

The **HY**pertension in the **V**ery **E**lderly **T**rial

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on behalf of the HYVET committees and
investigators**



ClinicalTrials.gov: NCT00122811



Disclosure Information

The Hypertension in the Very Elderly Trial – main results

Disclosure Information...

The following relationships exist related to this presentation:

<i>Dr . Nigel Beckett MD</i>	}	<i>University Salaries supported by</i>
<i>Dr. Ruth Peters PhD</i>		<i>Servier/British Heart Foundation</i>
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Blood Pressure & The Very Elderly (aged 80 or more)

- Epidemiologic population studies suggest better survival with higher levels of blood pressure
- Clinical trials recruited too few.
- Meta-analysis (n=1670) (Gueyffier et al. 1997)
 - 36% reduction in the risk of stroke (BENEFIT)
 - 14% (p=0.05) increase in total mortality (RISK)
- Hypertension in the Very Elderly Trial (HYVET) pilot results (n=1273) similar to meta-analysis (Bulpitt et al. 2003)

The Trial:

International, multi-centre, randomised double-blind placebo controlled

Inclusion Criteria:

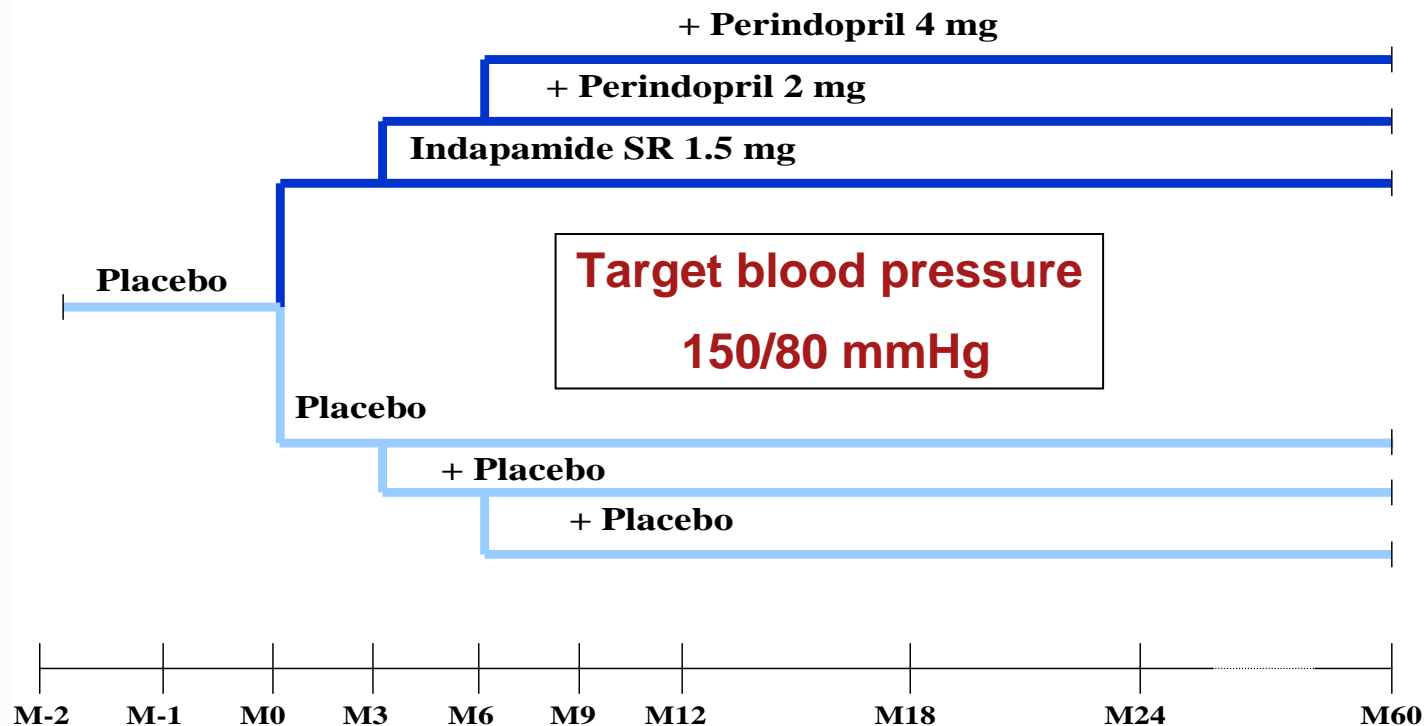
Aged 80 or more,
Systolic BP; 160 -199mmHg
+ diastolic BP; <110 mmHg,
Informed consent

