CORONARY RISK FACTORS

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CARDIOVASCULAR DISEASE DIMENSION OF THE PROBLEM

- First cause of death in the world, but for Sub-Saharan Africa.
- It killed 14.7 millions of people in 1990 and 17 millions in 1999 (WHO).
- 30% of all deaths are cardiovascular.
- 80% of these deaths occur in poor countries (China, Russia, Poland, Mauritania, Argentina, India, etc.)

Circulation 2002; 106: 1602.

Mortality by ischemic heart disease by gender and region. 1990-2020 projection.

	Women			Men		
Region	1990	2020	% Increase	1990	2020	% Increase
EME	838	1107	32	829	1209	46
FSE	559	702	26	468	712	52
Total developed countries	1397	1809	29	1297	1921	48
India	556	1197	115	619	1405	127
China	377	684	81	386	811	110
OAI	227	552	143	233	581	149
SSA	117	263	125	92	222	141
Latin America	169	412	144	179	444	148
Middle East	291	717	146	319	874	174
Total developing countries	1737	3825	120	1828	4337	137
World	3134	5634	80	3125	6258	100

Yusuf et al. Circulation Nov. 2001

Mortality by cerebrovascular disease by gender and region. 1990-2020 projection.

	Women			Men		
Region	1990	2020	% Increase	1990	2020	% Increase
EME	467	618	32	322	477	59
FSE	400	495	24	239	364	52
Total developed countries	867	1113	28	539	841	56
India	220	463	104	227	493	124
China	601	1087	81	672	1413	110
OAI	200	458	129	190	446	135
SSA	231	521	126	152	356	134
Latin America	127	302	138	121	297	145
Middle East	113	269	138	99	255	158
Total developing countries	1499	3100	107	1454	3260	124
World	2366	4213	78	1993	4101	106

Yusuf et al. Circulation Nov. 2001

Percentages of urban population from 1970 through 2025

Region	1970	1994	2025
World	36.6	44.8	61.1
Developed countries	67.5	74.4	84.0
Economies in transition*	25.1	37.0	57.0
Developing countries	12.6	21.9	43.5

*Current term for Eastern Europe.

Yusuf et al. Circulation Nov. 2001

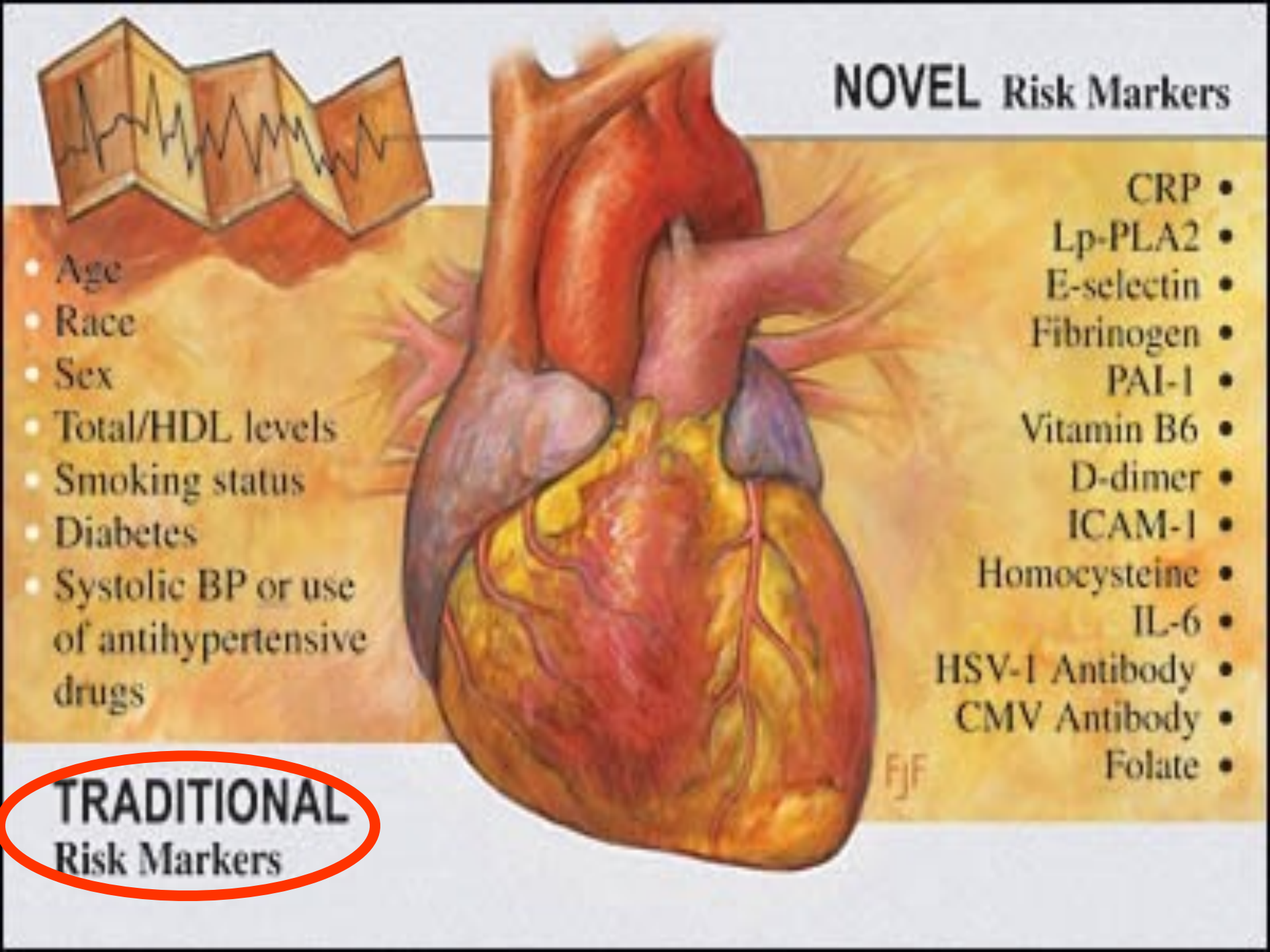
The stages of epidemiological transition

- 1) Sub-Saharan Africa; South American rural areas: Infectiones. Malnutrition.
- 2) China: ↑Hypertension. ↓Infections and malnutrition.
- 3) India; South America: ↑Coronary risk factors (CRF). ↑Ischemic heart disease.
- 4) Europe; North America; Australia: ↓CRF. ↓Ischemic heart disease.
- 5) Russia: ↑Ischemic heart disease. ↑Infections. ↑Accidents.

MAJOR RISK FACTORS
(Hypertension, smoking, dyslipemia, or diabetes)
AS BACKGROUND OF CORONARY EVENTS

- **3 prospective studies: CHICAGO, MRFIT & FRAMINGHAM**
- **N= 386,915 (18 to 59 years old)**
- **Fatal coronary disease: 1 or more CRF present in 87 to 100% of the cases.**
- **Nonfatal AMI: 1 or more CRF present in 92% of men and 87% of women.**

Greenland et al.; JAMA August 2003.


NOVEL Risk Markers
CRP
Lp-PLA2
E-selectin
Fibrinogen
PAI-1
Vitamin B6
D-dimer
ICAM-1
Homocysteine
IL-6
HSV-1 Antibody
CMV Antibody
Folate
Age
Race
Sex
Total/HDL levels
Smoking status
Diabetes
Systolic BP or use of antihypertensive drugs
TRADITIONAL
Risk Markers
FJF

OBESITY: A MODERN EPIDEMICS

- In USA:
- 35% of adults are overweight (BMI 25 to 30 $kg/m^{2)}$
- 26% are obese (BMI ≥ 30)
- 29% does not perform any physical activity
- 46% performs suboptimal activities

Circulation 2002; 106: 1602.

METABOLIC SYNDROME
(ATP III)

- A) Abdominal obesity (waist circumference): Men ≥ 102 cm

  Women ≥ 88 cm
- B) Triglycerides ≥ 150 mg%
- C) HDL cholesterol

  Men < 40 mg%

  Women < 50 mg%
- D) Blood pressure ≥ 130 / 85 mmHg
- E) Fasting glycemia ≥ 110 mg%

Metabolic syndrome as predictor of CAD and diabetes *WOSCOPS Study*

Disease	Hazard ratio	95% CI	p
CAD	1.76	1.44-2.15	<0.001
Diab	3.51	2.48-4.98	<0.001

Follow up: 5 years

Sattar N et al. *Circulation* 2003.

Risk of CAD and diabetes according to the number of components present in the MS

Nº of factors	HR for CAD (95% CI)	HR for diab (95% CI)
1	1.79 (1.11-2.89)	2.36 (0.71-7.93)
2	2.25 (1.40-3.60)	4.50 (1.39-14.6)
3	3.19 (1.98-5.12)	7.26 (2.25-23.4)
4-5	3.65 (2.11-6.33)	24.4 (7.53-79.6)

Sattar N et al. *Circulation* 2003.

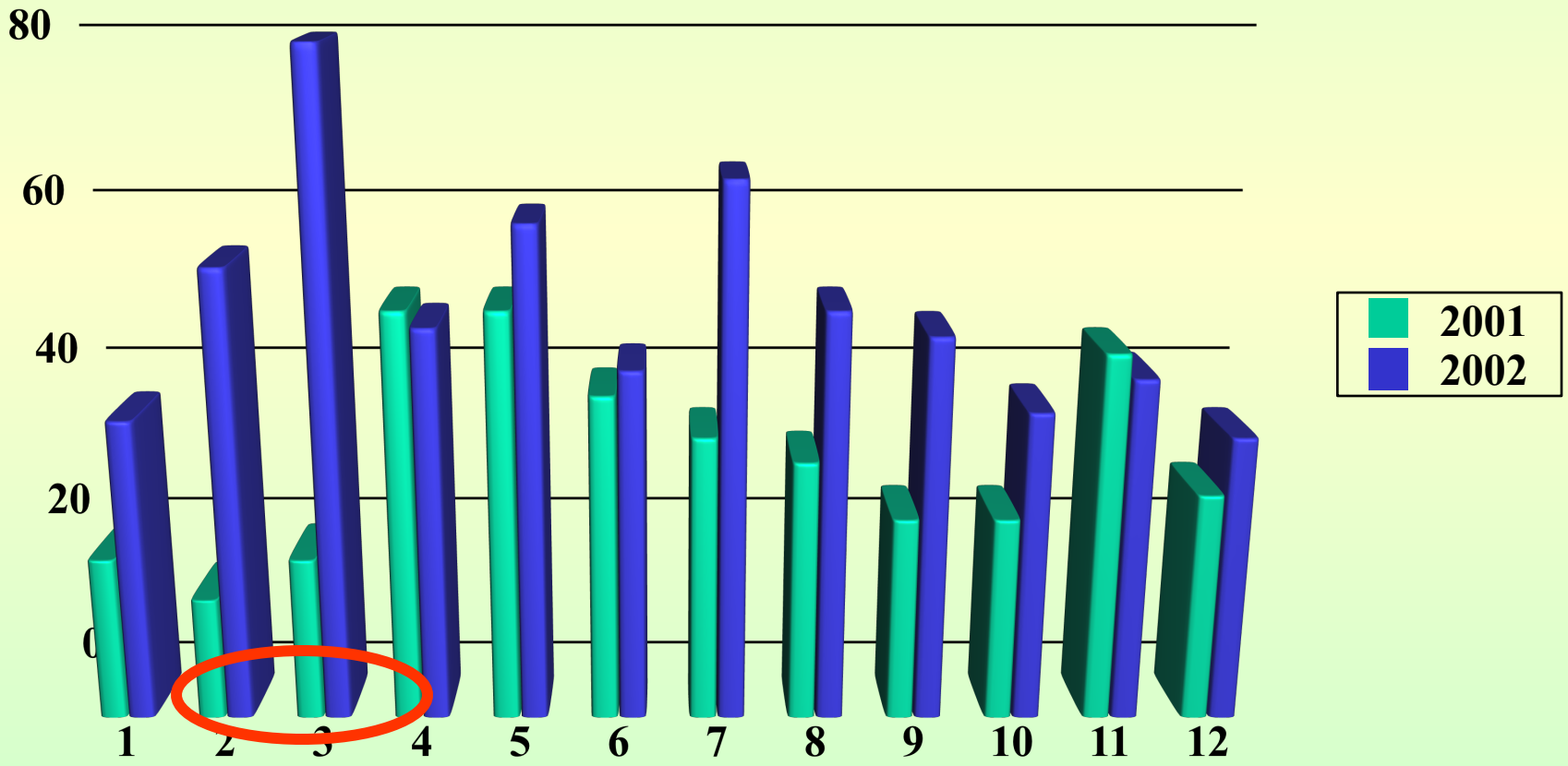
"HEREDOFAMILIAL" BACKGROUND THE GENECARD PROJECT

- Frequency of CRF in patients with familial premature coronary artery disease:
- Hypertension: 43%
- Hypercholesterolemia: 58%
- Smoking: 72%
- Obesity: 21%
- **Only 4% did not have any classical CRF**

