Maximizing Hypertension Therapy in Elderly Patients

Konkuk University Hospital
KyuHyung Ryu, MD, PhD, FACC

노인의료비 지출 10년간 8배 증가

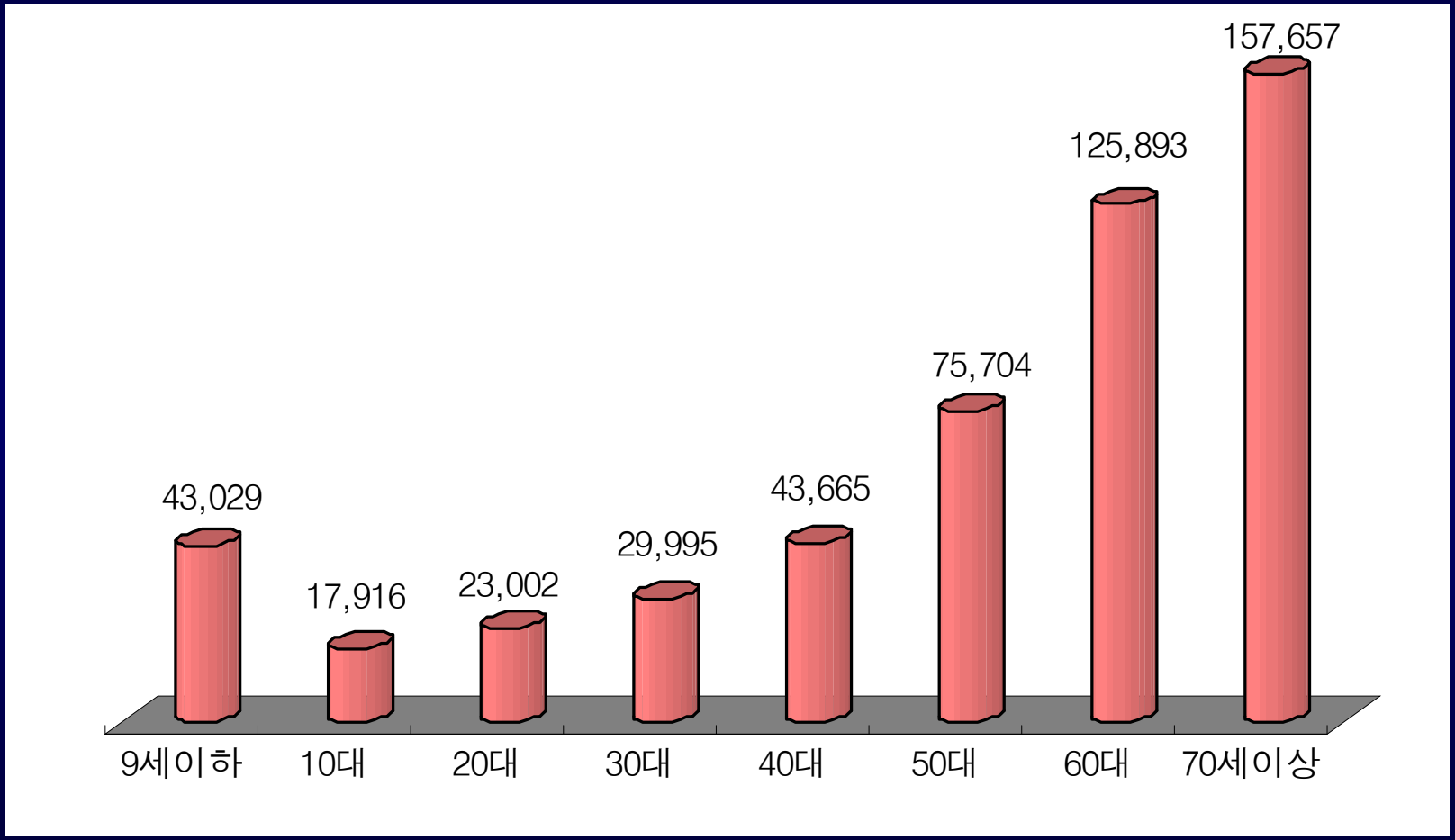
- 『국민건강보험공단 www.nhic.or.kr, 2006 건강보험주요통계 발간』
- ▶지난해 총 20조 9,316억원 중 5조 5,989억 원을 노인 급여비로 사용
- ▶노인인구 5.8%(1996)⇒8.6%(2006),
- 노인급여비 지출 13.5%(1996)⇒26.7%(2006)
- ▶매년 1조원씩 증가추세, 고령사회에 대비한 노인의료대책 법제화 시급

- 연령 증가에 따라 건강보험 재정(건강보험 비적용 제외)
- 지출 크게 증가

- 특히 65세 이상 노인은 10년 동안 8.3배 증가

	'96년	'06년	증가지수
- 건강보험급여비(계)	4조 9,644억원	20조 9,316억원	4.2배 ↑
. 65세이상	6,716억원	5조 5,989억원	8.3배 ↑
. 65세미만	4조 2,928억원	15조 3,327억원	3.6배 ↑

연령대별 2006년1인당건강보험 진료비



연령증가에 따른 심장혈관계변화

- 심장비대-좌심실 확장기능저하
- 판막과 지지조직의 변성-대동맥판막 협착증, 승모판막 폐쇄부전증
- 동방결절 주위의 섬유화-부정맥
- 운동에 따른 맥박수 변화-조절능력 감소
- 압력수용체 반사기능 저하
- 자율신경계장애

혈관 변화

- 혈관벽 탄성섬유 감소
- 죽상경화증, 석회화
- 동맥의 예비기능 감소
- 수축기 고혈압과 맥압 증가

- 좌심실 비후의 주된 원인

노인성 주요 심혈관질환

- 고혈압
- 심부전
- 부정맥(심방 세동, 동성기능저하)

- 판막질환
- 허혈성 심장질환
- 뇌졸증

고혈압

- 연령증가에 따라 증가
- 국내 성인의 30%, 65세 이상 50%이상

원인

- 동맥경화
- 죽상동맥경화성 신동맥 고혈압
- 일차성 알도스테론혈증
- 가성 고혈압(심한 혈관 경화)

특징

- 수축기 고혈압
  (관상동맥 질환, 심부전,뇌졸증 등의 사망 예측지표)
- 맥압 증가
  (혈관의 순응도 저하—심혈관계합병증의 위험지표)

아침 고혈압, 오후 정상혈압

약물에 의한 기립성 저혈압

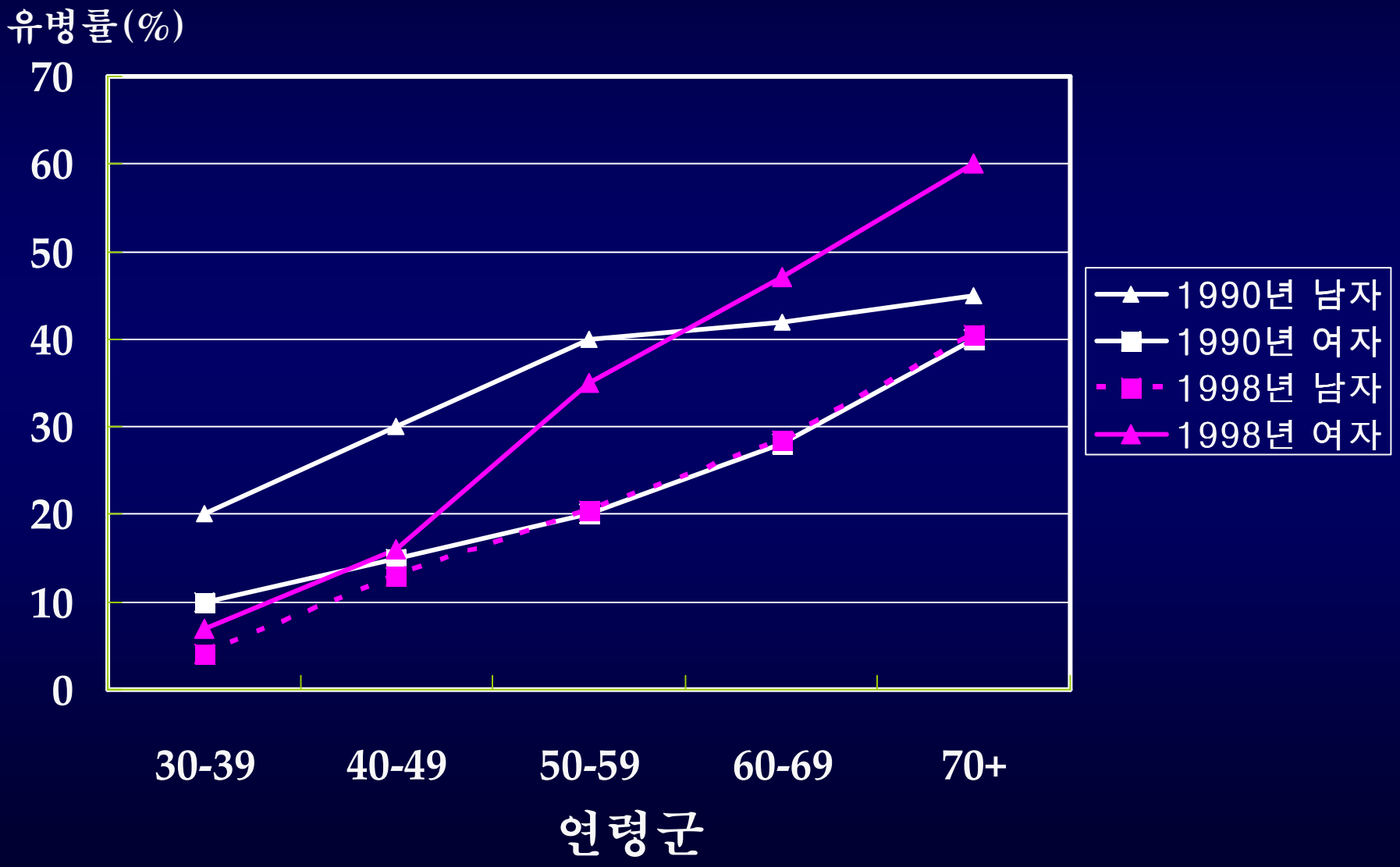
- 동반질환(당뇨병, 신장기능장애, 만성 폐쇄성 폐질환)
- 심장의 예비능 감소
- 작은 부하에 쉽게 심부전 발생

치료효과

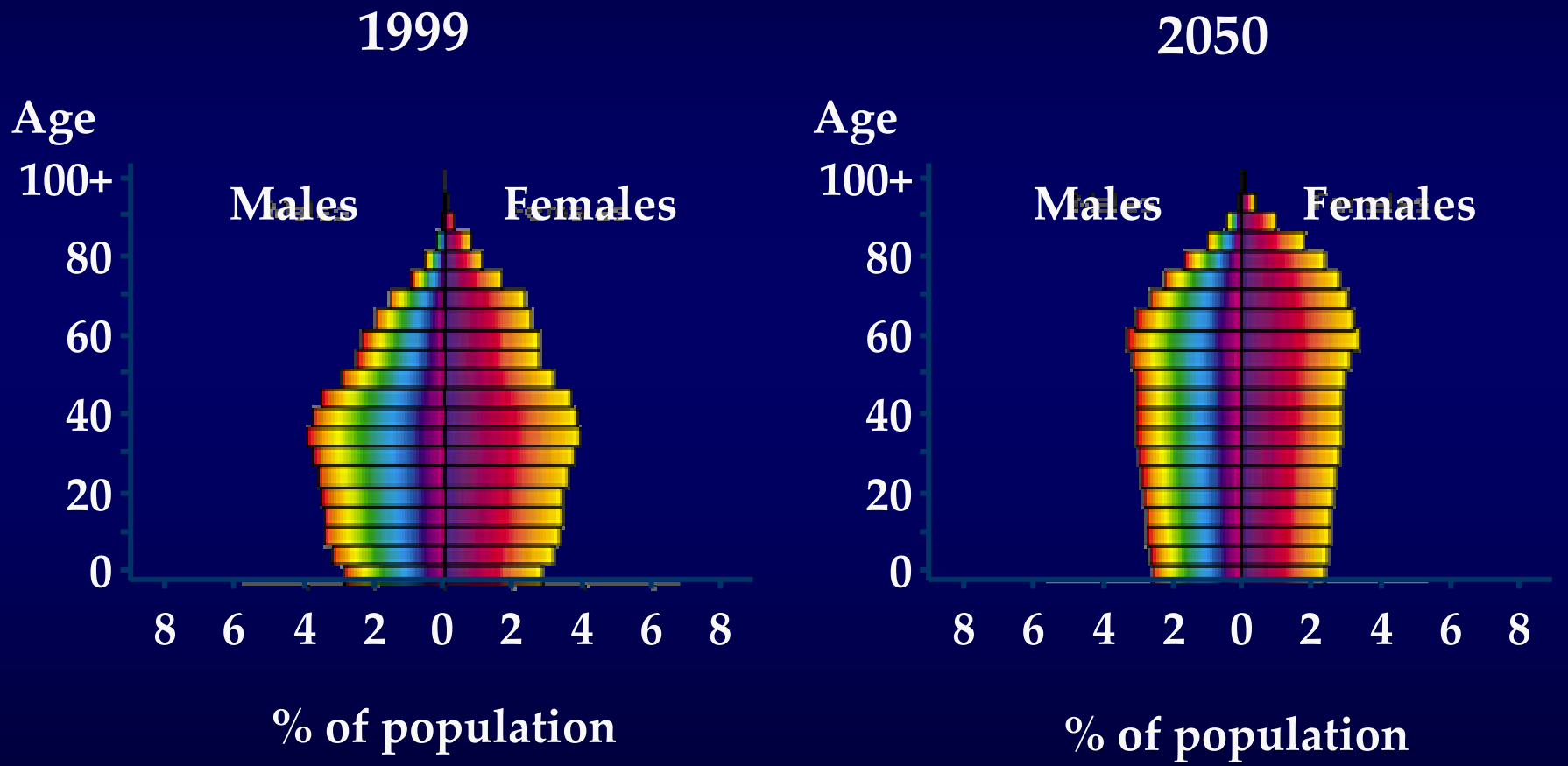
- 높은 연령일수록 사망률과 유병율 감소효과가 크다.

- 생활개선 요법(염분, 알코올 섭취 감소, 야채식이 요법,금연,규칙적인 유산소 운동)

국내 고혈압의 성별, 연령별 유병률(JNC 6기준)



The world population is aging

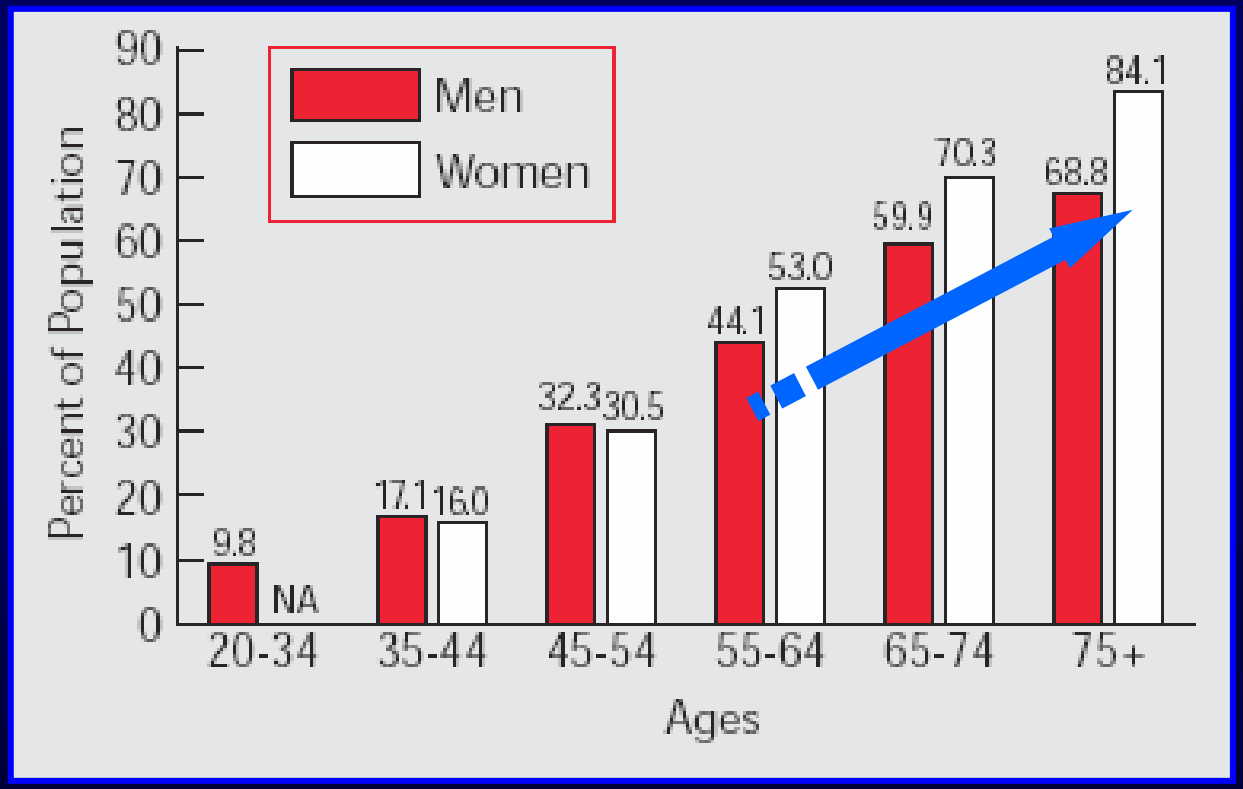


United Nations 1999

미국 고혈압 유병율

Prevalence of High Blood Pressure in USA
Age 20 and Older by Age and Sex

NHANES IV: 1999-2000

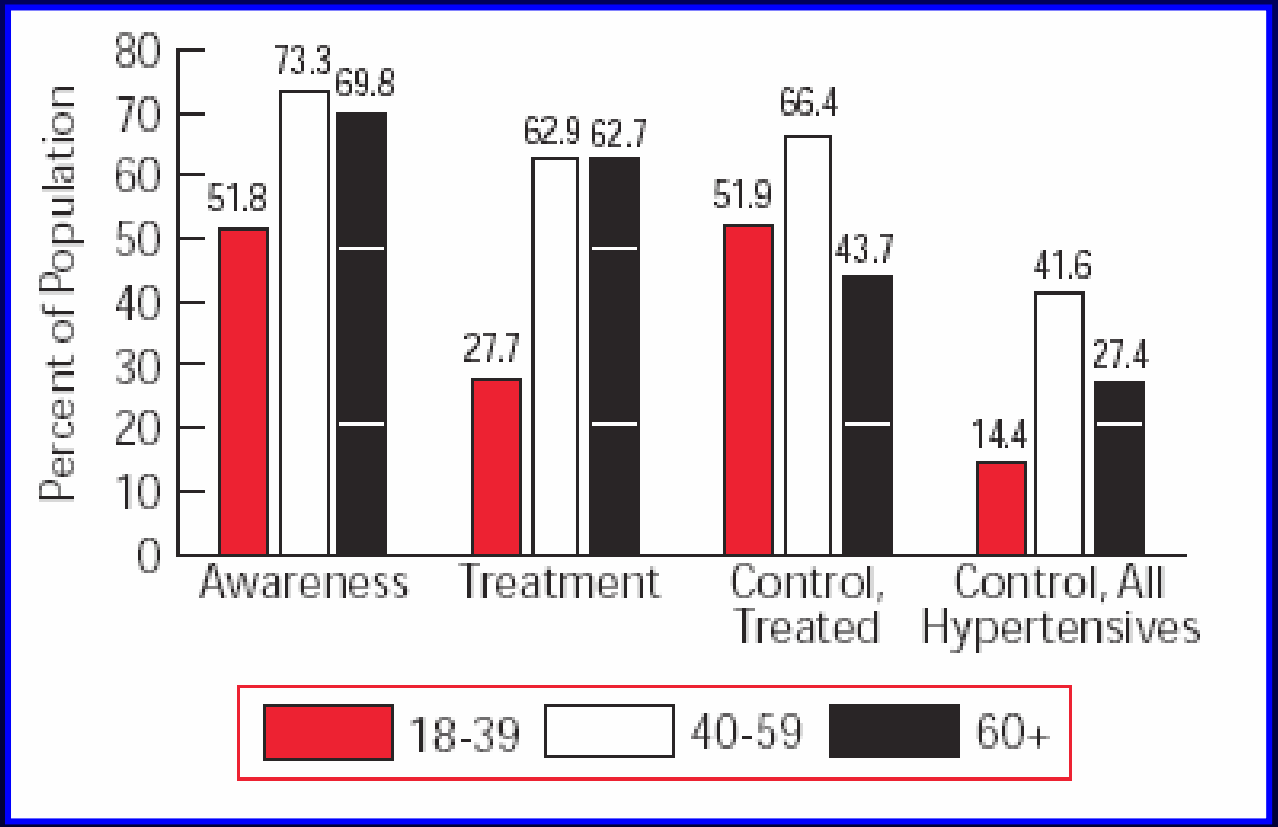


Source: Health, United States, 2003, CDC/NCHS.

미국 고혈압 치료율

Extent of Awareness, Treatment and Control of High Blood Pressure by Age

NHANES IV: 1999-2000



Source: JAMA 2003; 290: 199–206.

노년기 고혈압

- 연령의 증가와 함께
  고혈압 유병율도 증가
- 55세에 혈압이 정상인 경우도
  이후 고혈압이 발생할 확률은 90% 이상
- 수축기 혈압을 140 mmHg 이하로 조절하는 것은 50세 이상에서 심혈관계 합병증 예방을 위해 더욱 중요

옛날이야기

허봉사 나리
제 혈압이 160/90
이라는데 어찌해야
하나요?

나이가 들면 당연히
윗자리 혈압이 오르는
것이니 너무
근심치 말게...

U.S. Department of Health and Human Services

National Institutes of Health

National Heart, Lung, and Blood Institute

Jonit National Committee-7 (JNC-7, 2003)

-노인에서 수축기 혈압의 중요성을 강조-

New Features & Key massage

- **For persons over age 50, SBP is a more important than DBP as CVD risk factor.**
- Starting at 115/75 mmHg, CVD risk doubles with each increment of 20/10 mmHg throughout the BP range.
- Persons who are normotensive at age 55 have a 90% lifetime risk for developing HTN.
- Those with SBP 120–139 mmHg or DBP 80–89 mmHg should be considered prehypertensive who require health-promoting lifestyle modifications to prevent CVD.

노인 고혈압
-2가지 임상형태-

- 수축기 고혈압과 이완기 고혈압의 혼합 형태 (일차성 고혈압의 연장)

- *고립성 수축기 고혈압* ***(ISH, isolated systolic hypertension in old age)***
  노인에서 중요한 문제!

노인 고립성 수축기 고혈압
-isolated systolic hypertension in old age-

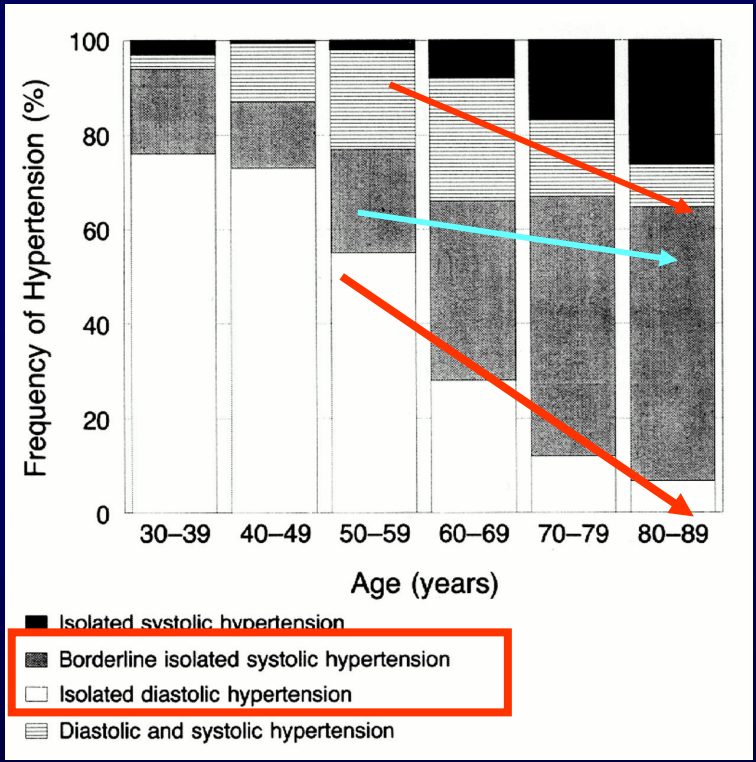
- 나이가 많아질수록 ISH의 유병률은 증가한다
- 과거 정상적인 반응으로 간주 → 소극적 치료
- 큰 수용혈관(large capacitance vessel)의 신전성(distensibilty)과 탄성도(elasticity)의 감소
- 맥압의 상승 – 미만성 동맥경화를 시사

연령 증가에 따른 유병률의 증가

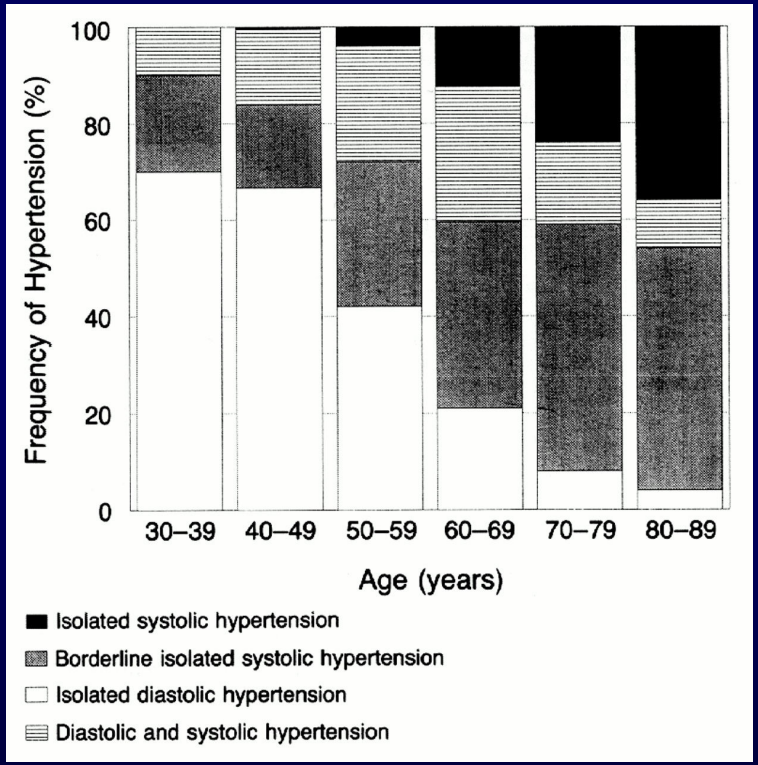
The Natural History of Borderline Isolated Systolic Hypertension

Sagie A, et al. N Engl J Med 1993;329

Men



Women



Borderline isolated systolic hypertension: SBP 140-159, DBP <90mmHg

Isolated systolic hypertension: SBP ≥ 160, DBP <90mmHg

기타 노인고혈압의 특성

- 기립성 저혈압
- 식사후 저혈압
- 백의효과 (White-coat effect)
- 가성 고혈압(pseudohypertension)

기립성 저혈압

Prevalence of Postural Hypotension at Baseline in the Systolic Hypertension in Elderly Patients (SHEP) Cohort

Applegate WB, et al. J Am Geriatr Soci 1991;39

- 4,736 명의 참가자
- 기립성 저혈압 : 기상시 SBP ≥ 20mmHg 감소
- 기립후 1분 : 10.4% , 3 분 : 12%

- 고혈압과 관련
- 기저 혈압이 높을 수록 혈압 하강이 크다
- 정맥의 저류
- 자율신경계 기능부전

***JNC-7에서는 증상을 동반하고 ≥ 10mmHg 감소하는 경우로 설정**

노인 고혈압 치료의 근거
-2 가지 의문-

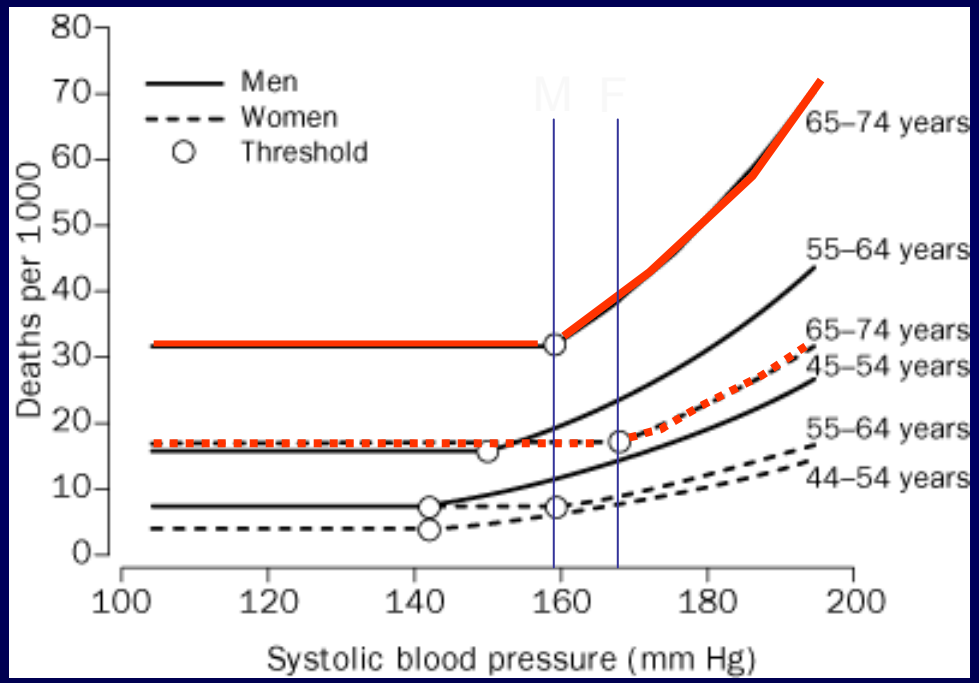
- 고혈압(고립성 수축기 고혈압 포함)이 노인에서도 위험한가?

- 치료를 하면 효과가 있는가?
  -더 해가 되는 것이 아닌가?