Exclusion Criteria:

Standing SBP < 140mmHg
Stroke in last 6 months
Dementia
Need daily nursing care

Primary Endpoint:

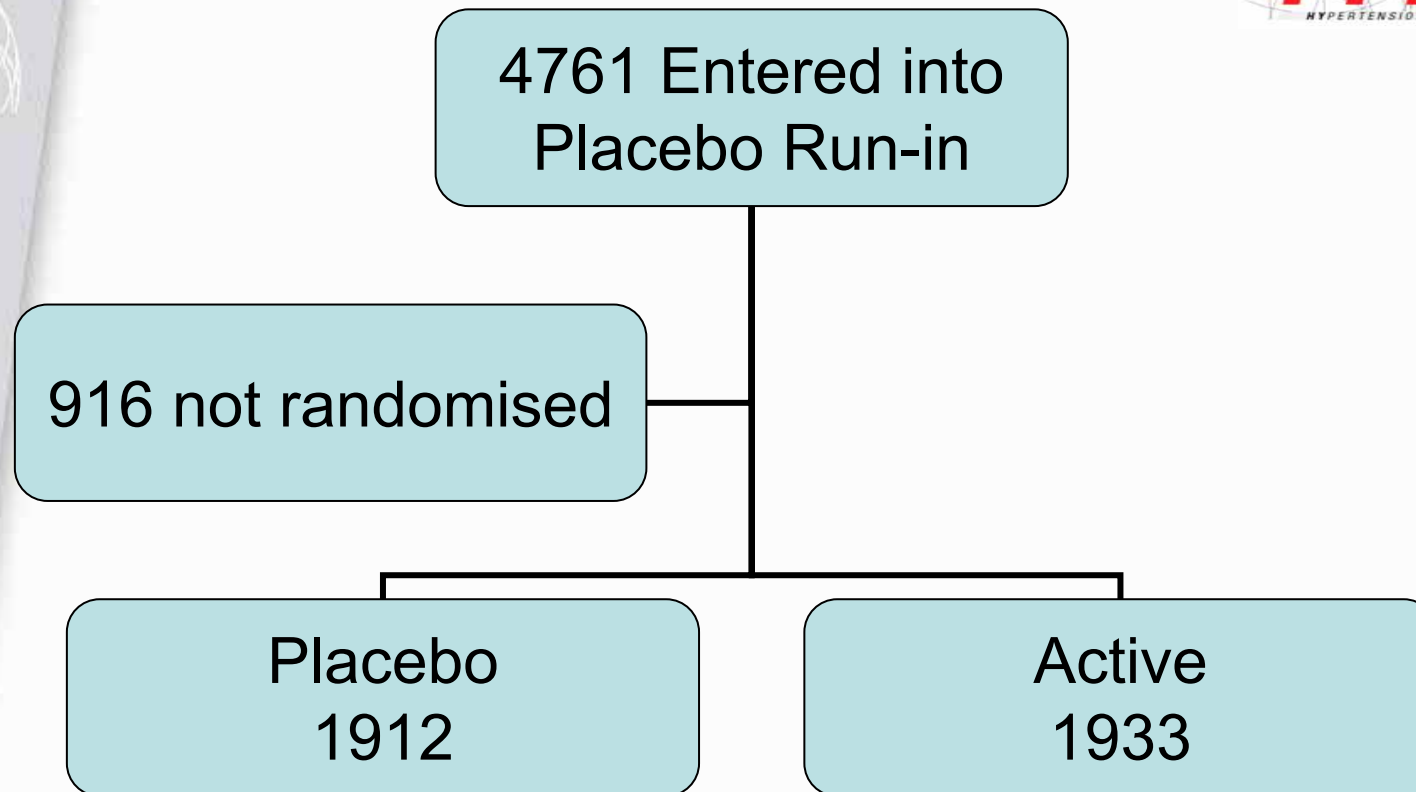
All strokes (fatal and non-fatal)





