

New Antihypertensive Strategies to Improve Blood Pressure Control

Antonio Coca, MD, PhD, FRCP, FESC

Hypertension and Vascular Risk Unit

Department of Internal Medicine. Hospital Clínic (IDIBAPS)

University of Barcelona, Spain

Conflict of interest concerning this presentation: None

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Treatment Strategies Based BP Values and Total Cardiovascular Risk

	High normal SBP 130-139 or DBP 85-89	Grade 1 SBP 140-159 or DBP 90-99	Grade 2 SBP 160-179 or DBP 100-109	Grade 3 SBP ≥180 or DBP ≥110
Recommendations	Class		Level	
It is recommended that decisions on treatment strategies depend on the initial level of total cardiovascular risk	I		B	
OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥ 4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

Absolute 10 year
risk of CV death

SCORE



< 4%



4-5%



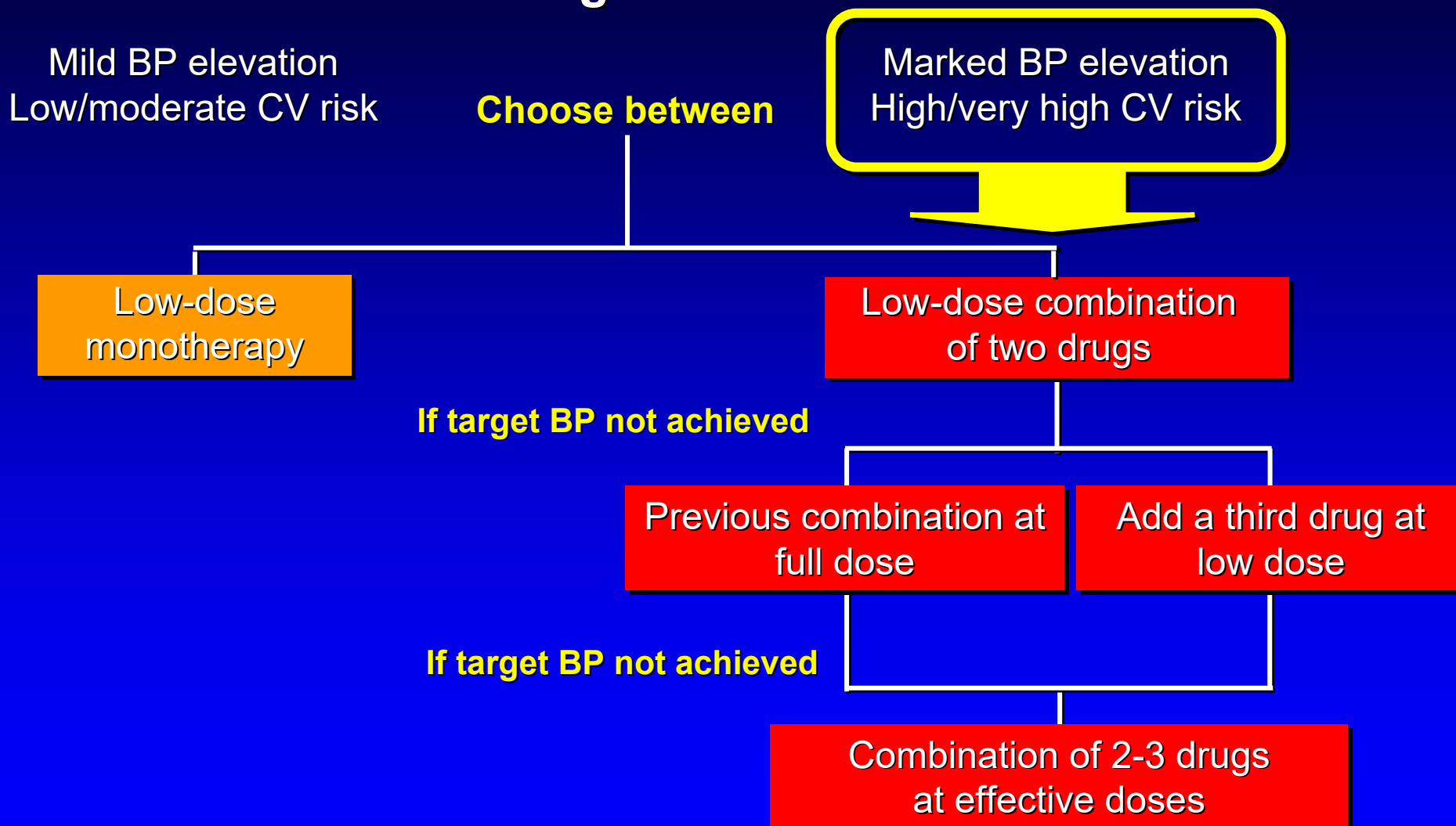
5-8%



> 8%

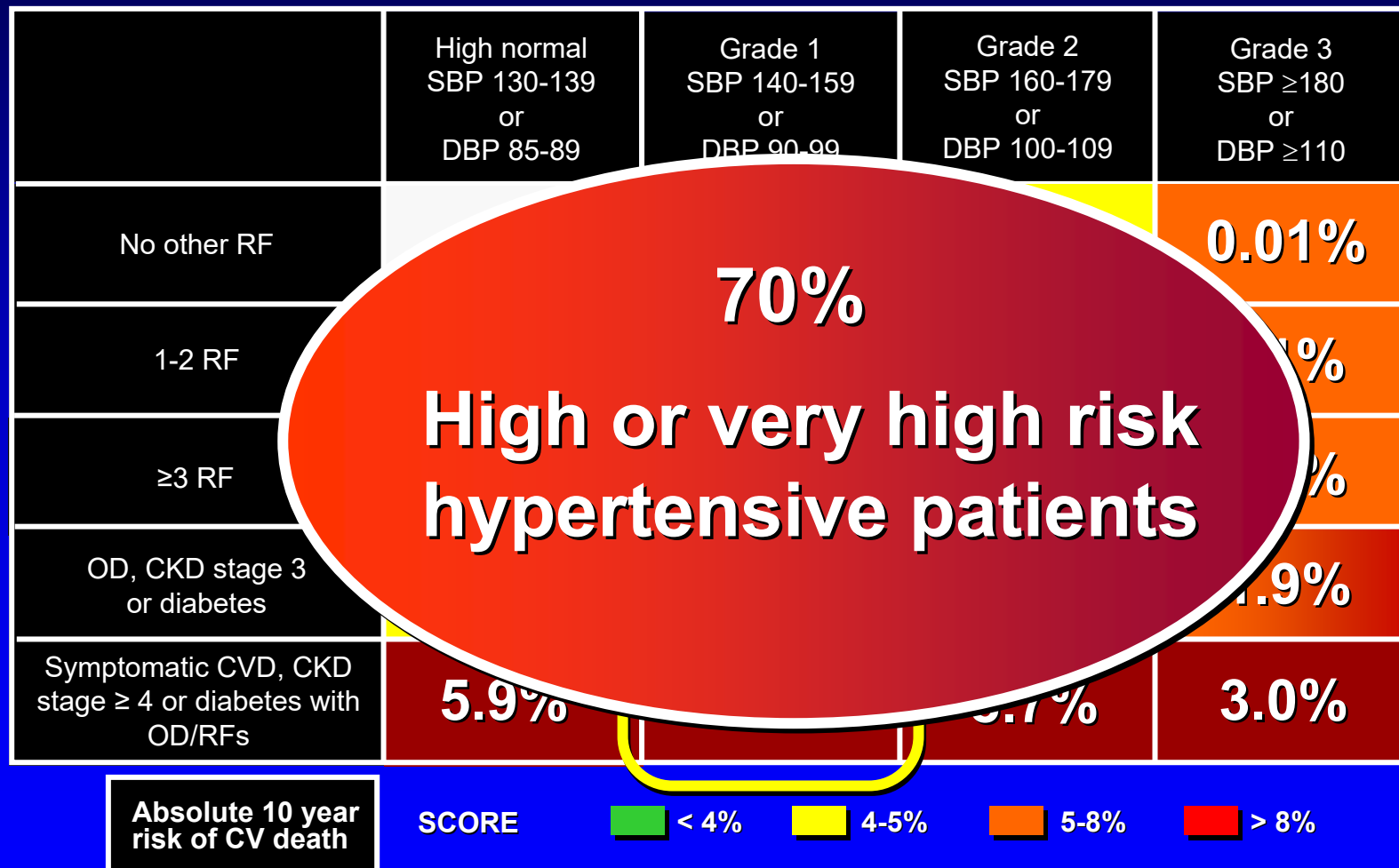
ESH/ESC 2013 Guidelines

Pharmacological Treatment

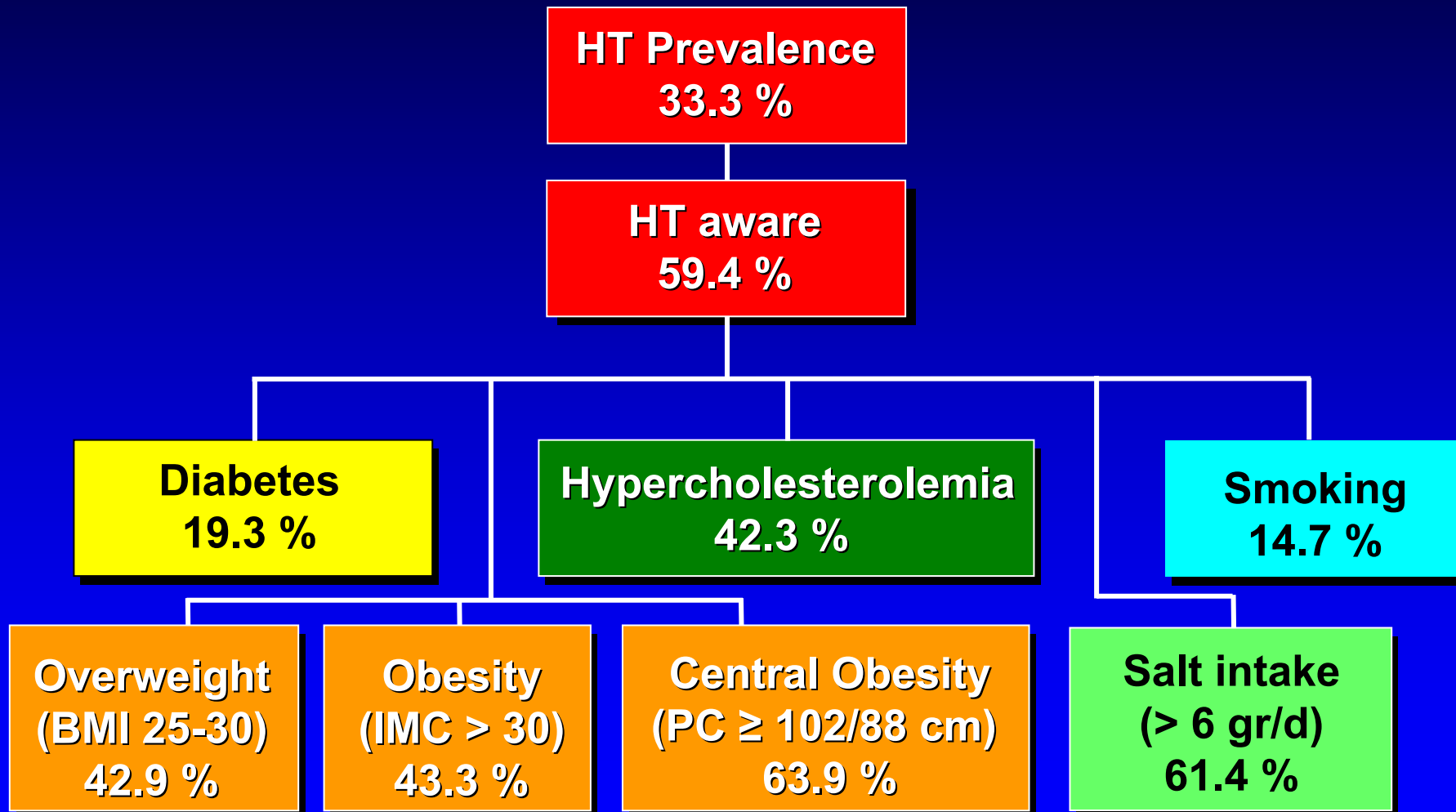


Cardiovascular Risk Stratification

DICOPRESS Study: 22,639 patients (>18 years) seen by GPs in Spain



