Αρτηριακή υπέρταση και καρδιαγγειακός κίνδυνος

Ιωάννης Γ. Στυλιάδης
ΚΑΡΔΙΟΛΟΓΟΣ
Επιμελητής Α΄
ΓΝΘ 'ΠΑΠΑΓΕΩΡΓΙΟΥ'

"The world is living dangerously either because it has little choice, or because it is making the wrong choices"

http://www.who.int/whr/2002

"The world is living dangerously either because it has little choice, or because it is making the wrong choices"

1. Υποσιτισμός
2. Σεξουαλικά μεταδιδόμενα νοσήματα

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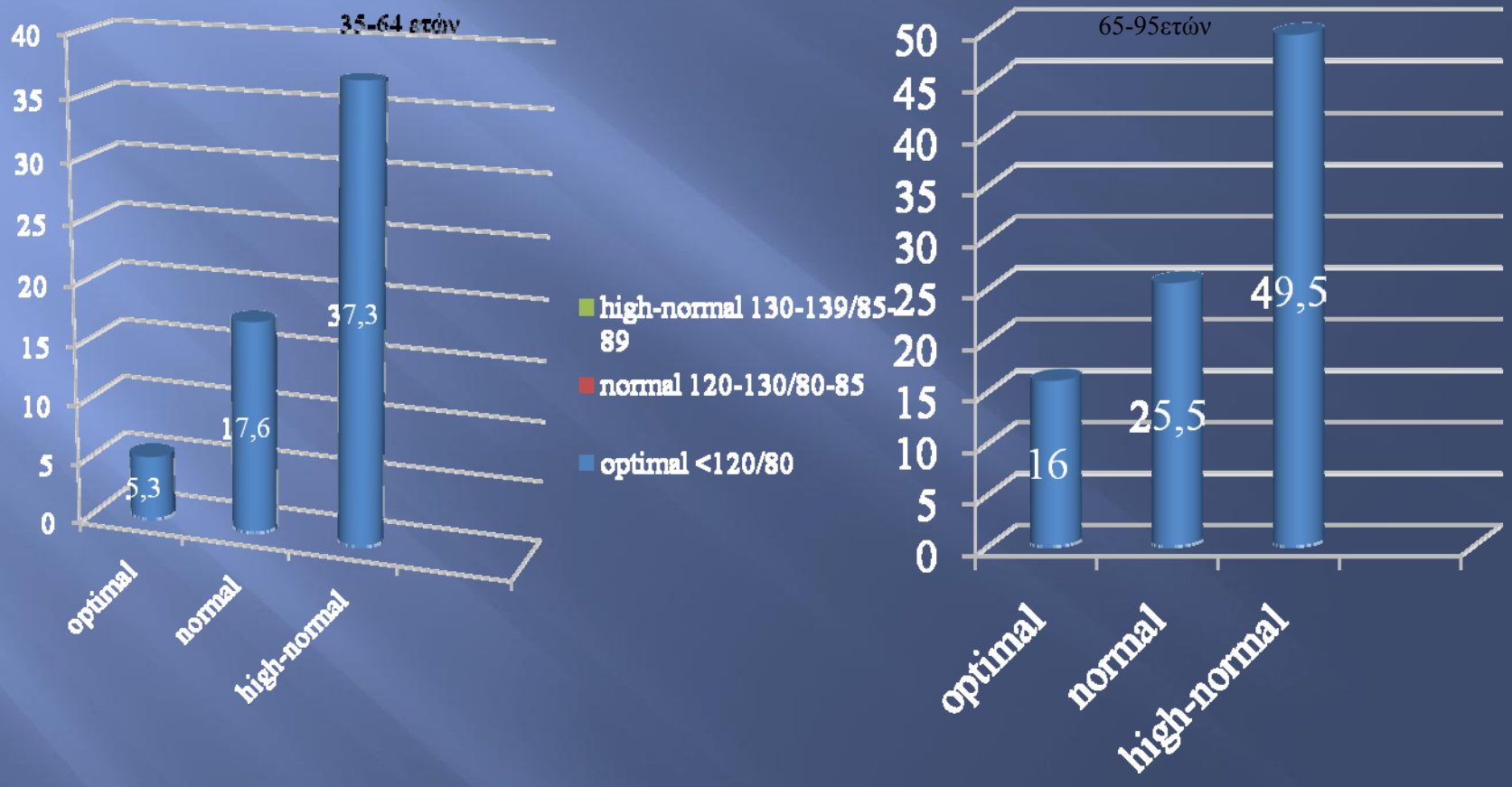
2. Σεξουαλικά μεταδιδόμενα νοσήματα
3. Υπέρταση

http://www.who.int/whr/2002

Definitions and Classification of Blood Pressure Levels (mmHg)

Category	Systolic		Diastolic
Optimal	<120	and	<80
Normal	120-129	and/or	80-84
High Normal	130-139	and/or	85-89
Grade 1 Hypertension	140-159	and/or	90-99
Grade 2 Hypertension	160-179	and/or	100-109
Grade 3 Hypertension	≥180	and/or	≥110
Isolated Systolic Hypertension	≥140	and	<90

4ετήςπιθανότητα αύξηση της ΑΠ



Vasan Lancet 2001

- **2002**

- 1/3 από το σύνολο των θανάτων CVD
- 17.000.000

- **2002**

- 1/3 από το σύνολο των θανάτων CVD
- 17.000.000

- **2020**

- Καρδιαγγειακά νοσήματα 1η αιτία θανάτου
- ↑ 20.000.000 ασθενών

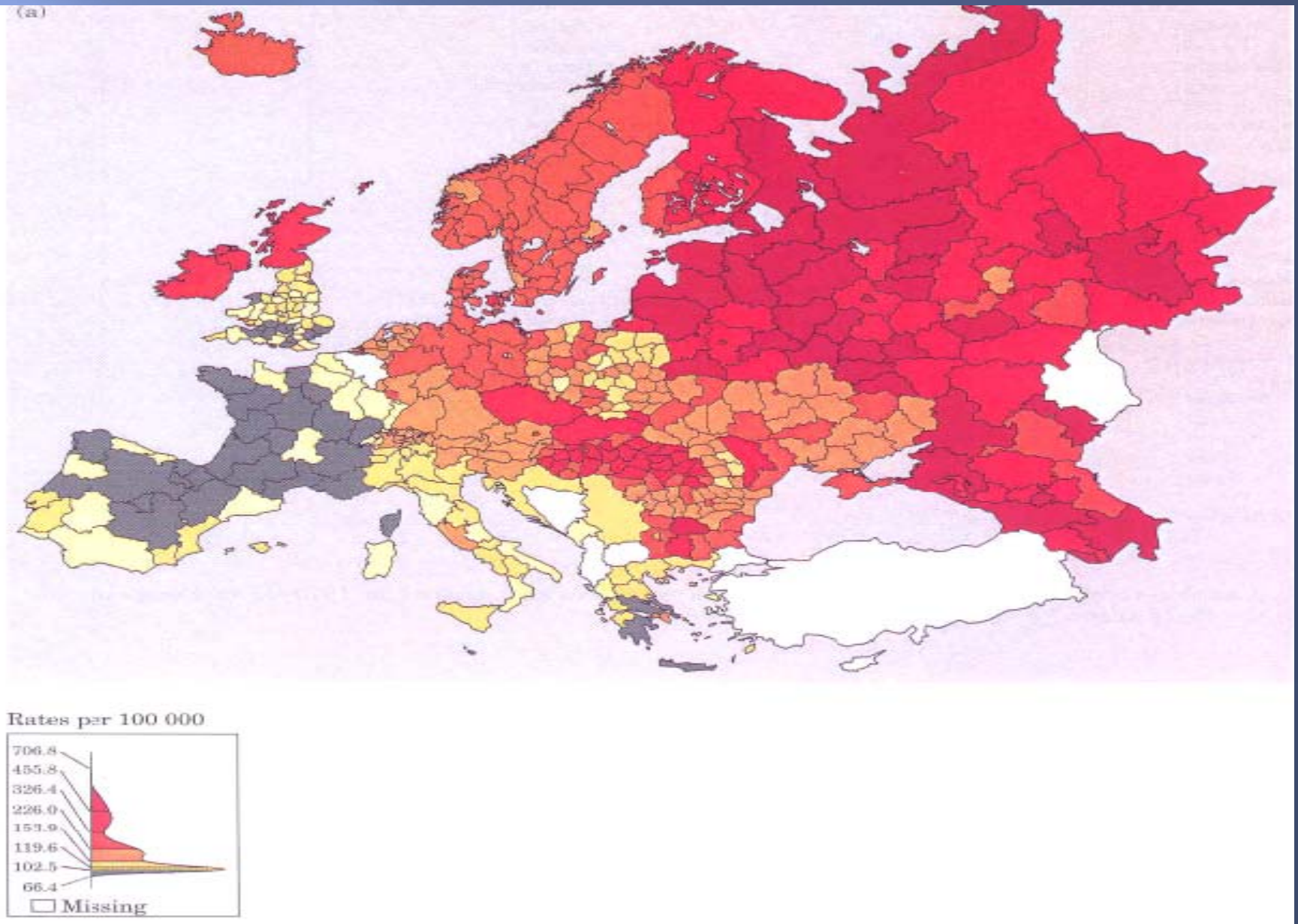
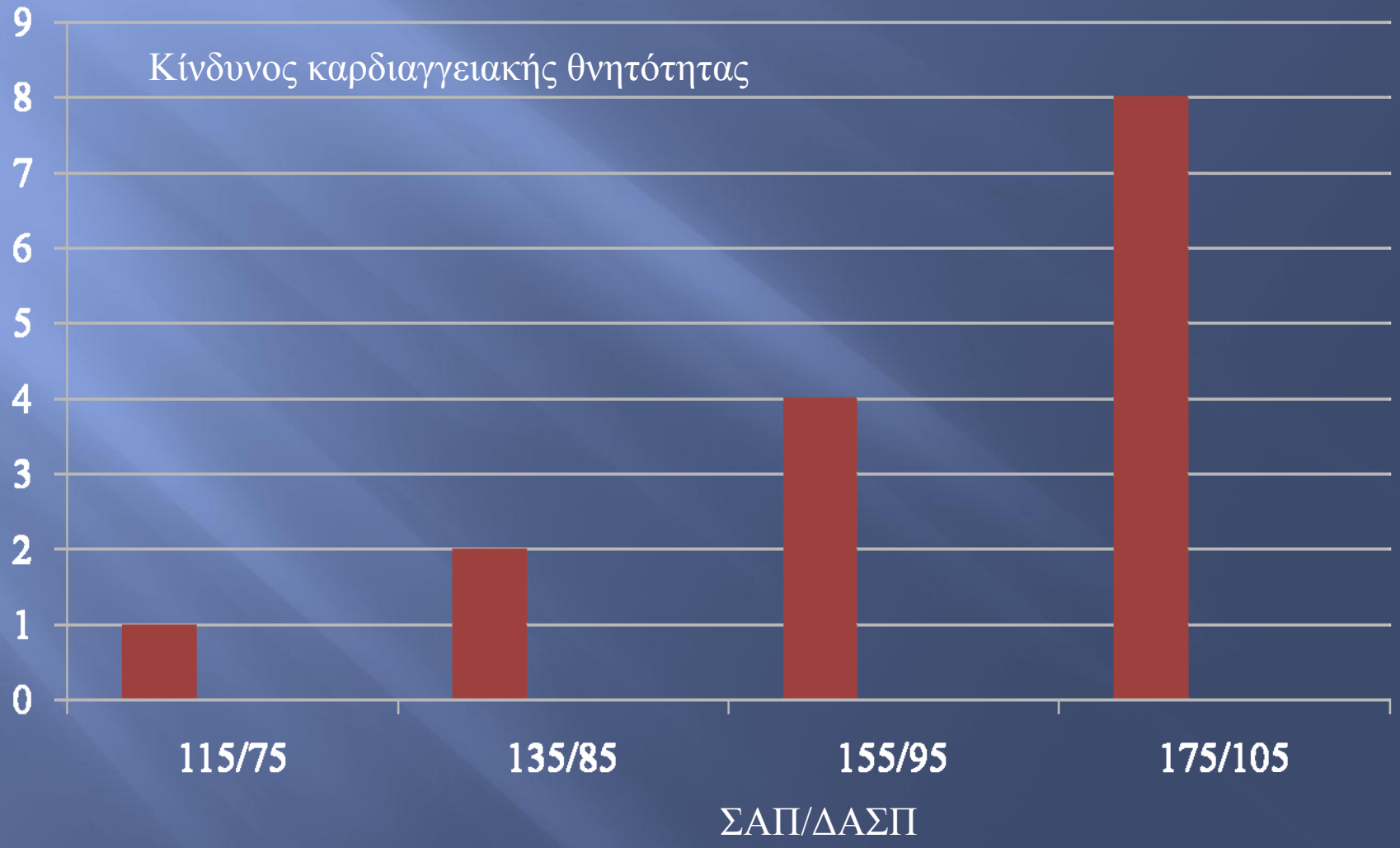
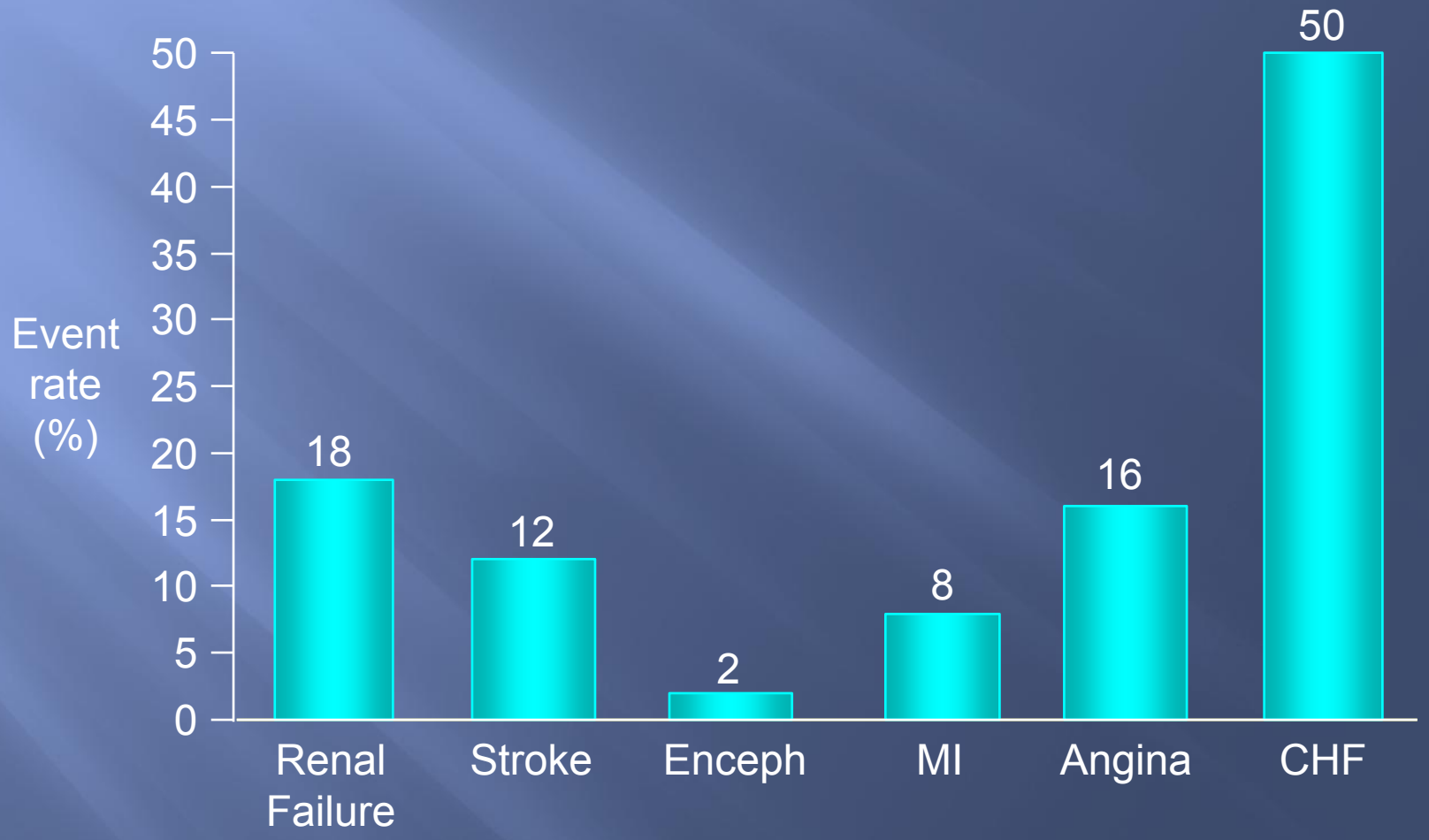


Figure 7(a) **Age-standardized mortality from ischaemic heart diseases (ICD410–414) in European regions 1990–91. Age 0–64 years. Men.**

Ο κίνδυνος καρδιαγγειακής θνητότητας διπλασιάζεται με κάθε αύξηση 20/10mmHg της ΣΑΠ και ΔΑΠ



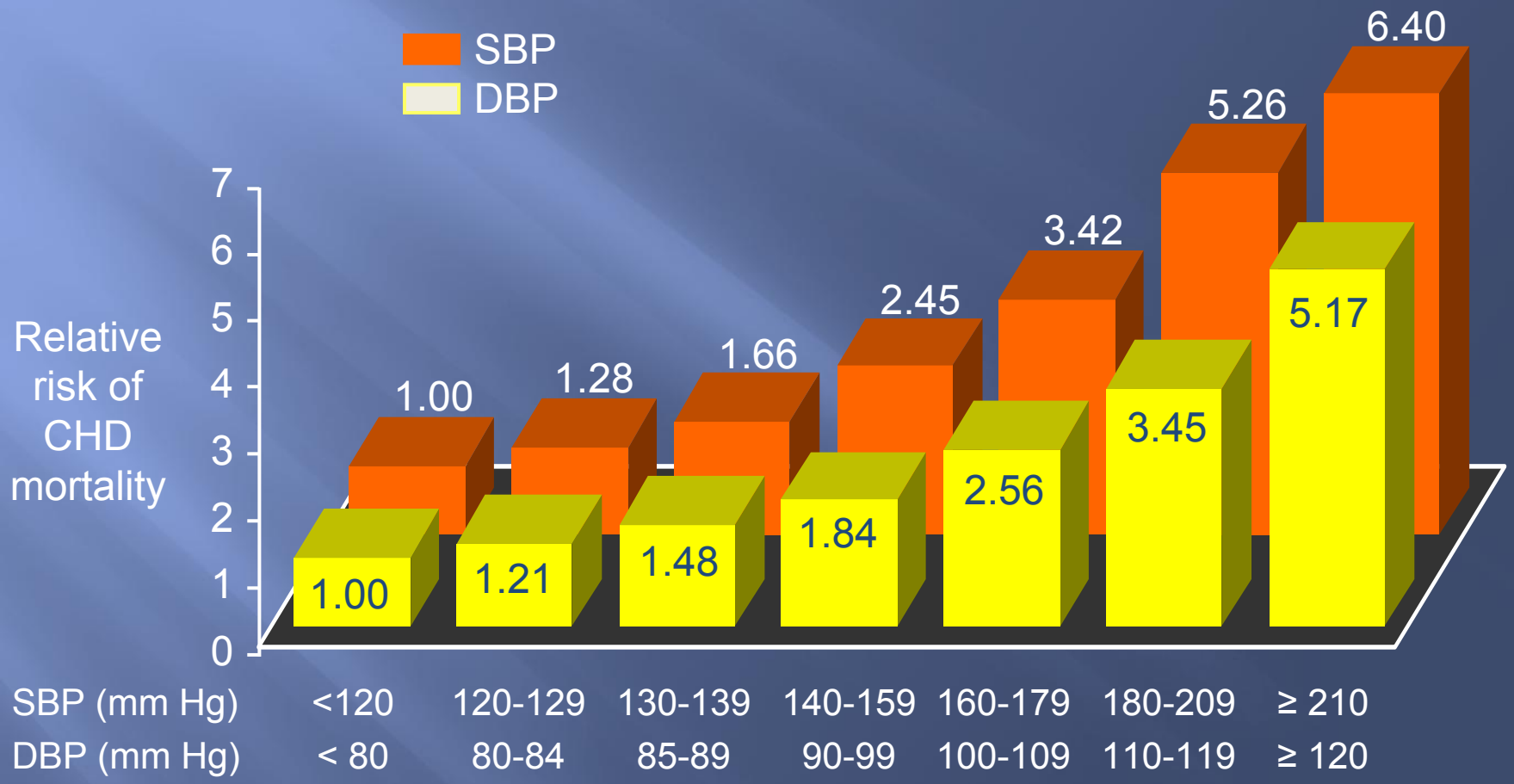
CV Complications of Untreated Hypertension (N=500)



MI, myocardial infarction; CHF, chronic heart failure.

