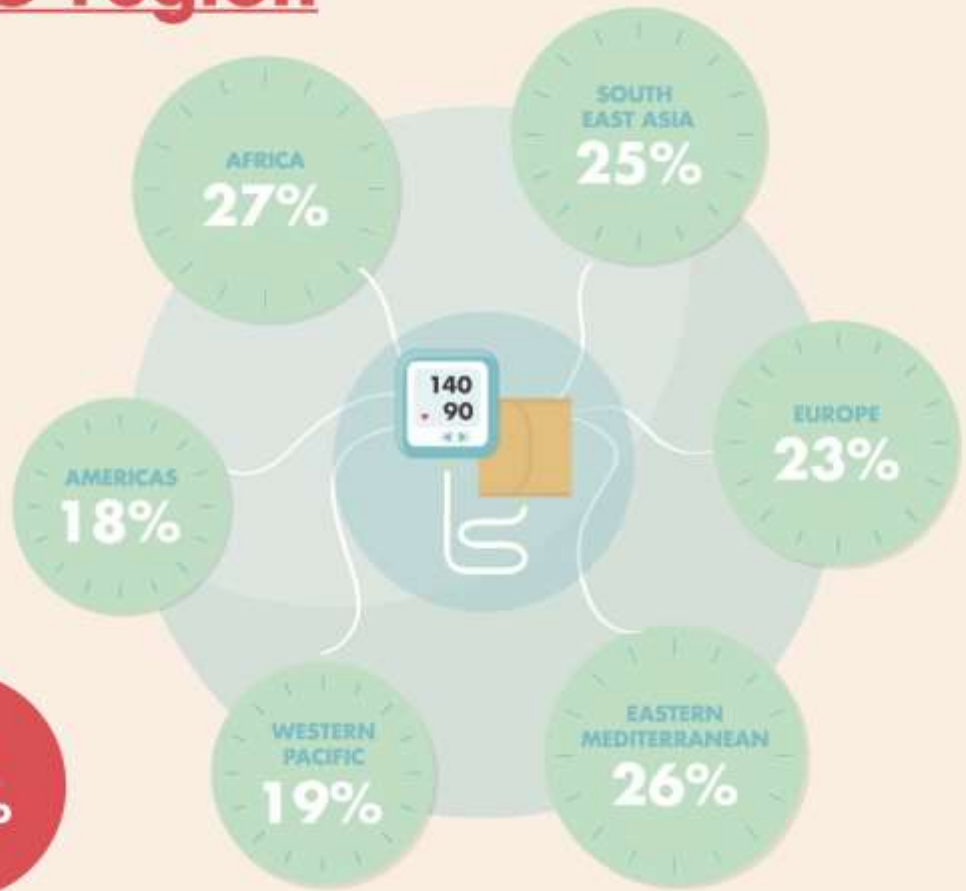
Athero**S**clerotic **C**ardio**V**ascular **D**isease

Prevention

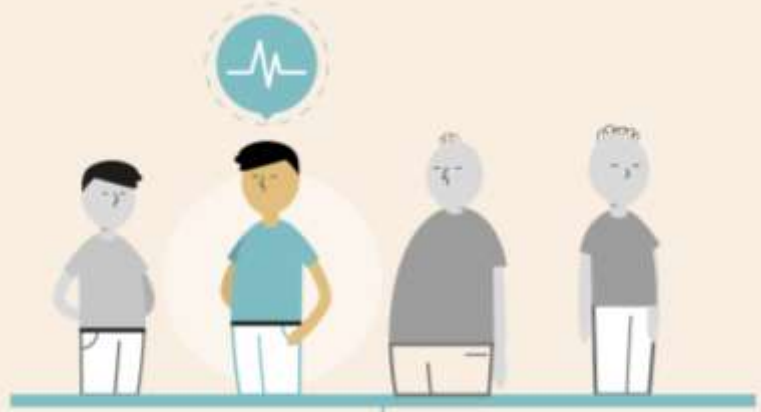
Cardio Thrombosis

Hypertension prevalence by WHO region

World Health Organization



GLOBAL
22%



1 in 4

men have hypertension

1 in 5

women have hypertension

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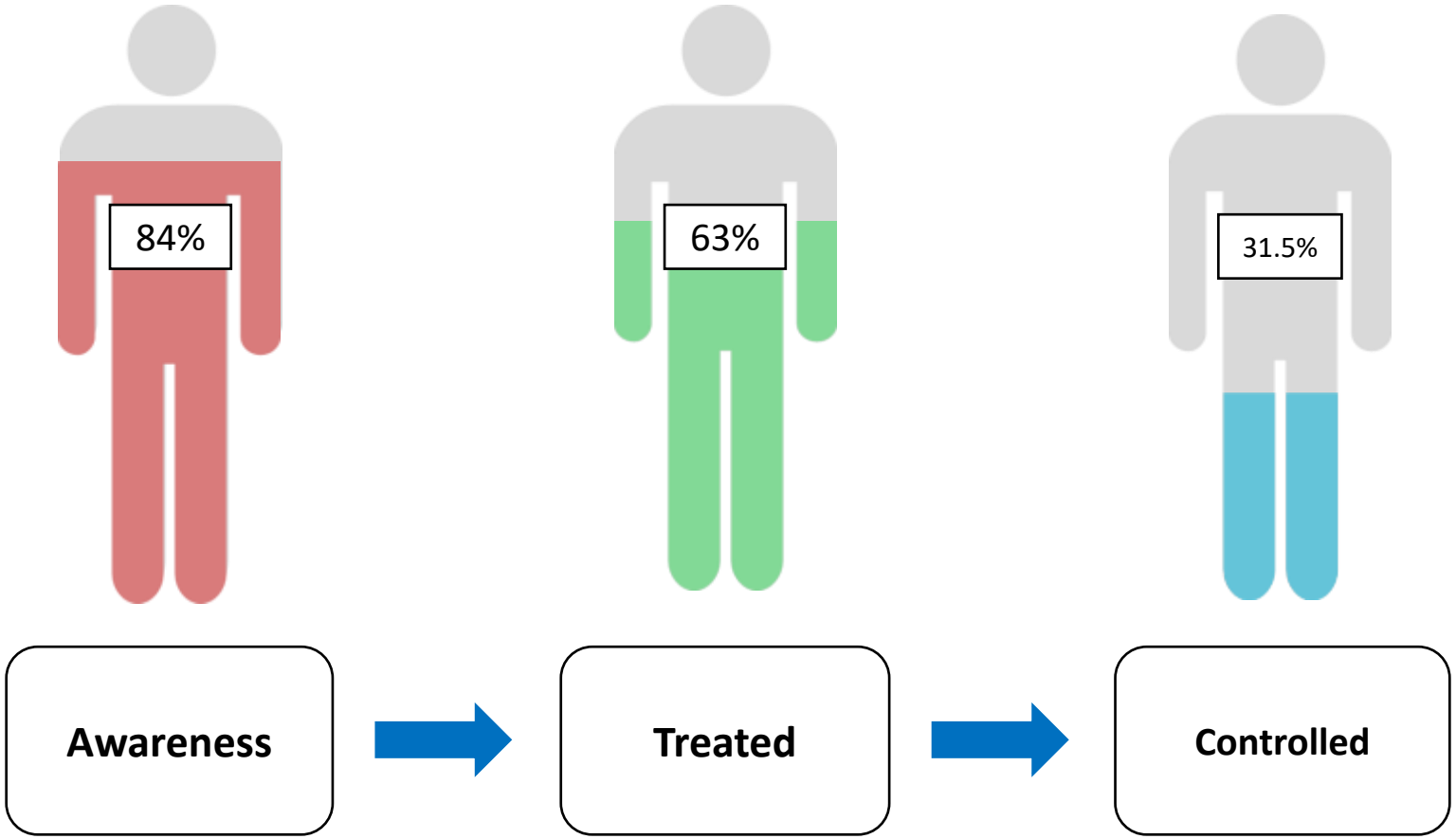
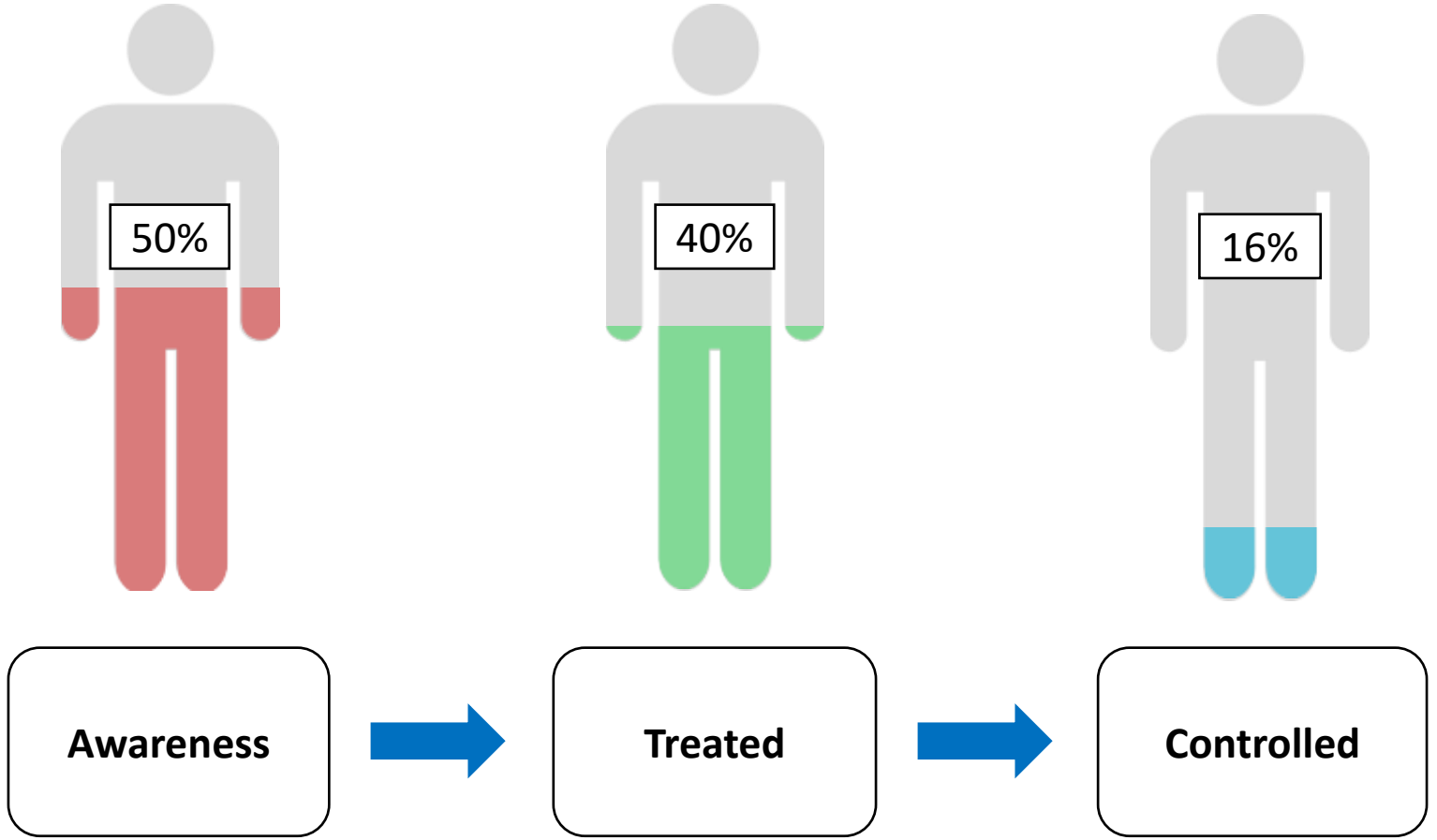
Hypertension in the U.S.



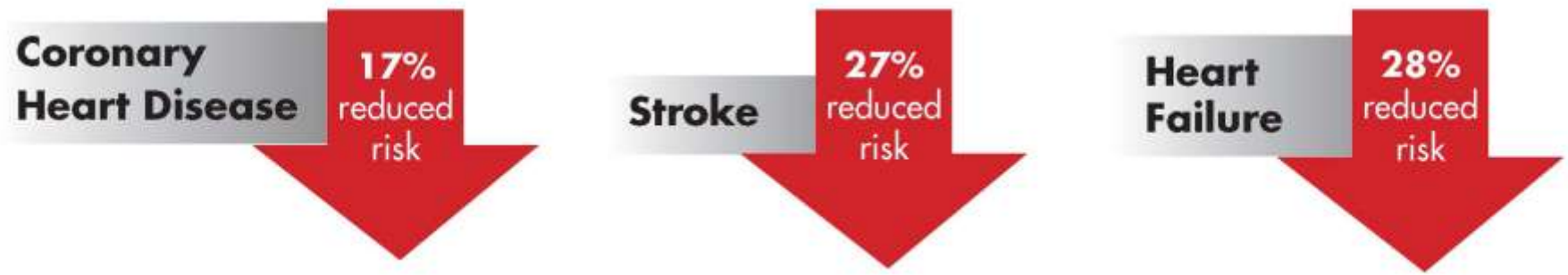
- JAMA November 6, 2018

Hypertension in Iran



- BMC Cardiovasc Disord 2010; 10: 61

A 10 mm Hg reduction in systolic blood pressure can significantly reduce risk of several conditions:



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Hypertension and total cardiovascular risk assessment

Hypertension **rarely** occurs in **isolation**, and often clusters with other cardiovascular risk factors such as dyslipidemia and glucose intolerance.

This metabolic risk factor clustering has a multiplicative effect on cardiovascular risk

Quantification of total cardiovascular risk is an important part of the risk stratification process for patients with hypertension.