Prevalence of Hypertension and Associated CV Risk Factors in Spain



Effects of Obesity, Sedentarism and Diabetes on Blood Pressure Control

PREVENCAT Study: 2,092 hypertensive patients (64 ± 11.3 years)

**Predictors of strict blood pressure control
(BP < 140/90 or < 130/85 in DM-2)**

Factor	OR [IC del 95%]	p
Type 2 Diabetes	0.29 [0.23 – 0.37]	< 0.001
Obesity	0.65 [0.49 – 0.85]	0.002
Sedentary life	0.78 [0.64 – 0.95]	0.014

ESH/ESC 2013 Guidelines

Pharmacological Treatment

Mild BP elevation
Low/moderate CV risk

Choose between

Marked BP elevation
High/very high CV risk

Low-dose
monotherapy

**100%
in
Diabetics**

Low-dose combination
of two drugs

Not achieved

Previous combination at
full dose

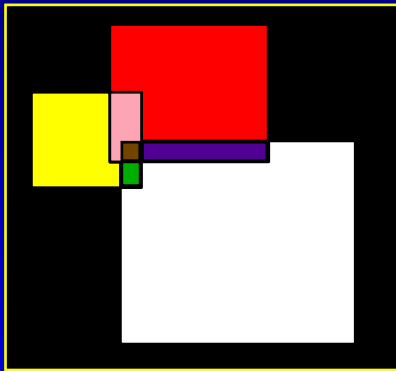
Add a third drug at
low dose

If target BP not achieved

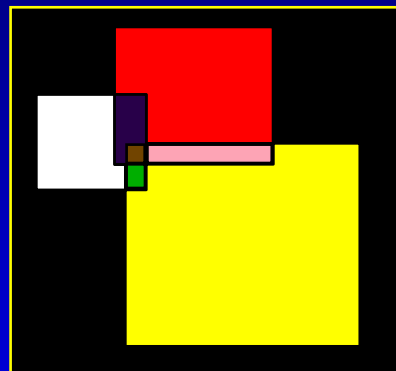
Combination of 2-3 drugs
at effective doses

Pathogenic Mechanisms of Hypertension in Humans

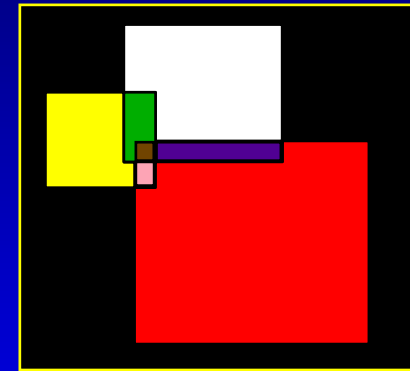
Patient A



Patient B

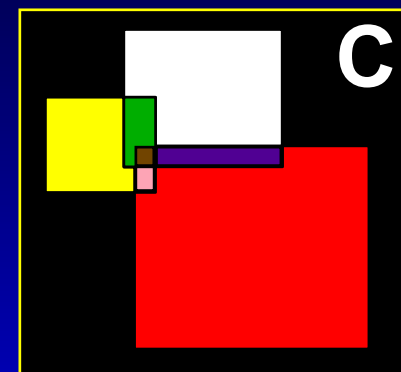
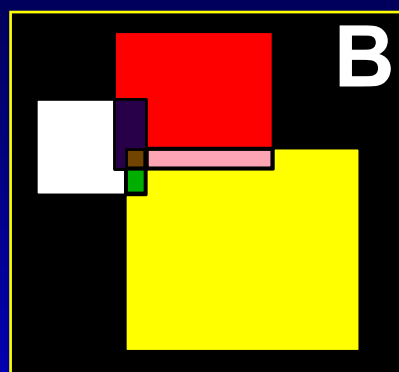
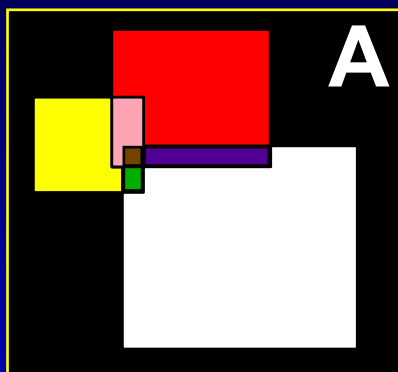