Jomini et al; JACC August 2002

ADMITTANCES IN CV EMERGENCY

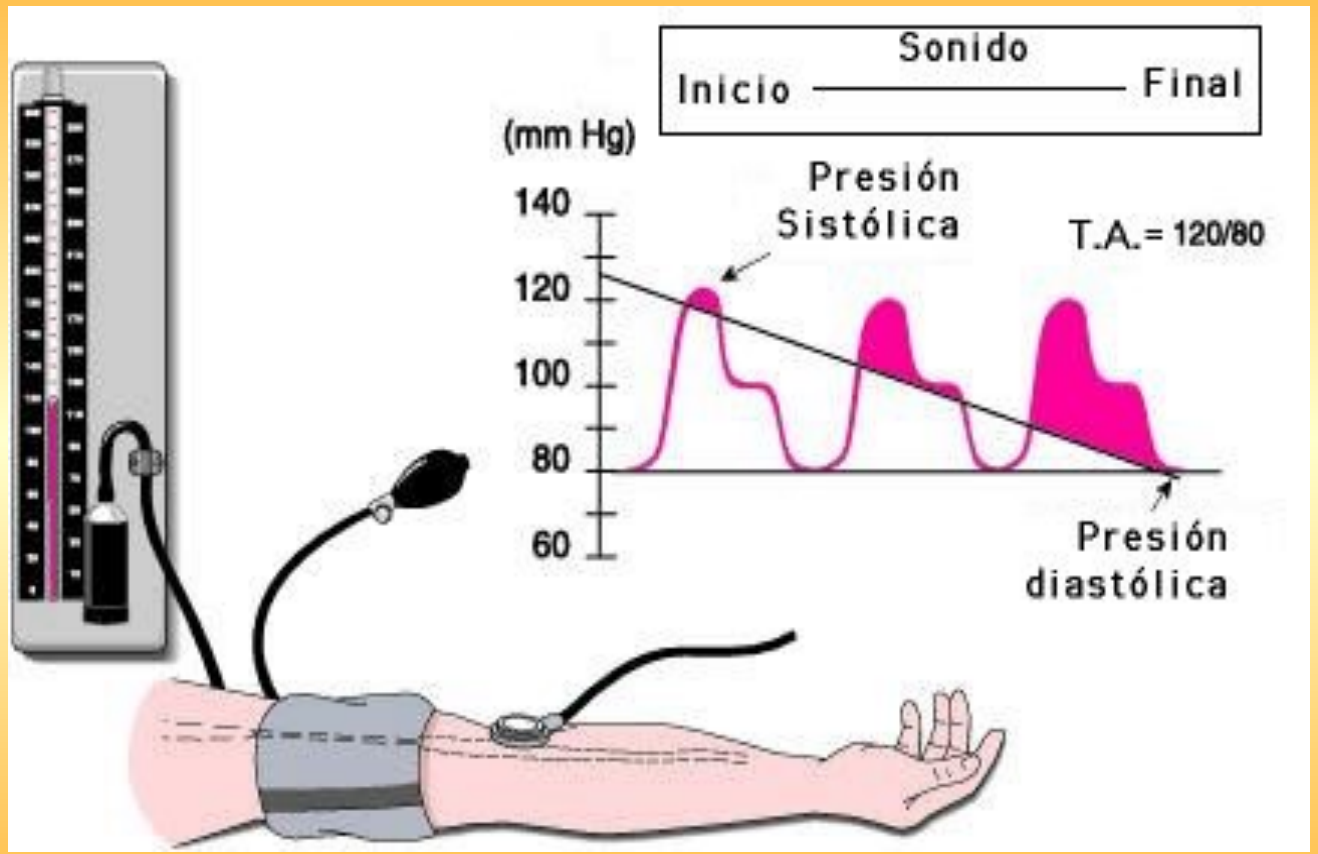
SANTOJANNI HOSPITAL
2001-2002 COMPARISON



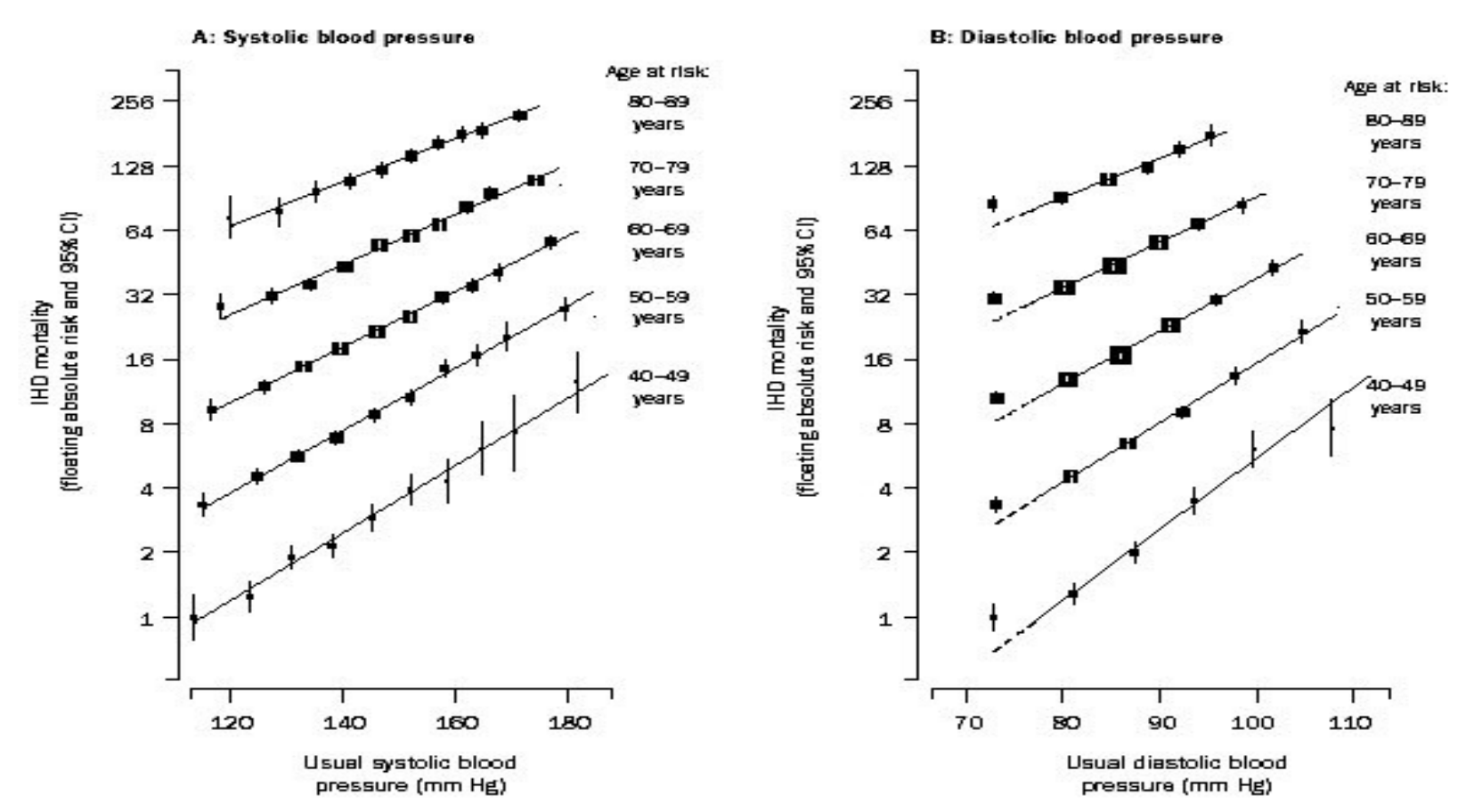
Auger et al; Congreso SAME 2003

REDUCTION OF CRF

- SHOULD WE?
- COULD WE?
- HOW MUCH?
- DOES IT WORK?


Sonido
Inicio
Final
(mm Hg)
140
120
100
80
60
Presión
Sistólica
T.A.= 120/80
Presión
diastólica

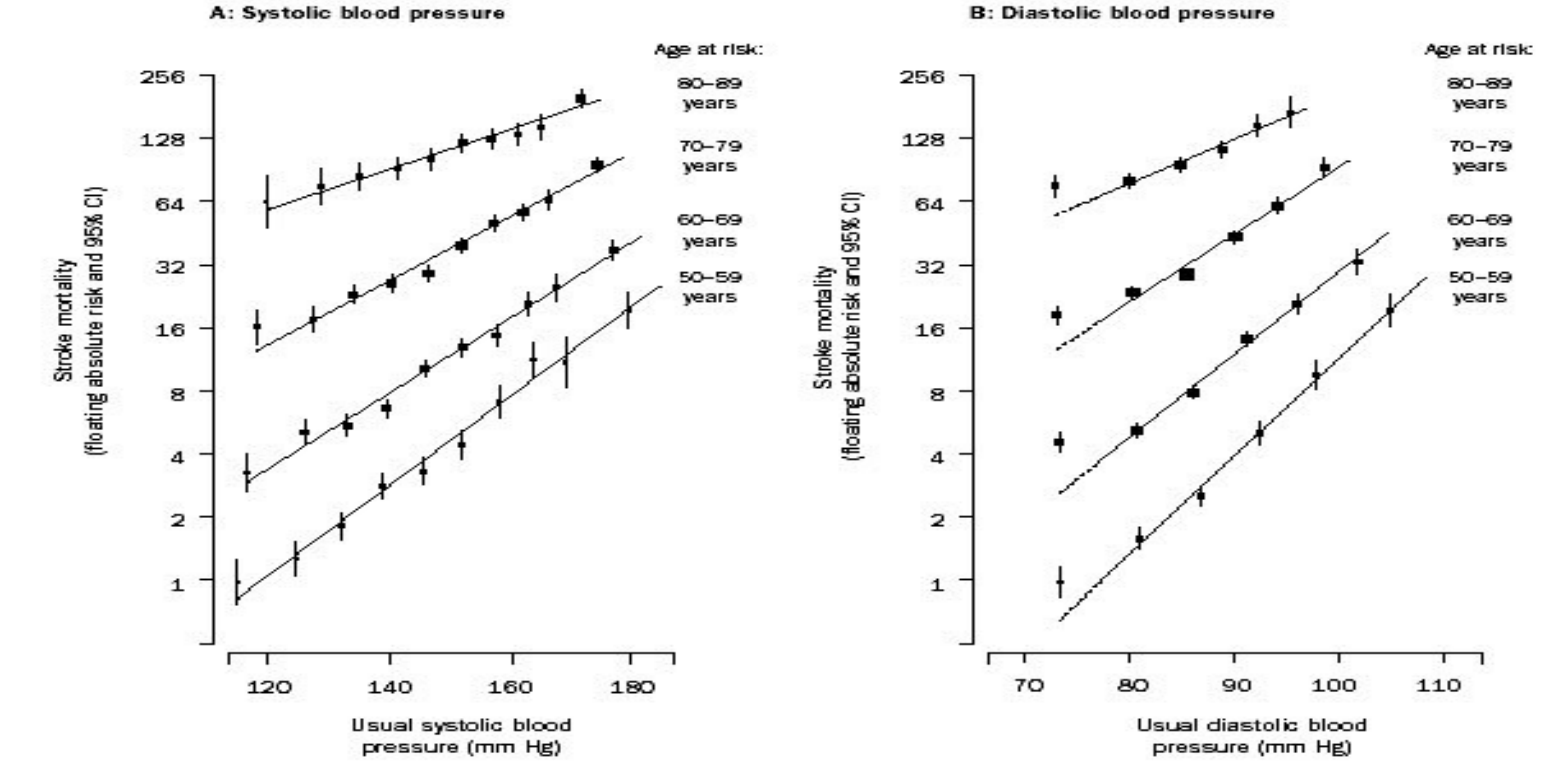
RELATIONSHIP BETWEEN BP, AGE, AND CORONARY MORTALITY



Threshold: 115/75

Lancet 2002; 360:1903

RELATIONSHIP BETWEEN BP, AGE, AND MORTALITY BY STROKE



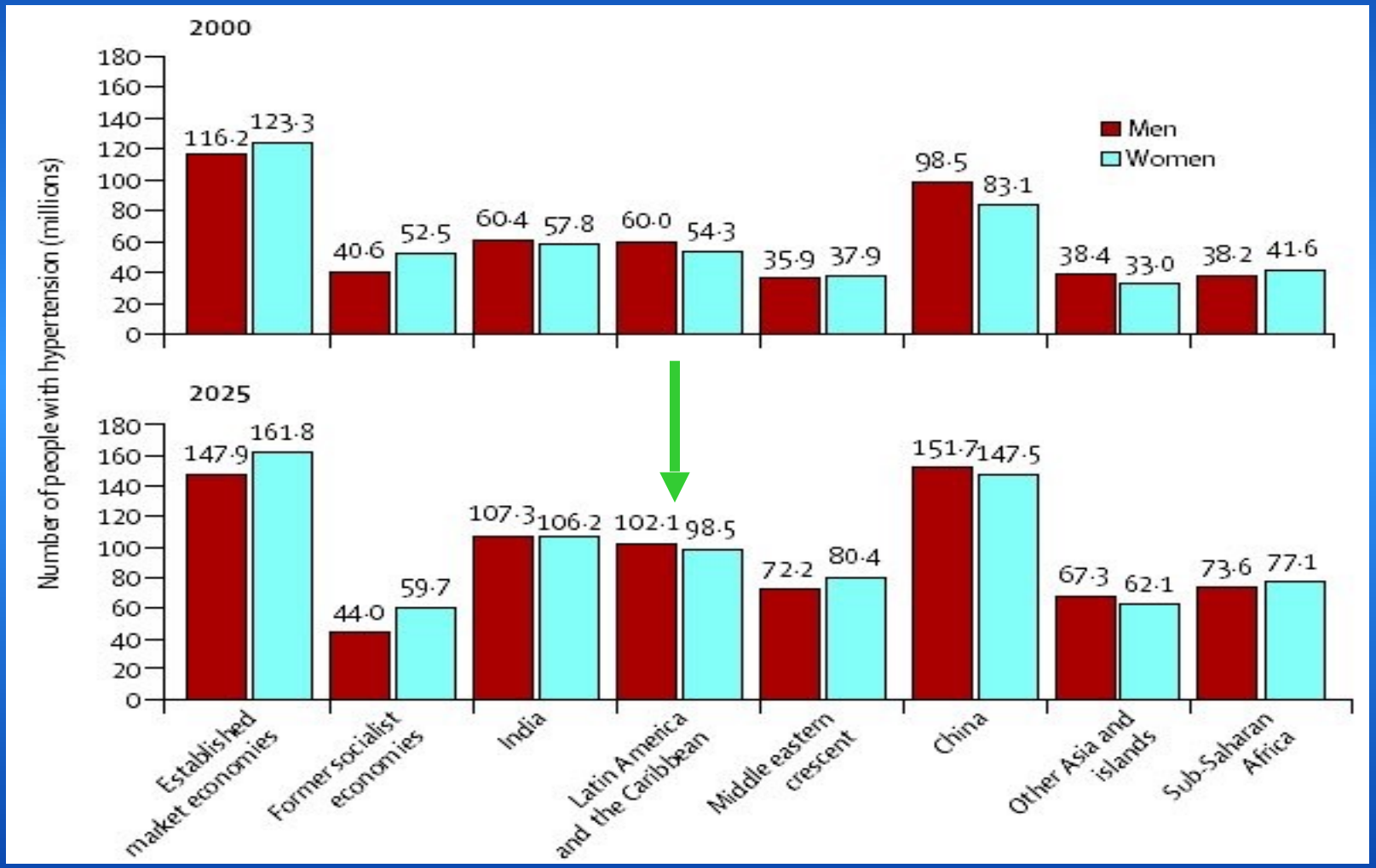
Threshold: 115/75

Lancet 2002; 360:1903

Knowledge, management, and control of hypertension in USA (1976-1994)

