

Randomized Evidence on Rosuvastatin for Primary Prevention in Individuals 70 Years of Age or Older: The JUPITER Trial

Discussant

Ph. Gabriel Steg

INSERM U-698 and Centre Hospitalier Bichat-Claude Bernard

Université Paris 7

AP-HP, Paris, France

Disclosures

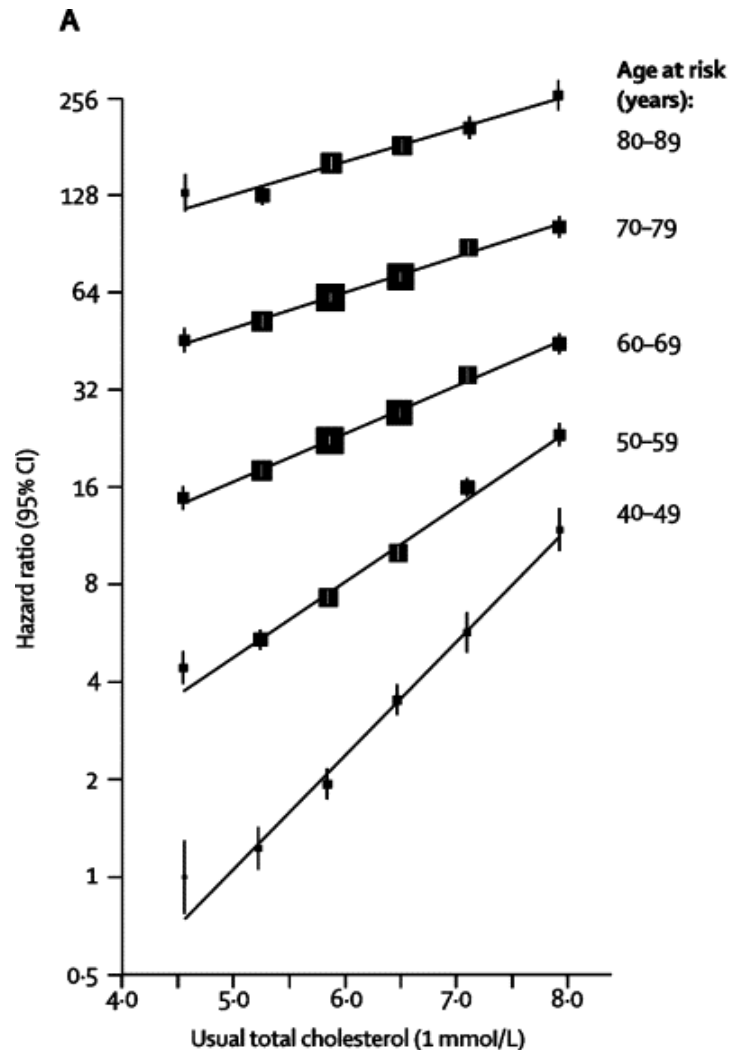
- **Research Grant:** sanofi-aventis
- **Speakers bureau:** Boehringer-Ingelheim, BMS, GSK, Medtronic, sanofi-aventis, Servier, The Medicines Company
- **Consulting/advisory board:** Astellas, AstraZeneca, Bayer, Boehringer-Ingelheim, BMS, Daiichi-Sankyo, GSK, MSD, sanofi-aventis, Servier, Takeda, The Medicines Company
- **Stockholding:** Aterovax

