

# Relationship Between Brain and Cardiac Silent Damage in Hypertension

**Antonio Coca, MD, PhD**

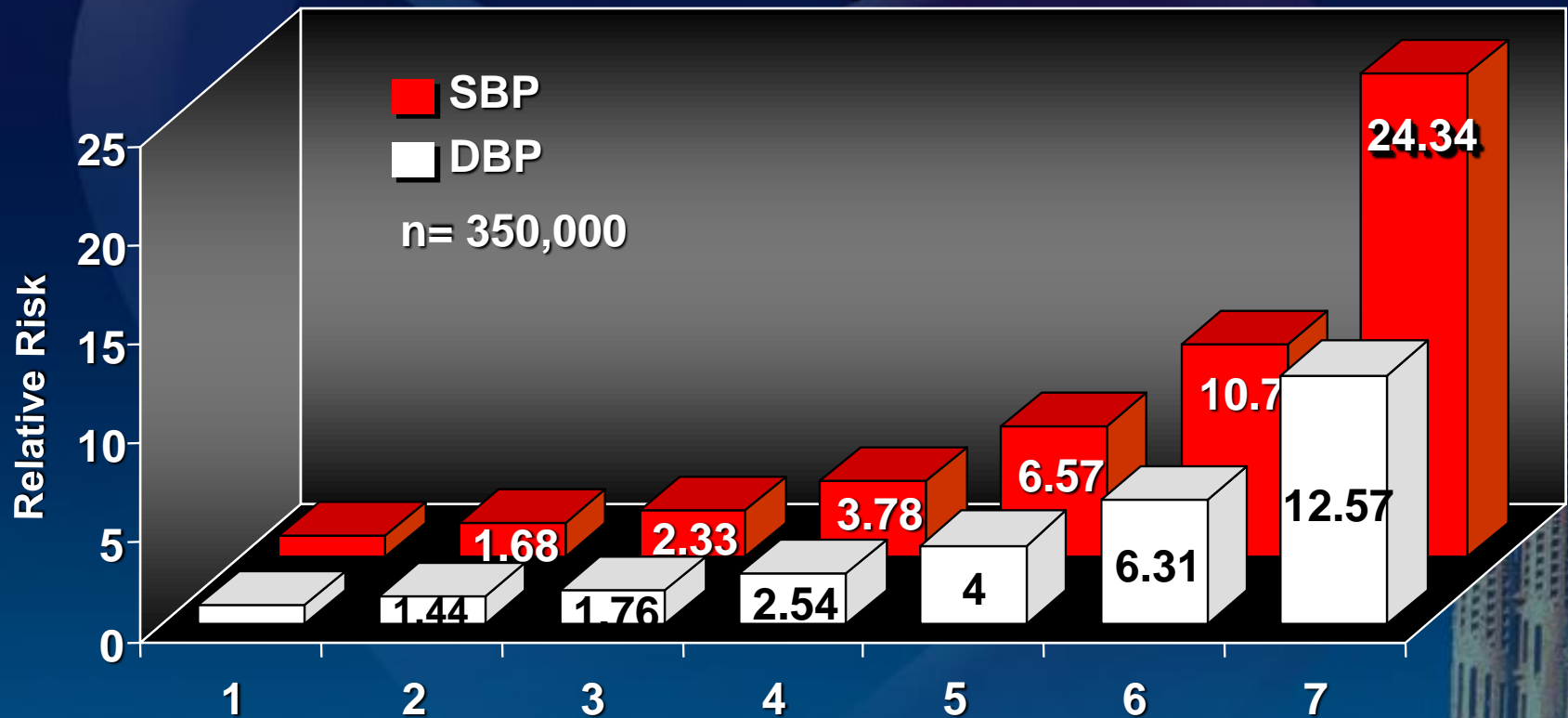
*Hypertension Unit. Hospital Clinic. Instituto de  
Investigaciones Biomédicas August Pi i Sunyer (IDIBAPS).  
University of Barcelona, Spain*