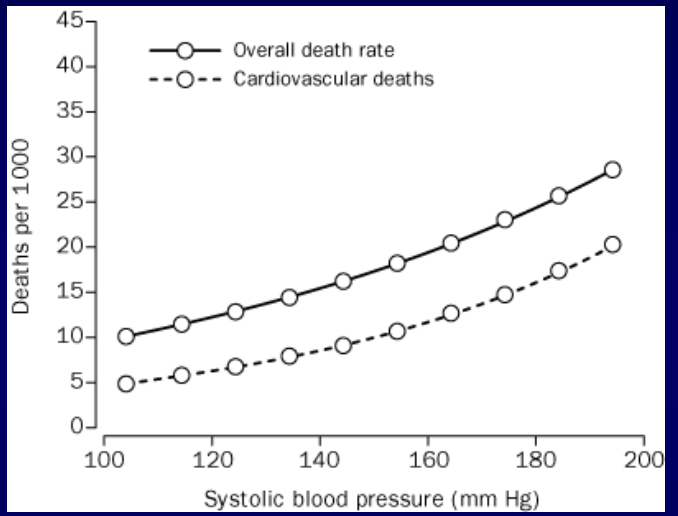
노인에서 수축기혈압과 사망률

Systolic Blood Pressure and Mortality

Port S, et al. Lancet 2000;355



Reduced horizontal-logistic-spline fits
: From pooled data of Framingham study

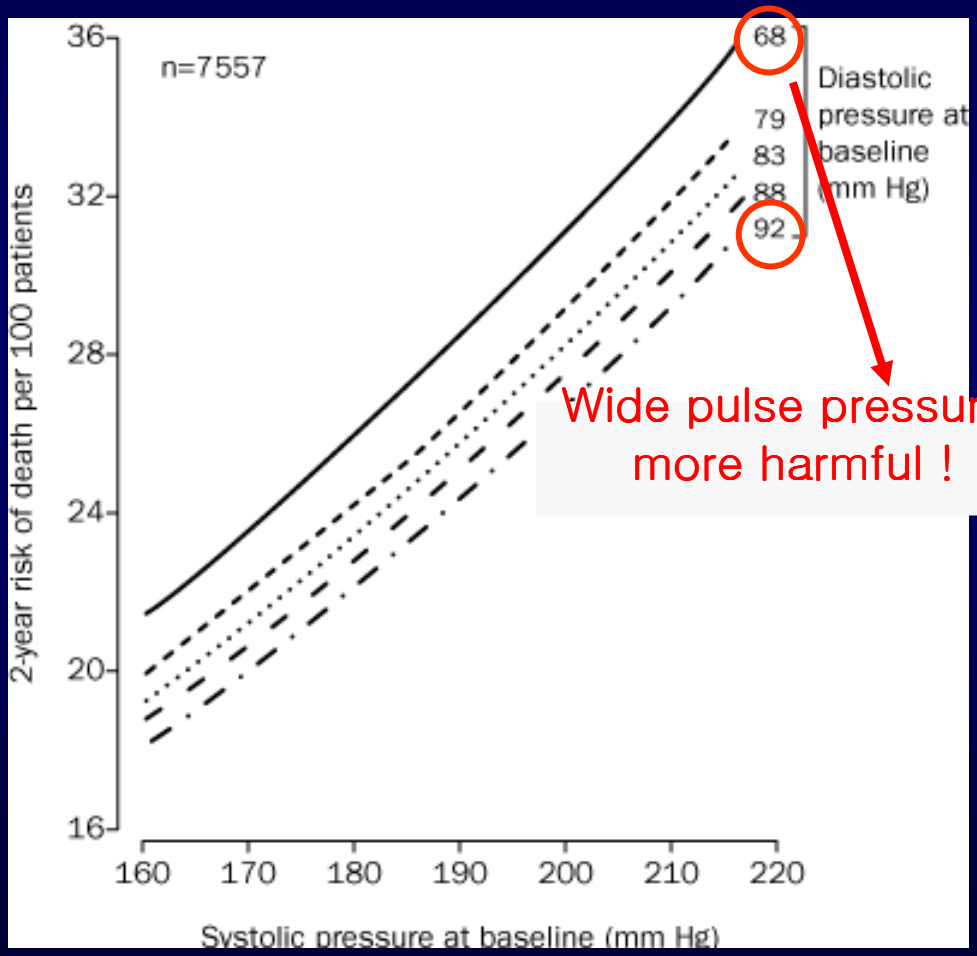


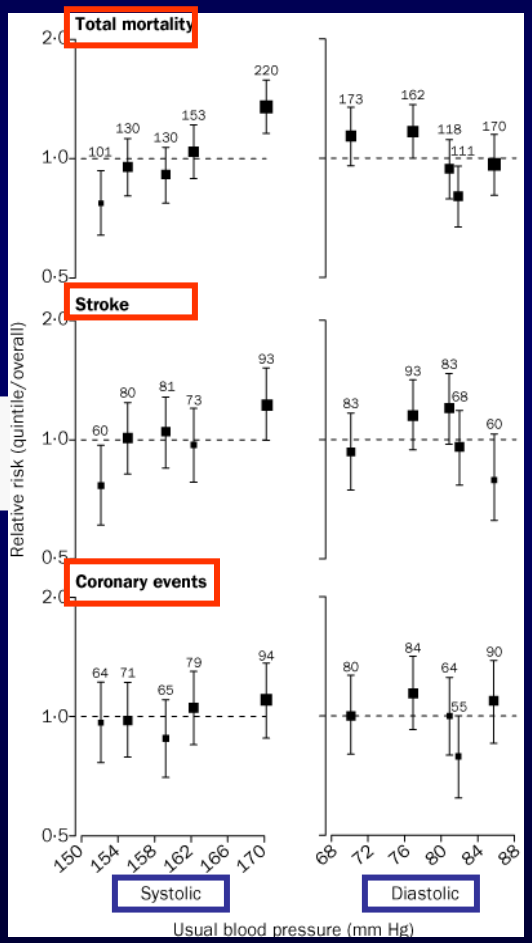
cf. Framingam age-adjusted rates for men aged 45-74 yrs related to SBP (simple linear regression model)

노인에서 수축기혈압과 사망률

Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials

Staessen JA, et al. Lancet 2000;355



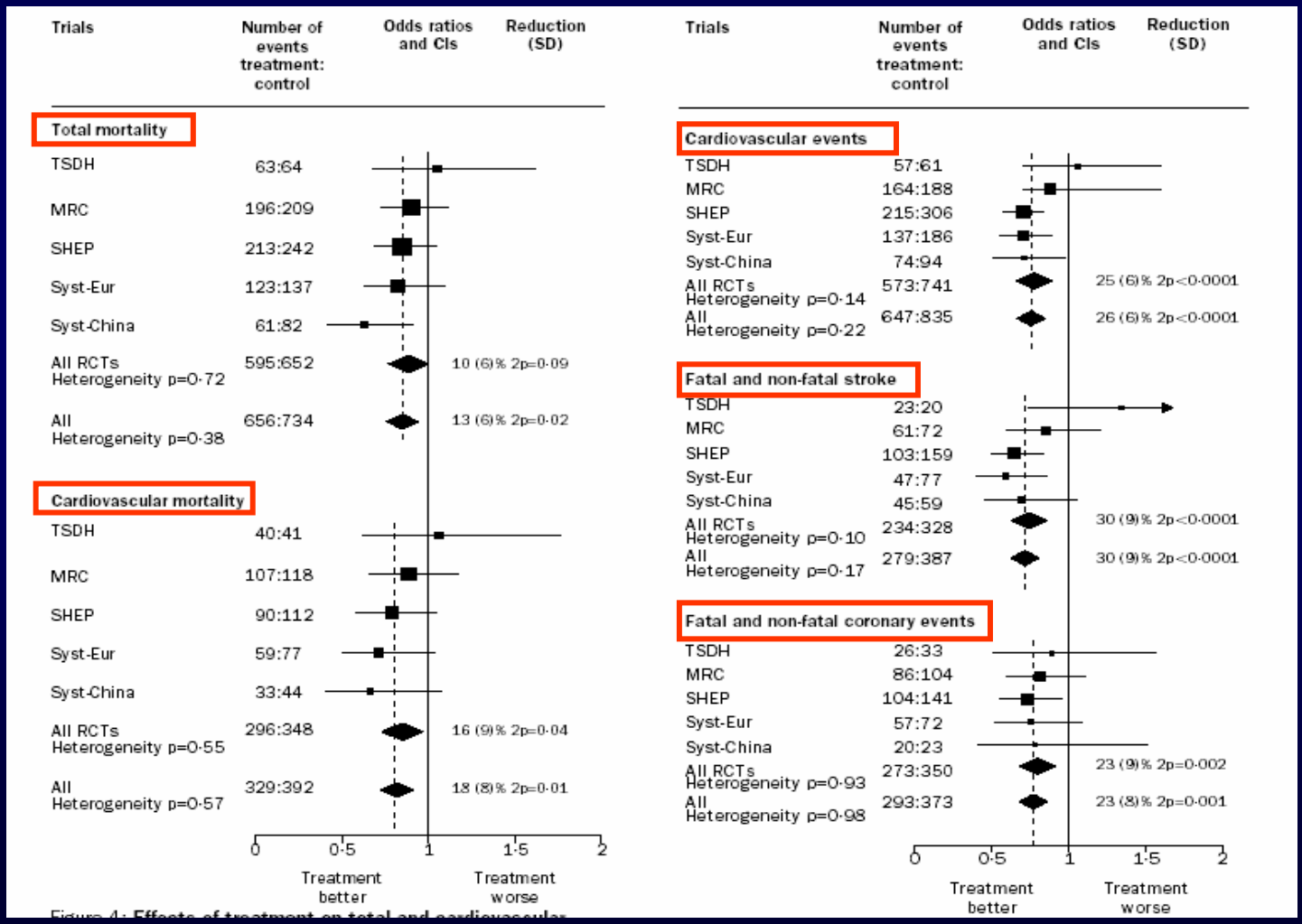


노인 수축기 고혈압의 치료효과

Risks of untreated and treated isolated systolic hypertension in the elderly: meta-analysis of outcome trials

Staessen JA, et al. Lancet 2000;355

TSDH: three smaller trials in systolic and diastolic hypertension



노인 고혈압의 치료효과
주요 합병증의 억제 효과

	EWPHE	MRC	SHEP	STOP-H	Syst-China	Syst-Eur
뇌졸중 감소 (%)	-36	-25	-33	-47	-47	-42
관동맥질환 억제 (%)	-20	-19	-27	-13	+6	-26
심부전 감소 (%)	-22	NA	-55	-51	-58	-27
복합투여(%)	35	52/38	44	67	11-26	26-36

노인 고혈압 치료의 실제
-몇 가지 의문-

- 얼마나 혈압을 낮추어야 하나?
- 어떤 약을 써야 하나?
- 부작용은 ?
- 주의할 점은 ?

노인 고혈압의 치료가 더 이득이 크다!

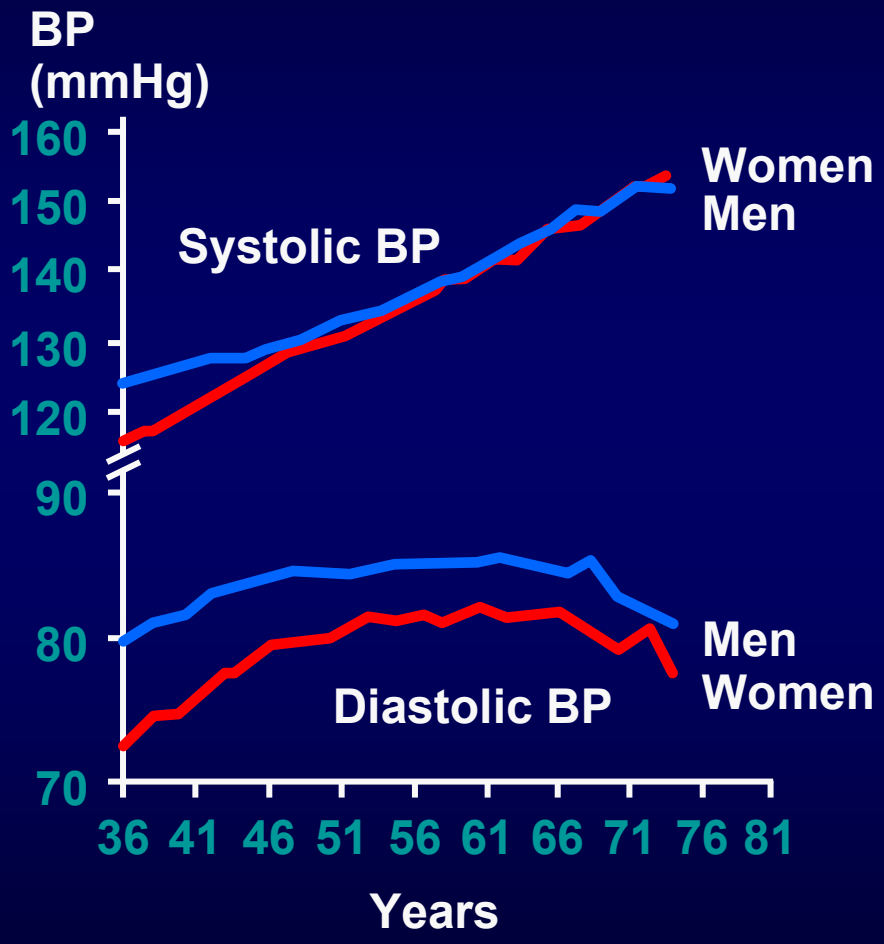
- **5년의 고혈압 치료: 노인 58명당 1명의 사망을 줄인다.**
  젊은 사람 205명당 1명
- 치료 시작 전에 이미 더 큰 위험에 노출
- 흡연률이 낮다(임상연구에 포함된 환자들)
- 최근에 시행된 연구들로 **thiazide** 등의 효과가 입증된 약제들을 사용

노인 고혈압의 치료목표

JNC-7 (2003): 노인도 같은 기준을 적용해야 한다

- 혈압 목표치 **140/90mmHg**
- **130/80mmHg:** 당뇨병이나 신장질환이 있는 경우
- 노인의 경우 수축기 혈압을 목표치까지 도달하는 것이 바람직
- 이완기 혈압이 지나치게 감소하는 경우는?

수축기 고혈압

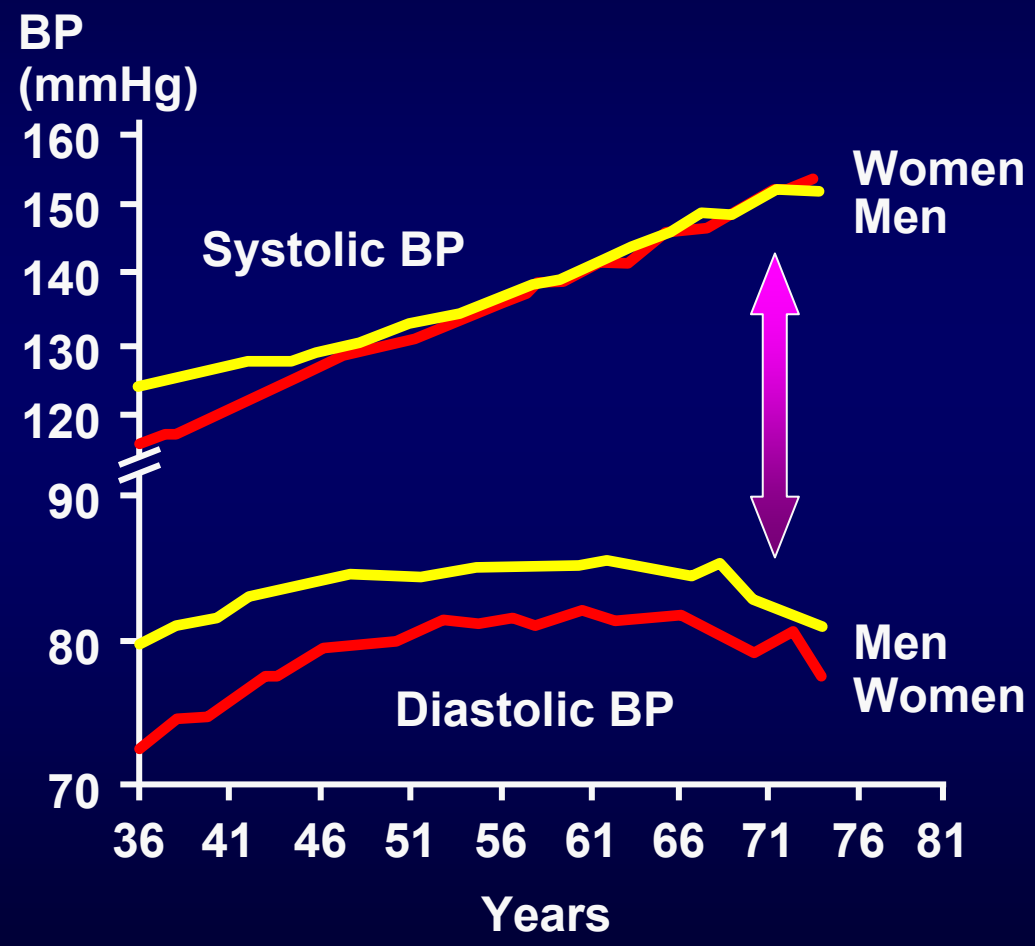


나이에 따라 SBP는 상승하고 DBP는 감소한다.

- SBP는 거의 일직선으로 상승
- DBP는 완만하게 상승하다, 70세 이후는 천천히 감소

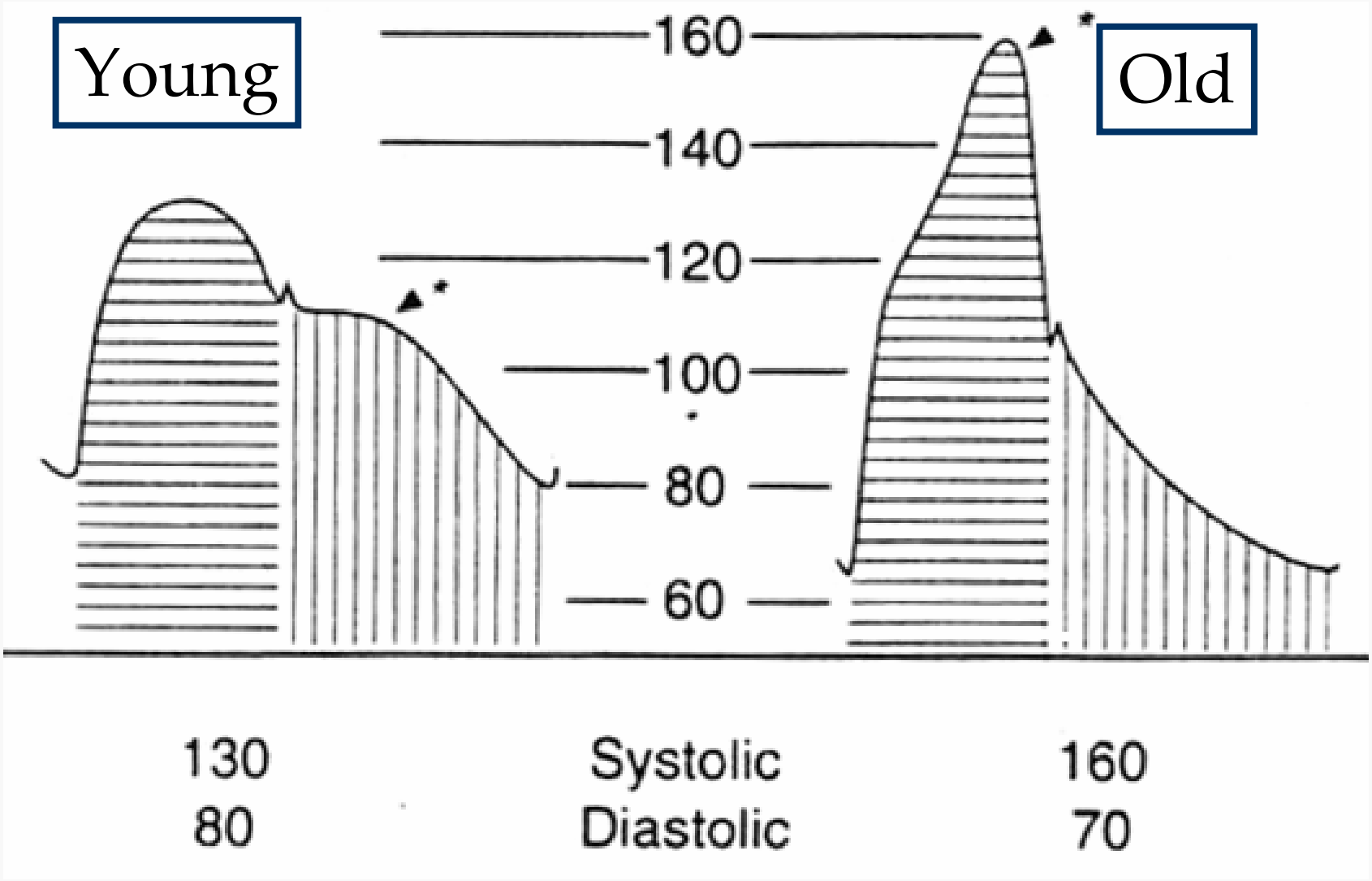
Galarza CR et al. Hypertension. 1997;30:809-816

Wide Pulse Pressure with Aging

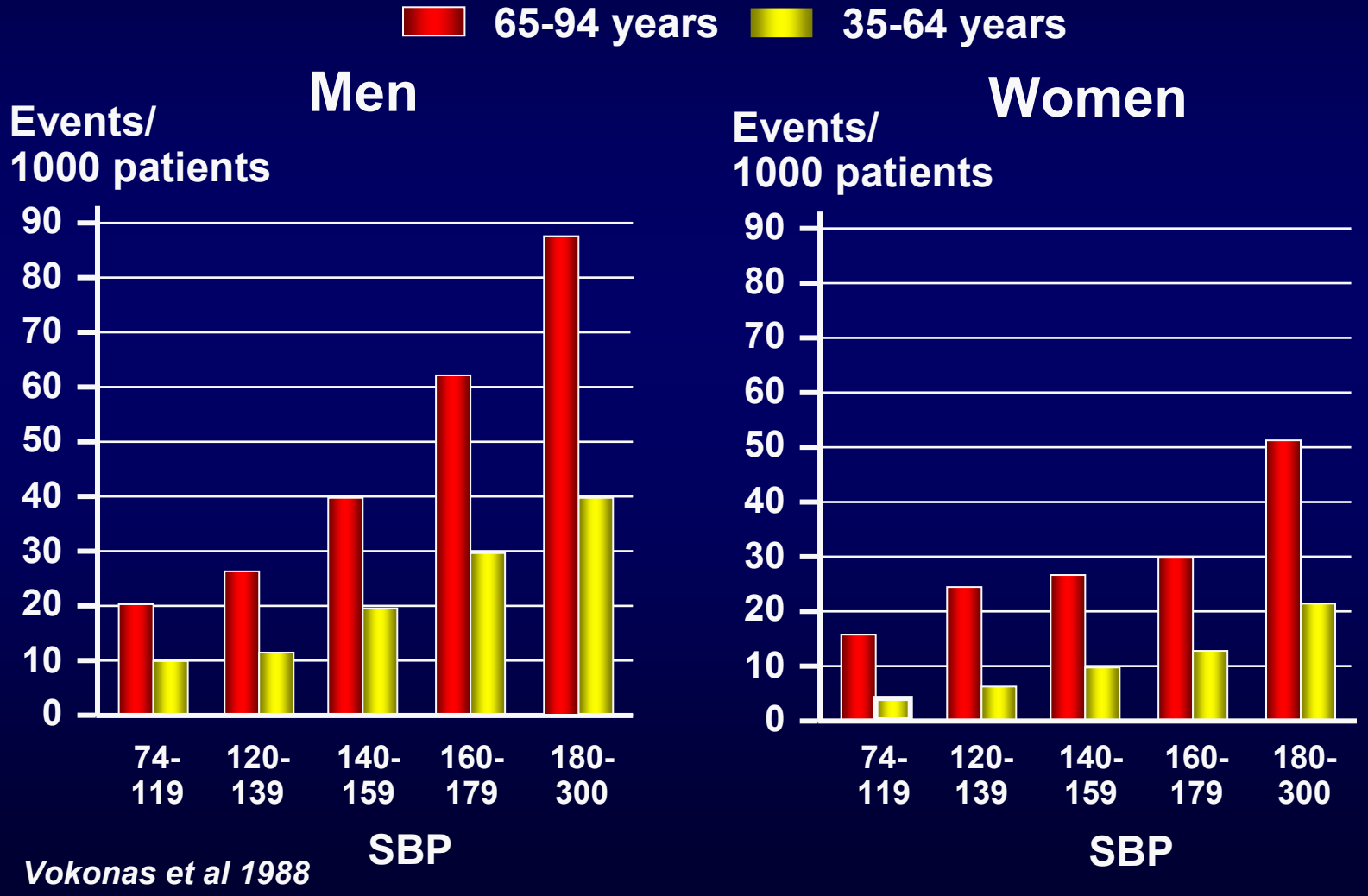


Galarza CR et al. Hypertension. 1997;30:809-816

Systolic Hypertension
Characteristic finding of elderly HT



노인에서 맥압과 심혈관사망률 (framingham study)

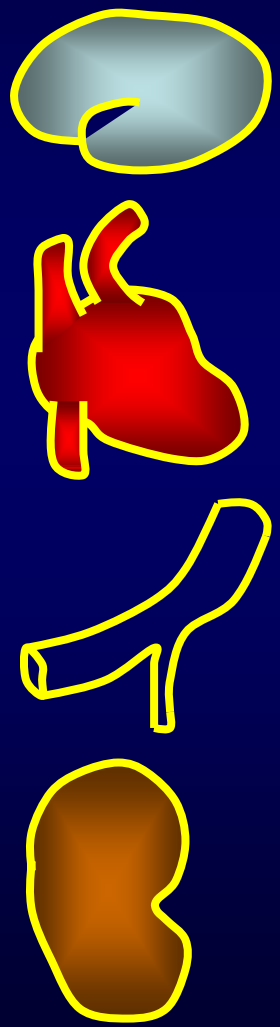


Vokonas et al 1988

맥압 증가의 영향

- 수축기압 증가에 의한 좌심실 비대의 유발; 산소소모량의 증가와 동맥경화의 촉진
- 확장기압력의 감소에 의한 심장관류압력의 감소
- 이상에 의해서 심장의 산소요구량은 증가되나 공급은 감소된다.

Target organ of Hypertension
Endpoints of Clinical Trials

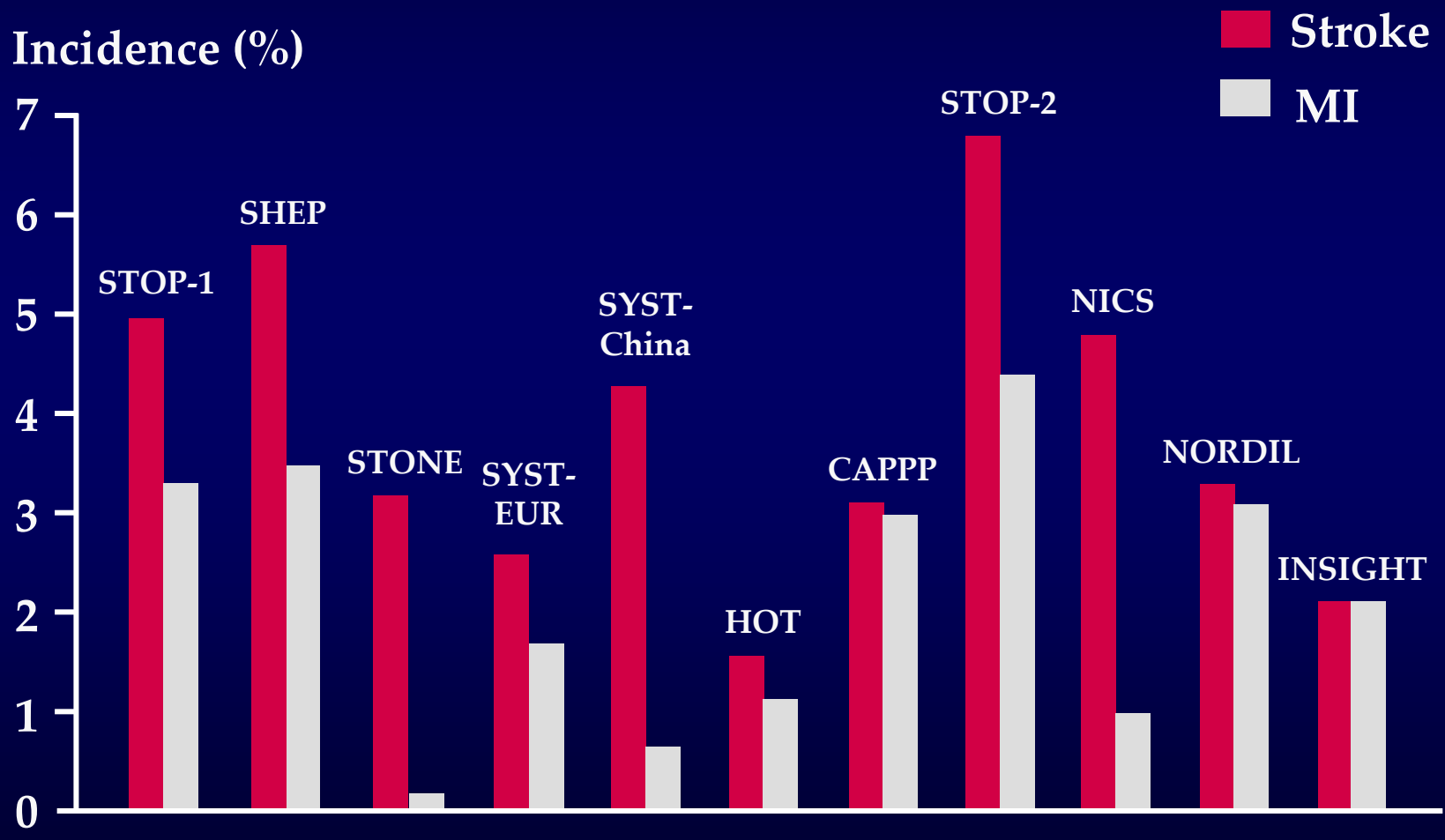


- Stroke
- Coronary heart disease
- Heart failure (fatal or hospitalized)
- Total cardiovascular events (composite of all above)
- Declining renal function
- Cardiovascular mortality
- Total mortality