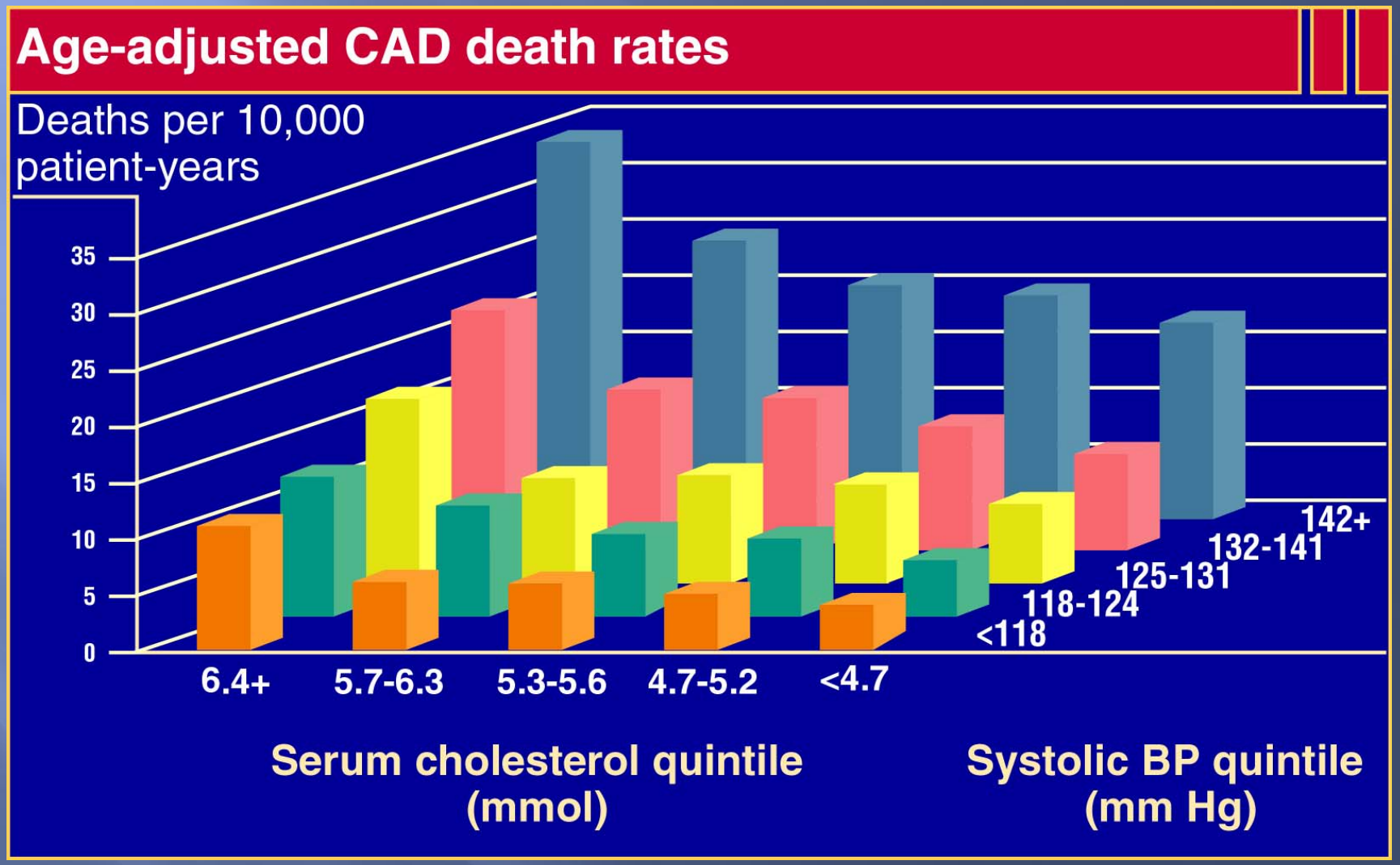
Perera GA J. *Chron Dis.* 1955;1:33-42.

BP and Risk of CHD Mortality



CHD, coronary heart disease.
Multiple Risk Factor Intervention Trial (MRFIT); n=347,978 men without previous myocardial infarction.
Neaton JD et al. In: *Hypertension: Pathophysiology, Diagnosis, and Management*. 1995:127-144.

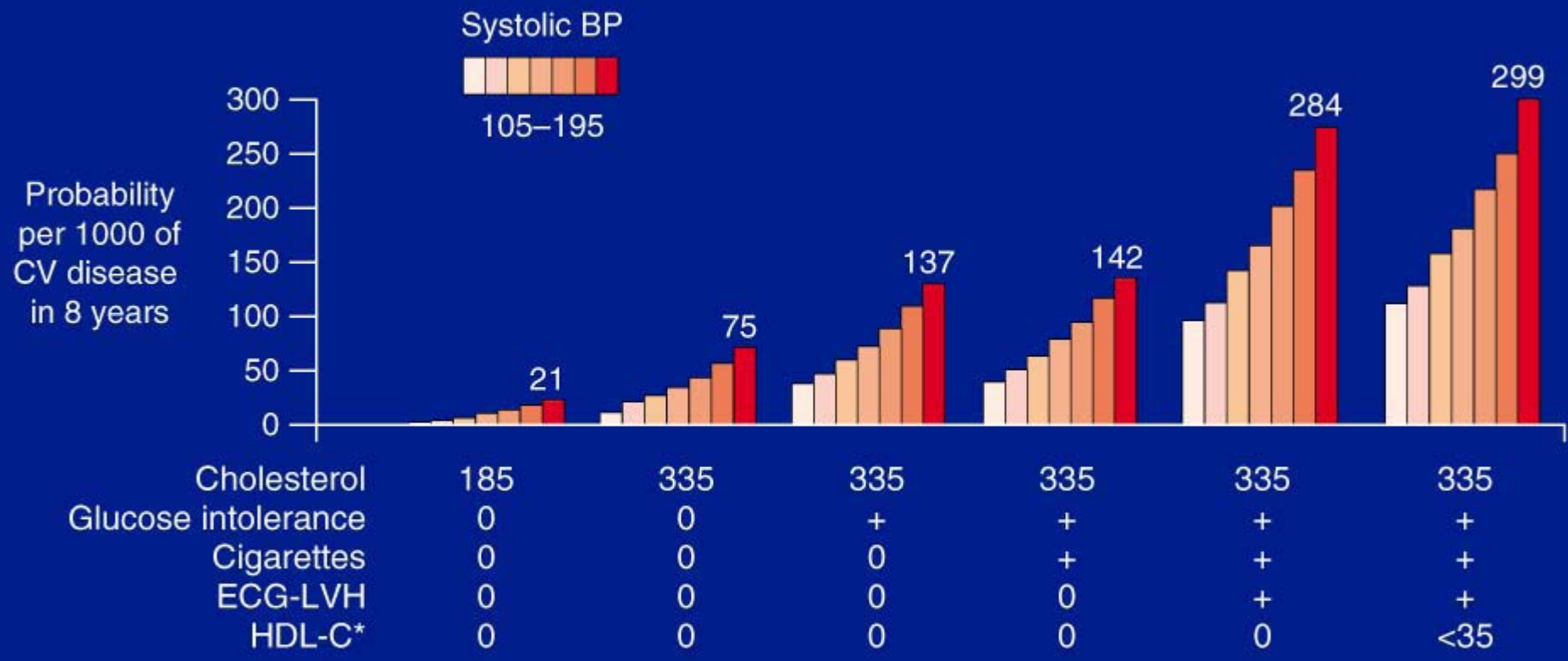
CAD Risk Is Incremental



(Adapted from Neaton et al.)

Neaton JD et al, *Arch Intern Med*, 1992.

Risk of cardiovascular disease



*Age-adjusted 10-year rate, data extrapolated for blood pressure (BP) categories.

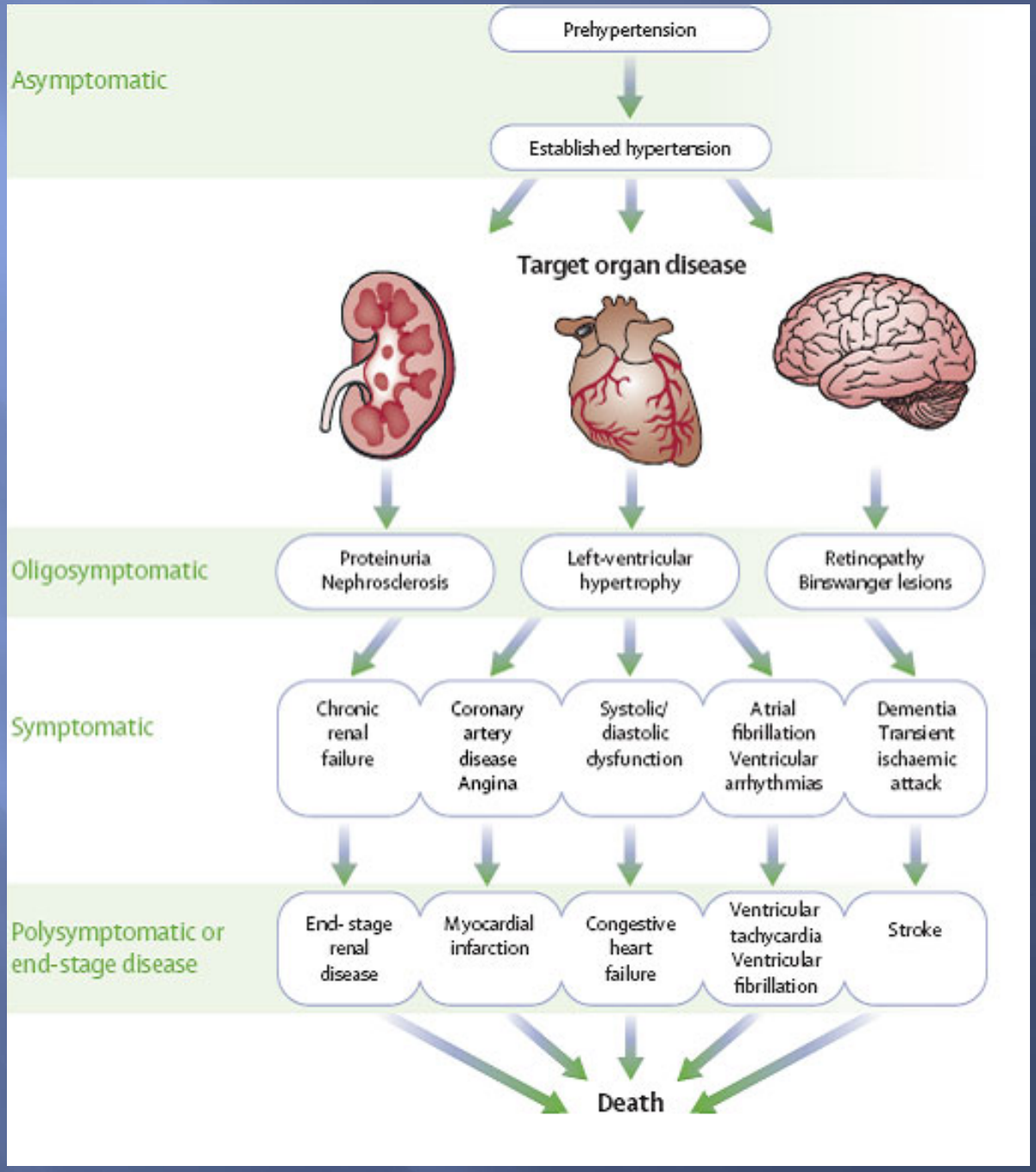
Kannel WB. *J Cardiovasc Pharmacol.* 1989;13:(suppl 1):S4-S10.
Wilson PWF, et al. *Circulation.* 1998;97:1837-1847.

ΑΡΤΗΡΙΑΚΗ ΥΠΕΡΤΑΣΗ

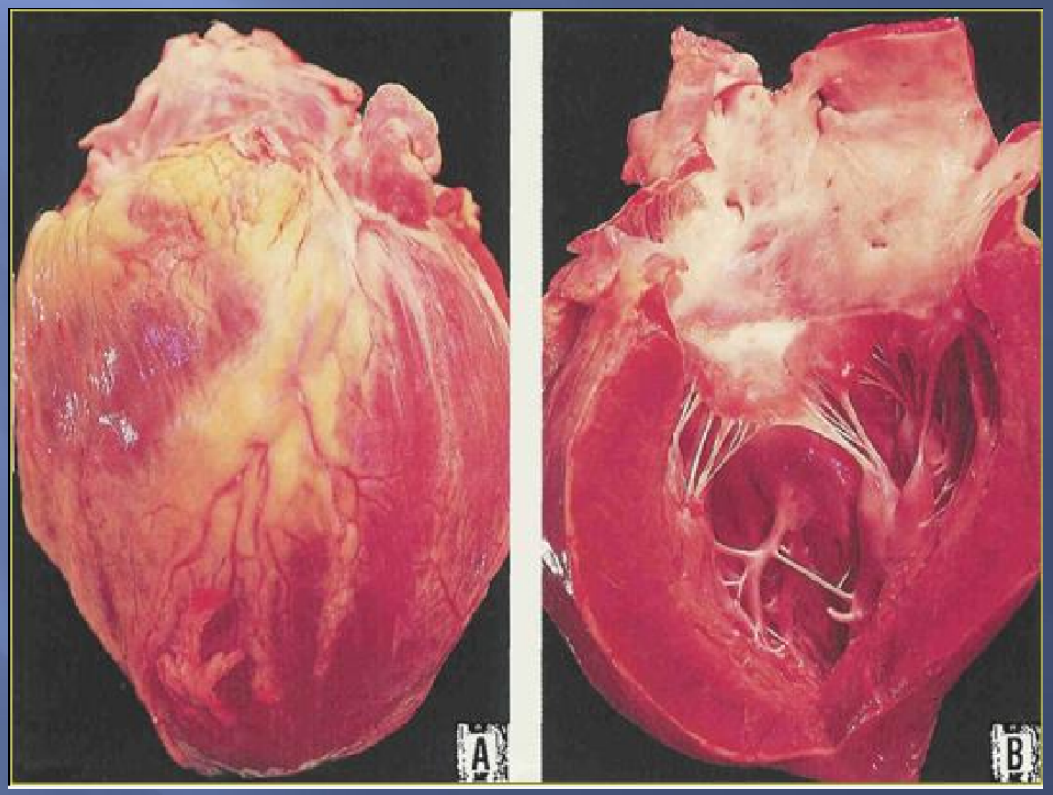
↑αιμοδυναμικό Φορτιο

↑ Ang II
↓NO
υποκλινική φλεγμονή

βλάβες οργάνων στόχων


Asymptomatic
Prehypertension
Established hypertension
Target organ disease
Oligosymptomatic
Proteinuria
Nephrosclerosis
Left-ventricular
hypertrophy
Retinopathy
Bineswanger lesions
Symptomatic
Chronic
renal
failure
Coronary
artery
disease
Angina
Systolic/
diastolic
dysfunction
Atrial
fibrillation
Ventricular
arrhythmias
Dementia
Transient
ischaemic
attack
Polysymptomatic or
end-stage disease
End- stage
renal
disease
Myocardial
infarction
Congestive
heart
failure
Ventricular
tachycardia
Ventricular
fibrillation
Stroke
Death

