Terapia antiipertensiva aggressiva: quando e perchè

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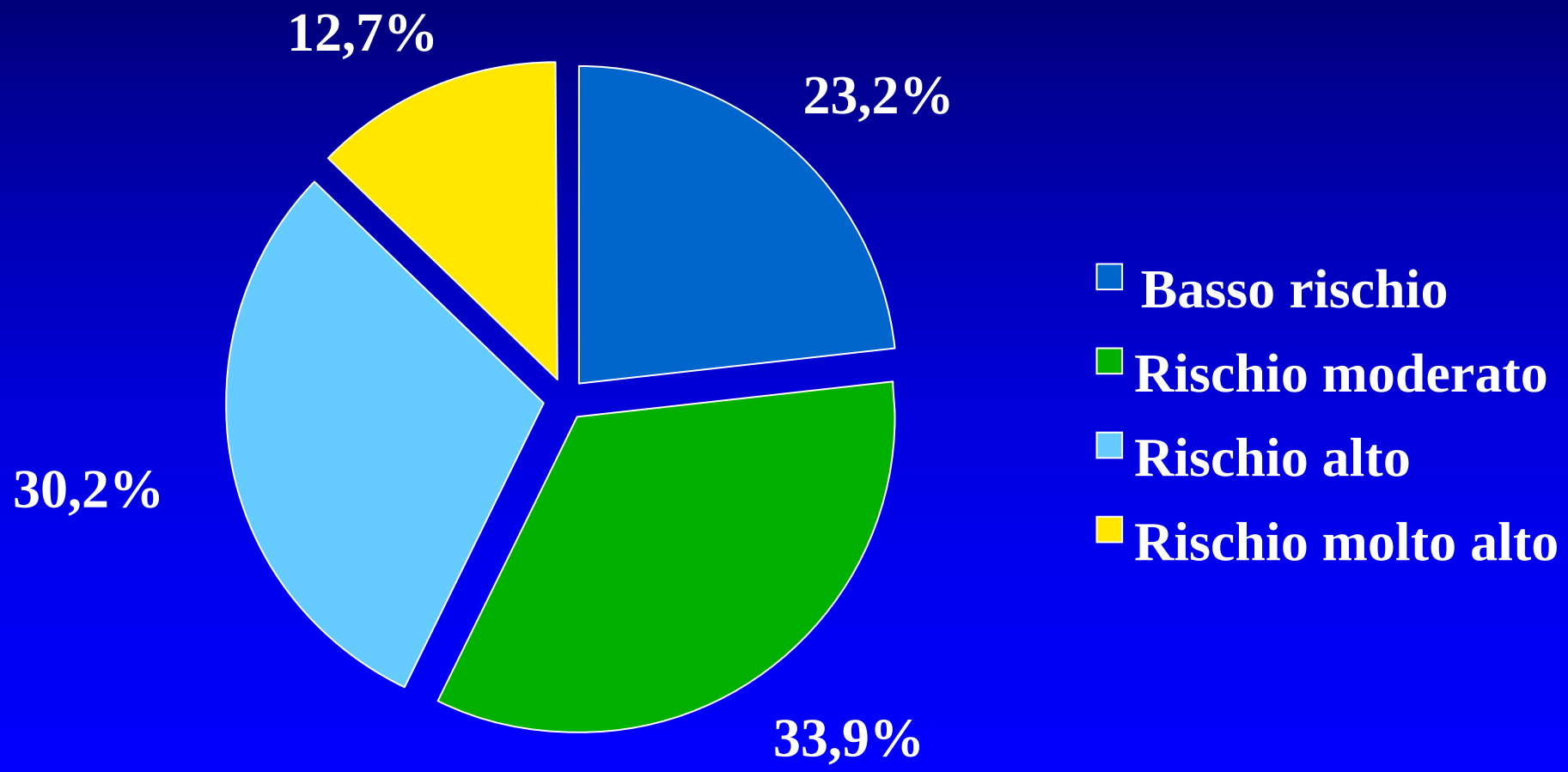
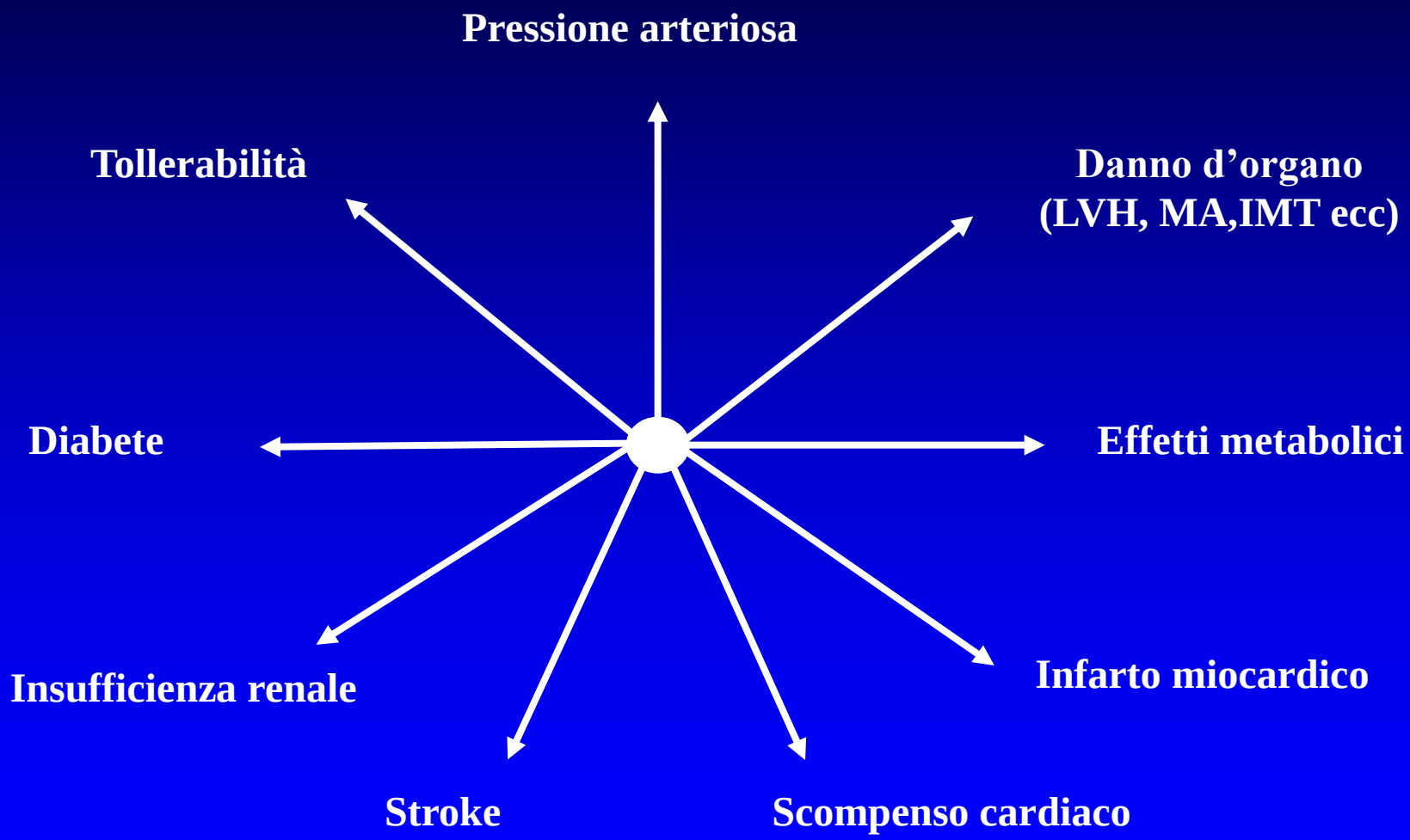
Stratificazione del rischio cardiovascolare globale in accordo con le linee guida ESH/ESC 2013 in pazienti italiani ipertesi inclusi in una survey clinica



A cosa bisogna prestare attenzione nella gestione del paziente iperteso?



