



“First Stroke Reduced 44 Percent by Well Tolerated Medication”

Stroke Outcomes From the Heart Outcomes Prevention Evaluation 3 Study

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Presenter Disclosure Information

Jackie Bosch, PhD

Stroke Outcomes From HOPE-3

FINANCIAL DISCLOSURE:

The study was funded by Unrestricted grants from the Canadian Institutes of Health Research and AstraZeneca

UNLABELED/UNAPPROVED USES DISCLOSURE:

Use of candesartan/HCTZ or rosuvastatin for primary stroke prevention

Strategies to reduce the burden of stroke



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- >76% are first strokes, often result in permanent disability or death
- To decrease burden, must focus on primary prevention
- BP lowering & statins recommended for those at high-risk; data uncertain for those at moderate or low risk
- Interventions must be safe, easy to administer and monitor and effective

HOPE- 3 Objectives



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In an intermediate-risk population without CVD, to evaluate the effects on CV events of:

1. BP lowering with a fixed dose combination of Candesartan 16 mg and HCTZ 12.5 mg daily
2. Cholesterol lowering with Rosuvastatin 10 mg daily
3. Combined BP and cholesterol lowering

Participants received lifestyle advice and necessary therapies

Intermediate-Risk Population



Inclusion Criteria (Target Risk 1.0%/yr)

Women \geq 60 yrs, men \geq 55 yrs with at least one additional Risk Factor

- Increased WHR
- Smoking
- Low HDL-C
- Dysglycemia
- Mild renal dysfunction
- Family history of CHD

Exclusion Criteria:

CVD or indication(s) or contraindication(s) to study drugs

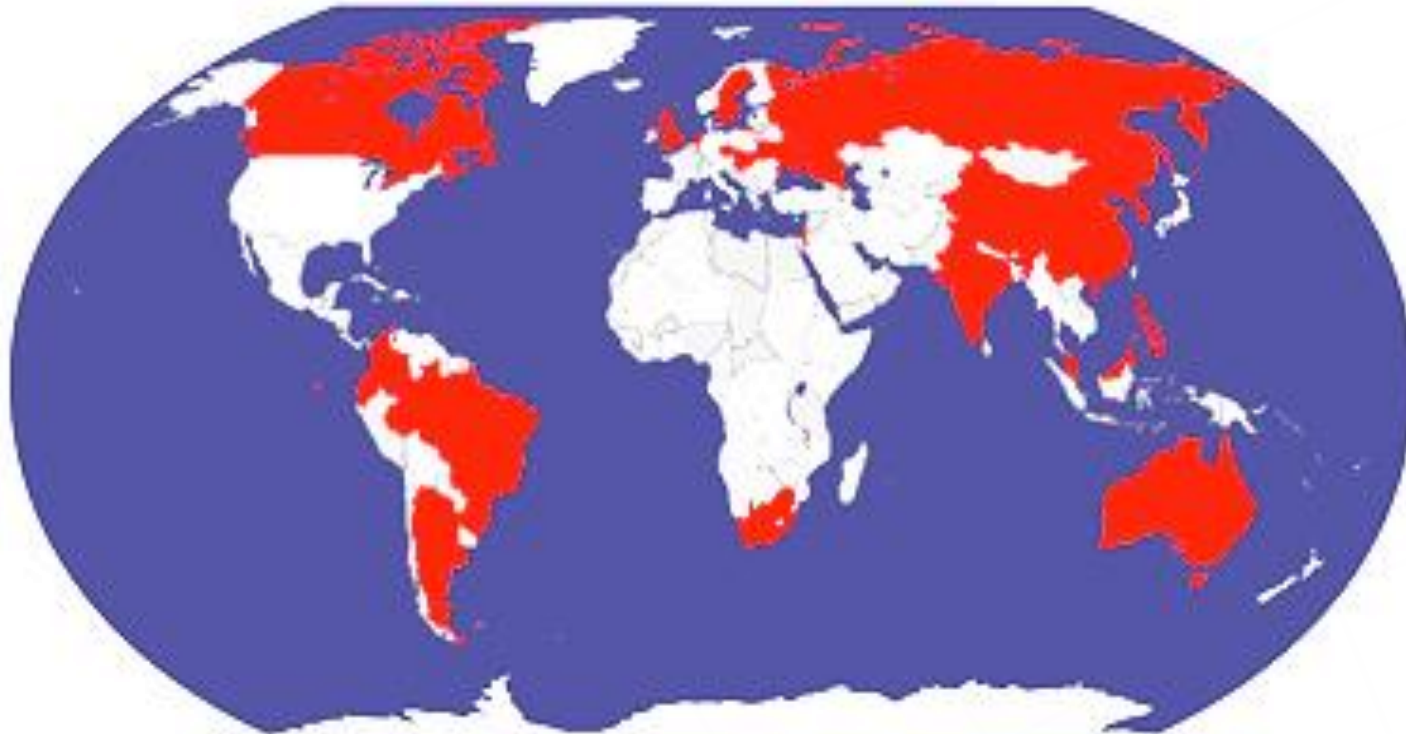
No strict BP or LDL-C criteria for entry
Uncertainty principle

