Traitements associés chez l'hypertendu:

Statines, Aspirine

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DU HTA, Mars 2013

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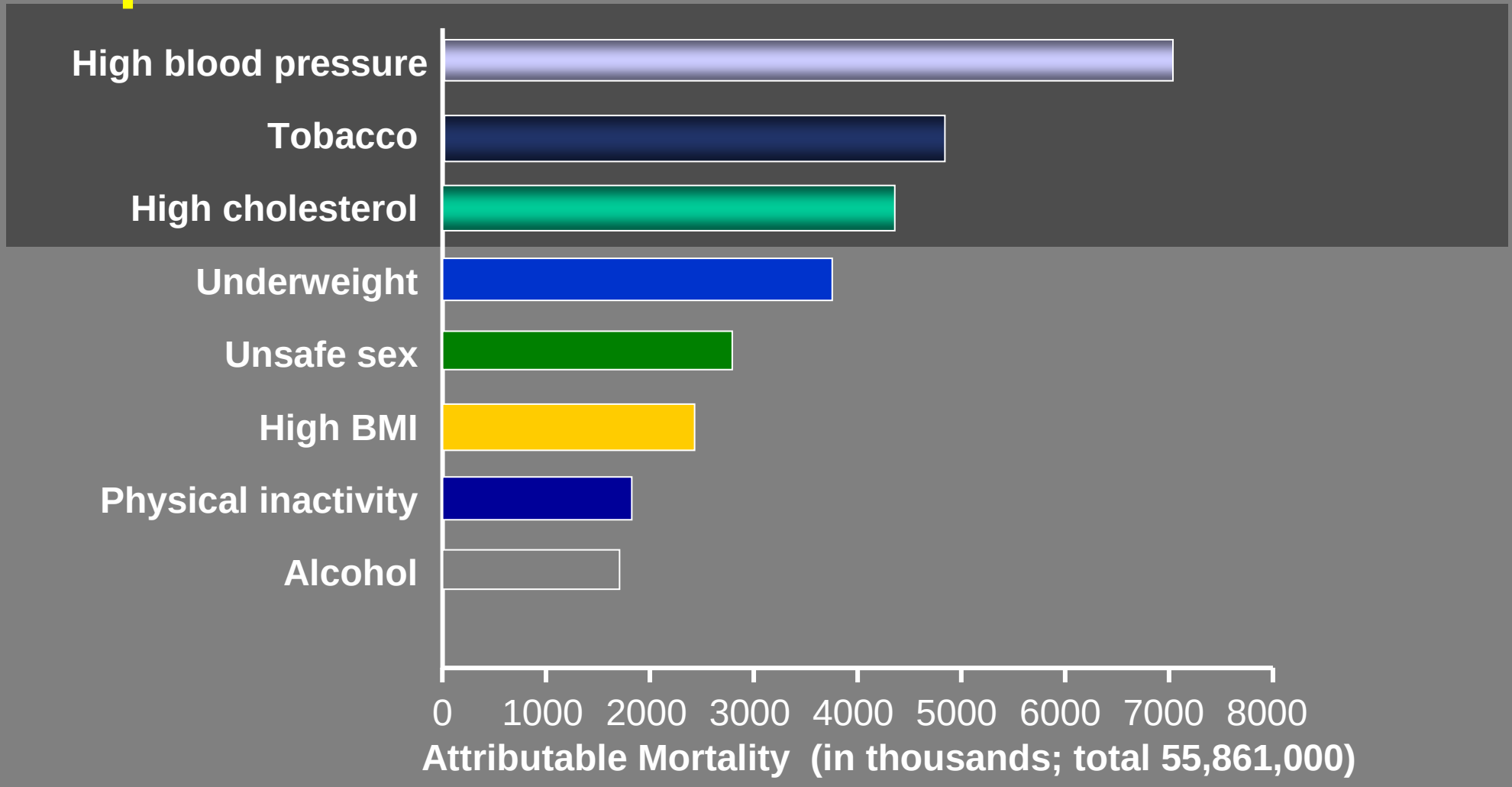
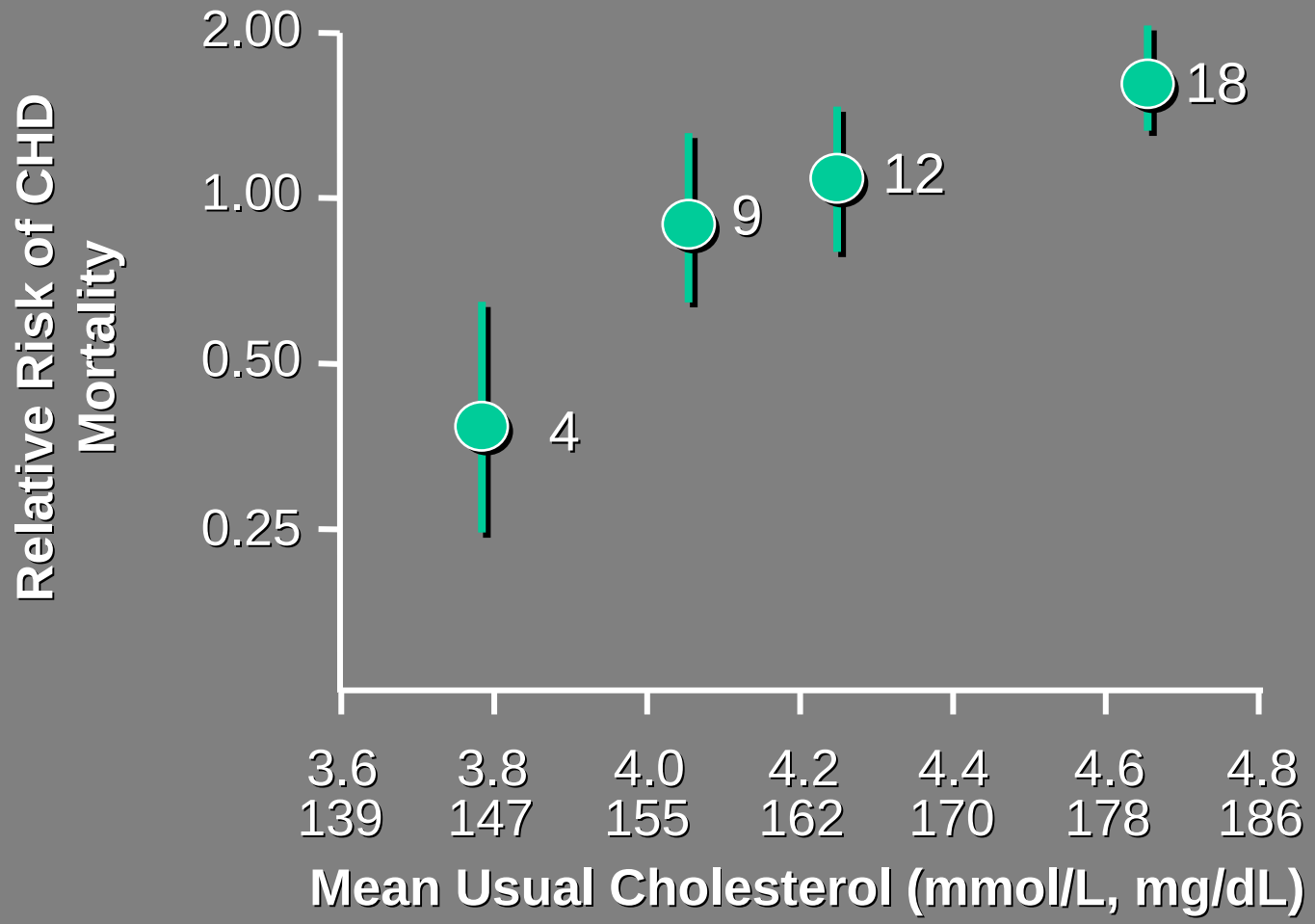
Global Mortality 2000: Impact of Blood Pressure and Cholesterol



Ezzati M, et al. *Lancet*. 2002;360:1347-1360.

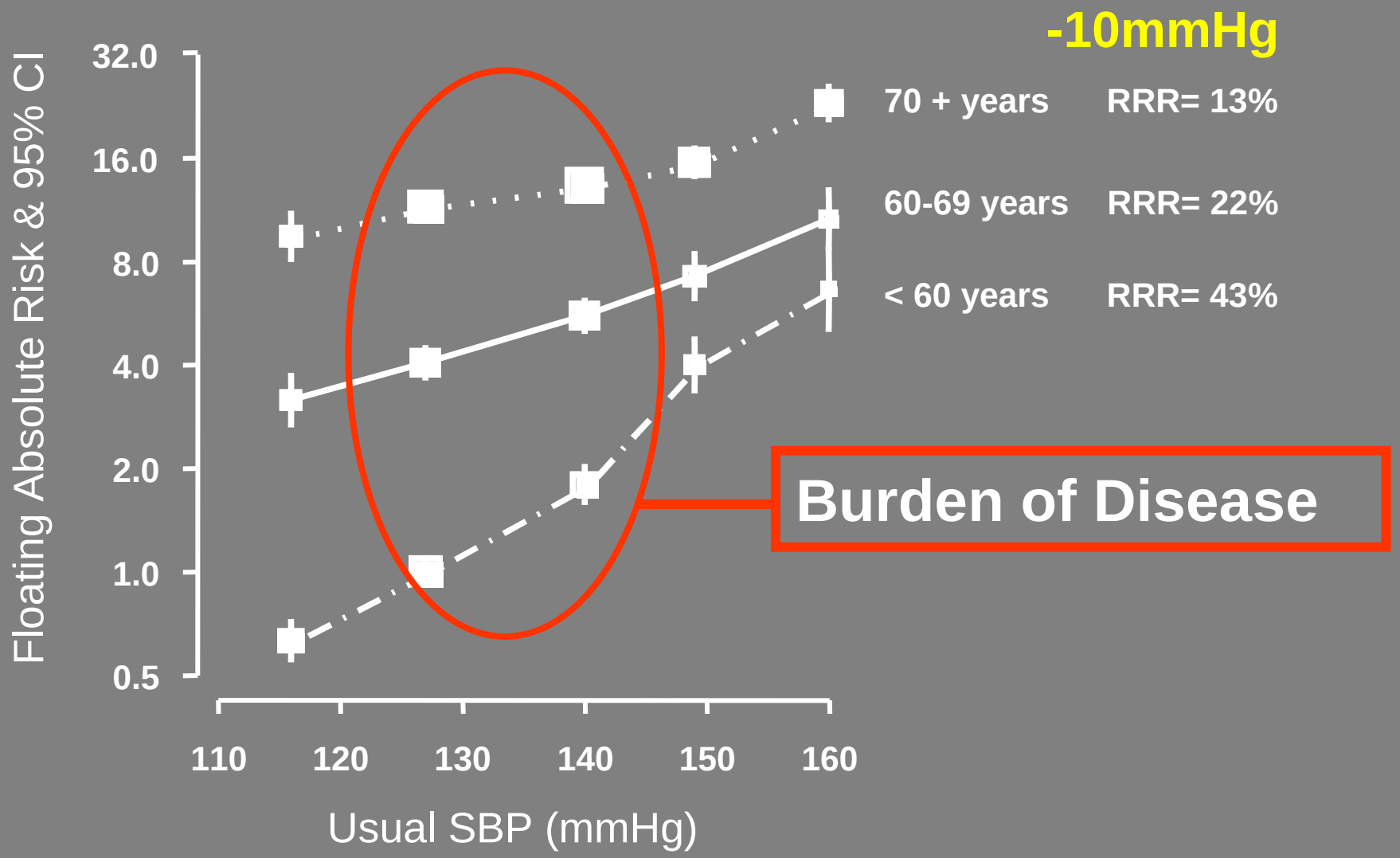
What Is Normal Cholesterol?



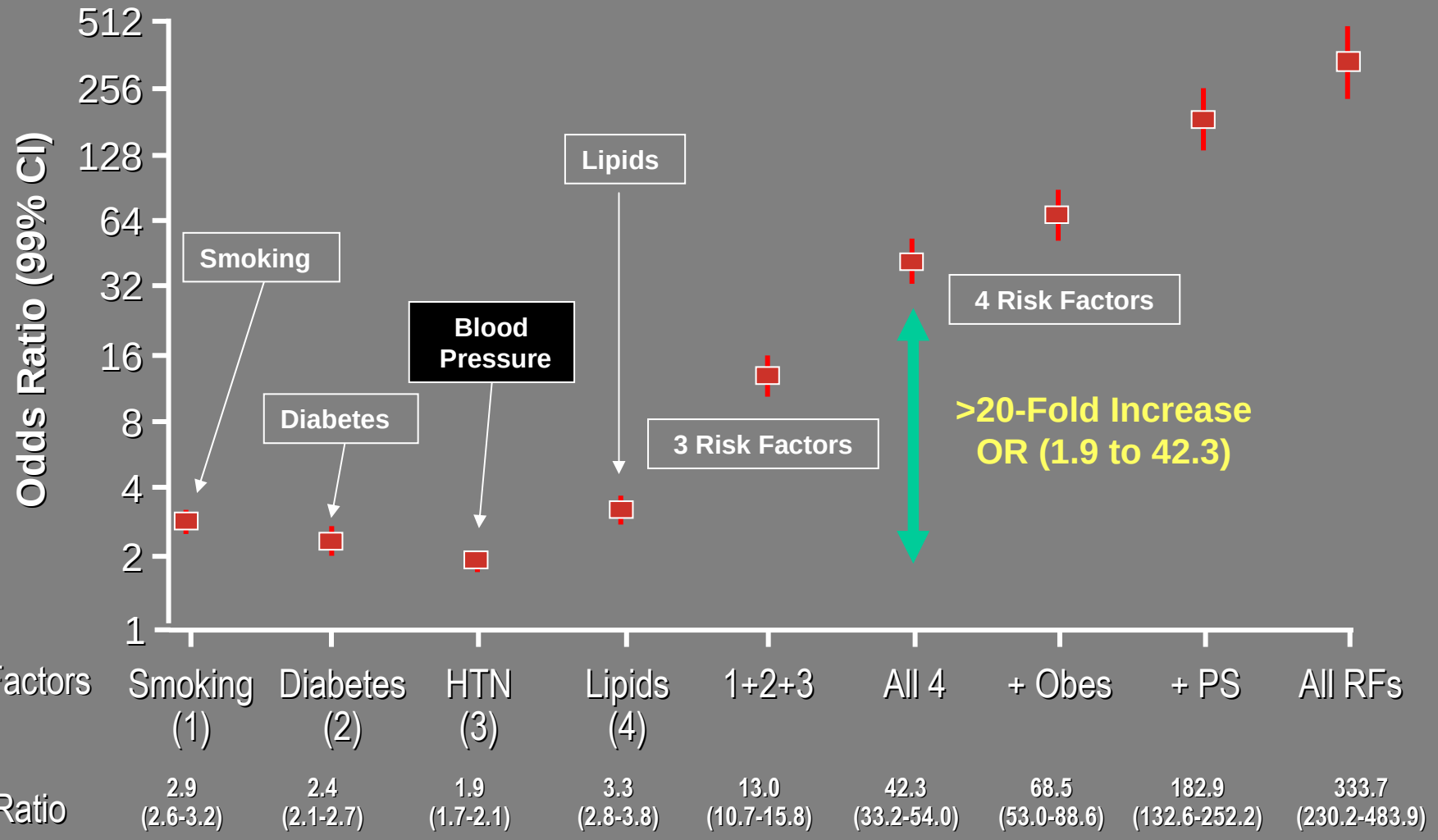
Relative risk of death (± SD) from CHD by quartiles of baseline total cholesterol in 9021 Chinese people with 8-13 years' follow-up.

Chen Z, et al. *BMJ*. 1991;303:276-282.