Patient C



-  Sympathetic nervous system
-  Renin-angiotensin-aldosterone system
-  Intravascular volume (Na⁺ and water)

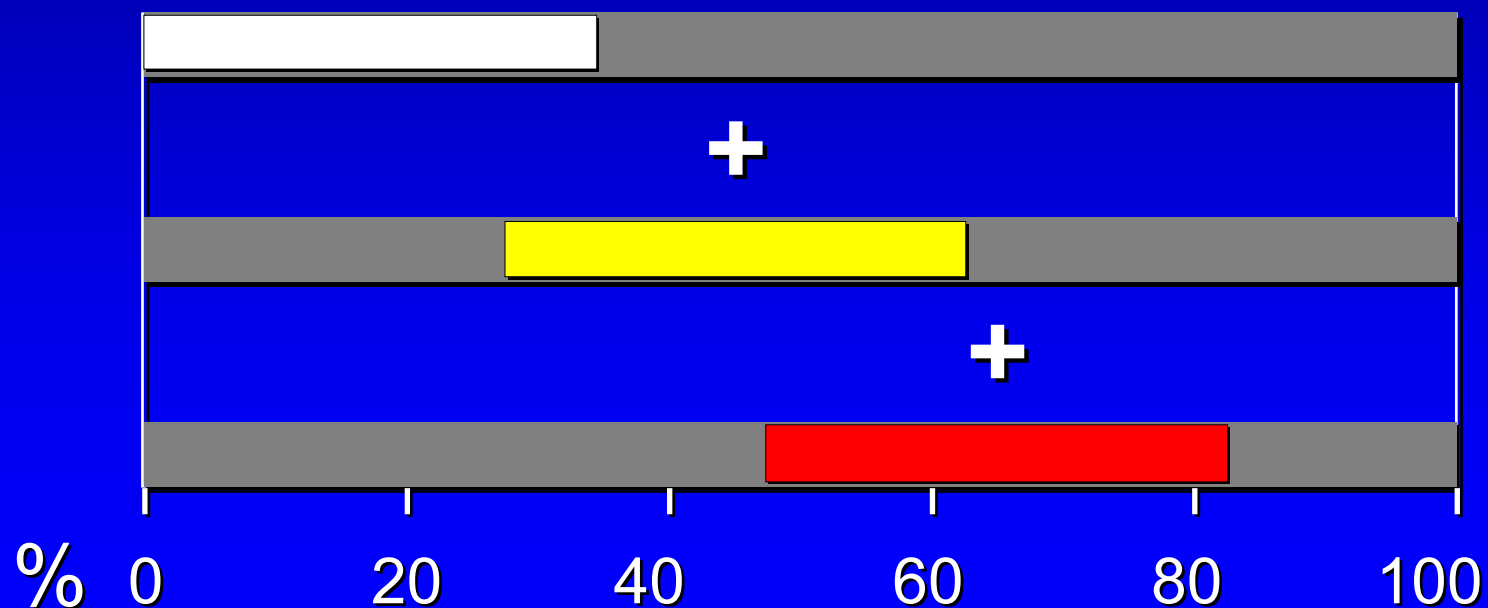
Blood Pressure Control Achieved by Different Antihypertensive Drugs



