



TURIN, 20<sup>TH</sup>—21<sup>ST</sup> NOVEMBER 2008

# GREAT INNOVATIONS IN CARDIOLOGY

4<sup>TH</sup> JOINT MEETING WITH MAYO CLINIC

4<sup>TH</sup> TURIN CARDIOVASCULAR NURSING CONVENTION



**SESSION III: HOT SESSION**  
**NEW THERAPIES AND NEW TREATMENTS**

**G. Grassi (Milano)**

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**Part I** Cardiovascular high risk patient and blood pressure reduction: when and how to get it

## Stratification of CV Risk in Four Categories

### Blood Pressure (mmHg)

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 $\geq$ 180 or DBP $\geq$ 110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1-2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very high added risk
3 or more Risk Factors, MS, OD or Diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very high added risk
Established CV or renal disease	Very high added risk	Very high added risk	Very high added risk	Very high added risk	Very high added risk

SBP: systolic blood pressure; DBP: diastolic blood pressure; CV: cardiovascular; HT: hypertension. Low, moderate, high, very high risk refer to 10-year risk of a CV fatal or non-fatal event. The term "added" indicates that in all categories risk is greater than average. OD: subclinical organ damage; MS: metabolic syndrome.

# High / Very High Risk Patients

● BP  $\geq$  180/110 mmHg

● BP  $\geq$  130/ 85 mmHg if:

- Risk factors  $\geq$  3
- Diabetes
- Associated CVD
- TOD



LVH

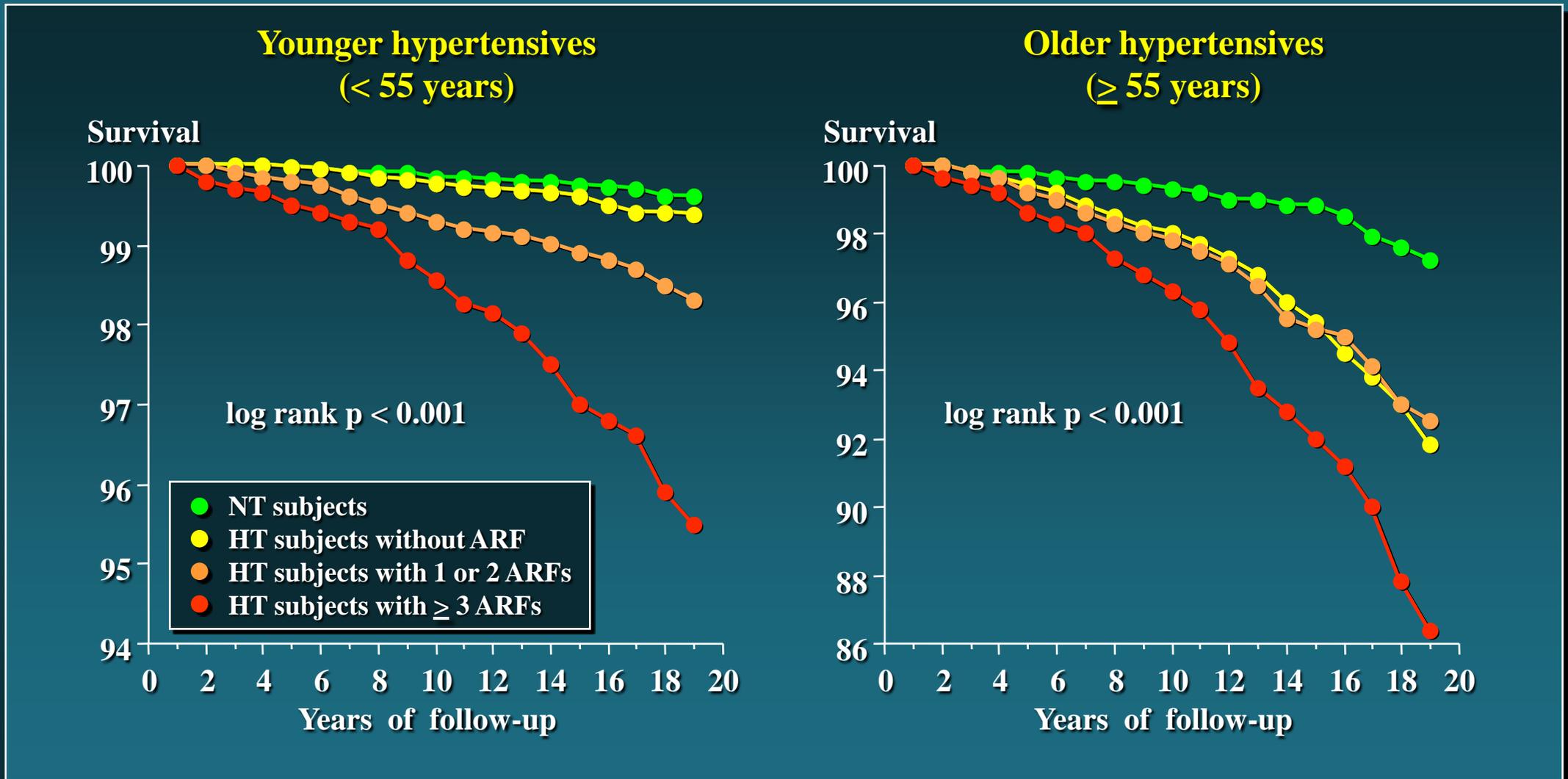
CA thickening

Microalbuminuria

Mild renal damage

→ SCr > 1.3-1.5 mg/dl (M) / 1.2-1.4 mg/dl (F)  
(routine examination)

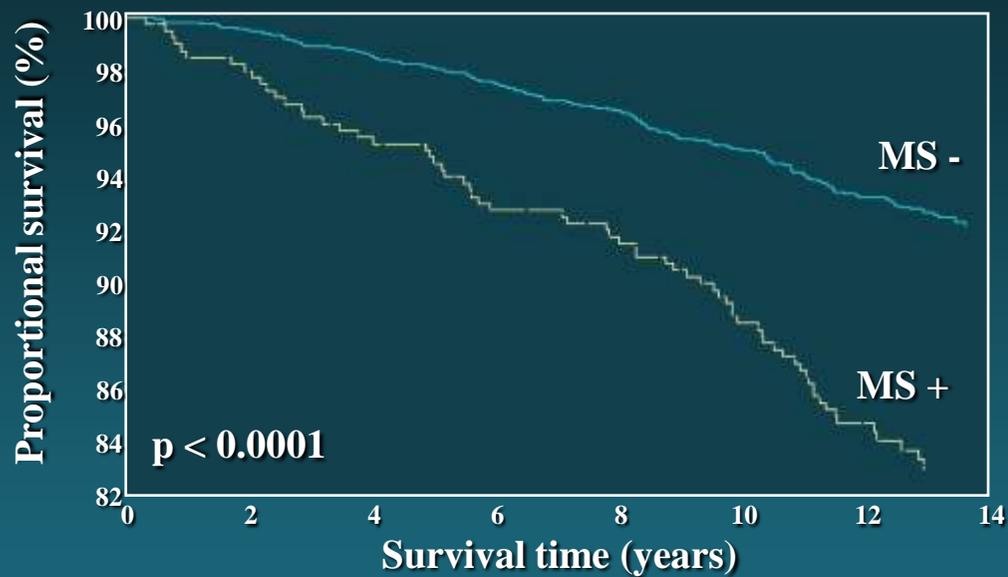
# Survival Probability for CVD Mortality in Younger and Older Men according to the Presence of Hypertension and Associated Risk Factors



