# Traitements associés chez l'hypertendu:

# Statines, Aspirine

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DU HTA, Mars 2012

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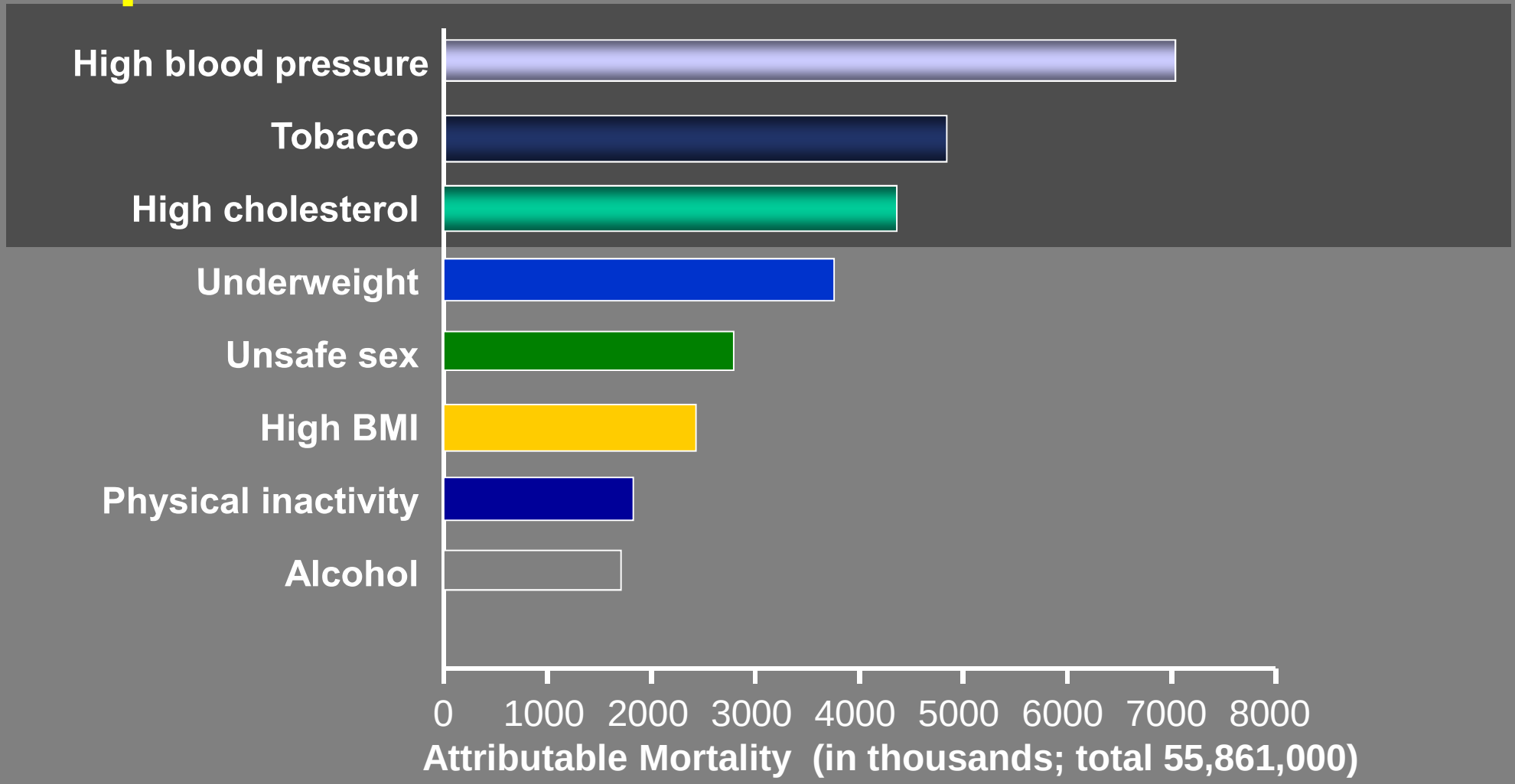
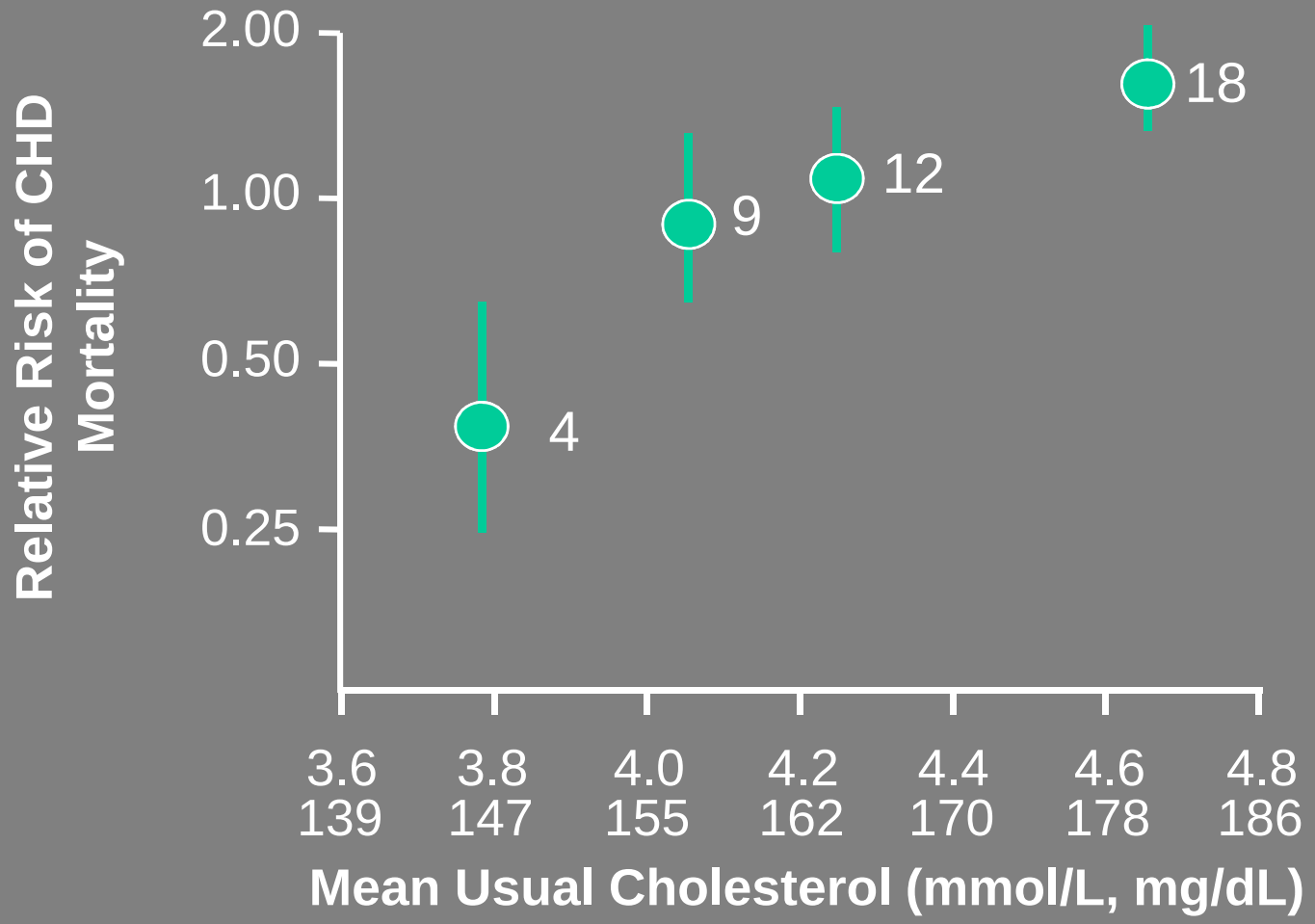
# Global Mortality 2000: Impact of Blood Pressure and Cholesterol




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

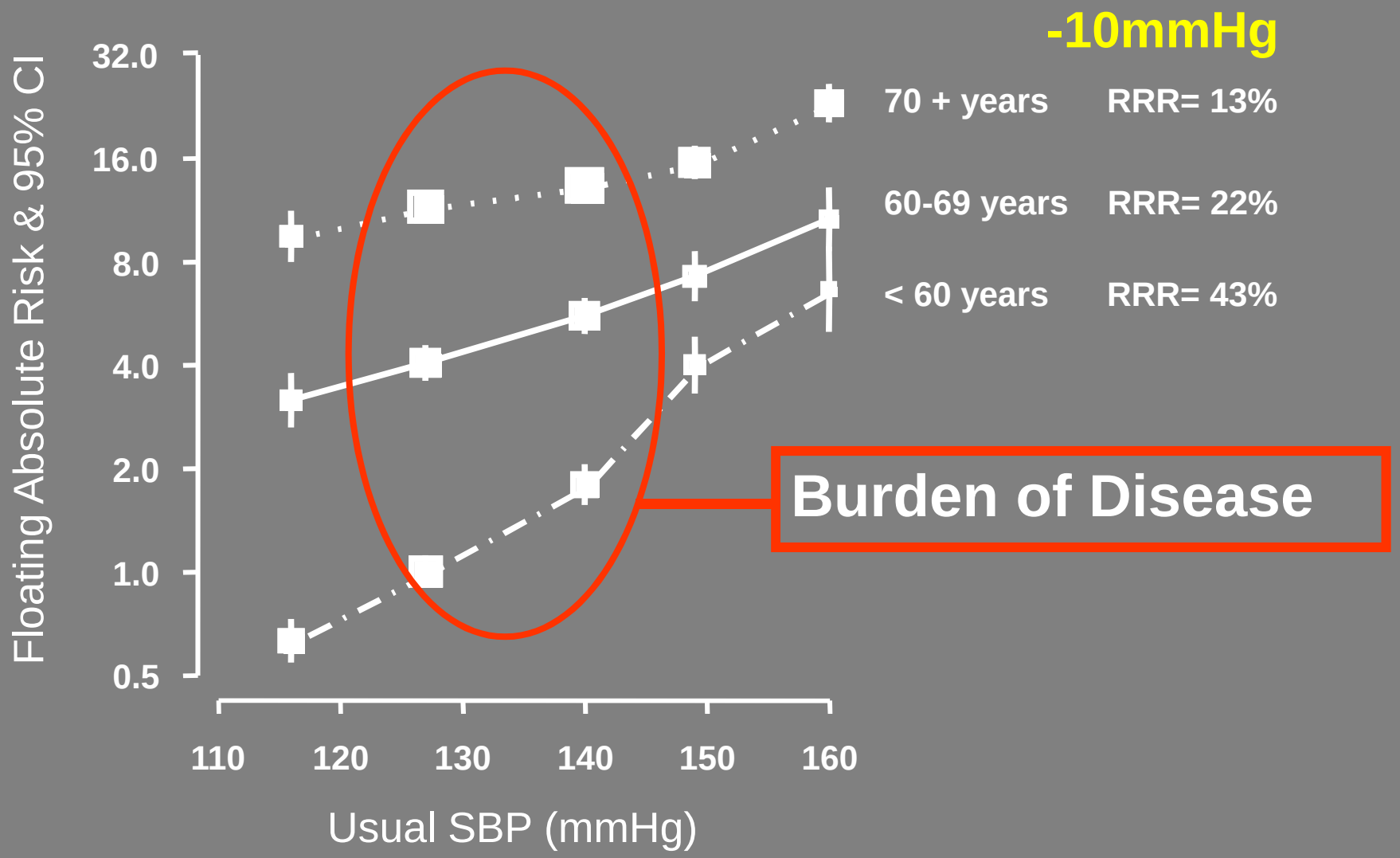
# What Is Normal Cholesterol?