*1st International Meeting on Nitric Oxide  
Barcelona, May 10th, 2003*



# Stroke Mortality and Blood Pressure

Relative Risk associated with Systolic and Diastolic BP

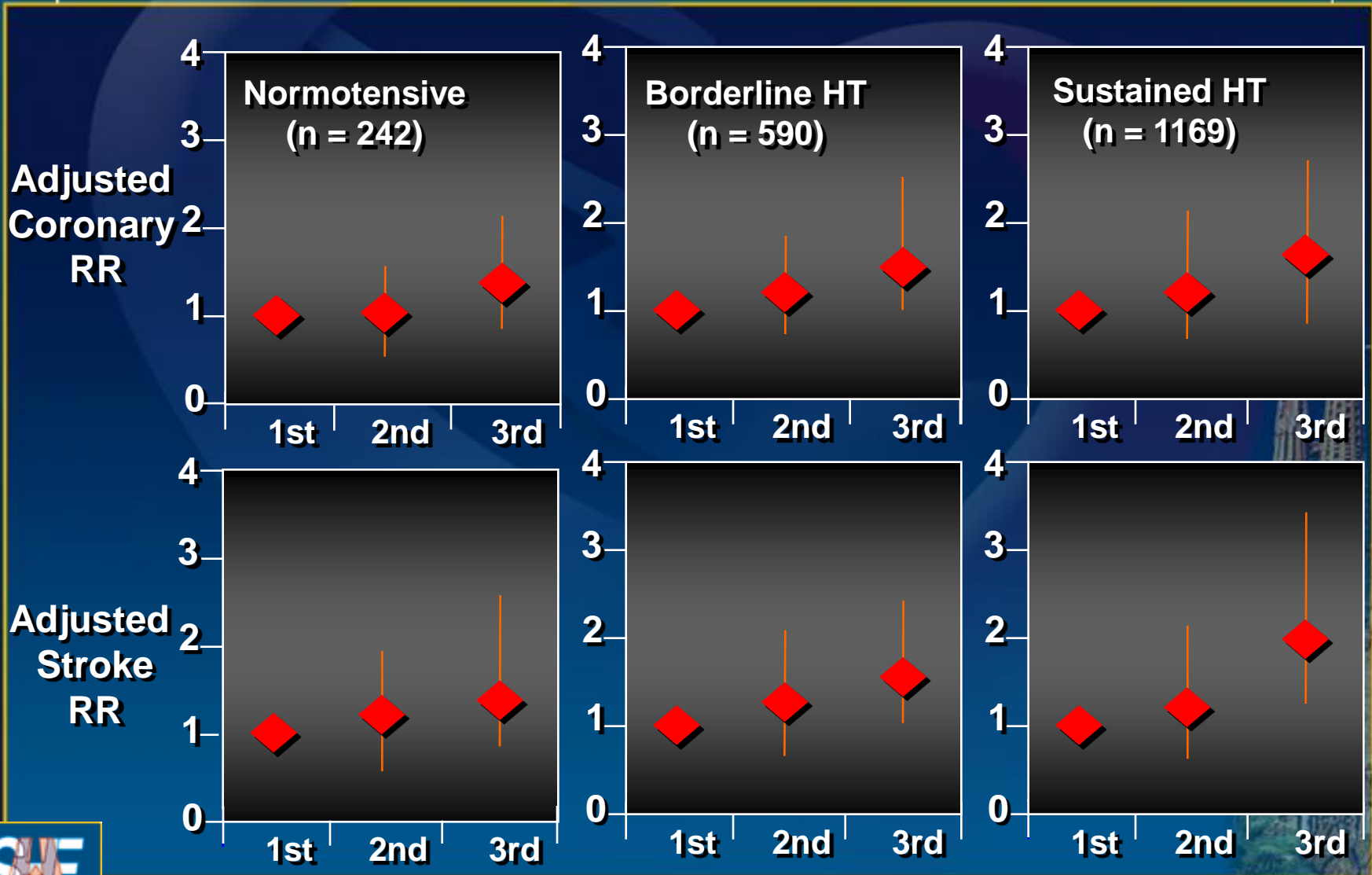


SBP	<120	120-129	130-139	140-159	160-179	180-209	≥ 210
DBP	<80	80-84	85-89	90-99	100-109	110-119	≥ 120



3

# Coronary and Stroke Mortality according to Tertiles of Pulse Pressure



## Stroke and Myocardial infarction in Large Prospective Hypertension Trials

### 11 STUDIES

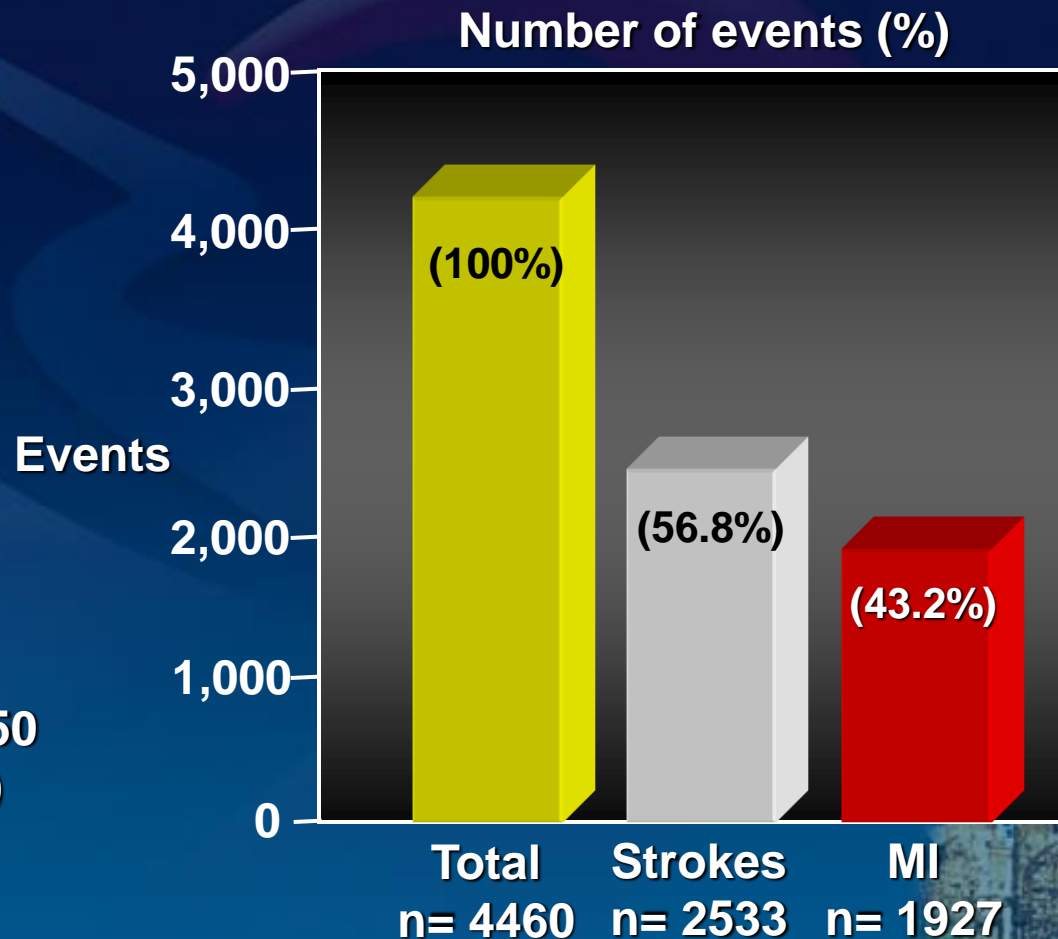
Publication 1991-2000

STOP-1; SHEP  
STONE; SYST-EUR  
SYST-CHINA  
HOT; CAPPP  
STOP-2; NICS  
NORDIL; INSIGHT

Patients randomized: 59,550

Total strokes: 2533 (56.8%)

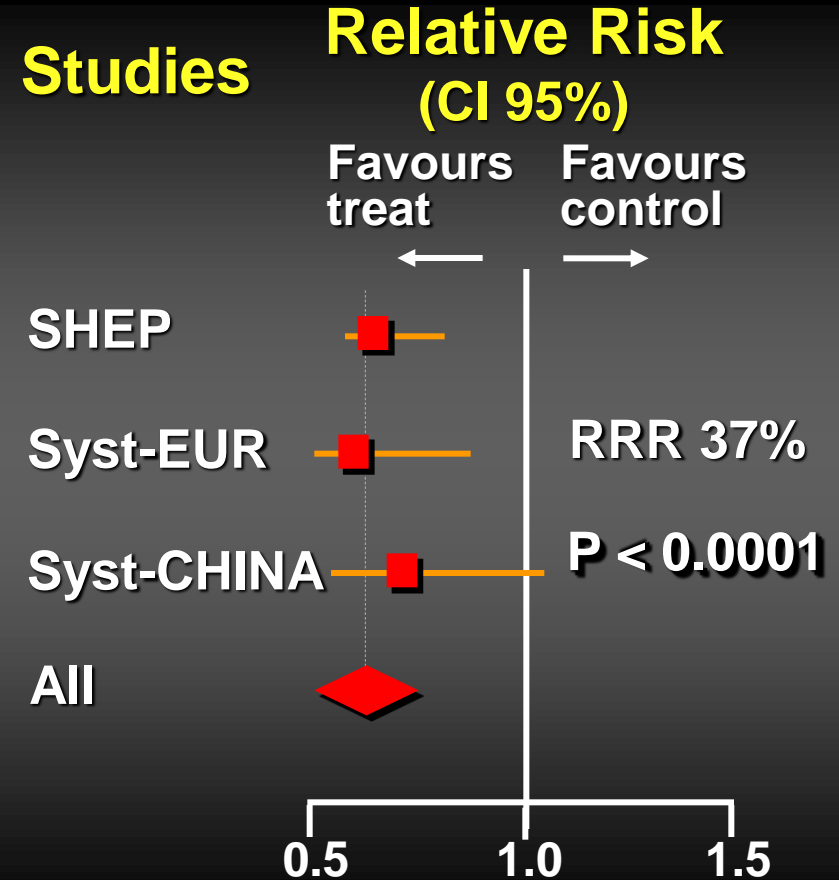
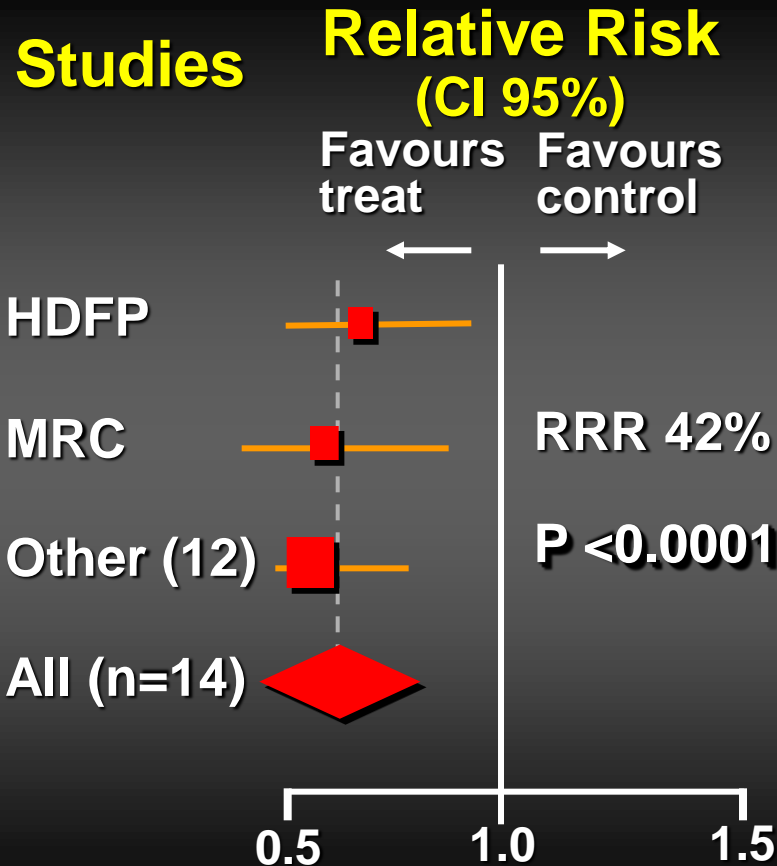
Total MI: 1927 (43.2%)



# Stroke and Antihypertensive Treatment

Sustained Reduction of 5-6 mmHg  
DBP for 5 years

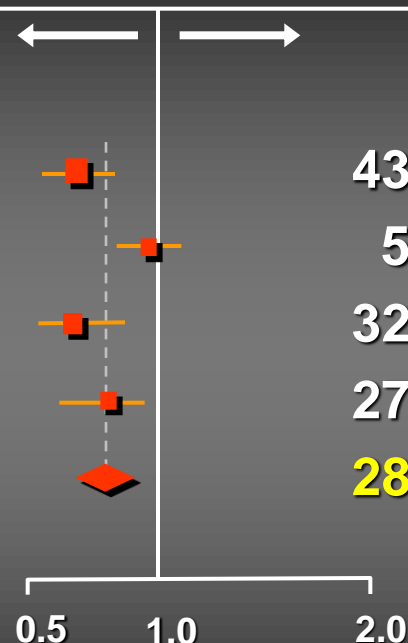
Sustained Reduction of 10-12 mmHg  
SBP for 3-5 years



