

Making an Impact on Cardiovascular Disease in Your Patients

**A New Indication for Simvastatin Based on
the Heart Protection Study**

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MRC/BHF Heart Protection Study - unique data

- **Large study: 20,000 patients**
- **Many patients with “low” cholesterol**
 - 33% had LDL < 116mg/dl (3.0 mmol/l)
- **Over 5,000 women**
- **Almost 6,000 diabetic patients**
- **2,701 patients with PVD only**
- **1,263 patients over age 74**

ELIGIBILITY: MRC/BHF Heart Protection Study

- **Increased risk of CHD death due to prior disease:**
 - **Myocardial infarction or other coronary heart disease;**
 - **Occlusive disease of non-coronary arteries; or**
 - **Diabetes mellitus or treated hypertension**
- **Age 40-80 years**
- **Total cholesterol >3.5 mmol/l (>135mg/dl)**
- **Statin or vitamins not considered clearly indicated or contraindicated by patient's own doctors**

PRIOR DISEASE at BASELINE

Prior disease	Number	Percentage
Any MI	8510	41%
Other CHD	4876	24%
No CHD*	7150	35%
Cerebrovascular	1820	
Peripheral vascular	2701	
Diabetes	3982	
ALL PATIENTS	20,536	100%

* Overlap between categories within "No CHD" group

FACTORIAL TREATMENT COMPARISONS

Simvastatin
(40 mg daily)

vs

Placebo
tablets

Vitamins
(600 mg E, 250 mg C
& 20 mg beta-carotene)