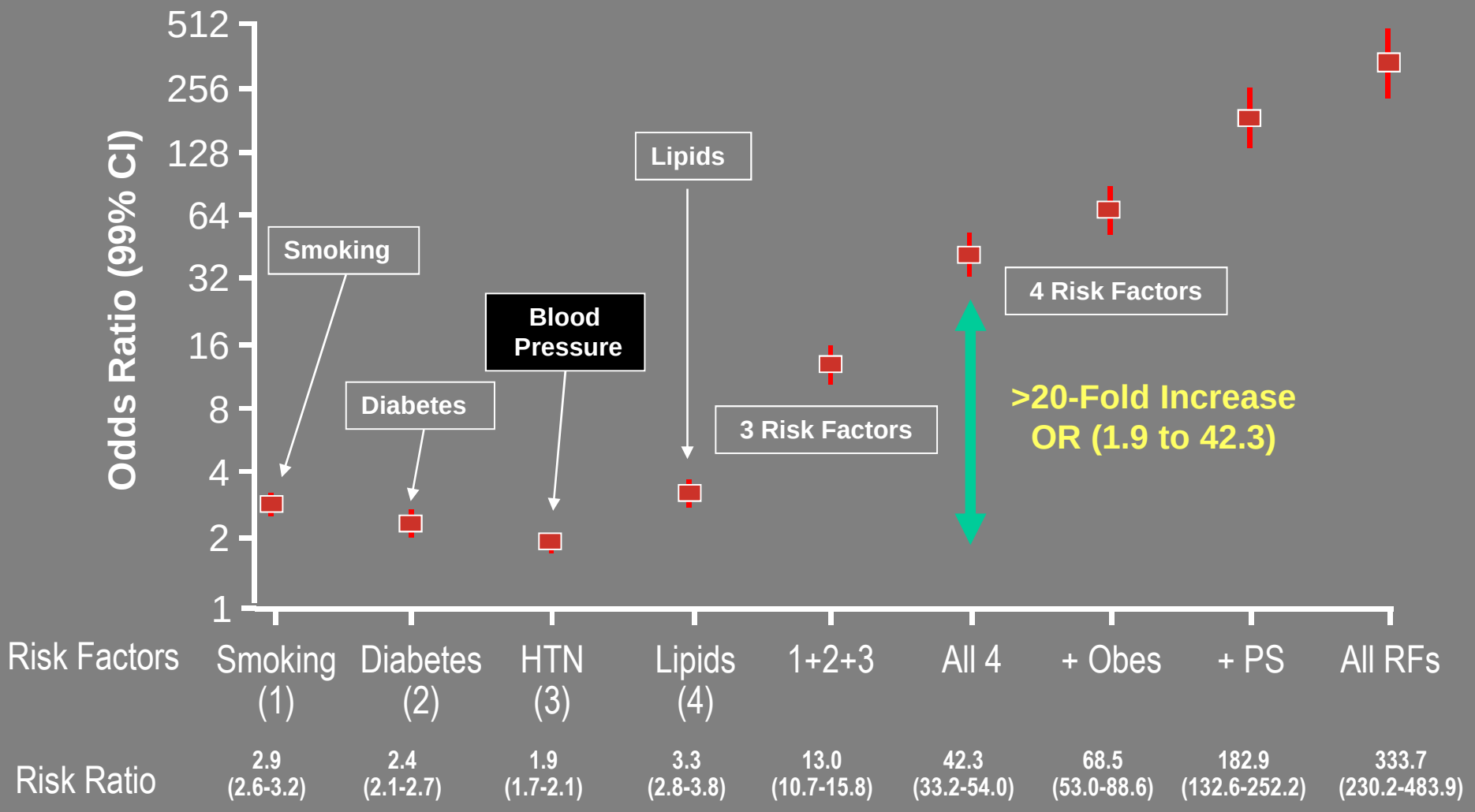

**Relative risk of death (± SD) from CHD by quartiles of baseline total cholesterol in 9021 Chinese people with 8-13 years' follow-up.**