Statins in the elderly

Relative Risk Reduction vs Absolute Risk

Cholesterol as a risk factor for CV death as a function of age

IHD mortality (33 744 deaths) versus usual total cholesterol



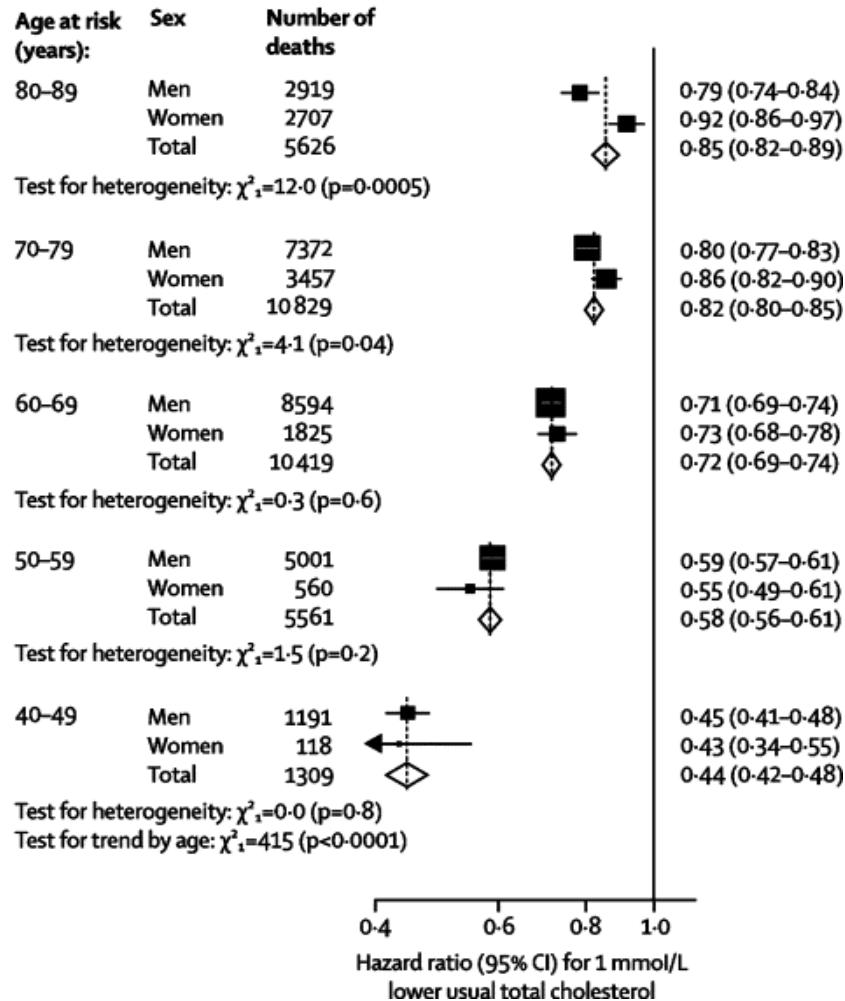
Age-specific associations

Impact of reducing cholesterol on risk of CV death

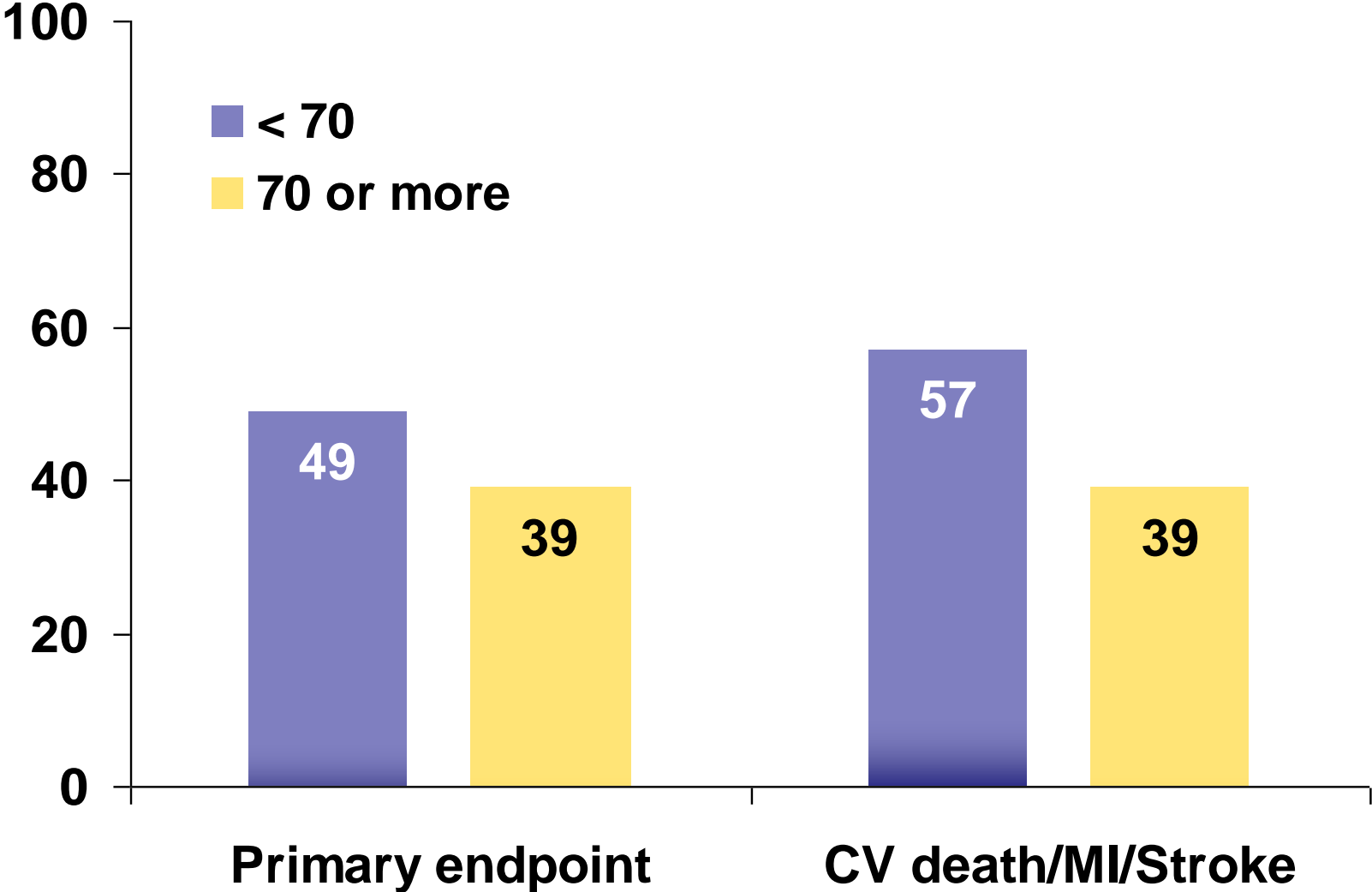
IHD mortality (33 744 deaths) versus usual total cholesterol