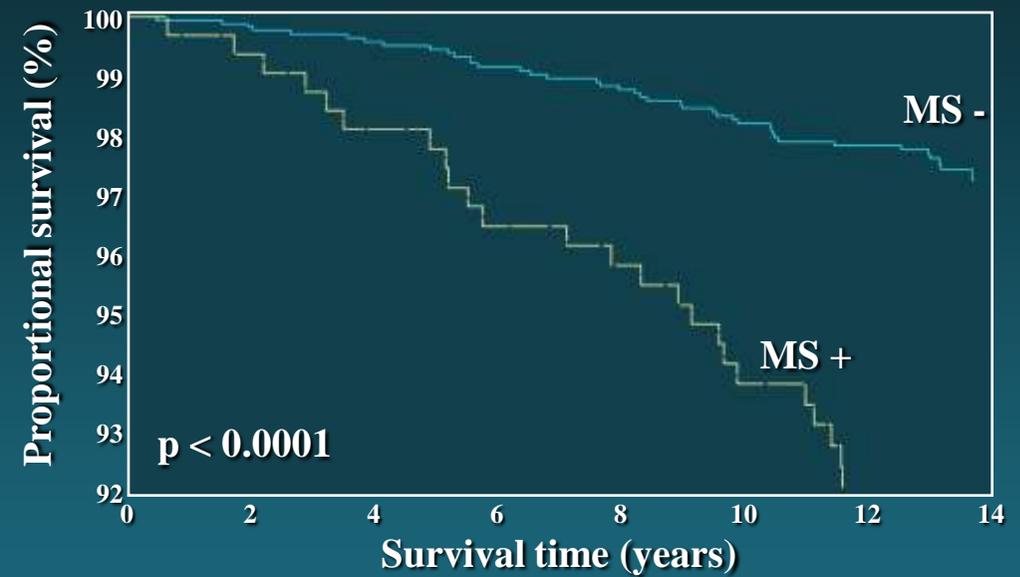
Thomas F et al., Hypertension 2001; 37: 1256-1261

# Kaplan-Meier Survival Curves for CV Death and All Cause Death in Subjects Without and With Metabolic Syndrome

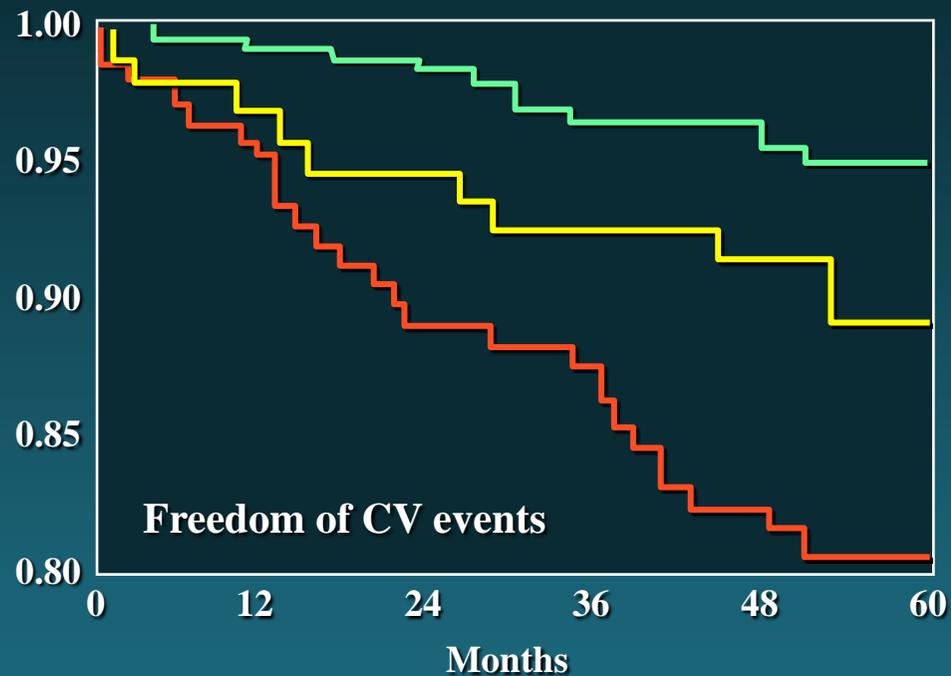
### All cause death



### Cardiovascular death

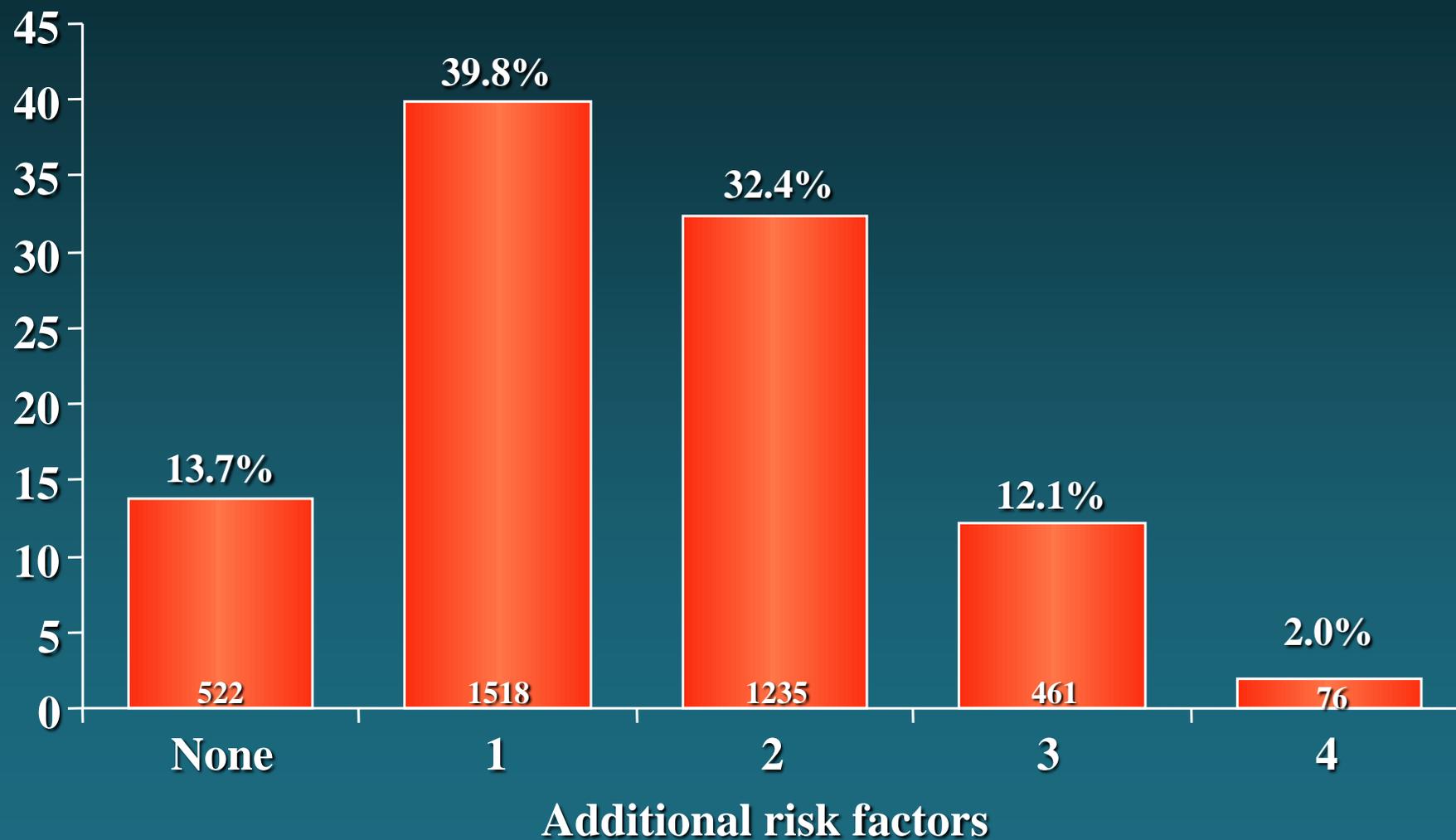


## LIFE Substudy: Kaplan-Meier Plots on Accumulated Freedom of CV events according to Urine Albumin/Creatinine Ratio (UACR) and LV Mass