Diagnosis of high blood pressure

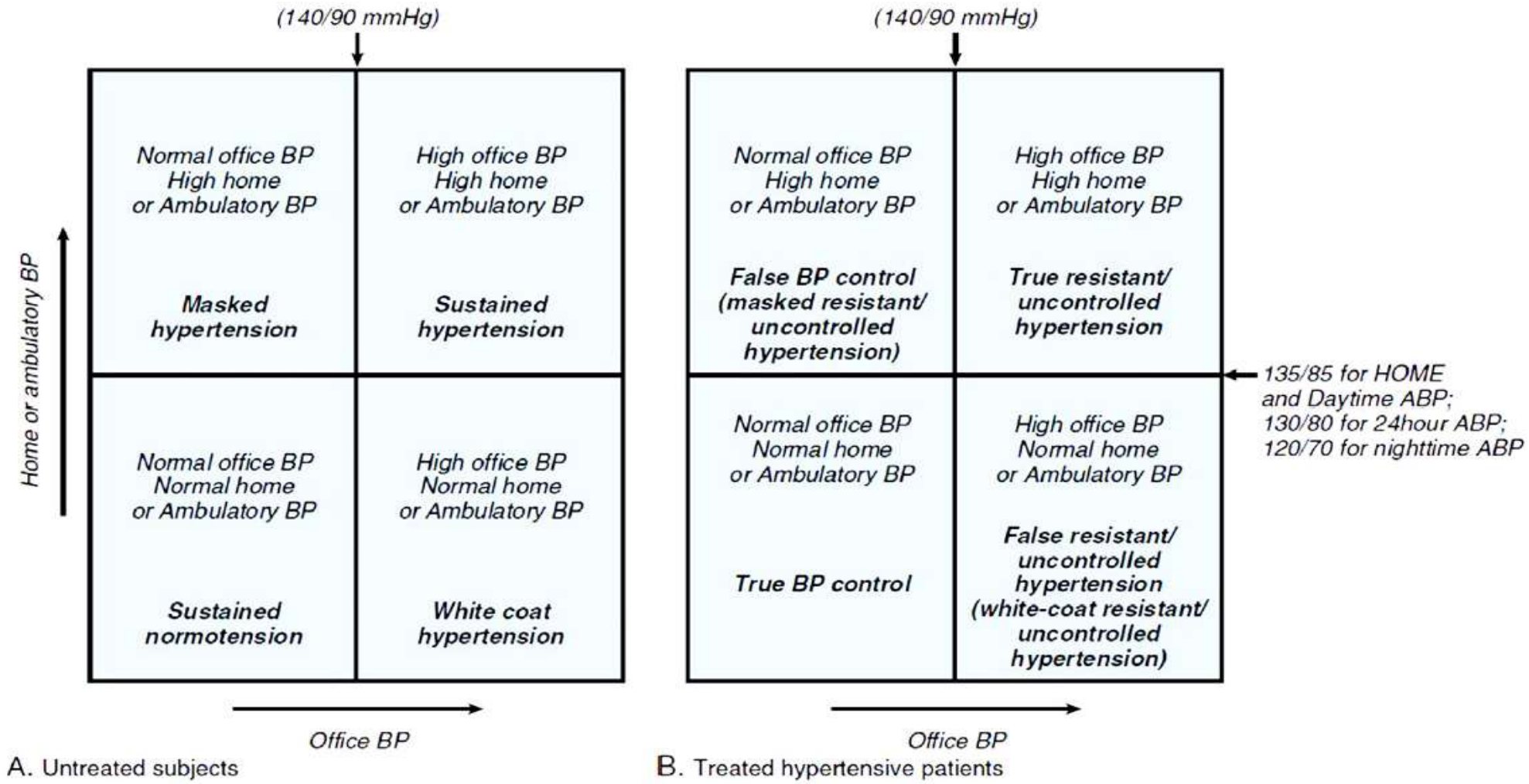
Identification of a number of specific BP patterns

- Combined use of office and out-of-office blood pressure measurements allows identification of a number of specific BP patterns, characterized by discrepant levels of office and out-of-office BP.

- Evidence has been provided in this regard showing that both WCH and MH in untreated individuals and WCUH and MUCH in treated patients are associated to an increased risk of major cardiovascular outcomes and hypertension related hospitalization.

nternational Journal of Cardiology 331 (2021) 262–269

Identification of a number of specific BP patterns



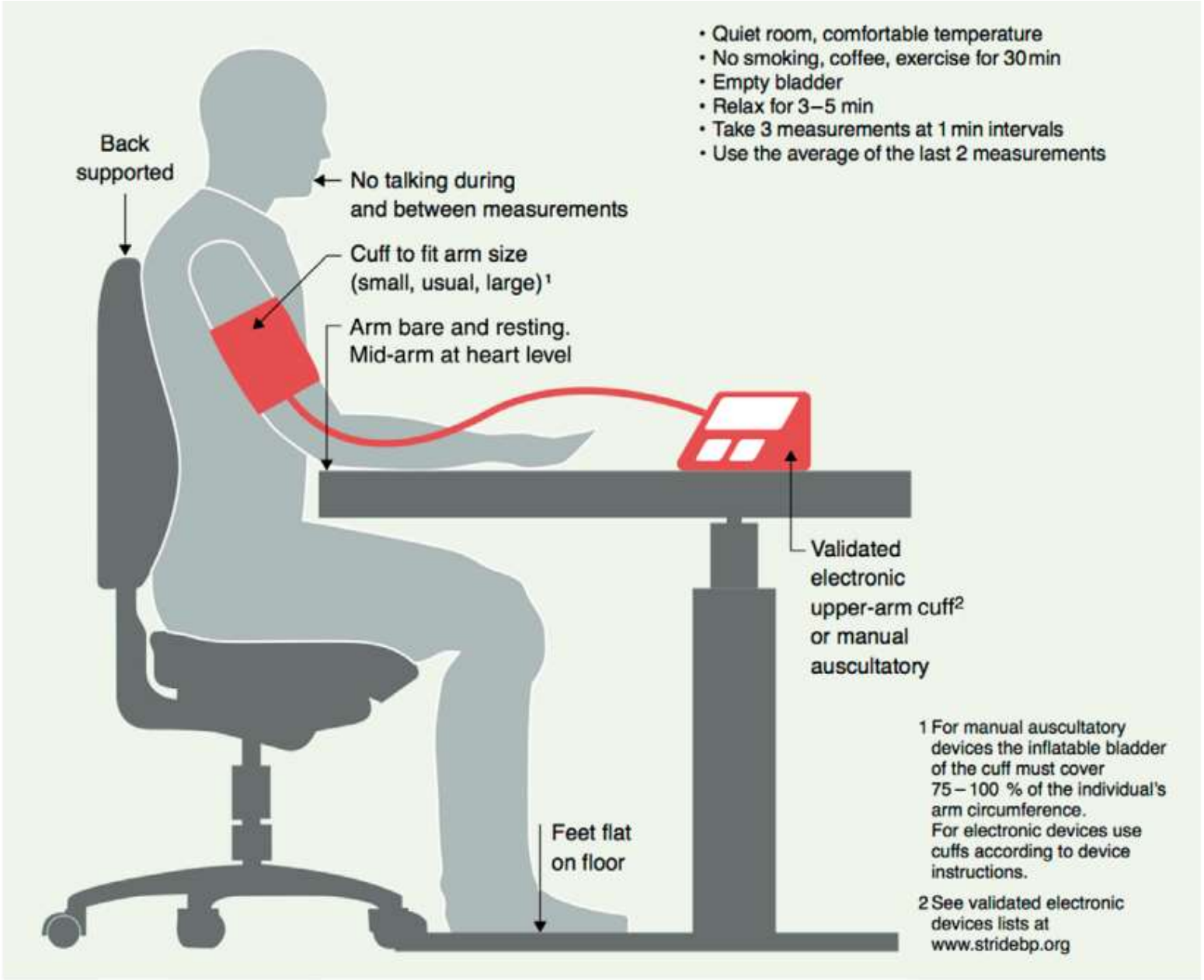
International Journal of Cardiology 331 (2021) 262–269

Hypertension Diagnosis

ESSENTIAL

- The measurement of BP in the office or clinic is most commonly the basis for hypertension diagnosis and follow-up.
- Whenever possible, the diagnosis should not be made on a single office visit. Usually 2–3 office visits at 1–4-week intervals are required. The diagnosis might be made on a single visit, if BP is ≥180/110 mmHg and there is evidence of CVD.
- If possible and available, the diagnosis of hypertension should be confirmed by **out-of-office** BP measurement.

Blood Pressure Measurement



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Blood Pressure Measurement Plan

Office Blood Pressure Levels (mm Hg)		
<130/85	130–159/85–99	>160/100
Remeasure within 3 years (1 year in those with other risk factors)	If possible confirm with out-of-office blood pressure measurement (high possibility of white coat or masked hypertension). Alternatively confirm with repeated office visits.	Confirm within a few days or weeks

Diagnostic/ Clinical Tests

Medical History ESSENTIAL

1. Blood pressure:

- New onset hypertension
- duration
- previous BP levels
- current and previous antihypertensive medication
- other medications
- history of intolerance of antihypertensive medications
- adherence to antihypertensive treatment
- previous hypertension with oral contraceptives or pregnancy

Diagnostic/ Clinical Tests

Medical History ESSENTIAL

2. Risk factors / Assessment of overall CV risk:

- Personal history of CVD
  - MI
  - HF
  - Stroke
  - TIA
  - DM
  - Dyslipidemia
  - CKD
- Lifestyle habits
  - smoking status
  - Diet
  - alcohol intake
  - physical activity
  - psychosocial aspects
  - history of depression
- Family history of
  - Hypertension
  - premature CVD
  - (familial) hypercholesterolemia
  - diabetes.

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Diagnostic / Clinical Tests

Medical History

ESSENTIAL

3. Symptoms/signs of hypertension/coexistent illnesses:

- Chest pain
- shortness of breath
- Palpitations
- Claudication
- peripheral edema
- Headaches
- blurred vision
- Nocturia
- Hematuria
- dizziness

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Medical History ESSENTIAL

Diagnostic / Clinical Tests

4. Symptoms suggestive of secondary hypertension:

- Muscle weakness/tetany
- Cramps
- arrhythmias (hypokalemia/primary aldosteronism)
- flash pulmonary edema (renal artery stenosis)
- Sweating
- palpitations
- frequent headaches (pheochromocytoma)
- snoring,
- daytime sleepiness (obstructive sleep apnea)
- symptoms suggestive of thyroid disease

Diagnostic/ Clinical Tests

Physical Examination ESSENTIAL

1. Circulation and heart:

- Pulse rate/rhythm/character
- jugular venous pulse/pressure
- apex beat
- extra heart sounds
- basal crackles, peripheral edema
- bruits (carotid, abdominal, femoral)
- radio-femoral delay

2. Other organs/systems:

- Enlarged kidneys
- neck circumference >40 cm (obstructive sleep apnea)
- enlarged thyroid
- BMI / waist circumference
- fatty deposits and colored striae (Cushing disease/syndrome).

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Diagnostic/ Clinical Tests

Laboratory Investigations and ECG ESSENTIAL

- **Blood tests:**
  - Sodium, potassium, serum creatinine and eGFR. If available, lipid profile and fasting glucose.
- **Urine test:**
  - Dipstick urine test.
- **12-lead ECG:**
  - Detection of AF, LVH, ischemic heart disease.

Cardiovascular Risk Factors

- 50% < hypertensive patients have additional CV risk factors.
- The most common additional risk factors are:

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Treatment of Hypertension

Classification of office BP and definitions of hypertension grade

Category	Systolic (mmHg)		Diastolic (mmHg)
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[b]	≥140	and	<90

- European Heart Journal (2018) 39, 3021–3104

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10 Year CV risk Categories

Very high risk	**People with any of the following:**
	Documented CVD, either clinical or unequivocal on imaging. • **Clinical CVD** includes acute myocardial infarction, acute coronary syndrome, coronary or other arterial revascularization, stroke, TIA, aortic aneurysm, and PAD • **Unequivocal documented CVD on imaging** includes significant plaque (i.e. ≥50% stenosis) on angiography or ultrasound; it does not include increase in carotid intima-media thickness • **Diabetes mellitus with target organ damage**, e.g. proteinuria or a with a major risk factor such as grade 3 hypertension or hypercholesterolaemia • **Severe CKD** (eGFR <30 mL/min/1.73 m^2) • **A calculated 10 year SCORE of ≥10%**
High risk	**People with any of the following:** • **Marked elevation of a single risk factor**, particularly cholesterol >8 mmol/L (>310 mg/dL), e.g. familial hypercholesterolaemia or grade 3 hypertension (BP ≥180/110 mmHg) • **Most other people with diabetes mellitus** (except some young people with type 1 diabetes mellitus and without major risk factors, who may be at moderate-risk)
	Hypertensive LVH
	Moderate CKD eGFR 30-59 mL/min/1.73 m^2)
	A calculated 10 year SCORE of 5-10%

- European Heart Journal (2018) 39, 3021–3104

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10 Year CV risk Categories

Moderate risk	**People with:** • **A calculated 10 year SCORE of ≥1 to <5%** • **Grade 2 hypertension** • **Many middle-aged people belong to this category**
Low risk	**People with:** • **A calculated 10 year SCORE of <1%**