Coronary disease by usual SBP



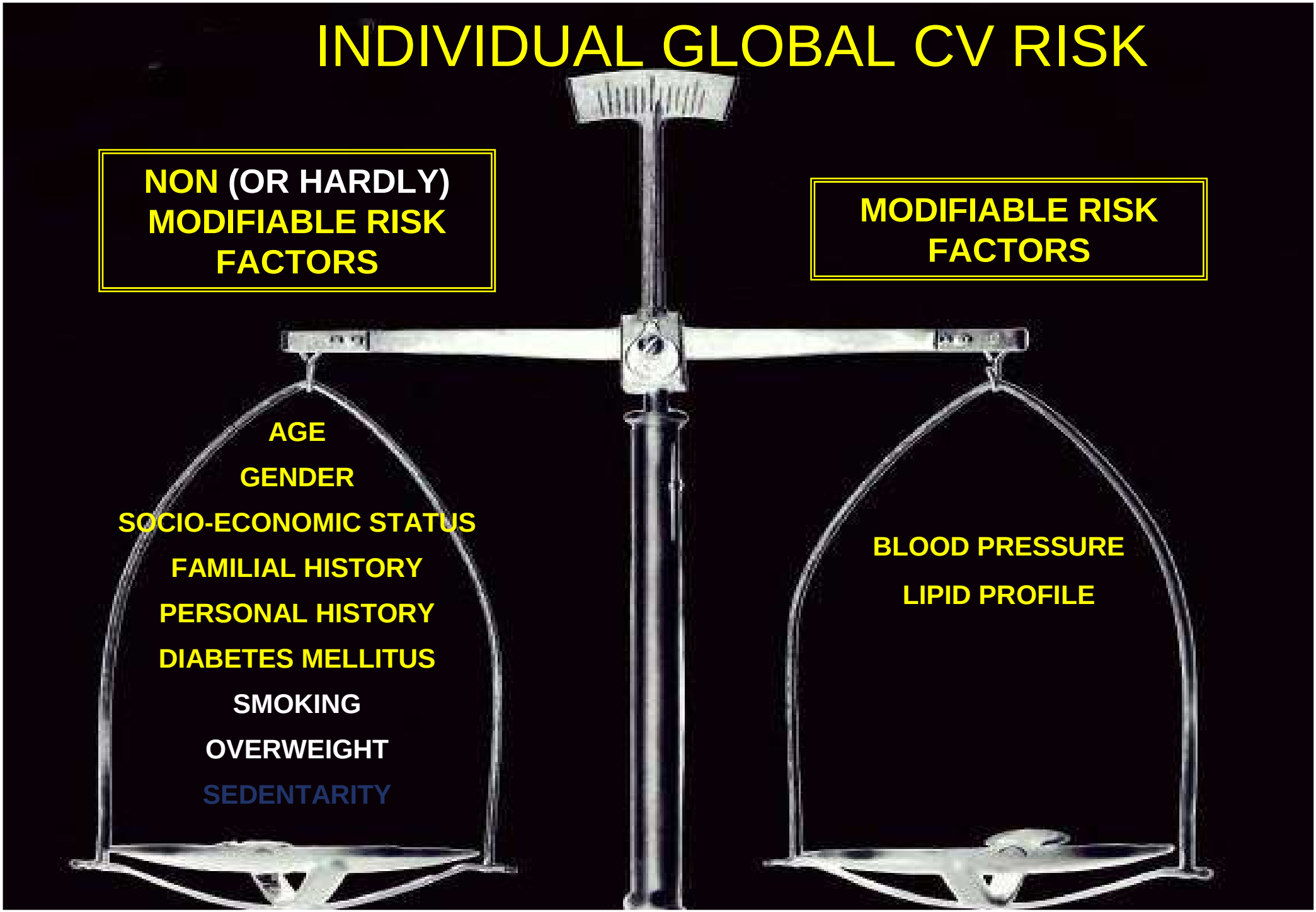
Increased Number of CV Events (MI) in Patients With Hypertension Plus Other CV Risk Factors



HTN = hypertension; MI = myocardial infarction; PS = psychosocial.

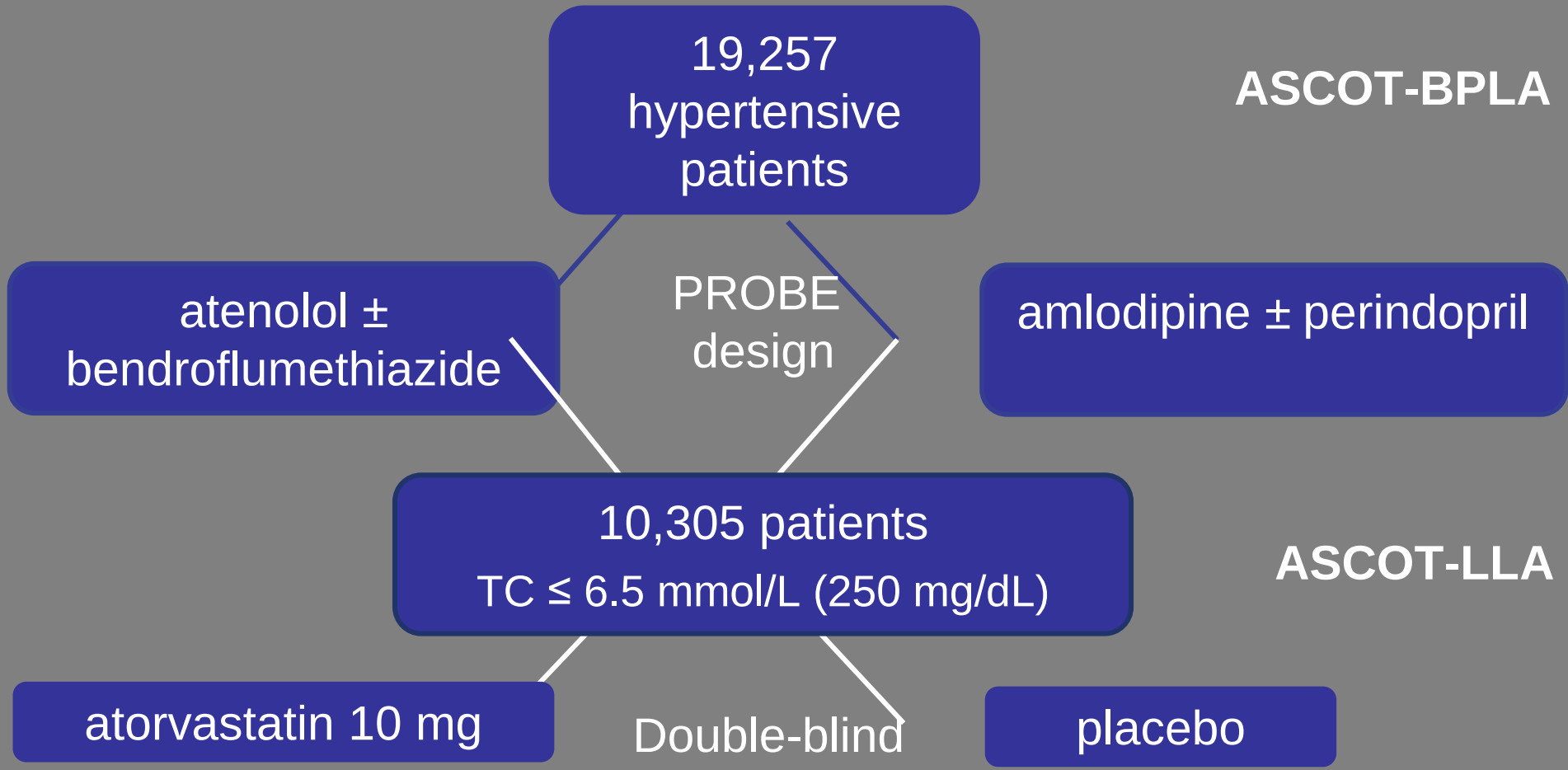
Reproduced with permission from Yusuf S, et al. *Lancet.* 2004;364:937-952.

INDIVIDUAL GLOBAL CV RISK



STATINES

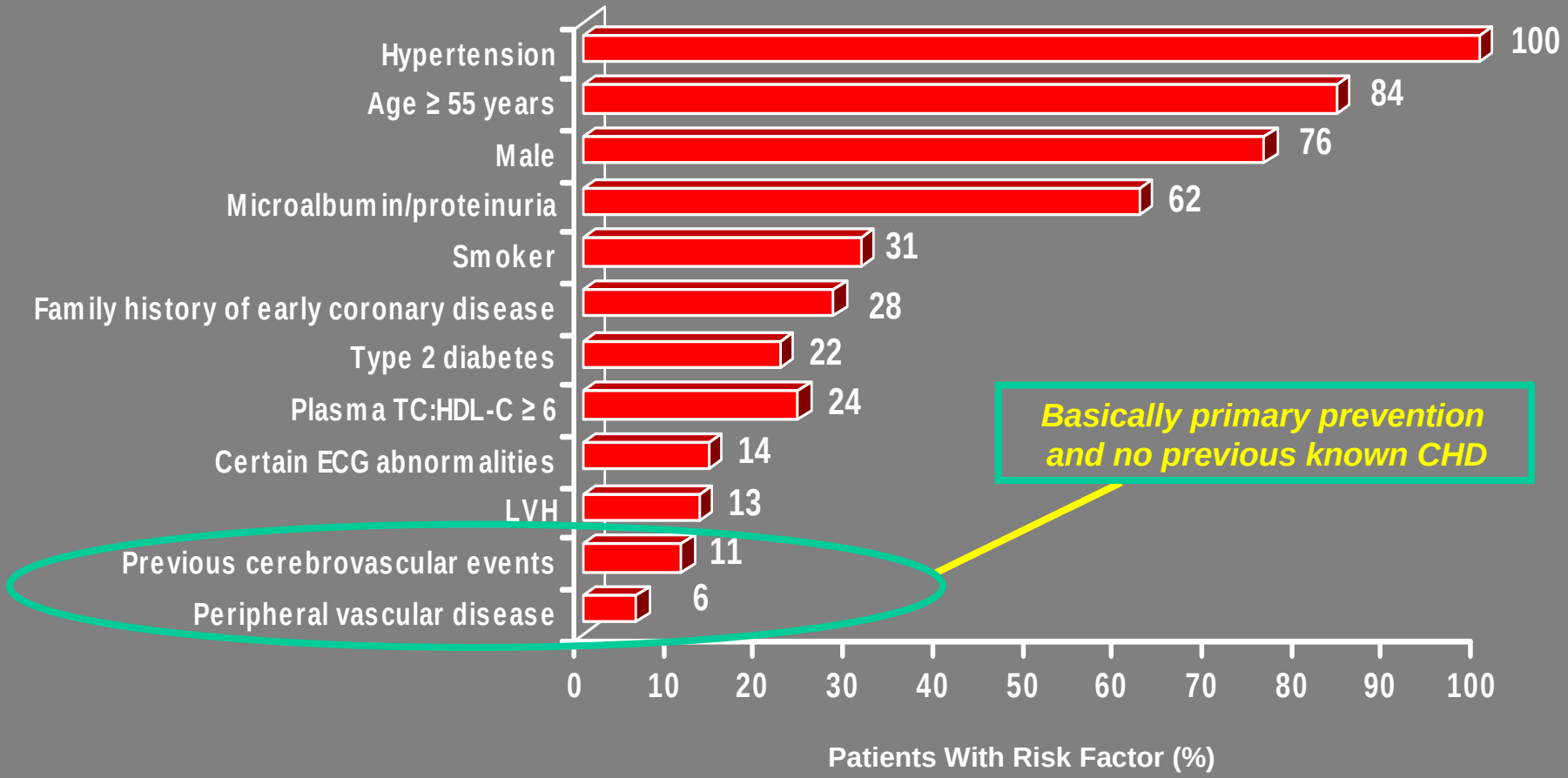
ASCOT Study design



Investigator-lead, multinational randomised controlled trial

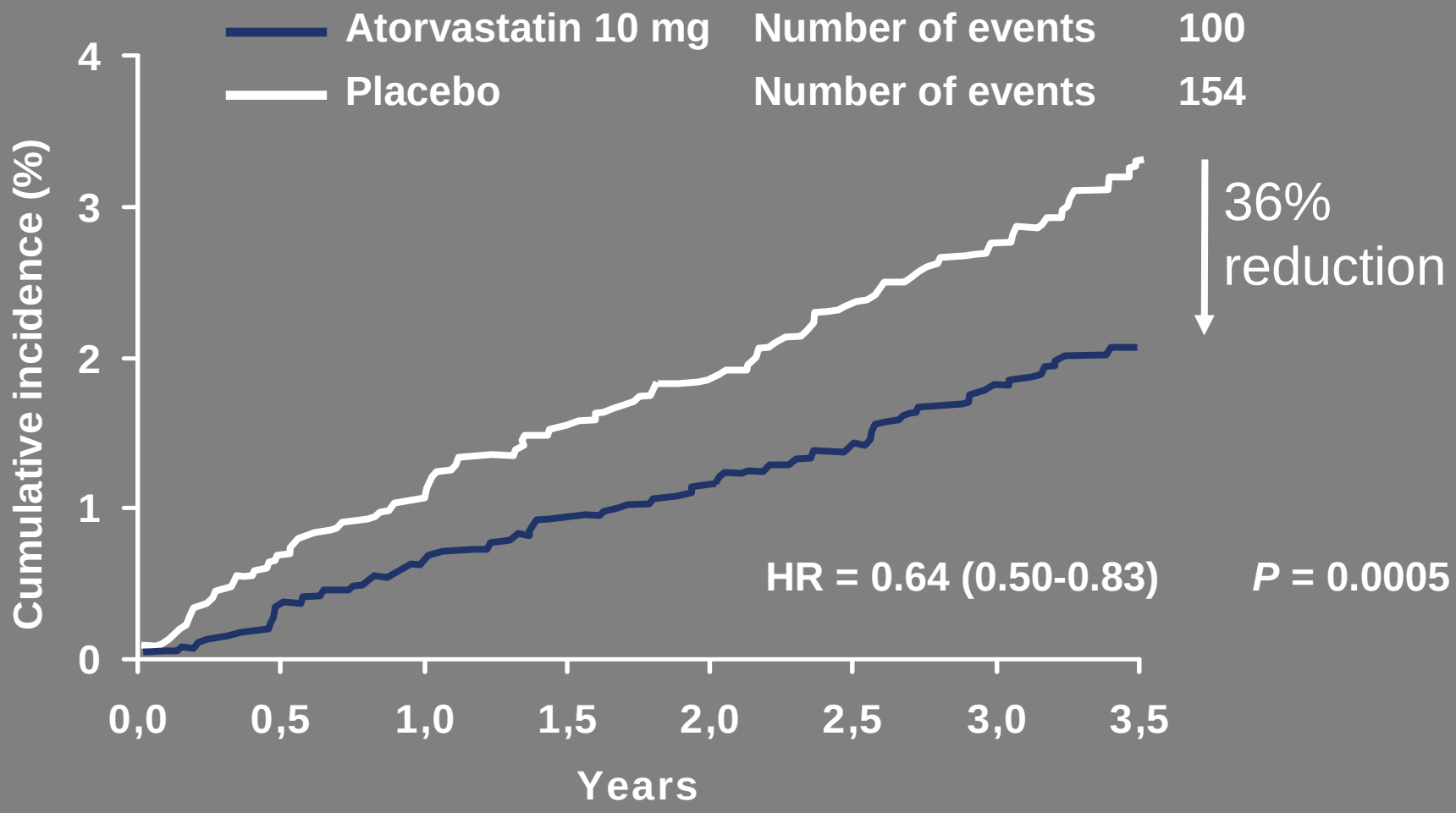
ASCOT LLA: Patient Population Risk Factor Profile