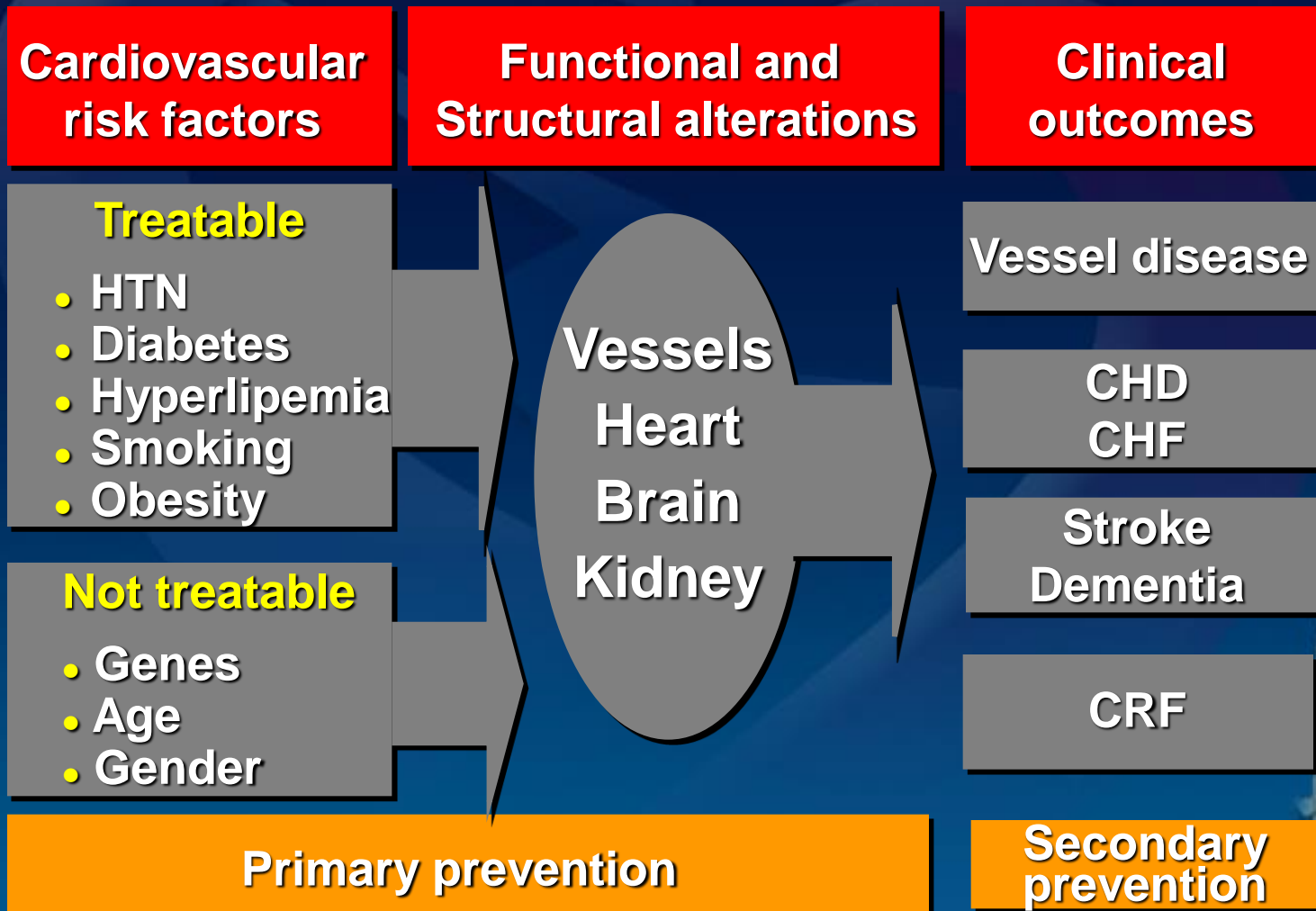
# PROGRESS Study

## Lowering of BP and Secondary Prevention of Stroke

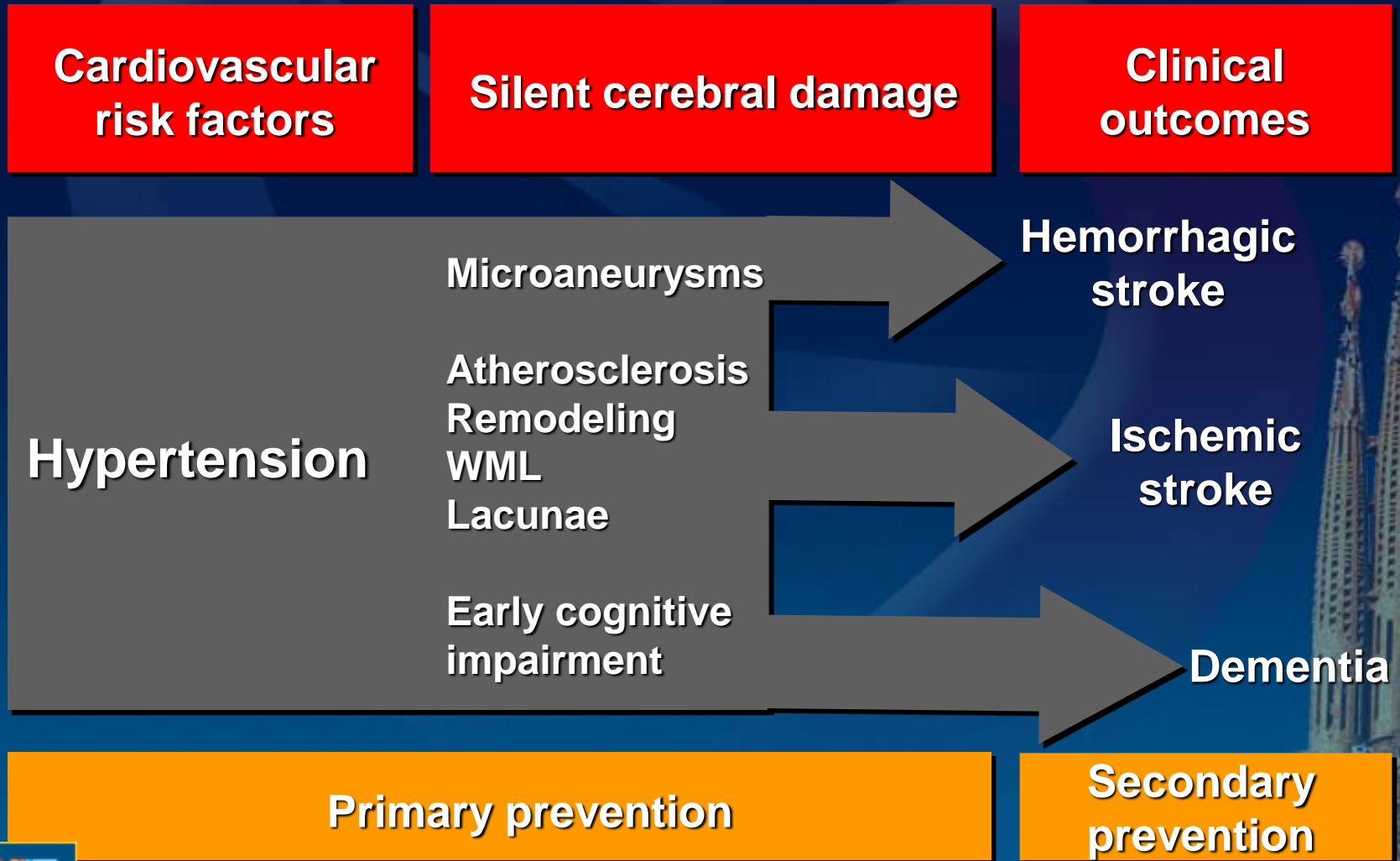
Stroke Prevention	Treat (n= 2051)	Placebo (n= 3054)	Favours treat	Favours placebo	RR (CI 95%) reduction
Combination	150	255	←	→	43% (30 - 54)
Monotherapy	157	165	←	→	5% (-19 - 23)
Hypertensive	163	235	←	→	32% (17 - 44)
Non-Hypertensive	144	185	←	→	27% (8 - 42)
<b>Total</b>	<b>307</b>	<b>420</b>	←	→	<b>28% (17 - 38)</b>



# Pathophysiology of Cardiovascular Damage



# Silent Cerebral Damage in Hypertension





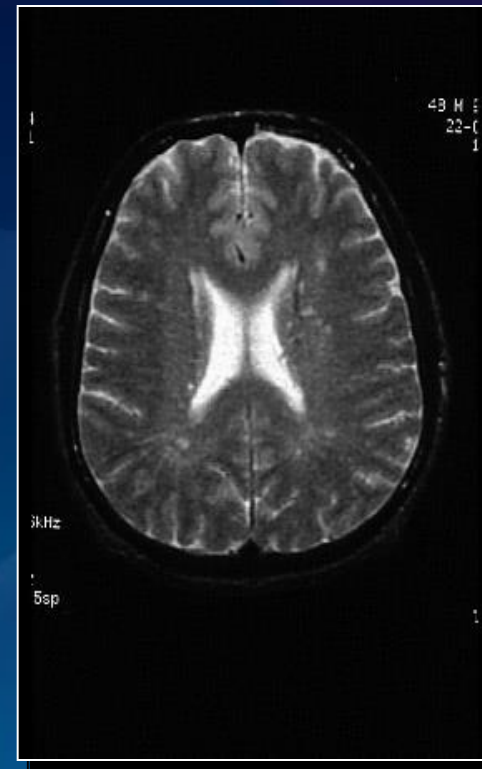
# Silent Cerebral Damage in Hypertension

