

HEART RATE IN CAD- risk marker or risk factor

European Society of Cardiology - EuroPRevent 2009

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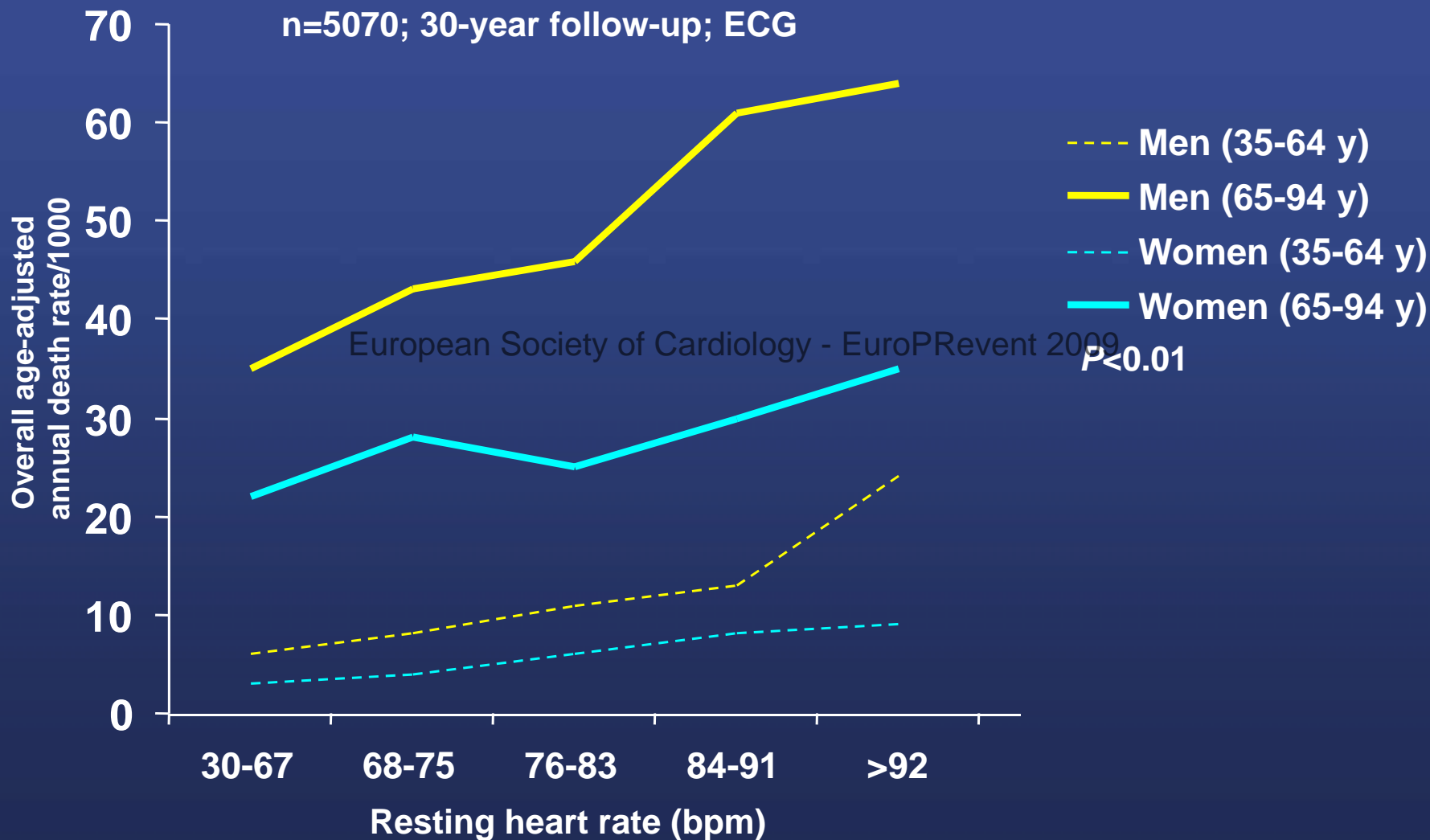
Prognostic importance of resting heart rate: epidemiological evidence (in general population and hypertensives)

| Study | Population | Follow-up | Cardiovascular mortality RR |
|--------------------------------|---------------|-----------|---|
| Chicago Gas Company '80 | 1 233 M | 15 y | >94 vs. ≤60 bpm 2.3 |
| Chicago Heart Ass. Project '80 | 33 781 M&W | 22 y | ≥90 vs. <70 bpm M: 1.6 W: 1.1 (ns) |
| Framingham '93 | 4 530 M&W HTN | 36 y | >100 vs. <60 bpm M: 1.5 W: 1.4 (ns) |
| British Regional Heart '93 | 735 M | 8 y | >90 vs. ≤ 90 bpm IHD death 3.3 |
| Spandau '97 | 4 756 M&W | 12 y | Sudden death 5.2 per 20 bpm |
| Benetos '99 | 19 386 M&W | 18.2 y | >100 vs. <60 bpm M: 2.2 W: 1.1 (ns) |
| Castel '99 | 1 938 M&W | 12 y | 5th vs. 3rd quintile M: 1.6 W: 1.1 |
| Cordis '00 | 3 257 M | 8 y | ≥90 vs. <70 bpm 2.0 |
| Reunanen '00 | 10 717 M&W | 23 y | M: 1.4 (>84 vs. <60) W: 1.5 (>94 vs. <66) |
| Thomas '01 | 60 343 M HTN | 14 y | >80 vs. ≤ 80 bpm <55y:1.5 >55y:1.3 |
| Matiss '01 | 2 533 M | 9 y | per 20 bpm: 1.5 ≥90 vs. <60 bpm: 2.7 |
| Ohasama '04 | 1 780 M&W | 10 y | M: 1.2 W: 1.1 (ns) per 5 bpm |
| Okamura '04 | 8 800 M&W | 16.5 y | per 11 bpm (1 SD) M: 1.3 W: 1.2 |
| Jouven '05 | 5 713 M | 23 y | Sudden death from AMI 3.92 (>75 bpm) |

During 25 years - more than 155 000 patients, follow-up 8-36 years

Resting heart rate and all-cause mortality

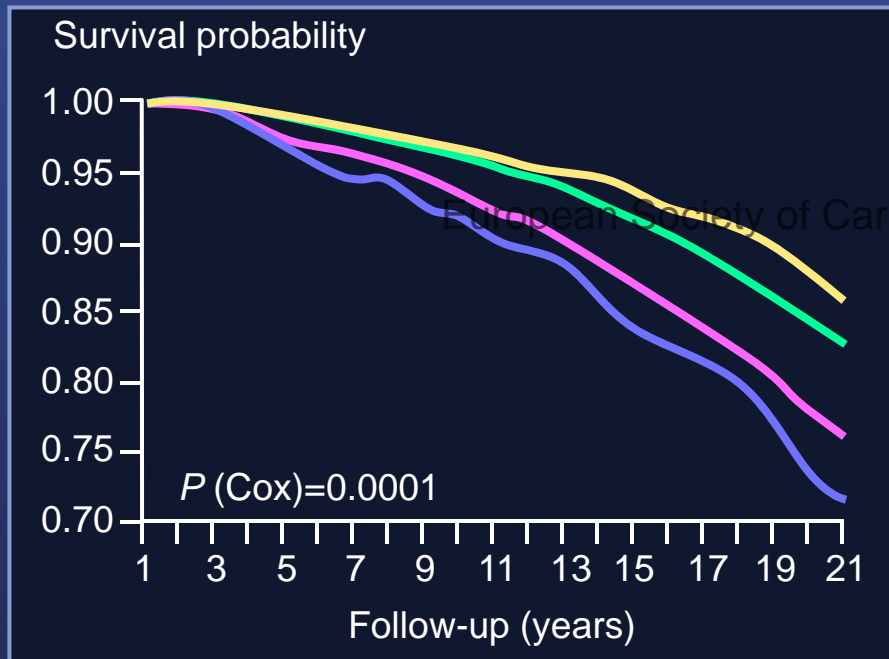
The Framingham Study



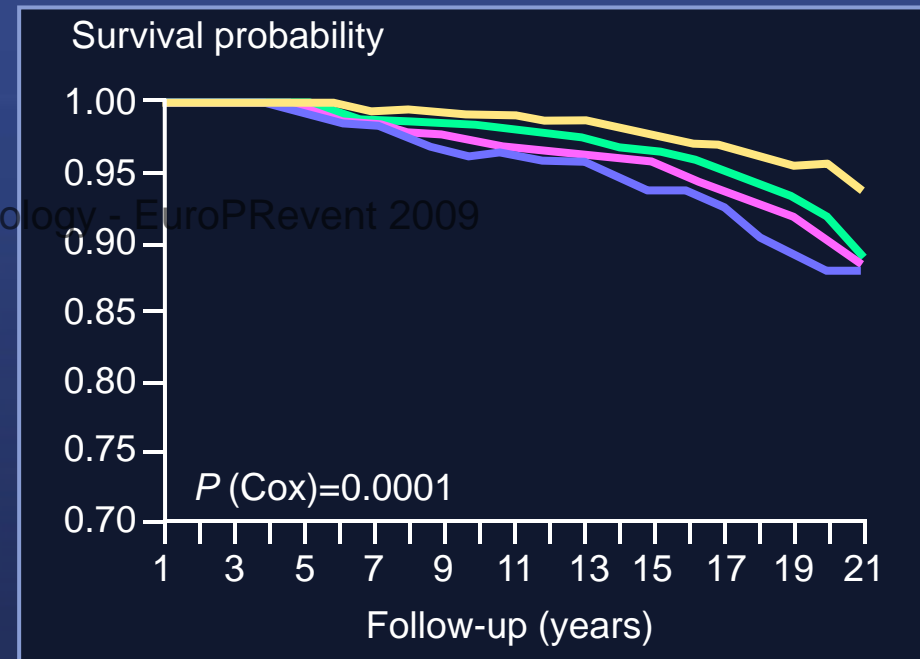
Resting heart rate independently predicts total and CV mortality in men and women