	NHANES II 1976-1980	NHANES III (Stage 1) 1988-1991	NHANES III (Stage 2) 1991-1994
They know (%)	51	73	68
Are managed (%)	31	55	54
Controlled (%)	10	29	27

Number of adults with HBP according to regions of the world and gender in 2000 (up) and 2025 (down)

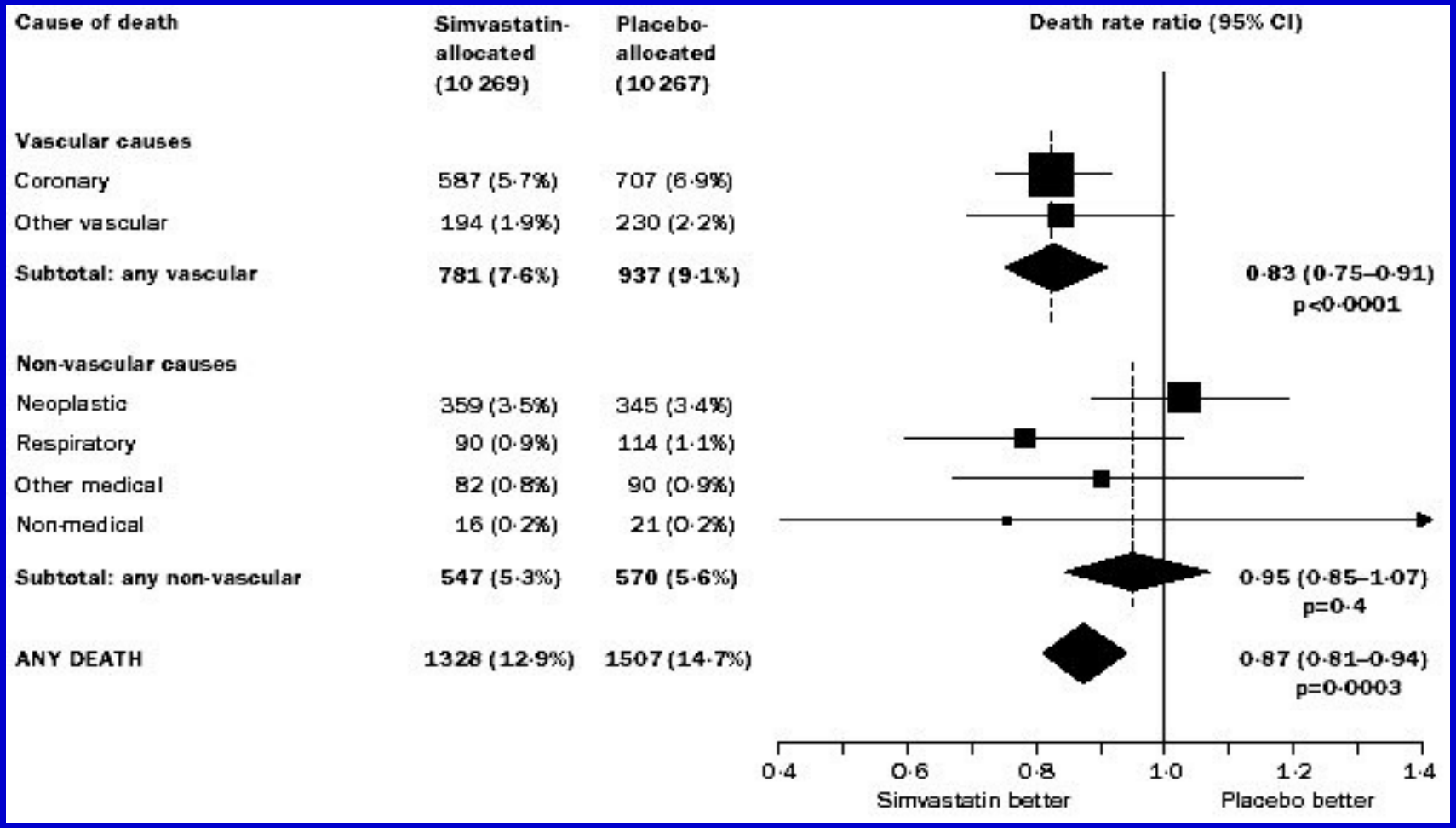


Lancet January 2005

HEART PROTECTION STUDY
REDUCTION OF CHOLESTEROL with SIMVASTATIN in 20536 HIGH-RISK INDIVIDUALS

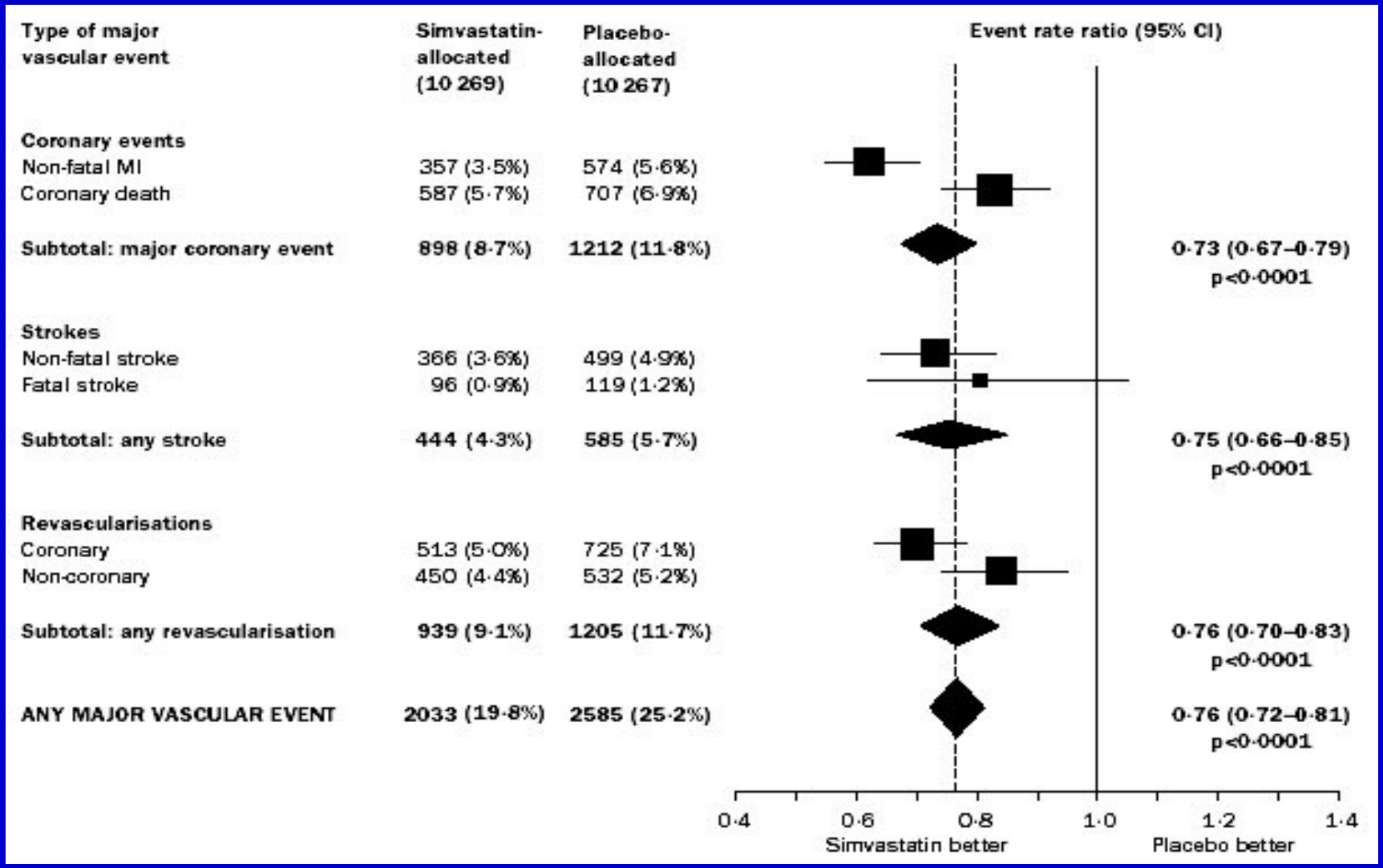
- **Randomized, placebo-controlled study.**
- **Patients with CAD, other vascular disease, or diabetes.**
- **40 mg/day of simvastatin or placebo.**
- **End point: mortality and fatal or nonfatal vascular events.**

HPS STUDY
EFFECTS OF SIMVASTATIN ON MORTALITY



Lancet 2002; 360: 7.

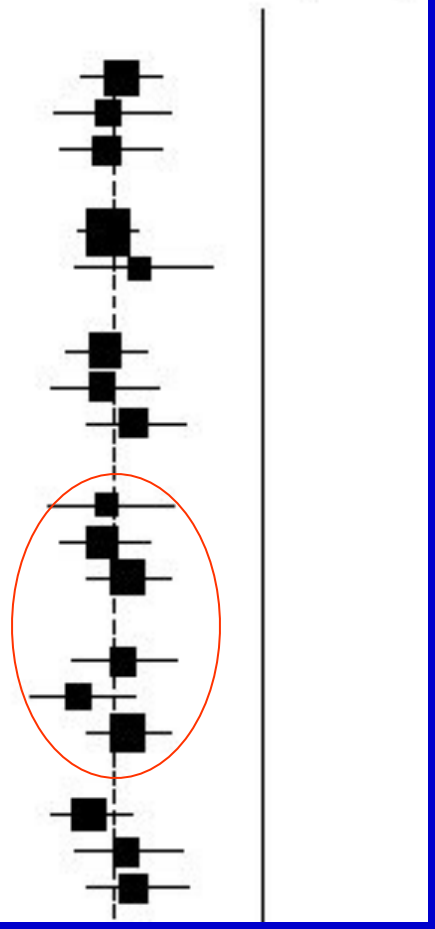
HPS STUDY
EFFECTS OF SIMVASTATIN ON VASCULAR EVENTS



Lancet 2002; 360: 7.

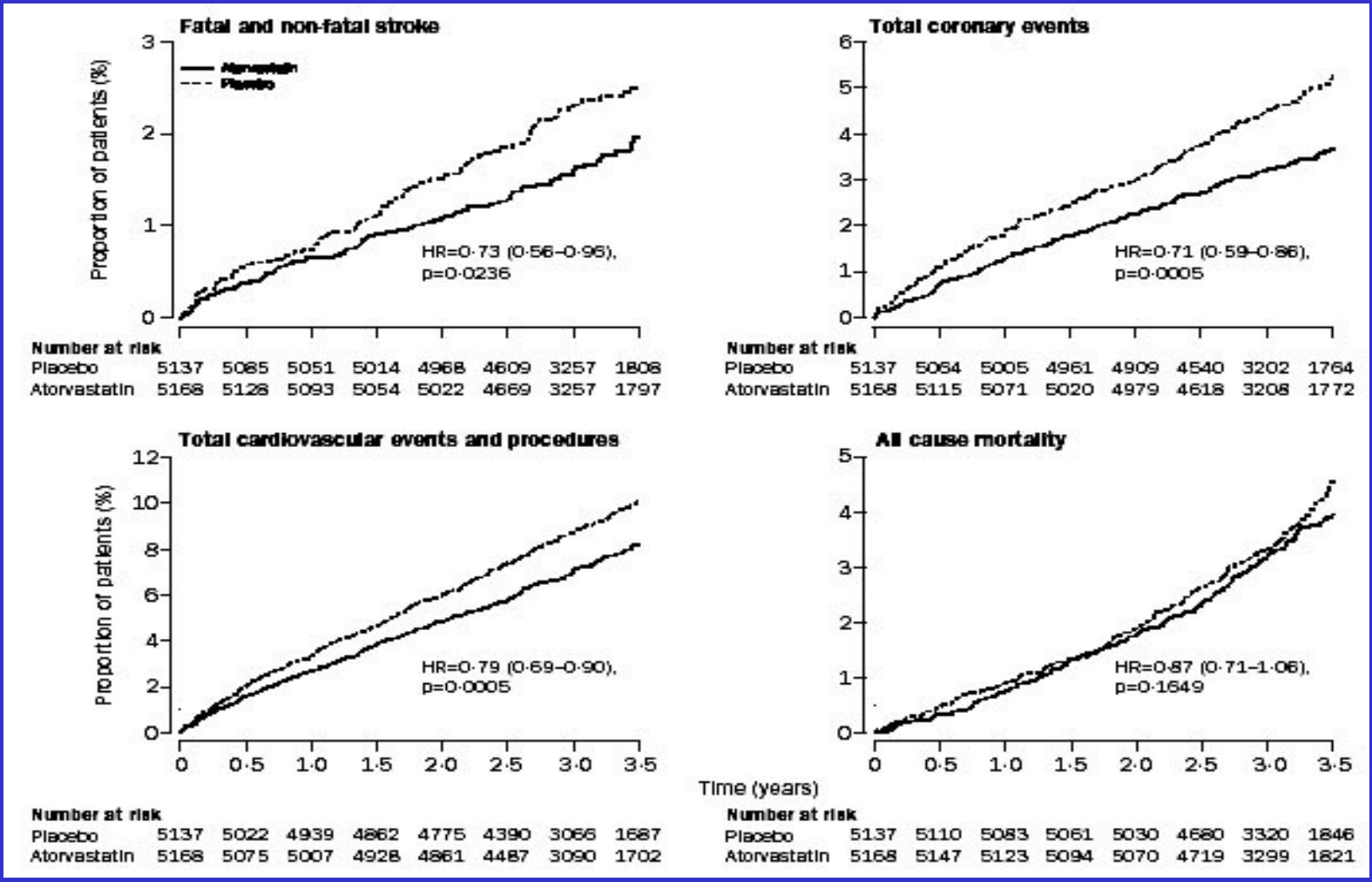
HPS STUDY
EFFECTS OF SIMVASTATIN ON VASCULAR EVENTS IN SUBSETS