- European Heart Journal (2018) 39, 3021–3104

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Hypertension disease staging	Other risk factors, HMOD, or disease	BP (mmHg) grading			
		High normal SBP 130-139 DBP 85-89	Grade 1 SBP 140-159 DBP 90-99	Grade 2 SBP 160-179 DBP 100-109	Grade 3 SBP ≥180 or DBP ≥110
Stage 1 (uncomplicated)	No other risk factors	Low risk	Low risk	Moderate risk	High risk
	1 or 2 risk factors	Low risk	Moderate risk	Moderate to high risk	High risk
	≥3 risk factors	Low to Moderate risk	Moderate to high risk	High Risk	High risk
Stage 2 (asymptomatic disease)	HMOD, CKD grade 3, or diabetes mellitus without organ damage	Moderate to high risk	High risk	High risk	High to very high risk
Stage 3 (established disease)	Established CVD, CKD grade ≥4, or diabetes mellitus with organ damage	Very high risk	Very high risk	Very high risk	Very high risk

- European Heart Journal (2018) 39, 3021–3104

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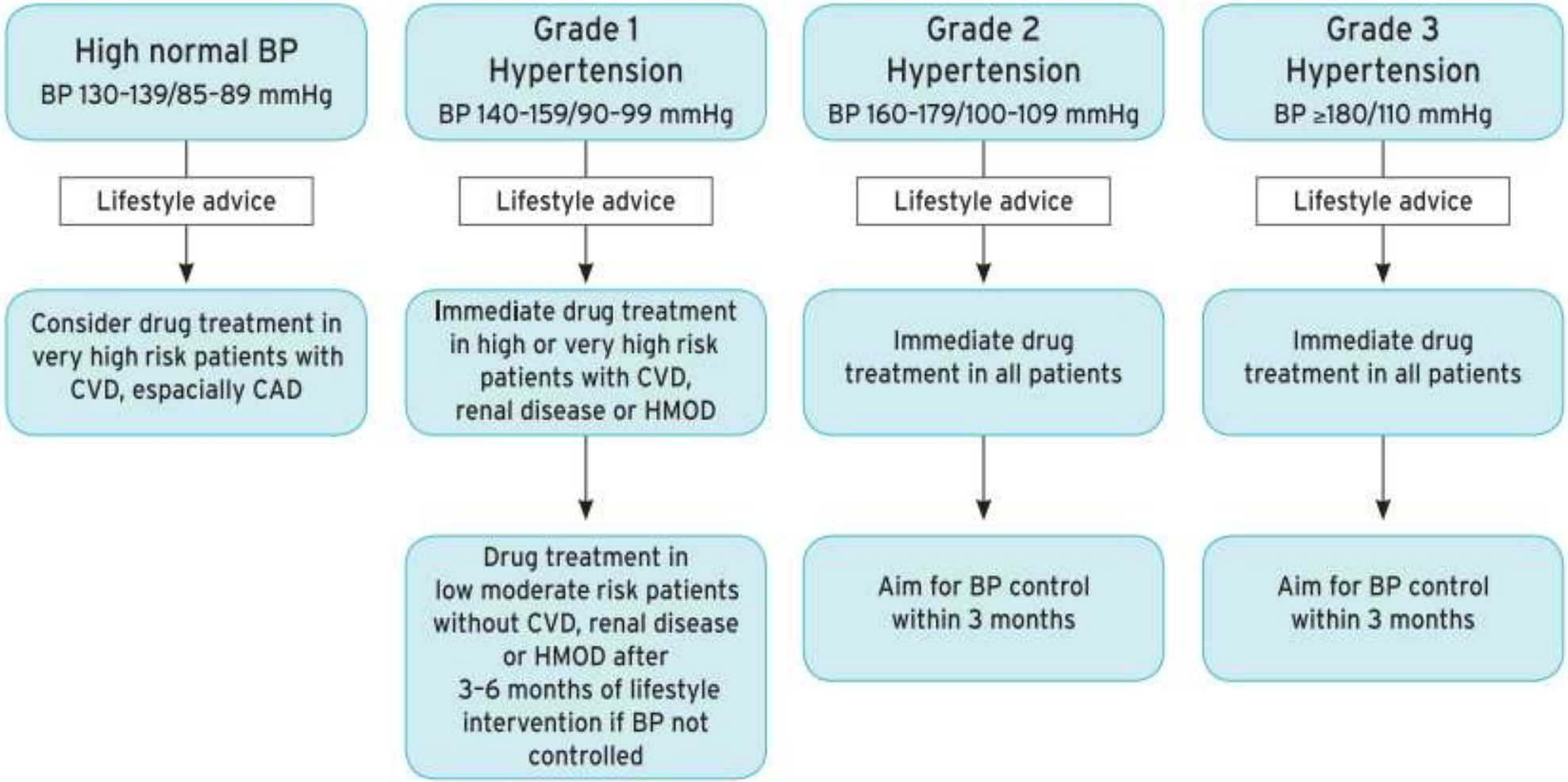
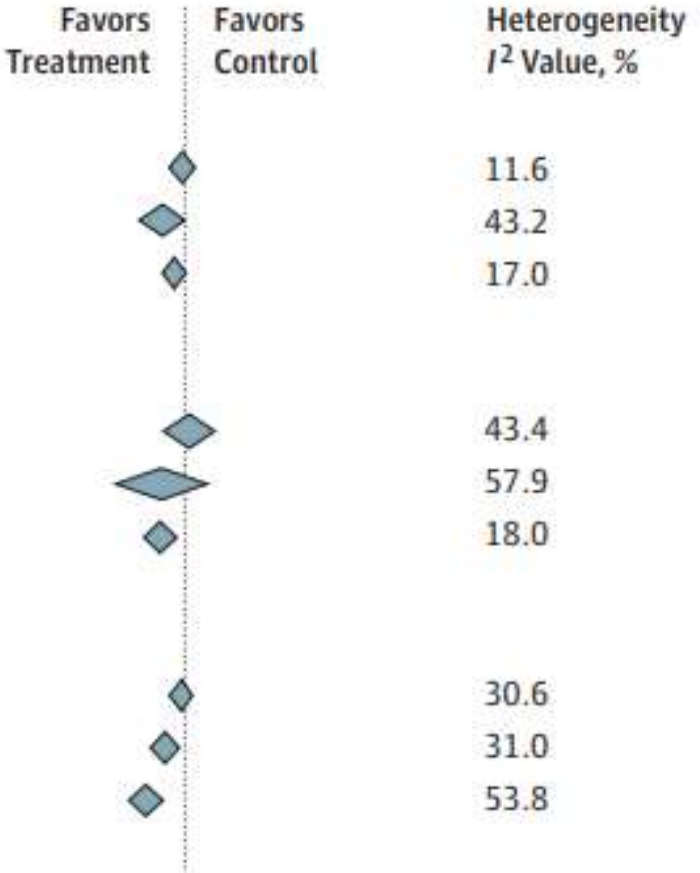
When to initiate antihypertensive treatment?



- European Heart Journal (2018) 39, 3021–3104

Baseline SBP, mm Hg	No. of Events/ Participants/Trials	RR (95% CI)	Heterogeneity I^2 Value, %
All-cause mortality			
<140	4897/68 816/16	0.98 (0.90-1.06)	11.6
140-159	2731/41 049/15	0.87 (0.75-1.00)	43.2
≥160	4361/79 900/18	0.93 (0.87-1.00)	17.0
SBP interaction, $P=.18$			
Cardiovascular mortality			
<140	2633/66 480/12	1.03 (0.87-1.20)	43.4
140-159	1465/42 587/15	0.86 (0.65-1.14)	57.9
≥160	2290/78 789/17	0.85 (0.77-0.95)	18.0
SBP interaction, $P=.02$			
Major cardiovascular events			
<140	7354/67 928/13	0.97 (0.90-1.04)	30.6
140-159	3951/43 489/16	0.88 (0.80-0.96)	31.0
≥160	4627/77 733/16	0.78 (0.70-0.87)	53.8
SBP interaction, $P=.004$			



- Primary preventive BP lowering is associated with reduced risk for death and CVD if baseline SBP is 140 mm Hg or higher.
- At lower BP levels, treatment is not associated with any benefit in primary prevention but might offer additional protection *in patients with CHD*.

- JAMA Intern Med. 2018;178(1):28-36.

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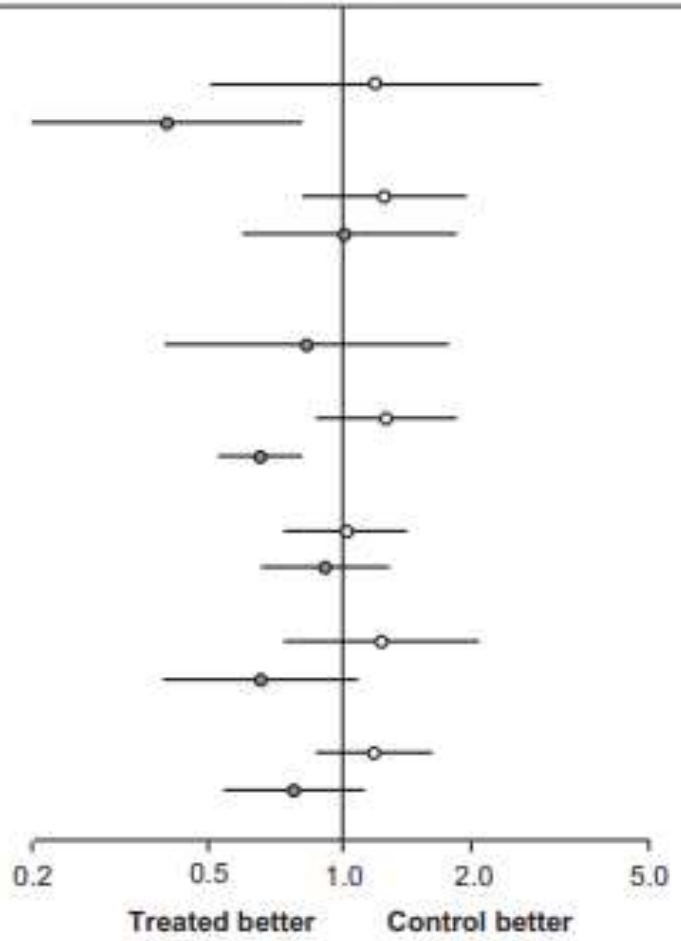
Outcome	CV risk	Trials (n)	Standardized RR (95% CI)	P-value homogeneity
Stroke	L-M	4	1.20 (0.51-2.78)	0.006
	H-VH	8	0.40 (0.20-0.81)	
CHD	L-M	4	1.25 (0.82-1.92)	0.089
	H-VH	6	1.00 (0.60-1.84)	
HF	L-M	1	-	-
	H-VH	5	0.82 (0.38-1.81)	
Stroke + CHD	L-M	3	1.27 (0.88-1.81)	<0.001
	H-VH	8	0.65 (0.52-0.80)	
Stroke + CHD + HF	L-M	5	1.02 (0.73-1.39)	0.32
	H-VH	6	0.91 (0.66-1.29)	
CV Death	L-M	3	1.23 (0.74-2.06)	0.001
	H-VH	6	0.66 (0.40-1.09)	
All Death	L-M	10	1.18 (0.88-1.60)	0.016
	H-VH	6	0.77 (0.54-1.13)	



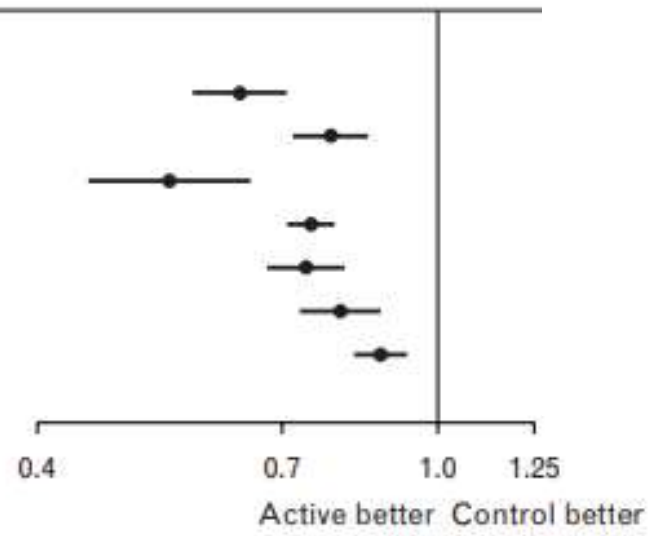
Individuals with *very high cardiovascular risk* due to symptomatic cardiovascular disease should consider BP-lowering treatment *even when their BP is in the high-normal range*.

- J Hypertens 2017;35:2150–2160.

Initiation of treatment In Patients with Grade 2 or 3 HTN

Prompt initiation of BP-lowering drug treatment is recommended in patients with grade 2 or 3 HTN **at any level of CV risk**, simultaneous with the initiation of lifestyle changes.