Statistical Analysis

- Numbers based on a 35% reduction in all strokes
 - $\alpha = 0.01$ $\beta = 0.1$
 - Stroke event rate of 40/1000
 - 10,500 patient-years of follow-up required
- 3 interim analyses planned
 - Stopped at 2nd as decrease in stroke and all-cause mortality
- Independent Steering, Ethics and Data Monitoring Committees
- Independent Endpoints Committee (blinded evaluation)
- ITT and PP analyses
- Other main trial endpoints: total mortality, cardiovascular mortality, cardiac mortality, stroke mortality, heart failure



- 3845 randomised; Western Europe (86) Eastern Europe (2144), China (1526), Australasia (19), Tunisia (70)
- At end of trial; 1882 still in double blind, 17 vital status not known, 220 in open follow-up

Baseline data



	Placebo (n= 1912)	Active (n= 1933)
Age (years)	83.5	83.6
Female	60.3%	60.7%
<u>Blood Pressure:</u>		
Sitting SBP (mmHg)	173.0	173.0
Sitting DBP (mmHg)	90.8	90.8
Orthostatic Hypotension [‡]	8.8%	7.9%
Isolated Systolic Hypertension	32.6%	32.3%

[‡] Fall in SBP \geq 20mmHg and/or fall in DBP \geq 10mmHg

Baseline Data

(Previous Cardiovascular History)

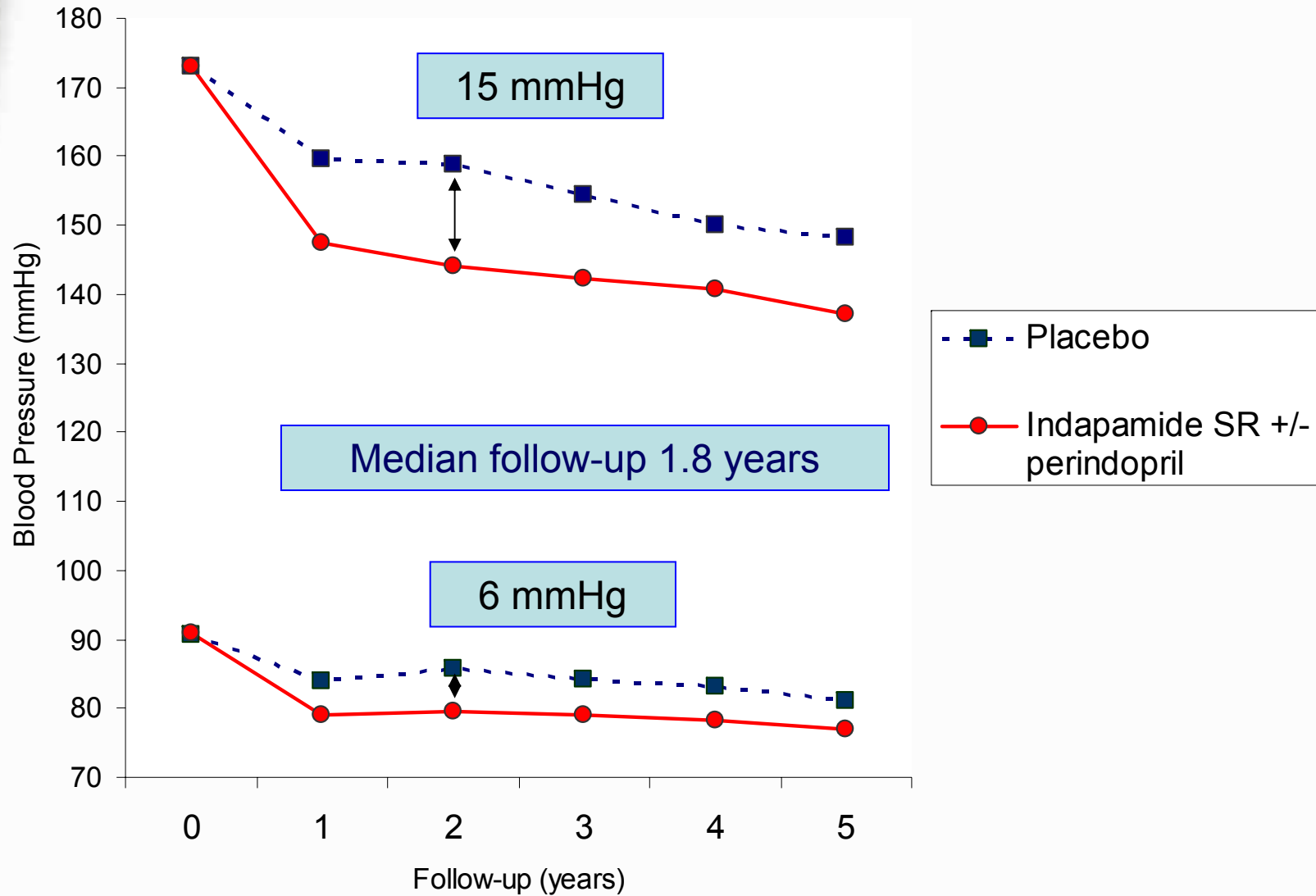
	Placebo (%)	Active (%)
Cardiovascular disease	12.0	11.5
Known Hypertension	89.9	89.9
Anti-hypertensive treatment	65.1	64.2
Stroke	6.9	6.7
Myocardial Infarction	3.2	3.1
Heart Failure	2.9	2.9