Age and sex-specific HRs for 1 mmol/L lower total cholesterol

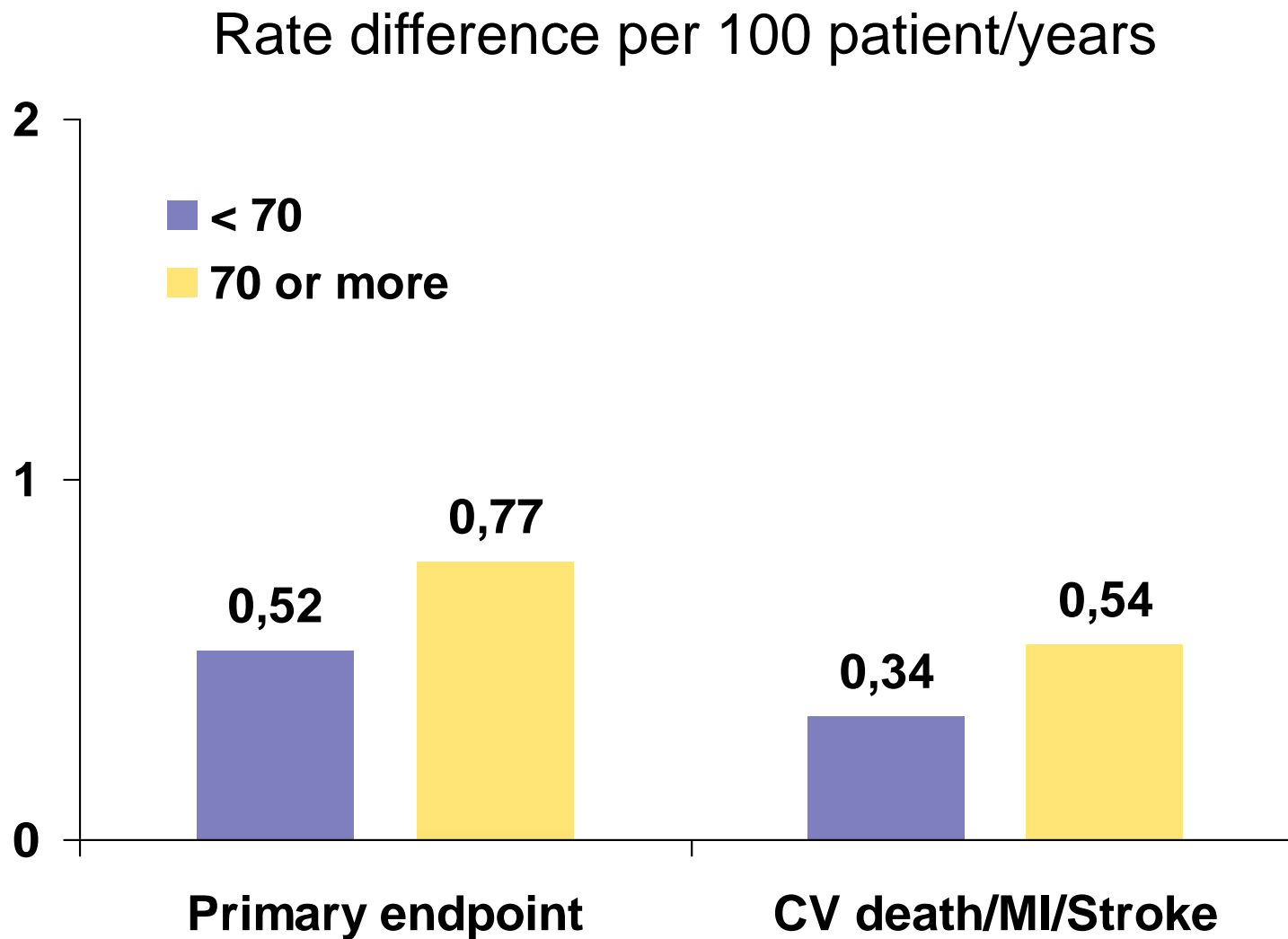
B



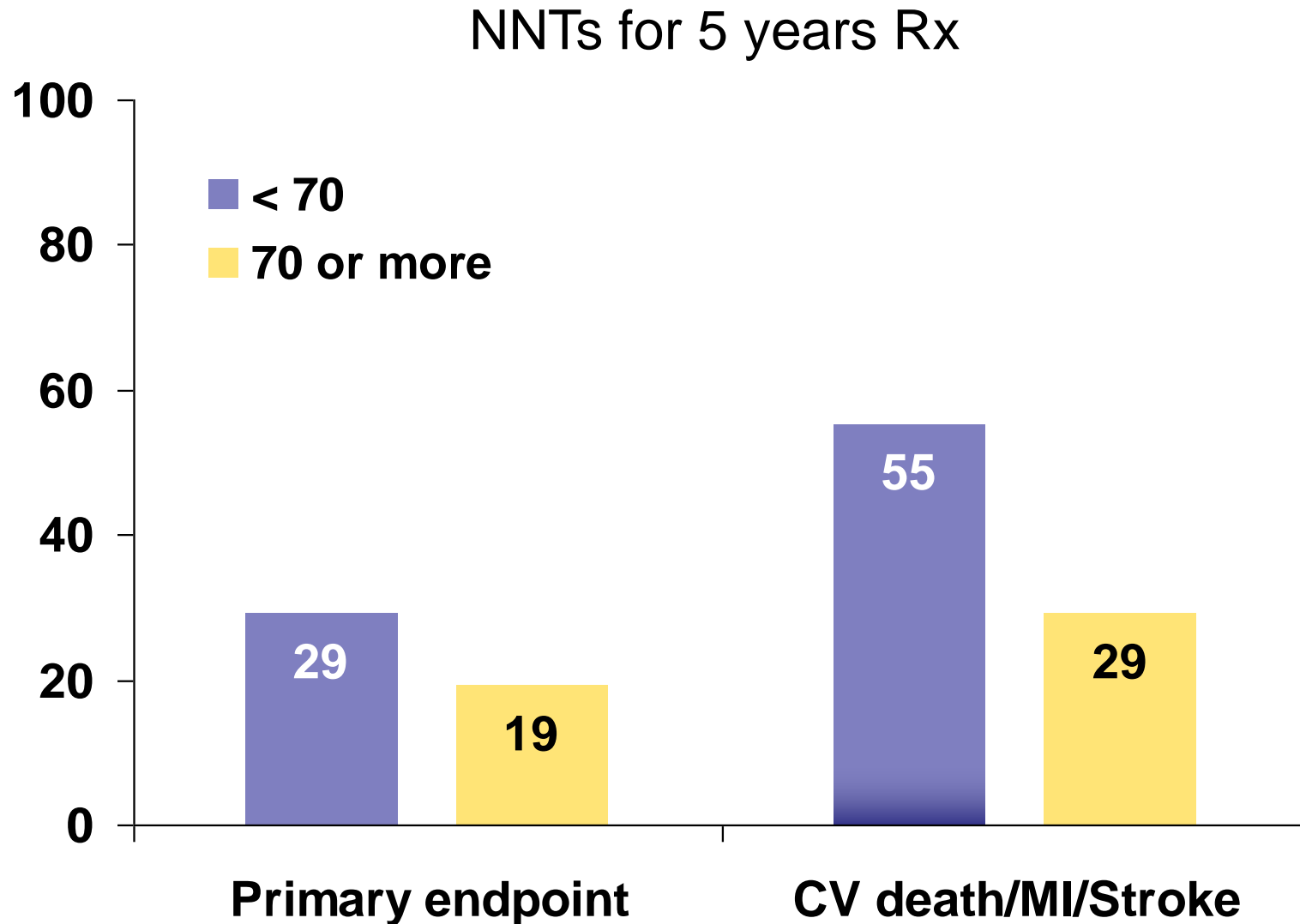
The RRR from rosuvastatin in JUPITER was smaller in older vs younger patients



The Absolute Risk reduction in JUPITER was *greater* in older vs younger patients