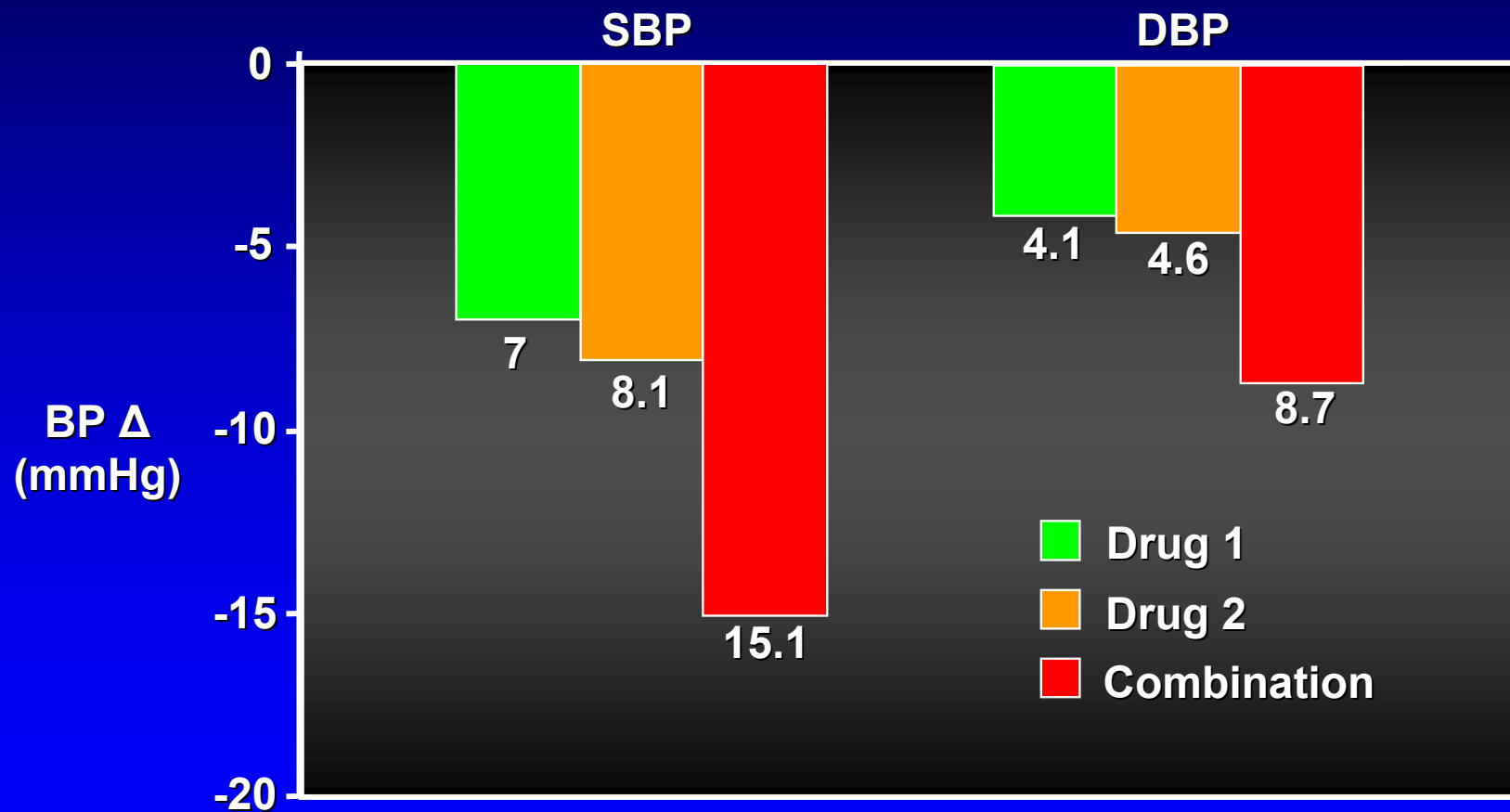
Drug A

Drug B

Drug C



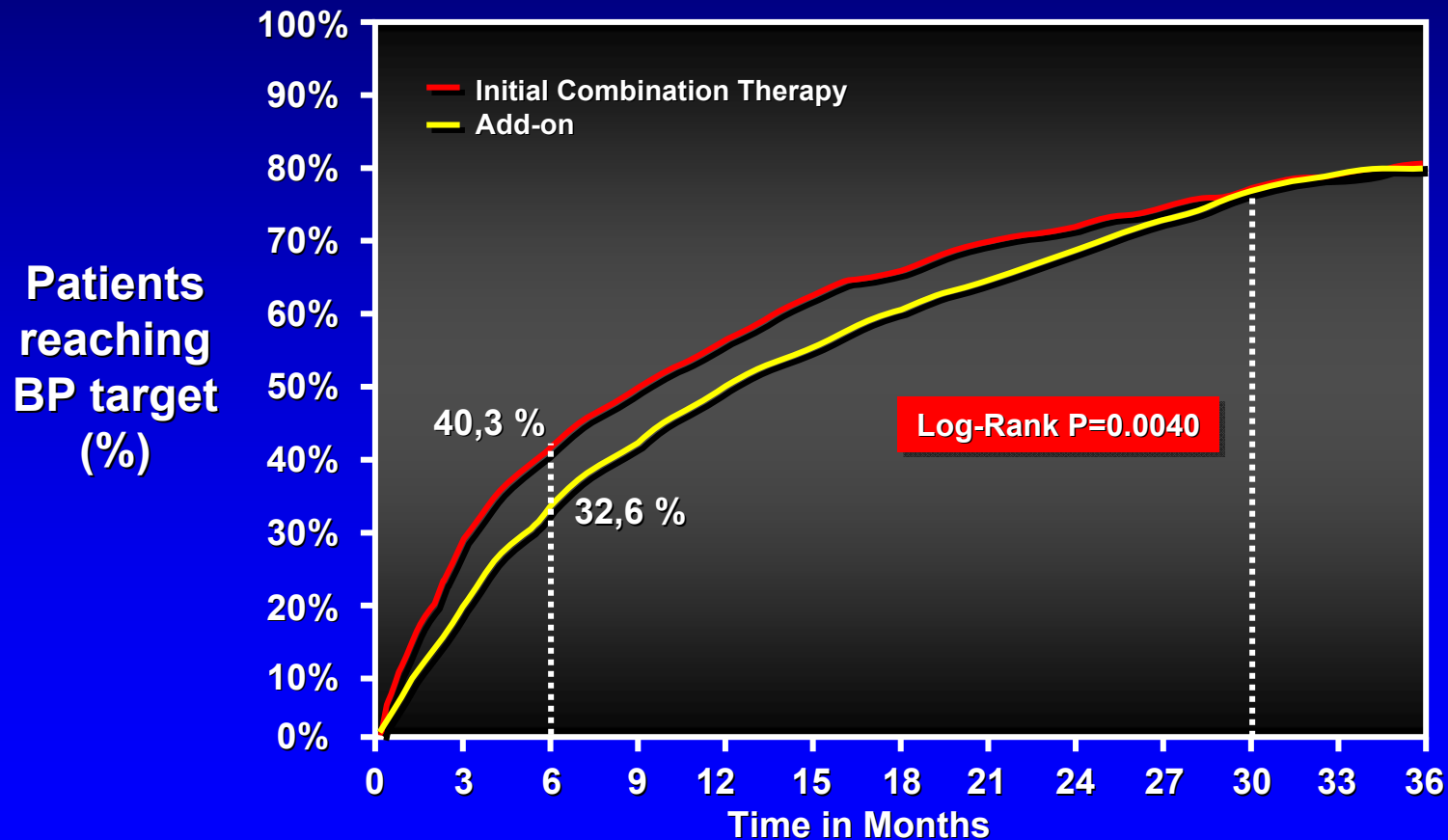
BP Reduction in Monotherapy vs Combined Therapy in 119 Placebo-controlled Studies



Initial Combination Therapy and Achievement of Blood Pressure Target

Retrospective analysis of 1762 patients who initiate combination therapy vs those starting in monotherapy and later shifted to combined therapy

Kaplan-Meier estimates of achieving BP target with initial combination therapy

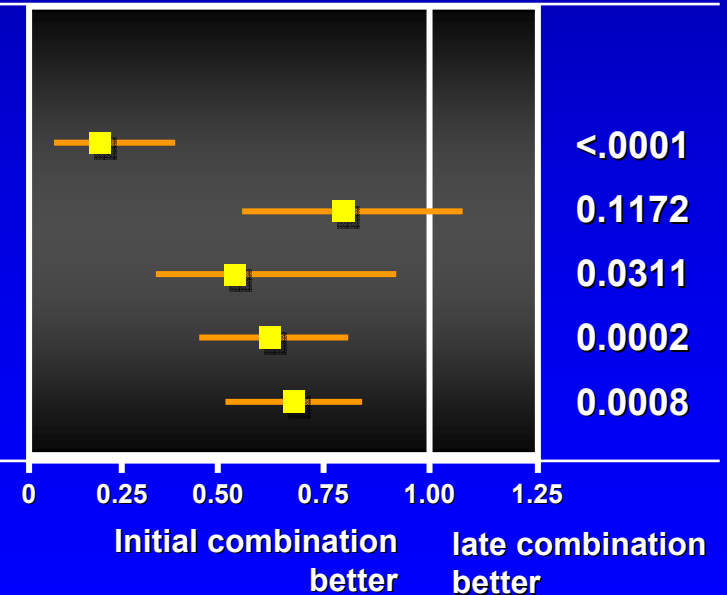


Initial Combination Therapy and Reduction of Cardiovascular Events

Retrospective analysis of 1762 patients who initiate combination therapy vs those starting in monotherapy and later shifted to combined therapy

Incident Rate of Cardiovascular Events (IRCVE)

	Incident rates (Initial vs. late combination)	IRCVE (95% CI)	P
All patients (1762 patients in each cohort)			
Acute Myocardial Infarct	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
CHF Hospitalization	0.55 vs. 0.78	0.54 (0.31-0.95)	0.0311
All	3.34 vs. 4.10	0.62 (0.48-0.80)	0.0002
All (including death)	3.58 vs. 4.28	0.66 (0.52-0.84)	0.0008