The HOPE-3 Trial



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228 centers in 21 countries
Coordinated by PHRI, Hamilton, Canada



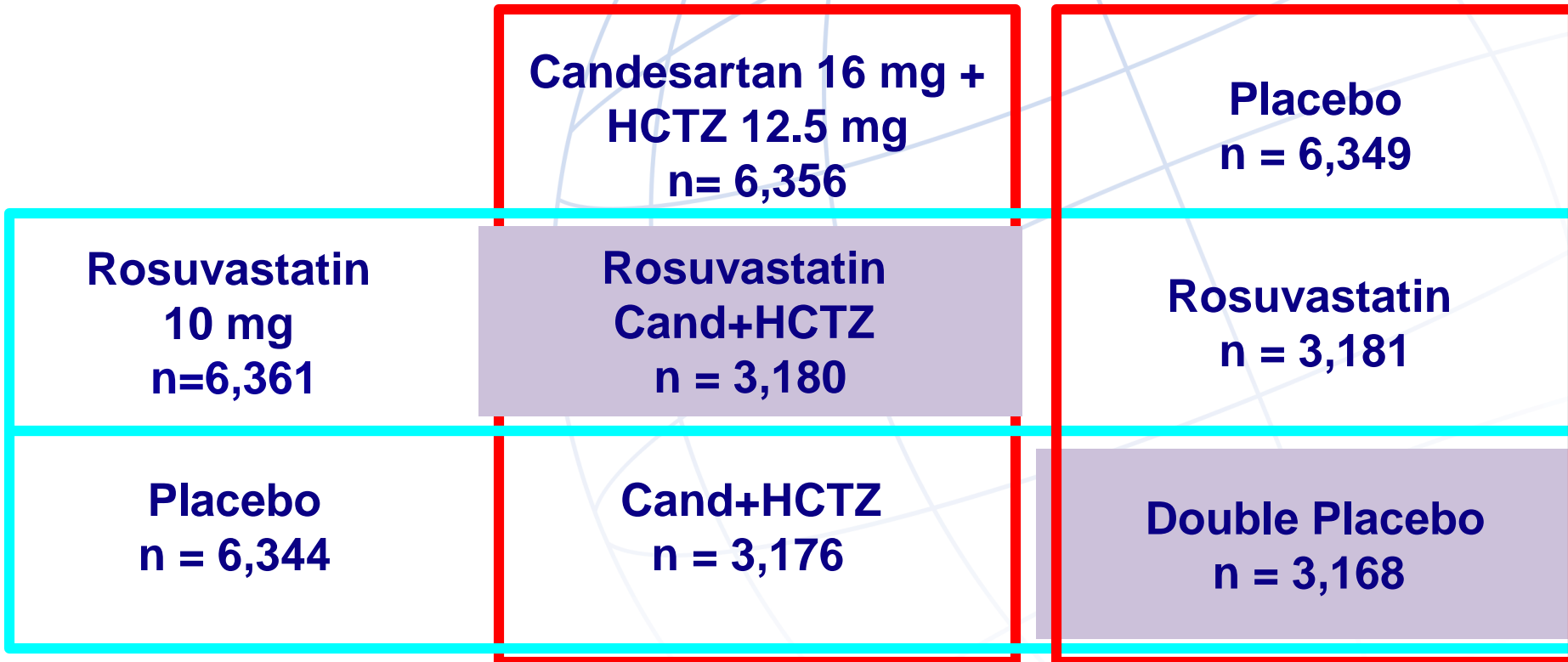
Argentina, Australia, Brazil, Canada, China, Colombia, Czech
Republic, Ecuador, Hungary, India, Israel, Korea, Malaysia,
Netherlands, Philippines, Russia, Slovakia, South Africa, Sweden,
United Kingdom, Ukraine