Presenting feature	Simvastatin-allocated	Placebo-allocated
Prior disease		
Prior MI	999/4257(23·5%)	1250/4253(29·4%)
Other CHD	460/2437(18·9%)	591/2439(24·2%)
No prior CHD	574/3575(16·1%)	744/3575(20·8%)
Sex		
Male	1666/7727(21·6%)	2135/7727(27·6%)
Female	367/2542(14·4%)	450/2540(17·7%)
Age (years)		
<65	831/4903(16·9%)	1091/4936(22·1%)
≥65 <70	512/2447(20·9%)	665/2444(27·2%)
≥70	690/2919(23·6%)	829/2887(28·7%)
Total cholesterol (mmol/L)		
<5·0	360/2030(17·7%)	472/2042(23·1%)
≥5·0 <6·0	744/3942(18·9%)	964/3941(24·5%)
≥6·0	929/4297(21·6%)	1149/4284(26·8%)
LDL cholesterol (mmol/L)		
<3·0	598/3389(17·6%)	756/3404(22·2%)
≥3·0 <3·5	484/2549(19·0%)	646/2514(25·7%)
≥3·5	951/4331(22·0%)	1183/4349(27·2%)
HDL cholesterol (mmol/L)		
<0·9	818/3617(22·6%)	1064/3559(29·9%)
≥0·9 <1·1	560/2795(20·0%)	720/2871(25·1%)
≥1·1	655/3857(17·0%)	801/3837(20·9%)



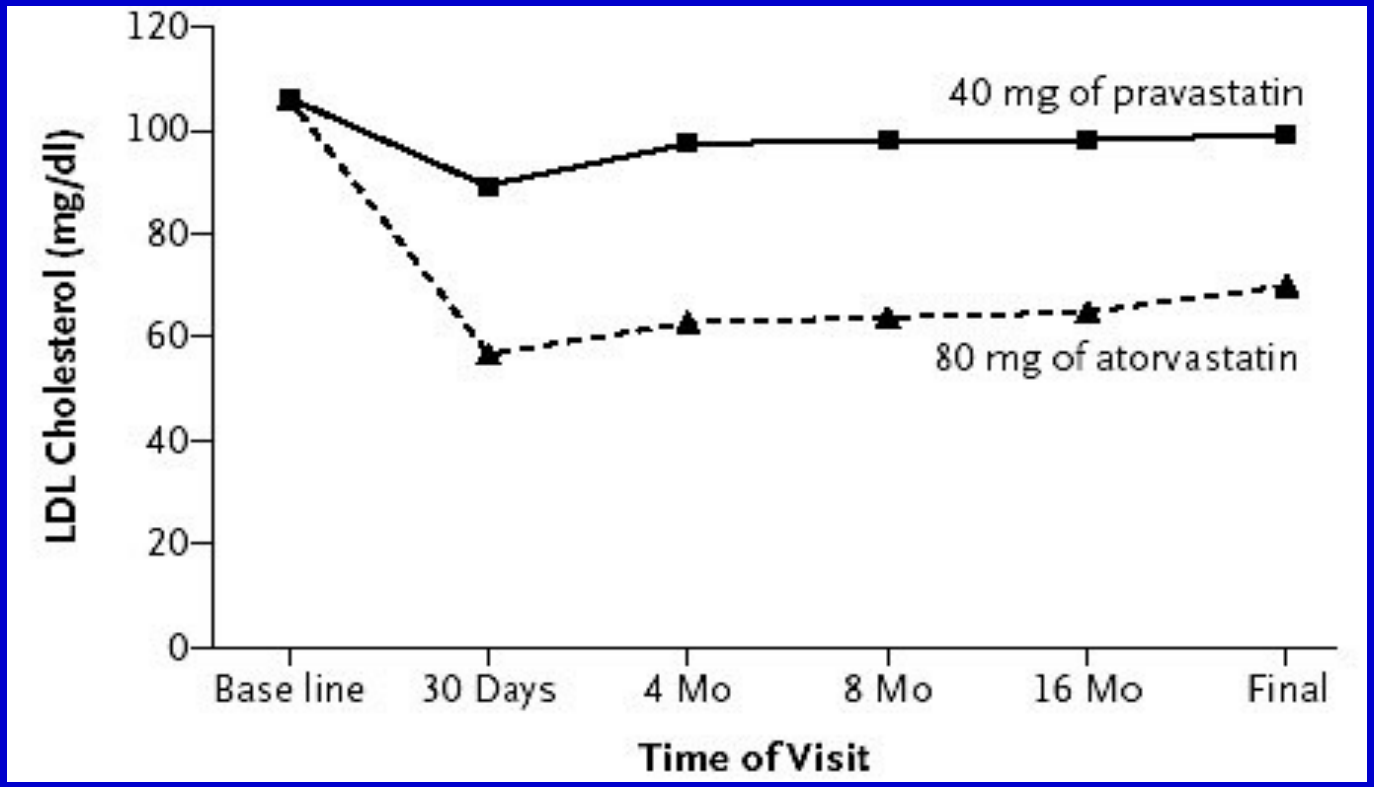
Lancet 2002; 360: 7.

Prevention of vascular events in hypertensive patients with "normal" cholesterol: ASCOT-LLA