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

# Coronary disease by usual SBP

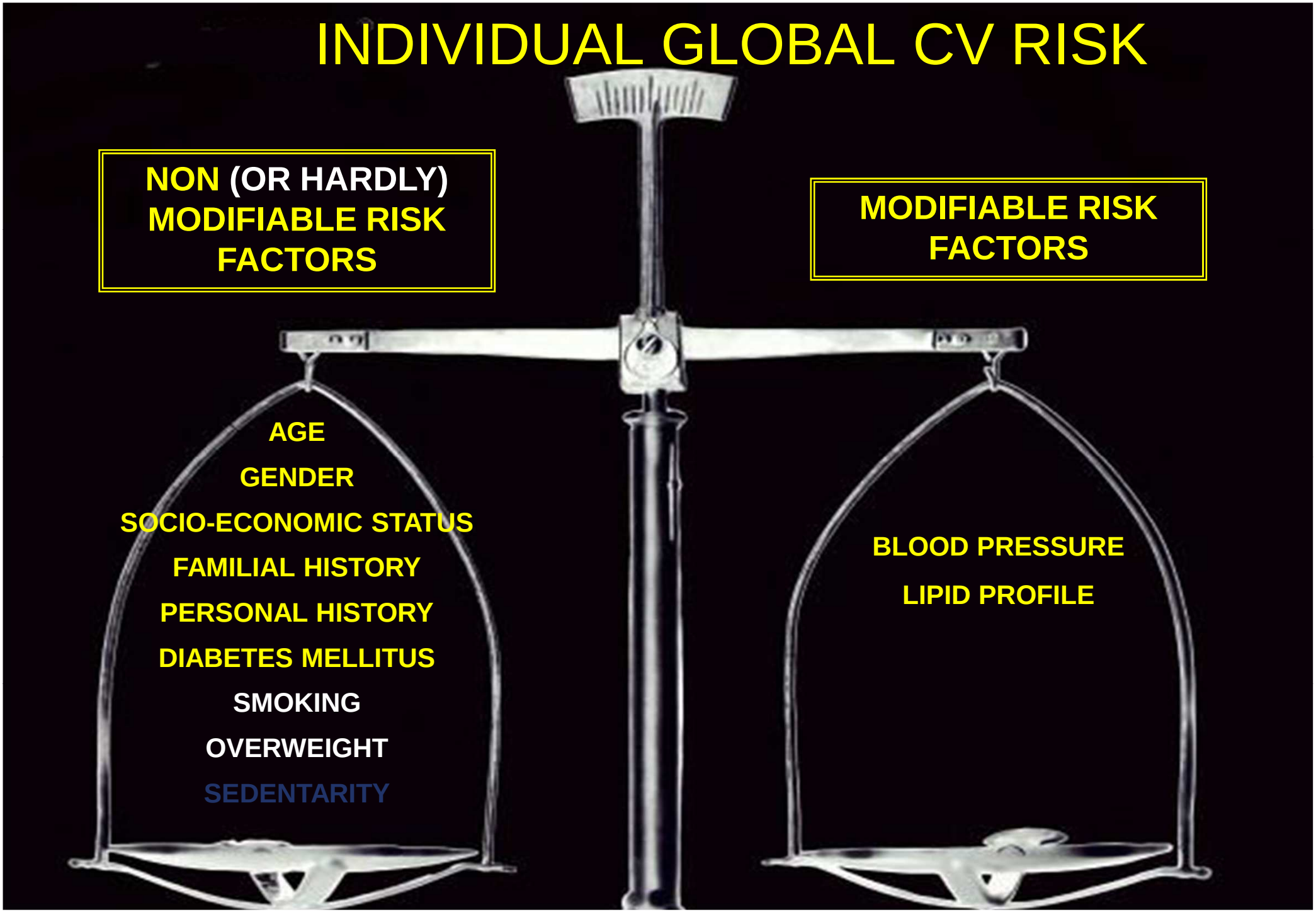


# Increased Number of CV Events (MI) in Patients With Hypertension Plus Other CV Risk Factors



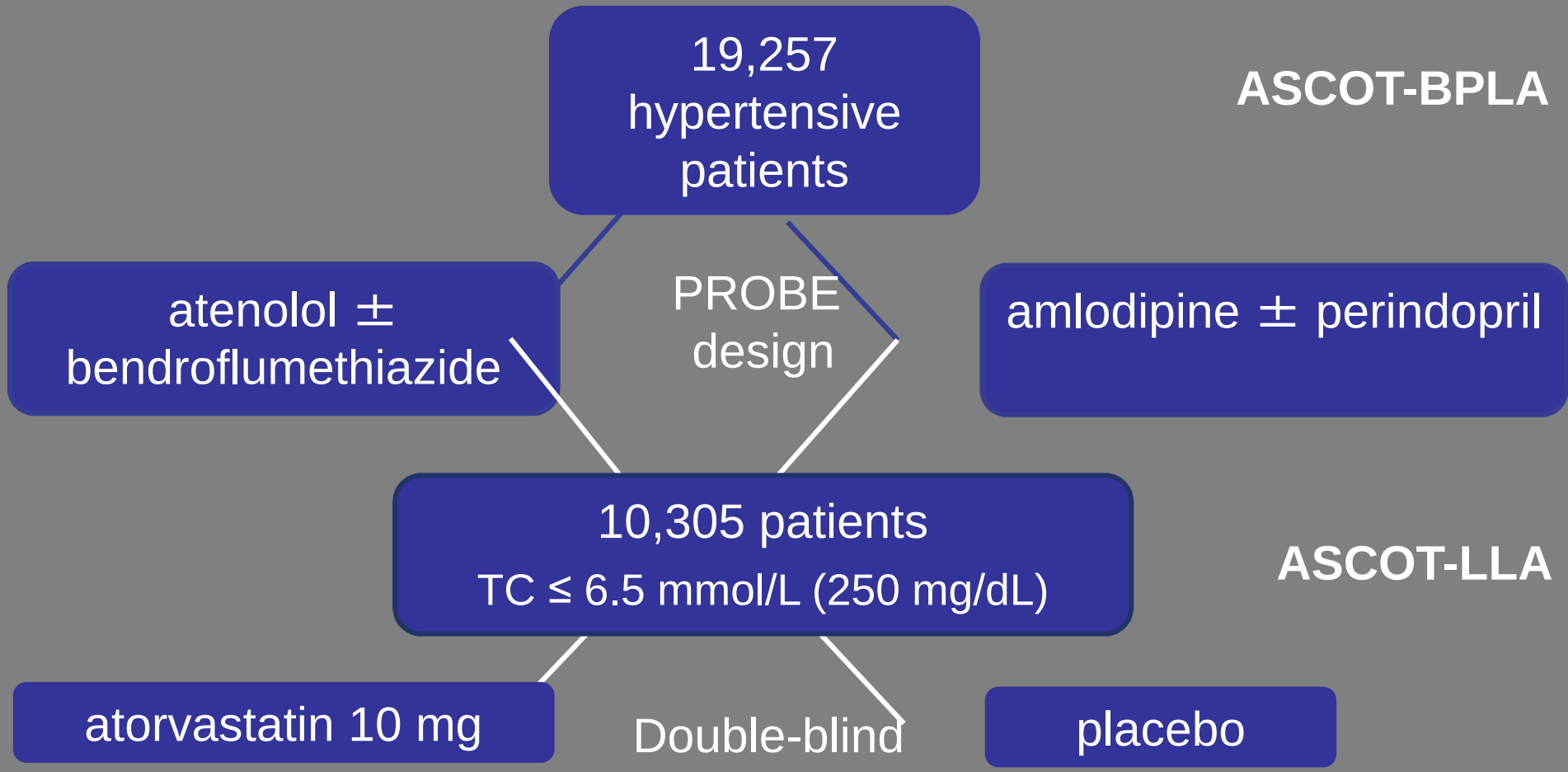

**HTN = hypertension; MI = myocardial infarction; PS = psychosocial.**

# INDIVIDUAL GLOBAL CV RISK



# STATINES

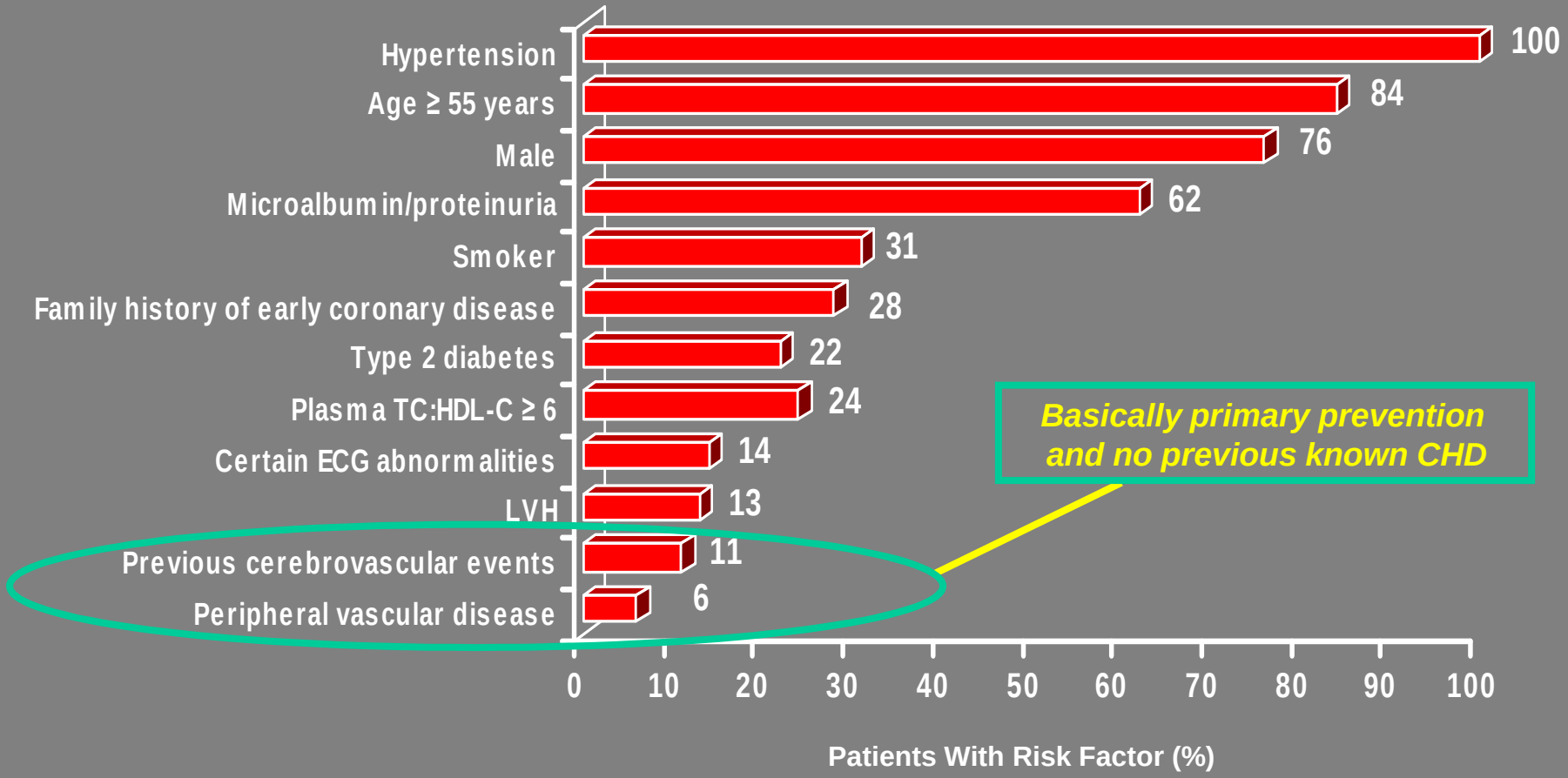
# ASCOT Study design




**Investigator-lead, multinational randomised controlled trial**

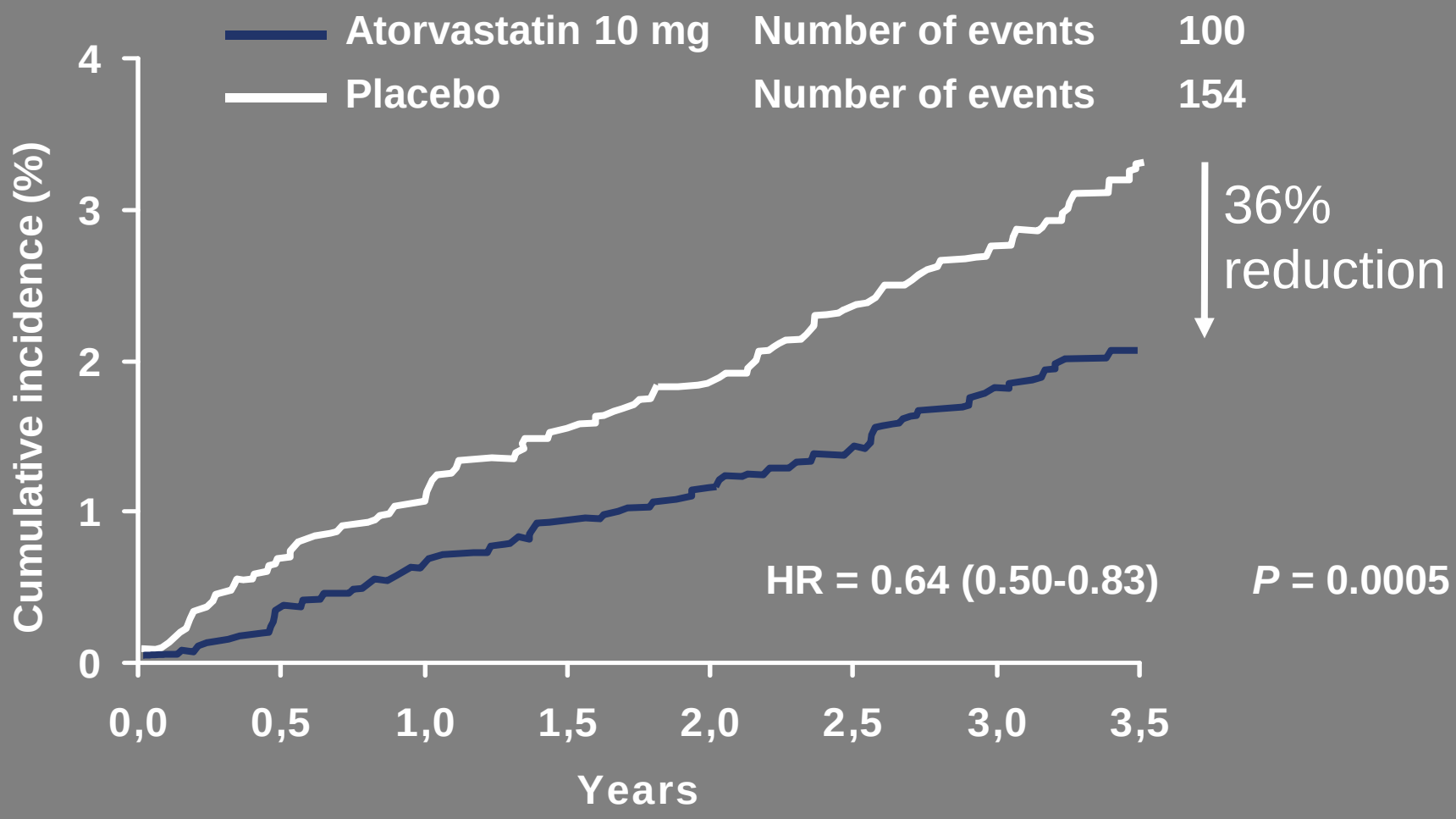
# ASCOT LLA: Patient Population Risk Factor Profile

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



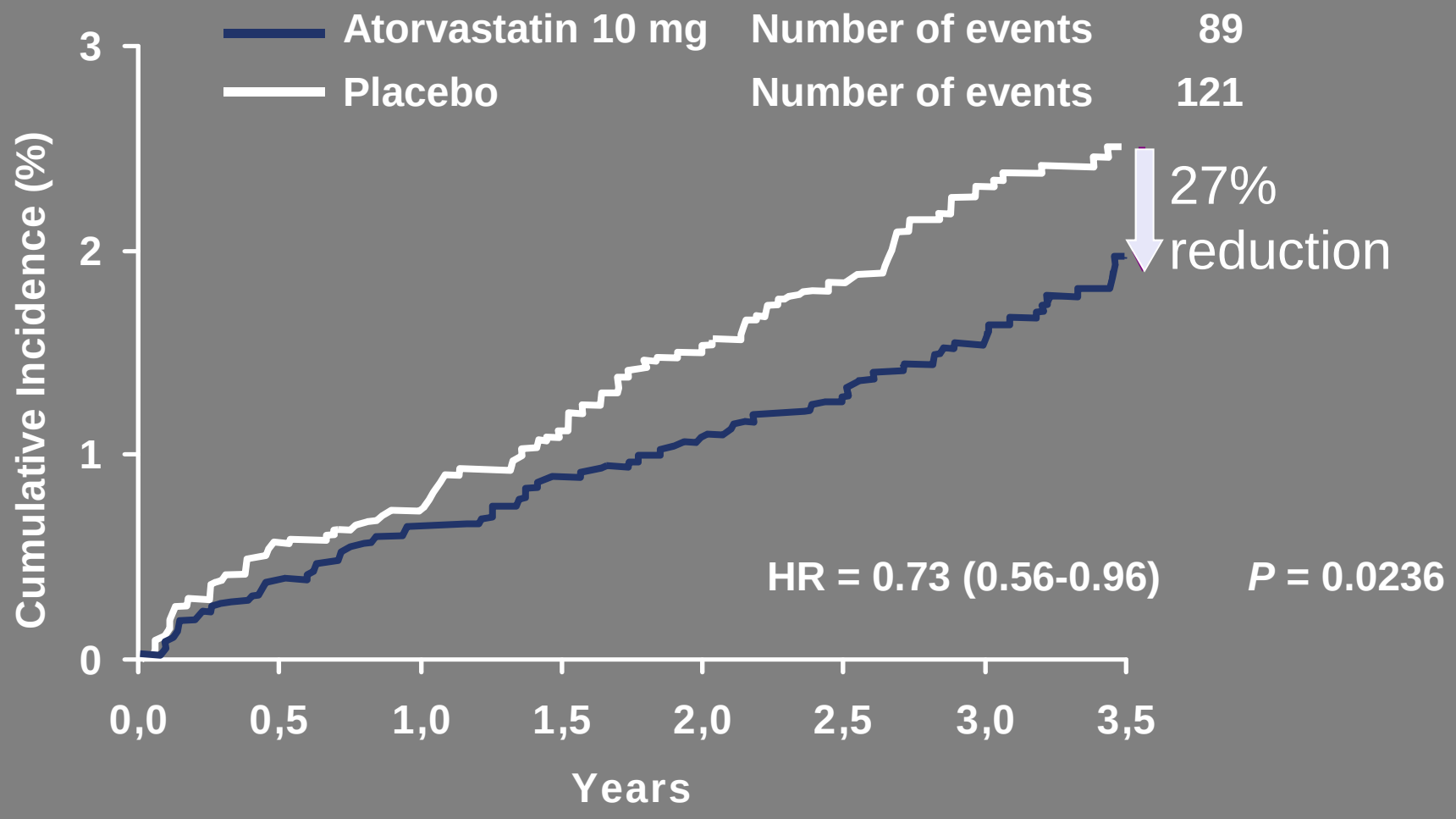

Sever PS, et al. *J Hypertens*. 2001;19:1139-1147.

# 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.

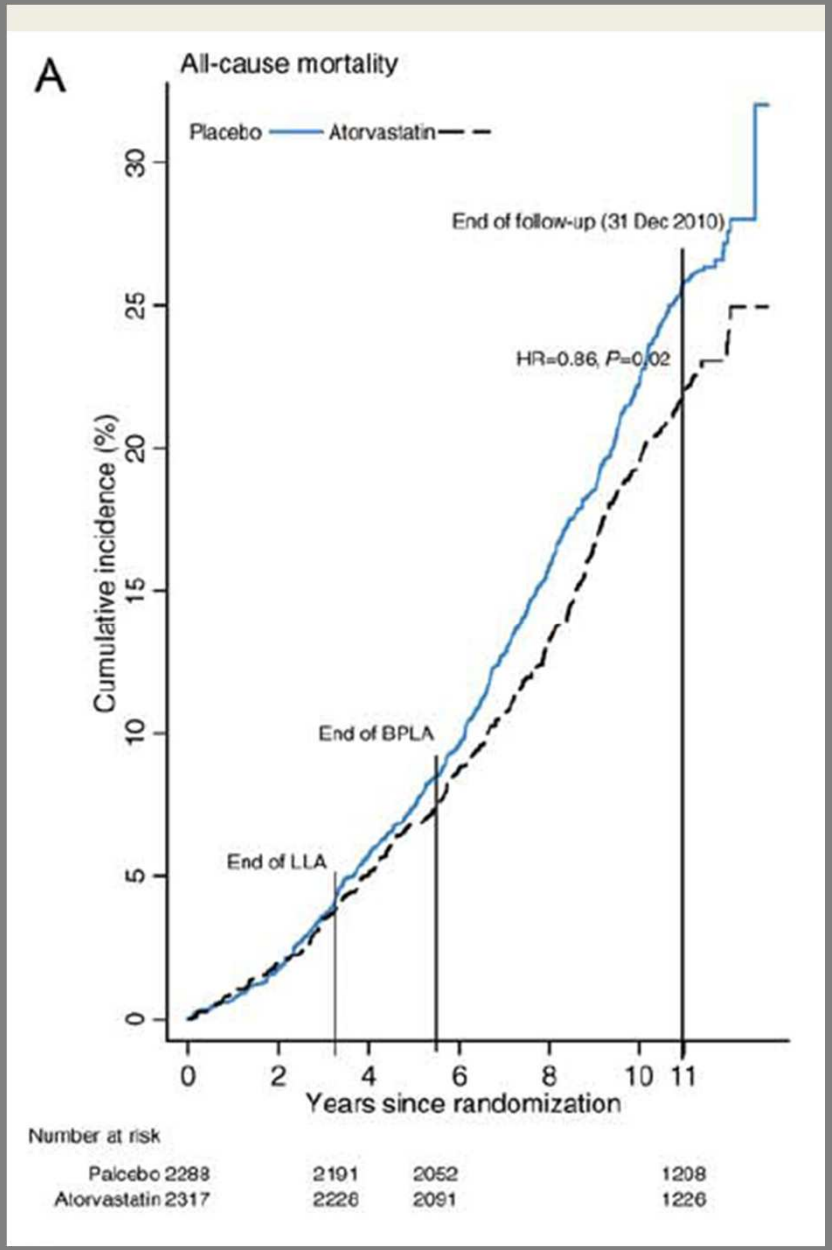
# ASCOT-LLA: Secondary End Point: Fatal and Nonfatal Stroke




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

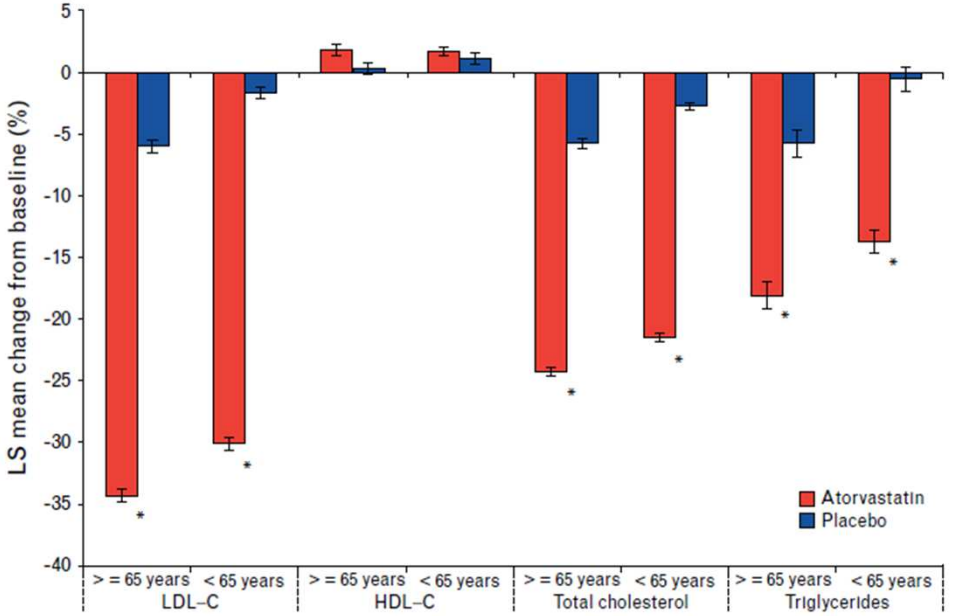
# Impact of atorvastatin among older and younger patients in the Anglo-Scandinavian Cardiac Outcomes Trial Lipid-Lowering Arm

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.