Treatment of Elderly Hypertension

Stroke

Stroke more common than MI in 11 major hypertension trials

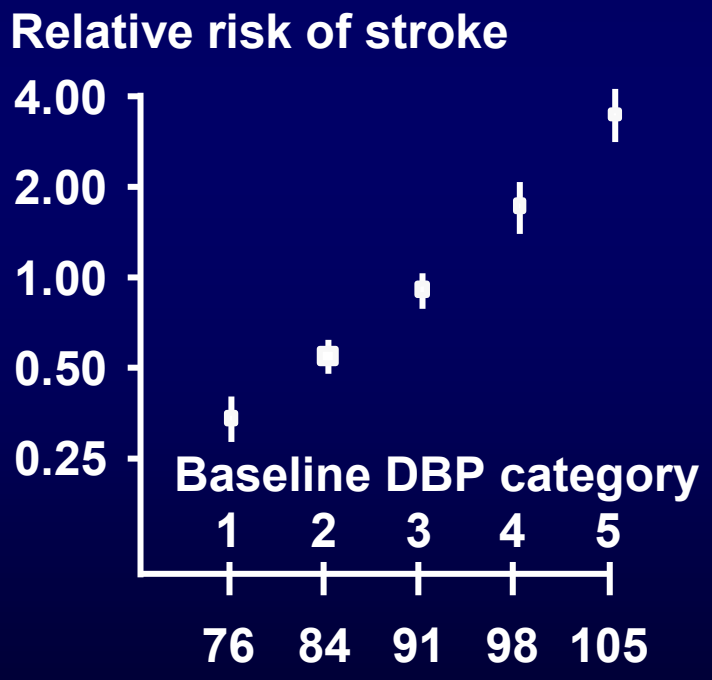


Kjeldsen Blood Press 2001;10(4):190

The higher the blood pressure, the greater the risk of stroke and CHD

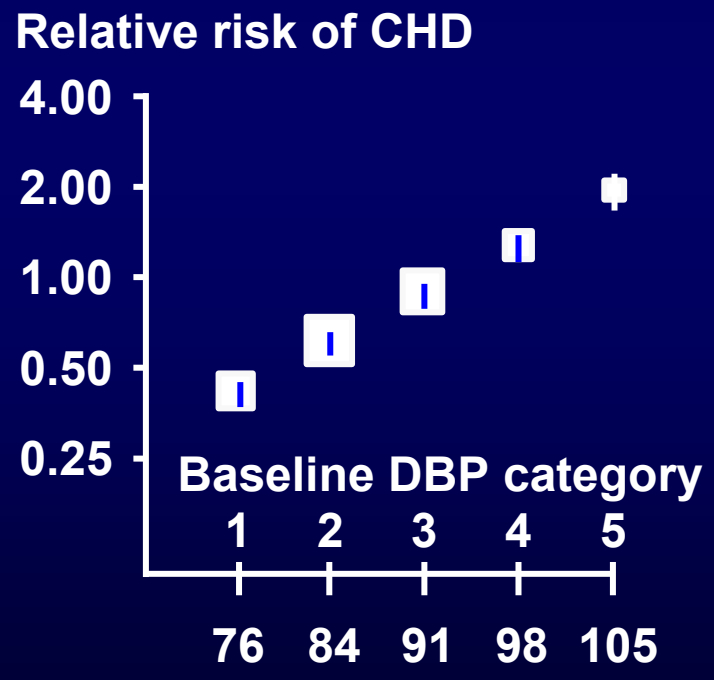
Stroke

7 prospective observational studies:
843 events



CHD

9 prospective observational studies:
4856 events

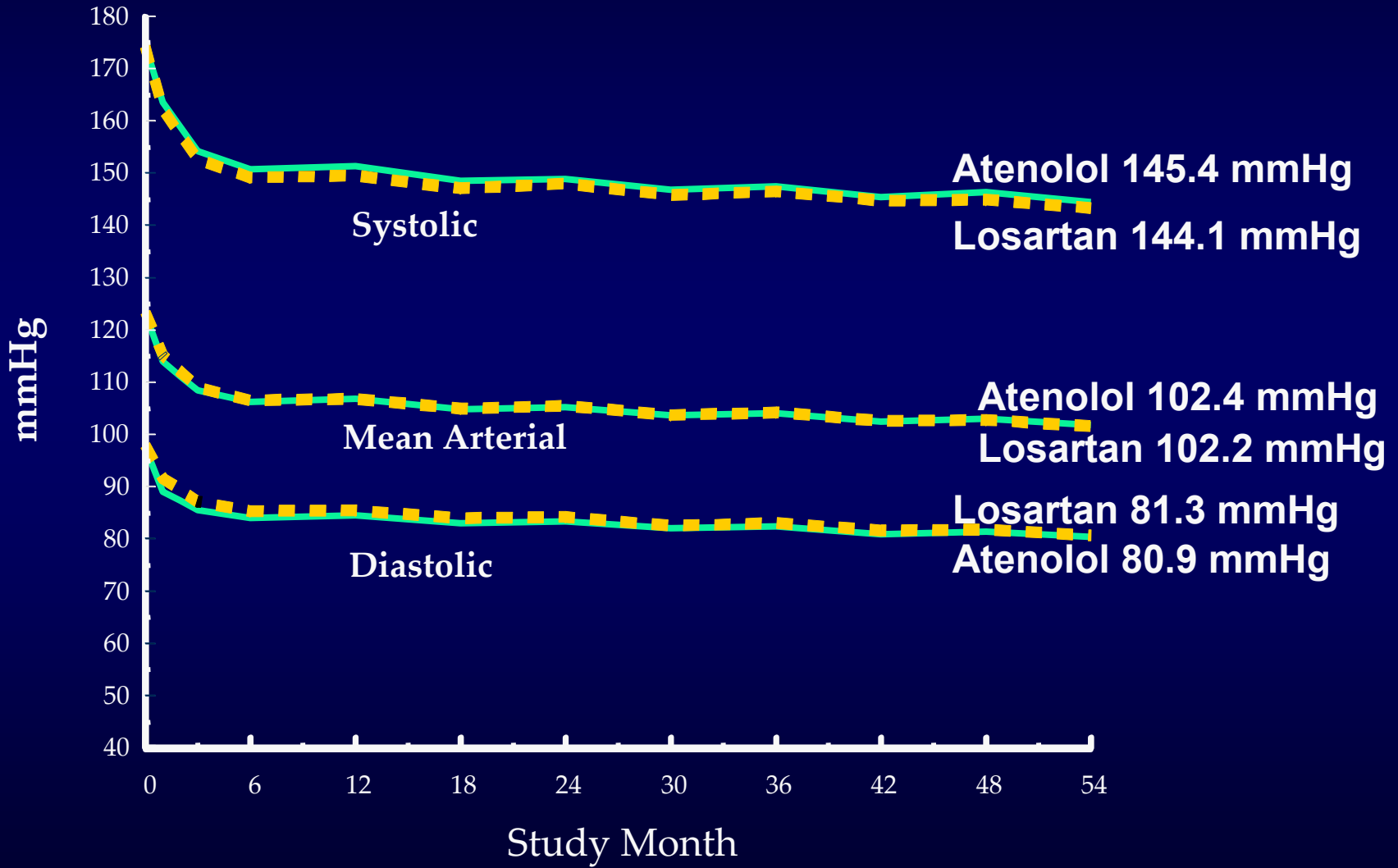


Approximate mean usual DBP (mmHg)

MacMahon et al 1990

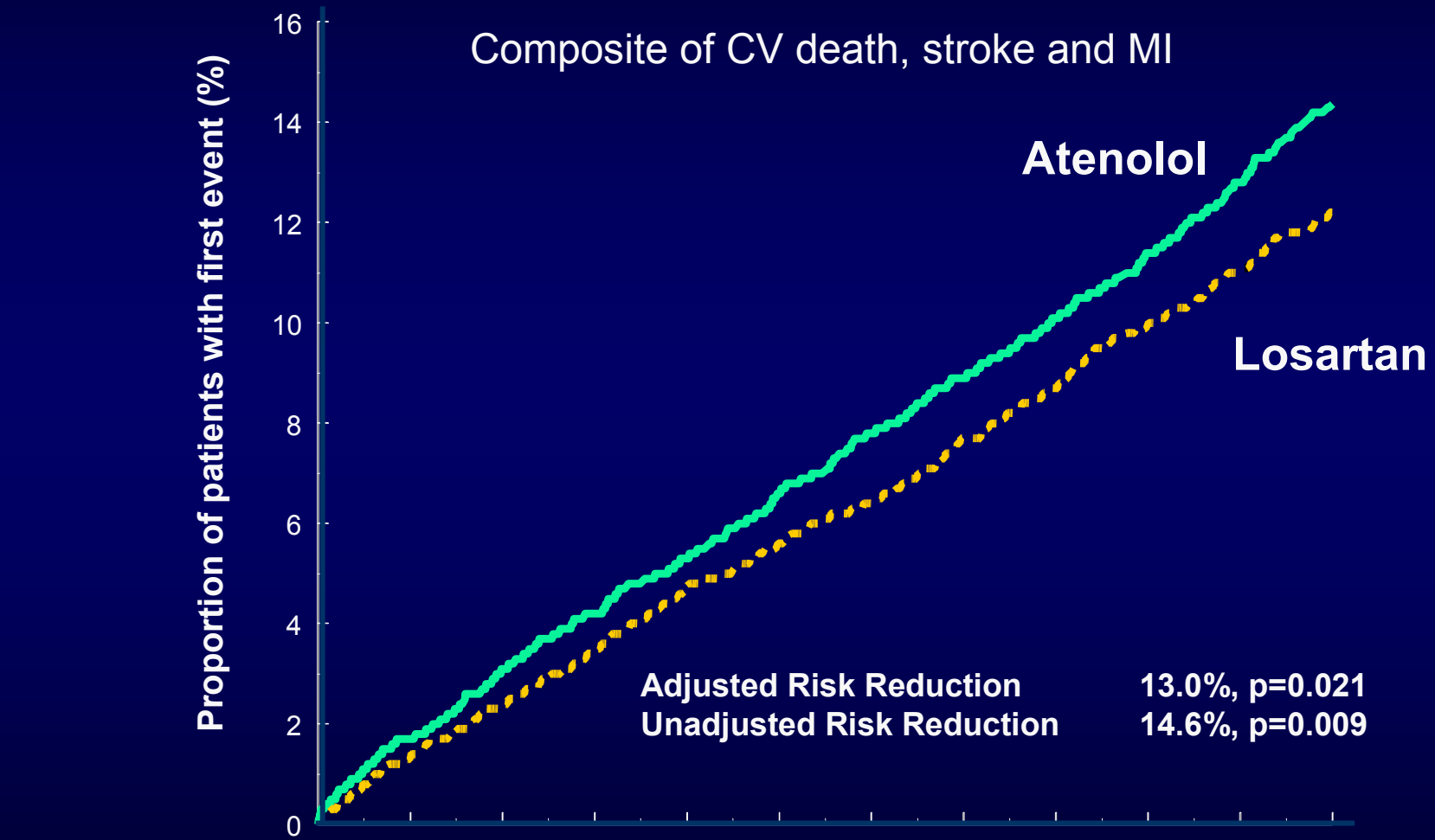
Prevention of Stroke, General Population

LIFE: Comparable Blood Pressure Reductions



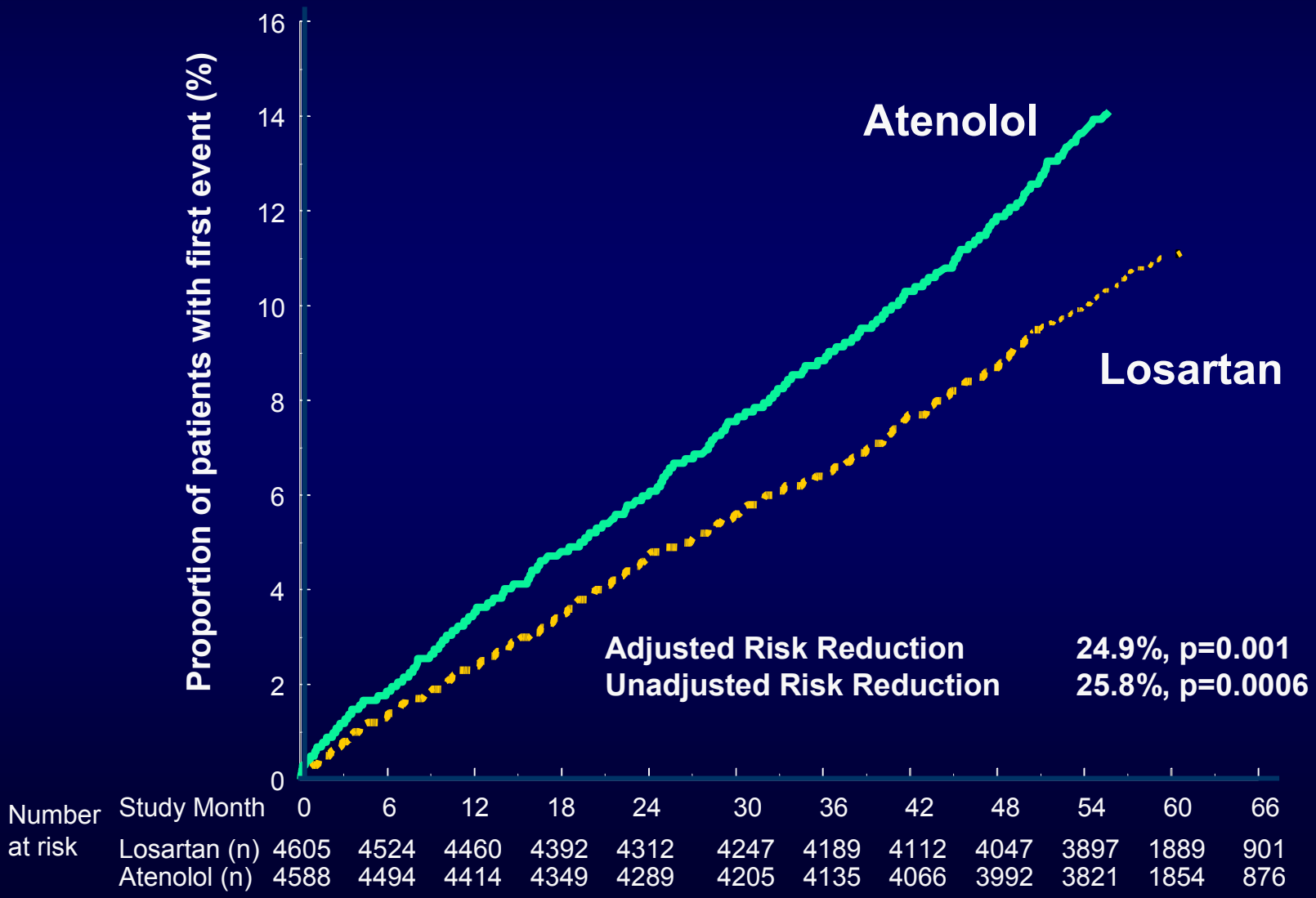
Dahlöf B et al *Lancet* 2002;359:995

LIFE: Primary Composite Endpoint

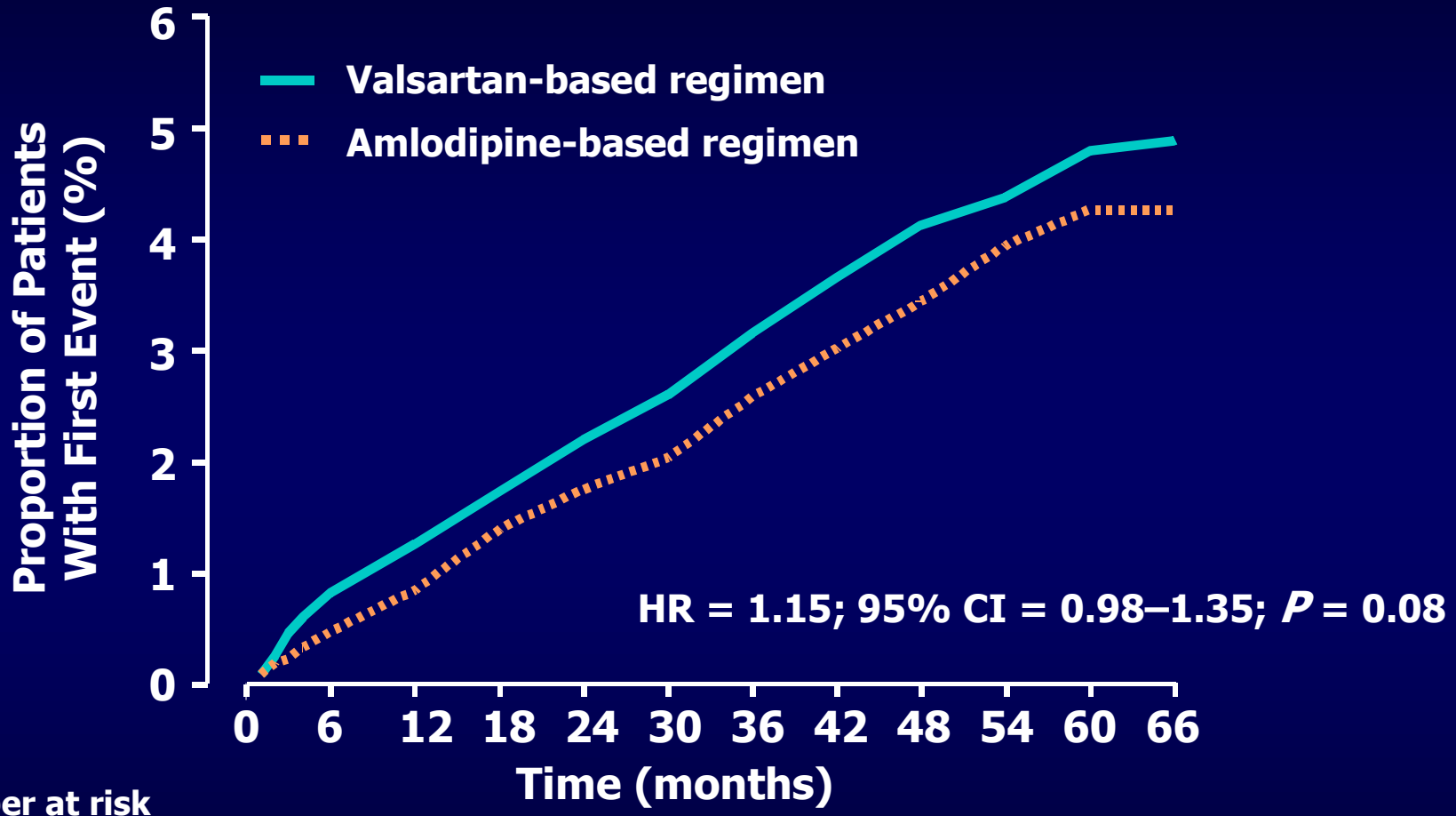


Dahlöf B et al *Lancet* 2002;359:995-1003.

LIFE: Fatal & Non-fatal stroke



VALUE: Fatal and Non-fatal Stroke



Number at risk												
Valsartan	7649	7494	7448	7312	7170	7022	6877	6692	6515	6093	3859	1516
Amlodipine	7596	7499	7455	7334	7195	7055	6918	6744	6587	6163	3846	1532

Julius S et al. *Lancet*. June 2004;363.

Prevention of Stroke in Elderly Hypertension

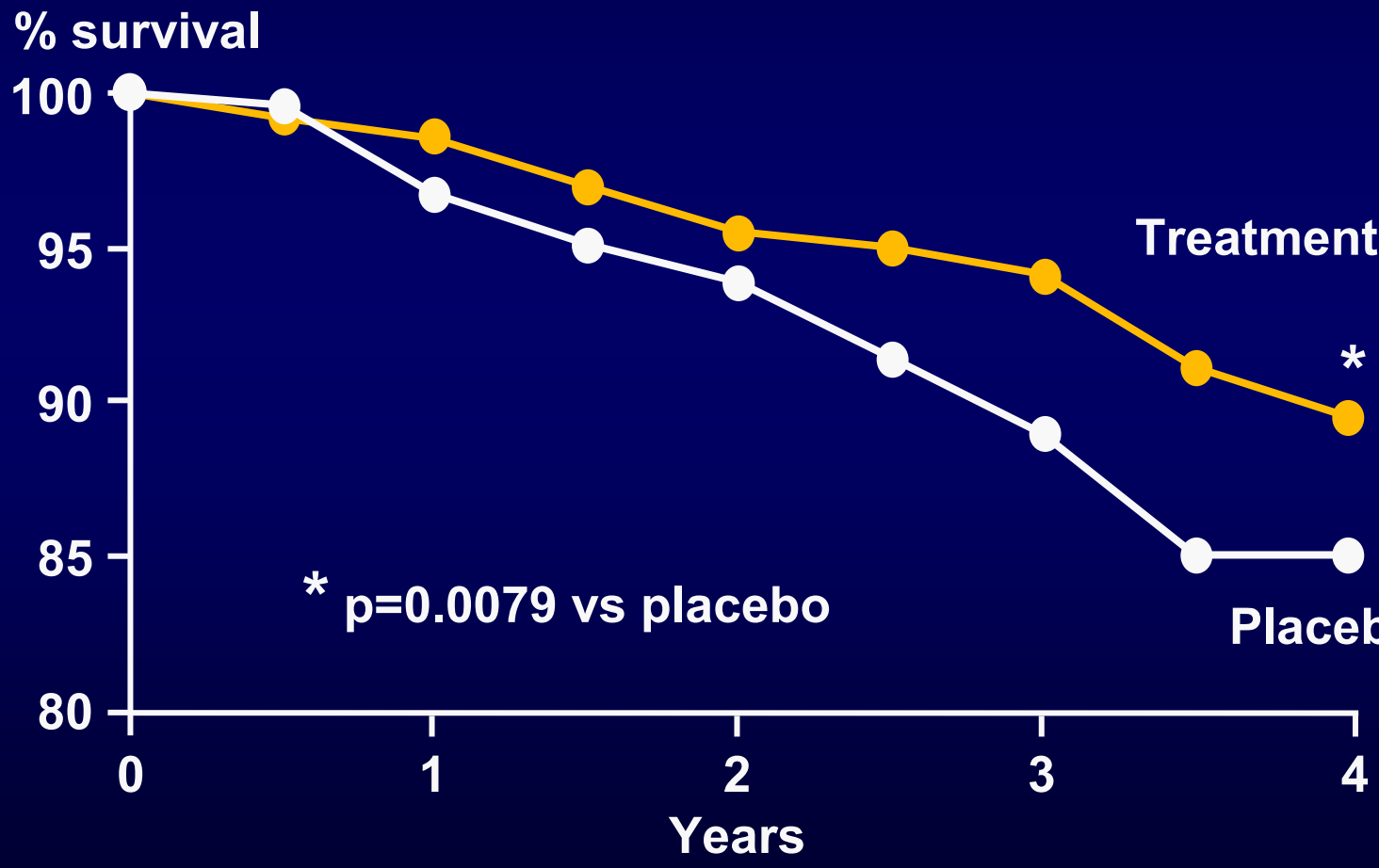
Is There Evidence for Treatment in Elderly Hypertension?

Swedish Trial in Old Patients with Hypertension (STOP-Hypertension) ,1991

Cohort	4,736; 43% men
Age	70-84 yrs old; mean 71.6 yrs old
Eligibility	Systolic BP 180-230 mmHg and Diastolic BP 105-120 mmHg
Design	Double blind; placebo control
Therapy	3 beta blockers, 1 diuretics
Duration	25 months
BP change	-19.5/8.1mmHg

Dahlöf et al Lancet 1991;338(8778):1281

STOP – Hypertension
Survival benefit with antihypertensive treatment in elderly patients



Dahlöf et al Lancet 1991;338(8778):1281

The Systolic Hypertension in the Elderly Program, 1991

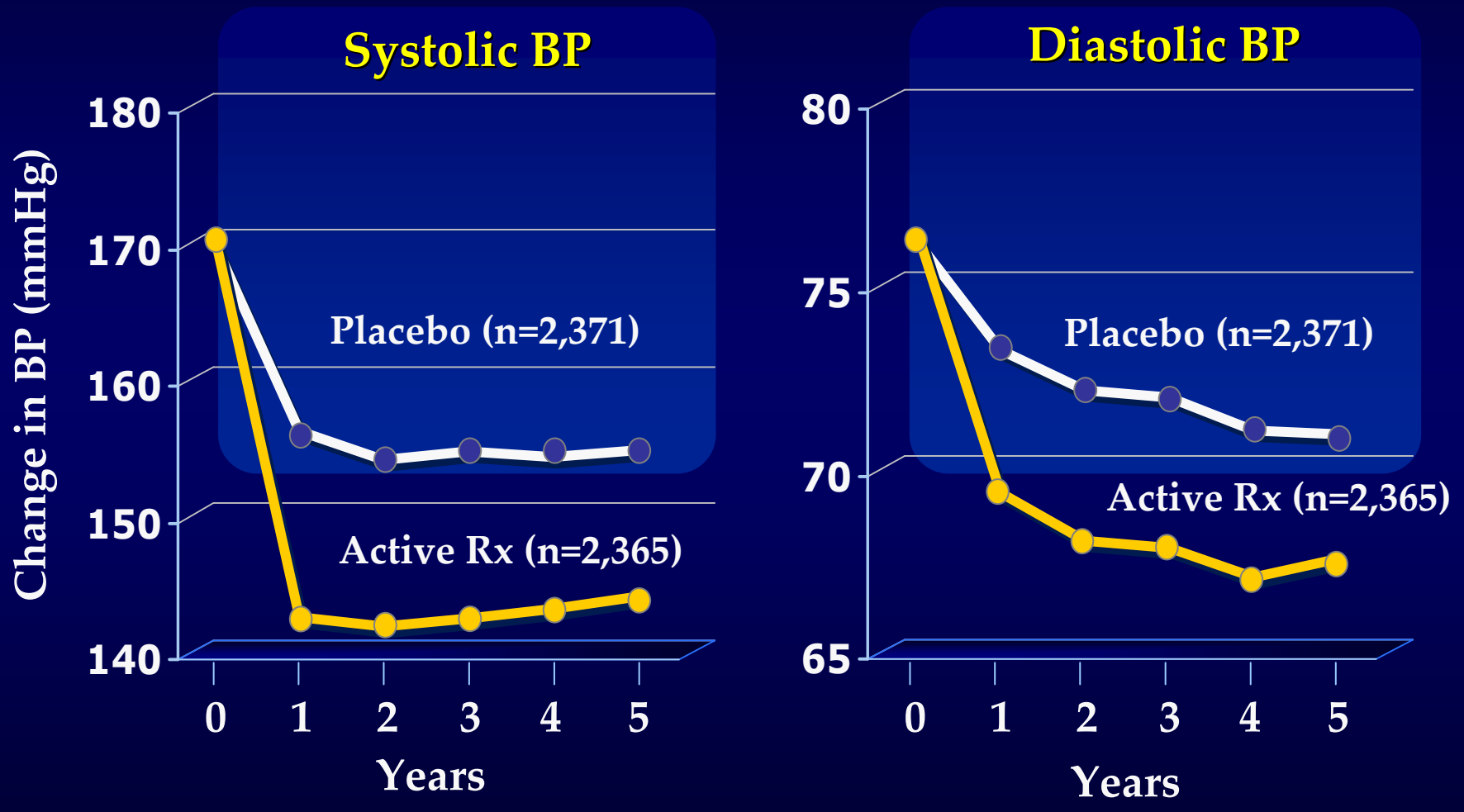
The Systolic Hypertension in the Elderly (SHEP) Program

Cohort	4,736; 43% men
Age	≥ 60 yrs old; mean 71.6 yrs old
Eligibility	Systolic BP 160–219 mmHg and Diastolic BP <90 mmHg
Design	Double blind; placebo control
Therapy	Chlorthalidone (atenolol as step 2)
Duration	4.5 years
BP change	Systolic BP –12 mmHg

SHEP Research Group. JAMA. 1991;265:3255-3264.

SHEP

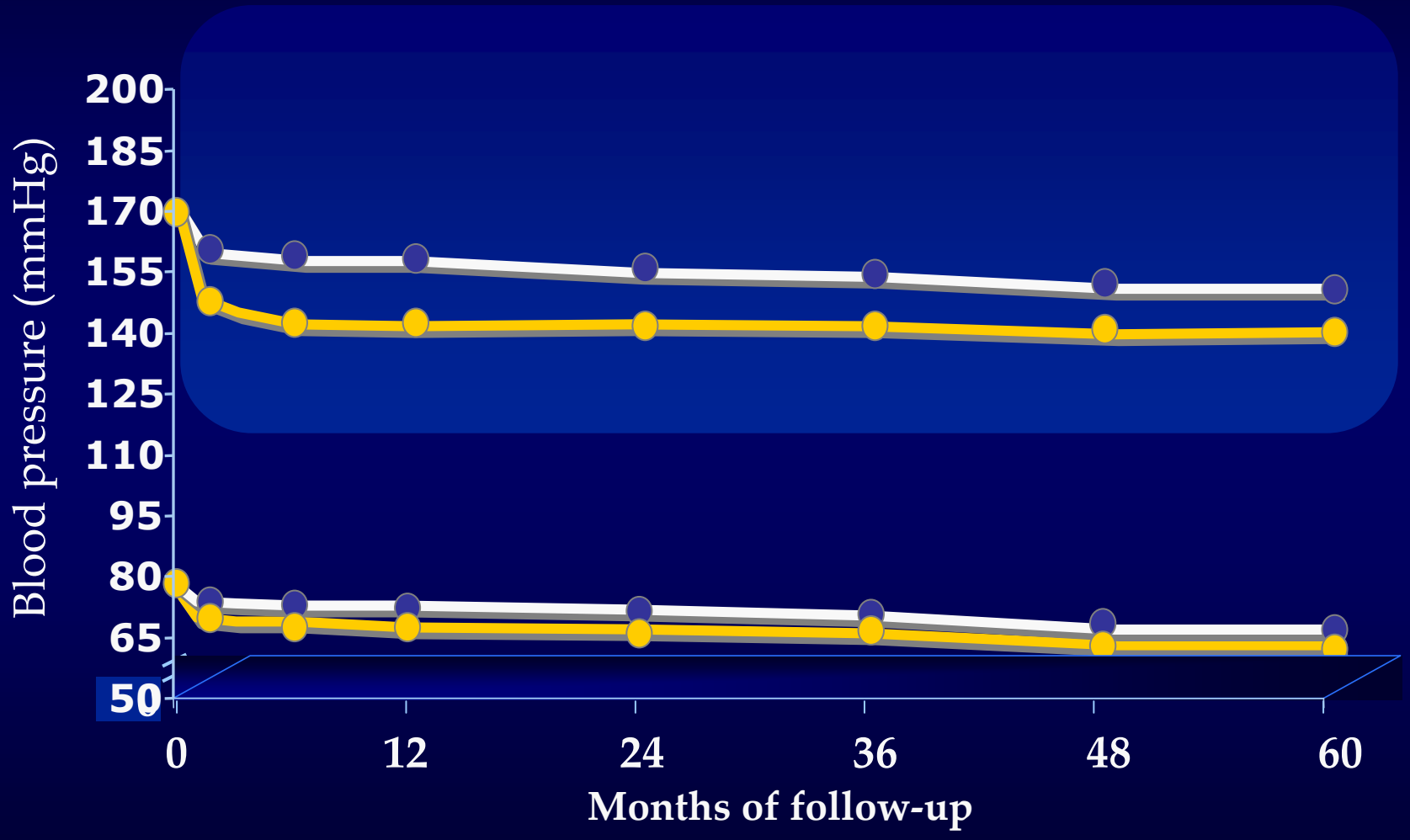
Change in Blood Pressure



SHEP Research Group. JAMA. 1991;265:3255-3264

SHEP

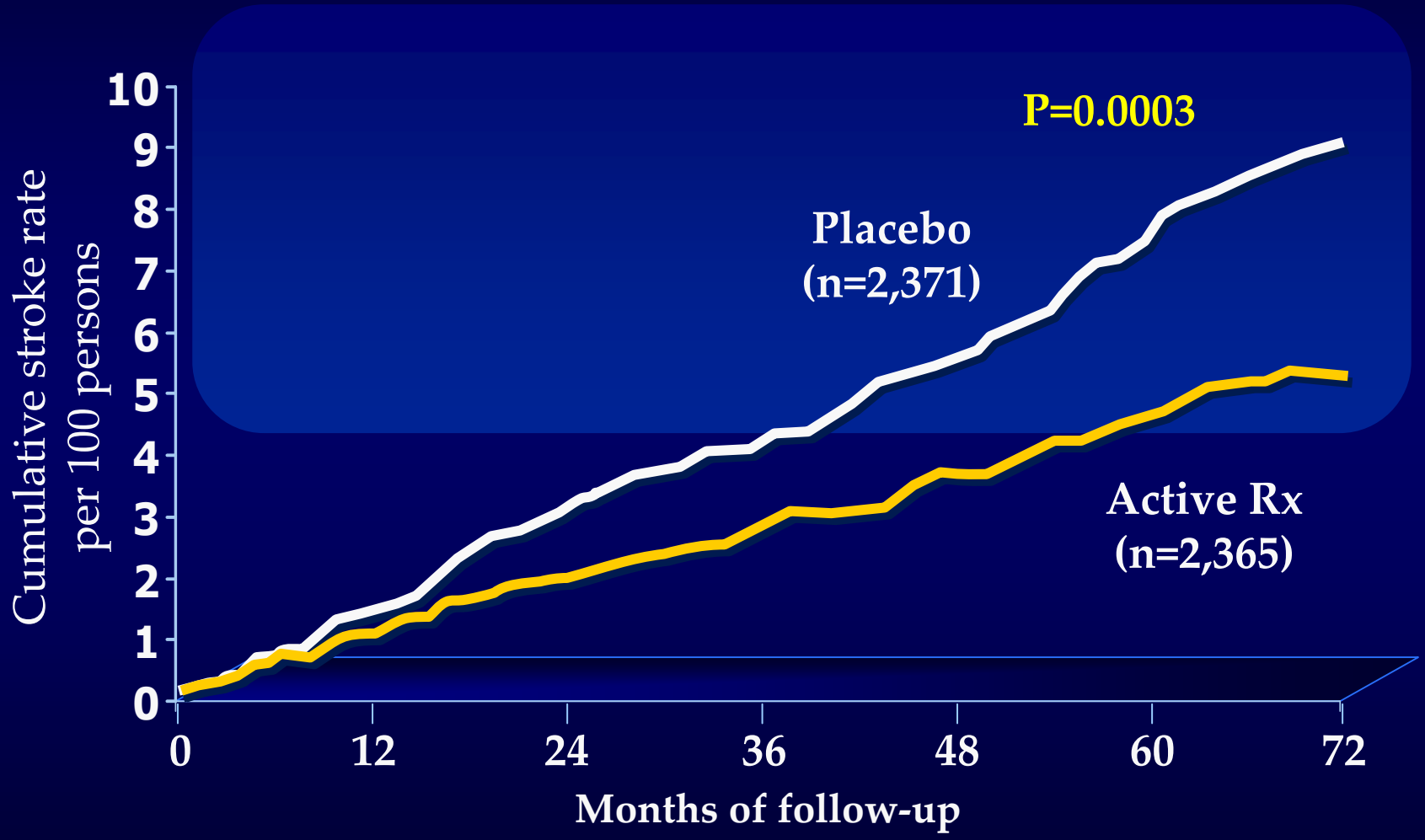
Average Blood Pressure During Follow-up



SHEP Research Group. JAMA. 1991;265:3255-3264.