All patients in ASCOT have hypertension plus ≥3 risk factors for CHD



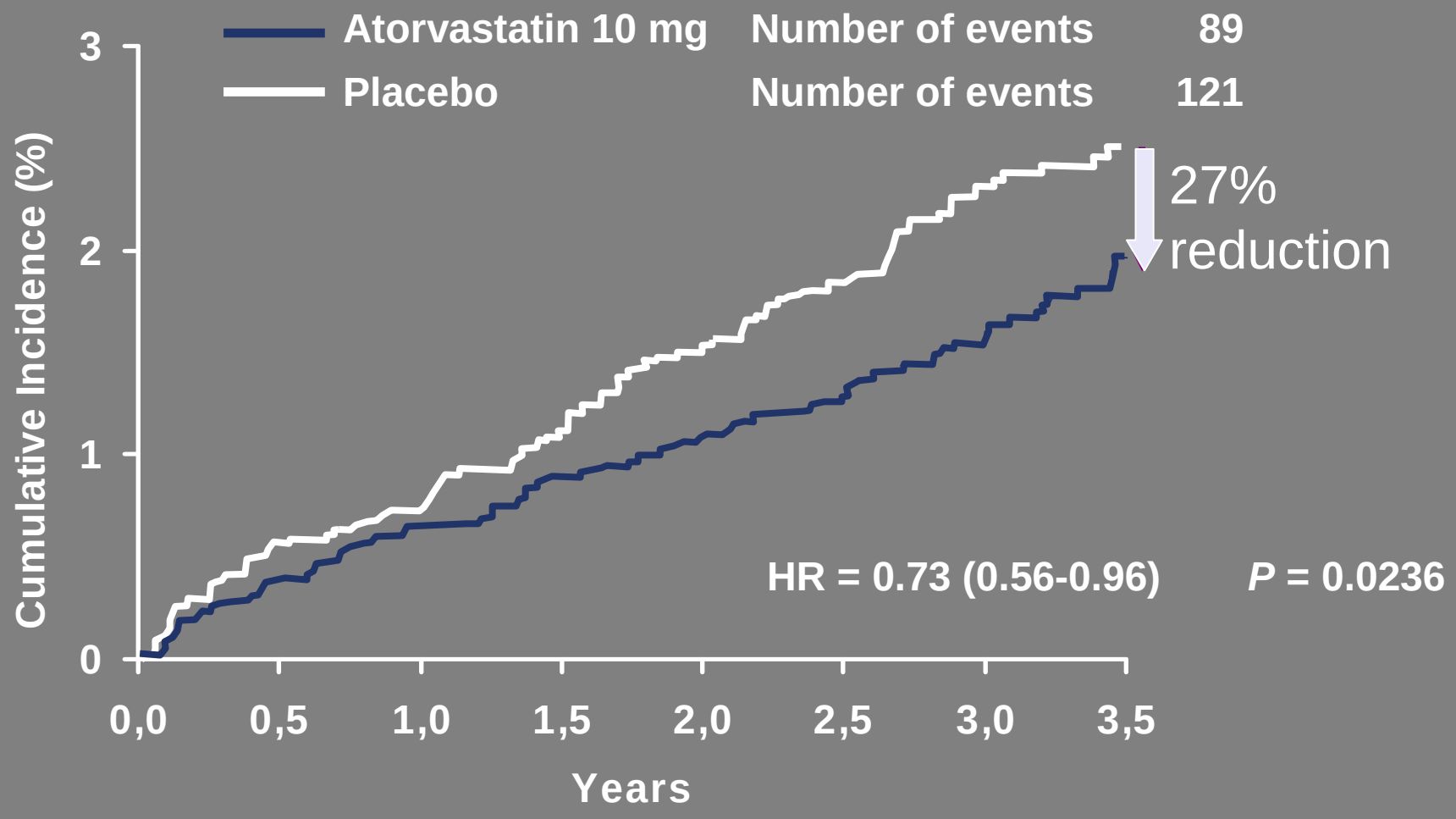
Sever PS, et al. *J Hypertens*. 2001;19:1139-1147.

ASCOT-LLA: Primary End Point: Nonfatal MI and Fatal CHD



Sever PS, Dahlöf B, Poulter N, Wedel H, et al, for the ASCOT Investigators. *Lancet.* 2003;361:1149-58.

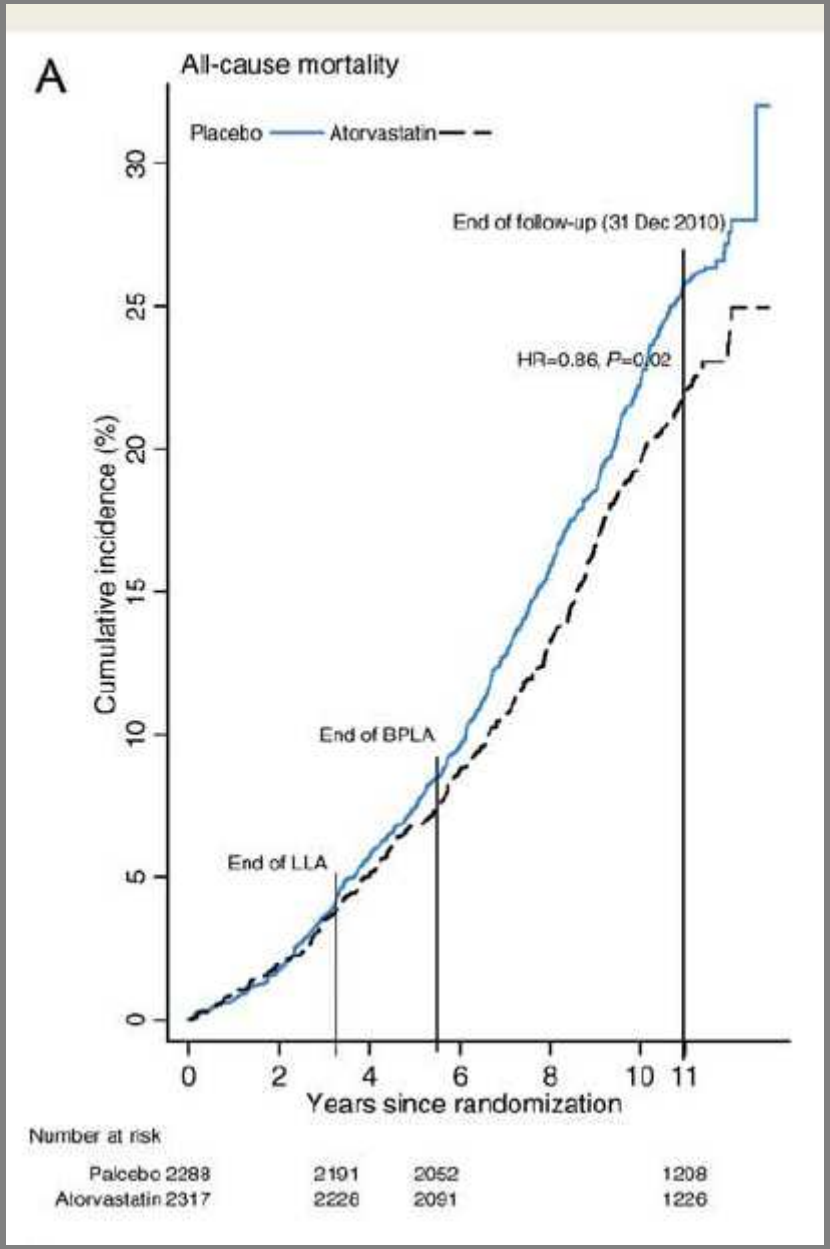
ASCOT-LLA: Secondary End Point: Fatal and Nonfatal Stroke



Sever PS, Dahlöf B, Poulter N, Wedel H, et al, for the ASCOT Investigators. *Lancet.* 2003;361:1149-58.

The Anglo-Scandinavian Cardiac Outcomes Trial: 11-year mortality follow-up of the lipid-lowering arm in the UK

Peter S. Sever*, Choon L. Chang, Ajay K. Gupta, Andrew Whitehouse, and Neil R. Poulter, on behalf of the ASCOT Investigators



European Heart Journal (2011) 32, 2525–2532

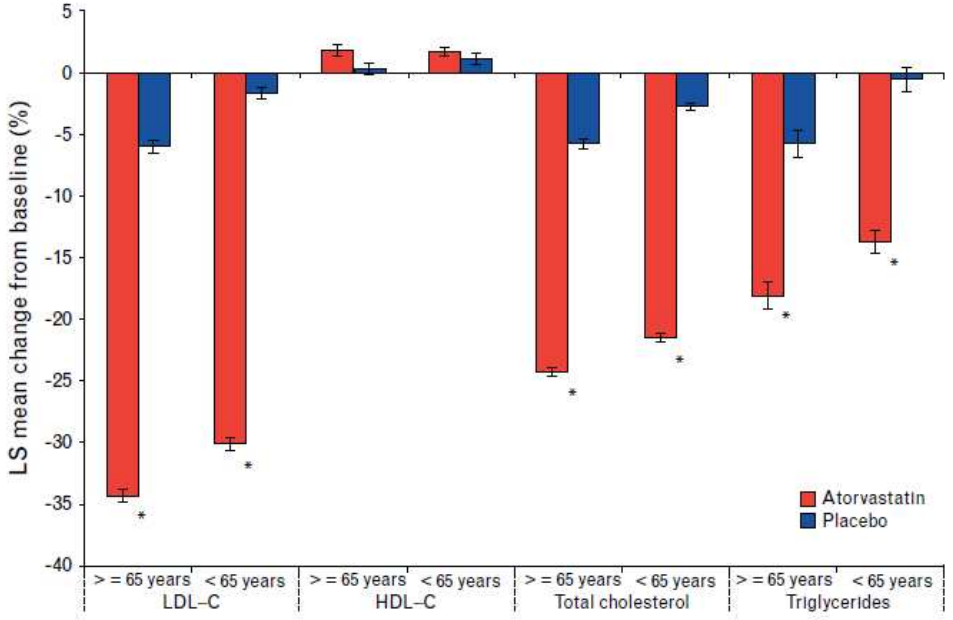
Impact of atorvastatin among older and younger patients in the Anglo-Scandinavian Cardiac Outcomes Trial Lipid-Lowering Arm

David J. Collier[a], Neil R. Poulter[b], Björn Dahlöf[c], Peter S. Sever[b], Hans Wedel[d], Jan Buch[e], Mark J. Caulfield[a], on behalf of the ASCOT Investigators

Table 1 Baseline characteristics

	Patients aged ≥65 years		Patients aged <65 years	
	Atorvastatin ($n=2189$)	Placebo ($n=2256$)	Atorvastatin ($n=2979$)	Placebo ($n=2881$)
Demographic and clinical characteristics				
Men, *n* (%)	1780 (81.3)	1792 (79.4)	2409 (80.9)	2382 (82.7)
Age, years, mean (SD)	71.1 (4.1)	71.1 (4.0)	57.2 (5.6)	57.0 (5.7)
White, *n* (%)	2105 (96.2)	2167 (96.1)	2784 (93.5)	2696 (93.6)
Current smoker, *n* (%)	524 (23.9)	529 (23.4)	1194 (40.1)	1127 (39.1)
Alcohol consumption, mean units/week, (SD)	6.9 (10.4)	6.7 (10.3)	8.8 (11.9)	9.3 (13.1)
SBP, mean mmHg (SD)	168.2 (18.6)	168.2 (18.4)	161.2 (16.5)	161.1 (17.0)
DBP, mean mmHg (SD)	92.3 (10.4)	92.2 (10.3)	97.0 (9.8)	97.2 (9.7)
Heart rate, mean beats/min (SD)	69.8 (12.5)	70.2 (12.4)	72.4 (12.8)	73.1 (12.6)
BMI, mean kg/m^2 (SD)	27.9 (4.4)	28.0 (4.3)	29.2 (4.9)	29.2 (4.7)
TC, mean mg/dl (SD)	210.9 (30.8)	211.8 (30.4)	212.4 (29.9)	211.5 (30.2)
LDL-C, mean mg/dl (SD)	132.8 (28.0)	134.2 (28.2)	133.0 (27.7)	132.1 (27.8)
HDL-C, mean mg/dl (SD)	51.6 (14.4)	51.3 (13.6)	49.9 (13.9)	49.7 (13.8)
Triglycerides, mean mg/dl (SD)	135.9 (68.7)	136.1 (64.9)	154.7 (88.5)	153.2 (85.0)
Glucose, mean mg/dl (SD)	111.7 (37.8)	113.5 (37.8)	111.7 (37.8)	111.7 (37.8)
Creatinine, mean mg/dl (SD)	1.2 (0.2)	1.1 (0.2)	1.1 (0.2)	1.1 (0.2)
Medical history				
Previous stroke or TIA, *n* (%)	285 (13.0)	319 (14.1)	200 (6.7)	197 (6.8)
Diabetes mellitus, *n* (%)	570 (26.0)	620 (27.5)	688 (23.1)	654 (22.7)
LVH (on ECG or ECHO), *n* (%)	340 (15.5)	314 (13.9)	404 (13.6)	415 (14.4)
ECG abnormalities (not LVH), *n* (%)	383 (17.5)	378 (16.8)	358 (12.0)	351 (12.2)
Peripheral vascular disease, *n* (%)	155 (7.1)	142 (6.3)	106 (3.6)	111 (3.9)
Number of risk factors, mean (SD)	3.7 (0.9)	3.7 (0.9)	3.6 (0.8)	3.6 (0.8)
Drug therapy				
No previous antihypertensive use, *n* (%)	378 (17.3)	387 (17.2)	643 (21.6)	609 (21.1)
Prior lipid-lowering therapy, *n* (%)	20 (0.9)	26 (1.2)	21 (0.7)	26 (0.9)
Aspirin use, *n* (%)	534 (24.4)	542 (24.0)	395 (13.3)	360 (12.5)

CVD, cardiovascular disease; ECHO, echocardiogram; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVH, left ventricular hypertrophy; TC, total cholesterol; TIA, transient ischemic attack.



J Hypertens 2011; 29:592–599

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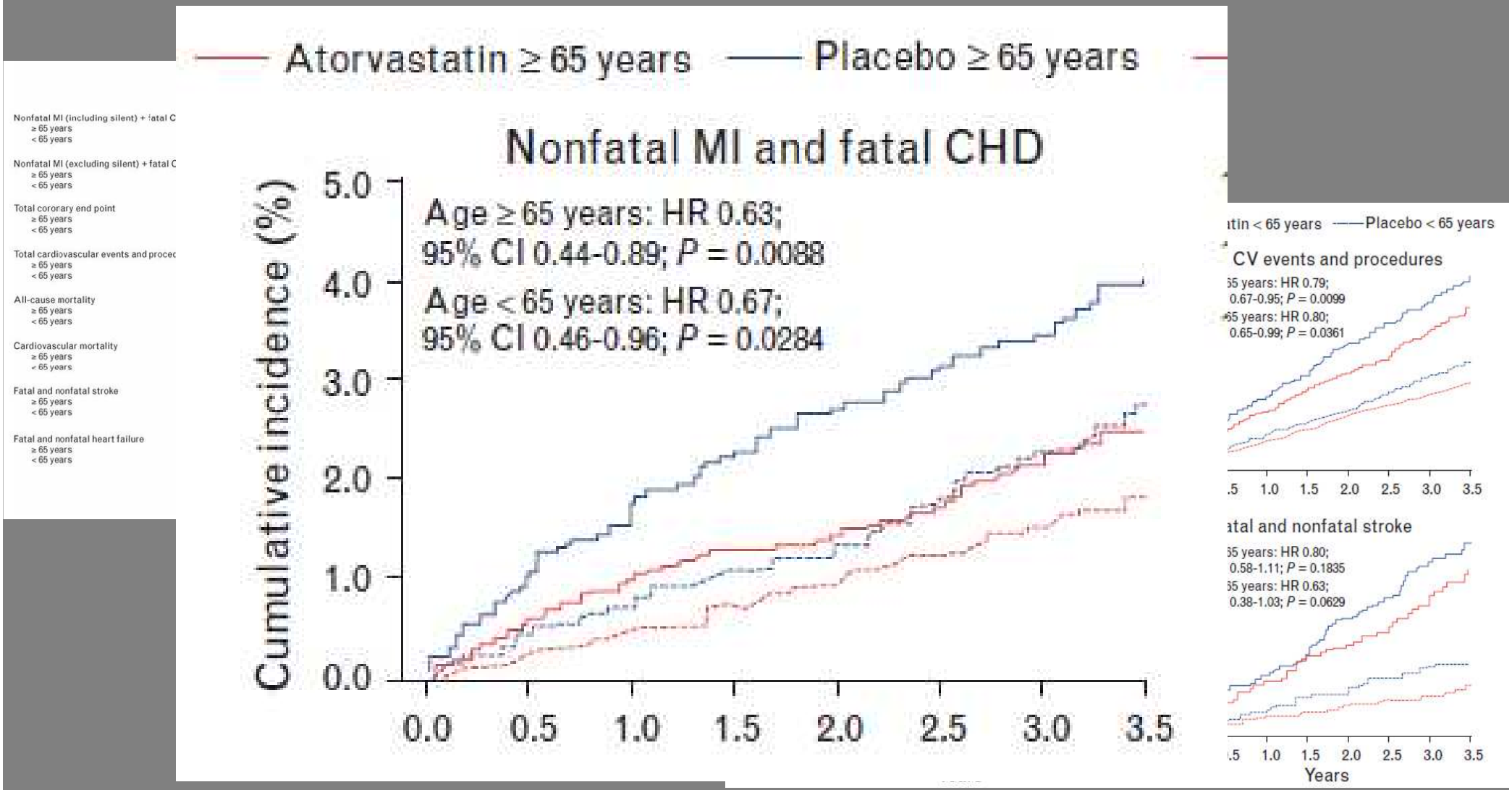
David J. Collier[a], Neil R. Poulter[b], Björn Dahlöf[c], Peter S. Sever[b], Hans Wedel[d], Jan Buch[e], Mark J. Caulfield[a], on behalf of the ASCOT Investigators