Volpe M, 2004

1. **Più bassi sono gli obiettivi di pressione arteriosa, migliore è l'*outcome* del paziente: la differenza di pochi mmHg può impattare sugli eventi clinici**

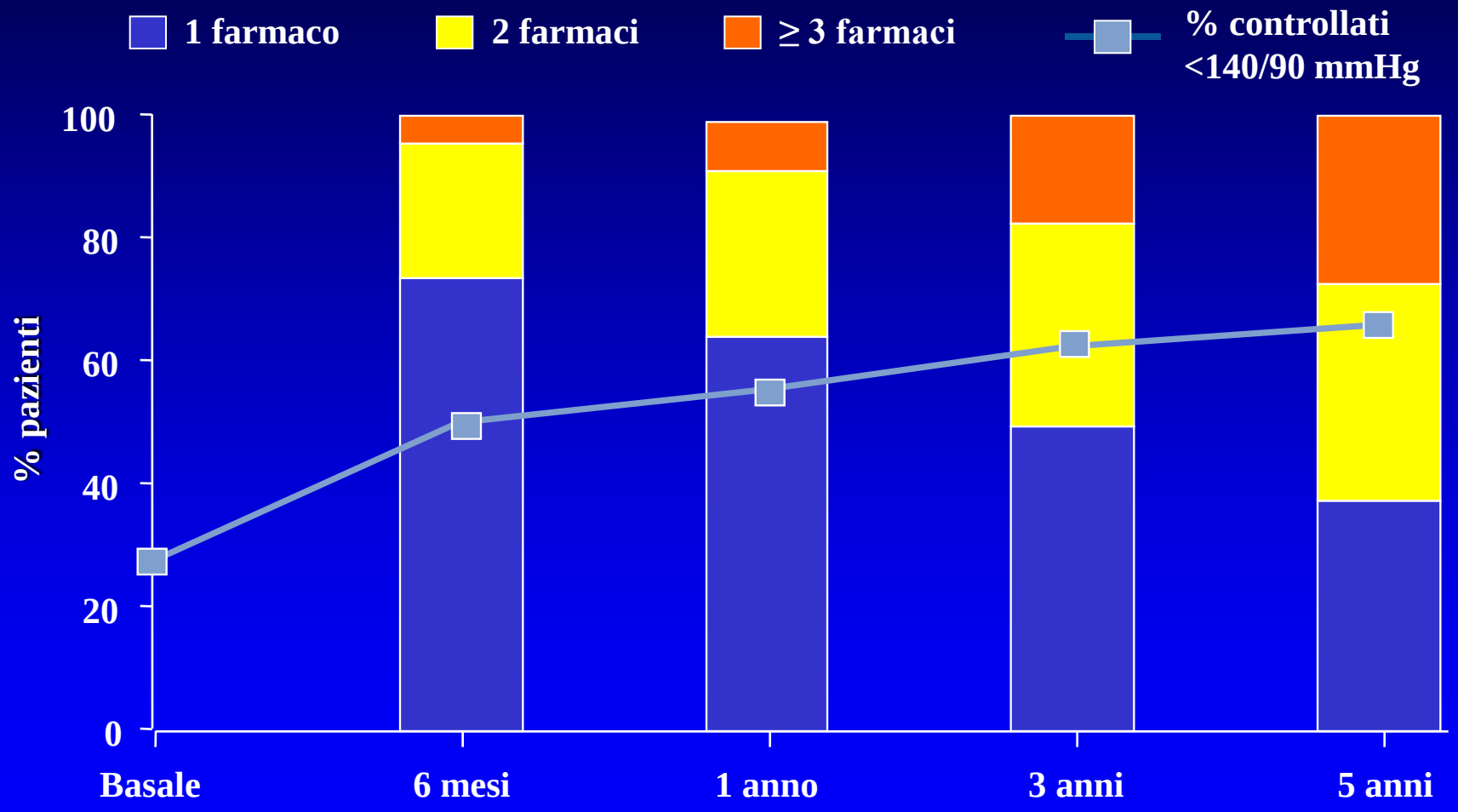
2. **Più precoce è l'ottenimento dei risultati, migliore è l'*outcome***

3. **In 2 casi su 3, sono necessarie le combinazioni per ottenere il controllo dei valori pressori**

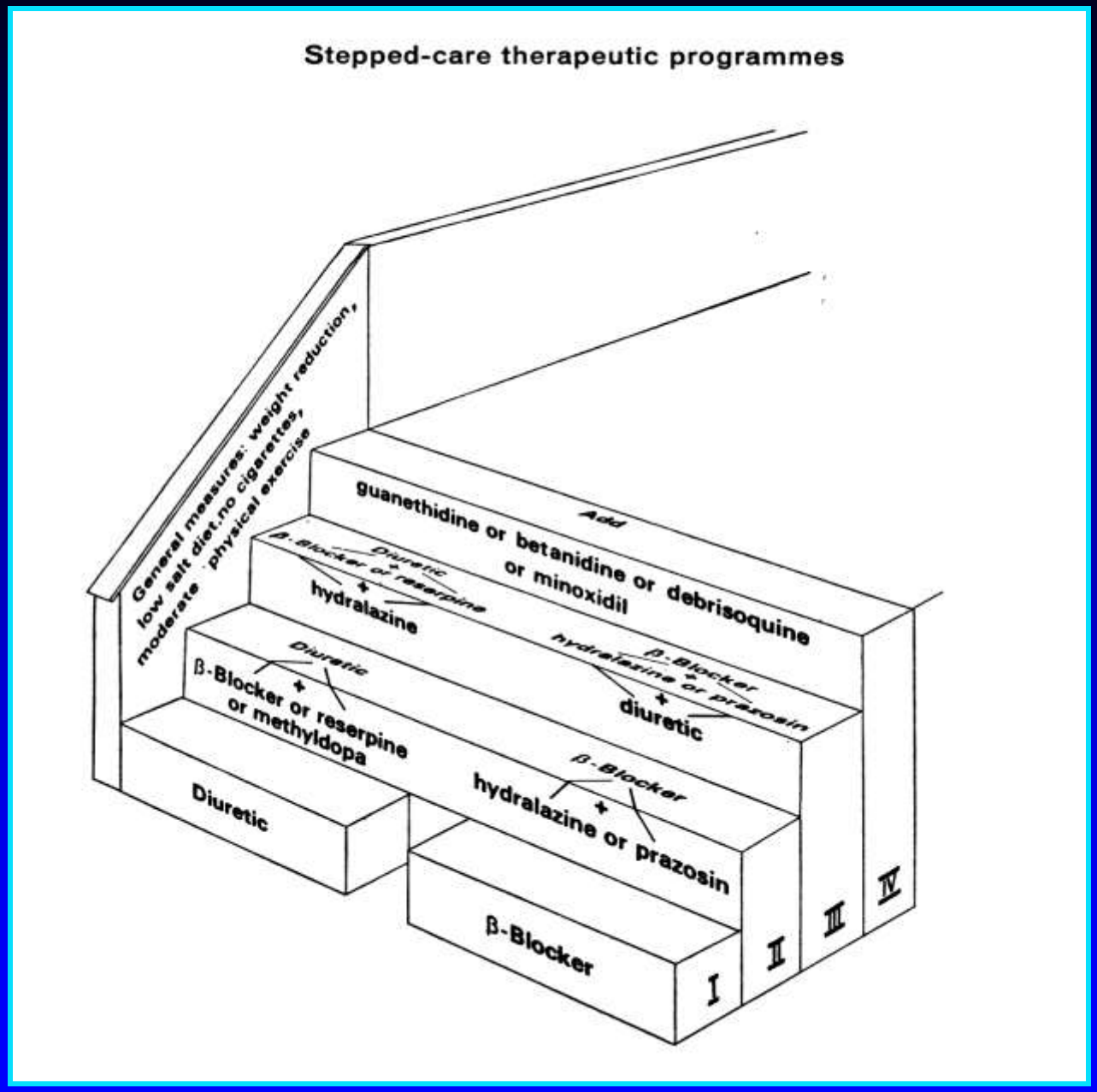
4. **La terapia antipertensiva può impattare sullo status metabolico dei pazienti**