Cardiovascular Prevention in Early Blood Pressure Control: the VALUE Study

All treatment groups

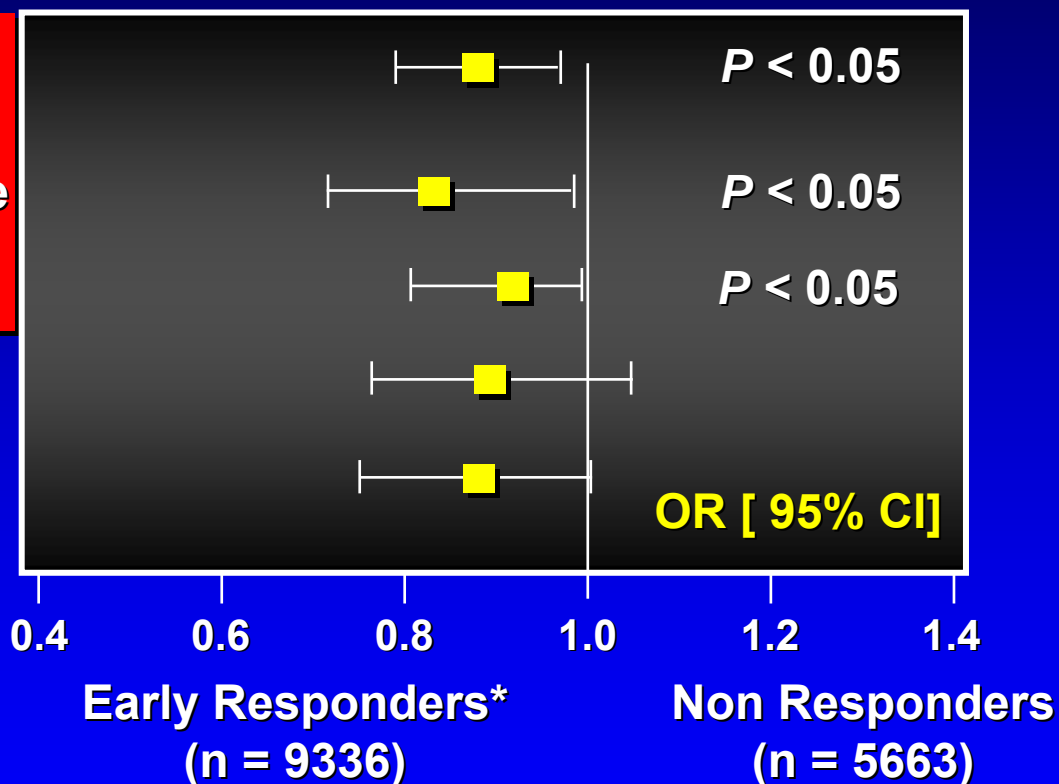
Fatal and nonfatal
Cardiac events

Fatal and nonfatal stroke

All cause mortality

Myocardial infarction

Hospitalization for
heart failure



*Previously untreated: SBP reduction > 10 mmHg at first month
Previously treated: Any SBP Reduction PAS at first month

Hypertension Treatment and Blood Pressure Control

The National Health and Nutrition Examination Survey, 2005 to 2010

Adjusted Odds Ratio for BP control in the USA 2005 - 2010

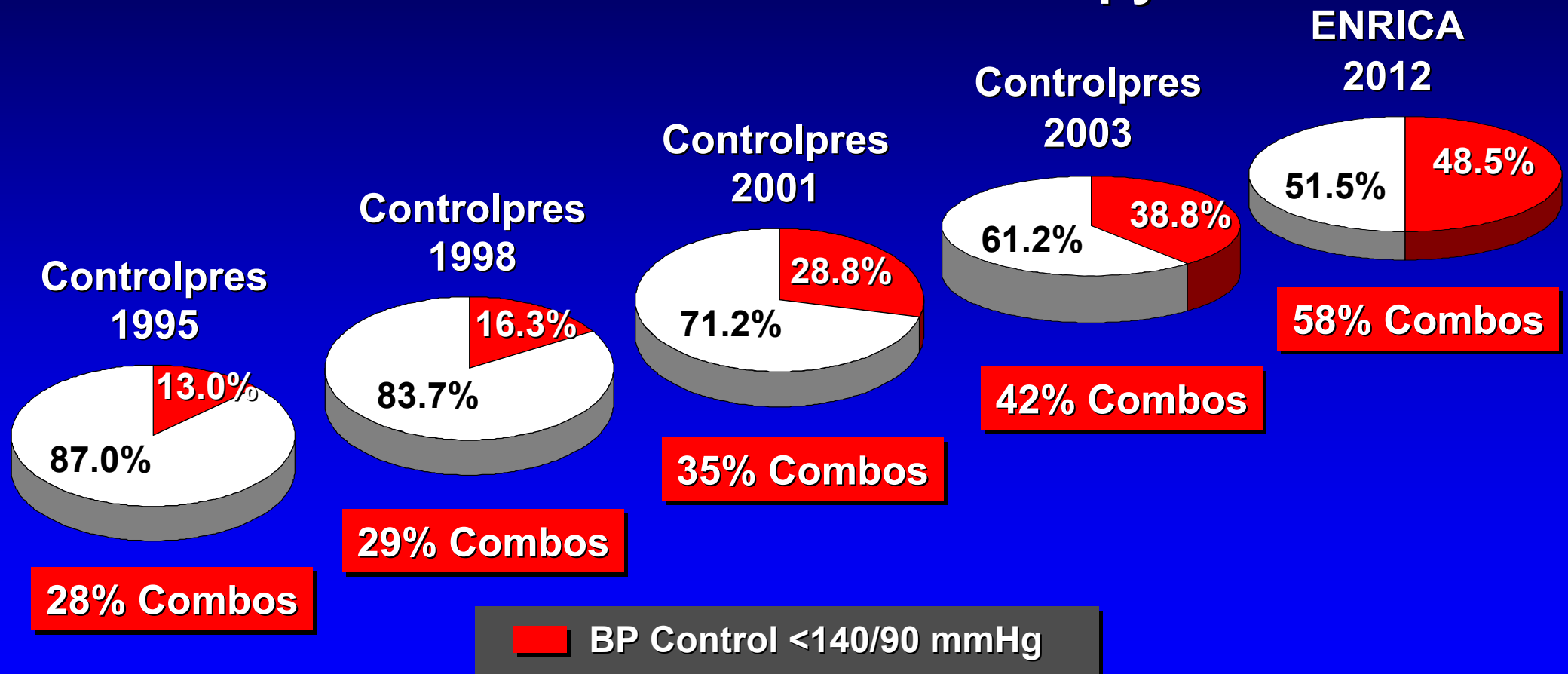
Treatment strategy and BP control	BP control
	Treated patients
Monotherapy	1.00 (ref)
Fixed-dose combination in a single pill	1.55 (1.20-2.00)*
Multiple pill combination	1.26 (1.03-1.55)†

* Significant difference compared to reference, $P < 0.01$

† Significant difference compared to reference, $P < 0.05$

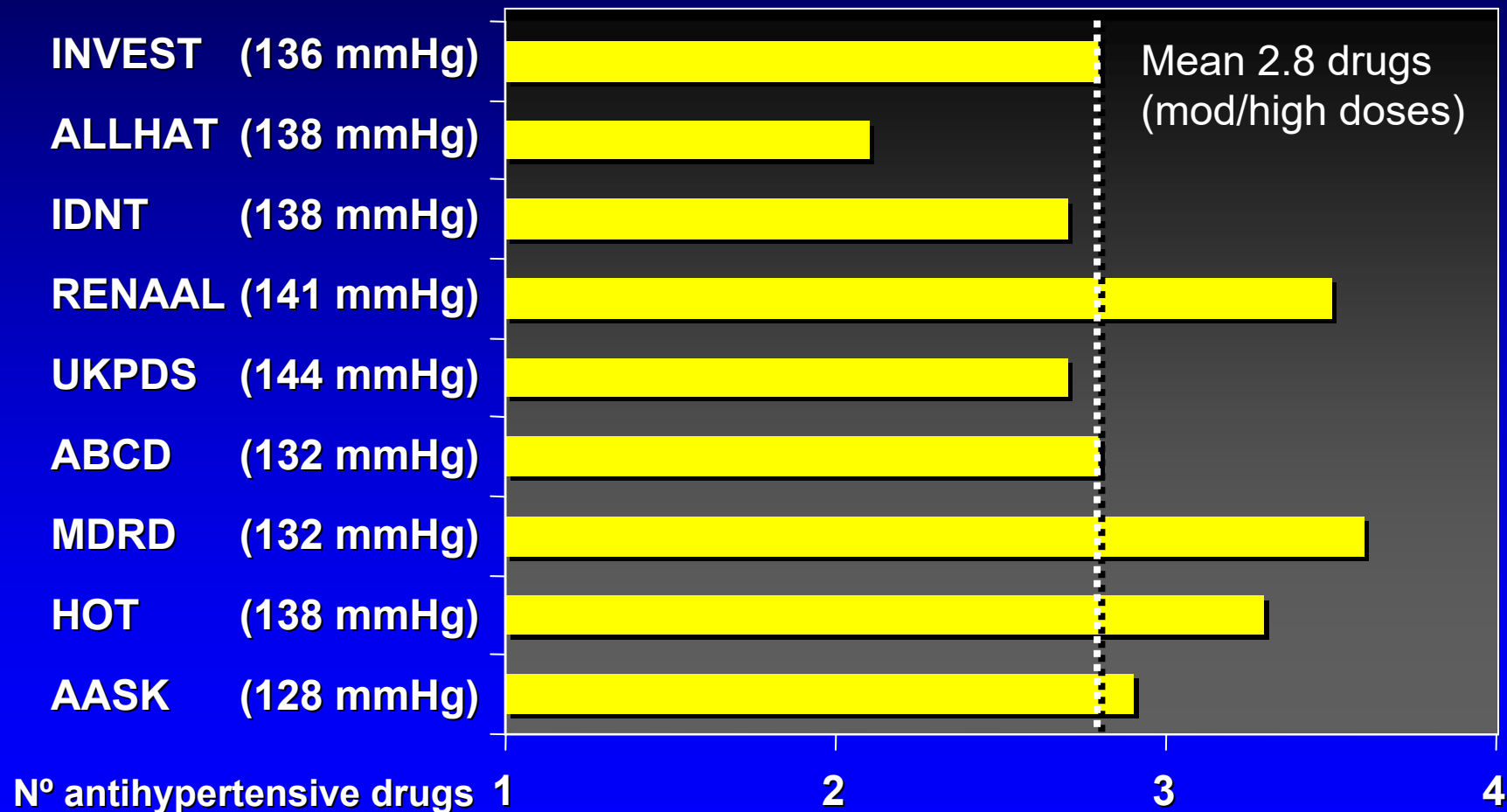
Blood Pressure Control in Hypertensive Patients Treated by GPs in Spain