French cohort study, n=19 386 (12 123 men, 7 263 women), 18-year follow-up

Men: all-cause mortality



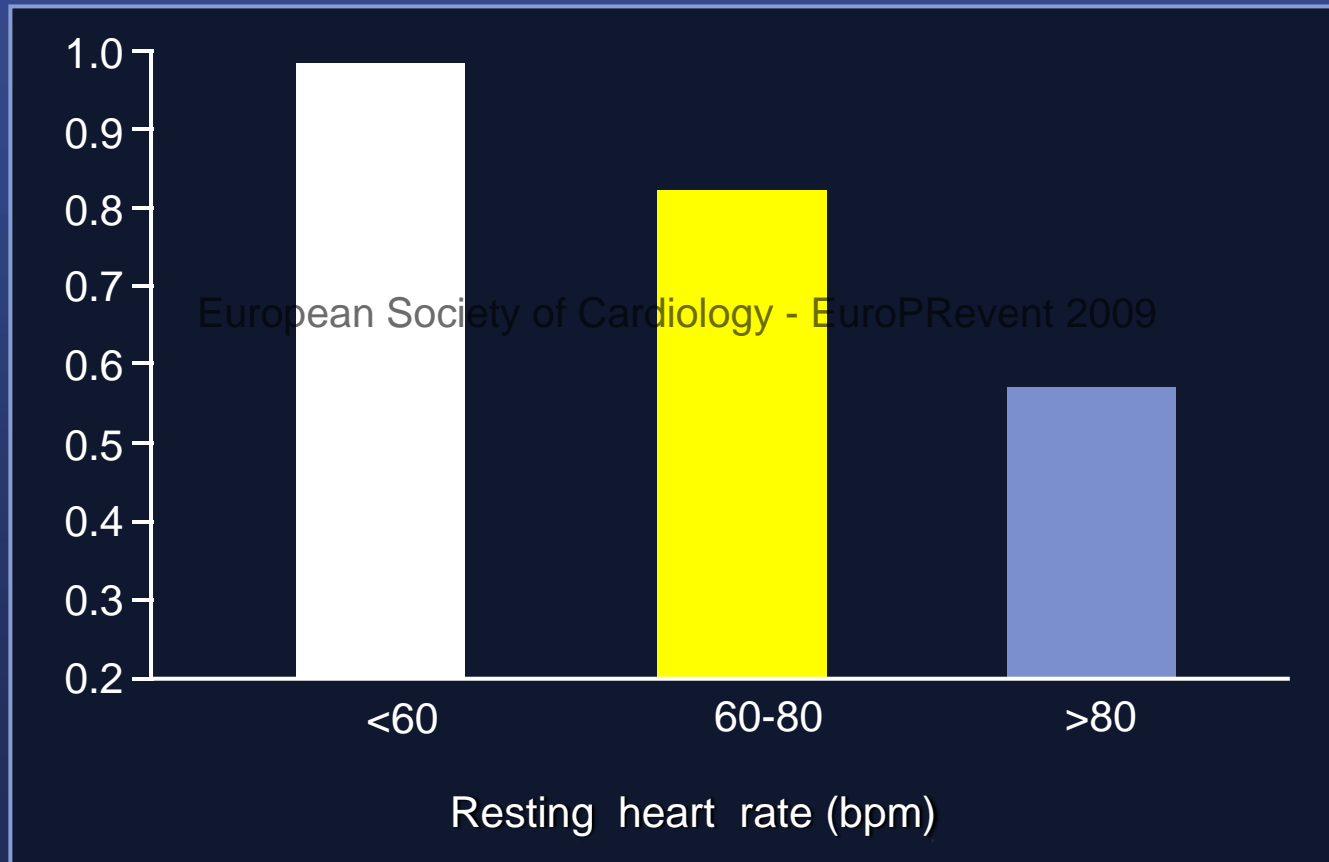
Women: all-cause mortality



— HR < 60 — 60 ≤ HR ≤ 80 — 80 < HR ≤ 100 — HR > 100 bpm

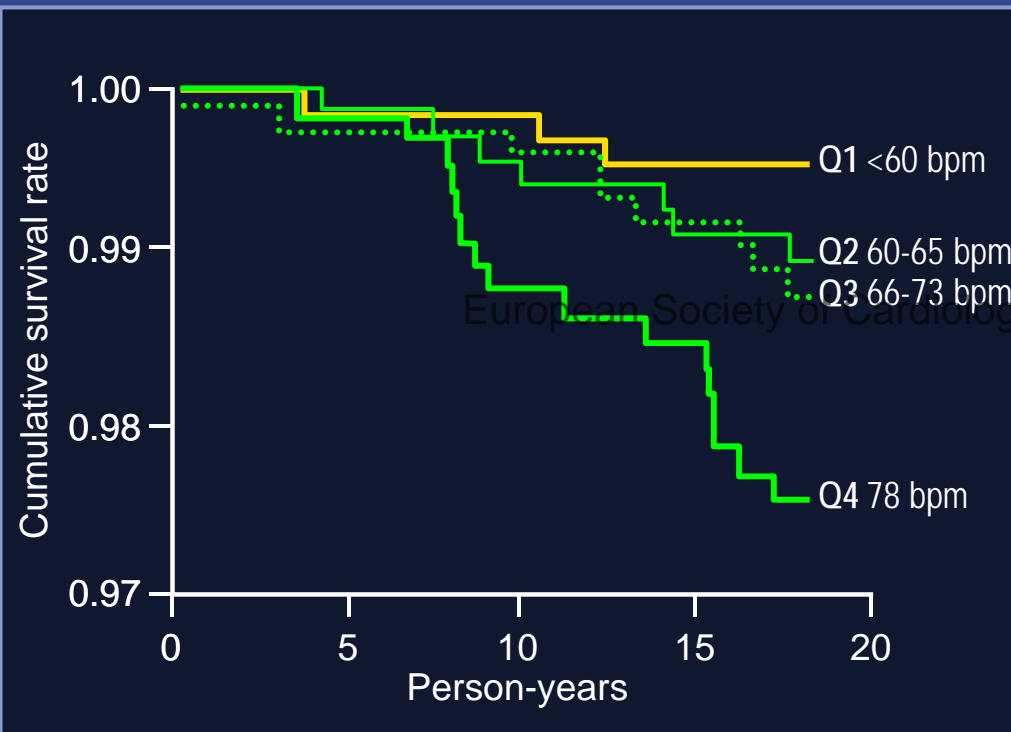
Resting heart rate: predicts survival in people aged >65years

Cohort study in 1 407 men aged from 65 to 70 years, follow-up 18 years

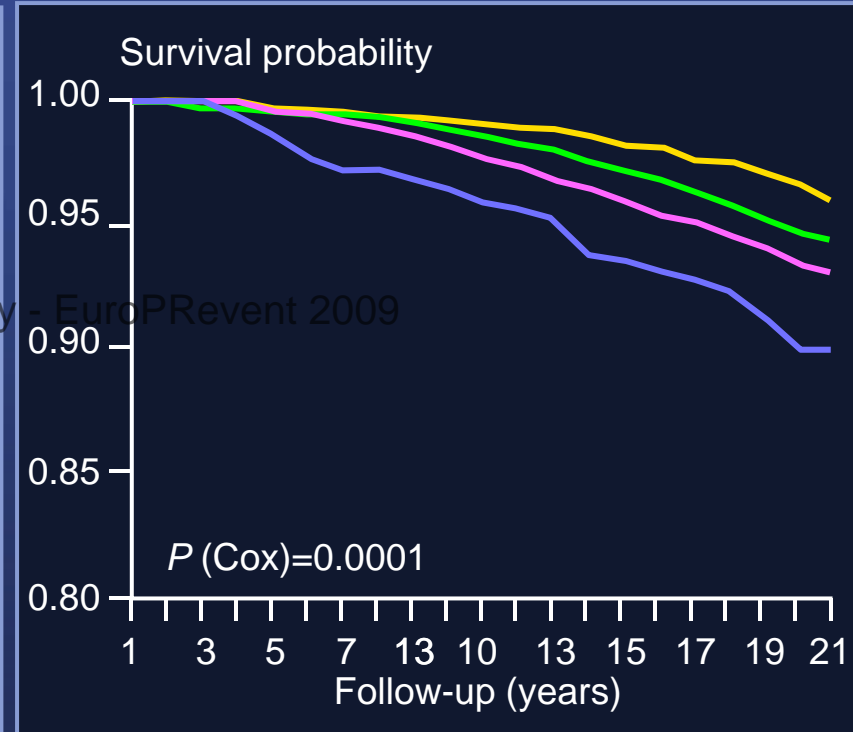


Resting heart rate independently predicts mortality in Western and Asian populations

Cumulative survival rates due to cardiac events in Japanese men (n=3 856)



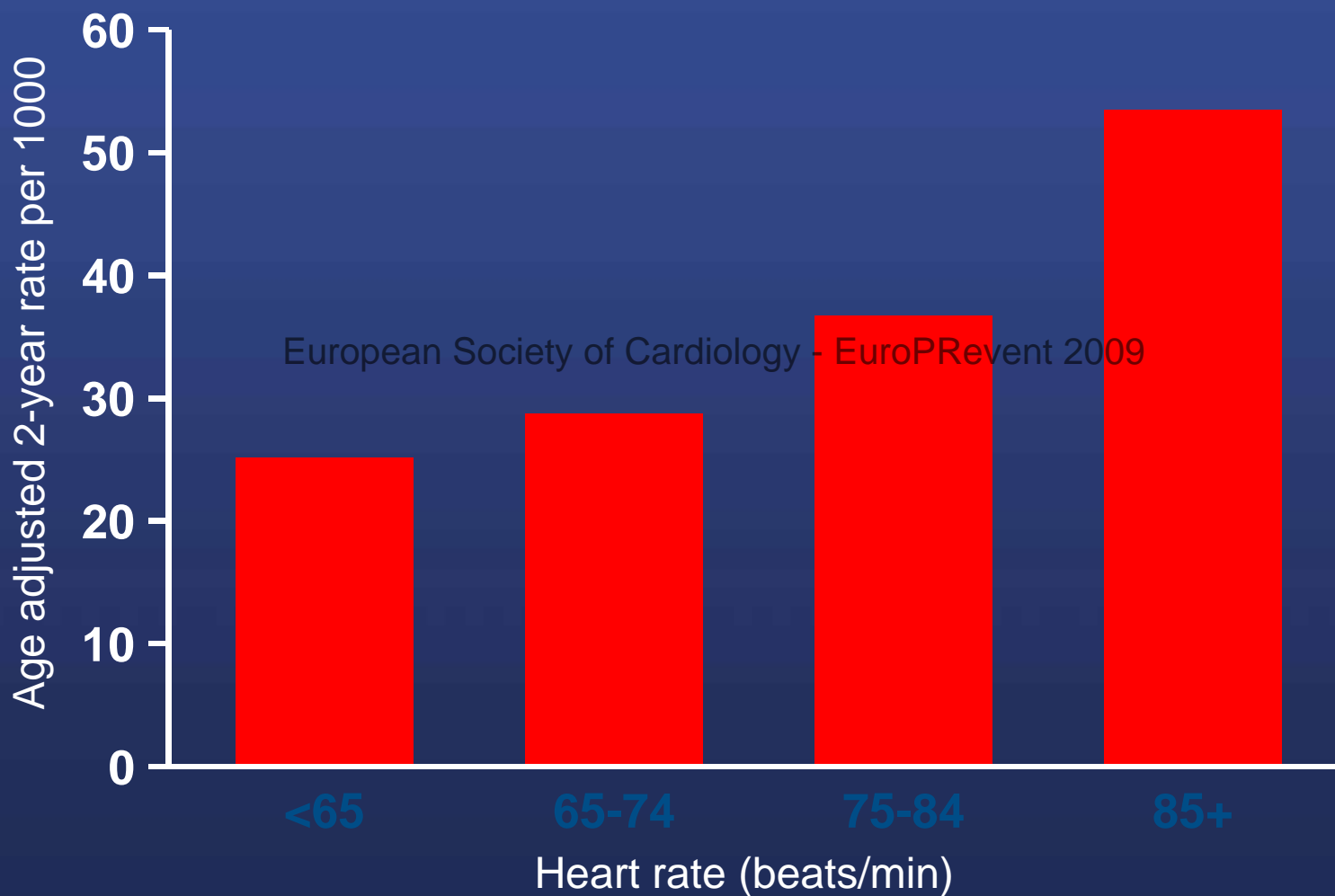
Survival probability curves for CV mortality in French men (n=12 123)



— HR <60 — 60 ≤ HR ≤ 80 — 80 < HR ≤ 100 — HR > 100 bpm

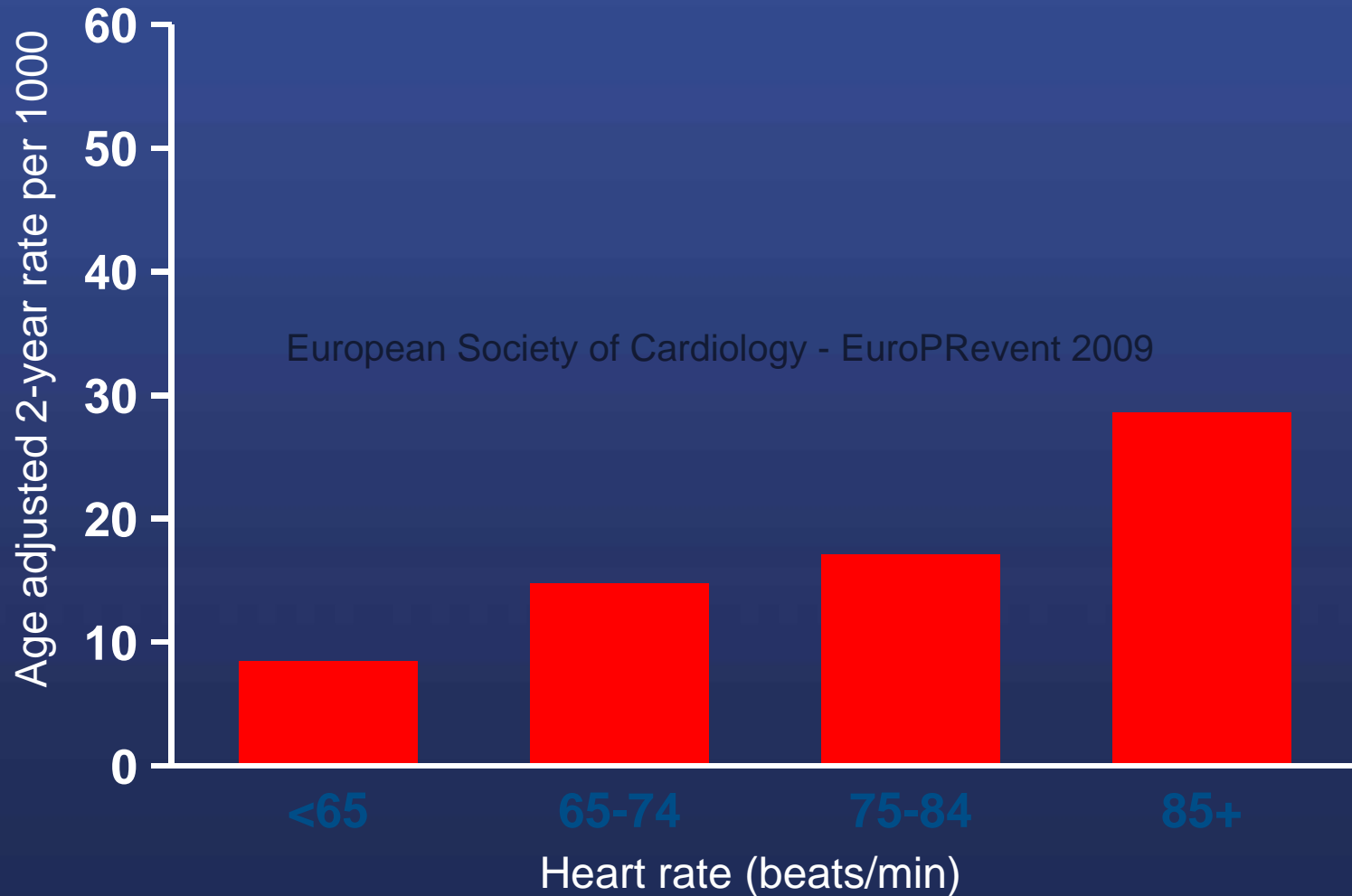
All Cause Mortality - men With Hypertension