YAK



Determinants for LV Hypertrophy

Υπόβαθρο

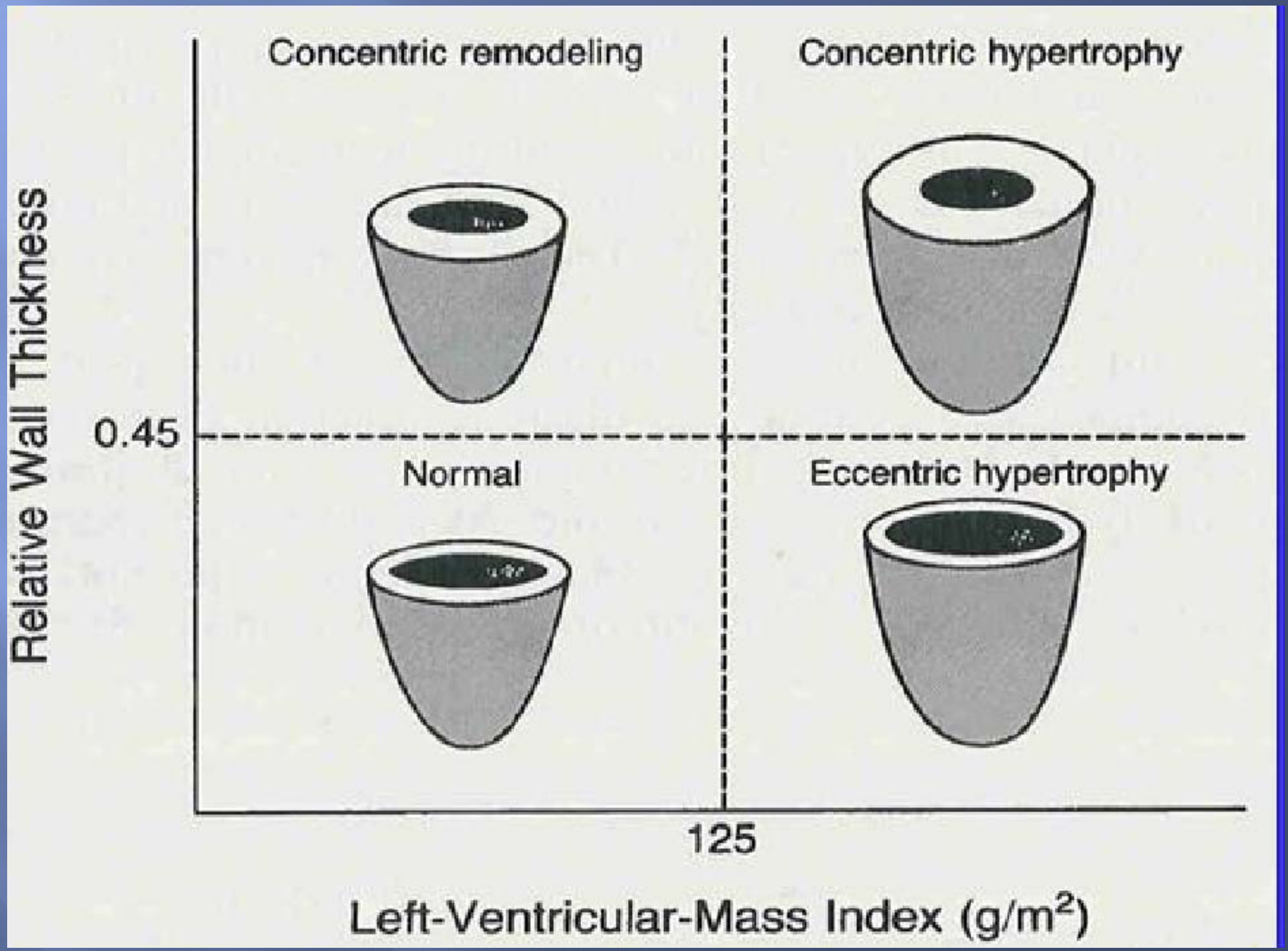
- Ηλικία
- Φύλο
- Φυλή
- Παχυσαρκία
- Αλάτι
- Αλκοόλ
- Λοιπές παθήσεις

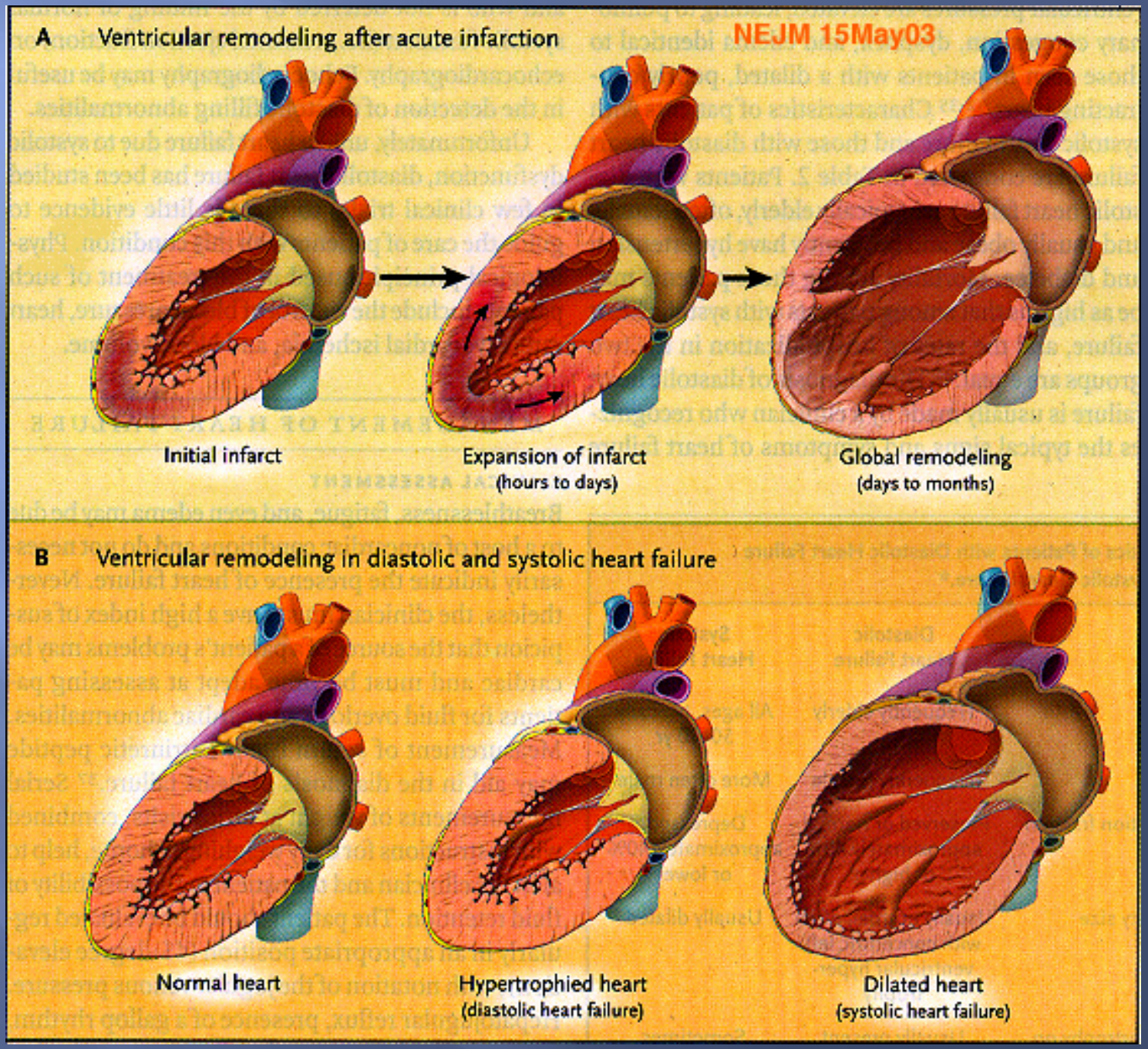
Αιμοδυναμικές παράμετροι

- Αρτ. Πίεση
- Φόρτιση όγκου
- Αρτηριακή δομή
- Γλοιότητα αίματος

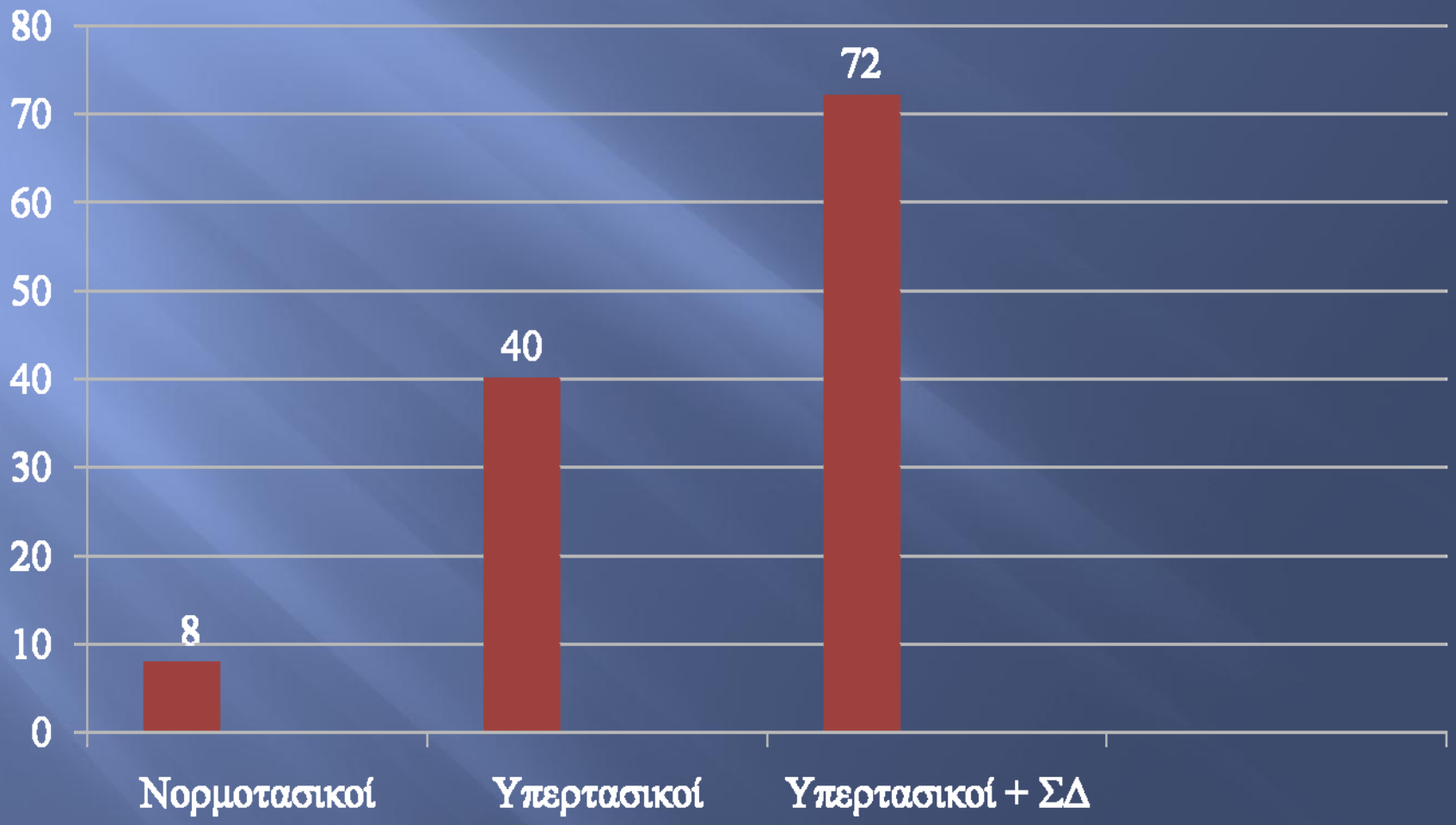
Μη-αιμοδυναμικές παράμετροι

- Τροφικοί παράγοντες:
  - -Συμπαθητικό ΝΣ
  - -RAAS
  - -Ινσουλίνη
- Γενετικοί παράγοντες και άλλα ενδοκυττάρια σήματα

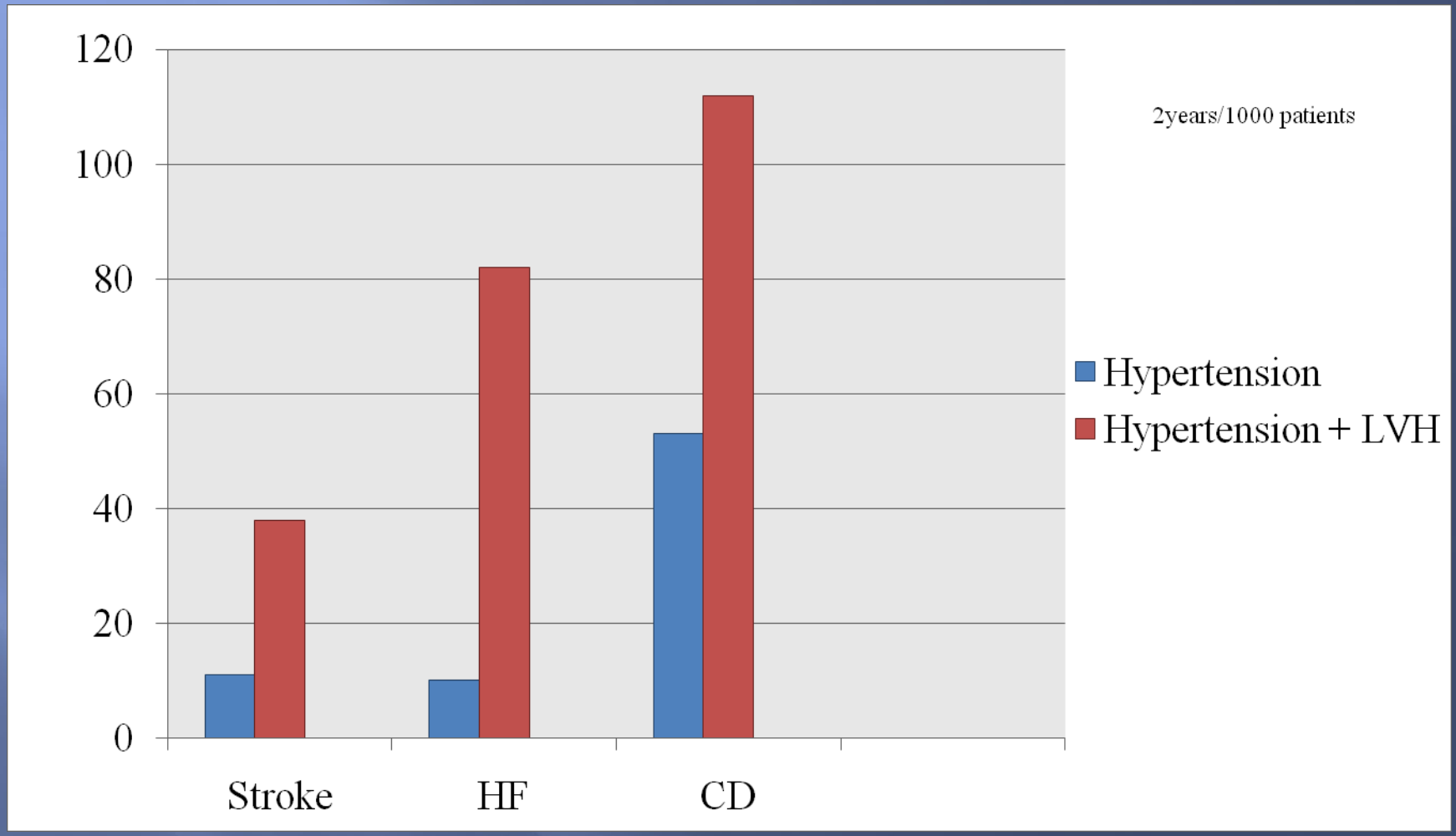

Concentric remodeling
Concentric hypertrophy
Normal
Eccentric hypertrophy
Relative Wall Thickness
0.45
125
Left-Ventricular-Mass Index (g/m²)


A Ventricular remodeling after acute infarction
NEJM 15May03
Initial infarct
Expansion of infarct
(hours to days)
Global remodeling
(days to months)
B Ventricular remodeling in diastolic and systolic heart failure
Normal heart
Hypertrophied heart
(diastolic heart failure)
Dilated heart
(systolic heart failure)