Use of Combination Therapy



Number of Drugs to Achieve Target SBP

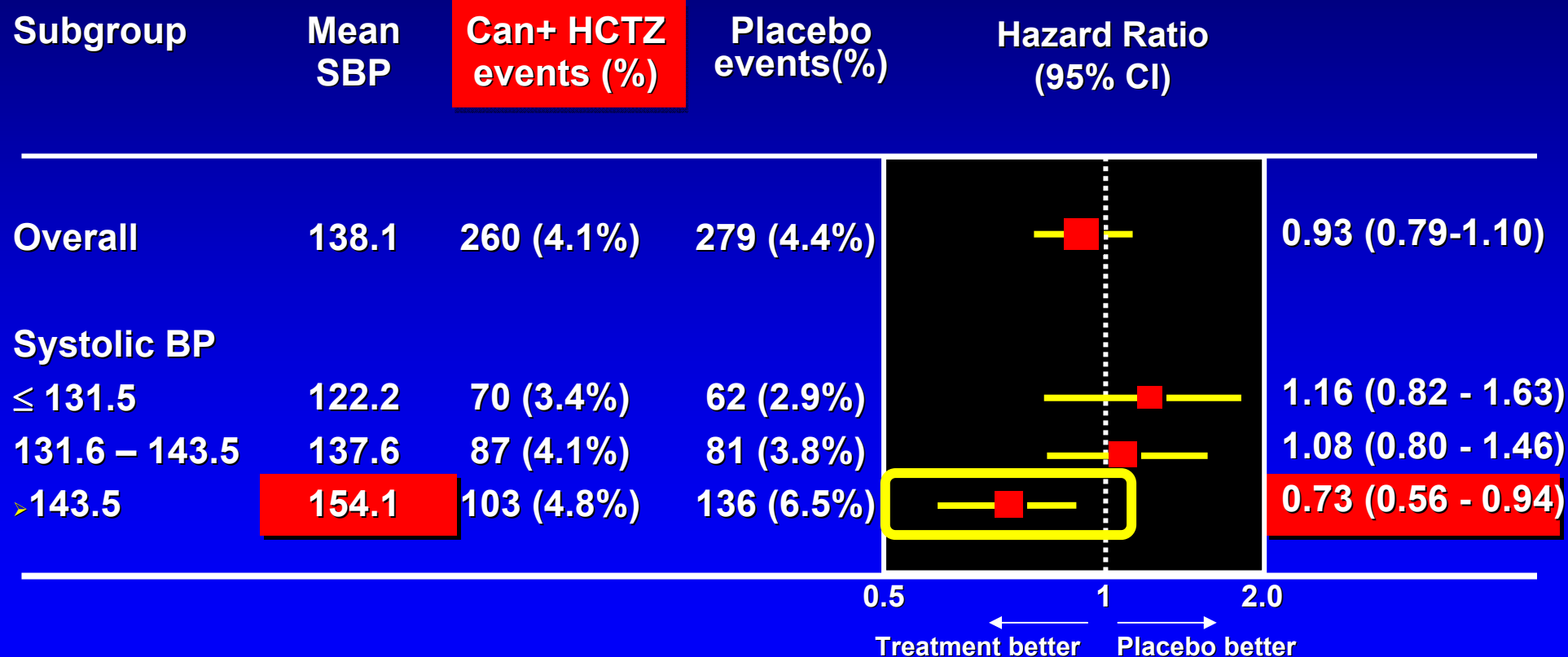
Trial/SBP Achieved



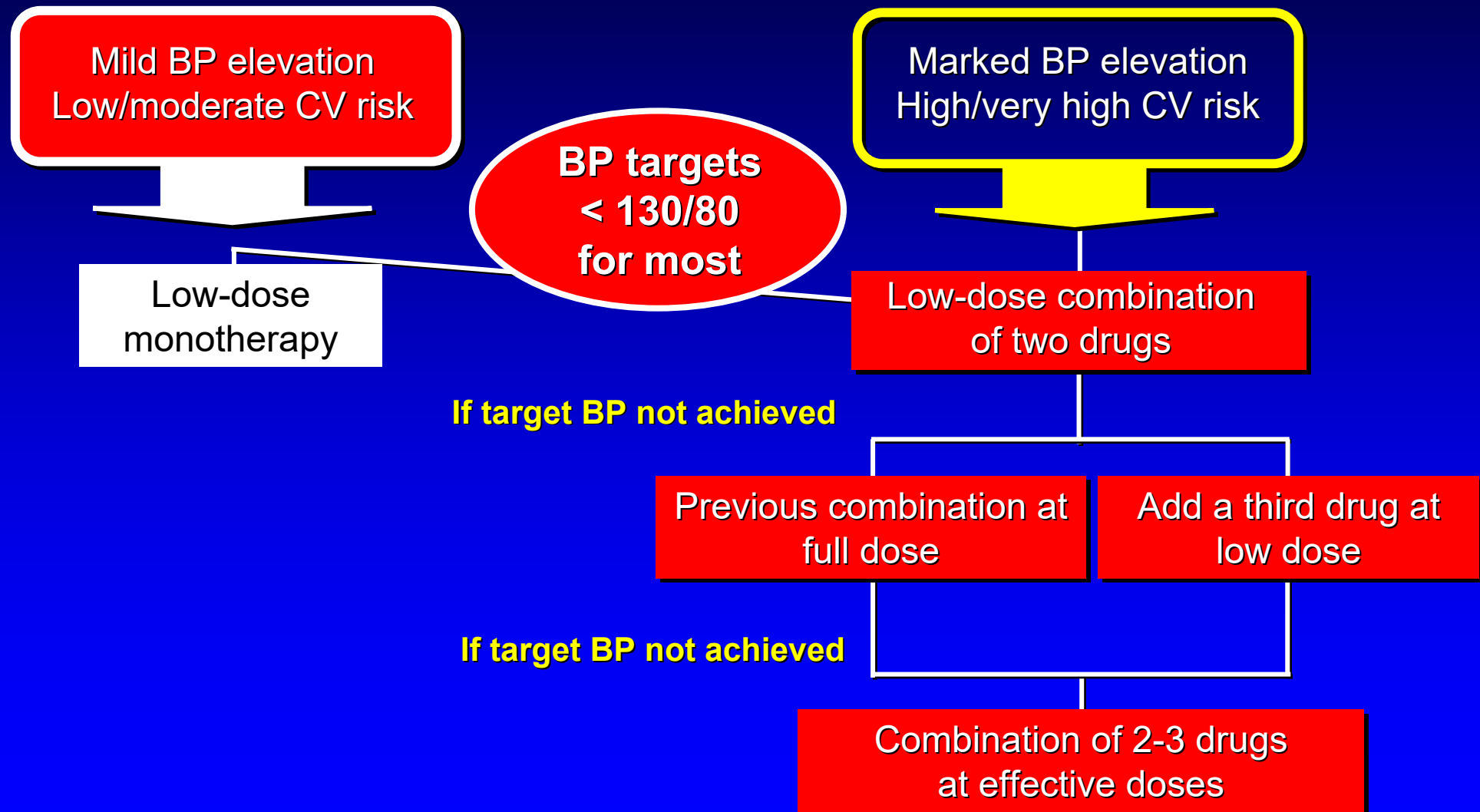
New Evidence in Low and Moderate CV Risk

