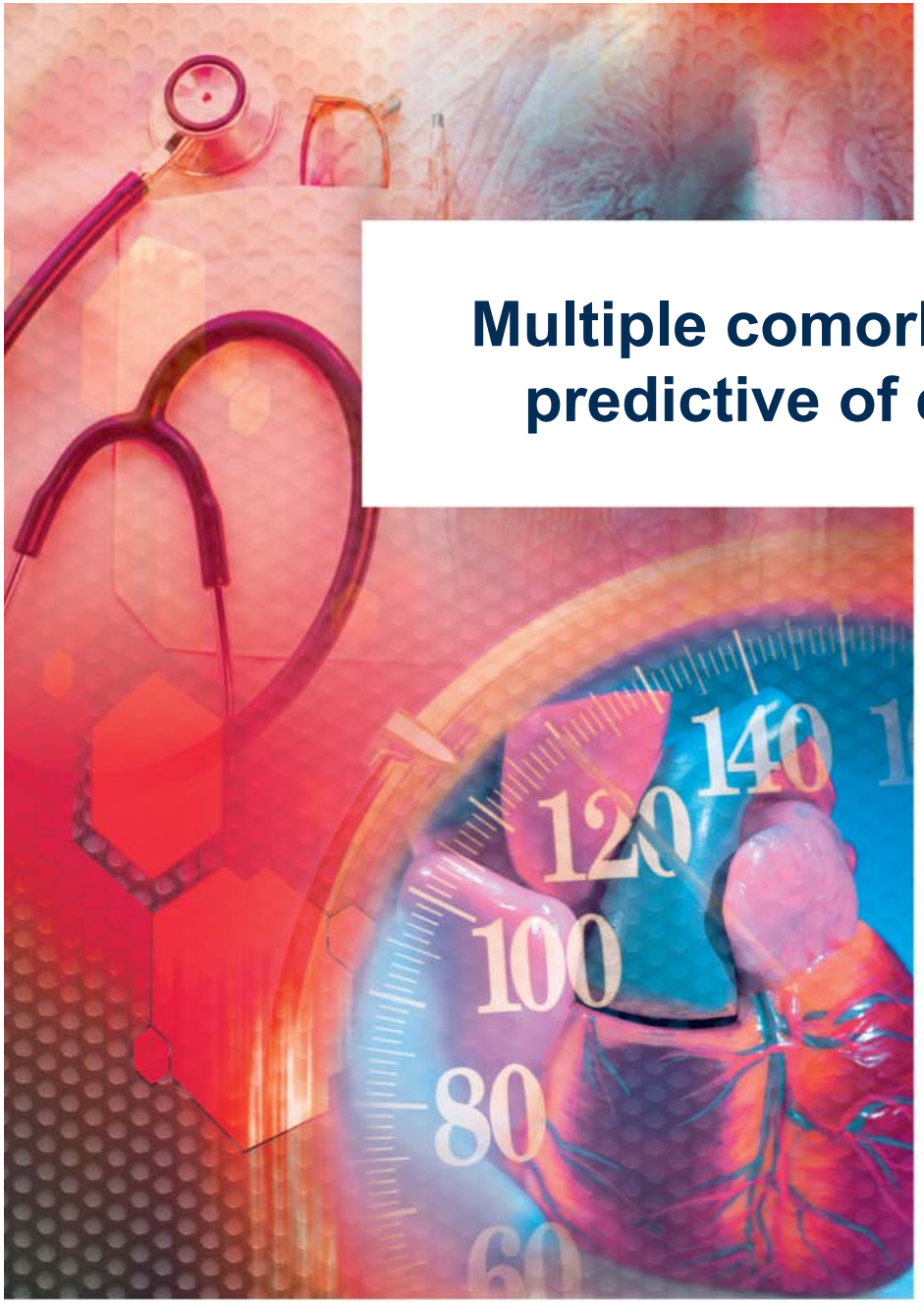


Multiple comorbidities: additive and predictive of cardiovascular risk

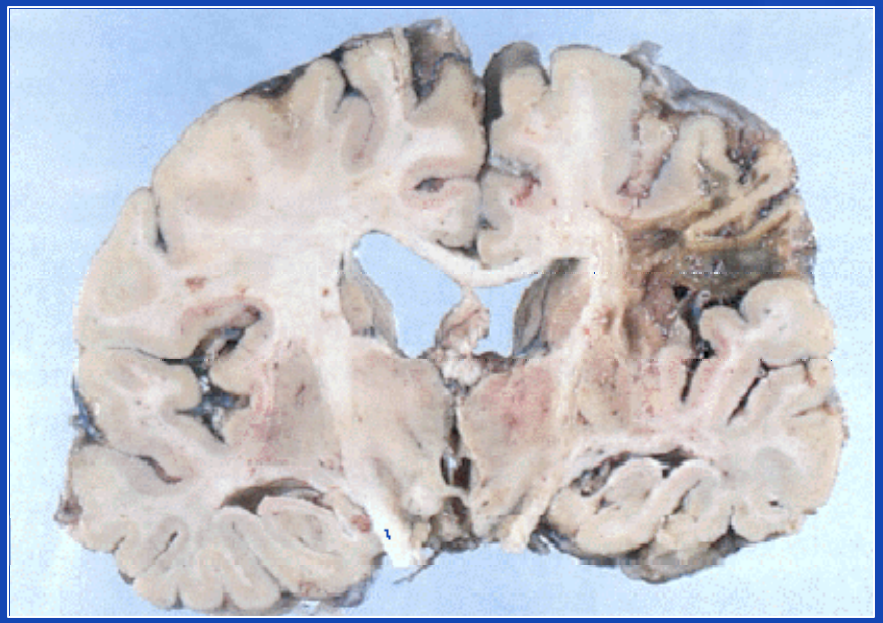
Peter M. Nilsson

Lund University
University Hospital
Malmö, Sweden

Clinical outcomes: major complications of CVD

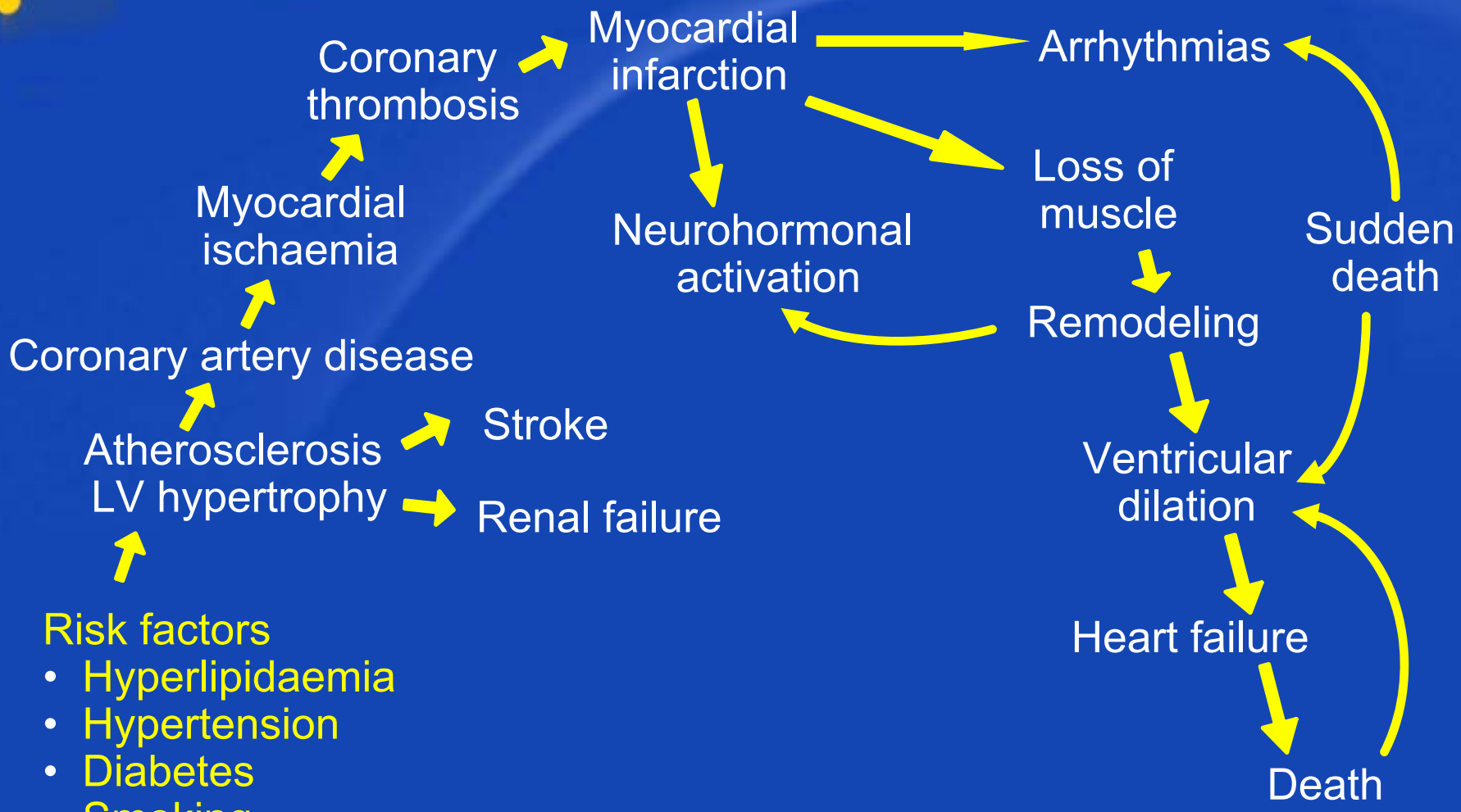
Heart Attack/ACS

Stroke/TIA



ACS=acute coronary syndrome; CVD=cardiovascular disease; TIA=transient ischaemic attack

Chain of events leading to cardiovascular mortality

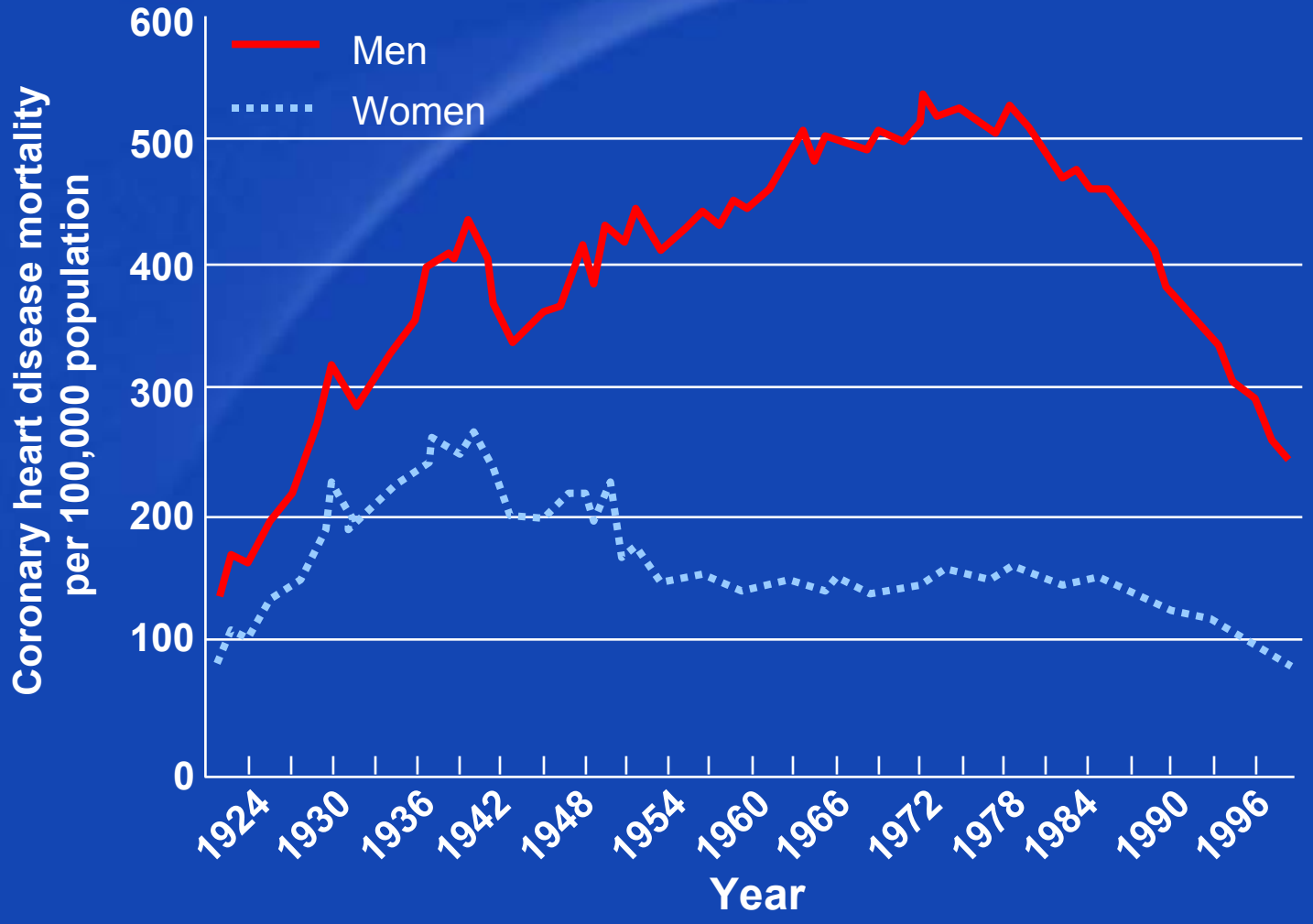


Risk factors
- Hyperlipidaemia
- Hypertension
- Diabetes
- Smoking
- Psychosocial stress

Dzau, Braunwald. *Am Heart J.* 1991

Genetic influences on CVD risk and Type 2 diabetes

Secular trends in CVD in the UK



Secular trends in age-standardised mortality per 100,000 population from coronary heart disease for men and women, 1921-1998, England and Wales
Lawlor et al. *BMJ*. 2001

The challenge: the clustering of related risk factors

- Hypertension
- Obesity
- Hyperinsulinaemia
- Type 2 diabetes
- Hypertriglyceridaemia
- Small, dense LDL
- Low HDL

Atherosclerosis

Type 2 diabetes

HDL=high-density lipoprotein; LDL=low-density lipoprotein

Deedwania. *Am J Med.* 1998

Es kil Kylin

(1886-1975)

Kylin E. Studien über das Hypertonie-Hyperurikemie-syndrom. Zentralblatt für Innere Medizin 1923;7:105

Metabolic syndrome: does it exist? arguments – PRO

- **Historical observations** of the syndrome; it has been around for a long time!
- **Logical clustering** of risk factors for the metabolic syndrome is based on evolutionary selection and brain reward systems
- **Risk prediction** of CVD is possible based on the metabolic syndrome
- **Treatment** of metabolic syndrome/insulin resistance and associated risk factors is beneficial