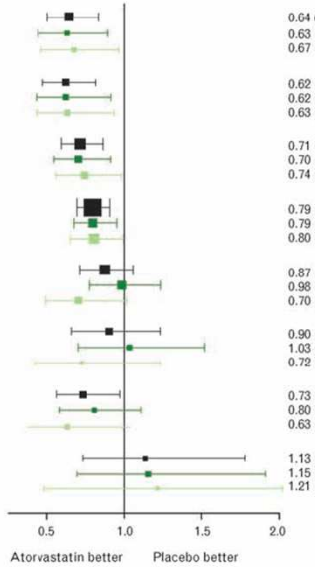


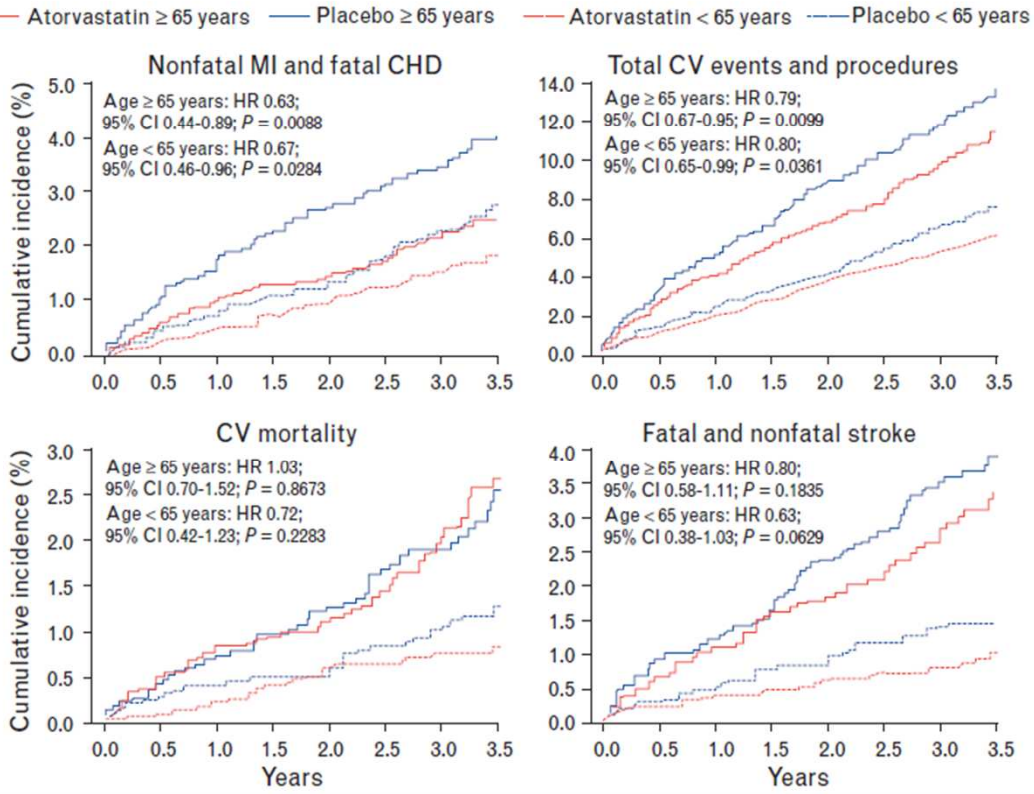

J Hypertens 2011; 29:592–599

# 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

| | Atorvastatin Number (%) | Rate/1000 | Placebo Number (%) | Rate/1000 | HR (95% CI) | P | Hetero-geneity P* |
|---|---|---|---|---|---|---|---|
| Nonfatal MI (including silent) + fatal CHD | 100 (1.9%) | 6.0 | 154 (3.0%) | 9.4 | 0.64 (0.50-0.83) | < 0.01 | |
| ≥ 65 years | 51 (2.3%) | 7.4 | 83 (3.7%) | 11.7 | 0.63 (0.44-0.89) | < 0.01 | 0.82 |
| < 65 years | 51 (2.3%) | 7.4 | 71 (2.5%) | 7.6 | 0.67 (0.46-0.96) | 0.03 | |
| Nonfatal MI (excluding silent) + fatal CHD | 86 (1.7%) | 5.2 | 137 (2.7%) | 8.3 | 0.62 (0.47-0.81) | < 0.01 | |
| ≥ 65 years | 43 (2.0%) | 6.2 | 71 (3.1%) | 10.0 | 0.62 (0.43-0.91) | 0.01 | 0.96 |
| < 65 years | 43 (1.4%) | 4.4 | 66 (2.3%) | 7.1 | 0.63 (0.43-0.93) | 0.02 | |
| Total cororary end point | 178 (3.4%) | 10.8 | 247 (4.8%) | 15.2 | 0.71 (0.59-0.86) | < 0.01 | |
| ≥ 65 years | 92 (4.2%) | 13.4 | 135 (6.0%) | 19.3 | 0.70 (0.54-0.91) | < 0.01 | 0.76 |
| < 65 years | 86 (2.9%) | 9.0 | 112 (3.9%) | 12.1 | 0.74 (0.56-0.98) | 0.04 | |
| Total cardiovascular events and procedures | 389 (7.5%) | 24.1 | 486 (9.5%) | 30.6 | 0.79 (0.69-0.90) | < 0.01 | |
| ≥ 65 years | 223 (10.2%) | 33.6 | 286 (12.7%) | 42.3 | 0.79 (0.67-0.95) | < 0.01 | 0.95 |
| < 65 years | 166 (5.9%) | 17.5 | 200 (6.9%) | 21.9 | 0.80 (0.65-0.99) | 0.04 | |
| All-cause mortality | 185 (3.5%) | 11.1 | 212 (4.1%) | 12.8 | 0.87 (0.71-1.06) | 0.17 | |
| ≥ 65 years | 135 (6.2%) | 19.3 | 143 (6.3%) | 19.8 | 0.98 (0.77-1.23) | 0.84 | 0.14 |
| < 65 years | 50 (1.7%) | 5.1 | 69 (2.4%) | 7.3 | 0.70 (0.49-1.01) | 0.06 | |
| Cardiovascular mortality | 74 (1.4%) | 4.4 | 82 (1.6%) | 4.9 | 0.90 (0.66-1.23) | 0.51 | |
| ≥ 65 years | 51 (2.3%) | 7.3 | 51 (2.3%) | 7.1 | 1.03 (0.70-1.52) | 0.87 | 0.29 |
| < 65 years | 23 (0.8%) | 2.4 | 31 (1.1%) | 3.3 | 0.72 (0.42-1.23) | 0.23 | |
| Fatal and nonfatal stroke | 89 (1.7%) | 5.4 | 121 (2.4%) | 7.4 | 0.73 (0.56-0.96) | 0.02 | |
| ≥ 65 years | 63 (2.9%) | 9.1 | 81 (3.6%) | 11.4 | 0.80 (0.58-1.11) | 0.18 | 0.43 |
| < 65 years | 26 (0.9%) | 2.7 | 40 (1.4%) | 4.3 | 0.63 (0.38-1.03) | 0.06 | |
| Fatal and nonfatal heart failure | 41 (0.8%) | 2.5 | 36 (0.7%) | 2.2 | 1.13 (0.73-1.78) | 0.58 | |
| ≥ 65 years | 31 (1.4%) | 4.5 | 28 (1.2%) | 3.9 | 1.15 (0.69-1.91) | 0.60 | 0.92 |
| < 65 years | 10 (0.3%) | 1.0 | 8 (0.3%) | 0.9 | 1.21 (0.48-3.07) | 0.69 | |




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

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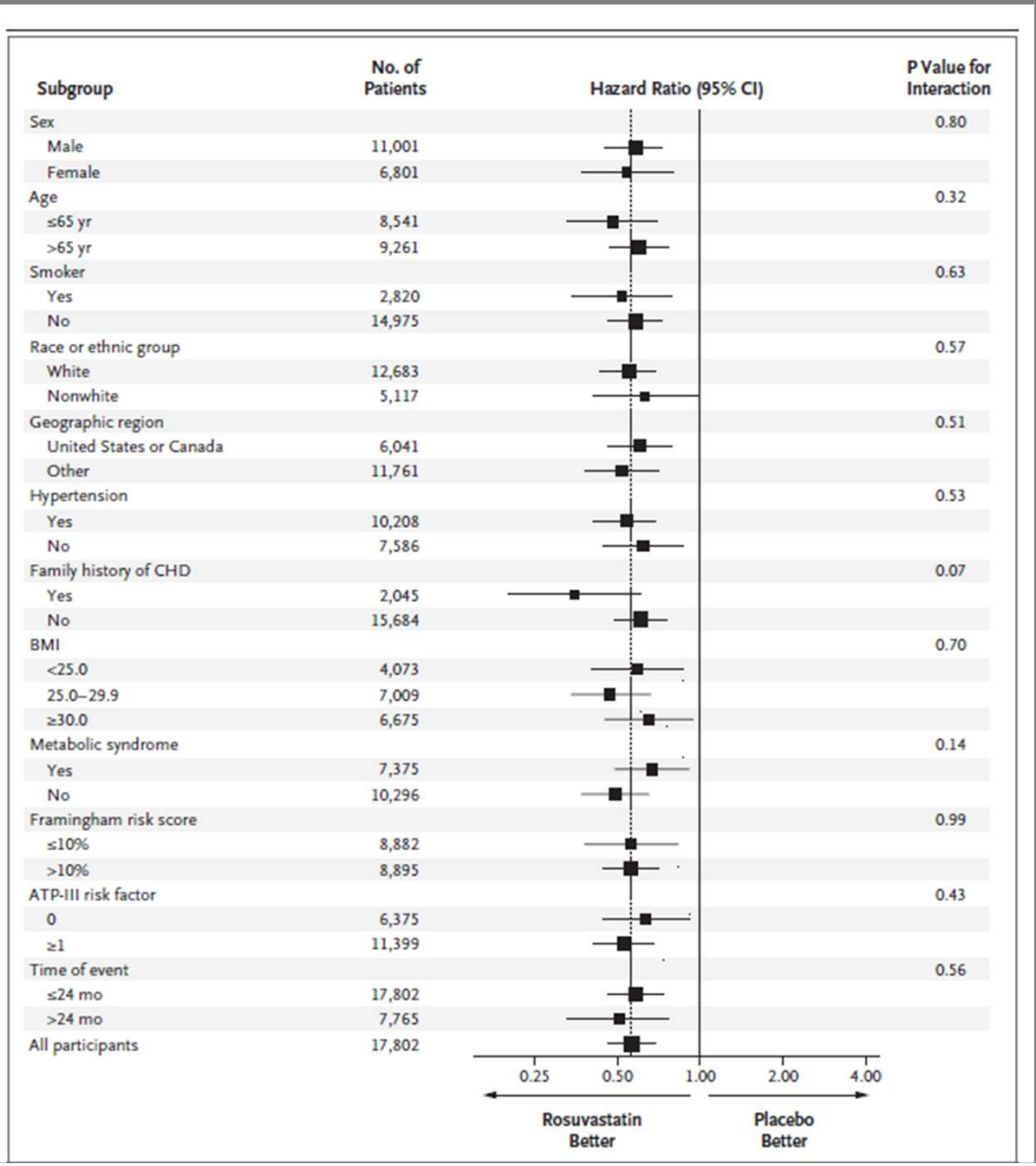
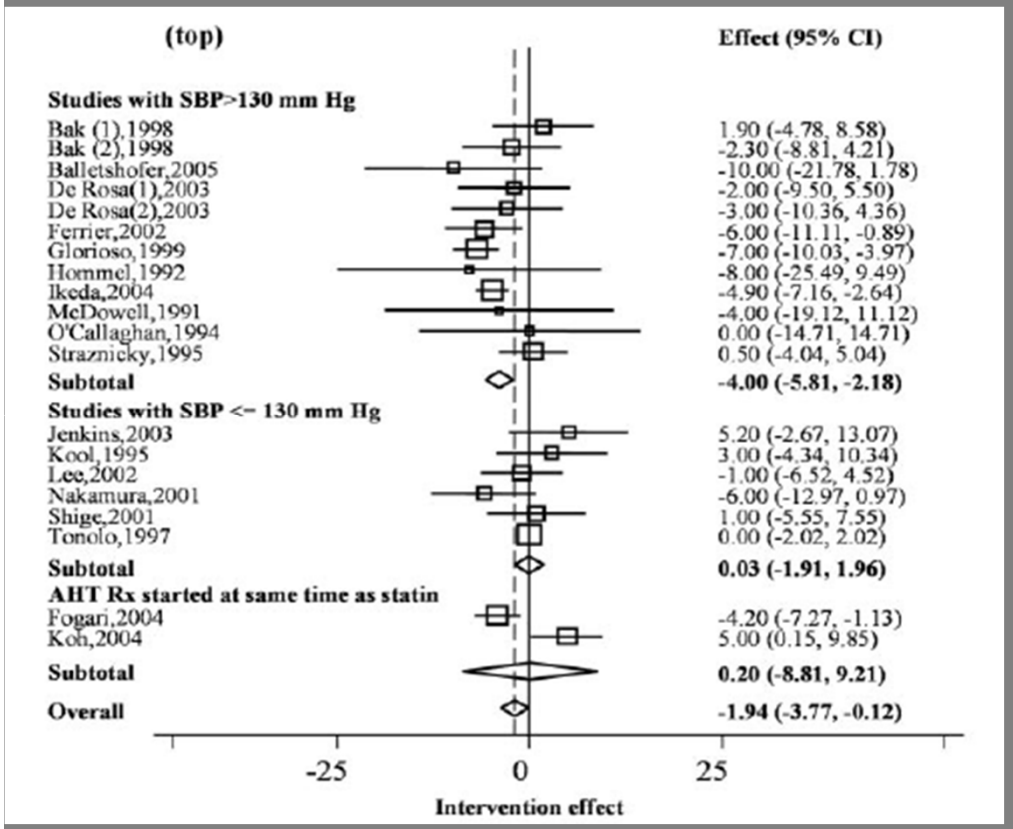


