

Nieuwigheden in de benadering van arteriële hypertensie

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2013 ESH/ESC guidelines for the management of arterial hypertension

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Overzicht

1. Definitie en classificatie
2. Epidemiologie
3. Risicostratificatie
4. Orgaanschade
5. Behandeling
6. Specifieke subgroepen

Overzicht

1. Definitie en classificatie

2. Epidemiologie

3. Risicofactoren

4. Orgaanschade

5. Behandeling

6. Specifieke subgroepen

Definitions and Classification of Office 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

The BP category is defined by the highest level of BP, whether systolic or diastolic.

Isolated systolic hypertension should be graded 1, 2, or 3 according to systolic BP values in the ranges indicated.

Office BP is the average of at least 2 BP measurements (with a validated device), spaced 1-2 min apart, after the patient has been sitting for 3-5 min, on at least 2 visits.

Definitions of hypertension by office and out-of-office blood pressure levels (mmHg)

Category	Systolic		Diastolic
Office BP	≥ 140	and/or	≥ 90
Ambulatory BP			
- Daytime (or awake)	≥ 135	and/or	≥ 85
- Nighttime (or asleep)	≥ 120	and/or	≥ 70
- 24-hour	≥ 130	and/or	≥ 80
Home BP	≥ 135	and/or	≥ 85

Diagnostic evaluation

ABPM: Derived variables

- Night-to-day BP ratio: ratio between average night-time BP and average day-time BP.
- Night-time dipping pattern:

Category	Night/day ratio
Absence of dipping	> 1.0
Mild dipping	$> 0.9 \text{ and } \leq 1.0$
Dipping	$> 0.8 \text{ and } \leq 0.9$
Extreme dipping	≤ 0.8

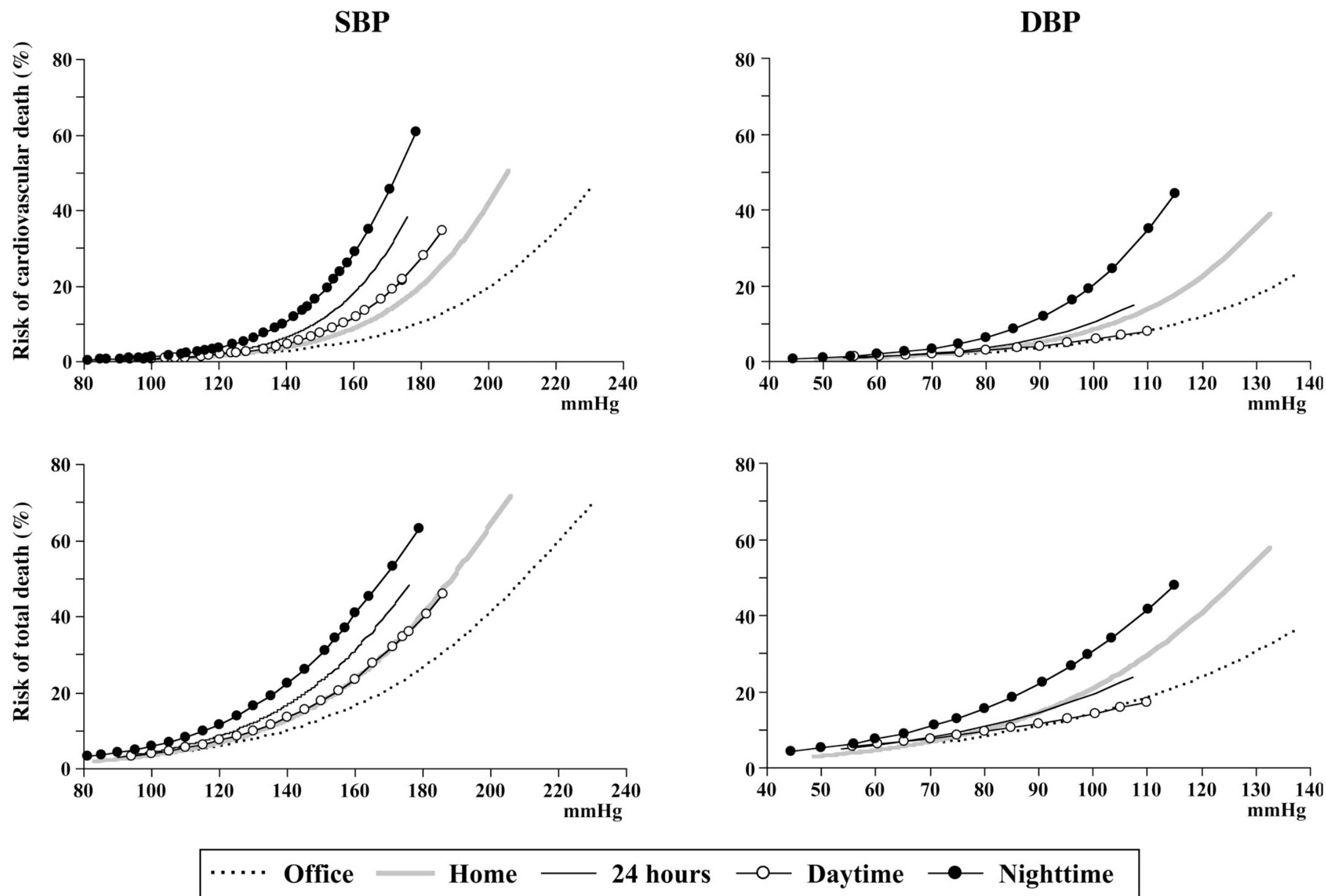
- Additional diagnostic indices such as BP variability, morning BP surge, BP load and ambulatory arterial stiffness index should be regarded as experimental with no routine clinical use, and are discussed in detail in ESH position papers and guidelines.

Diagnostic evaluation

HBPM: Methodological aspects

- The technique usually involves self-measurement of BP, but in some patients the support of a trained health provider or family member may be needed.
- BP should be measured daily on at least 3 to 4 days and preferably on 7 consecutive days.
- BP is measured twice in the morning and twice in the evening, after 5 min rest in the sitting position, and 1-2 min between measurements.
- Home BP is the average of these readings, with exclusion of the first monitoring day.

Figure 1. Office, home, 24-hour, daytime, and nighttime systolic (S) and diastolic (D) BP as predictors of 11-year risk of cardiovascular or all-cause deaths.



Sega R et al. Circulation. 2005;111:1777-1783



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Prediction of total mortality and all cardiovascular events from ambulatory blood pressure measurement at baseline in cohorts of hypertensive patients.

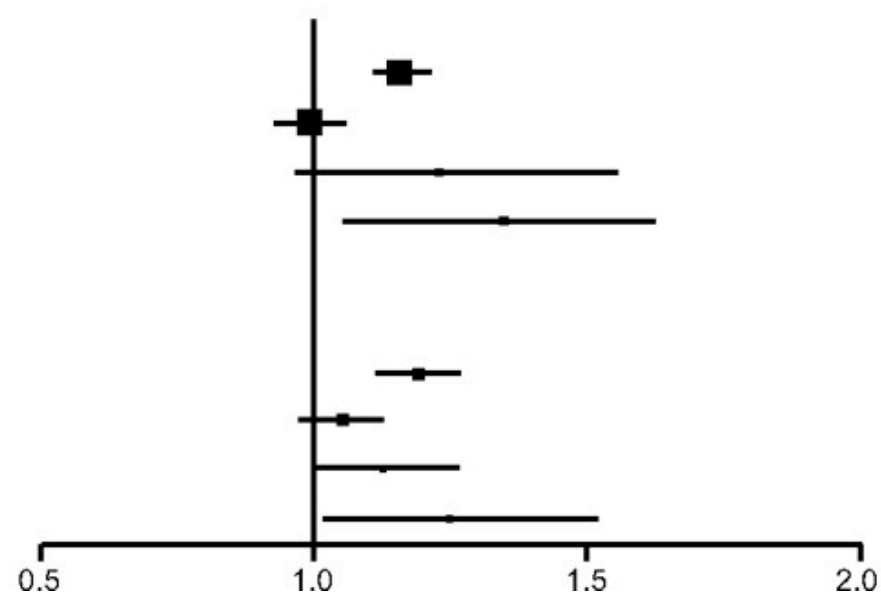
B Fully adjusted

Total mortality

Nighttime (+10 mm Hg)	5	1231/13566
Daytime (+10 mm Hg)	5	1231/13566
Night-to-day ratio (+0.1)	3	307/4111
Nondipping (0.1)	4	345/4686

Cardiovascular events

Nighttime (+10 mm Hg)	5	706/6212
Daytime (+10 mm Hg)	5	706/6212
Night-to-day ratio (+0.1)	2	442/3325
Nondipping (0.1)	2	422/3745



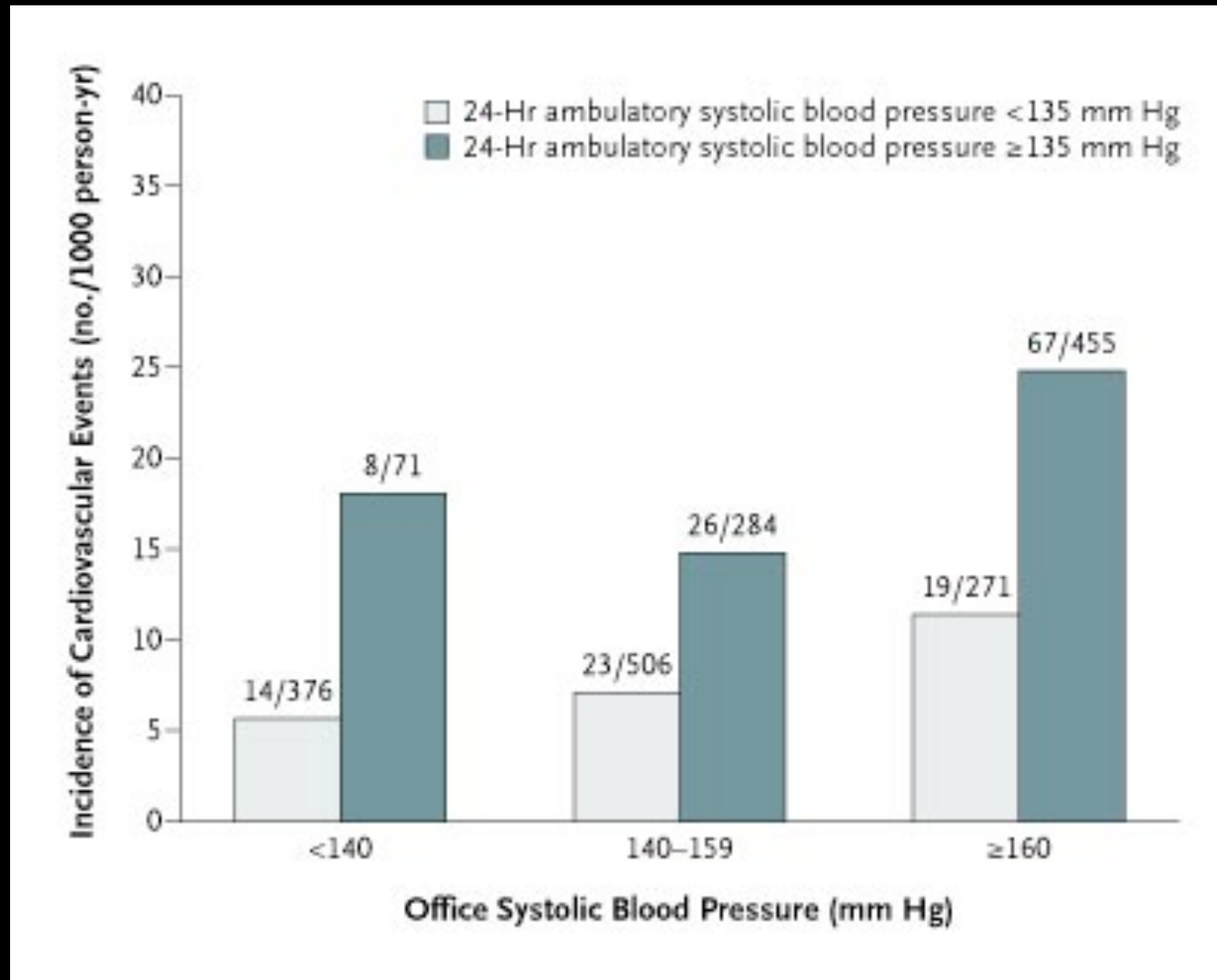
1.16 (1.12 - 1.22)	62.0	<0.001	<0.001
0.99 (0.93 - 1.06)	2.3	0.68	0.84
1.23 (0.96 - 1.57)	9.4	0.009	0.10
1.30 (1.06 - 1.60)	8.5	0.04	0.01
1.19 (1.12 - 1.27)	32.4	0.04	<0.001
1.06 (0.98 - 1.13)	5.4	0.35	0.13
1.13 (1.00 - 1.27)	4.1	0.04	0.04
1.25 (1.02 - 1.52)	4.7	0.03	0.03

Hansen T W et al. Hypertension. 2011;57:3-10



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Incidence of Cardiovascular Events According to Category of Office Systolic Blood Pressure



Clement, D. et al. N Engl J Med 2003;348:2407-2415



The NEW ENGLAND
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Diagnostic evaluation White-coat and masked hypertension

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Eur Heart J, 2013; 34: 2159-2219
J Hypertens, 2013; 31: 1281-1357
Blood Pressure, 2013: 193-278



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Definitions according to office BP and out-of-office BP (daytime ambulatory or home BP)

		Office BP (mmHg)	
		SBP <140 and DBP <90	SBP ≥140 or DBP ≥90
Daytime ABP or home BP (mmHg)	SBP <135 and DBP <85	True normotension (NT)	White-coat hypertension (WCHT)
	SBP ≥135 or DBP ≥85	Masked hypertension (MHT)	Sustained hypertension (SHT)

Diagnostic evaluation

WCHT: Prevalence and determinants

- Based on population-based studies, the overall prevalence of WCHT averages about 13% (range: 9-16%) in the population and about 32% (range: 25-46%) among hypertensive patients in these surveys.
- Factors related to the prevalence of WCHT:
 - **higher prevalence:** older age, female gender, non-smoking, no organ damage, grade 1 hypertension,
 - **lower prevalence:** repeated office BP measurements, measurements by a nurse or another healthcare provider, grade 3 hypertension.
- It is recommended that the diagnosis of WCHT be confirmed within 3 to 6 months.