36 Year Follow-up Framingham Study (n=2037)



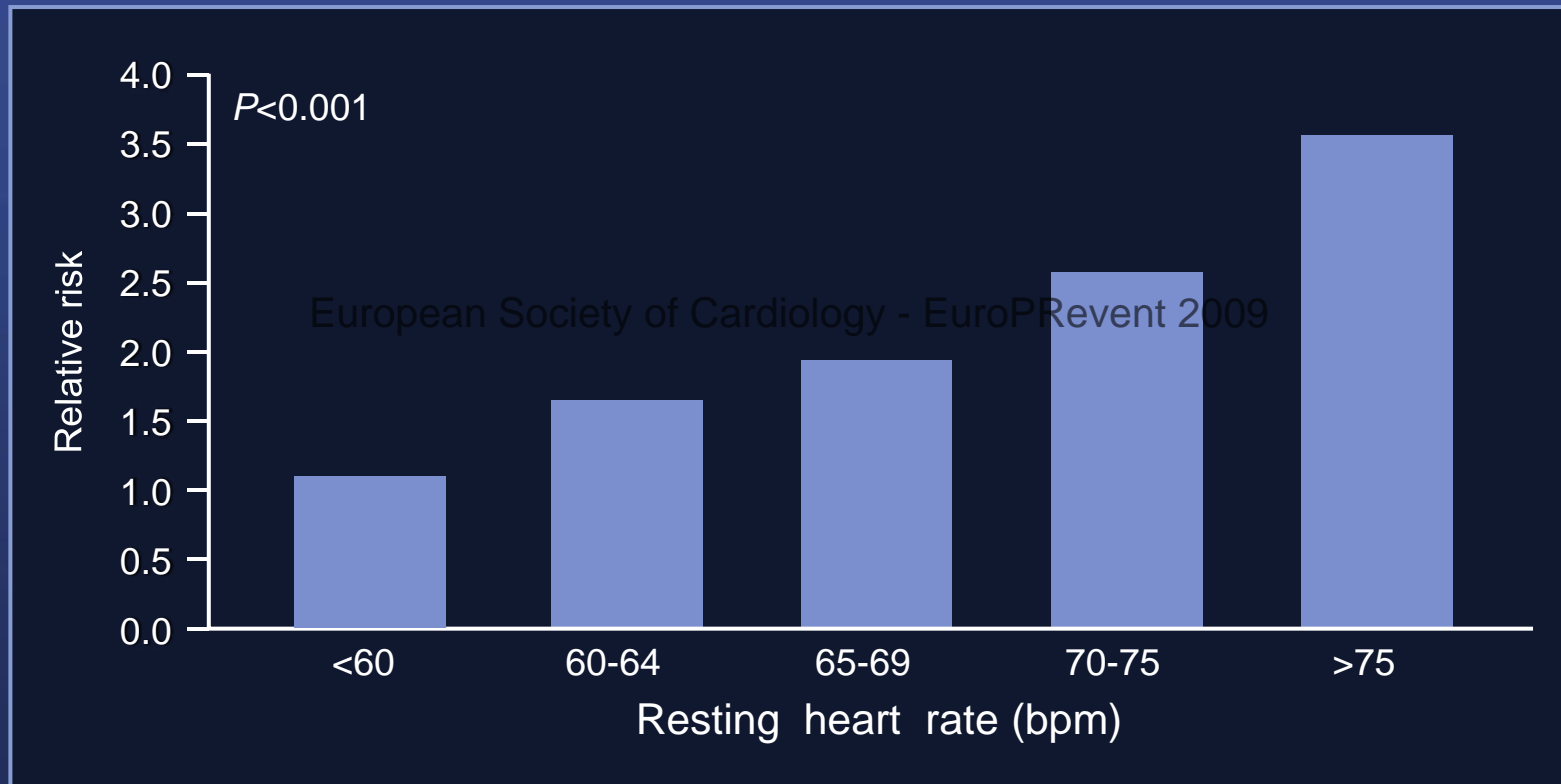
All Cause Mortality - Women With Hypertension

36 Year Follow-up Framingham Study (n=2493)



Sudden death risk increases progressively with resting HR in the general population

The Paris Prospective Study, general population, 5 713 men; 23-year follow-up

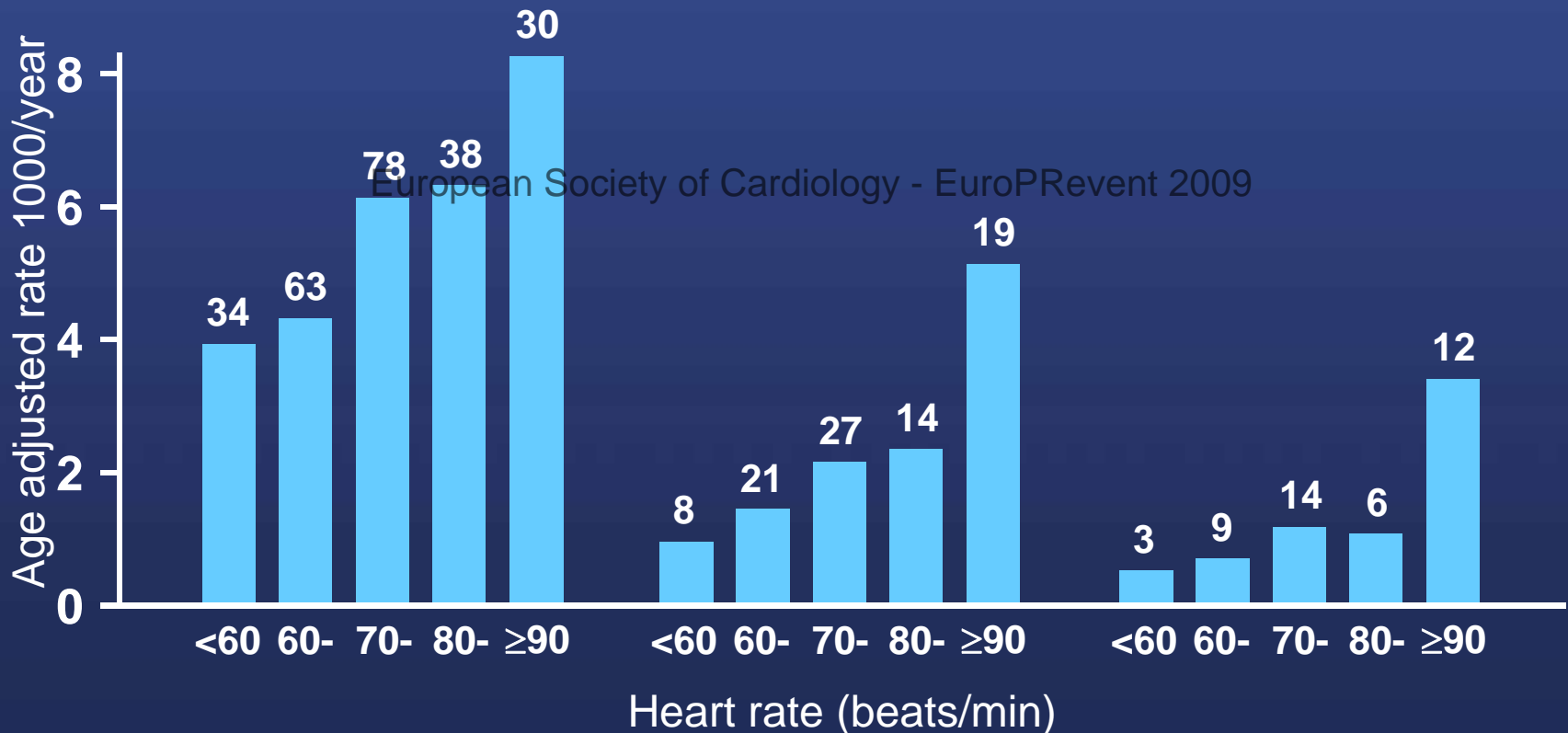


Age Adjusted Rates for Major Ischaemic Heart Disease (IHD), Mortality from IHD and Sudden Death (5769 healthy men, 40-59 yrs)

Major IHD events

IHD mortality

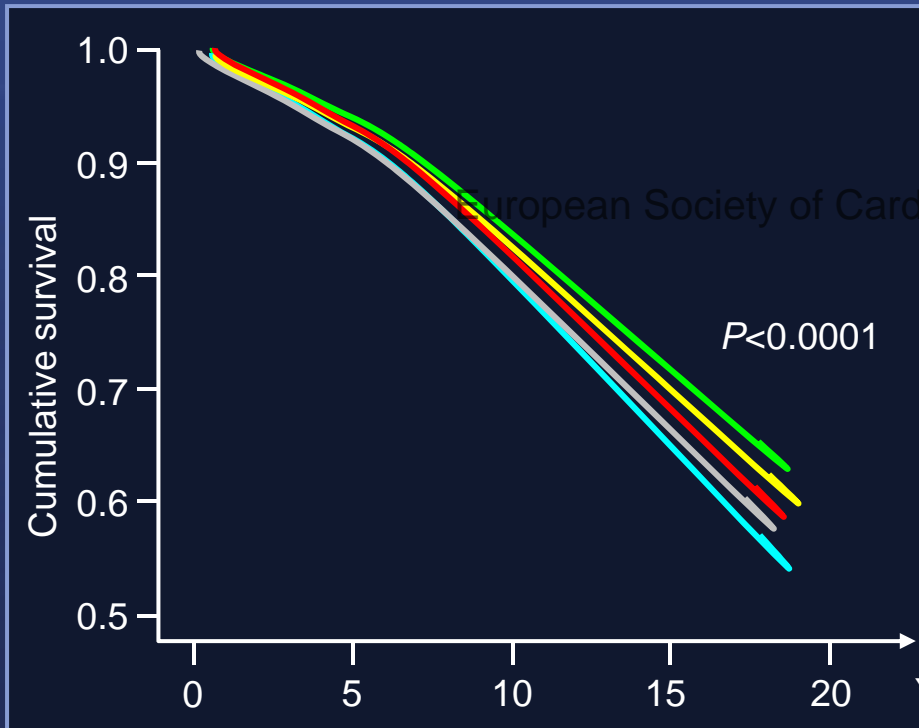
Sudden cardiac death



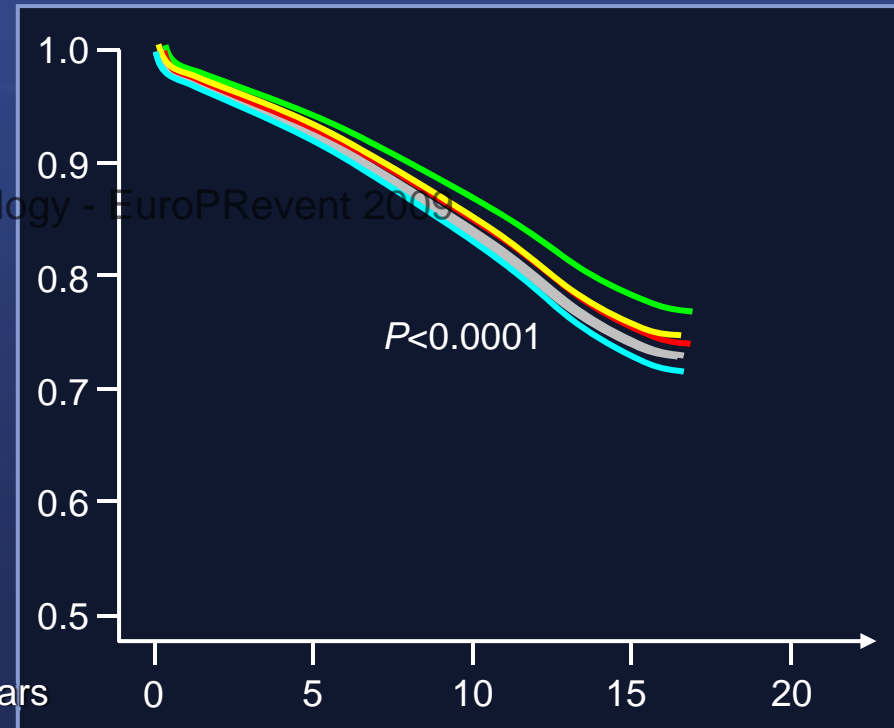
Resting heart rate as a predictor of mortality in patients with CAD