5. **La scelta della terapia è un momento critico nella gestione del paziente**

Studio ALLHAT - Utilizzo dei farmaci e controllo dell'ipertensione



Cushman et al. J Clin Hypertens 2002;4:393-404



WHO Tech Rep 628,1978

Farmaci Tradizionali

Diuretici

Beta-bloccanti

Metil-dopa

Clonidina

Reserpina

Idralazina

Alfa bloccanti

Inibitori RAAS

Farmaci Nuovi 2015

Inibitori Renina

LCZ !

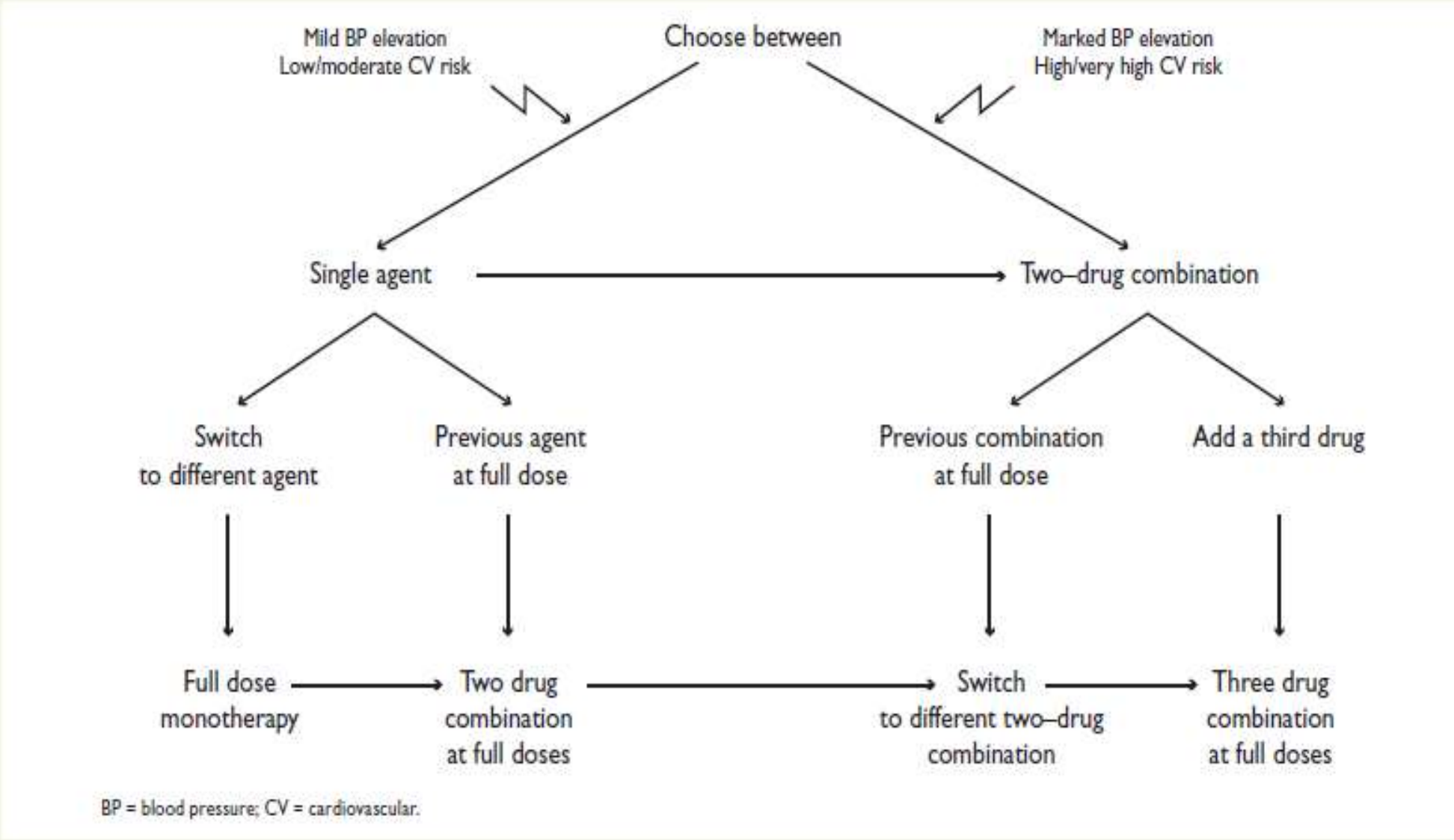


Figure 3 Monotherapy vs. drug combination strategies to achieve target BP. Moving from a less intensive to a more intensive therapeutic strategy should be done whenever BP target is not achieved.