vs

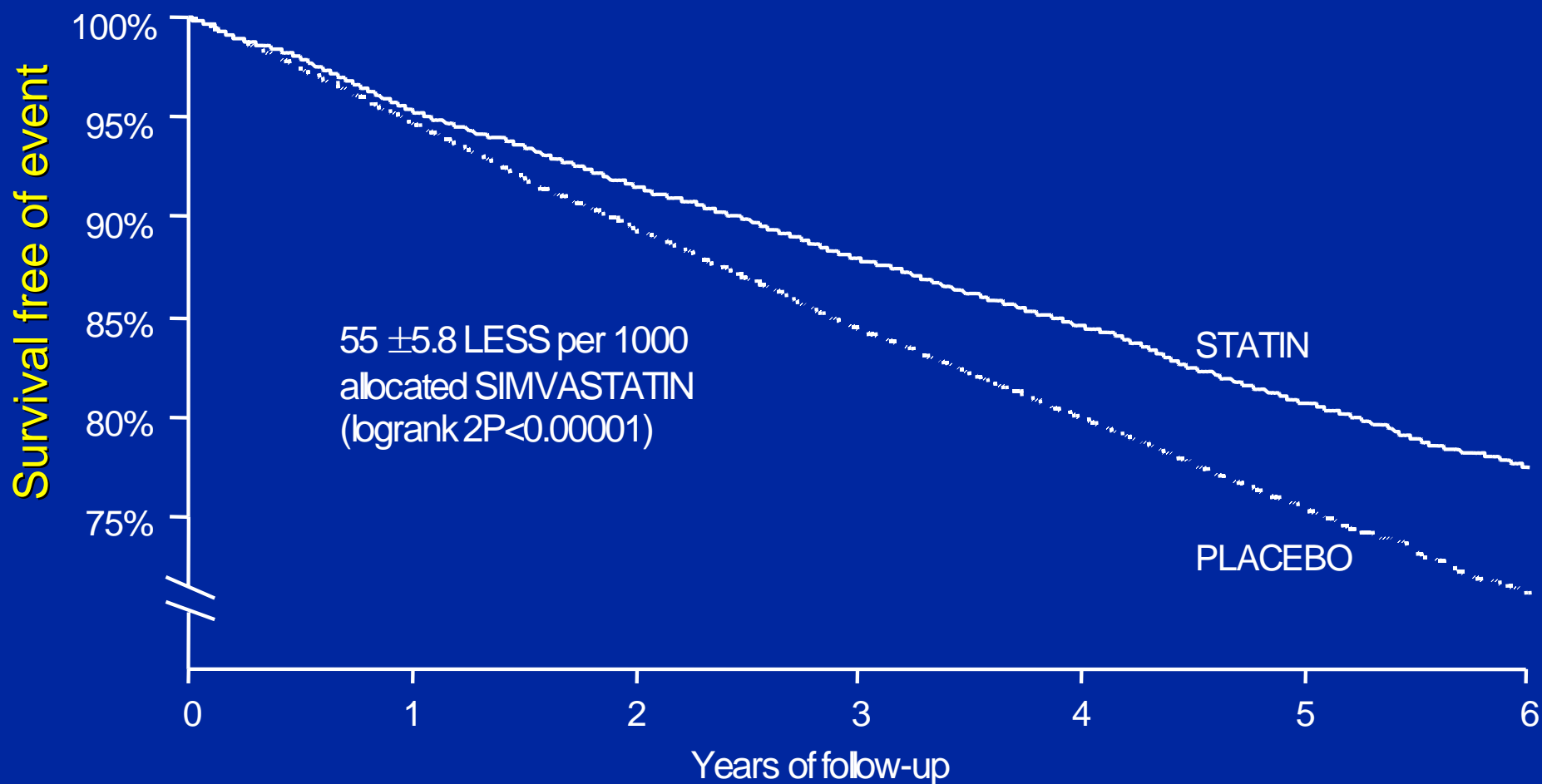
Placebo
capsules

Planned mean duration: At least 5 years

STATIN USE: Compliance ($\geq 80\%$) with study simvastatin or non-study statin use

Years of follow-up	Approx. no. of patients	SIMVASTATIN ALLOCATION	
		Active	Placebo
1	20,000	89%	4%
2	20,000	85%	9%
3	19,000	84%	17%
4	18,500	83%	24%
5	14,500	82%	32%
6	4,500	81%	38%
STUDY AVERAGE		85%	18%

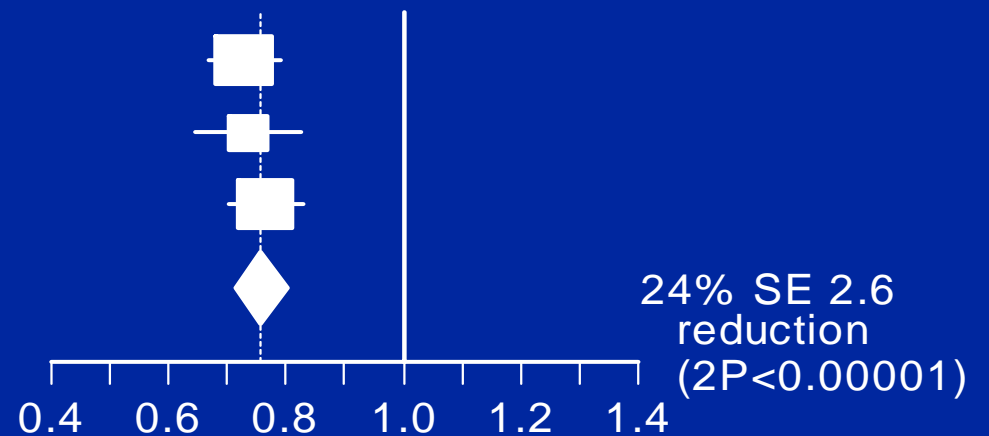
HPS: Vascular events by follow up duration