NCEP ATP III criteria for the metabolic syndrome

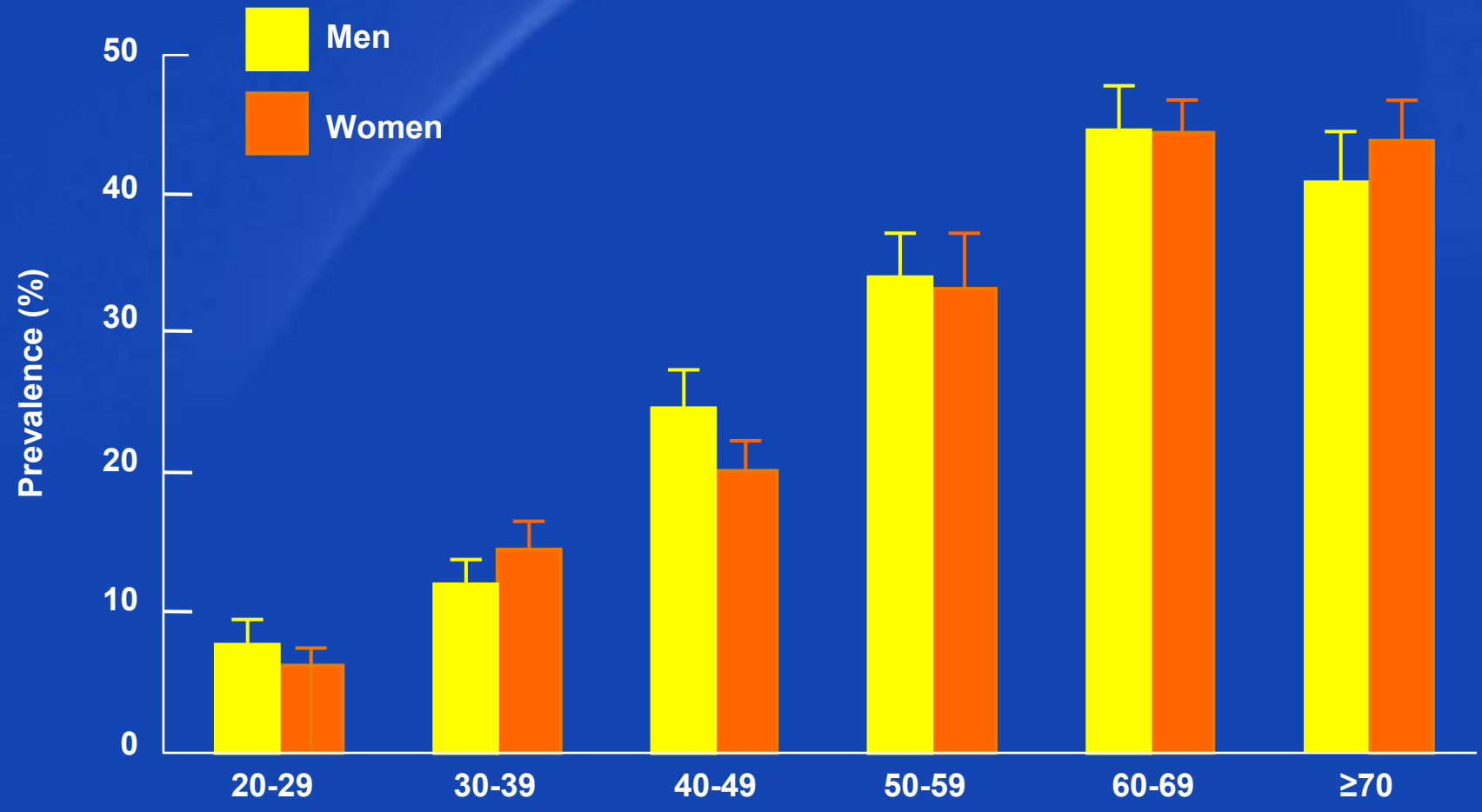
≥3 of the following:

- Fasting plasma glucose ≥6.1 mmol/l
- Abdominal obesity: waist circumference >88 cm (women) or >102 cm (men)
- Triglycerides ≥1.7 mmol/l
- HDL cholesterol <1.29 mmol/l (women) or <1.03 mmol/l (men)
- Blood pressure ≥130/≥85 mmHg

NCEP ATP III=National Cholesterol Education Program Adult Treatment Panel III
Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Available at: http://www.nhlbi.nih.gov/guidelines/cholesterol/

Age-specific prevalence of the metabolic syndrome among 8814 US adults

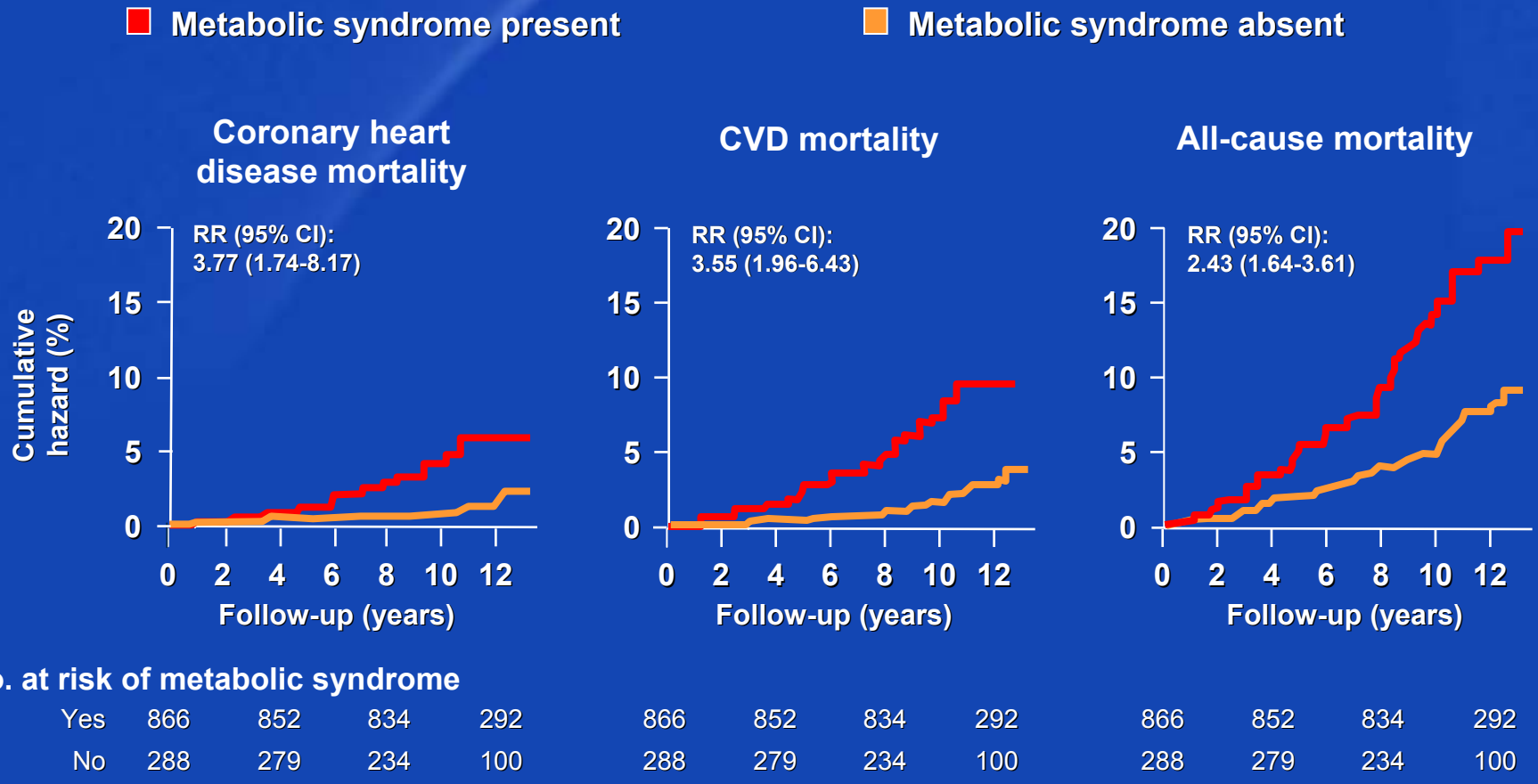
Third National Health and Nutrition Examination Survey (NHANES III)



Ford et al. *JAMA*. 2002

Adverse prognostic implications of cardiovascular metabolic syndrome

Population-based observational study in 1209 Finnish men



No. at risk of metabolic syndrome

Yes	866	852	834	292	866	852	834	292	866	852	834	292
No	288	279	234	100	288	279	234	100	288	279	234	100