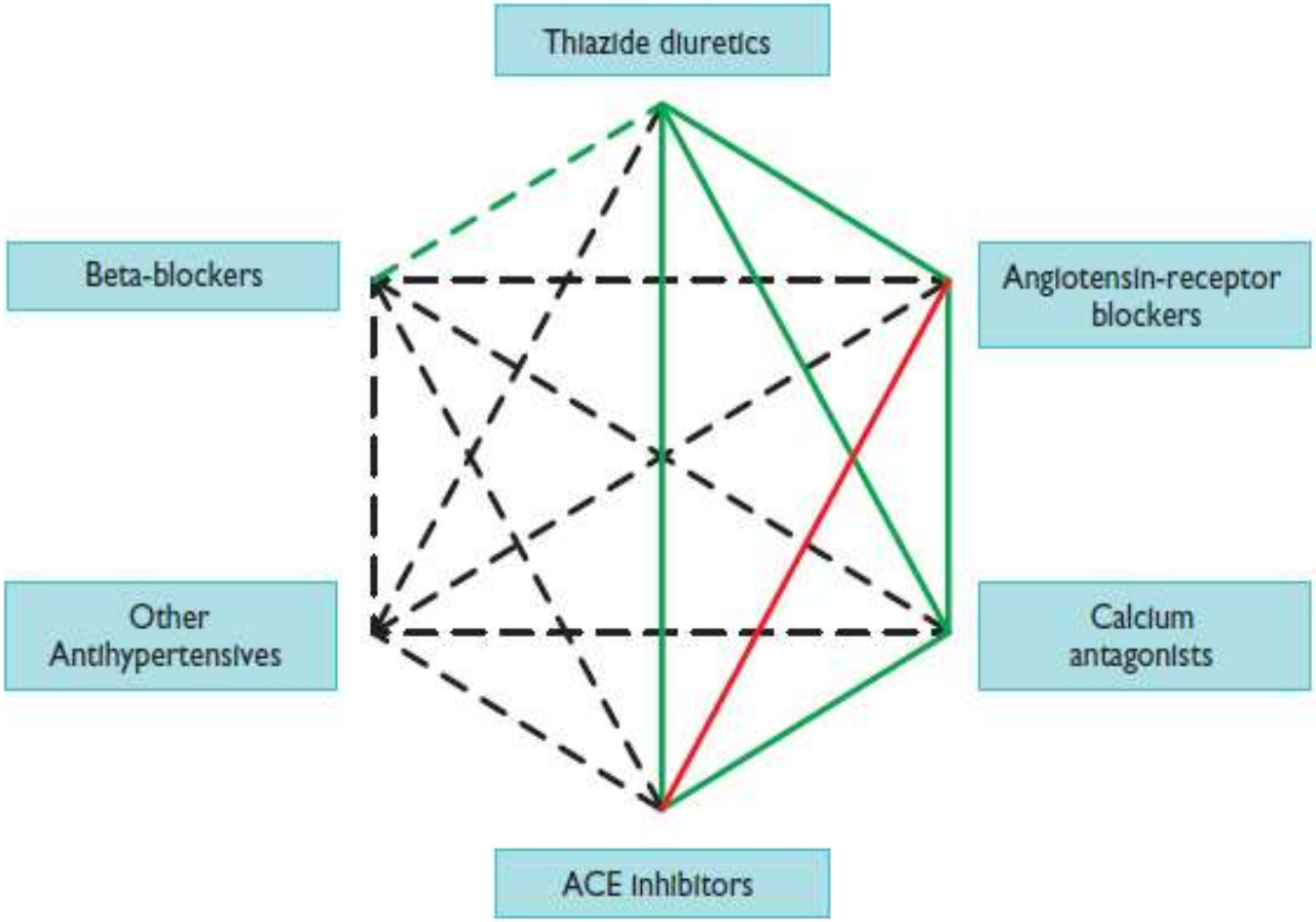
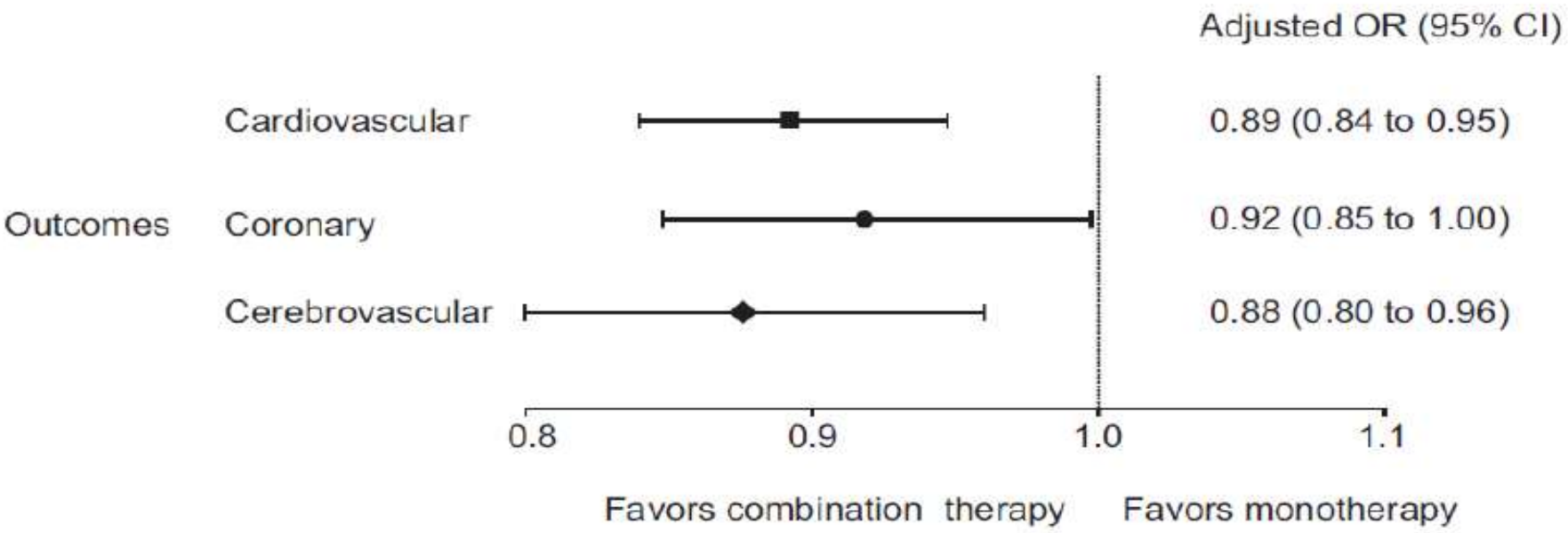


Figure 4 Possible combinations of classes of antihypertensive drugs. Green continuous lines: preferred combinations; green dashed line: useful combination (with some limitations); black dashed lines: possible but less well-tested combinations; red continuous line: not recommended combination. Although verapamil and diltiazem are sometimes used with a beta-blocker to improve ventricular rate control in permanent atrial fibrillation, only dihydropyridine calcium antagonists should normally be combined with beta-blockers.

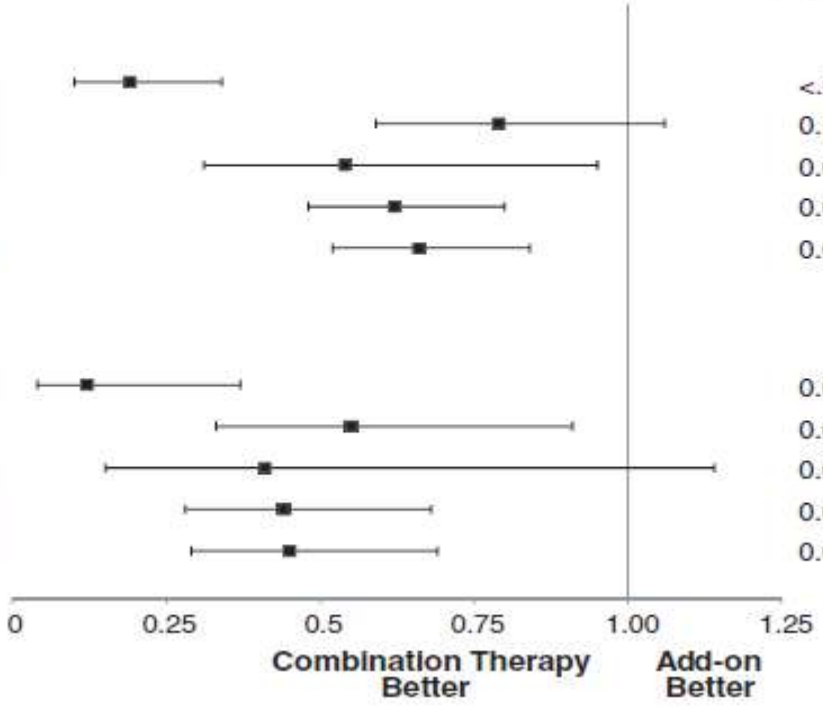
Efficacy of combination therapy in the clinical practi