The NNT in JUPITER was smaller in older vs younger patients



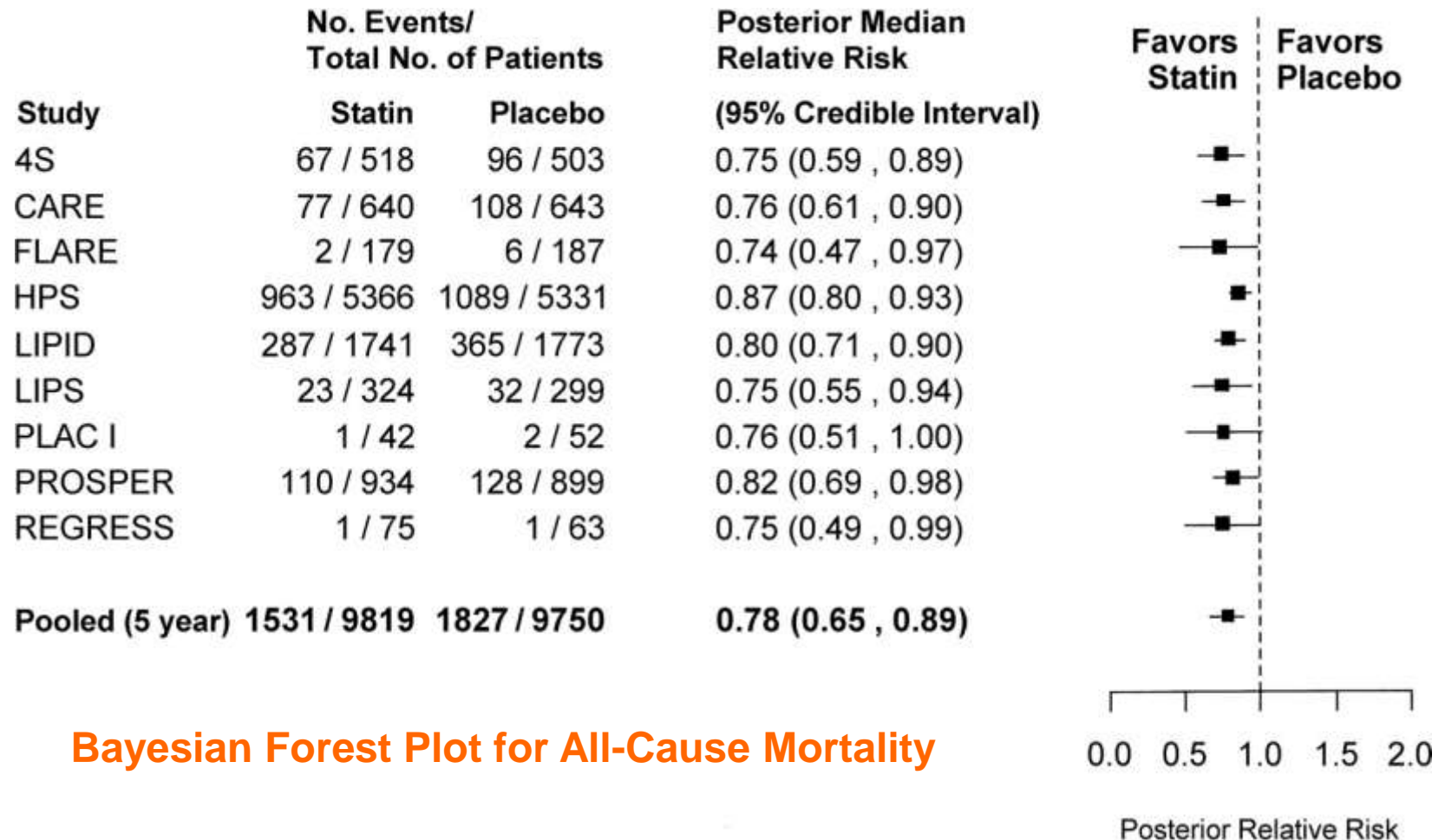
Primary endpoint: Nonfatal MI, nonfatal stroke, revascularization, unstable angina, CV death

Statins in the Elderly

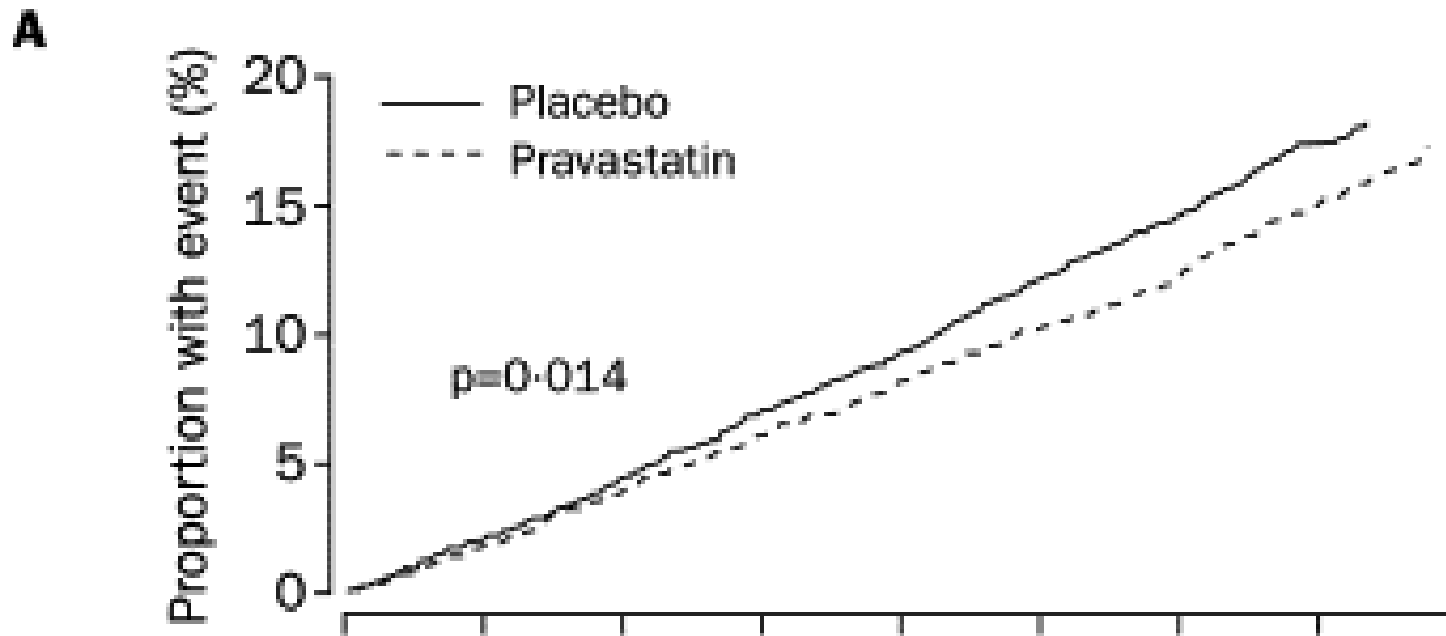
- Statins are underused for secondary prevention in elderly patients
- Evidence for using statins in primary prevention in the elderly is limited