Diagnostic evaluation

WCHT: Organ damage and prognosis

- The prevalence of organ damage and the incidence of CV events is lower than in sustained hypertension.
- Meta-analyses concluded that prognosis is not significantly different from true normotension after adjustment for age, gender and other covariates.
- However, other factors to consider are that, compared with true normotension, out-of-office BP is higher, organ damage and metabolic risk factors may be more frequent, and the risk of new-onset diabetes and progression to sustained hypertension may be increased.

Diagnostic evaluation

Masked HT: Prevalence, determinants, organ damage and prognosis

- Based on population-based studies, the overall prevalence of masked hypertension averages about 13% (range: 10-17%).
- Factors related to the higher prevalence of masked HT: younger age, male gender, smoking, alcohol consumption, exercise-induced hypertension, physical activity, anxiety, job stress, obesity, diabetes, chronic kidney disease, family history of hypertension, high normal BP.
- The condition is frequently associated with other risk factors, organ damage, increased risk of diabetes and sustained hypertension.
- Meta-analyses indicate that the incidence of CV events is about two times higher than in true normotension and is similar to the incidence in sustained hypertension.

Overzicht

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3. Risicostratificatie

4. Orgaanschade

5. Behandeling

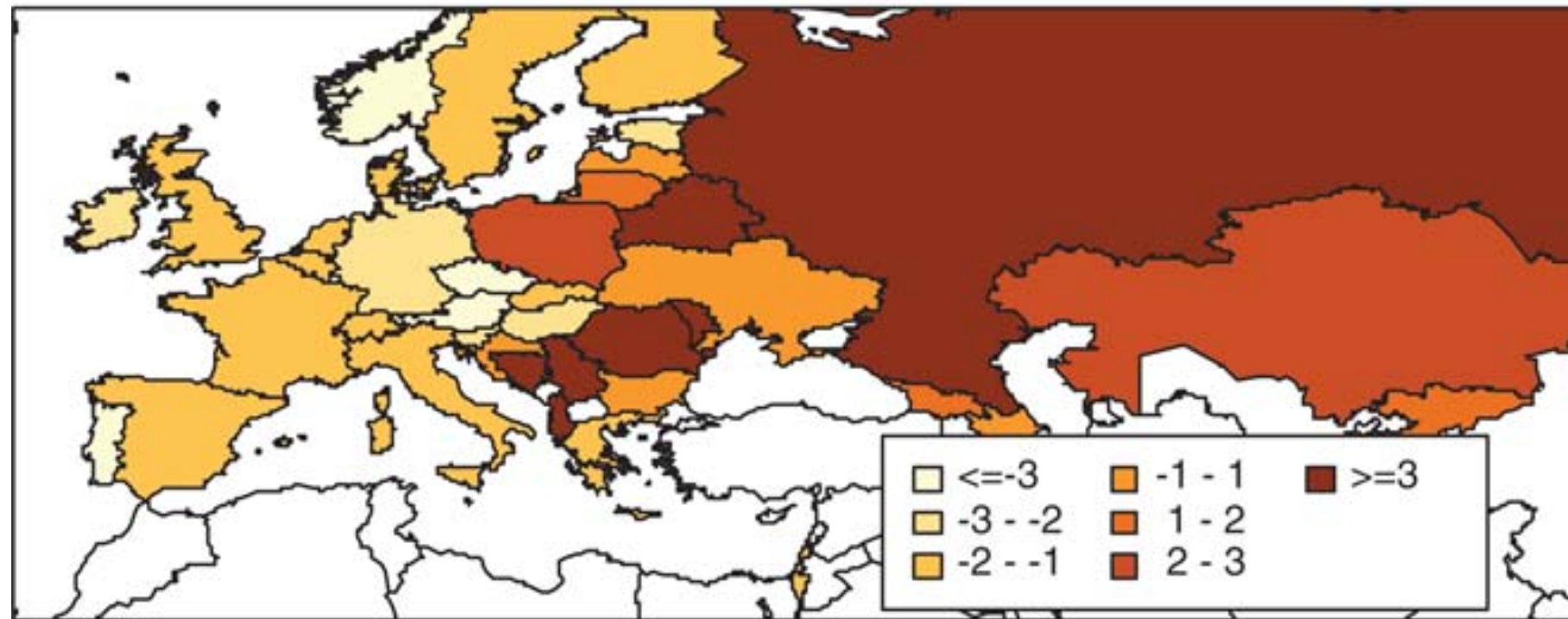
6. Specifieke subgroepen

Epidemiological aspects

- Based on 21 reports from the last decade the prevalence of hypertension appears to be around 30-45% of the general population, with a steep increase with ageing.
- There also appear to be noticeable differences in the average BP levels across countries with no systematic trends towards BP changes in the last decade.
- However, it is difficult to obtain comparable results on BP among countries and over time, and therefore the use of a surrogate of hypertension status, such as stroke mortality, has been suggested.
- Based on WHO statistics, western European countries exhibit a downward trend in stroke mortality, whereas eastern European countries show a clear-cut increase.

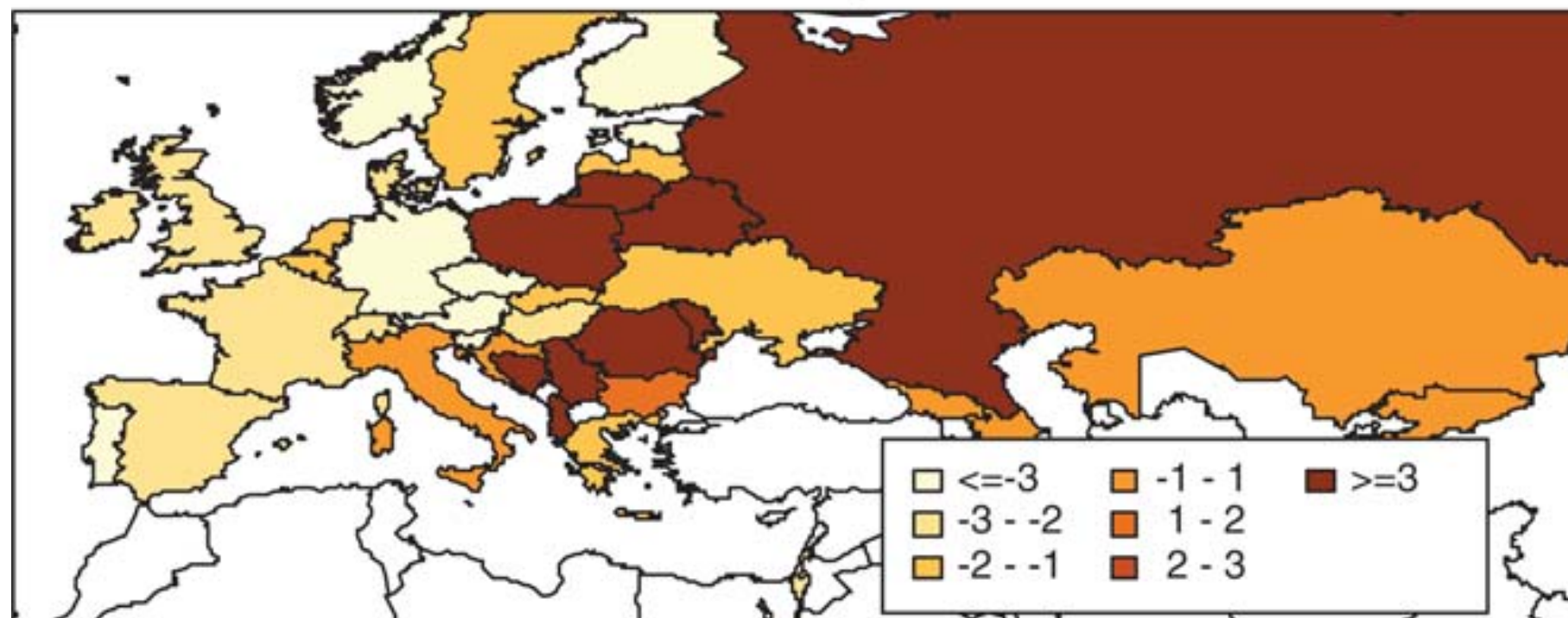
Stroke mortality and trends in Europe and Central Asia

Annual variation of the rate per 100 000 men



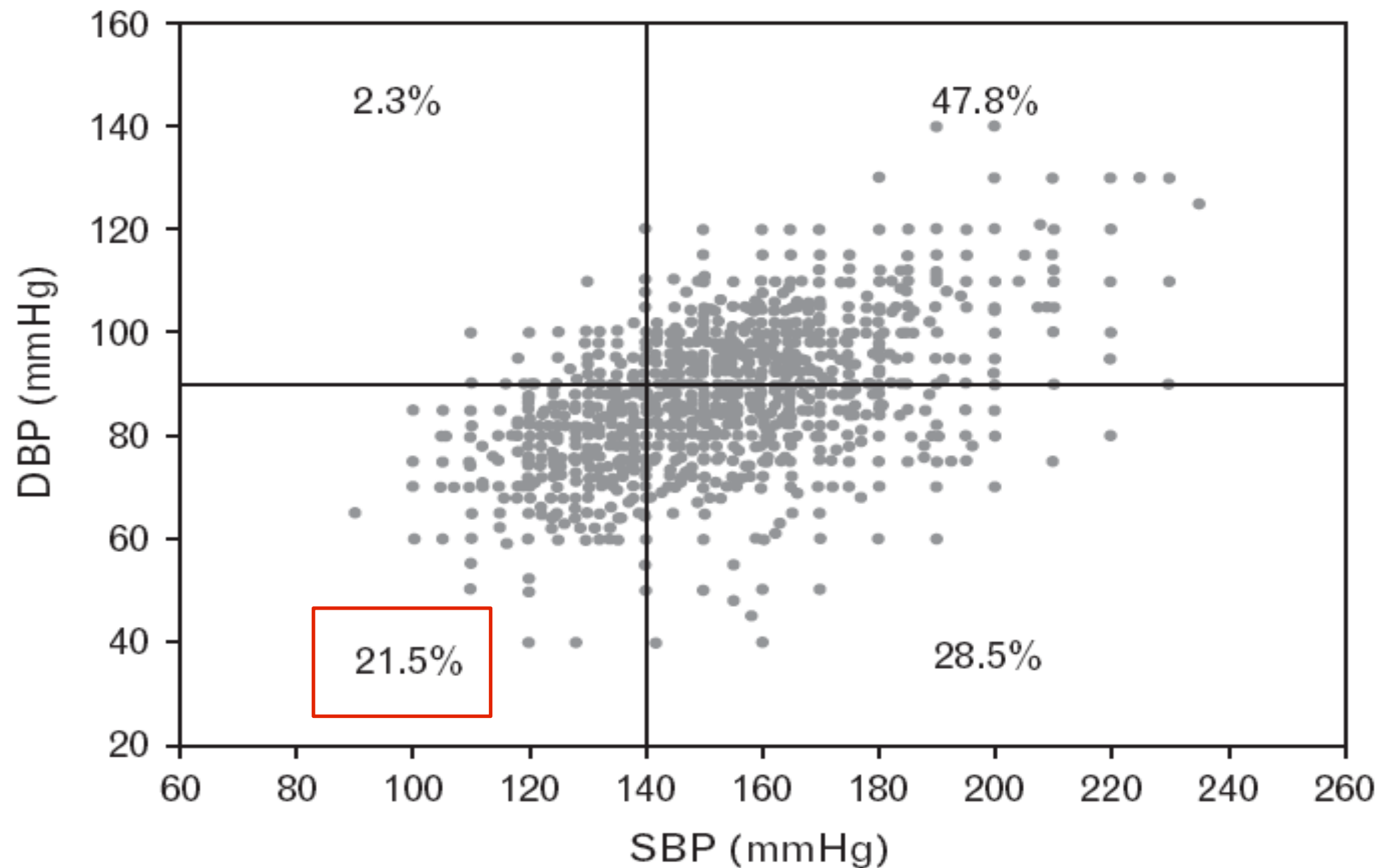
Belgian men
-2/100.000/jaar
Lithuanian men
+2/100.000/jaar