Επιπολασμός ΥΑΚ σε διαφορετικές ομάδες πληθυσμού

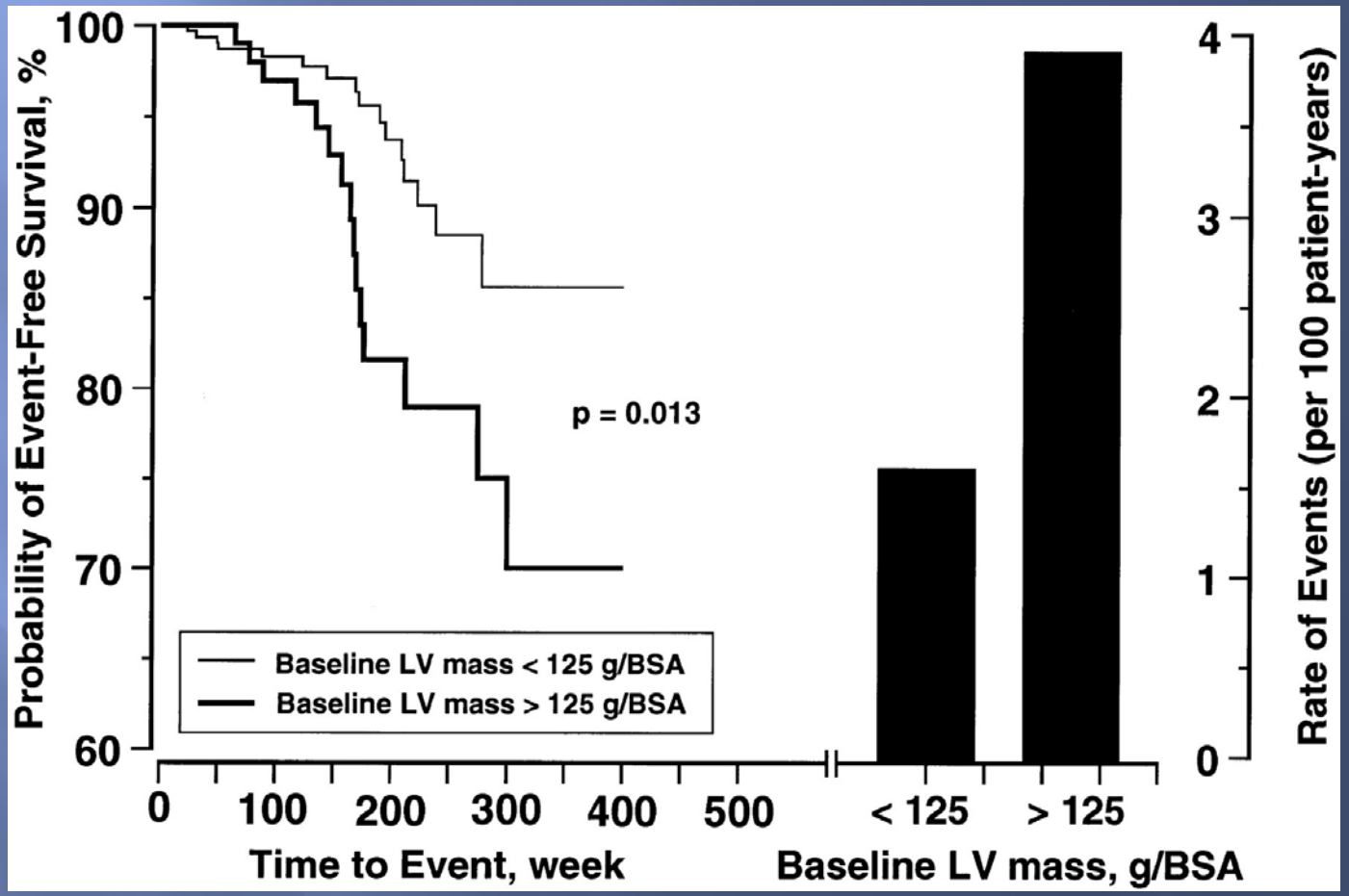


Target-organ damage increases cardiovascular risk



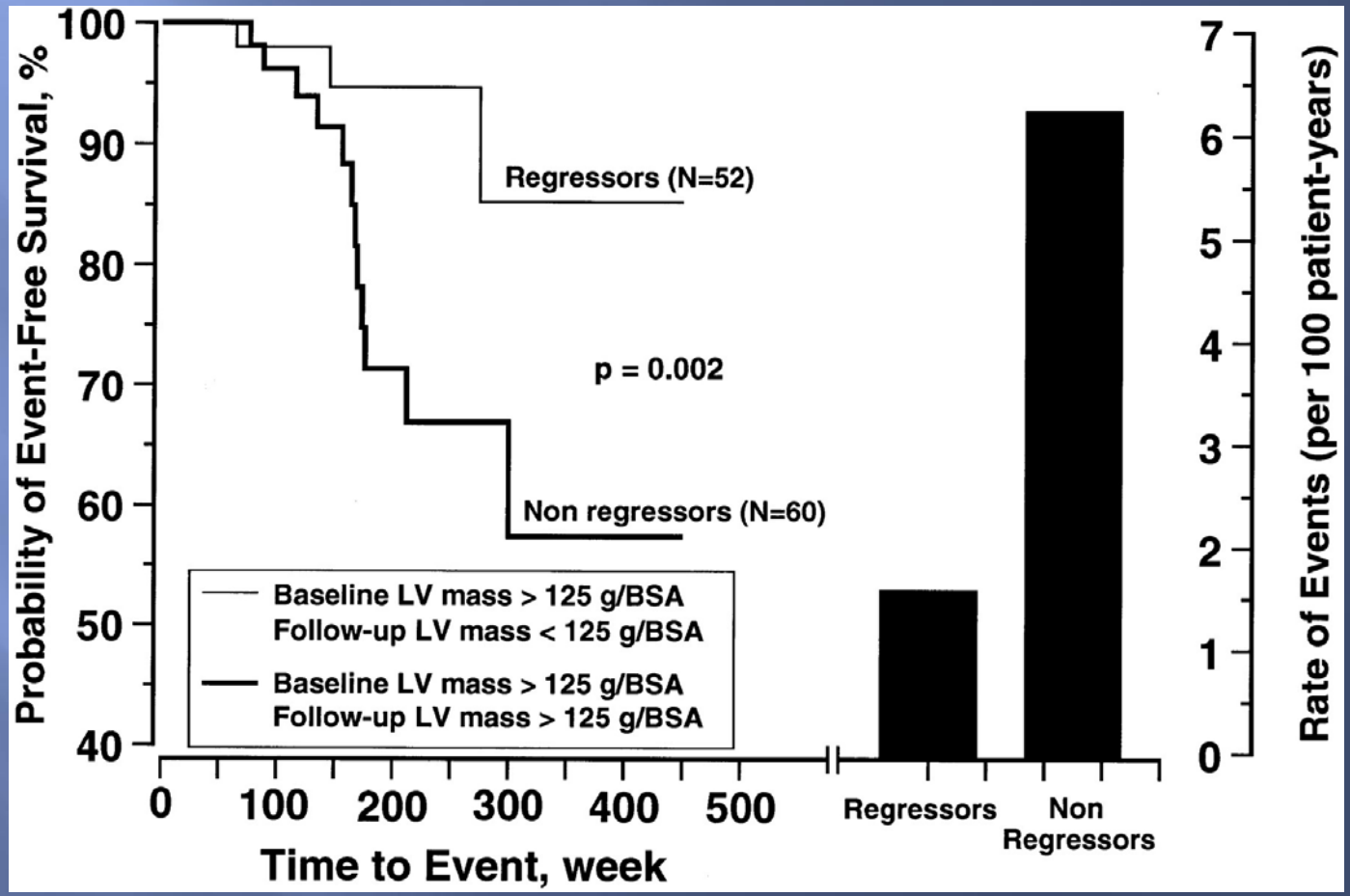
Kannel. Eur Heart J 1992;13 (Suppl D):82–88

Event-free survival in the two groups with (thick line) and without (thin line) echocardiographic LVH at the baseline visit



Verdecchia, P. et al. Circulation 1998;97:48-54

Event rate in subset with echocardiographic LVH at baseline visit



Verdecchia, P. et al. Circulation 1998;97:48-54

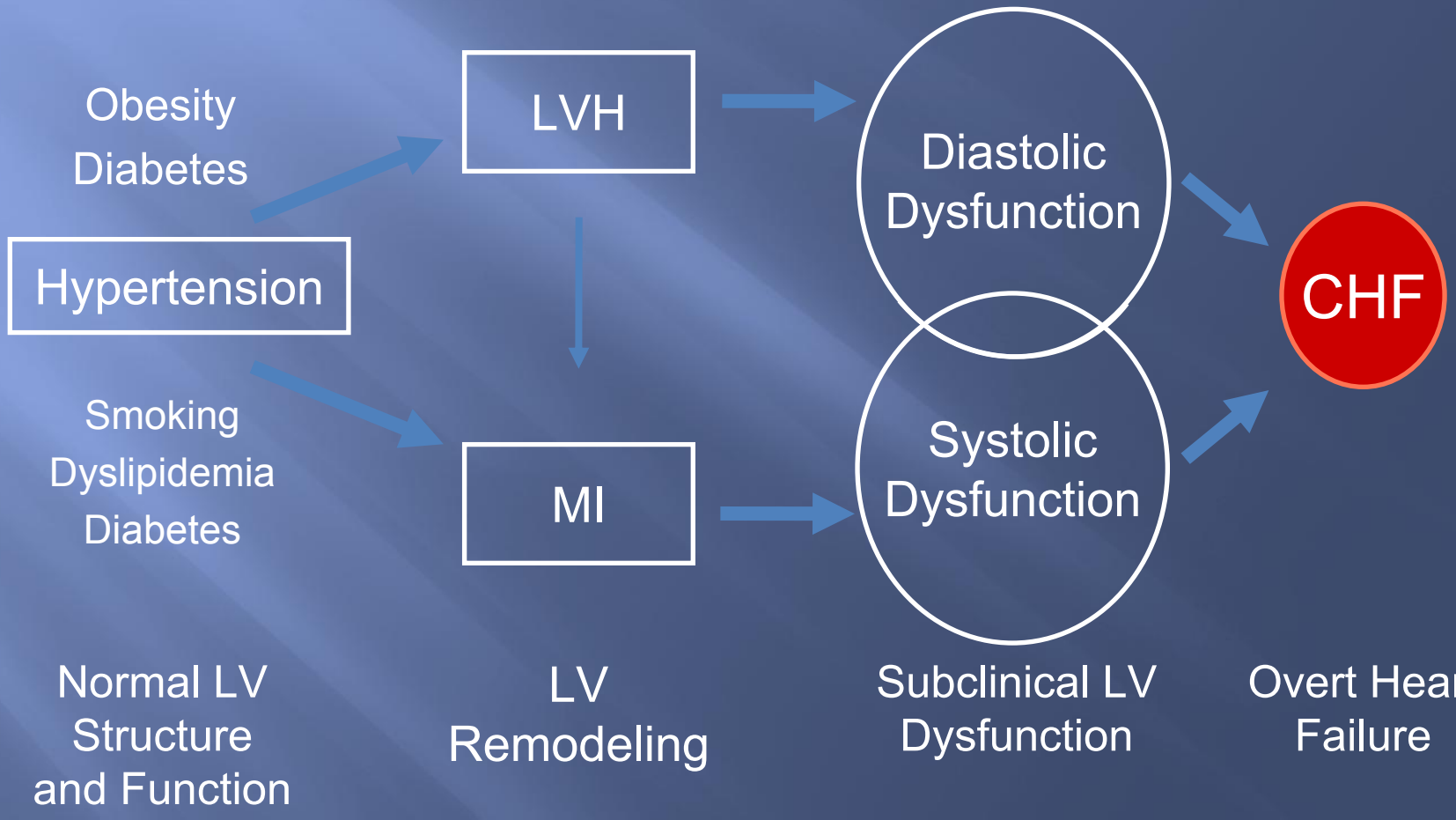
Relative risk of non- invasive parameters concerning cardiac mortality and sudden cardiac death (univariate analysis).

Parameter	Mortality		Sudden cardiac death	
	P	RR	P	RR
Age > 65 years	0.001	5.31	0.002	12.1
Lown lvb	0.0024	4.37	0.0004	17.1
QTd> 80 ms	0.0002	5.87	0.01	4.8
LVEF < 65%	0.43	1.82	0.32	1.7
VLP	0.53	1.52	0.97	1.04
LVH (echo)	0.002	4.97	0.34	1.93

VLP: Ventricular Late Potentials; QTd: QT-dispersion

Galinier M et al. Eur Heart J 1997;18:1484

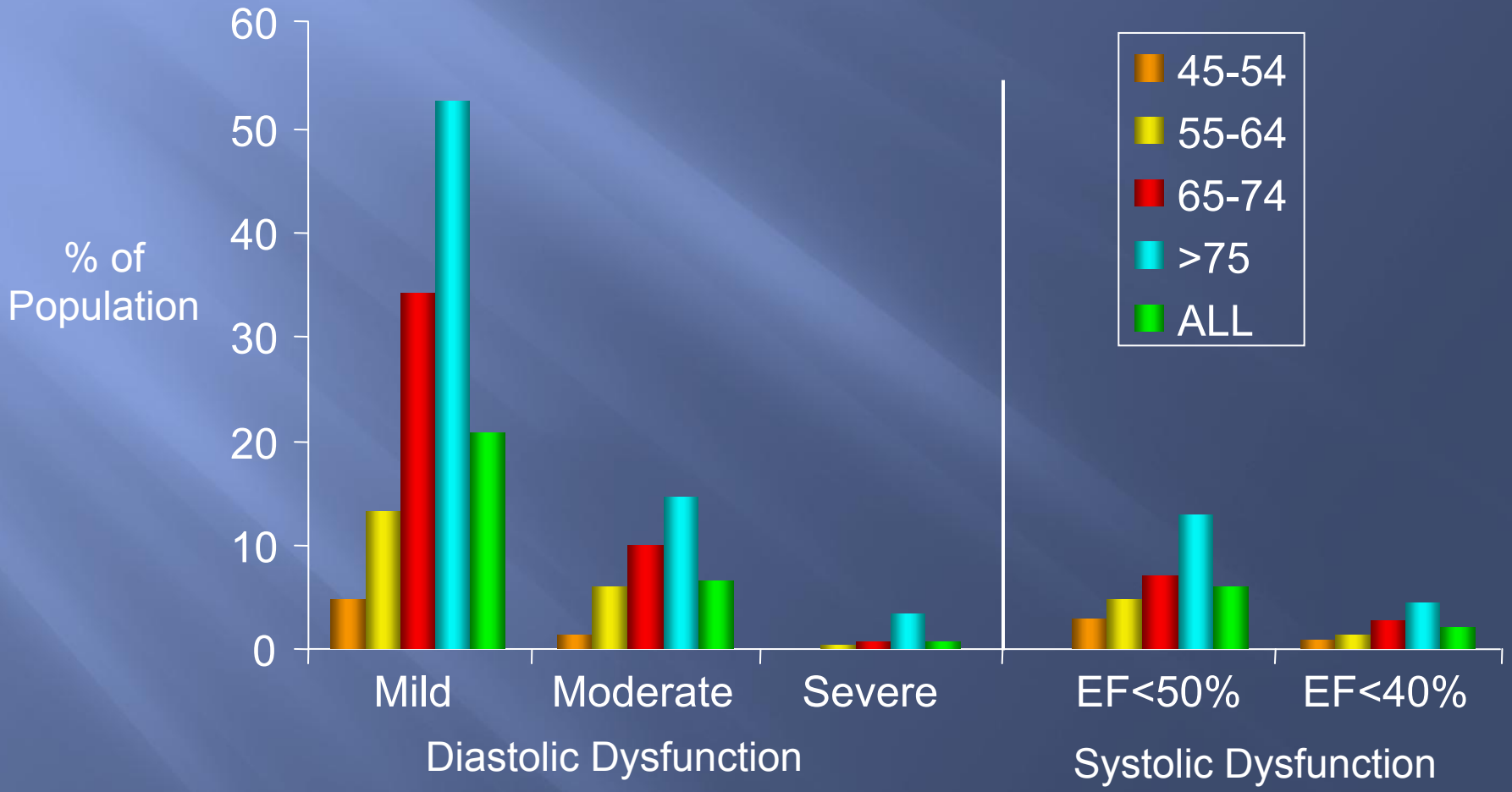
Progression From Hypertension to Heart Failure



LVH, left ventricular hypertrophy; MI, myocardial infarction; CHF, chronic heart failure.

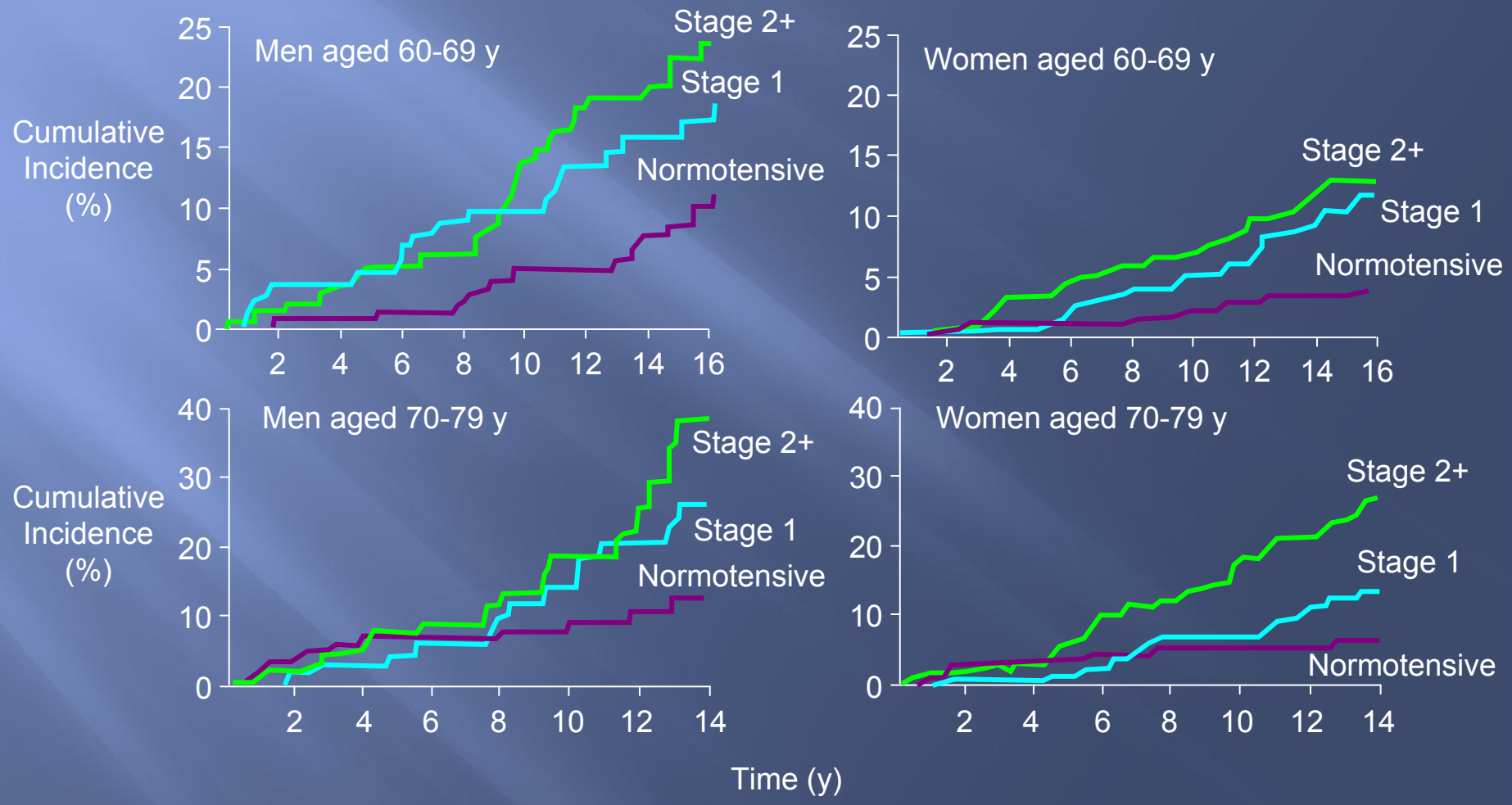
Vasan RS and Levy D. *Arch Intern Med.* 1996;156:1789-1796.

Prevalence of Systolic and Diastolic Dysfunction by Age



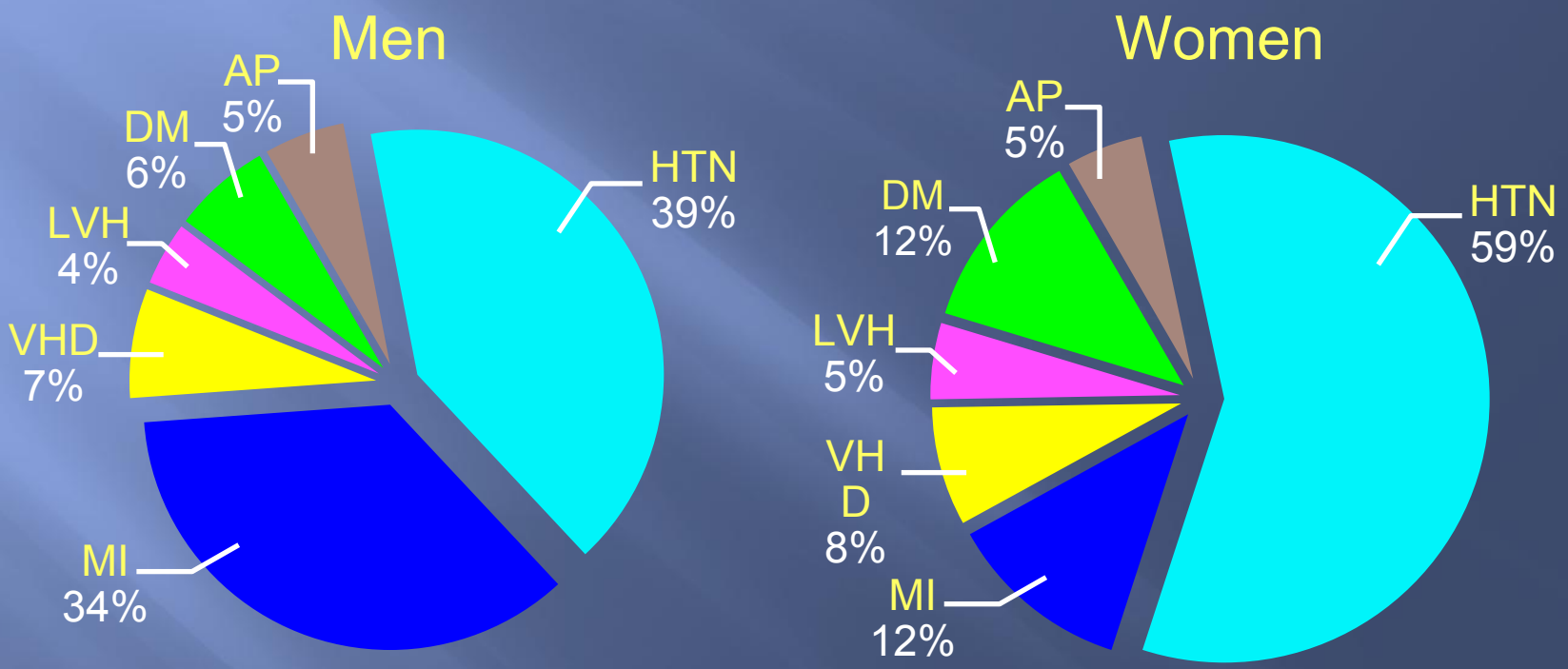
Redfield MM et al. *JAMA*. 2003;289:194-202.