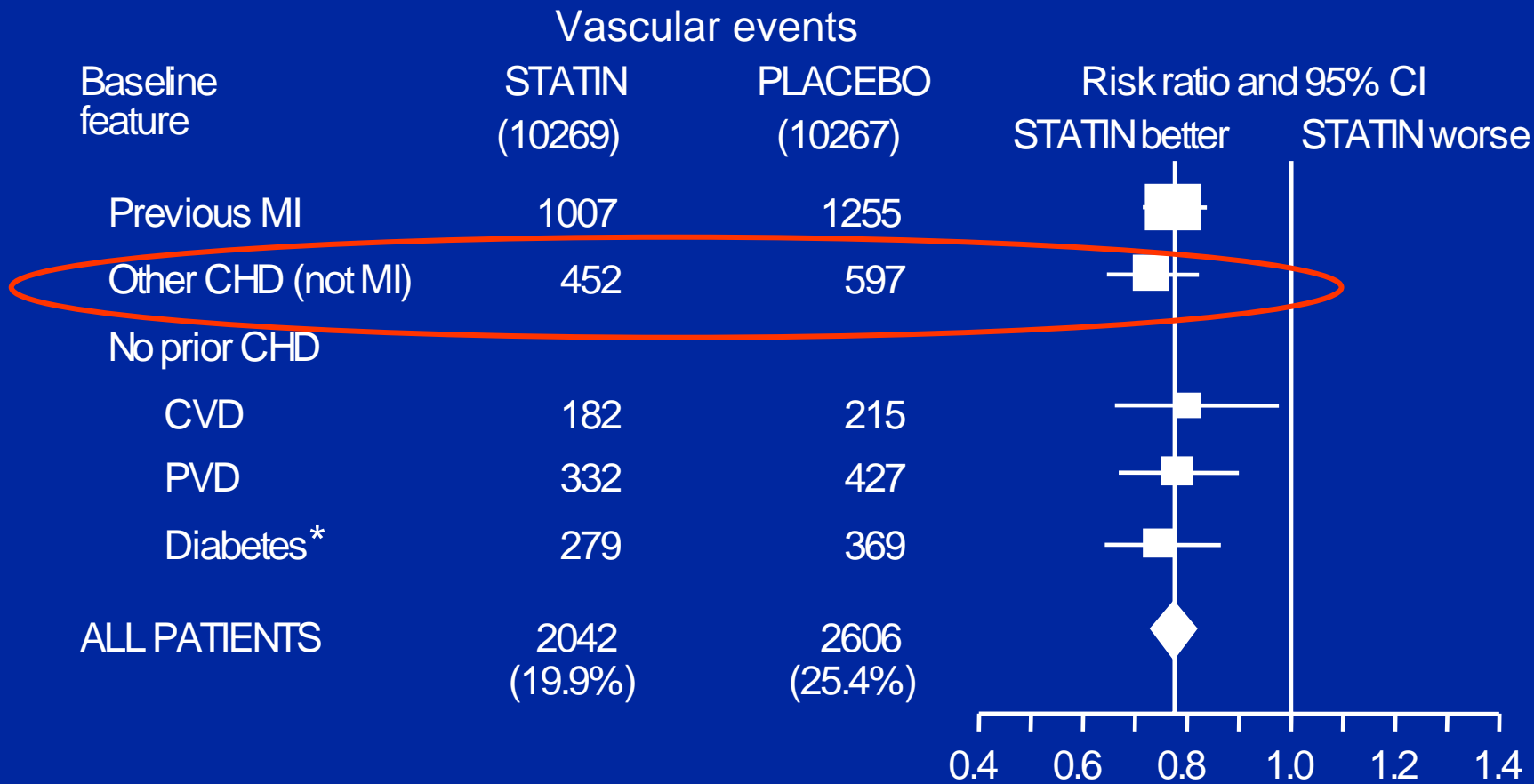
SIMVASTATIN: MAJOR VASCULAR EVENTS

Vascular event	STATIN (10269)	PLACEBO (10267)	Risk ratio and 95% CI STATIN better STATIN worse
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Total CHD	914	1234
Total stroke	456	613
Revascularisation	926	1185
ANY OF ABOVE	2042 (19.9%)	2606 (25.4%)



HPS: Effect of prior disease

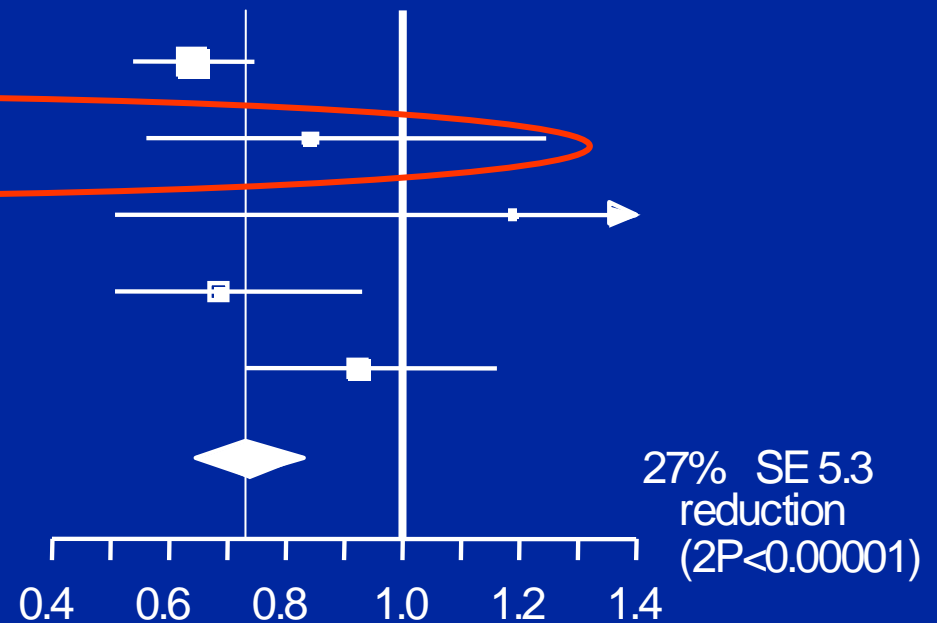


* Some of these diabetic patients had PVD or prev. stroke

SIMVASTATIN: STROKE by AETIOLOGY

Stroke aetiology	STATIN (10269)	PLACEBO (10267)	Risk ratio and 95% CI	
			STATIN better	STATIN worse