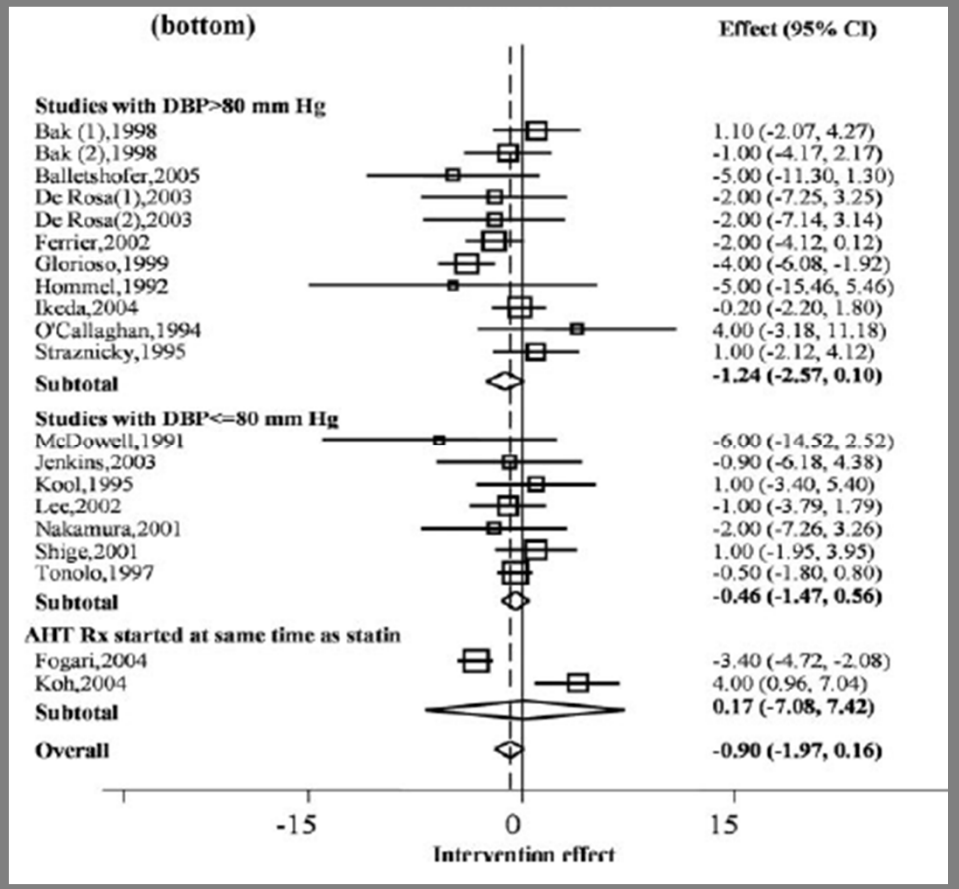

N Engl J Med 2008;359:2195-207

# 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, Drl*
*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*

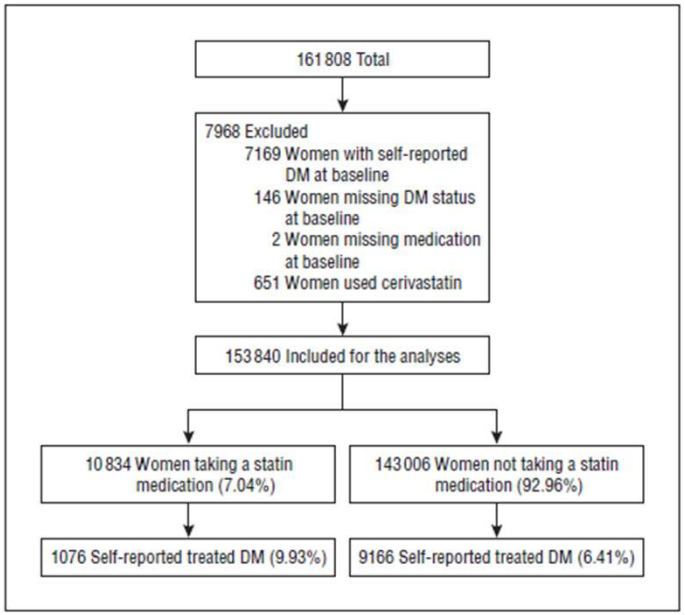



**Figure.** Flowchart for statin users and diabetes mellitus (DM) analyses using data sets from the Women's Health Initiative.

**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*

# 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 C. Olendzki, RD, MPH; Deidre M. Sepavich, MBA; Jean Wactawski-Wende, PhD; JoAnn E. Manson, MD, DrPH; Yongxia Qiao, MD; Simin Liu, MD, ScD; Philip A. Merriam, MSPH; Catherine Rahilly-Tierny, MD, MPH; Fridtjof Thomas, PhD; Jeffrey S. Berger, MD, MS; Judith K. Ockene, PhD, MEd, MA; J. David Curb, MD; Yunsheng Ma, MD, PhD*

| 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] |

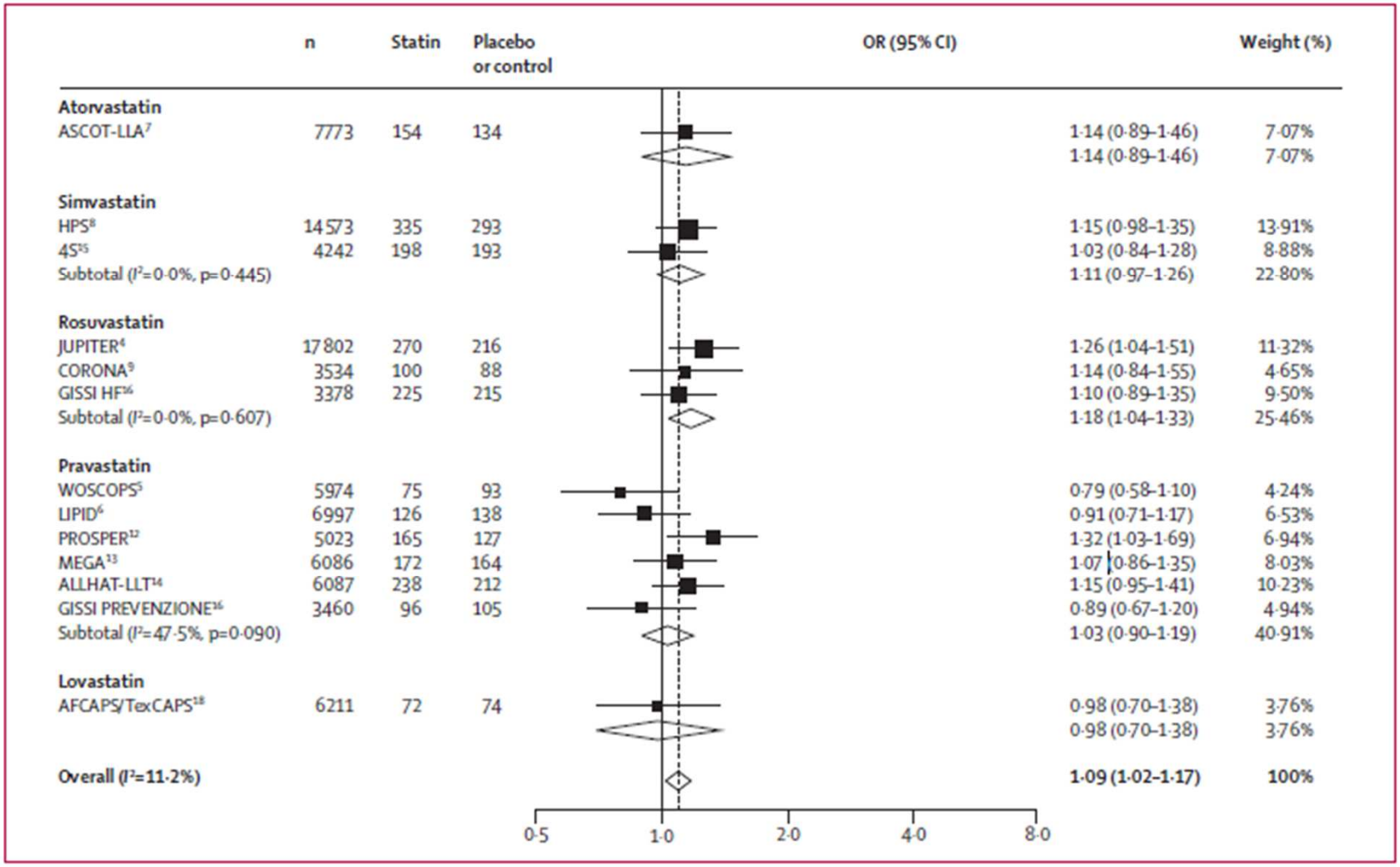
Abbreviations: HR, hazard ratio; PH, proportional hazards.