## White Matter Lesions

Normal



Confluent periventricular hyperintensities



Brain MRI: axial plane T<sub>2</sub> - weighted image

## Silent Cerebral White Matter Lesions Related to Age in the Rotterdam Study

Age (years)	Subjects	White Matter Lesions in MRI (%)		
		No / Mild	Moderate	Severe
65-69	36	89	8	3
70-74	23	78	17	4
75-79	26	73	19	8
80-84	26	46	27	27

# Silent Cerebral White Matter Lesions and Hypertension

## The ARIC Study (Atherosclerosis Risk in Communities)

### Prevalence of Silent Cerebral WML

	No lesions (%) (n= 1673)	WML (%) (n= 236)
Normotensive (n= 975)	92.4	7.6
Hypertensive (n= 934)	83	17
Untreated (n= 204)	85	15
Treated controlled (n= 425)	86	14
Treated uncontrolled (n= 303)	76	24

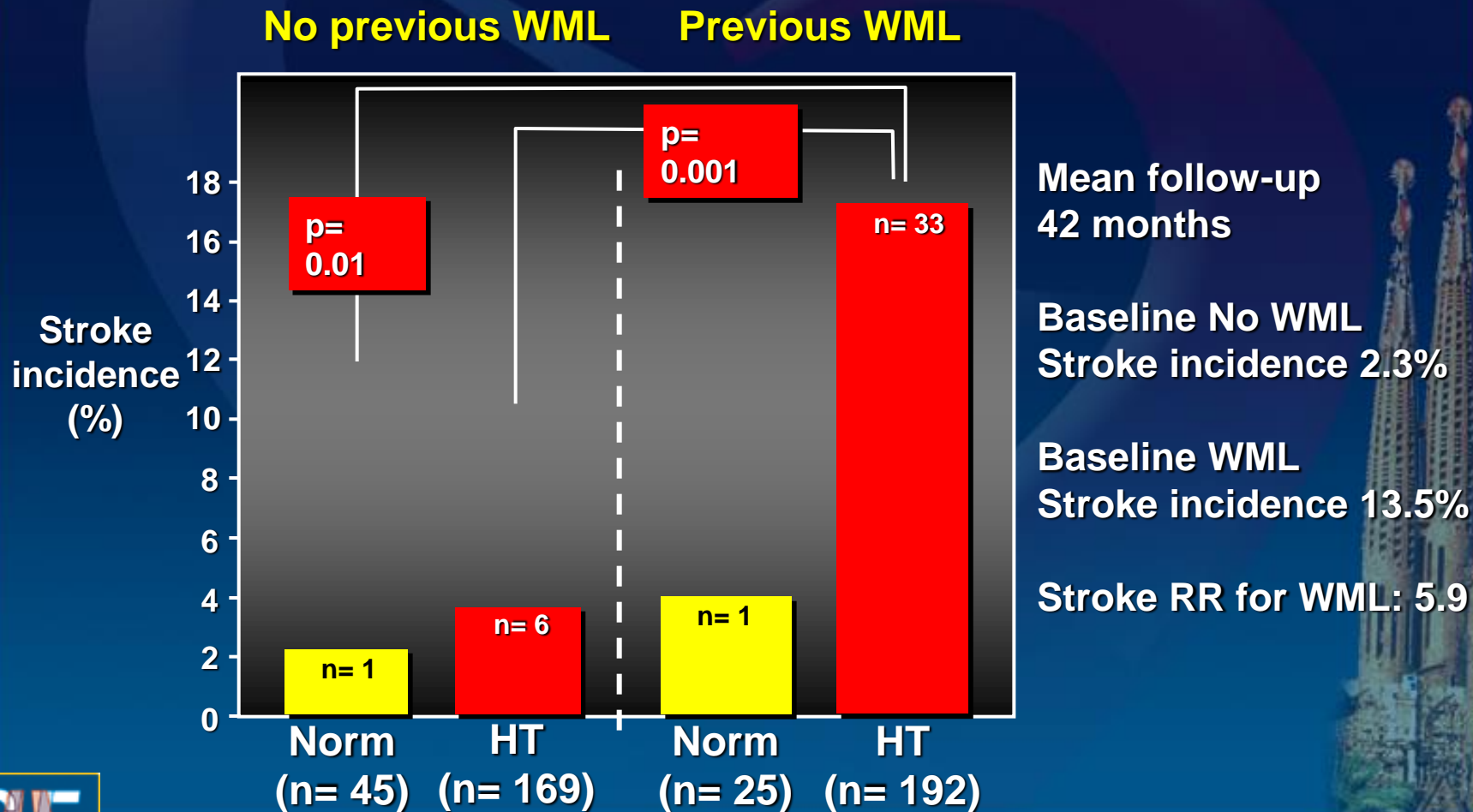
■ p < 0.001 \*Age 55 - 72 años

\*50% African-American, 40% male



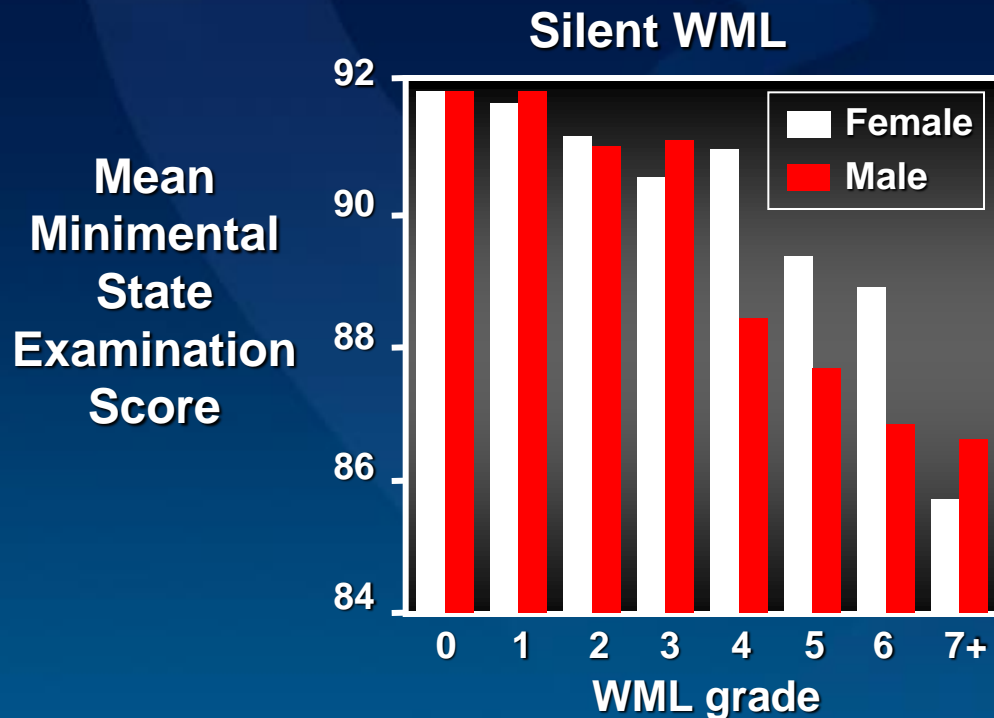
## Stroke and White Matter Lesions in Hypertension

### Stroke Incidence and baseline White Matter Lesions



# Silent Cerebral White Matter Lesions and Cognitive Impairment

## The Cardiovascular Health Study



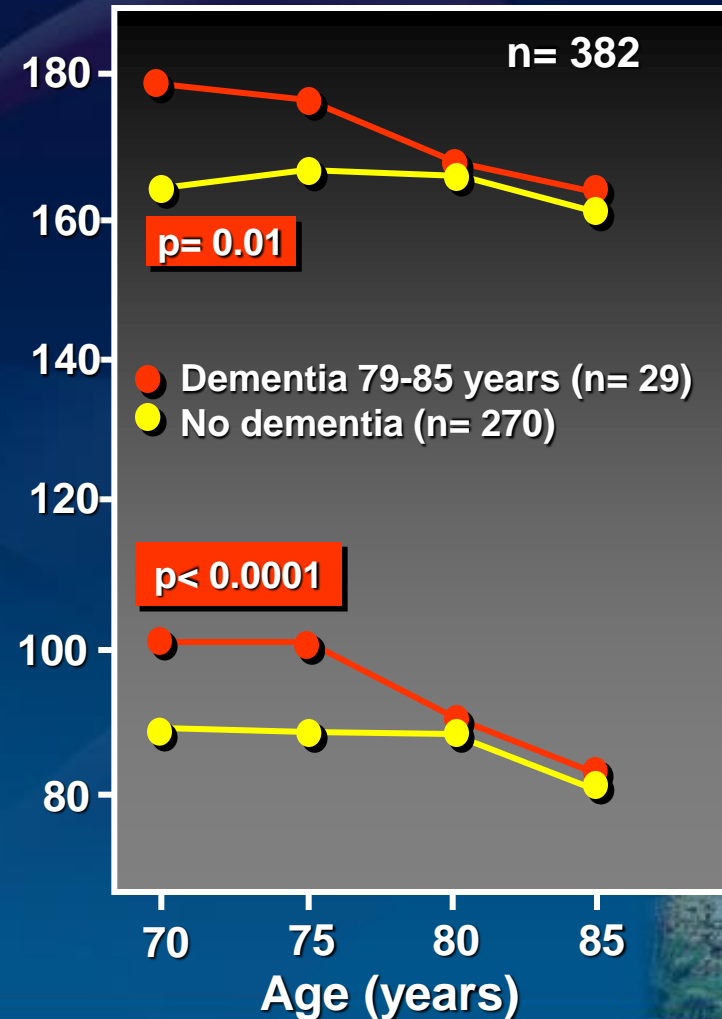
- 1107 subjects > 65 years (33.5%) with WML
- 2194 subjects >65 years (66.5%) without WML