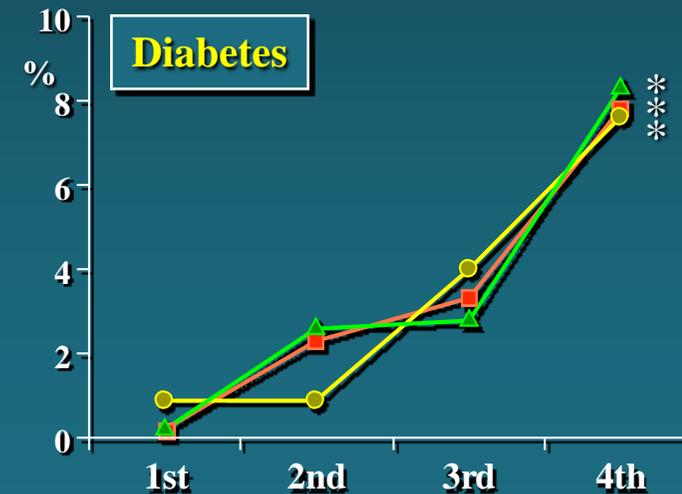
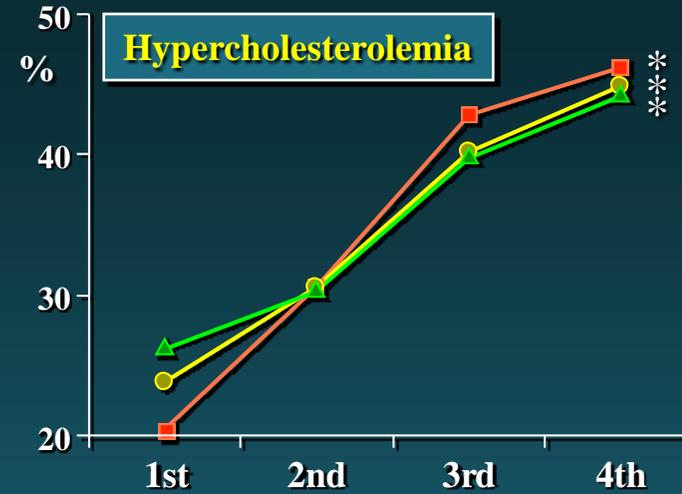
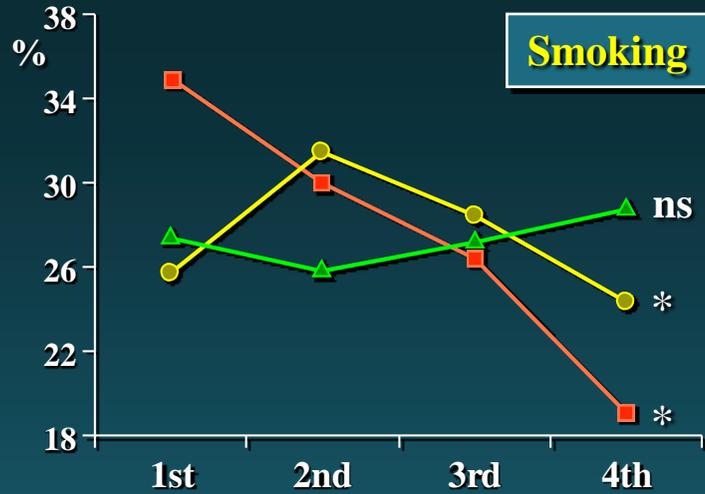


- UACR < 1.406, LV mass < 194
- UACR ≥ 1.406, LV mass < 194
- UACR ≥ 1.406, LV mass ≥ 264

## Percentage of hypertensive patients



# Relationship of Smoking Habit, Hypercholesterolemia, IFG and Diabetes to Office, Home, 24h SBP Quartiles



—■— Office SBP  
—●— Home SBP  
—▲— 24h SBP

\* P < 0.05 for trend

# Assessment of Total (Global) CV Risk

JNC 7

→ No

European Task Force

2003 ESH / ESC

WHO / ISH

2007 ESH / ESC

→ Yes

Continuous /  
Colorimetric scales

Discontinuous risk categories

# ESH/ESC Guidelines and Search for Subclinical Organ Damage

2003  
GLs

↑ SCr (> 1.4-1.5 mg/dl)

LVH (EKG/Echo)  
CA thickening / plaques  
MA

Routine

Recommended

Mentioned

2007  
GLs

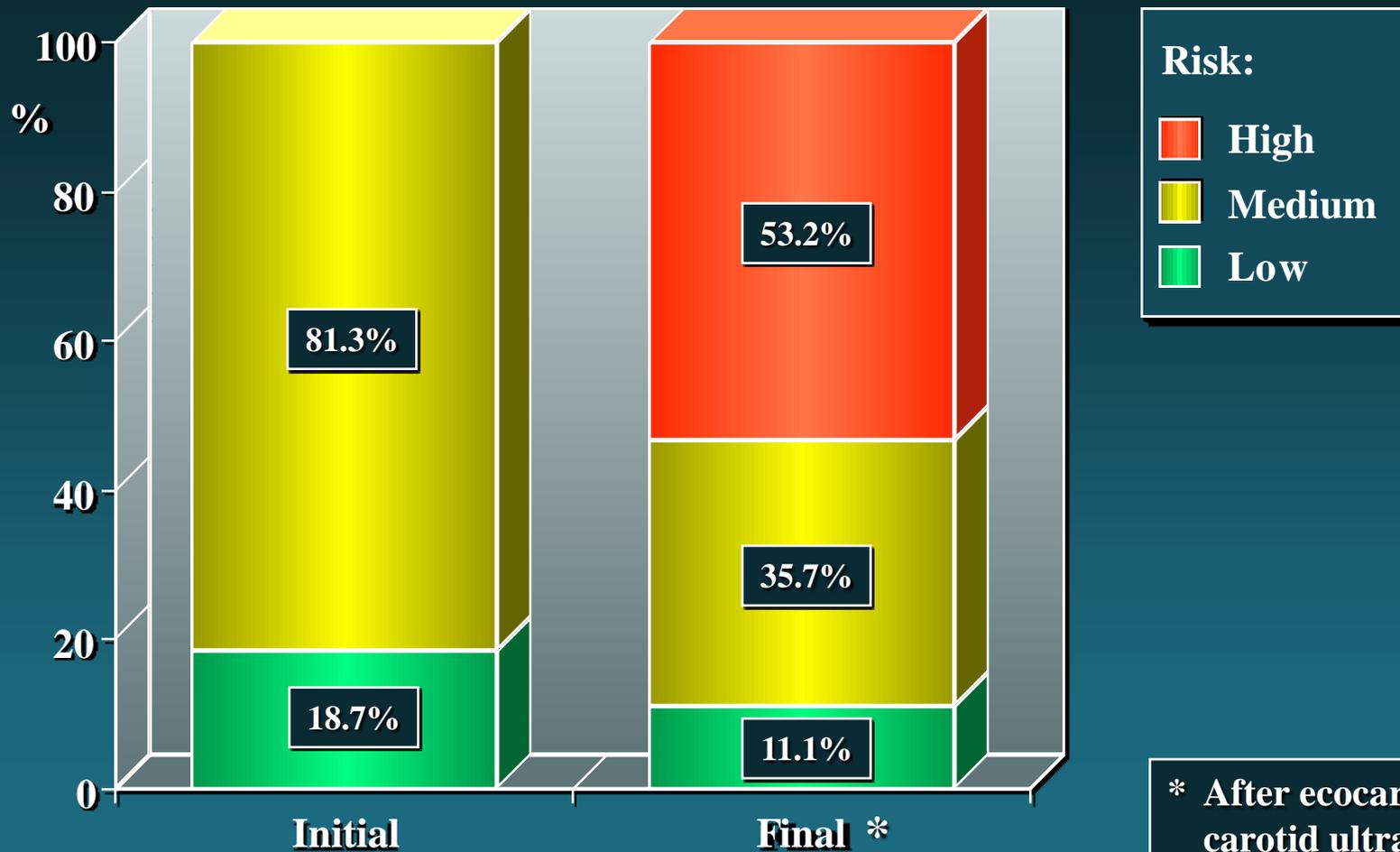
↑ SCr (> 1.4-1.5 mg/dl)  
↓ eCrCl / GFR  
MA

LVH (EKG/Echo)  
Concentric LVH  
LA enlargement  
CA thickening / plaques  
Ankle/Brachial ratio  
Arterial stiffening (PWV)\*

Systolic dysfunction  
Diastolic dysfunction  
Coronary Ca<sup>++</sup>  
Arteriolar remodelling  
Collagen markers  
Endothelial dysfunction  
Cerebral lacunae / WMLs  
Cognitive dysfunction  
Retinopathy

\* Depending on availability / also shown by high SBP / low DBP

# Risk Reclassification in APROS Study



## Treatment of Hypertensives at High / Very High Risk

- Intensive life-style changes (use of specific professionals)
  - Drug treatment in the high-normal BP range
  - Target BP < 130/80 mmHg
  - BP control without delay
  - Antiplatelet / lipid lowering treatment
  - **Drugs more effective on regression of organ damage to be included**
- Combination treatment as first step