[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



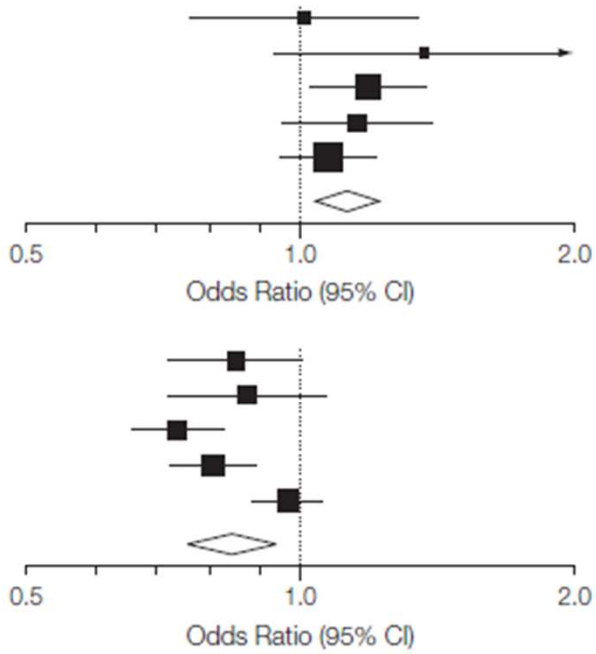

*Lancet* 2010; 375: 735–42

# 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*

# 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%.**

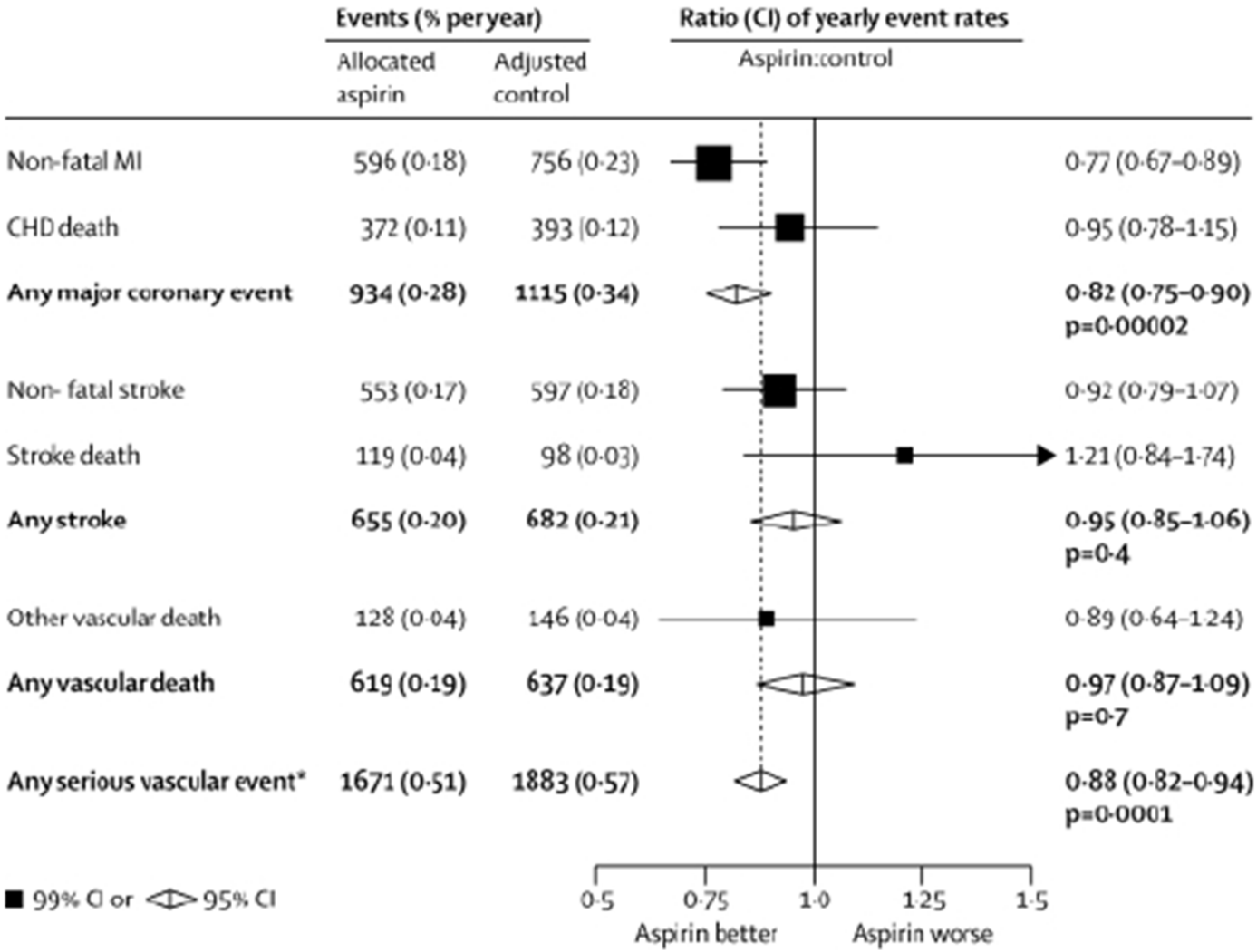
**In conclusion, the recommendation given in the 2007 guidelines to consider statin therapy in hypertensive patients who have an estimated 10-year risk of cardiovascular events more than 20% can be reconfirmed, but the JUPITER study suggests that statin benefits can be observed also in patients with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

# ASPIRINE

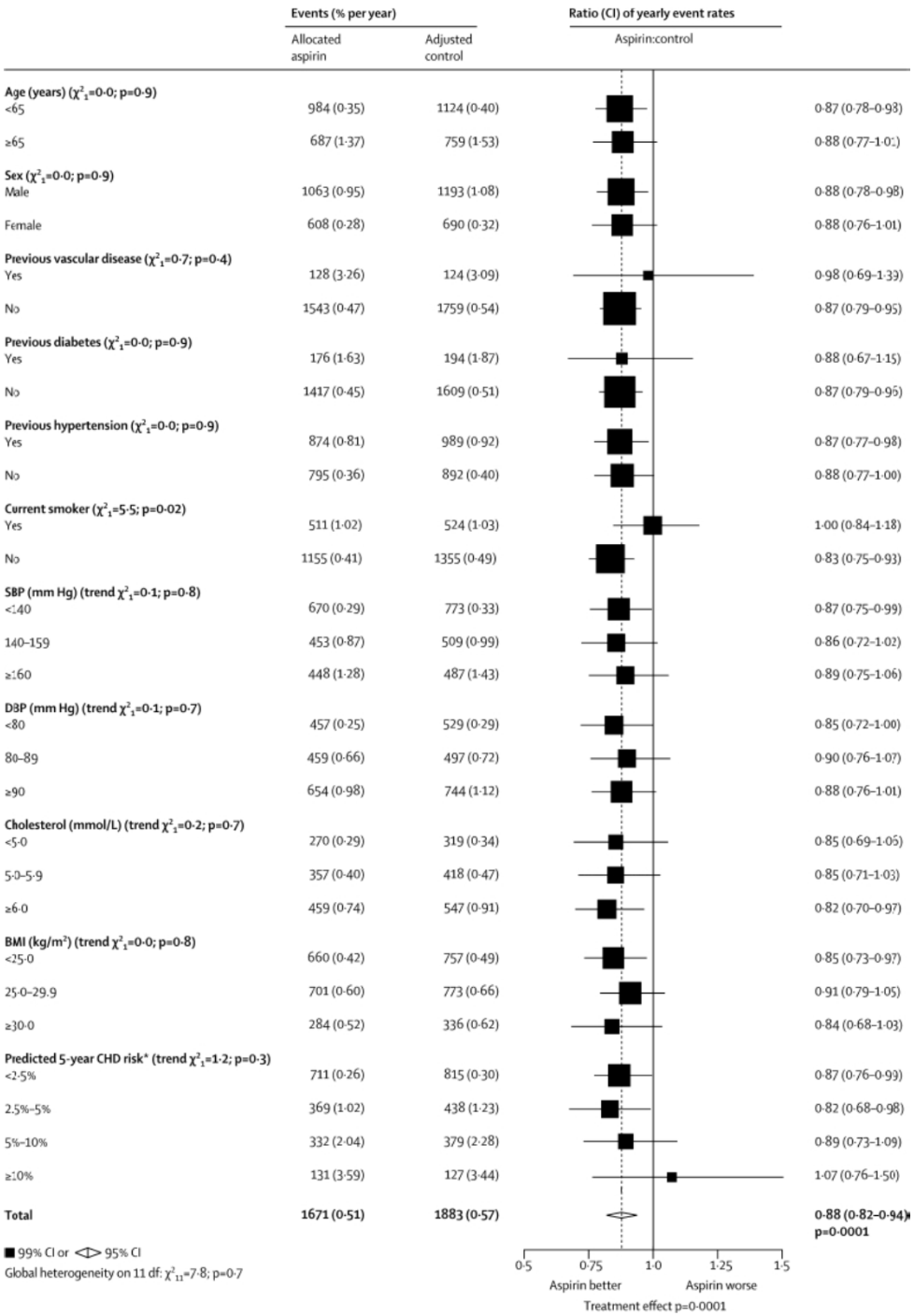
# Problème nosologique: Qu’appelle-on prévention primaire??

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

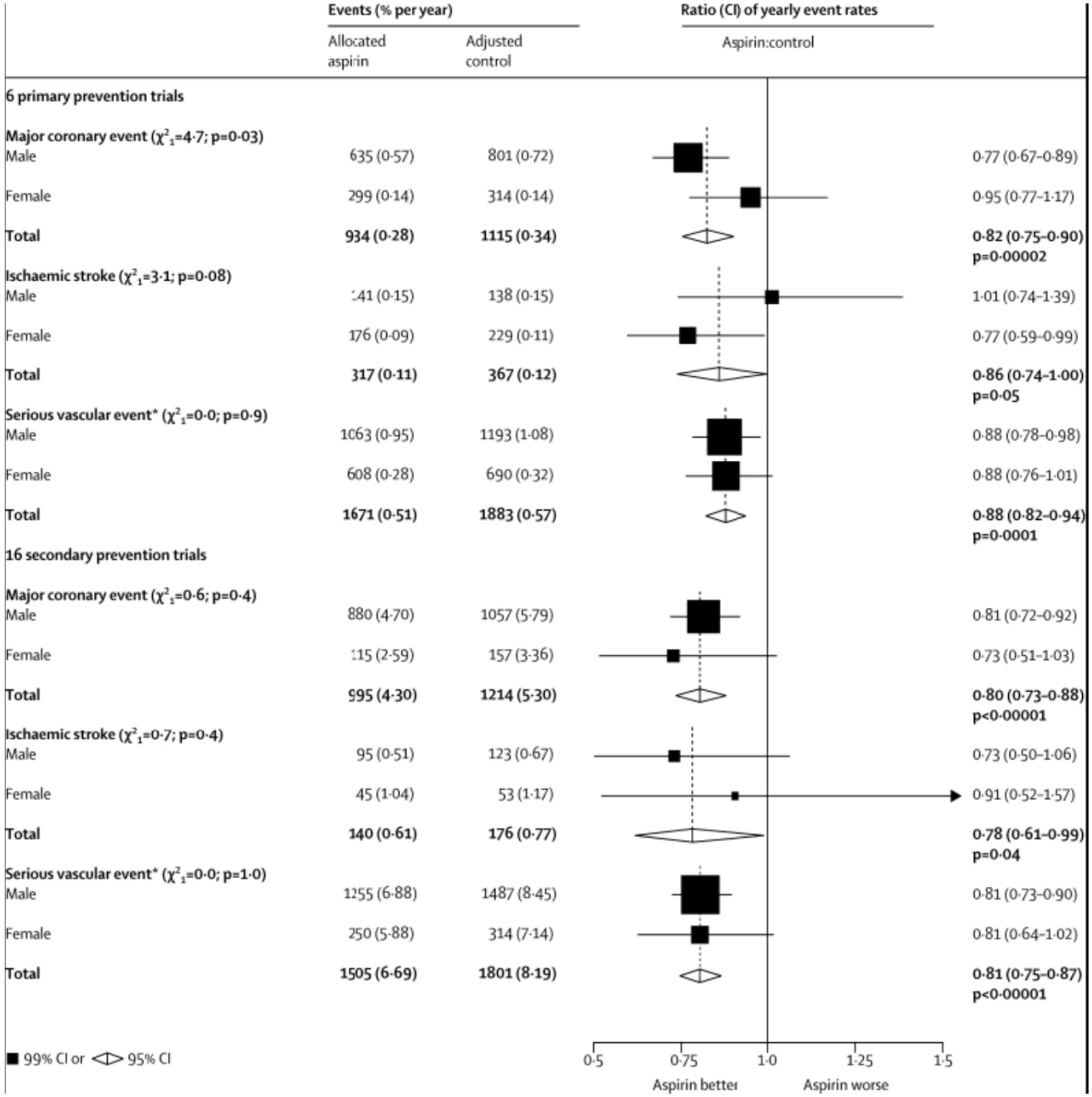
**Antithrombotic Trialists' (ATT) Collaboration**[‡,*]
Antithrombotic Trialists' (ATT) Collaboration: colin.baigent@ctsu.ox.ac.uk