# Dementia and Blood Pressure

## The Göteborg Study (follow-up 15 years)

Blood Pressure at  
age 70 years related  
to the onset of  
dementia at age  
79 - 85 years

BP  
(mmHg)



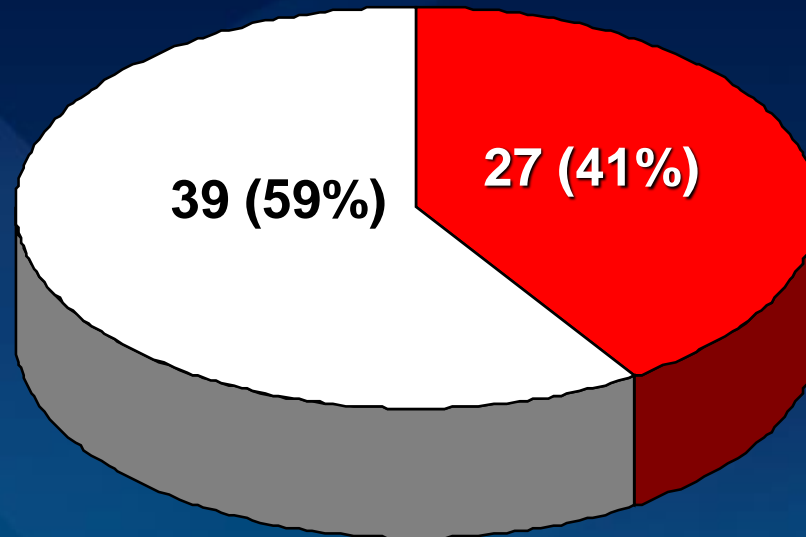
# Silent Cerebral Damage in Hypertension

## Study Patients

- 66 untreated, mild-to-moderate HT (41m, 25w) aged 50-60 years
- No clinical evidence of cerebral or cardiovascular disease
- Diabetes, daily alcohol intake > 30g, or carotid atheromatosis with stenosis > 50% excluded
- Tests performed:
  - Brain MRI scanning
  - 24-h ABPM
  - Echocardiography
  - Cognitive function test

# Silent Cerebral Damage in Hypertension

White Matter Lesions (grades 1- 2)  
n= 66



■ WML   ■ No WML



## Silent Cerebral Damage in Hypertension

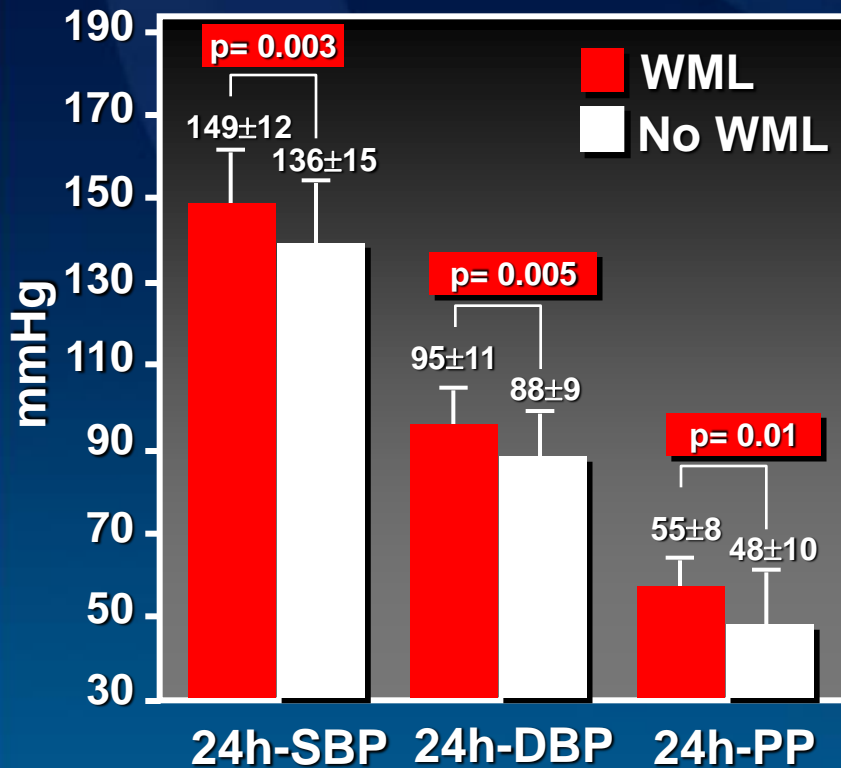
### Anthropometric and Clinical Characteristics of Patients

Parameter	WML (n= 27)	No WML (n= 39)	p
Gender (M/F)	16/11	25/14	0.033
Age (years)	55.4 ± 4.8	53.7 ± 3.5	n.s.
Smokers (%)	22.2	30.8	n.s.
BMI (kg/m ) <sup>2</sup>	29.5 ± 4.0	28.6 ± 2.9	n.s.
Office SBP	171.5 ± 12.8	161.0 ± 13.2	0.01
Office DBP	101.2 ± 6.7	97.5 ± 6.2	0.02
Office PP	70.6 ± 8.0	63.5 ± 8.9	0.01

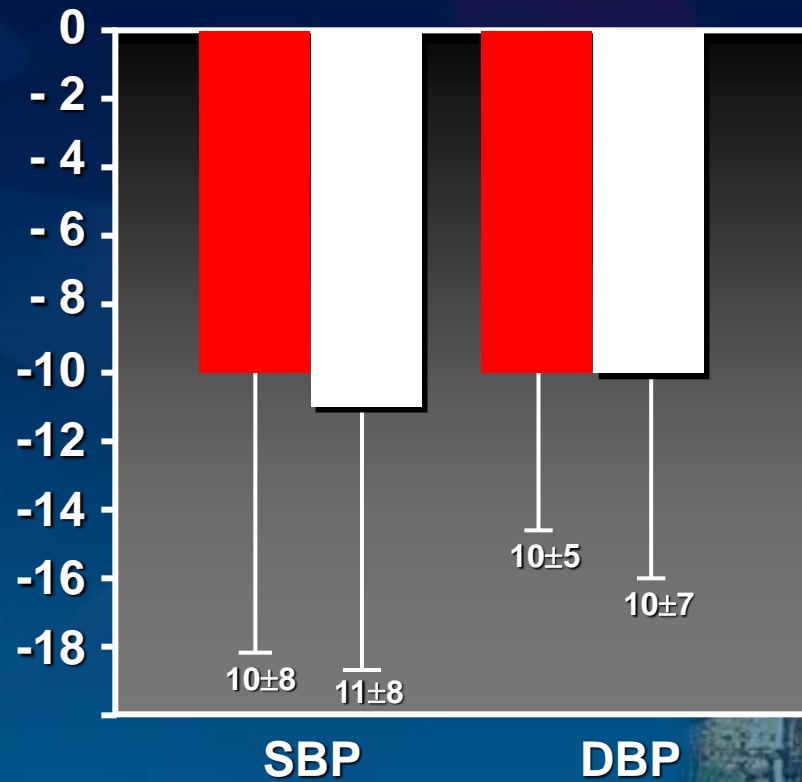
# Silent Cerebral Damage in Hypertension

