

Hope-3



The Heart Outcomes Prevention Evaluation (HOPE) – 3 Trial

Eva Lonn, Jackie Bosch, Salim Yusuf

For the HOPE-3 Investigators

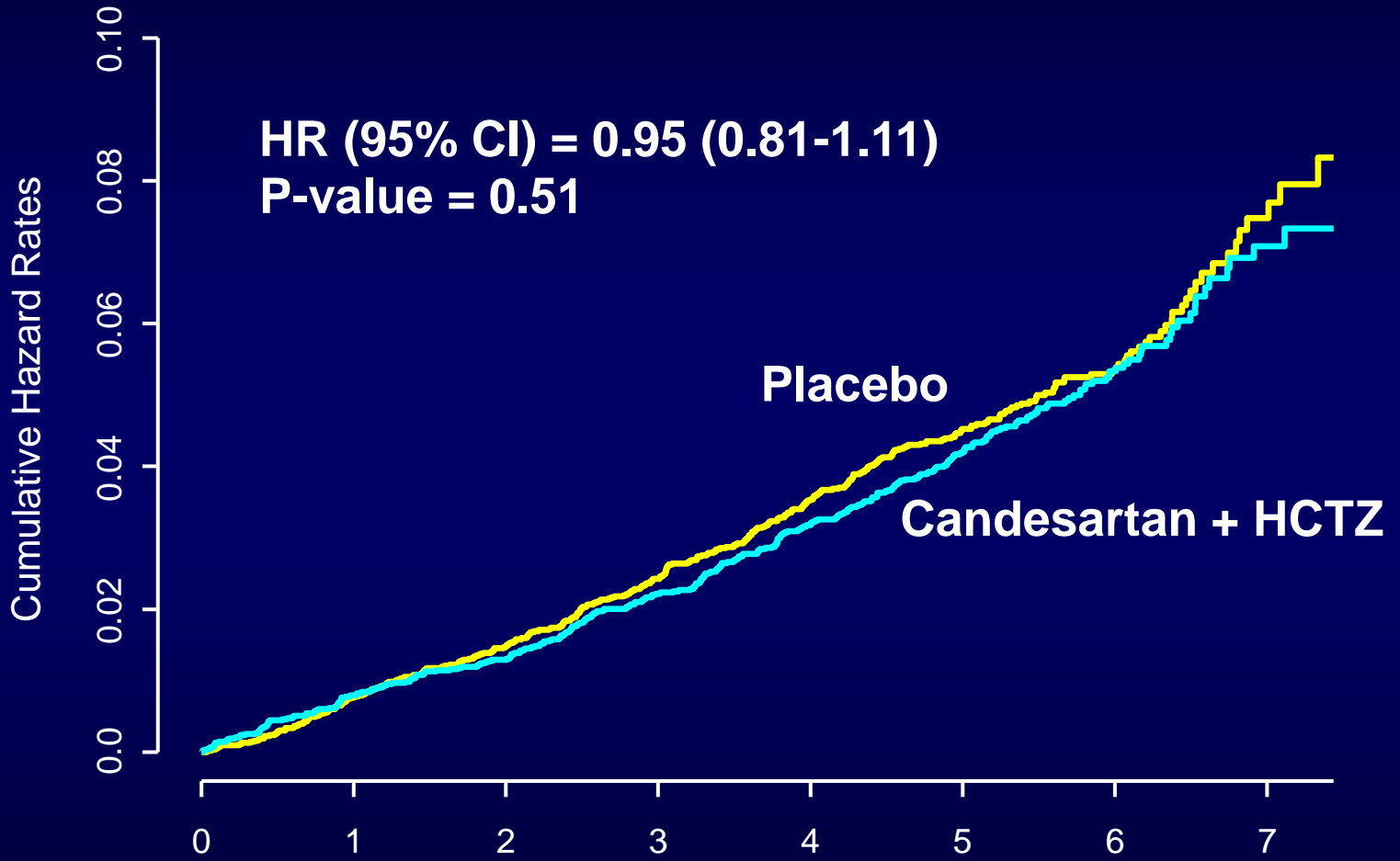
Population Health Research Institute, (PHRI)
McMaster University and Hamilton Health Sciences,
Hamilton, Canada

*Unrestricted grants from the Canadian Institutes of Health
Research and AstraZeneca*

Unique Aspects of HOPE-3

- BP lowering trial with wide range of BP entry criteria
- Cholesterol lowering treatment based on risk opposed to baseline LDL or HDL measurement
- Diverse population