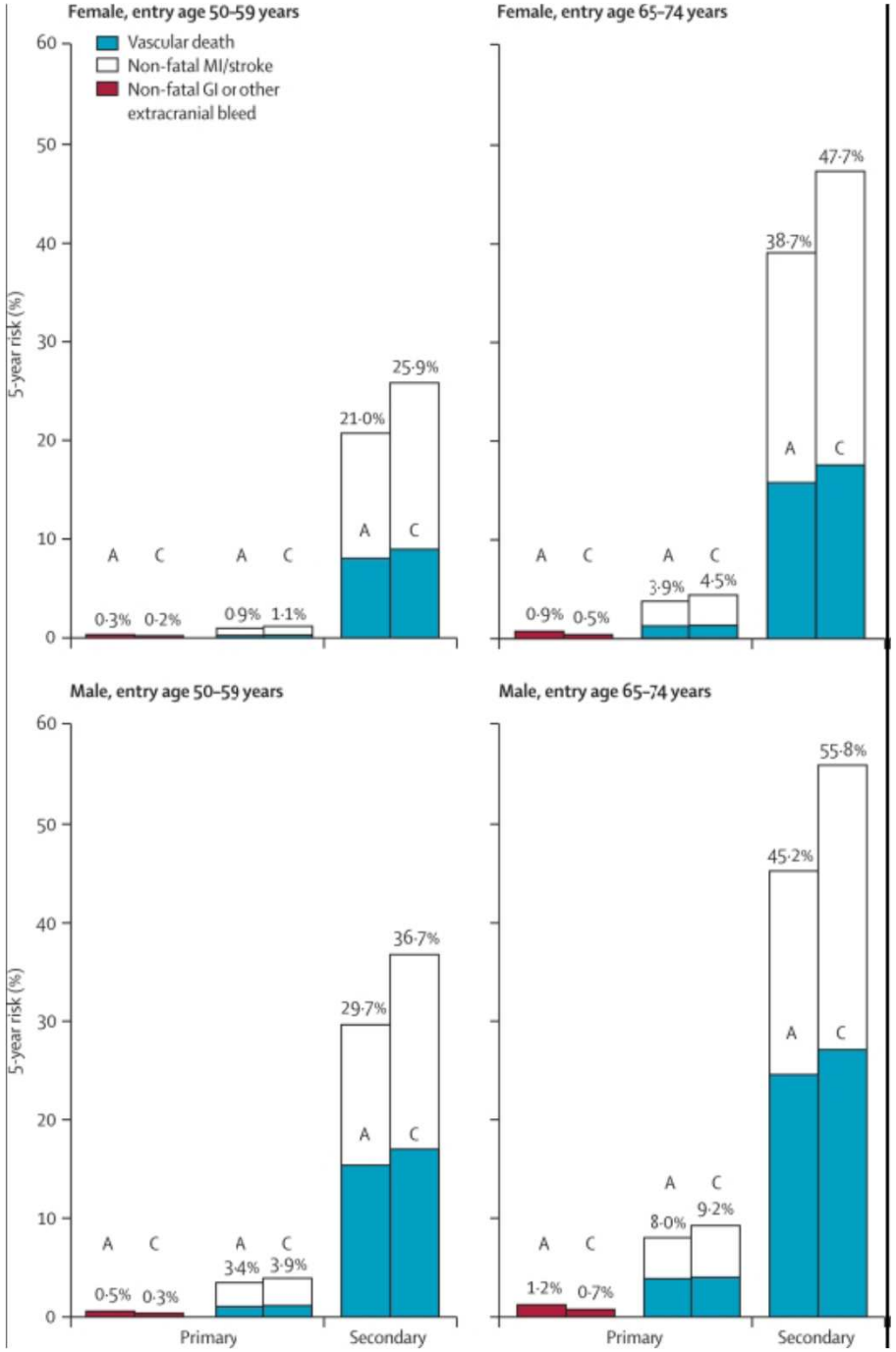

Lancet 2009;373:1849



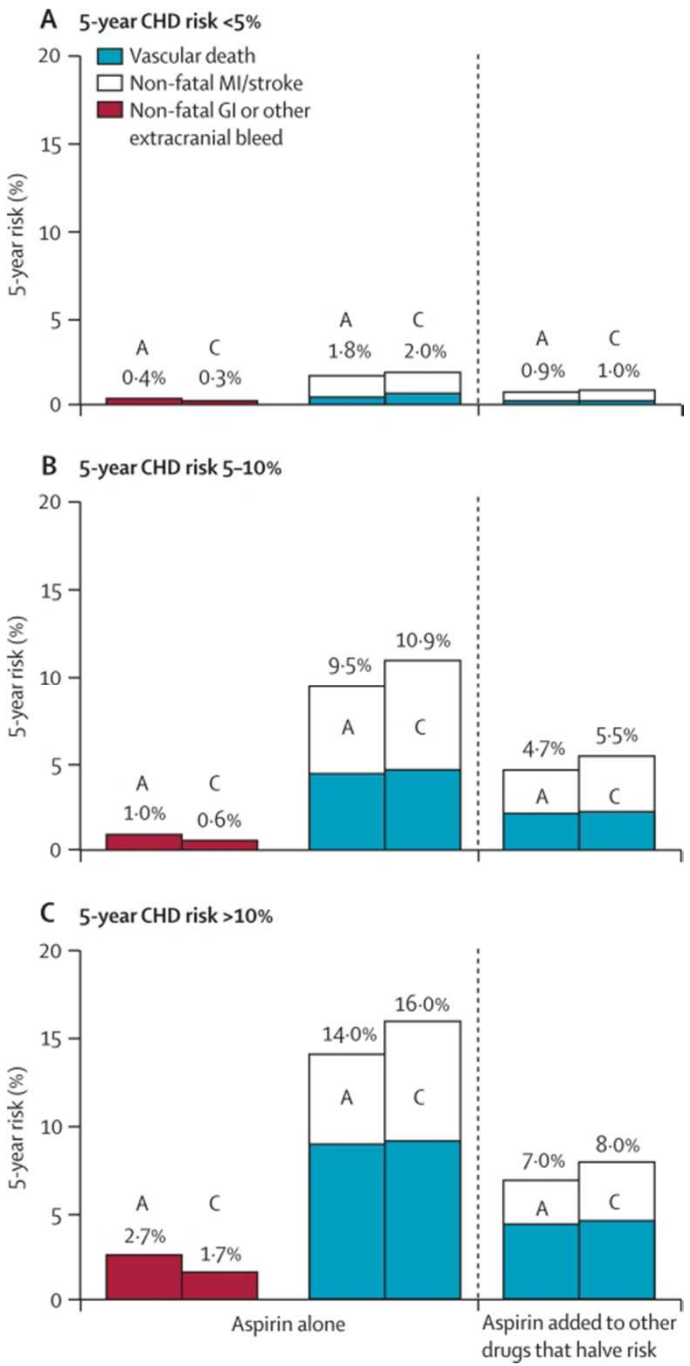

Lancet 2009;373:1849




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

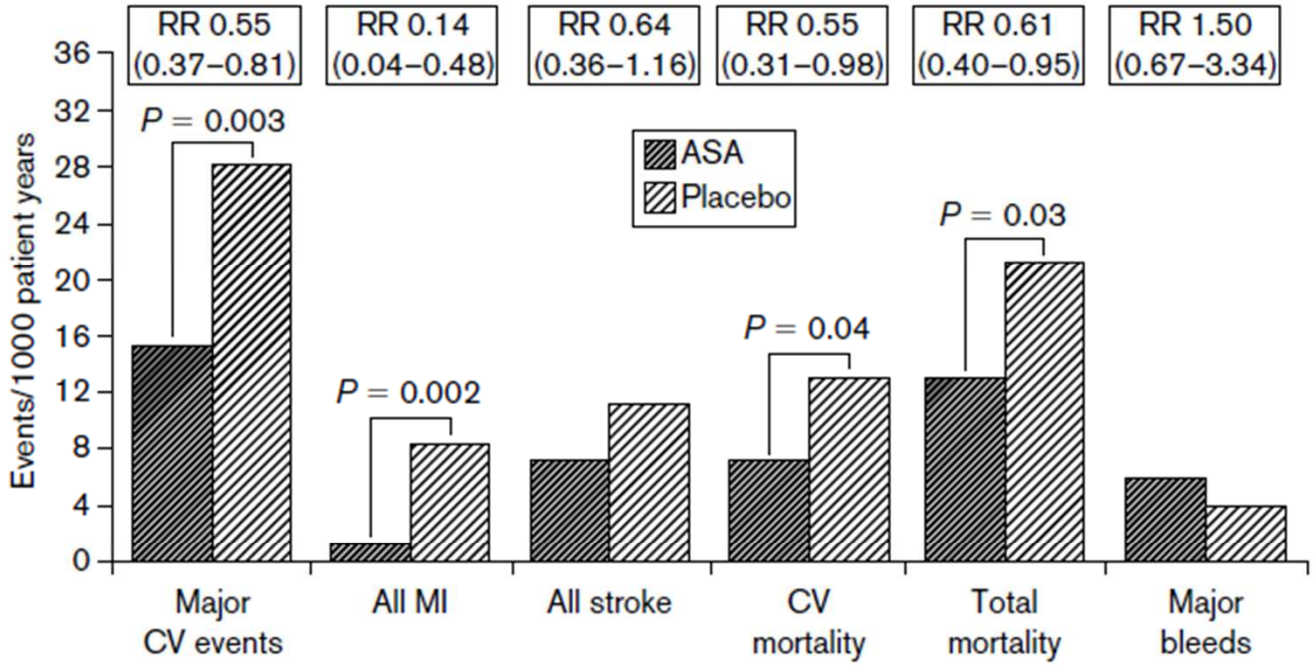
| Risk group | Event (*n*) | | Events/1000 patient-years | | Absolute risk increase/1000 patient-years | Relative risk (95% CI) | NNH (95% CI) |
|---|---|---|---|---|---|---|---|
| | Aspirin | Placebo | Aspirin | Placebo | | | |
| All patients | 127 | 77 | 3.6 | 2.2 | 1.4 | 1.65 (1.24–2.19) | 188 (121–425) |
| 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*

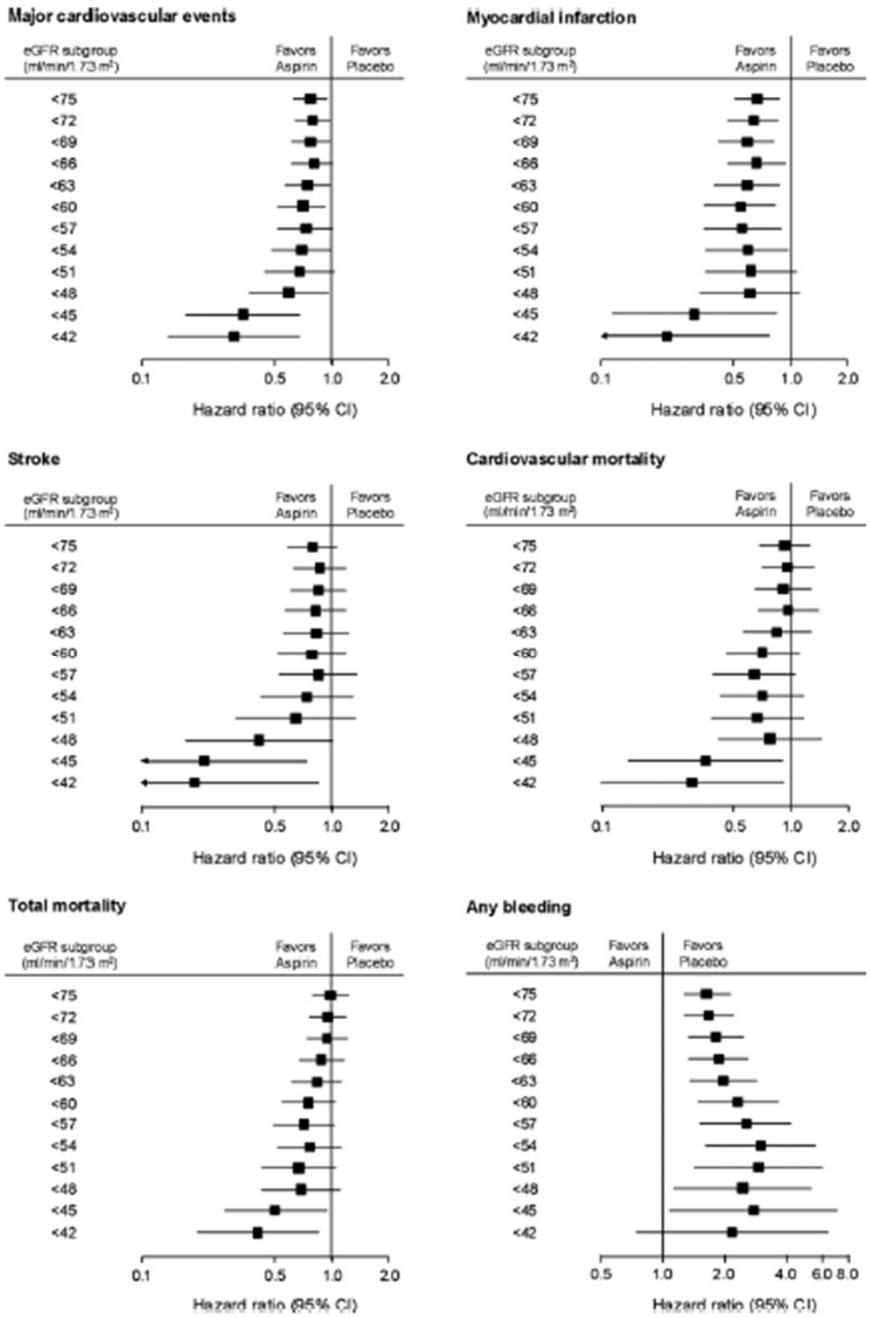



Effects of aspirin (ASA) in patients with high serum creatinine. Events in patients randomized to ASA or placebo, with baseline serum creatinine > 1.3 mg/dl (> 115 μmol/l). On the vertical axis, events per 1000 patient-years. RR, relative risk (95% confidence intervals); CV, cardiovascular; MI, myocardial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