CASS registry (Coronary Artery Surgery Study) n=24 913; 14.1 years follow-up

Adjusted survival for all cause mortality

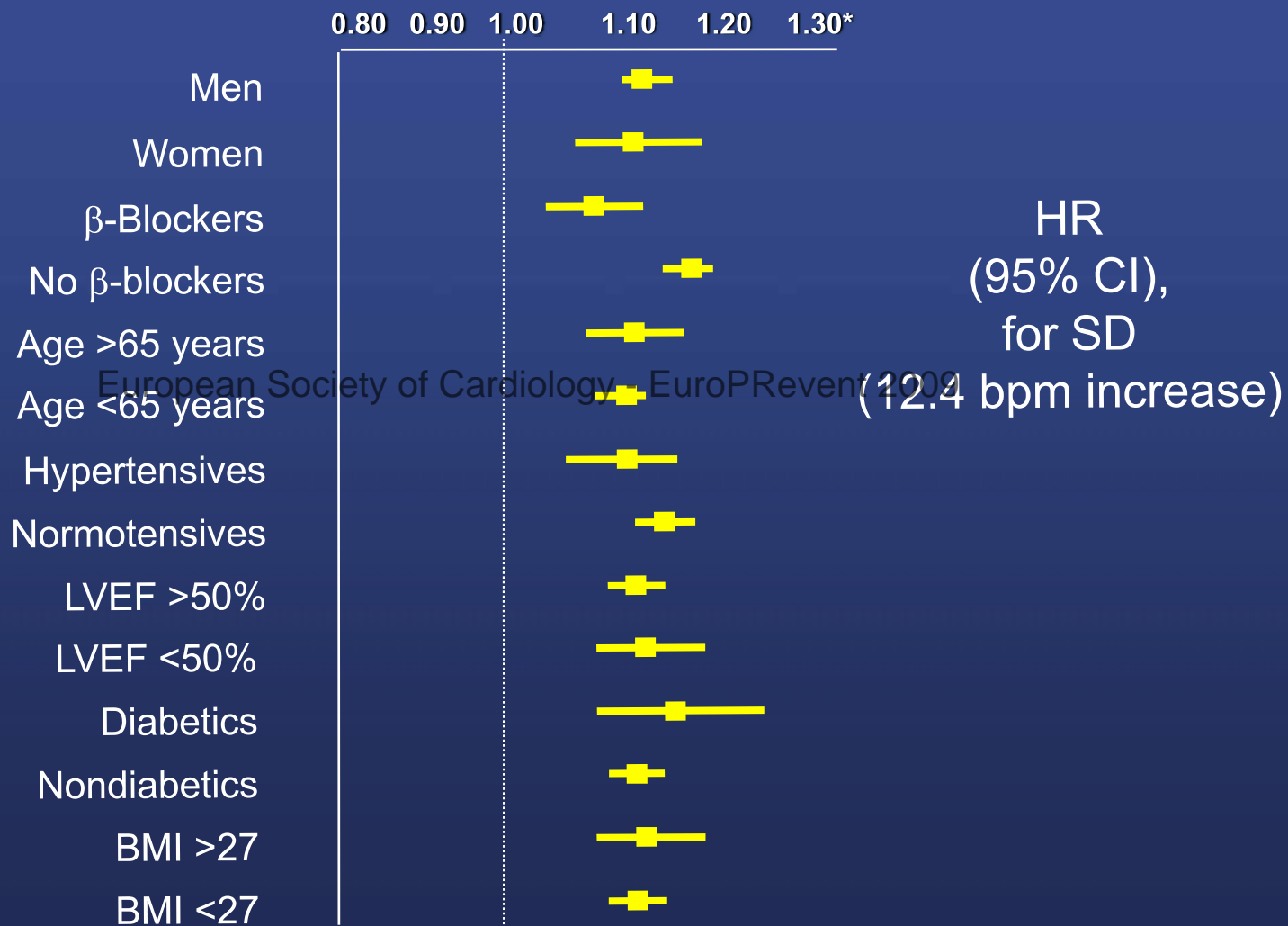


Adjusted survival for cardiovascular mortality



— ≤62 — 63-70 — 71-76 — 77-82 — ≥83 bpm

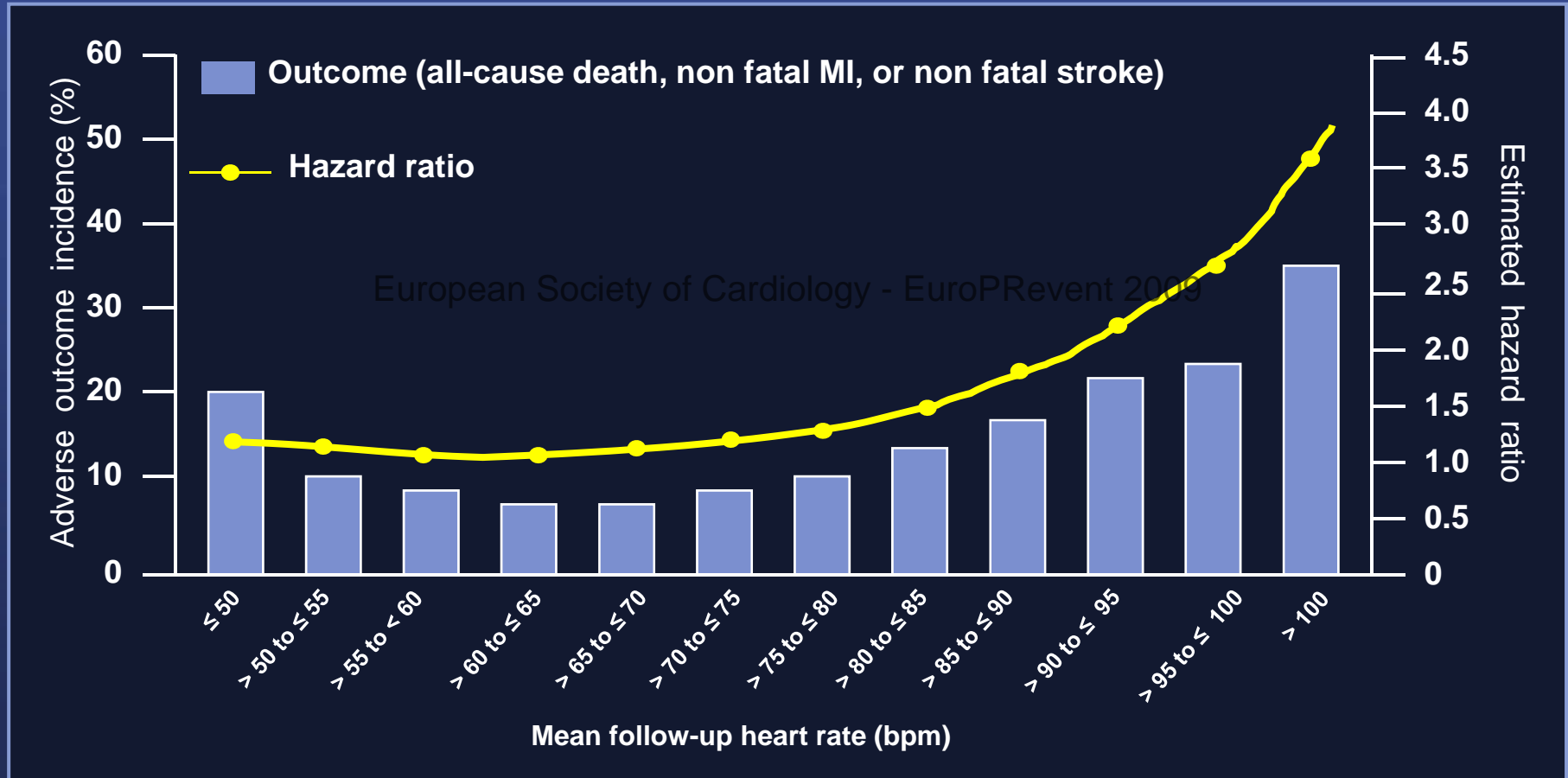
Subgroup analysis of total mortality



European Society of Cardiology, EuroPRevent (2009)

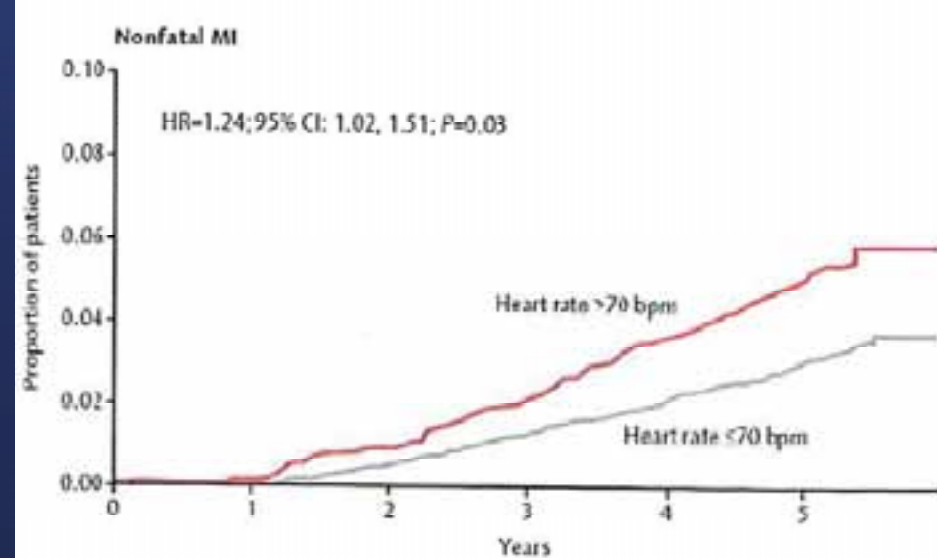
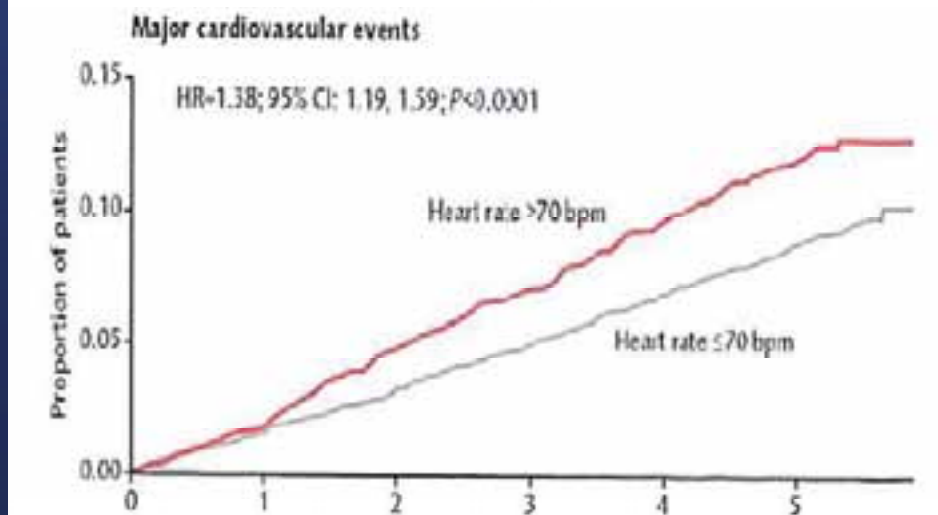
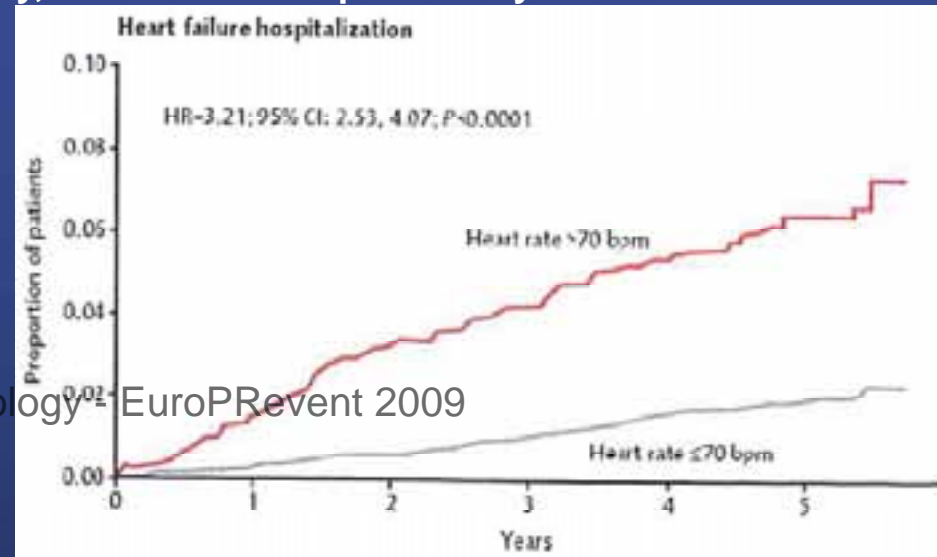
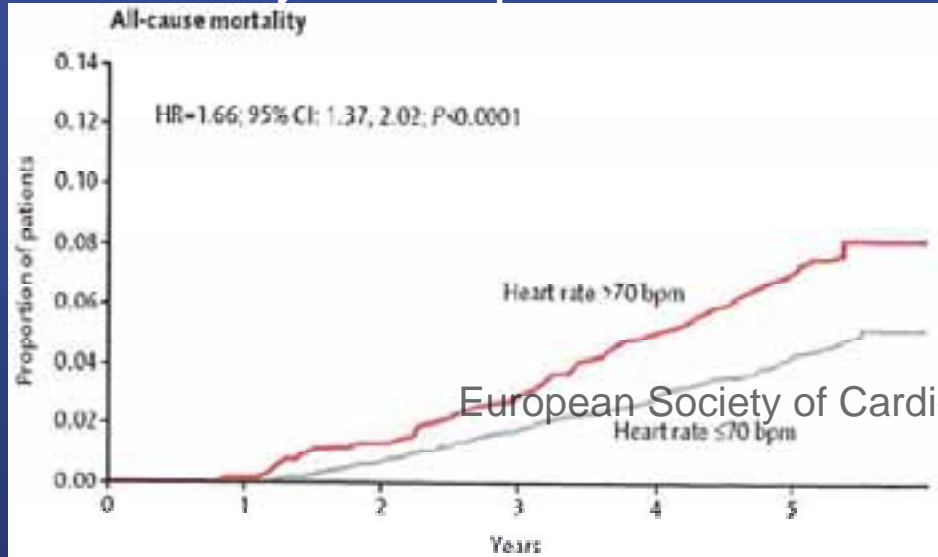
...and CV events are directly related to resting HR in patients with CAD and hypertension