Baseline data

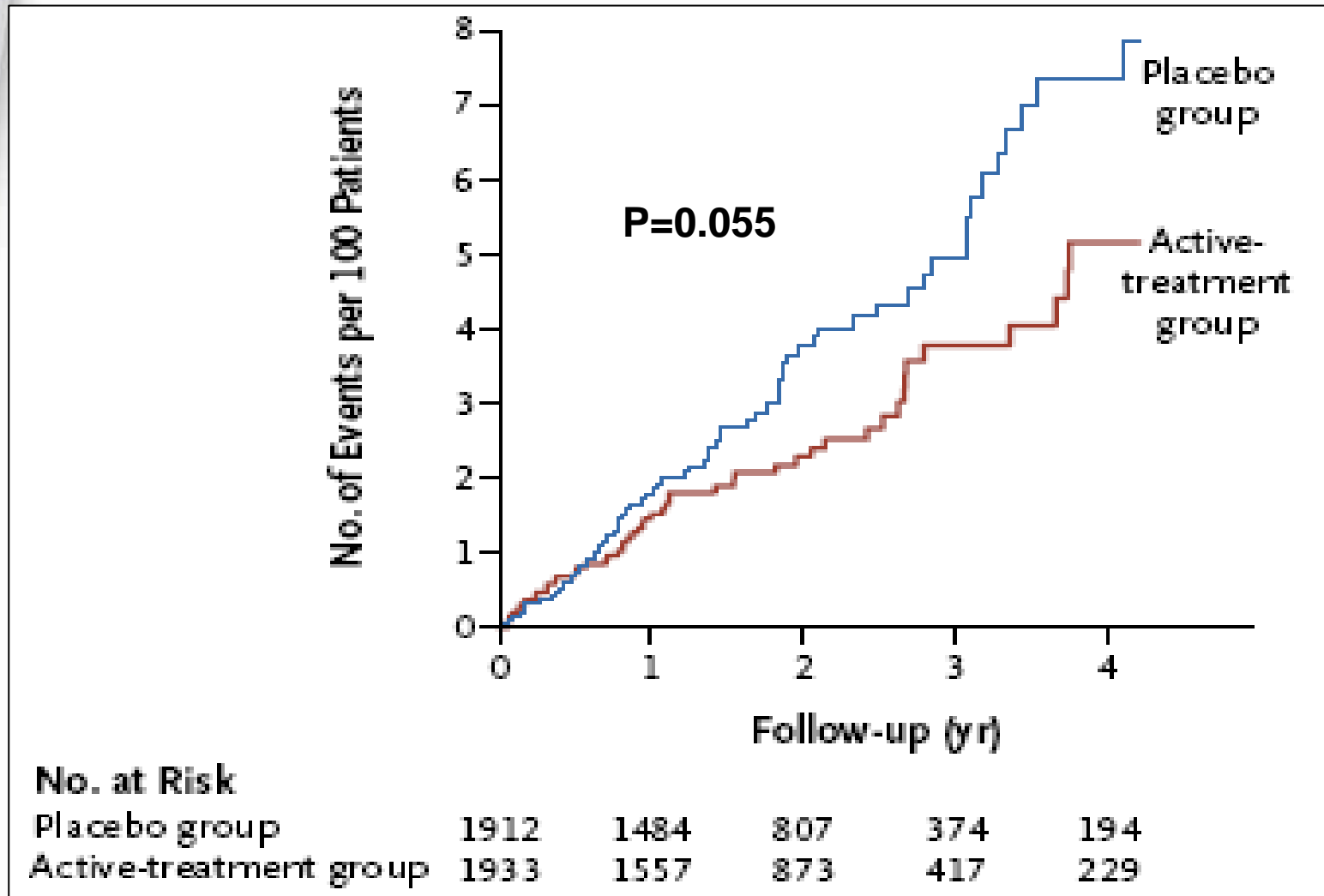
(Cardiovascular Risk factors)