Ischaemic	242	376
Hæmorrhagic	45	53
Subarachnoid	12	10
Unknown	69	100
Unadjudicated	136	146
ALL STROKE	456 (4.4%)	613 (6.0%)



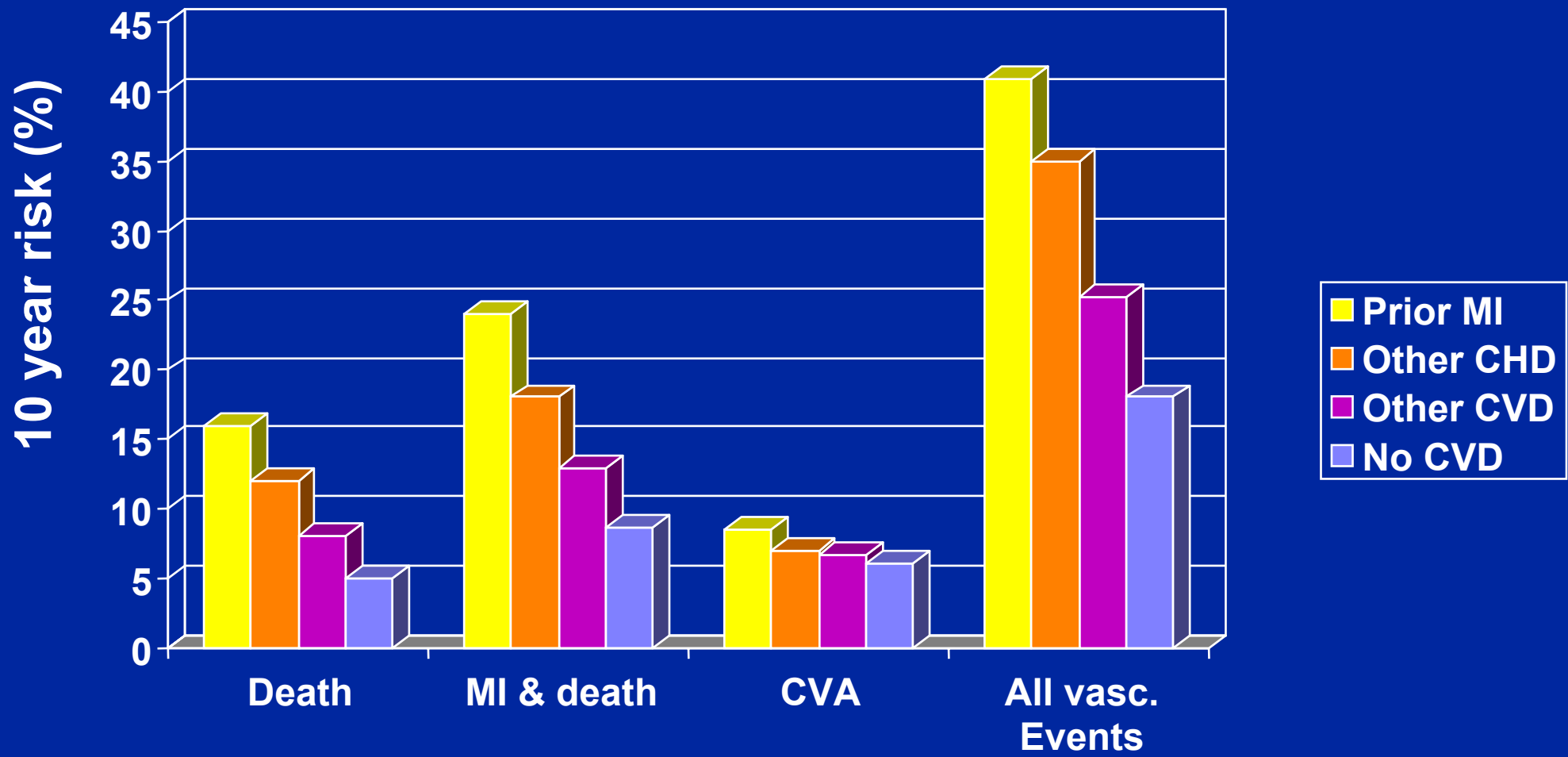
MRC/BHF Heart Protection Study

A true landmark study for diabetic patients

