Κάπνισμα και καρδιαγγειακός κίνδυνος

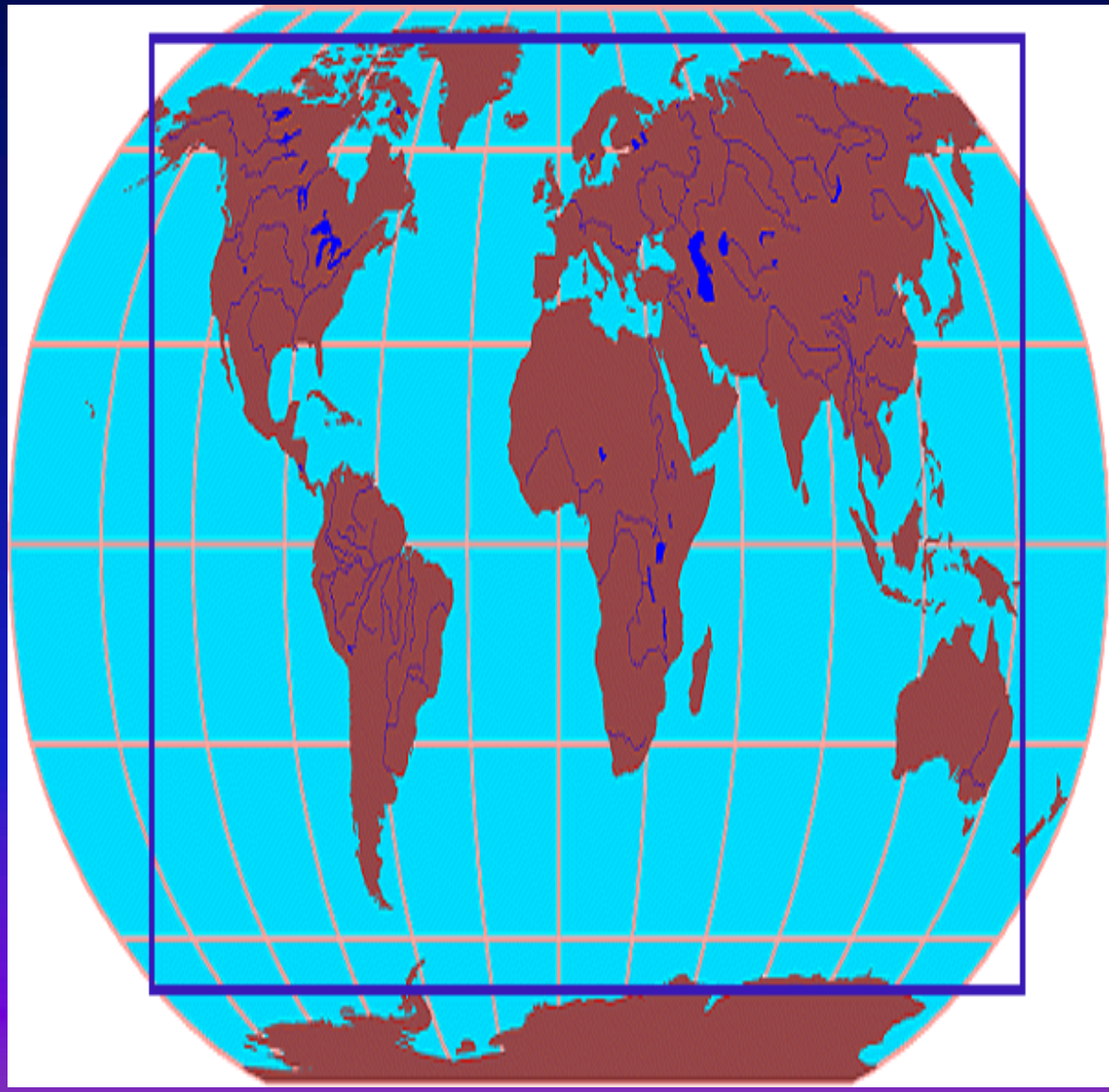
Dr. Παπαστεφάνου Εμμ. Στέφανος

Επιμελητής Α! Καρδιολογικής Κλινικής

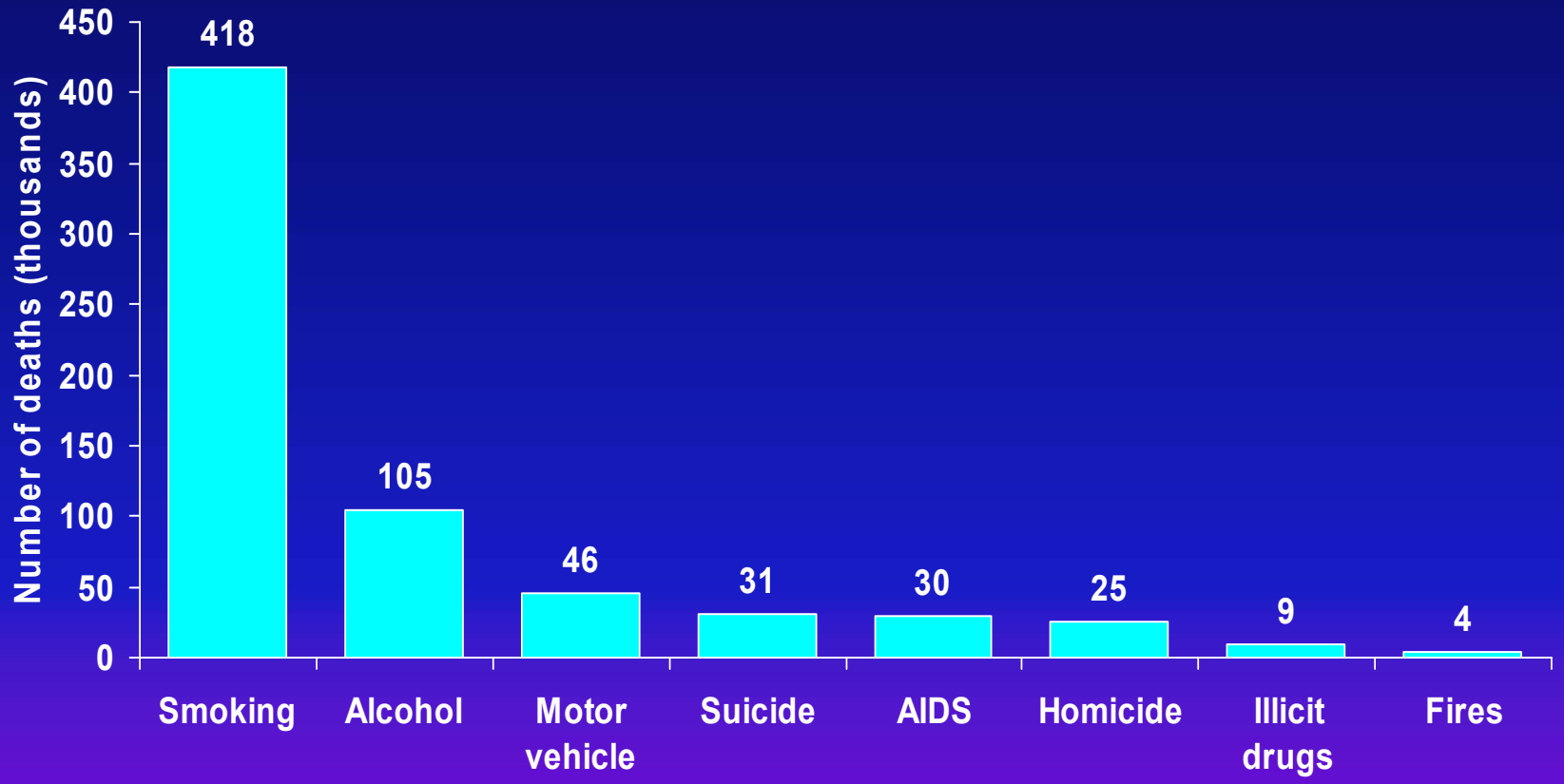
Γ.Ν. ΄΄ΑΓΙΟΣ ΠΑΥΛΟΣ΄΄

1.3 Billion

- Tobacco use is one of the most important modifiable causes of CVD worldwide.
- Each year tobacco kills 3 million people worldwide.
- WHO estimates that by 2020–2030, tobacco will be responsible for 10 million deaths per year 70% will occur in developing countries.



Comparative Causes of Annual Deaths in the US



McGinnis and Foege, 1993

Επιπολασμός καπνίσματος στους άνδρες

60% and above

30% – 39.9%

50% – 59.9%

20% – 29.9%

40% – 49.9%

below 20%

♂

Mackay J, et al The Tobacco Atlas, 2006

Επιπολασμός καπνίσματος στις γυναίκες

60% and above

30% – 39.9%

50% – 59.9%

20% – 29.9%

40% – 49.9%

below 20%

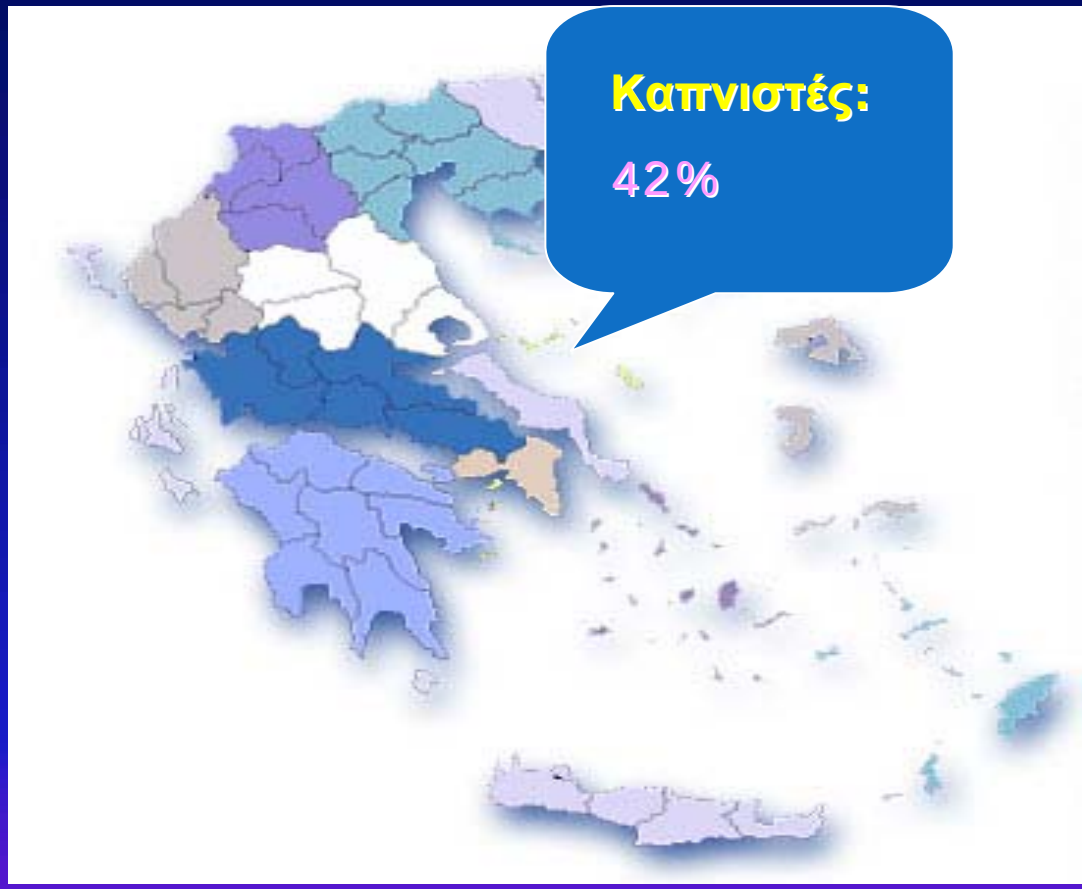
countries where women smoke more than men

Mackay J, et al The Tobacco Atlas, 2006

Επιπολασμός του καπνίσματος στην Ελλάδα (2006)

Μη καπνιστές: 41%

Πρώην καπνιστές: 17%



ΕΕ:

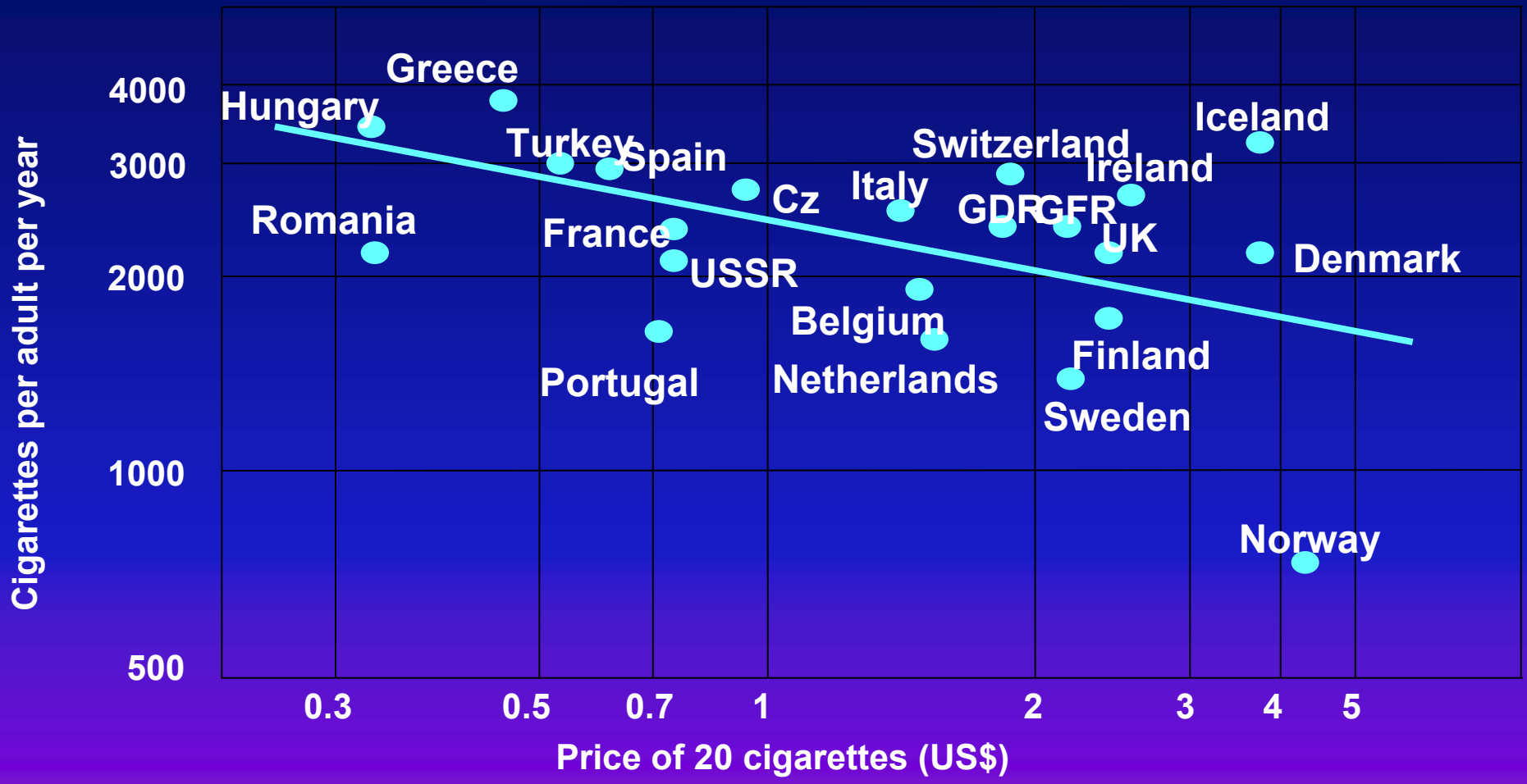
Καπνιστές: 32%

Μη Καπνιστές: 47%

Πρώην Καπνιστές: 21%

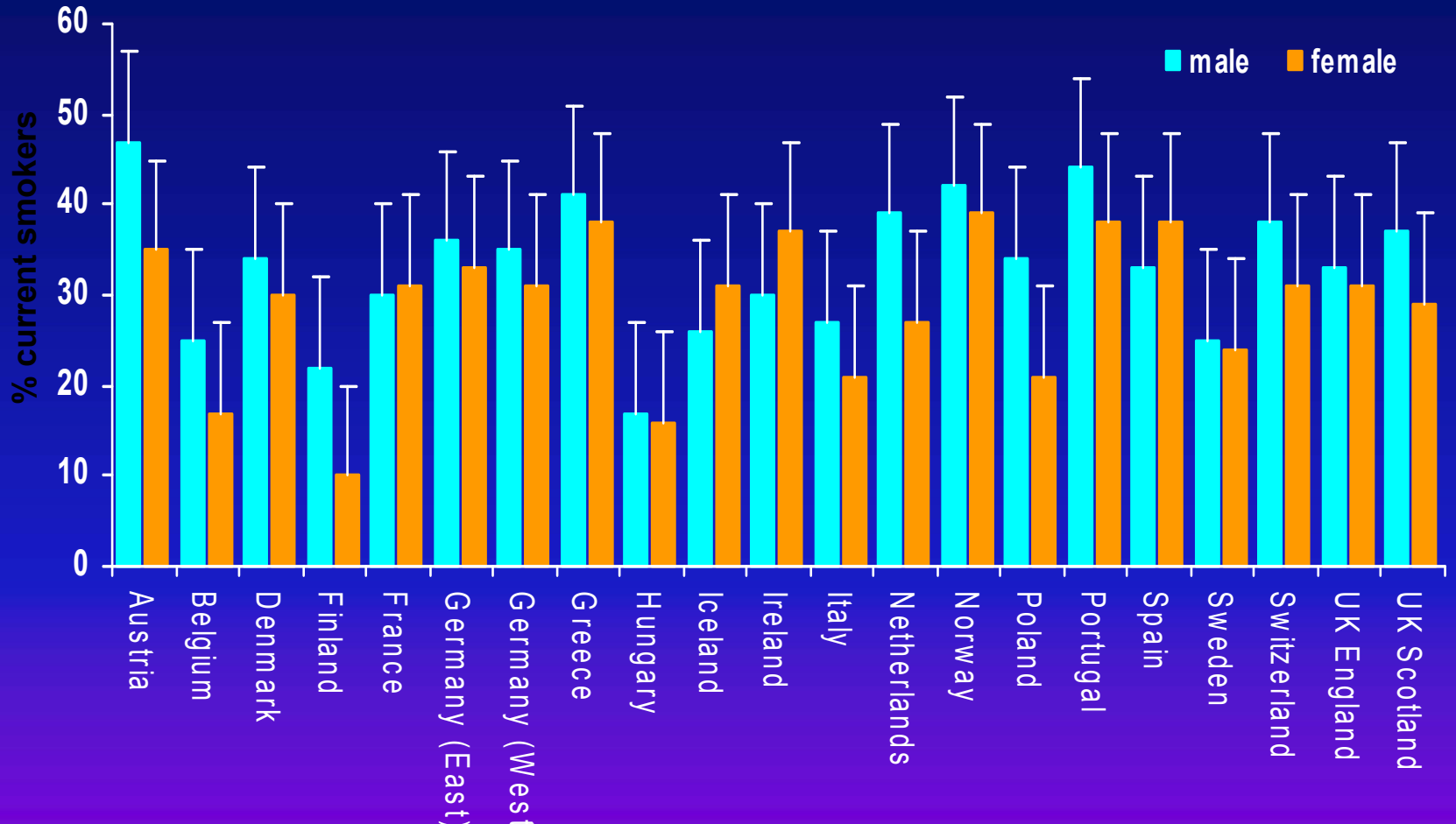
ec.europa.eu/public_opinion/archives/ebs/ebs_272c_en.pdf

Cigarette Price and Consumption in 22 European Countries



Townsend, 1998

Age-adjusted Prevalence of Smoking Among Men and Women in Europe



The overall age-adjusted prevalence of smoking ♂ 33% ♀ 29%

Steptoe, Wardle and Smith, 1995

The association between smoking and cardiovascular disease was first elucidated in large epidemiological studies, in particular the British Doctors Study and the Framingham Heart Study.

Doll R, Peto R, Wheatley K, Gray R,Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors. *Br. Med. J. 309(6959),*901–911 (1994).


FRAMINGHAM HEART STUDY

CVD Risk by Cigarette Smoking Framingham Study 36-yr. Follow-up

Age-adjusted Rate per 1000			Risk Ratio		Excess Risk per 1000	
Age	Men	Women	Men	Women	Men	Women
35-64	164	135	4.7***	7.4***	129	117
65-94	234	235	2.8***	4.1***	51	178

Biennial Rate per 1000. CVD=CHD, stroke, peripheral vascular disease, heart failure ***P<0.001

Risk Factors

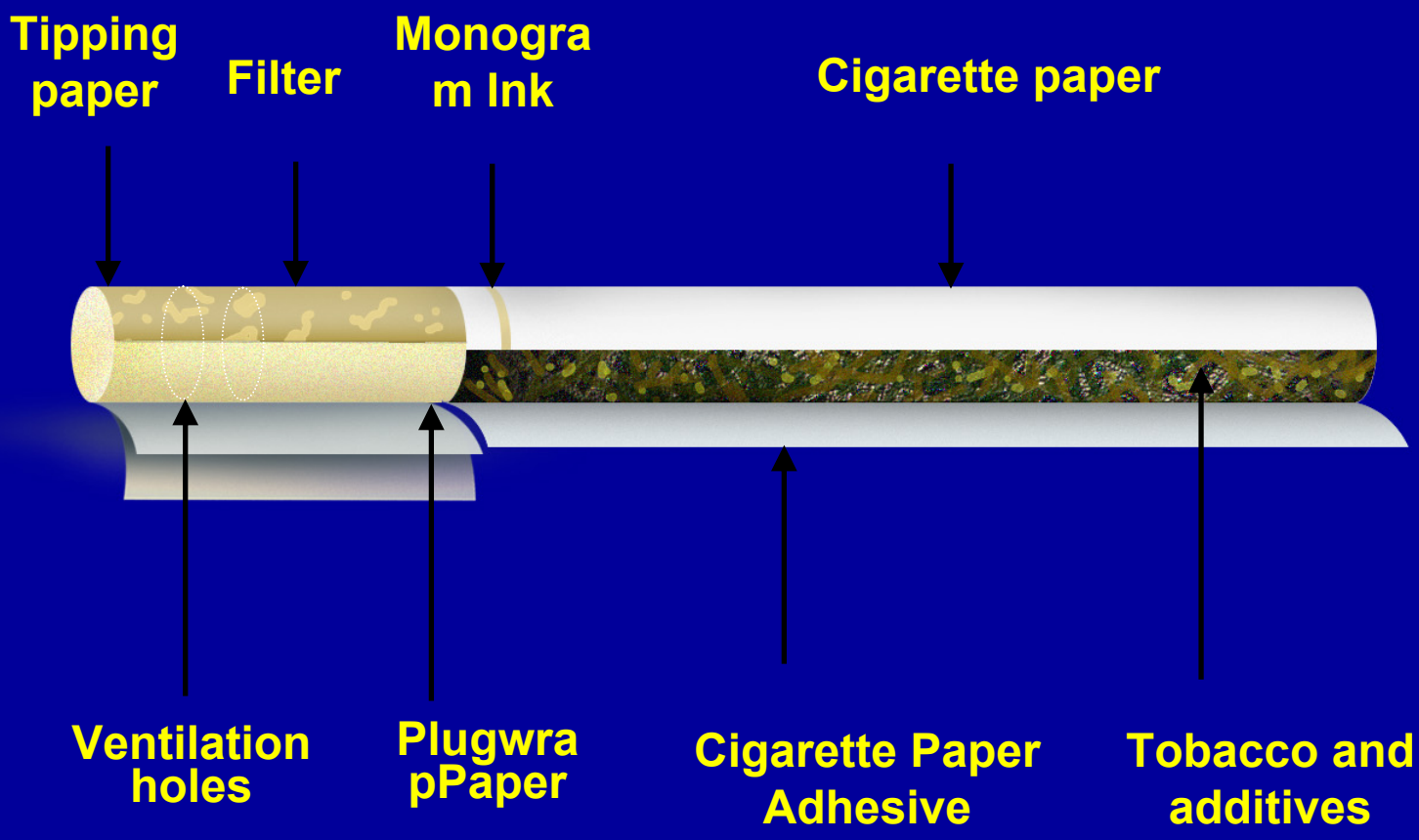
- Modifiable
  - Hypertension
  - **Smoking**
  - Obesity
  - Diabetes
  - Cardiac Disease
  - Dyslipidemia
  - Excessive Alcohol Intake
  - Physical Inactivity
  - Stress
  - Diet
- Non-Modifiable
  - Age
  - Gender
  - Family History
  - Ethnicity

Epidemiology

- Smoking has a greater impact on acute, typically thrombotic events, than on atherogenesis.

  This is most marked in young and middle-aged adults, where smoking is responsible for approximately 50% of premature acute myocardial infarctions (AMIs) .
- The relative risk (RR) of cardiovascular events is much greater in younger than in older smokers principally because such events are extremely rare in young nonsmokers.

The Manufactured Cigarette



Tobacco contains over 4,000 chemicals, many of which are harmful. These include:

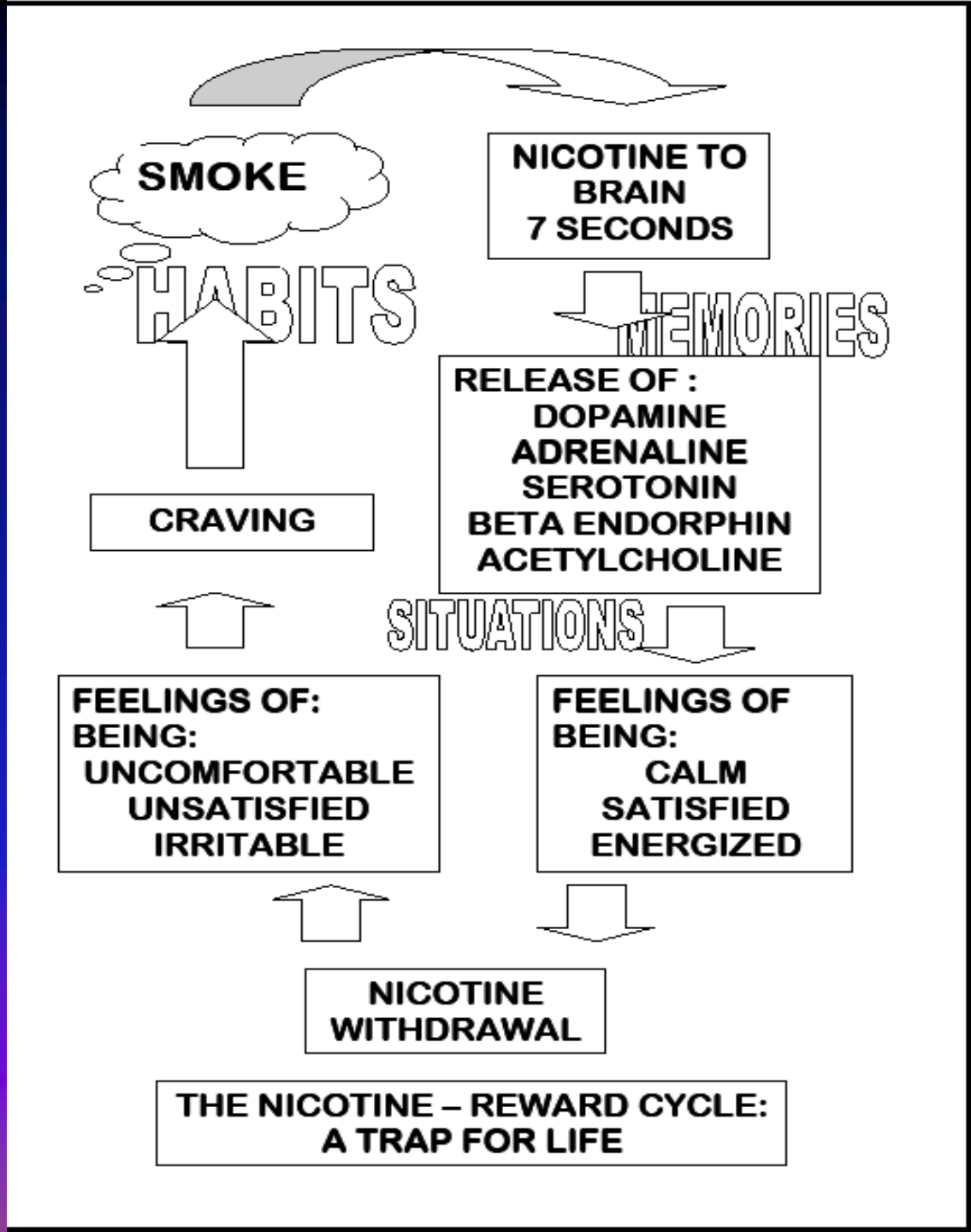
- **Benzene** - solvent used in fuel and chemical manufacture
- **Formaldehyde** - highly poisonous, colourless liquid used to preserve dead bodies
- **Ammonia** - chemical found in cleaning fluids. Used in cigarettes to increase the delivery of nicotine
- **Hydrogen cyanide** - poisonous gas used in the manufacture of plastics, dyes, and pesticides. Often used as a fumigant to kill rats
- **Cadmium** - extremely poisonous metal found in batteries
- **Acetone** - solvent found in nail polish remover
- **Arsenic** - ingredient in rat poison

The three main components of inhaled smoke are :

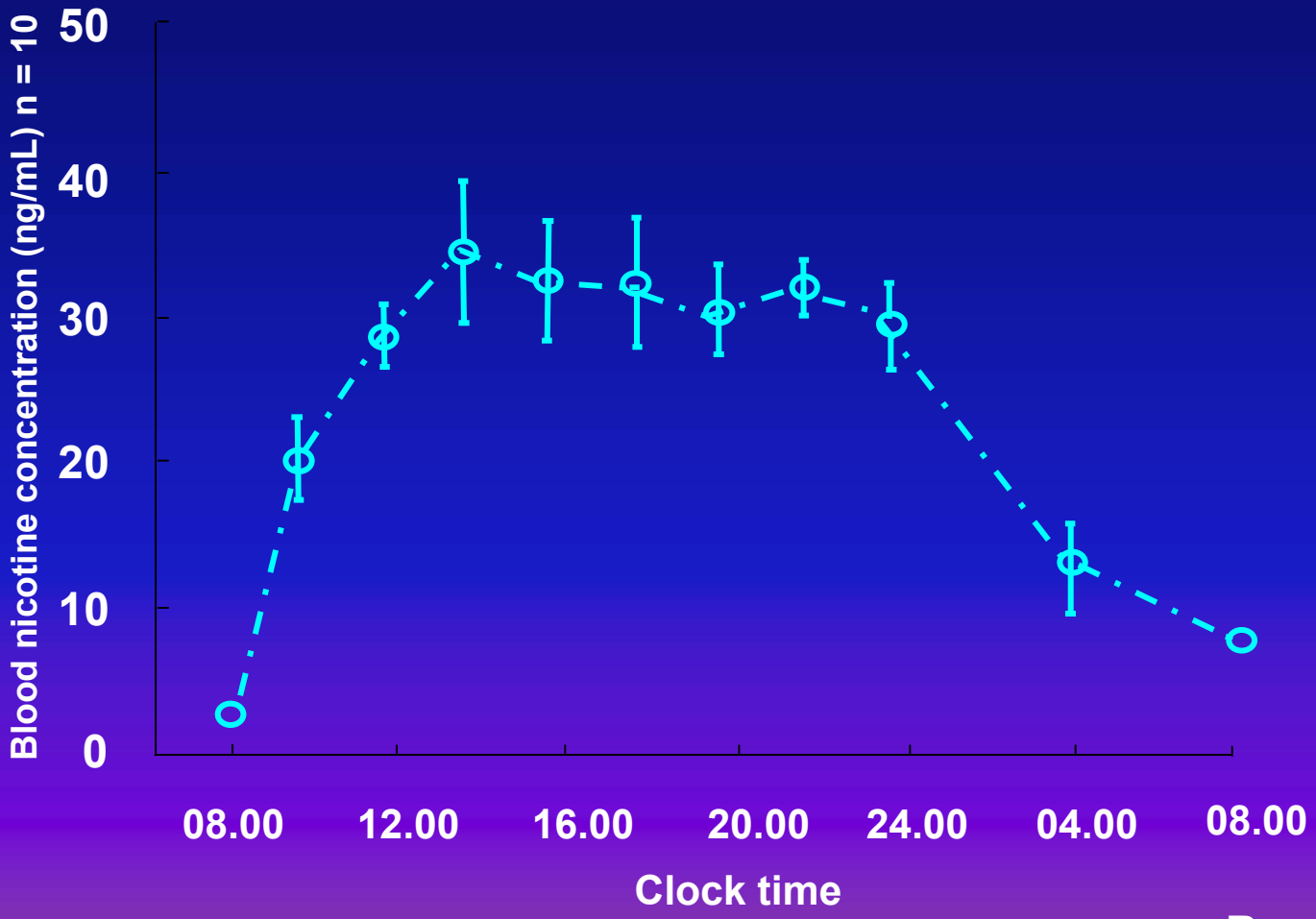
- **Nicotine**
- **Carbon monoxide**
- **Tar**

all of which can cause disease.