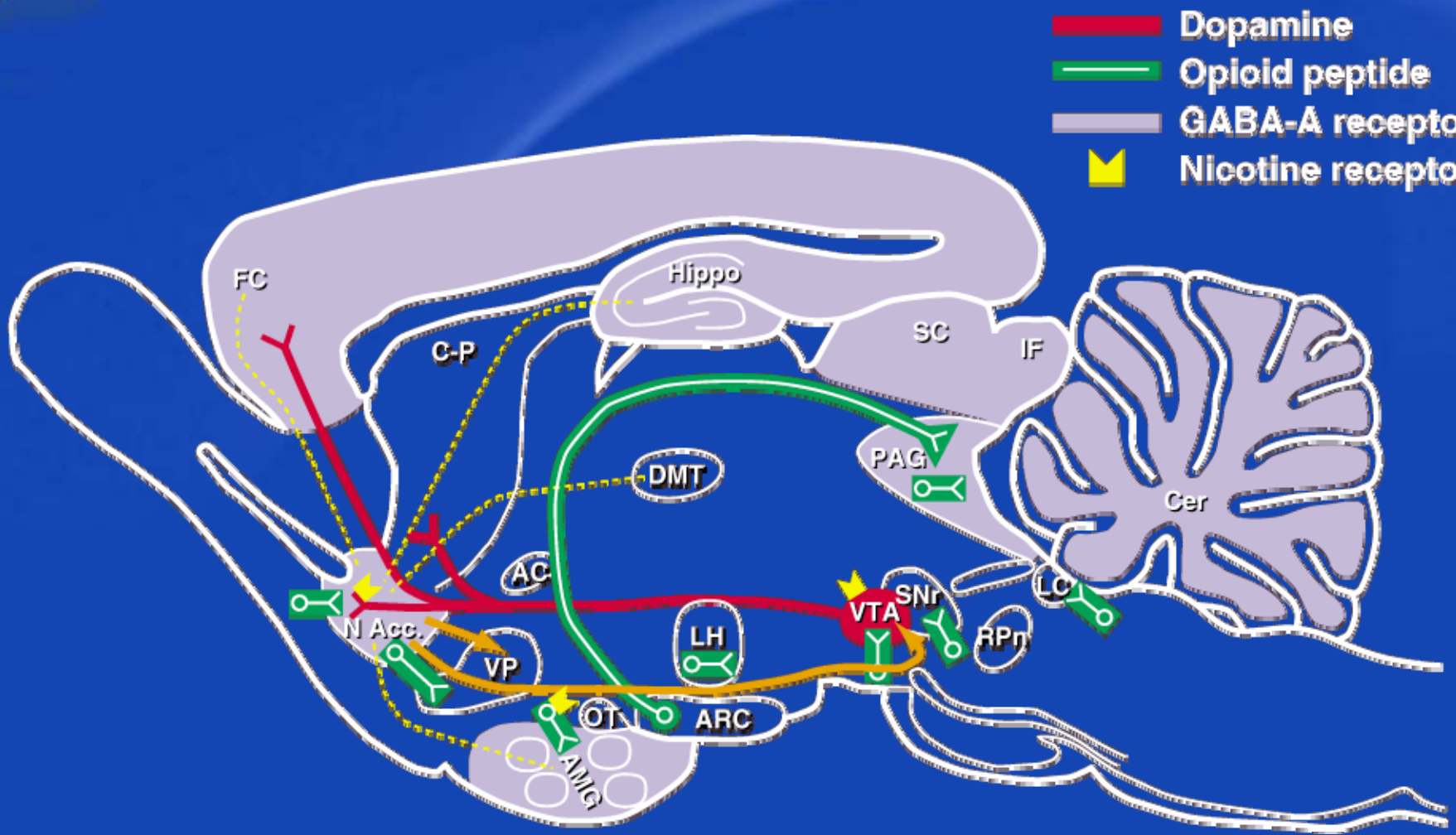
Lakka et al. *JAMA*. 2002

Incidence of cardiovascular events in non-diabetic subjects with the metabolic syndrome

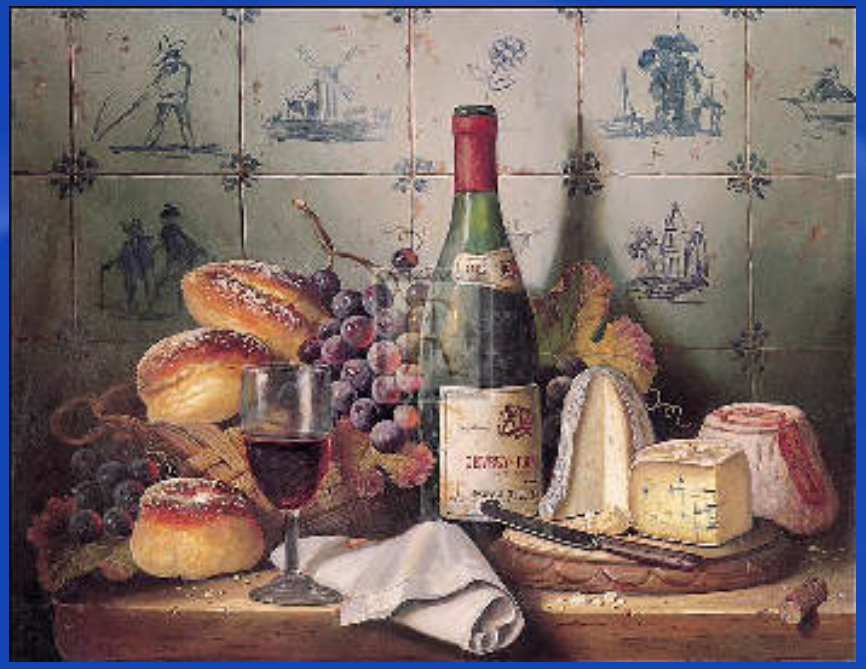
	NCEP ATP III	EGIR	IDF	No metabolic syndrome
Number (N)	774	949	1105	
Incident MI / stroke (n/n)	33 / 38 10.9 / 1000	38 / 40 9.8 / 1000	35 / 38 7.7 / 1000	70 / 67 4.4 / 1000
Age + sex (adjusted hazard ratio)	1.95 (1.48-2.58)	1.62 (1.23-2.12)	1.27 (0.96-1.67)	
Risk factors (adjusted * hazard ratio)	1.66 (1.22-2.25)	1.46 (1.09-1.97)	1.06 (0.78-1.44)	
+C-reactive protein (adjusted**hazard ratio)	1.47 (1.04-1.88)	1.36 (0.98-1.90)	1.02 (0.73-1.42)	

EGIR=European Group for the Study of Insulin Resistance
IDF=International Diabetes Federation
MI=myocardial infarction
Nilsson P. et al. *Diabetic Med*. 2006, in press