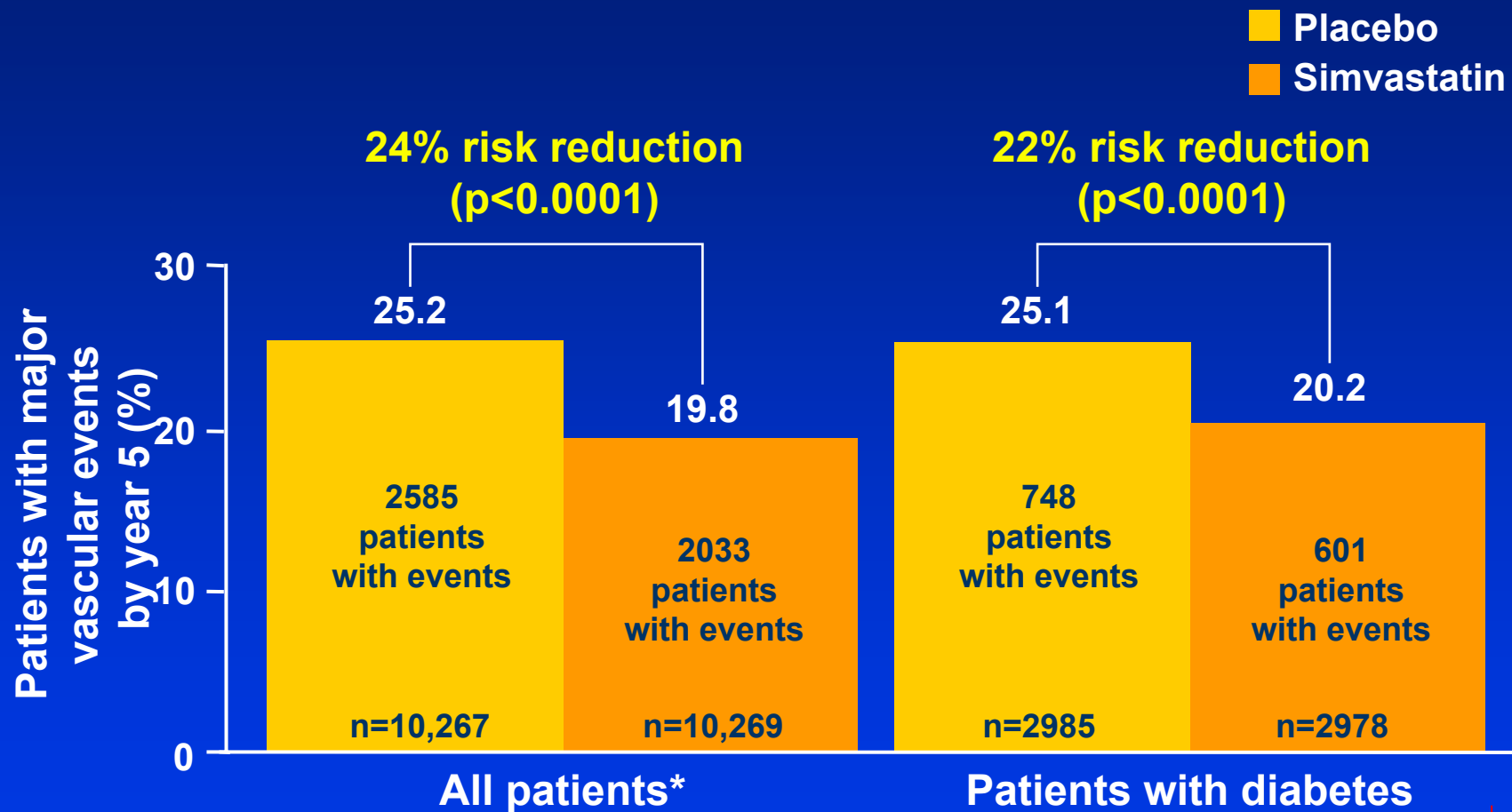
- All previous statin trials: 2006 diabetic patients
- **HPS:** 5963 diabetic patients

hps

HPS diabetes: event rates in the placebo group



Impact of Simvastatin on First Major Vascular Events All Patients and Patients with Diabetes