- Συμπαθητικομιμητική ουσία που προάγει την απελευθέρωση κατεχολαμινών και άλλων νευρομεταβιβαστών δρώντας κεντρικά και περιφερικά.



Blood Nicotine Concentrations in Smokers



Benowitz *et al*, 1983

Smoking and the Cardiovascular system

Effects of Nicotine

- Increase in BP
- Increase in HR
- Increase in SVR

} Due to the release of catecholamines from adrenal meddula 30 min after smoking

Also increases coronary artery vascular resistance

↓

Myocardial oxygen supply-demand imbalance

↓

Myocardial ischemia

Smoking and the Cardiovascular system

Effcts of Carbon monoxide (CO)

- Increase in COHb levels lead to a decrease in oxygen content
- Shift of the oxygen dissociation curve to the left
- Weak, direct negative ionotropic effect on the heart

↓

Myocardial oxygen supply-demand imbalance

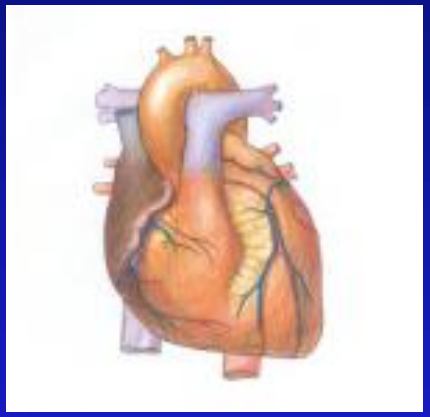
↓

Myocardial ischemia

Harmful effects of smoking

Cardiovascular Complications

- Increased myocardial work
- Decreased oxygen supply
- Coronary vasocontriction
- Increased catecholamine release



Increased concentrations of CO has been correlated to frequency of ST-depression during general anaesthesia

Κάπνισμα και καρδιαγγειακό σύστημα

Cardiovascular Diseases

Cigarette smoking predisposes the individual to several different clinical atherosclerotic syndromes

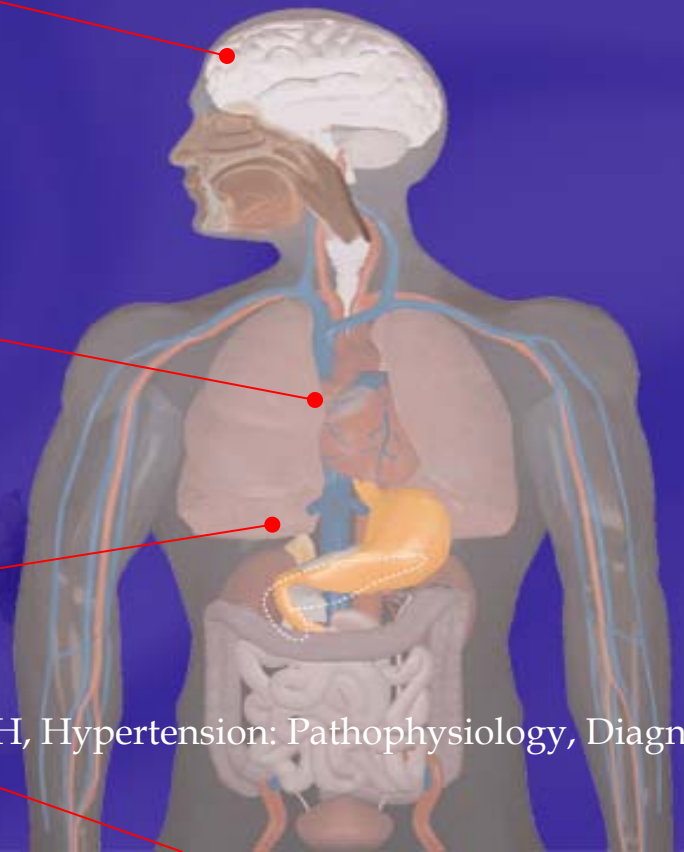
Includes:

Cerebral vascular disease
(stroke)

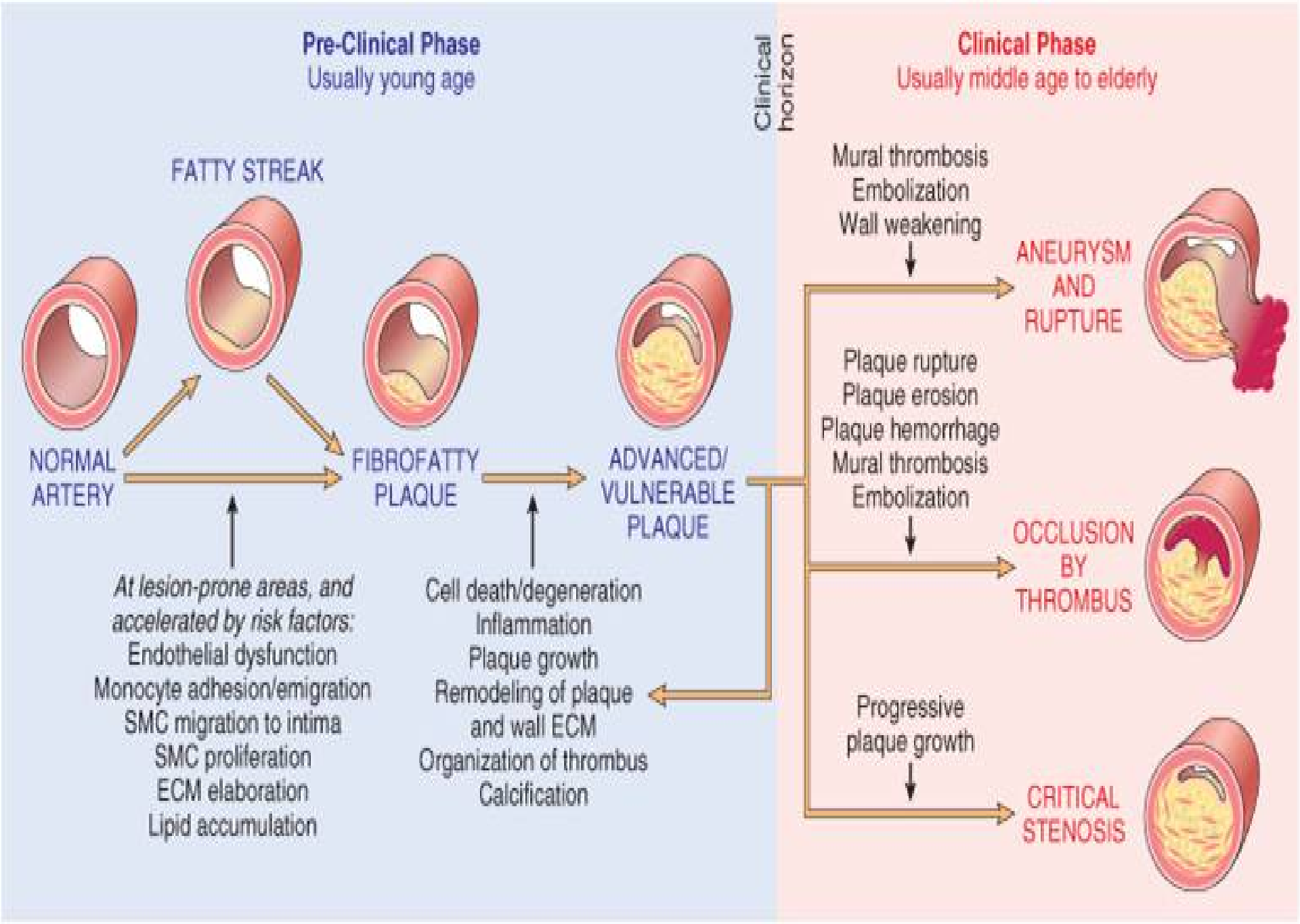
Coronary heart disease
(angina pectoris,
myocardial infarction,
sudden cardiac death)

Aortic and peripheral atherosclerosis are also increased,
leading to

(abdominal aortic aneurysm
Intermittent claudication,**)**



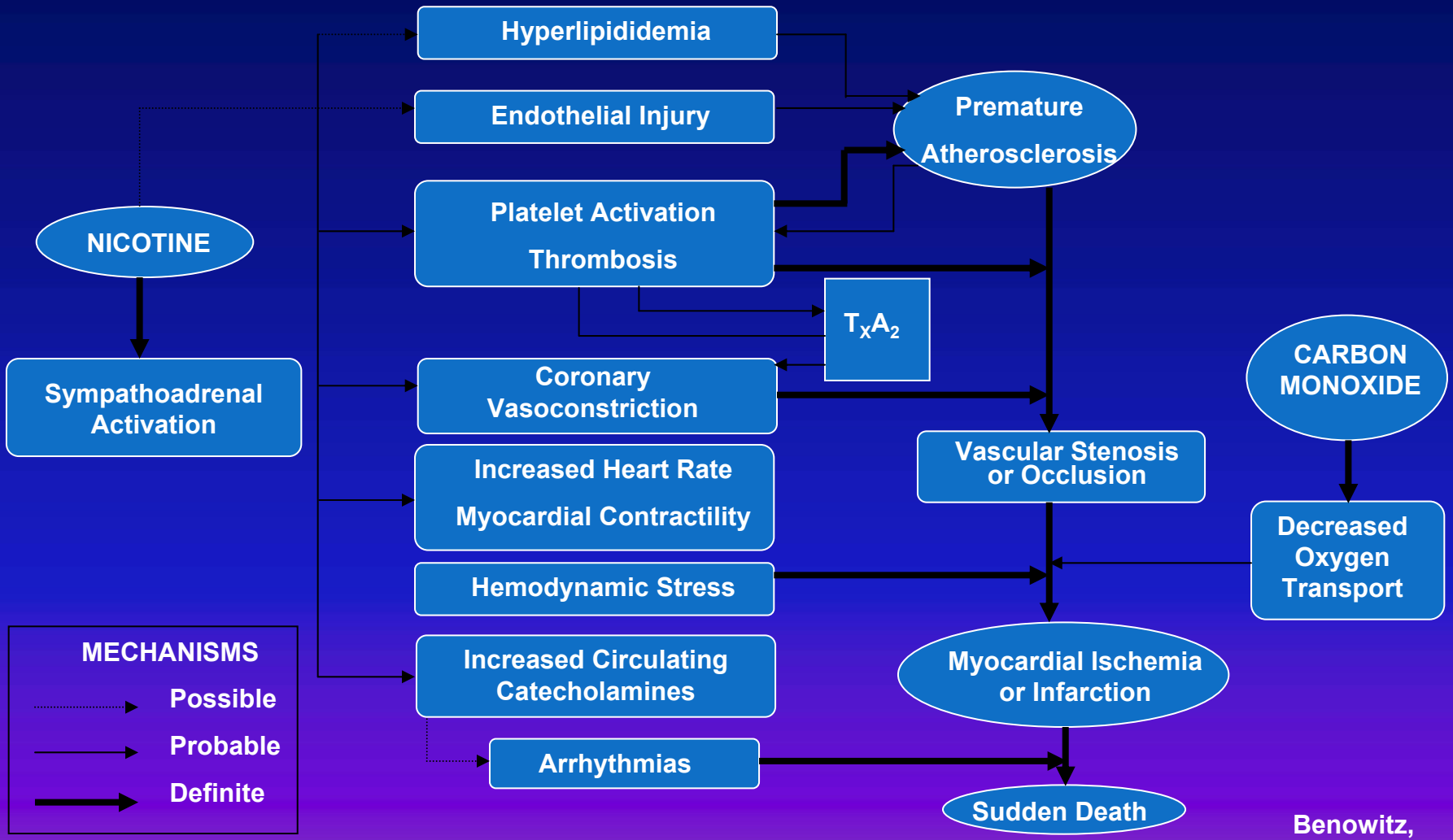
Black HR. Smoking and cardiovascular disease. In: Laragh JH, Hypertension: Pathophysiology, Diagnosis and Management. 1995:2621–47



Coronary Heart Disease Pathogenesis

- Atherosclerosis
- Thrombosis
- Coronary artery spasm
- Cardiac arrhythmia
- Reduced capacity of the blood to deliver oxygen

Mechanisms by which Nicotine may Contribute to Coronary Heart Disease



Benowitz, 1991

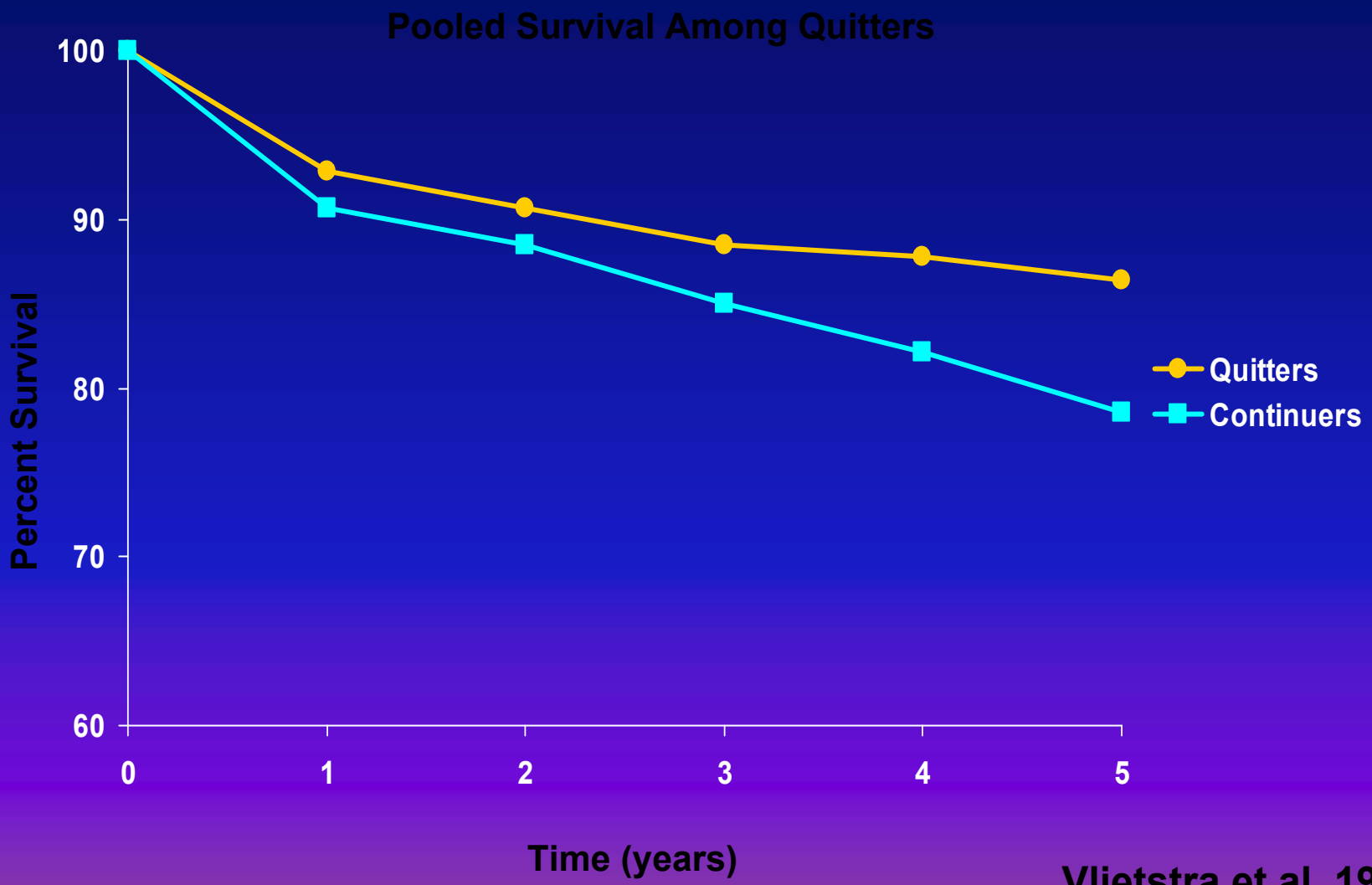
Fatal Coronary Heart Disease, Non-fatal Myocardial Infarction and Angina Pectoris

Epidemiological Evidence: The Nurses' Health Study
Age-adjusted Relative Risks in Relation to Smoking

	Non-smoker	Ex-smoker	Current smoker (cigarettes/day)		
			1-14	15-24	≥25
Coronary heart disease	1	1.3	1.7	3.7	5.4
Non- fatal M.I	1	1.3	2.3	4.3	5.8
Angina	1	1.6	1.6	2.0	2.6

Willet et al, 1987

Effect of Smoking Cessation on Survival among Men with Documented Coronary Atherosclerosis



Vlietstra et al, 1986

Cerebrovascular Disease

Two major types:

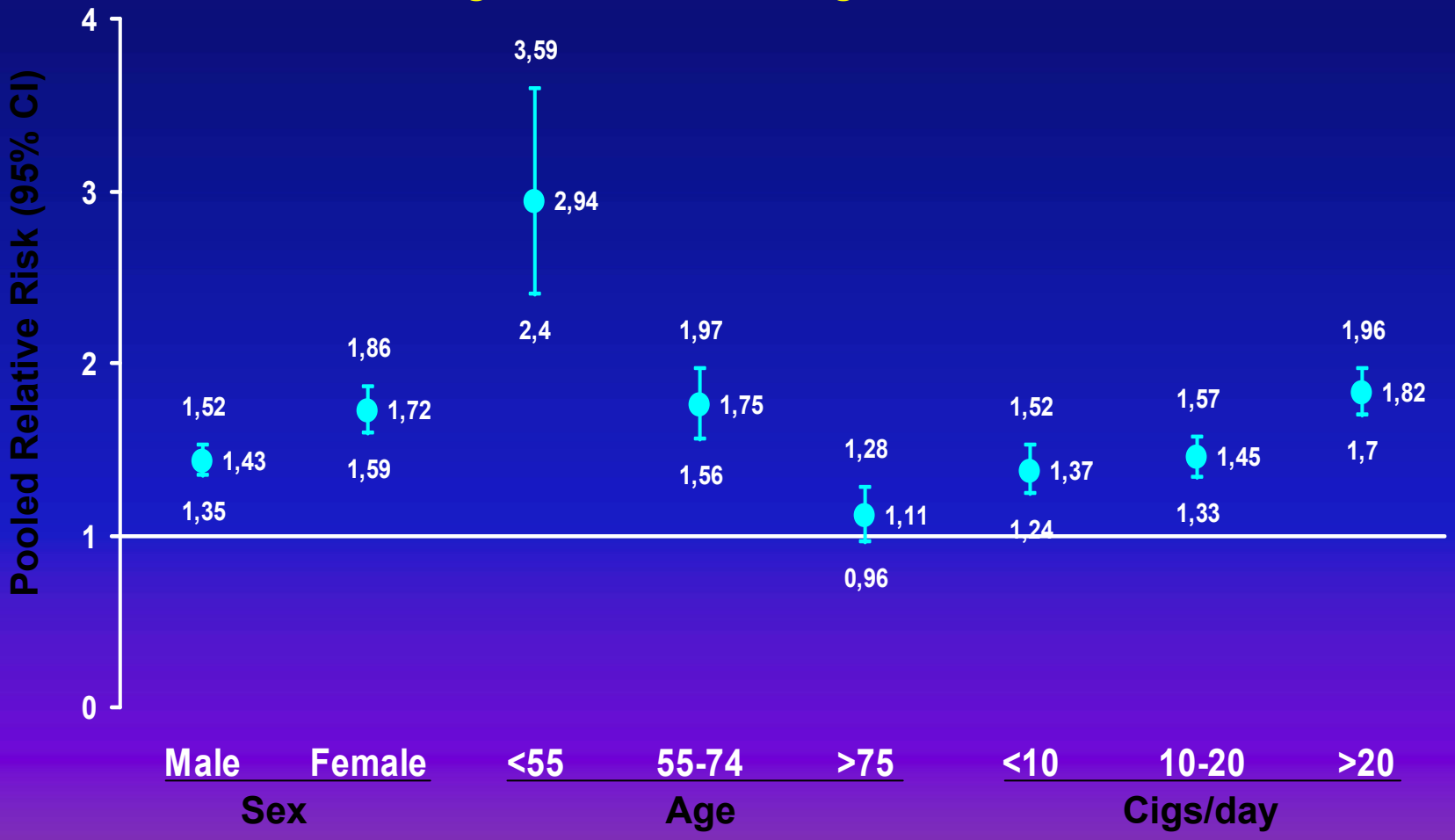
- cerebral infarction
- cerebral hemorrhage
  - subarachnoid
  - parenchymal

Based on data from the CPS-II study, the 1989 Report of the Surgeon General

Smokers		
Male deaths	< 65	51%
Female deaths	<65	55%
Male deaths	>65	24%
Female deaths	>65	6%

Stroke

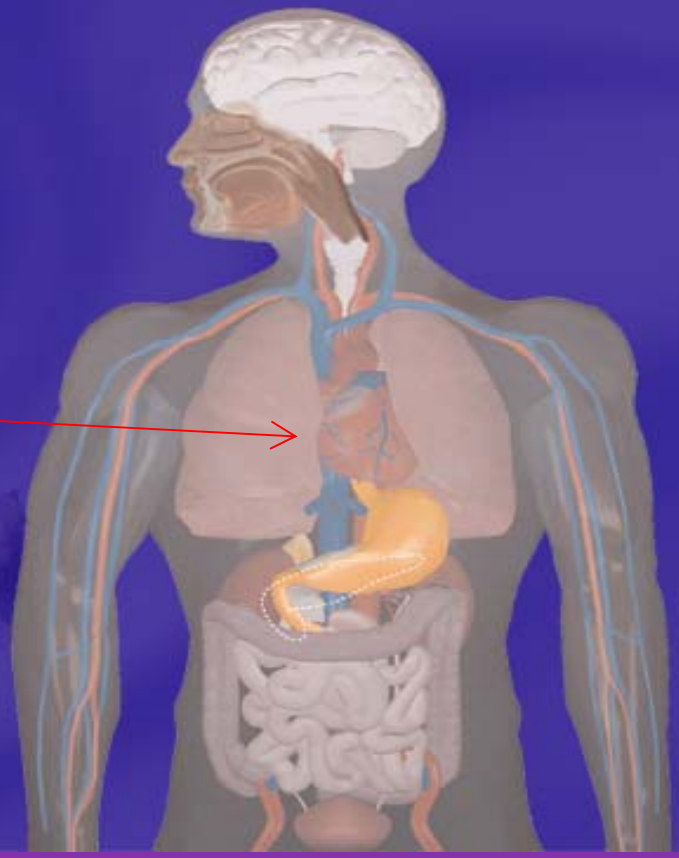
Estimated relative risk of stroke in cigarette smokers compared with non-smokers by sex, age, and number of cigarettes smoked



Shinton & Beevers,

Atherosclerotic Peripheral Vascular Disease

Atherosclerotic Peripheral Vascular Disease



Peripheral vascular disease

Peripheral vascular disease (PVD) affects approximately 20% of adults older than 55 years of age, half of whom are asymptomatic. Of these, 5–10% progress to symptomatic PVD within 5 years.

Cigarette smoking increases the risk of PVD 7 fold and progression to symptomatic disease occurs a decade earlier than in non smokers.

The risk of developing claudication increases with the intensity of smoking. The 5-year mortality for patients with claudication who continue to smoke is 40–50% .

Price JF, Mowbray PI, Lee AJ *et al.* Relationship between smoking and cardiovascular risk factors in the development of peripheral arterial diseaseand coronary artery disease: Edinburgh Artery Study. *Eur. Heart J. 20(5), 344–353 \9199)*

Abdominal aortic aneurysm

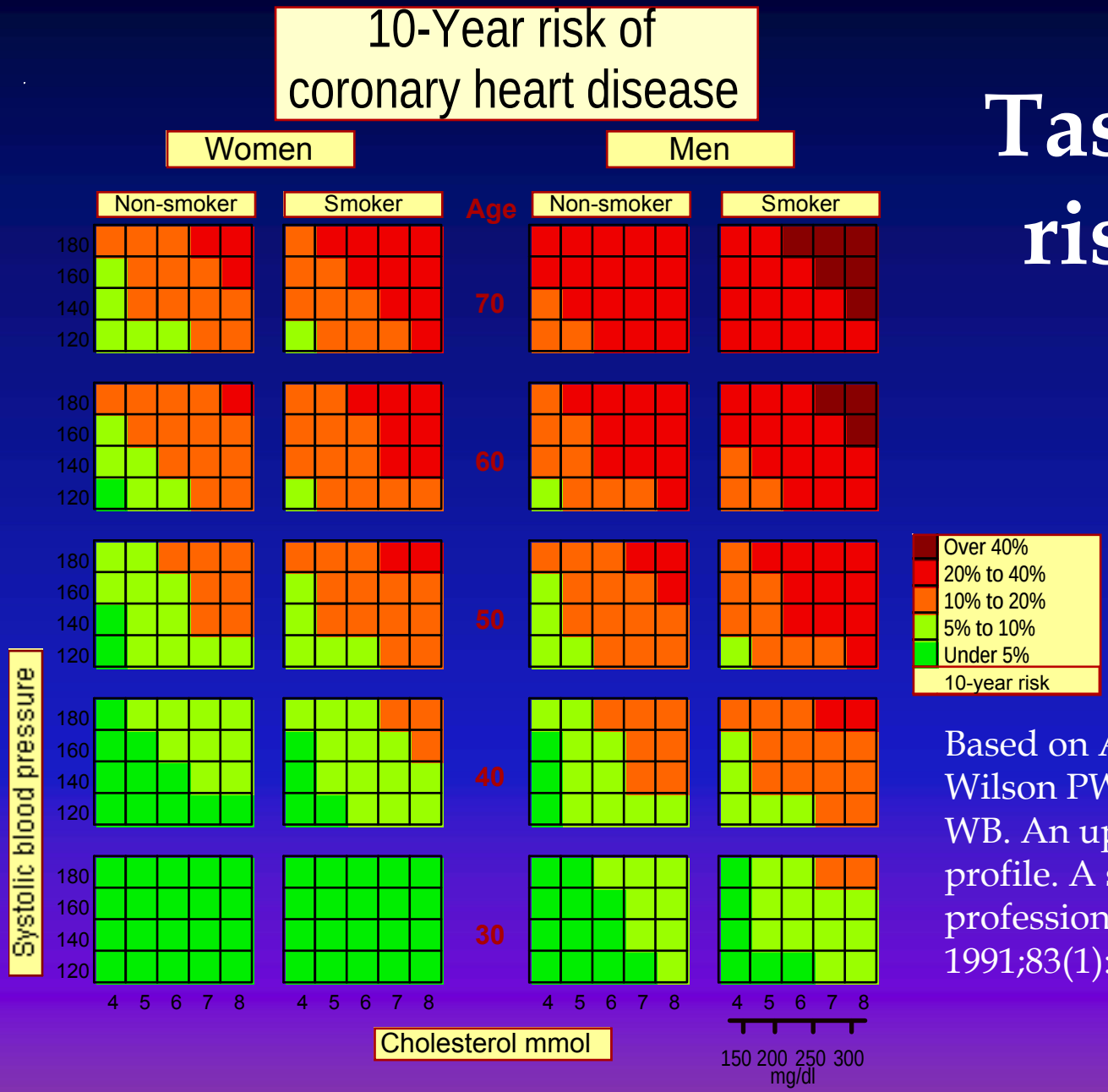
Smoking is the most important modifiable risk factor for development of abdominal aortic aneurysm (AAA) and not only leads to progression of aortic atherosclerosis, but also increases the risk of AAA formation and expansion .

Smoking - Smoking Duration and Risk of AAA: The Tromsø Study: Tromsø, Norway, 1994–2001

	Subjects, n	AAA, n	AAA, %	OR*	95% CI
Smoking status					
Never-smoker	1506	12	0.8	1.0	Reference
Stopped smoking 20 y ago	718	11	1.5	1.17	0.50–2.74
Stopped smoking 10–19 y ago	391	12	3.1	2.99	1.31–6.85
Stopped smoking <10 y ago	465	11	2.4	2.66	1.14–6.20
Current smoker <10 cigarettes/d	394	17	4.3	5.62	2.62–12.04
Current smoker 10 cigarettes/d	628	37	5.9	8.73	4.41–17.25
Current smoker 20 cigarettes/d	201	18	9.0	12.47	5.66–27.49
P for linear trend				<0.001	
Duration of smoking					
Never-smoker	1506	12	0.8	1.0	Reference
Smoked <20 y	800	3	0.4	0.44	0.12–1.58
Smoked 20–29 y	678	15	2.2	2.56	1.17–5.58
Smoked 30 y	1343	88	6.6	7.01	3.73–13.16
P for linear trend				<0.001	

*Adjusted for age and sex.

Task force risk chart



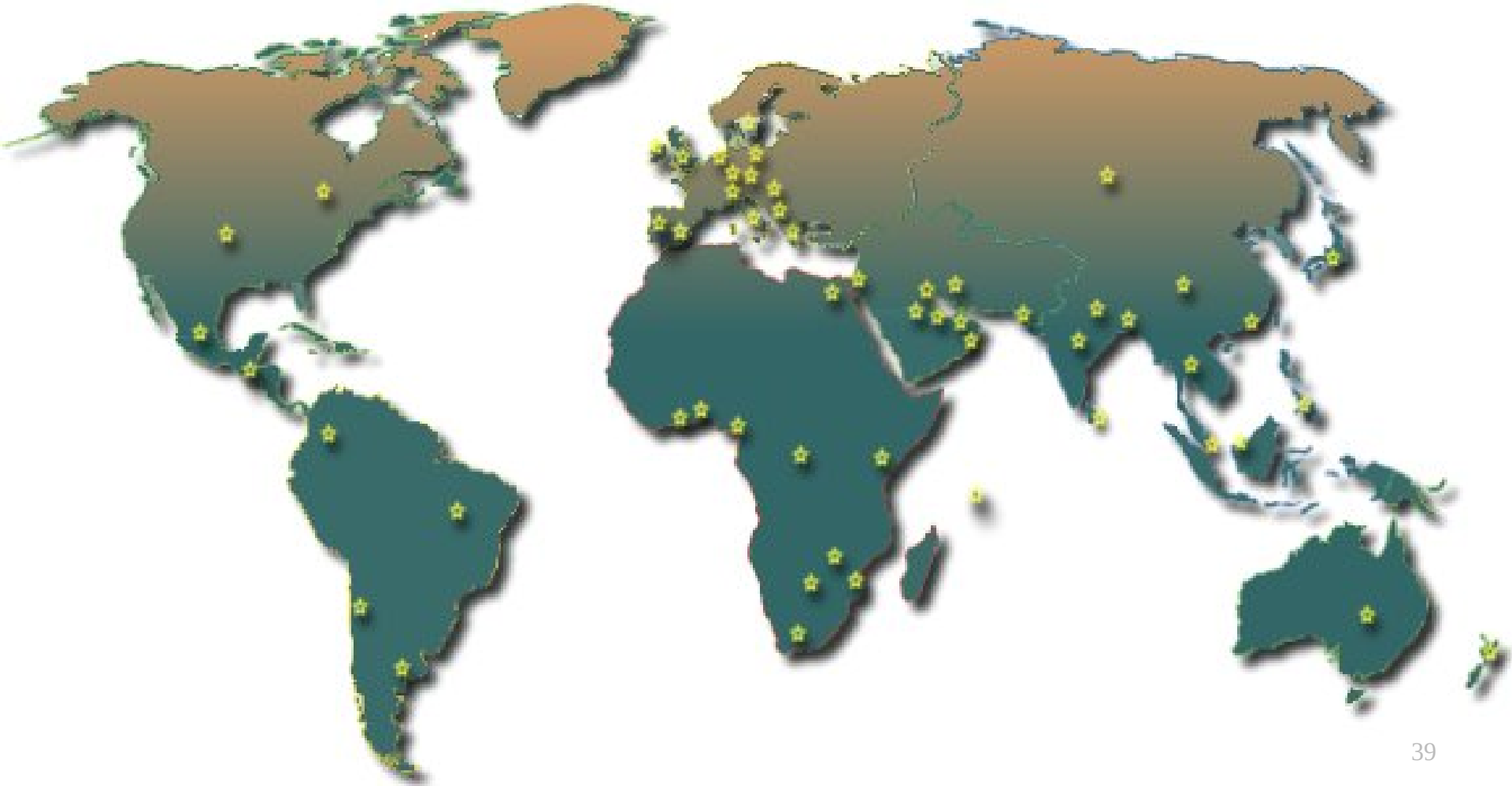
Based on Anderson KM, Wilson PW, Odell PM, Kannel WB. An updated coronary risk profile. A statement for health professionals. Circulation 1991;83(1):356-62

Tobacco use and risk of myocardial infarction in 52 countries in the INTERHEART study: a case-control study

Koon K Teo, Stephanie Ounpuu, Steven Hawken, MR Pandey, Vicent Valentin, David Hunt, Rafael Diaz, Wafa Rashed, Rosario Freeman, Lixin Jiang, Xiaofei Zhang, Salim Yusuf, on behalf of the INTERHEART Study Investigators