Outcome	Trials (n)	Difference SBP/DBP (mmHg)	Events (n/patients) Treated	Events (n/patients) Controls	RR (95% CI)	Standardized RR (95% CI)
Stroke	31	–9.0/–4.8	1262/51179	1870/56326	0.68 (0.62–0.75)	0.63 (0.56–0.71)
CHD	35	–9.0/–4.8	1443/52168	1723/56868	0.82 (0.77–0.88)	0.78 (0.72–0.85)
HF	20	–10.6/–4.8	231/21517	415/20605	0.55 (0.46–0.65)	0.54 (0.45–0.64)
Stroke + CHD	32	–9.0/–4.8	2632/50705	3472/55848	0.77 (0.73–0.81)	0.75 (0.71–0.79)
Stroke + CHD + HF	22	–11.2/–5.4	1969/31902	2536/30979	0.73 (0.68–0.80)	0.74 (0.69–0.81)
CV death	33	–9.1/–4.8	1473/51245	1778/56402	0.82 (0.76–0.89)	0.80 (0.73–0.88)
All-cause death	37	–9.0/–4.8	2913/53140	3336/58288	0.89 (0.84–0.94)	0.88 (0.82–0.93)



- European Heart Journal (2018) 39, 3021–3104 , Journal of Hypertension (2014) 32:2285–2295

Office BP treatment targets in hypertensive patients

Age group	Office SBP treatment target ranges (mmHg)					Office DBP treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke[a]/TIA	
18 - 65 years	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120	**Target to <140 to 130** *if tolerated*	**Target to 130** *or lower if tolerated* Not <120	**Target to 130** *or lower if tolerated* Not <120	70–79
65 - 79 years[b]	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	70–79
≥80 years[b]	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	**Target to 130-139** *if tolerated*	70–79
Office DBP treatment target range (mmHg)	70–79	70–79	70–79	70–79	70–79	

- European Heart Journal (2018) 39, 3021–3104

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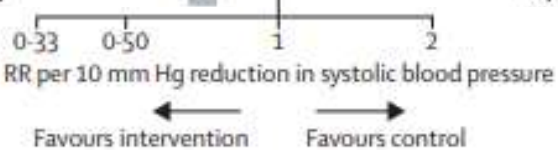
	Studies	Intervention		Control		RR (95% CI) per 10 mm Hg reduction in systolic blood pressure	p_{trend}
		Events	Participants	Events	Participants		
Major cardiovascular events							0·22
<130	4	542	4547	530	3881	0·63 (0·50–0·80)	
130–139	17	5375	47103	5856	47167	0·87 (0·82–0·92)	
140–149	7	4365	33333	4694	33062	0·79 (0·72–0·87)	
150–159	13	1289	21290	1257	20088	0·80 (0·71–0·91)	
≥160	14	1638	31045	1731	24060	0·74 (0·69–0·79)	
Total						**0·80 (0·77–0·83)**	
Coronary heart disease							0·93
<130	5	489	6071	620	5395	0·55 (0·42–0·72)	
130–139	18	2258	47608	2461	47670	0·88 (0·80–0·96)	
140–149	8	1225	34834	1307	34581	0·80 (0·69–0·94)	
150–159	12	409	20386	442	19788	0·84 (0·68–1·05)	
≥160	13	481	28086	471	21113	0·82 (0·73–0·92)	
Total						**0·83 (0·78–0·88)**	
Stroke							0·38
<130	3	48	3669	47	2984	0·65 (0·27–1·57)	
130–139	18	1191	47608	1403	47670	0·73 (0·62–0·85)	
140–149	7	2130	34166	2381	34347	0·78 (0·70–0·87)	
150–159	11	538	19636	702	19026	0·65 (0·54–0·78)	
≥160	15	728	31603	845	24613	0·70 (0·64–0·78)	



- Lancet 2016; 387: 957–67

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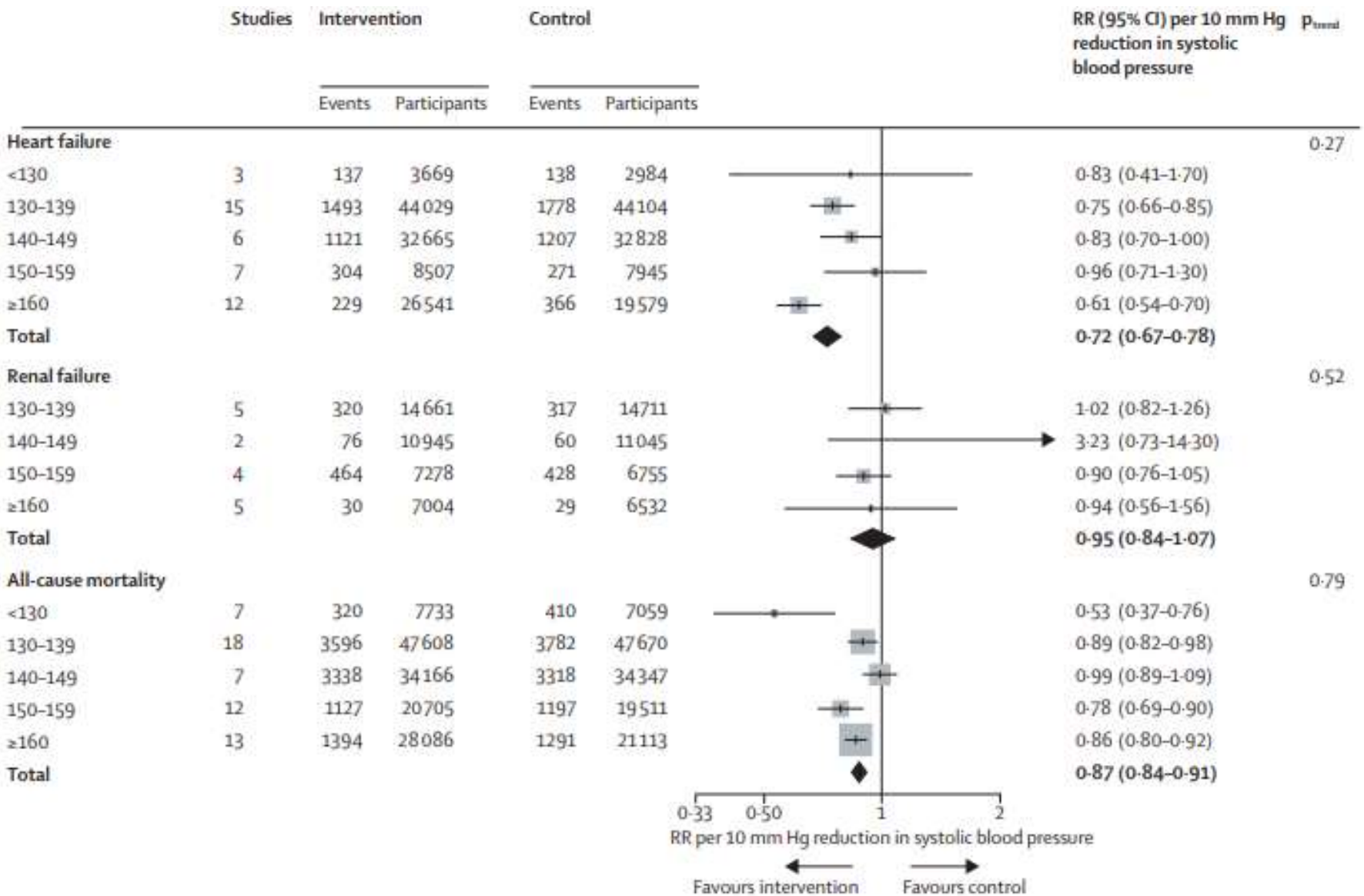

- Lancet 2016; 387: 957–67

Cardio Thrombosis

Treatment of hypertension

- Lifestyle changes
- Pharmacological therapy

- European Heart Journal (2018) 39, 3021–3104

Lifestyle Modification

	Modification	Recommendation	Approximate SBP Reduction Range
	Weight reduction	Maintain normal body weight (BMI=18.5-24.9 kg/m²)	5 mm Hg
	DASH eating plan	Diet rich in fruits, vegetables, low fat dairy and reduced in fat	11 mm Hg
	Restrict sodium intake	<1500 mg of sodium per day	5-6 mm Hg
	Physical activity	Be more physically active. Aim for at least 90 to 150 minutes of aerobic exercise per week.	5-8 mm Hg
	Moderation of alcohol consumption	No more than 2 drinks/day for men and 1 drink/day for women	4 mm Hg

BP = Blood pressure, BMI = Body mass index, SBP = Systolic blood pressure, DASH = Dietary Approaches to Stop Hypertension

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Ideal Characteristics of Drug Treatment

1	Treatments should be evidence-based in relation to morbidity/mortality prevention.
2	Use a once-daily regimen which provides 24-hour blood pressure control.
3	Treatment should be affordable and/or cost-effective relative to other agents.
4	Treatments should be well-tolerated.
5	Evidence of benefits of use of the medication in populations to which it is to be applied.

- Hypertension. 2020;75:1334-1357

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Oral Antihypertensive Drugs

Primary agents

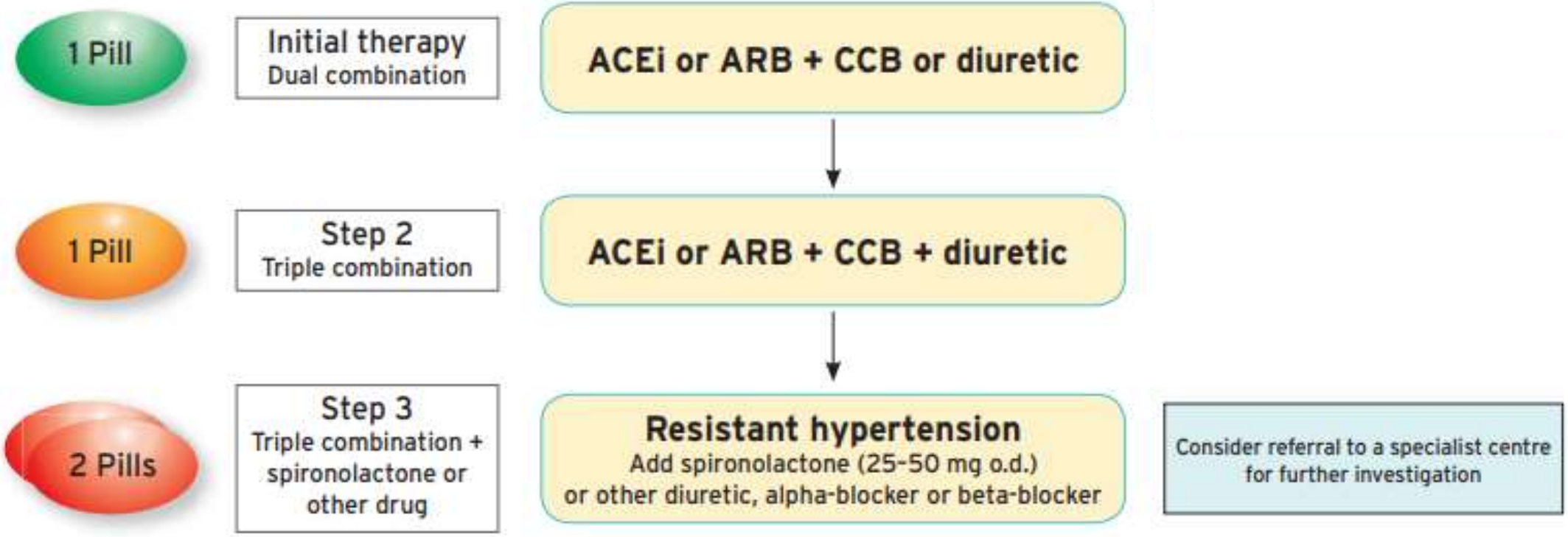
	Class	Drug	Daily Freq.
1	**Thiazide or Thiazide-type diuretics**	Chlorthalidone	1
		Hydrochlorothiazide	1
		Indapamide	1
2	**ACE inhibitors**	Benazepril	1 or 2
		Captopril	2 or 3
		Enalapril	1 or 2
3	**ARBs**	Losartan	1 or 2
		Telmisartan	1
		Valsartan	1
4	**CCB dihydropyridines**	Amlodipine	1
		Nifedipine LA	1
	CCB nondihydropyridines	Diltiazem SR	2
		Verapamil SR	1 or 2

Secondary agents

Class	Drug	Daily Freq.
Diuretics— loop	Furosemide	2
Diuretics potassium sparing	Amiloride	1 or 2
	Triamterene	1 or 2
Aldosterone antagonists	Spironolactone	1
Beta blockers	Atenolol	
	Bisoprolol	1
	Metoprolol tartrate	2
	Nebivolol	1
	Propranolol IR	2
	Carvedilol	2
Alpha-1 blockers	Terazosin	1 or 2
Central alpha1 agonist	Clonidine oral	2
	Methyldopa	2
Direct vasodilators	Hydralazine	2 or 3

- Hypertension. 2018;71:e13-e115.

Core drug treatment strategy for uncomplicated HTN



- European Heart Journal (2018) 39, 3021–3104

The drug treatment algorithm for HTN

1. The initiation of treatment in most patients with an SPC comprising two drugs, to improve the speed, efficiency, and predictability of BP control.

2. A beta-blocker in combination with a diuretic or any drug from the other major classes is an alternative when there is a specific indication for a beta-blocker, e.g. angina, post-myocardial infarction, heart failure, or heart rate control.

3. Use monotherapy for:
   a) low-risk patients with stage 1 hypertension
   b) very high-risk patients with high–normal BP
   c) frail older patients

- European Heart Journal (2018) 39, 3021–3104

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Combination Therapy

Patients initiated with combination:

- Required less titration steps
- Reached the goal of BP in a shorter period of time
- Achieve higher BP control rates and greater reductions in both systolic and diastolic BP from baseline

- Journal of Human Hypertension (2010) 24, 483–491

Adherence to Antihypertensive Treatment

- Nonadherence to antihypertensive treatment affects 10%–80% of hypertensive patients and is one of the key drivers of suboptimal BP control.