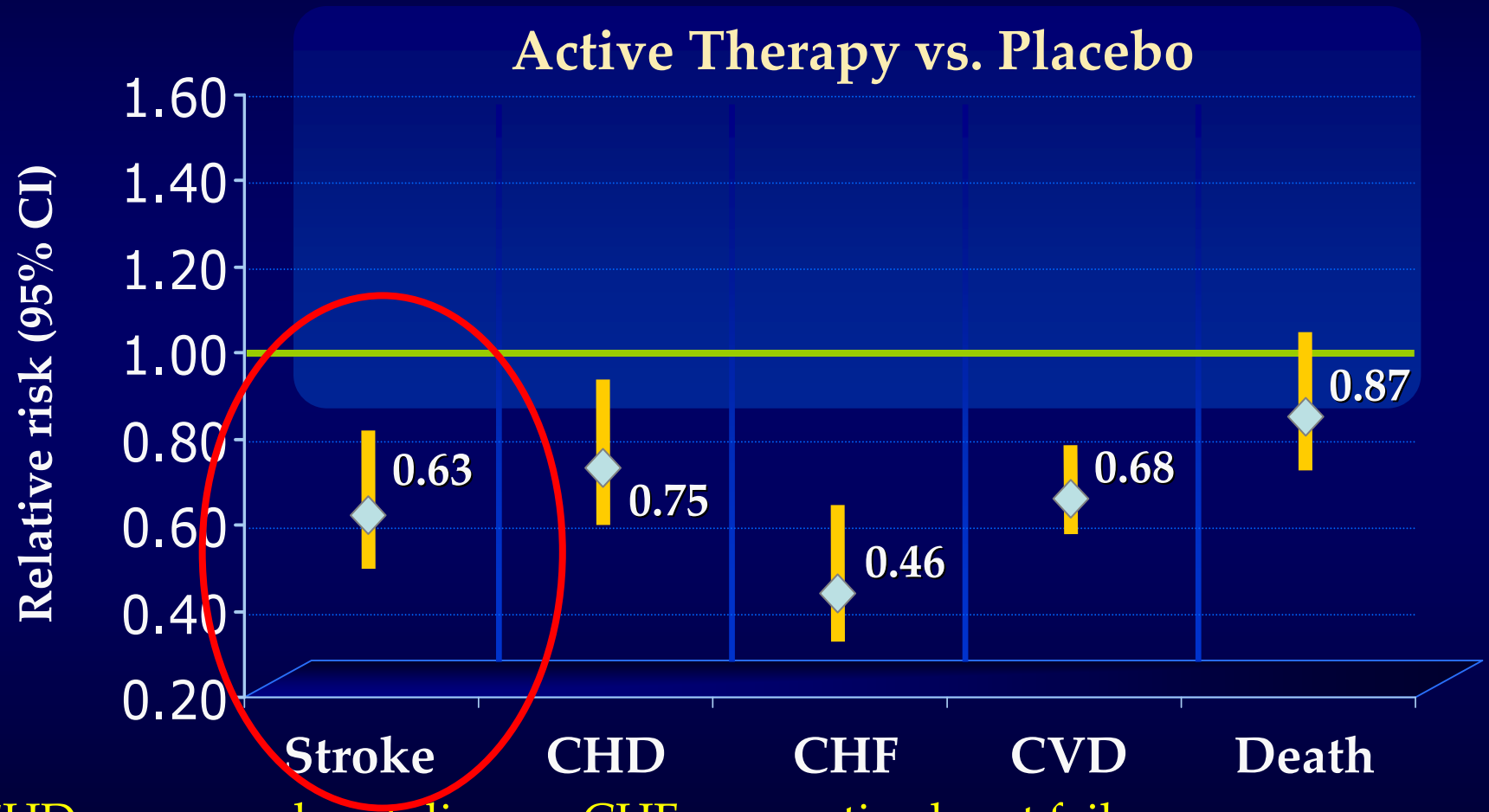
SHEP

Cumulative Stroke Rate



SHEP Research Group. JAMA. 1991;265:3255-3264.

SHEP
Cardiovascular Disease Endpoints



CHD=coronary heart disease; CHF=congestive heart failure;
CVD=cardiovascular disease

SHEP Research Group. JAMA. 1991;265:3255-3264.

SHEP
Conclusions

- SHEP was the first clinical trial to demonstrate that reduction of blood pressure in patients with isolated systolic hypertension reduced cardiovascular (CV) mortality
- The relative risk of stroke was reduced by 36% with therapy compared to placebo (P=0.0003)
- The 5-year absolute benefits were a reduction in 30 strokes and 55 major CV disease events per 1,000 persons

SHEP Research Group. JAMA. 1991;265:3255-3264.

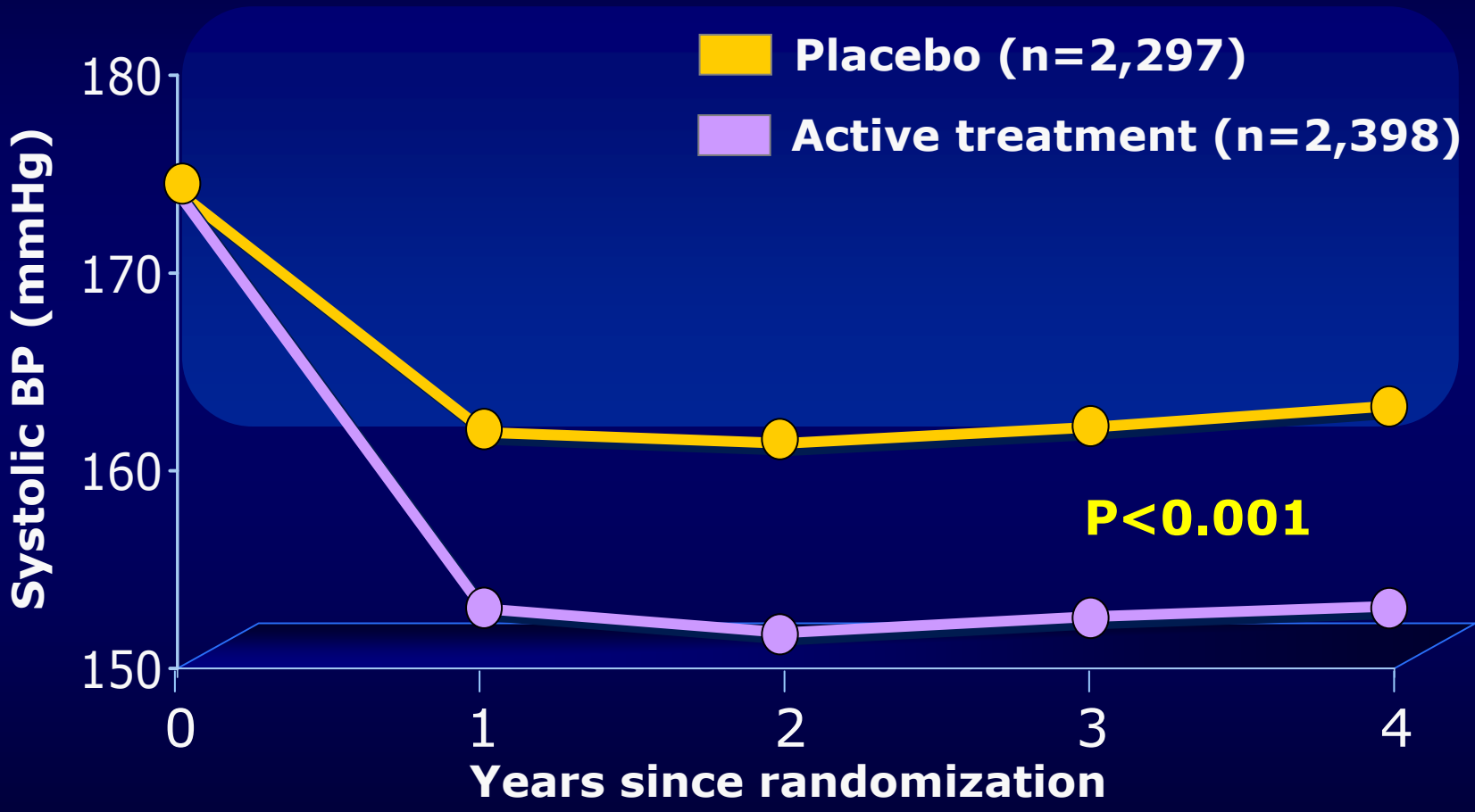
The Systolic Hypertension in Europe (Syst-Eur) Trial, 1997

The Systolic Hypertension in Europe Trial, 1997

Cohort	4,695; 67% women
Age	≥ 60 yrs old
Eligibility	Systolic BP 160–219 mmHg and diastolic BP <95 mmHg
Design	Double blind; placebo control
Therapy	Nitrendipine (enalapril, HCTZ as Step 2)
Duration	Median 2 yrs (1-97 months)
BP difference	-10/5 mmHg

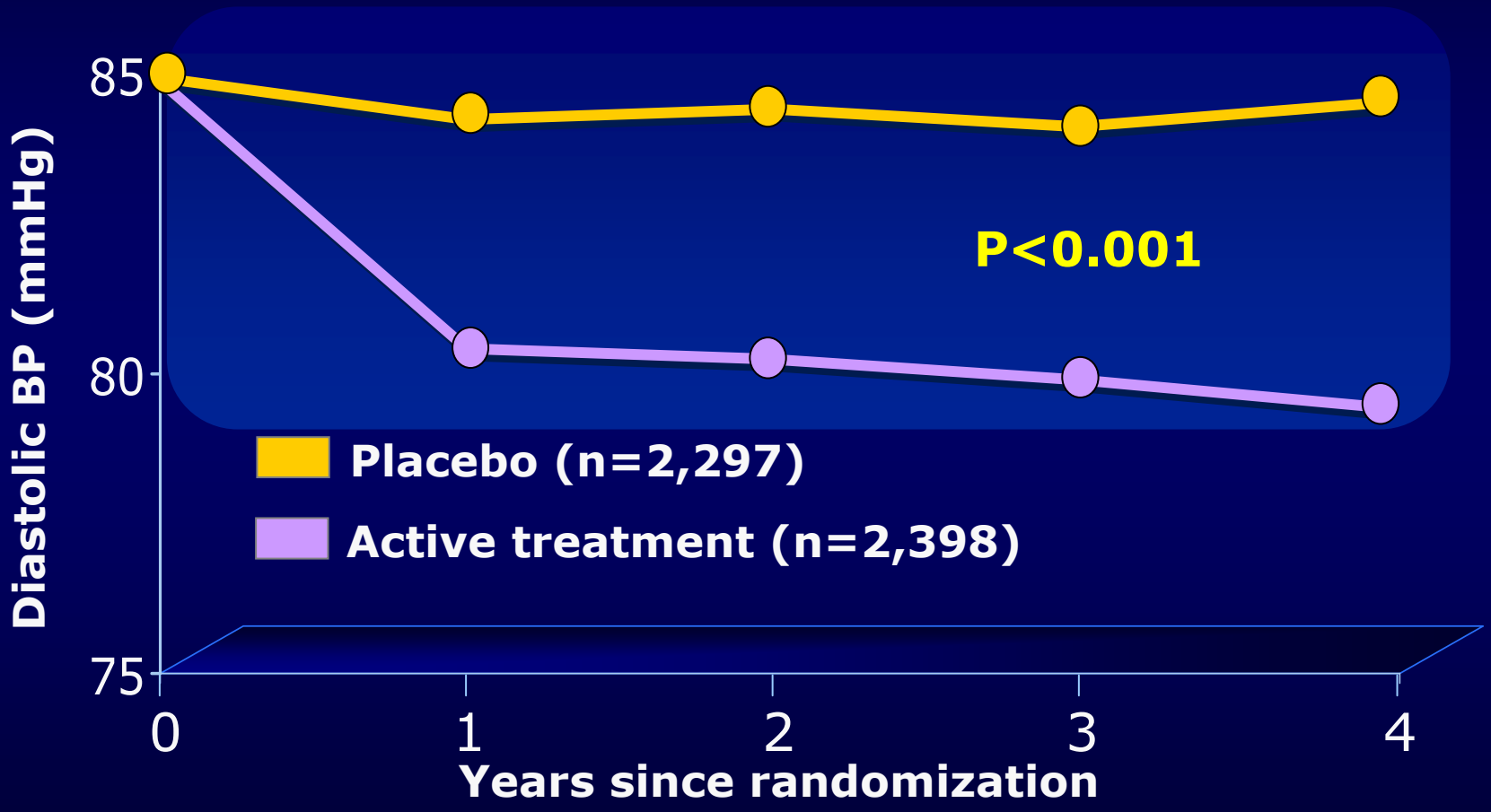
Staessen JA, et al. Lancet. 1997;350:757-764.

Syst-Eur
Mean Sitting Systolic Blood Pressure



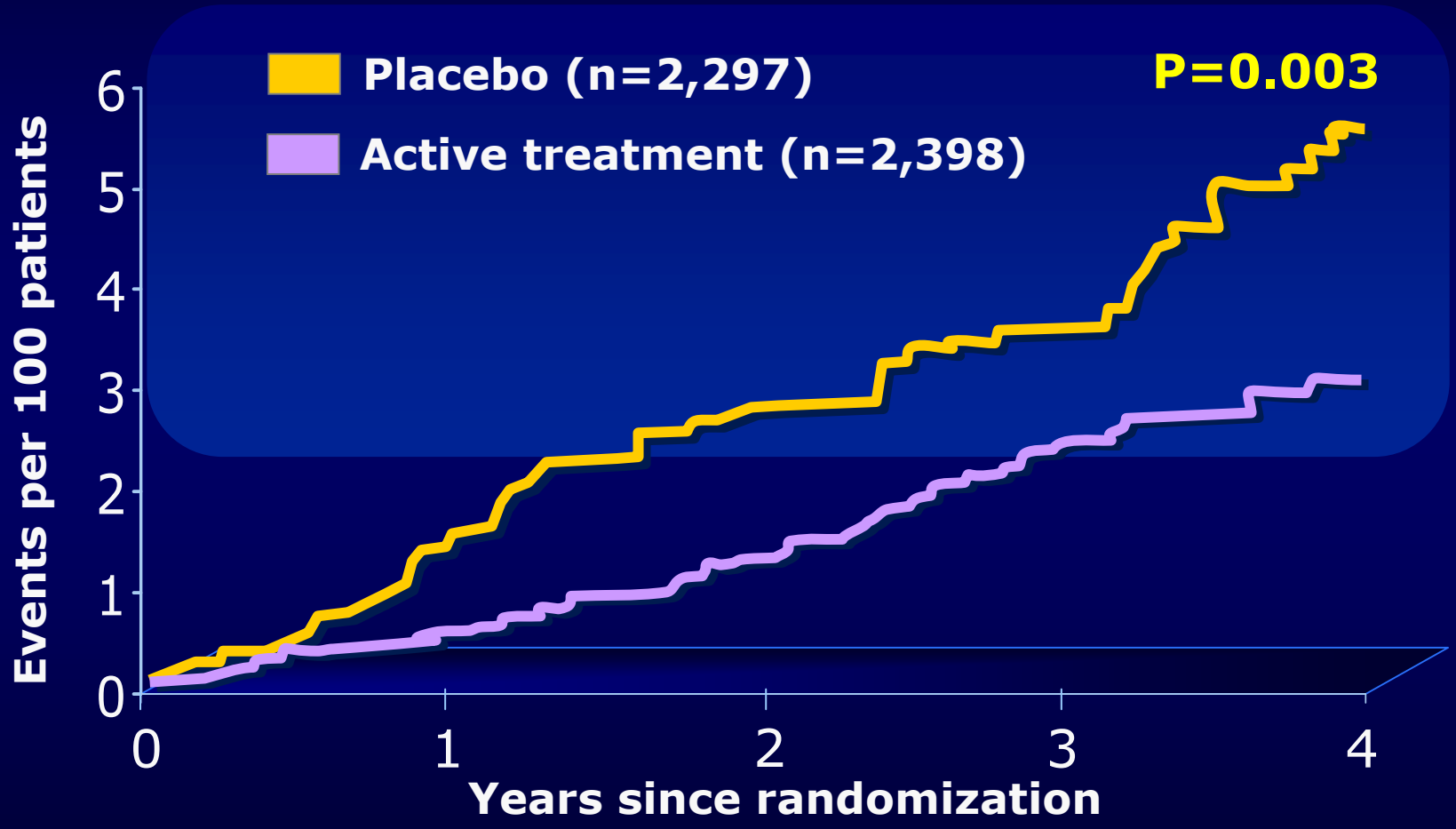
Staessen JA, et al. Lancet. 1997;350:757-764.

Syst-Eur
Mean Sitting Diastolic Blood Pressure



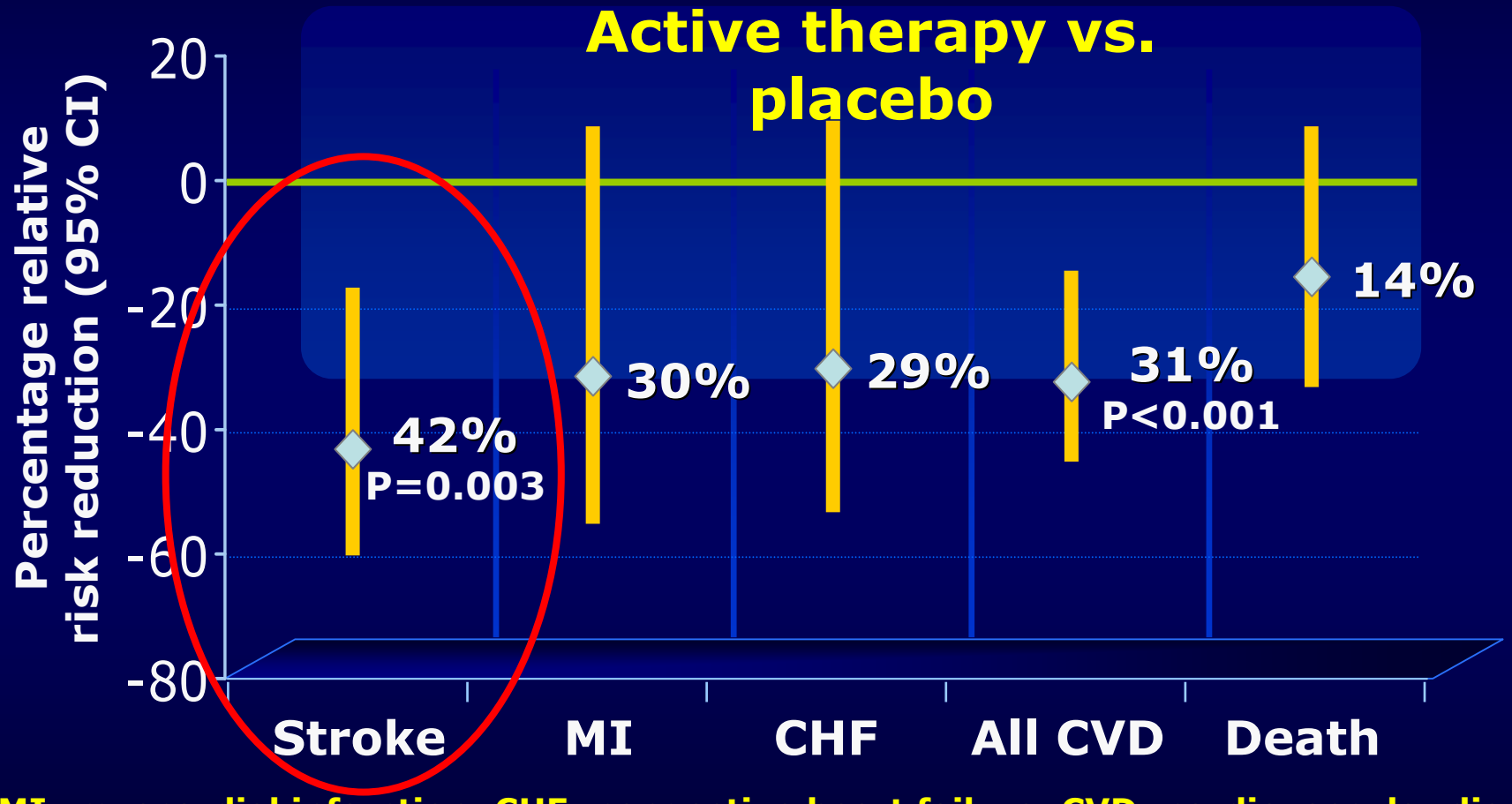
Staessen JA, et al. Lancet. 1997;350:757-764.

Syst-Eur
Primary Endpoint, Fatal and Nonfatal Stroke



Staessen JA, et al. Lancet. 1997;350:757-764.

Syst-Eur
Cardiovascular Disease Endpoints



MI=myocardial infarction; CHF=congestive heart failure; CVD=cardiovascular disease

Syst-Eur=Systolic Hypertension in Europe Trial

Staessen JA, et al. Lancet. 1997;350:757-764.

Syst-Eur
Conclusions

- Older men and women with isolated systolic hypertension who received active treatment with a dihydropyridine calcium channel blocker experienced fewer strokes and cardiovascular disease (CVD) events than those receiving placebo.

- Treatment of 1,000 patients for 5 years with this type of regimen could prevent 29 strokes or 53 major CVD endpoints.

Staessen JA, et al. Lancet. 1997;350:757-764.

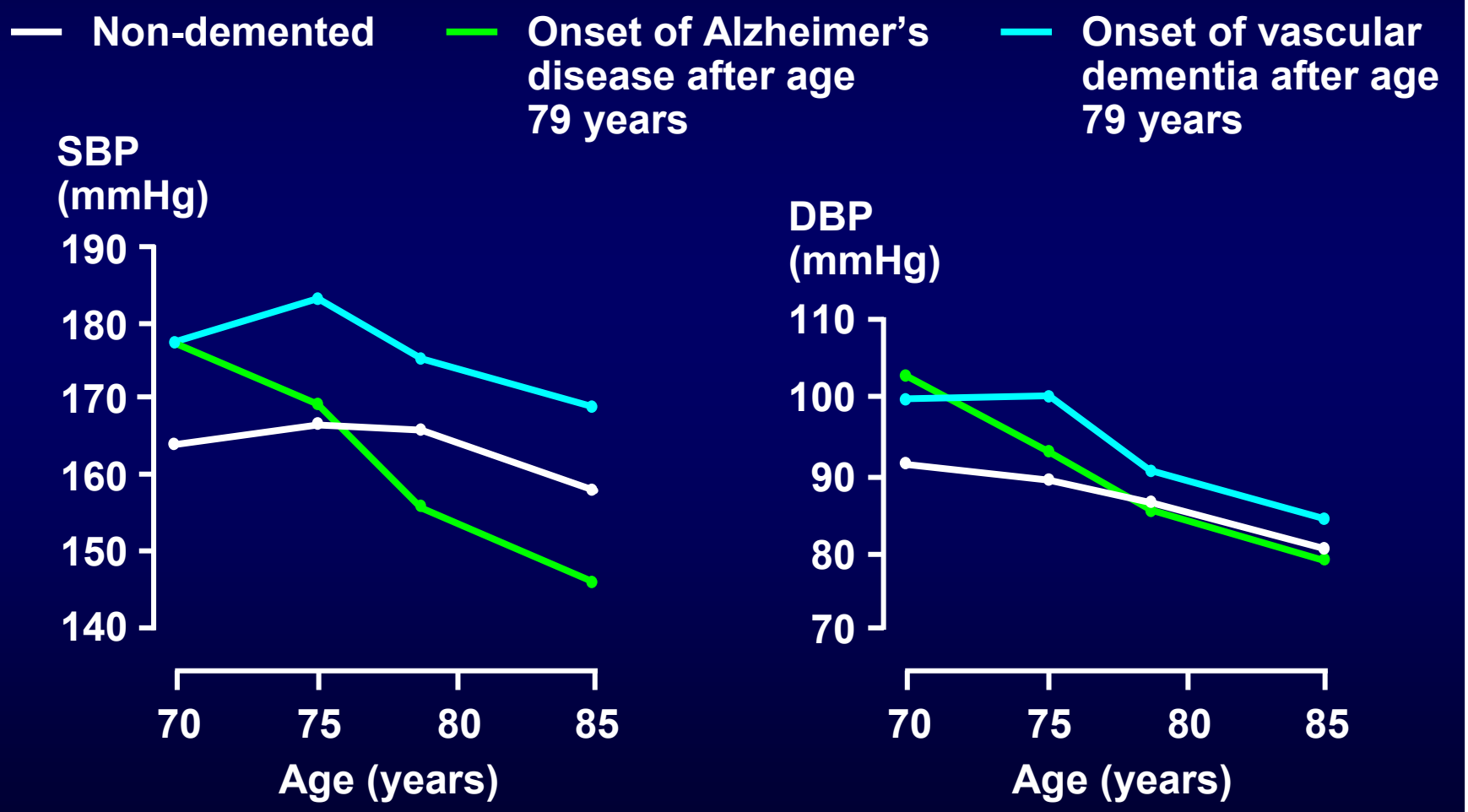
Dementia

Alzheimer's disease (AD)

Vascular dementia (VD)

Mixed AD+VD Accounts for 80% of all cases of dementia

High blood pressure precedes development of dementia



Skoog et al 1996

Hypertension and cognitive decline: white matter lesions suggest a mechanism

- Elevated blood pressure causes hyalinisation of vascular walls
- Hyalinisation coupled with episodes of hypotension may lead to hypoperfusion and ischaemia in vulnerable brain areas, such as deep white matter
- Subsequent demyelinisation may lead to disconnection of subcortical-cortical pathways, resulting in cognitive decline and dementia

Antihypertensive treatment halves dementia rate in Syst-Eur

- 2418 patients aged ≥60 years
- Median MMSE=29
- ≥1 year follow up

New cases of dementia (defined as MMSE £23)	
placebo	active treatment
21	**11**
7.7 / 1000 patient years	**3.8 / 1000 patient years**
p=0.05	

Forette et al Lancet 1998;352:1347

Study on COgnition and Prognosis in the Elderly (SCOPE)

Rationale for SCOPE

- Hypertension is a risk factor for both CV disease and dementia
- Antihypertensive treatment reduces CV risk and may reduce risk of dementia
- However, data are inconclusive with regard to elderly patients with mild-to-moderate hypertension

Objectives

Primary

- Major cardiovascular events (cardiovascular death, no n-fatal myocardial infarction, non-fatal stroke)

Secondary

- Cognitive function
- Dementia
- Total mortality
- Cardiovascular mortality
- Fatal MI
- Non-fatal MI
- All MI
- Fatal stroke
- Non-fatal stroke
- All stroke
- Development of diabetes mellitus
- Discontinuation of study drug

Lithell et al, J Hypertens 2003

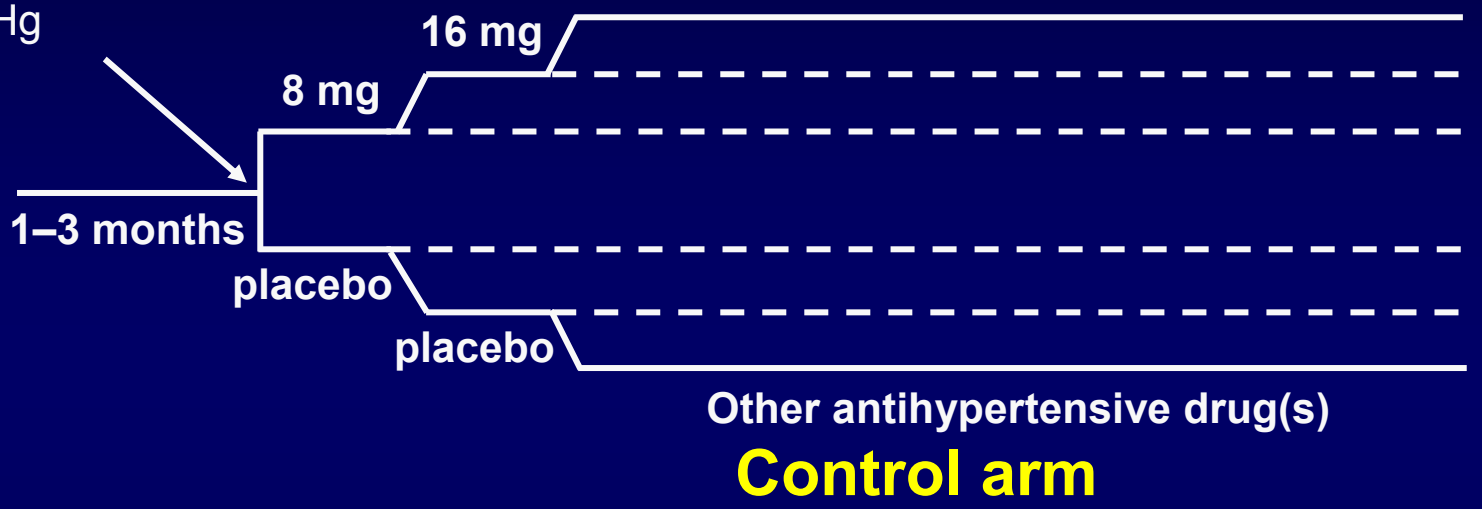
Inclusion criteria

- Men and women, aged 70–89 years
- Previously treated or untreated hypertension
- Previous treatment standardised to HCT 12.5 mg
- SBP 160–179 mmHg or DBP 90–99 mmHg, or both
- MMSE score ≥24