INVEST study, 22 192 CAD patients; 2.7-year follow-up



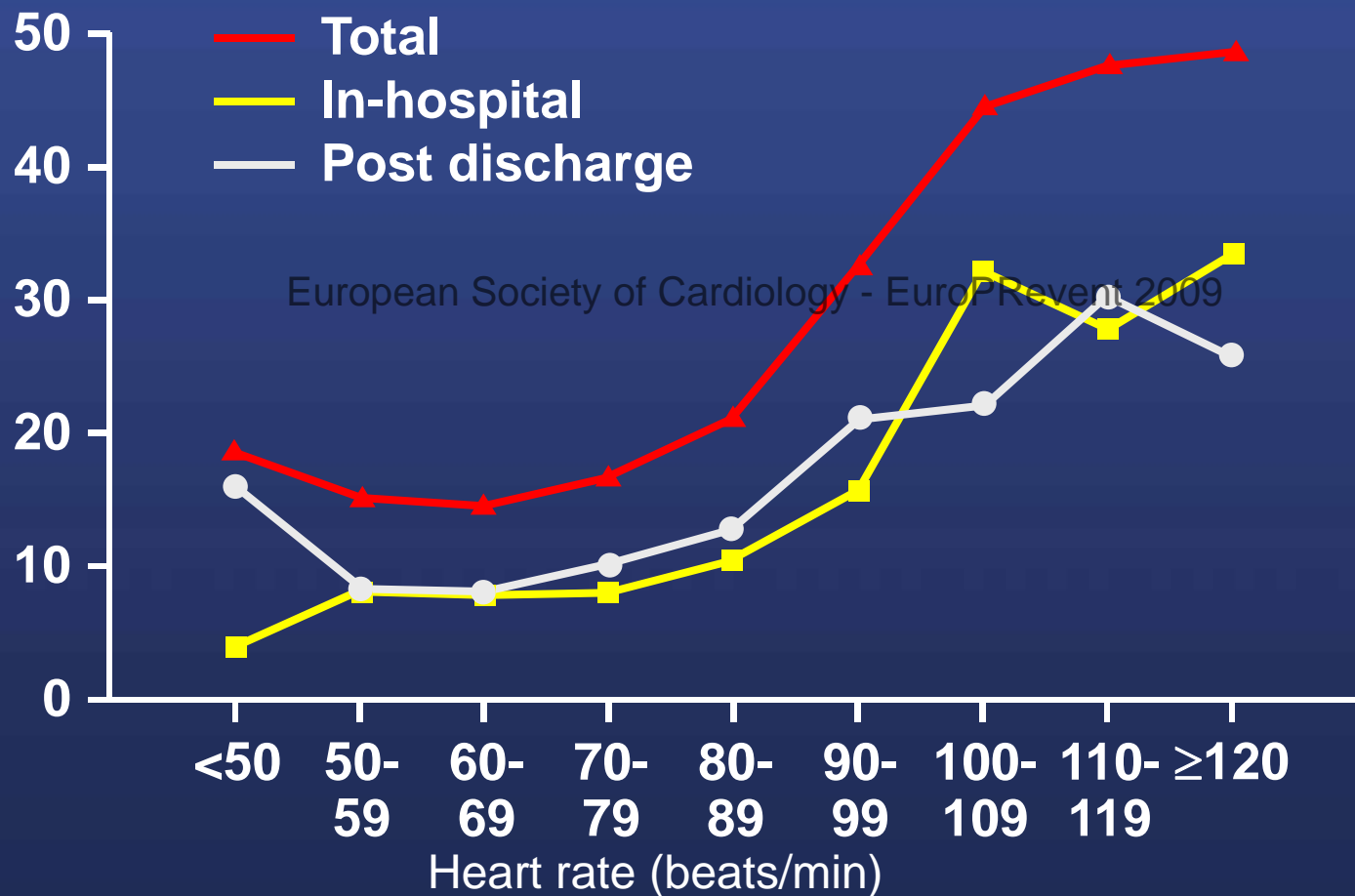
Resting heart rate as a predictor of prognosis in patients with stable CAD

Post hoc analysis in 9580 patients from the TNT study, median follow-up was 4.9 years



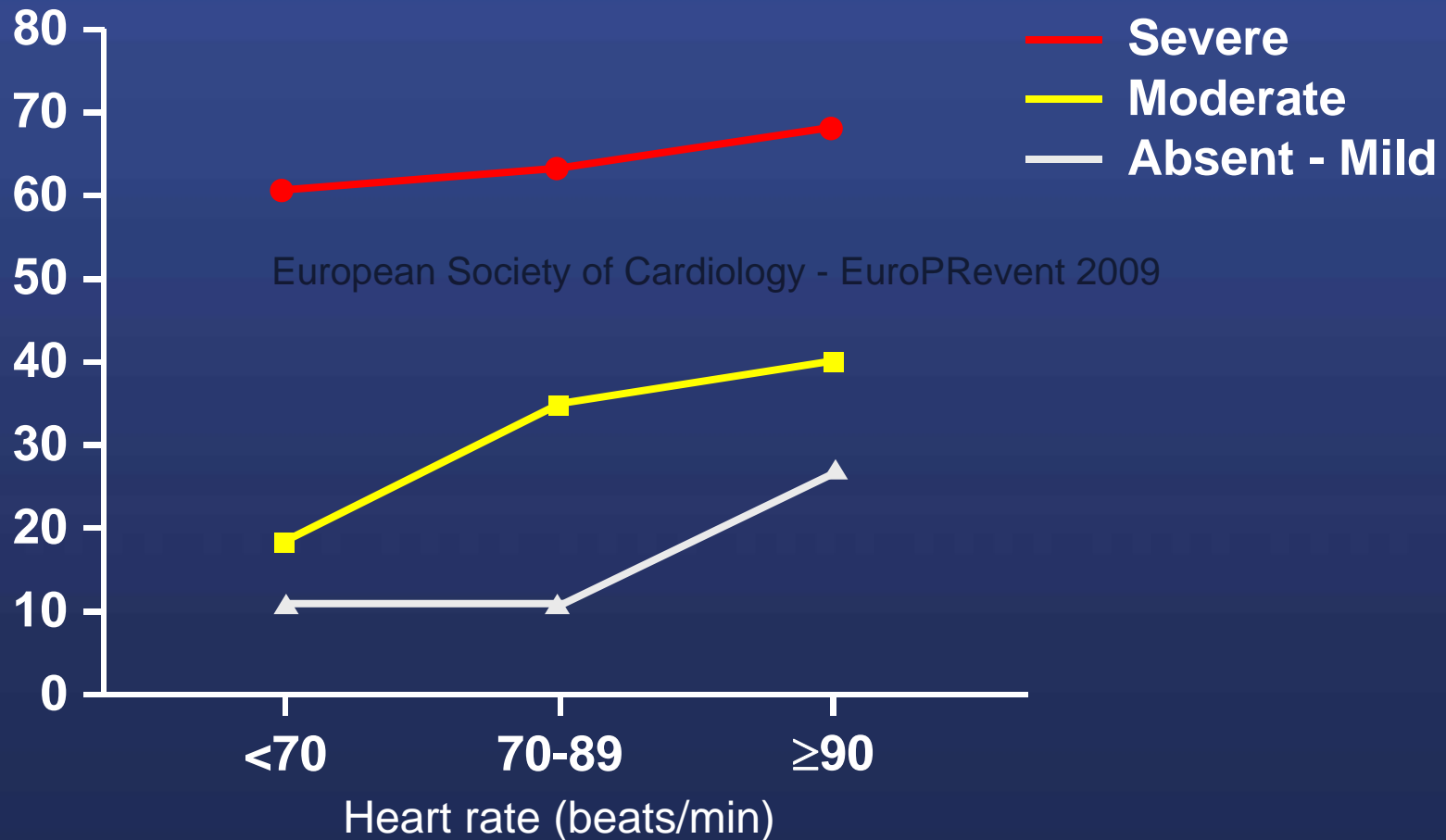
Mortality With different heart rate on hospital admission for AMI (n=1807)

Mortality %

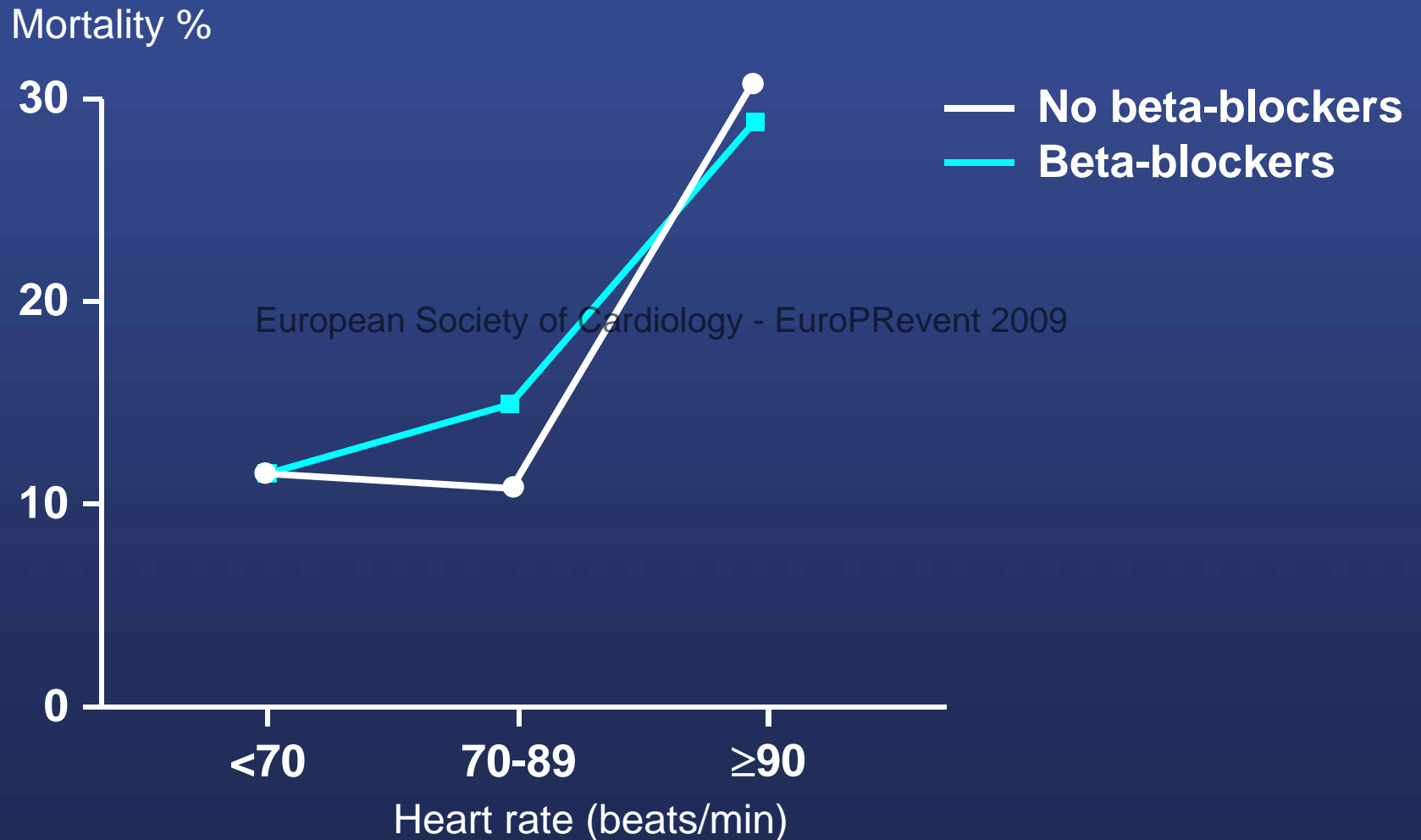


Total mortality from day 2 to 1 year related to admission HR in patients with or without HF (n=1807)