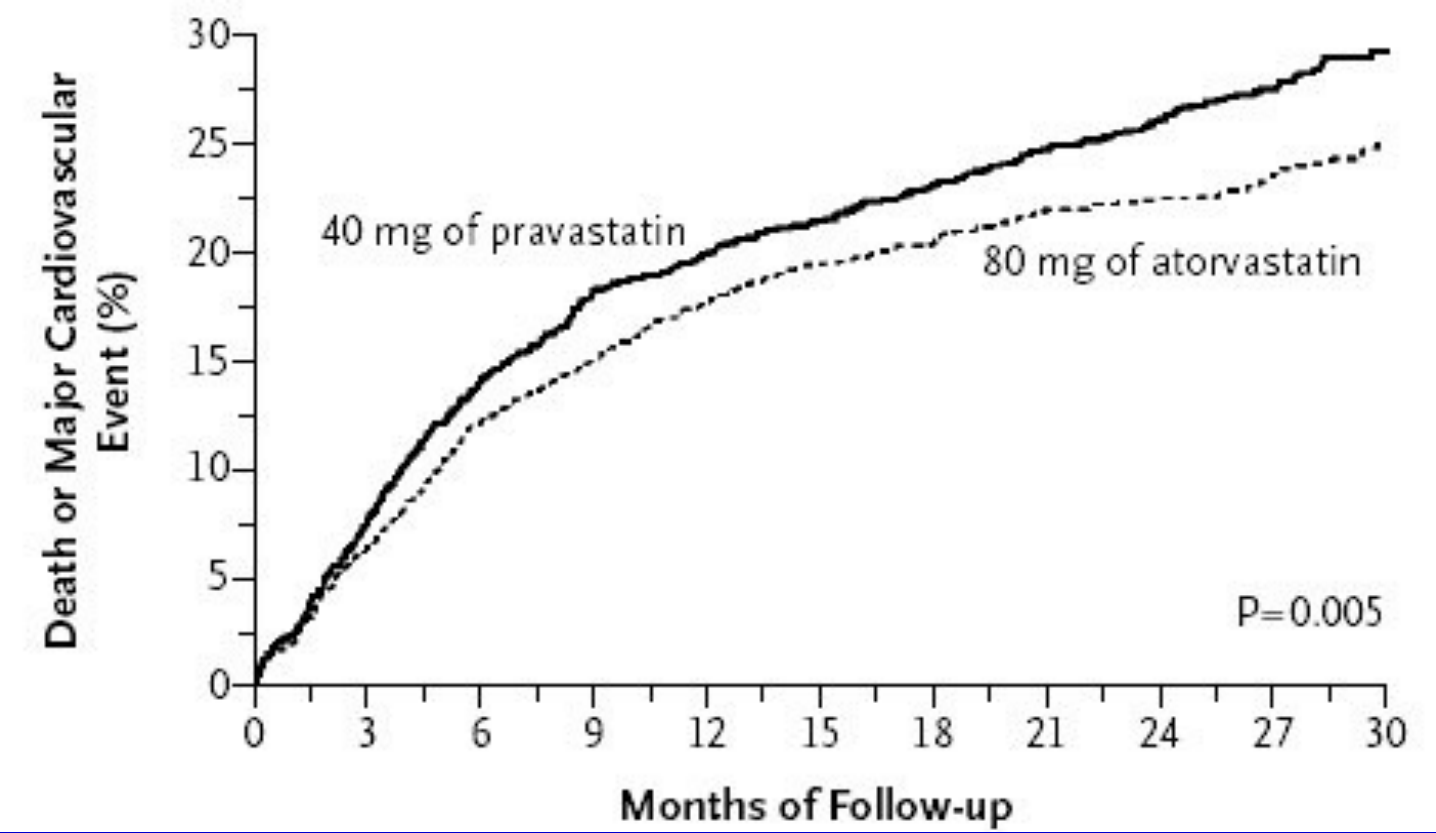
Sever et al; Lancet April 2003

MODERATE OR INTENSIVE REDUCTION OF CHOLESTEROL IN ACS
PROVE-IT STUDY: LEVELS OF LDL



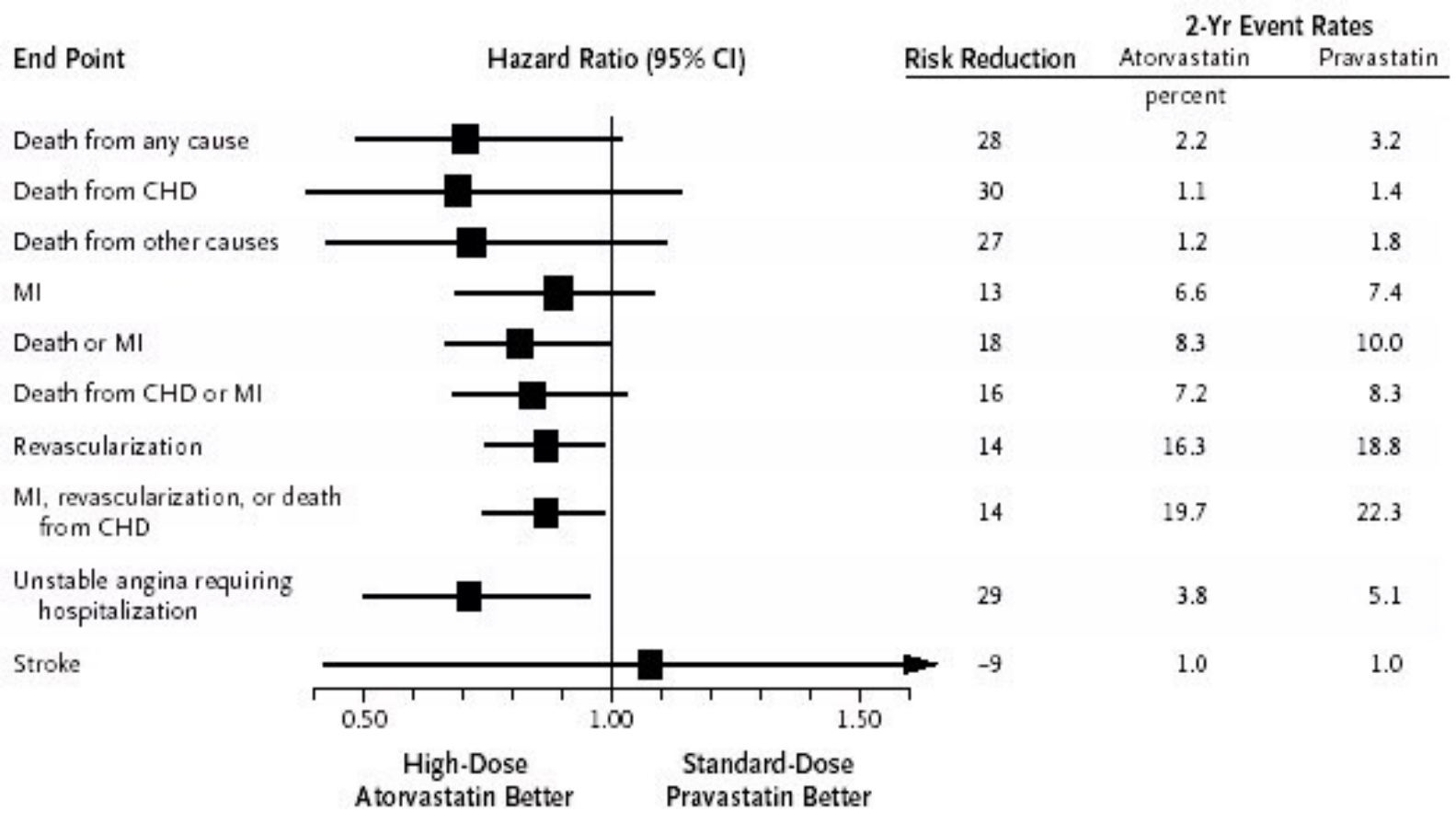
Cannon et al; N Engl J Med April 2004

MODERATE OR INTENSIVE REDUCTION OF CHOLESTEROL IN ACS
PROVE-IT STUDY: CV EVENTS



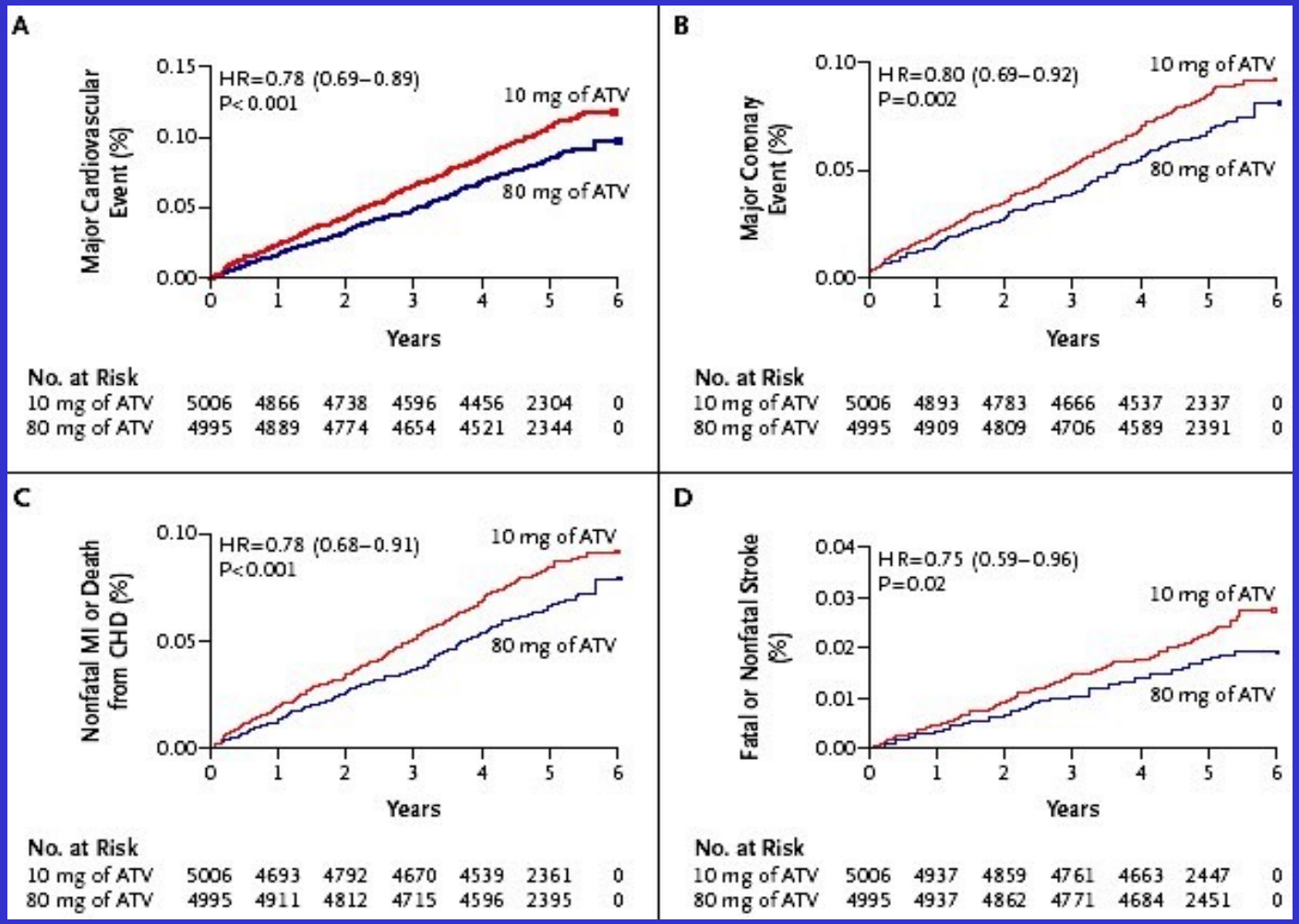
Cannon et al; N Engl J Med April 2004

MODERATE OR INTENSIVE REDUCTION OF CHOLESTEROL IN ACS
PROVE-IT STUDY: CV EVENTS



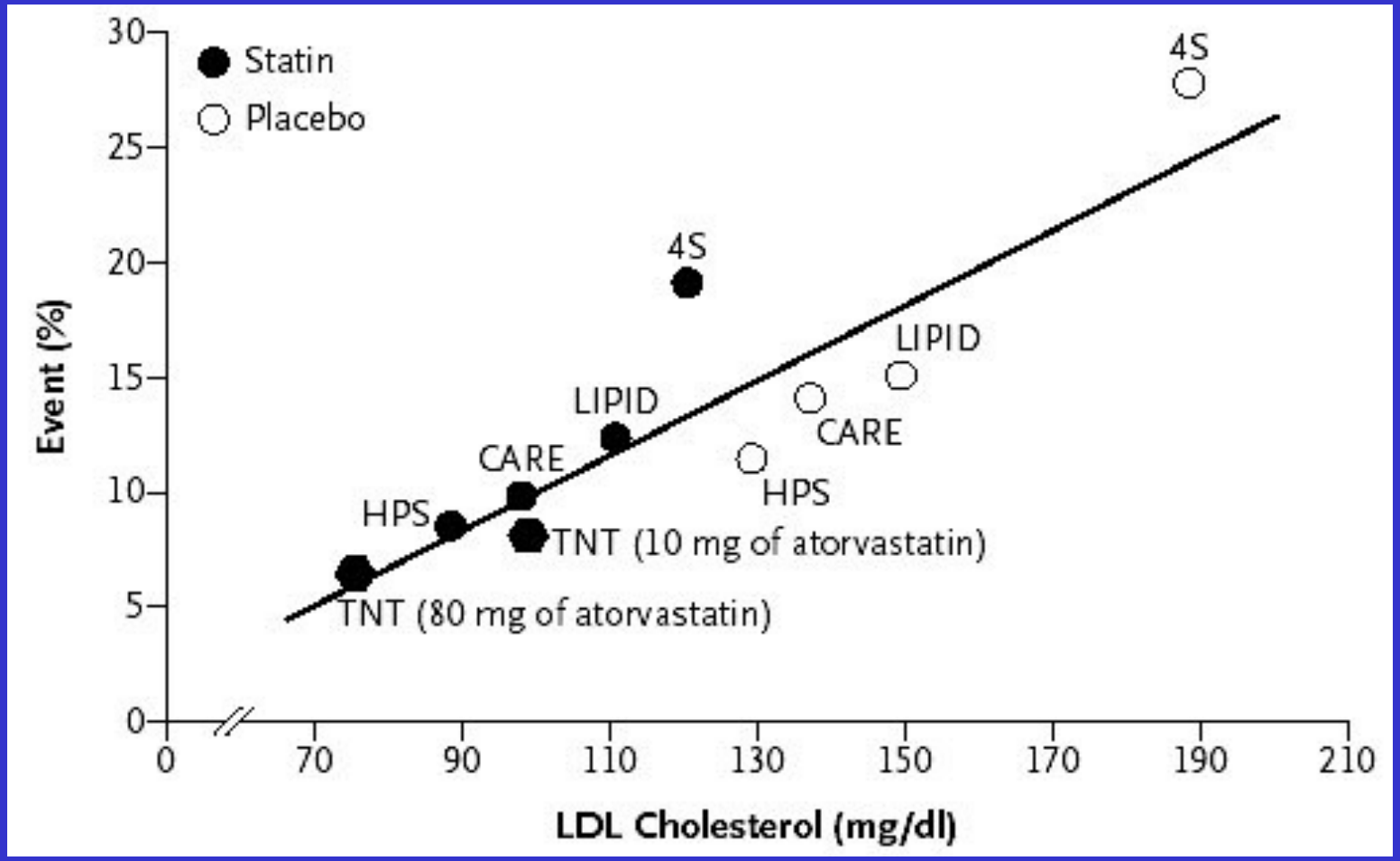
Cannon et al; N Engl J Med April 2004

INTENSIVE REDUCTION OF LIPIDS WITH ATORVASTATIN IN PATIENTS WITH STABLE CAD
TNT STUDY



La Rosa et al; N Engl J Med Abril 2005

MAJOR EVENTS ACCORDING TO LDLc LEVELS IN STUDIES OF SECONDARY PREVENTION WITH STATINS



La Rosa et al; N Engl J Med April 2005


Diabetes

RELATIONSHIP BETWEEN GLYCOSYLATED HEMOGLOBIN AND CARDIOVASCULAR DISEASE: NORFOLK STUDY.

Variable	Hemoglobin A_{1c} Concentration						Known Diabetes
	<5%	5%–5.4%	5.5%–5.9%	6%–6.4%	6.5%–6.9%	≥7%	
Men, *n*	1204	1606	1153	374	84	81	160
Coronary heart disease events							
Events/100 persons	3.8	6.4	8.7	10.2	16.7	28.4	21.9
Events, *n*	46	102	100	38	14	23	35
Age-adjusted relative risk (95% CI)	1.00	1.56 (1.09–2.24)	2.00 (1.39–2.88)	2.13 (1.35–3.35)	3.44 (1.78–6.63)	7.07 (3.96–12.62)	4.82 (2.96–7.85)
Cardiovascular disease events							
Events/100 persons	6.7	9.0	12.1	15.2	25.0	34.8	26.9
Events, *n*	81	144	140	57	21	28	43
Age-adjusted relative risk (95% CI)	1.00	1.23 (0.92–1.64)	1.56 (1.16–2.09)	1.79 (1.24–2.60)	3.03 (1.73–5.31)	5.01 (2.95–8.51)	3.32 (2.16–5.10)
All-cause mortality							
Events/100 persons	3.8	5.5	7.5	9.9	19.0	18.5	20.0
Events, *n*	46	88	87	37	16	15	32
Age-adjusted relative risk (95% CI)	1.00	1.25 (0.88–1.82)	1.57 (1.08–2.29)	1.80 (1.13–2.86)	3.49 (1.83–6.66)	3.38 (1.74–6.53)	3.68 (2.22–6.09)

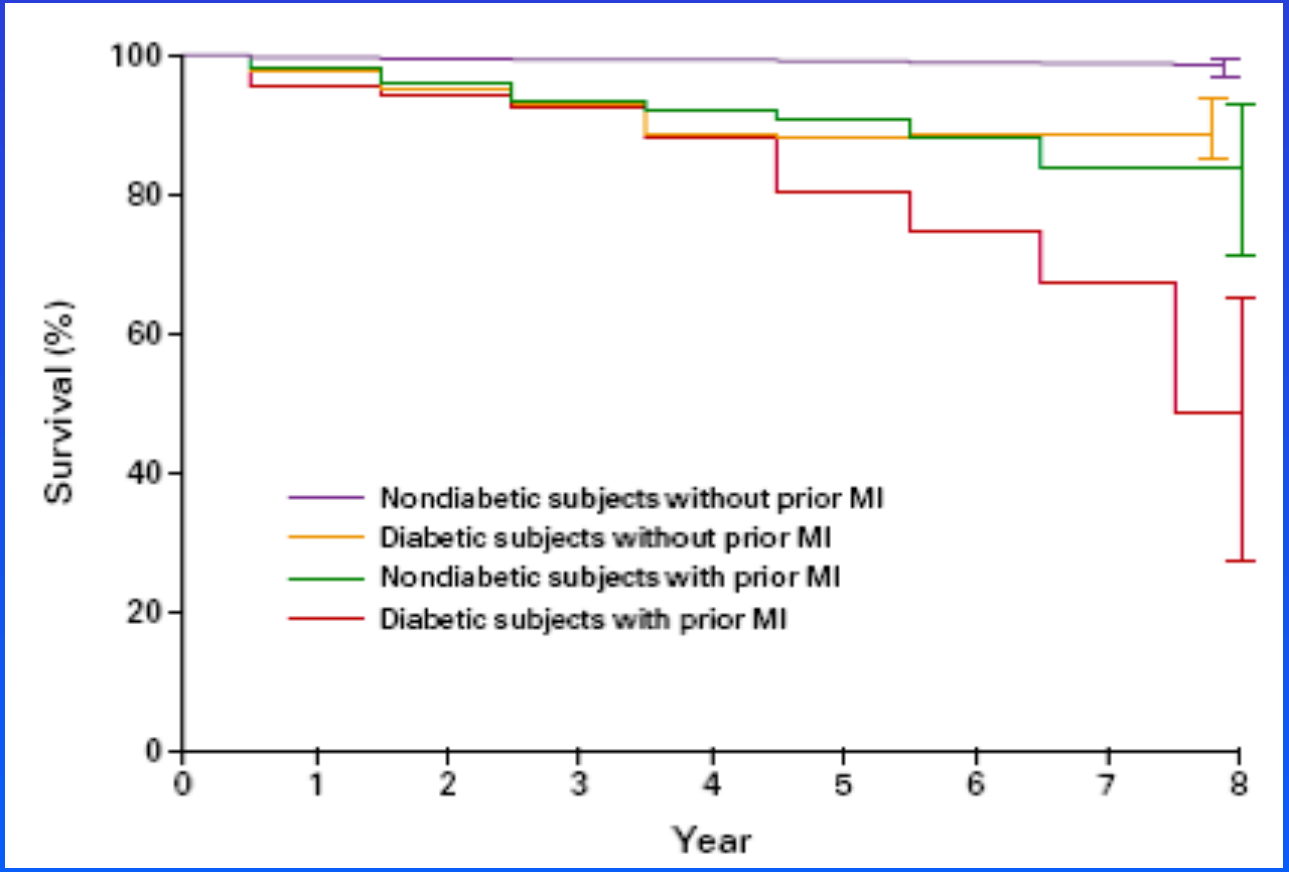
Ann Intern Med 2004; 141:413.

RELATIONSHIP BETWEEN GLYCOSYLATED HEMOGLOBIN AND CARDIOVASCULAR DISEASE: NORFOLK STUDY.