CV Death, MI, Stroke, Cardiac Arrest, Revascularization, Heart Failure

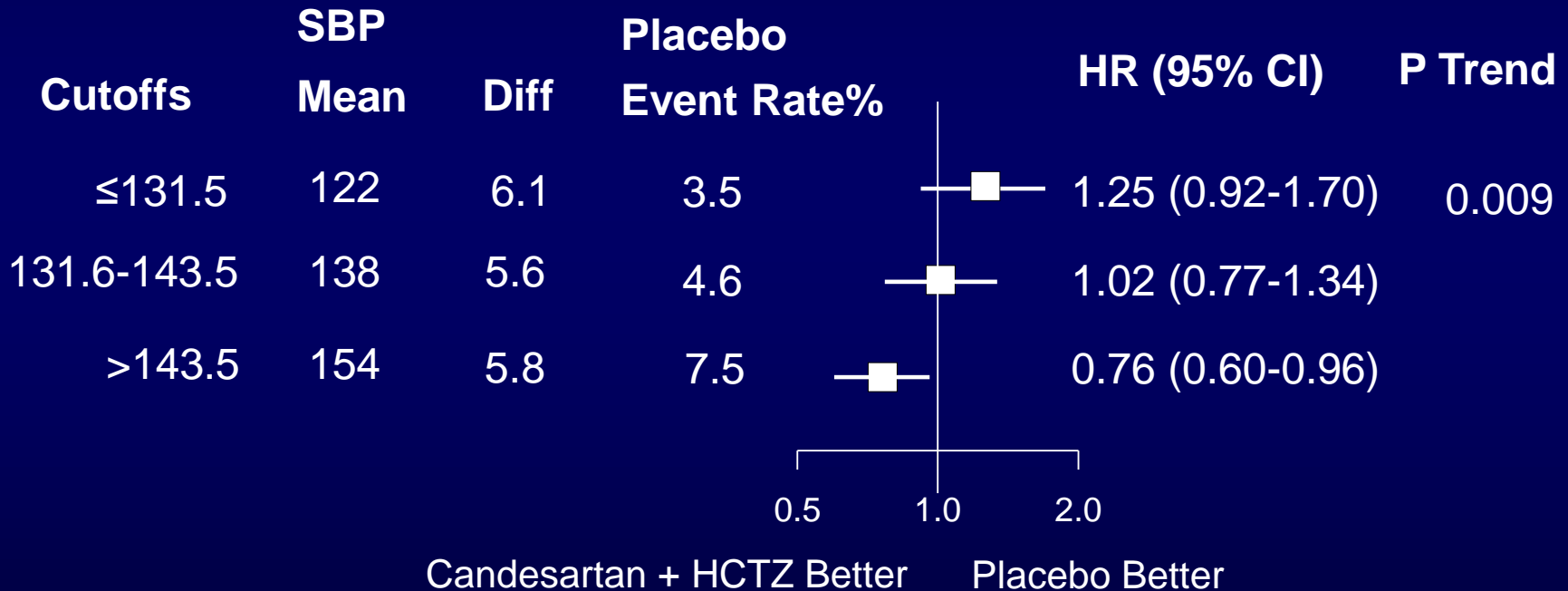


No. at Risk
Cand + HCTZ
Placebo

Years	0	1	2	3	4	5	6	7
Cand + HCTZ	6356	6272	6200	6103	5968	4969	2076	522
Placebo	6349	6270	6198	6096	5967	4970	2075	488