- Evaluate adherence to antihypertensive treatment as appropriate at each visit and prior to escalation of antihypertensive treatment

- Hypertension. 2020;75:1334-1357

Adherence to Antihypertensive Treatment

Consider the following strategies to improve medication adherence:

1. reducing polypharmacy – use of **single pill combinations**
2. **once-daily dosing** over multiple times per day dosing
3. linking adherence behavior with daily habits
4. providing adherence feedback to patients
5. home BP monitoring
6. reminder packaging of medications
7. empowerment-based counseling for self-management
8. electronic adherence aids such as mobile phones or short messages services
9. multidisciplinary healthcare team approach to improve monitoring for adherence

- Hypertension. 2020;75:1334-1357

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Treatment strategies in people with diabetes

Recommendations	Class	Level
In people with diabetes receiving BP-lowering drugs it is recommended: • To target SBP to 130 mmHg and <130mmHg if tolerated, but not <120 mmHg. • In older people (aged >_65 years aged), to target to an SBP range of 130–139 mmHg. • To target the DBP to <80 mmHg, but not <70 mmHg.	I	A
It is recommended to initiate treatment with a combination of a RAS blocker with a CCB or thiazide/thiazide-like diuretic.	I	A
Simultaneous administration of two RAS blockers, e.g. an ACE inhibitor and ARB, is not indicated.	III	A

- European Heart Journal (2018) 39, 3021–3104

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Treatment strategies in people with CKD

Recommendations	Class	Level
In patients with diabetic or non-diabetic CKD: • It is recommended to lower SBP to a range of 130–139 mmHg. • Individualized treatment should be considered according to its tolerability and impact on renal function and electrolytes.	I	A
	IIa	C
RAS blockers are more effective at reducing albuminuria than other antihypertensive agents, and are recommended as part of the treatment strategy in hypertensive patients in the presence of microalbuminuria or proteinuria.	I	A
A combination of a RAS blocker with a CCB or a diuretic is recommended as initial therapy.	I	A

- European Heart Journal (2018) 39, 3021–3104

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Treatment strategies in secondary stroke prevention

Recommendations	Class	Level
In all hypertensive patients with ischemic stroke or TIA, an SBP target range of 120–130 mmHg should be considered.	IIa	B
The recommended antihypertensive drug treatment strategy for stroke prevention is a RAS blocker plus a CCB or a thiazide-like diuretic.	I	A

- European Heart Journal (2018) 39, 3021–3104

Diuretics

Consider ACEIs or ARBs + Thiazide-**like** diuretic in:

- Post-stroke
- Very elderly
- Incipient HF
- CCB intolerance

- Hypertension. 2020;75:1334-1357

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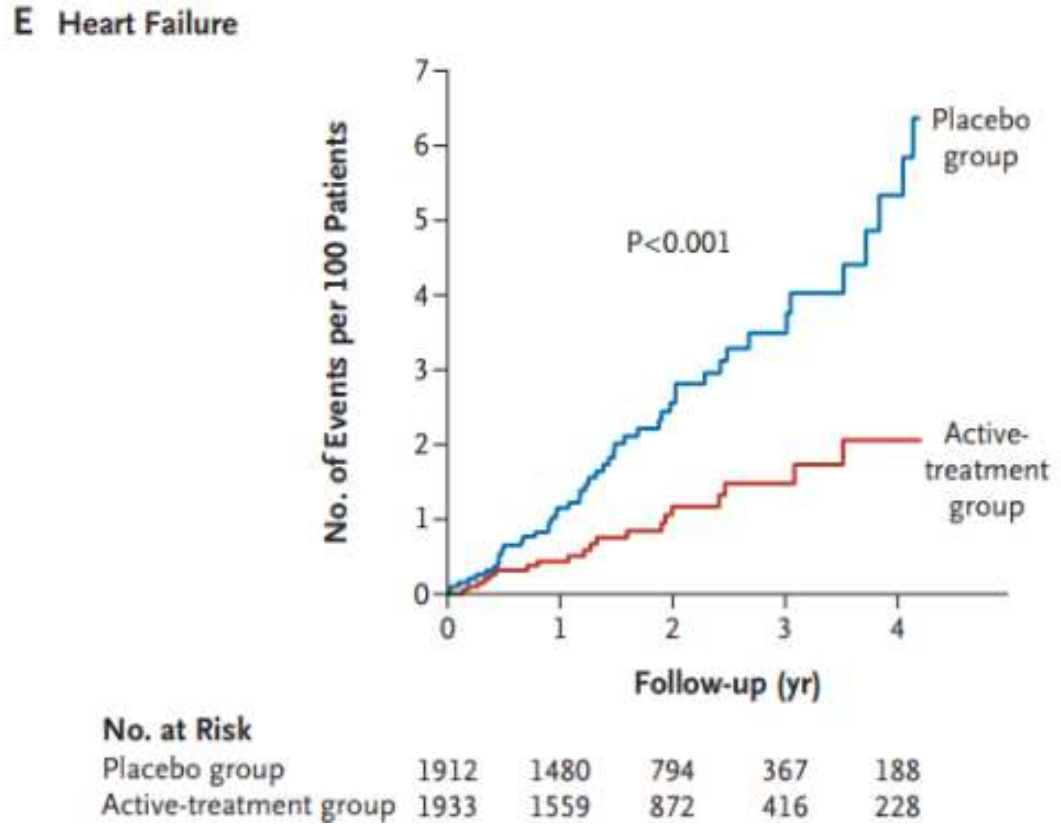
Choice of diuretic therapy

Hypertension in the Very Elderly Trial (HYVET)



Antihypertensive treatment with indapamide ER, with or without perindopril, in persons 80 years of age or older is beneficial.

- N Engl J Med 2008;358:1887-98

Blood Pressure Goals

BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General		
Clinical CVD or 10-year ASCVD risk ≥10%	≥130/80	<130/80
No clinical CVD and 10-year ASCVD risk <10%	≥140/90	<130/80
Older persons (≥65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥130 (SBP)	<130 (SBP)
Specific comorbidities		
Diabetes mellitus	≥130/80	<130/80
Chronic kidney disease	≥130/80	<130/80
Chronic kidney disease after renal transplantation	≥130/80	<130/80
Heart failure	≥130/80	<130/80
Stable ischemic heart disease	≥130/80	<130/80
Secondary stroke prevention	≥140/90	<130/80
Secondary stroke prevention (lacunar)	≥130/80	<130/80
Peripheral arterial disease	≥130/80	<130/80

Hypertension. 2018;71:e13–e115

Why is Single Pill Combination recommended for initial therapy?

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Advantages of Combination Drug Therapy

- Most patients with hypertension require multiple agents for control of their blood pressure.
- Many patients started on a single agent will subsequently require ≥2 drugs from different pharmacological classes to reach their BP goals.
- Patients with higher blood pressures are at greater risk and more rapid titration of antihypertensive medications began to be recommended in patients with BP >20/10 mm Hg above their target.
- Initial combination therapy leads to reduced hypertension-related cardiovascular complications more effectively than monotherapy.
- Fixed-dose combinations simplify therapeutic regimen.
- Use of combination therapy may also improve adherence.

Hypertension. 2018;71:e13–e115 American Journal of Hypertension 31(3) March 2018/International Journal of Cardiology 331 (2021) 262–269

Advantages of Combination Drug Therapy

Combination therapy is the suggested way to increase treatment efficacy while combined agents also may minimize the adverse effects of each individual agent.

- Thiazide diuretics may stimulate the RAAS. By adding an ACEI or ARB to the thiazide, an additive BP-lowering effect may be obtained.

- Studies show treatment with amlodipine/valsartan 5/160 mg induced significantly less peripheral **edema** than amlodipine 10 mg for similar BP reduction.

Hypertension. 2018;71:e13–e115

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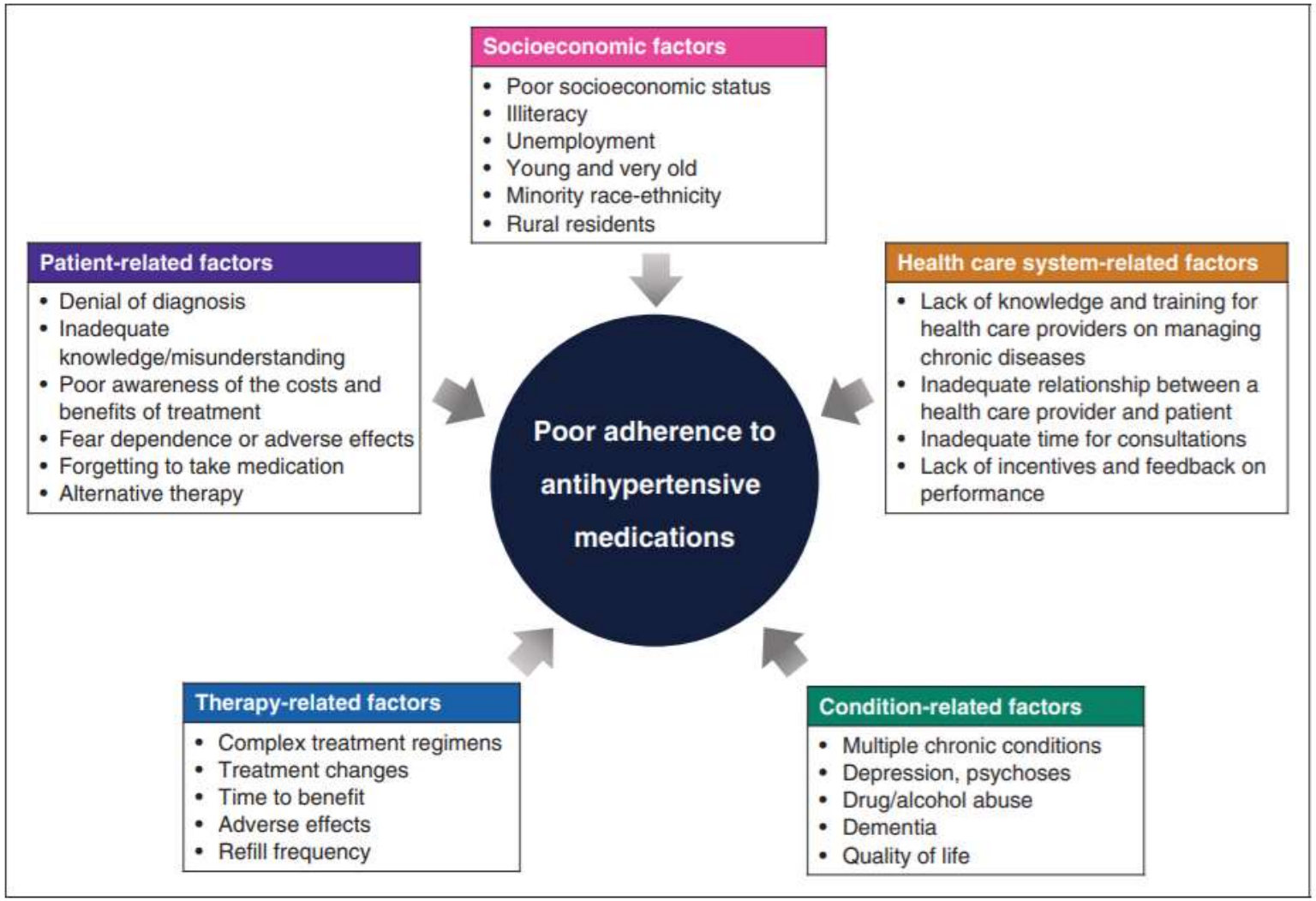
Factors affecting adherence to antihypertensive treatment



Consequences of Suboptimal Adherence to Antihypertensive Medications

1. Uncontrolled hypertension
2. Progression to hypertensive crisis
3. Vascular stiffness
4. Left ventricular hypertrophy
5. Microalbuminuria
6. Myocardial infarction
7. Stroke
8. Chronic heart failure
9. Chronic kidney and end-stage renal disease
10. Cognitive dysfunction, dementia
11. Excess emergency department and hospital admissions
12. Reduced quality of life
13. Impaired work productivity, disability
14. Increased healthcare costs
15. Death

Advantages of Combination Drug Therapy: Adherence Improvement

Therapeutic non-adherence is a major contributor to poor control of hypertension and a key barrier to reducing CVD deaths.

Up to 25% of patients do not fill their initial prescription for antihypertensive therapy.

During the first year of treatment, the average patient has possession of antihypertensive medications only 50% of the time, and only 1 in 5 patients has sufficiently high adherence to achieve the benefits observed in clinical trials.

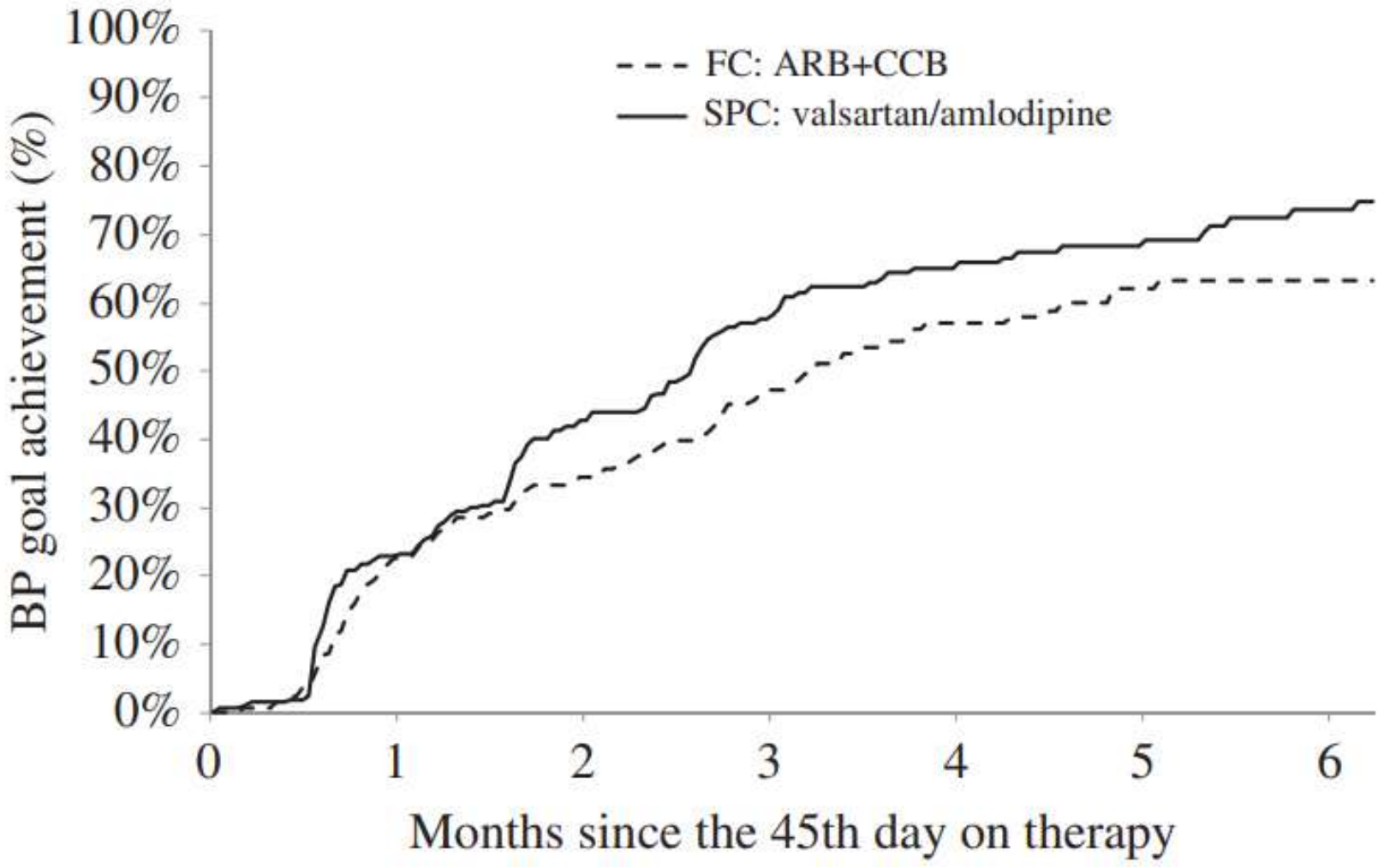
Taking medications several times throughout the day requires greater attention to scheduling, as well as additional issues such as transportation or storage, which can be challenging for some patients.