Annual variation of the rate per 100 000 women



Belgian women
-2/100.000/jaar
Lithuanian women
+ ≥3/100.000/jaar

Blood pressure distribution in Belgium : room for improvement

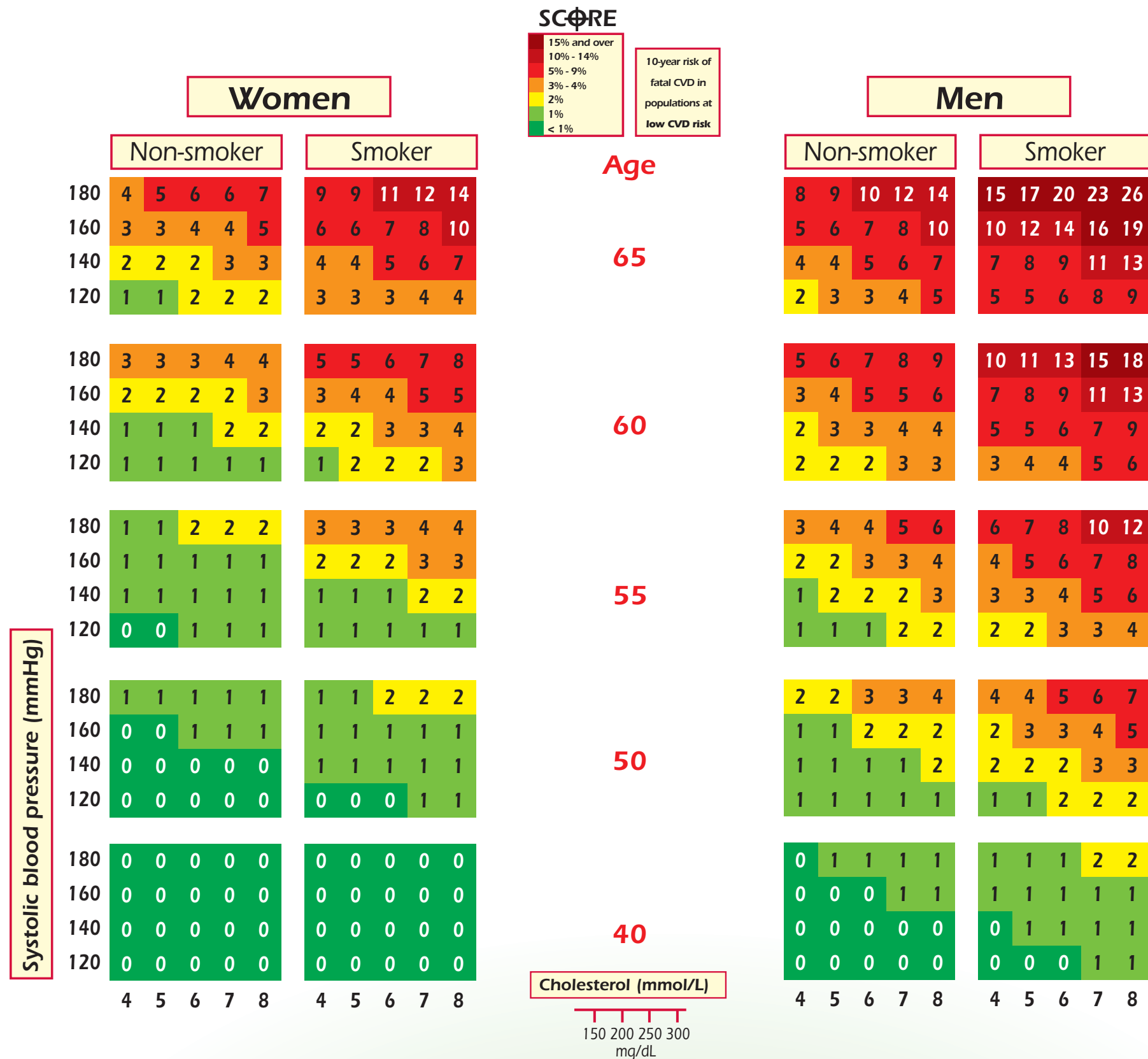


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SCORE - European Low Risk Chart

10 year risk of fatal CVD in low risk regions of Europe by gender, age, systolic blood pressure, total cholesterol and smoking status



Total cardiovascular risk stratification

Other risk factors (RF), asymptomatic organ damage (OD) or disease	Blood Pressure (mmHg)			
	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 RF		Low risk	Moderate risk	High risk
1-2 RF	Low risk	Moderate risk	Moderate to High risk	High risk
≥ 3 RF	Low to moderate risk	Moderate to high risk	High risk	High risk
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

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Total cardiovascular risk stratification

- **Factors other than blood pressure influencing prognosis:**
 - other cardiovascular risk factors,
 - asymptomatic organ damage,
 - presence of diabetes mellitus,
 - symptomatic cardiovascular disease or chronic kidney disease.

Total cardiovascular risk stratification

Risk factors

- Male sex.
- Age (≥ 55 yrs in men; ≥ 65 yrs in women).
- Smoking.
- Dyslipidaemia:
 - TC >4.9 mmol/L (190 mg/dL), and/or
 - LDL-C >3.0 mmol/L (115 mg/dL), and/or
 - HDL-C <1.0 mmol/L (40 mg/dL) in men; <1.2 mmol/L (46 mg/dL) in women, and/or
 - TG >1.7 mmol/L (150 mg/dL)
- Fasting plasma glucose 5.6-6.9 mmol/L (102-125 mg/dL).
- Abnormal glucose tolerance test.
- Obesity (BMI ≥ 30 kg/m²).
- Abdominal obesity: waist circumference ≥ 102 cm in men; ≥ 88 cm in women (in Caucasians).
- Family history of premature CV disease (<55 yrs in men; <65 yrs in women).

Total cardiovascular risk stratification

Asymptomatic organ damage

- Pulse pressure ≥ 60 mmHg (in the elderly).
- Electrocardiographic LVH (Sokolow-Lyon index >3.5 mV; RaVL >1.1 mV; Cornell voltage duration product >244 mm*ms), or
- Echocardiographic LVH (LVM index >115 g/m² in men; >95 g/m² in women).
- Carotid wall thickening (IMT >0.9 mm) or plaque.
- Carotid-femoral pulse wave velocity >10 m/s.
- Ankle-brachial index <0.9 .
- Chronic kidney disease stage 3 (eGFR: 30-60 mL/min/1.73 m²).
- Microalbuminuria (30-300 mg/24 h), or albumin-creatinine ratio (30-300 mg/g or 3.4-34 mg/mmol) (preferentially on morning spot urine).

Total cardiovascular risk stratification

Diabetes mellitus

- Fasting plasma glucose ≥ 7.0 mmol/L (126 mg/dL) on two repeated measurements, and/or
- HbA_{1c} $> 7\%$ (53 mmol/mol), and/or
- Post-load plasma glucose > 11.0 mmol/L (198 mg/dL).

Total cardiovascular risk stratification

Established CV or renal disease

- Cerebrovascular disease: ischaemic stroke; cerebral haemorrhage; transient ischaemic attack.
- Coronary heart disease: angina; myocardial infarction; revascularization with PCI or CABG.
- Heart failure, including heart failure with preserved ejection fraction.
- Symptomatic lower extremities peripheral artery disease.
- Chronic kidney disease stage 4 (eGFR <30 mL/min/1.73 m²).
- Proteinuria >300 mg/24 h.
- Advanced retinopathy: haemorrhages or exudates, papilloedema.

Total cardiovascular risk stratification

Other risk factors (RF), asymptomatic organ damage (OD) or disease	Blood Pressure (mmHg)			
	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 RF		Low risk	Moderate risk	High risk
1-2 RF	Low risk	Moderate risk	Moderate to High risk	High risk
≥ 3 RF	Low to moderate risk	Moderate to high risk	High risk	High risk
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

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Initiation of lifestyle changes and antihypertensive drug treatment based on total CV risk

Other risk factors (RF), asymptomatic organ damage (OD) or disease	Blood Pressure (mmHg)			
	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 RF	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting $<140/90$	• Lifestyle changes for several weeks • Then add BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$
1-2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting $<140/90$	• Lifestyle changes for several weeks • Then add BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$
≥ 3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting $<140/90$	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$
Symptomatic CVD, CKD stage ≥ 4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$

(In patients with diabetes, the optimal diastolic BP target is 80-85 mmHg)

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Treatment strategies Lifestyle changes

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Treatment strategies

Lifestyle changes

- Appropriate lifestyle changes are the cornerstone for the prevention of hypertension and are also important for its treatment.
- They may safely and effectively delay or prevent hypertension in non-hypertensive subjects, delay or prevent medical therapy in grade I hypertension and contribute to BP reduction in hypertensive individuals already on antihypertensive drug therapy.
- Beside the BP-lowering effect, they contribute to the control of other CV risk factors and clinical conditions.
- The major drawback is the low level of adherence over time, which requires special action to be overcome.

Recommendations on lifestyle changes

Are recommended	Class	LoE ^a	LoE ^b
Salt restriction to 5-6 g per day.	I	A	B
Moderation of alcohol consumption to no more than 20-30 g of ethanol per day in men and 10-20 g of ethanol per day in women.	I	A	B
Increased consumption of vegetables, fruits, and low-fat dairy products.	I	A	B
Reduction of weight to BMI of 25 kg/m ² and of waist circumference to <102 cm in men and <88 cm in women, unless contraindicated.	I	A	B
Regular exercise, i.e. at least 30 min of moderate dynamic exercise on 5 to 7 days per week.	I	A	B
Advice to quit smoking and to offer assistance to all smokers.	I	A	B

^a LoE: based on the effect on BP and/or CV risk profile

^b LoE: based on outcome studies

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Treatment strategies

Initiation of antihypertensive drug treatment

*‘The initiation of antihypertensive drug treatment is based
on the initial level of total cardiovascular risk’*

Initiation of lifestyle changes and antihypertensive drug treatment based on total CV risk

Other risk factors (RF), asymptomatic organ damage (OD) or disease	Blood Pressure (mmHg)			
	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 RF	• No BP intervention	• Lifestyle changes for several months • Then add BP drugs targeting $<140/90$	• Lifestyle changes for several weeks • Then add BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$
1-2 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting $<140/90$	• Lifestyle changes for several weeks • Then add BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$
≥ 3 RF	• Lifestyle changes • No BP intervention	• Lifestyle changes for several weeks • Then add BP drugs targeting $<140/90$	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$
OD, CKD stage 3 or diabetes	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$
Symptomatic CVD, CKD stage ≥ 4 or diabetes with OD/RFs	• Lifestyle changes • No BP intervention	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • BP drugs targeting $<140/90$	• Lifestyle changes • Immediate BP drugs targeting $<140/90$

(In patients with diabetes, the optimal diastolic BP target is 80-85 mmHg)

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Treatment strategies Blood pressure goals

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Blood pressure goals in hypertensive patients*

Recommendations	Class	Level
A systolic BP goal of <140 mmHg:		
a) is recommended in patients at low-moderate CV risk,	I	B
b) is recommended in patients with diabetes,	I	A
c) should be considered in patients with previous stroke or TIA,	Ila	B
d) should be considered in patients with coronary heart disease,	Ila	B
e) should be considered in patients with diabetic or non-diabetic chronic kidney disease.	Ila	B
A diastolic BP target of <90 mmHg is always recommended, except in patients with diabetes, in whom values <85 mmHg are recommended. It should nevertheless be considered that DBP values between 80 and 85 mmHg are safe and well tolerated.	I	A

*See dedicated section for recommendations in special conditions and populations

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Treatment strategies

- Choice of drugs
- Monotherapy vs combination therapy

Recommendations on treatment strategies and choice of drugs (1)