J Hypertens 2011; 29:592–599

Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

Characteristic	Rosuvastatin (N=8901)	Placebo (N=8901)
Age — yr		
Median	66.0	66.0
Interquartile range	60.0–71.0	60.0–71.0
Female sex — no. (%)	3426 (38.5)	3375 (37.9)
Race or ethnic group — no. (%)†		
White	6358 (71.4)	6325 (71.1)
Black	1100 (12.4)	1124 (12.6)
Hispanic	1121 (12.6)	1140 (12.8)
Other or unknown	322 (3.6)	312 (3.5)
Body-mass index‡		
Median	28.3	28.4
Interquartile range	25.3–32.0	25.3–32.0
Blood pressure — mm Hg		
Systolic		
Median	134	134
Interquartile range	124–145	124–145
Diastolic		
Median	80	80
Interquartile range	75–87	75–87
Current smoker — no. (%)	1400 (15.7)	1420 (16.0)
Family history of premature CHD — no. (%)§	997 (11.2)	1048 (11.8)
Metabolic syndrome — no. (%)¶	3652 (41.0)	3723 (41.8)
Aspirin use — no. (%)	1481 (16.6)	1477 (16.6)
High-sensitivity C-reactive protein — mg/liter‖		
Median	4.2	4.3
Interquartile range	2.8–7.1	2.8–7.2
LDL cholesterol — mg/dl		
Median	108	108

NEJM 2008;359:2195

Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

Paul M Ridker, M.D., Eleanor Danielson, M.I.A., Francisco A.H. Fonseca, M.D., Jacques Genest, M.D., Antonio M. Gotto, Jr., M.D., John J.P. Kastelein, M.D., Wolfgang Koenig, M.D., Peter Libby, M.D., Alberto J. Lorenzatti, M.D., Jean G. MacFadyen, B.A., Børge G. Nordestgaard, M.D., James Shepherd, M.D., James T. Willerson, M.D., and Robert J. Glynn, Sc.D., for the JUPITER Study Group*

We randomly assigned 17,802 apparently healthy men and women with low-density lipoprotein (LDL) cholesterol levels of less than 130 mg per deciliter (3.4 mmol per liter) and high-sensitivity C-reactive protein levels of 2.0 mg per liter or higher to rosuvastatin, 20 mg daily, or placebo

Table 3. Outcomes According to Study Group.

End Point	Rosuvastatin (N=8901)		Placebo (N=8901)		Hazard Ratio (95% CI)	P Value
	No. of Patients	Rate per 100 person-yr	No. of Patients	Rate per 100 person-yr		
Primary end point	142	0.77	251	1.36	0.56 (0.46–0.69)	<0.00001
Nonfatal myocardial infarction	22	0.12	62	0.33	0.35 (0.22–0.58)	<0.00001
Any myocardial infarction	31	0.17	68	0.37	0.46 (0.30–0.70)	0.0002
Nonfatal stroke	30	0.16	58	0.31	0.52 (0.33–0.80)	0.003
Any stroke	33	0.18	64	0.34	0.52 (0.34–0.79)	0.002
Arterial revascularization	71	0.38	131	0.71	0.54 (0.41–0.72)	<0.0001
Hospitalization for unstable angina	16	0.09	27	0.14	0.59 (0.32–1.10)	0.09
Arterial revascularization or hospitalization for unstable angina	76	0.41	143	0.77	0.53 (0.40–0.70)	<0.00001
Myocardial infarction, stroke, or confirmed death from cardiovascular causes	83	0.45	157	0.85	0.53 (0.40–0.69)	<0.00001
Death from any cause						
Death on known date	190	0.96	235	1.19	0.81 (0.67–0.98)	0.03
Any death	198	1.00	247	1.25	0.80 (0.67-0.97)	0.02

N Engl J Med 2008;359:2195-207

Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein

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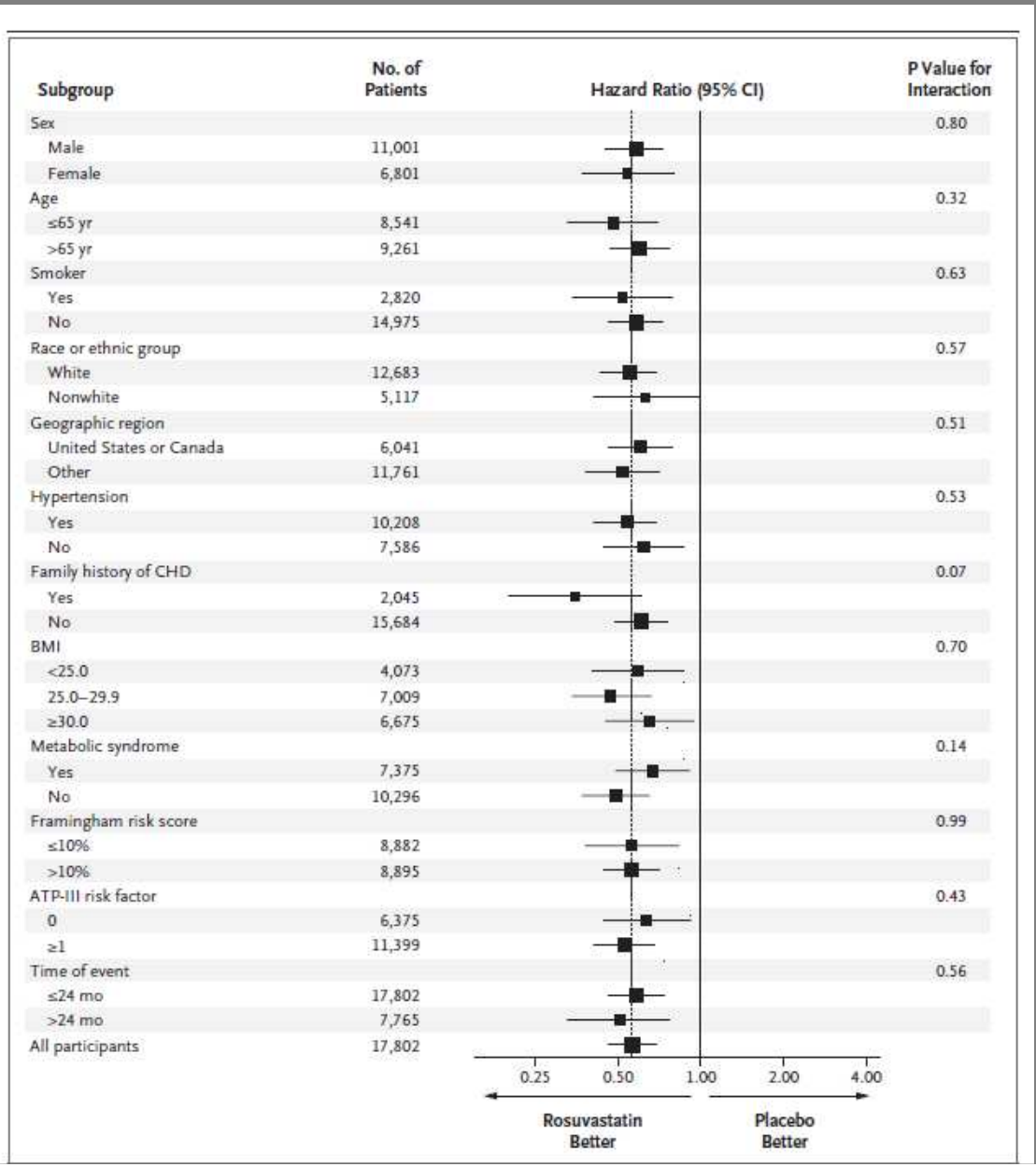
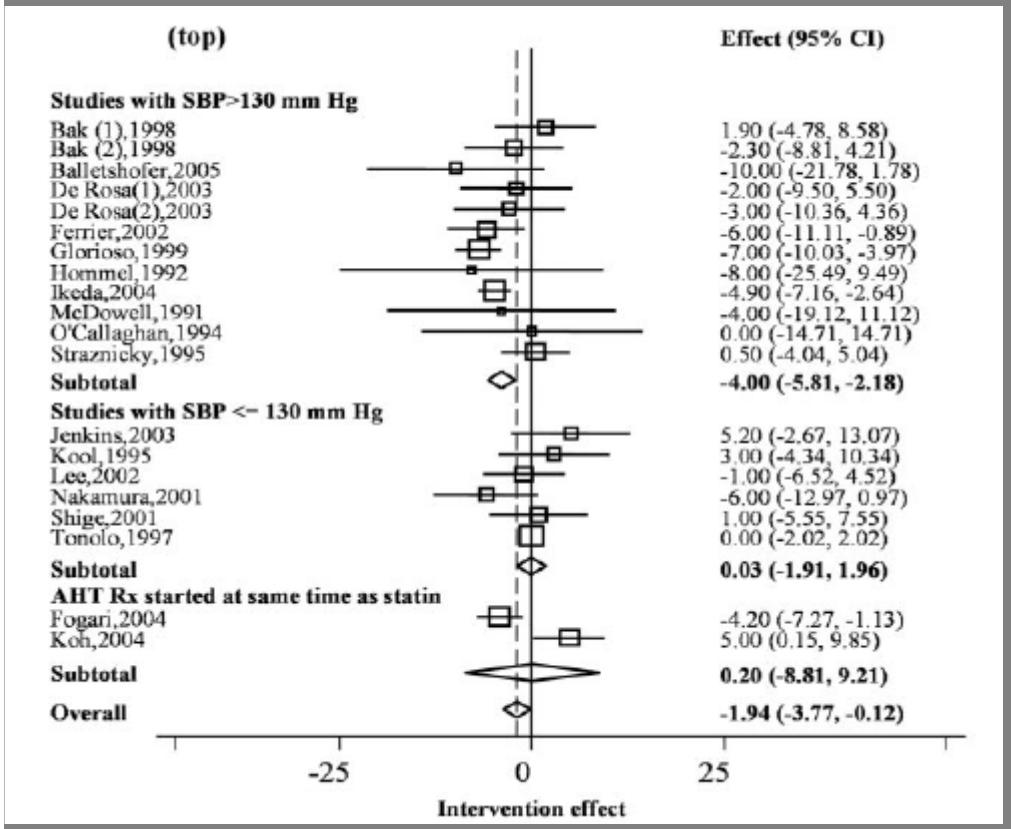


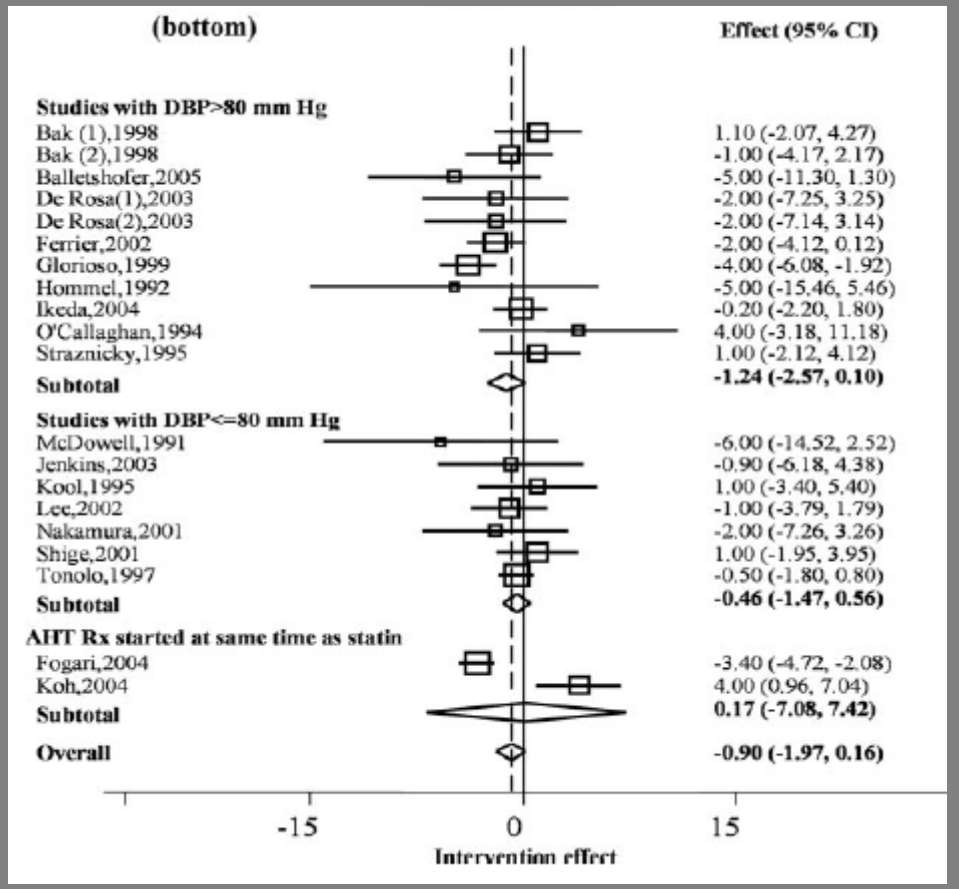
N Engl J Med 2008;359:2195-207

Do Statins Reduce Blood Pressure?

A Meta-Analysis of Randomized, Controlled Trials

Pasquale Strazzullo, Sally M. Kerry, Antonio Barbato, Marco Versiero, Lanfranco D'Elia, Francesco P. Cappuccio





Hypertension. 2007;49:792-798

Statin Use and Risk of Diabetes Mellitus in Postmenopausal Women in the Women's Health Initiative

Annie L. Culver, BPharm; Ira S. Ockene, MD; Raji Balasubramanian, ScD; Barbara
Deidre M. Sepavich, MBA; Jean Wactawski-Wende, PhD; JoAnn E. Manson, MD, Dr
Simin Liu, MD, ScD; Philip A. Merriam, MSPH; Catherine Rahilly-Tierny, MD, MPH
Jeffrey S. Berger, MD, MS; Judith K. Ockene, PhD, MEd, MA; J. David Curb, MD; Yu

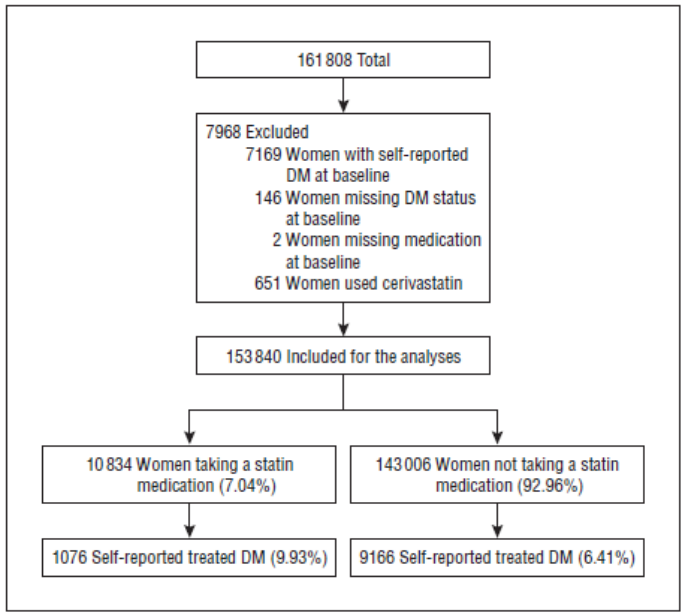


Figure. Flowchart for statin users and diabetes mellitus (DM) analyses using data sets from the Women's Health Initiative.