Cumulative Incidence of Heart Failure by Baseline Hypertension Status



Levy D et al. *JAMA.* 1996;275:1557-1562.

Population-Attributable Risks for Development of CHF



Population-attributable risk defined as:
(100 x prevalence x [hazard ratio – 1])/(prevalence x [hazard ratio – 1] + 1)

CHF, chronic heart failure; AP, angina pectoris; DM, diabetes mellitus; LVH, left ventricular hypertrophy; VHD, valvular heart disease; HTN, hypertension; MI, myocardial infarction.

Levy D et al. *JAMA.* 1996;275:1557-1562.

Figure 4

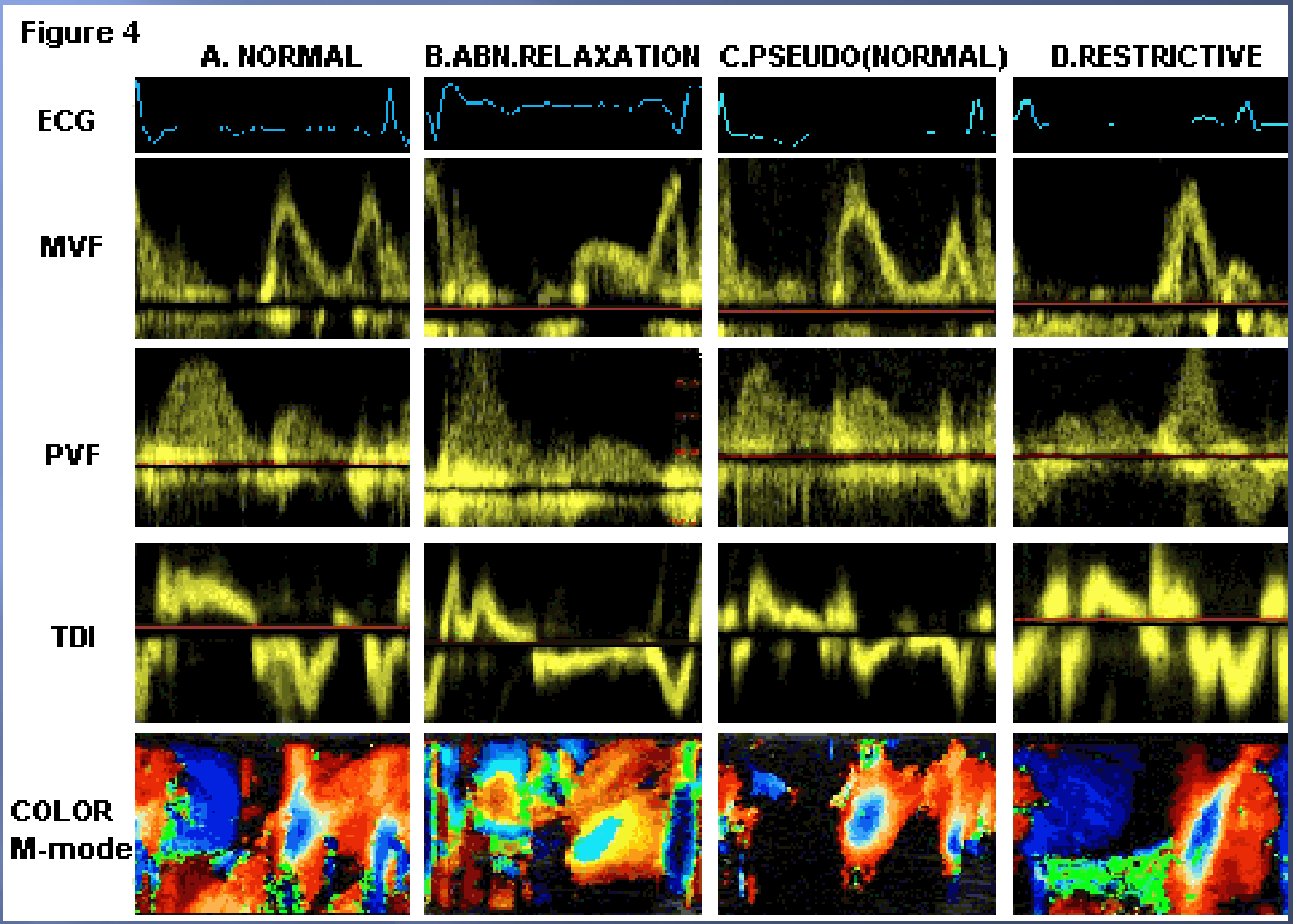

A. NORMAL
B.ABN.RELAXATION
C.PSEUDO(NORMAL)
D.RESTRICTIVE
ECG
MVF
PVF
TDI
COLOR
M-mode

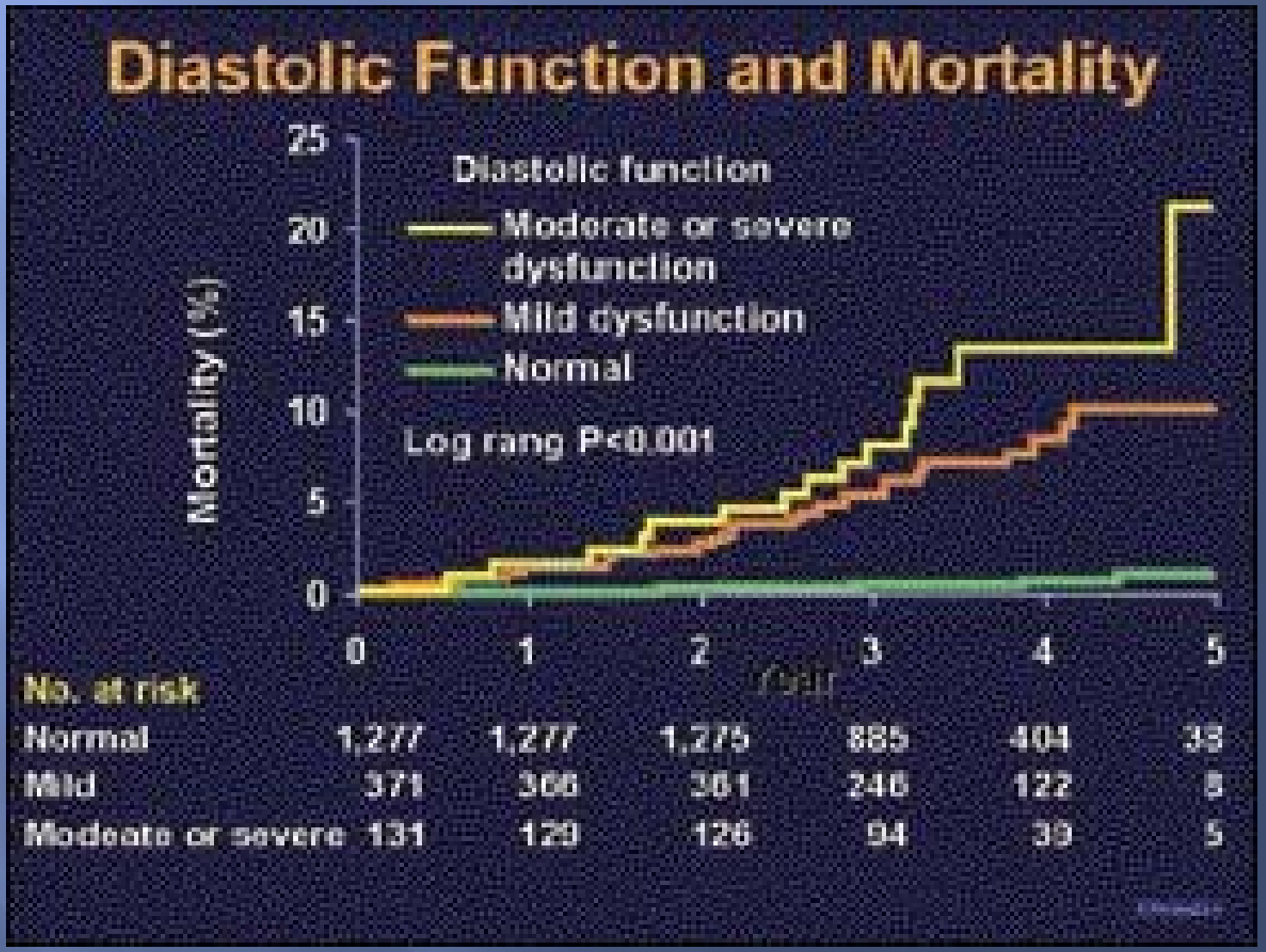
Table 4. Predictive Value of Various Echocardiographic Parameters

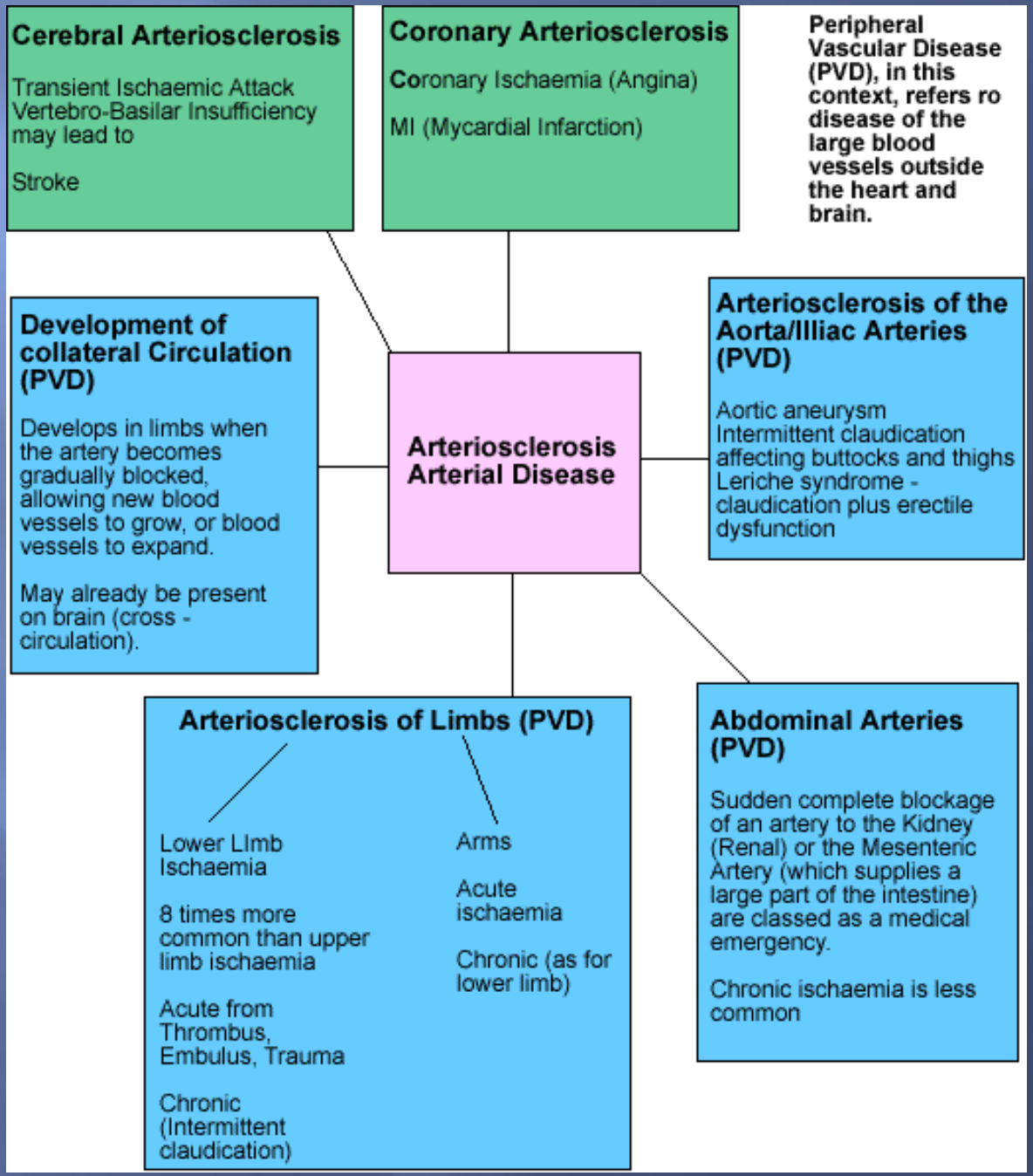
	Sensitivity (%)	Specificity	+ Predictive Value	− Predictive Value
LVH	24	92	18	95
Depressed FSmw	11	94	11	94
Depressed FSendo	13	95	15	94
E/A > 1.5 or < 0.7	40	83	14	95

Numbers given are percents. LVH (left ventricular hypertrophy) = LV mass index exceeding 95% of the healthy reference population. *Depressed shortening = stress adjusted shortening below 5th percentile of the healthy reference population.
FSendo = fractional shortening measured at the endocardium; FSmw = fractional shortening measured at the midwall.

JACC Vol. 37, No. 4, 2001 **Aurigemma *et al.***
Predictive Value of Echocardiography in CHF

Diastolic Function and Mortality



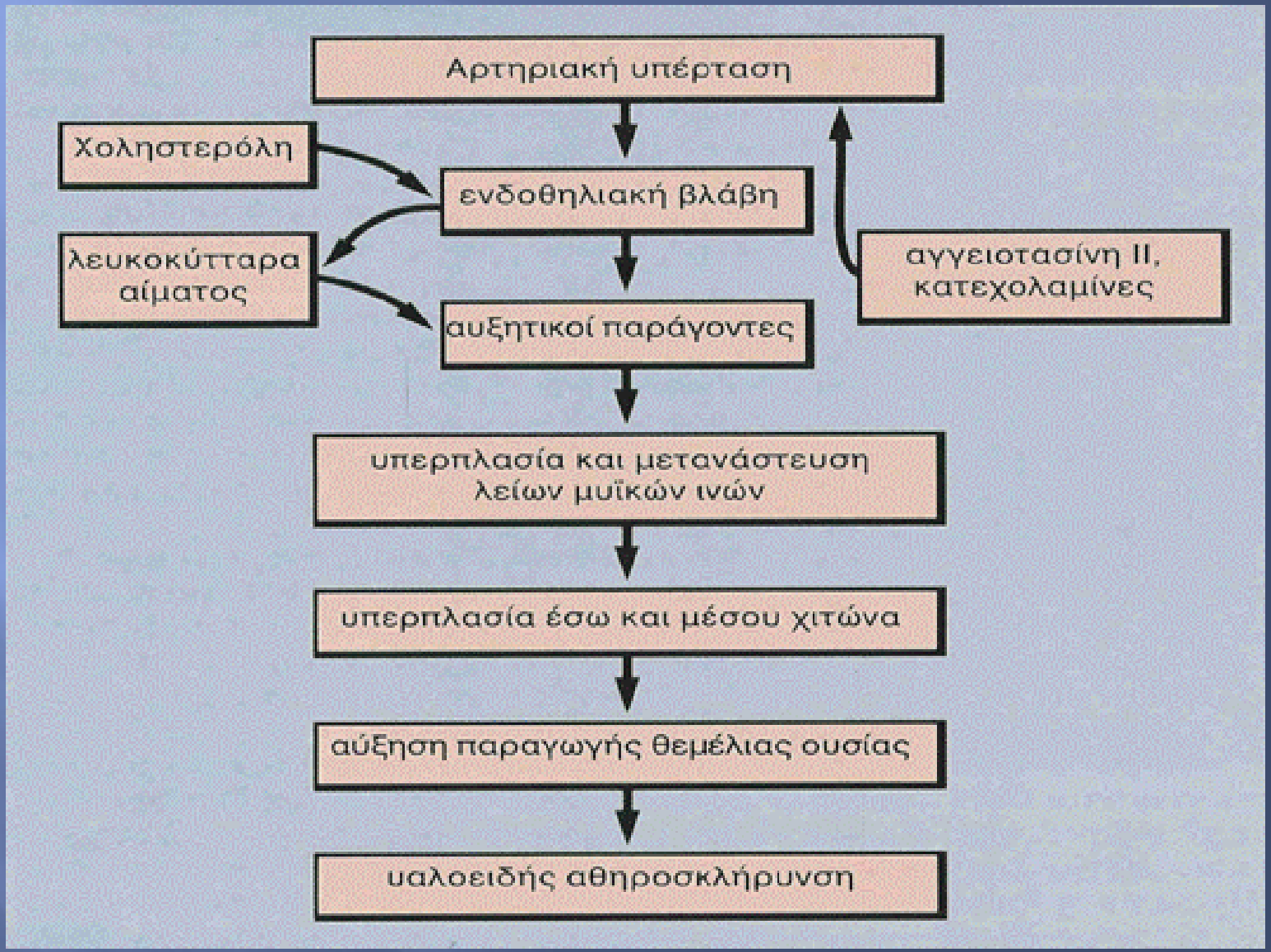

Cerebral Arteriosclerosis
Transient Ischaemic Attack
Vertebro-Basilar Insufficiency may lead to
Stroke
Coronary Arteriosclerosis
Coronary Ischaemia (Angina)
MI (Mycardial Infarction)
Peripheral Vascular Disease (PVD), in this context, refers ro disease of the large blood vessels outside the heart and brain.
Development of collateral Circulation (PVD)
Develops in limbs when the artery becomes gradually blocked, allowing new blood vessels to grow, or blood vessels to expand.
May already be present on brain (cross - circulation).
Arteriosclerosis Arterial Disease
Arteriosclerosis of the Aorta/Illiac Arteries (PVD)
Aortic aneurysm
Intermittent claudication affecting buttocks and thighs
Leriche syndrome - claudication plus erectile dysfunction
Arteriosclerosis of Limbs (PVD)
Lower LImb Ischaemia
8 times more common than upper limb ischaemia
Acute from Thrombus, Embulus, Trauma
Chronic (Intermittent claudication)
Arms
Acute ischaemia
Chronic (as for lower limb)
Abdominal Arteries (PVD)
Sudden complete blockage of an artery to the Kidney (Renal) or the Mesenteric Artery (which supplies a large part of the intestine) are classed as a medical emergency.
Chronic ischaemia is less common