Mortality %

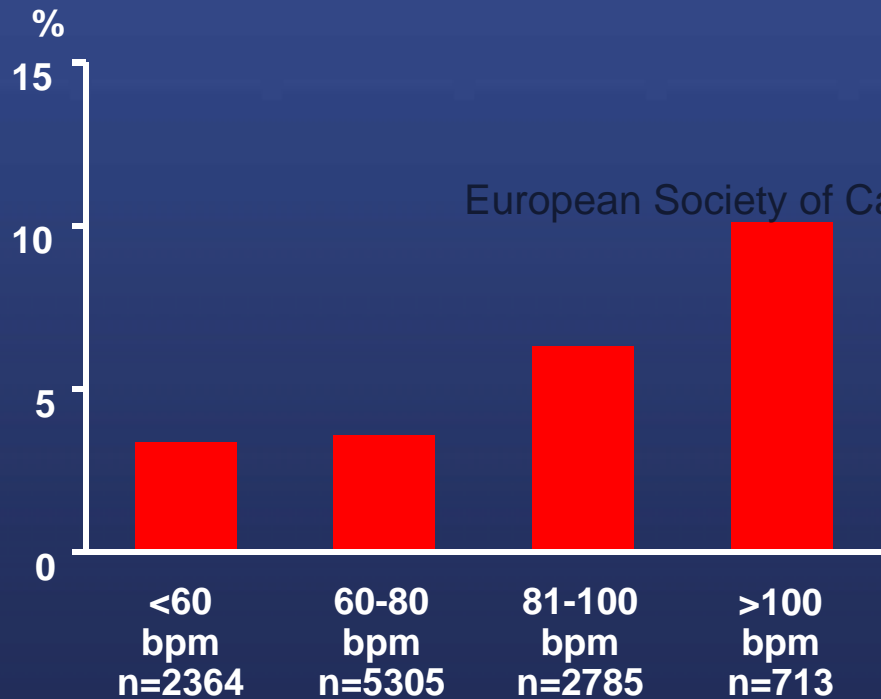


Total Mortality From Day 2 to 1 Year for Patients With Absent to Mild Heart Failure (n=1355)

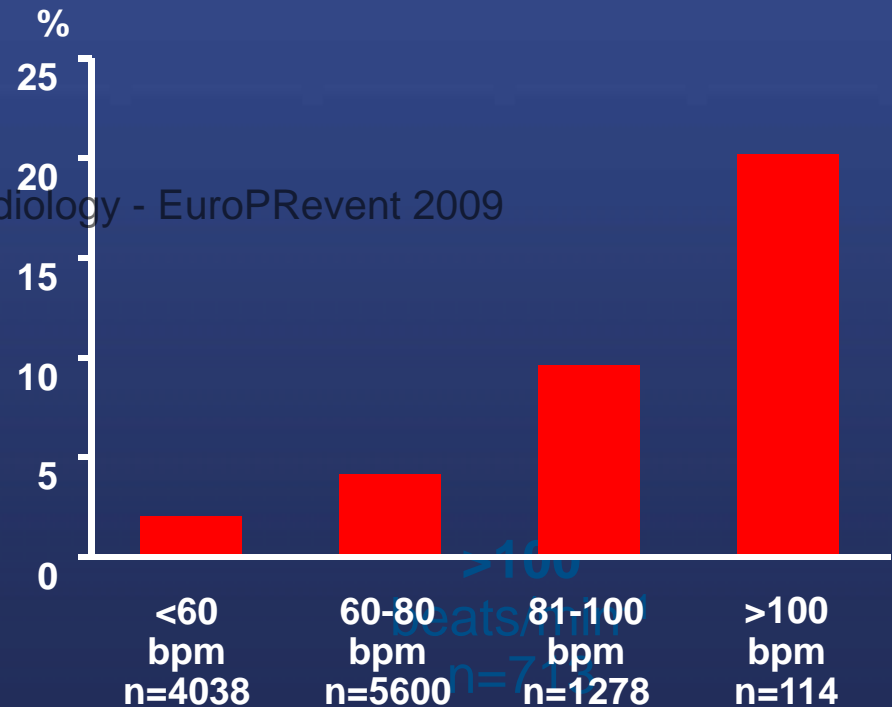


Heart rate and mortality in the GISSI-3 Study

HR at admission and in-hospital mortality
(n=11020 with AMI)



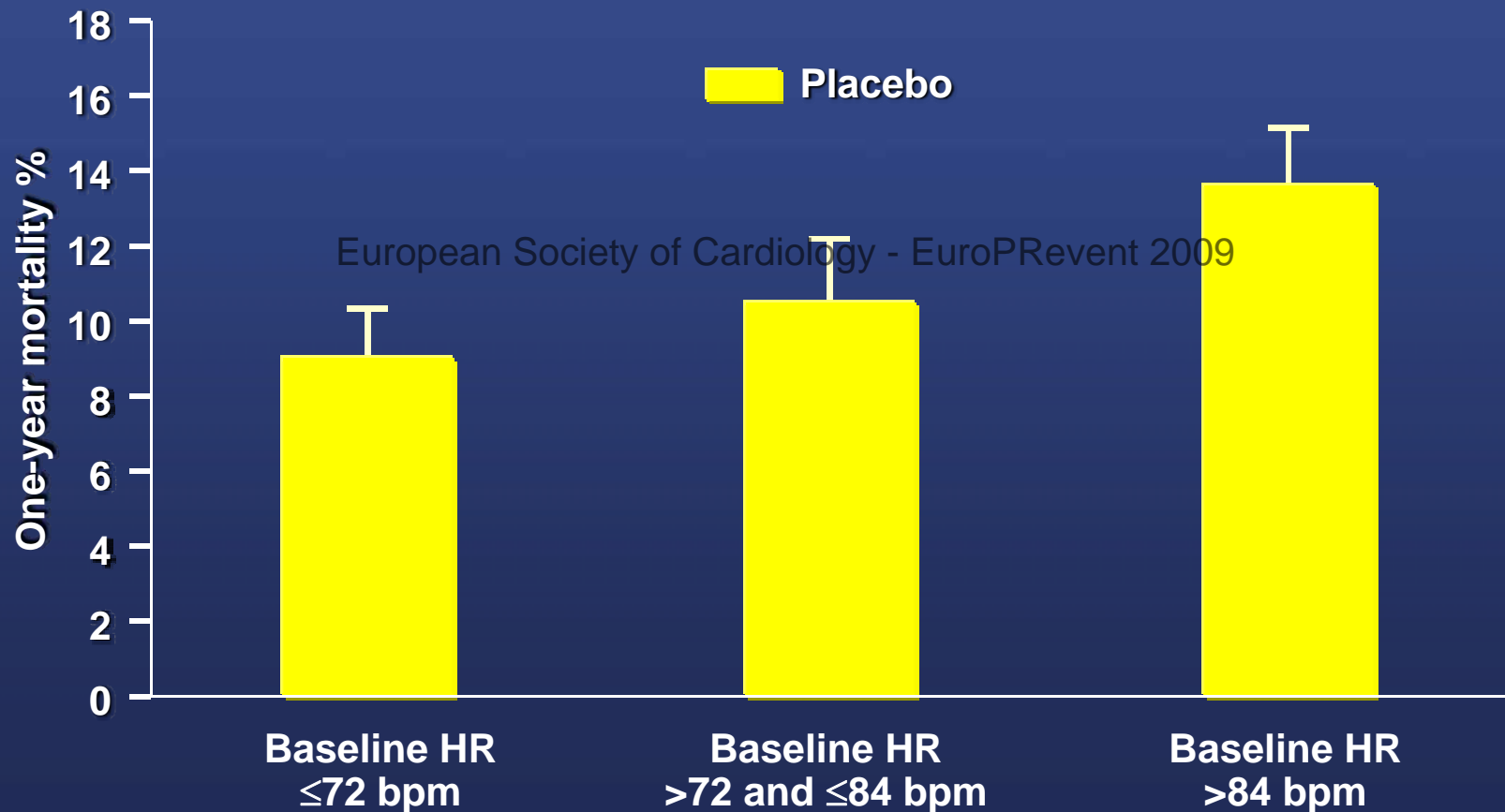
HR at discharge and 6-month mortality
(n=11020 with AMI)



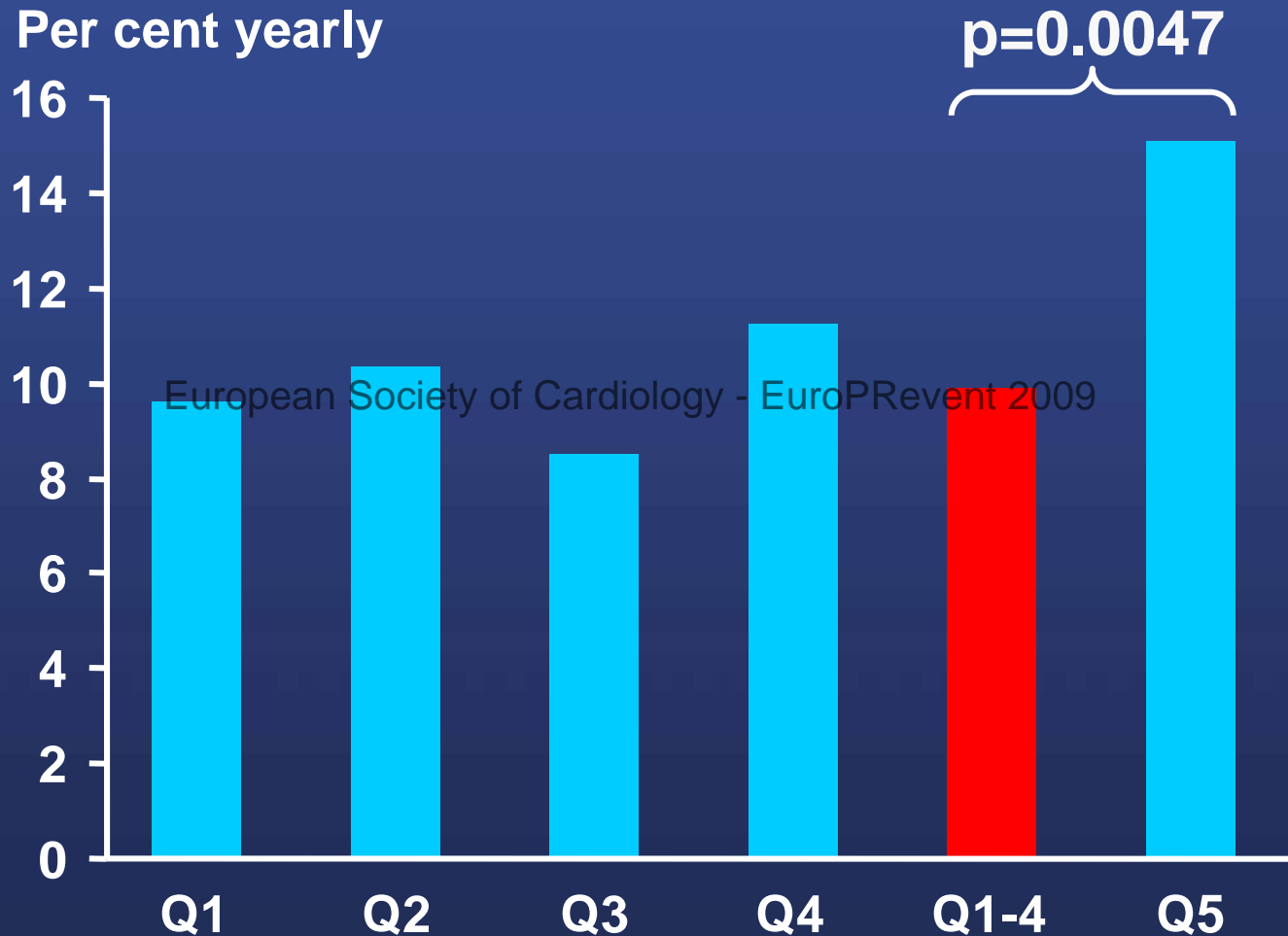
European Society of Cardiology - EuroPREvent 2009