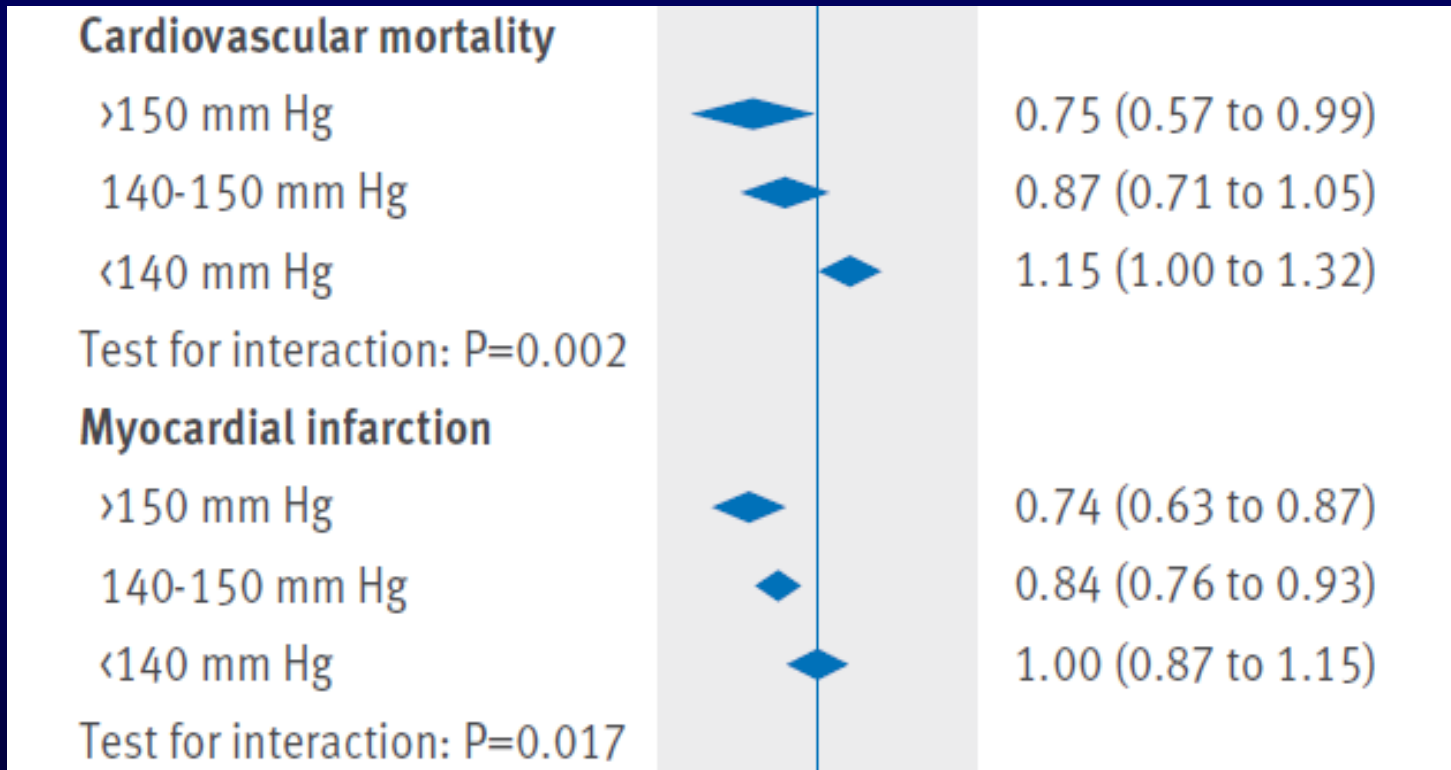
Prespecified Subgroups: By Thirds of SBP

CV Death, MI, Stroke, Cardiac Arrest, Revasc, HF



Meta analysis of BP Lowering Trials in DM

Results by Baseline Levels



BP Lowering Arm: Conclusions

- Fixed dose combination of Candesartan 16 mg + HCTZ 12.5 mg/day reduced BP by 6.0/3.0 mmHg, but did not reduce CV events
- CV events were significantly reduced in the highest third of SBP
 - SBP >143.5 mmHg, mean 154 mmHg
- Results were neutral in the middle third, and trended towards harm in the lowest third of SBP
- Treatment increased lightheadedness, but not syncope or renal dysfunction

Hope-3



Cholesterol Lowering Arm Results

Jackie Bosch

Hope-3

Unique Aspects of Cholesterol Lowering Arm



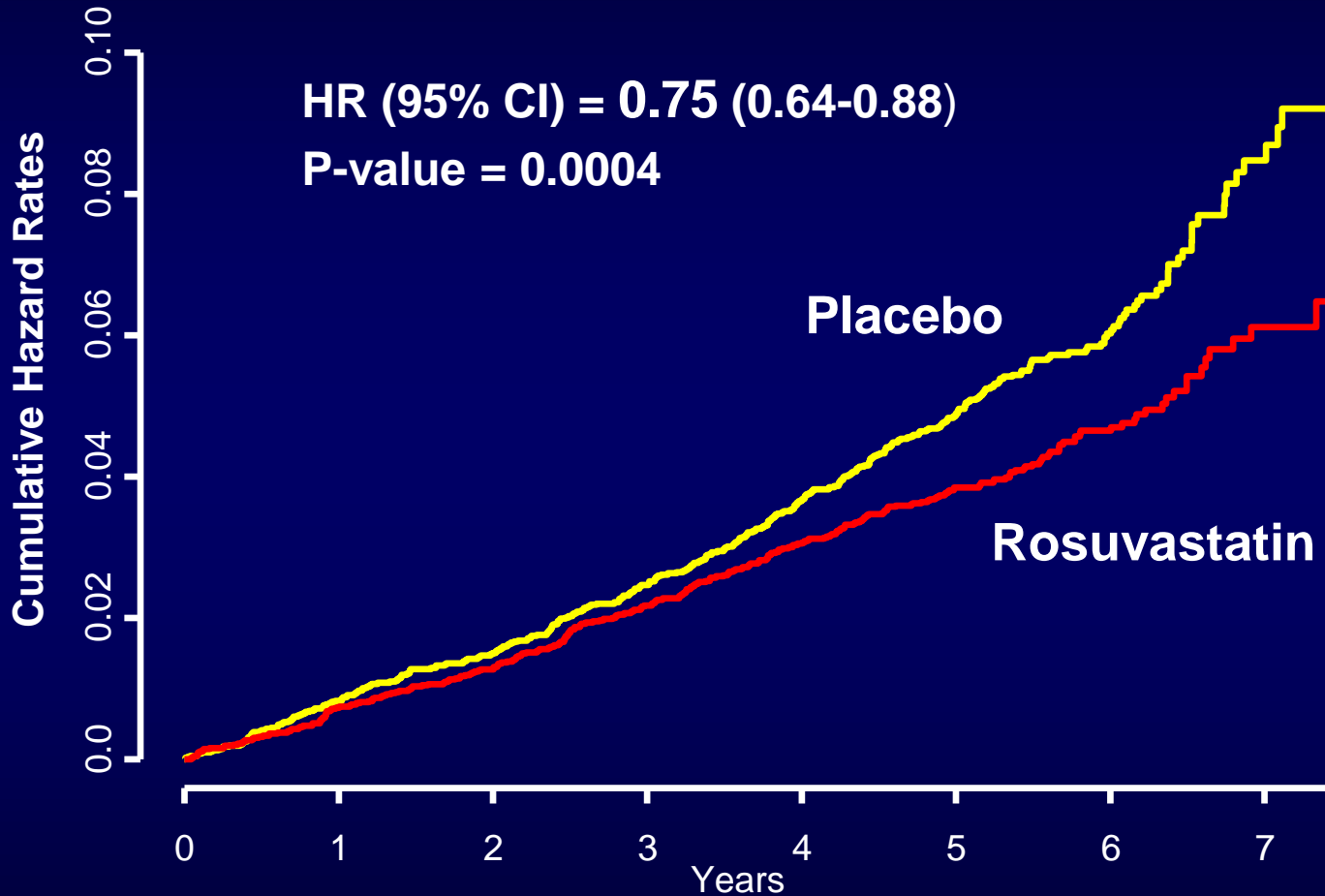
- No entry criteria based on lipid level
- No routine monitoring
- No dose titration
- Low dose of rosuvastatin