Statins reduce mortality in the elderly in secondary prevention

Nine trials with a total of 19 569 patients aged 65–82 years



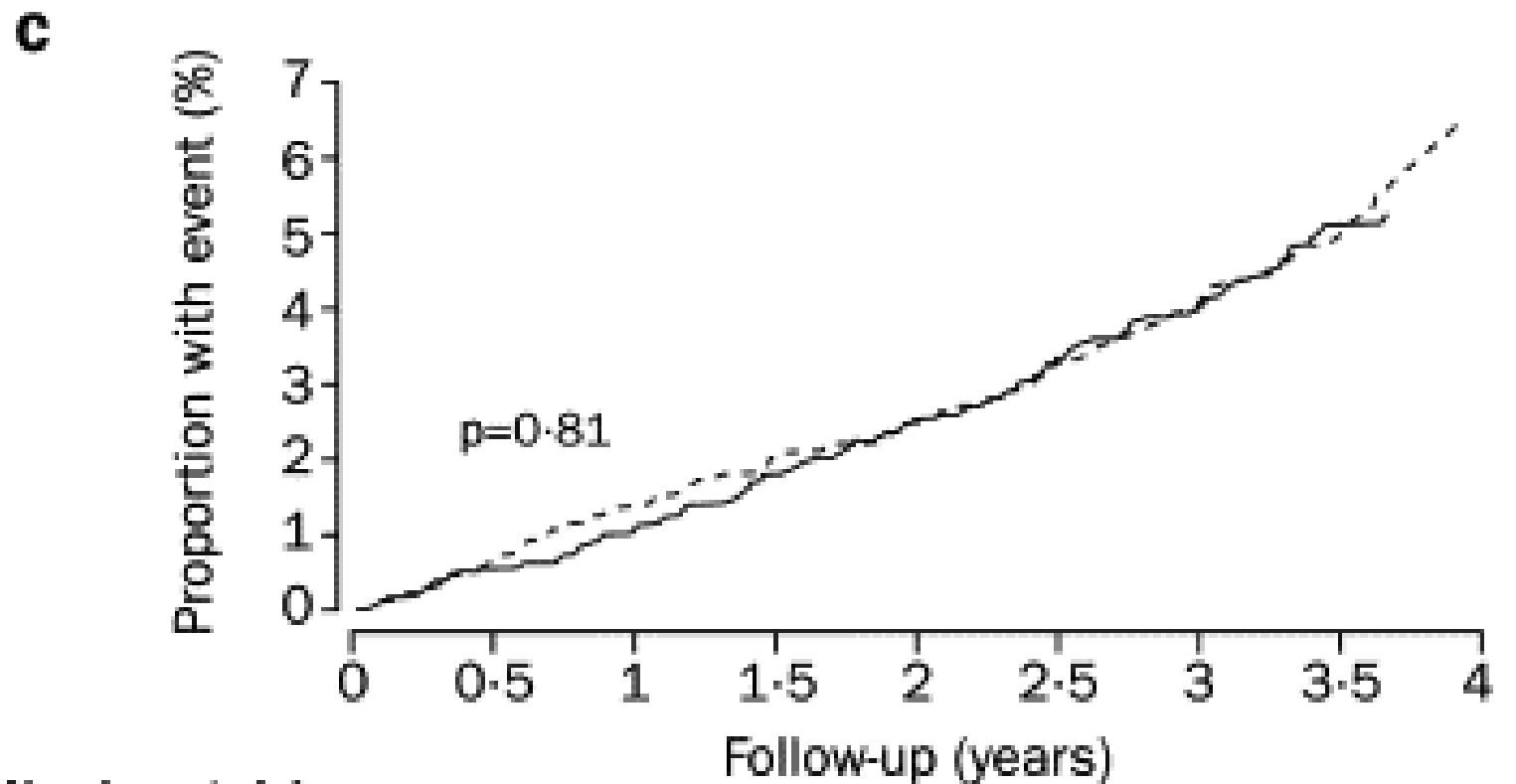
PROSPER: Pravastatin in the elderly : reduction of the composite of CV death/MI/Stroke



Number at risk

Placebo	2913	2832	2748	2651	2560	2458	2128	730	44
Pravastatin	2891	2812	2738	2655	2562	2483	2167	770	40