Simplifying medication regimens, either by less frequent dosing or use of combination drug therapy, improves adherence.

Hypertension. 2018;71:e13–e115

Combination Therapy

More Adherence, More BP Goal Achievements



Curr Med Res Opin 2010; 26:2203–12

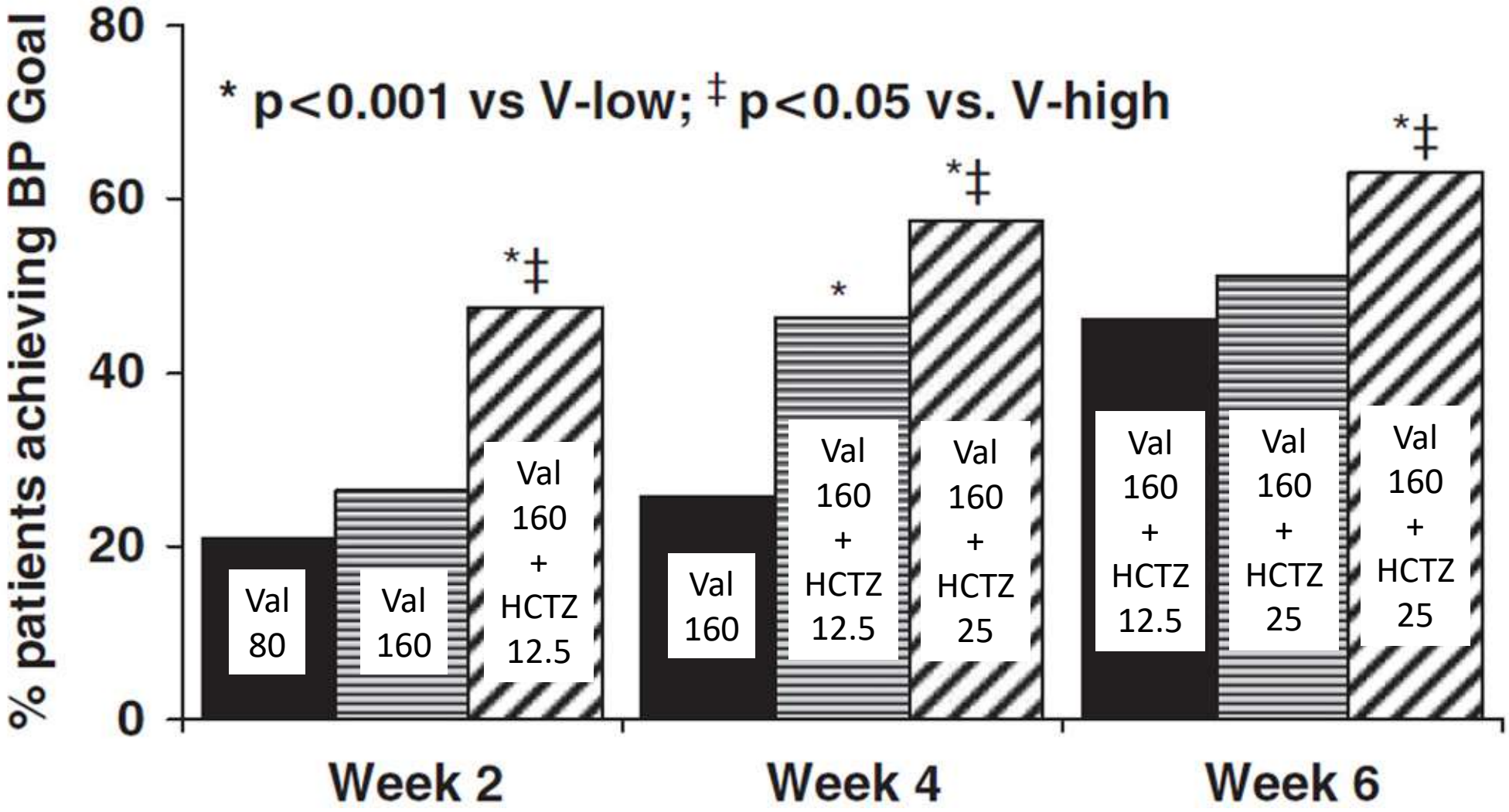
Antihypertensive Medication Adherence Strategies

COR	LOE	Recommendations for Antihypertensive Medication Adherence Strategies
I	B-R	In adults with hypertension, dosing of antihypertensive medication **once daily** rather than multiple times daily is beneficial to improve adherence.
IIa	B-NR	Use of **combination pills** rather than free individual components can be useful to improve adherence to antihypertensive therapy.

Hypertension. 2018;71:e13–e115

Combination Therapy

More Efficacy, Less Titration Steps

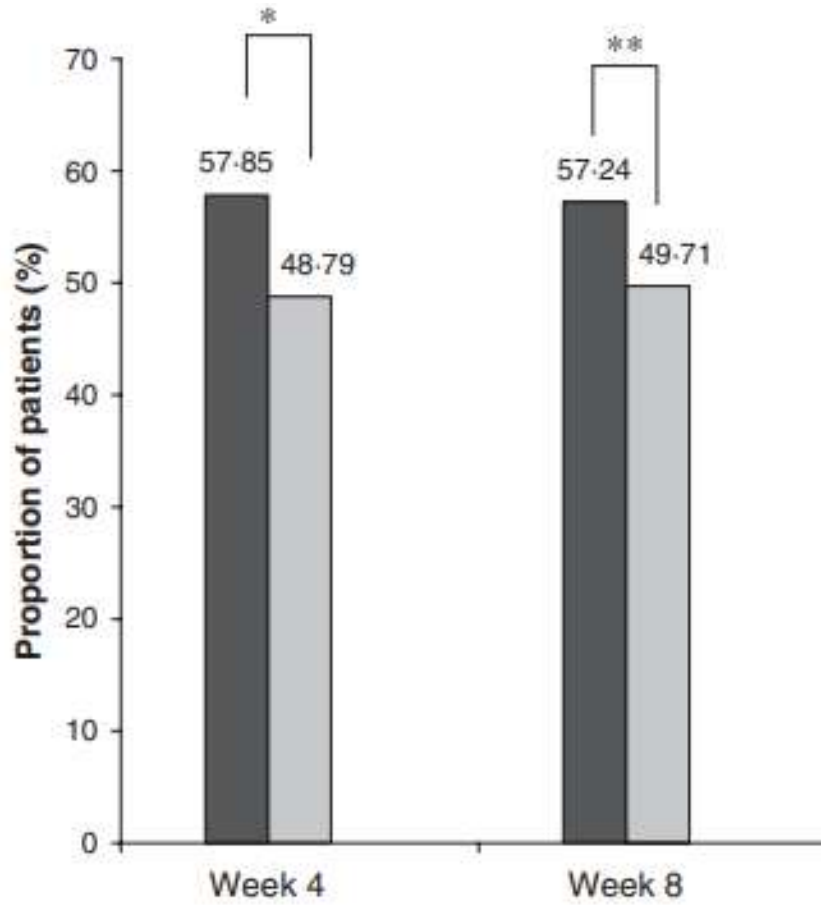


Journal of Human Hypertension (2010) 24, 483–491

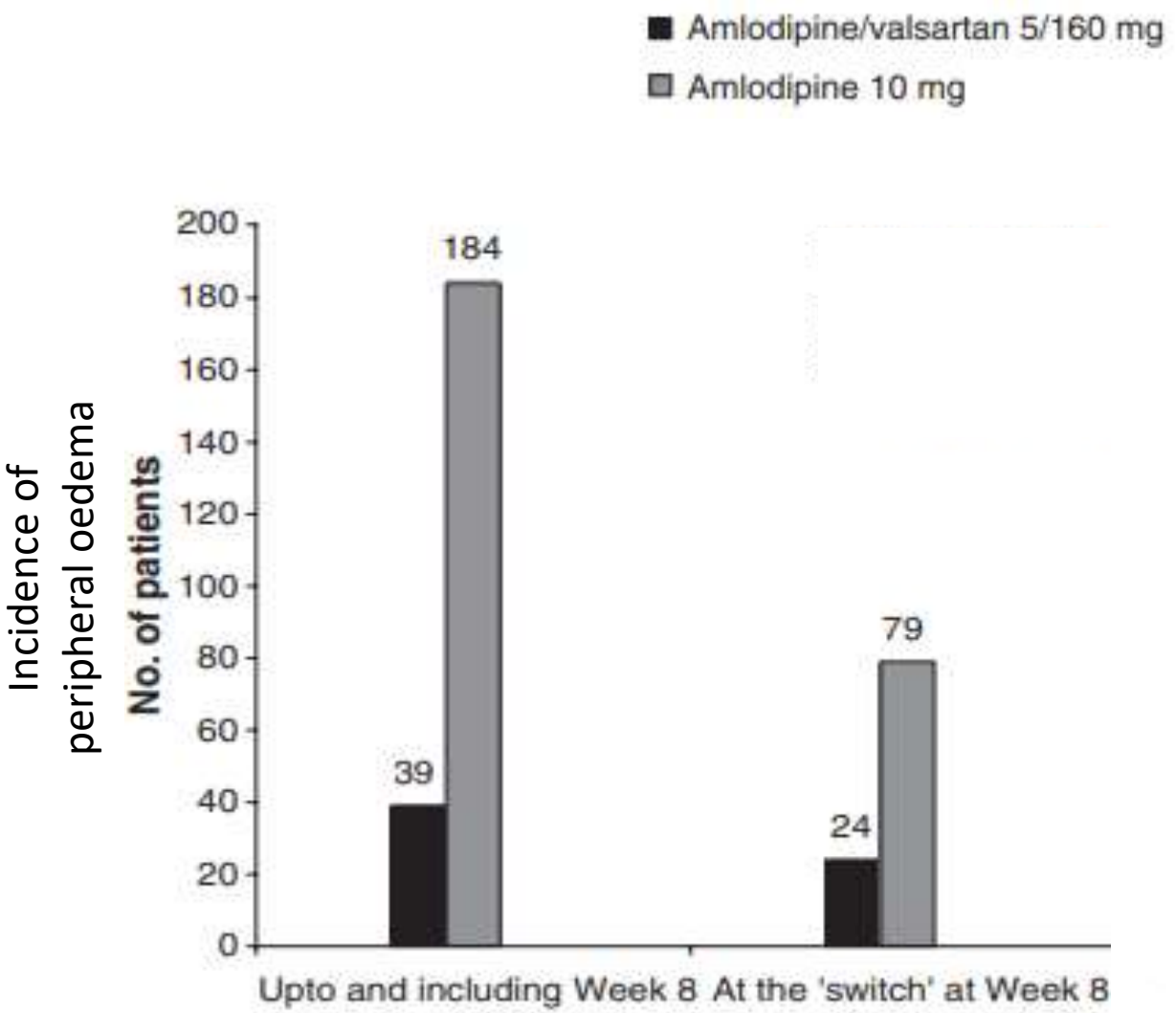
Combination Therapy

More Efficacy, Less Adverse Reaction

overall BP control



Incidence of peripheral oedema



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Int J Clin Pract, February 2009, 63, 2, 217–225