## Stratification of CV Risk in Four Categories

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# BP Threshold / Target in the General Hypertensive Population



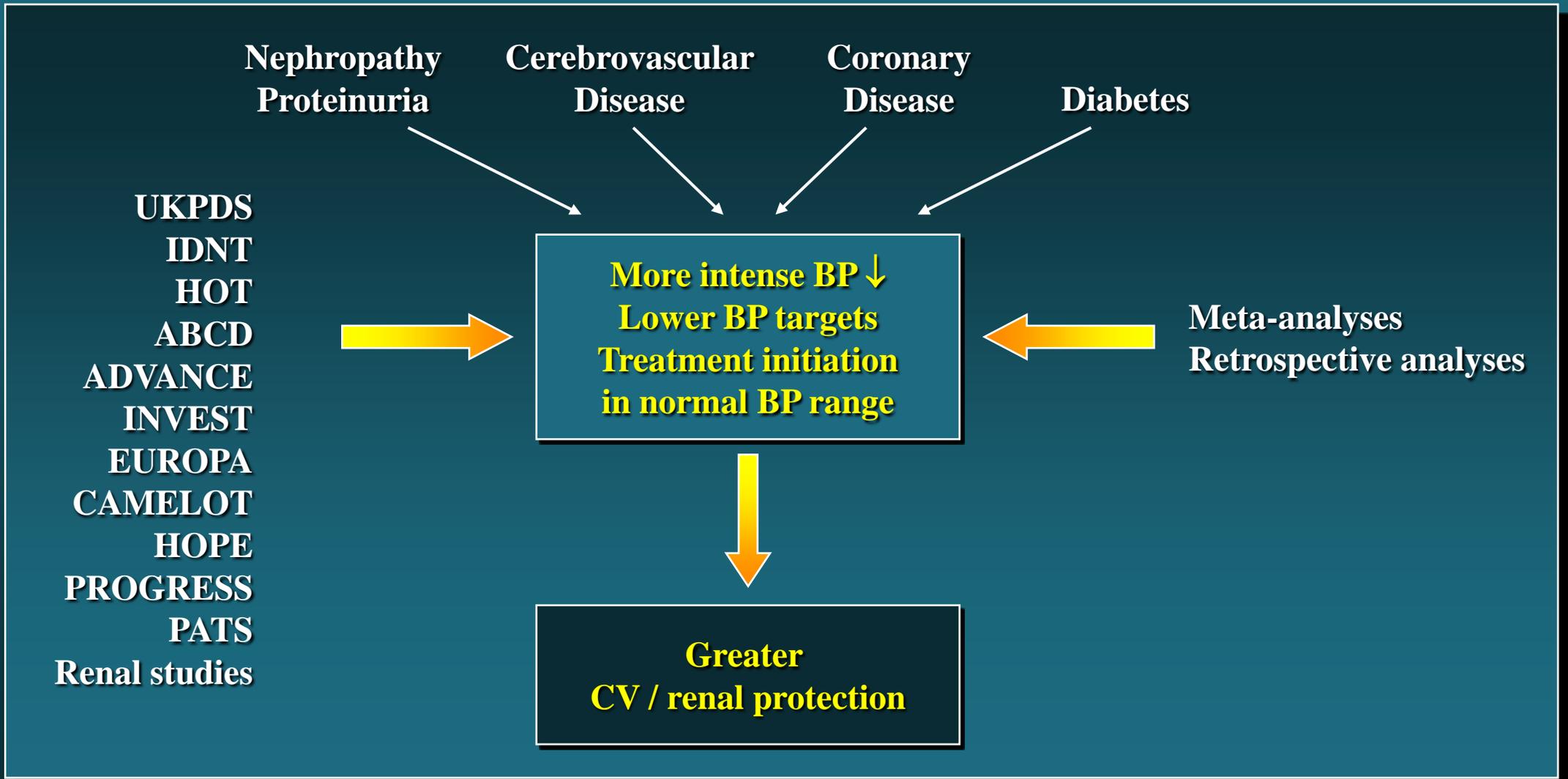
**BP threshold**

**$\geq 140/90$  mmHg**

**BP target**

**$< 140/90$  mmHg  
(and lower values  
if tolerated)**

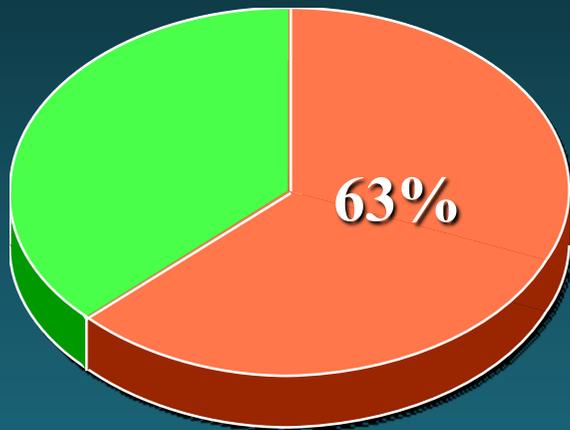
# Beneficial Effects of Tighter BP Control



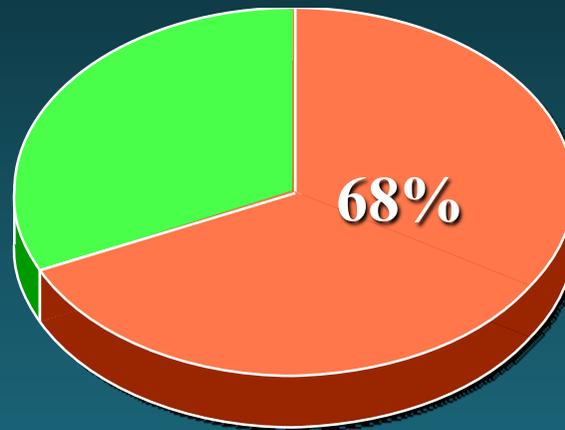
# HOT Study: % of Patients on Combination Reaching Target