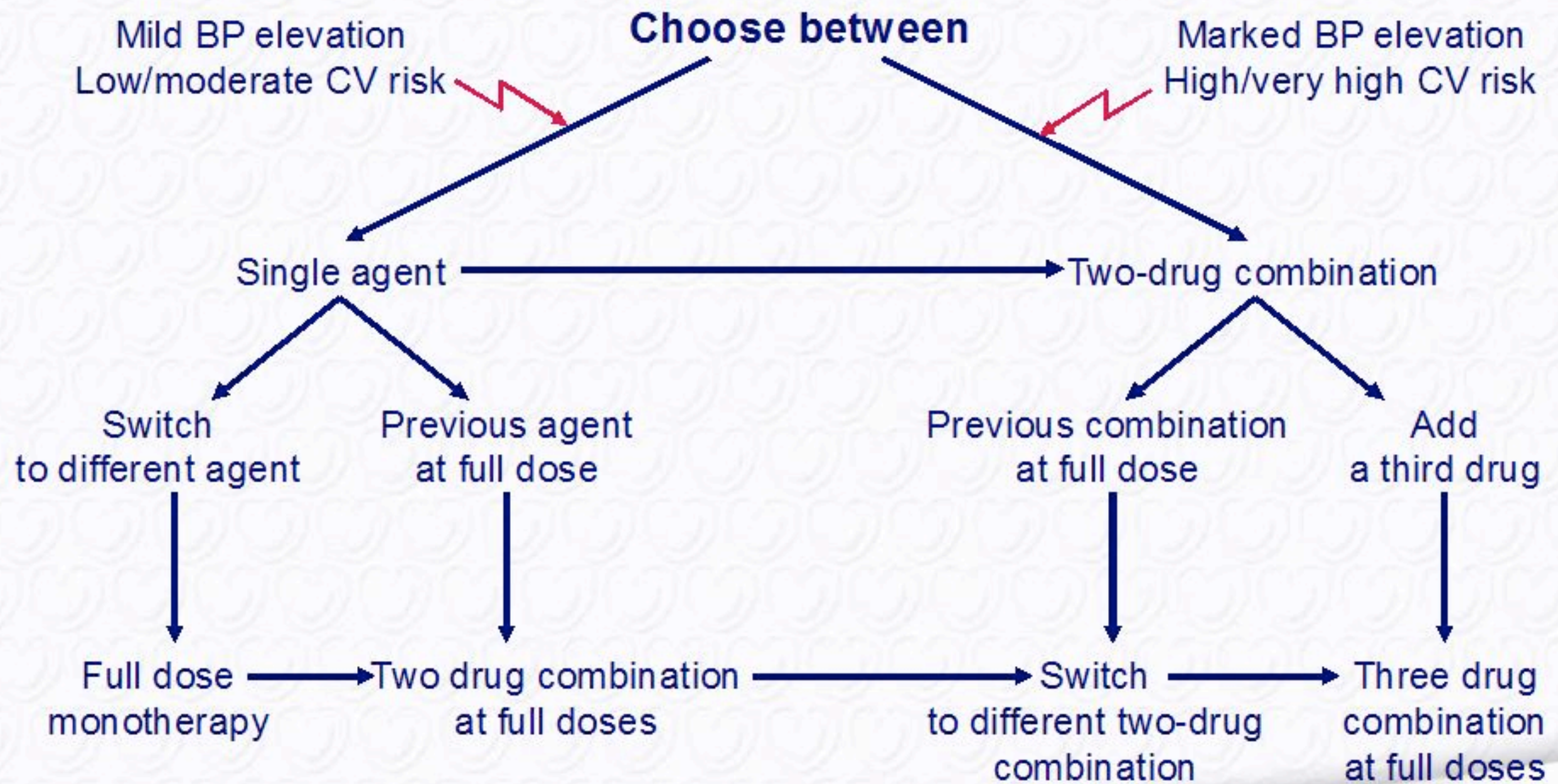
Recommendations	Class	Level
Diuretics (thiazides, chlorthalidone and indapamide), beta-blockers, calcium antagonists, ACE inhibitors, and angiotensin receptor blockers are all suitable and recommended for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combination with each other.	I	A
Some agents should be considered as the preferential choice in specific conditions because used in trials in those conditions or because of greater effectiveness in specific types of organ damage.	Ila	C

Recommendations on treatment strategies and choice of drugs (2)

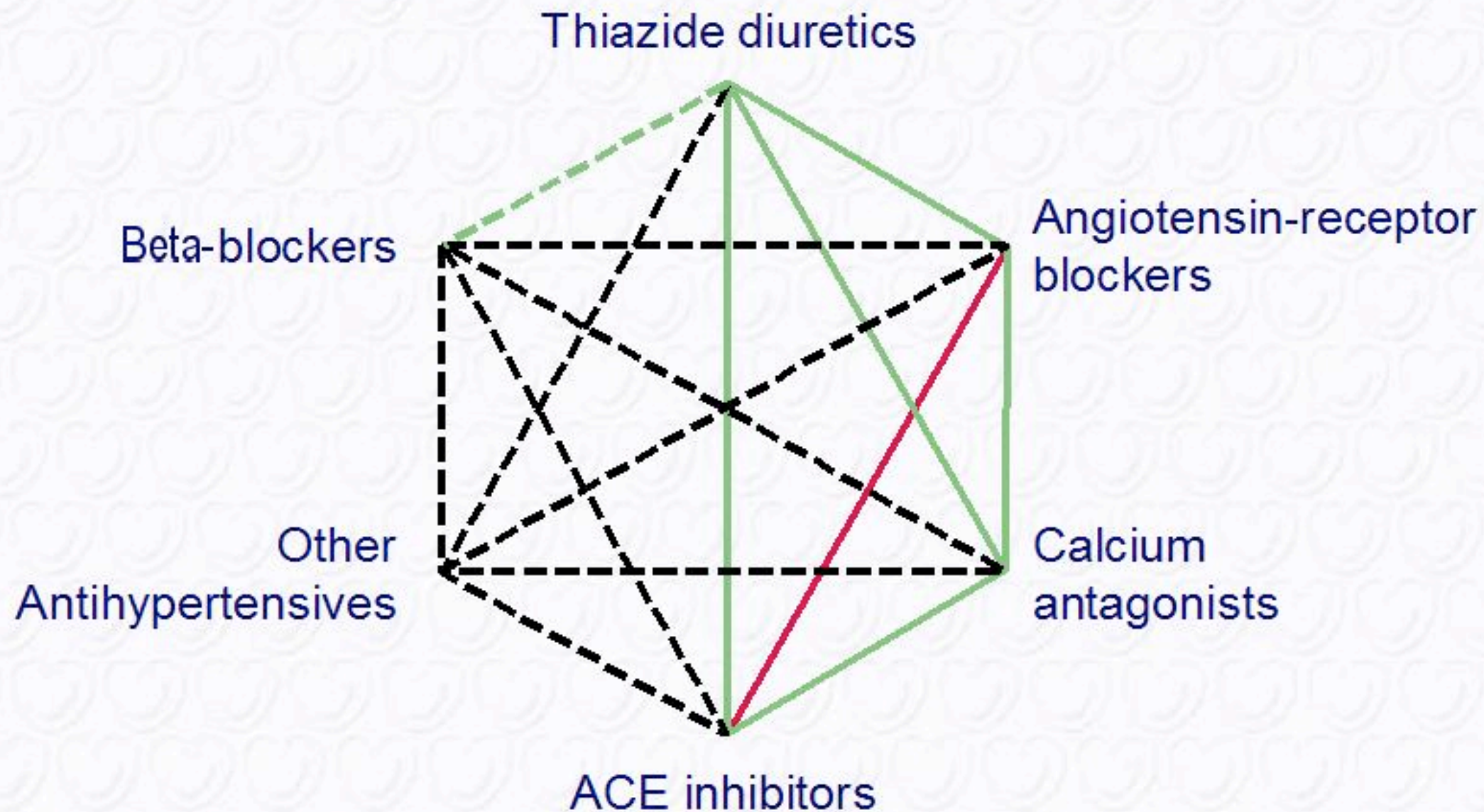
Recommendations	Class	Level
Initiation of antihypertensive therapy with a two-drug combination may be considered in patients with markedly high baseline BP or at high CV risk.	IIb	C
The combination of two antagonists of the renin-angiotensin system is not recommended and should be discouraged.	III	A
Other drug combinations should be considered and probably are beneficial in proportion to the extent of BP reduction. However, combinations that have been successfully used in trials may be preferable.	IIa	C
Combinations of two antihypertensive drugs at fixed doses in a single tablet may be recommended and favoured, because reducing the number of daily pills improves adherence, which is low in patients with hypertension.	IIb	B

Monotherapy vs drug combination therapy

Moving from a less intense to a more intense therapeutic strategy to achieve target blood pressure

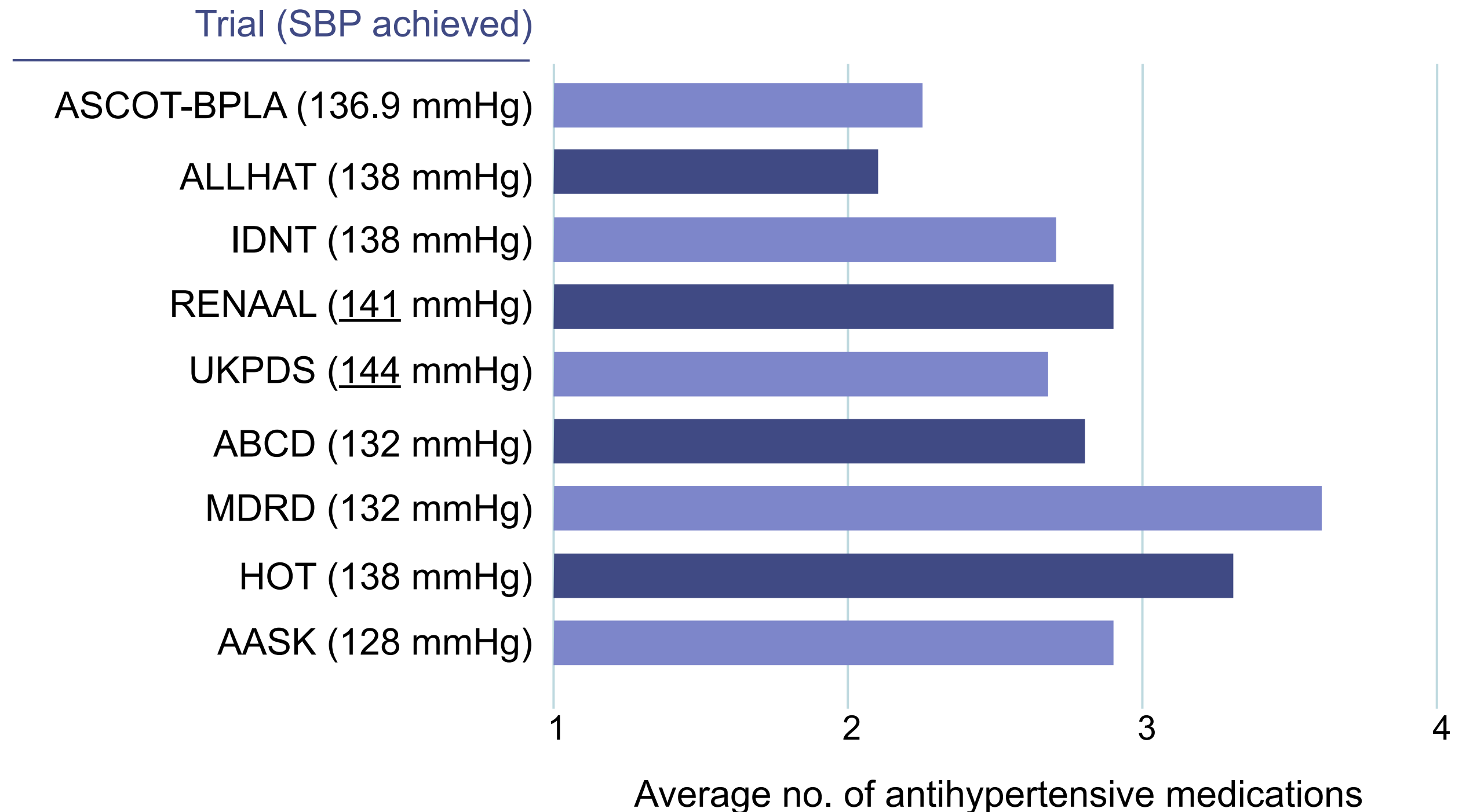


Possible combinations of classes of antihypertensive drugs



Green continuous lines: preferred. **Green dashed lines:** useful combinations with some limitations
Black dashed line: possible combinations (only DHP calcium antagonists should normally be combined with beta-blockers)
Red continuous line: not recommended combination