Key neurochemical systems comprising the brain reward circuitry



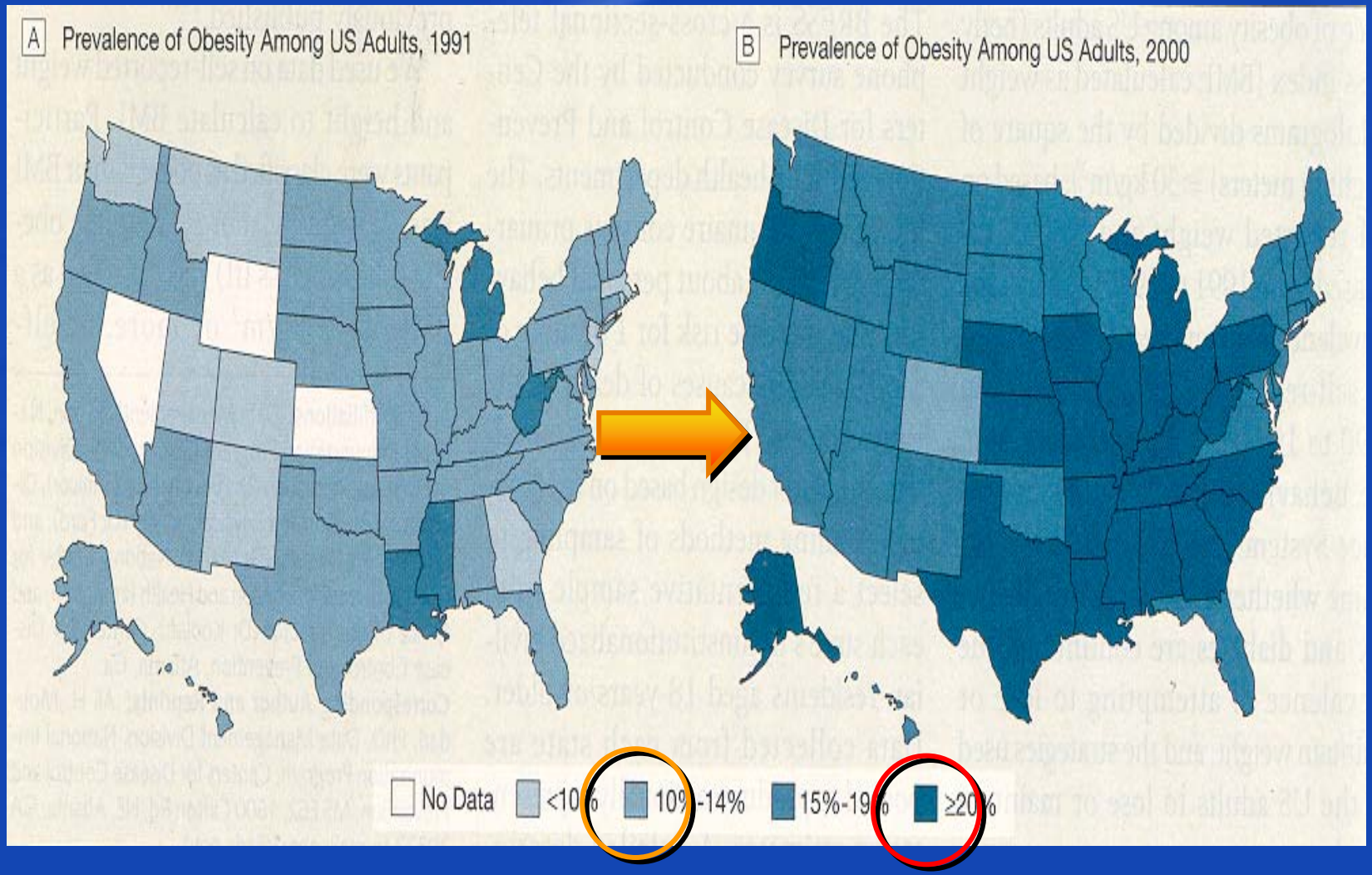
Gardner. In: Lowinson et al, eds. *Substance Abuse*. 4th ed. Lippincott Williams and Wilkins; 2005. Kruger et al. *Photographic Atlas of the Rat Brain*. Cambridge Press; 1995



Brain reward system triggered…

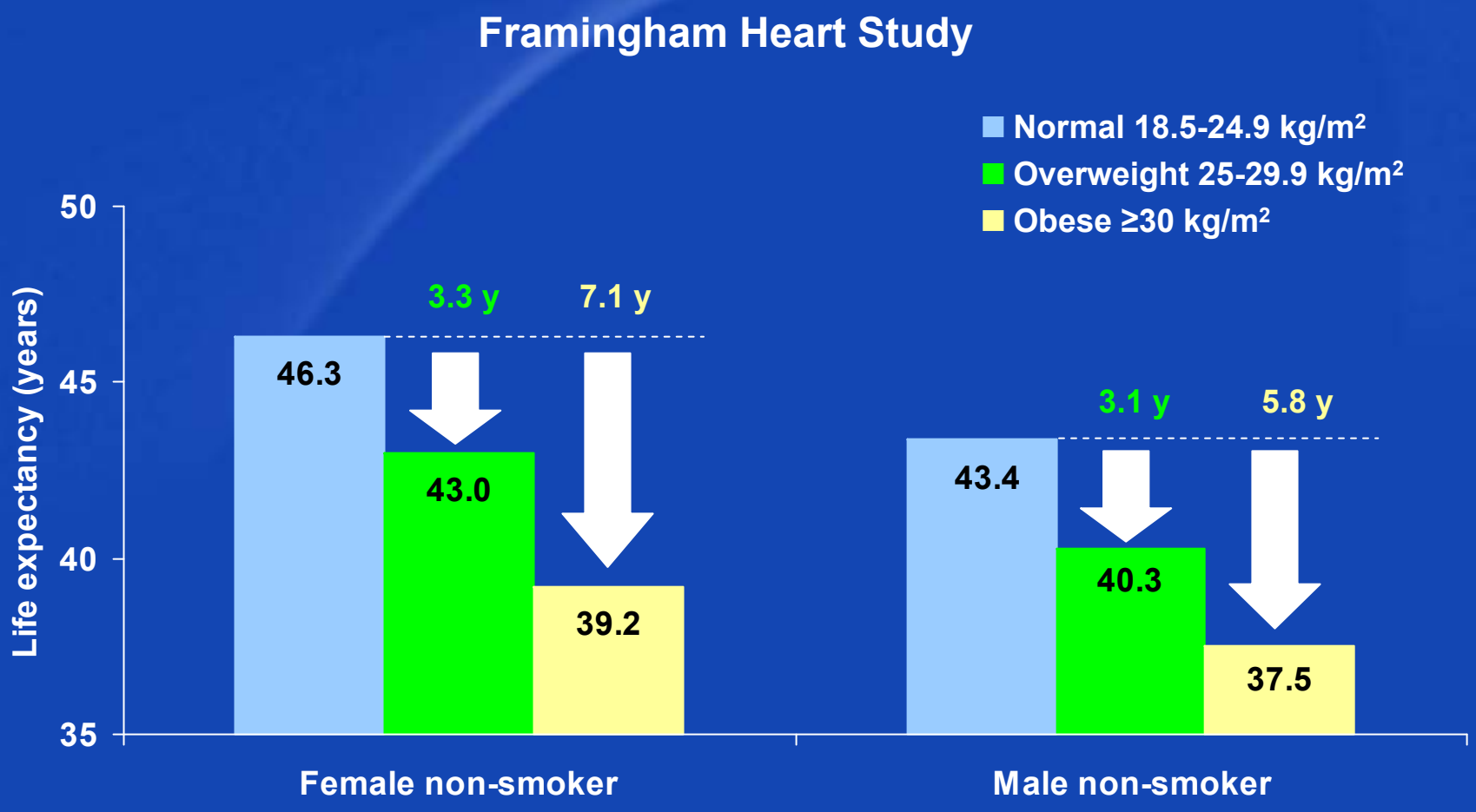
…but also by these things!