HOPE - 3 Trial

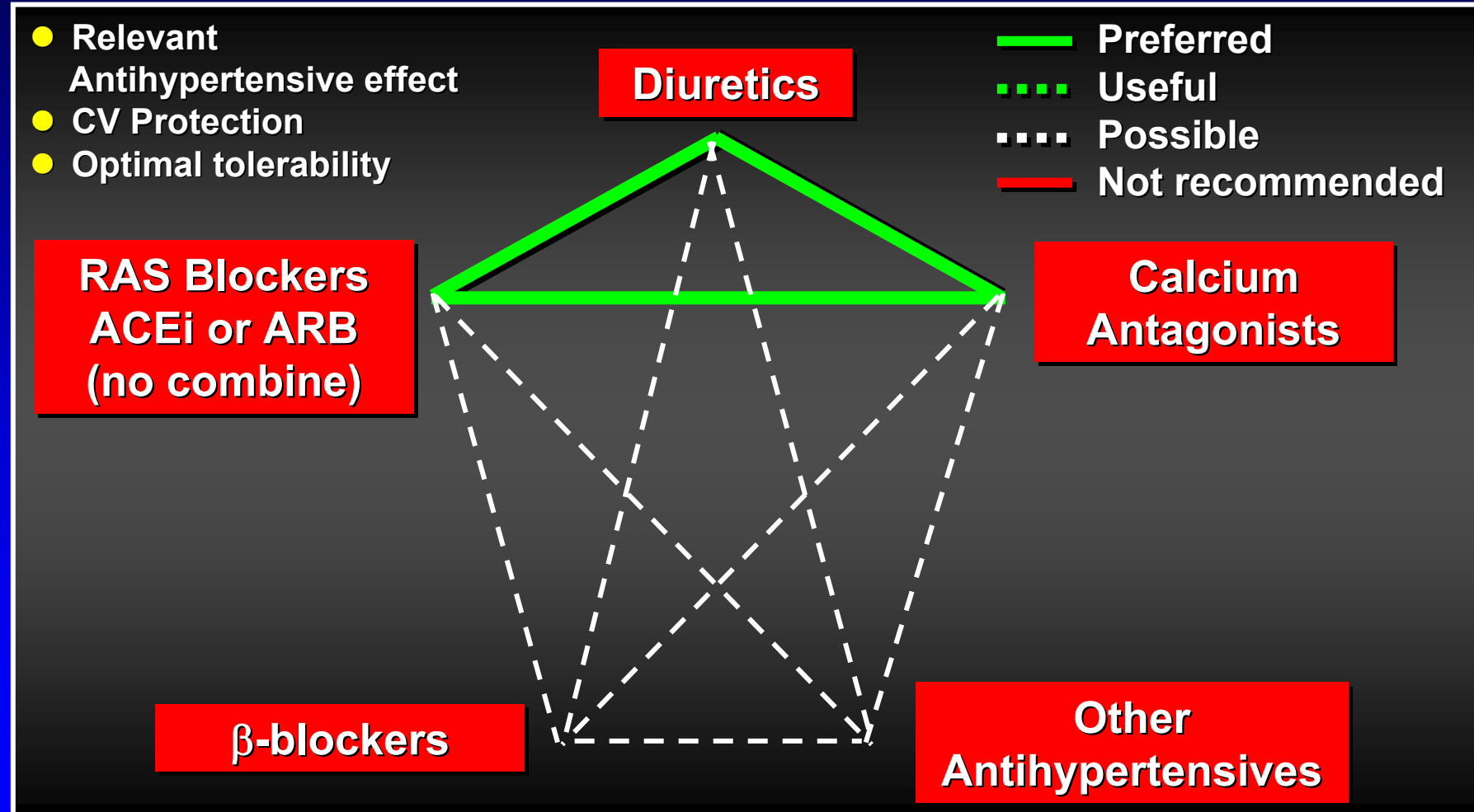
First Co-primary Outcome: composite of CV death, nonfatal MI, or nonfatal stroke



Treatment Strategies: The 2018 European Vision



Treatment Strategies: The 2018 European Vision



Fixed-dose Combination Therapy Increases Compliance with Treatment

Study

Clinical trials

Schweizer et al, 2007

Asplund et al, 1984

Subtotal (I-squared=45.6%, p=0.175)

Cohort studies

Taylor et al, 2003

Gerbino et al, 2004

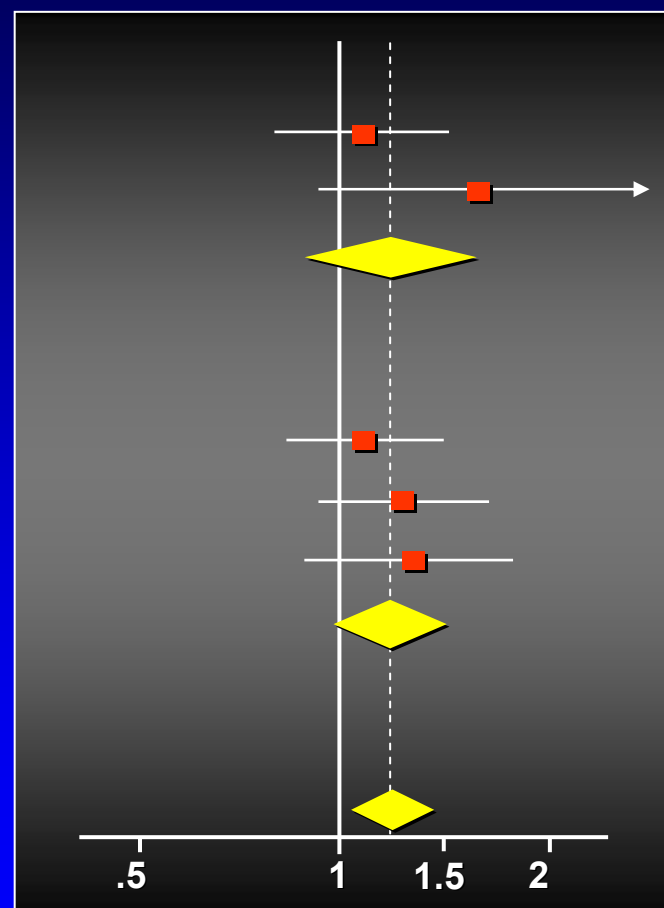
Dickson et al, 2008

Subtotal (I-squared=0.0%, p=0.740)

Heterogeneity between groups: p= 0.9

Total (I-squared=0.0%, p=0.655)

Antihypertensive drugs



OR (IC 95%)

1.08 (0.75 - 1.54)

1.74 (0.96 - 3.15)

1.22 (0.90 - 1.66)

1.09 (0.80 - 1.51)

1.28 (0.93 - 1.75)