Corrao et al. *Hypertension* 2011

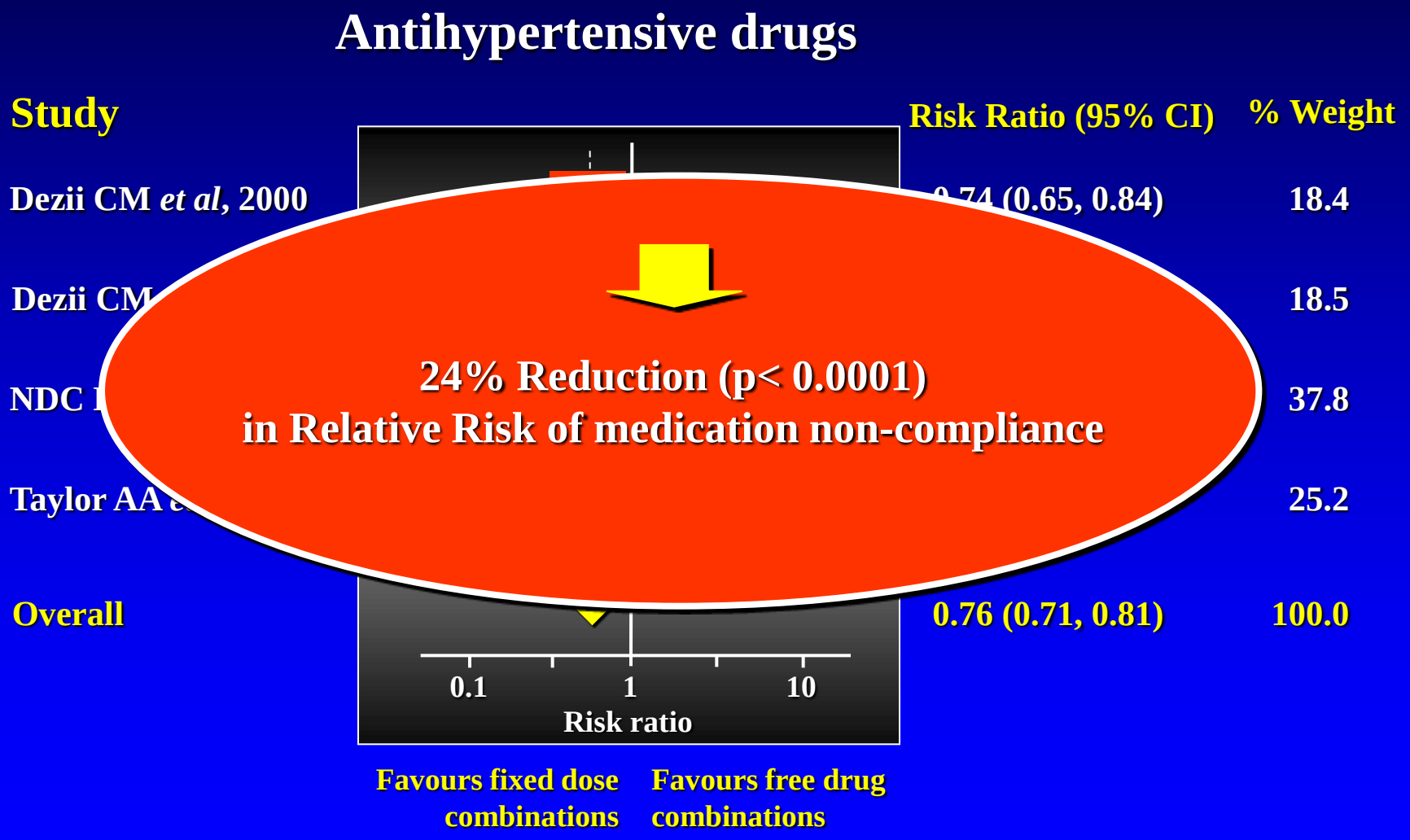
Associazione fissa: minor rischio di eventi CV e morte

	Incidence Rate* (Combination Therapy vs. Add-on)	IRR (95% CI)†	*P*-Value†
All Patients (1762 Patients In Each Cohort)			
Acute Myocardial Infarction	0.45 vs. 0.99	0.19 (0.10 - 0.34)	<.0001
Stroke/TIA	2.57 vs. 2.84	0.79 (0.59 - 1.06)	0.1172
Hospitalization for Heart Failure	0.55 vs. 0.78	0.54 (0.31 - 0.95)	0.0311
Overall	3.34 vs. 4.10	0.62 (0.48 - 0.80)	0.0002
Overall (With Death)	3.58 vs. 4.28	0.66 (0.52 - 0.84)	0.0008
Excluding Patients with Diabetes or CKD (803 Patients In Each Cohort)			
Acute Myocardial Infarction	0.24 vs. 0.68	0.12 (0.04 - 0.37)	0.0002
Stroke/TIA	1.89 vs. 2.58	0.55 (0.33 - 0.91)	0.0200
Hospitalization for Heart Failure	0.34 vs. 0.63	0.41 (0.15 - 1.14)	0.0875
Overall	2.39 vs. 3.55	0.44 (0.28 - 0.68)	0.0002
Overall (With Death)	2.49 vs. 3.68	0.45 (0.29 - 0.69)	0.0002



Gradman A.H. et al Hypertension 2013; 61: 309-318

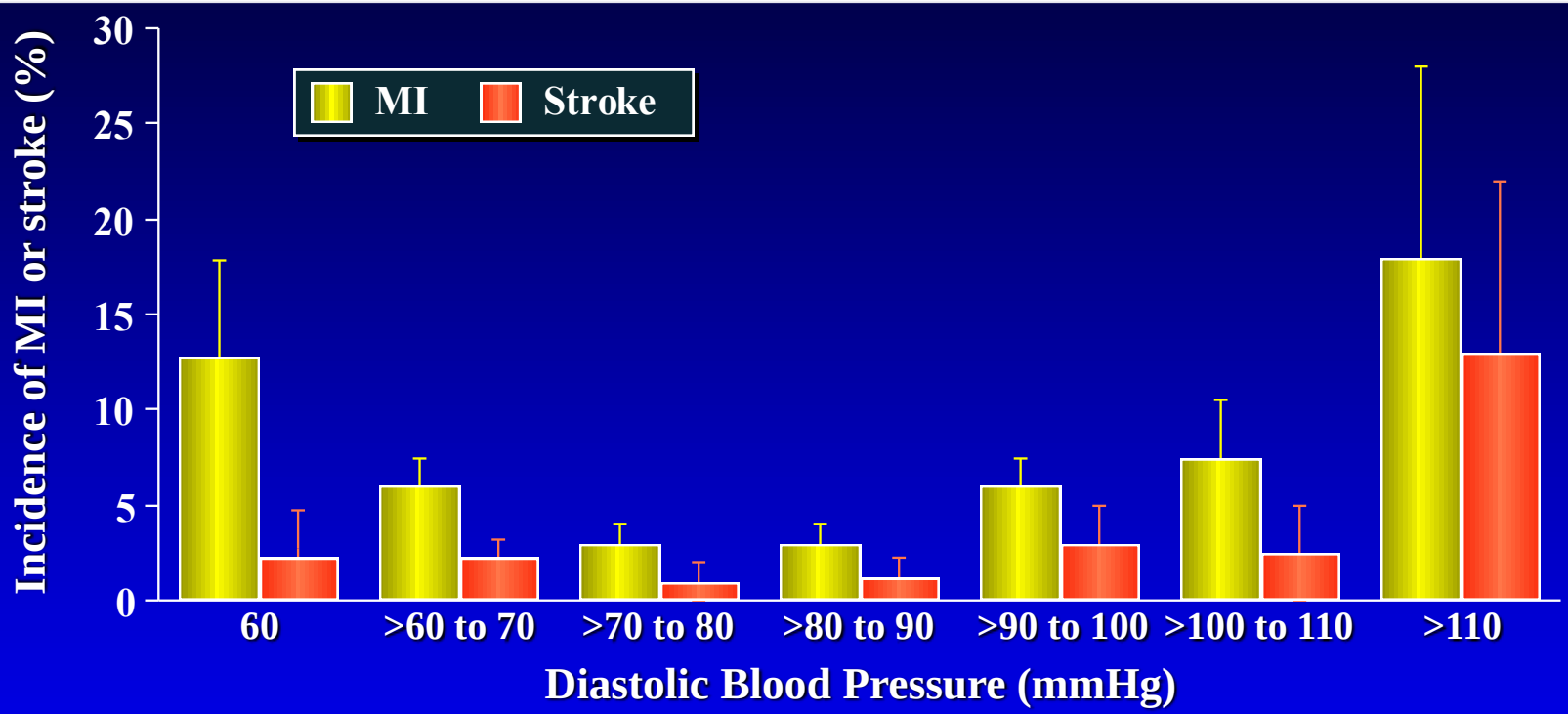
Fixed-dose Combination Therapy Increases Compliance with Treatment



Bangalore et al. Am J Med 2007; 120: 713-719

E' utile una terapia aggressiva dell'ipertensione?