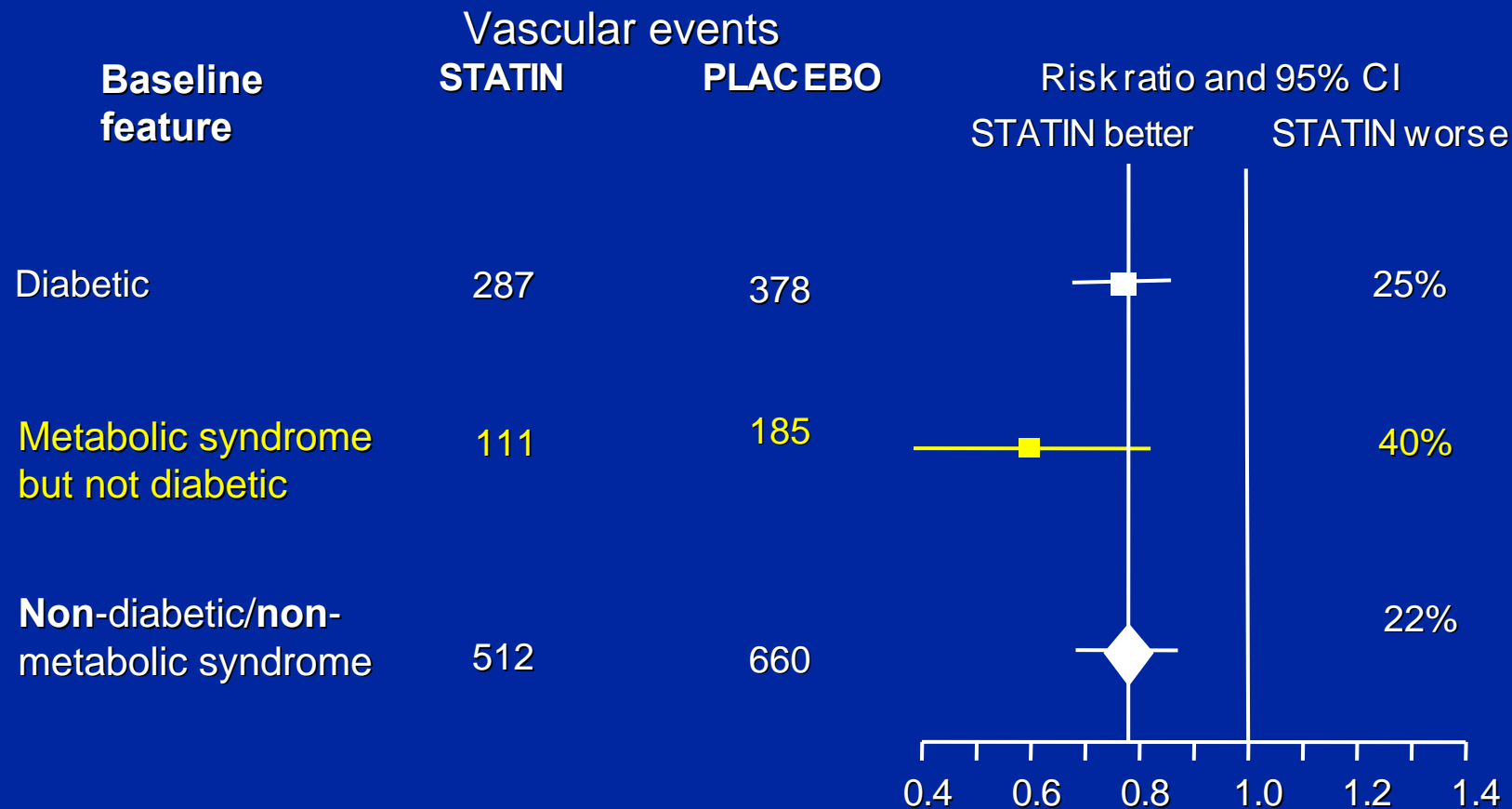
*Includes patients with CHD, occlusive disease of noncoronary arteries, diabetes, or treated hypertension

Adapted from Heart Protection Study Collaborative Group *Lancet* 2002;360:7-22; Heart Protection Study Collaborative Group *Lancet* 2003;361:2005-2016.