## Silent WML and 24-h Ambulatory Blood Pressure

### 24-hours ABPM

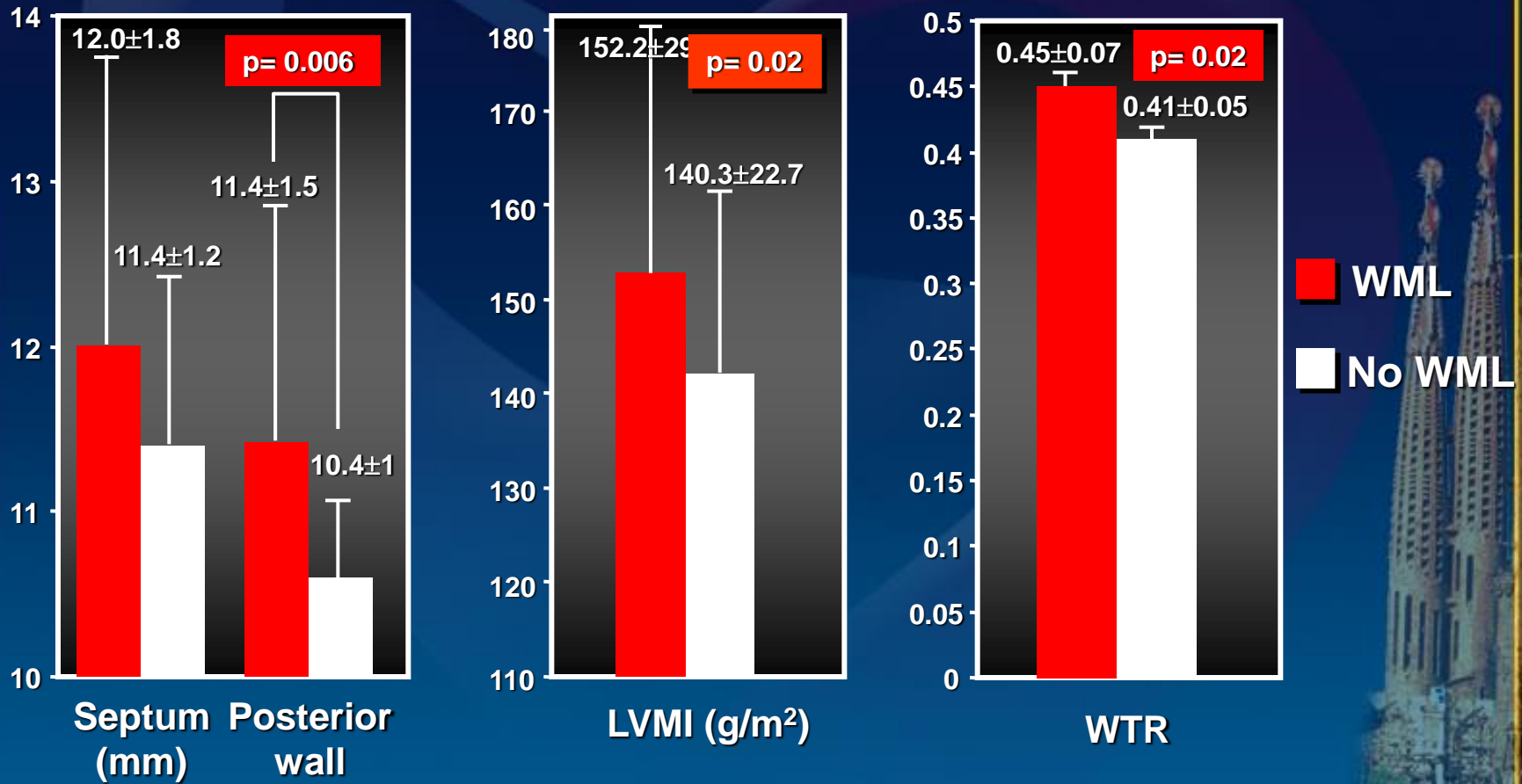


### Nocturnal reduction



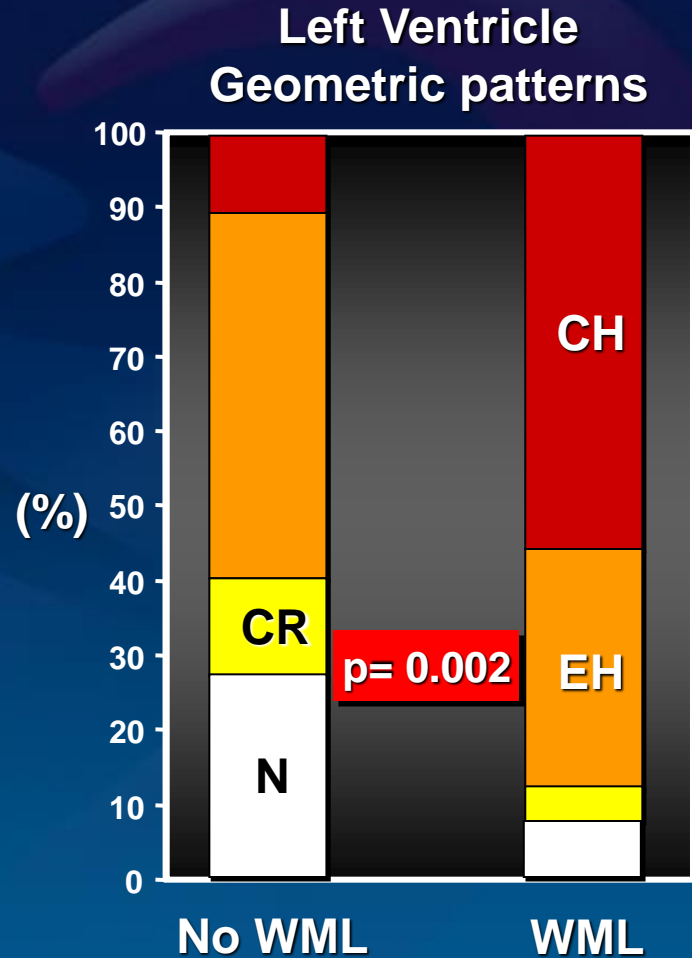
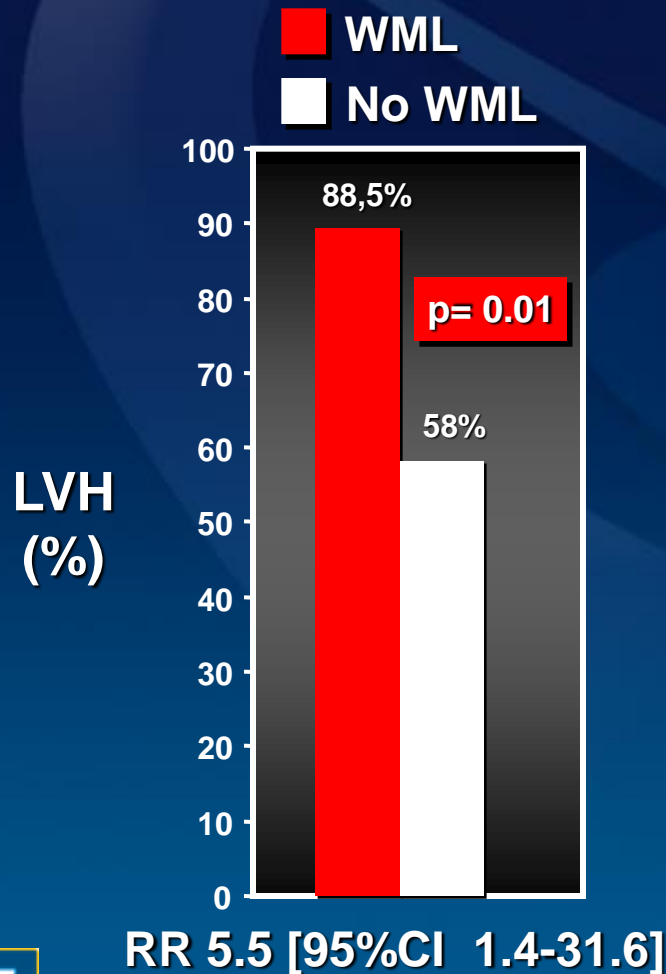
# Silent Cerebral Damage in Hypertension

## Echocardiography



# Silent Cerebral Damage in Hypertension

## Echocardiography



# Silent Cerebral Damage in Hypertension

Echocardiography

## Left Ventricle Geometric Patterns

### Logistic Regression

LVH Relative Risk

Odds Ratio [95% CI]

5.5 [95% CI 1.4 – 31.6]

LVH Relative Risk  
(BP adjusted)

3.4 [95% CI 0.8 – 14.8]