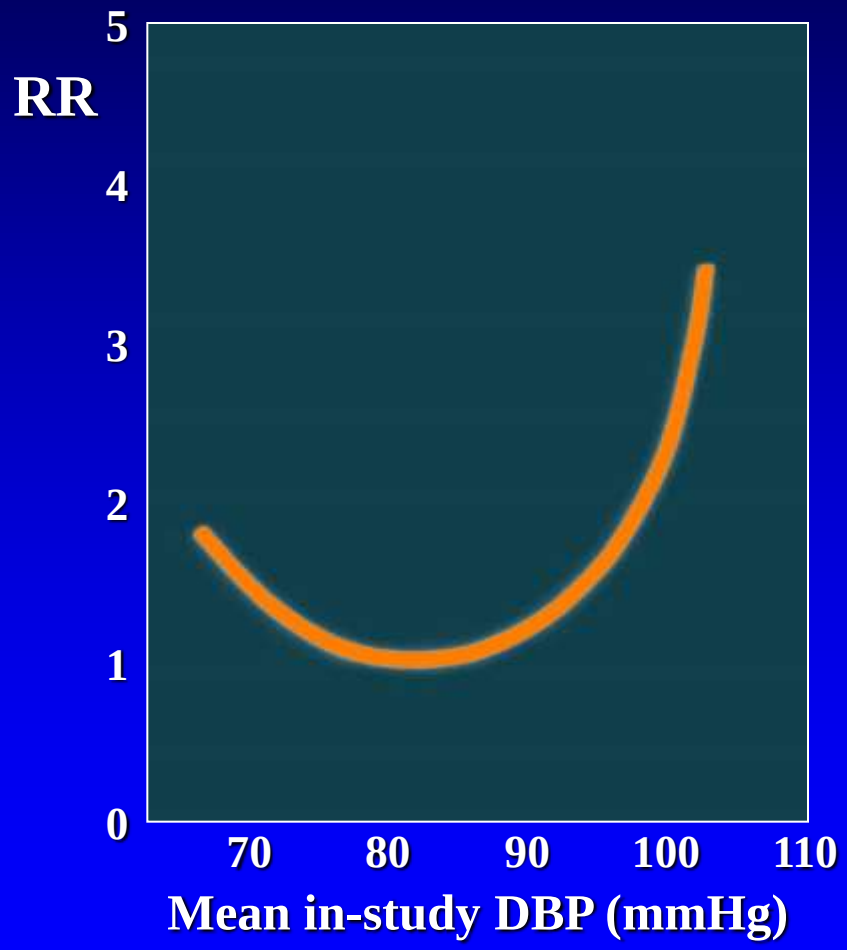
Incidence of Total Myocardial Infarction and Total Stroke by DBP Strata



MI							
Patients with MI (n)	29	135	387	255	71	14	8
Total patients (n)	177	2239	11324	7376	1214	201	43
Mean SBP (mmHg)							
Patients with MI	127.0	131.9	135.2	143.8	158.3	166.9	191.4
Patients without MI	126.2	129.6	131.4	139.3	155.2	170.3	85.7
Stroke							
Patients with stroke (n)	4	50	151	116	44	5	6
Total patients (n)	175	2253	11320	7366	1217	199	45
Mean SBP (mmHg)							
Patients with stroke	112.2	132.7	136.3	143.8	161.1	171.1	177.9
Patients without stroke	126.7	129.6	131.5	139.3	155.2	169.9	187.9

Messerli, Mancia et al., Ann Intern Med 2006; 144: 884-893

J-Curve - 12 Years Follow-Up



Samuelsson et al., J Hypertens

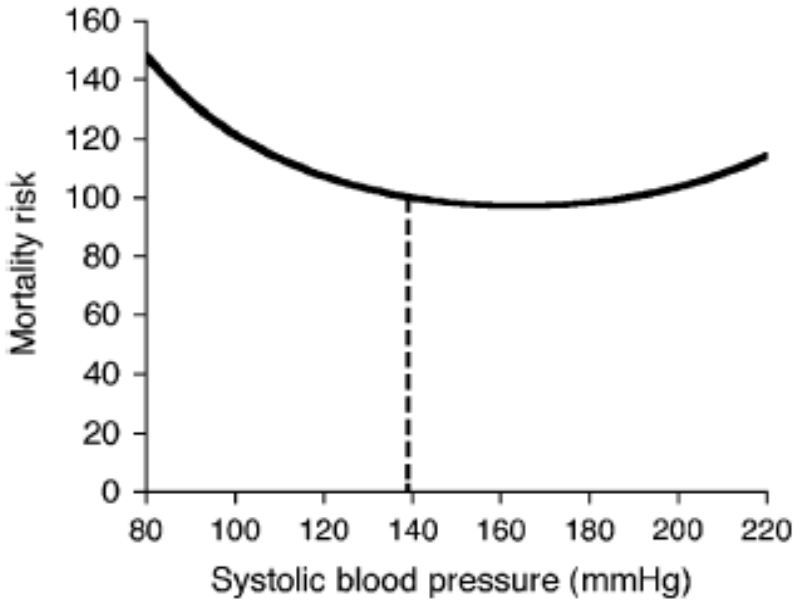


Figure 2. Graph of multivariate Cox regression. Adjusted for sex, age, Mini-Mental State Examination score, activities of daily living according to Barthel score, atrial fibrillation, and diabetes mellitus. Risk associated with systolic blood pressure 140 mmHg (dotted line) was used as index (=100).

CONCLUSION: Lower SBP seems to be associated with greater mortality in people aged 85 and older, irrespective of health status. There are indications of a U-shaped correlation between SBP and mortality, and the optimal SBP for this age group could be above 140 mmHg. J Am Geriatr Soc 56:1853–1859, 2008.

JAGS 2008 1853-59

New Directions for Treating NSTE-ACS Patients: ESC

Heart Disease: What's Bad for the Goose Is Bad for the Gander

Debating NO Warfarin for Boxing Matc

Heartwire from Medscape

BP Targets Far Below Guidelines Cut Mortality, CV Events: SPRINT Trial

Michael O'Riordan

September 11, 2015

In the first treatment arm, patients were randomized to intensive blood-pressure control, the goal being a systolic blood **pressure less than 120 mm Hg**. In the intensive-therapy arm, patients were treated with three or more antihypertensive medications, including diuretics, such as chlorthalidone; the calcium-channel blocker amlodipine; and the ACE inhibitor lisinopril.

With the second strategy, patients were randomized to standard blood-pressure control, the aim of which was to achieve a target **of less than 140 mm Hg.** Patients were treated with an average of two antihypertensive medications.