Lithell et al, J Hypertens 2003

Design

Randomisation:
Patients untreated or HCT 12.5 mg with SBP 160–179 mmHg and/or DBP 90–99 mmHg



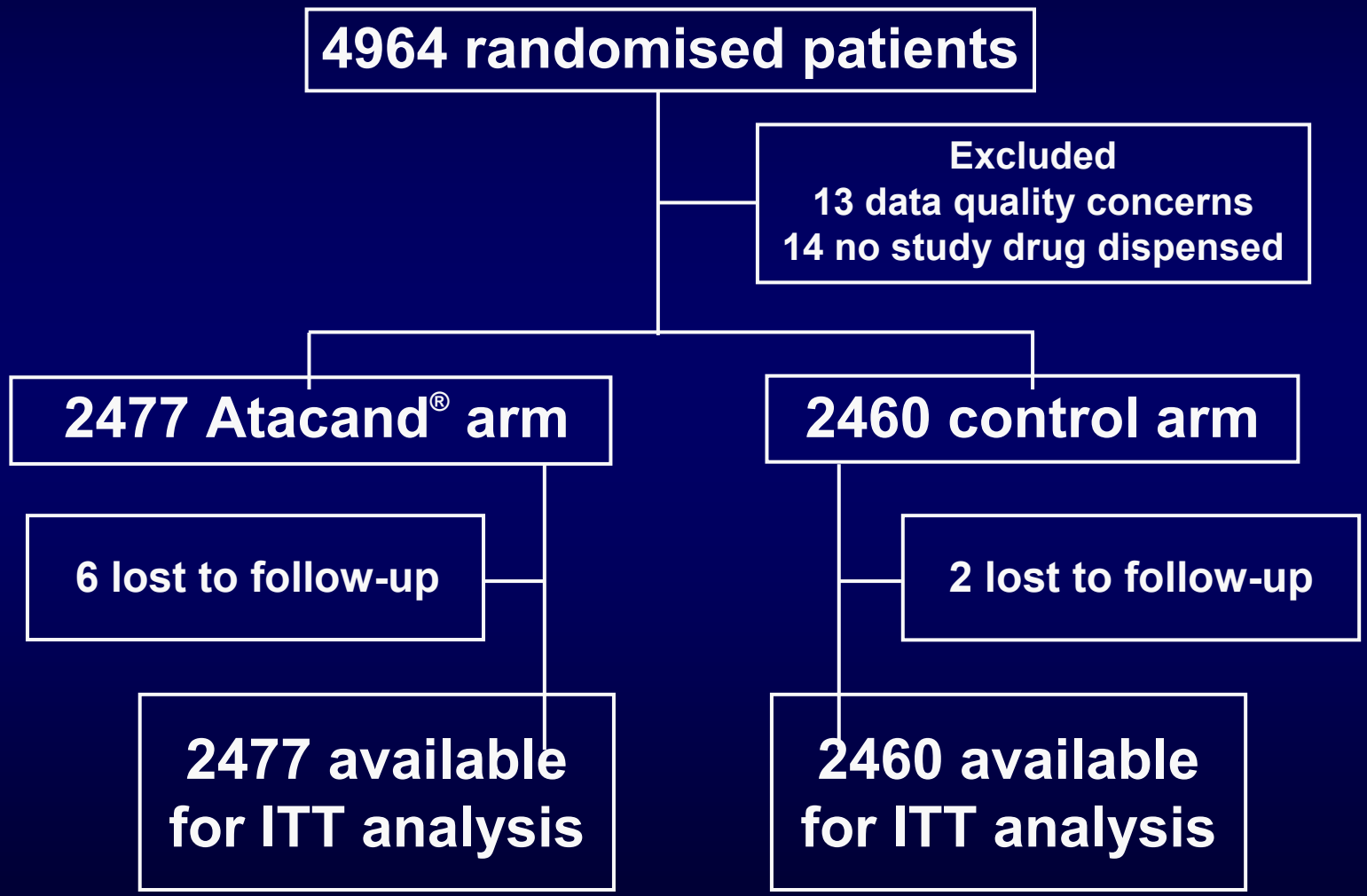
Step 1: candesartan 8 mg, or placebo, once daily

Step 2: If SBP >160 mmHg or DBP >85 mmHg – dose doubled

Step 3: If SBP remains ≥160 mmHg or DBP remains ≥90 mmHg – other antihypertensive drug (not ACE inhibitor or AT_1-receptor blocker) added

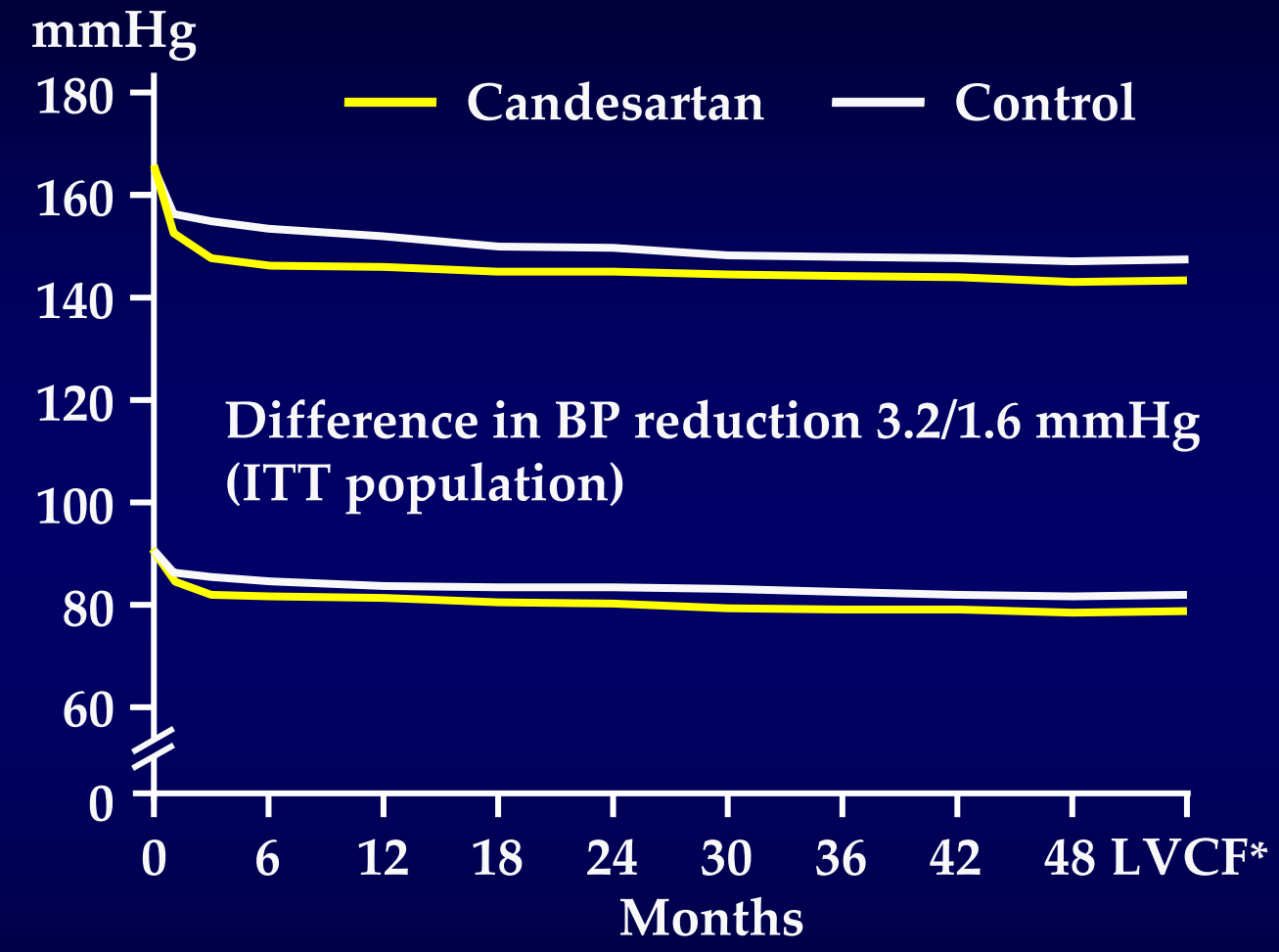
Lithell et al, J Hypertens 2003

SCOPE analysed data from 4937 patients



Lithell et al, J Hypertens 2003

Blood pressure reductions



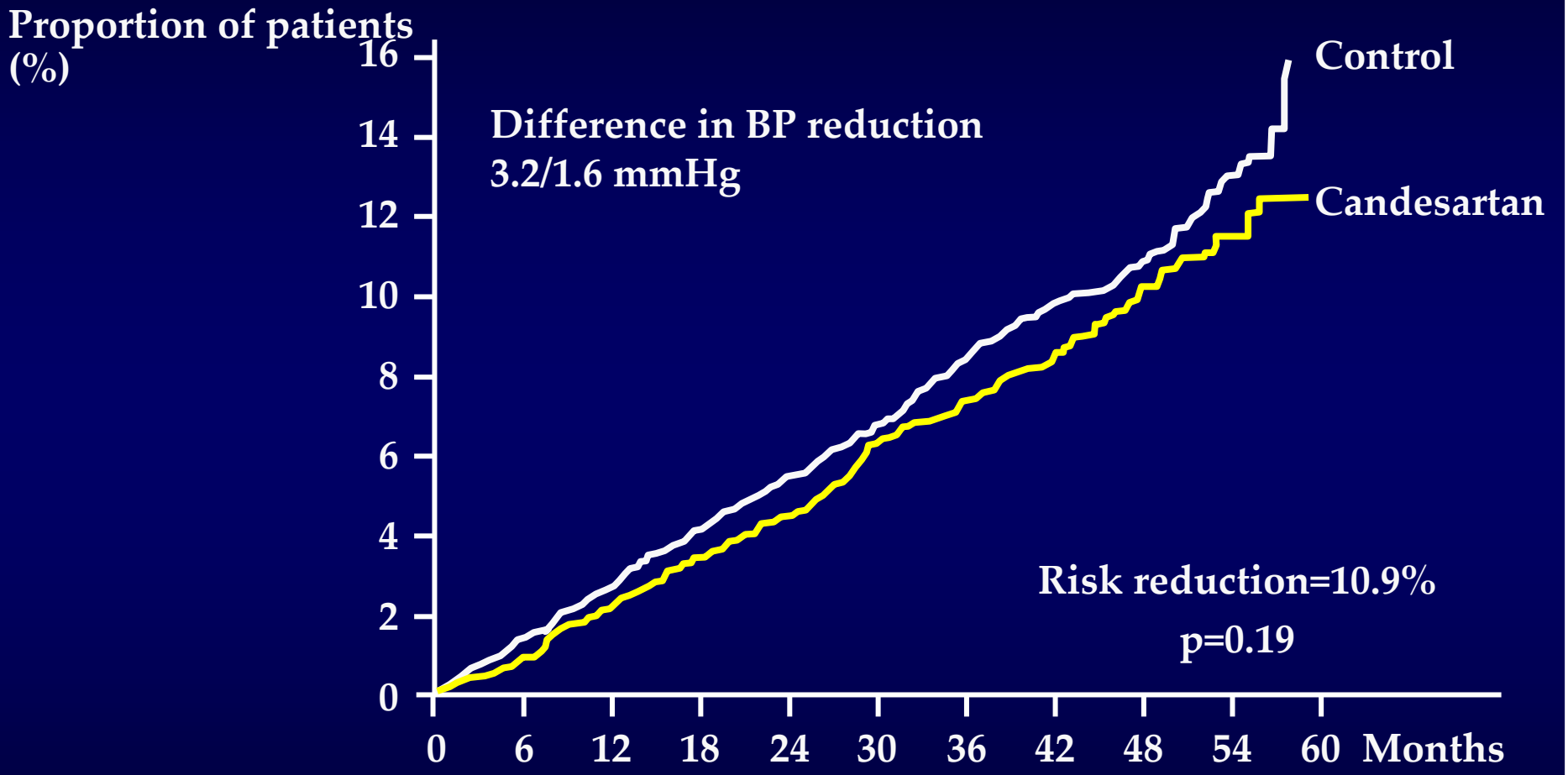
Candesartna (n)	2477	2317	2217	1703	646	2468
Control (n)	2460	2296	2192	1656	635	2455

* LVCF=last value carried forward

* LVCF=last value carried forward

Lithell et al, J Hypertens 2003

First major cardiovascular event



Atacand®	(n)	2477	2454	2371	2262	1587	406
Control	(n)	2460	2423	2333	2239	1542	401

Lithell et al, J Hypertens 2003

Incidences of significant cognitive decline and dementia

Number of patients (events per 1000 patient years)

	Candesartan	Control	p value
Significant cognitive decline	113 (13.5) (n=2416)	125 (15.2) (n=2409)	>0.20
Dementia	62 (6.8) (n=2477)	57 (6.3) (n=2460)	>0.20

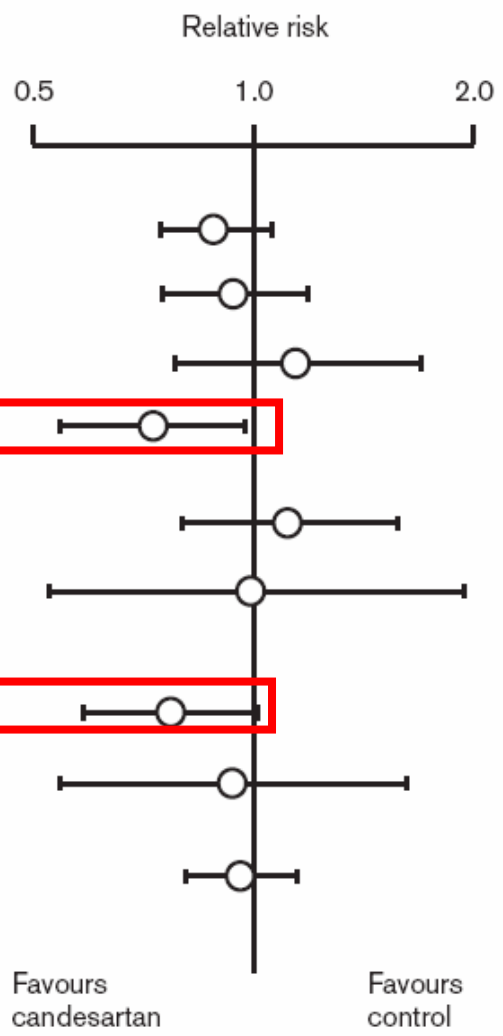
Lithell et al, J Hypertens 2003

SCOPE: Fatal & All stroke

	Candesartan (*n* = 2477)		Control (*n* = 2460)	
	n	rate	*n*	rate
Major CV events	242	26.7	268	30.0
CV deaths	145	15.6	152	16.6
Non-fatal MI	54	5.9	47	5.2
Non-fatal stroke	68	7.4	93	10.3
All MI	70	7.6	63	6.9
Fatal MI	18	1.9	18	2.0
All stroke	89	9.7	115	12.8
Fatal stroke	24	2.6	26	2.8
Total mortality	259	27.9	266	29.0

Non-fatal stroke 27.8% reduction (p=0.04)

All stroke 23.6% reduction (p=0.056)



Study on Cognition and Prognosis in the Elderly (SCOPE) Subdata Analysis

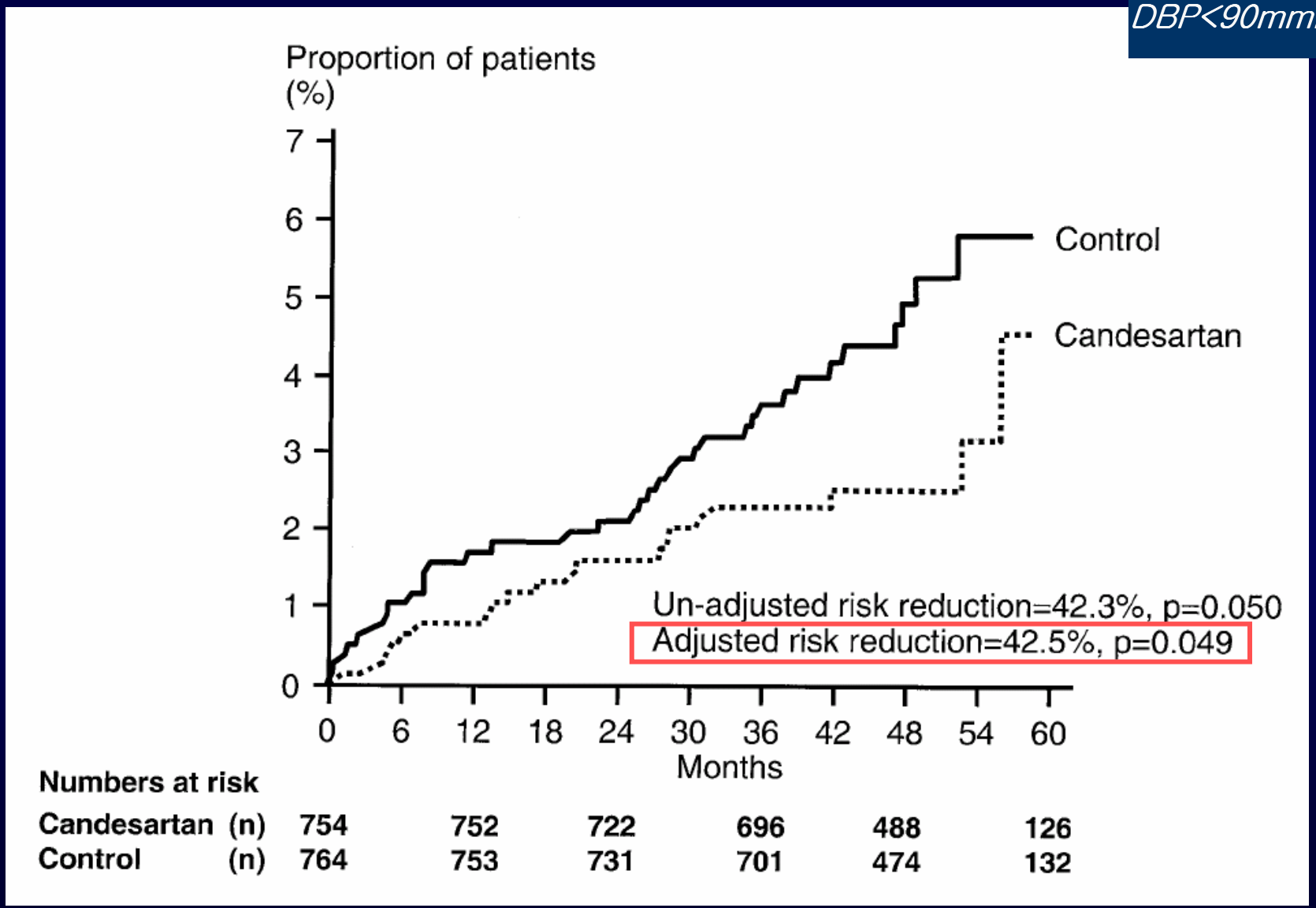
Isolated systolic hypertension group

SCOPE:ISH

Fatal or Non-fatal Stroke

patients with isolated systolic hypertension(ISH)

SBP≥160mmHg
DBP<90mmHg



Conclusions

- Considerable blood pressure reductions achieved in both treatment groups
- For major CV events, there was an 11% risk reduction in the Atacand®-based treatment group (p=0.19)
- Marked risk reduction of 28% in non-fatal stroke with Atacand® (p=0.04)
- For all stroke, there was a 24% risk reduction in the Atacand® group (p=0.056)

Lithell et al, J Hypertens 2003

Beta-blocker as 1st line drug in Elderly Patients

The time of withhold?

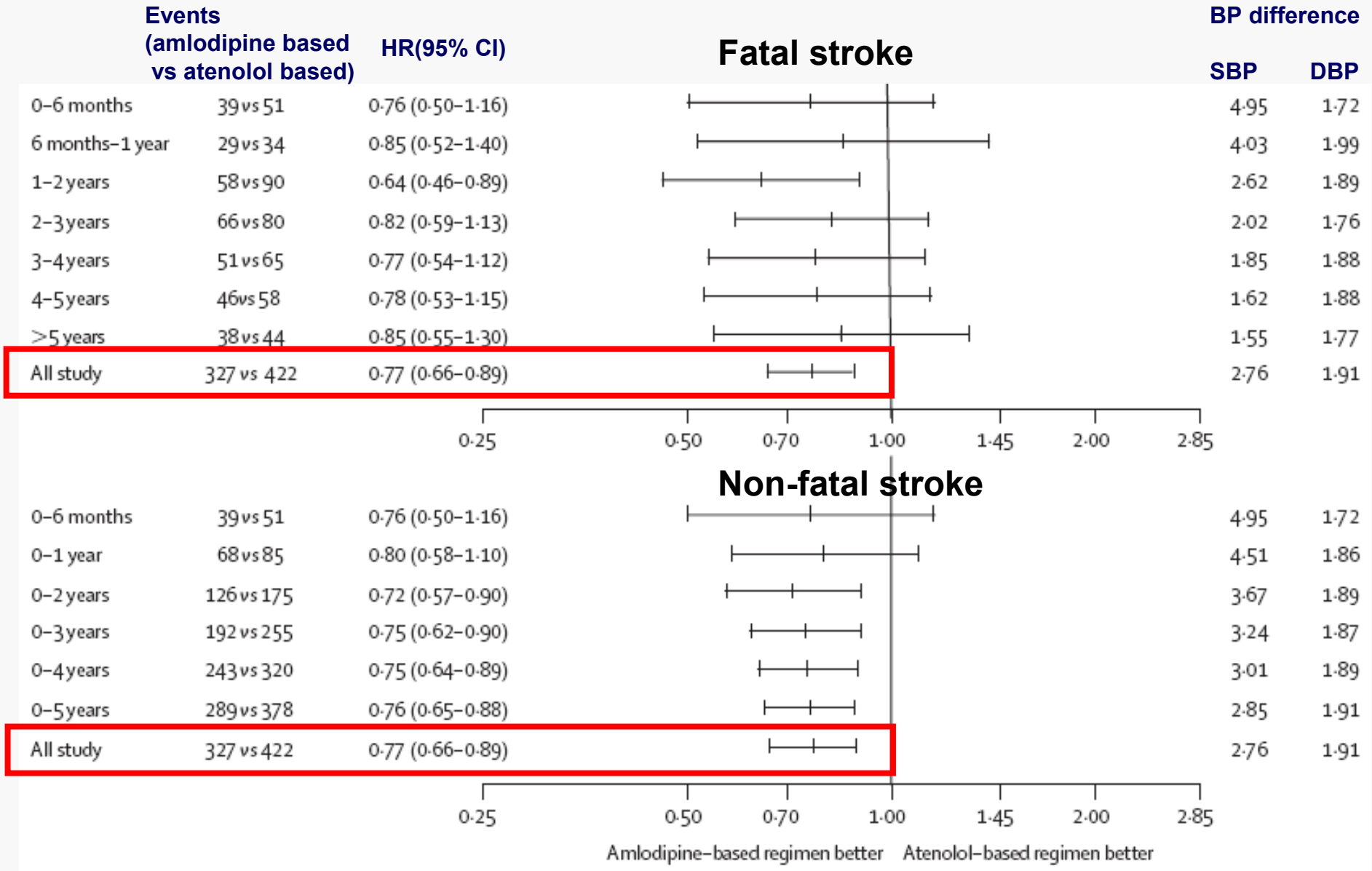
Beta-blocker, No Strong Evidence for Survival Benefit

Overview of Major Meta-Analyses of Randomized Controlled Trials of Beta-Blockers vs. Placebo for Patients with Hypertension

Meta-Analysis	Parameter	No. of Trials	Mortality	Myocardial Infarction	Stroke
Cochrane (2007)	Overall	4	0.99 (0.88-1.11)	0.93 (0.81-1.07)	0.80 (0.66-0.96)
Bradley et al. (2006)	Overall	4	0.99 (0.88-1.11)	0.93 (0.81-1.07)	0.80 (0.66-0.96)
Khan et al. (2006)	Younger	2	0.94 (0.79-1.10)	0.85 (0.71-1.03)	0.84 (0.65-1.10)
Khan et al. (2006)	Elderly	5	0.91 (0.74-1.12)	0.98 (0.83-1.16)	0.78 (0.63-0.98)
Lindholm et al. (2005)	Overall	7	0.95 (0.86-1.04)	0.93 (0.83-1.05)	0.81 (0.71-0.93)
Carlberg et al. (2004)	Overall	4	1.01 (0.89-1.15)	0.99 (0.83-1.19)	0.85 (0.72-1.01)

Numbers represent hazard ratio (95% confidence interval).

ASCOT-BPLA,2005
Fatal & Non-fatal stroke



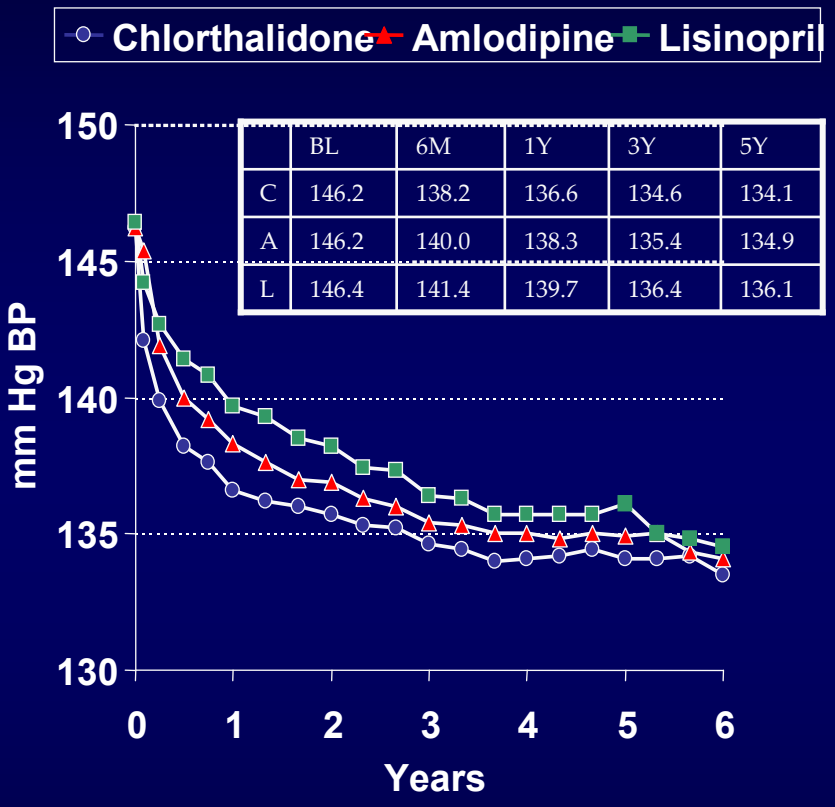
BRITISH HYPERTENSION SOCIETY GUIDELINES

Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004—BHS IV

Hypertension in the elderly

The routine use of beta-blockers to treat high BP in older people should be limited unless there are specific indications, for example, post MI, angina or heart failure.

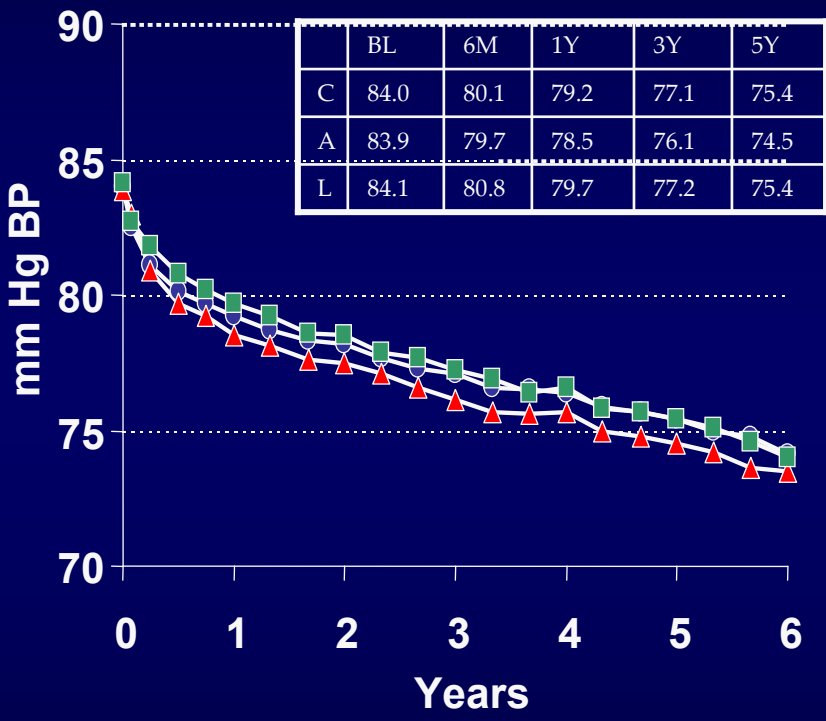
ALLHAT: BP Results by Treatment Group



	BL	6M	1Y	3Y	5Y
C	146.2	138.2	136.6	134.6	134.1
A	146.2	140.0	138.3	135.4	134.9
L	146.4	141.4	139.7	136.4	136.1

Compared to chlorthalidone:

SBP significantly higher in the amlodipine group (~1 mm Hg) and the lisinopril group (~2 mm Hg).