INTER-HEART

A Global Study of Risk Factors in Acute Myocardial Infarction

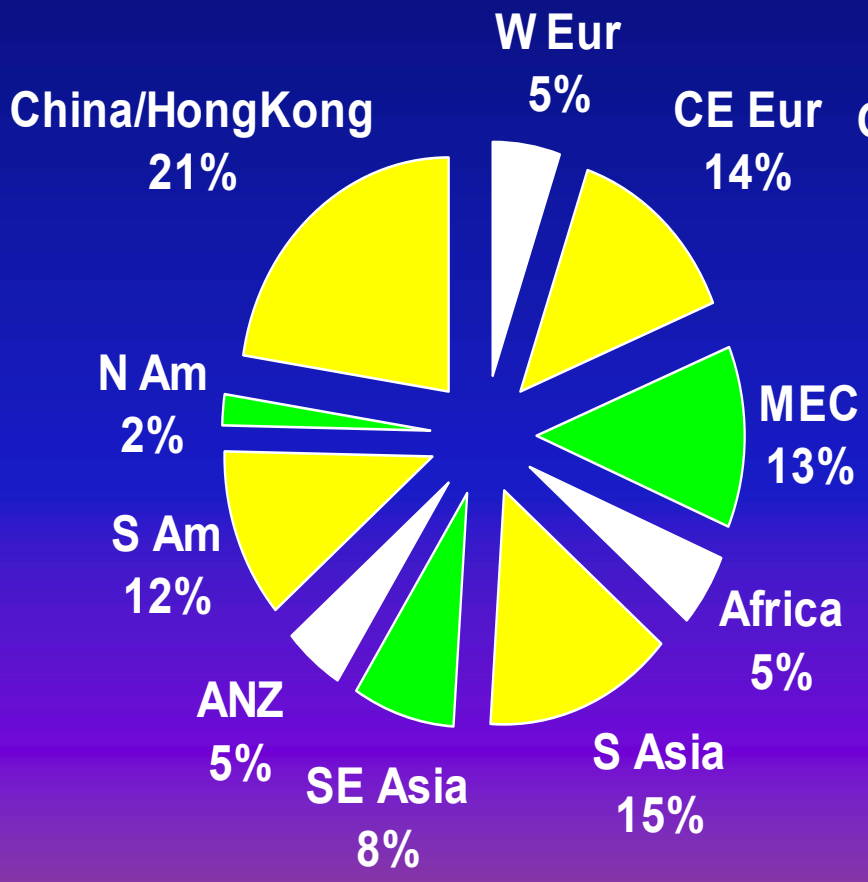


52 Countries Representing Every Inhabited Continent

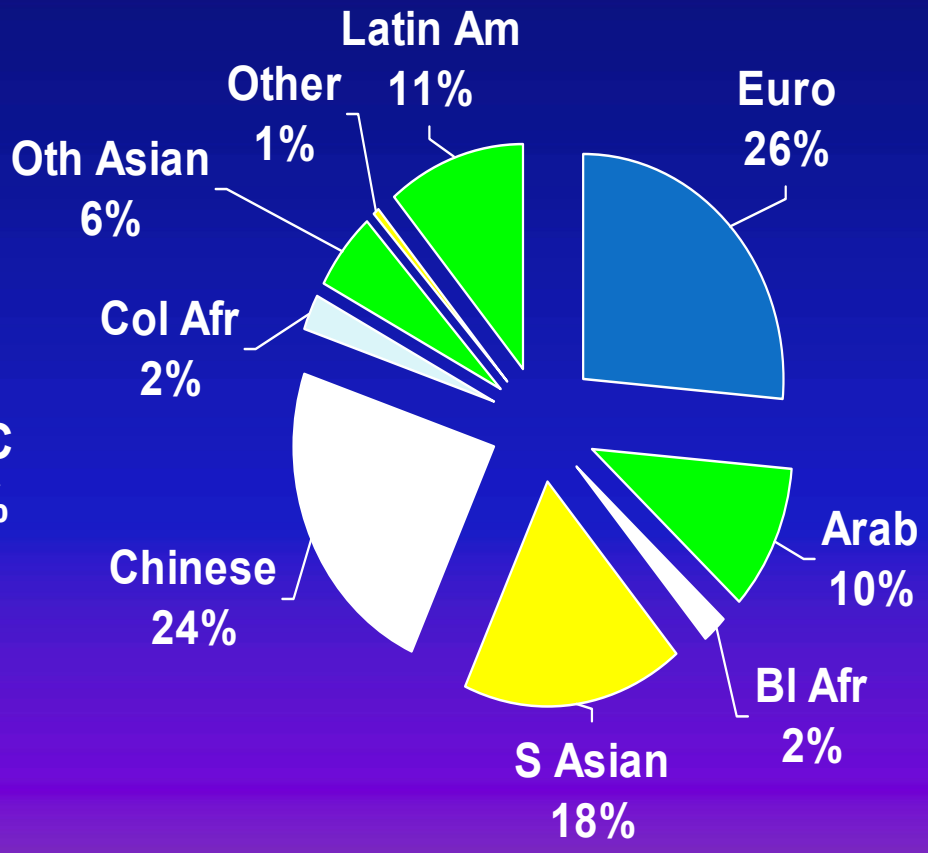
Argentina
Australia
Bahrain
Bangladesh
Benin
Botswana
Brazil
Cameroon
Canada
Chile
China/Hong Kong
Colombia
Croatia
Czech Rep
Egypt
Germany
Greece
Guatemala
Hungary
India
Iran
Israel
Italy
Japan
Kenya
Kuwait
Malaysia
Mexico
Mozambique
Nepal
New Zealand
Netherlands
Nigeria
Pakistan
Philippines
Poland
Portugal
Qatar
Russia
Seychelles
Singapore
S Africa
Spain
Sri Lanka
Sultanate of Oman
Sweden
Thailand
UAE
UK
USA
Zimbabwe

15,152 MI cases and 14,820 controls

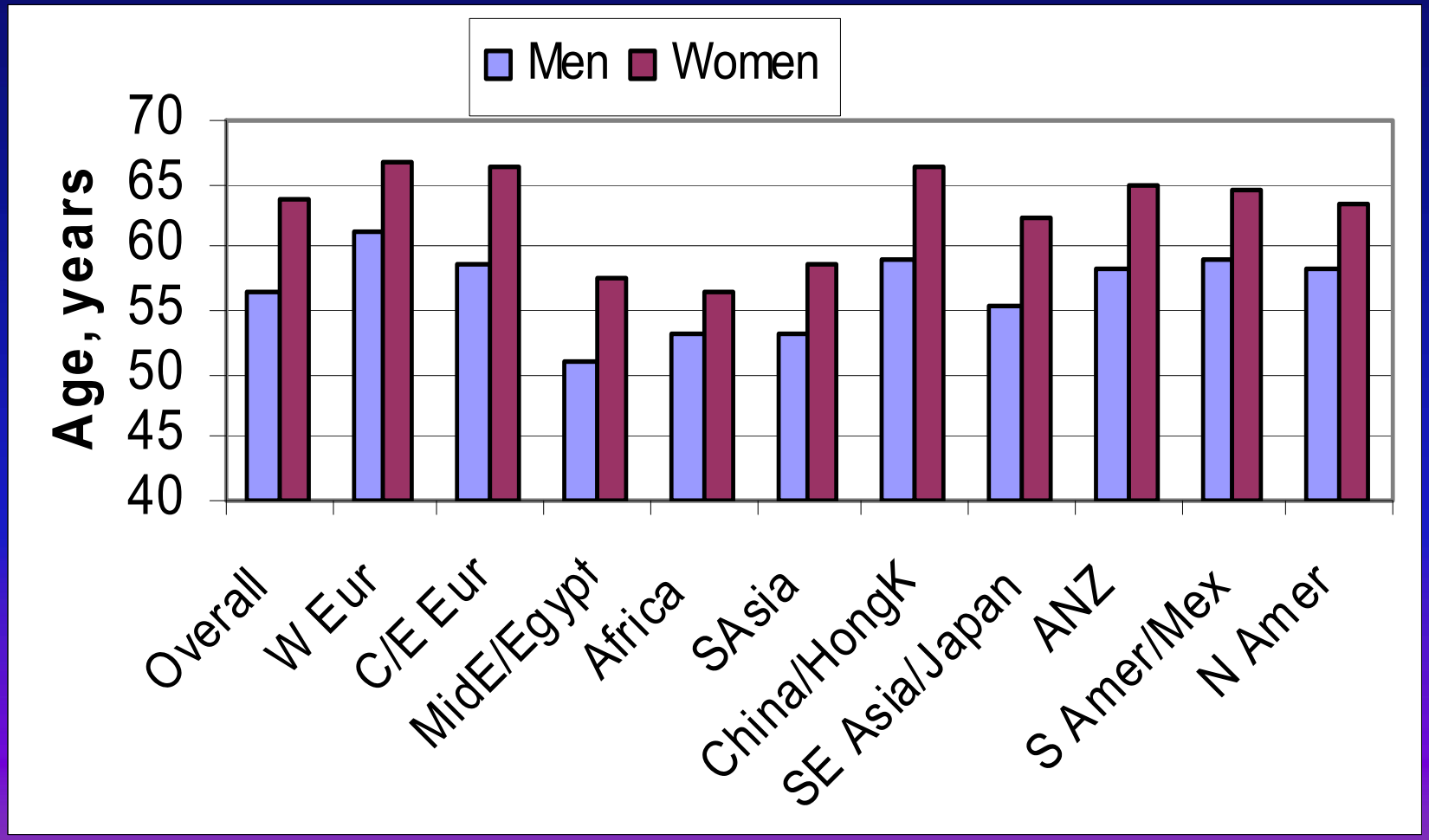
Distribution by region



Distribution by ethnicity



Mean age of male and female cases, overall and by region



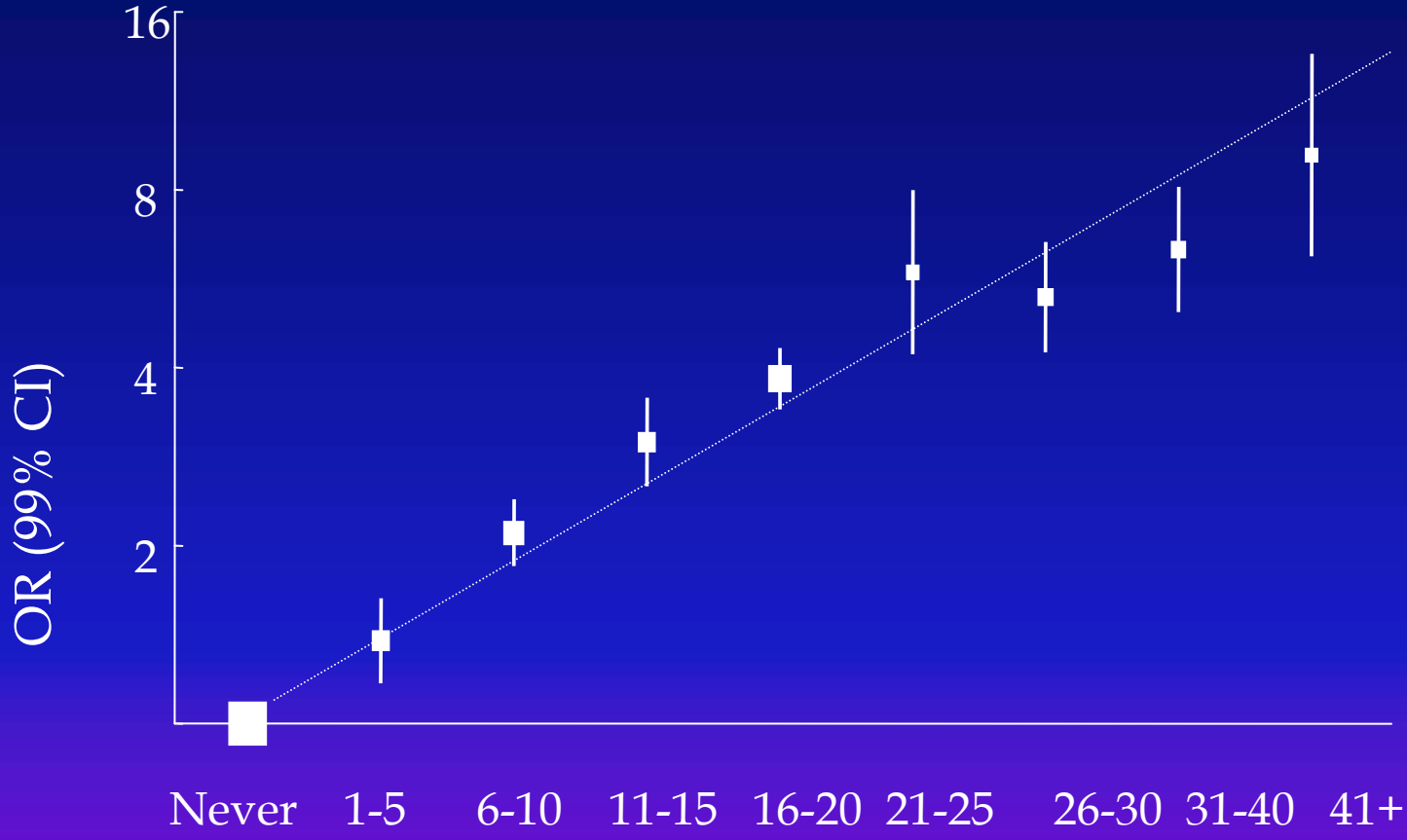
	Prevalence		Odds ratio (99% CI) adjusted for age, sex, and smoking (OR 1)	PAR (99% CI)	Odds ratio (99% CI) adjusted additionally for all other risk factors (OR 2)	PAR 2 (99% CI)
	Controls (%)	Cases (%)				
Risk factor						
Current smoking*	26·76	45·17	2·95 (2·72–3·20)	–	2·87 (2·58–3·19)	–
Current and former smoking*	48·12	65·19	2·27 (2·11–2·44)	36·4% (33·9–39·0)	2·04 (1·86–2·25)	35·7% (32·5–39·1)
Diabetes	7·52	18·45	3·08 (2·77–3·42)	12·3% (11·2–13·5)	2·37 (2·07–2·71)	9·9% (8·5–11·5)
Hypertension	21·91	39·02	2·48 (2·30–2·68)	23·4% (21·7–25·1)	1·91 (1·74–2·10)	17·9% (15·7–20·4)
Abdominal obesity (2 vs 1)†	33·40	30·21	1·36 (1·24–1·48)	–	1·12 (1·01–1·25)	–
Abdominal obesity (3 vs 1)†	33·32	46·31	2·24 (2·06–2·45)	33·7% (30·2–37·4)	1·62 (1·45–1·80)	20·1% (15·3–26·0)
All psychosocial‡	–	–	2·51 (2·15–2·93)	28·8% (22·6–35·8)	2·67 (2·21–3·22)	32·5% (25·1–40·8)
Vegetables and fruit daily*	42·36	35·79	0·70 (0·64–0·77)	12·9% (10·0–16·6)	0·70 (0·62–0·79)	13·7% (9·9–18·6)
Exercise*	19·28	14·27	0·72 (0·65–0·79)	25·5% (20·1–31·8)	0·86 (0·76–0·97)	12·2% (5·5–25·1)
Alcohol intake*	24·45	24·01	0·79 (0·73–0·86)	13·9% (9·3–20·2)	0·91 (o·82–1·02)	6·7% (2·0–20·2)
ApoB/ApoA1 ratio (2 vs 1)§	19·99	14·26	1·47 (1·28–1·68)	–	1·42 (1·22–1·65)	–
ApoB/ApoA1 ratio (3 vs 1)§	20·02	18·05	2·00 (1·74–2·29)	–	1·84 (1·58–2·13)	–
ApoB/ApoA1 ratio (4 vs 1)§	19·99	24·22	2·72 (2·38–3·10)	–	2·41 (2·09–2·79)	–
ApoB/ApoA1 ratio (5 vs 1)§	20·00	33·49	3·87 (3·39–4·42)	54·1% (49·6–58·6)	3·25 (2·81–3·76)	49·2% (43·8–54·5)
All above risk factors combined¶	–	–	129·20 (90·24–184·99)	90·4% (88·1–92·4)	129·20 (90·24–184·99)	90·4% (88·1–92·4)

The median waist /hip ratio was 0·93 in cases and 0·91 in controls (p<0·0001), and the median ApoB/ApoA1 ratio was 0·85 in cases and 0·80 in controls (p<0·0001). Percentage of controls with four or five factors positive is 22·2% compared with 29·2% in cases. *PARs for smoking, abdominal obesity, and ApoB/ApoA1 ratio are based on a comparison of all smokers vs never, top two tertiles vs lowest tertile, and top four quintiles vs lowest quintile. For protective factors (diet, exercise, and alcohol), PARs are provided for the group without these factors. †Top two tertiles vs lowest tertile. ‡A model-dependent index combining positive exposure to depression, perceived stress at home or work (general stress), low locus of control, and major life events, all referenced against non-exposure for all five factors. §Second, third, fourth, or fifth quintiles vs lowest quintile. ¶The model is saturated, so adjusted and unadjusted estimates are identical for all risk factors. The odds ratio of 129·20 is derived from combining all risk factors together, including current and former smoking vs never smoking, top two tertiles vs lowest tertile of abdominal obesity, and top four quintiles vs lowest quintile of ApoB/ApoA1. If, however, the model includes only current smoking vs never smoking, the top vs lowest tertile for abdominal obesity, and the top vs lowest quintile for ApoB/ApoA1, the odds ratio for the combined risk factors increases to 333·7 (99% CI 230·2–483·9).