9300 pazienti
No diabetici
No pregresso ictus
25% > 75 aa

Conclusion

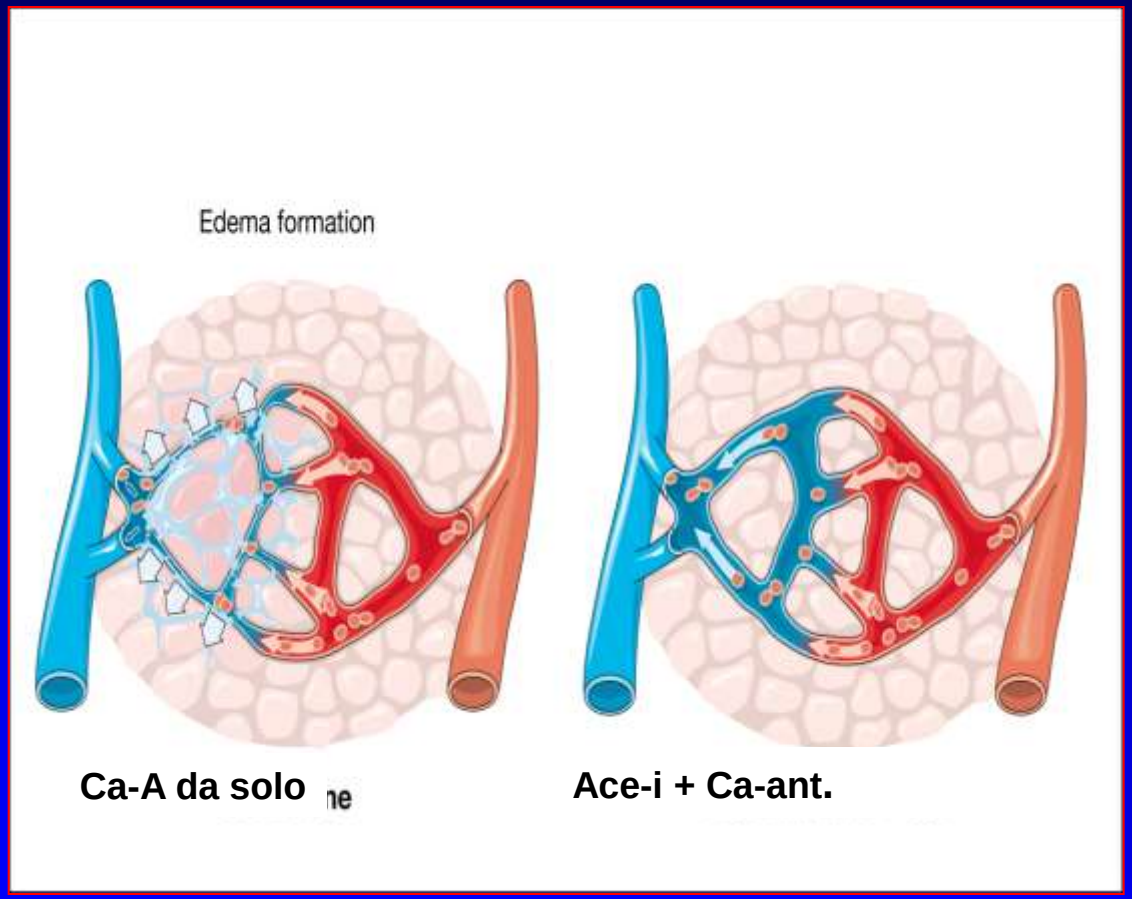
In the Systolic Blood Pressure Intervention Trial (SPRINT), investigators report that treating high-risk hypertensive adults 50 years of age and older to a target of 120 mm Hg significantly reduced cardiovascular events by 30% and reduced all-cause mortality by nearly 25% when compared with patients treated to a target of 140 mm Hg.

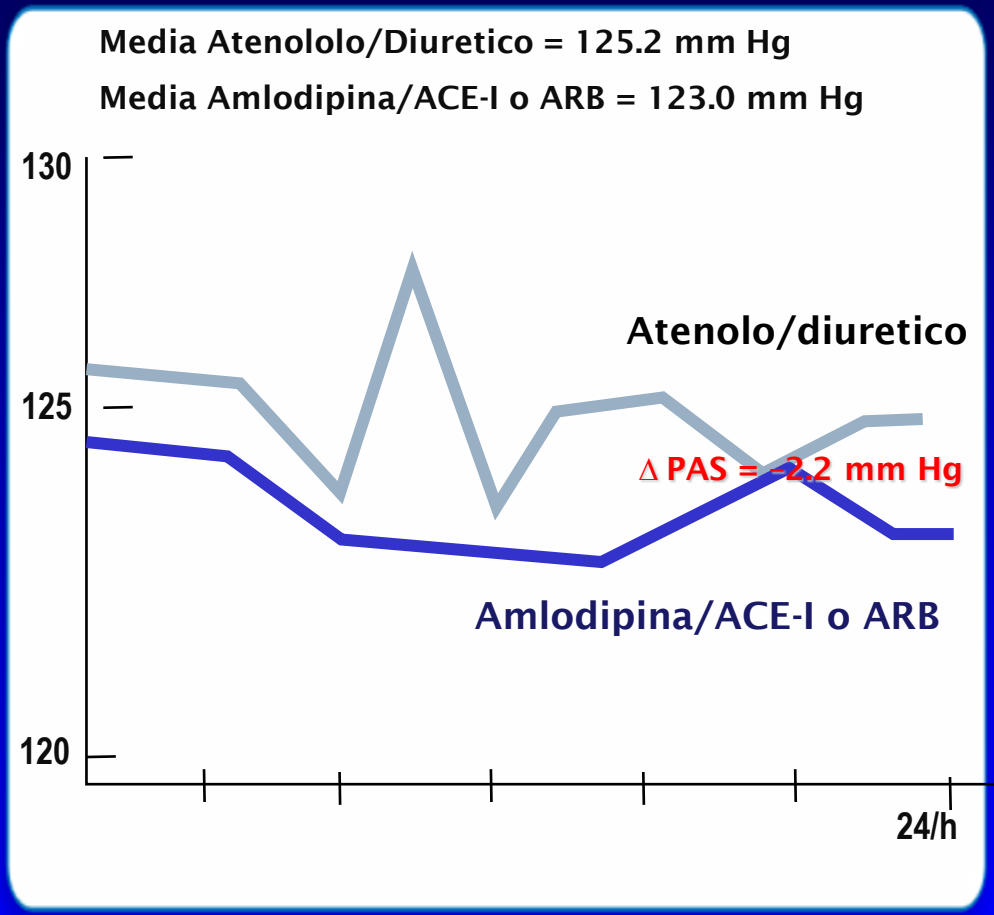
Messerli said this does not mean that the J-curve—an inverse relationship between cardiovascular events and mortality at low blood pressures—has disappeared altogether, noting that a systolic blood pressure of zero will still result in death, but the "optimal on-treatment blood pressure is obviously lower than what was previously documented in many post hoc studies, including some of our own."

ACE + CCB

Associazione Ace-inibitori con Ca-Antagonisti

Migliore tollerabilità (ridotta incidenza di edemi ai malleoli rispetto al solo Ca ed efficacia/24 ore