	BL	6M	1Y	3Y	5Y
C	84.0	80.1	79.2	77.1	75.4
A	83.9	79.7	78.5	76.1	74.5
L	84.1	80.8	79.7	77.2	75.4

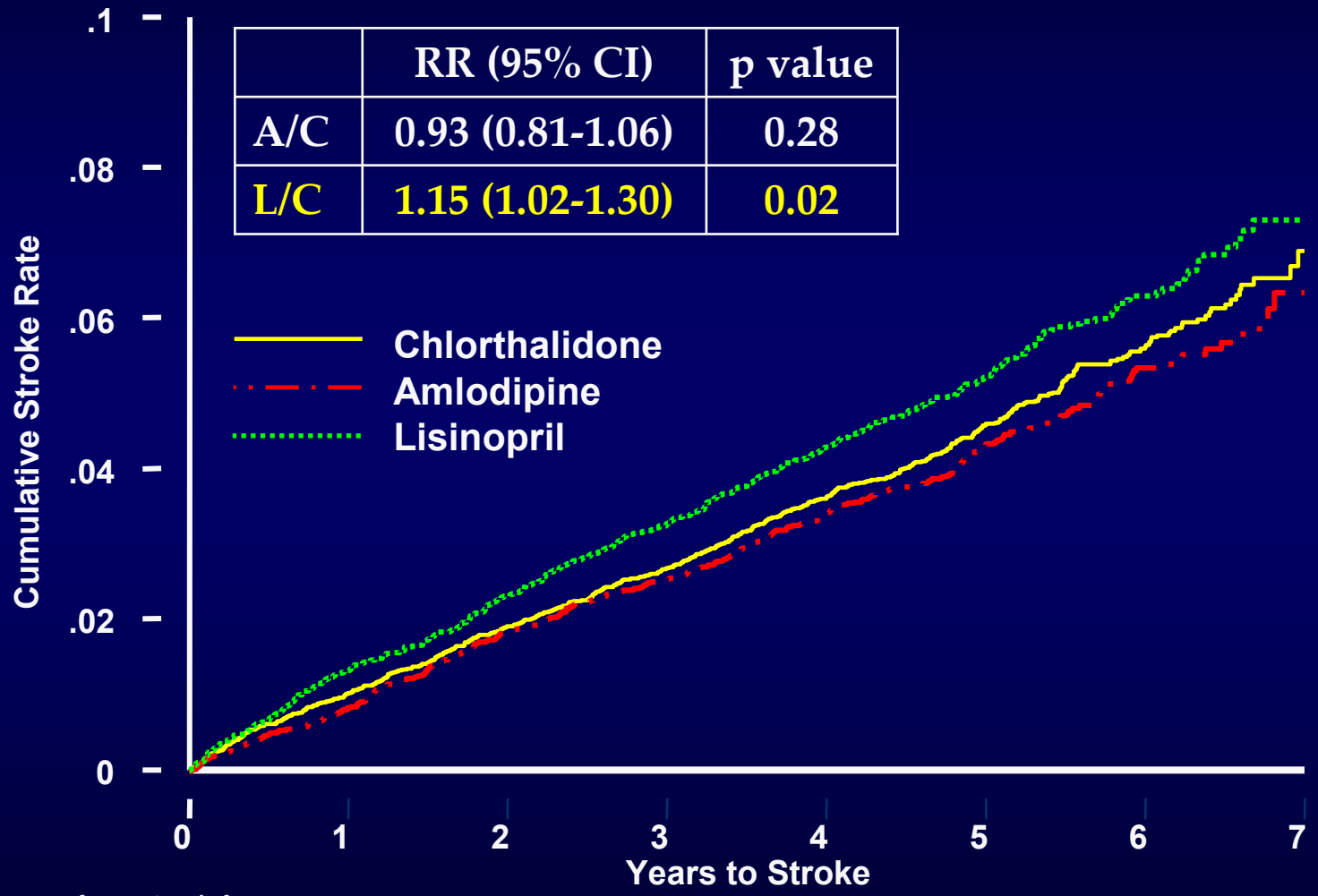
Compared to chlorthalidone:

DBP significantly lower in the amlodipine group (~1 mm Hg).

JAMA 2002;288:2981-2997

ALLHAT : Risk of Stroke

	RR (95% CI)	p value
A/C	0.93 (0.81-1.06)	0.28
L/C	1.15 (1.02-1.30)	0.02



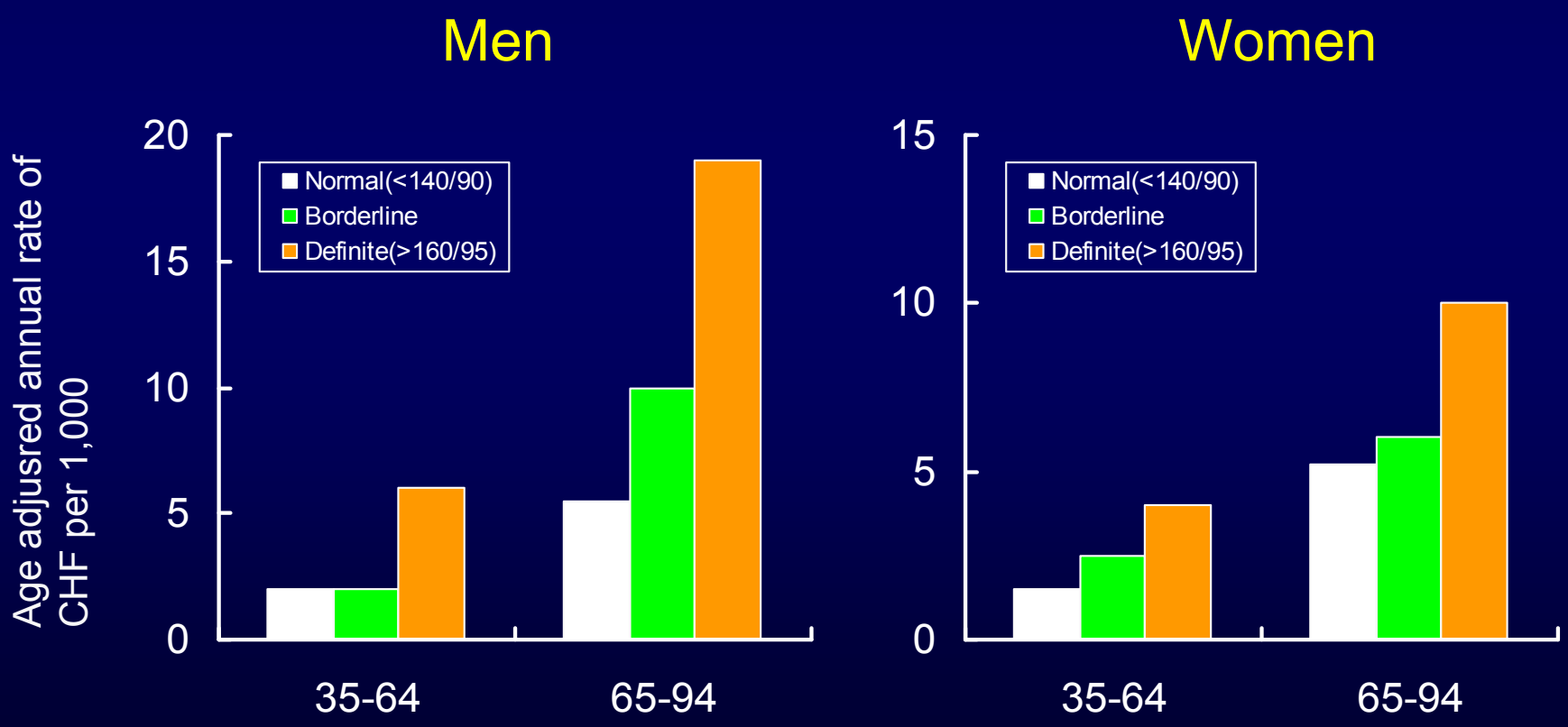
Number at risk:							
Chlor	15,255	14,515	13,934	13,309	11,570	6,385	3,217	567
Amlo	9,048	8,617	8,271	7,949	6,937	3,845	1,813	506
Lisin	9,054	8,543	8,172	7,784	6,765	3,891	1,828	949

Prevention of Heart Failure in Elderly Hypertension

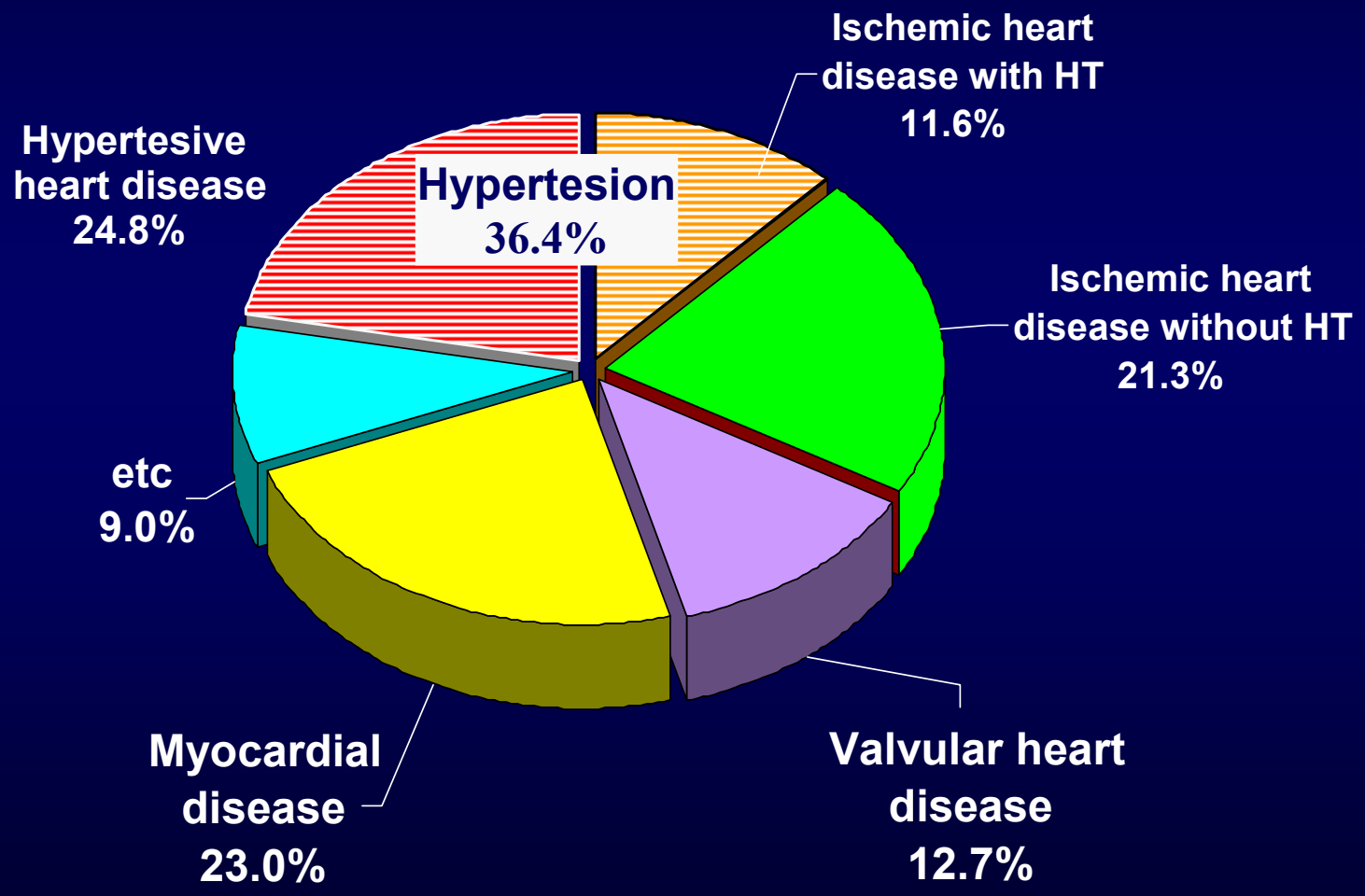
Hypertension, still leading cause of heart failure

Effect of hypertension on the risk of heart failure (Framingham Study)
Levy D et al. *JAMA 1996*

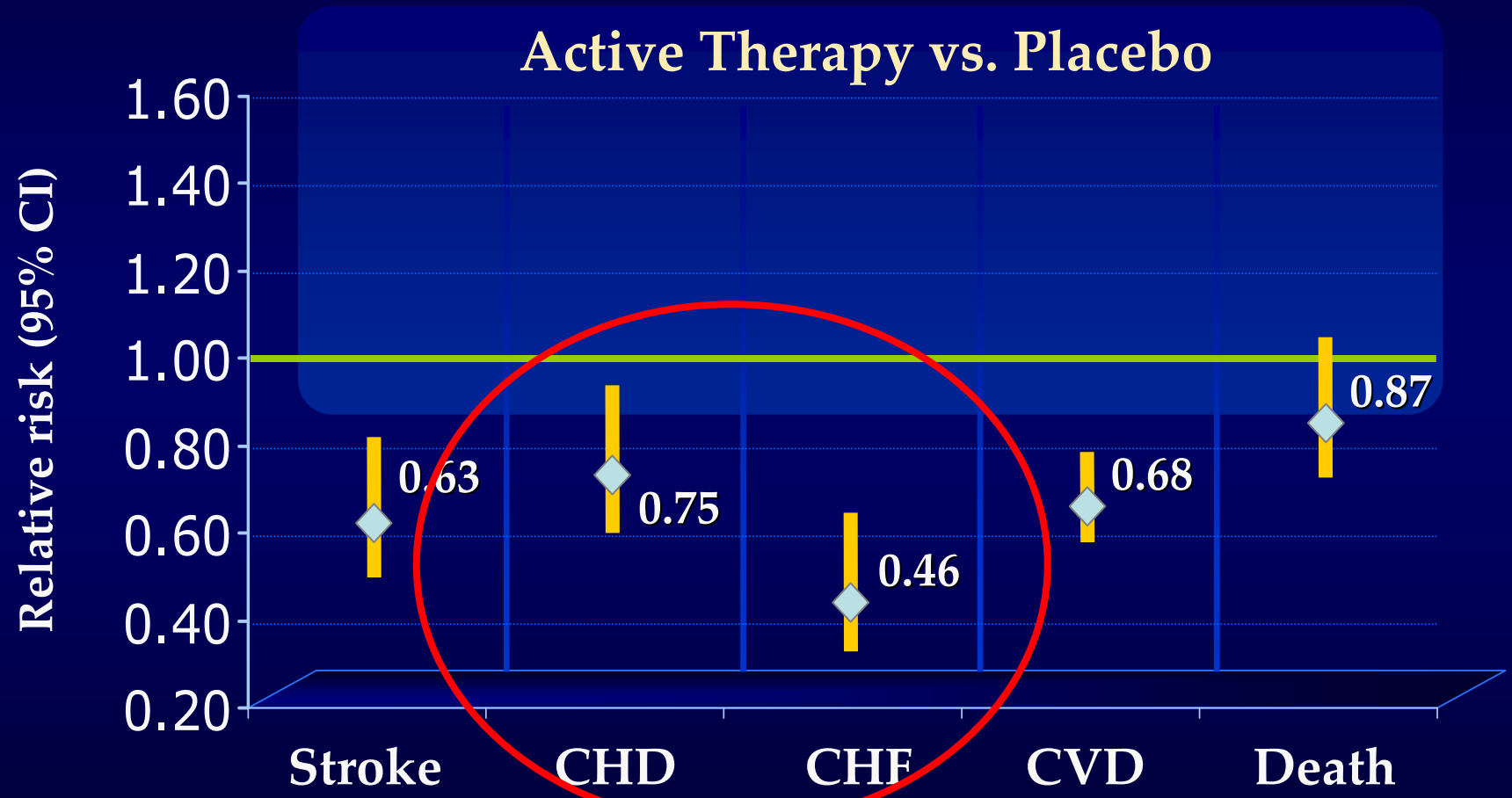
375/392(91%) prior hypertension



Underlying cause of CHF in Korea (multicenter survey) *Korean J Circ 2003*



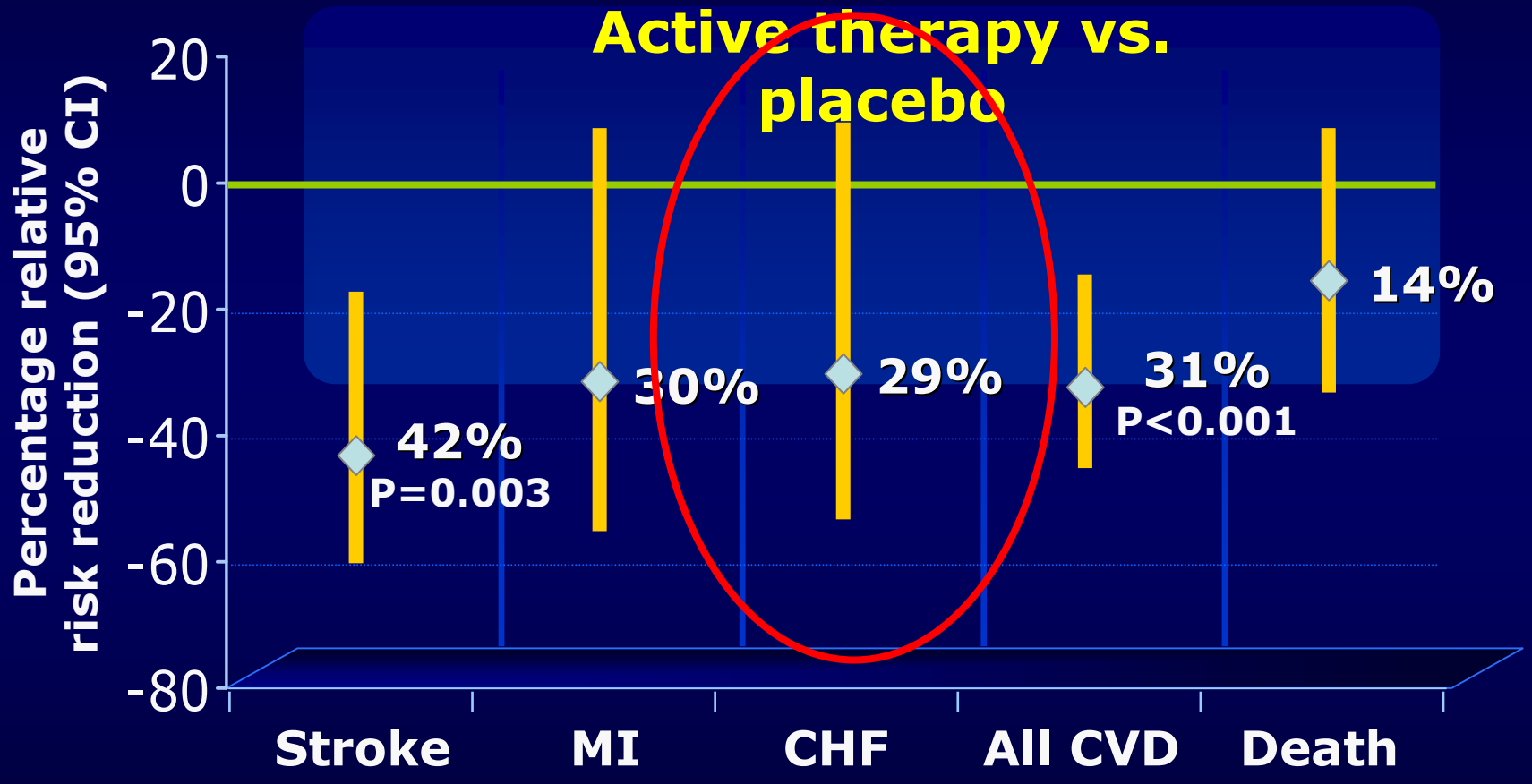
SHEP
Cardiovascular Disease Endpoints



CHD=coronary heart disease; CHF=congestive heart failure;
CVD=cardiovascular disease

SHEP Research Group. JAMA. 1991;265:3255-3264.

Syst-Eur
Cardiovascular Disease Endpoints



MI=myocardial infarction; CHF=congestive heart failure; CVD=cardiovascular disease

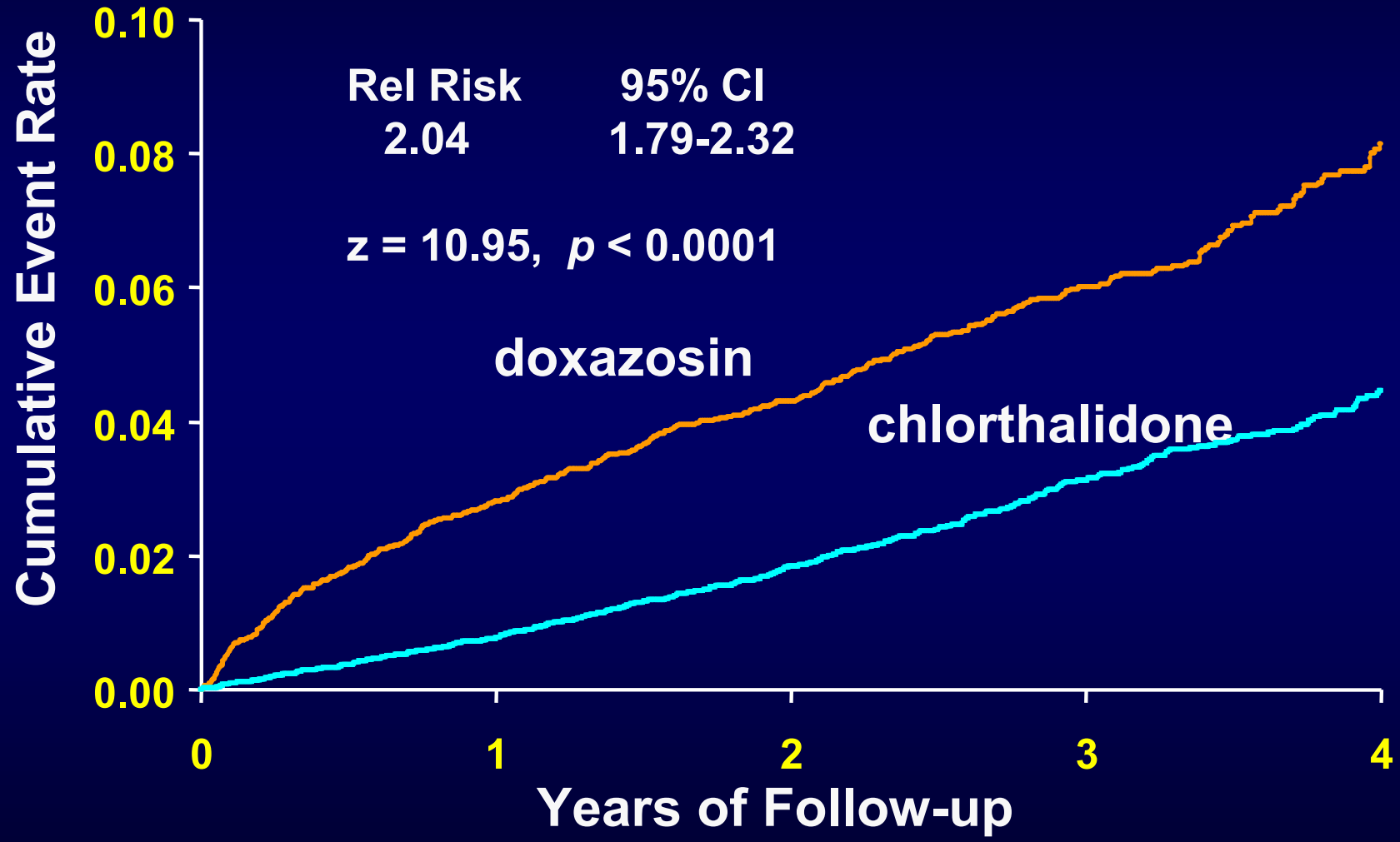
Syst-Eur=Systolic Hypertension in Europe Trial

Staessen JA, et al. Lancet. 1997;350:757-764.

ACE inhibitor, ARB in Heart Failure Prevention

ALLHAT: Doxazosin arm withdrawn

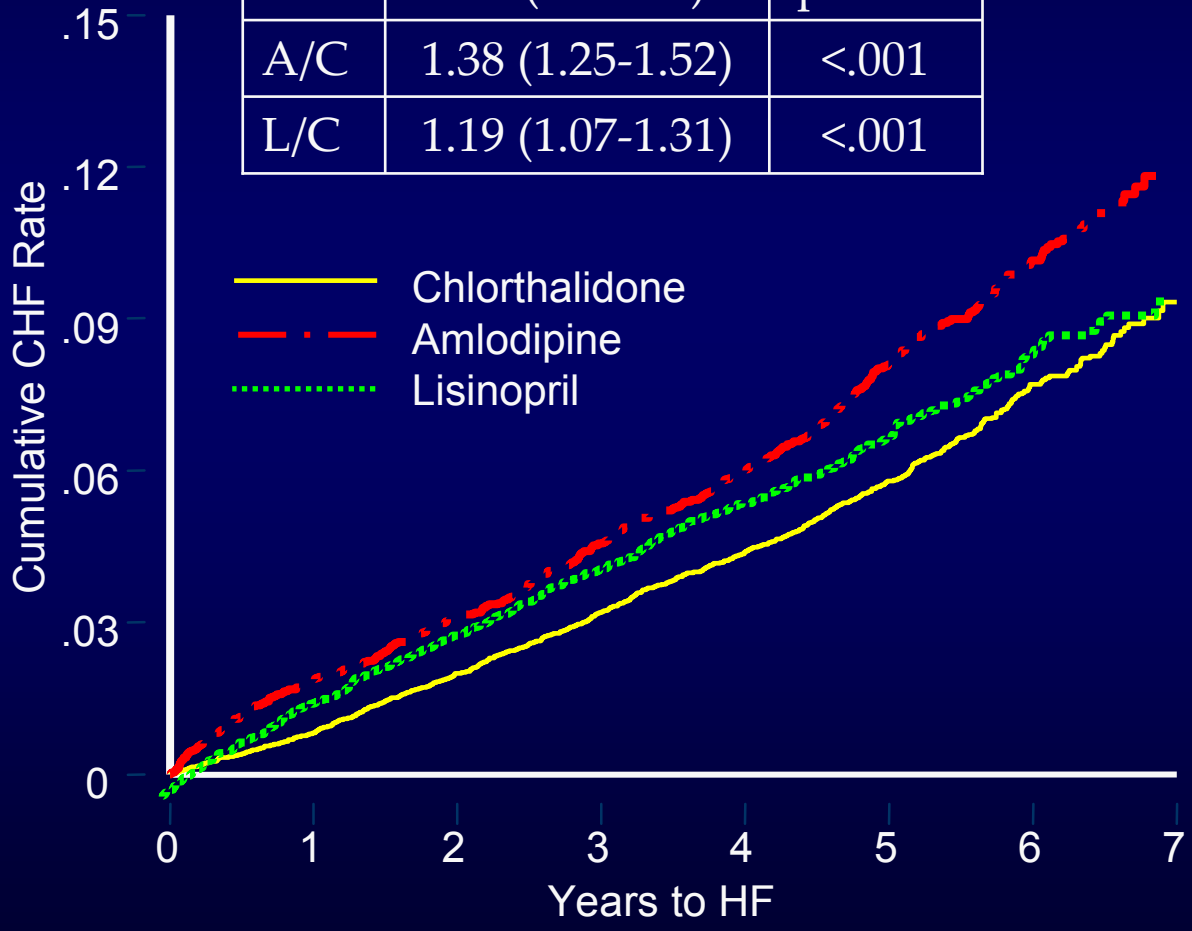
Heart Failure



JAMA. 2000;283:1967-1975

ALLHAT : Heart Failure

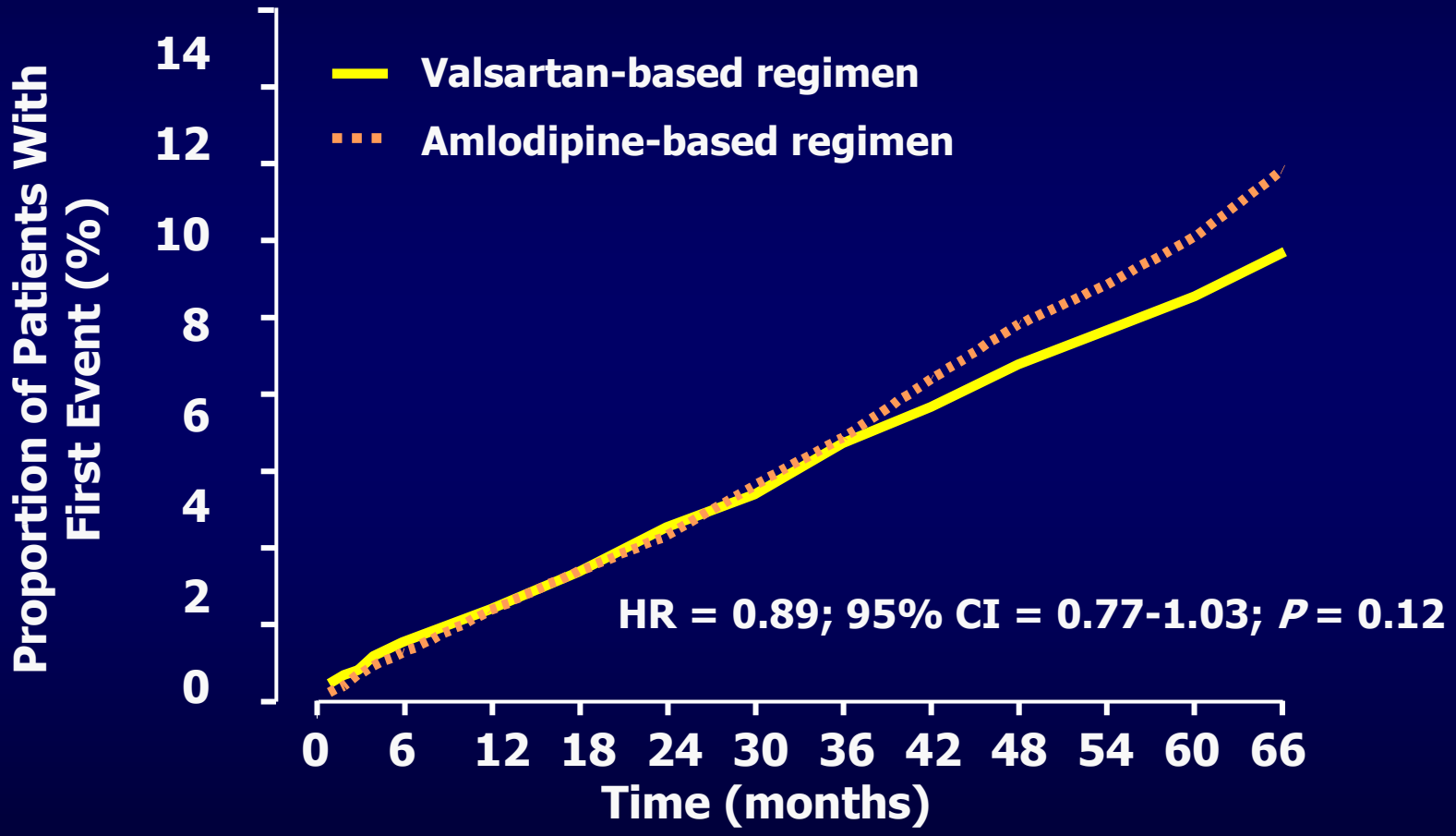
	RR (95% CI)	p value
A/C	1.38 (1.25-1.52)	<.001
L/C	1.19 (1.07-1.31)	<.001



ALLHAT study group JAMA 2002

VALUE: Heart Failure

Hospitalisation for HF or death from HF

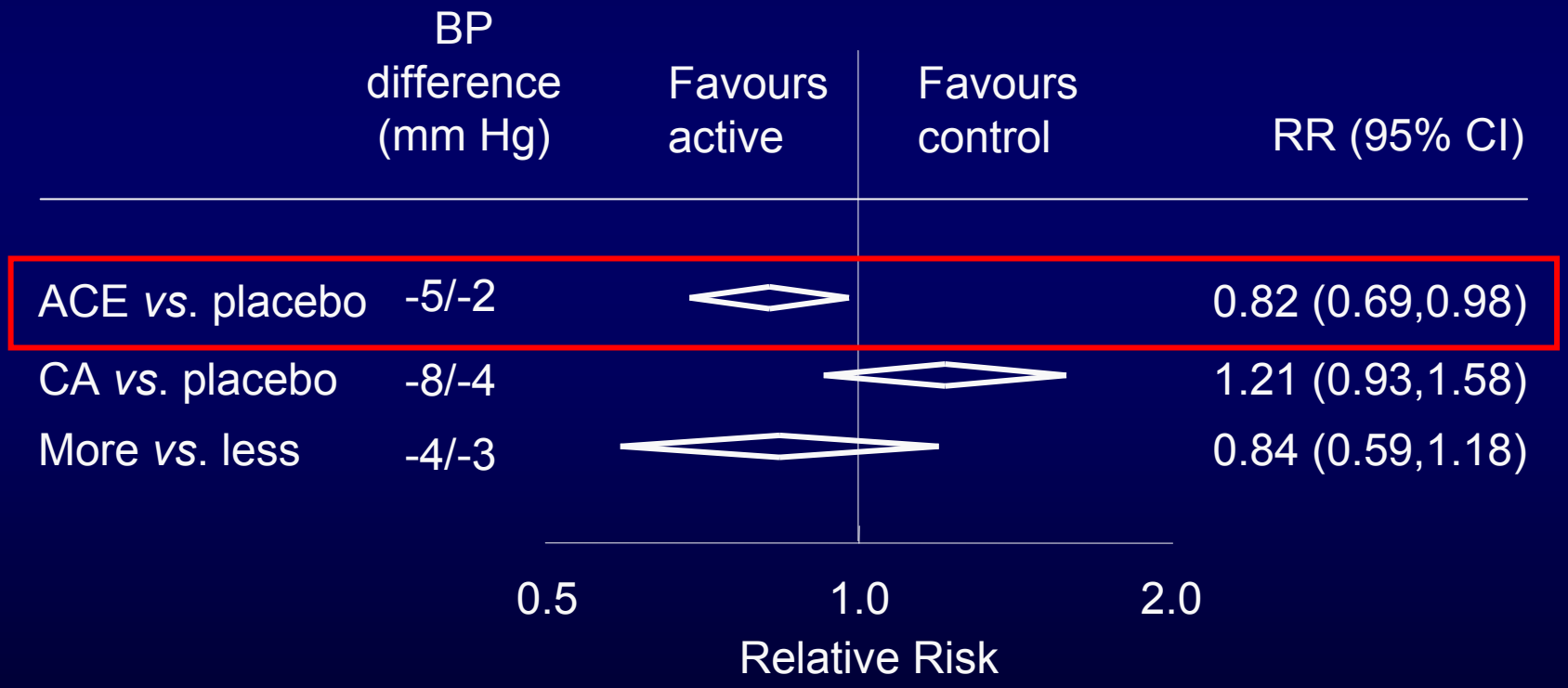


Julius S et al. *Lancet*. June 2004;363.

Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTT)

HEART FAILURE

Treatment vs Placebo

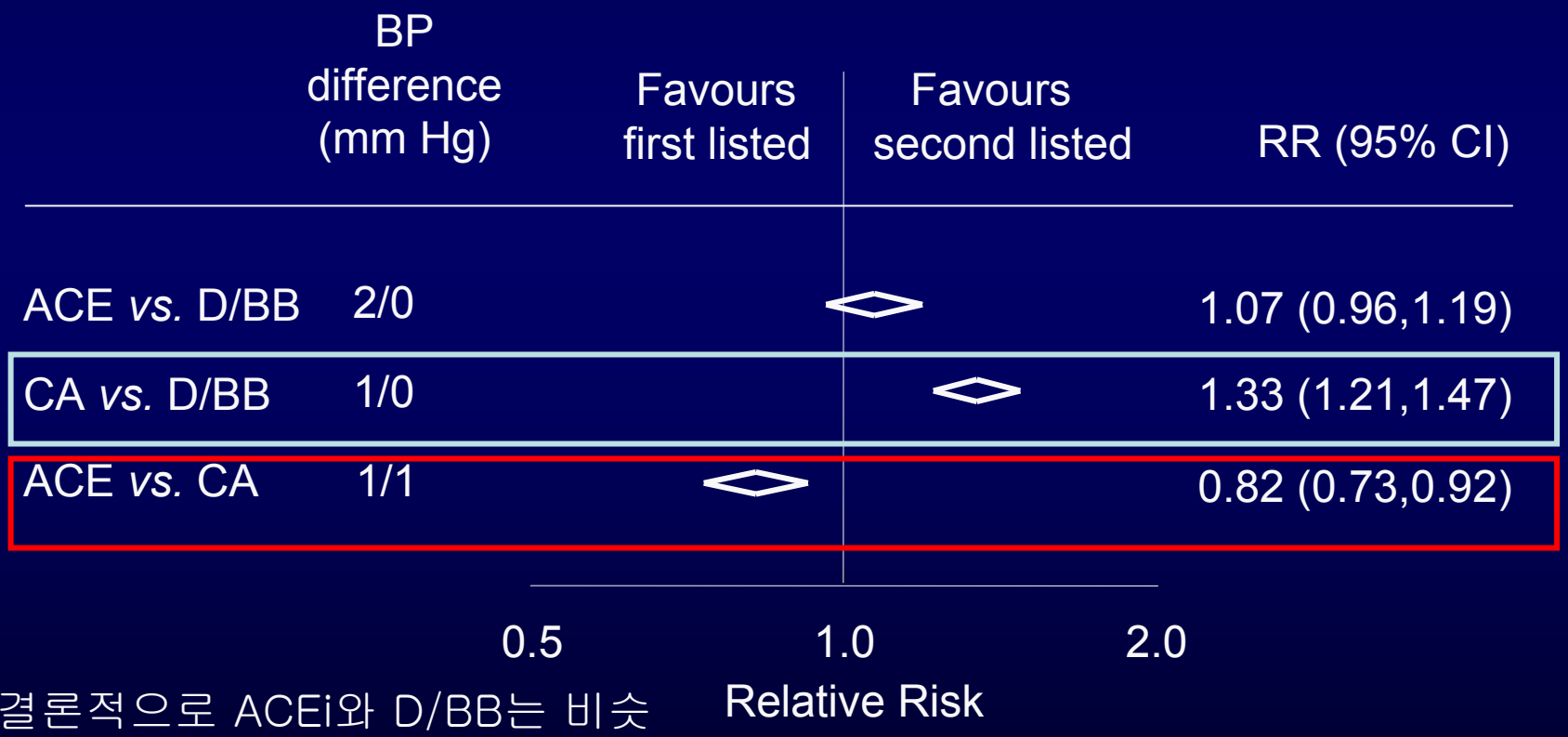


BPLTT collaboration group Lancet 2003

Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTT)

HEART FAILURE

Different Agents



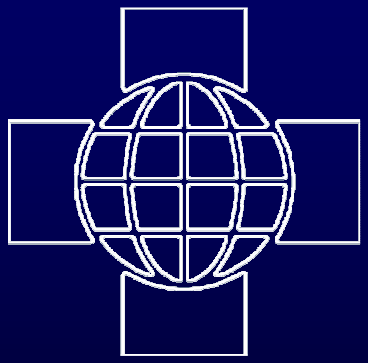
결론적으로 ACEi와 D/BB는 비슷

BPLTT collaboration group Lancet 2003

Blood Pressure Lowering Treatment Trialists' Collaboration

Second cycle of overview analyses

BLOOD
PRESSURE
LOWERING
TREATMENT
TRIALISTS'
COLLABORATION



Institute
for
International
Health

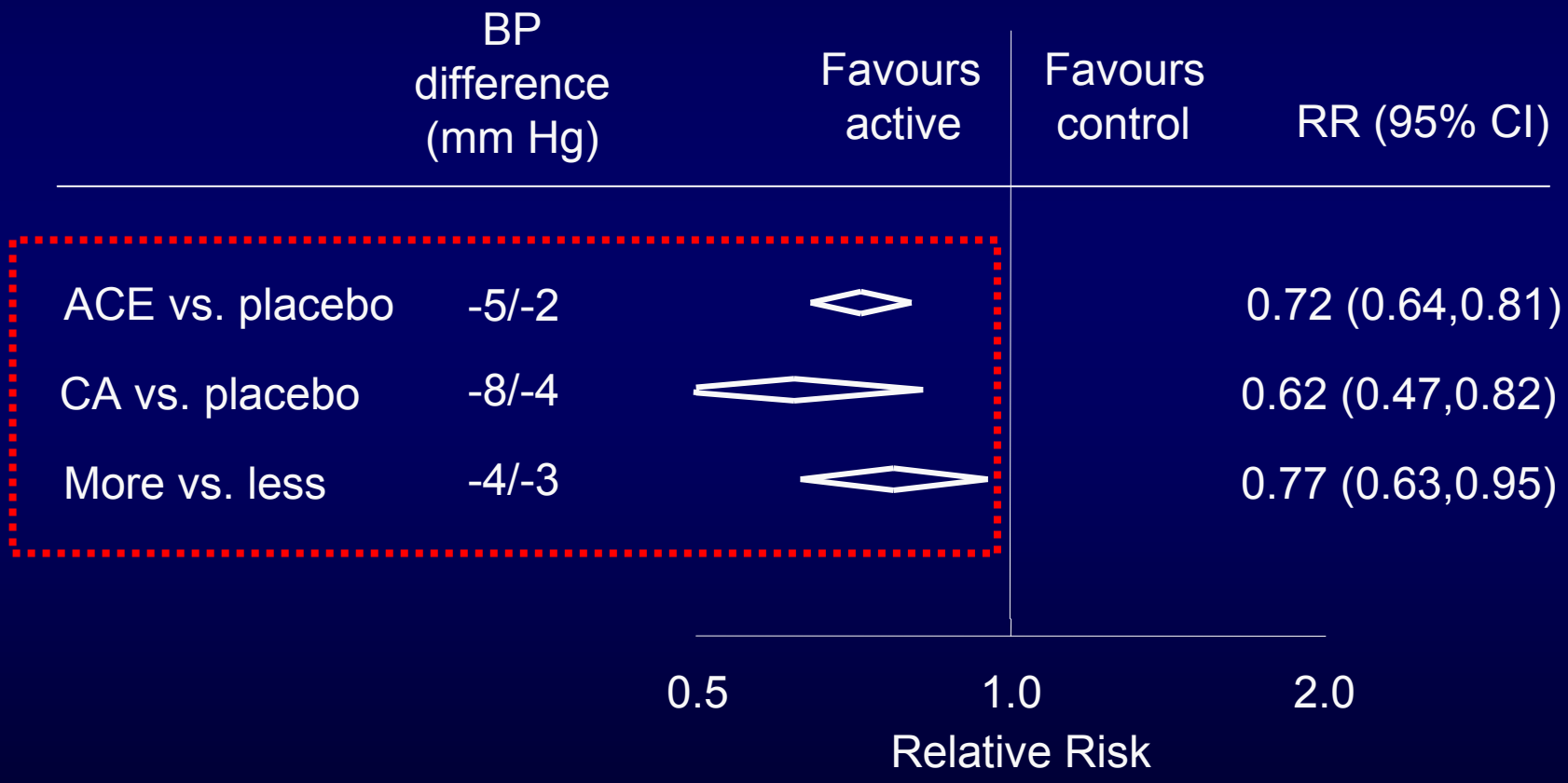
Contributing trials

Second cycle (29 trials, n= 162,341)

AASK
ABCD (H)
ABCD (N)
ALLHAT
ANBP2
CAPPP
CONVINCE
ELSA
HOPE
HOT
IDNT
INSIGHT
JMIC-B
LIFE
NICOLE
NICS-EH
NORDIL
PART-2
PREVENT
PROGRESS
QUIET
RENAAL
SCAT
SCOPE
SHELL
STOP-2
SYST-EUR
UKPDS-HDS
VHAS

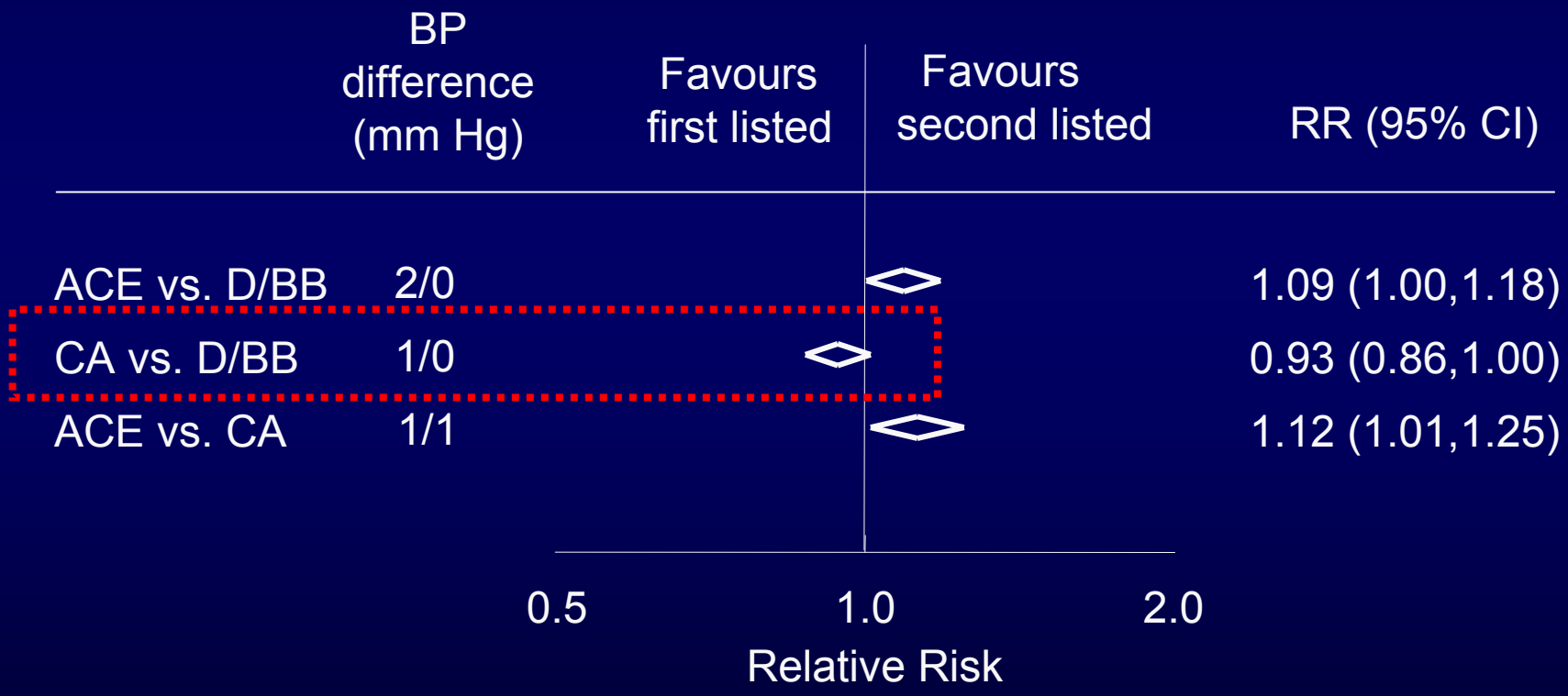
STROKE

active treatments vs control



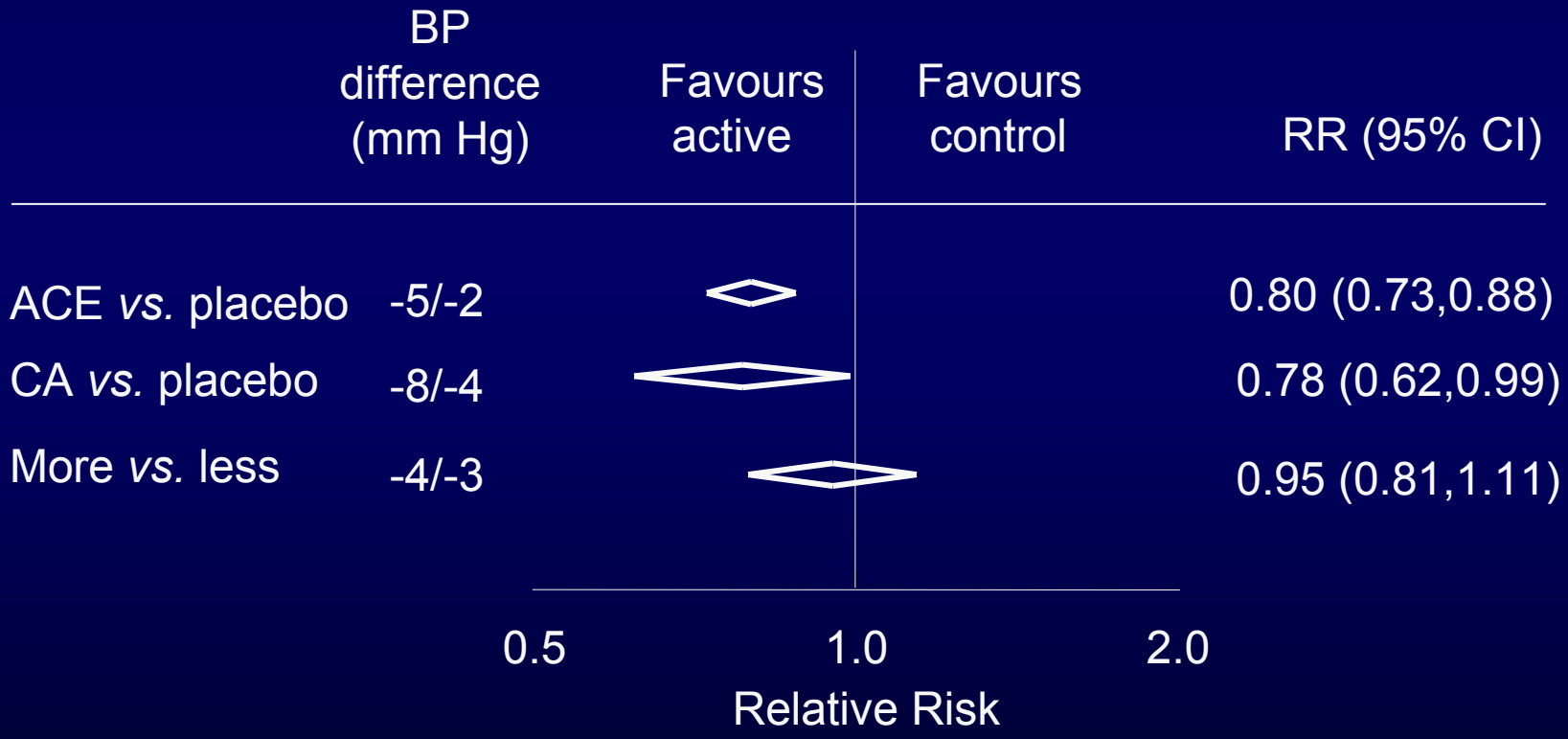
STROKE

Comparisons of different active treatments



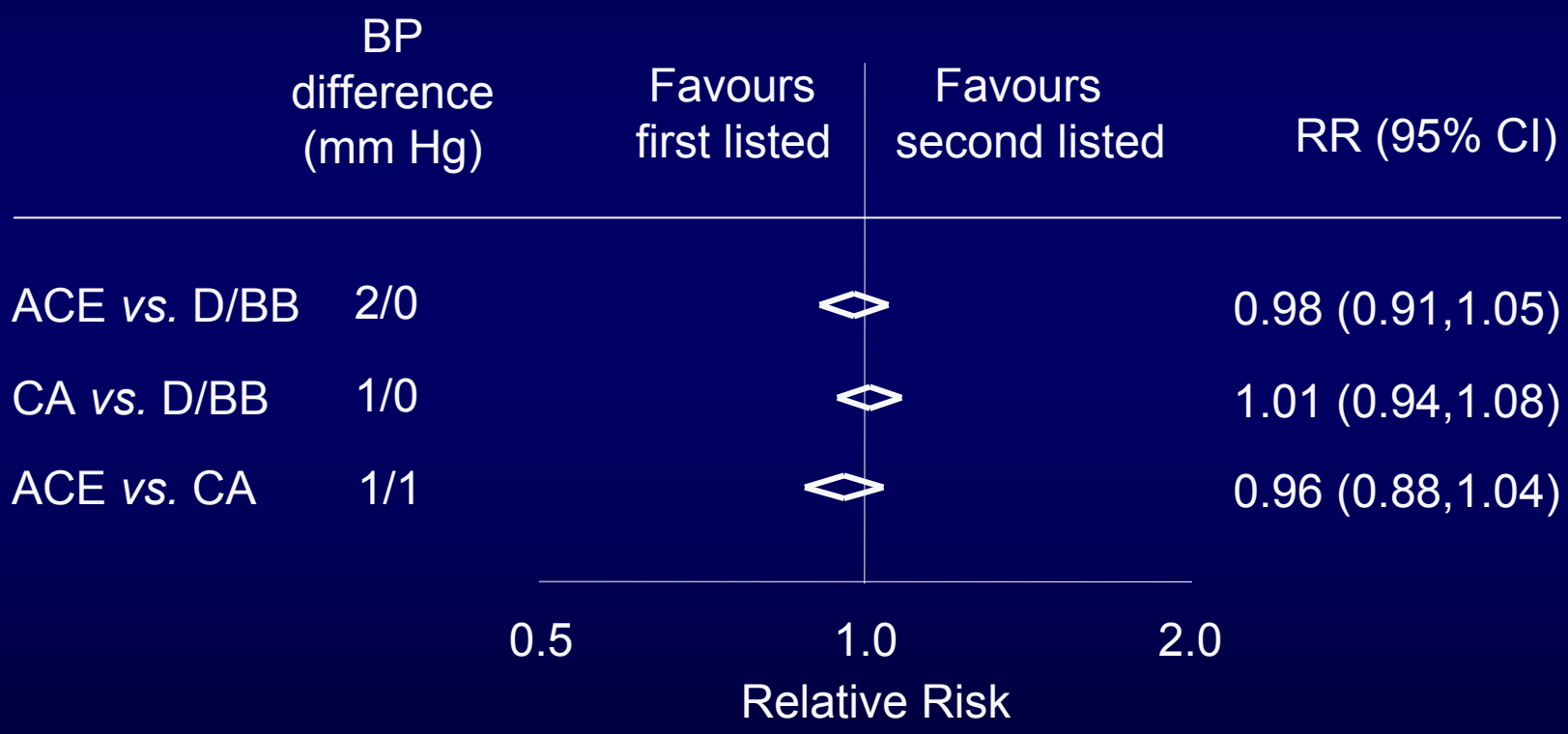
CORONARY HEART DISEASE

active treatments vs control



CORONARY HEART DISEASE

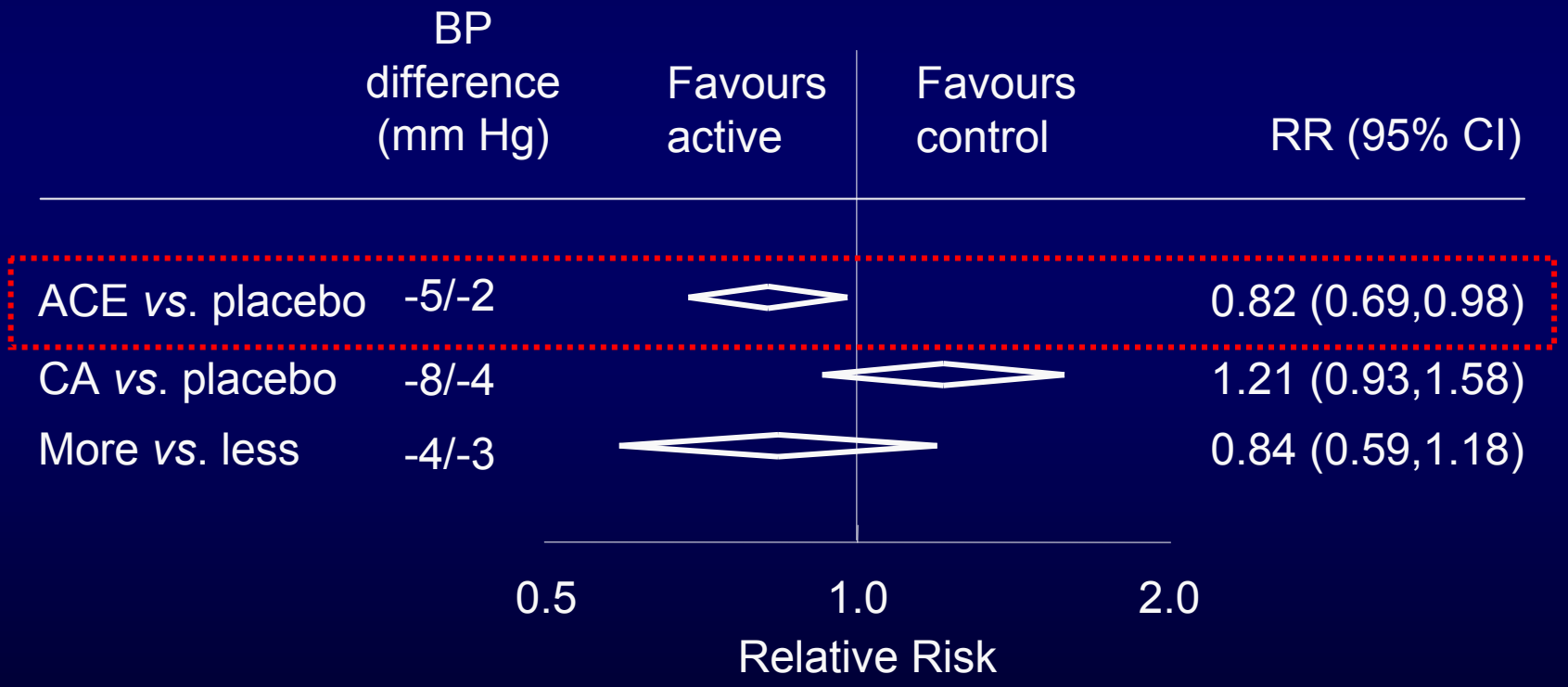
Comparisons of different active treatments



Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTT)

HEART FAILURE

Treatment vs Placebo

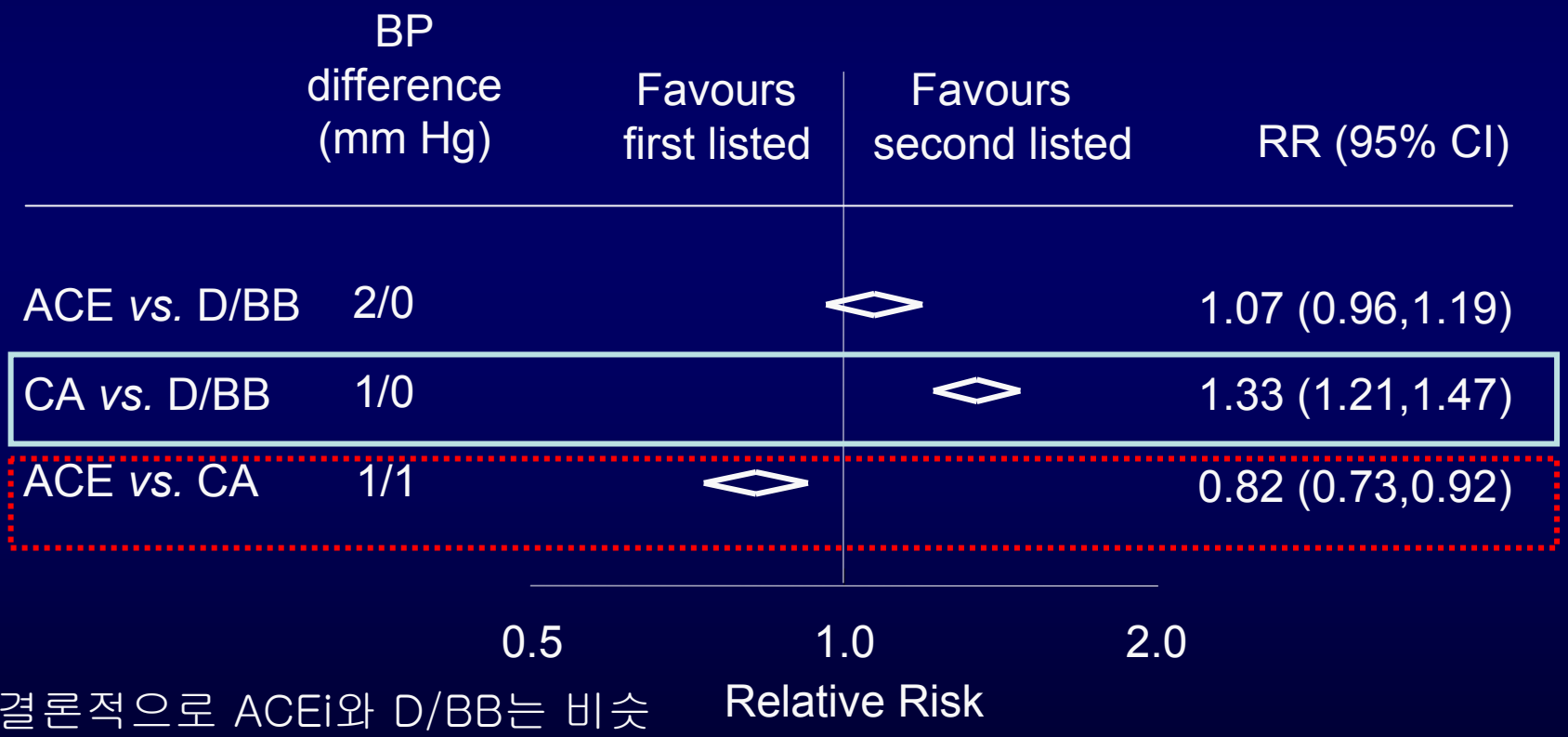


BPLTT collaboration group Lancet 2003

Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTT)