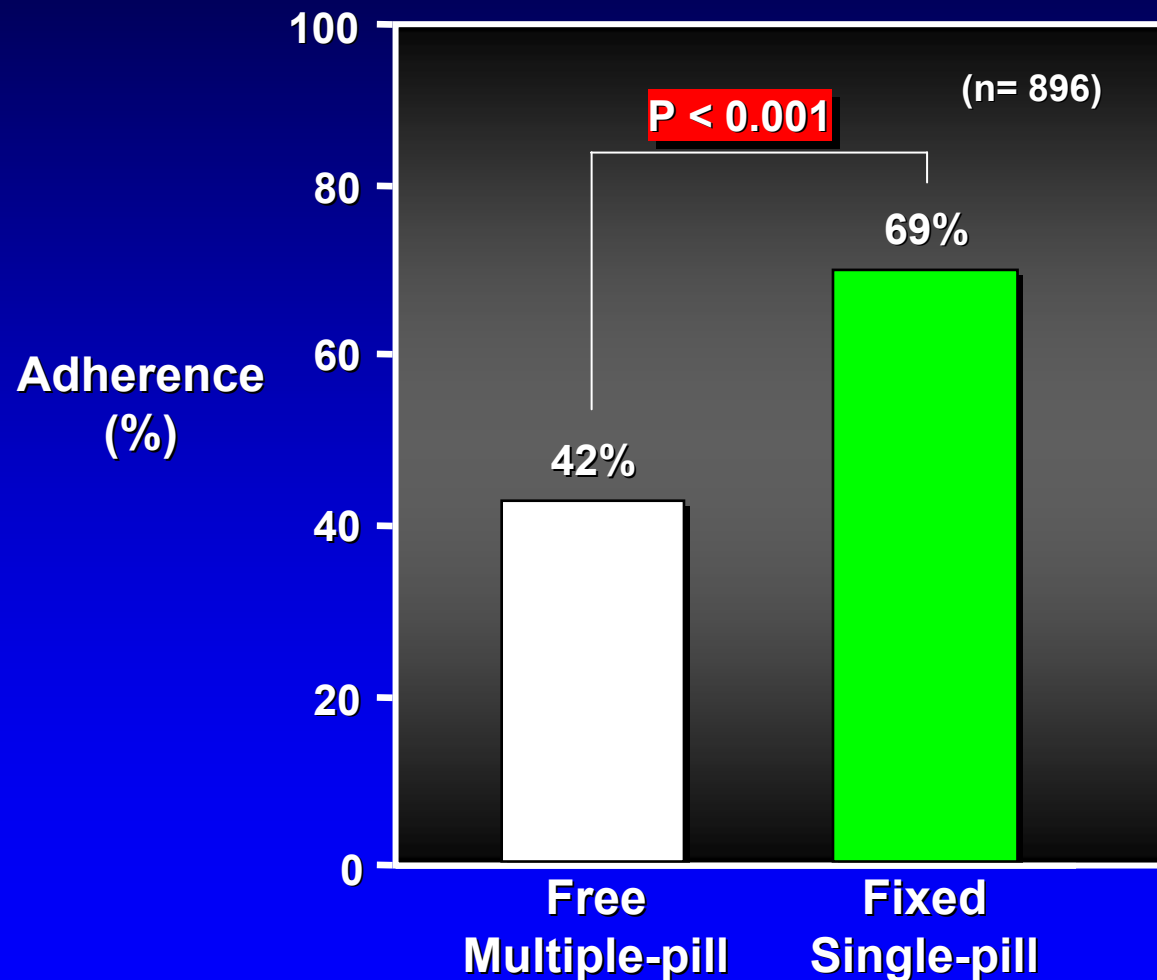
1.29 (0.89 - 1.89)

1.21 (1.00 - 1.47)

1.21 (1.03 - 1.43)

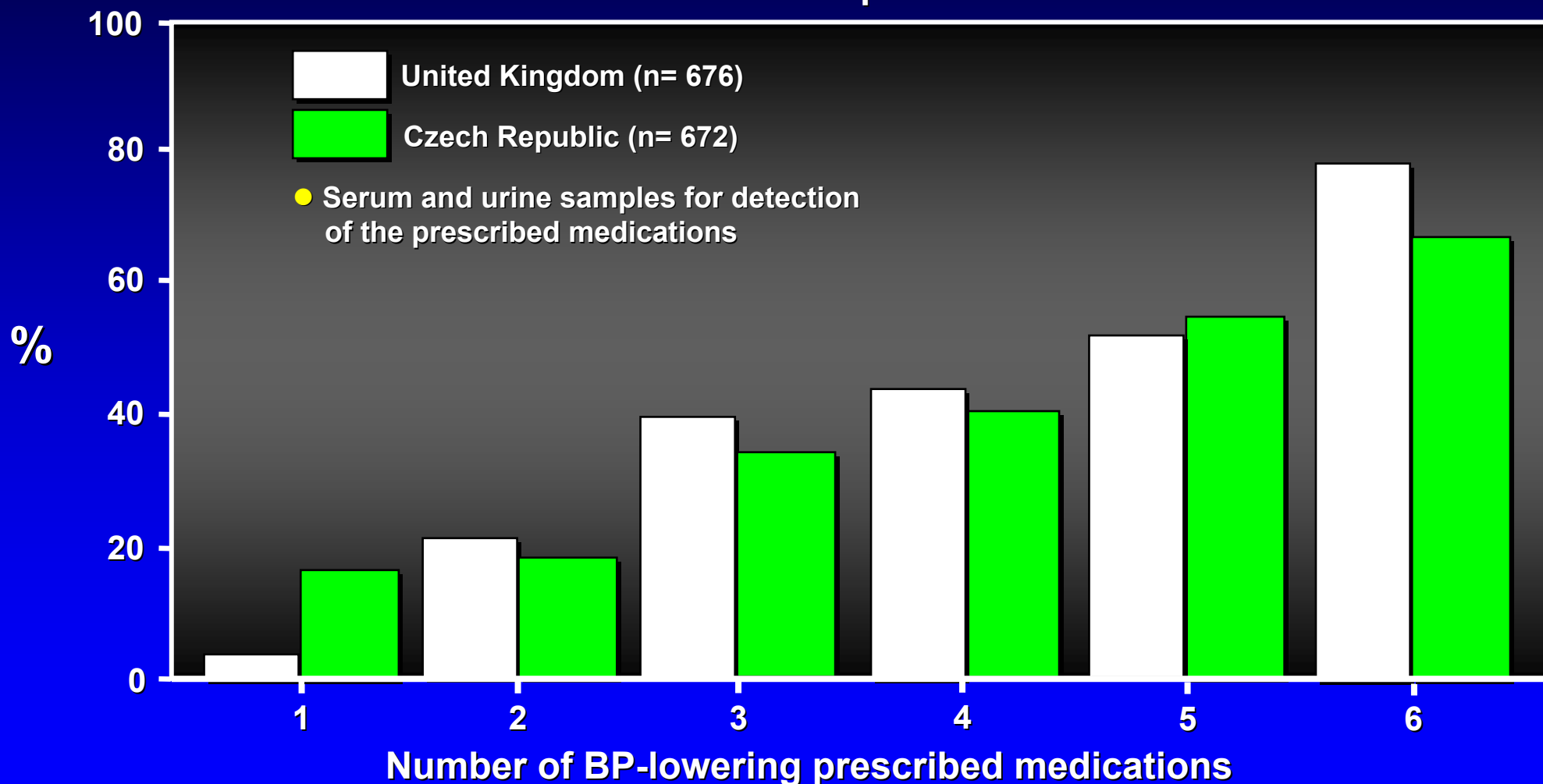
Favours ← → Favours
free-drug combinations fixed-dose combinations

Changes in Adherence to Treatment when Shifting from Free to Fixed Combinations



Number of Prescribed Antihypertensive Medications and the Risk of Nonadherence

Patients nonadherent to prescribed treatment



Adherence to Cardiovascular Therapy, and Mortality: Meta-analysis

Relative risks (RR) for all cause mortality in good ($\geq 80\%$) vs. poor ($< 80\%$) adherence to cardiovascular disease medications

	No. of studies	No. of participants	No. of deaths		RR (95% CI)
Adherence to statins	11	291,864	29,605		0.55 (0.46, 0.67)
Adherence to antihypertensive agents	11	205,598	12,288		0,71 (0.64, 0.78)
Adherence to aspirin	3	12,980	1573		0.45 (0.16, 1.29)
Adherence to any CVD medication	23	533,381	94,126		0.62 (0.57, 0.67)
				0,3 0,5 0,7 1 1,2	
				Good adherence Poor adherence	