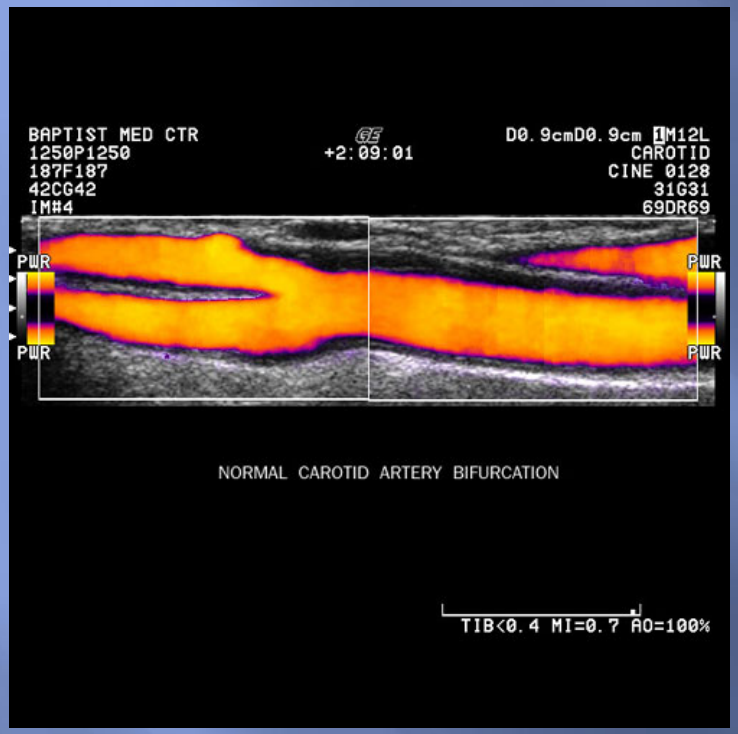
ΥΠΕΡΤΑΣΗ - ΑΘΗΡΩΜΑΤΩΣΗ

- Πνευμονικές αρτηρίες
- Φλέβες
- Στένωση Ισθμού αορτής

Πνευμονική υπέρταση

Φλεβικό μοσχευμα


Αρτηριακή υπέρταση
Χοληστερόλη
ενδοθηλιακή βλάβη
λευκοκύτταρα αίματος
αγγειοτασίνη ΙΙ, κατεχολαμίνες
αυξητικοί παράγοντες
υπερπλασία και μετανάστευση λείων μυϊκών ινών
υπερπλασία έσω και μέσου χιτώνα
αύξηση παραγωγής θεμέλιας ουσίας
υαλοειδής αθηροσκλήρυνση


BAPTIST MED CTR
1250P1250
187F187
42CG42
IM#4
+2:09:01
D0.9cmD0.9cm IM12L
CAROTID
CINE 0128
31G31
69DR69
PWR
PWR
PWR
PWR
NORMAL CAROTID ARTERY BIFURCATION
TIB<0.4 MI=0.7 AO=100%

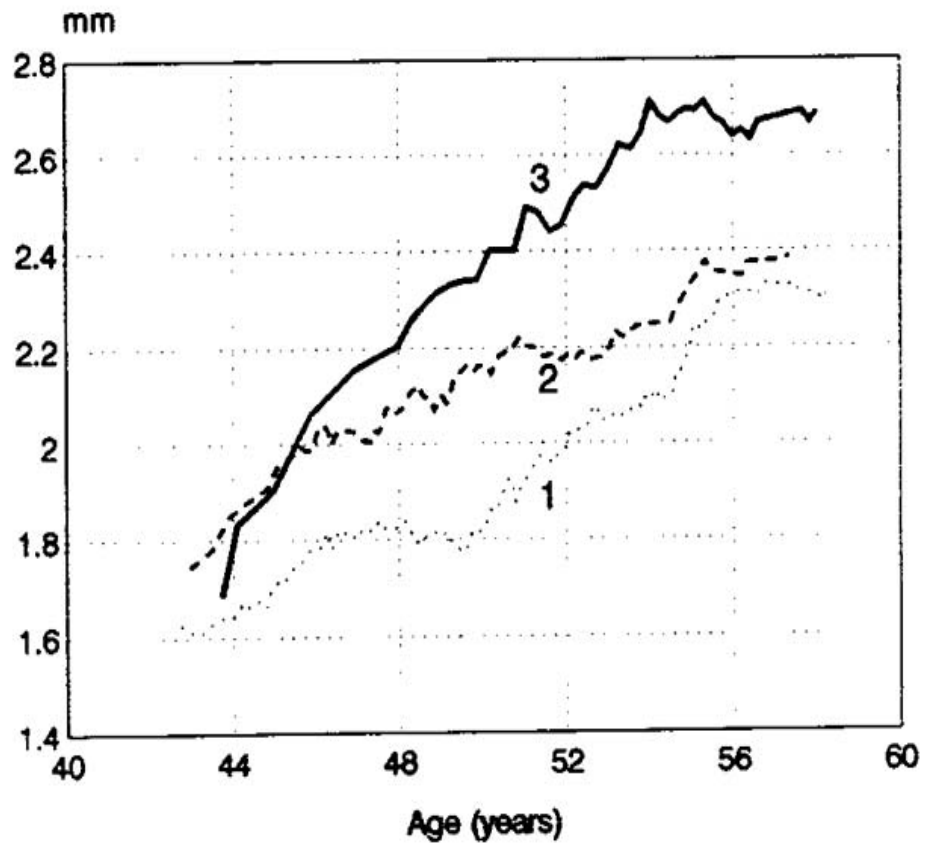
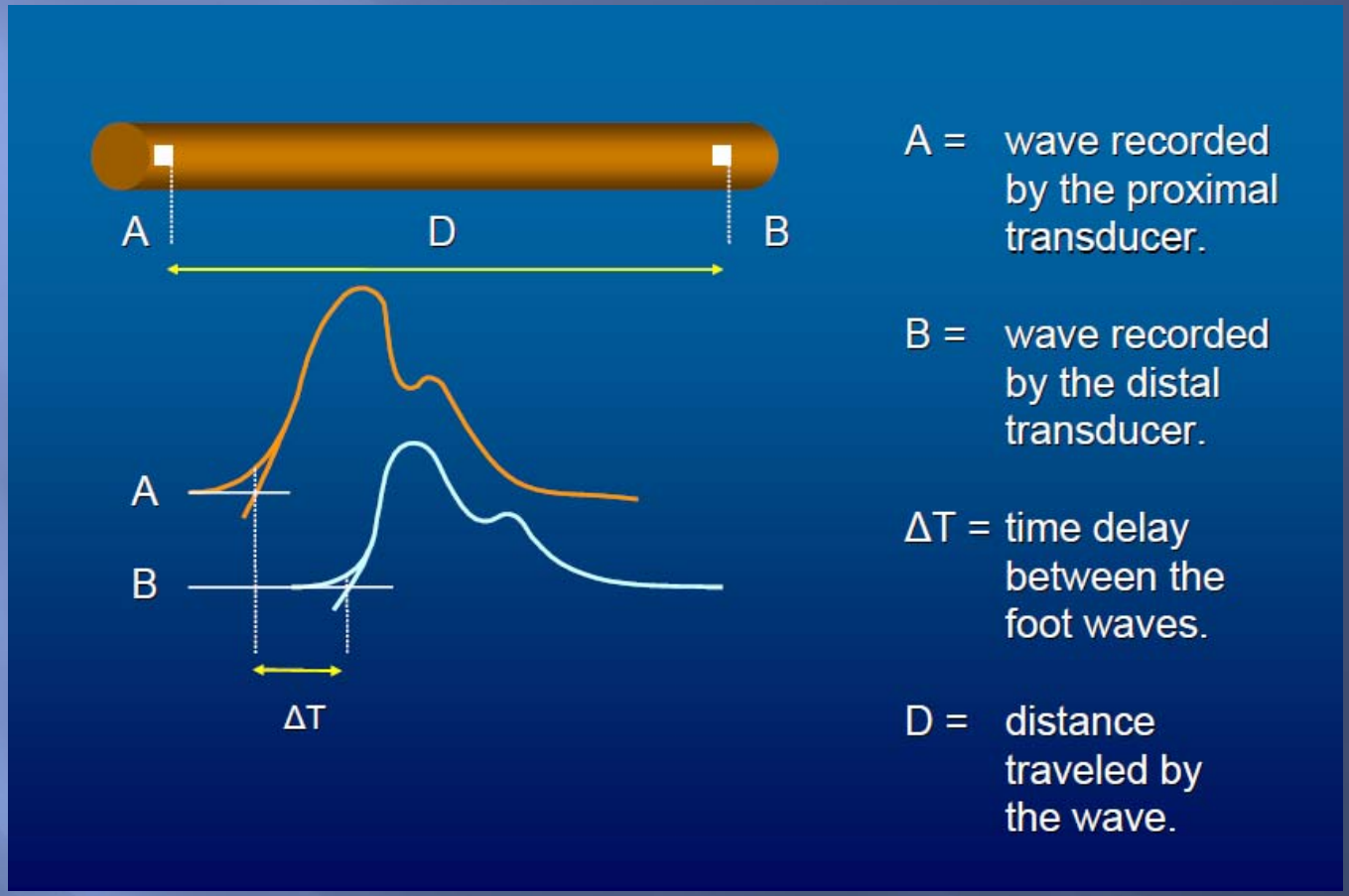


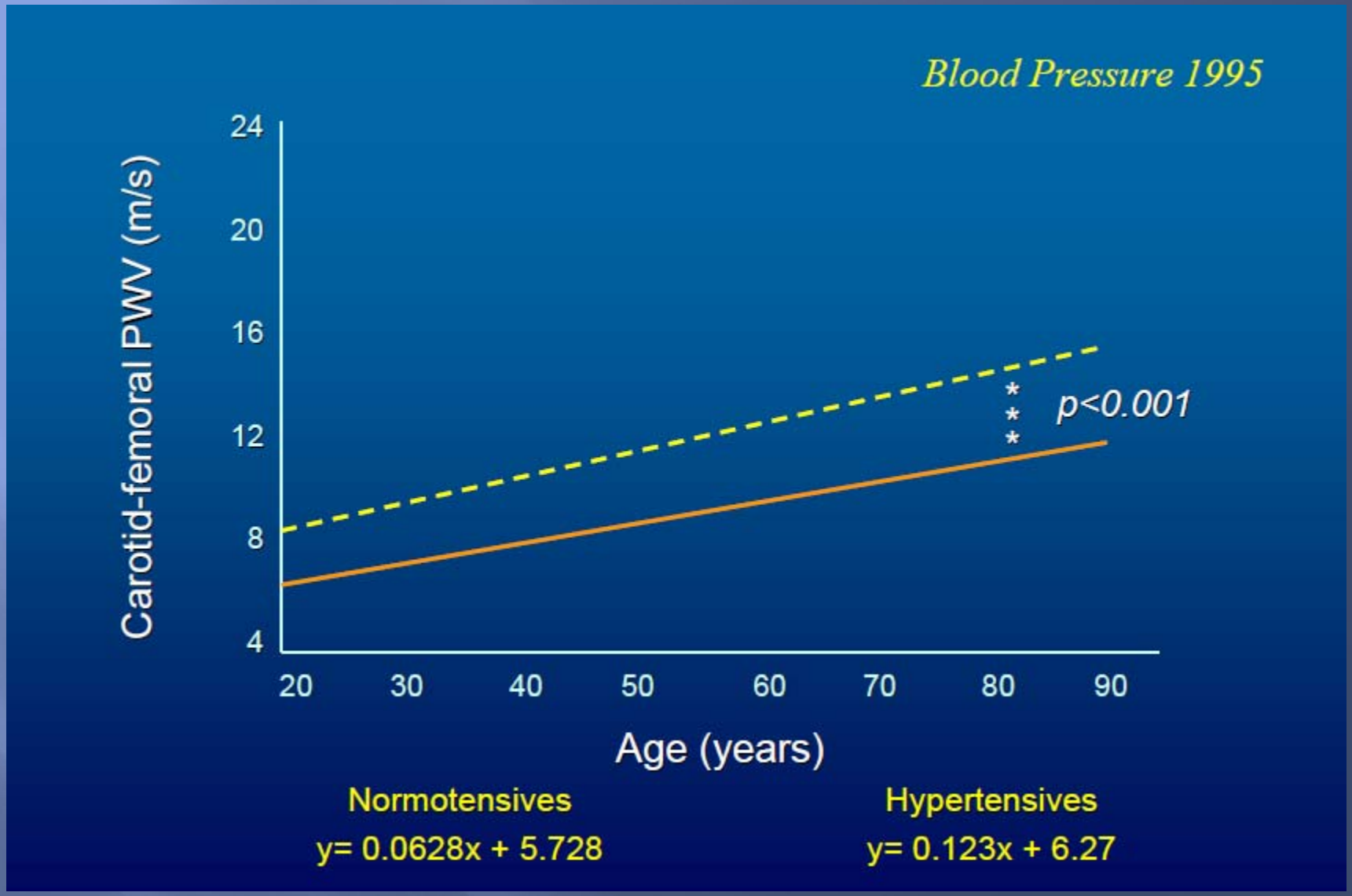
Figure 4. Maximal intima-media and plaque thickness in control men (1) and in men with hypertension of duration < 7 years (2) and ≥ 7 years (3).



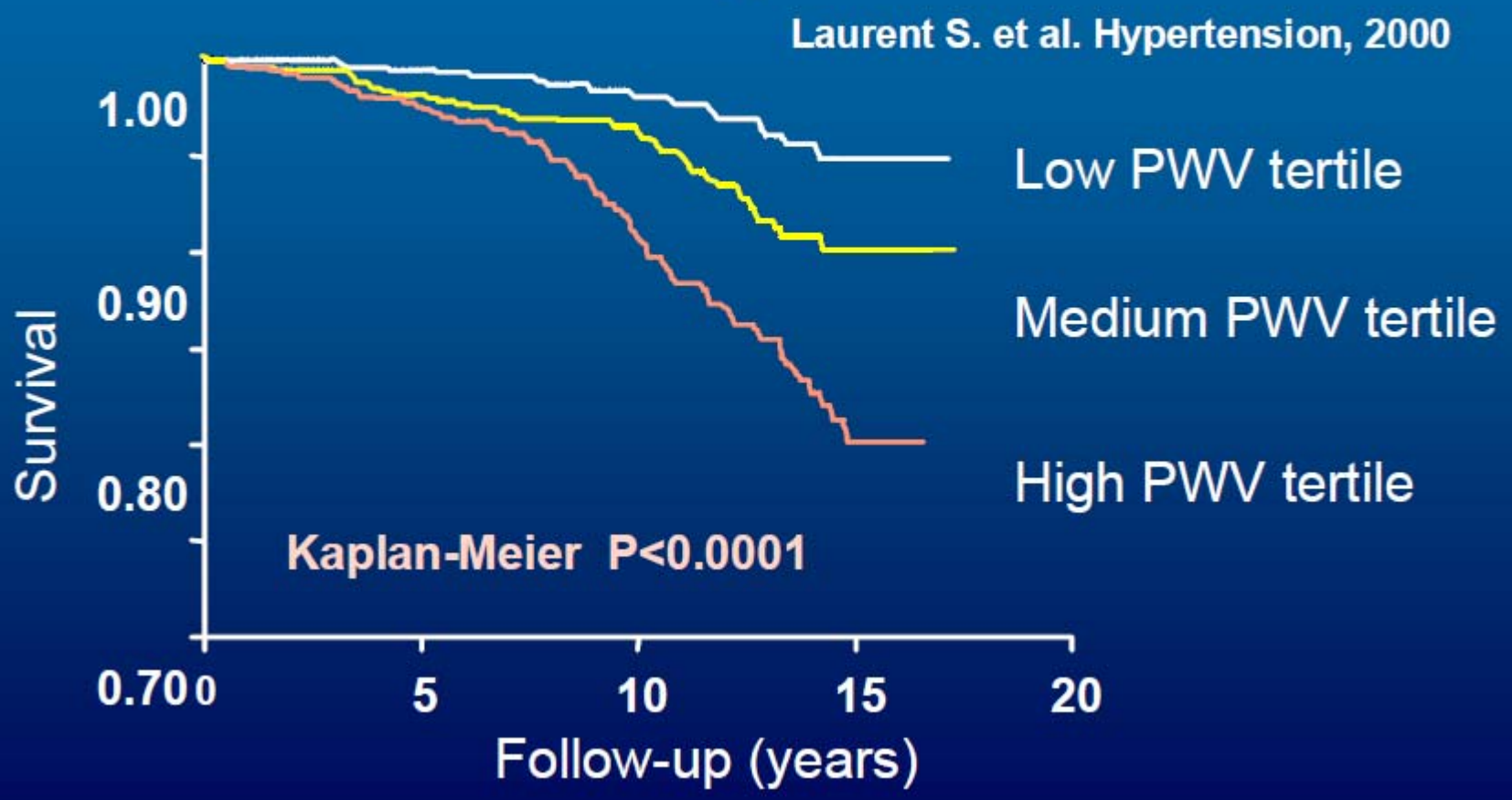
Η ταχύτητα του σφυγμικού κύματος είναι μια απλή εξέταση που βασίζεται στη μέτρηση της ταχύτητας (απόσταση από ένα σημείο του αρτηριακού δένδρου σε ένα άλλο / χρόνο) που χρειάζεται το σφυγμικό κύμα για να διανύσει τη συγκεκριμένη απόσταση.

Η φυσιολογική ταχύτητα (αρτηρίες χωρίς σκλήρυνση) στο καρωτιδο-μηριαίο αρτηριακό τμήμα είναι 770-980 cm/sec

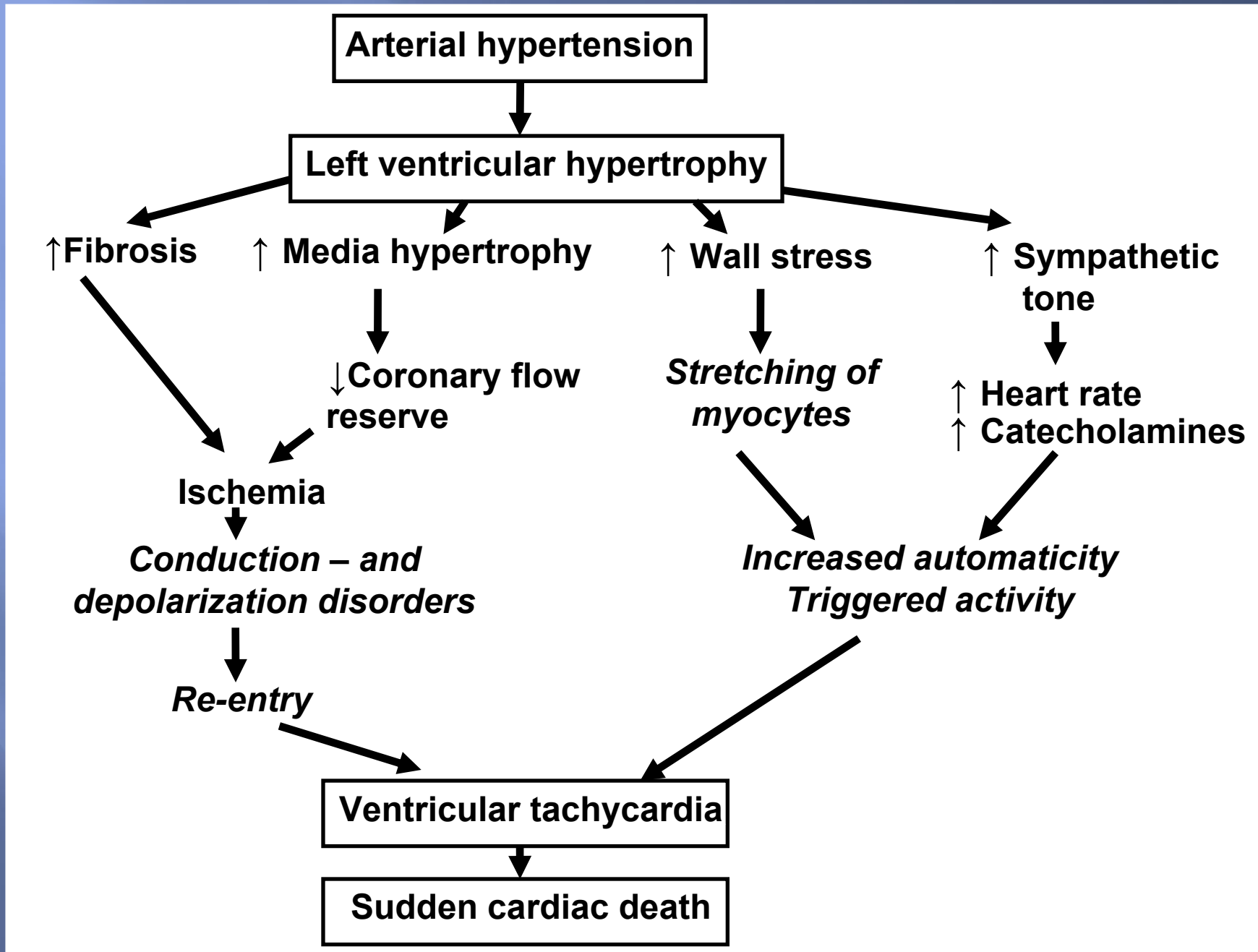
(0.06 Συστολική Α.Π. (mmHg) + 0.09 ηλικία (έτη) - $2.3.10^2$ m/sec).