One-year mortality according to baseline heart rate in the CIBIS-II Trial

n=1268 CHF patients

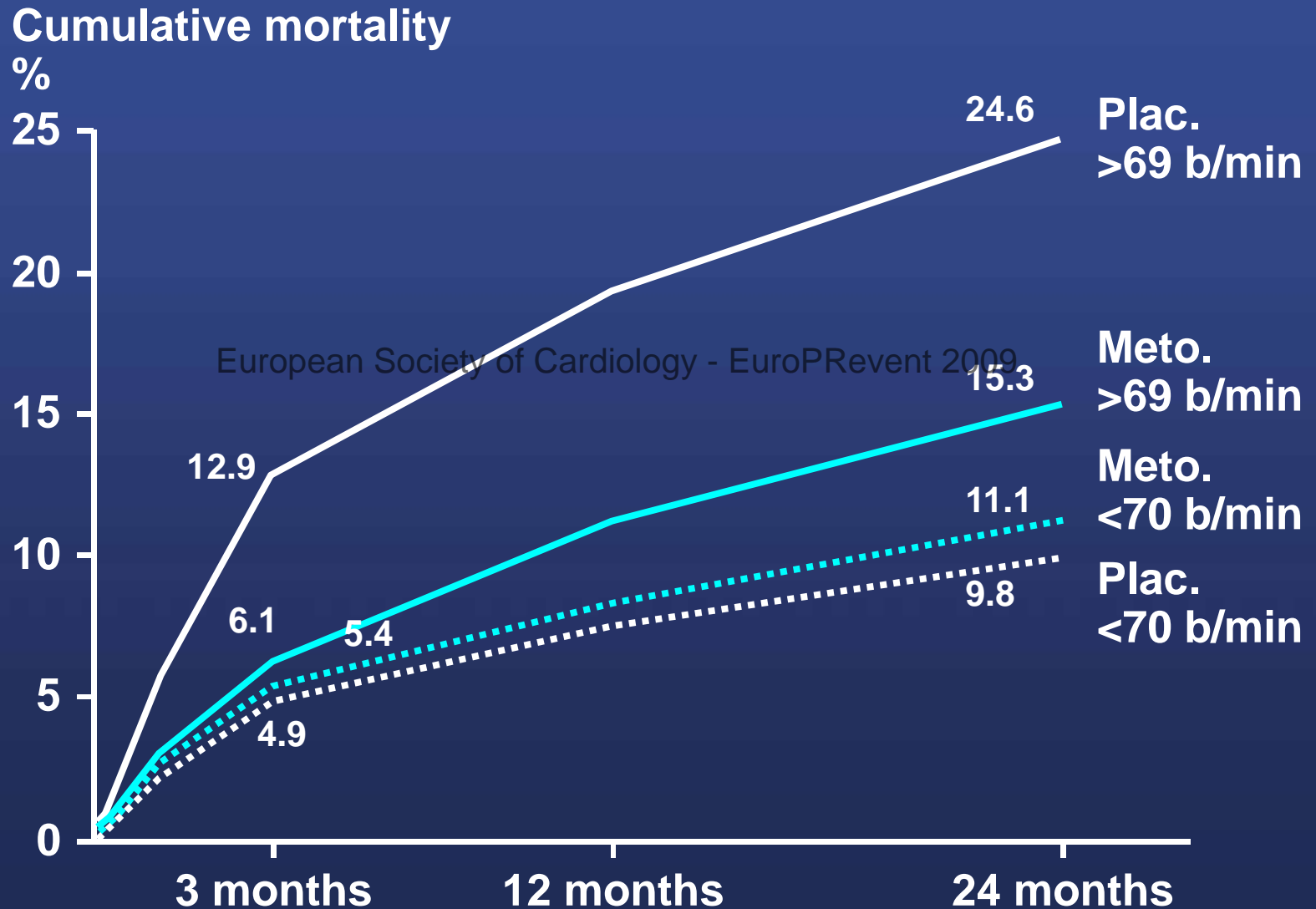


Total Mortality by Baseline HR in the MERIT-HF Trial Placebo Group (n=2001)



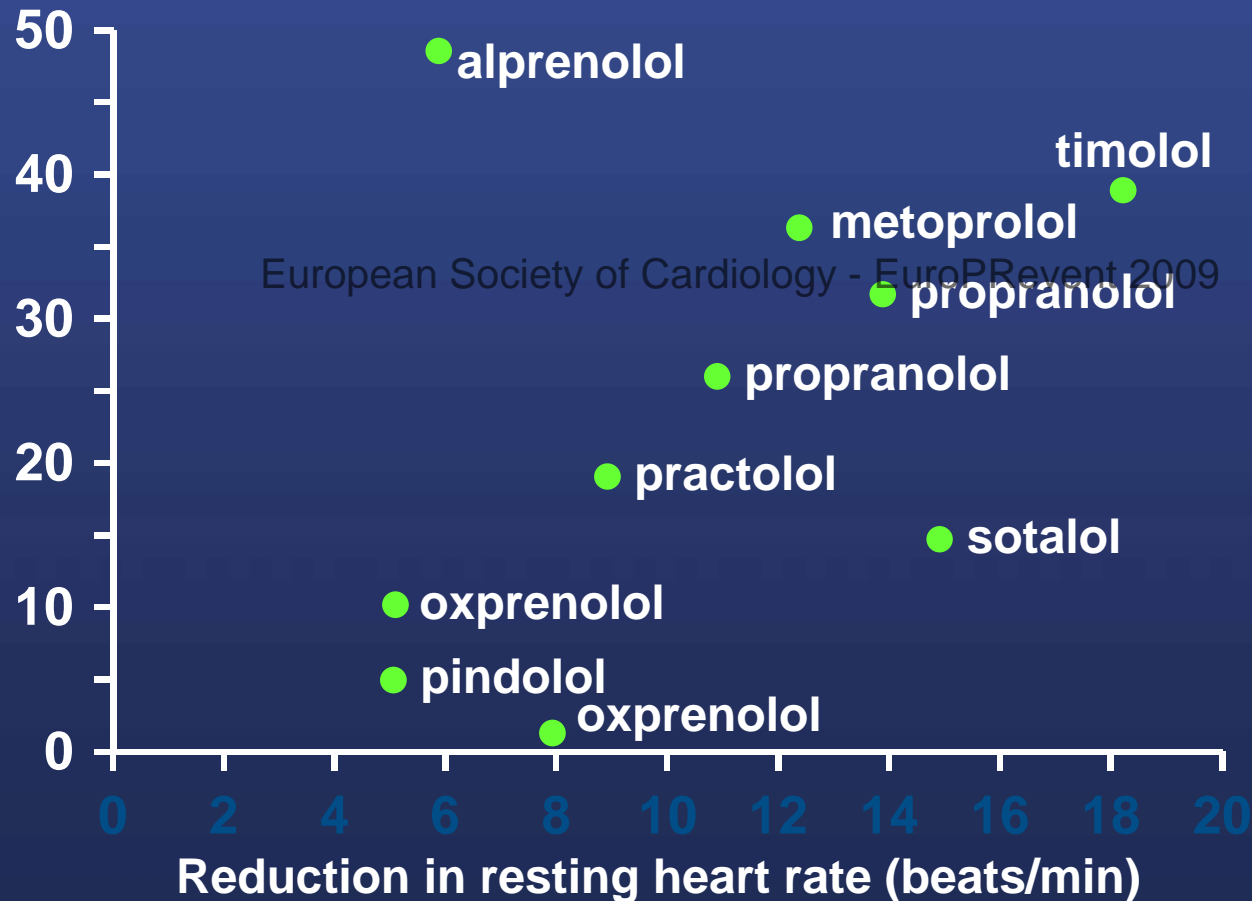
Göteborg Metoprolol Trial in AMI

Mortality Related to Admission Heart Rate (n=1395)

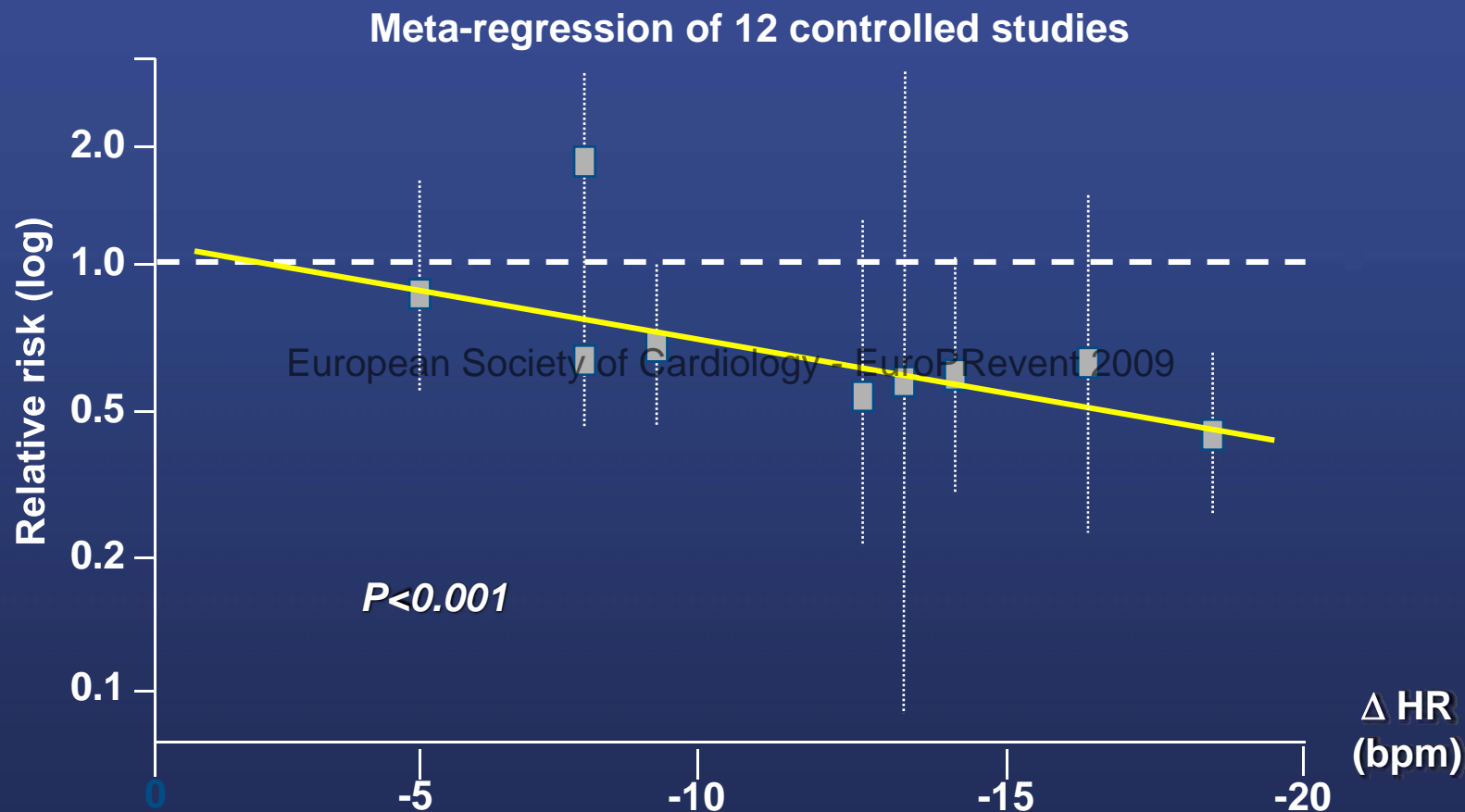


Relationship Between Reduction of Resting Heart Rate and Reduction in Mortality From Beta-blocker Trials

Reduction in mortality %

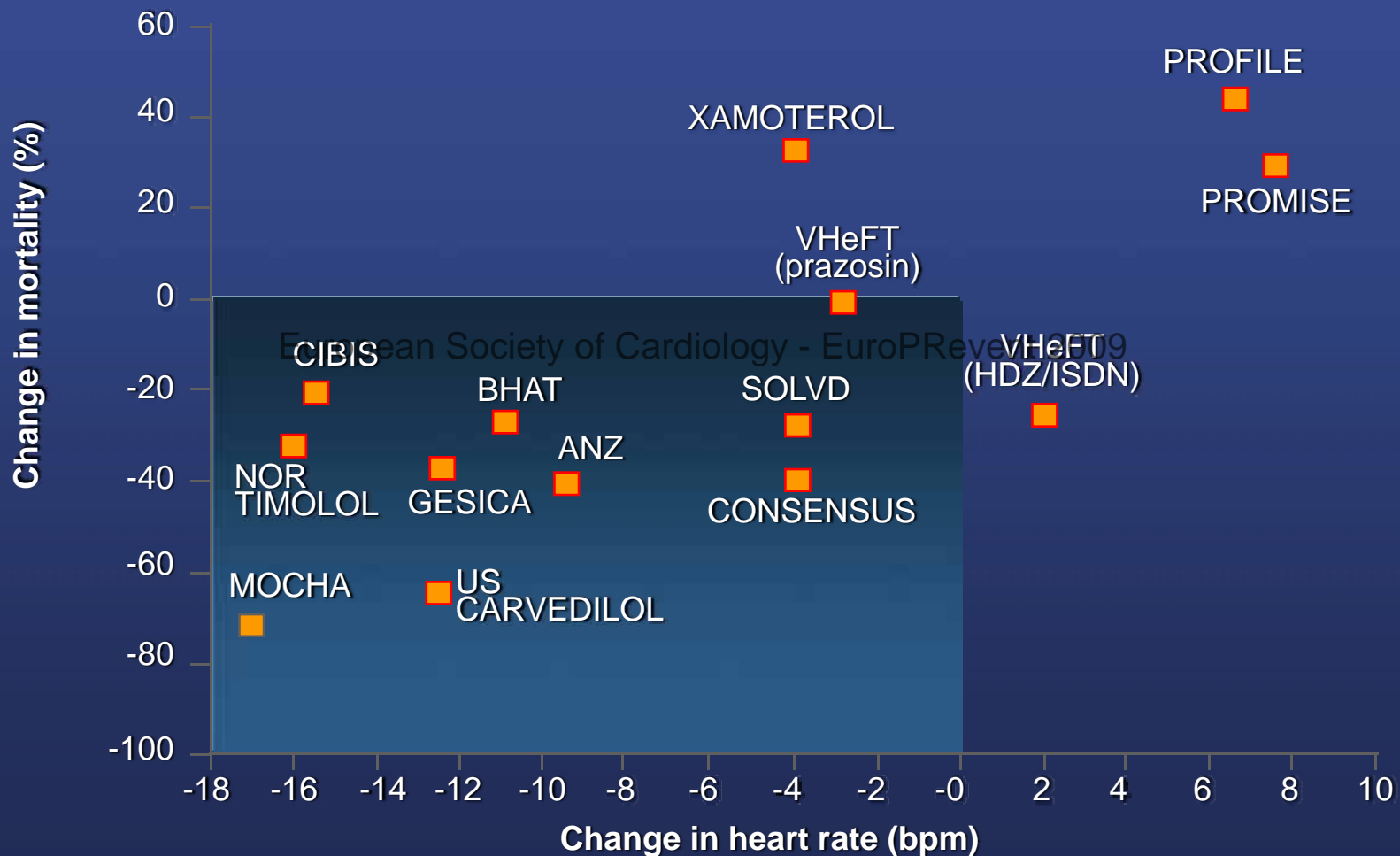


Heart rate lowering is associated with a reduction in cardiac deaths in post-myocardial infarction patients