Women, *n*	1562	1967	1378	439	73	68	83
Coronary heart disease events							
Events/100 persons	1.7	2.1	3.0	7.3	9.6	16.2	15.7
Events, *n*	26	41	41	32	7	11	13
Age-adjusted relative risk (95% CI)	1.00	0.96 (0.58–1.59)	1.04 (0.62–1.63)	2.29 (1.34–3.96)	3.06 (1.25–7.49)	4.73 (2.16–10.34)	6.00 (2.90–12.44)
Cardiovascular disease events							
Events/100 persons	3.3	3.8	5.4	9.8	13.7	36.8	18.1
Events, *n*	51	74	74	43	10	25	15
Age-adjusted relative risk (95% CI)	1.00	0.89 (0.62–1.29)	0.98 (0.68–1.44)	1.63 (1.05–2.52)	2.37 (1.13–5.01)	7.96 (4.38–14.5)	3.63 (1.90–6.93)
All-cause mortality							
Events/100 persons	2.0	2.7	4.4	6.4	6.8	25.0	4.9
Events, *n*	32	53	61	28	5	17	4
Age-adjusted relative risk (95% CI)	1.00	1.02 (0.65–1.60)	1.28 (0.82–2.01)	1.61 (0.94–2.75)	1.70 (0.63–4.60)	6.91 (3.50–13.67)	1.26 (0.43–3.72)

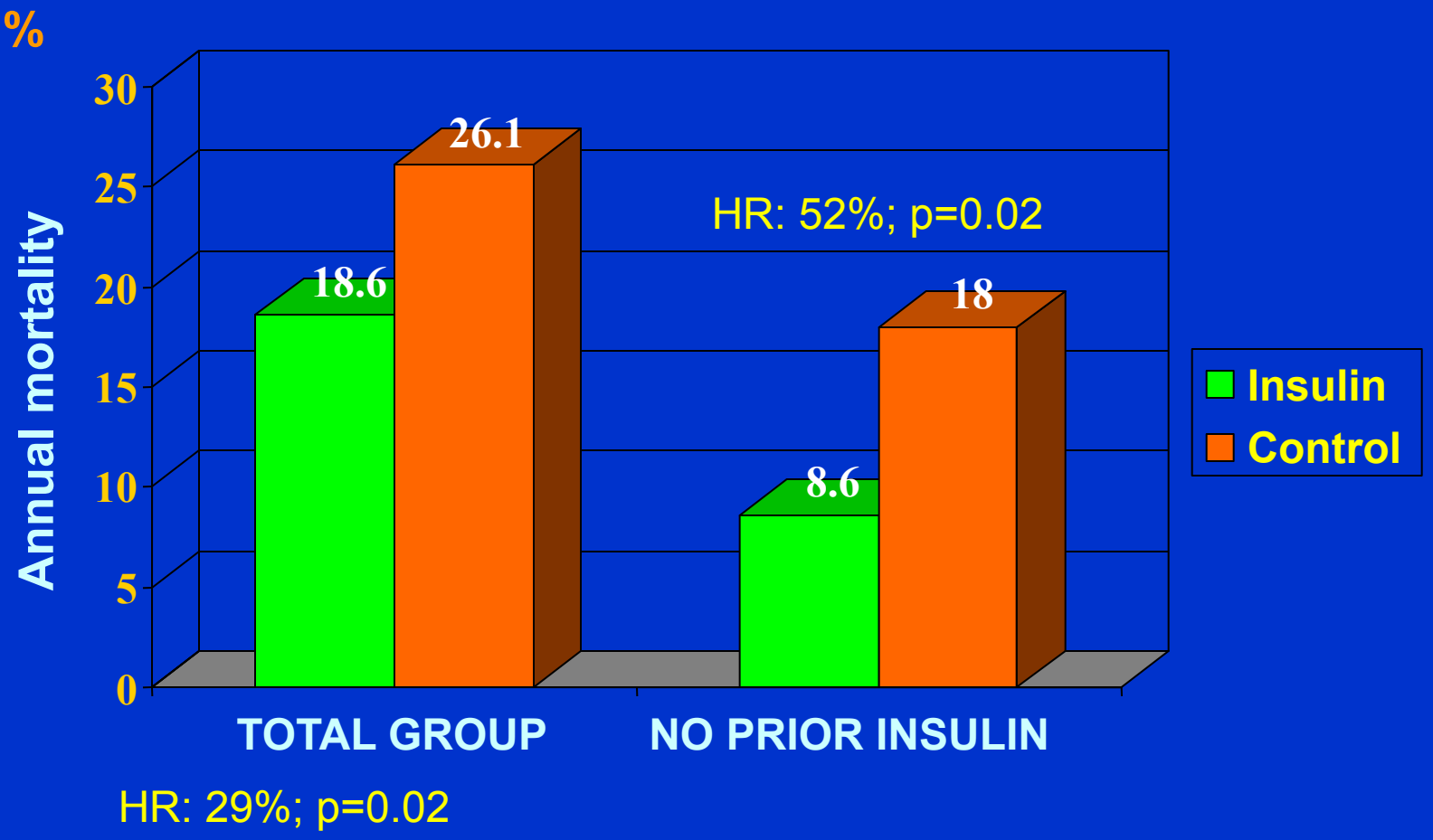
Ann Intern Med 2004; 141:413.

PROBABILITY OF DEATH BY CAD IN DIABETIC (n: 1059) AND NONDIABETIC PATIENTS (n: 1373) WITH AND W/O PRIOR INFARCTION



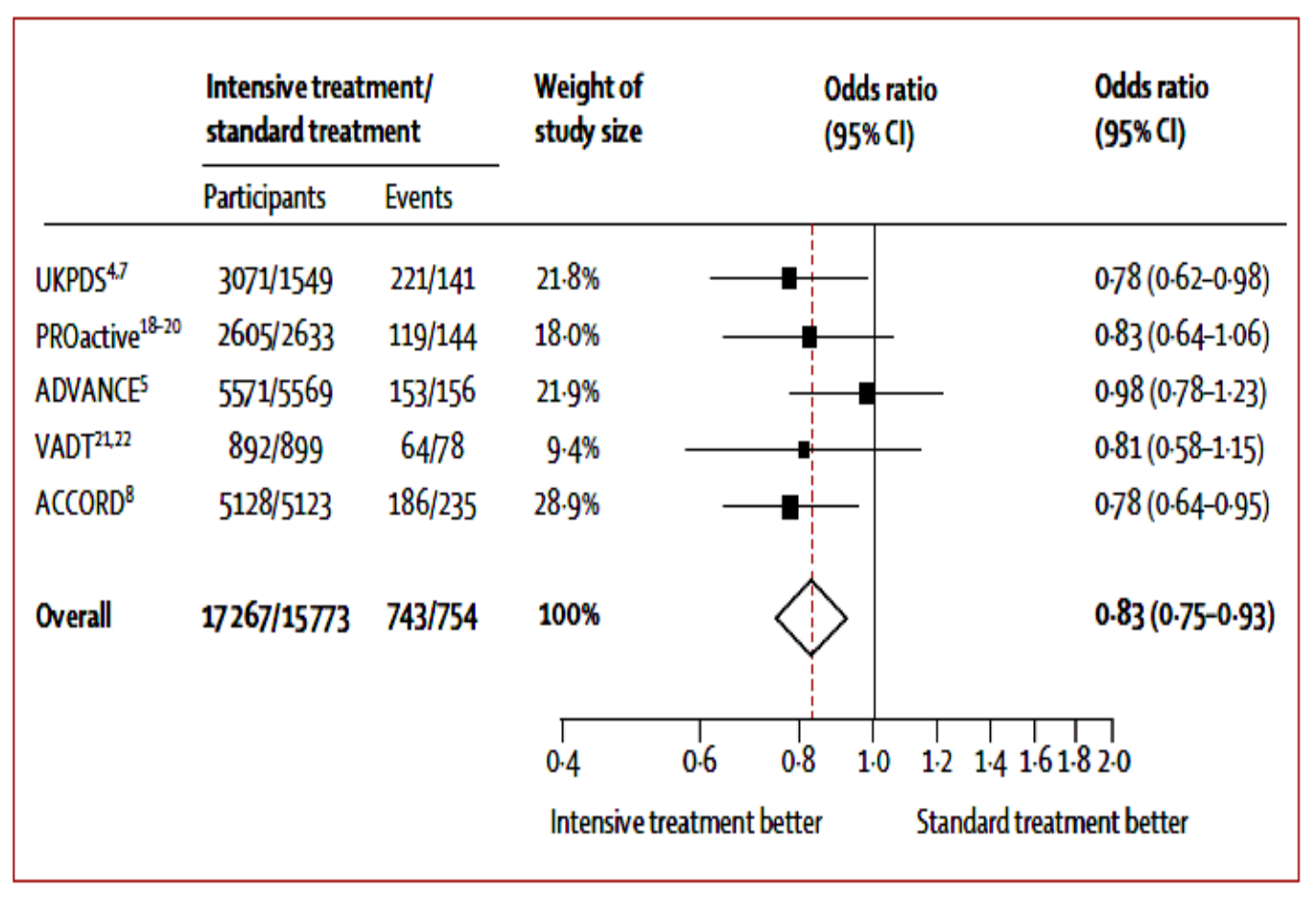
Haffner et al; N Engl J Med July 1998

MANAGEMENT with INSULIN (3 months) in POST-AMI DIABETIC PATIENTS DIGAMI STUDY (n: 620)



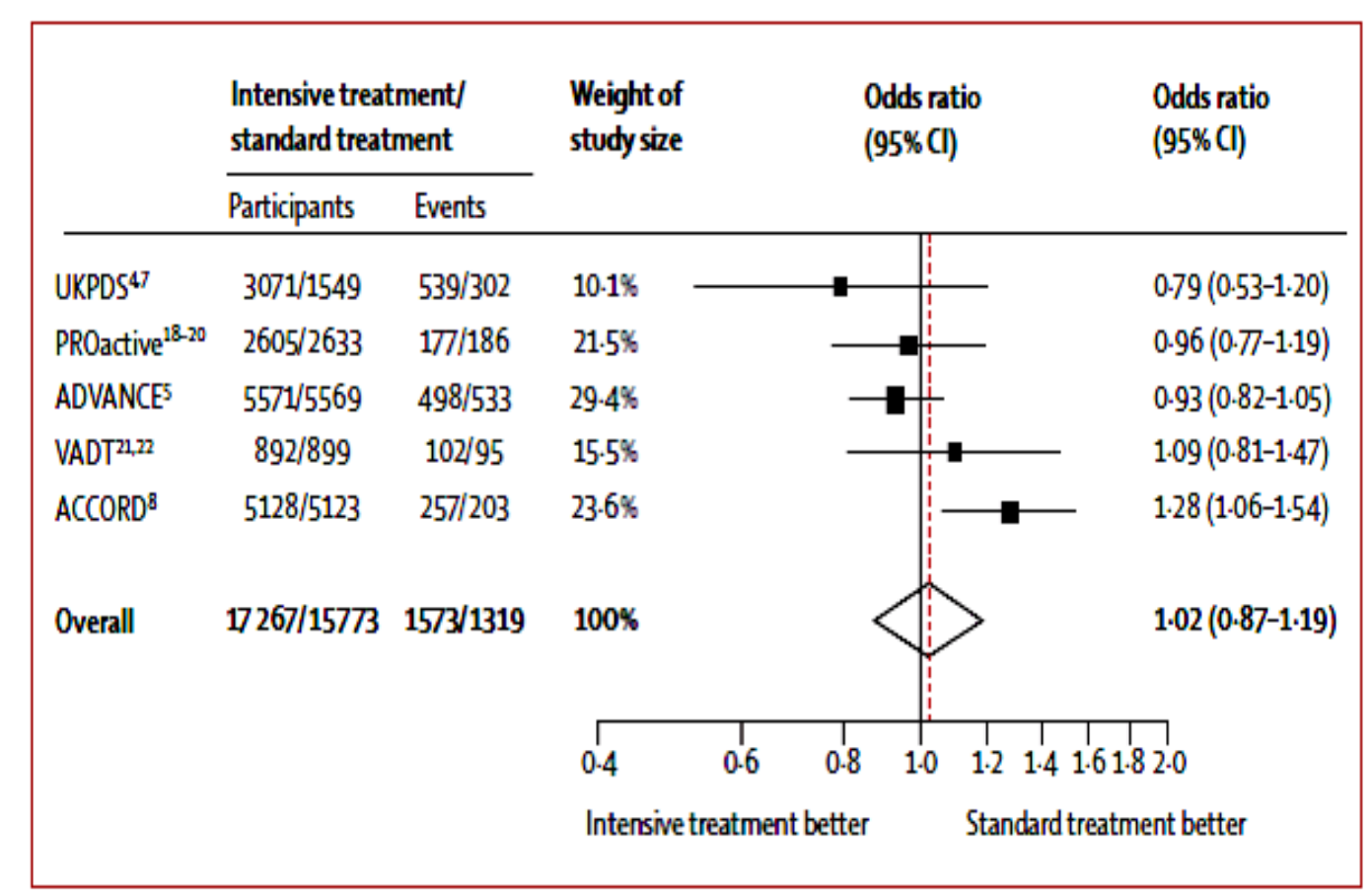
Malmberg et al; JACC July 1995

INTENSIVE CONTROL OF GLYCEMIA vs. STANDARD CONTROL: INFARCTION



Lancet May 2009

INTENSIVE GLYCEMIA CONTROL vs. STANDARD CONTROL: MORTALITY



Lancet May 2009

Epidemiology of smoking

- 1100 million people smoke in the world
- 1965 → USA → 42% of smokers → anti-smoking campaigns → 26% current
- Argentina → 38% of smokers (adults) → 1500 cigarettes/adult/year
- 80% starts smoking before reaching 18 years of age
- 5 million deaths per year are attributed to smoking.
- Year 2025 → 10 million deaths.