Prevalence of obesity in the USA, 1991-2000



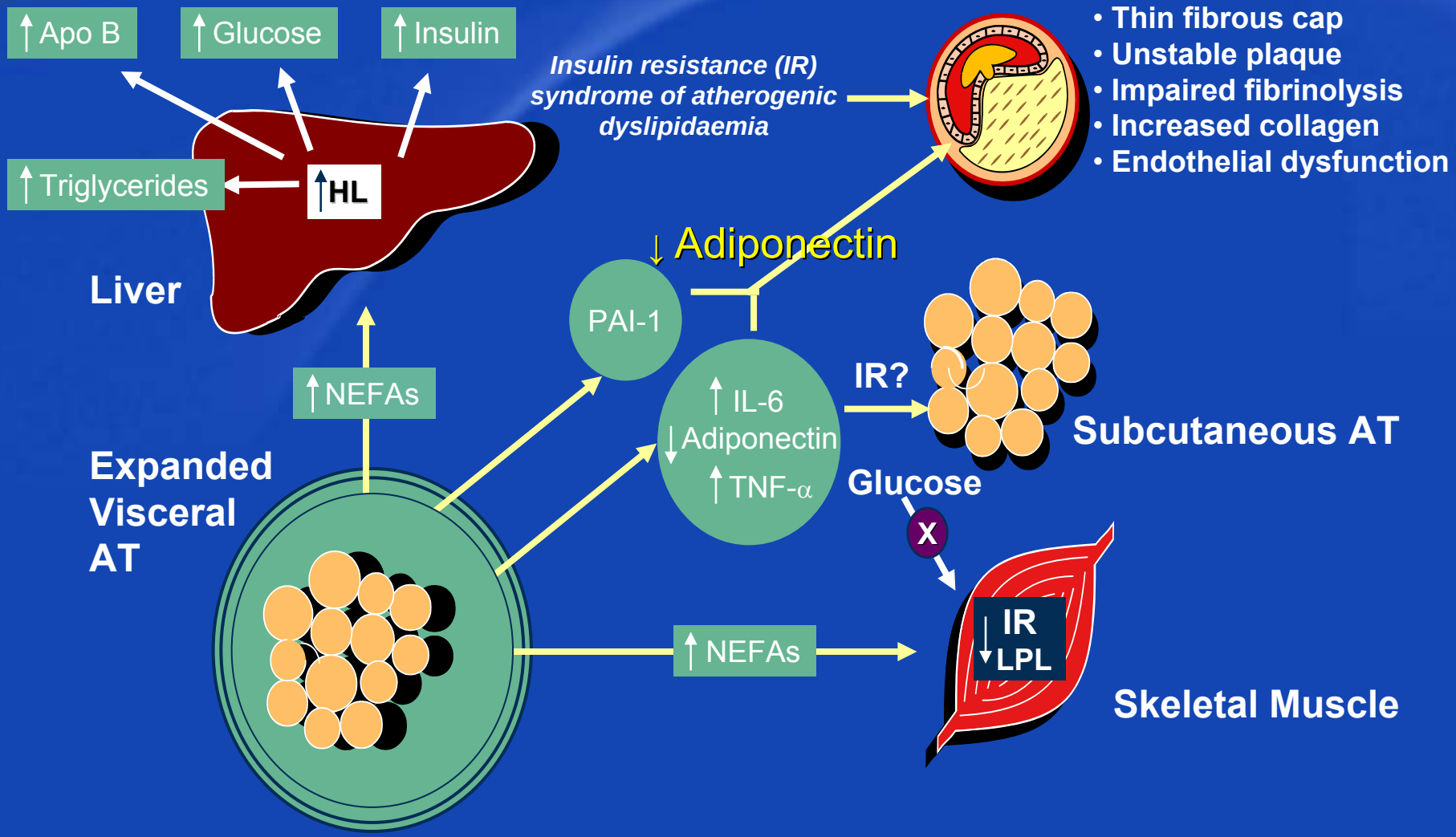
Mokdad et al. *JAMA*. 2001

Life expectancy at age 40: impact of excess body weight



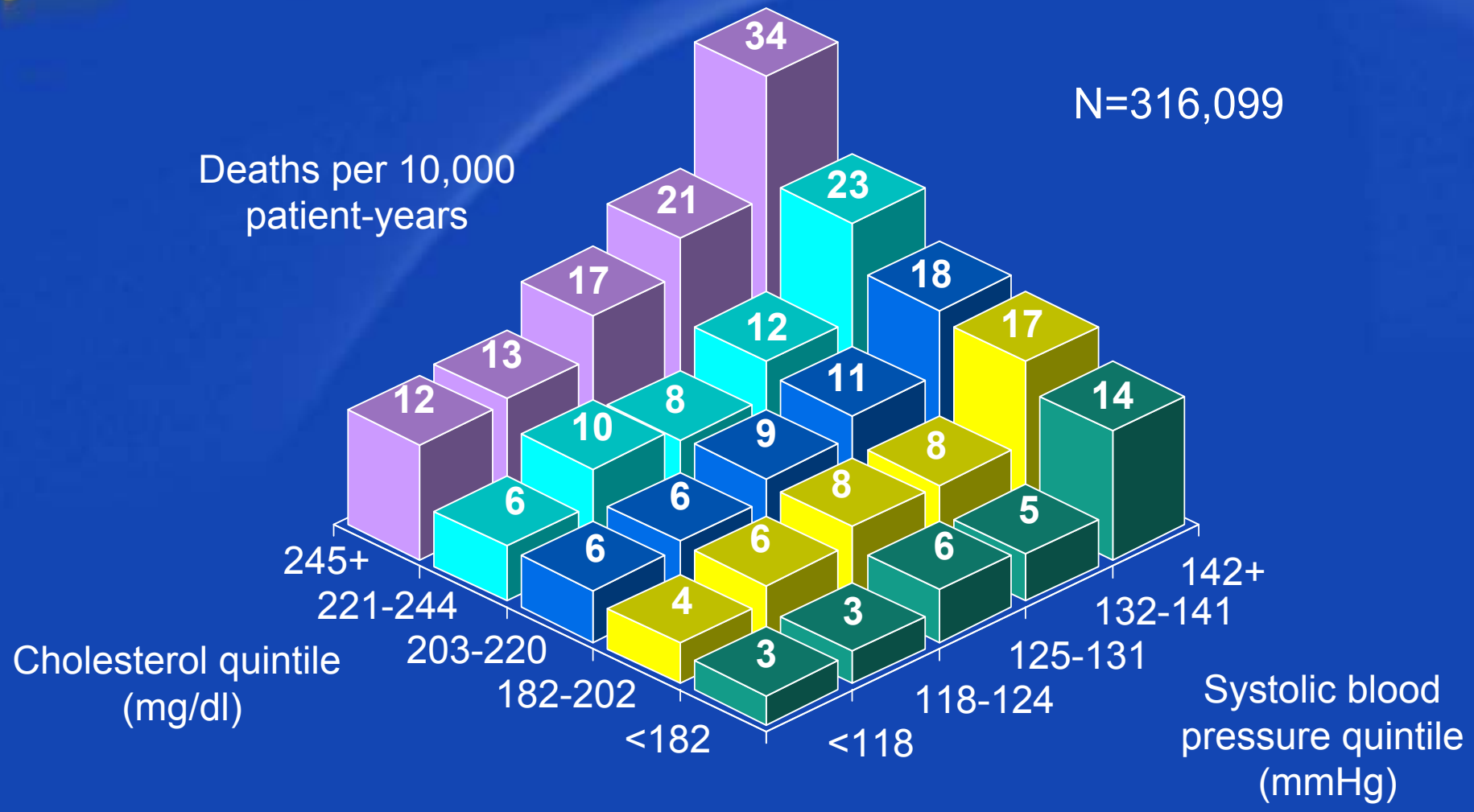
Peeters et al. *Ann Intern Med*. 2003

Potential contribution of expanded visceral adipose tissue to the atherothrombotic pro-inflammatory profile of abdominally obese patients