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2 by 2 Factorial Design

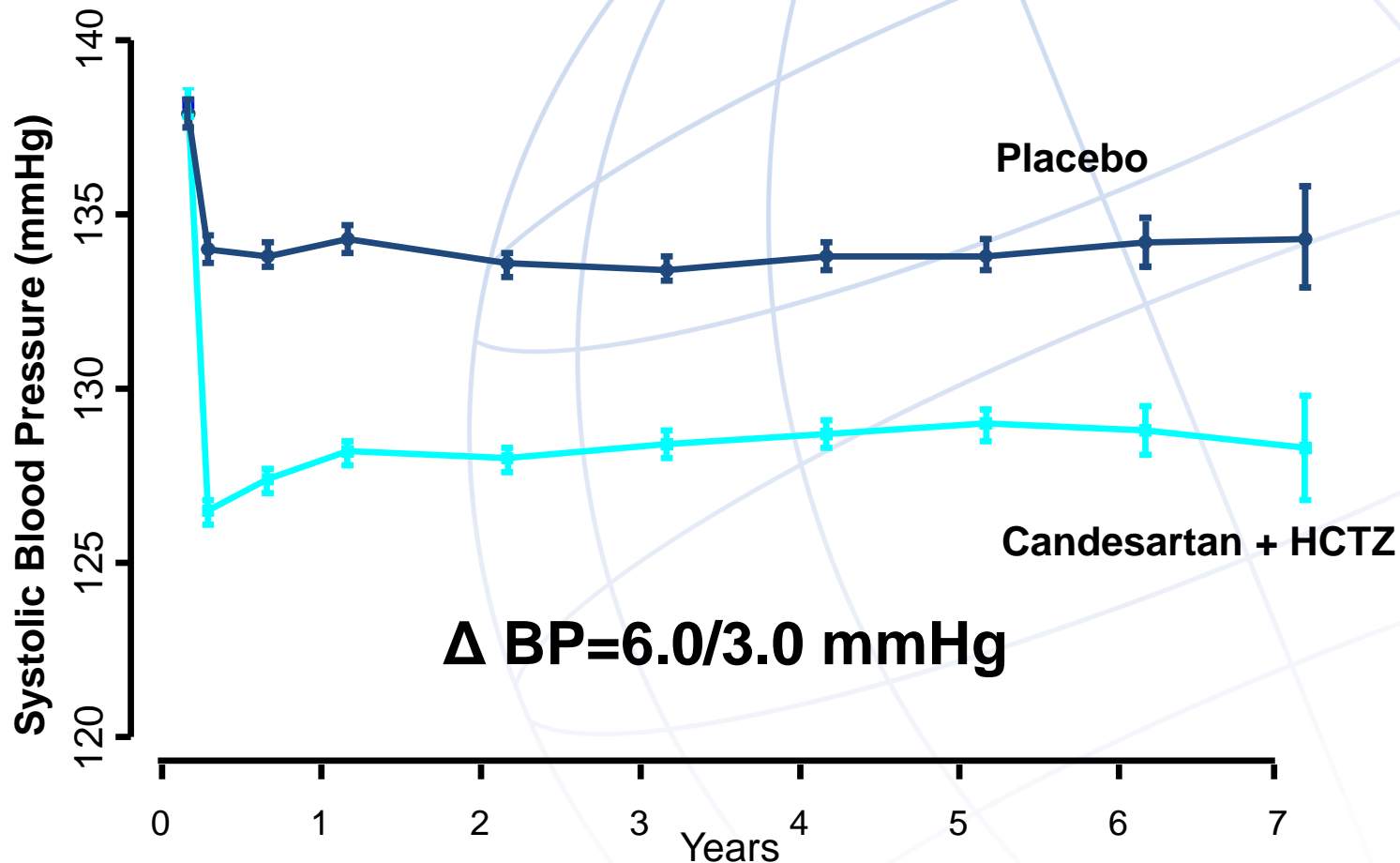


14,682 Entered Single-blind 4 week Active Run-in
12,705 (87%) Randomized



Simple follow-up and few blood tests

BP Lowering vs. Placebo: SBP Changes

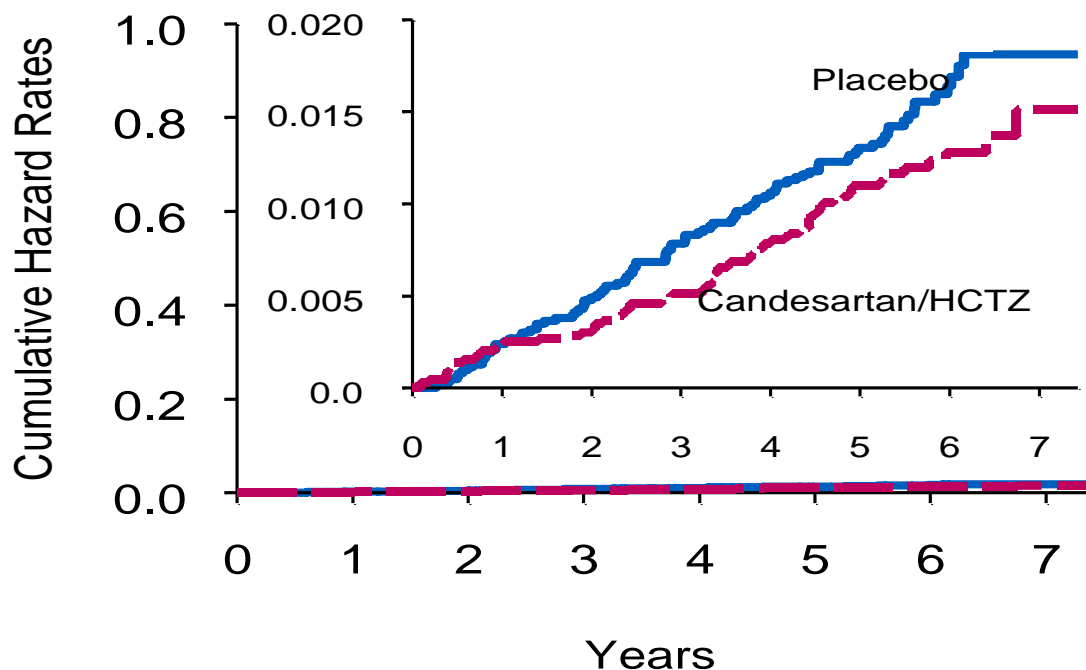


Cand+HCTZ	6356	5907	5667	5446	5213	3862	1437	350
Placebo	6347	5879	5623	5442	5186	3822	1424	334