Blood Pressure 1995
Carotid-femoral PWV (m/s)
24
20
16
12
8
4
20
30
40
50
60
70
80
90
Age (years)
***
p<0.001
Normotensives
y= 0.0628x + 5.728
Hypertensives
y= 0.123x + 6.27

Aortic stiffness and all-cause mortality in 1980 hypertensives



ΥΠΕΡΤΑΣΗ ΚΑΙ ΑΡΡΥΘΜΙΕΣ


Arterial hypertension
Left ventricular hypertrophy
↑Fibrosis
↑ Media hypertrophy
↑ Wall stress
↑ Sympathetic tone
↓Coronary flow reserve
Stretching of myocytes
↑ Heart rate
↑ Catecholamines
Ischemia
Conduction – and depolarization disorders
Increased automaticity
Triggered activity
Re-entry
Ventricular tachycardia
Sudden cardiac death

Μηχανισμοί αρρυθμιογένεσης στην υπέρταση

- Duration of the action potential is increased
- The plateau phase of the action potential is more labile than non-LVH
- Disorders of the cytosolic calcium concentrations
- The normal regional differences of action potential duration are reversed
- Reentry seems to be directly linked with fibrosis
- Link of LV wall stress and arrhythmias
- The HRV is decreased
- Electrolyte imbalance such as disorders of calcium and potassium channels

Ventricular ectopy in patients with normal left ventricular (LV) mass and left ventricular hypertrophy

		Normal LV-mass		Left ventricular hypertrophy	
Reference	Criterion	PVC/24 h	Patients with PVC (%)	PVC/24 h	Patients with PVC (%)
Messerli (1984) [53]	PVC/24 h	10		475*	
	Lown ⩾ 2		0		63*
McLenachan (1987) [8]	Couplets		16		36*
Lavie (1988) [54]	PVC/h > 1	24		291*	
	Lown ⩾ 2		0		35*
Szlachic (1989) [30]	PVC/h > 30		29		47*
Ghali (1991) [55]	PVC 1–4/h		1		6*
	PVC 5–30/h		0		5*
	PVC > 30/h		0		5*
Galinier (1997) [56]	PVC/24 h	23		826*	
	Lown ⩾ 2		4		50*
Schannwell (1998) [29]	Lown I/II		23		39*
	Lown ⩾ 3		0		29*
Kulan (1998) [57]	Lown > 2		8		19*

Percentage of Patients with Supraventricular and Ventricular Arrhythmias in Hypertensives with or without LVH

	With LVH	Without LVH
PSVB > 30/h	22.7%†	4.8%
PSVB	2736 ± 284†	720 ± 417
SVC (%)	36.4%	16.1%
SVC, 24-h mean	110 ± 97†	30 ± 19
SVT (%)	27.3%*	12.9%
SVT, 24-h mean	2.4 ± 0.7‡	1.2 ± 0.6
Beats	45 ± 27†	15 ± 11
PVB < 30/h	25.6%†	8.0%
PVB	3728 ± 319**	237 ± 129
VC	30.3%†	12.9%
PVC	172 ± 95‡	12 ± 7
VT (%)	12.1%*	3.2%
VT, 24-h mean	1.9 ± 1.2†	1.5 ± 0.5
Beats	45 ± 35*	16 ± 9

Novo S. et al. Am J Hypertens 1997;10:843

Coefficients of Correlation (R) Between SBP, DBP, HR and Supraventricular and Ventricular Arrhythmias in two Groups of Hypertensives with or without LVH

	With LVH		Without LVH	
	PSVB	PVB	PSVB	PVB
ASBP	0.34	0.83*	0.88*	0.38
ADBP	0.39	0.74*	0.49*	0.31
AHR	0.55*	0.87*	0.76*	0.36

** p<.01*

Novo S. et al. Am J hypertens 1997;10:843

Associations of Systolic and Diastolic Blood Pressure with Prevalence of Atrial Fibrillation

Variables	OR (95% CI) Systolic BP (per 10mm Hg)	Diastolic BP (per 10mm Hg)	Pulse Pressure (per 9 mm Hg)
Unadjusted	1.46*	1.07	1.52*
Adjustment			
Age (5 yrs)	1.25*	1.05	1.23*
Age and gender (men)	1.21*	1.04	1.19*
Age, gender and BMI (>28kg/m^2)	1.16*	1.02	1.18*
Age, gender, BMI and systolic BP	-	1.01	1.17
Age, gender, BMI and pulse pressure	1.15*	0.91	-

*$p < 0.001$

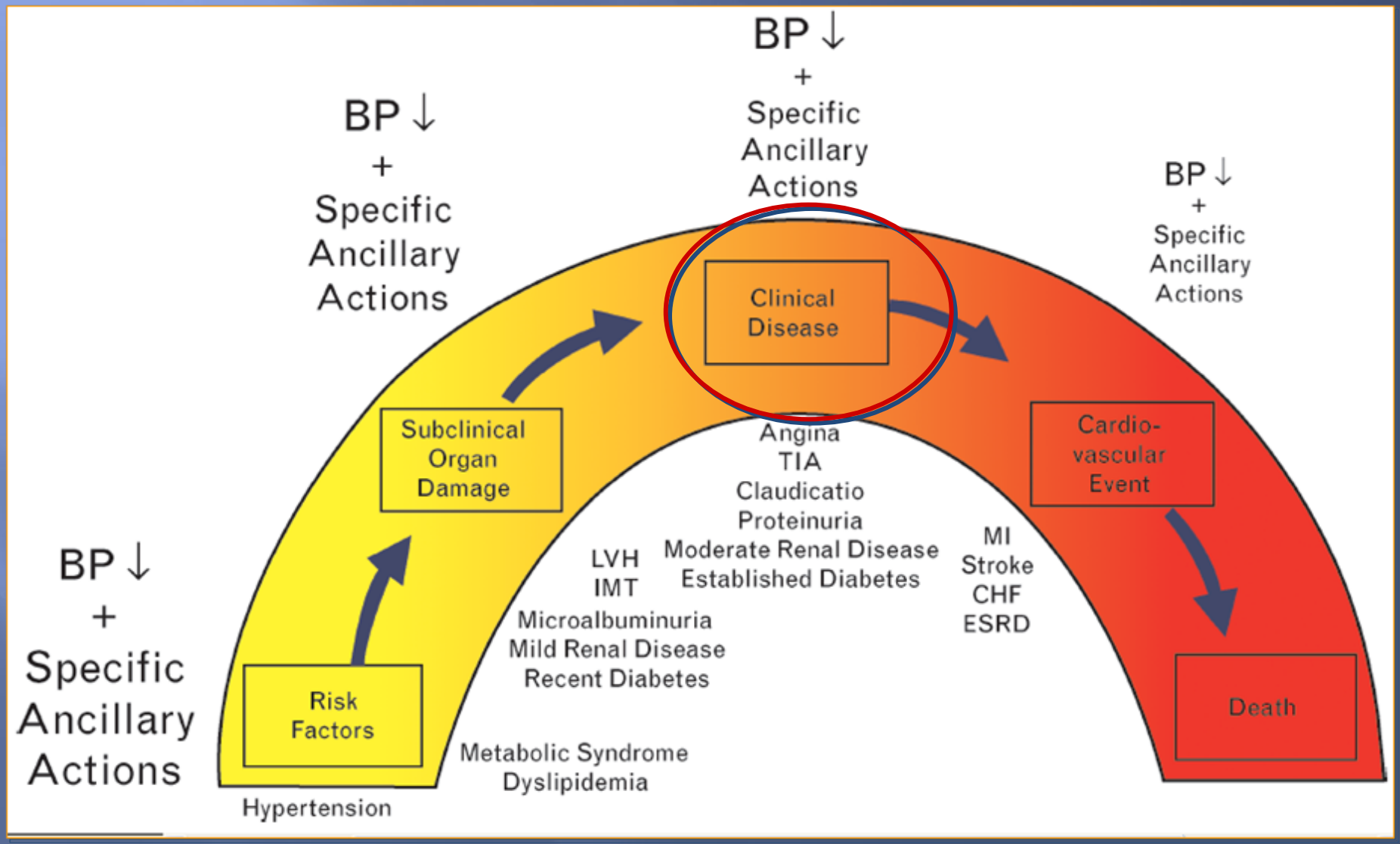
Ciaroni S et al. Am J Cardiol 2004;94:2566

Factors Associated With Ischemic Stroke Multivariate Analysis SPAF I-III Trial

	All Participants (n=2012)		Primary Prevention* (n=1853)	
	Adjusted RR	*P*	Adjusted RR	*P*
Features				
Age (per decade)	1.8	<0.001	2.0	<0.001
Female sex	1.6	0.01	NA†	NA†
History of hypertension	2.0	<0.001	2.2	<0.001
Systolic BP >160 mm Hg	2.3	<0.001	2.6	<0.001
Alcohol use (≥14/wk)	0.4‡	0.04	0.2‡	0.003
Prior stroke or TIA	2.9	<0.001	NA	NA

Hart R.G. et al. Stroke. 1999; 30: 1223-1229

The CV continuum in HTN and the relative prevention of BP lowering and the ancillary action of drugs.



Zanchetti A. J Hypertens 2005;23:113

Initiation of antihypertensive treatment

Other risk factors, OD or disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP ≥180 or DBP ≥110
No other risk factors	No BP intervention	No BP intervention	Lifestyle changes for several months then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + immediate drug treatment
1-2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes + immediate drug treatment
3 or more risk factors, MS, OD or diabetes	Lifestyle changes	Lifestyle changes and consider drug treatment	Lifestyle changes + drug treatment	Lifestyle changes + drug treatment	Lifestyle changes + immediate drug treatment
Diabetes	Lifestyle changes	Lifestyle changes + drug treatment			
Established CV or renal disease	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment	Lifestyle changes + immediate drug treatment

Conditions favoring use of some antihypertensive drugs versus others

ACE Inhibitors	Angiotensin receptor antagonists	Diuretics (antialdosterone)	Loop diuretics
Heart failure	Heart failure	Heart failure	End stage renal disease
LV dysfunction	Post-myocardial infarction	Post-myocardial infarction	Heart failure
Post-myocardial infarction	Diabetic nephropathy		
Diabetic nephropathy	Proteinuria/ Microalbuminuria		
Non-diabetic nephropathy	LV hypertrophy		
LV hypertrophy	Atrial fibrillation		
Carotid atherosclerosis	Metabolic syndrome		
Proteinuria/ Microalbuminuria	ACEI - induced cough		
Atrial fibrillation			
Metabolic syndrome			

Conditions favoring use of some antihypertensive drugs versus others

Thiaside diuretics	Beta-blockers	Calcium antagonists (dihydropyridines)	Calcium antagonists (verapamil/diltiazem)
Isolated systolic hypertension (elderly)	Angina pectoris	Isolated systolic hypertension (elderly)	Angina pectoris
Heart failure	Post-myocardial infarction	Angina pectoris	Carotid atherosclerosis
Hypertension in blacks	Heart failure	LV hypertrophy	Supraventricular tachycardia
	Tachyarrhythmias	Carotid/ Coronary Atherosclerosis	
	Glaucoma	Pregnancy	
	Pregnancy	Hypertension in blacks	

Antihypertensive Treatment: Preferred Drugs

- **General rules**: lower SBP and DBP to goal. Use any effective agent at adequate doses, if useful in combination. Use long acting agents to lower BP throughout 24 hours. Avoid or minimize adverse effects.

- **Subclinical organ damage**

Left ventricular hypertrophy	**ACE inhibitors, calcium antagonists, angiotensin receptor antagonists**
Asymptomatic atherosclerosis	Calcium antagonists, ACE inhibitors
Microalbuminuria	ACE inhibitors, angiotensin receptor antagonists
Renal dysfunction	ACE inhibitors, angiotensin receptor antagonists

- **Clinical event**

Previous stroke	Any BP lowering agent
Previous MI	β-blockers, ACE inhibitors, angiotensin receptor antagonists
Angina pectoris	β-blockers, calcium antagonists
Heart failure	diuretics, β-blockers, ACE inhibitors, angiotensin receptor antagonists, antialdosterone agents
Atrial fibrillation	
Recurrent	ACE inhibitors, angiotensin receptor antagonists
Continuous	β-blockers, non-dihydropiridine calcium antagonists
Renal failure/proteinuria	ACE inhibitors, angiotensin receptor antagonists, loop diuretics
Peripheral artery disease	Calcium antagonists

- **Condition**

Isolated systolic hypertension (elderly)	Duretics, calcium antagonists
Metabolic syndrome	ACE inhibitors, angiotensin receptor antagonists, calcium antagonists
Diabetes mellitus	ACE inhibitors, angiotensin receptor antagonists
Pregnancy	calcium antagonists, methyldopa, β-blockers
Blacks	diuretics, calcium antagonists

BP-Lowering Treatment Trialists: Contributing Trials (N=29)

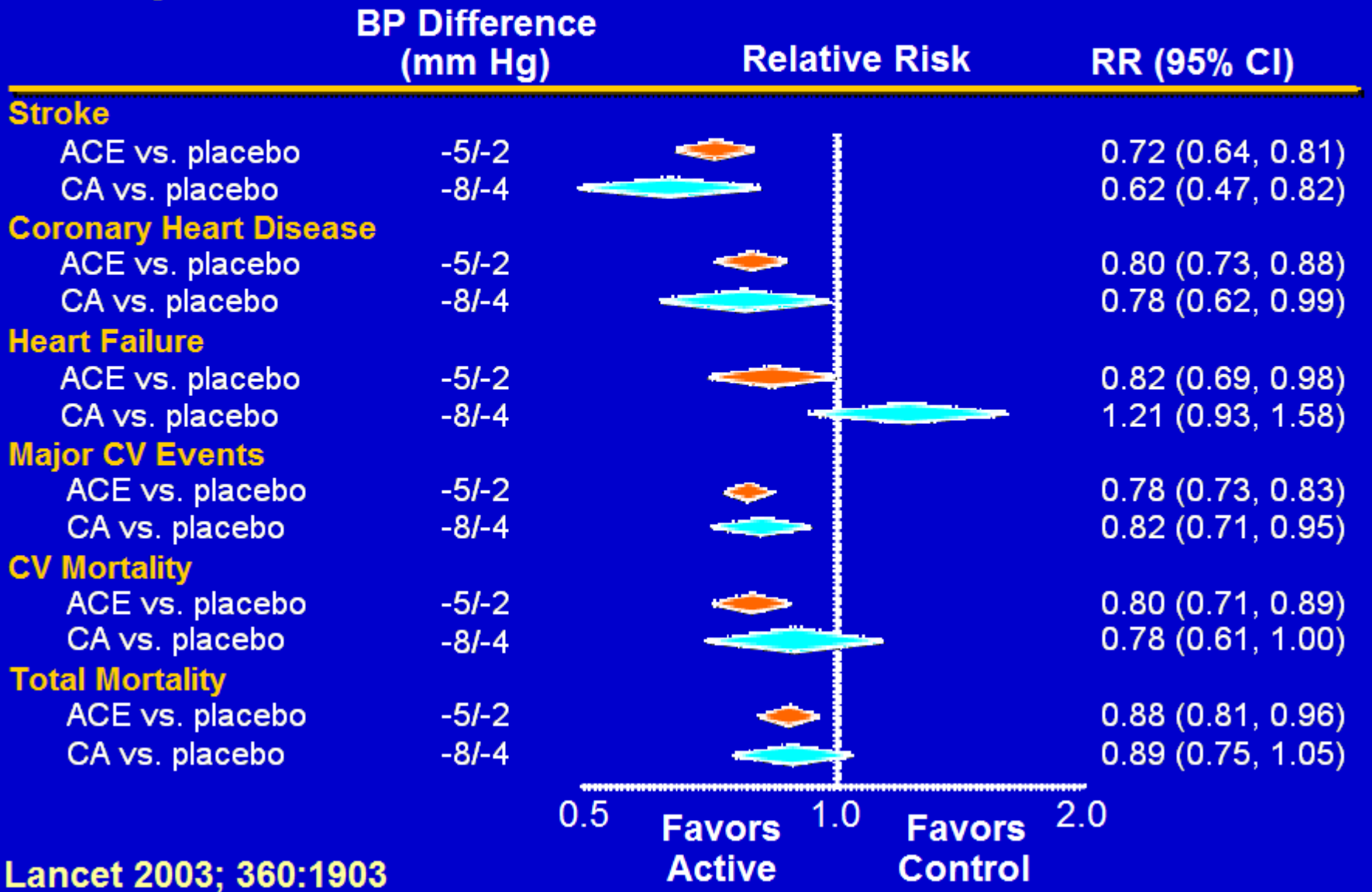
Second cycle (n=162,341)

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

Blood Pressure Lowering Treatment Trialists' Collaboration. *Lancet*. 2003;362:1527-1535.