Multiple Antihypertensive Agents are Needed to Reach BP Goal



Bakris et al. Am J Med 2004;116(5A):30S–8
Adapted from Dahlöf et al. Lancet 2005;366:895–906

Compelling and possible contra-indications to the use of antihypertensive drugs

Drug	Compelling	Possible
Thiazide diuretics	Gout	Metabolic syndrome, Glucose intolerance, Pregnancy, Hypercalcaemia, Hypokalaemia
Beta-blockers	Asthma A-V block (grade 2 or 3)	Metabolic syndrome, Glucose intolerance, Athletes and physically active patients, Chronic obstructive pulmonary disease (except for vasodilator beta-blockers)
Calcium antagonists (dihydropiridines)		Tachyarrhythmias, Heart failure
Calcium antagonists (verapamil, diltiazem)	A-V block (grade 2 or 3) Severe LV dysfunction Heart failure	
ACE inhibitors	Pregnancy Angioneurotic oedema Hyperkalaemia Bilateral renal artery stenosis	Women with childbearing potential
Angiotensin receptor blockers	Pregnancy, Hyperkalaemia Bilateral renal artery stenosis	Women with child bearing potential
Mineralocorticoid receptor antagonists	Acute or severe renal failure (eGFR <30 mL/min) Hyperkalaemia	

Conditions favouring the use of some antihypertensive drugs versus others

■ Subclinical Organ Damage

- LVH: ACEI, CA, ARB
- Asympt. ath.scl.: CA, ACEI
- Microalbuminuria: ACEI, ARB
- Renal dysfunction: ACEI, ARB

■ Condition

- ISH (elderly): diur, CA
- Met Syndr: ACE, ARB, CA
- DM: ACEI, ARB
- Pregn: CA, methyldopa, BB
- Black: diur, CA
- Glaucoma: BB
- ACEI induced cough: ARB

■ Clinical Event

- Previous stroke: any
- Previous MI: BB, ACEI, ARB
- Angina pectoris: BB, CA
- Heart Failure: diur, BB, ACEI, ARB, ant-aldost
- AFIB recurr: ARB, ACEI
- AFIB perm: BB, nondihydropir CA
- Tachyarrhythmias: BB
- ESRD/proteinuria: ACEI, ARB, loop diur
- PAOD: CA
- LV dysfunction: ACEI

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Treatment strategies in special conditions

- White-coat and masked hypertension
- Young adults
- Elderly
- Women
- Metabolic syndrome
- Diabetes mellitus
- Heart disease
- Cerebrovascular disease
- Atherosclerosis, arteriosclerosis and peripheral artery disease
- Nephropathy
- Resistant hypertension
- Renovascular hypertension
- Obstructive sleep apnoea
- Malignant hypertension

Young adults

Recommendations	Class	Level
Despite absence of evidence from randomized controlled trials, antihypertensive drug treatment may be considered prudent in young hypertensives and, especially when other risk factors are present.	-	-
Young individuals with white-coat hypertension can be followed with lifestyle measures only.	-	-
Lack of evidence does also not allow recommending to initiate antihypertensive drug therapy in young individuals with isolated elevation of brachial SBP, but these individuals should be followed closely with lifestyle recommendations.	III	A

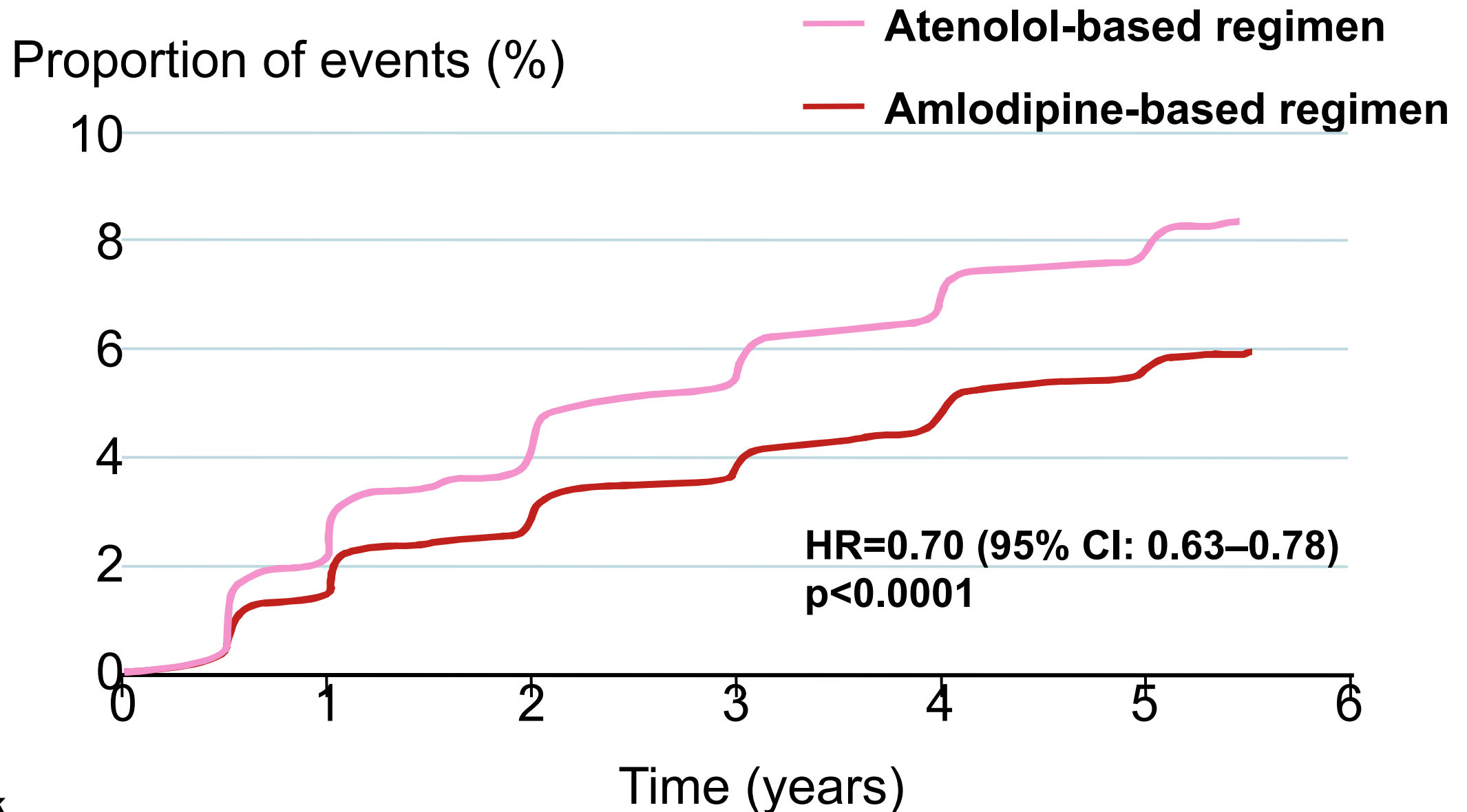
Elderly

Recommendations	Class	Level
In elderly hypertensives with SBP ≥ 160 mmHg there is solid evidence to recommend reducing SBP to between 150 and 140 mmHg.	I	A
In fit elderly patients <80 years old antihypertensive treatment may be considered at SBP values ≥ 140 mmHg with a target SBP <140 mmHg if treatment is well tolerated.	IIb	C
In individuals older than 80 years with an initial SBP ≥ 160 mmHg it is recommended to reduce SBP to between 150 and 140 mmHg, provided they are in good physical and mental conditions.	I	B
In frail elderly patients, it is recommended to leave decisions on anti-hypertensive therapy to the treating physician, and based on monitoring of the clinical effects of treatment.	I	C
Continuation of well-tolerated antihypertensive treatment should be considered when a treated individual becomes octogenarian.	IIa	C
All hypertensive agents are recommended and can be used in the elderly, although diuretics and calcium antagonists may be preferred in isolated systolic hypertension.	I	A

Metabolic syndrome

Recommendations	Class	Level
Lifestyle changes, particularly weight loss and physical exercise, are to be recommended to all individuals with the metabolic syndrome. These interventions improve not only BP, but also the metabolic components of the syndrome, and delay diabetes onset.	I	B
As the metabolic syndrome can be considered a 'pre-diabetic' state, antihypertensive agents potentially improving or at least not worsening insulin sensitivity, such as blockers of the renin-angiotensin system and calcium antagonists, should be considered as the preferred drugs. Beta-blockers (with the exception of vasodilating beta-blockers) and diuretics should be considered only as additional drugs, preferably in association with a potassium-sparing agent.	IIa	C
It is recommended to prescribe antihypertensive drugs with particular care in hypertensive patients with metabolic disturbances when BP is $\geq 140/90$ mmHg after a suitable period of lifestyle changes, and to maintain BP $< 140/90$ mmHg.	I	B
BP lowering drugs are not recommended in individuals with metabolic syndrome and high normal BP.	III	A

Amlodipine prevents New-onset Diabetes Compared with Atenolol (ASCOT)



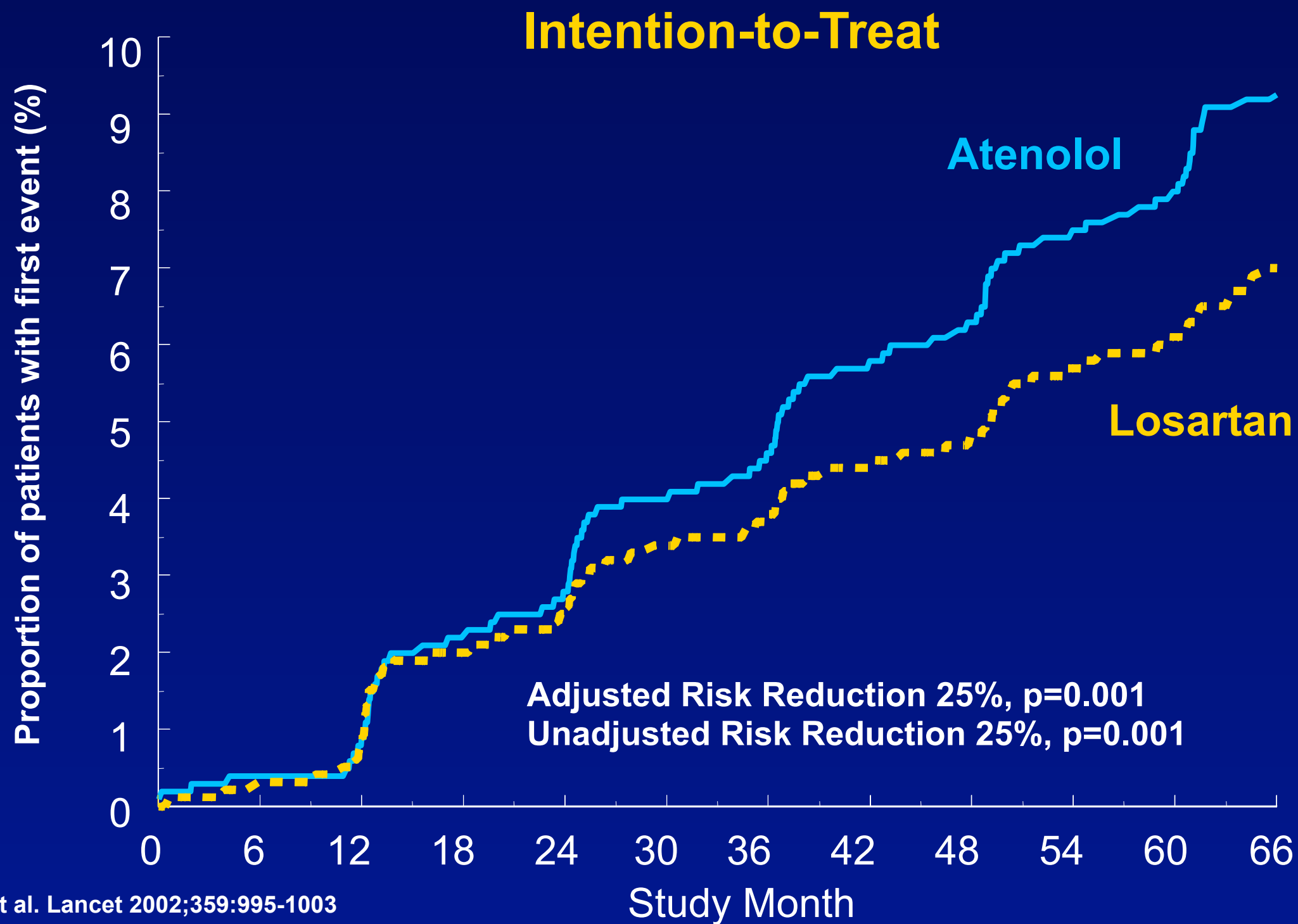
Number at risk

Amlodipine
(567 events)