Effects of BP Lowering on Stroke



MI/stroke/CV death: HR (95% CI), 0.93 (0.79-1.10); p=0.40
stroke: HR (95% CI), 0.80 (0.59-1.08); p=0.14

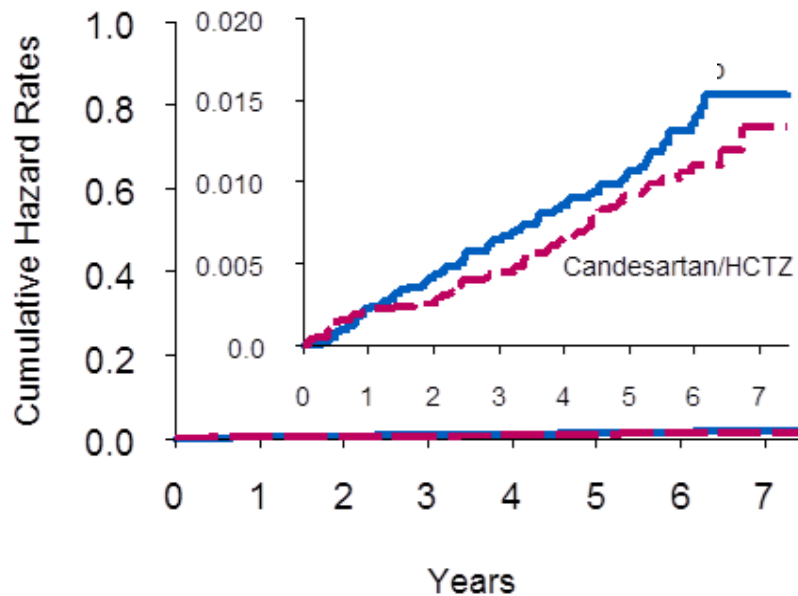


No. at Risk	0	1	2	3	4	5	6	7
Cand/HCTZ	6356	6292	6235	6155	6038	5042	2111	534
Placebo	6349	6291	6234	6147	6041	5045	2115	505

Effects of BP Lowering on Stroke

Ischemic

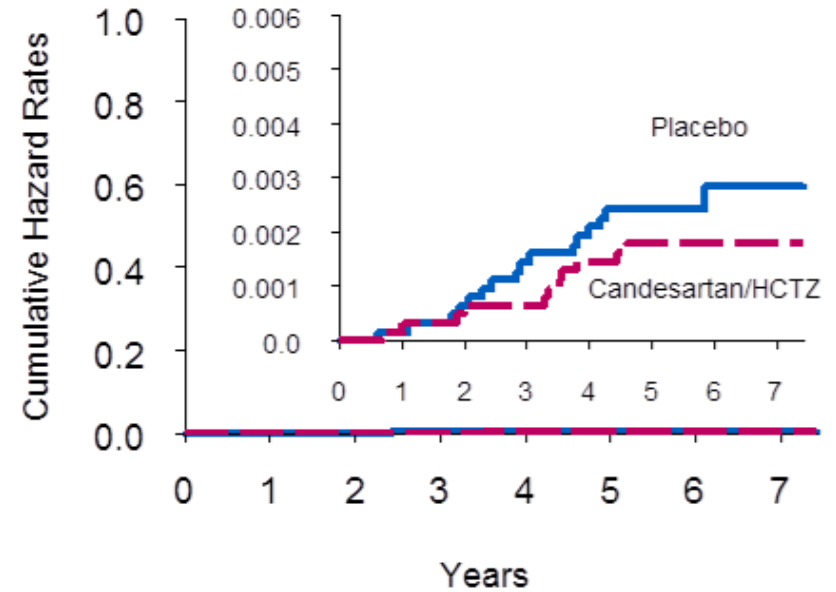
HR (95% CI), 0.82 (0.59-1.14); p=0.24



No. at Risk	0	1	2	3	4	5	6	7
Cand/HCTZ	6356	6293	6237	6157	6043	5047	2114	536
Placebo	6349	6291	6236	6152	6048	5053	2117	506