Table 1. Characteristics of 153 840 Study Participants, Women's Health Initiative[a]

Variable	Total (N = 153 840)	Statin Users (n = 10 834)	Non–Statin Users (n = 143 006)	*P* Value
Age, y	63.17 (7.25)	65.66 (6.48)	62.98 (7.27)	<.001
BMI	27.77 (5.81)	28.56 (5.32)	27.70 (5.84)	<.001
Dietary variable				
Energy intake, kcal/d	1625.24 (711.56)	1541.81 (690.42)	1631.56 (712.75)	<.001
Carbohydrate, % of energy	50.34 (9.37)	52.12 (9.34)	50.21 (9.36)	<.001
Protein, % of energy	16.71 (3.21)	17.06 (3.31)	16.68 (3.20)	<.001
Fat, % of energy	32.53 (8.39)	30.79 (8.37)	32.66 (8.38)	.81
Saturated fat, % of energy	10.84 (3.33)	9.94 (3.15)	10.91 (3.34)	<.001
Trans fat, g/d	4.29 (3.22)	4.02 (3.08)	4.31 (3.23)	<.001
Fiber, g/d	15.88 (7.14)	15.63 (7.07)	15.90 (7.14)	.18
Alcohol intake, g/d	5.32 (10.58)	4.47 (9.44)	5.38 (10.65)	<.001
Physical activity				
Minutes of recreational physical activity per week[b]	183.40 (180.53)	177.50 (167.28)	183.86 (181.52)	<.001
Categorical variable, No. (%)				
Race/ethnicity				
Asian or Pacific Islander	3922 (2.56)	401 (3.71)	3521 (2.47)	<.001
African American	12 772 (8.32)	862 (7.97)	11 910 (8.35)	
Hispanic/Latino	5978 (3.90)	322 (2.98)	5656 (3.96)	
European American, not of Hispanic origin	12 8458 (83.71)	9065 (83.87)	119 393 (83.69)	
Education				
<High school	7711 (5.05)	651 (6.05)	7060 (4.97)	<.001
High school/GED	25 955 (17.0)	2241 (20.83)	23 714 (16.71)	
>High school, <4 y college	57 740 (37.81)	4205 (39.08)	53 535 (37.72)	
≥4 y college	61 285 (40.14)	3663 (34.04)	57 622 (40.60)	
Smoking status				
Never	77 364 (50.94)	5178 (48.48)	72 186 (51.13)	<.001
Former	63 893 (42.07)	4858 (45.49)	59 035 (41.81)	
Current	10 605 (6.98)	644 (6.03)	9961 (7.06)	
Hormone therapy use				
Never	49 198 (32.94)	3654 (34.42)	45 544 (32.83)	<.001
Former	34 430 (23.05)	2633 (24.80)	31 797 (22.92)	
Current	65 720 (44.0)	4330 (40.78)	61 390 (44.25)	
Family history of DM				
Yes	47 329 (30.93)	3653 (33.91)	43 676 (30.70)	<.001
No	98 686 (64.48)	6599 (61.26)	92 087 (64.73)	
Type of statin medication use at baseline				
Lovastatin	2957 (27.29)	2957 (27.29)	NA	NA
Simvastatin	3282 (30.29)	3282 (30.29)	NA	NA
Fluvastatin	1316 (12.15)	1316 (12.15)	NA	NA
Atorvastatin	839 (7.74)	839 (7.74)	NA	NA
Pravastatin	2440 (22.52)	2440 (22.52)	NA	NA

Arch Intern Med. 2012;172(2):144-152

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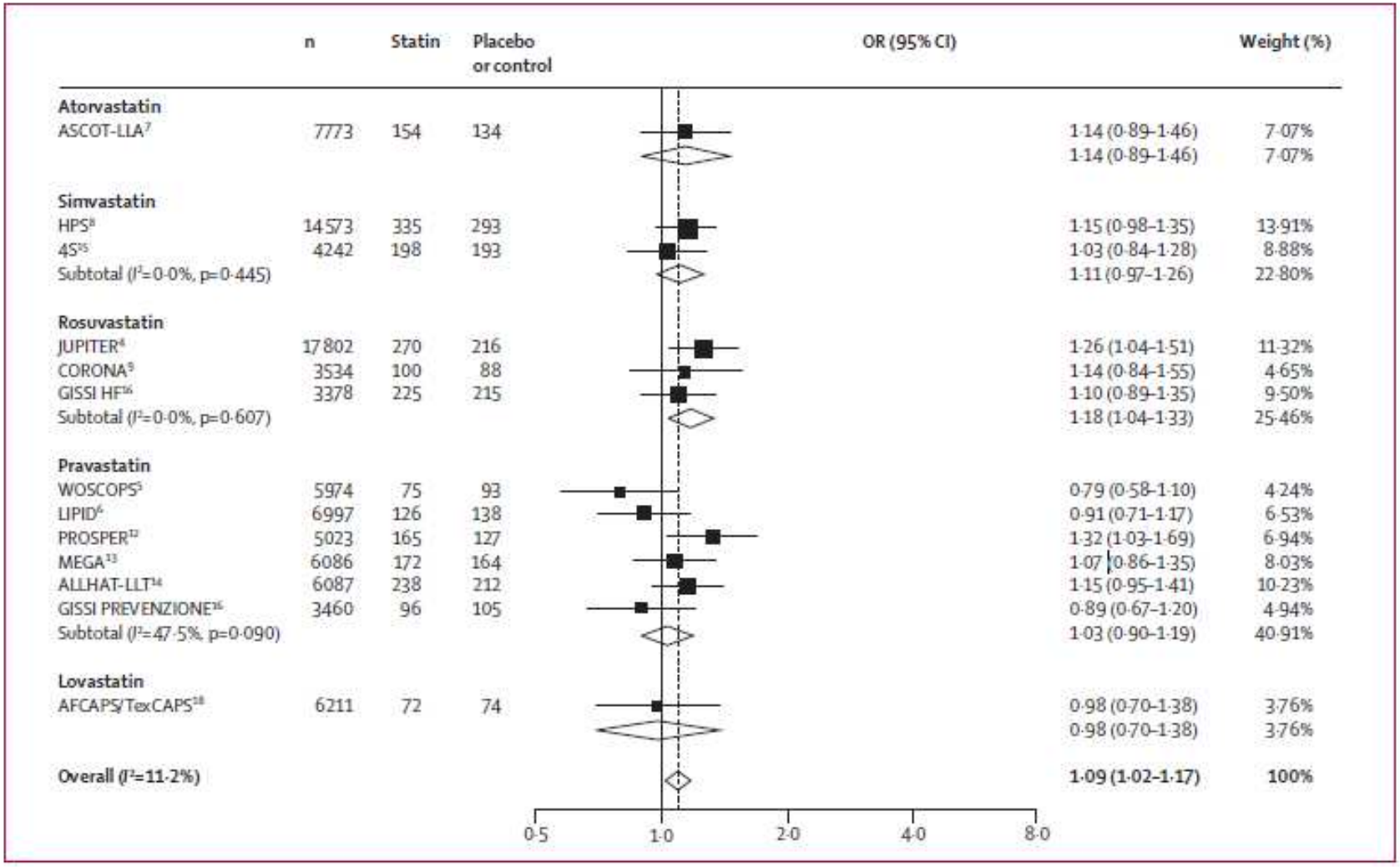
Variable	Patients, No.	Cases of New-Onset DM	Unadjusted HR	Age- and Race/Ethnicity-Adjusted HR[a]	Multivariate-Adjusted HR[b]
Taking statin medications at baseline					
Yes	10 834	1076 (9.93)	1.71 (1.61-1.83)	1.69 (1.58-1.80)	1.48 (1.38-1.59)
No	143 006	9166 (6.41)	1 [Reference]	1 [Reference]	1 [Reference]
Years of statin medication use					
<1.0	3614	360 (9.96)	1.74 (1.57-1.94)	1.71 (1.54-1.90)	1.46 (1.30-1.64)
1.0-2.9	3650	365 (10.00)	1.72 (1.55-1.91)	1.67 (1.51-1.86)	1.42 (1.26-1.59)
≥3.0	3570	351 (9.83)	1.68 (1.51-1.87)	1.68 (1.51-1.87)	1.57 (1.40-1.77)
Nonuser	143 006	9166 (6.41)	1 [Reference]	1 [Reference]	1 [Reference]
Type of statin medications at baseline					
Lovastatin					
Yes	2949	281 (9.53)	1.52 (1.35-1.71)	1.51 (1.33-1.70)	1.35 (1.19-1.55)
Other statins	7885	795 (10.08)	1.85 (1.72-1.99)	1.82 (1.69-1.97)	1.56 (1.43-1.69)
Nonuser	143 006	9166 (6.41)	1 [Reference]	1 [Reference]	1 [Reference]
Simvastatin					
Yes	3247	310 (9.55)	1.71 (1.52-1.92)	1.72 (1.53-1.93)	1.41 (1.25-1.61)
Other statins	7587	766 (10.10)	1.77 (1.64-1.91)	1.73 (1.61-1.87)	1.54 (1.41-1.67)
Nonuser	143 006	9166 (6.41)	1 [Reference]	1 [Reference]	1 [Reference]
Fluvastatin					
Yes	1313	145 (11.04)	1.99 (1.69-2.35)	1.90 (1.61-2.24)	1.61 (1.35-1.92)
Other statins	9521	931 (9.78)	1.72 (1.60-1.84)	1.71 (1.59-1.83)	1.48 (1.37-1.60)
Nonuser	143 006	9166 (6.41)	1 [Reference]	1 [Reference]	1 [Reference]
Atorvastatin					
Yes	839	79 (9.42)	1.99 (1.58-2.49)	1.99 (1.58-2.49)	1.61 (1.26-2.06)
Other statins	9995	997 (9.97)	1.74 (1.63-1.86)	1.72 (1.61-1.84)	1.49 (1.39-1.61)
Nonuser	143 006	9166 (6.41)	1 [Reference]	1 [Reference]	1 [Reference]
Pravastatin					
Yes	2423	256 (10.57)	1.87 (1.65-2.13)	1.83 (1.61-2.07)	1.63 (1.43-1.87)
Other statins	8411	820 (9.75)	1.71 (1.59-1.84)	1.70 (1.58-1.83)	1.46 (1.34-1.58)
Nonuser	143 006	9166 (6.41)	1 [Reference]	1 [Reference]	1 [Reference]
Potency of statin at baseline					
Low potency: lovastatin, fluvastatin and pravastatin	6701	682 (10.18)	1.68 (1.56-1.82)	1.64 (1.52-1.78)	1.48 (1.36-1.61)
High-potency: simvastatin and atorvastatin	4133	394 (9.53)	1.74 (1.58-1.93)	1.75 (1.58-1.93)	1.45 (1.36-1.61)
Nonuser	143 006	9166 (6.41)	1 [Reference]	1 [Reference]	1 [Reference]

Abbreviations: HR, hazard ratio; PH, proportional hazards.
[a] The HRs were estimated from Cox PH models adjusting for age and race/ethnicity.
[b] The HRs were estimated from Cox PH models, adjusting for age, race/ethnicity, education, cigarette smoking, BMI, physical activity, alcohol intake, energy intake, family history of DM, hormone therapy use, study arms, and self-report of cardiovascular disease at baseline.

Arch Intern Med. 2012;172(2):144-152

Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials



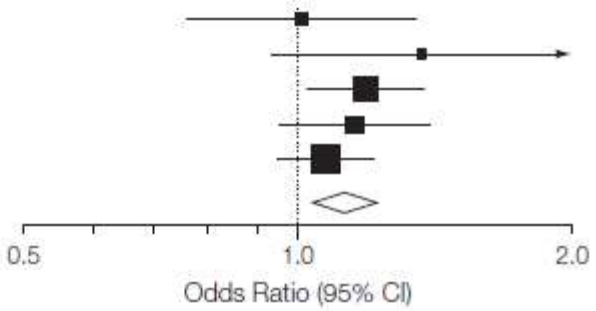
Lancet 2010; 375: 735–42

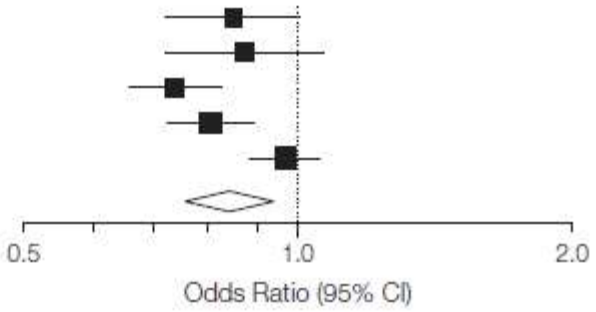
Risk of Incident Diabetes With Intensive-Dose Compared With Moderate-Dose Statin Therapy

A Meta-analysis

Figure 2. Meta-analysis of New-Onset Diabetes and First Major Cardiovascular Events in 5 Large Trials Comparing Intensive-Dose to Moderate-Dose Statin Therapy

	Cases/Total No. (%)		
	Intensive Dose	Moderate Dose	OR (95% CI)
Incident Diabetes			
PROVE IT–TIMI 22,[18] 2004	101/1707 (5.9)	99/1688 (5.9)	1.01 (0.76-1.34)
A to Z,[17] 2004	65/1768 (3.7)	47/1736 (2.7)	1.37 (0.94-2.01)
TNT,[15] 2005	418/3798 (11.0)	358/3797 (9.4)	1.19 (1.02-1.38)
IDEAL,[16] 2005	240/3737 (6.4)	209/3724 (5.6)	1.15 (0.95-1.40)
SEARCH,[5] 2010	625/5398 (11.6)	587/5399 (10.9)	1.07 (0.95-1.21)
Pooled odds ratio	**1449/16408 (8.8)**	**1300/16344 (8.0)**	**1.12 (1.04-1.22)**
Heterogeneity: $I^2 = 0\%$; $P = .60$			
Incident CVD			
PROVE IT–TIMI 22,[18] 2004	315/1707 (18.4)	355/1688 (21.0)	0.85 (0.72-1.01)
A to Z,[17] 2004	212/1768 (12.0)	234/1736 (13.5)	0.87 (0.72-1.07)
TNT,[15] 2005	647/3798 (17.0)	830/3797 (21.9)	0.73 (0.65-0.82)
IDEAL,[16] 2005	776/3737 (20.8)	917/3724 (24.6)	0.80 (0.72-0.89)
SEARCH,[5] 2010	1184/5398 (21.9)	1214/5399 (22.5)	0.97 (0.88-1.06)
Pooled odds ratio	**3134/16408 (19.1)**	**3550/16344 (21.7)**	**0.84 (0.75-0.94)**
Heterogeneity: $I^2 = 74\%$; $P = .004$			





Data marker size indicates relative weight of the studies; OR, odds ratio; and CI, confidence interval.