HEART FAILURE

Different Agents

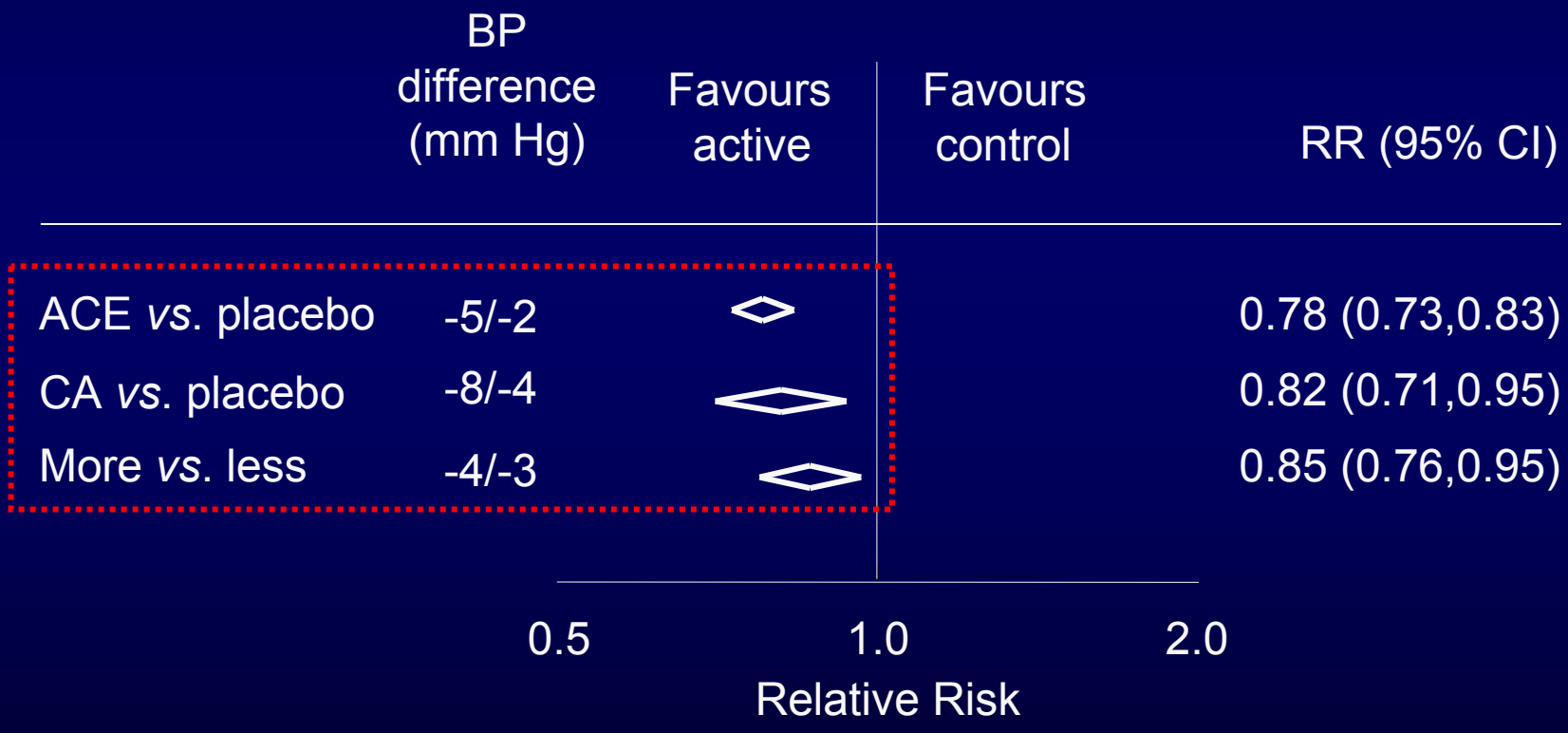


결론적으로 ACEi와 D/BB는 비슷

BPLTT collaboration group Lancet 2003

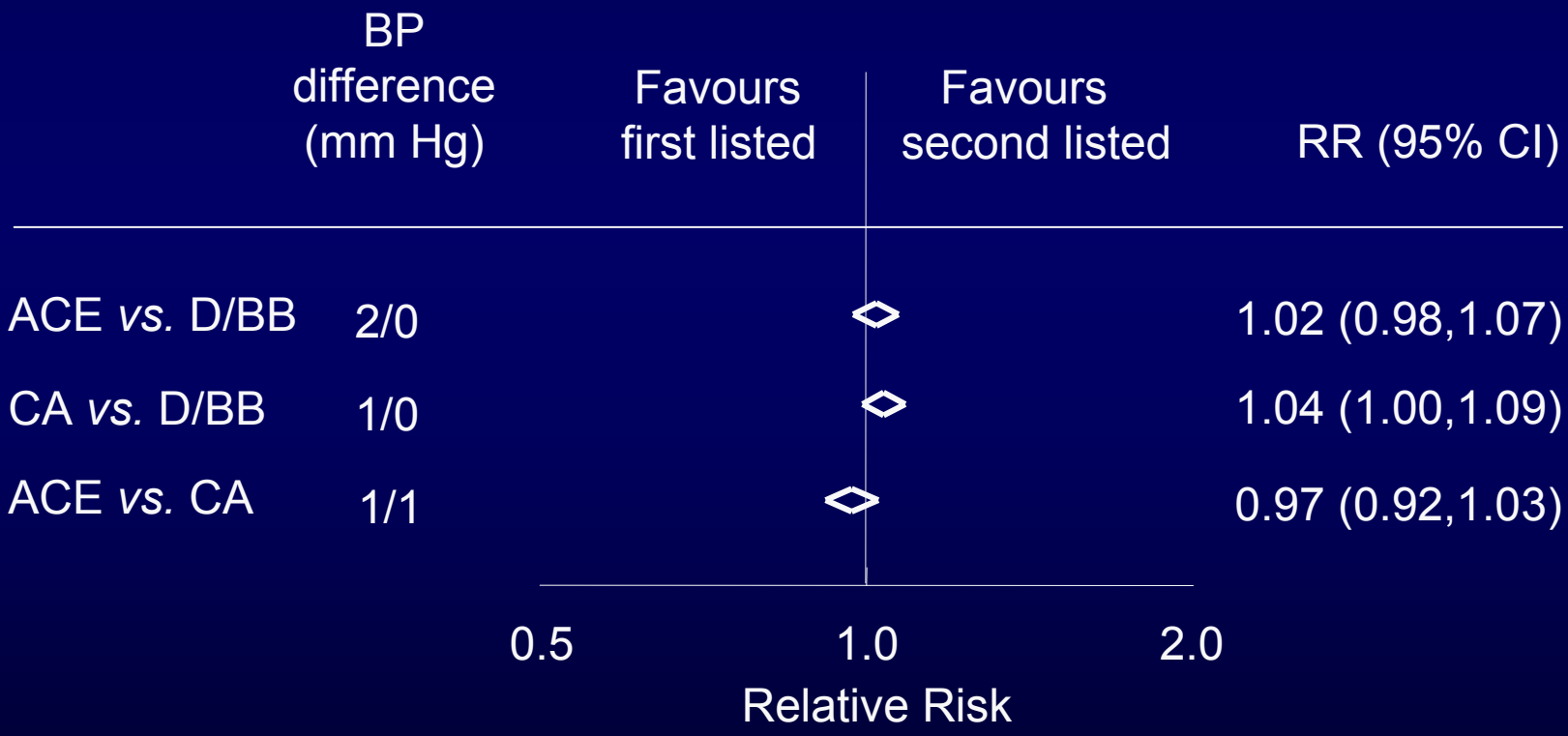
MAJOR CARDIOVASCULAR EVENTS

active treatments vs control



MAJOR CARDIOVASCULAR EVENTS

Comparisons of different active treatments



Pivotal studies demonstrate benefits of treating elderly hypertensive patients

Study	n	Age (mean)	Inclusion BP (mmHg) SBP	DBP
SCOPE	4937	70–89 (76)	160–179	90–99
SHEP	4736	≥60 (72)	160–219	<90
Syst-Eur	4695	≥60 (70)	160–219	<95
STOP	1627	70–84 (76)	180–230	105–120
STOP-2	6614	70–84 (76)	≥180	105
MRC elderly	4396	65–74 (69)	160–209	<115
EWPHE	840	≥60 (72)	160–239	90–119

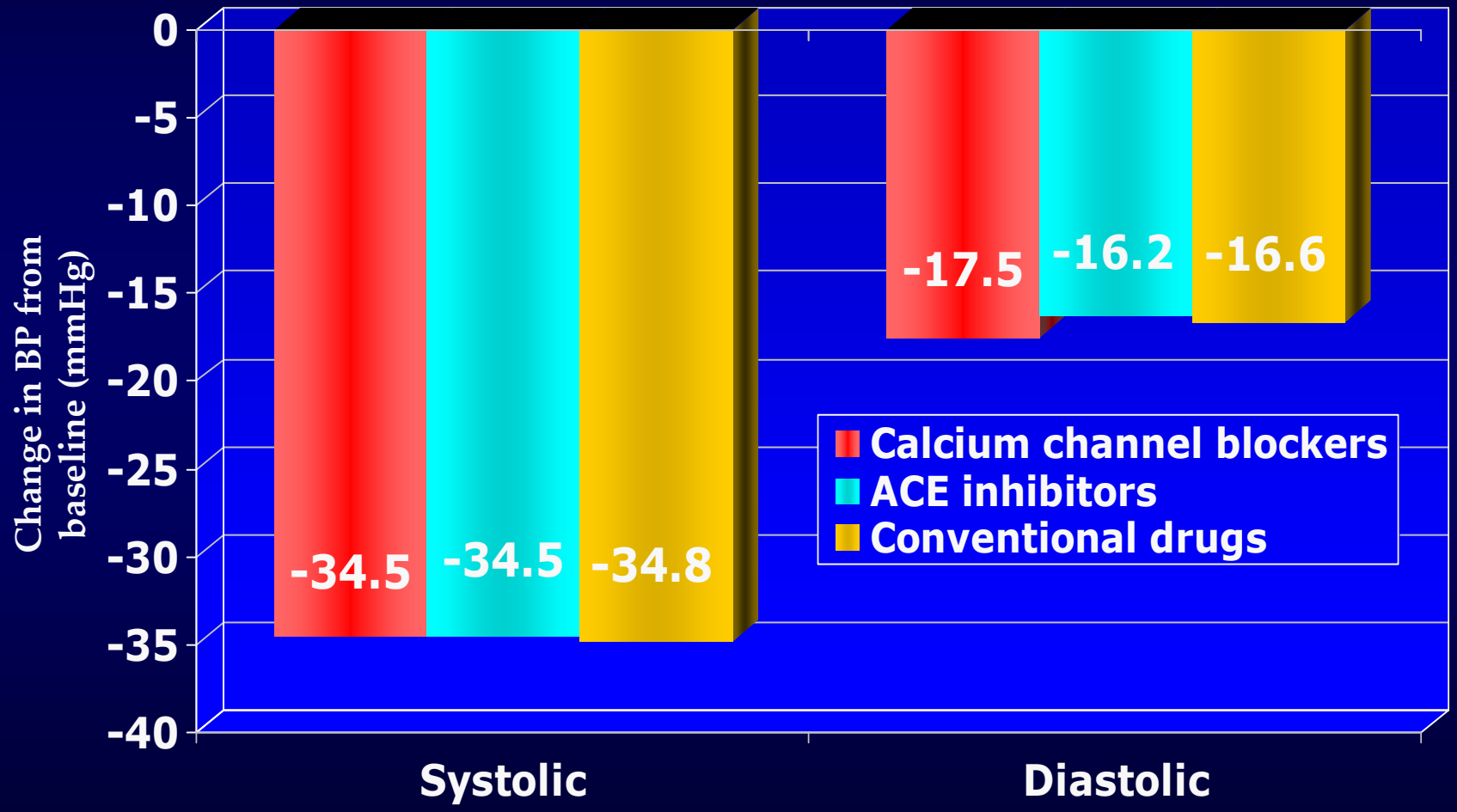
In extremely old age (>80 yrs), high BP should be treated?

STOP-2

Cohort	6.614
Age	70-84 yrs old
Eligibility	Systolic BP≥180 mmHg, diastolic BP ≥105 mmHg, or both
Design	Double blind; placebo control
Therapy	Conventional antihypertensive drug (beta-blocker+diuretics, n=2,213), ACE inhibitors (n=2,205), or Calcium channel blockers (n=2,196)

Hansson L, et al. Lancet. 1999;354:1751-1756.

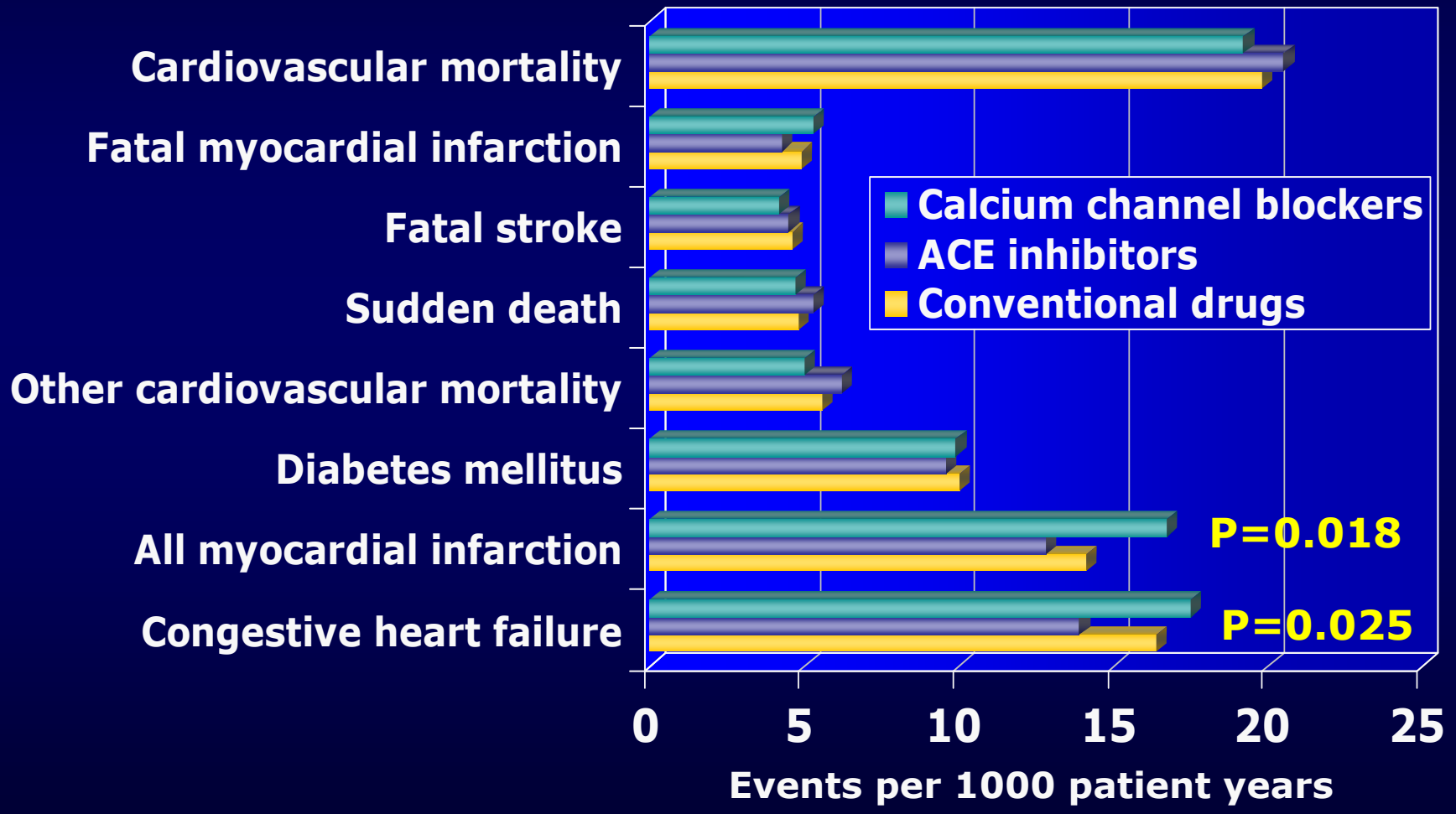
STOP-2 Change in Supine Blood Pressure From Baseline*



*Among patients who survived at least 24 months

Hansson L, et al. Lancet. 1999;354:1751-1756.

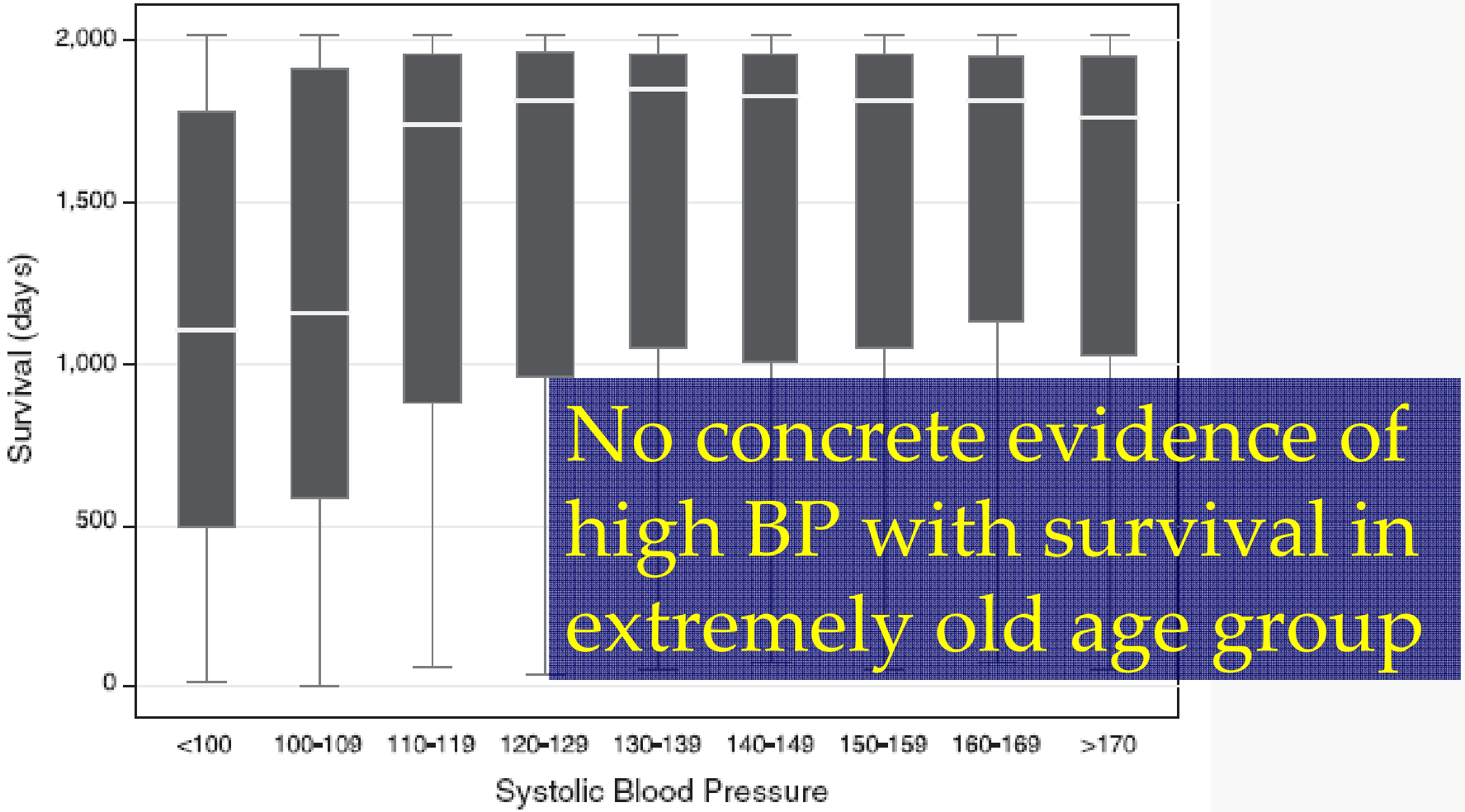
STOP-2 Frequency of Events Per 1000 Patient Years



Hansson L, et al. Lancet. 1999;354:1751-1756.

Blood Pressure and Survival in the Oldest Old

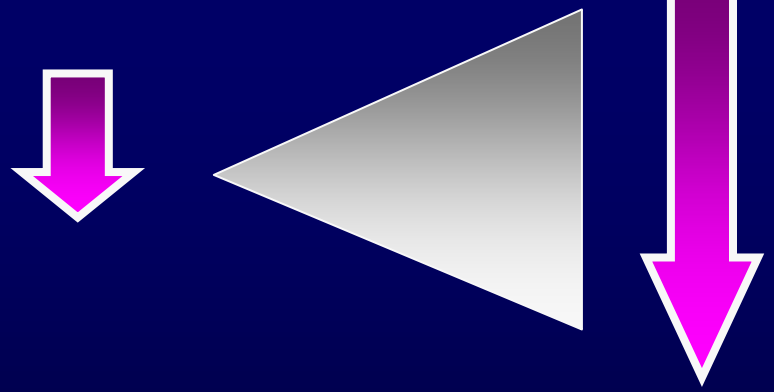
Daniel J. Oates, MD, MSc,[*†] *Dan R. Berlowitz, MD, MPH,*[‡‖] *Mark E. Glickman, PhD,*[‡‖] *Rebecca A. Silliman, MD, PhD,*[*†§] *and Ann M. Borzecki, MD, MPH*[‡‖]



Amplification of Benefit

Meta-analysis for
61 prospective &
observational studies

Mean BP
2mmHg



7% mortality
Risk reduction
By CAD

10% mortality
Risk reduction
By Stroke

Lewington S et al. Lancet 2002

Benefit of Hypertension Treatment in old age

	EWPHE	MRC	SHEP	STOP-H	Syst-China	Syst-Eur
Stroke (%)	**-36**	**-25**	**-33**	**-47**	**-47**	**-42**
CAD (%)	**-20**	**-19**	**-27**	**-13**	**+6**	**-26**
Heart Failure (%)	**-22**	**NA**	**-55**	**-51**	**-58**	**-27**

치 료

- 노년기 고혈압: 반듯이 치료 해야된다

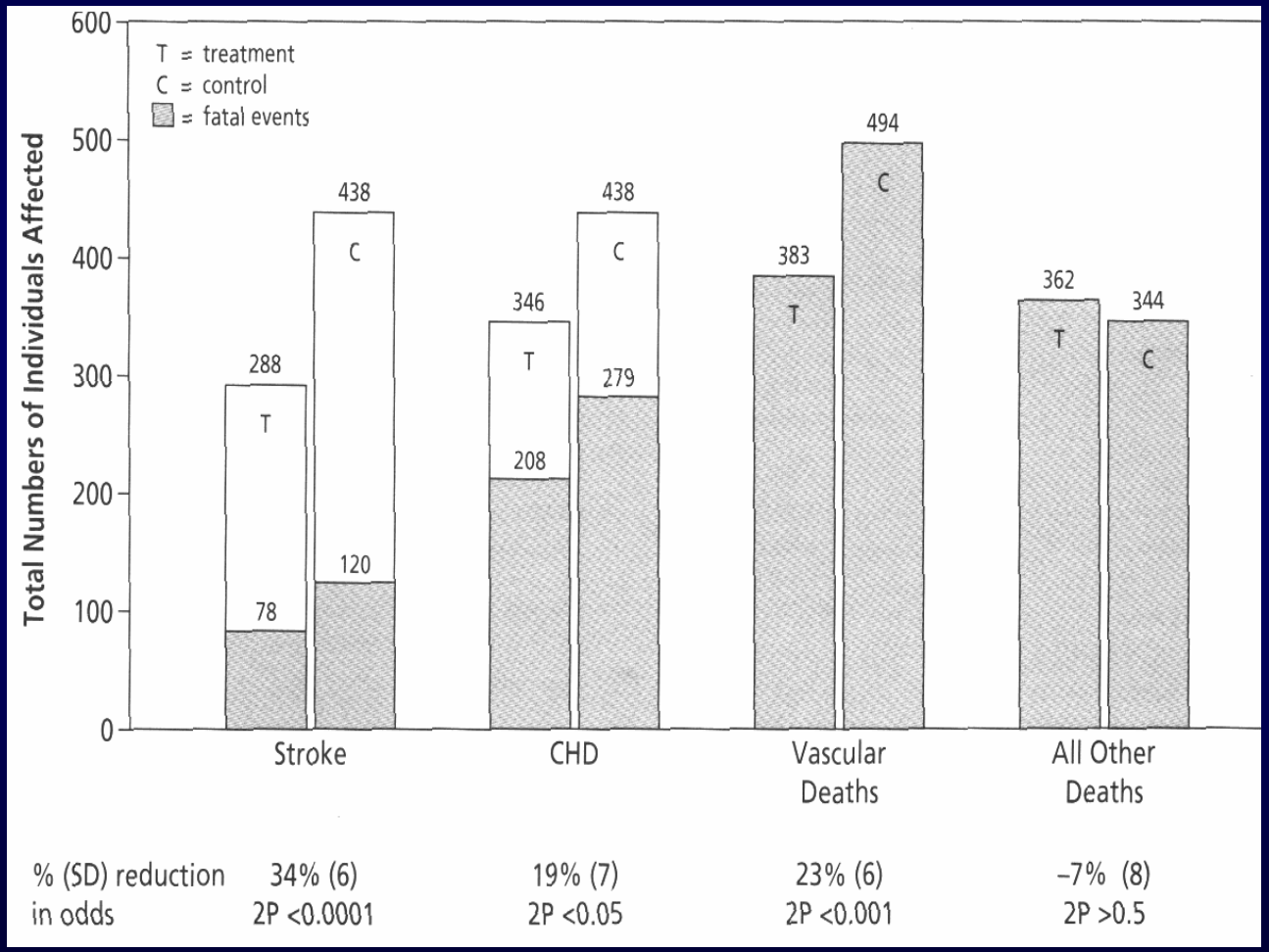
  ⇒ 심혈관질환: 젊은 환자보다 3-4배 높다

- 수축기 고혈압도 치료효과 유사

- 남자/ 70세 이상/ 맥압이 큰 환자

  ⇒ 치료효과 더욱 크다

노년기 고혈압의 치료 효과



치 료

- 일차목표는 수축기혈압과 맥압 조절에 둔다
- 치료목표

  ⇒ 135-140/85-90 mmHg 이하
- 중간목표 설정

  초기혈압이 매우 높고 표적장기 손상 없으면

  ⇒ 일단 160mmHg이하로 조절

노년기 고혈압의 일반적 치료원칙

- 비약물치료법부터 시작한다
- 처음 치료의 일차 약제는 저용량 이뇨제부터 투여한다
- 환자의 동반 질병에 따라 일차 약제 혹은 복합제제를 선택한다.
- 처음 사용하는 약제는 일반 용량의 반으로 시작하여, 천천히 증량한다
- 치료목표는 수축기 혈압 140에서 135mmHg 이하로 한다
- 확장기 혈압의 지나친 하강은 피한다 (70mmHg 이하)
- 기립성 저혈압을 유발할 정도의 지나친 치료는 피한다

비약물치료

- 초기 고혈압 치료
- 치료약제의 용량 감소
- 다른 위험인자 조절 효과
- 처음 수축기 혈압<160mmHg/(-)

  ⇒ 처음 6개월은 비약물치료
- 과체중/활동이 적은 환자에서 반듯이 시행

비약물치료 (Lifestyle Modifications)

Modification	Recommendation	Systolic BP Reduction
Weight reduction	Maintain normal body weight(BMI,18.5-24.9)	5-20 mmHg/10-kg
Adopt DASH eating plan	Consume a diet rich in **fruits, vegetables, and low-fat** dairy products with a reduced content of saturated and total fat	8-14 mm Hg
Dietary sodium reduction	Reduced dietary sodium intake to no more than 100mEq/L (2.4g sodium or 6 g sodium chloride)	2-8 mm Hg
Physical activity	Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)	4-9 mm Hg
Moderation of alcohol consumption	Limit consumption to no more than 2 drinks per day(1 o or 30 ml ethanol [eg, 24 oz beer, 10 oz wine, or 3 oz 80-proof whiskey]) in most men and no more than 1 drink per day in women and lighter-weight persons	2-4 mm Hg

약물치료

- 일반 고혈압 치료와 동일
- 동반질환 여부: 당뇨, CAD, HF, BPH 등
- 단순히 고혈압만 있는 경우

  ⇒ Thiazide 이뇨제를 처음 사용
- 기립성 저혈압을 잘 유발하는 clonidine, reserpine 등은 피한다

어떤 약제를 선택할 것인가?

- 위약에 비해서 효과적인 것은 이뇨제와 칼슘차단제이며 베타차단제도 효과적이나 이뇨제보다는 못하다
- 새로운 약제들은 이뇨제와 비슷한 효과가 있다

약물치료

- 초기 용량은 절반으로 시작
  (신장기능저하, 약물의 감수성 증대)
- 이뇨제-→칼슘 길항제→ACE I, ARB
- 베타 차단제는 관상동맥질환과 심부전에 만 선택적으로 투여
- 치료목표: 초기 수축기160→140mmHg 미만

고려사항

- 대부분의 연구는 건강한 노인을 대상으로 시행
- 기립성 저혈압의 출현
- 저포타슘혈증의 출현: 이뇨제는 저용량으로
- 인지기능의 변화에 대한 고려: 뇌혈류의 저하
- 정서기능의 변화: 과거의 약제들
- 미각의 변화
- 요량의 증가에 따른 요실금의 발생

추적과 관찰

- 치료 순응도 파악
- 부작용에 대한 평가 (특히 기립성 저혈압)
- 앙와위와 기립 혈압 측정
- 자가 혈압 측정 권장
- 비약물치료법 권장 (식이요법, 운동)
- 혈압 강하제 용량 결정에 주의
- Refractory HT의 평가

Summary

JNC 7 – COMPLETE VERSION

SEVENTH REPORT OF THE JOINT NATIONAL COMMITTEE ON PREVENTION, DETECTION, EVALUATION, AND TREATMENT OF HIGH BLOOD PRESSURE

2007 Guidelines for the management of arterial hypertension

The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC)

Use of specific drug classes in older people is largely similar to that recommended in the general algorithm and for individual compelling indications. Combination therapy with two or more drugs is generally needed to achieve optimal BP control. In routine practice, if the systolic goal is achieved, the diastolic goal will almost always be reached as well.

A significant number of elderly individuals have widely variable BP with exaggerated high and low extremes. Such individuals deserve consideration for a slow titration approach, as do individuals with a history of medication side effects and those with orthostatic hypotension. Unfortunately, the misperception that many elderly have "brittle hypertension" has contributed to widespread inadequacy of drug titration and to poor BP control.

[58] Benefits of therapy have been demonstrated even in individuals over 80 years old.[116,259] Analyses of treatment trials in the elderly by the Hypertension Trialists group have suggested that the choice of initial agent is less important than the degree of BP reduction achieved.[90]

Box 13 Antihypertensive treatment in the elderly

- Randomized trials in patients with systolic-diastolic or isolated systolic hypertension aged ≥ 60 years have shown that a marked reduction in cardiovascular morbidity and mortality can be achieved with antihypertensive treatment.
- Drug treatment can be initiated with thiazide diuretics, calcium antagonists, angiotensin receptor antagonists, ACE inhibitors, and β-blockers, in line with general guidelines. Trials specifically addressing treatment of isolated systolic hypertension have shown the benefit of thiazides and calcium antagonists but subanalysis of other trials also shows efficacy of angiotensin receptor antagonists.
- Initial doses and subsequent dose titration should be more gradual because of a greater chance of undesirable effects, especially in very old and frail subjects.
- BP goal is the same as in younger patients, i.e. <140/90 mmHg or below, if tolerated. Many elderly patients need two or more drugs to control blood pressure and reductions to <140 mmHg systolic may be particularly difficult to obtain.
- Drug treatment should be tailored to the risk factors, target organ damage and associated cardiovascular and non-cardiovascular conditions that are frequent in the elderly. Because of the increased risk of postural hypotension, BP should always be measured also in the erect posture.
- In subjects aged 80 years and over, evidence for benefits of antihypertensive treatment is as yet inconclusive. However, there is no reason for interrupting a successful and well tolerated therapy when a patient reaches 80 years of age.

Thank for your attention!