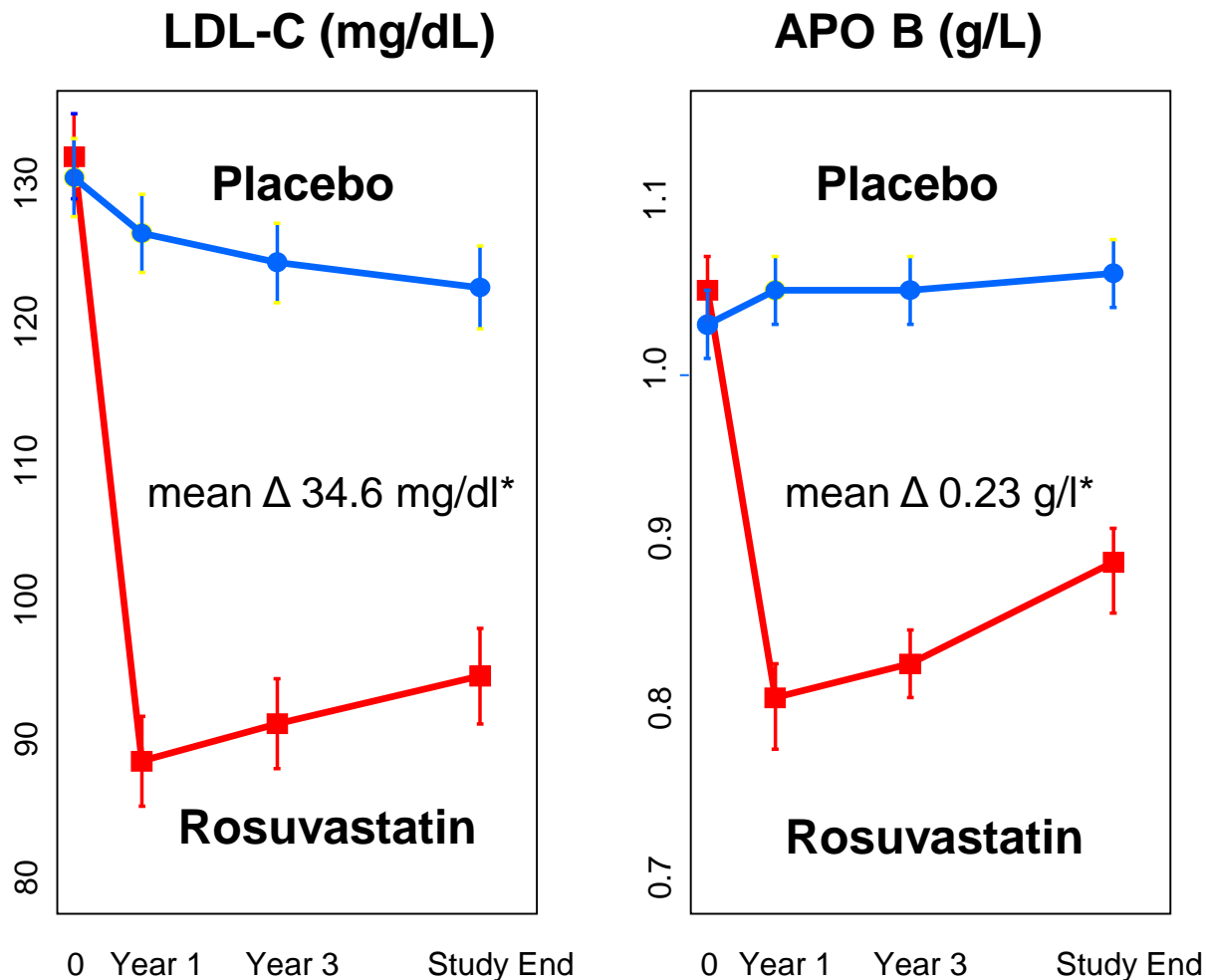
Hemorrhagic

HR (95% CI), 0.69 (0.32-1.48); p=0.34



No. at Risk	0	1	2	3	4	5	6	7
Cand/HCTZ	6356	6304	6250	6180	6071	5080	2123	534
Placebo	6349	6302	6254	6173	6075	5079	2130	509