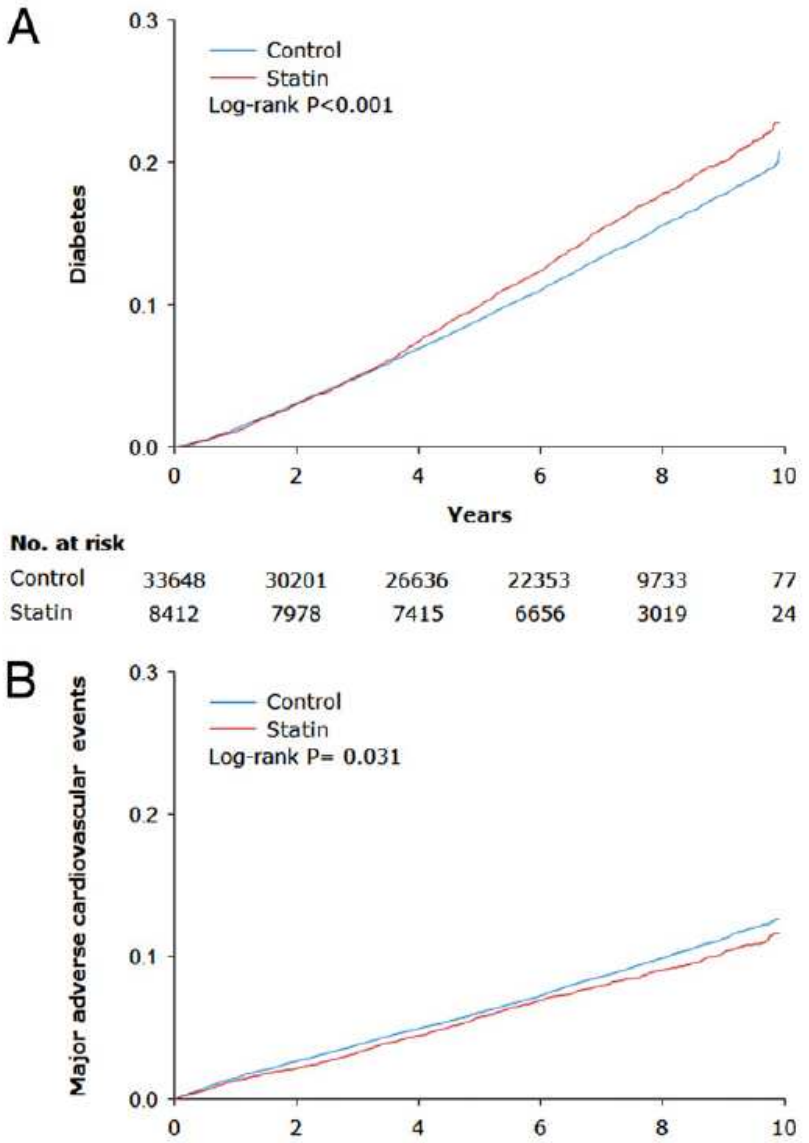
JAMA. 2011;305(24):2556-2564

Statins, Risk of Diabetes, and Implications on Outcomes in the General Population

Kang-Ling Wang, MD,*†‡ Chia-Jen Liu, MD,† Tze-Fan Chao, MD,†‡ Chi-Ming Huang, Cheng-Hsueh Wu, MD,†‡ Su-Jung Chen, MD,†‡ Tzeng-Ji Chen, MD, PHD,§‖ Shing-Jong Lin, MD, PHD,*†‡¶ Chern-En Chiang, MD, PHD*†‡¶#

Taipei, Taiwan

During the median follow-up of 7.2 years (interquartile range: 6.1 to 8.7 years), there were 5,754 cases of incident diabetes. Kaplan-Meier curves suggested statin use increased the hazards of diabetes occurrence (HR: 1.15; 95% CI: 1.08 to 1.22; p 0.001).



J Am Coll Cardiol 2012;60:1231–8

ESH 2009

The benefit of combining a statin with antihypertensive treatment in hypertensive patients was well established by the ASCOT-LLA study, as summarized in the 2007 ESH/ESC guidelines.

The negative results obtained with another statin in the ALLHAT study can be attributed to insufficient lowering of total cholesterol (11% in ALLHAT as compared with 20% in ASCOT).

The beneficial effect of statin administration to patients without previous cardiovascular events has been strengthened by the findings of the JUPITER study, showing that lowering LDL-cholesterol by 50% in patients with baseline values less than 130 mg/dl (3.4 mmol/l), but elevated C-reactive protein (CRP), reduced cardiovascular events by 44%.

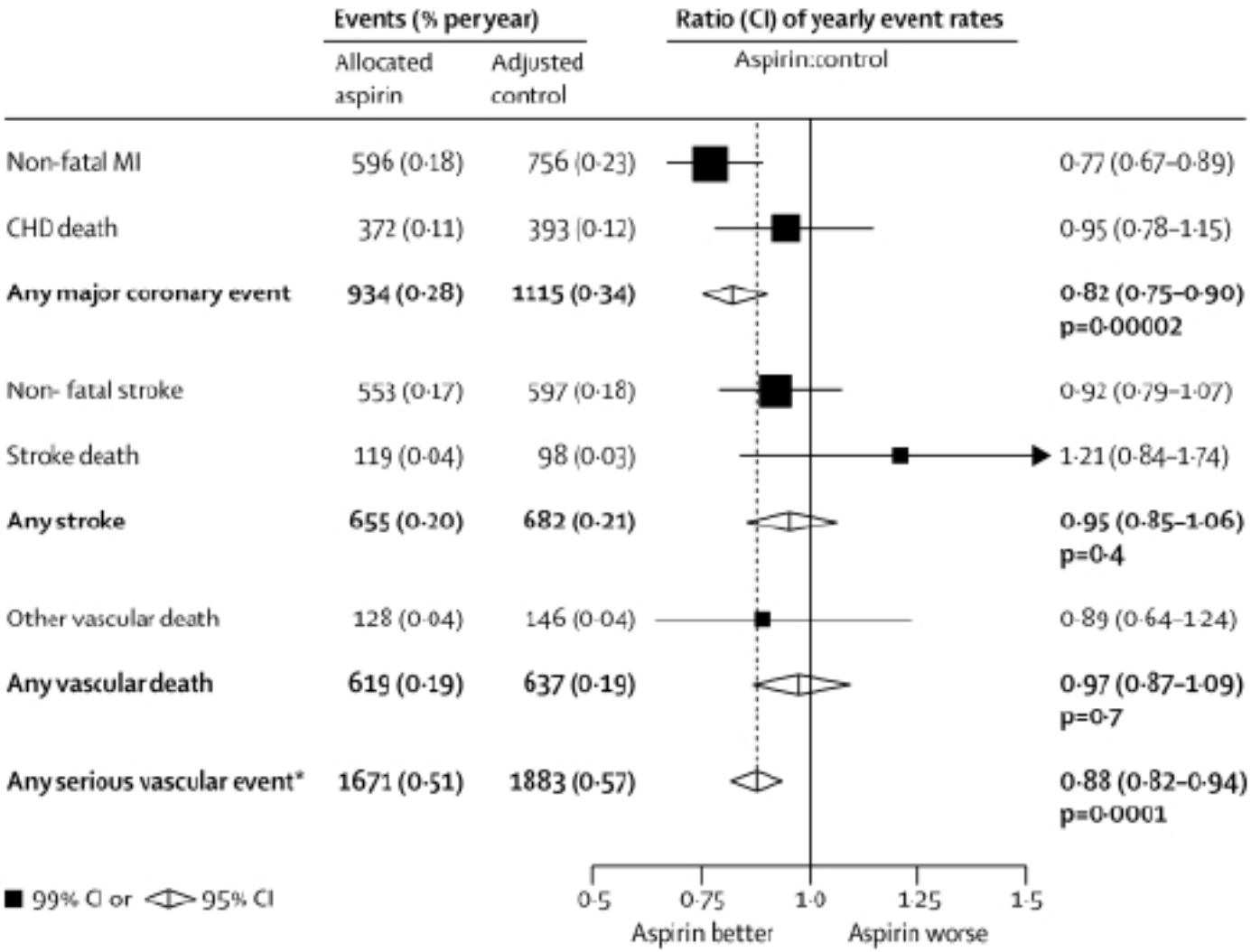
In conclusion, the recommendation given in the 2007 guidelines to consider statin therapy in hypertensive patients who have an estimated 10-year risk of cardiovascular events more than 20% can be reconfirmed, but the JUPITER study suggests that statin benefits can be observed also in patients with elevated CRP and at moderate cardiovascular risk (about 15% cardiovascular events in 10 years).

ASPIRINE

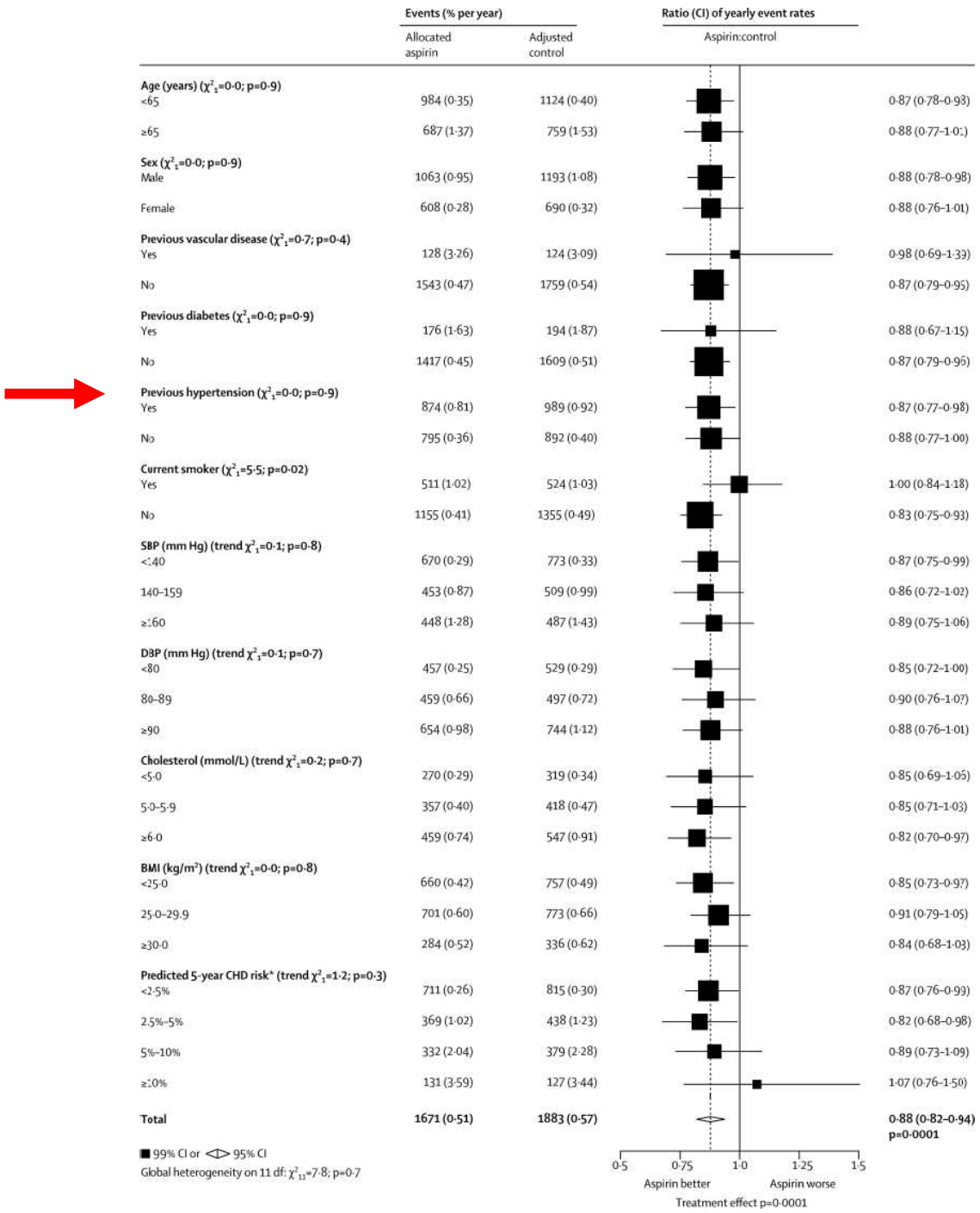
Problème nosologique: Qu’appelle-on prévention primaire??

Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials

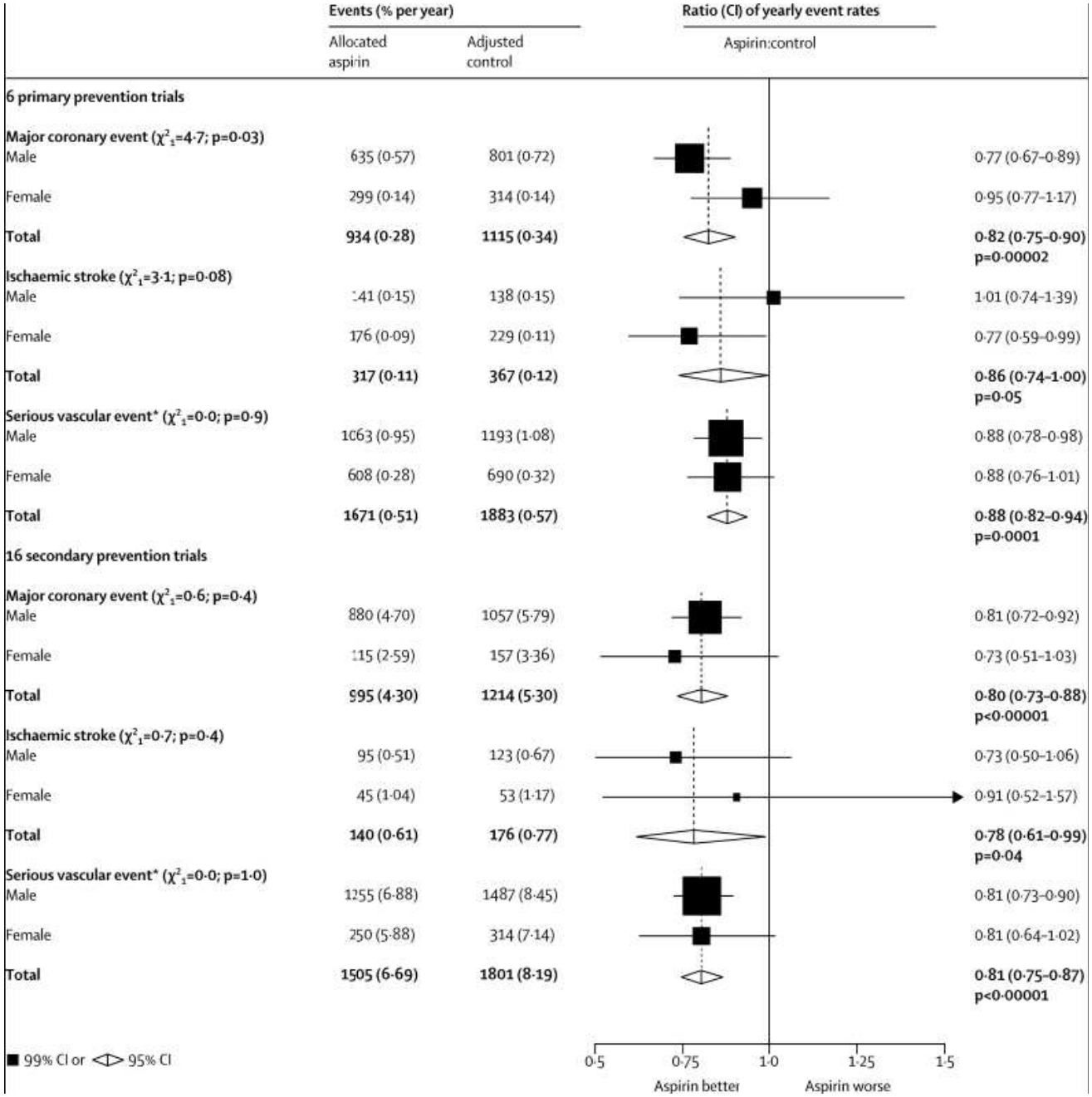
Antithrombotic Trialists' (ATT) Collaboration[‡,*]
Antithrombotic Trialists' (ATT) Collaboration: colin.baigent@ctsu.ox.ac.uk