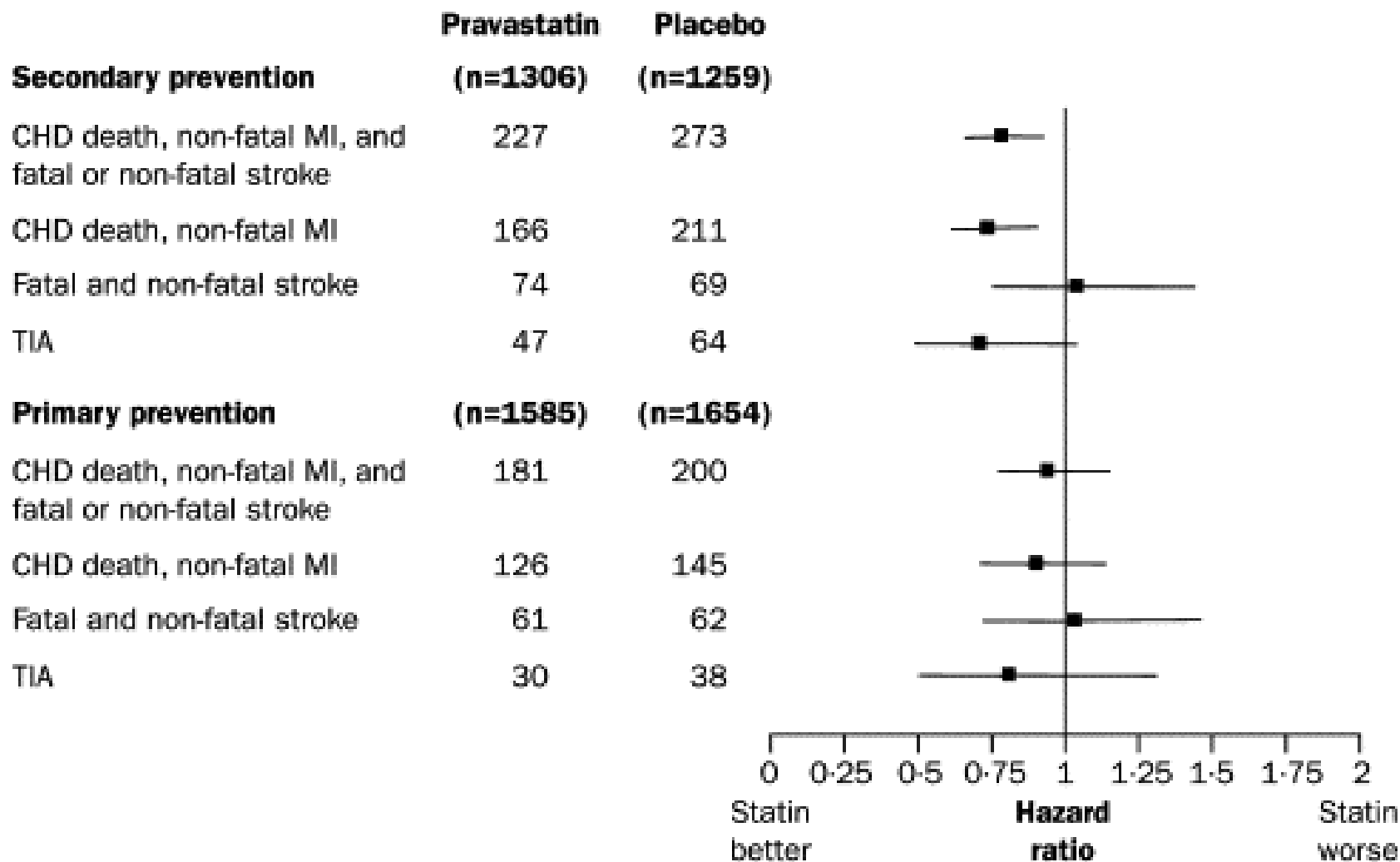
PROSPER: Pravastatin in the elderly : no effect on Stroke



Number at risk

Placebo	2913	2871	2812	2744	2685	2621	2291	796	48
Pravastatin	2891	2848	2795	2730	2673	2618	2295	822	45

Effect of pravastatin in the elderly as a function of clinical setting in PROSPER



What this study adds

- Solid evidence that the benefit seen from rosuvastatin in the overall trial is seen in the elderly subgroup, including a reduction in stroke
- Evidence that while the RR may be smaller than among younger pts, the absolute benefit is actually *higher* among elderly
- No evidence for a major increase in side effects with age
- Therefore, strong evidence for not depriving elderly patients of the benefits of statins

Caveats

This study pertains to a special population : high-risk CV patients with low LDL and elevated hs-CRP

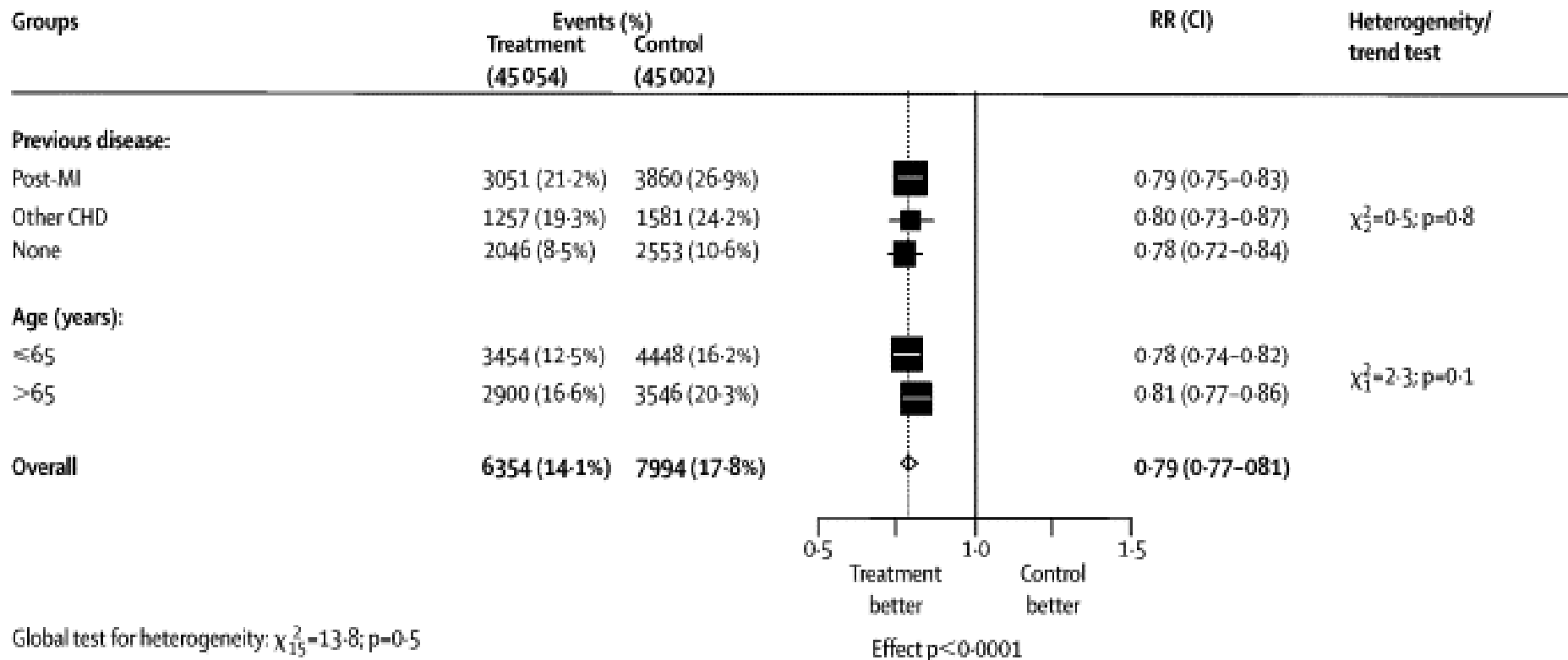
Can we extend the results to

- patients without elevated CRP ?
- very elderly patients (above 80 years) ?