hps

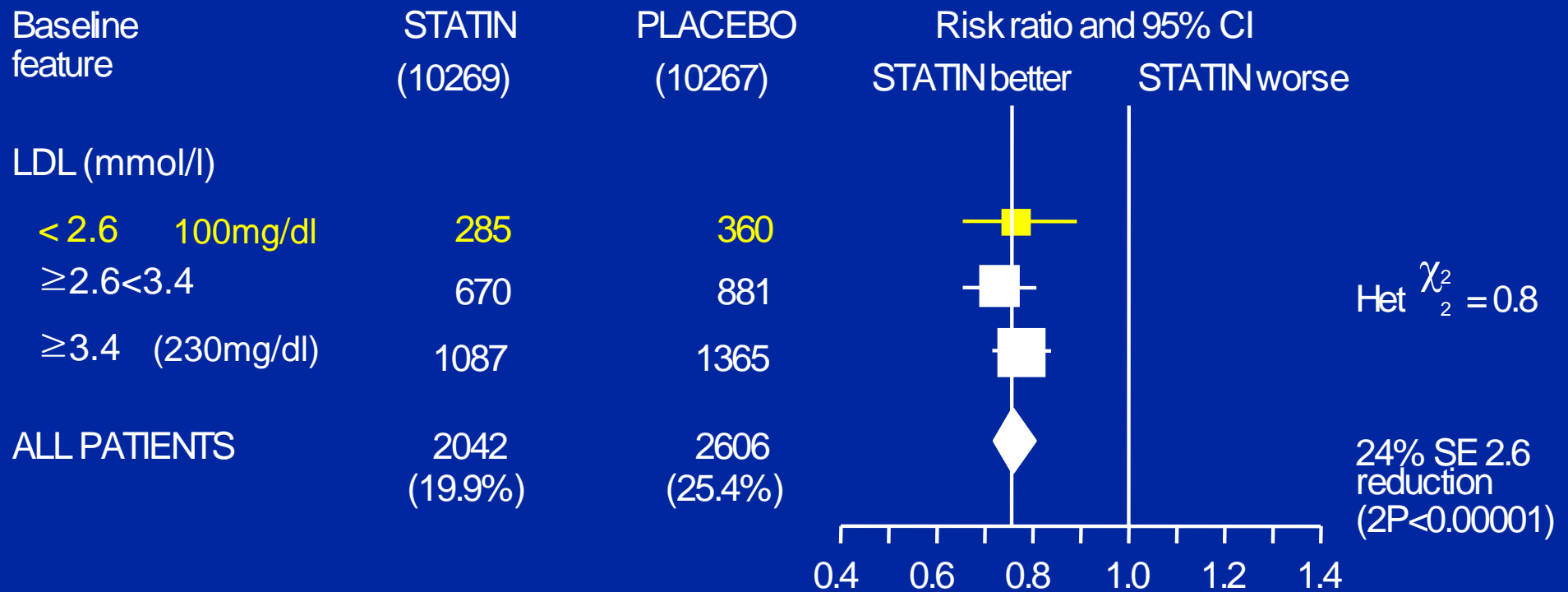
HPS:

Risk reduction in diabetes and the metabolic syndrome



HPS: effect of baseline LDL on response to simvastatin

Vascular events



New concept in simvastatin therapy

Risk reduction is independent of the baseline LDL

Therefore

**The decision to treat should be based
on the risk of vascular disease rather
than on LDL level**

Who should receive statin therapy?

- Patients with coronary disease
- Patients with cerebrovascular disease
- Patients with peripheral vascular disease
- Diabetic patients

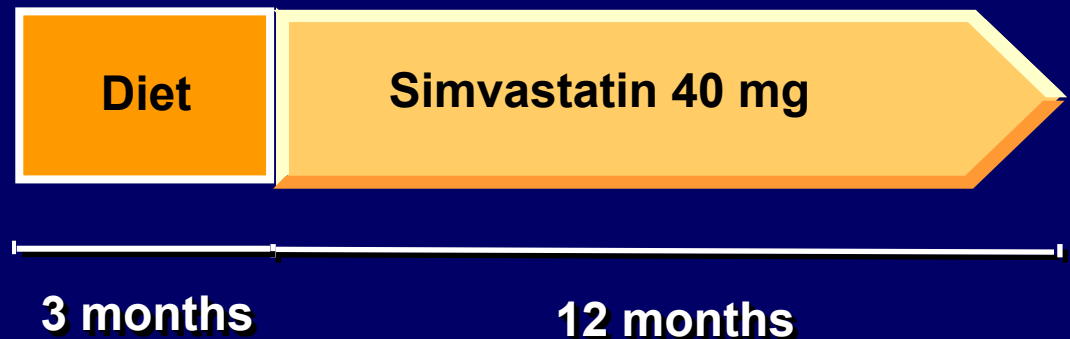
- In others - calculate the risk of vascular disease

Simvastatin IVUS study

Patient population

- History of CAD
- Cholesterol > 190 (5.0)
- LDL > 115 (3.0)
- Coronary lesion < 50%