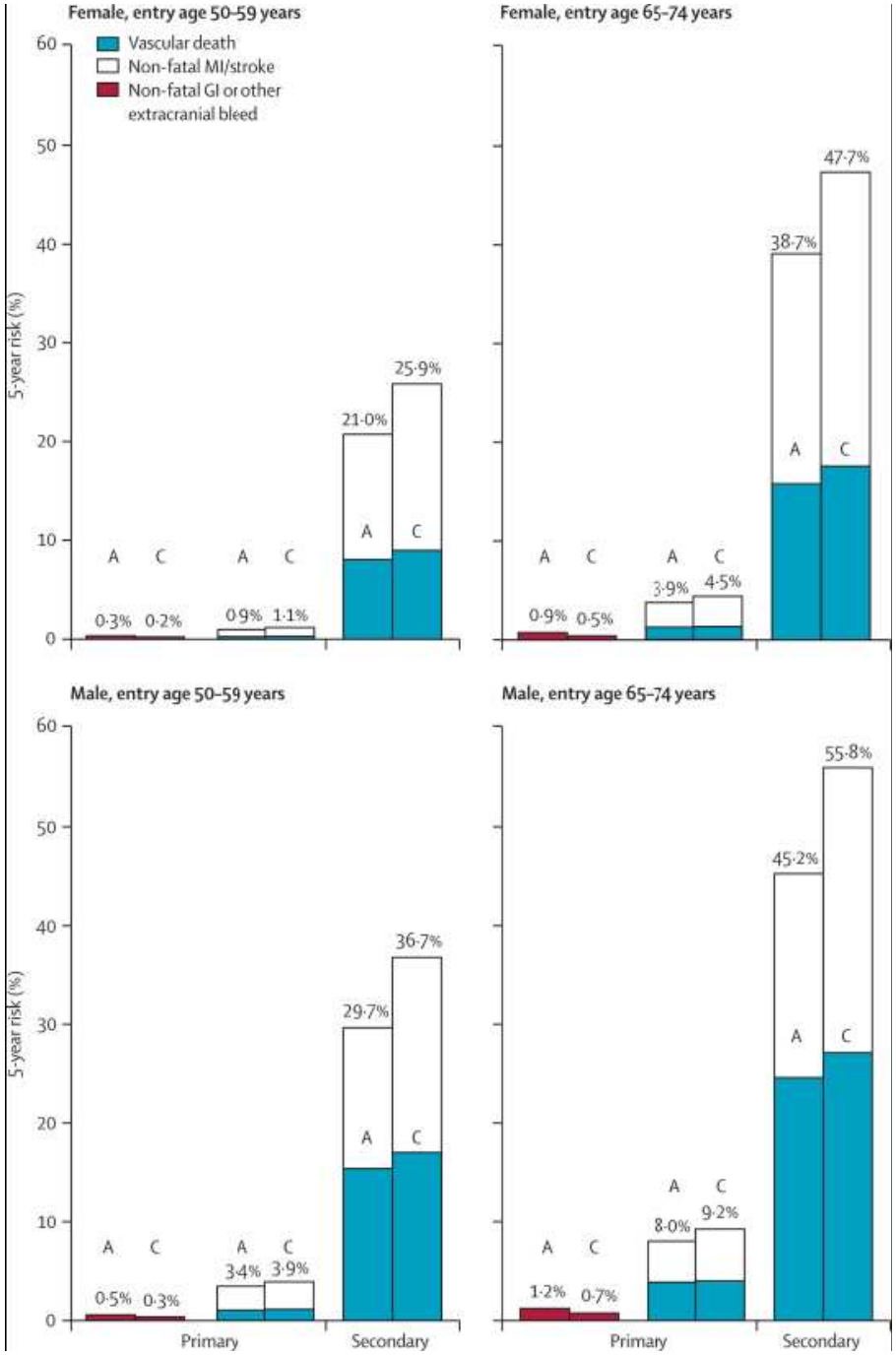
Lancet 2009;373:1849



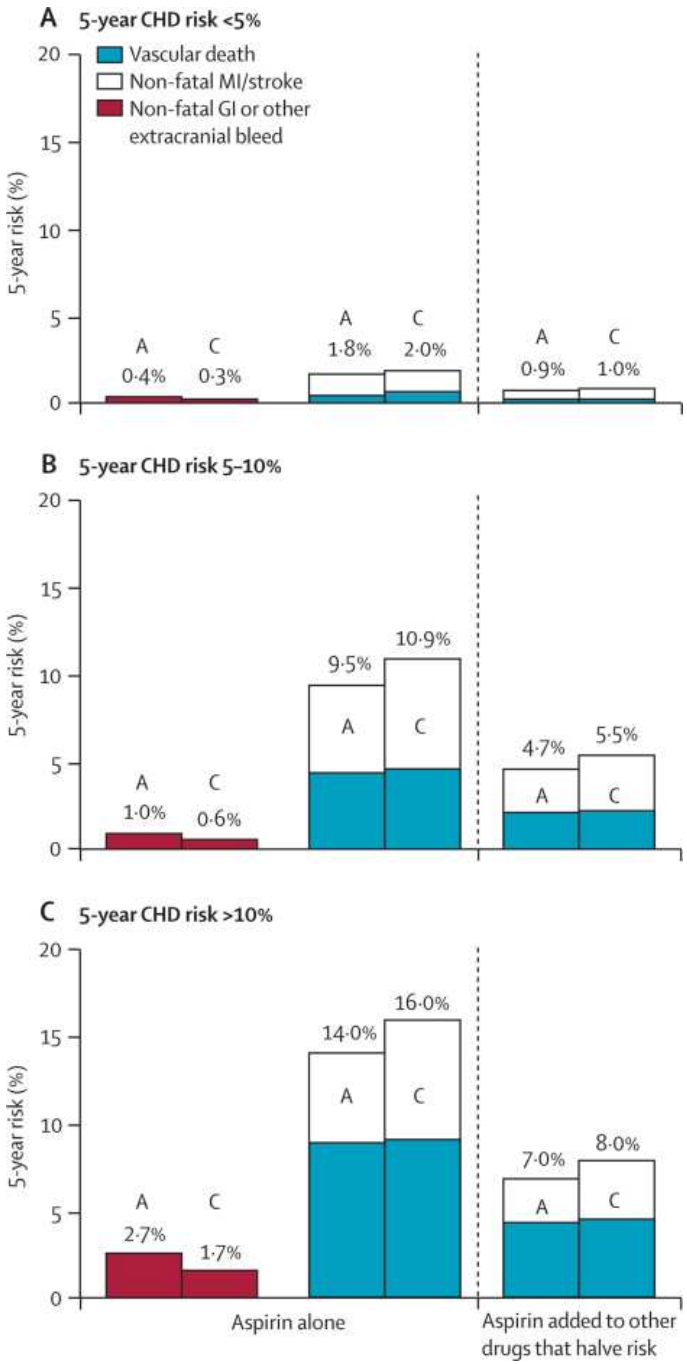
Lancet 2009;373:1849



Lancet 2009;373:1849



Lancet 2009;373:1849



Lancet 2009;373:1849

Rate ratios (95% CI) associated with risk factors for selected outcomes in people with no known vascular disease in primary prevention trials

	Major coronary event	Probably ischaemic stroke	Haemorrhagic stroke	Major extracranial bleed
Age (per decade)	1·84 (1·74–1·95)	2·46 (2·27–2·65)	1·59 (1·33–1·90)	2·15 (1·93–2·39)
Male sex*	2·43 (1·94–3·04)	1·44 (1·14–1·82)	1·11 (0·52–2·34)	1·99 (1·45–2·73)
Diabetes mellitus	2·66 (2·28–3·12)	2·06 (1·67–2·54)	1·74 (0·95–3·17)	1·55 (1·13–2·14)
Current smoker	2·05 (1·85–2·28)	2·00 (1·72–2·31)	2·18 (1·57–3·02)	1·56 (1·25–1·94)
Mean blood pressure (per 20 mm Hg)†	1·73 (1·59–1·89)	2·00 (1·77–2·26)	2·18 (1·65–2·87)	1·32 (1·09–1·58)
Cholesterol (per 1 mmol/L)	1·18 (1·12–1·24)	1·02 (0·95–1·09)	0·90 (0·77–1·07)	0·99 (0·90–1·08)
Body-mass index (per 5 kg/m^2)	1·09 (1·03–1·15)	1·06 (0·98–1·14)	0·85 (0·71–1·02)	1·24 (1·13–1·35)

*Analyses are stratified by trial. The relevance of male sex can therefore be assessed only in the two trials that included both men and women, so the 95% CIs for it are wide, particularly for stroke.

†Mean of systolic and diastolic blood pressure. Associations with measured values are not corrected for the effects of regression dilution.

Lancet 2009;373:1849

Benefit and harm of low-dose aspirin in well-treated hypertensives at different baseline cardiovascular risk

Alberto Zanchetti[a], Lennart Hansson[b], Björn Dahlöf[c], Stevo Julius[d], Joël Ménard[e], Ingrid Warnold[f], Hans Wedel[g], on behalf of the HOT Study Group*

Table 2 Effects of aspirin on all myocardial infarctions

Risk group	Event (*n*)		Events/1000 patient-years		Absolute risk reduction/1000 patient-years	Relative risk (95% CI)	NNT (95% CI)
	Aspirin	Placebo	Aspirin	Placebo			
All patients	82	127	2.3	3.6	1.3	0.64 (0.49–0.85)	208 (128–555)
High to very high risk	50	78	2.8	4.5	1.6	0.64 (0.45–0.91)	167 (94–771)
Medium risk	32	49	1.8	2.8	1.0	0.65 (0.42–1.01)	276 (136–∞)
SBP ⩾ 180 mmHg	23	41	3.1	5.2	2.2	0.59 (0.35–0.98)	125 (65–2194)
SBP 160 to < 180 mmHg	41	62	2.1	3.4	1.2	0.64 (0.43–0.94)	220 (117–1756)
SBP < 160 mmHg	18	24	2.1	2.7	0.6	0.77 (0.42–1.41)	423 (129–∞)
DBP ⩾ 107 mmHg	21	35	1.9	3.2	1.4	0.58 (0.34–1.00)	199 (100–42404)
DBP 104 to < 107 mmHg	25	46	2.4	4.5	2.1	0.53 (0.32–0.86)	128 (73–513)
DBP < 104 mmHg	36	46	2.7	3.3	0.6	0.81 (0.52–1.25)	434 (141–∞)
Serum creatinine > 1.3 mg/dl	3	21	1.2	8.4	7.2	0.14 (0.04–0.48)	38 (25–81)

NNT, number needed to treat for the average duration of the trial (3.8 years) to prevent a myocardial infarction; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure.

J Hypertens 2002; 20:2301–2307

Benefit and harm of low-dose aspirin in well-treated hypertensives at different baseline cardiovascular risk

Alberto Zanchetti[a], Lennart Hansson[b], Björn Dahlöf[c], Stevo Julius[d], Joël Ménard[e], Ingrid Warnold[f], Hans Wedel[g], on behalf of the HOT Study Group*

Table 3 Effects of aspirin on fatal and non-fatal major bleeding

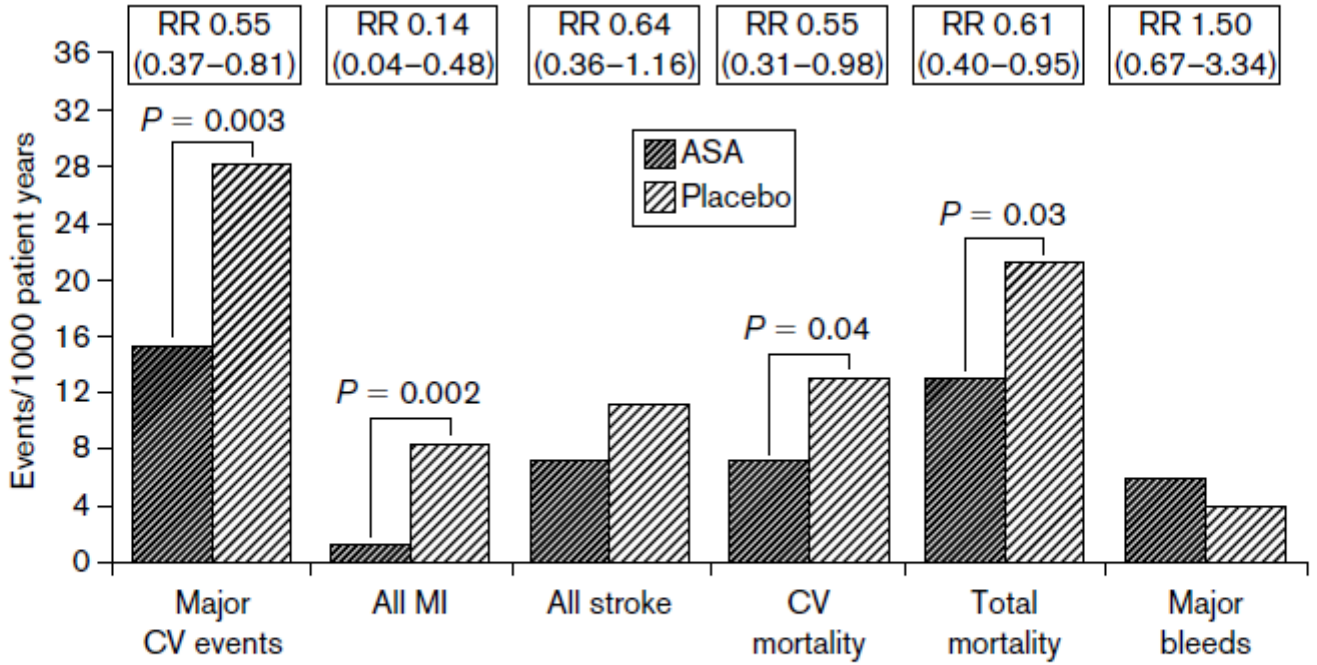
Risk group	Event (*n*)		Events/1000 patient-years		Absolute risk increase/1000 patient-years	Relative risk (95% CI)	NNH (95% CI)
	Aspirin	Placebo	Aspirin	Placebo			
All patients	127	77	3.6	2.2	1.4	1.65 (1.24–2.19)	188 (121–425)
High to very high risk	75	52	4.3	3.0	1.3	1.45 (1.01–2.06)	205 (105–4881)
Medium risk	52	25	2.9	1.4	1.5	2.08 (1.29–3.35)	174 (107–476)
SBP ⩾ 180 mmHg	36	27	4.8	3.4	1.4	1.41 (0.86–2.32)	194 (79–∝)
SBP 160 to < 180 mmHg	68	35	3.6	1.9	1.7	1.88 (1.25–2.82)	160 (98–430)
SBP < 160 mmHg	23	15	2.6	1.7	1.0	1.58 (0.82–3.02)	277 (114–∝)
DBP ⩾ 107 mmHg	41	29	3.7	2.7	1.0	1.38 (0.86–2.22)	263 (107–∝)
DBP 104 to < 107 mmHg	41	19	3.9	1.8	2.0	2.10 (1.22–3.62)	132 (77–450)
DBP < 104 mmHg	45	29	3.3	2.1	1.3	1.62 (1.01–2.58)	211 (107–6685)
Serum creatinine > 1.3 mg/dl	15	10	6.0	4.0	2.0	1.50 (0.67–3.34)	134 (46–∝)

NNH, number needed to treat (harm) for the average duration of the trial (3.8 years) to cause a major bleed; CI, confidence interval; SBP, systolic blood pressure; DBP, diastolic blood pressure.