Advantages of Combination Drug Therapy: Recap

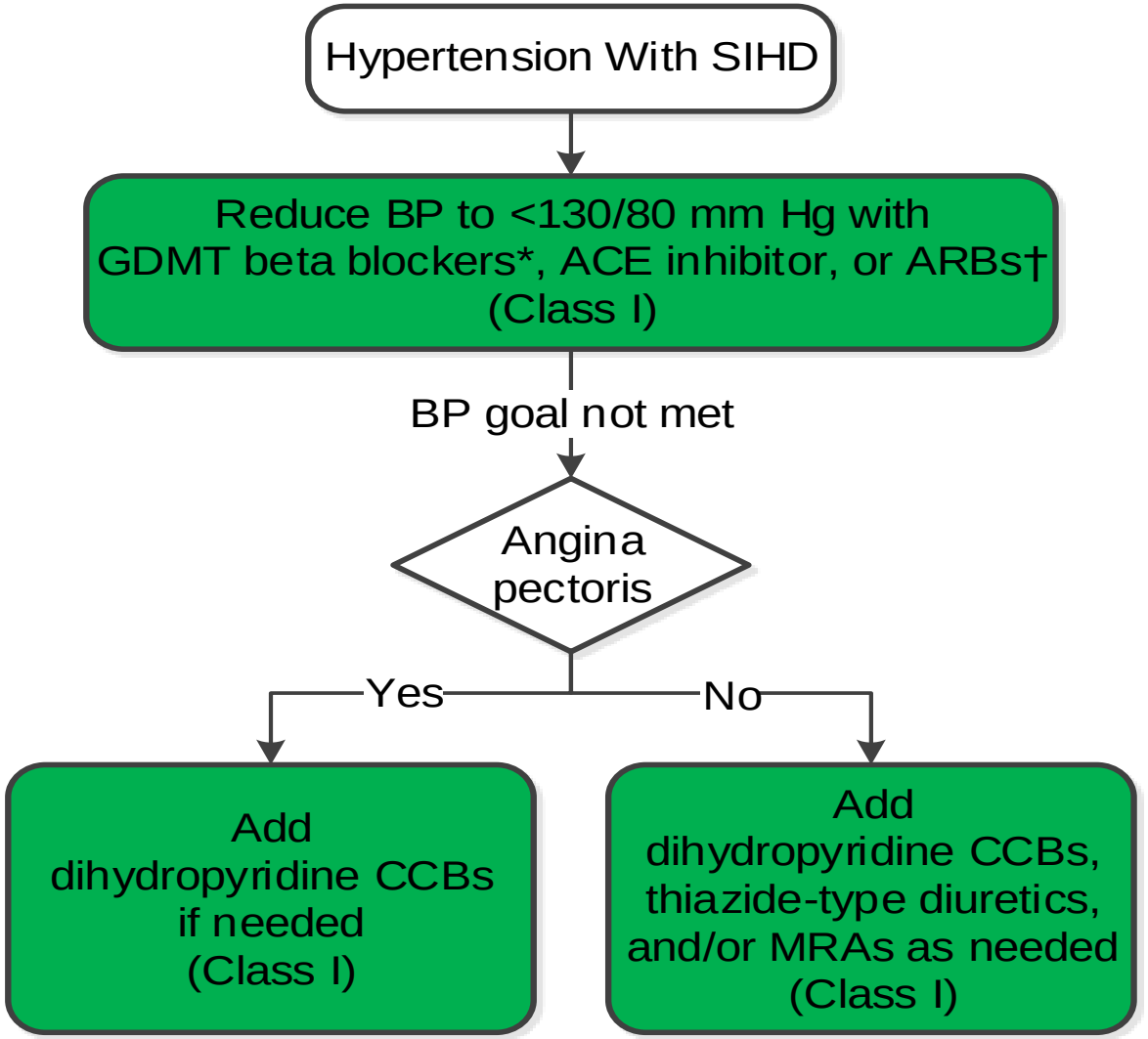
- From a guidelines perspective, SPCs as first line should now be viewed as having been met a reasonable minimum standard, i.e., demonstration of both reduction in BP and reduction in CV risk.

- With the appreciation of the ***greater effectiveness***, ***lesser rates of adverse effects***, ***greater adherence***, ***improved BP control rates***, and ***lower risks of hypertension-related cardiovascular complications,*** initial SPCs is an established if not preferred form of therapy in hypertension.

Hypertension. 2018;71:e13–e115

Which combination for which patient?

Management of Hypertension in Patients With SIHD



Hypertension. 2018;71:e13–e115

Management of Hypertension in Patients With Heart Failure

COR	LOE	Recommendations for Treatment of Hypertension in Patients With HF
III: No Benefit	B-R	**Nondihydropyridine CCBs** are not recommended in the treatment of hypertension in adults with HF*r*EF.

I	C-EO	In adults with HF*p*EF who present with symptoms of volume overload, **diuretics** should be prescribed to control hypertension.
I	C-LD	Adults with HF*p*EF and persistent hypertension after management of volume overload should be prescribed **ACEI** or **ARBs** and **beta blockers** titrated to attain SBP of less than 130 mm Hg.

Hypertension. 2018;71:e13–e115

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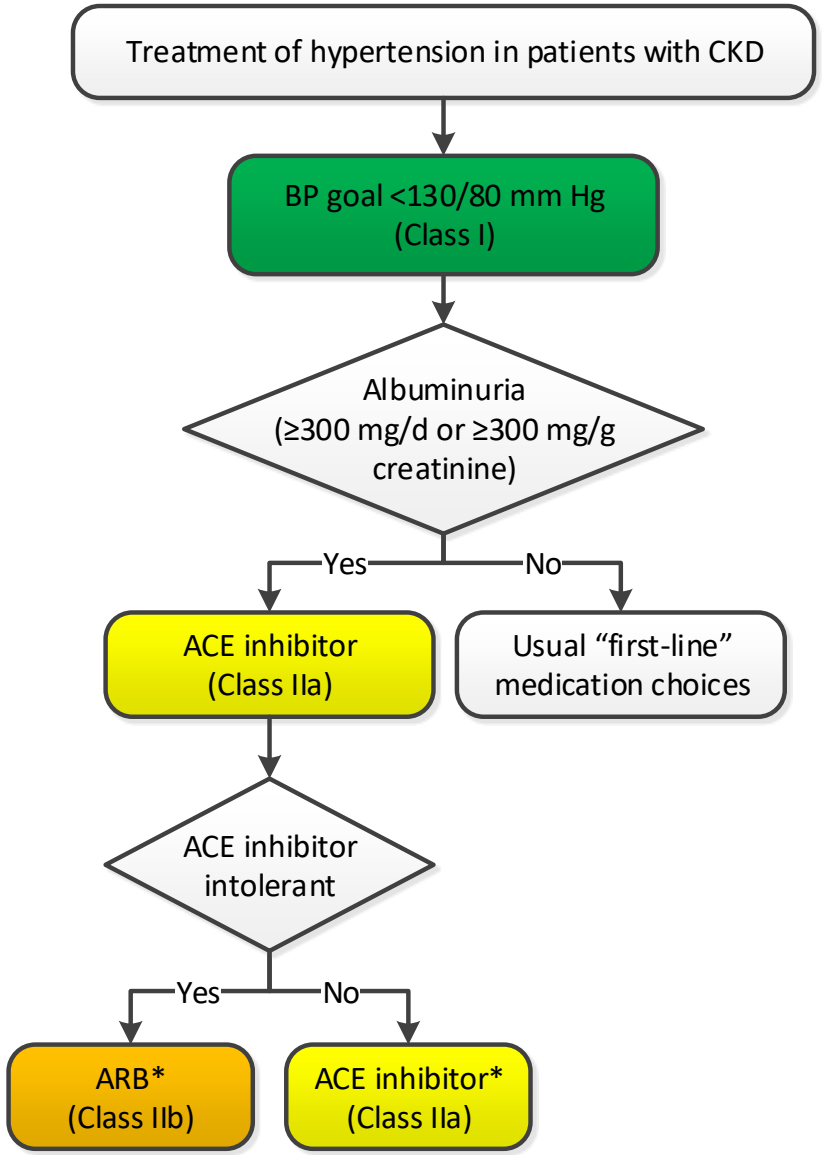
Management of Hypertension in Patients With CKD



Hypertension. 2018;71:e13–e115

Management of Hypertension in Patients With Diabetes Mellitus

COR	LOE	Recommendations for Treatment of Hypertension in Patients With DM
I	A^{SR}	In adults with DM and hypertension, all first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective.
IIb	B-NR	In adults with DM and hypertension, ACE inhibitors or ARBs may be considered in the presence of albuminuria.

Hypertension. 2018;71:e13–e115

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Management of Hypertension for Secondary Stroke Prevention

COR	LOE	Recommendations for Treatment of Hypertension for Secondary Stroke Prevention
I	A	For adults who experience a stroke or TIA, treatment with a **thiazide diuretic**, **ACE inhibitor**, or **ARB**, or combination treatment consisting of a thiazide diuretic plus ACE inhibitor, is useful.

Hypertension. 2018;71:e13–e115

Management of Hypertension in Patients With Atrial Fibrillation

COR	LOE	Recommendation for Treatment of Hypertension in Patients With AF
IIa	B-R	Treatment of hypertension with an **ARB** can be useful for prevention of recurrence of AF.

Hypertension. 2018;71:e13–e115

European Journal of Preventive Cardiology

ESC European Society of Cardiology

Research letter

European Journal of Preventive Cardiology
0(00) 1–4

DOI: 10.1177/2047487319900326
journals.sagepub.com/home/cpr
SAGE

Persistence and adherence to antihypertensive drugs in newly treated hypertensive patients according to initial prescription

Su-Min Jeong[1,2], Shinhye Kim[3,4], Dong Wook Shin[5,6], Kyungdo Han[7], Sang Hyun Park[7], Sang Hyuk Kim[8], Yul-Hee Kim[9] and Yong-Chol Kwon[9]

Study design

South Korea

N=2,919,162

Follow up=12 months

Explain persistence and adherence according to initial antihypertensive prescription

IR-1021-VLZ-6069-SP
Eur J Prev Cardiol.2020;2047487319900326

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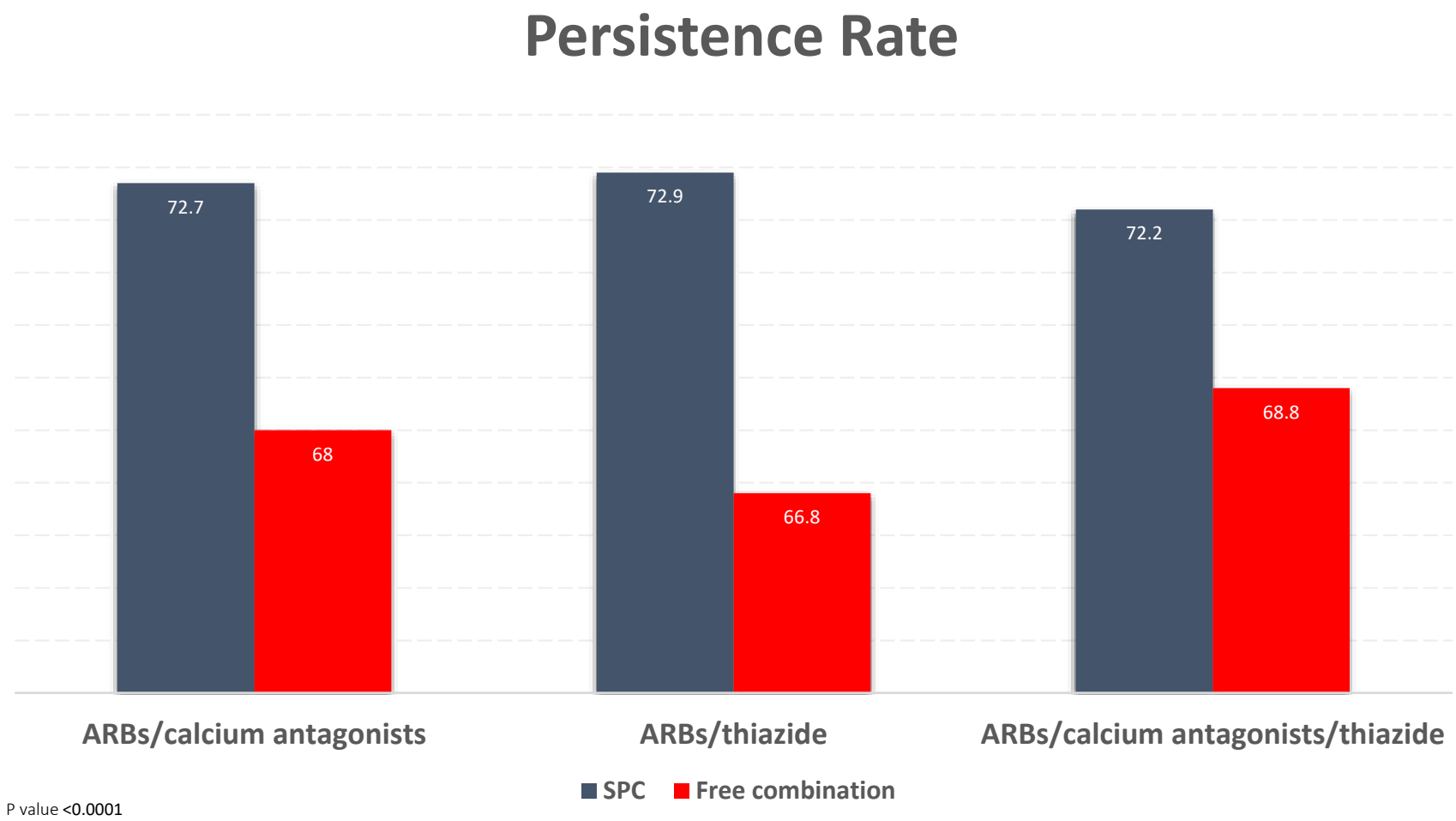
SPC vs Free combination