Time (years)	0	1	2	3	4	5
Amlodipine	9,639	9,383	9,165	8,966	8,726	7,618
Atenolol	9,618	9,295	9,014	8,735	8,455	7,319

Atenolol
(799 events)

LIFE: New Onset Diabetes



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

β -Blockers May Reduce Mortality and Risk of Exacerbations in Patients With Chronic Obstructive Pulmonary Disease

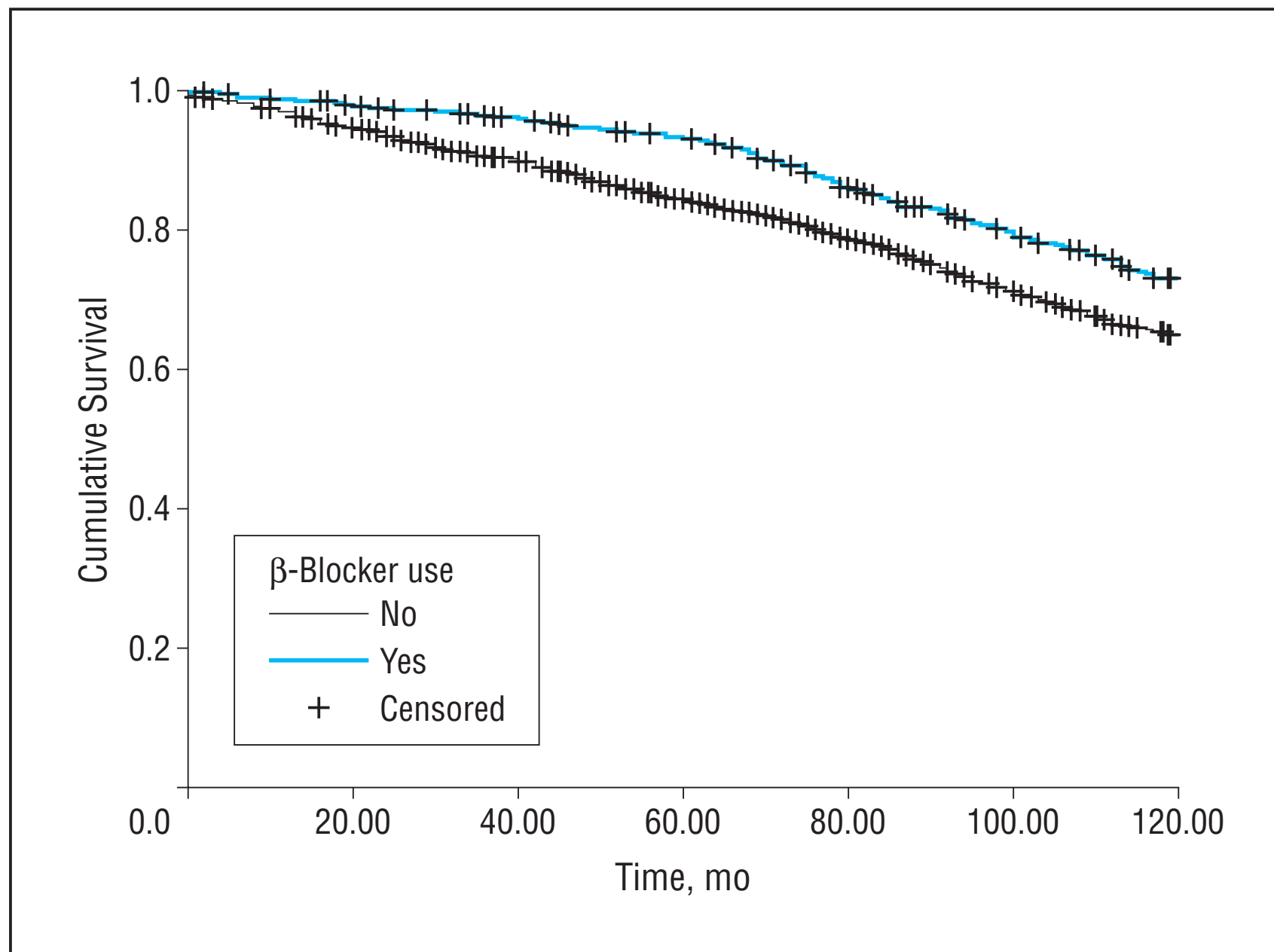


Figure 1. Cumulative survival of patients with chronic obstructive pulmonary disease according to β -blocker use.

β-Blockers May Reduce Mortality and Risk of Exacerbations in Patients With Chronic Obstructive Pulmonary Disease

Table 2. Crude and Adjusted Hazard Ratios (HRs) for Mortality According to β-Blocker Use in 2230 Patients With a Diagnosis of Chronic Obstructive Pulmonary Disease^a

Variable	HR (95% Confidence Interval)		
	Any β-Blocker	Cardioselective β-Blocker	Nonselective β-Blocker
Unadjusted (crude)	0.70 (0.59-0.84)	0.69 (0.57-0.83)	0.80 (0.61-1.06)
Covariates included in the Cox model to calculate adjusted HRs +			
Age	0.66 (0.56-0.79)	0.64 (0.54-0.78)	0.80 (0.61-1.05)
Sex	0.69 (0.58-0.82)	0.66 (0.55-0.80)	0.84 (0.63-1.11)
Current or former smoker	0.69 (0.58-0.81)	0.66 (0.55-0.79)	0.83 (0.63-1.10)
Diabetes, hypertension, cardiovascular diseases	0.65 (0.54-0.79)	0.64 (0.52-0.79)	0.77 (0.57-1.03)
Cardiovascular drugs other than β-blocker	0.67 (0.55-0.81)	0.64 (0.52-0.79)	0.82 (0.61-1.10)
Pulmonary drugs	0.67 (0.55-0.82)	0.65 (0.53-0.80)	0.82 (0.61-1.10)
Referral to a pulmonologist	0.68 (0.56-0.83)	0.67 (0.55-0.83)	0.82 (0.61-1.10)
Adjusted with propensity score ^b	0.64 (0.52-0.77)	0.63 (0.51-0.77)	0.80 (0.60-1.05)

^aAdjusted HRs based on the Cox proportional hazards model were calculated step by step after adjustment for age, sex, current or former smoking, diabetes, hypertension, cardiovascular diseases, cardiovascular drugs other than the one under study, use of pulmonary inhalation drugs, and referral to a pulmonologist. Cardiovascular drugs include β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, aldosterone antagonists, digoxin, loop and thiazide diuretics, nitrates, aspirin, vitamin K antagonists, and calcium channel blockers. Pulmonary drugs include inhalers of β₂-agonists, anticholinergic agents, corticosteroids, and oral xanthine derivatives.

^bAdjusted HRs of β-blocker use are conditional on the propensity score (based on covariates related to prescription of β-blockers).

Diabetes mellitus

Recommendations	Class	Level
While initiation of antihypertensive drug treatment in diabetic patients whose SBP is ≥ 160 mmHg is mandatory, it is strongly recommended to start drug treatment also when SBP is ≥ 140 mmHg.	I	A
A SBP goal < 140 mmHg is recommended in patients with diabetes.	I	A
The DBP target in patients with diabetes is recommended to be < 85 mmHg.	I	A
All classes of antihypertensive agents are recommended and can be used in patients with diabetes; blockers of the renin-angiotensin system may be preferred, especially in the presence of proteinuria or microalbuminuria.	I	A
It is recommended that individual drug choice takes comorbidities into account.	I	C
Simultaneous administration of two blockers of the renin-angiotensin system is not recommended and should be avoided in patients with diabetes.	III	B

Original Article

Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus

The ACCORD Study Group

N Engl J Med
Volume 362(17):1575-1585
April 29, 2010



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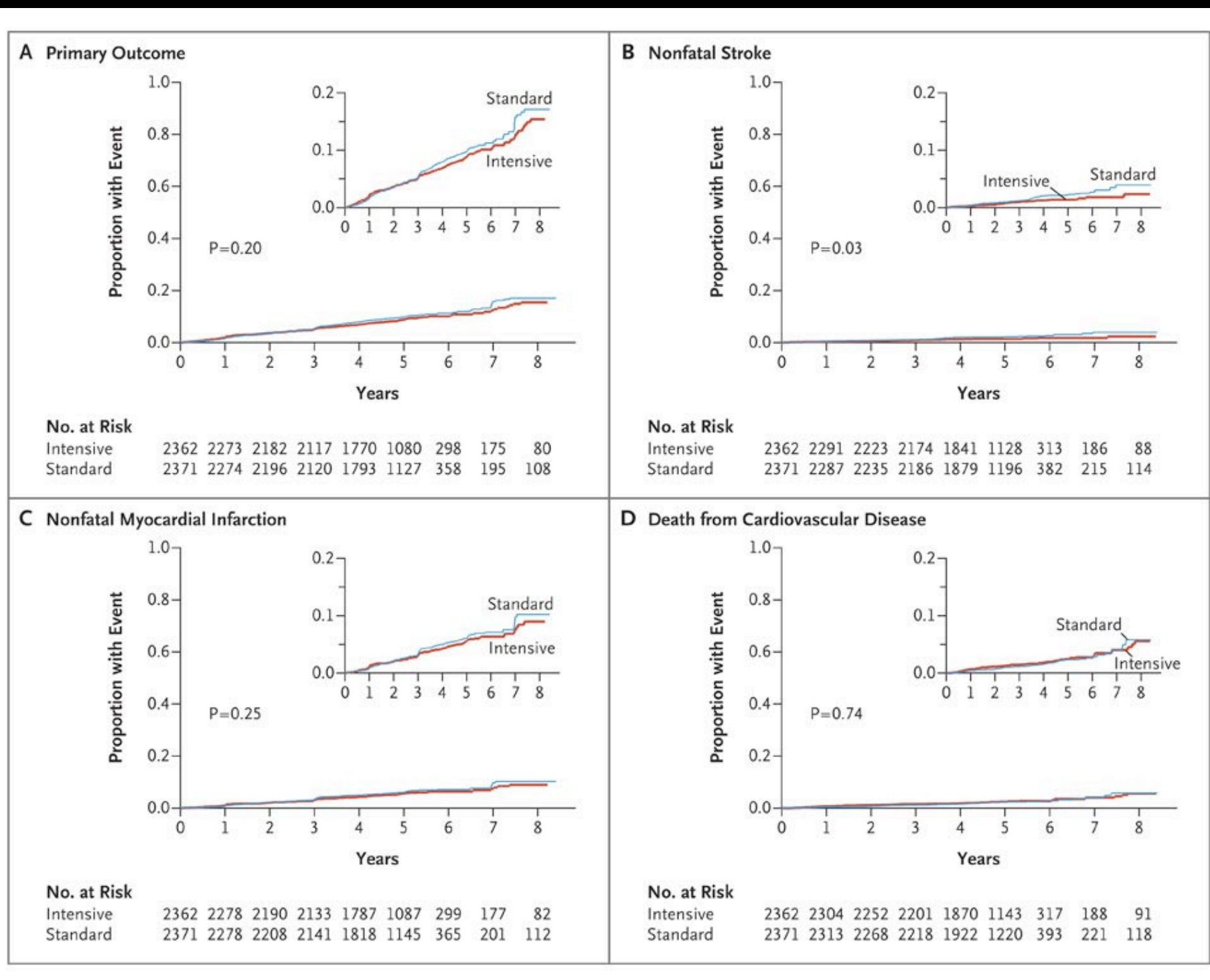
Study Overview

- In a randomized trial, 4733 patients with type 2 diabetes mellitus who were at high risk for cardiovascular events received treatment aimed at a target systolic blood pressure of less than 120 mm Hg or less than 140 mm Hg
- At a mean follow-up of 4.7 years, the rates of the primary end point (nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death) were not significantly different between the two trial groups



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Kaplan-Meier Analyses of Selected Outcomes



The ACCORD Study Group. N Engl J Med 2010;362:1575-1585



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Conclusion

- In patients with type 2 diabetes at high risk for cardiovascular events, targeting a systolic blood pressure of less than 120 mm Hg, as compared with less than 140 mm Hg, did not reduce the rate of a composite outcome of fatal and nonfatal major cardiovascular events



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Original Article

Cardiorenal End Points in a Trial of Aliskiren for Type 2 Diabetes

Hans-Henrik Parving, M.D., D.M.Sc., Barry M. Brenner, M.D., Ph.D., John J.V. McMurray, M.D., Dick de Zeeuw, M.D., Ph.D., Steven M. Haffner, M.D., Scott D. Solomon, M.D., Nish Chaturvedi, M.D., Frederik Persson, M.D., Akshay S. Desai, M.D., M.P.H., Maria Nicolaides, M.D., Alexia Richard, M.Sc., Zhihua Xiang, Ph.D., Patrick Brunel, M.D., Marc A. Pfeffer, M.D., Ph.D., for the ALTITUDE Investigators