## DBP target

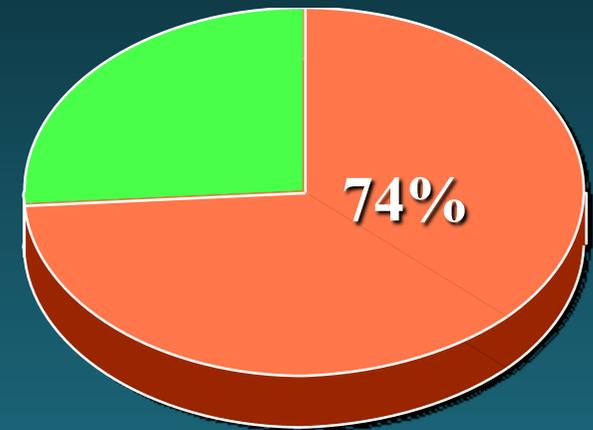
≤ 90 mmHg



≤ 85 mmHg

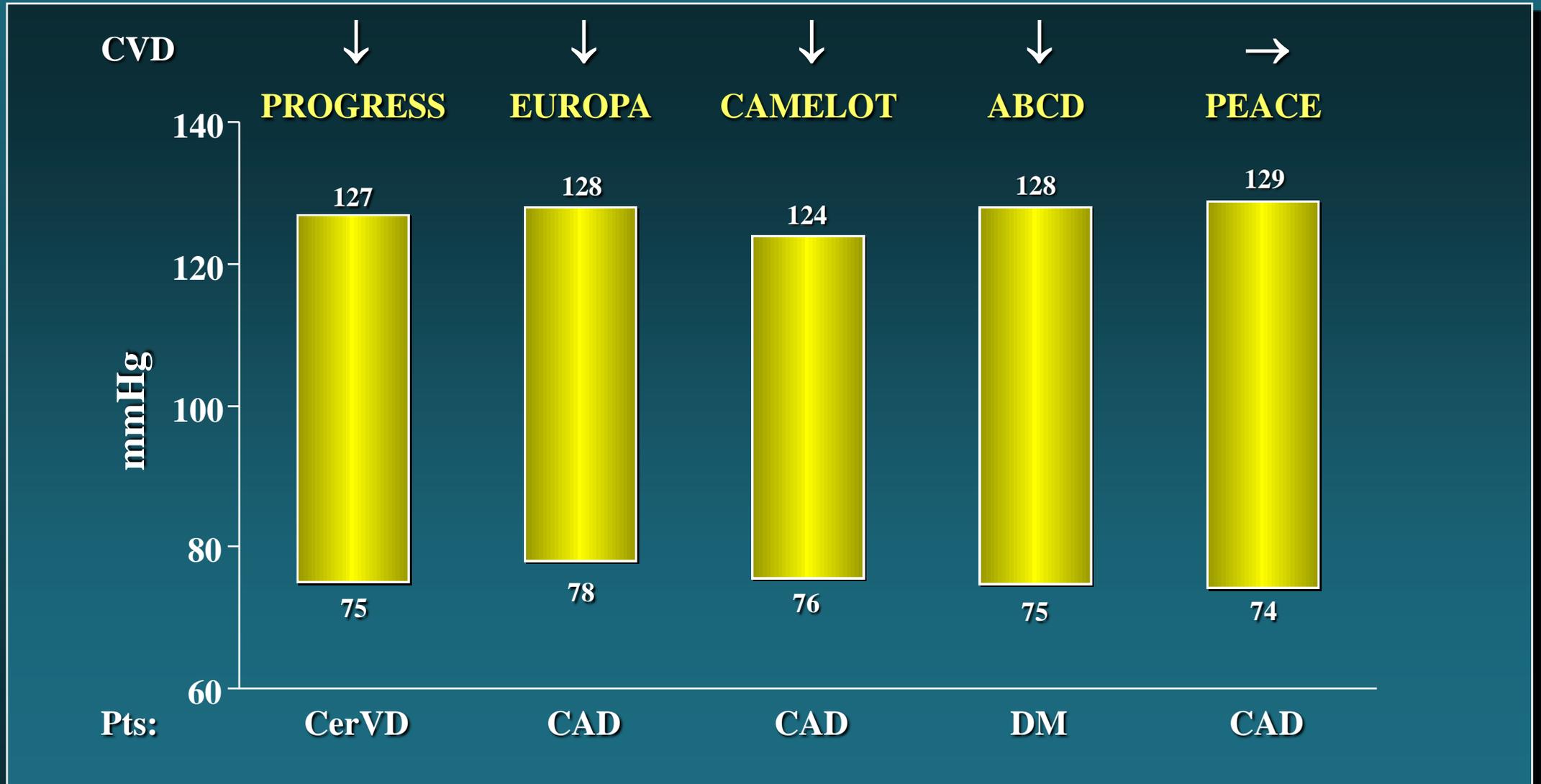


≤ 80 mmHg



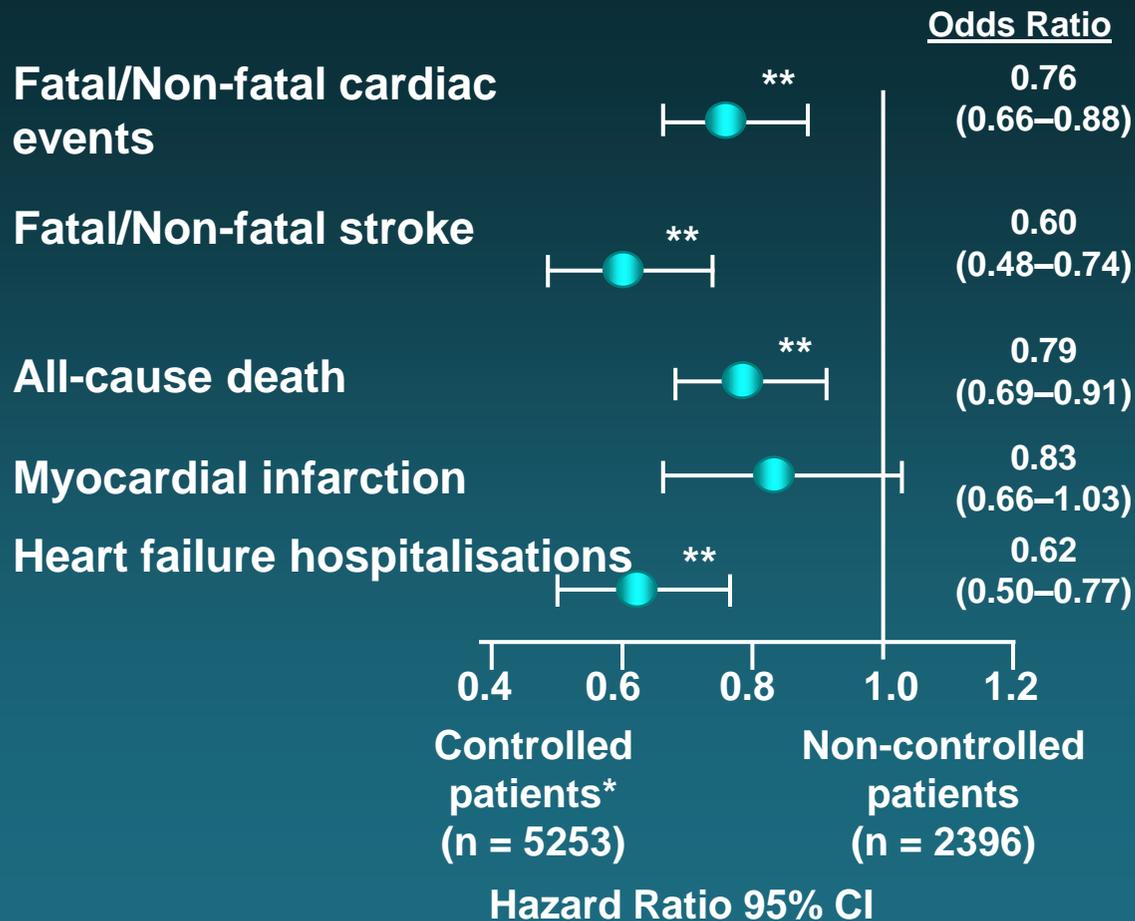
Combination therapy Monotherapy

# On-treatment BP in Recent Trials

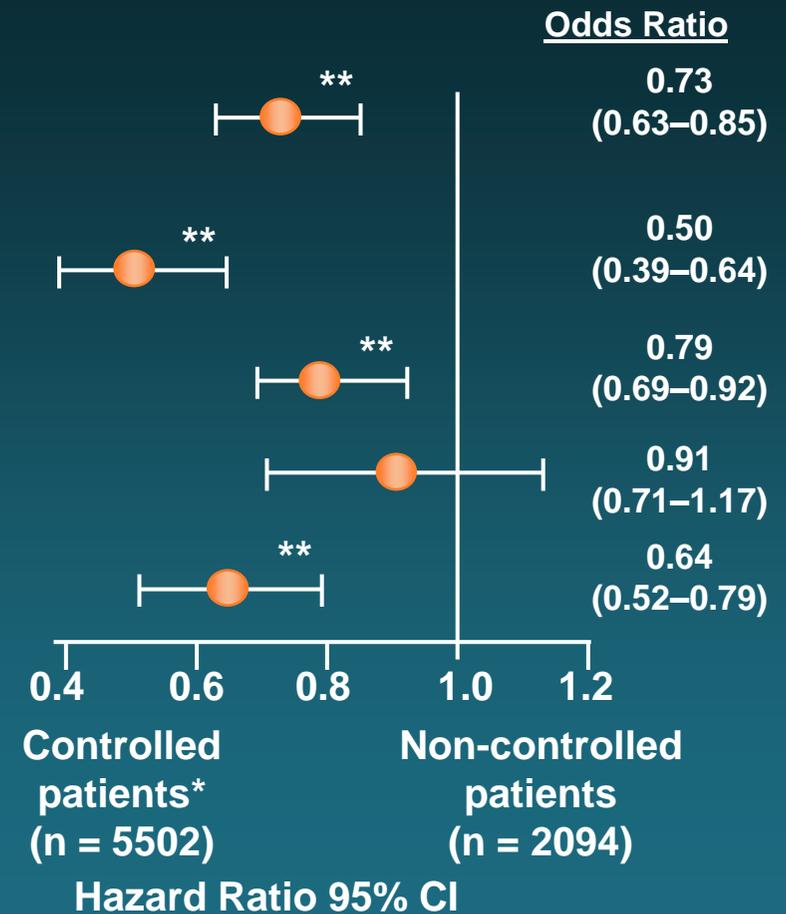


# VALUE: Analysis of Results Based on BP Control at 6 Months

## Patients Treated With Valsartan



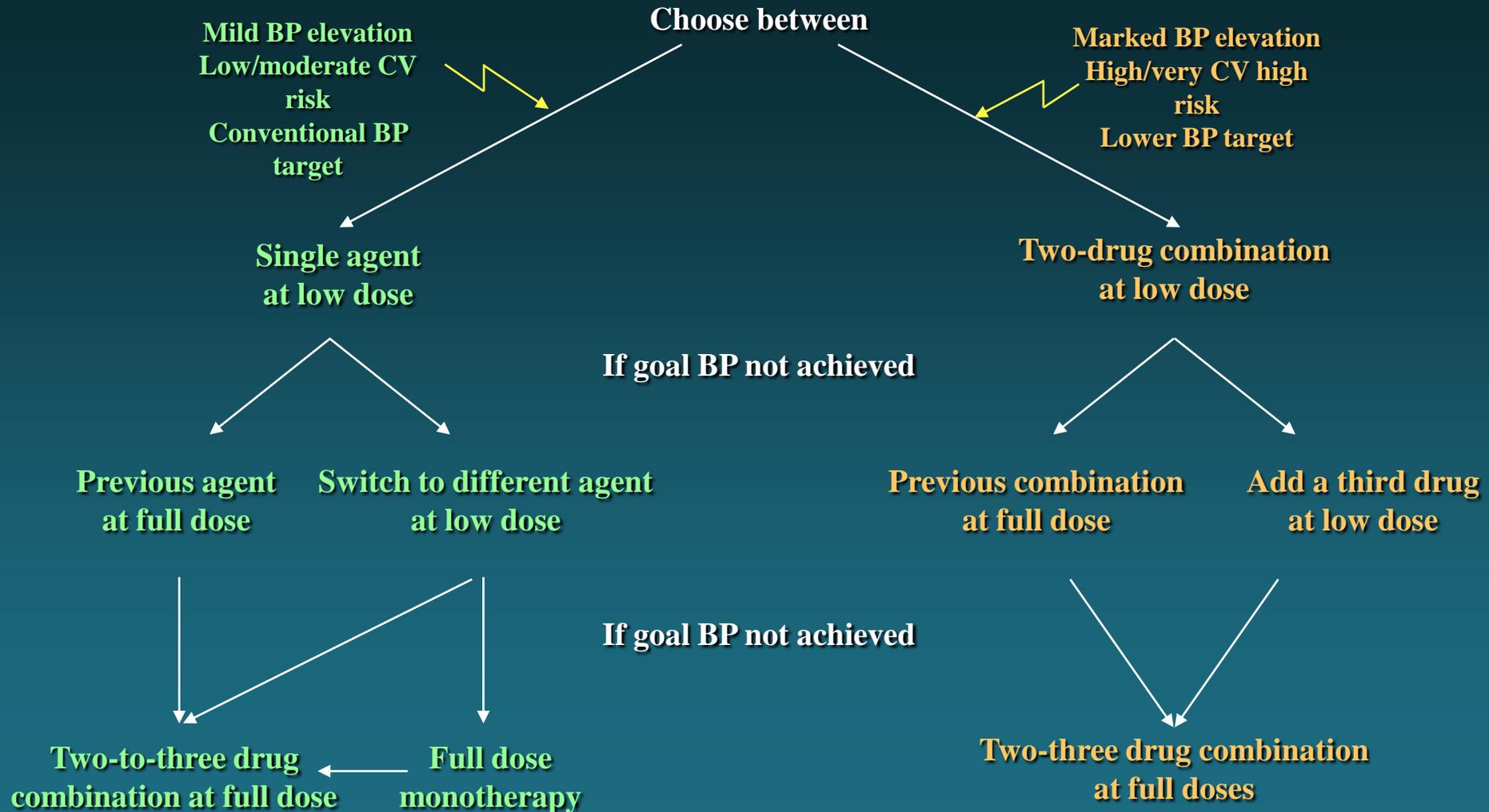
## Patients Treated With Amlodipine



\*SBP < 140 mmHg at 6 months.      \*\* $P < 0.01$ .