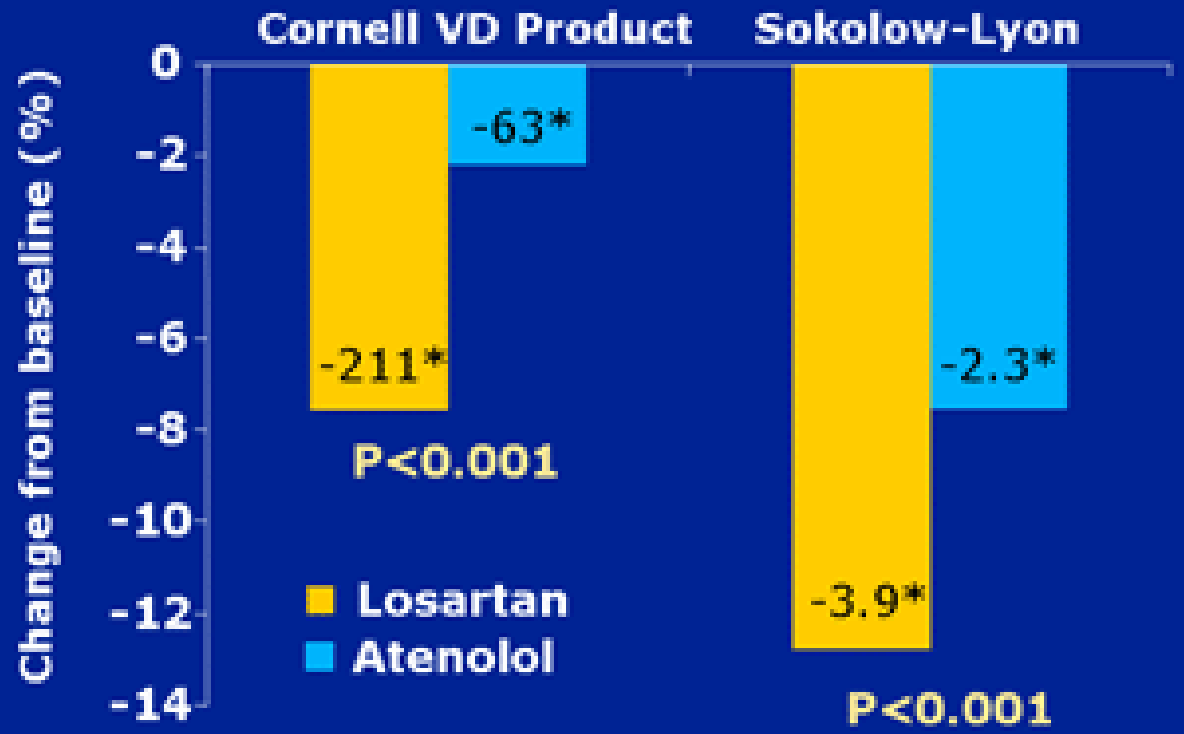
BP-Lowering Treatment Trialists

Comparisons of active treatments to PLACEBO



Lancet 2003; 360:1903

LIFE Study ISH Subgroup ECG-LVH Regression

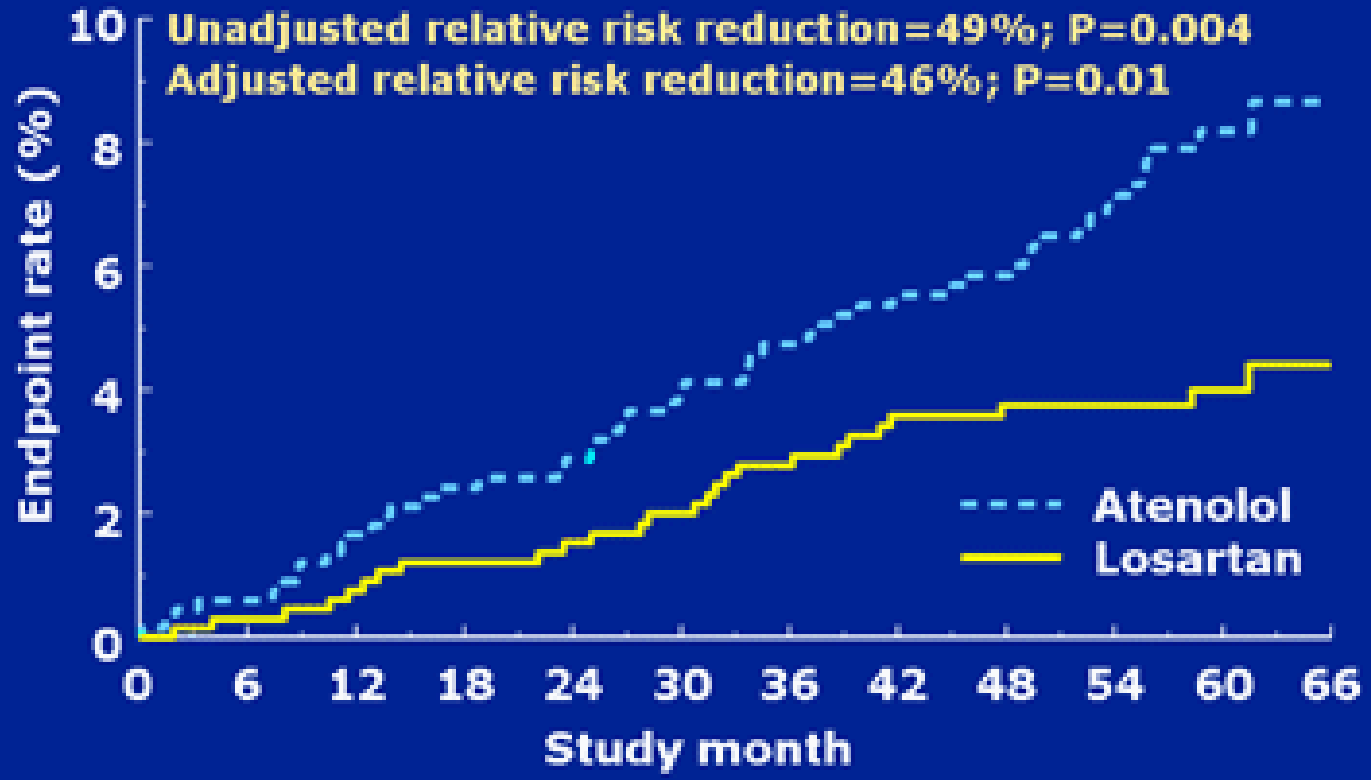


*absolute change from baseline

Kjeldsen SE, et al. JAMA. 2002;228:1491-1498.

www.hypertensiononline.org

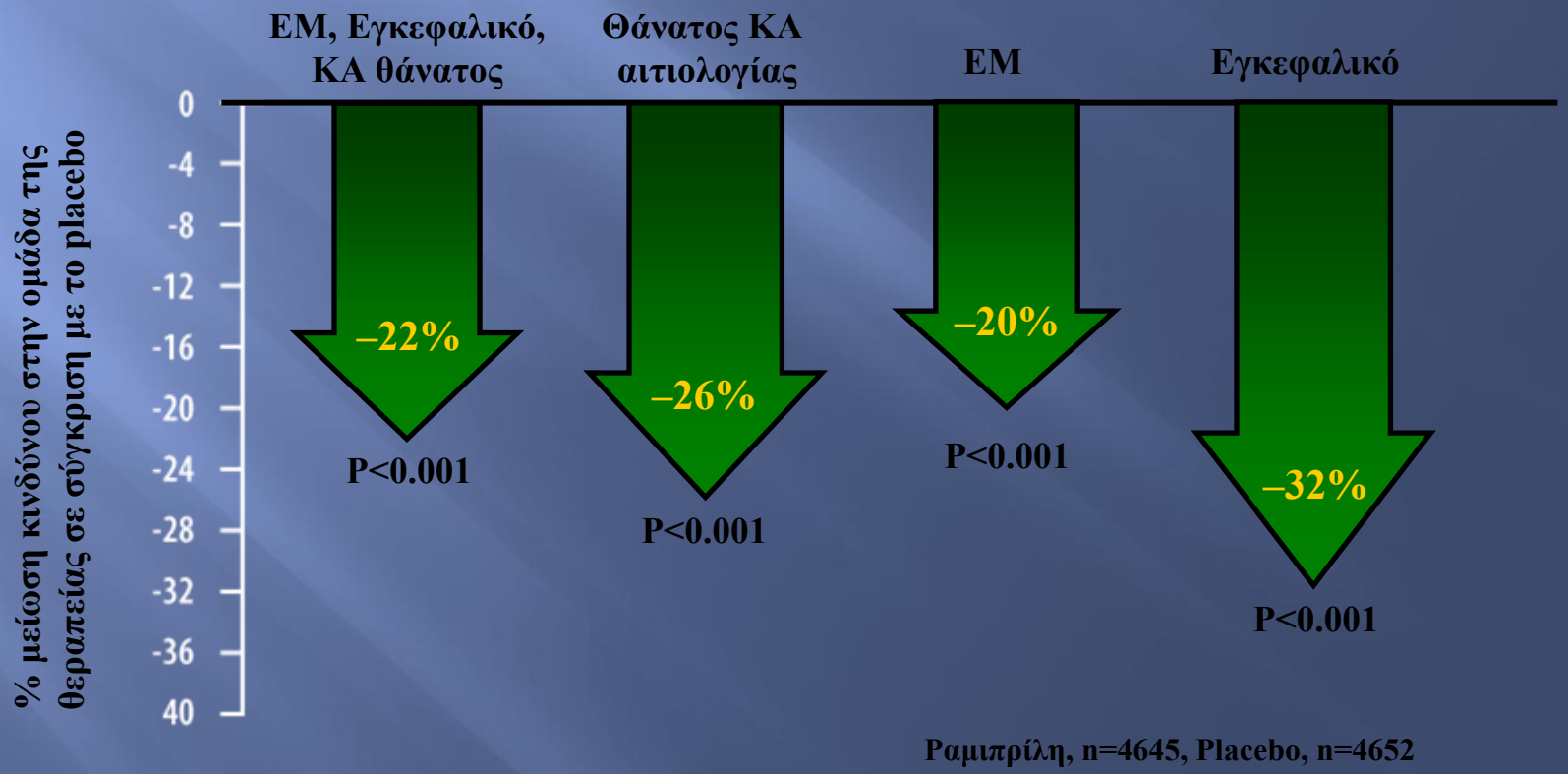
LIFE Study ISH Subgroup Cardiovascular Mortality



Kjeldsen SE, et al. JAMA. 2002;228:1491-1498.

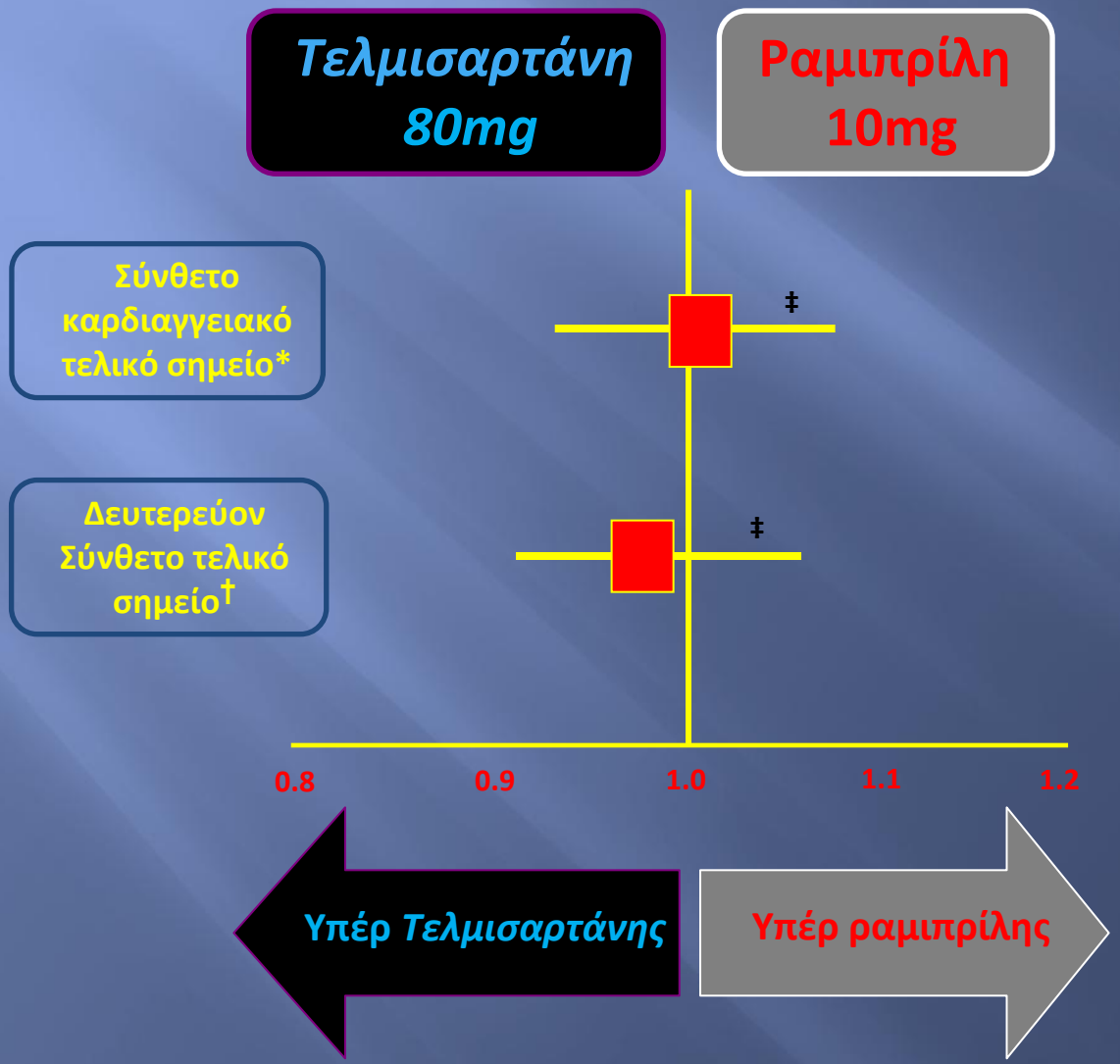
www.hypertensiononline.org

Αποτελεσματικότητα της ραμιπρίλης 10mg (n=4,645) έναντι placebo (n=4,652) στην πρόληψη μειζόνων καρδιαγγειακών επεισοδίων σε ασθενείς υψηλού κινδύνου με ή χωρίς υπέρταση



The HOPE Study Investigators. N Engl J Med 2000;342:145–153

Ισοδυναμία Αποτελεσματικότητας μεταξύ Τελμισαρτάνης 80mg και Ραμιπρίλης 10mg

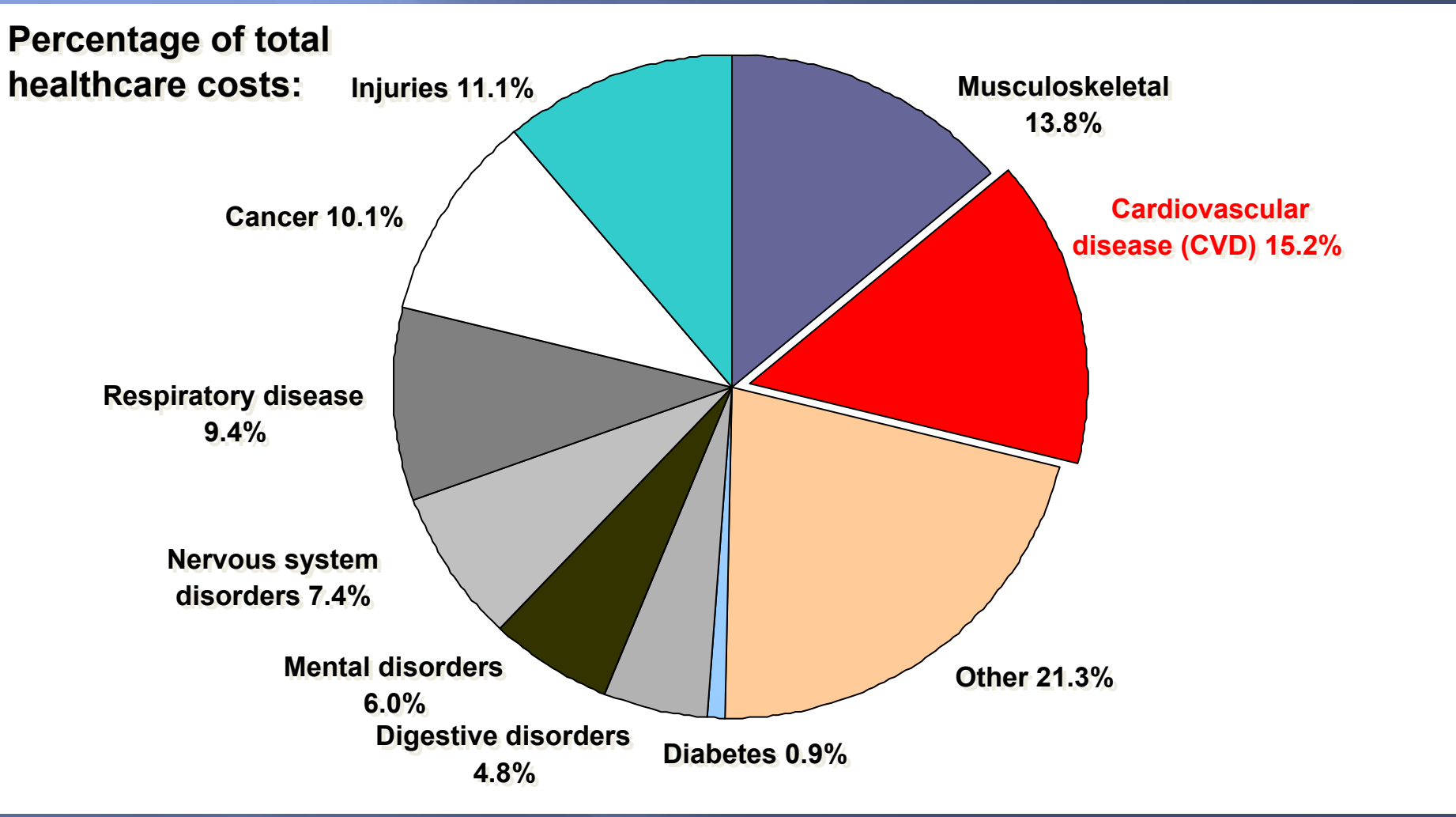


*** Σύνθετο Καρδιαγγειακό Τελικό Σημείο** = Καρδιαγγειακός θάνατος + μη θανατηφόρο έμφραγμα μυοκαρδίου + νοσηλεία για συμφορητική καρδιακή ανεπάρκεια + μη θανατηφόρο εγκεφαλικό

† Πρωτεύον τελικό σημείο μελέτης HOPE (Καρδιαγγειακός θάνατος + έμφραγμα μυοκαρδίου + εγκεφαλικό)

‡p< 0.01 vs. όριο μη-κατωτερότητας (1.13)

CVD has the highest economic impact of all diseases (15% of total healthcare costs)



Source: www.hc-sc.gc.ca/hpb/lcdc/publicat/burden/burd1_e.html