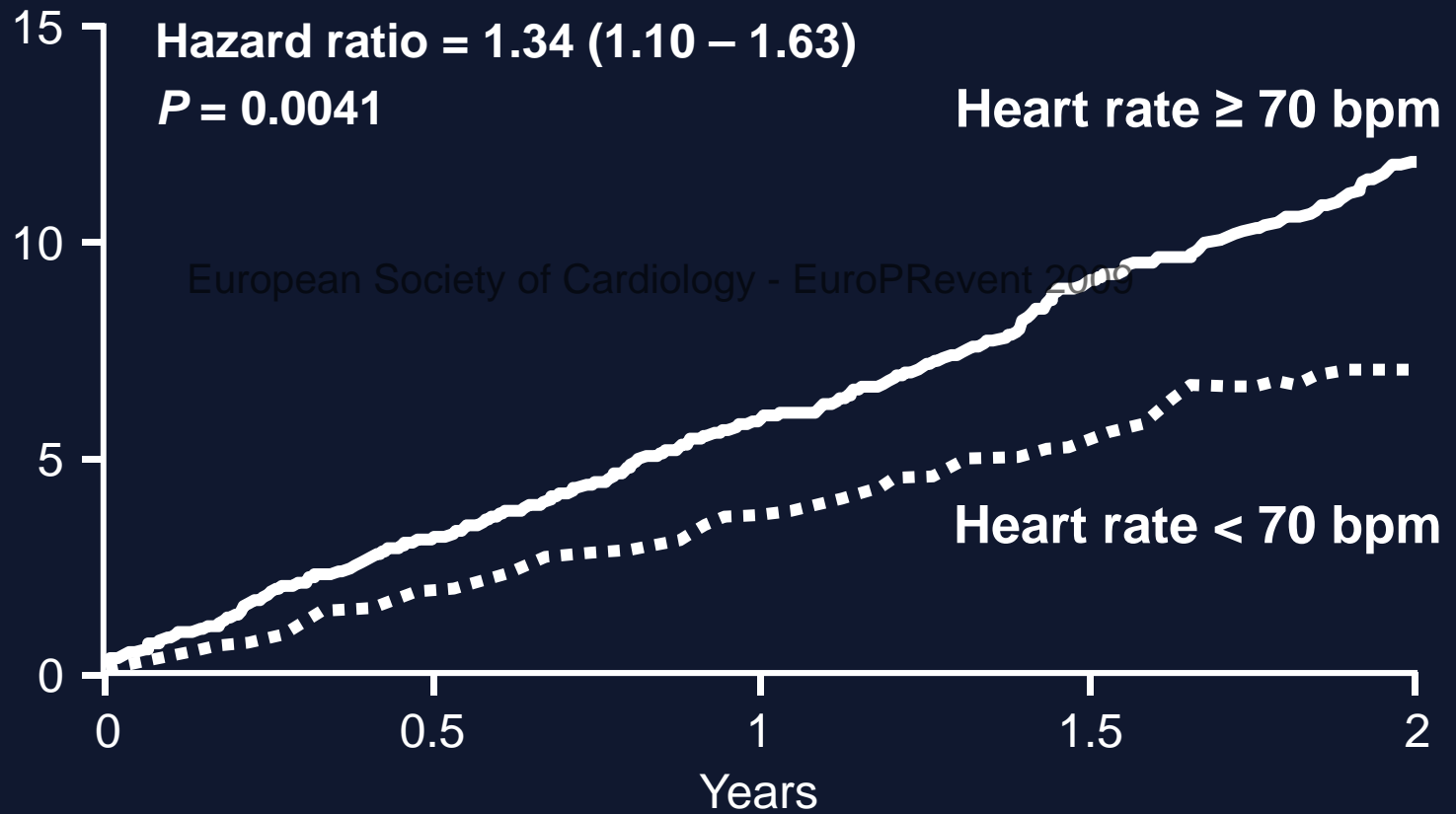
Each 10 bpm HR reduction = 26% cardiac death reduction

Relationship between changes in heart rate and mortality in CHF



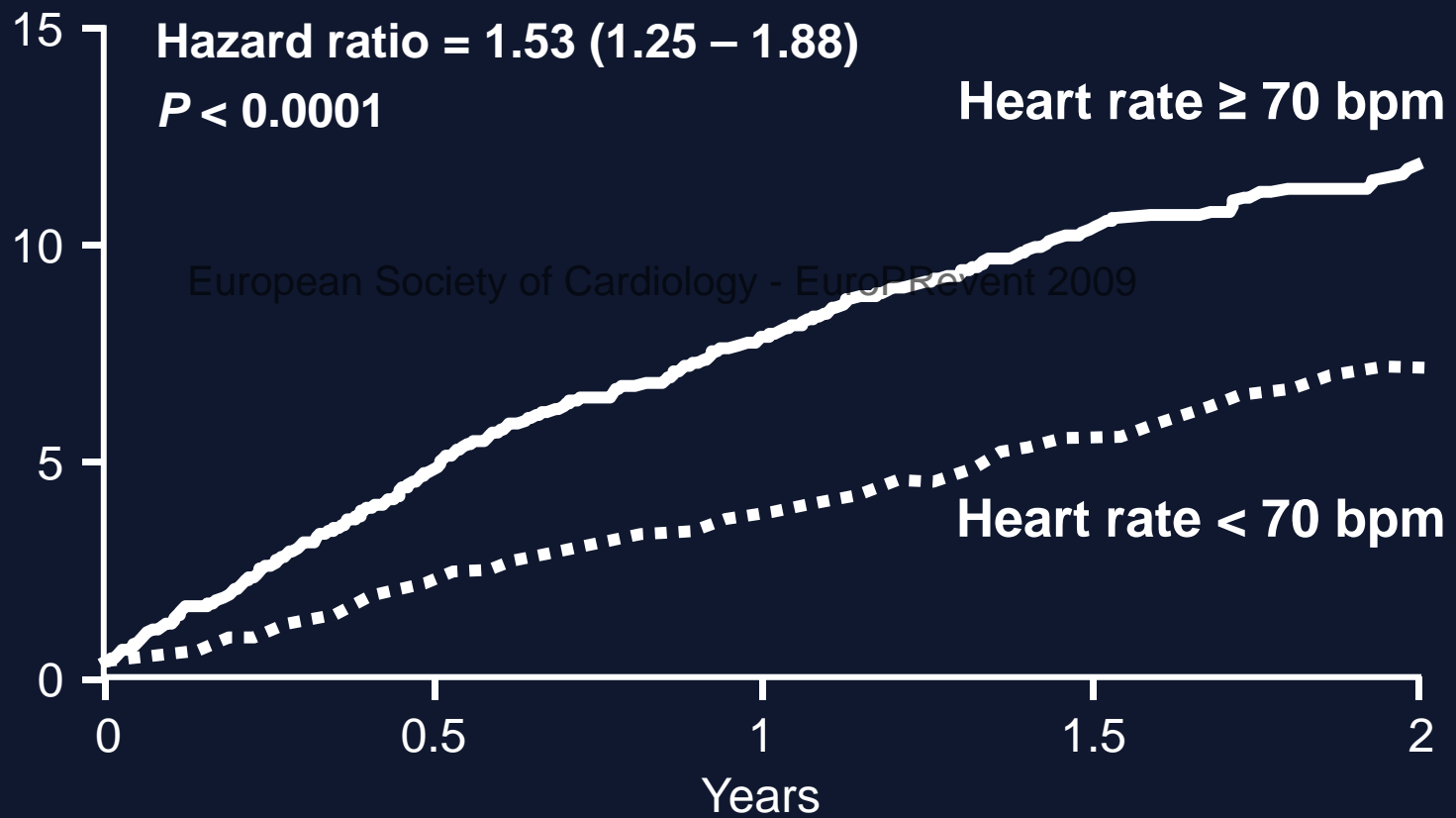
Heart rate a predictor of CV death on placebo (n=5.438)

% with cardiovascular death



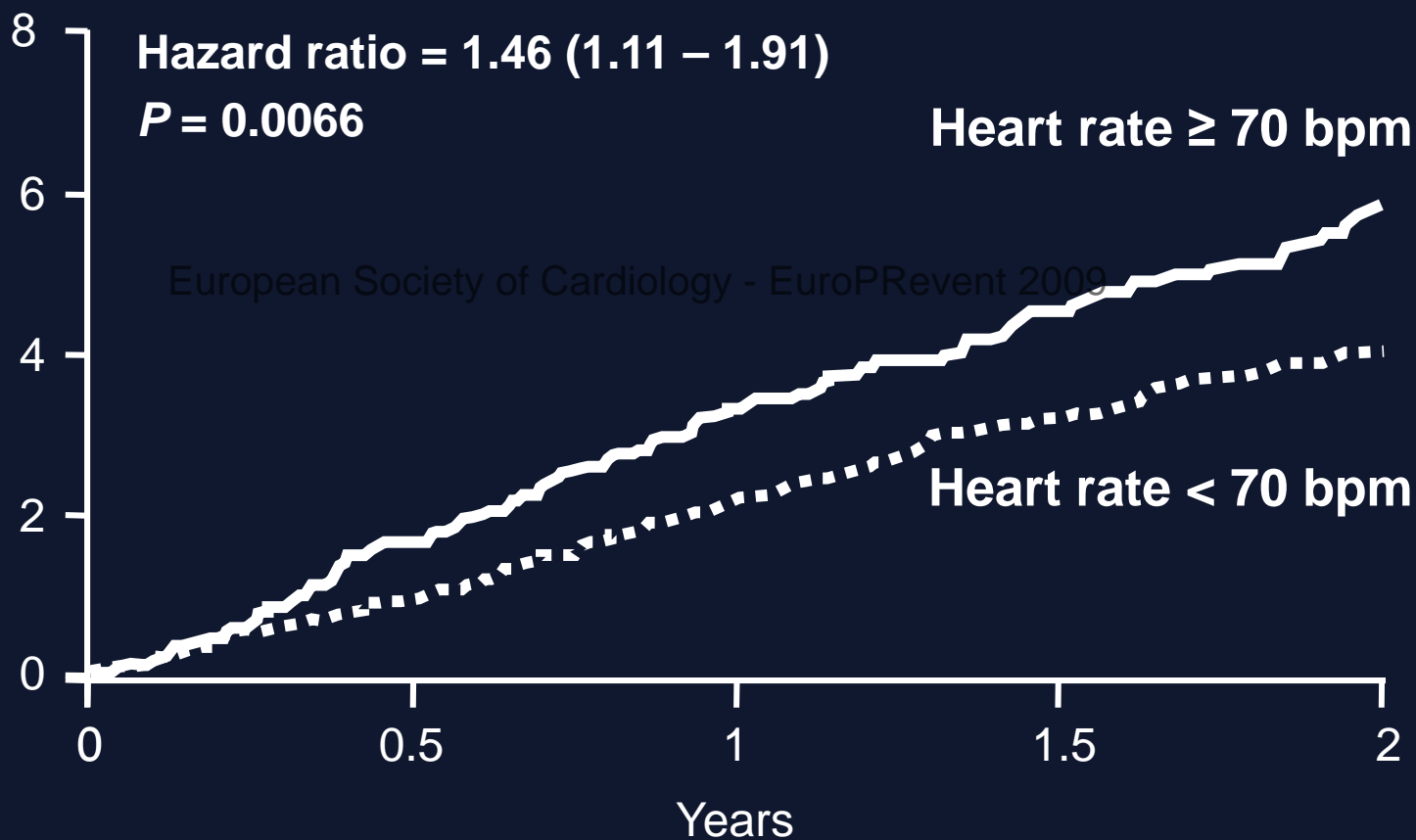
Heart rate a predictor of hospitalization for heart failure on placebo (n=5.438)

% with hospitalization for heart failure



BEAUTIFUL Heart rate a predictor of hospitalization for MI on placebo (n=5.438)

% with hospitalization for fatal and nonfatal MI



Lessons from BEAUTIFUL trial in stable coronary artery disease

- 10,917 patients randomized to ivabradine or placebo on top of optimal treatment (87% on betablockers)
- Heart rate > 70 bpm was related to higher morbidity and mortality as assumed European Society of Cardiology - EuroPRevent 2009
- Reduction of heart rate by 9 bpm (at 6 months) in these patients reduced significantly new coronary events by about 30%
- Ivabradine was well tolerated
- These effects are clinically relevant and ought to be part of clinical practice

Heart rate as a cardiovascular risk factor

- Heart rate is directly associated with total and/or CV mortality
- This association is present in different clinical setting
- The relationship is strong, graded, independent, and present at all ages and in both genders
- Direct relation of heart rate to development and progression of atherosclerosis is documented in experimental and clinical studies
- Heart rate reduction improves cardiovascular prognosis

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Heart rate is a risk factor, not merely a risk marker, and should be used to guide optimal medical therapy