* average age of the elderly in JUPITER was « only » 74. (IQR: 72-78)

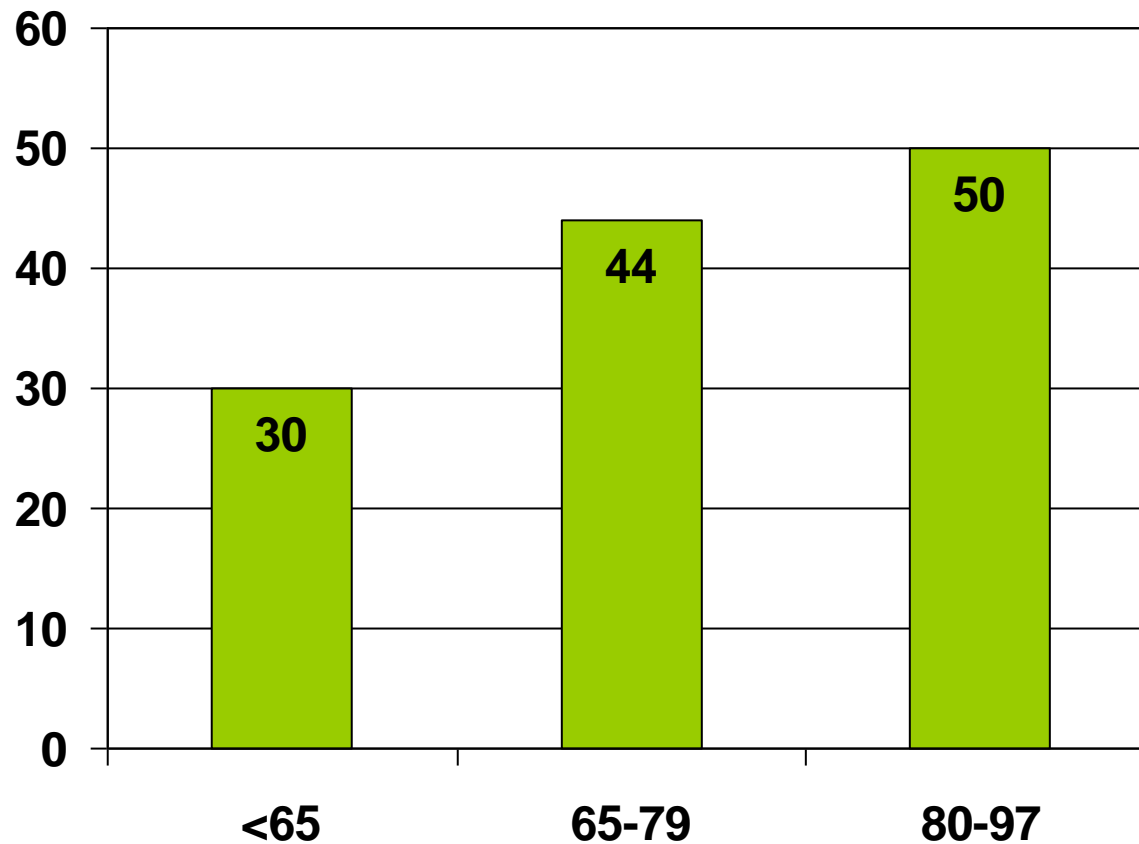
Thank you !

Reduction in coronary events with LDL lowering in the CTT collaboration analysis



The RRR of all-cause mortality from statins in secondary prevention trials was greater among older patients

Nine trials with a total of 19 569 patients aged 65–82 years

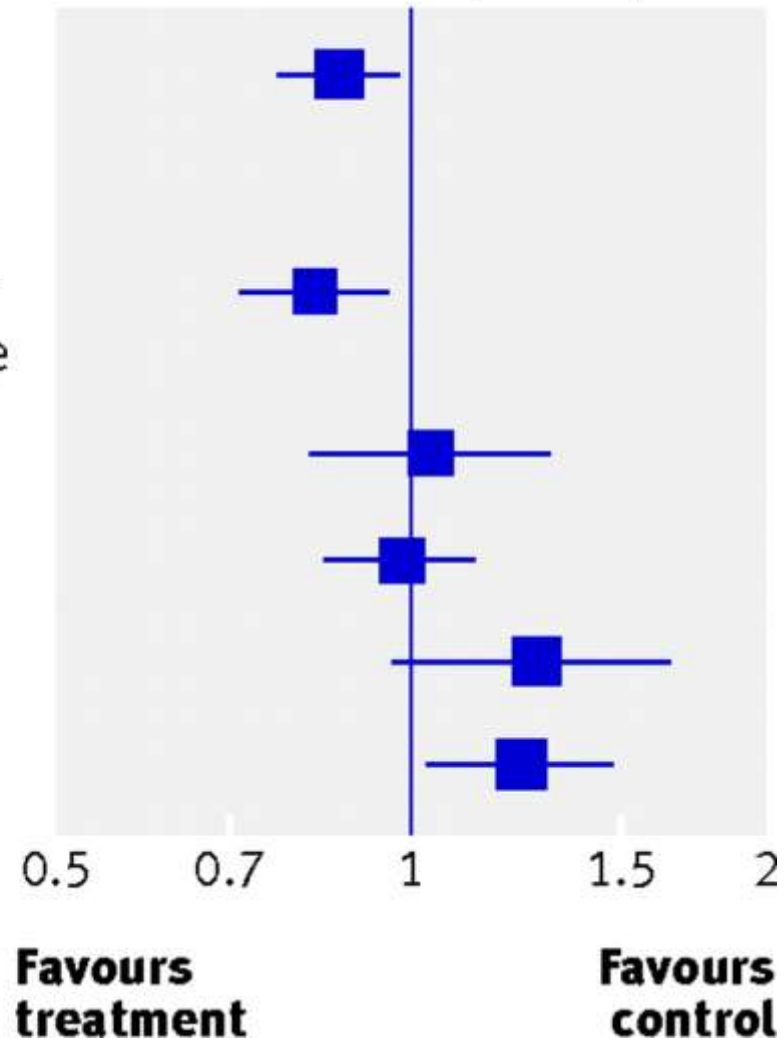


Cardiovascular outcomes, all cause mortality, and cancer outcomes in the PROSPER study

Outcome

- Non-fatal myocardial infarction, fatal/non-fatal stroke, or death from coronary heart disease
- Non-fatal myocardial infarction or death from coronary heart disease
- Fatal or non-fatal stroke
- All cause mortality
- Death from cancer
- New diagnosis of cancer

Hazard ratio (95% CI)



Mangin, D. et al. *BMJ* 2007;335:285-287

Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial.