2007 ESH/ESC Guidelines

# Monotherapy versus Combination Therapy Strategies



## RR of CVD with Low-Dose Aspirin (vs Placebo) in HOT

On-treatment BP (mmHg) ~ 140/83

Medium risk 1.00

High / very high risk 0.78 \*

\* statistically significant

## On-Treatment BP and $\Delta$ Events with Atorvastatin (vs Placebo) in ASCOT \*

- All patients with  $\geq 3$  risk factors
- BP (mmHg) ~ 138/80
- Stroke -27%
- CHD -29%
- CVD -21%
- Total mortality -13%

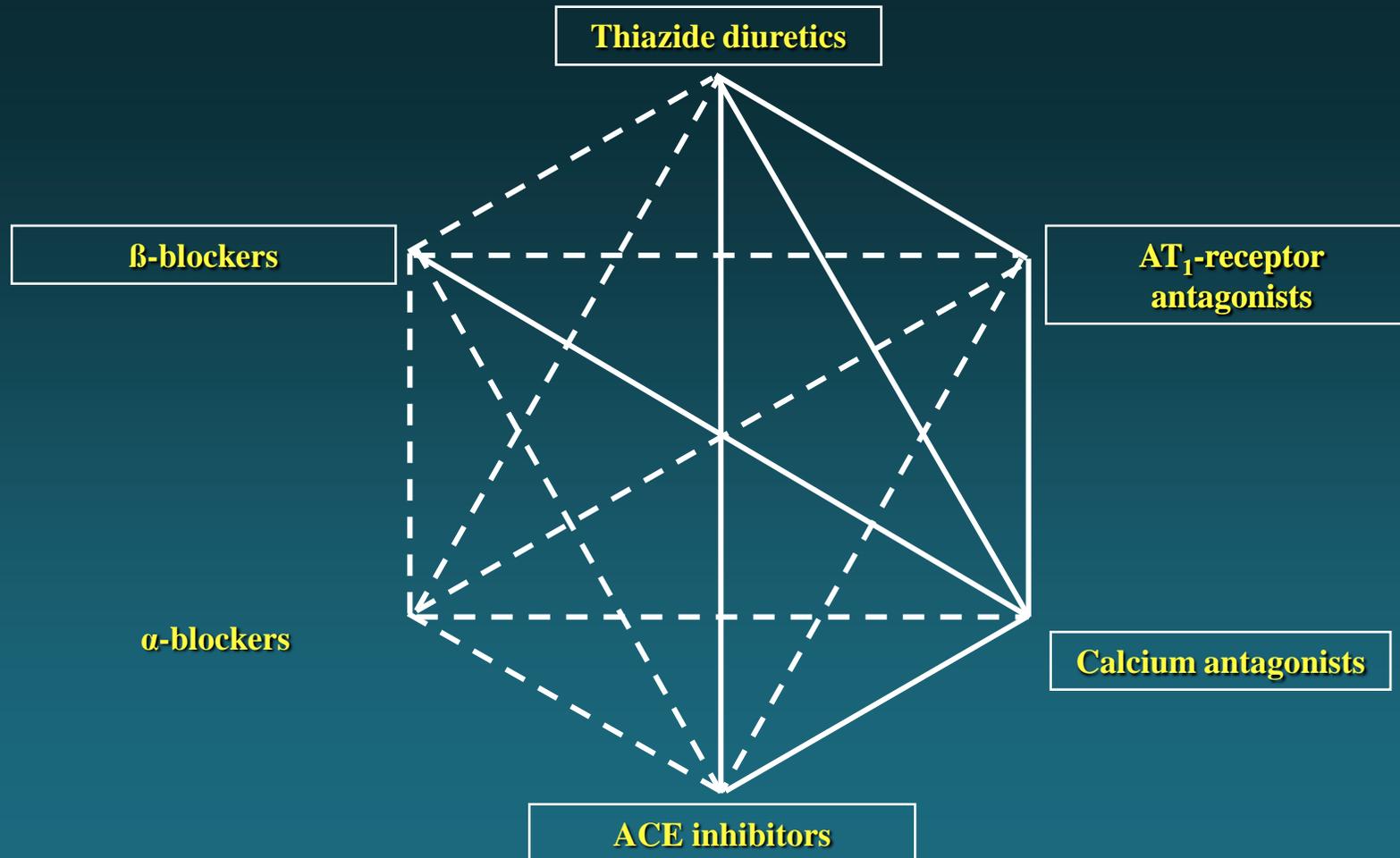
\* All changes statistically significant