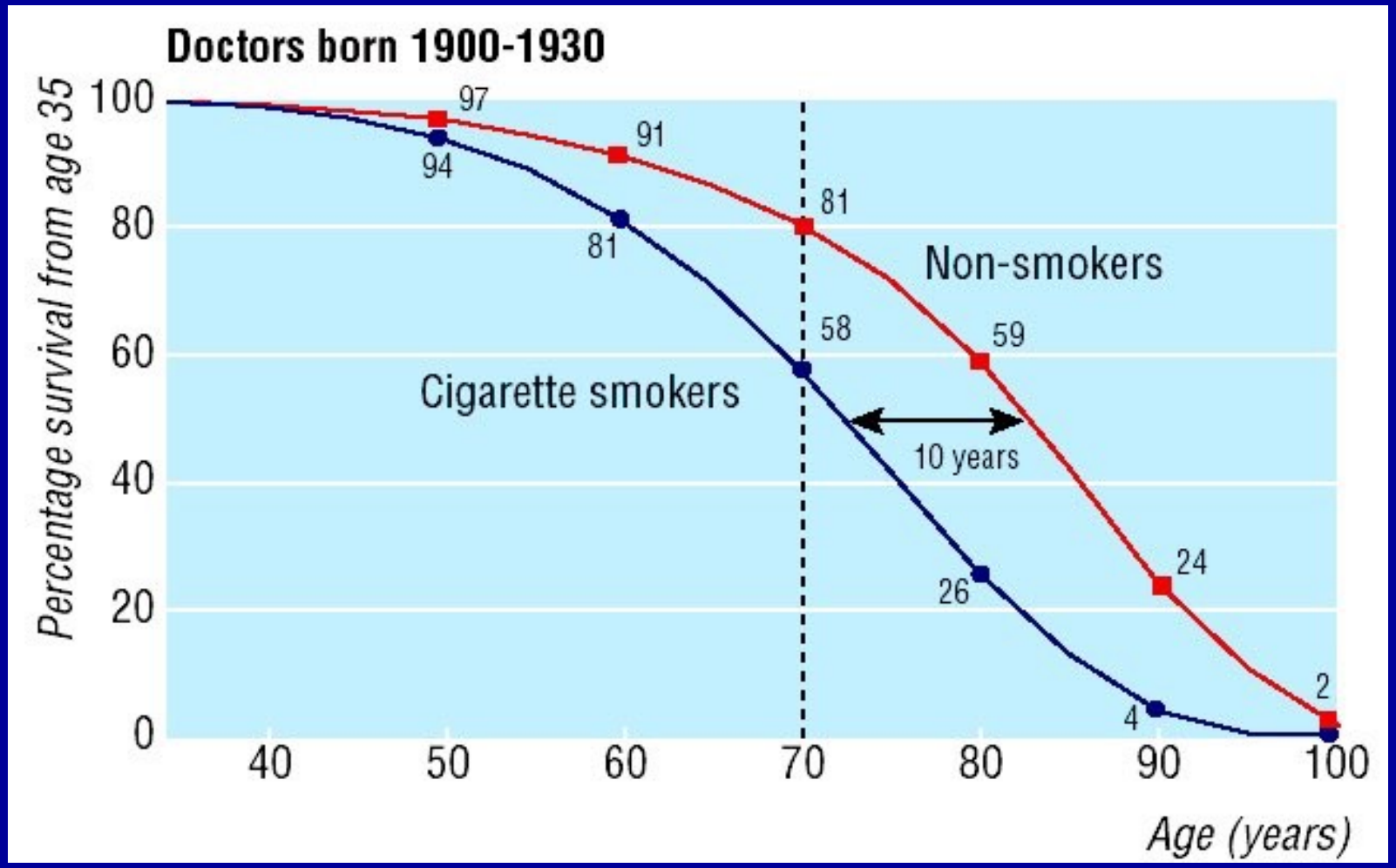
Sources: WHO – UATA
(Argentine Anti-Smoking Association)

Mortality in relation to smoking: 50 years' observations on male British doctors

Richard Doll, Richard Peto,

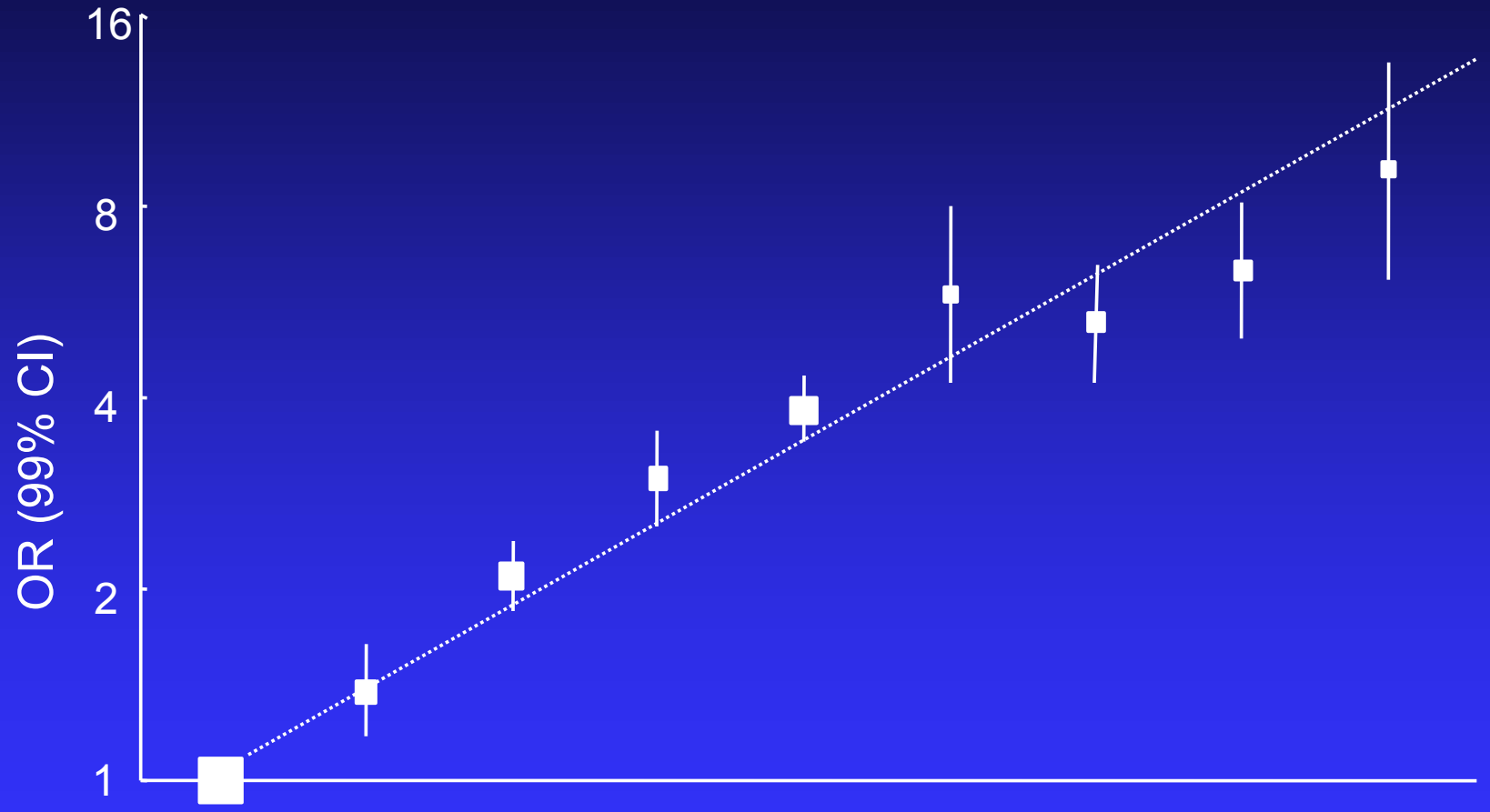
British Medical Journal, June 22nd, 2004

SURVIVAL SINCE 35 YEARS OF AGE FOR SMOKERS AND NONSMOKERS



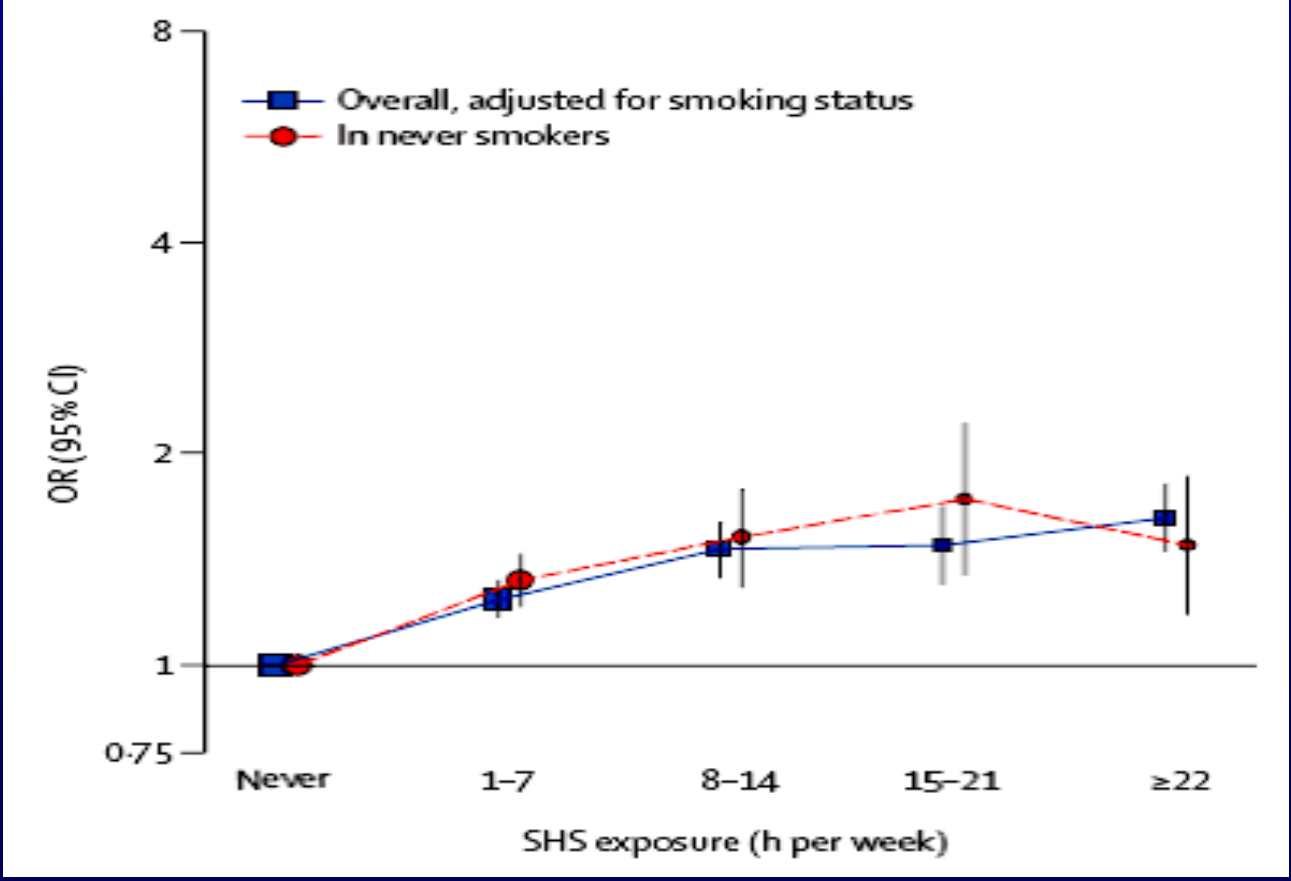
Doll, R et al; BMJ June 2004

INTERHEART: Smoking and AMI



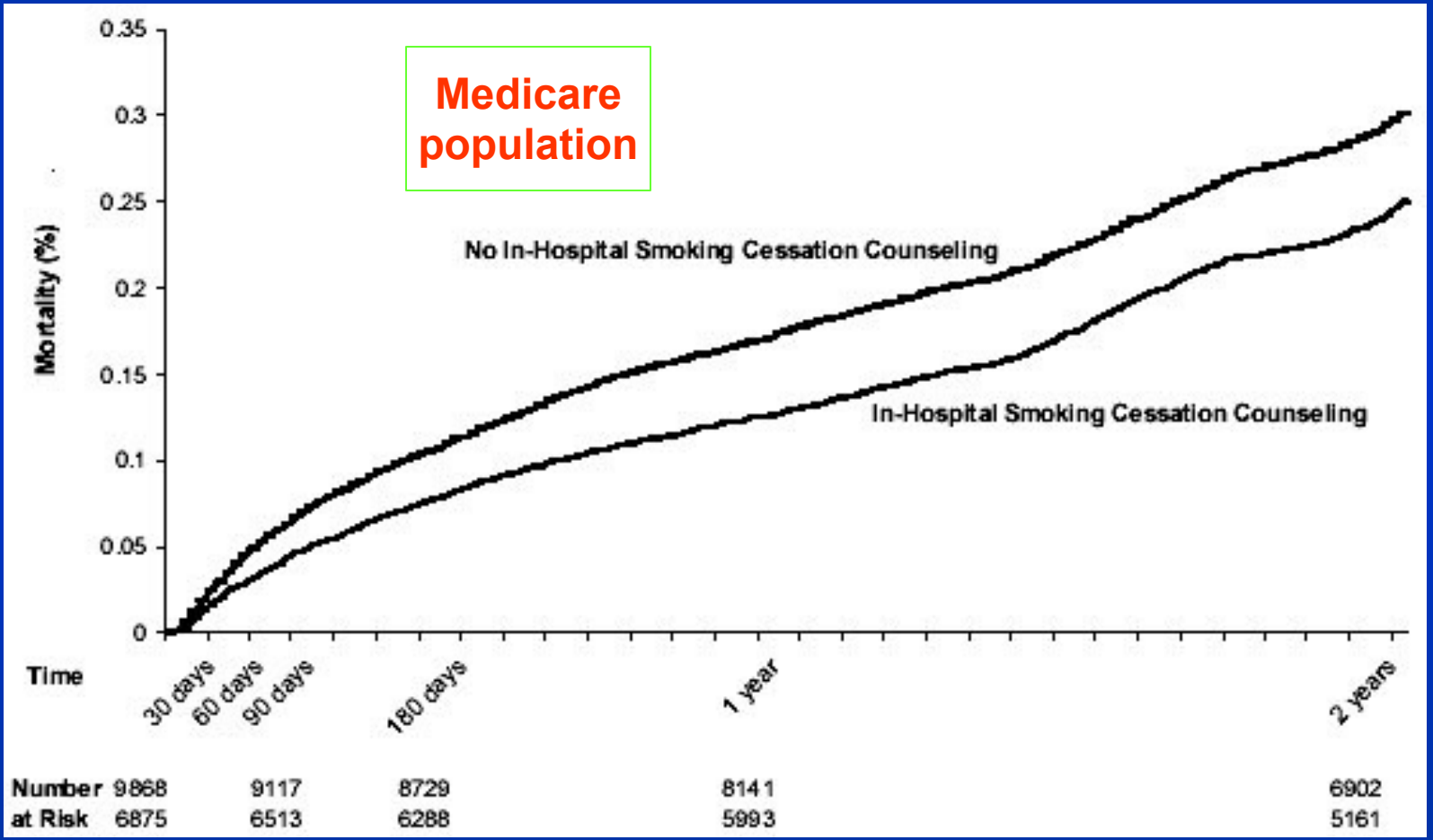
	Never	1-5	6-10	11-15	16-20	21-25	26-30	31-40	41+
Cont	7489	727	1031	446	1058	96	230 168	56	
Cases	4223	469	1021	623	1832	254	538 459	218	
OR	1	1.38	2.10	2.99	3.83	5.80	5.26 6.34	9.16	

RISK OF INFARCTION IN PASSIVE SMOKERS. INTERHEART STUDY.