Cholesterol Lowering Arm: Change in LDL-C, Apo-B, and CRP

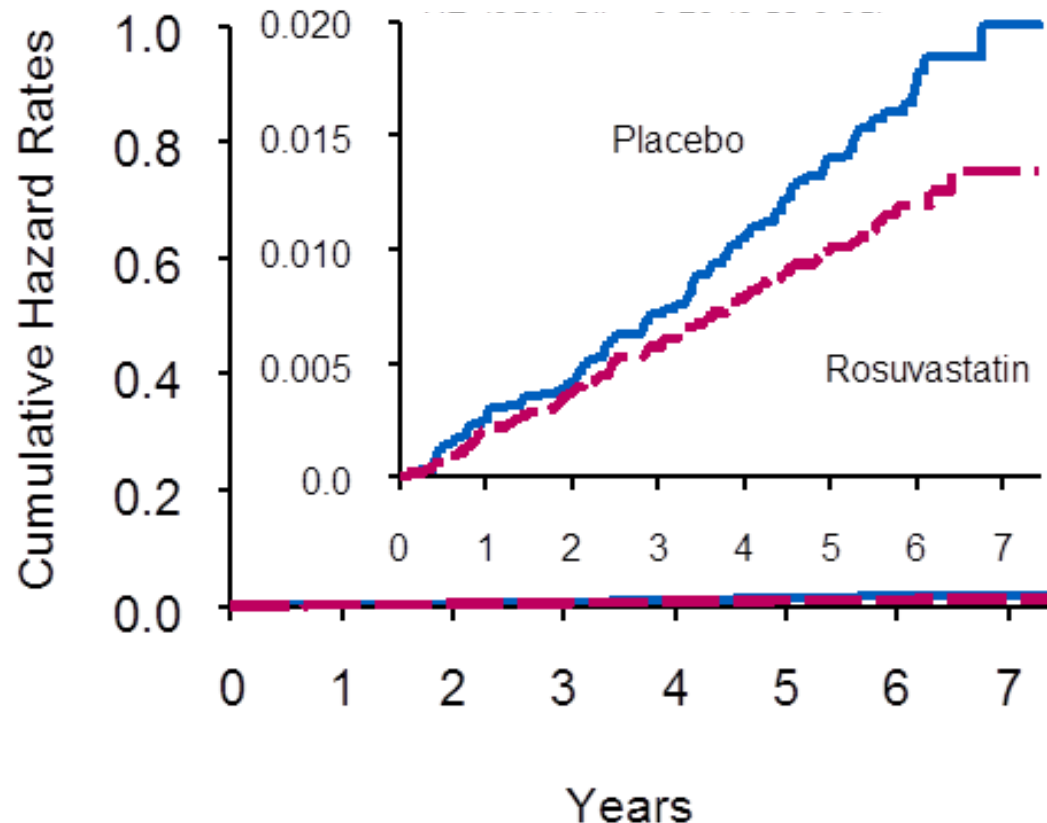


* P < 0.001

Effects of Rosuvastatin on Stroke



MI/stroke/CV death: HR (95% CI), 0.76 (0.64-0.91); p=0.002
stroke: HR (95% CI), 0.70 (0.52-0.95); p=0.02



No. at Risk

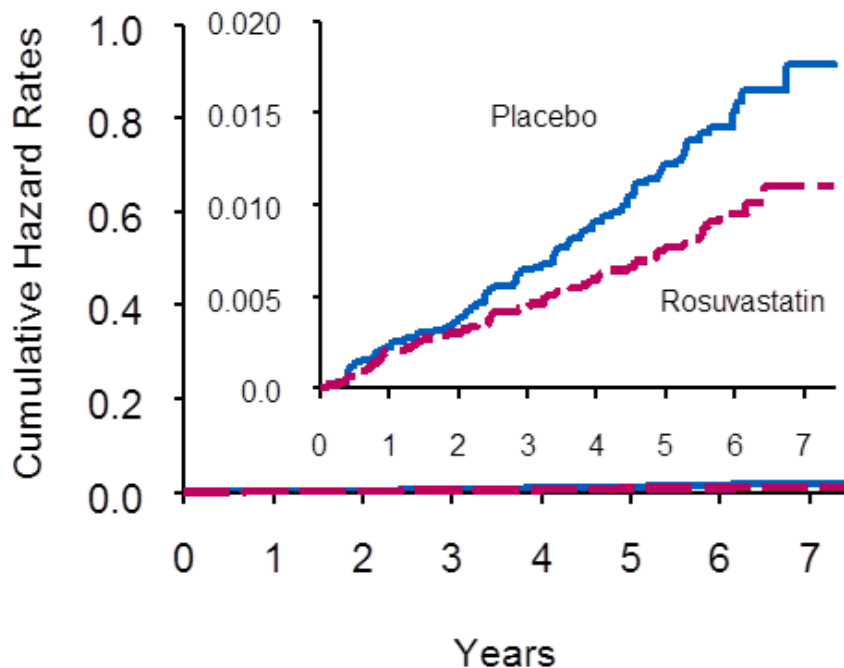
Rosuv	6361	6308	6259	6176	6069	5074	2132	534
Placebo	6344	6275	6210	6126	6010	5013	2094	505