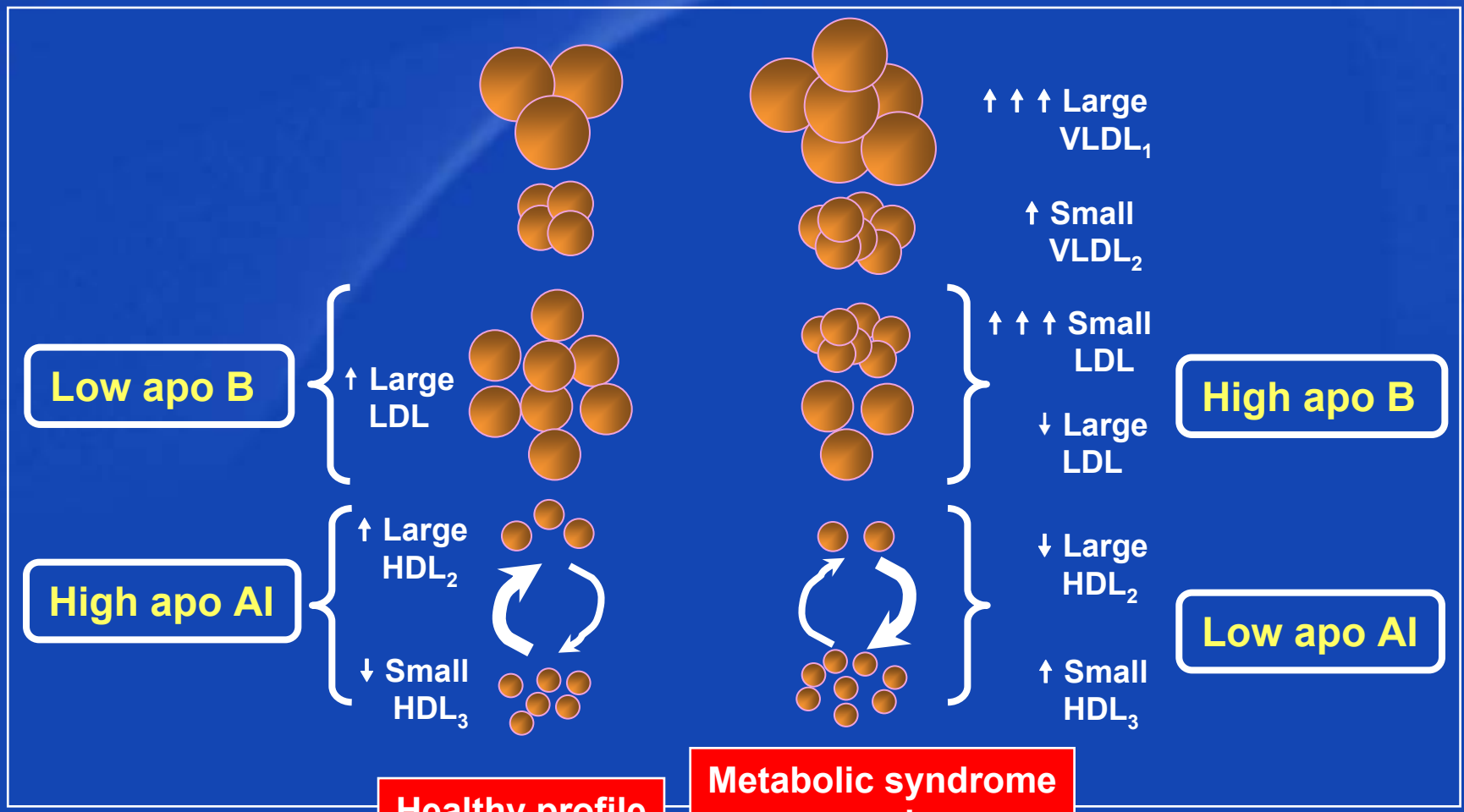
Després et al. *Ann Endocrinol*. 2001

Additive effect of cholesterol and systolic blood pressure on risk of coronary heart disease



Neaton et al. *Arch Intern Med*. 1992

INTERHEART: importance of APO B and AI levels



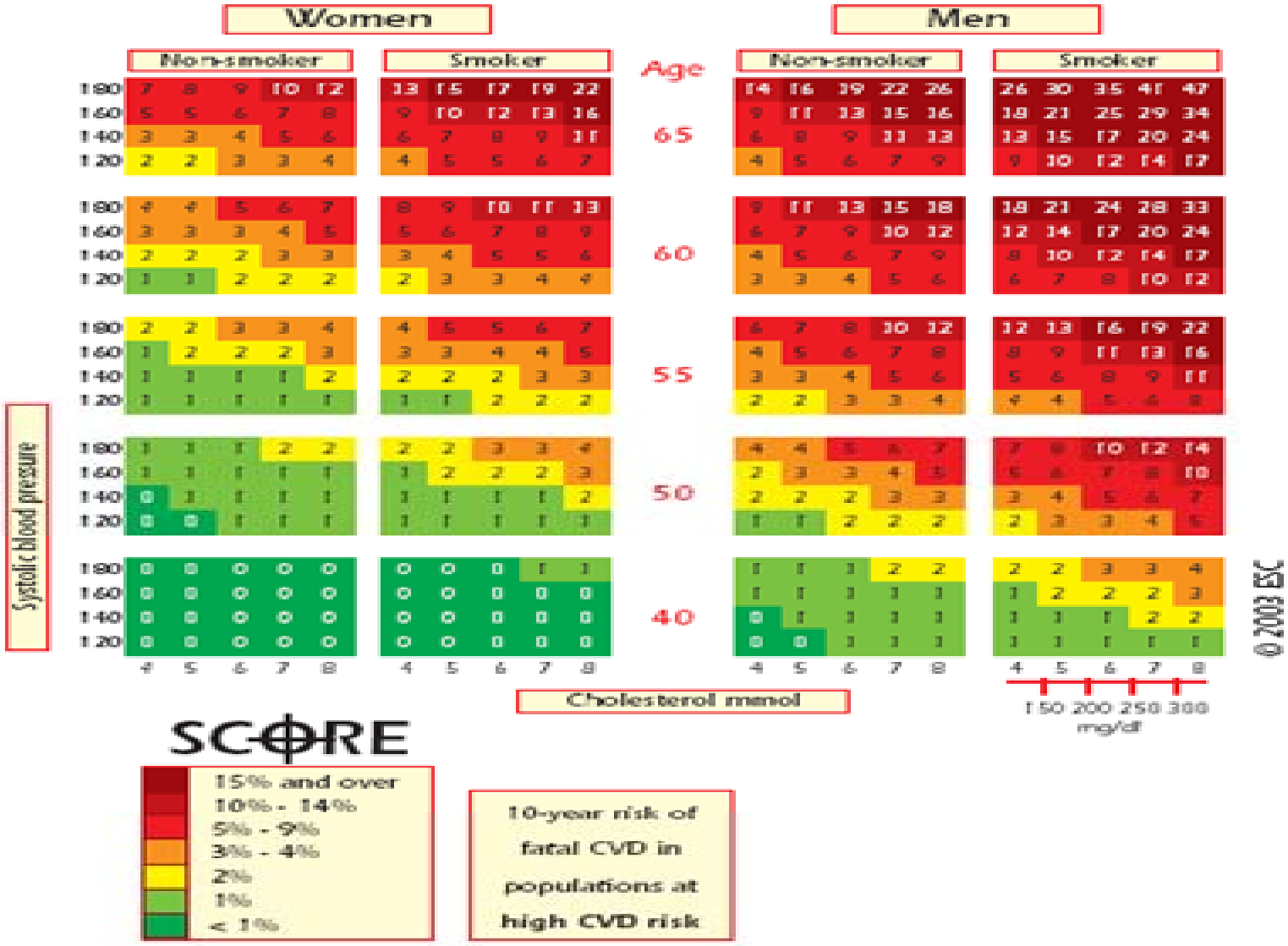
VLDL=very low-density lipoprotein

Yusuf et al. *Lancet*. 2004

- Fetal growth, retardation, and risk:
  - Arterial hypertension?
  - Type 2 diabetes?
  - Cardiovascular disease?
  - Insulin resistance syndrome?