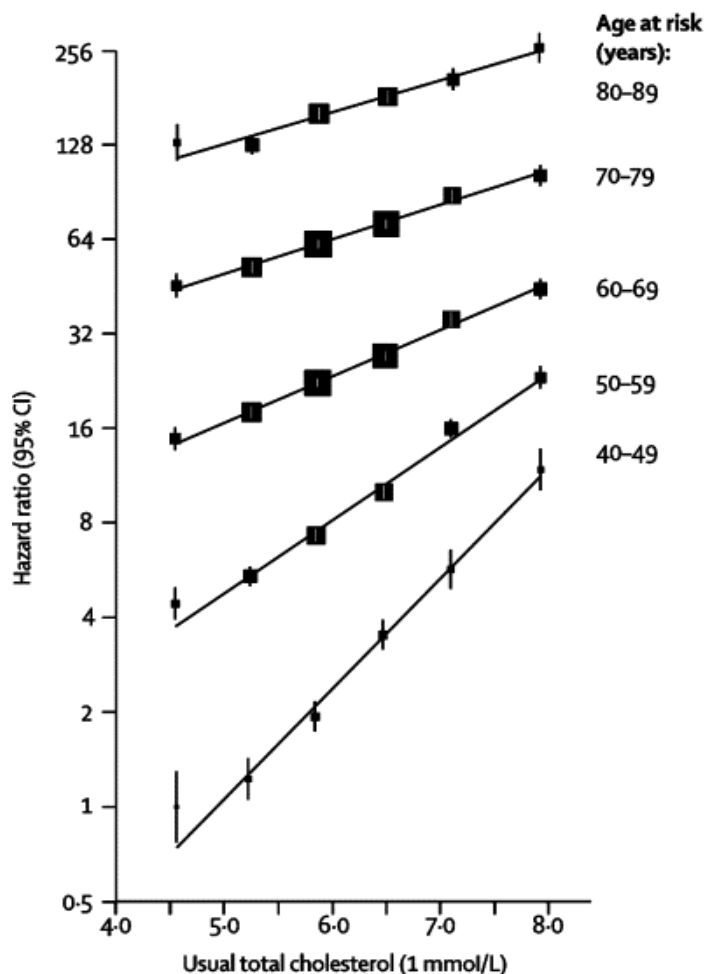
	Placebo (n, %) (n=2913)	Pravastatin (n, %) (n=2891)	Hazard ratio (95% CI)	p*
Primary endpoint				
Coronary heart disease death or non-fatal myocardial infarction or fatal or non-fatal stroke	473 (16.2)	408 (14.1)	0.85 (0.74–0.97)	0.014
Secondary endpoints				
Coronary heart disease death or non-fatal myocardial infarction	356 (12.2)	292 (10.1)	0.81 (0.69–0.94)	0.006
Fatal or non-fatal stroke	131 (4.5)	135 (4.7)	1.03 (0.81–1.31)	0.81
Other outcomes				
Non-fatal myocardial infarction	254 (8.7)	222 (7.7)	0.86 (0.72–1.03)	0.10
Coronary heart disease death or non-fatal myocardial infarction (excluding silent and unrecognised events)	246 (8.4)	193 (6.7)	0.77 (0.64–0.93)	0.007
Non-fatal stroke	119 (4.1)	116 (4.0)	0.98 (0.76–1.26)	0.85
Transient ischaemic attack	102 (3.5)	77 (2.7)	0.75 (0.55–1.00)	0.051
Percutaneous transluminal coronary angioplasty and coronary artery bypass graft	48 (1.6)	39 (1.3)	0.82 (0.54–1.26)	0.36
Peripheral arterial surgery/angioplasty	45 (1.5)	35 (1.2)	0.78 (0.50–1.21)	0.27
All cardiovascular events†	523 (18.0)	454 (15.7)	0.85 (0.75–0.97)	0.012
Fatal or non-fatal stroke or transient ischaemic attack	212 (7.3)	204 (7.1)	0.96 (0.79–1.16)	0.64
Heart failure hospitalisation	122 (4.2)	112 (3.9)	0.91 (0.71–1.18)	0.49
Deaths				
Coronary heart disease	122 (4.2)	94 (3.3)	0.76 (0.58–0.99)	0.043
Stroke	14 (0.5)	22 (0.8)	1.57 (0.80–3.08)	0.19
Vascular	157 (5.4)	135 (4.7)	0.85 (0.67–1.07)	0.16
Non-vascular	149 (5.1)	163 (5.6)	1.11 (0.89–1.38)	0.38
Cancer	91 (3.1)	115 (4.0)	1.28 (0.97–1.68)	0.082
Trauma or suicide	7 (0.2)	2 (0.1)	N/A	N/A
All causes	306 (10.5)	298 (10.3)	0.97 (0.83–1.14)	0.74

N/A=not analysed. *Significance of treatment effect in a Cox proportional hazard model adjusted for covariates presented in table 1. No formal analysis was done for events with a low incidence. †All cardiovascular events are primary endpoint or coronary artery bypass graft or percutaneous transluminal coronary angioplasty or peripheral arterial surgery or angioplasty.

Cholesterol as a risk factor for CV death as a function of age

IHD mortality (33 744 deaths) versus usual total cholesterol

A Age-specific associations



B Age and sex-specific HRs for 1 mmol/L lower total cholesterol