Table 3: Risk of acute myocardial infarction associated with risk factors in the overall population

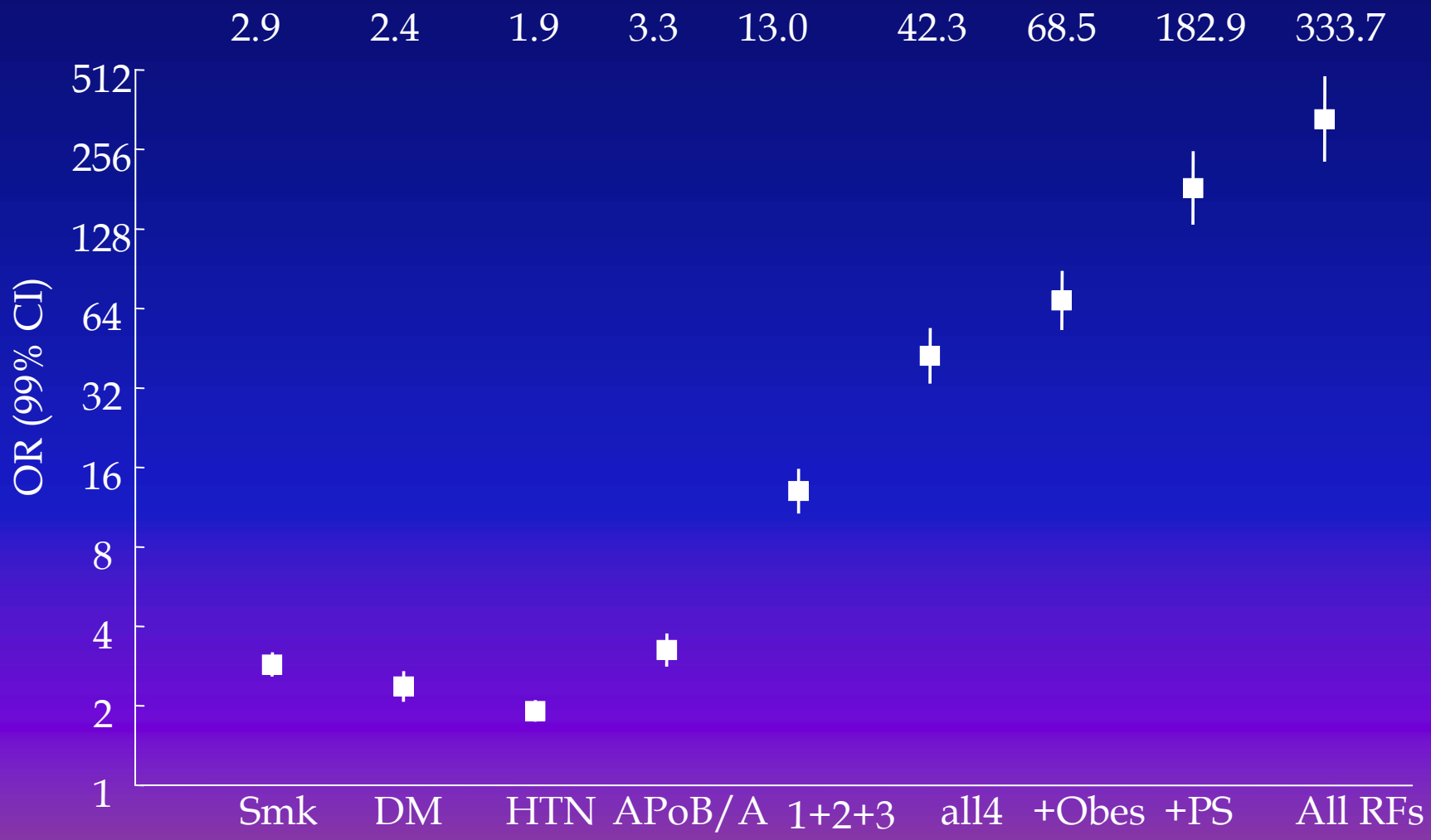
Cardiovascular risks increase with the number of cigarettes smoked each day, but the relationship is not straightforward.

INTERHEART: Smoking and MI

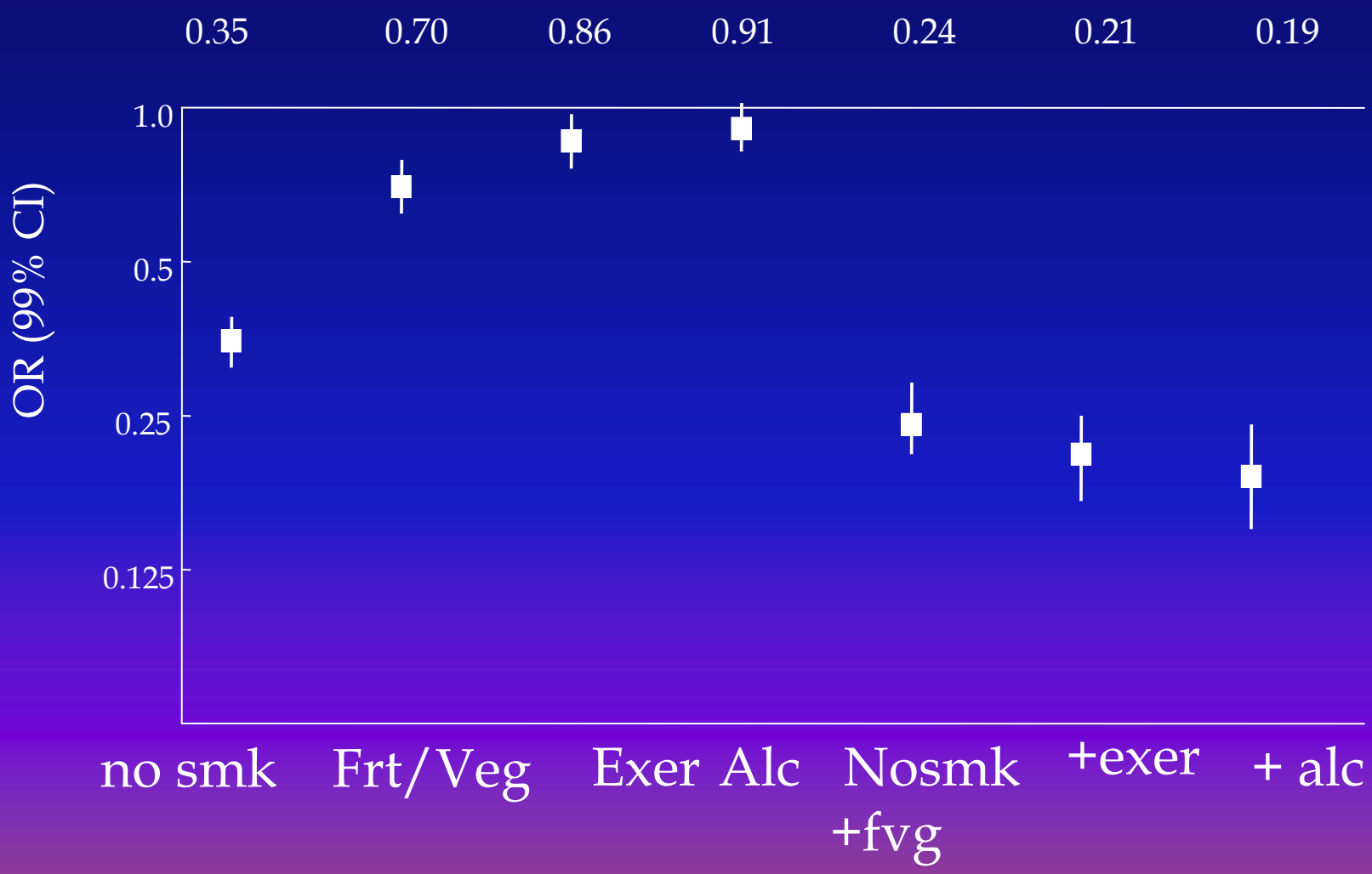


Cont	7489	727	1031	446	1058	96	230	168	56
Cases	4223	469	1021	623	1832	254	538	459	218
OR	1	1.38	2.10	2.99	3.83	5.80	5.26	6.34	9.16

INTERHEART:Risk of AMI with Multiple Risk Factors



INTERHEART: Decreased Risk of AMI with Avoidance of Smoking; Daily Fruits/Veg, Reg Phys Activity & Alcohol



Second hand smoke (SHS) increases the risk of heart disease by 30%, accounting for at least 35 000 deaths annually in the United States.

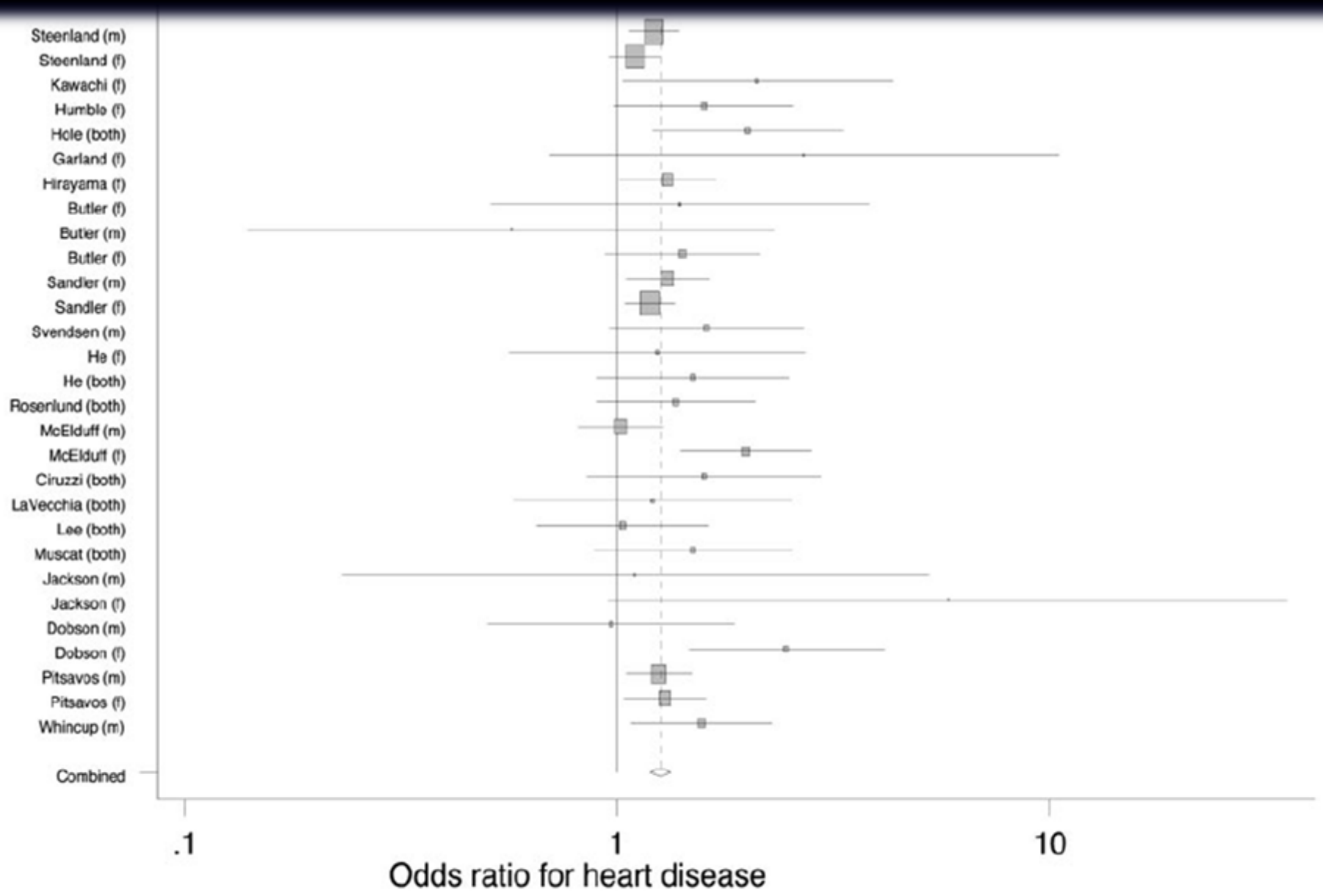


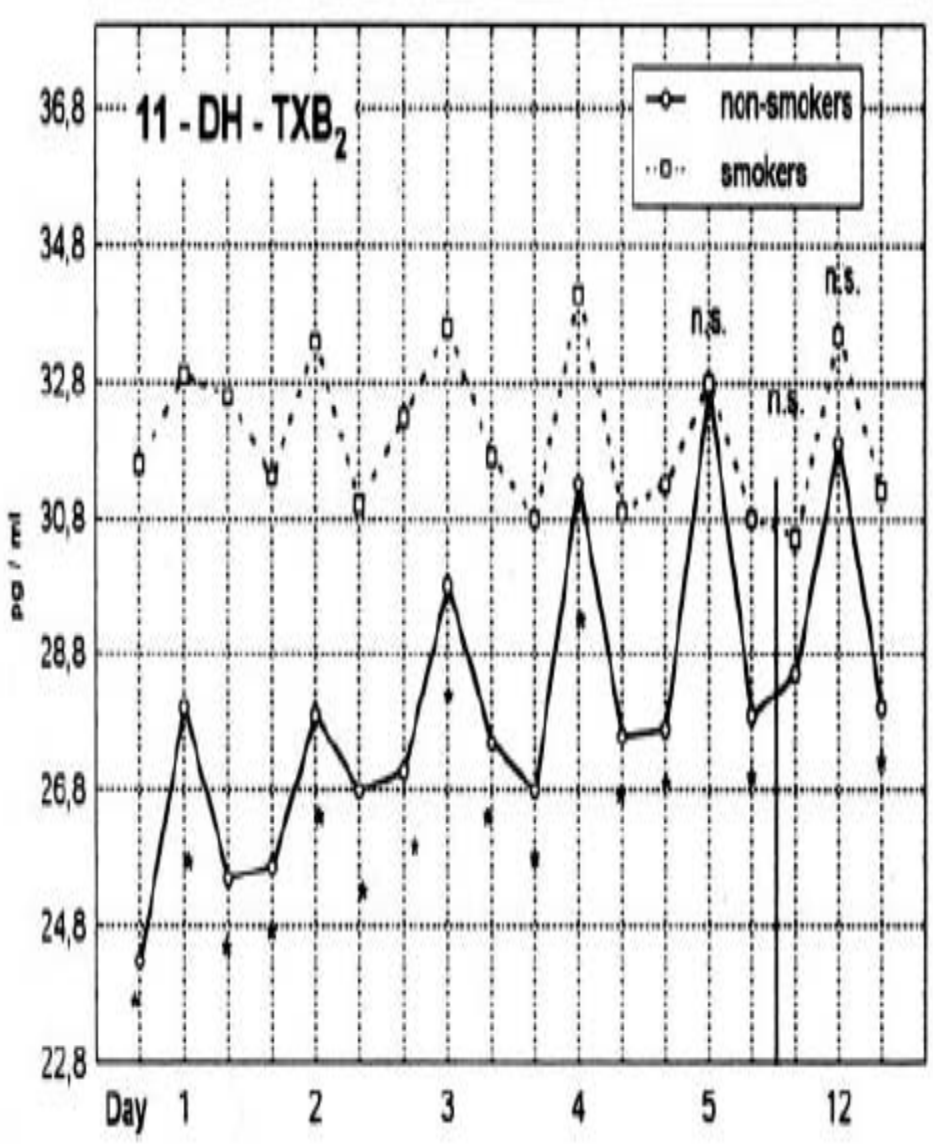
Figure 1. Summary of epidemiological studies on passive smoking and coronary heart disease, together with results of random-effects meta-analysis. There was no significant heterogeneity ($P=0.1$), but we used random-effects model to be conservative. Citations for individual studies are as follows: Steenland et al,[152] Kawachi et al,[153] Humble et al,[154] Hole et al,[155] Garland et al,[156] Hirayama,[157] Butler,[158] Sandler et al,[159] Svndsen et al,[160] He et al,[6] Roselund et al,[26] McElduff et al,[161] Ciruzzi et al,[162] LaVecchia et al,[163] Lee et al,[164] Muscat and Wynder,[165] Jackson,[166] Dobson et al,[167] Pitsavos et al,[24] and Whincup et al.[28]