Effects of Rosuvastatin on Stroke



Ischemic

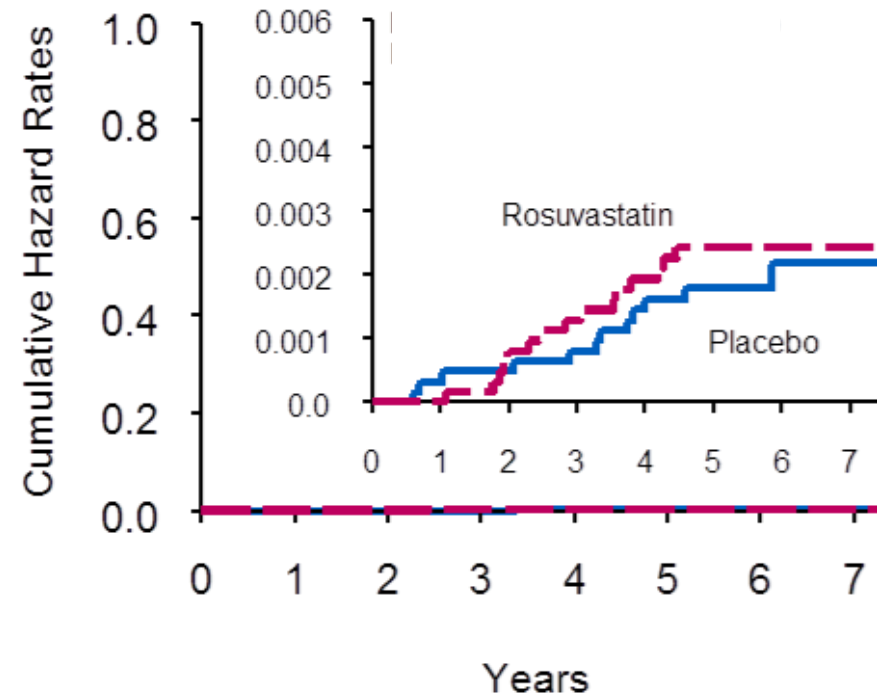
HR (95% CI), 0.63 (0.45-0.88); p=0.006



No. at Risk	0	1	2	3	4	5	6	7
Rosuv	6361	6308	6261	6181	6075	5082	2135	536
Placebo	6344	6276	6212	6128	6016	5018	2096	506

Hemorrhagic

HR (95% CI), 1.24 (0.58-2.65); p=0.57

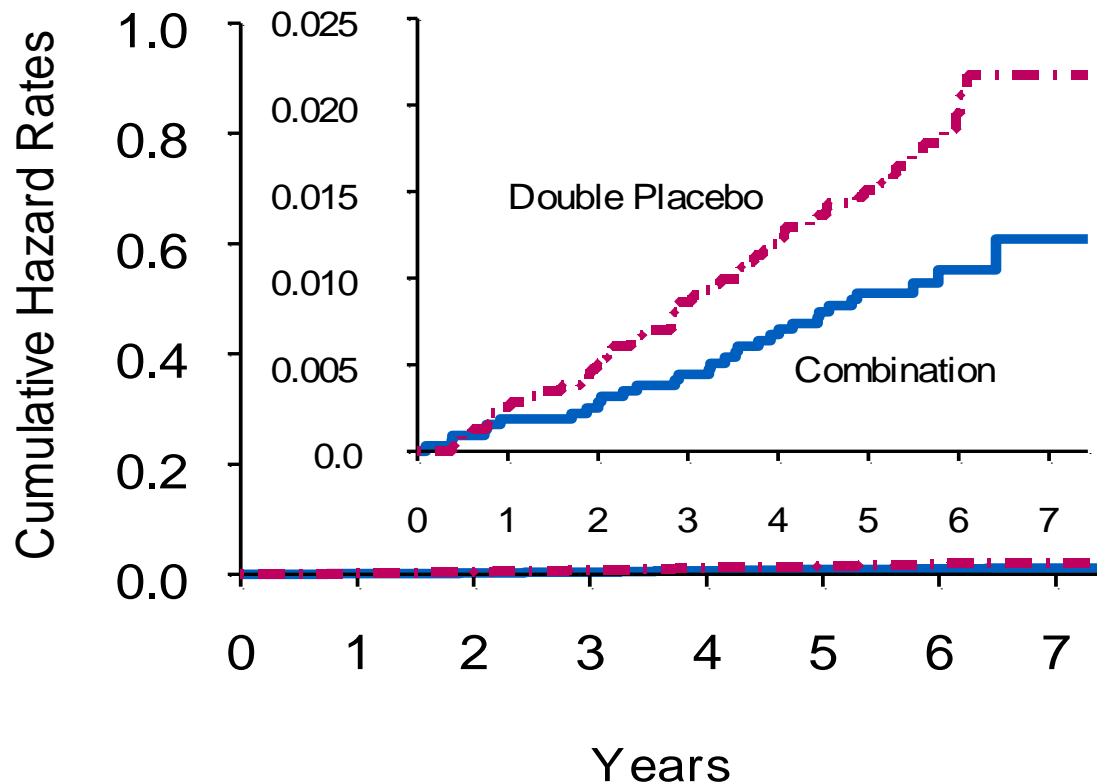


No. at Risk	0	1	2	3	4	5	6	7
Rosuv	6361	6318	6273	6196	6092	5096	2142	535
Placebo	6344	6288	6231	6157	6054	5063	2111	508

Effects of Combination on Stroke



MI/stroke/CV death: HR (95% CI), 0.71 (0.56-0.90); p=0.005
stroke: HR (95% CI), 0.56 (0.36-0.87); p=0.02