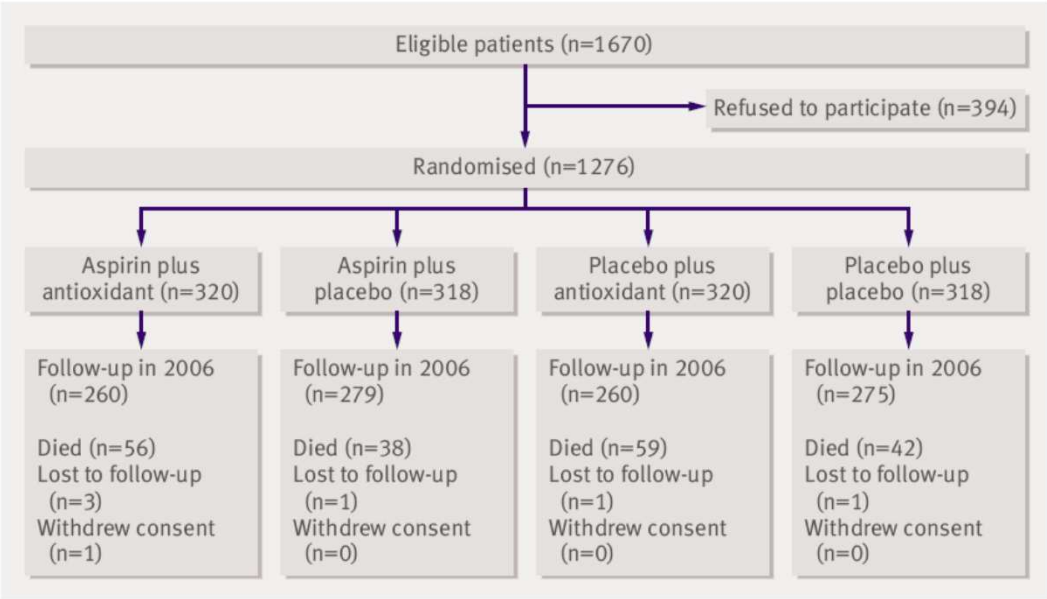

J Am Coll Cardiol 2010;56:956–65

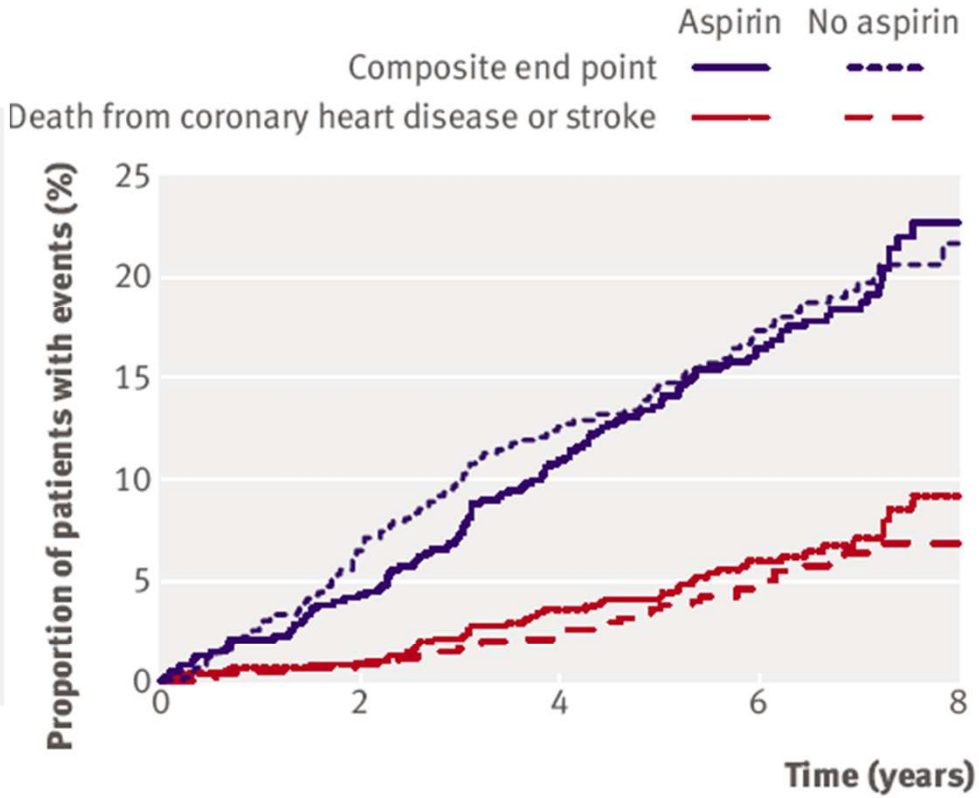
**Table 2** Events Prevented and Caused by Aspirin Therapy for Every 1,000 Patients Treated According to eGFR Category

| | 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



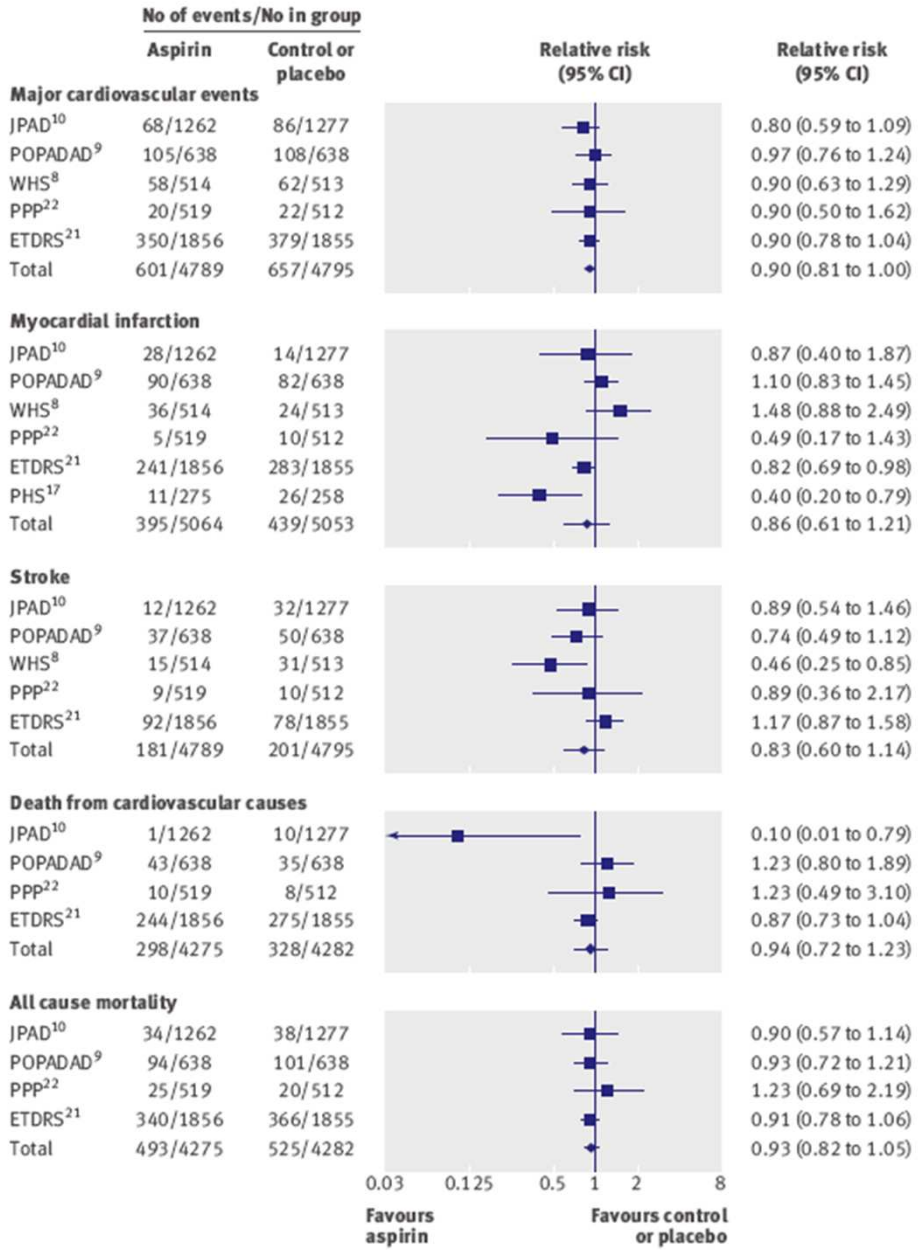



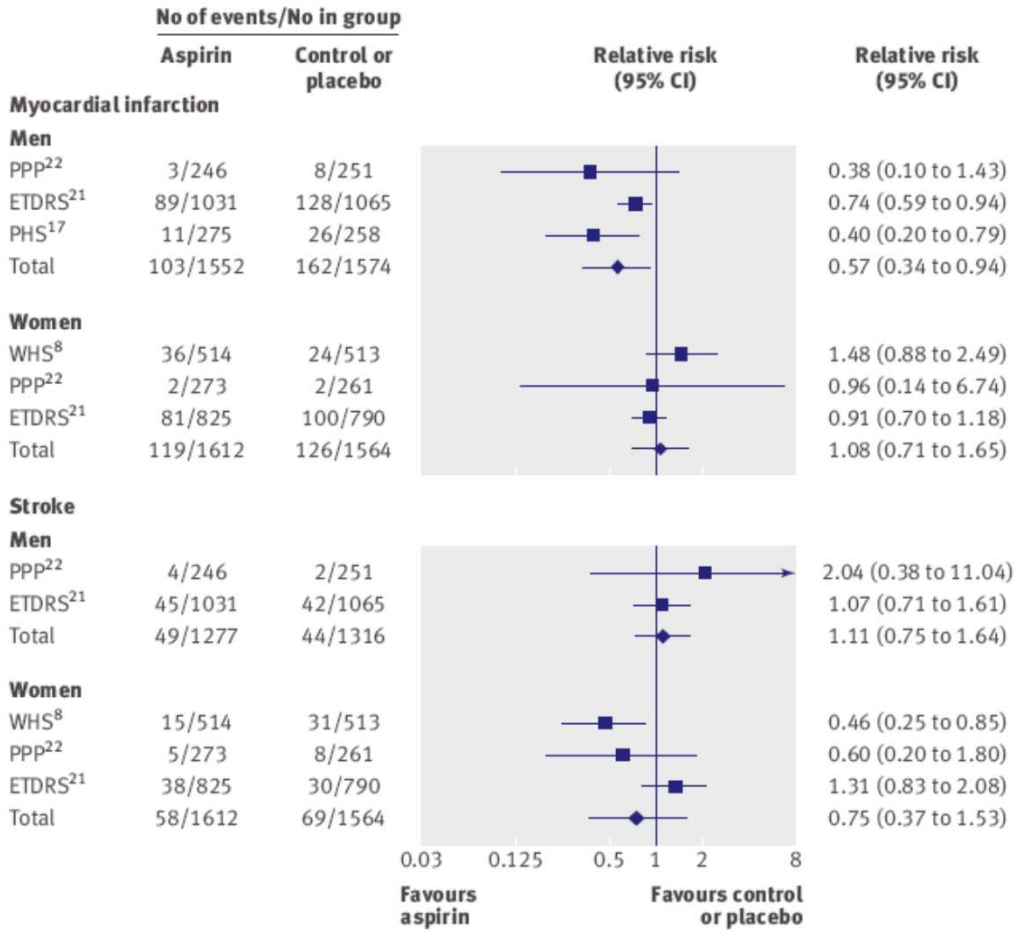

Numbers at risk for composite end point

| | | | | | |
|---|---|---|---|---|---|
| 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

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# A Randomized Trial of Low-Dose Aspirin in the Primary Prevention of Cardiovascular Disease in Women

Paul M Ridker, M.D., Nancy R. Cook, Sc.D., I-Min Lee, M.B., B.S., David Gordon, M.A., J. Michael Gaziano, M.D., JoAnn E. Manson, M.D., Charles H. Hennekens, M.D., and Julie E. Buring, Sc.D.

| End Point | Aspirin (N=19,934) | Placebo (N=19,942) | Relative Risk (95% CI)* | P Value |
|---|---|---|---|---|
| | *no. of events* | | | |
| Major cardiovascular event† | 477 | 522 | 0.91 (0.80–1.03) | 0.13 |
| Stroke | 221 | 266 | 0.83 (0.69–0.99) | 0.04 |
| Ischemic | 170 | 221 | 0.76 (0.63–0.93) | 0.009 |
| Hemorrhagic | 51 | 41 | 1.24 (0.82–1.87) | 0.31 |
| Fatal | 23 | 22 | 1.04 (0.58–1.86) | 0.90 |
| Nonfatal | 198 | 244 | 0.81 (0.67–0.97) | 0.02 |
| Myocardial infarction | 198 | 193 | 1.02 (0.84–1.25) | 0.83 |
| Fatal | 14 | 12 | 1.16 (0.54–2.51) | 0.70 |
| Nonfatal | 184 | 181 | 1.01 (0.83–1.24) | 0.90 |
| Death from cardiovascular causes | 120 | 126 | 0.95 (0.74–1.22) | 0.68 |
| Transient ischemic attack | 186 | 238 | 0.78 (0.64–0.94) | 0.01 |
| Coronary revascularization | 389 | 374 | 1.04 (0.90–1.20) | 0.61 |
| Death from any cause | 609 | 642 | 0.95 (0.85–1.06) | 0.32 |

39876 femmes; âge moyen 55ans;

HTA 26%; Tabagisme 13%; Obésité : 18.2%; Diabète 2.6%; Risque framingham <5% à 10 ans : 85%

NEJM 2005

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**Table 4. Incidence and Relative Risk of Side Effects.***

| Side Effect | Aspirin (N=19,934) | Placebo (N=19,942) | Relative Risk (95% CI) | P Value |
|---|---|---|---|---|
| | *no. of events (%)* | | | |
| Gastrointestinal bleeding | | | | |
| Any | 910 (4.6) | 751 (3.8) | 1.22 (1.10–1.34) | <0.001 |
| Requiring transfusion | 127 (0.6) | 91 (0.5) | 1.40 (1.07–1.83) | 0.02 |
| Peptic ulcer | 542 (2.7) | 413 (2.1) | 1.32 (1.16–1.50) | <0.001 |
| Hematuria | 3,039 (15.2) | 2,879 (14.4) | 1.06 (1.01–1.12) | 0.02 |
| Easy bruising | 10,561 (53.0) | 8,494 (42.6) | 1.40 (1.37–1.45) | <0.001 |
| Epistaxis | 3,801 (19.1) | 3,321 (16.7) | 1.16 (1.11–1.22) | <0.001 |
| Any report of gastric upset | 11,856 (59.5) | 11,915 (59.7) | 0.99 (0.97–1.02) | 0.59 |

NEJM 2005

# 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

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**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.**