Concentric LVH  
Relative Risk

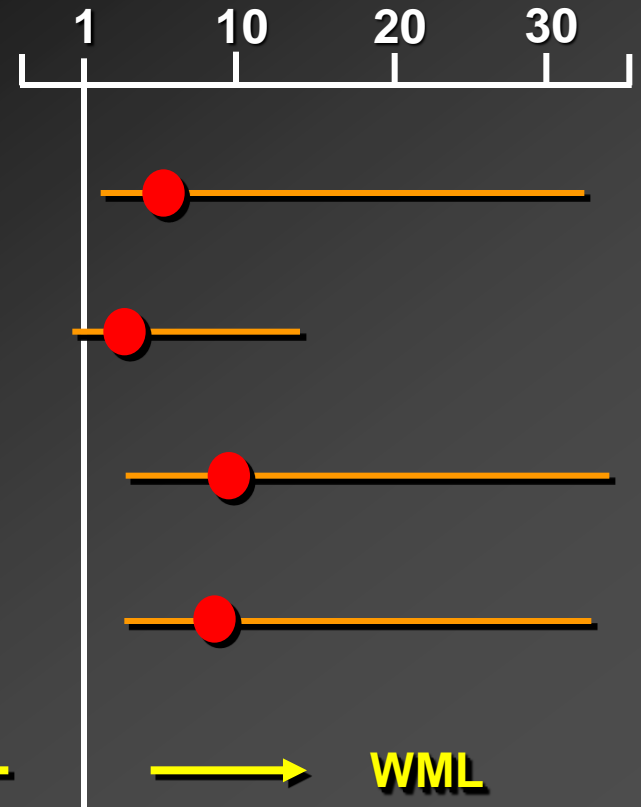
9.3 [95% CI 2.5 – 34]

Concentric LVH  
Relative Risk  
(BP adjusted)

8.2 [95% CI 2.1 – 32.8]

No WML ←

→ WML



## Early Cognitive Impairment in Hypertension

Wechsler Memory Scale (WMS) adjusted for age and education level

Neuropsychological test	WML (n= 27)	No WML (n= 39)	p
<b>Attention</b>			
WMS-Digit span forward	<b>4.8 ± 1.1</b>	5.5 ± 0.9	<b>0.02</b>
<b>Working Memory</b>			
WMS-Digit span backward	4.0 ± 0.4	4.1 ± 0.9	0.44
<b>Memory</b>			
WMS-Logical Memo(*)	82.3 ± 15.0	82.3 ± 16.0	0.99
WMS-Visual Memory(*)	83.8 ± 18.9	89.6 ± 15.7	0.21

(\*) % retention

# Silent Cerebral Damage in Hypertension

## Questions to be answered

- Can antihypertensive treatment and blood pressure control prevent cognitive impairment and dementia in hypertension?
- Can different antihypertensive drugs have differing effects on the prevention of Stroke, cognitive impairment and dementia?
  - Published Studies
    - SHEP study
    - Syst-Eur dementia substudy
    - SCOPE study
  - Forthcoming Studies
    - PROGRESS dementia substudy



## Incidence of Dementia in Major Randomized Placebo-Controlled Trials on Systolic Hypertension

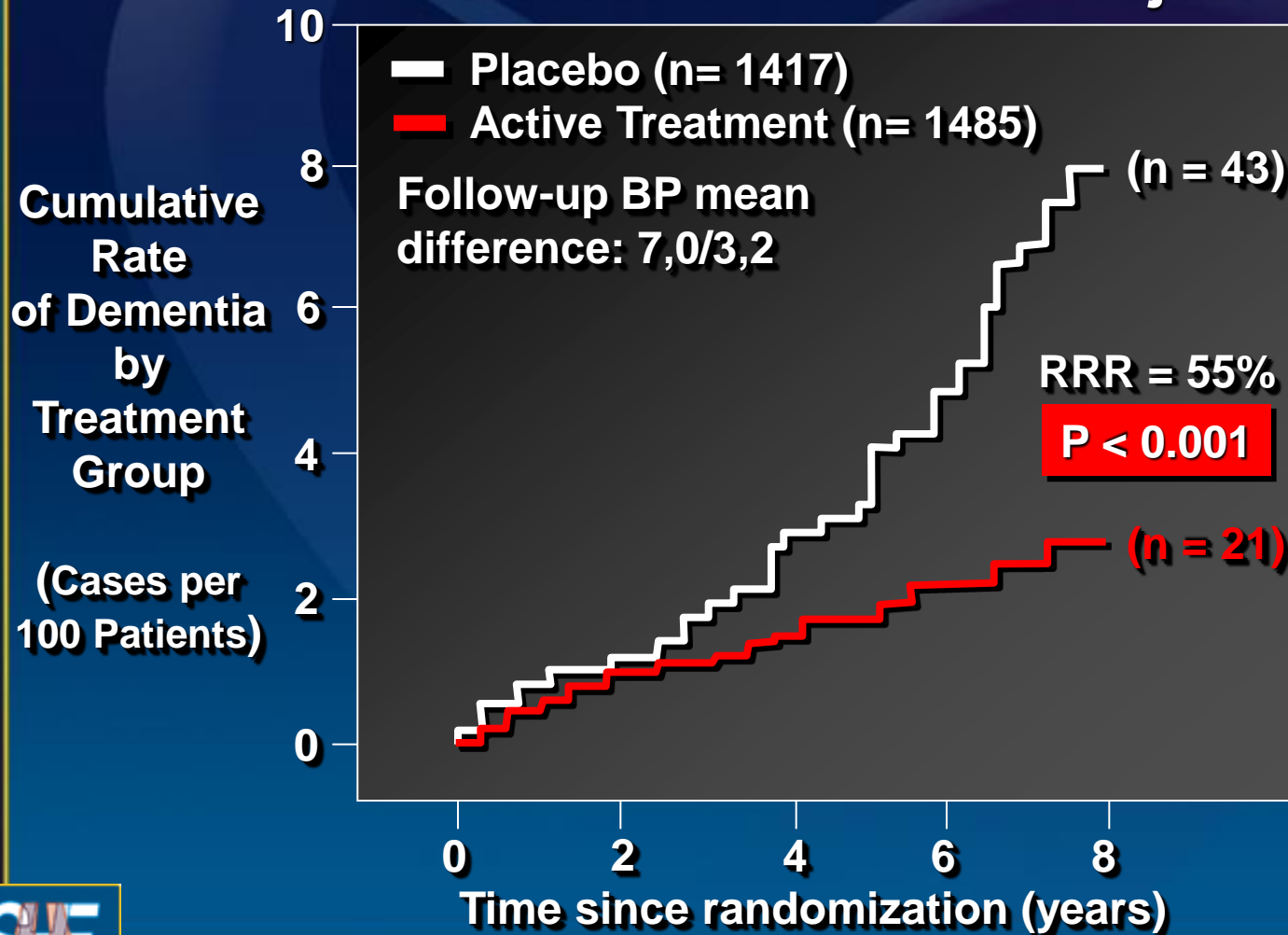
	<b>SHEP</b>	<b>Syst-Eur</b>
Number of patients	2034	2418
Follow-up (years)	5	2
Incidence of dementia in the placebo group (%)	1.9	1.8
Incidence of dementia in active treatment group (%)	1.6	<b>0.9</b>
Active treatment (based on)	Diuretic	Calcium antagonist