	Placebo	Active
Current smoker	6.6%	6.4%
Diabetes (Known DM/ DM treatment/glucose>11.1mmo/l)	6.9%	6.8%
Total cholesterol (mmol/l)	5.3	5.3
HDL Cholesterol (mmol/l)	1.35	1.35
Serum Creatinine ($\mu\text{mol/l}$)	89.2	88.6
Uric acid ($\mu\text{mol/l}$)	279	280
Body Mass Index (kg/m^2)	24.7	24.7

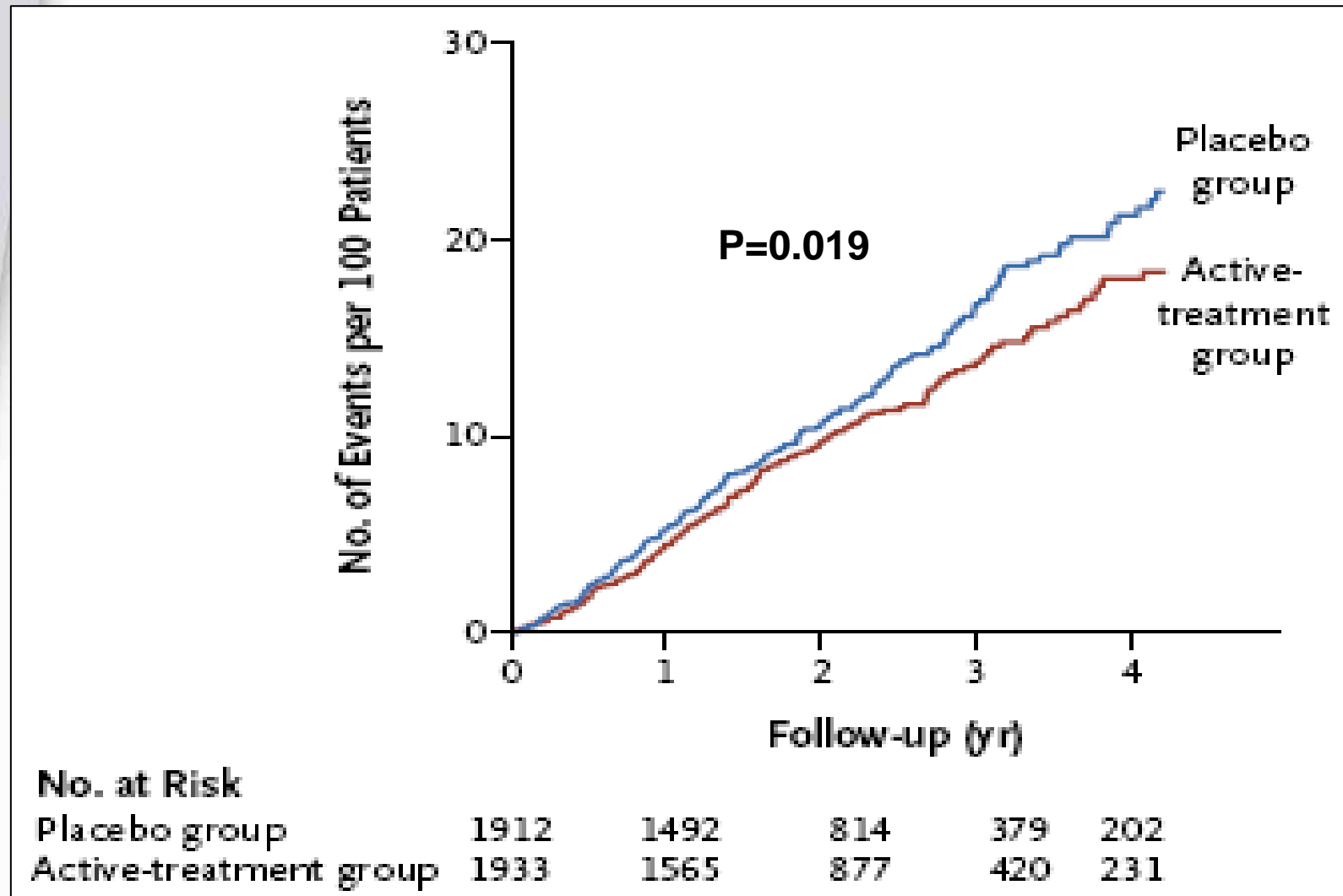
Blood pressure separation



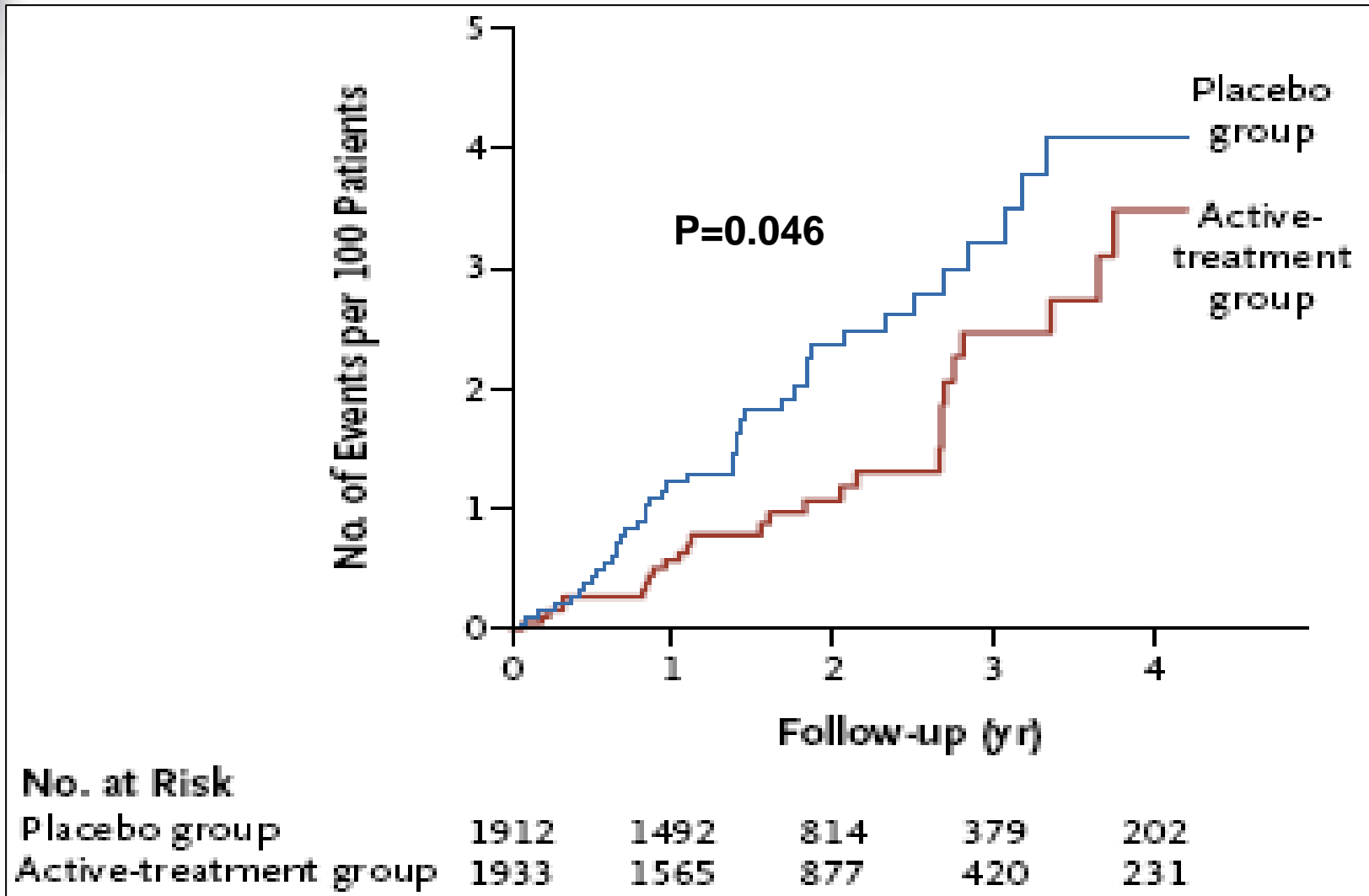
All stroke (30% reduction)