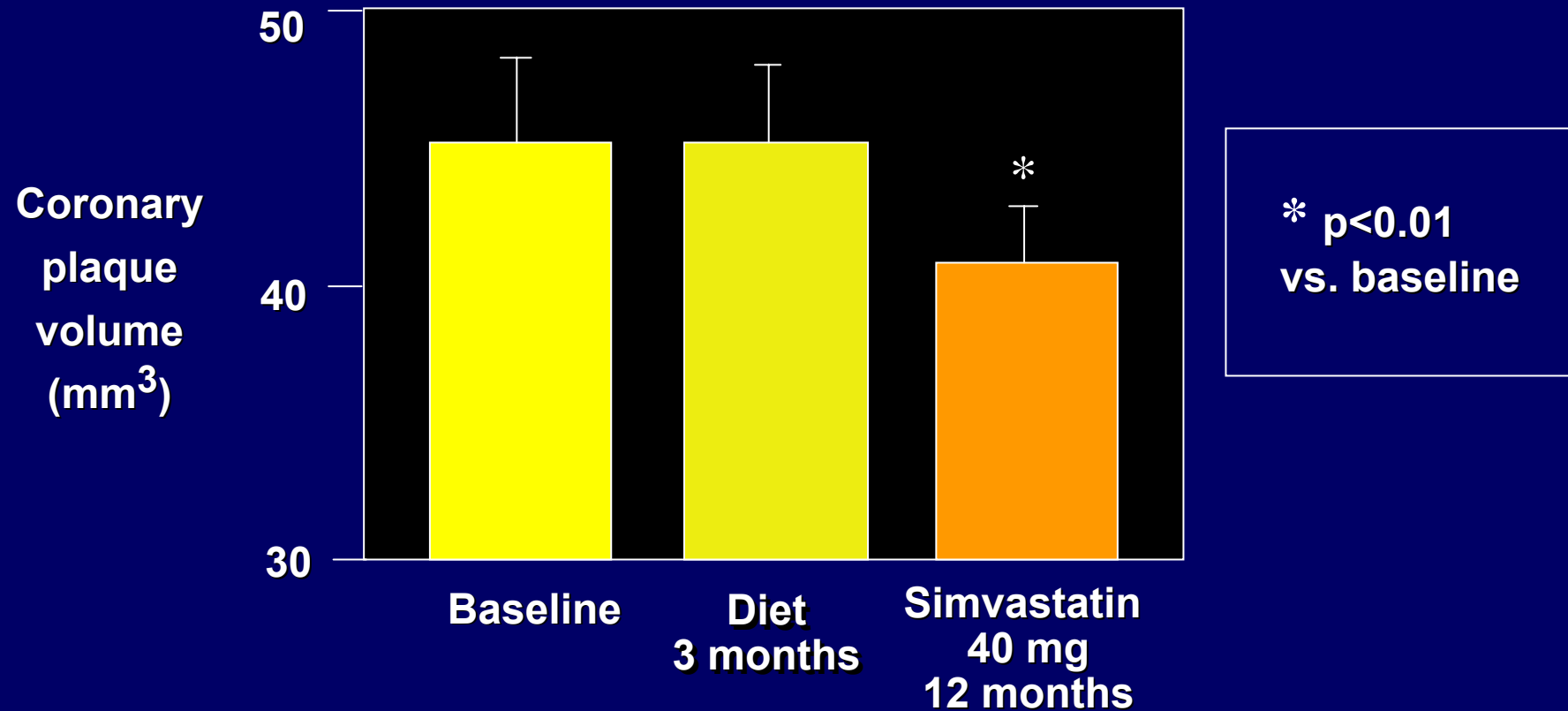
44
men



Primary end point:

- Change in coronary plaque volume measured by intravascular ultrasound

Simvastatin reduces plaque volume measured by IVUS



SIMVASTATIN: Safety monitoring

Blood enzymes (x upper limit of normal)	STATIN (10,269)	PLACEBO (10,267)
Liver: ALT > 3xULN	77 (0.8%)	65 (0.6%)
Muscle: CK > 10xULN	9 (0.09%)	5 (0.05%)

SIMVASTATIN 40mg daily: Muscle symptoms

Muscle pain or weakness	SIMVASTATIN (10,269)	PLACEBO (10,267)	P-value
Ever reported	3380 (33%)	3410 (33%)	NS
Stopped tablets	49 (0.5%)	50 (0.5%)	NS

HPS Key points

- Major benefit in all patients groups
- Large number of diabetic patients
- Major benefit in the metabolic syndrome
- Major benefit even if LDL \leq 100 (2.5)
- 40mg dose - excellent safety profile