## Importance of Identification of Patients at High / Very High CV Risk

1. Drug treatment to be promptly instituted
2. Combination treatment usually necessary
3. Specific antihypertensive agents may be needed
4. Lower BP threshold (<130/85 mmHg) and targets (<130/80 mmHg) for treatment
5. Use of aspirin and statins

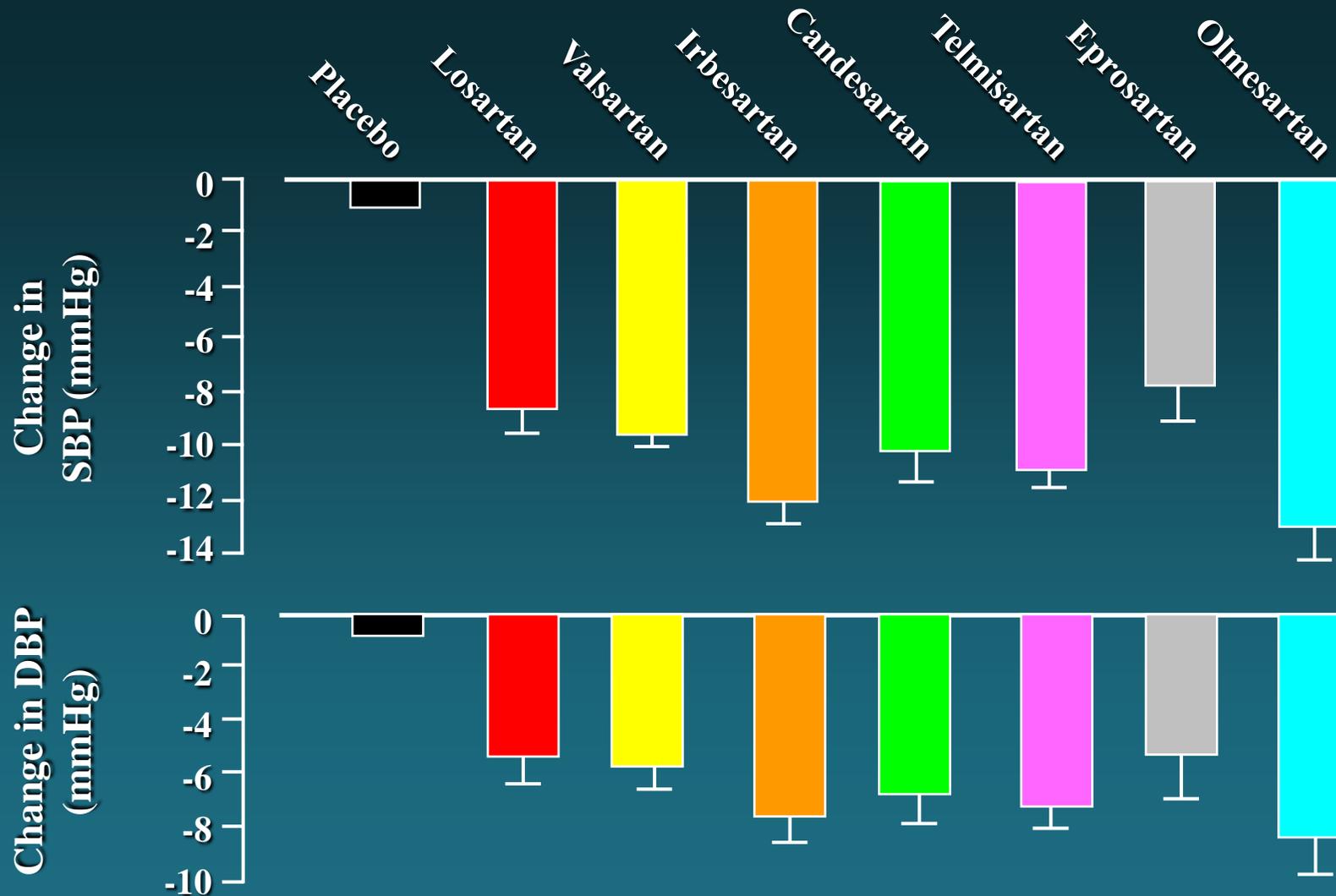
## 2007 ESH/ESC Guidelines

# Combinations between Some Classes of Antihypertensive Drugs



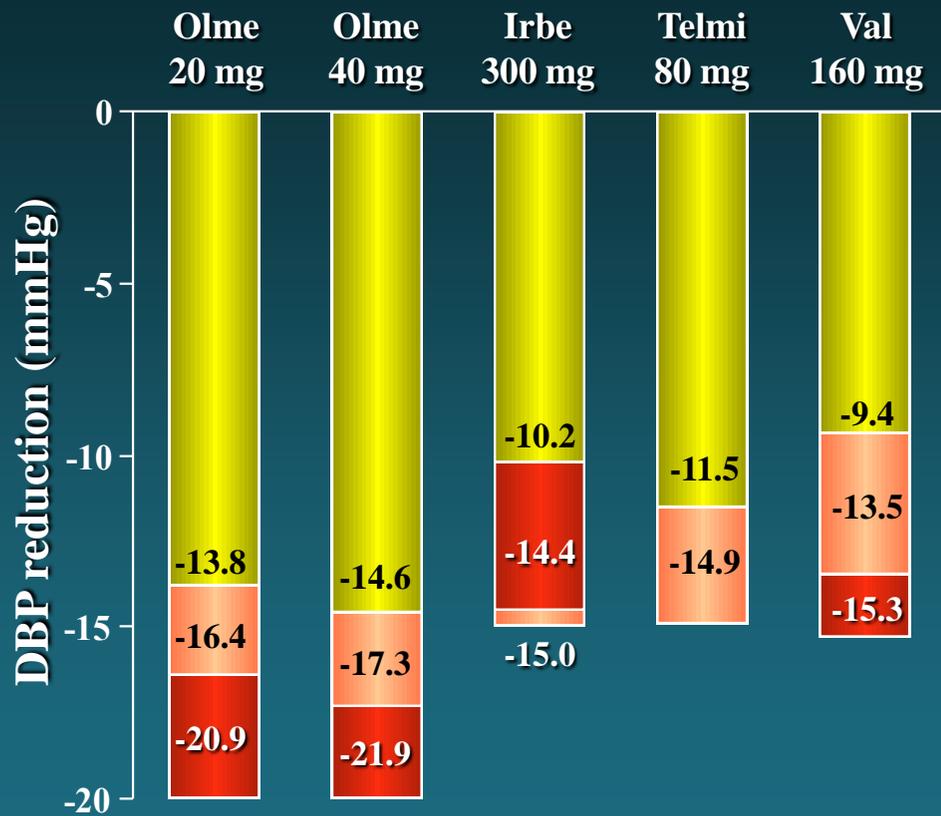
The preferred combinations in the general hypertensive population are represented as thick lines.  
The frames indicate classes of agents proven to be beneficial in controlled intervention trials.