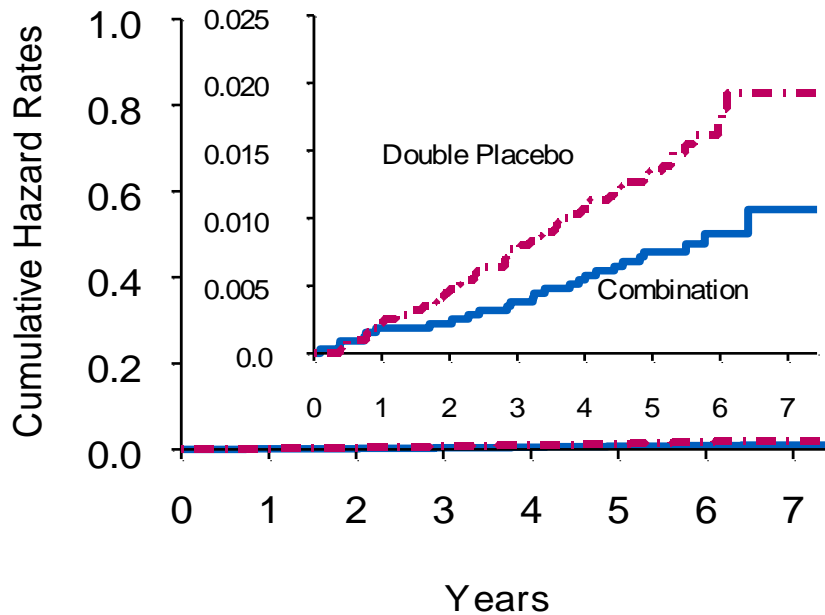
No. at Risk	0	1	2	3	4	5	6	7
Combination	3180	3155	3132	3088	3028	2538	1071	278
Dual Placebo	3168	3138	3107	3059	3000	2509	1054	249

Fatal or disabling stroke: HR (95% CI), 0.55 (0.32-0.95); p=0.03

Effects of Combination on Stroke

Ischemic

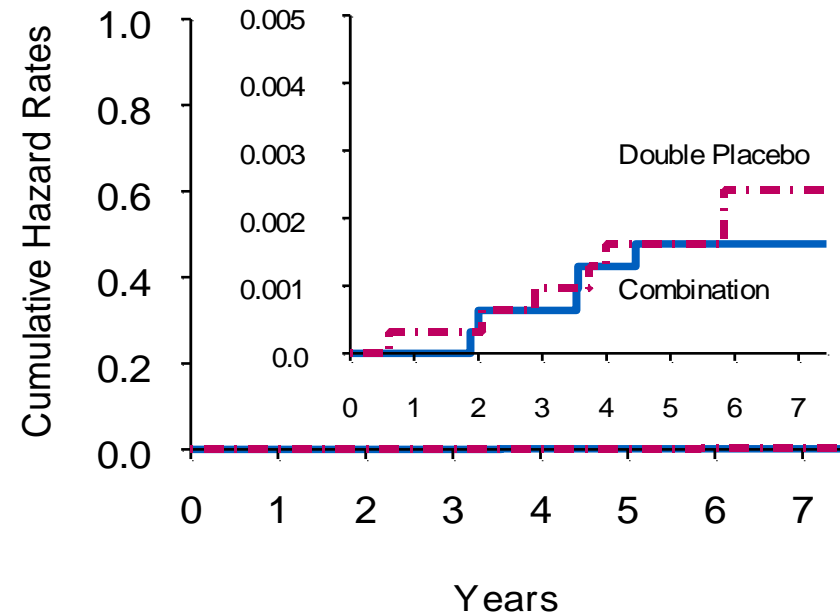
HR (95% CI), 0.53 (0.33-0.85); p=0.008



No. at Risk		Years							
		0	1	2	3	4	5	6	7
Combination	3180	3155	3132	3088	3029	2540	1072	279	
Dual Placebo	3168	3138	3107	3059	3002	2511	1054	249	

Hemorrhagic

HR (95% CI), 0.83 (0.25-2.72); p=0.75



No. at Risk		Years							
		0	1	2	3	4	5	6	7
Combination	3180	3160	3138	3099	3040	2551	1076	278	
Dual Placebo	3168	3144	3119	3076	3023	2534	1064	252	

HOPE-3 Stroke Results



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HEALTH THROUGH KNOWLEDGE

1. No statistically significant effect of candesartan 16 mg + HCTZ 12.5 mg daily
 - Trend for fewer events for both ischemic and hemorrhagic
2. 30% stroke reduction with rosuvastatin 10 mg daily
 - Larger effect than expected
 - Differed for ischemic vs. hemorrhagic strokes
3. 44% stroke reduction with combination
 - NNT for 1 year to prevent 1 stroke = 714

HOPE-3 Stroke Conclusions



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- Use of these well tolerated, simple to implement therapies has the potential to prevent 44% of first strokes
- The Public Health implications will require debate and consideration by guideline writers