 **p= 0.05 Rate of dementia reduced by 50%**



# Prevention of Dementia in the Syst-Eur Study

## “The Vascular Dementia Project”

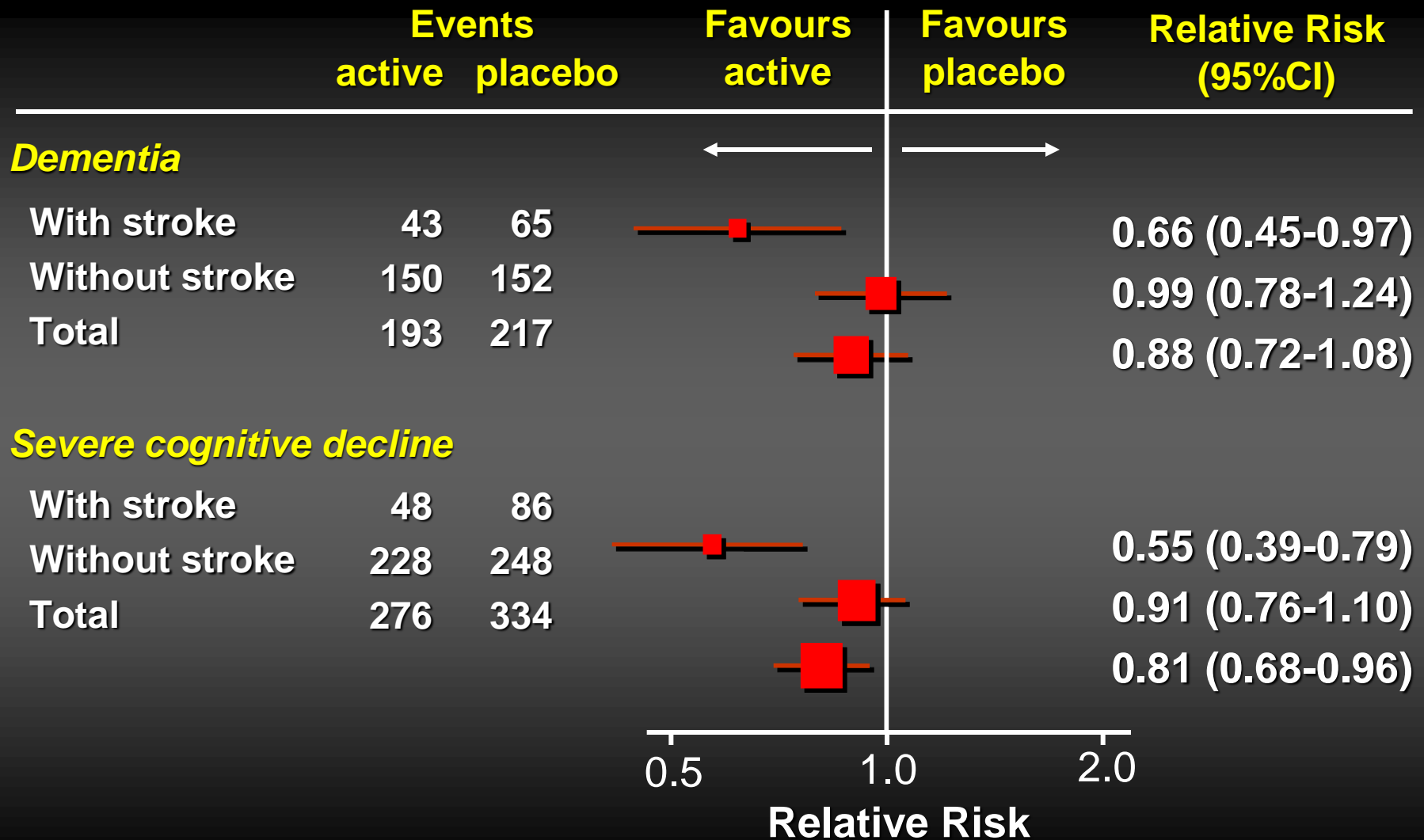


80.5% treated in 2nd phase from those initially randomized to placebo

Mean follow-up of 3.9 years

# PROGRESS Study

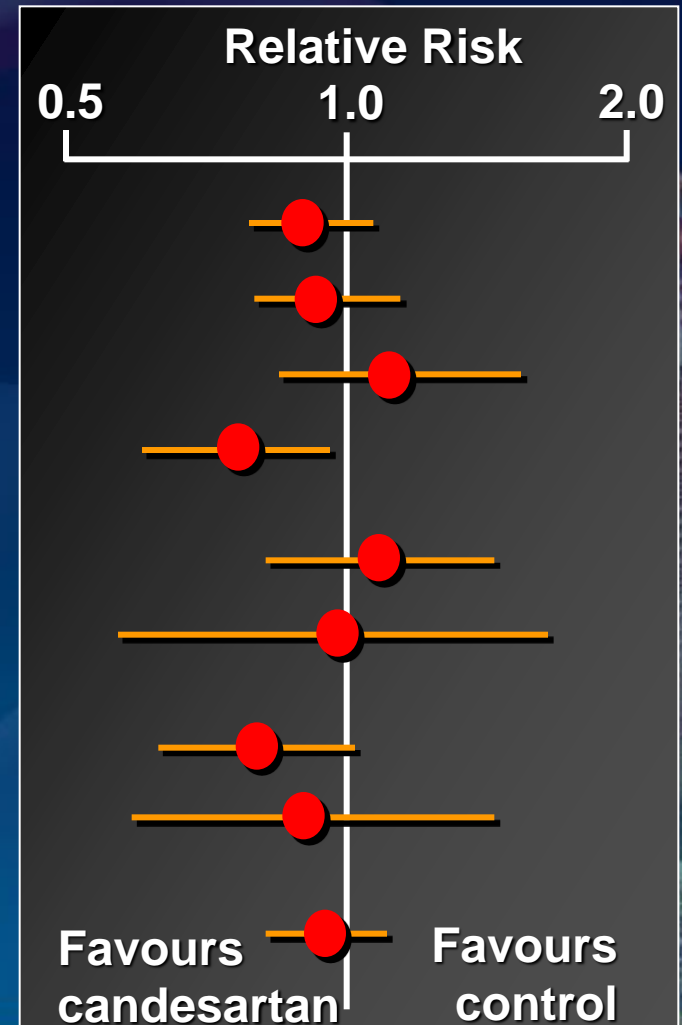
## Dementia and Severe Cognitive Decline (MMSE)



# SCOPE Study

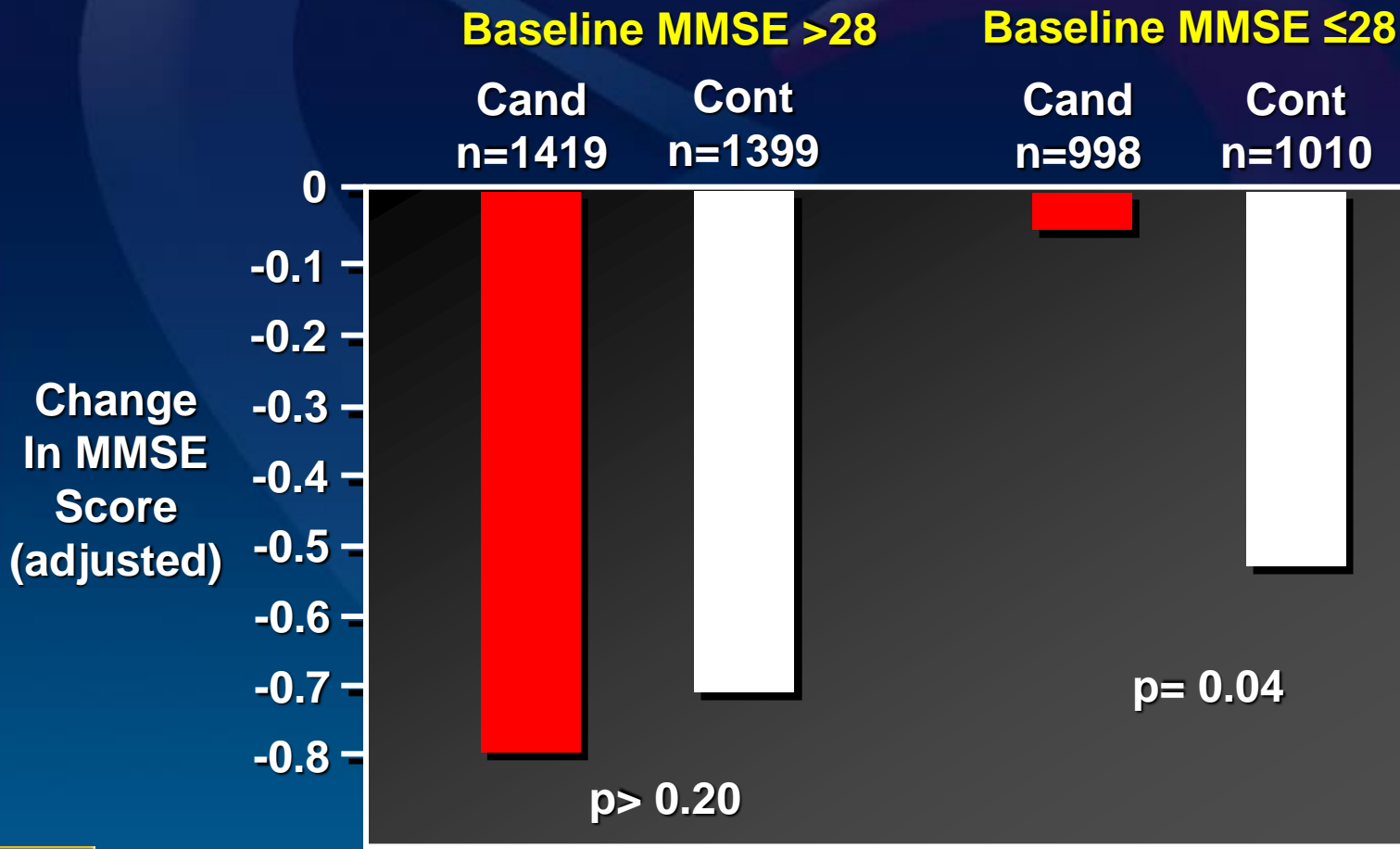
## Cardiovascular Events and Total Mortality, ITT

	No. of events	
	Candesartan	Control
Major CV events	238	266
CV deaths	141	150
Non-fatal MI	54	47
Non-fatal stroke	68	93
All MI	70	63
Fatal MI	18	18
All stroke	89	115
Fatal stroke	24	26
Total mortality	255	264



# SCOPE Study

## Change in MMSE Score, ITT



# Summary and Conclusions

- **There is a close relationship between silent cerebral damage (WML, cognitive impairment) and silent cardiac damage (LVH)**
- **Antihypertensive treatment reduces the risk of stroke more efficiently than the risk of coronary heart disease. Recent data also suggests that it may delay the progression of cognitive decline and dementia**
- **There is no definite evidence that one class of antihypertensive drug is superior to other in preventing cognitive decline**
- **Further mechanistic and clinical studies should provide insights into this subject**