Cholesterol Lowering: Outcomes



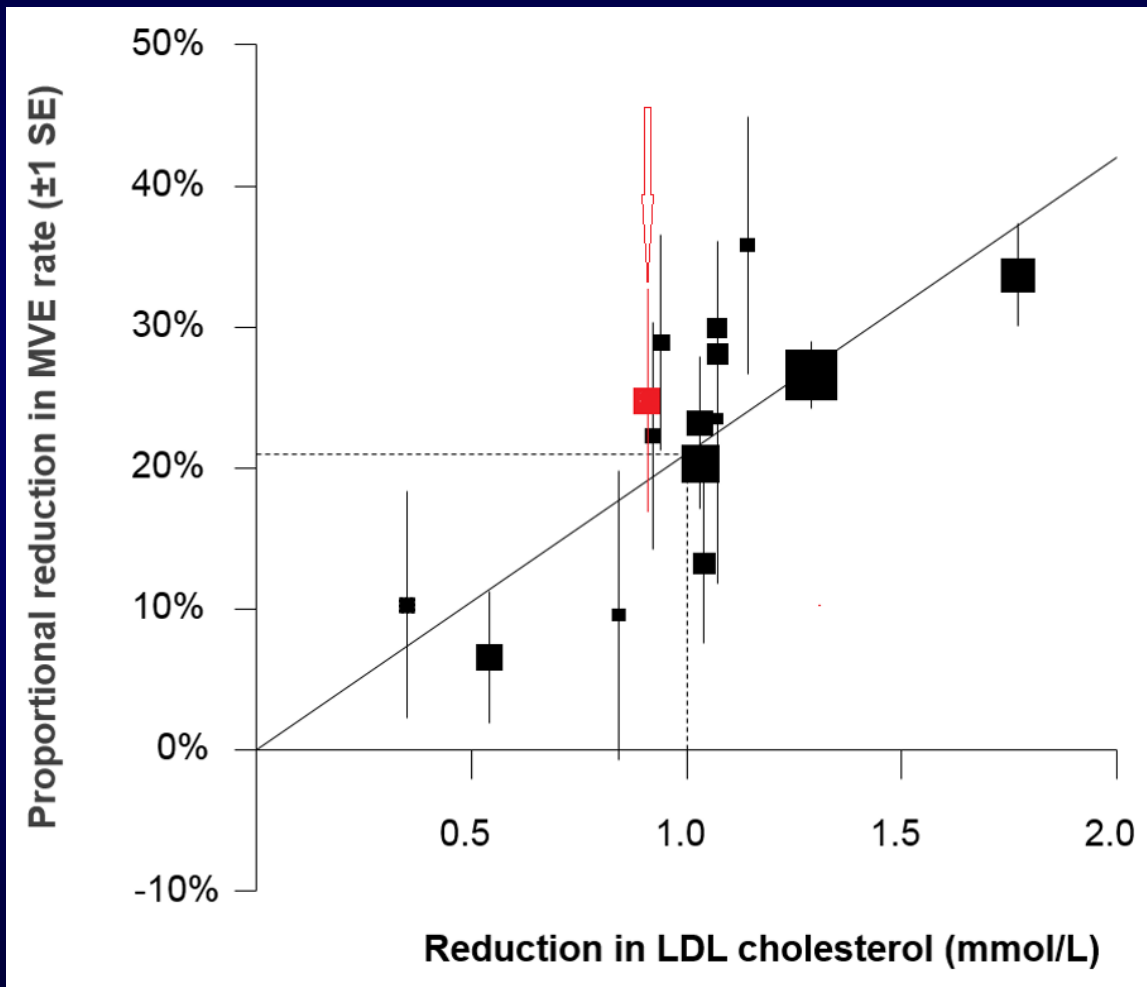
Outcome	Rosuvastatin N (%)	Placebo N (%)	HR (95% CI)	p
Co-Primary 1	235 (3.7)	304 (4.8)	0.76 (0.64-0.91)	0.002
Co-Primary 2	277 (4.4)	363 (5.7)	0.75 (0.64-0.88)	0.0004
Secondary 1	306(4.8)	393 (6.2)	0.77 (0.66-0.89)	0.0006
CV Death	154 (2.4)	171 (2.7)	0.89 (0.72-1.11)	0.31
MI	45 (0.7)	69 (1.1)	0.65 (0.44-0.94)	0.02
Stroke	70 (1.1)	99 (1.6)	0.70 (0.52-0.95)	0.02
CV Hosp.	281 (4.4)	369 (5.8)	0.75 (0.64-0.88)	0.0003