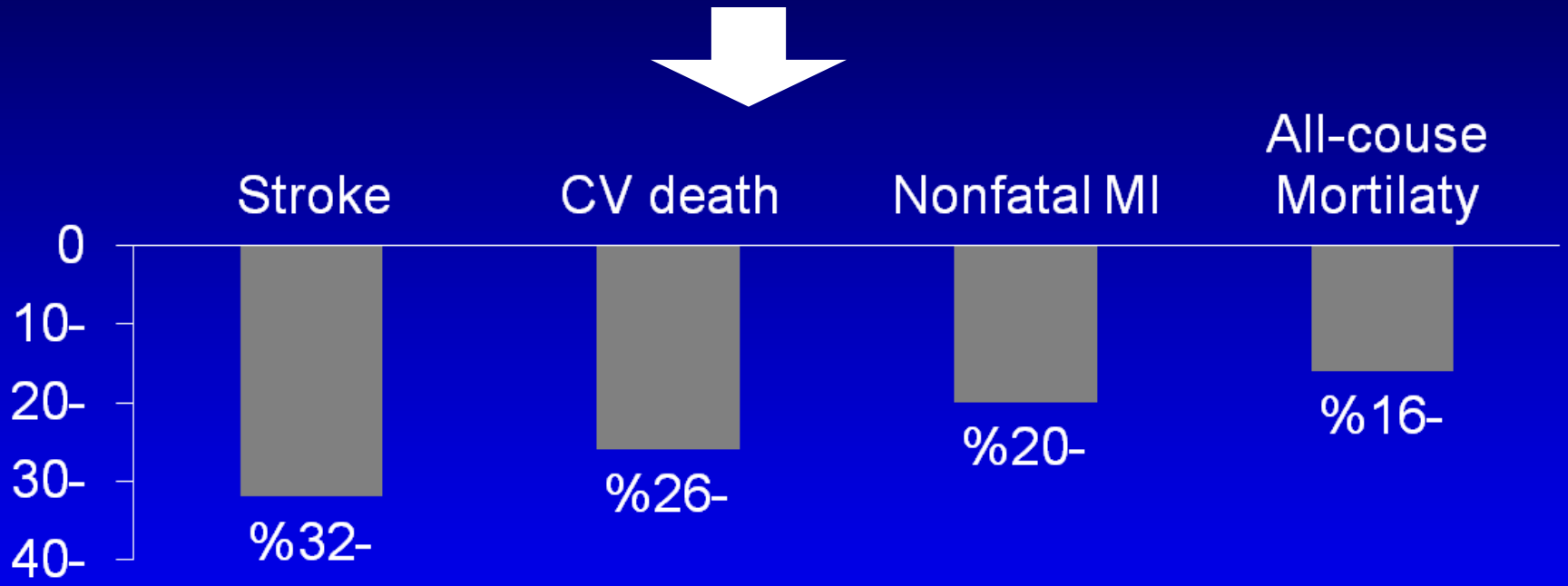


Ramipril o altro?

drug	HTN	CHF	ther uses
Captopril	25-100 mg/day Bid-tid	6.25-100 mg tid Maximum :450 mg/day	Diabetic nephropathy (DN), left ventricular dysfunction after acute MI
Enalapril	2.5-40 mg/day qd-bid	2.5-20 mg bid Maximum :20 mg bid	Asymptomatic left ventricular dysfunction , DN
Enalaprilat	0.625 mg , 1.25 mg , 2.5 mg q6h Maximum: 5 mg q6h	Not FDA approved	
Fosinopril	10-40 mg/day Maximum: 80 mg daily	10-40 mg/day Maximum: 40 mg daily	DN
Lisinopril	10-40 mg/day Maximum: 40 mg/day	5-40 mg/day	Hemodynamically stable pt within 24 hr of acute MI to improve survival , prevent DN
Ramipril	**2.5-20 mg/day Qd-bid**	**2.5-10 mg/day**	**DN , post AMI , to reduce of MI , stroke and death from CV causes**

Risk reduction with ramipril 10 mg

+ Ramipril 10 mg



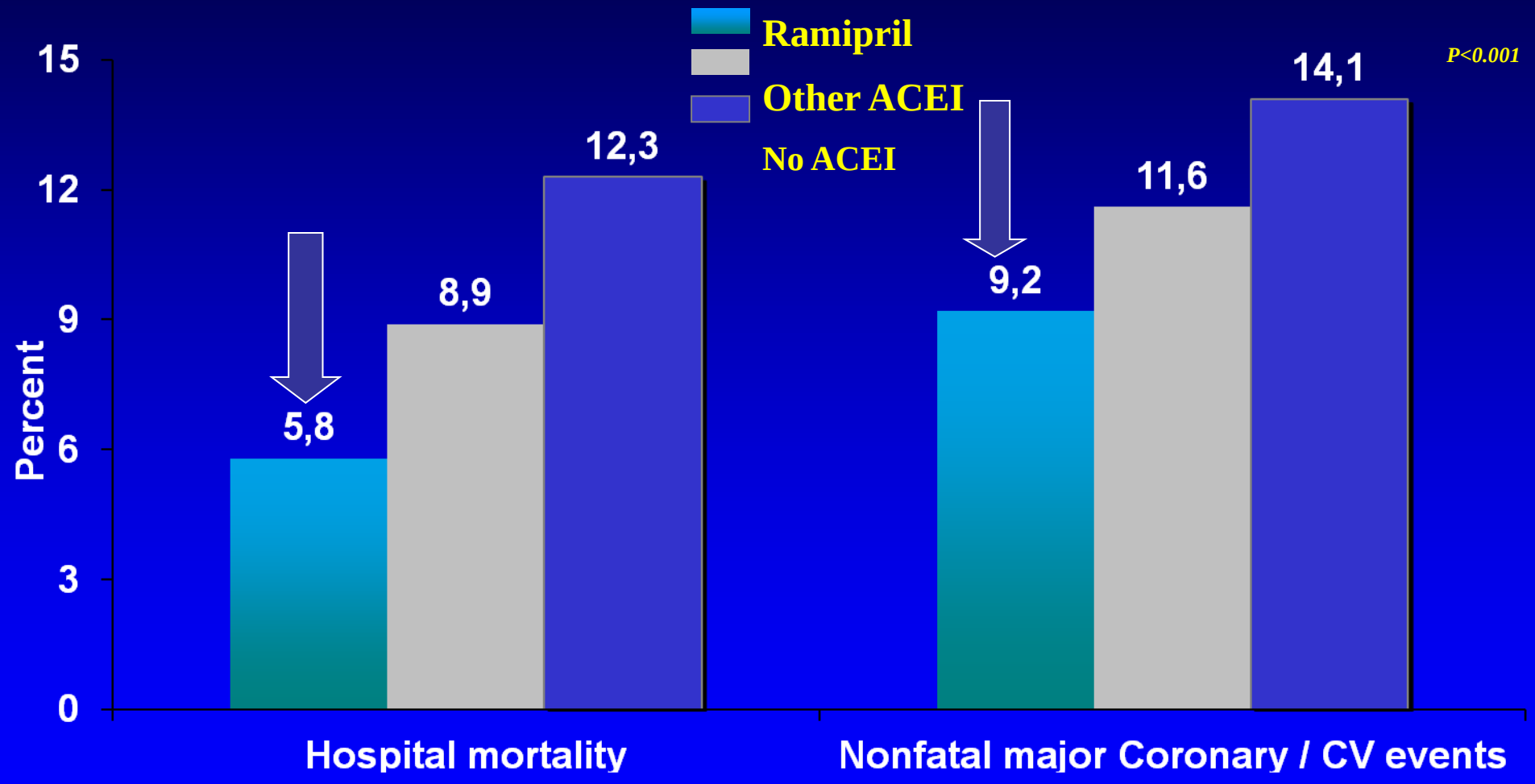
Effects beyond baseline therapy

Aspirin
- **b-blockade**
- **Lipid-lowering agents**
- **Diuretics**
- **Other antiplatelets**
- **Calcium channel blockade**

***P* = 0.0001**

†*P* = 0.005

Adding ACE Inhibitor reduces mortality and morbidity
Best results conferred by ramipril



*$P < 0.05$, ramipril vs no ACE inhibitor
Cor/CV = Coronary/cerebrovascular

Perché utilizzare proprio questa associazione?

- Efficace con scarsi effetti collaterali
- Semplice
- Monosomministrazione giornaliera
- Copertura vera 24 h
- Effetti positivi sul danno d'organo clinico e subclinico
- Efficace in: ipertesi (tutte le età), nefropatici , diabetici e obesi

Conclusioni

- La terapia di associazione è indispensabile per ottenere la normalizzazione dei valori pressori nella maggioranza dei pazienti ipertesi

- Fra gli ACE inibitori il Ramipril e fra e i CCB l'amlodipina hanno la migliore documentazione scientifica per quanto riguarda gli studi clinici controllati basati sugli eventi

- In ogni caso la scelta della terapia da utilizzare nella pratica clinica deve essere determinata, quando possibile, dai risultati degli studi clinici controllati basati su eventi e da una attenta conoscenza della letteratura scientifia

Grazie per l’attenzione!