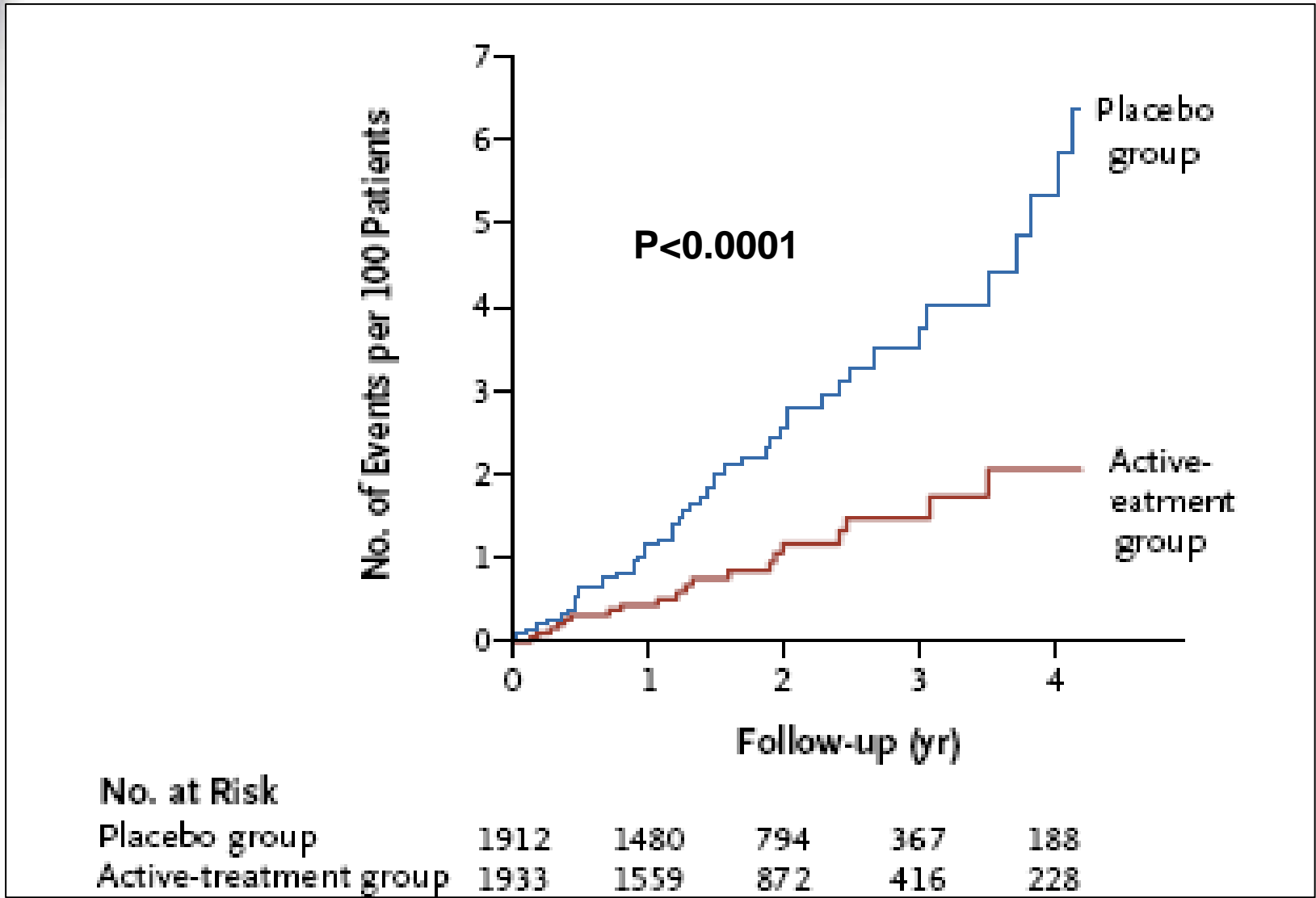
Total Mortality (21% reduction)