CV Death, MI, Stroke, Cardiac Arrest, Revasc, Heart Failure



Rosuva	6361	6241	6039	2122
Placebo	6344	6192	5970	2073

HOPE-3 & Other Studies of LDL Lowering and CVD



Cholesterol Lowering: Conclusions

- Rosuvastatin 10mg/day reduced:
 - LDL-C by 34.6 mg/dl (0.9 mmol/l; i.e. 27% in LDL-C)
 - **CVD by 25%**
- Consistent benefits regardless of:
 - LDL-C
 - SBP
 - Risk
 - CRP
 - Ethnicity
- Excess in muscle pain/weakness (reversible) and perhaps cataract surgery
- No excess in rhabdomyolysis, myopathy or new diabetes

Hope-3



Combined BP & Cholesterol Lowering vs Double Placebo

Salim Yusuf

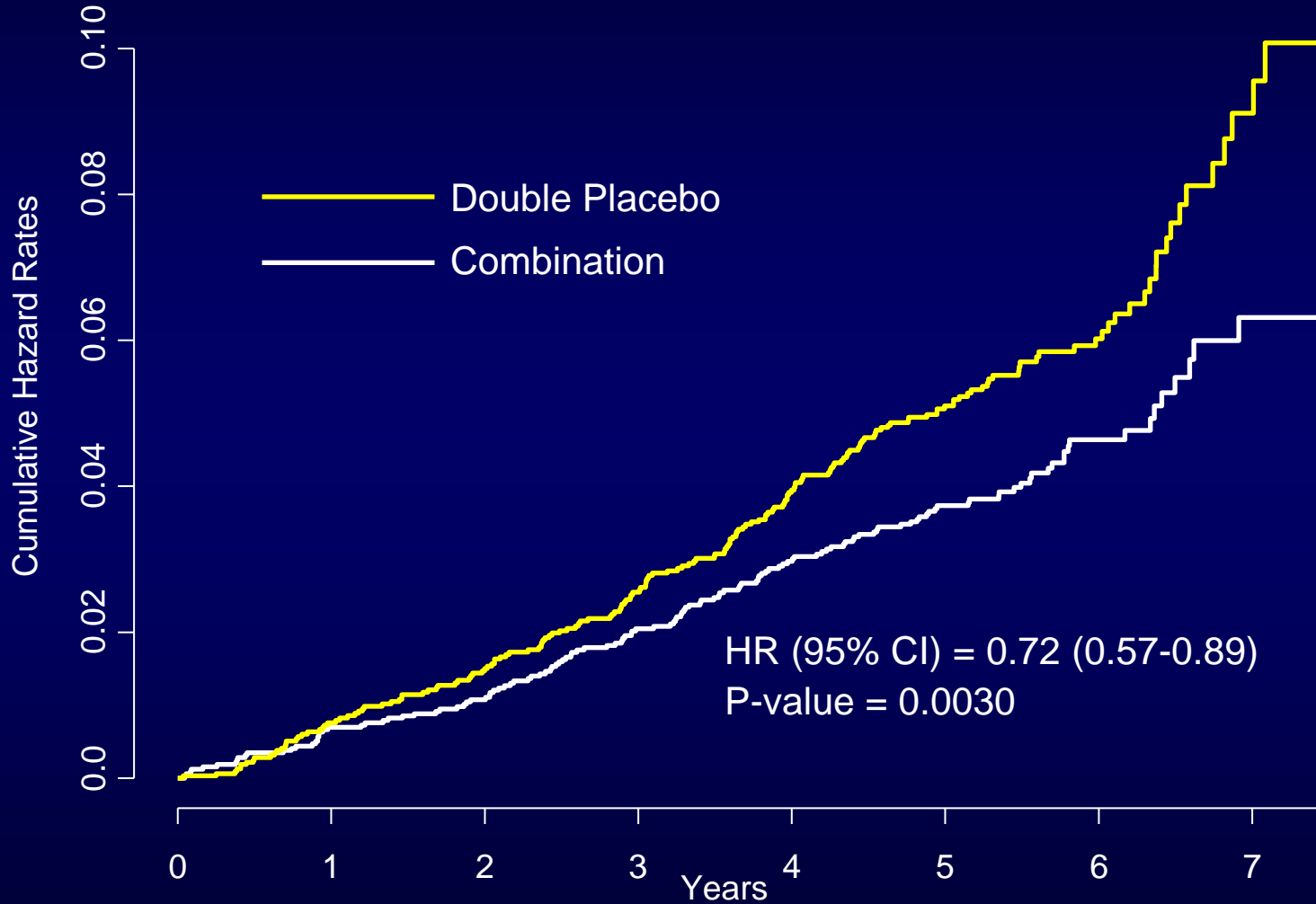
Hope-3

Unique Aspects of BP & Chol Lowering



- First formal testing of polypill concept on clinical events
- Demonstrates that the concept is valid in people with elevated BP; in others there is no benefit

CV Death, MI, Stroke, Cardiac Arrest, Revasc, Heart Failure

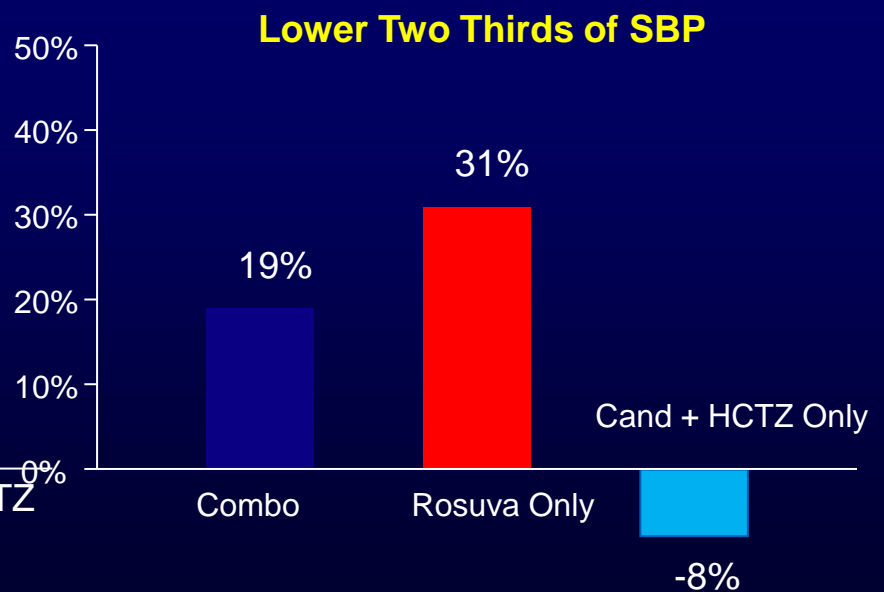
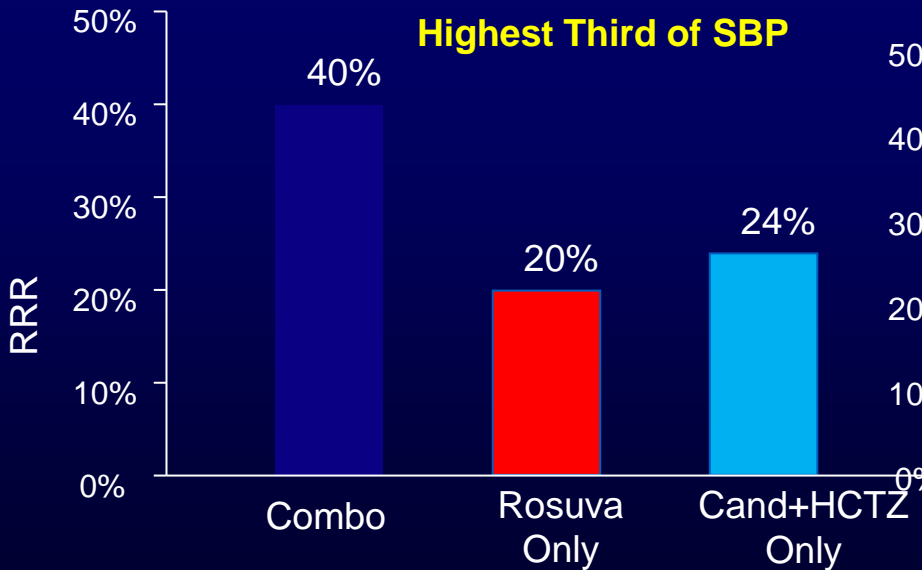
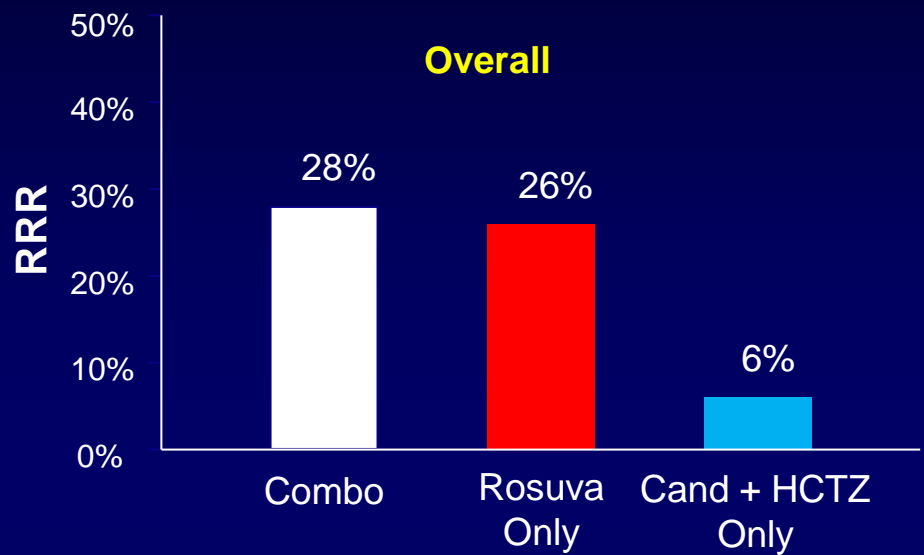