Effects of SHS on the Cardiovascular System

- Platelet activation
- Endothelial dysfunction
- Inflammation and infection
- Atherosclerosis
  - Low HDL levels
  - Plaque instability
  - Increased oxidized LDL
- Increased oxidative stress
- Decreased energy metabolism
- Increased insulin resistance
- Outcome measures
  - Increased infarct size
  - Decreased heart rate variability
  - Increased arterial stiffness
  - Increased risk of coronary disease events

TABLE 2. Comparative Effects of Passive and Active Smoking*

	SHS Effect†	Exposure	Active Effect‡	SHS/Active Effect,§ %
Risk of heart disease (95% CI)				
Figure 1	1.31 (1.21 to 1.41)	Chronic	1.78 (1.31 to 2.44)‖	40
20 y[28]	1.57 (1.08 to 2.28)¶	Cotinine at study entry	1.66 (1.04 to 2.68)	86
First 4 y[28]	3.73 (1.32 to 10.98)	Cotinine at study entry	3.32 (0.87 to 12.64)	122
Platelet function				
Platelet activation[31] (SI PGI_2)#	0.55±0.059	20 min	0.54±0.069	96
Platelet aggregate ratio[32,32a] (change)	−0.09	20 min	−0.15	60
Fibrinogen,[87] mg/dL (95% CI)	5.2 (−1.2 to 12)	Chronic	6.9 (−0.9 to 14)	75
Fibrinogen,[38] mg/dL (SE)	11.2±4.1	Chronic	18.1±6.7	62
Plasma thromboxane,[40] pg/mL	3.30±0.35	Acute	2.93±0.07	113
Plasma malondialdehyde,[40] nmol/L per 10^9 platelets	4.2±0.17	Acute	3.9±0.07	108
Endothelium and arterial function				
Endothelial cell count,[32,32a] mean No. of anuclear cell carcasses on 0.9-μL chamber (change)	0.9	20 min	2.0	45
Coronary flow velocity reserve,[43] cm/s	68.8±22.7	30 min	67.1±15.0	91
Flow-mediated dilation,[45] %	3.1±2.7	≥3 y	4.4±3.1	134
Aortic stiffness,[67,68] mm Hg/mm	58	4 minutes	49	110
HDL,[77] mg/dL	48.26±3.47	Chronic	45.59±4.6	73
Increase in IMT,[98] μm/3 y	5.9	Chronic	14.3	41
Inflammatory markers[87] (95% CI)				
White blood cells, $\times 10^3$ per 1 μL	0.6 (0.3 to 0.8)	Chronic	0.6 (0.5 to 0.7)	100
C-reactive protein, mg/dL	0.08 (0.02 to 0.1)	Chronic	0.1 (0.08 to 0.2)	80
Homocysteine, μmol/L	0.4 (0.2 to 0.6)	Chronic	0.5 (0.1 to 0.9)	80
Oxidized LDL, mg/dL	3.3 (0.5 to 6)	Chronic	3.9 (1.4 to 7)	85
Antioxidants				
Vitamin C,[120] median (interquartile range), μmol/L	53 (41 to 79)	Chronic	40 (25 to 58)	57



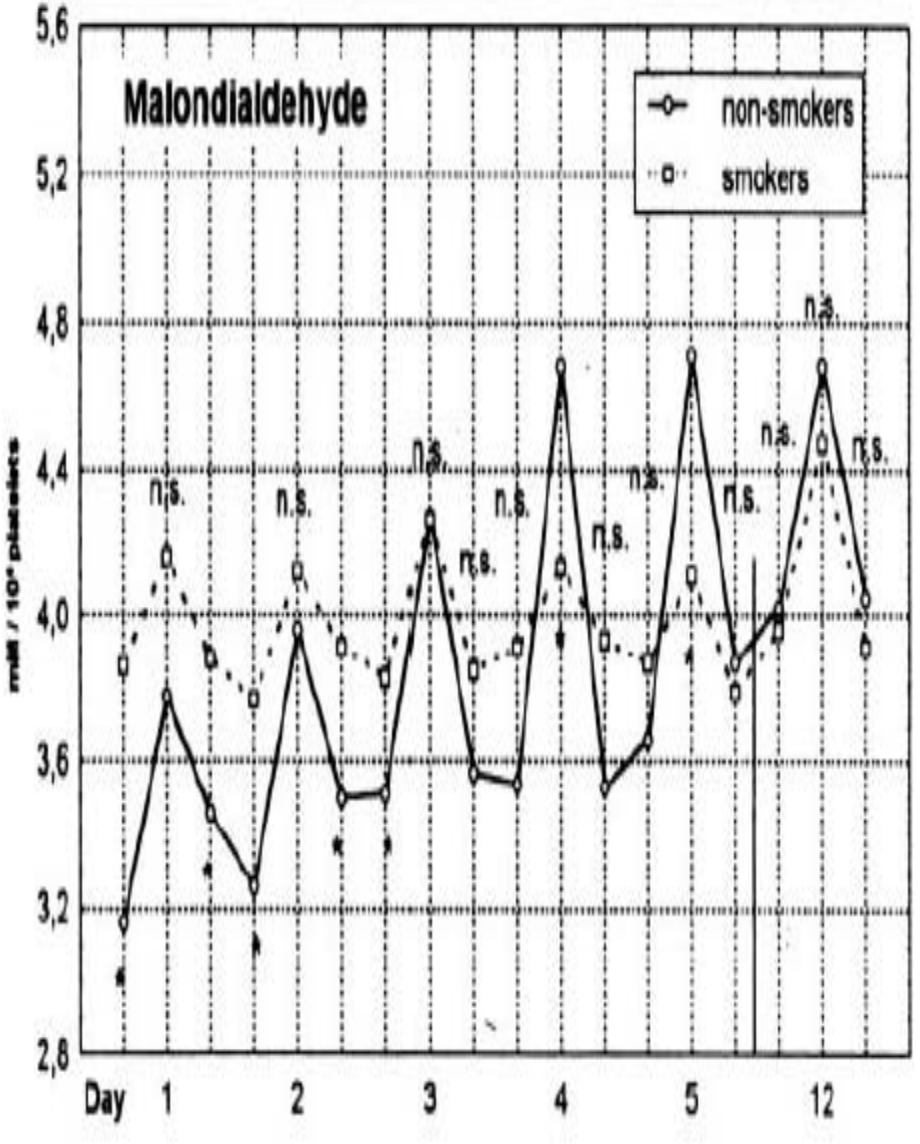
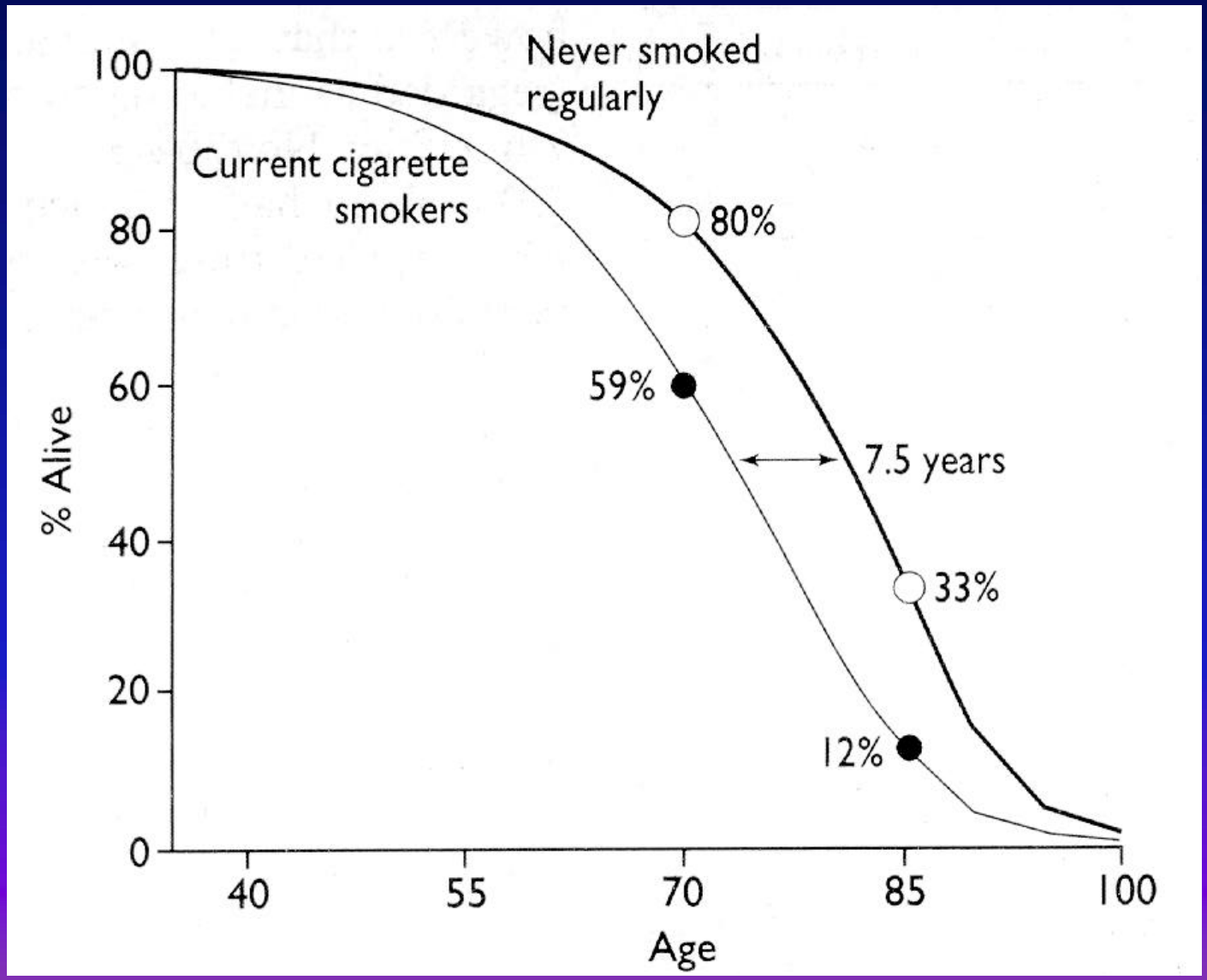
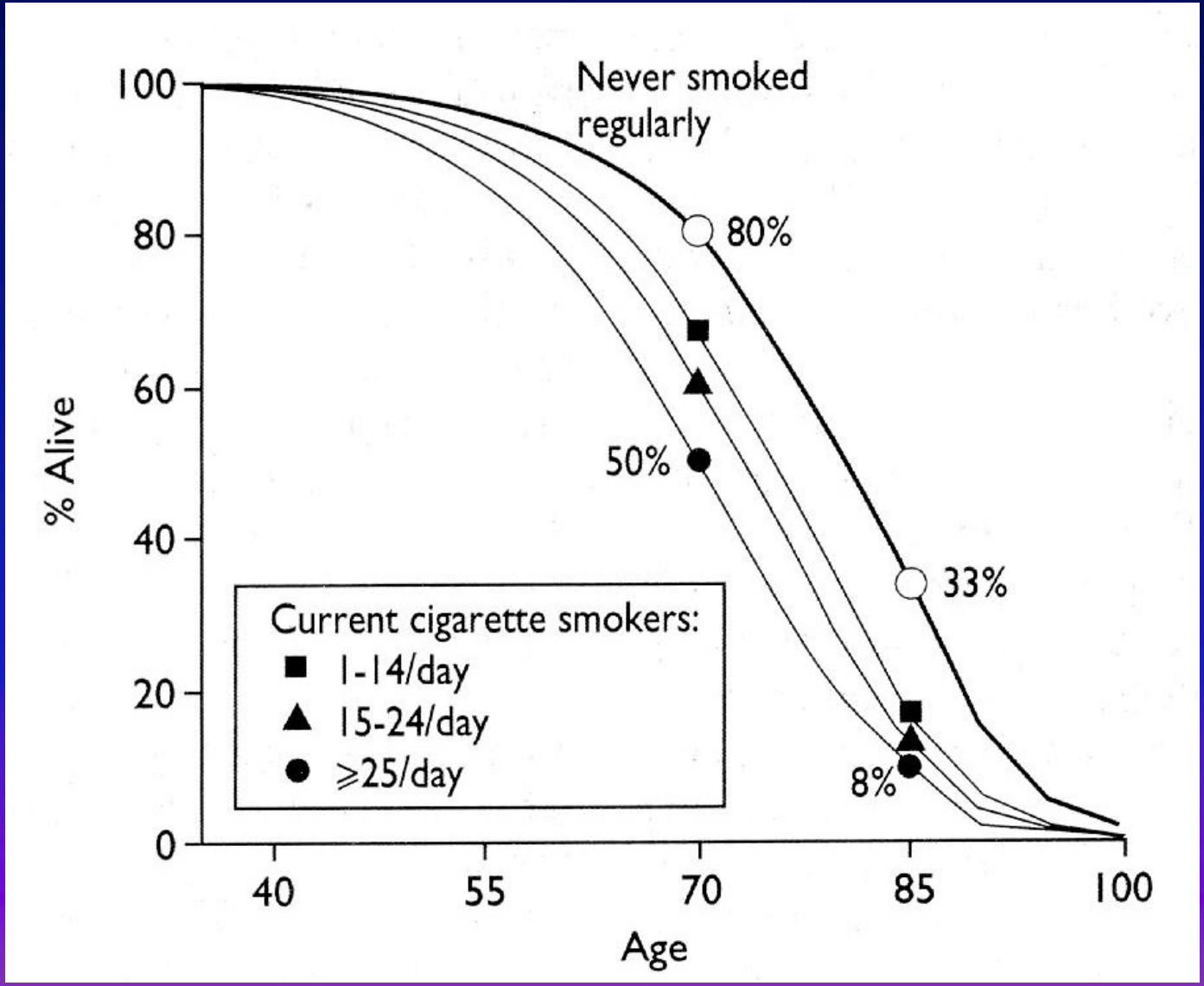


Figure 2. Exposure to 60 minutes of SHS increased measures of platelet activation; repeated exposures over several days led to levels in nonsmokers comparable to smokers. *$P<0.05$. Reproduced from Figure 1 of Schmid et al,[40] copyright 1996, with permission from Elsevier.

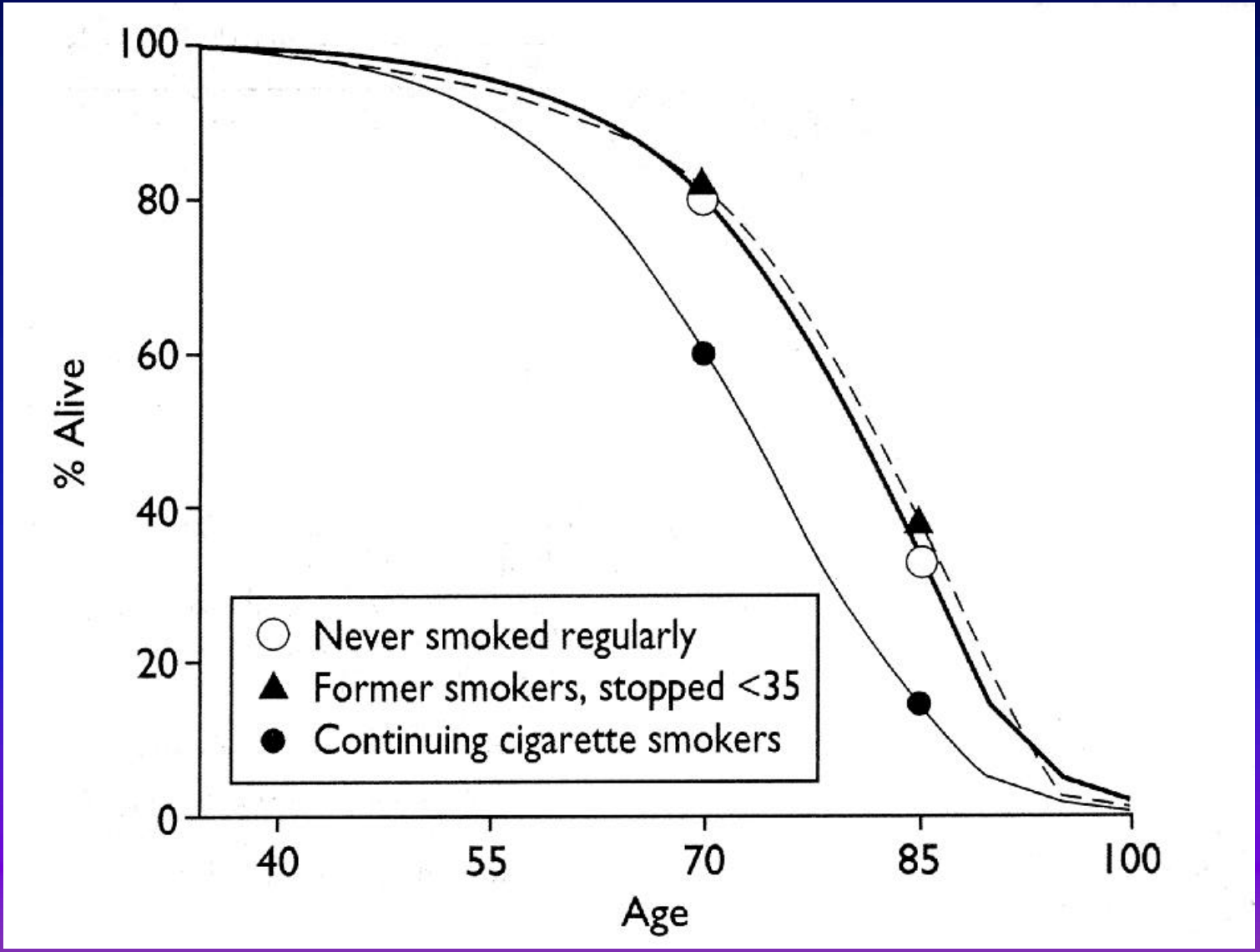
Overall survival after age 35 among cigarette smokers and non- smokers: life table estimates, based on age specific death rates for the entire 40 year period.