The Barker 'Fetal Origin Hypothesis'

Ten-year risk of fatal CVD in high-risk regions of Europe by gender, age, SBP, total cholesterol, and smoking status



Conroy et al. *Eur Heart J*. 2003

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Evidence Based Prevention of Cardiovascular Disease

EUROPEAN SOCIETY OF CARDIOLOGY

Based on PRECARD® technology
Developed by
Research Centre for Prevention and Health
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Copenhagen County, Denmark

Version 4.0

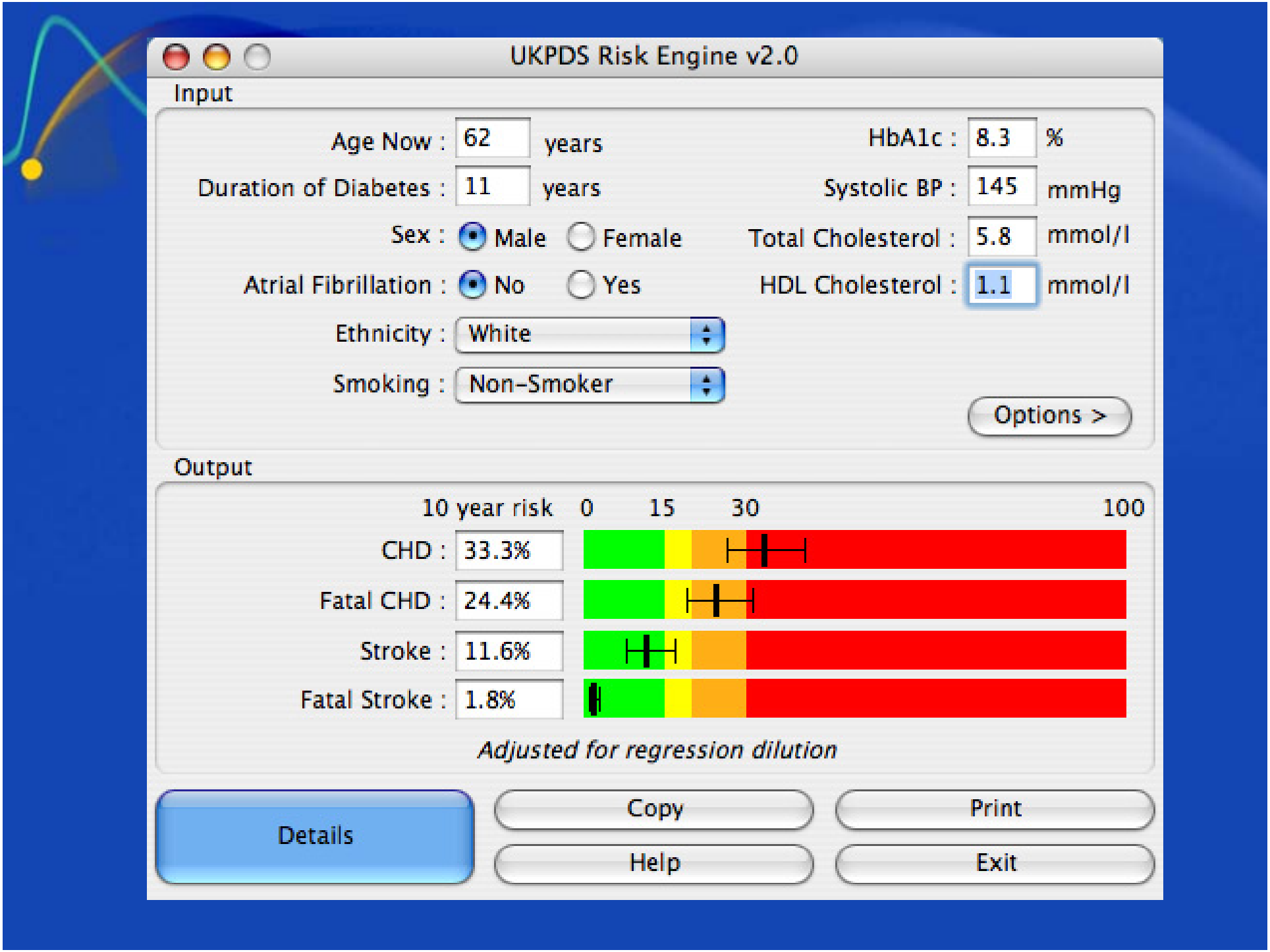
Update level 31 / 9

Design and development by Wind data

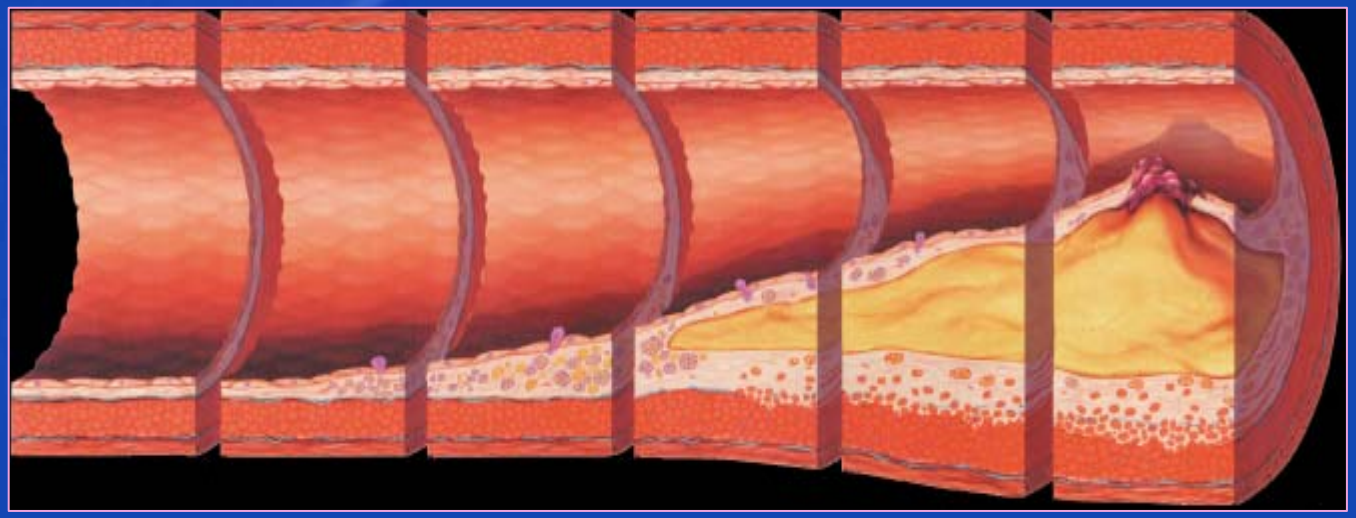
Branding: Hobby One.

EUROPEAN SOCIETY OF CARDIOLOGY

Development of this program has been made possible by unrestricted educational grants from Aventis, GlaxoSmithKline, Merck / Schering-Plough and Pfizer.


UKPDS Risk Engine v2.0
Input
Age Now : 62 years
Duration of Diabetes : 11 years
Sex : Male Female
Atrial Fibrillation : No Yes
Ethnicity : White
Smoking : Non-Smoker
HbA1c : 8.3 %
Systolic BP : 145 mmHg
Total Cholesterol : 5.8 mmol/l
HDL Cholesterol : 1.1 mmol/l
Options >
Output
10 year risk
0
15
30
100
CHD : 33.3%
Fatal CHD : 24.4%
Stroke : 11.6%
Fatal Stroke : 1.8%
Adjusted for regression dilution
Details
Copy
Print
Help
Exit

Vascular ageing: atherosclerosis and arterial stiffening



Butler et al. *Eur Heart J.* 1998

Conclusions

- Evolutionary biology and evolutionary medicine can provide new perspectives on the metabolic syndrome and clusters of CVD risk factors
- Survival genes do not match with modern lifestyle, resulting in abdominal obesity, chronic inflammation, and insulin resistance
- A life course approach takes into account the early programming (fetal life, catch-up post-natal growth) for prediction of cardiovascular risk and Type 2 diabetes
- Lifestyle programmes have to be tailored to brain reward systems and may prevent vascular ageing