J Hypertens 2002; 20:2301–2307

Benefit and harm of low-dose aspirin in well-treated hypertensives at different baseline cardiovascular risk

Alberto Zanchetti[a], Lennart Hansson[b], Björn Dahlöf[c], Stevo Julius[d], Joël Ménard[e], Ingrid Warnold[f], Hans Wedel[g], on behalf of the HOT Study Group*

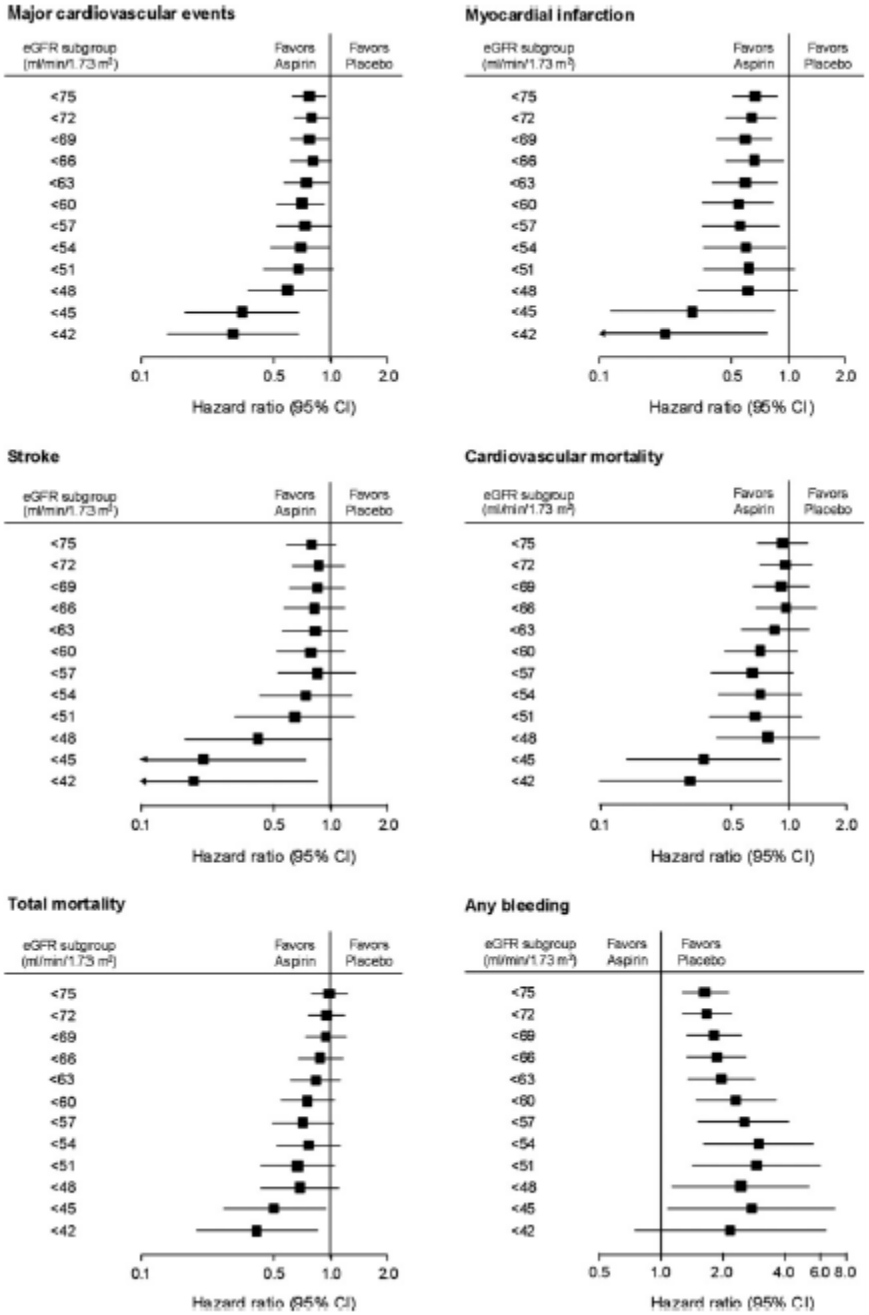


Effects of aspirin (ASA) in patients with high serum creatinine. Events in patients randomized to ASA or placebo, with baseline serum creatinine > 1.3 mg/dl (> 115 µmol/l). On the vertical axis, events per 1000 patient-years. RR, relative risk (95% confidence intervals); CV, cardiovascular; MI, myocardial infarction.

J Hypertens 2002; 20:2301–2307

Aspirin Is Beneficial in Hypertensive Patients With Chronic Kidney Disease

A Post-Hoc Subgroup Analysis of a Randomized Controlled Trial



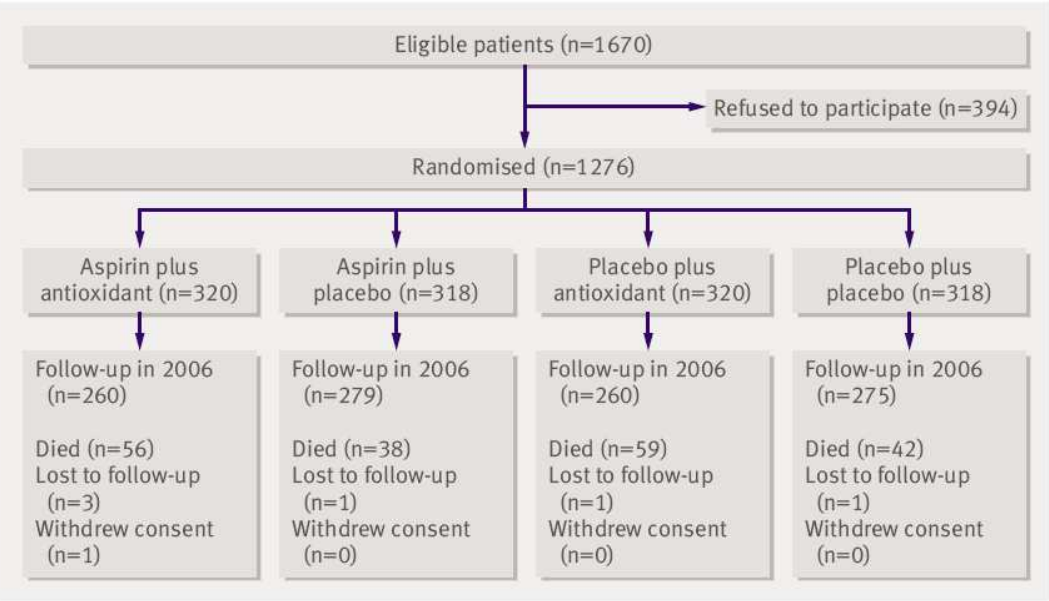
J Am Coll Cardiol 2010;56:956–65

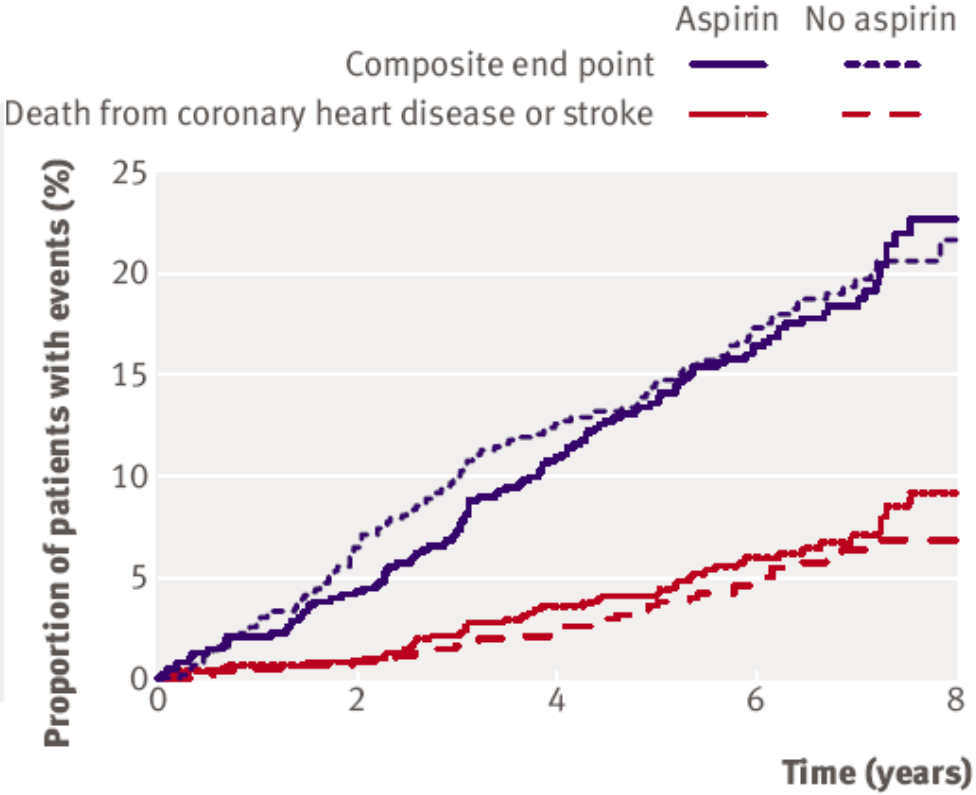
Table 2 Events Prevented and Caused by Aspirin Therapy for Every 1,000 Patients Treated According to eGFR Category

	eGFR, ml/min/1.73 m^2			
	≥60	45–59	<45	Overall
Events prevented by aspirin therapy				
Major cardiovascular events	3 (−3 to 8)	8 (−7 to 22)	76 (31 to 121)	6 (0 to 11)
Myocardial infarctions	4 (0 to 8)	10 (−1 to 20)	40 (7 to 72)	6 (2 to 10)
Stroke	−1 (−5 to 2)	0 (−11 to 10)	40 (11 to 69)	0 (−3 to 4)
Cardiovascular mortality	−1 (−5 to 3)	2 (−8 to 11)	40 (6 to 74)	1 (−3 to 4)
Total mortality	0 (−5 to 5)	4 (−9 to 17)	54 (7 to 100)	2 (−3 to 7)
Events caused by aspirin therapy				
Major bleeding	4 (1 to 8)	4 (−2 to 10)	27 (−1 to 55)	6 (3 to 8)
Minor bleeding	4 (1 to 8)	12 (3 to 21)	12 (−8 to 31)	6 (2 to 9)
Any bleeding	8 (3 to 12)	16 (5 to 27)	39 (5 to 72)	10 (6 to 14)

Values are absolute risk change (95% confidence interval) per 1,000 patients treated for an average of 3.8 years.
eGFR = estimated glomerular filtration rate.

The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease



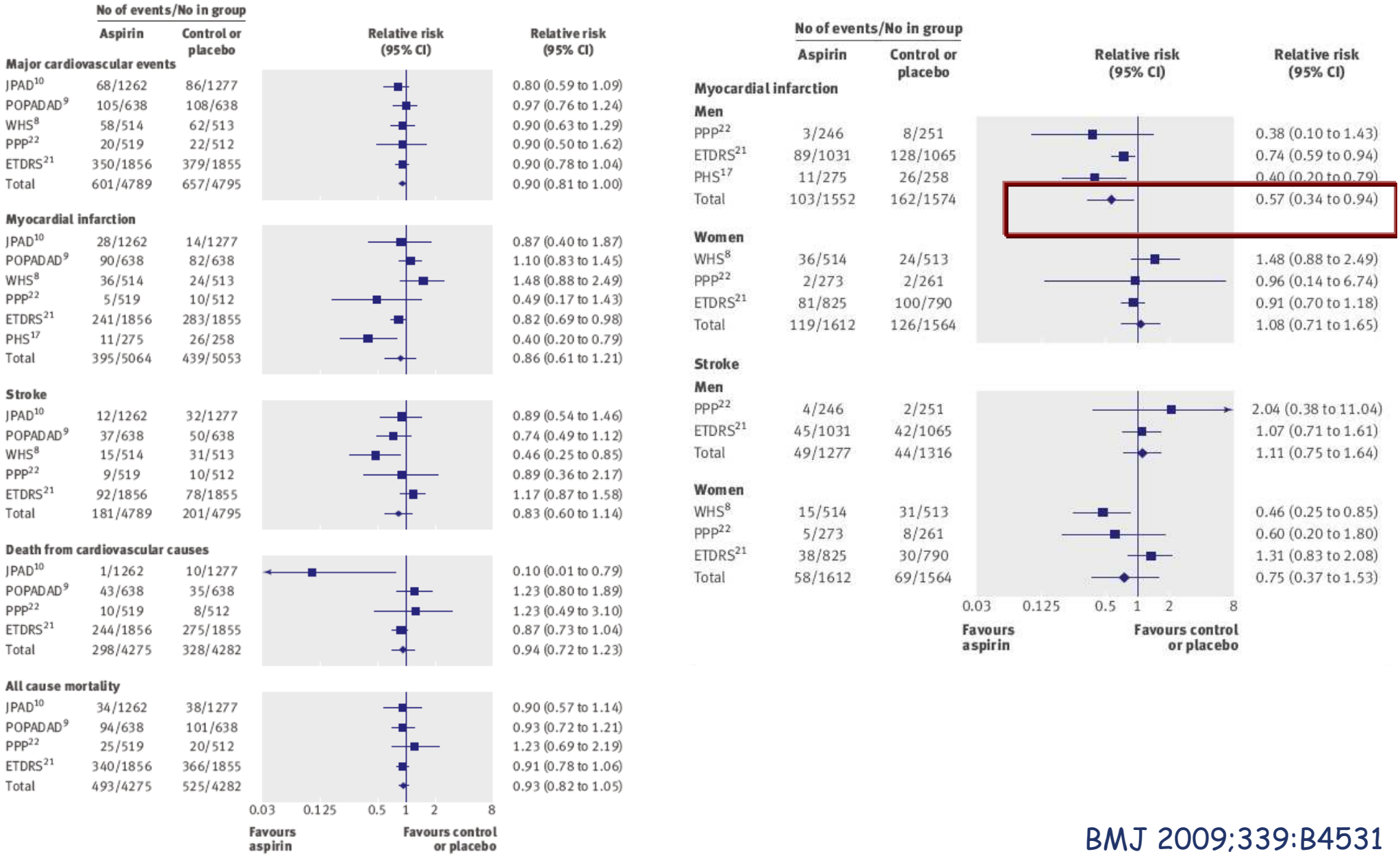


Numbers at risk for composite end point

Aspirin	638	599	543	399	48
No aspirin	638	590	534	381	48

BMJ 2008;337:a1840

Aspirin for primary prevention of cardiovascular events in people with diabetes: meta-analysis of randomised controlled trials



BMJ 2009;339:B4531

Rationale, design, and baseline data of the Japanese Primary Prevention Project (JPPP)—A randomized, open-label, controlled trial of aspirin versus no aspirin in patients with multiple risk factors for vascular events

Tamio Teramoto, MD, PhD,[a] Kazuyuki Shimada, MD, PhD,[b] Shinichiro Uchiyama, MD, PhD,[c] Masahiro Sugawara, MD,[d] Yoshio Goto, MD, PhD,[d] Nobuhiro Yamada, MD, PhD,[e] Shinichi Oikawa, MD, PhD,[f] Katsuyuki Ando, MD, PhD,[g] Naoki Ishizuka, PhD,[h] Tsutomu Yamazaki, MD, PhD,[i] Kenji Yokoyama, MD, PhD,[j] Mitsuru Murata, MD, PhD,[k] and Yasuo Ikeda, MD, PhD[l] *Tokyo, Tochigi, and Ibaraki, Japan*

Background Prevention of atherosclerotic disease has become an important public health priority in Japan due to the aging of the population and changes in diet and lifestyle factors.

Methods The Japanese Primary Prevention Project (JPPP) is a multicenter, open-label, randomized, parallel-group trial that is evaluating primary prevention with low-dose aspirin in Japanese patients aged 60 to 85 years with hypertension, dyslipidemia, or diabetes mellitus. The study cohort will be followed for a mean of 4 years. The primary end point is a composite of death from cardiovascular causes (including fatal myocardial infarction [MI], fatal stroke, and other cardiovascular death), nonfatal stroke (ischemic or hemorrhagic), and nonfatal MI. Key secondary end points include a composite of cardiovascular death, nonfatal stroke, nonfatal MI, transient ischemic attack, angina pectoris, or arteriosclerotic disease requiring surgery or intervention; each component of the primary end point; noncerebrovascular and noncardiovascular death; and extracranial hemorrhage requiring transfusion or hospitalization. End point assessment is done by a central adjudication committee that is blinded to treatment assignments.

Results Enrollment began in March 2005 and was completed in June 2007. A total of 14,466 patients were randomly allocated to receive enteric-coated aspirin, 100 mg/d, or no aspirin. At randomization, the study cohort had a mean (SD) age of 70.6 (6.2) years; 57.8% were women, 85.0% had hypertension, 71.7% had dyslipidemia, and 33.9% had diabetes. In the study cohort, 80.4% of patients had ≥3 risk factors.

ESH 2009

In conclusion, the prudent recommendations of the 2007 ESH/ESC guidelines can be reconfirmed: antiplatelet therapy, in particular low-dose aspirin, should be prescribed to hypertensive patients with previous cardiovascular events;

It can also be considered in hypertensive patients without a history of cardiovascular disease with reduced renal function or with a high cardiovascular risk.

In patients receiving aspirin, careful attention should always be given to the increased possibility of bleeding,particularly gastrointestinal.