N Engl J Med
Volume 367(23):2204-2213
December 6, 2012



The NEW ENGLAND
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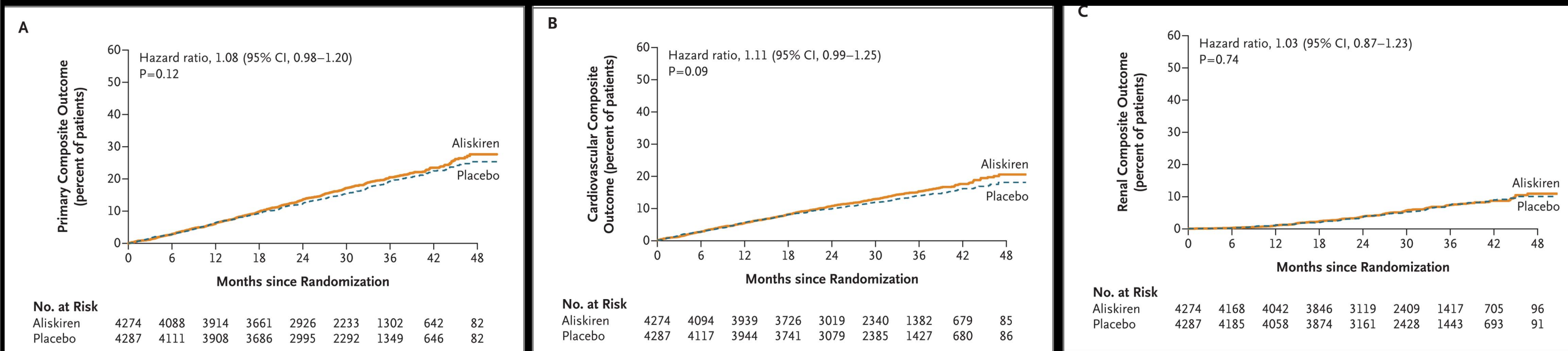
Study Overview

- Patients with type 2 diabetes at high risk for cardiovascular disease who were already taking a renin–angiotensin system blocker were randomly assigned to the direct renin inhibitor aliskiren or placebo.
- The study was discontinued early for no benefit, or even possible harm.



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Kaplan–Meier Curves for the Primary Composite Outcome, Secondary Cardiovascular Composite Outcome, and Secondary Renal Composite Outcome.



Primary Composite Outcome: death from cardiovascular causes or the first occurrence of cardiac arrest with resuscitation; nonfatal myo- cardiac infarction; nonfatal stroke; unplanned hospitalization for heart failure; end-stage renal disease, death attributable to kidney failure, or the need for renal-replacement therapy with no dialysis or transplantation available or initiated; or a serum creatinine value that was at least double the baseline value and that exceeded the upper limit of the normal range ($>80 \mu\text{mol}$ per liter [0.9 mg per deciliter] in women and $>106 \mu\text{mol}$ per liter [1.2 mg per deciliter] in men), sustained for at least a month.

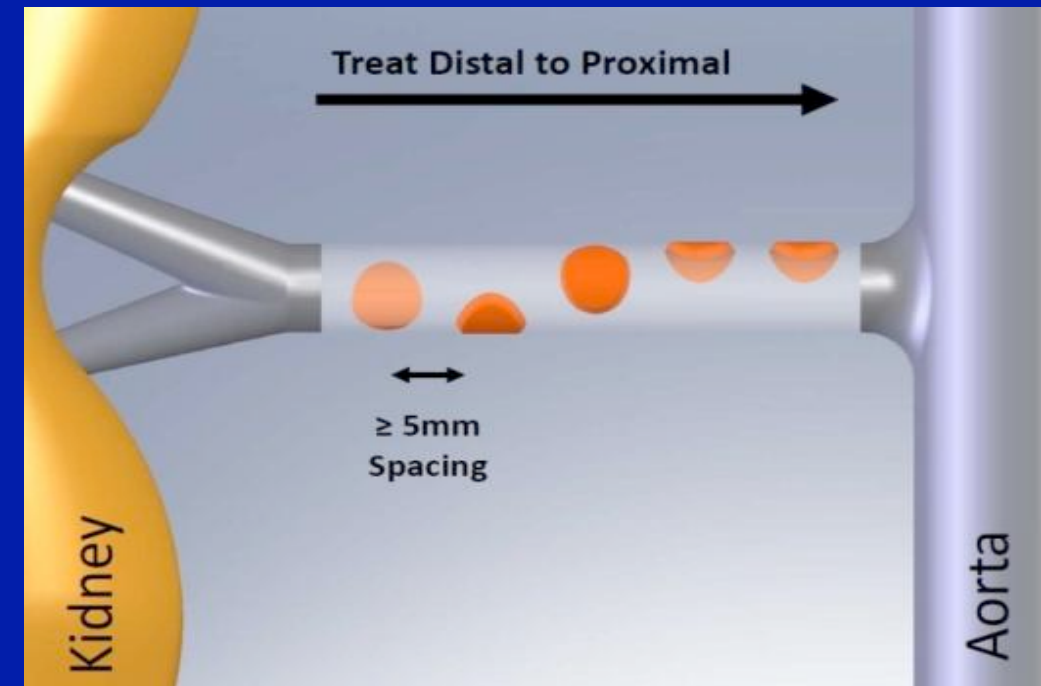
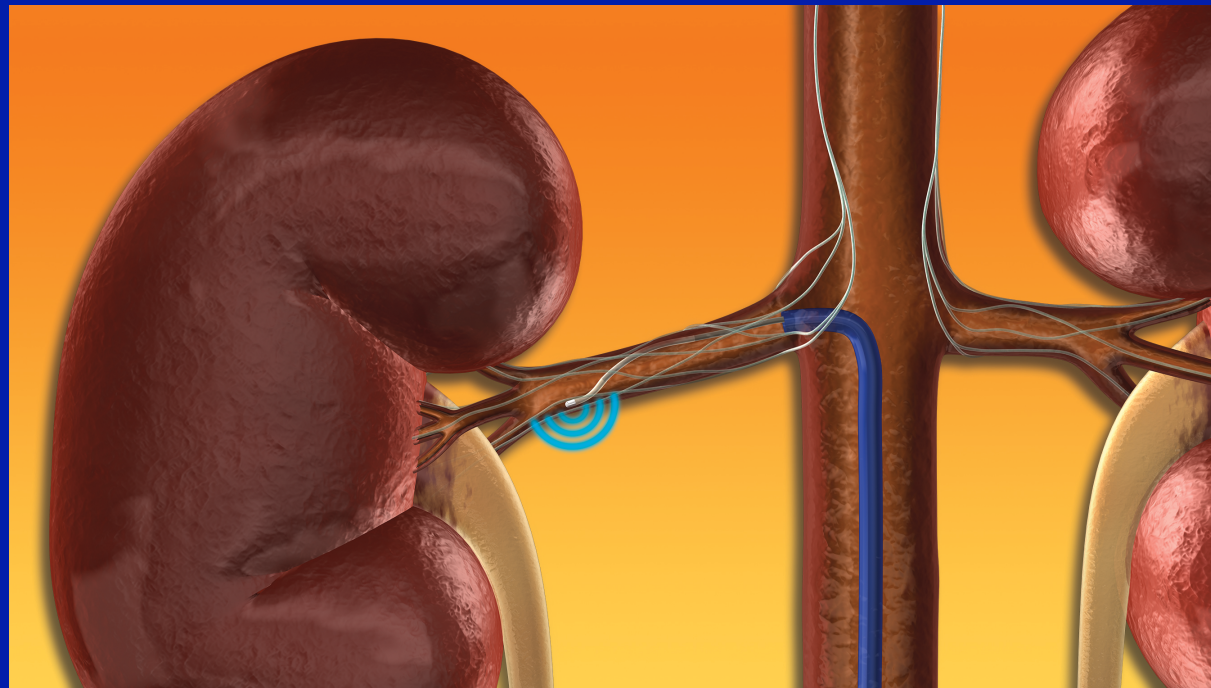
Secondary Cardiovascular Composite Outcome : a composite of all five cardio- vascular components of the primary composite end point

Secondary Renal Composite Outcome: composite of the renal components of the primary composite end point

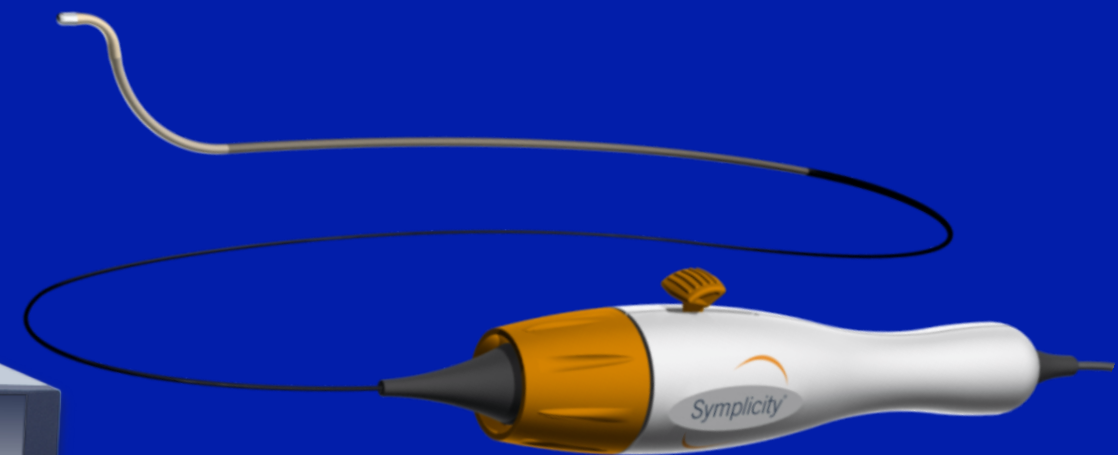
Resistant hypertension

Recommendations	Class	Level
In resistant hypertensive patients it is recommended that physicians check whether the drugs included in the existing multiple drug regimen have any BP lowering effect, and withdraw them if their effect is absent or minimal.	I	C
Mineralocorticoid receptor antagonists, amiloride, and the alpha-1-blocker doxazosin should be considered, if no contraindication exists.	IIa	B
In case of ineffectiveness of drug treatment invasive procedures such as renal denervation and baroreceptor stimulation may be considered.	IIb	C
Until more evidence is available on the long-term efficacy and safety of renal denervation and baroreceptor stimulation, it is recommended that these procedures remain in the hands of experienced operators and diagnosis and follow-up restricted to hypertension centers.	I	C
It is recommended that the invasive approaches are considered only for truly resistant hypertensive patients, with clinic values ≥ 160 mmHg SBP or ≥ 110 mmHg DBP and with BP elevation confirmed by ambulatory BP monitoring.	I	C