Combination	3180	4	3063	1057
Rosuvastatin	3181		3061	1045
Candesartan/HCTZ	3176		3040	1019
Double Placebo	3168		3035	1030

RRR of Combination and Each Intervention vs Double Placebo



Co-Primary 2



Clinical Implications

- Statins beneficial in *intermediate-risk* individuals without CVD
- BP lowering benefits only those with elevated BP
- Combined BP & cholesterol lowering:
 - Leads to a 40% risk reduction in hypertensives (benefits from *both* BP lowering and statin)
- In others, 30% RRR from statin alone
- Pragmatic strategy:
 - No Lipid or BP entry criteria or targets
 - No Dose titration
 - Infrequent safety monitoring

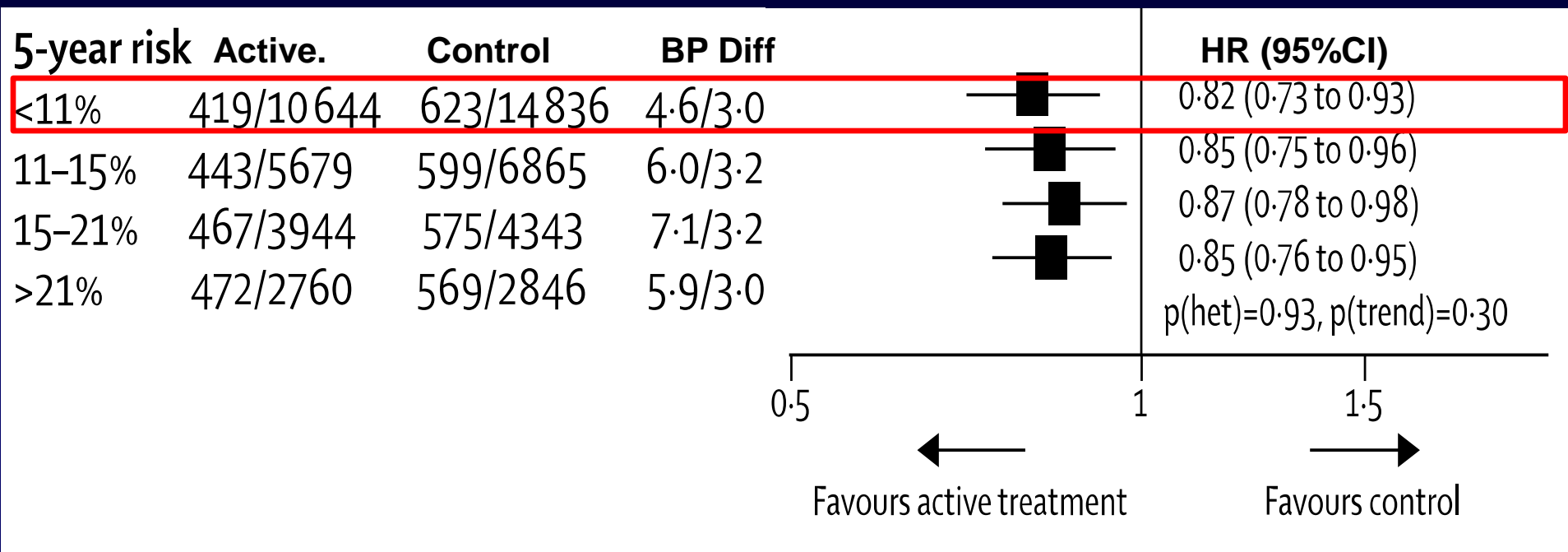
Strategy used in HOPE-3 is simple, safe and effective and widely applicable