Lancet, August 2006

ADVICE TO QUIT SMOKING AND MORTALITY IN POST-INFARCTION



Houston et al; Am J Med March 2005

INTER-HEART: Risk of AMI associated to risk factors in the global population

Risk factor	Odds ratio adjusted by age, gender, & smoking	Odds ratio adjusted by all (99% CI)
ApoB/ApoA-1 (5th quintile compared to the 1st)	3.87 (3.39-4.42)	3.25 (2.81-3.76)
Current smoking	2.95 (2.72-3.20)	2.87 (2.58-3.19)
Diabetes	3.08 (2.77-3.42)	2.37 (2.07-2.71)
Hypertension	2.48 (2.30-2.68)	1.91 (1.74-2.10)
Abdominal obesity	2.22 (2.03-2.42)	1.62 (1.45-1.80)
Psychosocial	2.51 (2.15-2.93)	2.67 (2.21-3.22)
Daily vegetables and fruits	0.70 (0.64-0.77)	0.70 (0.62-0.79)
Exercise	0.72 (0.65-0.79)	0.86 (0.76-0.97)
Alcohol consumption	0.79 (0.73-0.86)	0.91 (0.82-1.02)
All combined	129.2 (90.2-185.0)	129.2 (90.2-185.0)

Yusuf S. European Society of Cardiology Congress 2004; August 28-September 1, 2004; Munich, Germany.

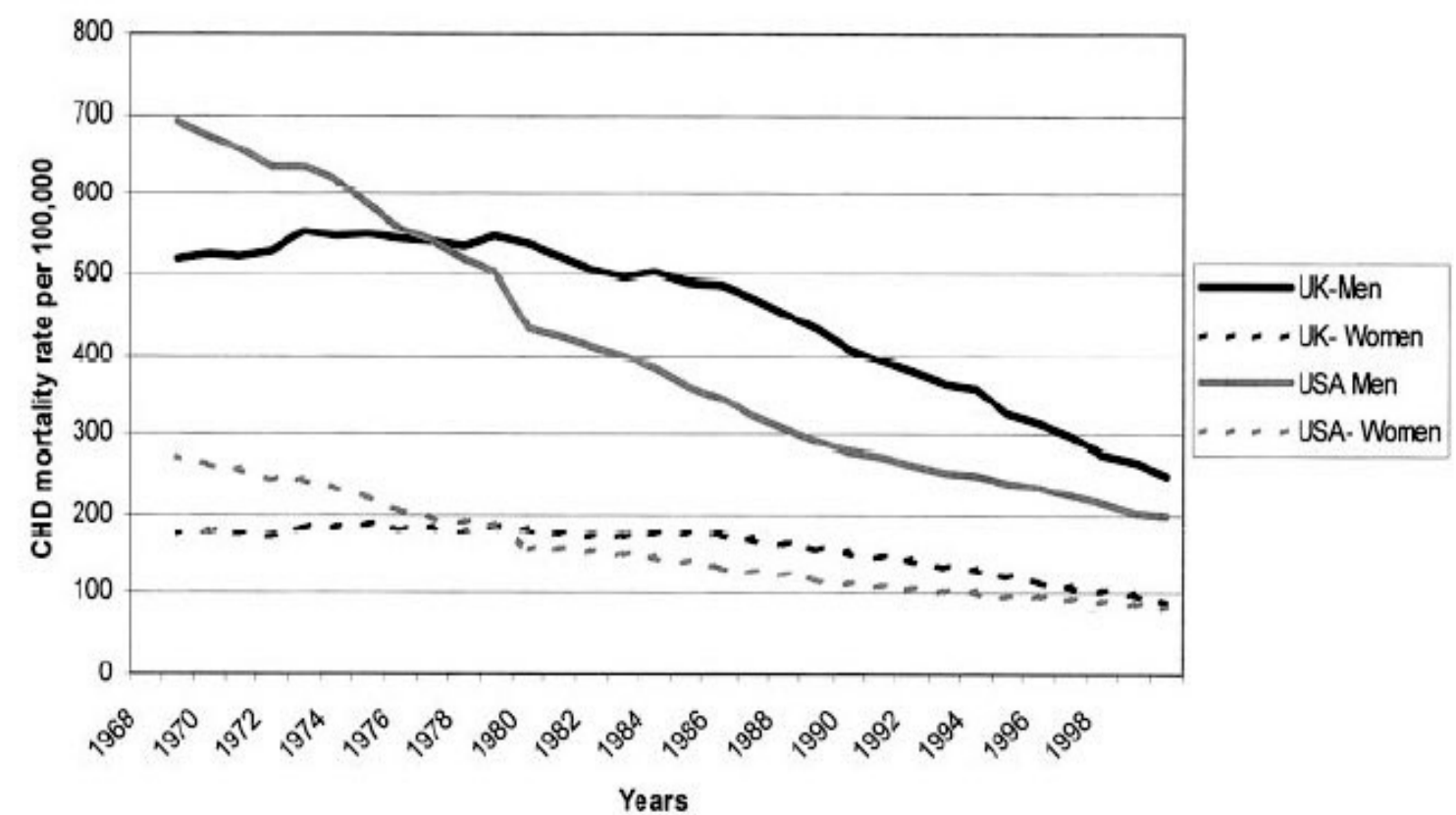
INTER-HEART: Risk of AMI attributable to the population (PAR) in the global population

Risk factor	PAR adjusted by age, gender, & smoking	PAR adjusted by all (99% CI)
ApoB/ApoA-1 (5th quintile compared to the 1st)	54.1 (49.6-58.6)	49.2 (43.8-54.5)
Current smoking	36.4 (33.9-39.0)	35.7 (32.5-39.1)
Diabetes	12.3 (11.2-13.5)	9.9 (8.5-11.5)
Hypertension	23.4 (21.7-25.1)	17.9 (15.7-20.4)
Abdominal obesity	33.7 (30.2-37.4)	20.1 (15.3-26.0)
Psychosocial	28.8 (22.6-35.8)	32.5 (25.1-40.8)
Daily vegetables & fruits	12.9 (10.0-16.6)	13.7 (9.9-18.6)
Exercise	25.5 (20.1-31.8)	12.2 (5.5-25.1)
Alcohol consumption	13.9 (9.3-20.2)	6.7 (2.0-20.2)
All combined	90.4 (88.1-92.4)	90.4 (88.1-92.4)

PAR=population-attributable risk

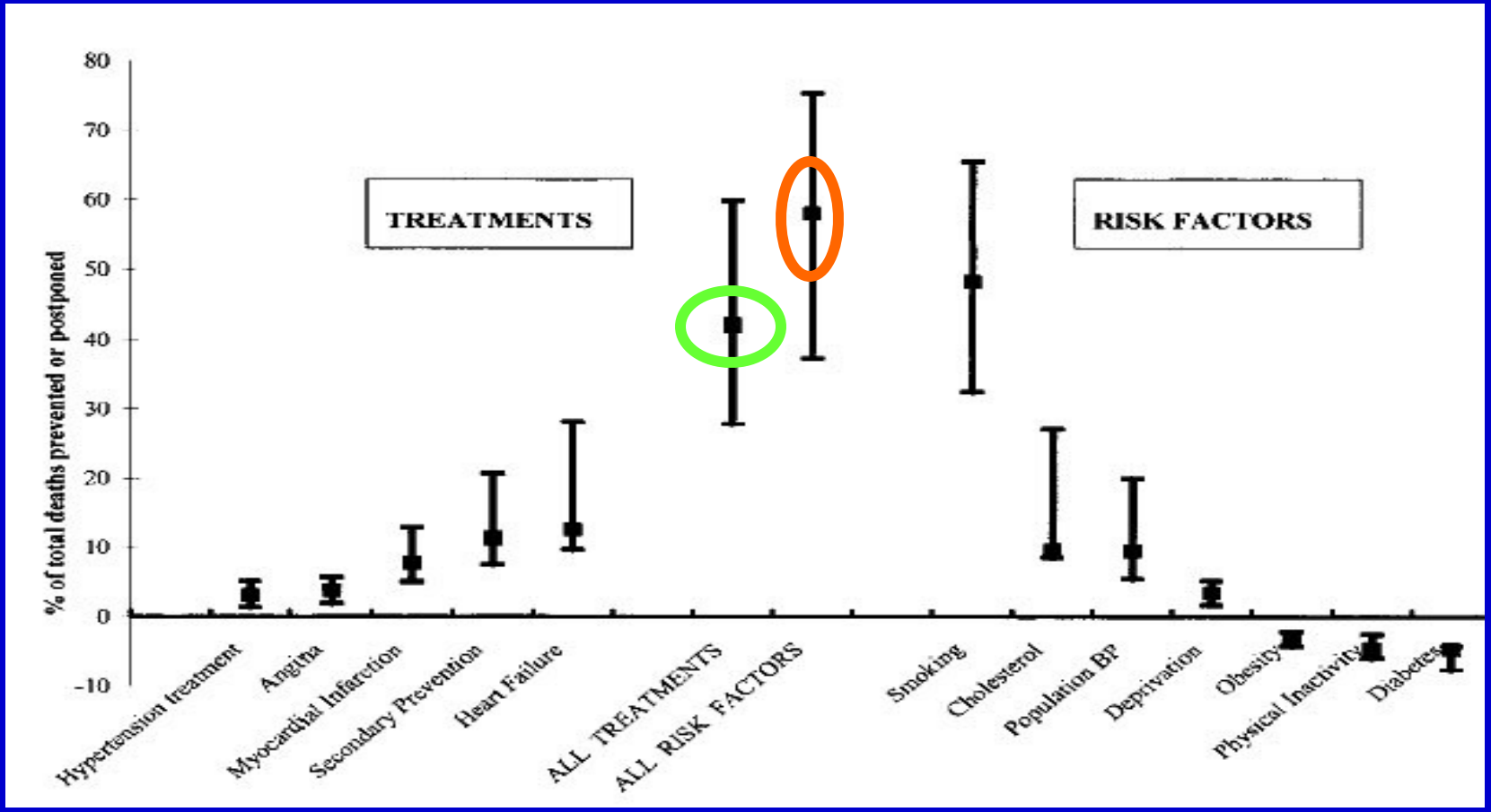
Yusuf S. European Society of Cardiology Congress 2004; August 28-September 1, 2004; Munich, Germany.

MORTALITY by CAD in USA & GREAT BRITAIN between 1968 and 2000



Unal et al; Circulation March 2004

CONTRIBUTION BY SEVERAL INTERVENTIONS TO REDUCING MORTALITY by CAD in ENGLAND & WALES between 1981 and 2000



Unal et al; Circulation March 2004

Deaths prevented according to changes in CRF of the population of England and Wales between 1981 and 2000

CRF	% of change	% prevented deaths
Smoking	- 34	48.1
HBP	- 7.7	9.5
Cholesterol	- 4.2	9.6
Socio-economic	- 6.6	3.4
Total CRF		58.2

Factors that contributed to a decrease in coronary mortality in Scotland (1975-1994) and in New Zealand (1982-1993)

	Scotland	New Zealand
Treatment, %	40	46
Acute myocardial infarction	10	12
Secondary prevention	8	12
Heart Failure	8	7
Aspirin for angina	2	3
CABG surgery	2	4
Hypertension treatment	9	7
Risk factor reduction, %	60	54
Population blood pressure*	15	11
Cholesterol	6	12
Deprivation	3	...
Other factors	9	4
Smoking	36	30

Capewell et al.; Circulation September 2000.

Deaths prevented by different treatments in England and Wales in 2000

- AMI
  - Defibrillation: 3.7 %
  - Thrombolytic agents: 2.1 %
  - Primary PTCA: 0.1 %
- Post-AMI secondary prevention: 6.2 %
- Post-PTCA secondary prevention: 4.9 %
- Unstable angina: 1.5 %
- Heart failure: 12.6 %
- Hypertension: 3.1 %
- Total: 41.8 %

Unal et al; Circulation March 2004


SAGRES

Effects of diet in secondary prevention
Lyon Diet Heart Study

- Post-infarction randomized study
- Mediterranean diet vs. control (N=605)
- 5-year follow up
- Reduction of cardiac death / nonfatal infarction: 73% (p=0.001)
- Reduction of total mortality: 70% (p=0.02)

De Lorgeril et al.; Lancet June 1994

Effects of diet in secondary prevention Indo-Mediterranean Diet Heart Study

- Randomized study in coronary patients
- Indo-mediterranean diet vs. control (N= 1000)
- Follow up in 2 years
- Reduction of coronary events: 50% (p= 0.001)
- Reduction of nonfatal infarction: 53% (p= 0.001)
- Reduction of sudden cardiac death: 67% (p= 0.01)

Singh et al; Lancet Nov. 2002

Effects of diet in primary prevention Greek study with mediterranean diet

- Randomized study in general population
- Mediterranean diet vs. control (N= 22043)
- Follow up in 4 years
- Reduction of coronary mortality: 33%
- Reduction of total mortality: 25%
- Reduction of death by cancer: 24%

Trichopoulou et al.; N Engl J Med Jun. 2003

REDUCTION OF CRF

- IT MUST BE DONE
- IT CAN BE DONE
- AS MUCH AS NECESSARY
- IT WORKS

Final reflections (I)

- 40-year-old patient. Smoker, hypertensive, known but not treated, ignores dyslipemia and diabetes (he suffers from both).
- He suffers extensive anterior infarction. Failed primary angioplasty. Evolves with shock and dies.
- Profession of the patient: physician.

Final reflections (II)

- Prevention of the disease is the most important task in the medical profession.
- Preventing is educating, both the population and health care professionals.
- Educating is not just providing knowledge, but also guaranteeing its feasibility.

THANK YOU FOR YOUR ATTENTION