# Systematic Review of the Antihypertensive Activity of ARBs: BP Reduction over 24 hours

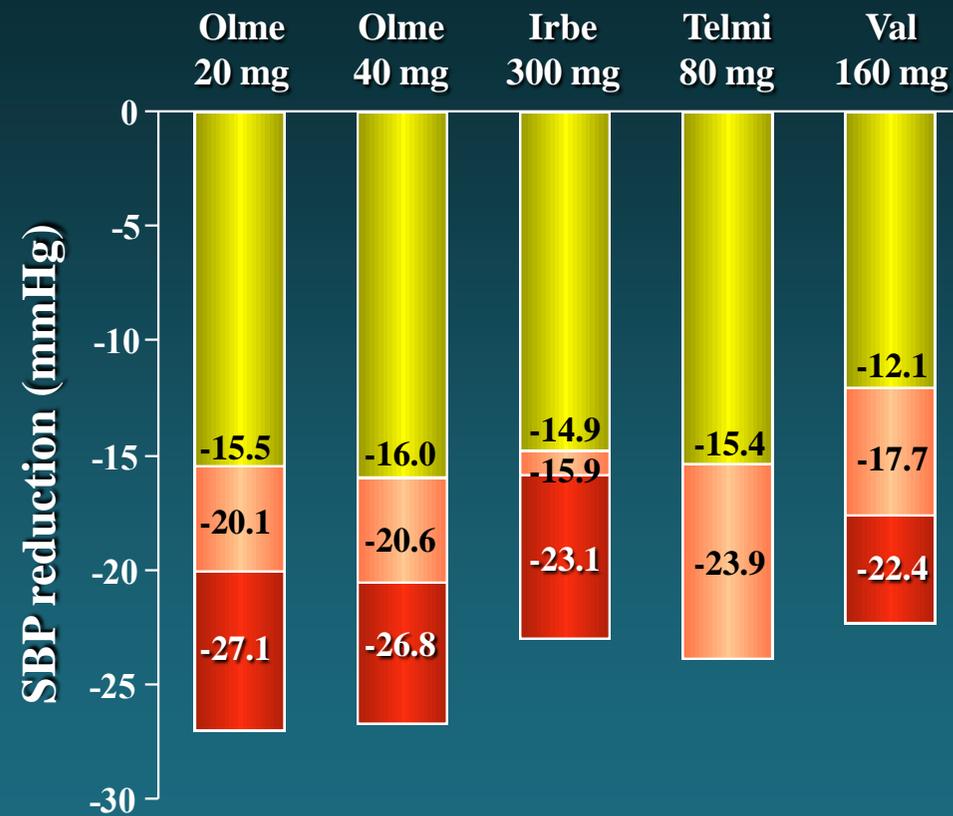


# Combination Treatment with ARB: Unique Position of Olmesartan

## Absolute DBP reductions



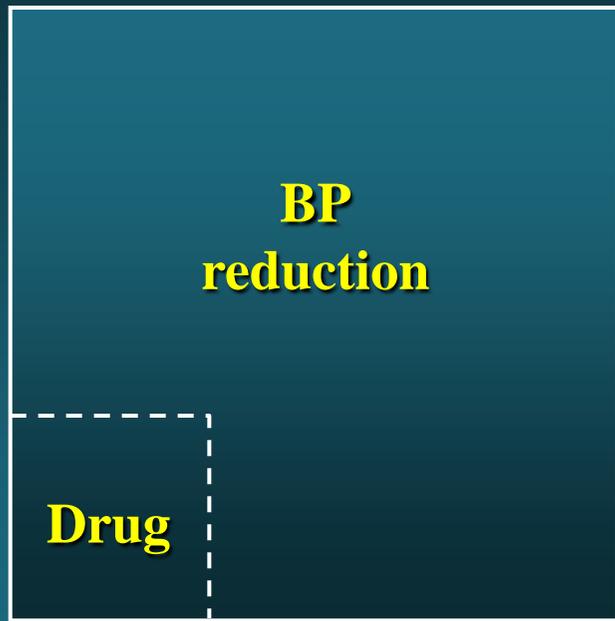
## Absolute SBP reductions



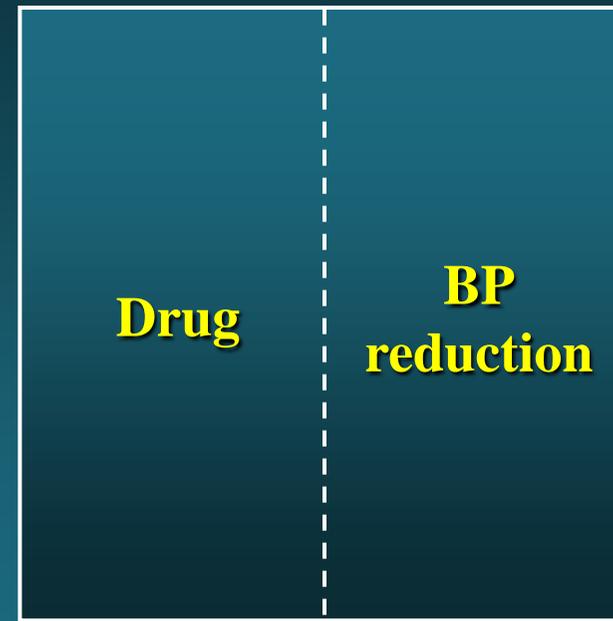
■ Monotherapy   
 ■ + HCTZ 12.5 mg   
 ■ + HCTZ 25 mg

# Role of Drugs' Specific Properties vs BP Reduction *per se* in CV Protection of Hypertensive Patients

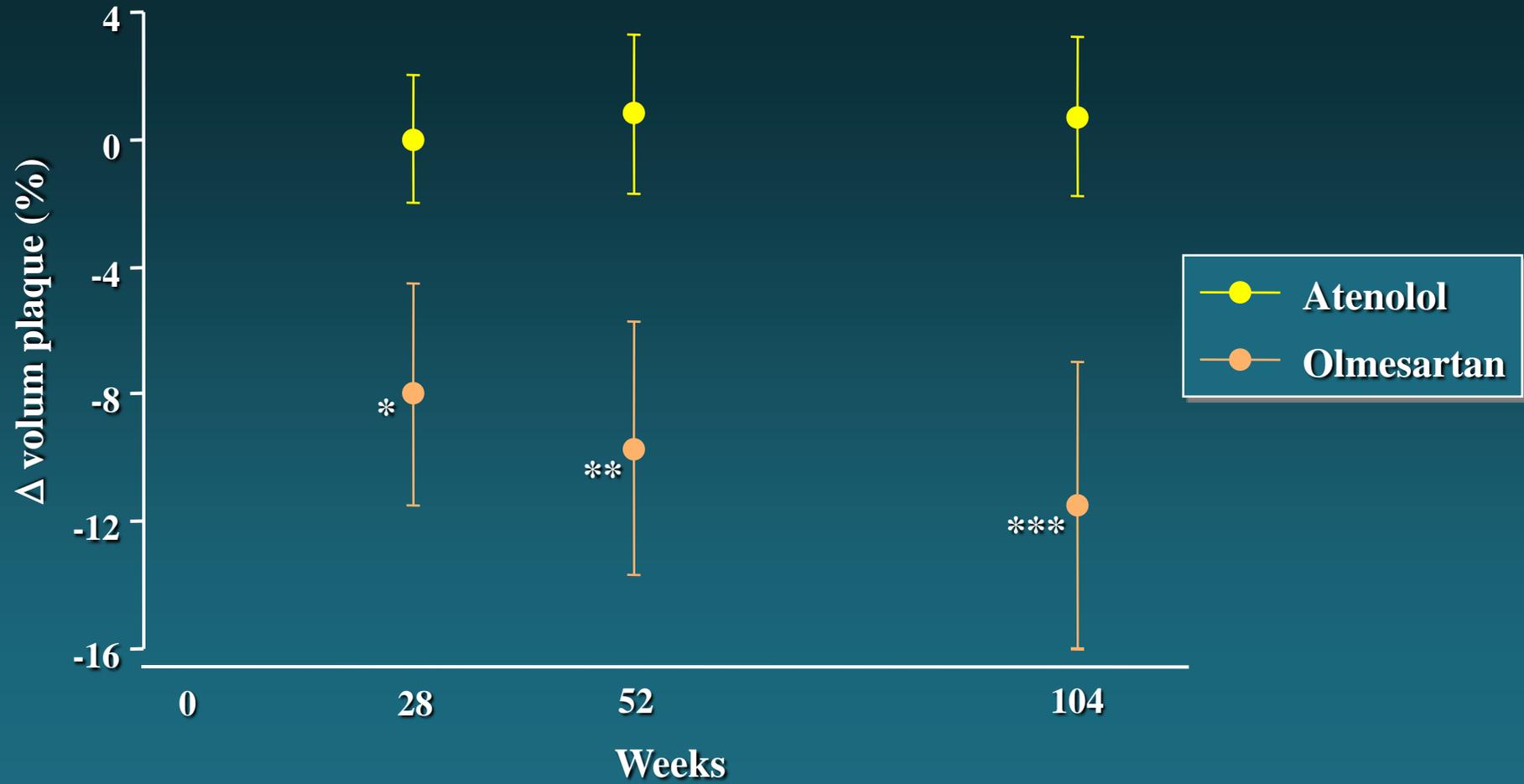
Short Term  
Protection



Long Term  
Protection



# Vascular Protection by Olmesartan vs. Atenolol: The MORE Study



# Average Changes in Wall-to-lumen Ratio in Normotensive Controls and in Stage 1 Hypertension Patients Before and After 1 Year of Treatment with Olmesartan or Atenolol