Renal Nerve Anatomy Allows a Catheter-Based Approach

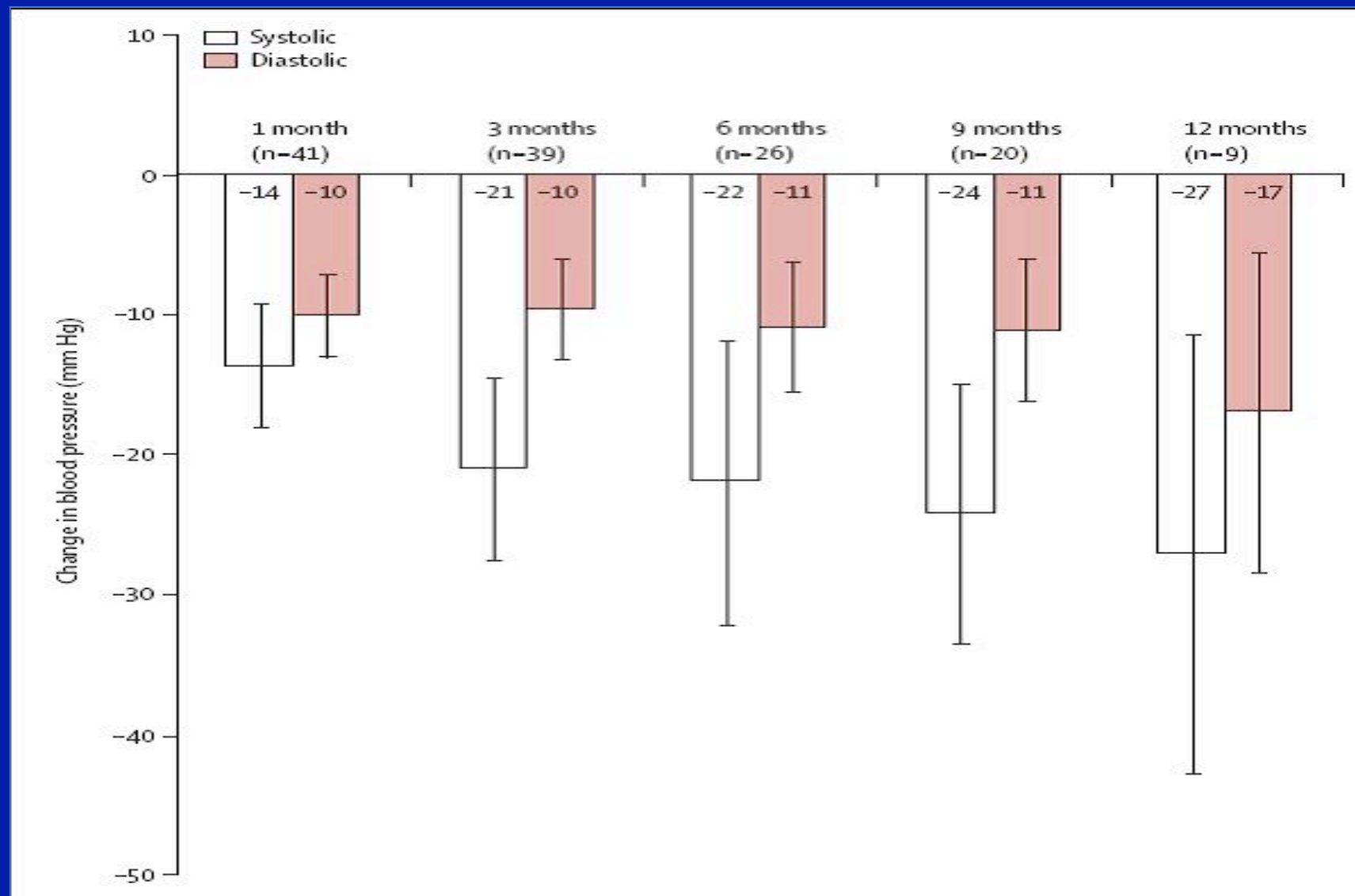


- Standard interventional technique
- 4-6 two-minute treatments per artery
- Proprietary RF Generator
 - Automated
 - Low-power
 - Built-in safety algorithms



Renal Denervation

Decrease of systolic and diastolic blood pressure after denervation of the renal nerves.



Lancet. 2009 Apr 11;373(9671):1275-81. Epub 2009 Mar 28.

Catheter-based renal sympathetic denervation for resistant hypertension: a multicentre safety and proof-of-principle cohort study.

Original Article

A Controlled Trial of Renal Denervation for Resistant Hypertension

Deepak L. Bhatt, M.D., M.P.H., David E. Kandzari, M.D., William W. O'Neill, M.D., Ralph D'Agostino, Ph.D., John M. Flack, M.D., M.P.H., Barry T. Katzen, M.D., Martin B. Leon, M.D., Minglei Liu, Ph.D., Laura Mauri, M.D., Manuela Negoita, M.D., Sidney A. Cohen, M.D., Ph.D., Suzanne Oparil, M.D., Krishna Rocha-Singh, M.D., Raymond R. Townsend, M.D., George L. Bakris, M.D., for the SYMPLICITY HTN-3 Investigators

N Engl J Med
Volume 370(15):1393-1401
April 10, 2014



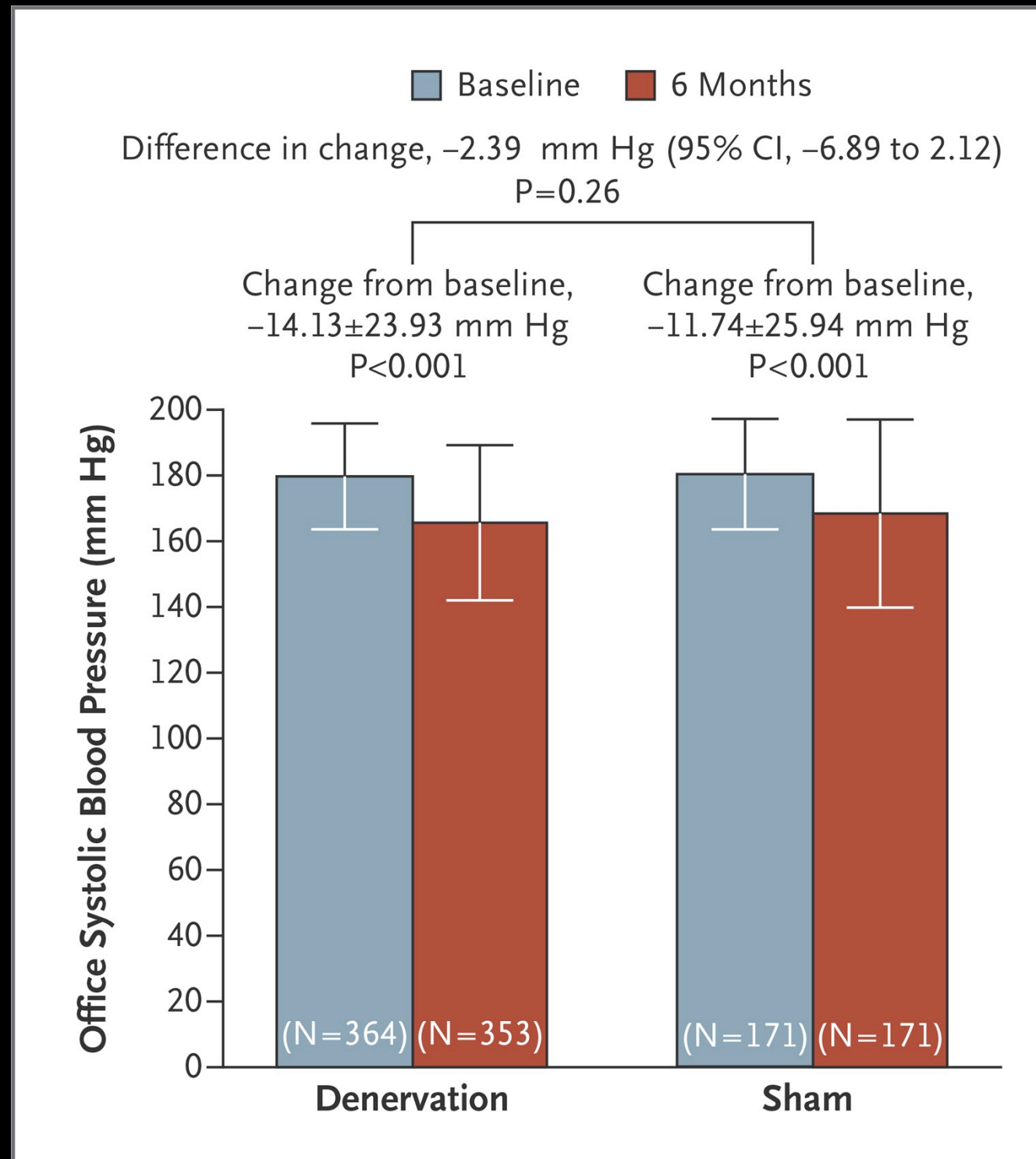
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Study Overview

- In this large trial, denervation of the kidneys with use of a radiofrequency ablation catheter in the renal arteries had no significant effect on blood pressure in patients with resistant hypertension.
- This contradicts results of smaller trials that did not include a sham control.



Primary Efficacy End Point.

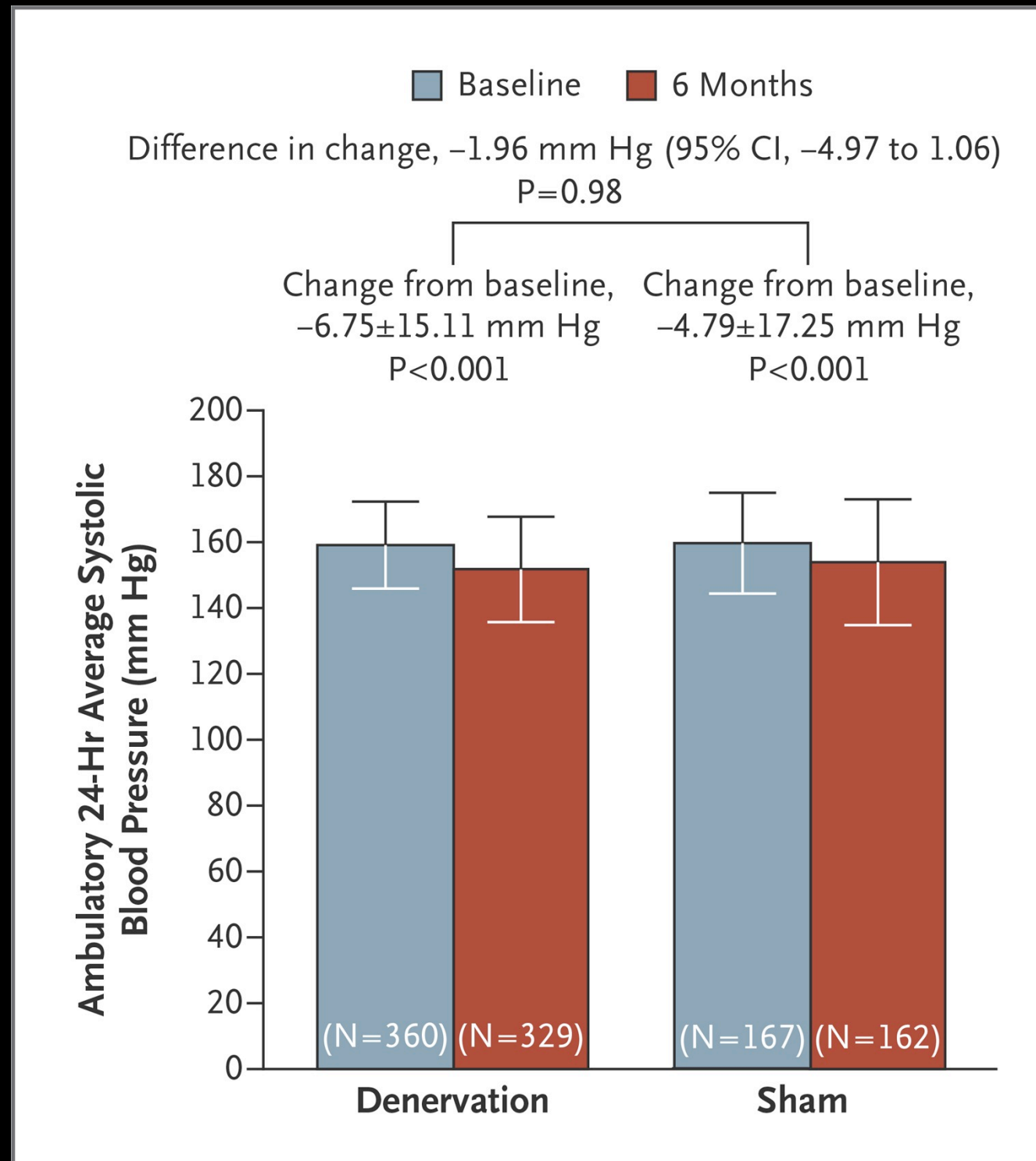


Bhatt DL et al. N Engl J Med 2014;370:1393-1401



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Secondary Efficacy End Point.



Bhatt DL et al. N Engl J Med 2014;370:1393-1401



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Renovascular hypertension

- Renovascular artery stenosis secondary to atherosclerosis is relatively frequent, especially in the elderly population.
- It is still debated whether these patients benefit from intervention, mostly percutaneous renal artery stenting.
- Intervention is not recommended if renal function has remained stable over the past 6-12 months and if hypertension is controlled by an acceptable medical regimen (Class III, LoE B).
- Fibromuscular dysplasia is more common in younger mostly female patients with uncontrolled hypertension, in whom there is convincing though uncontrolled information favouring the intervention (Class IIa, LoE B).

2013 ESH/ESC guidelines for the management of arterial hypertension

ESH/ESC Joint Task Force

Chairmen: Giuseppe Mancina (Italy), Robert Fagard (Belgium)

Section coordinators: Krzysztof Narkiewicz (Poland), Josep Redon (Spain), Alberto Zanchetti (Italy)

Members: Michael Böhm (Germany), Thierry Christiaens (Belgium), Renata Cifkova (Czech Republic), Guy De Backer (Belgium), Anna Dominiczak (UK), Maurizio Galderisi (Italy), Diederick E. Grobbee (Netherlands), Tiny Jaarsma (Sweden), Paulus Kirchhof (Germany/UK), Sverre E. Kjeldsen (Norway), Stéphane Laurent (France), Athanasios J. Manolis (Greece), Peter M. Nilsson (Sweden), Luis Miguel Ruilope (Spain), Roland E. Schmieder (Germany), Per Anton Simnes (Norway), Peter Sleight (UK), Margus Viigimaa (Estonia), Bernard Waeber (Switzerland), Faiez Zannad (France).