Fatal Stroke (39% reduction)



Heart Failure (64% reduction)





ITT – Summary

All Stroke

Stroke Death

All cause mortality

NCV/Unknown death

CV Death

Cardiac Death

Heart Failure

CV events



HR	95% CI
0.70	(0.49, 1.01)
0.61	(0.38, 0.99)
0.79	(0.65, 0.95)
0.81	(0.62, 1.06)
0.77	(0.60, 1.01)
0.71	(0.42, 1.19)
0.36	(0.22, 0.58)
0.66	(0.53, 0.82)

Per-Protocol

	HR	95% CI	P
All stroke	- 34%	0.46 - 0.95	0.025
Total mortality	- 28%	0.59 - 0.88	0.001
Fatal stroke	- 45%	0.33 - 0.93	0.021
Cardiovascular mortality	-27%	0.55-0.97	0.029
Heart failure	-72%	0.17-0.48	<0.001
Cardiovascular events	- 37%	0.51-0.71	<0.001



Biochemical Changes from Baseline (2 year cohort)

- In 2 year cohort there were no significant differences between the groups with regard to change in serum....
 - Potassium
 - Uric acid
 - Glucose
 - Creatinine
- At 2 years 73.4% on combination treatment in active group (85.2% placebo)

Safety

Reported serious adverse events (after randomisation)

- 448 in the placebo group vs 358 in active
($p=0.001$)
- Only 5 categorised by the local investigator
possible SADR (3 in placebo group, 2 being
in active)



Conclusions



- Antihypertensive treatment based on indapamide (SR) 1.5mg (\pm perindopril) reduced stroke mortality and total mortality in a very elderly cohort.
- NNT (2 years) = 94 for stroke and 40 for mortality
- Large and significant benefit in reduction of heart failure events and for combined endpoint of cardiovascular events
- Benefits seen early
- Treatment regime employed was safe



Cautions



- Subjects recruited generally healthier than those within a general population
- Benefit from treating systolic pressures less than 160mmHg requires further research
- Target blood pressure was 150/80 mmHg
 - Benefit from lower targets still needs to be established

- Professor C. Bulpitt (Principal investigator) & Professor A.E. Fletcher (Co-investigator)
- The HYVET co-ordinating office
- The members of the HYVET Committees
 - **Steering Committee** (Dr. T. McCormack, Prof. J. Potter, Prof. B.G. Extremera, Prof. P. Sever, Prof. F. Forette, Assoc. Prof. D. Dumitrascu, Prof. C. Swift, Prof. J. Tuomilehto)
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 - **Ethics Committee** (Prof. R. Fagard, Prof. J. Grimley Evans, Dr. B. Williams)
 - **Dementia Diagnosis Committee** (Prof. J. Tuomilehto, Dr R. Clarke, Dr I. Walton, Dr C. Ritchie, Dr A. Waldman)
- All the HYVET investigators
- All the HYVET national co-ordinators
 - R. Warne/I. Puddey (*Australia*), H. Celis (*Belgium*) V. Stoyanovsky (*Bulgaria*), L. Liu (*China*), R Antikainen (*Finland*), F. Forette (*France*), J. Duggan (*Ireland*), C.Anderson (*New Zealand*), T. Grodzicki (*Poland*), A. Belhani (*Tunisia*) C. Clara (*Portugal*), D. Dumitrascu (*Romania*), Y. Nikitin (*Russia*), C. Rajkumar (*UK*)
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