Hope-3



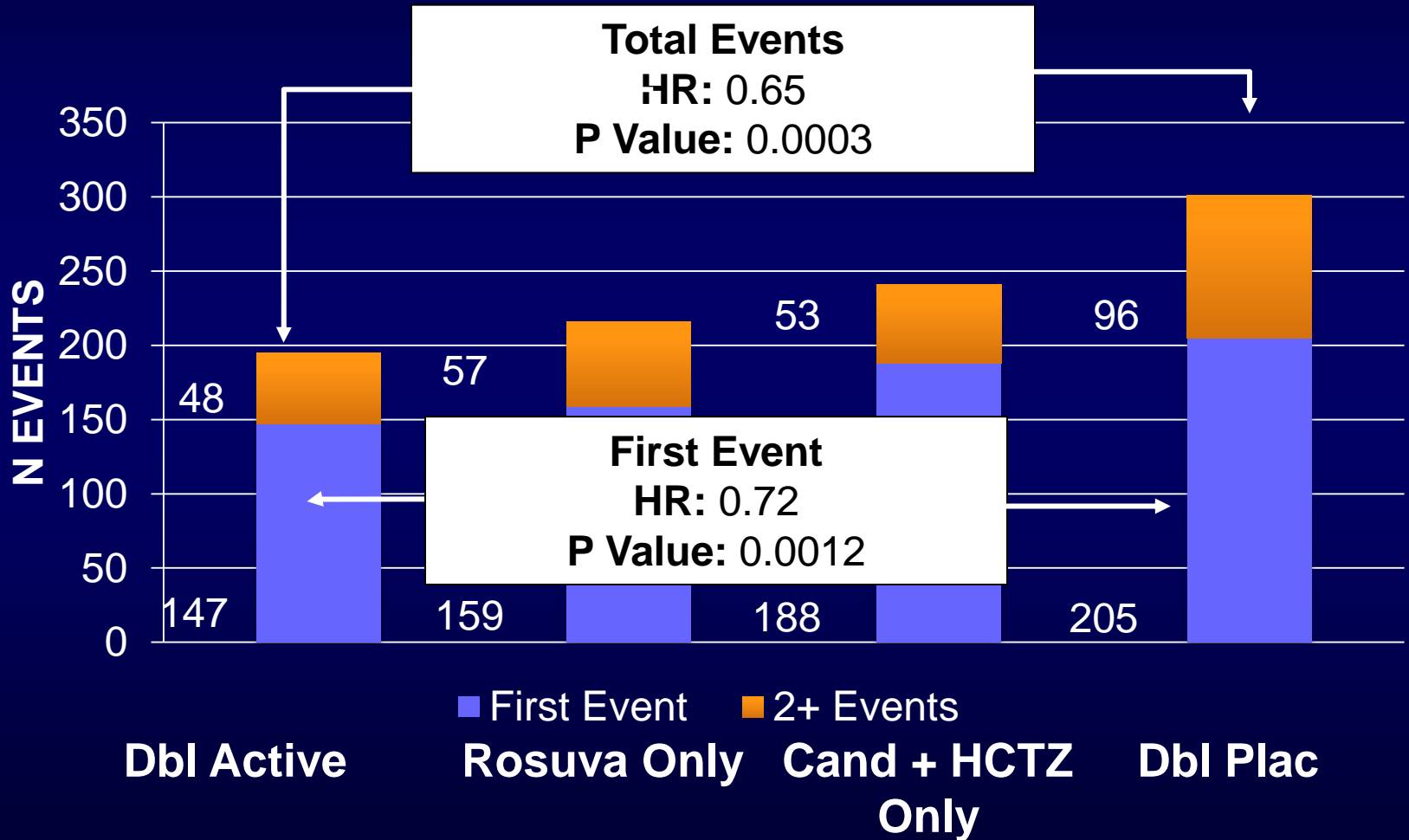
Back up

BP Lowering by CV Risk



5 yr Risk	<11% (6.5%)	11-15%	15-21%	>21%	Overall
SBP	155	159	162	165	158

1st & Recurrent CV Events



Hope-3



NNT Combination vs Double Placebo: Recurrent CV Events (Secondary)

Overall	30
Upper 1/3 rd	16
Lower 2/3 rd	41