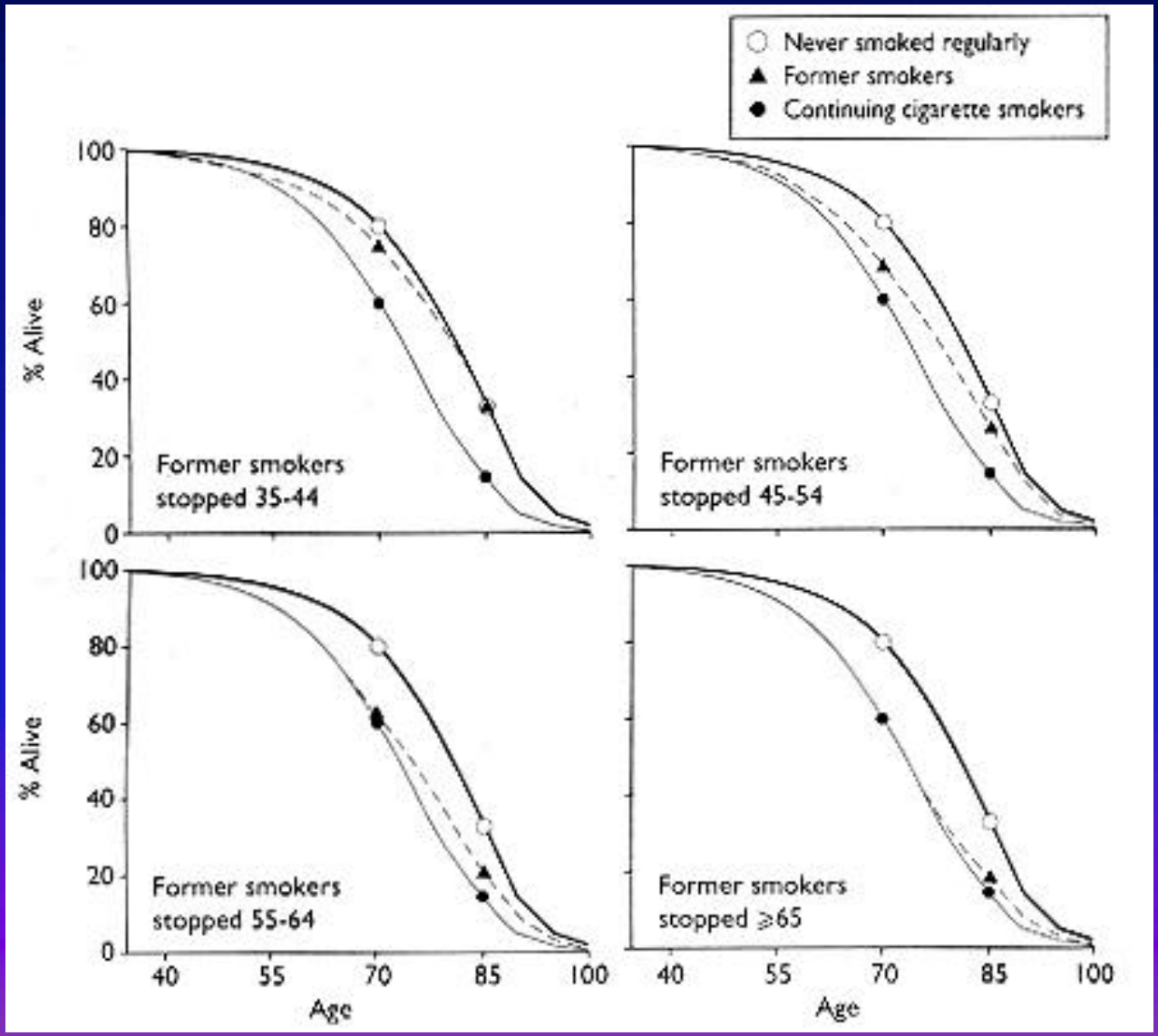
Overall survival (as fig 1), but with cigarette smokers subdivided by amount they were smoking at the time their last questionnaire was returned.



Effects on survival after age 35 of stopping smoking before age 35: life table estimates



Effects on survival after ages 45, 55, 65, and 75 of stopping smoking in previous decade: life table estimates .

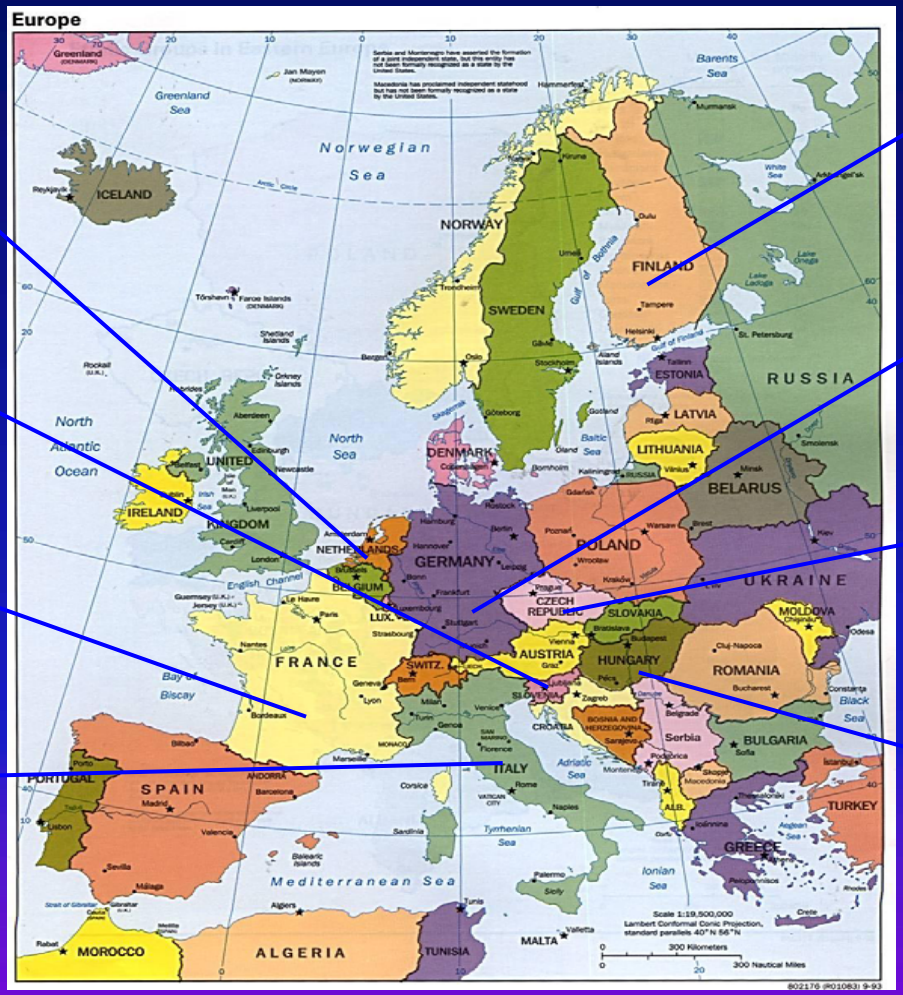


Risk factor management in coronary patients – results from a European wide survey

EUROASPIRE III

Professor David A Wood
on behalf of the EUROASPIRE Investigators

EUROASPIRE I, II and III



Netherlands

Slovenia

France

Italy

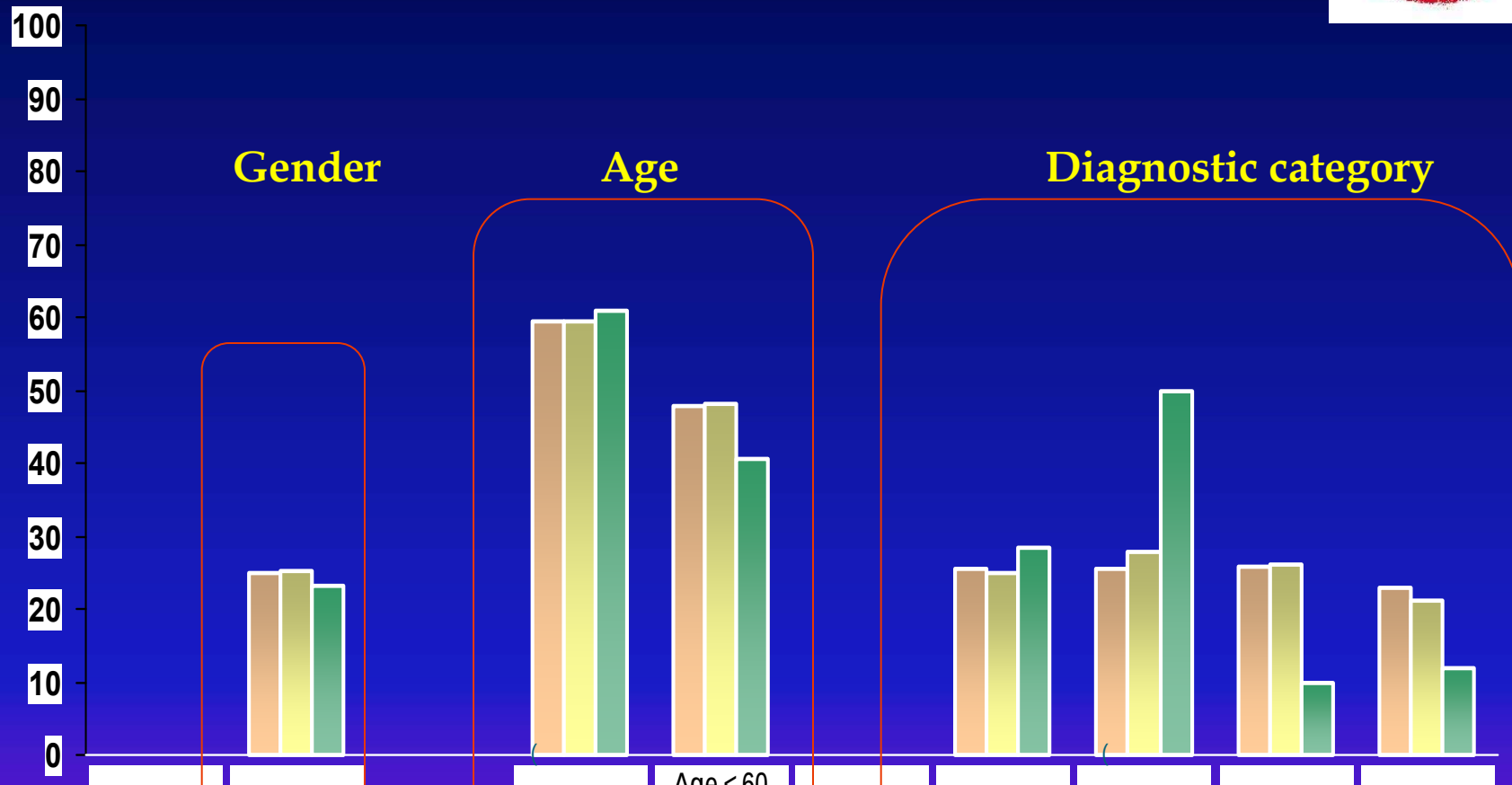
Finland

Germany

Czech Republic

Hungary

Distribution of Age, Gender and Diagnostic Category



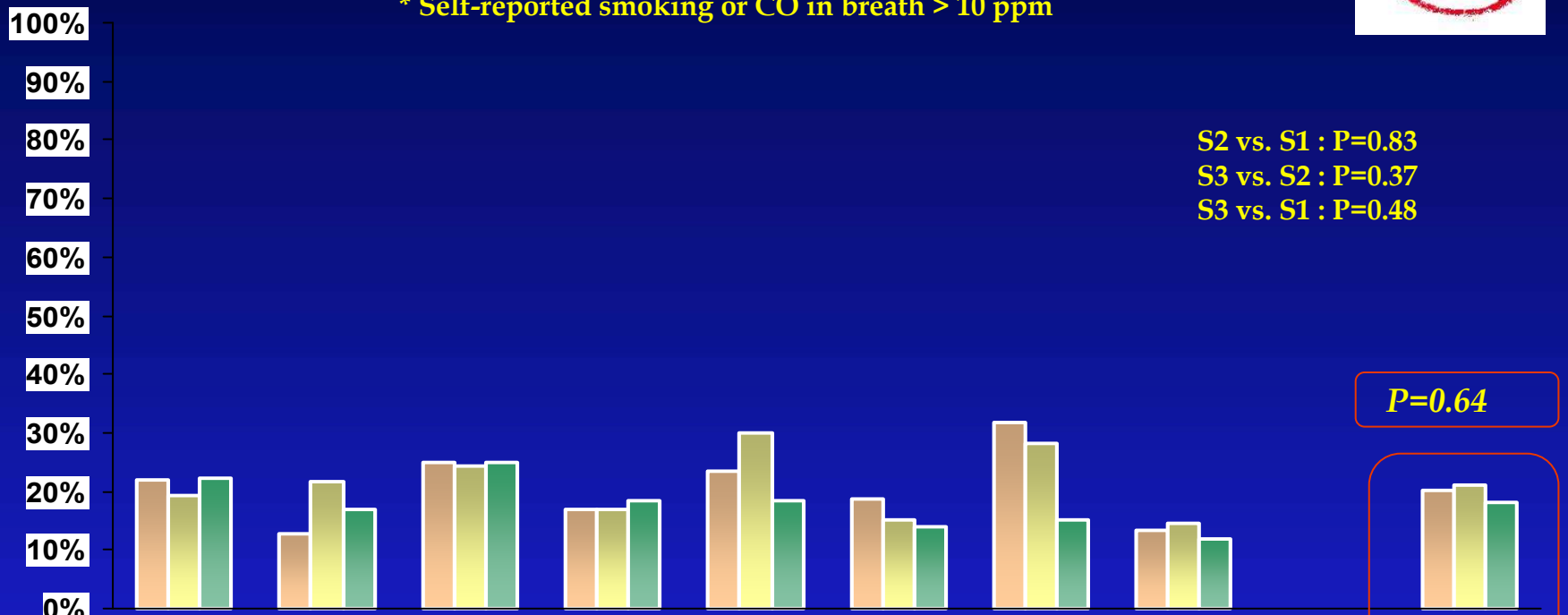
	Women (%)	Mean age (years)	Age < 60 yrs (%)	CABG (%)	PTCA (%)	AMI (%)	ISCHAEMIA (%)
Survey 1	24,9	59,3	47,8	25,6	25,6	25,8	23,0
Survey 2	25,2	59,4	48,1	24,8	27,8	26,1	21,2
Survey 3	23,1	60,9	40,6	28,3	49,8	9,9	12,0

Prevalence of Smoking*

* Self-reported smoking or CO in breath > 10 ppm

S2 vs. S1 : P=0.83
S3 vs. S2 : P=0.37
S3 vs. S1 : P=0.48

P=0.64



	Czech Rep.	Finland	France	Germany	Hungary	Italy	Nether-lands	Slovenia		ALL
Survey 1	22,0%	12,8%	25,0%	16,8%	23,3%	18,6%	31,8%	13,3%		20,3%
Survey 2	19,3%	21,6%	24,2%	16,8%	30,1%	15,1%	28,3%	14,6%		21,2%
Survey 3	22,2%	16,8%	24,8%	18,4%	18,3%	14,0%	15,1%	12,0%		18,2%

Some investigators have suggested that a pill that combines a statin, antihypertensive drugs, and aspirin, together with avoidance of smoking, could potentially reduce the risk of myocardial infarction by more than 80% to 90%.

Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. *BMJ 2003;* ***326: 1419–23.***