P value <0.0001

Eur J Prev Cardiol.2020;2047487319900326

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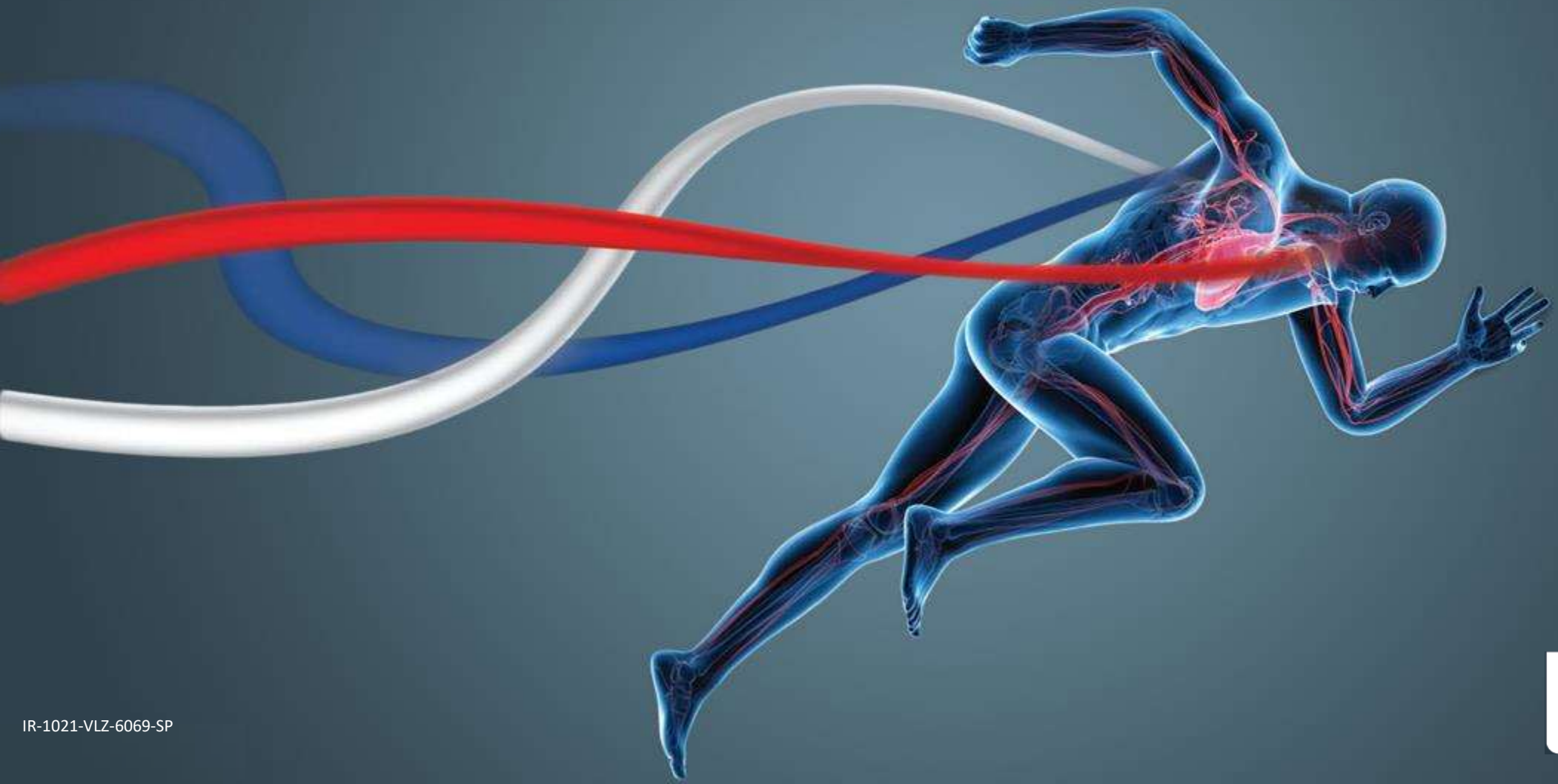
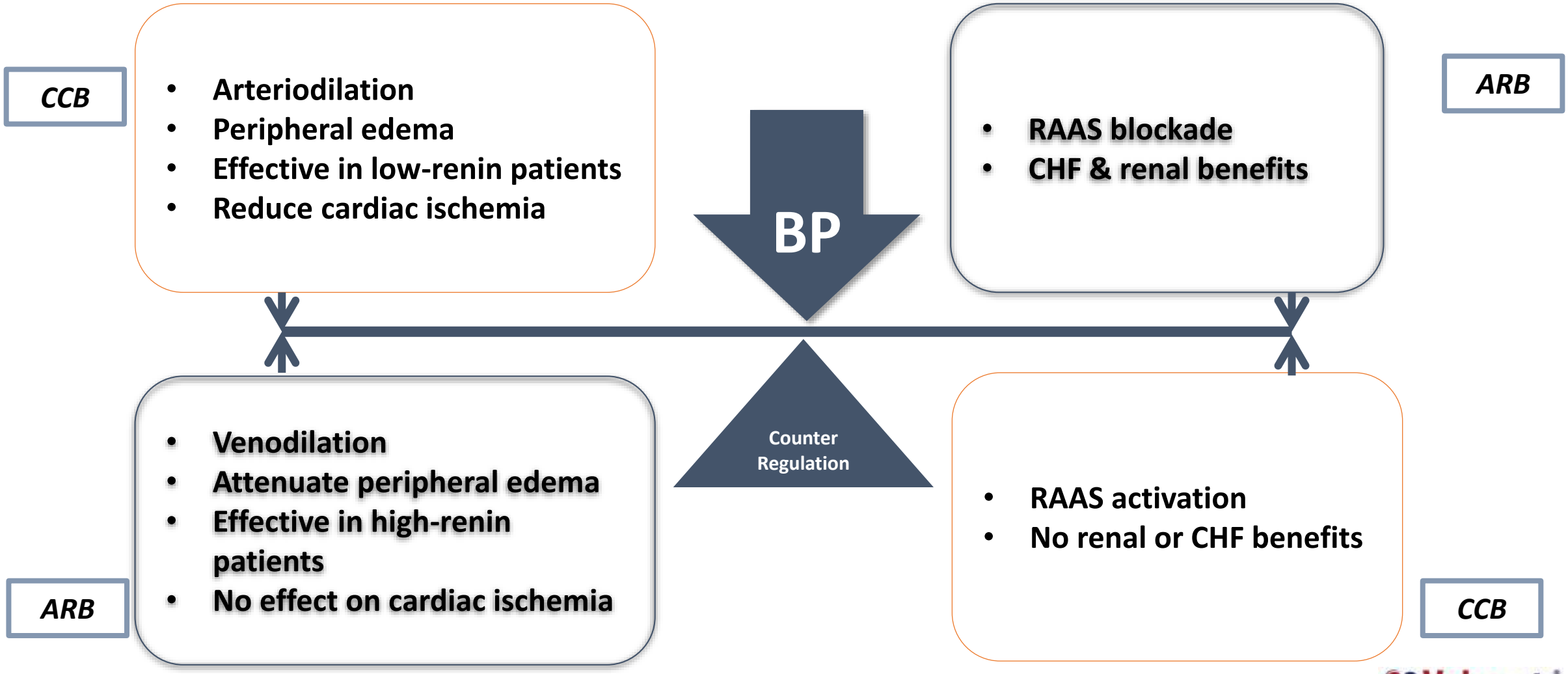
ARB/CCB Combination



IR-1021-VLZ-6069-SP

Valzomix®
Amlodipine / Valsartan

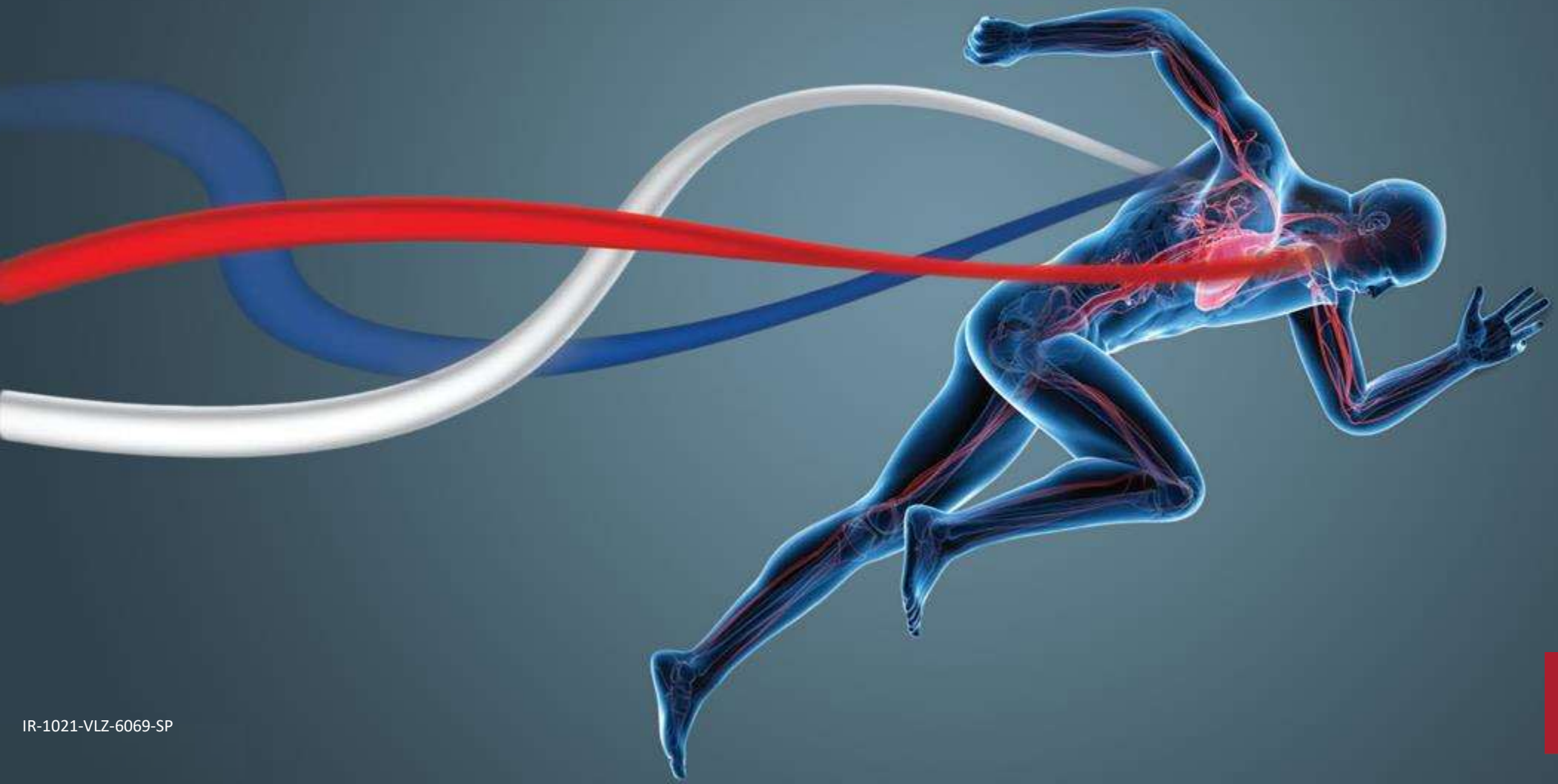
CCB/ARB(Amlodipine/Valsartan)



Vasc Health Risk Manag. 2010; 6: 253–260

Valzomix
Amlodipine / Valsartan

ARB/Diuretic Combination



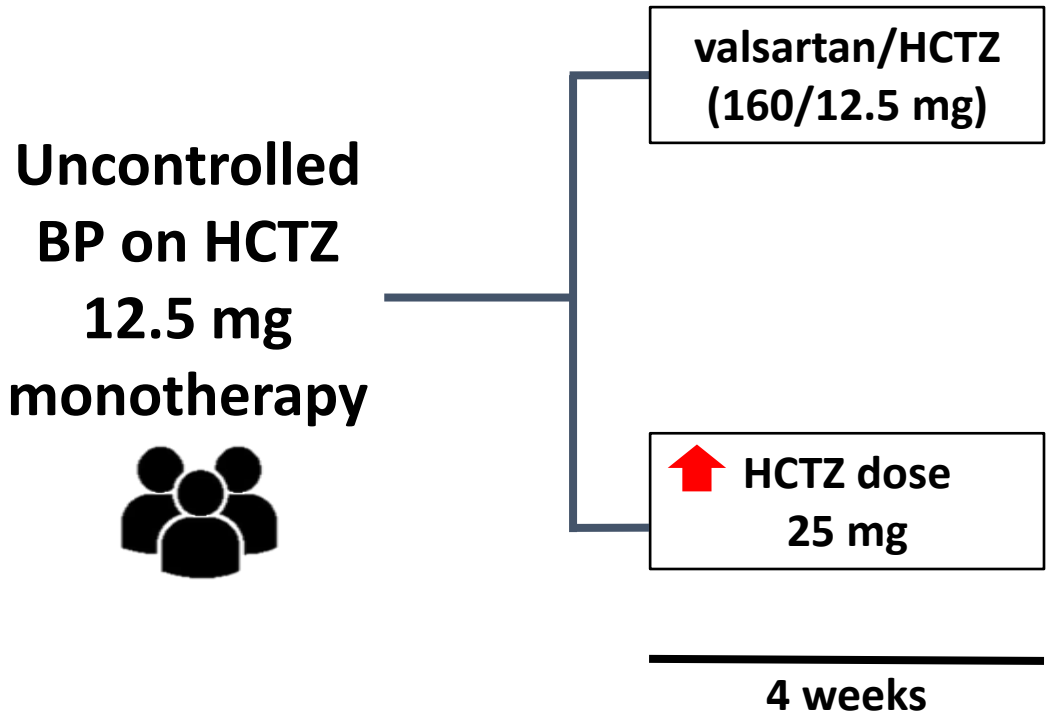
IR-1021-VLZ-6069-SP

Valzodec-HCT®
Valsartan / Hydrochlorothiazide

Val-DICTATE Trial

✓ **Multicenter**

✓ **Randomized**



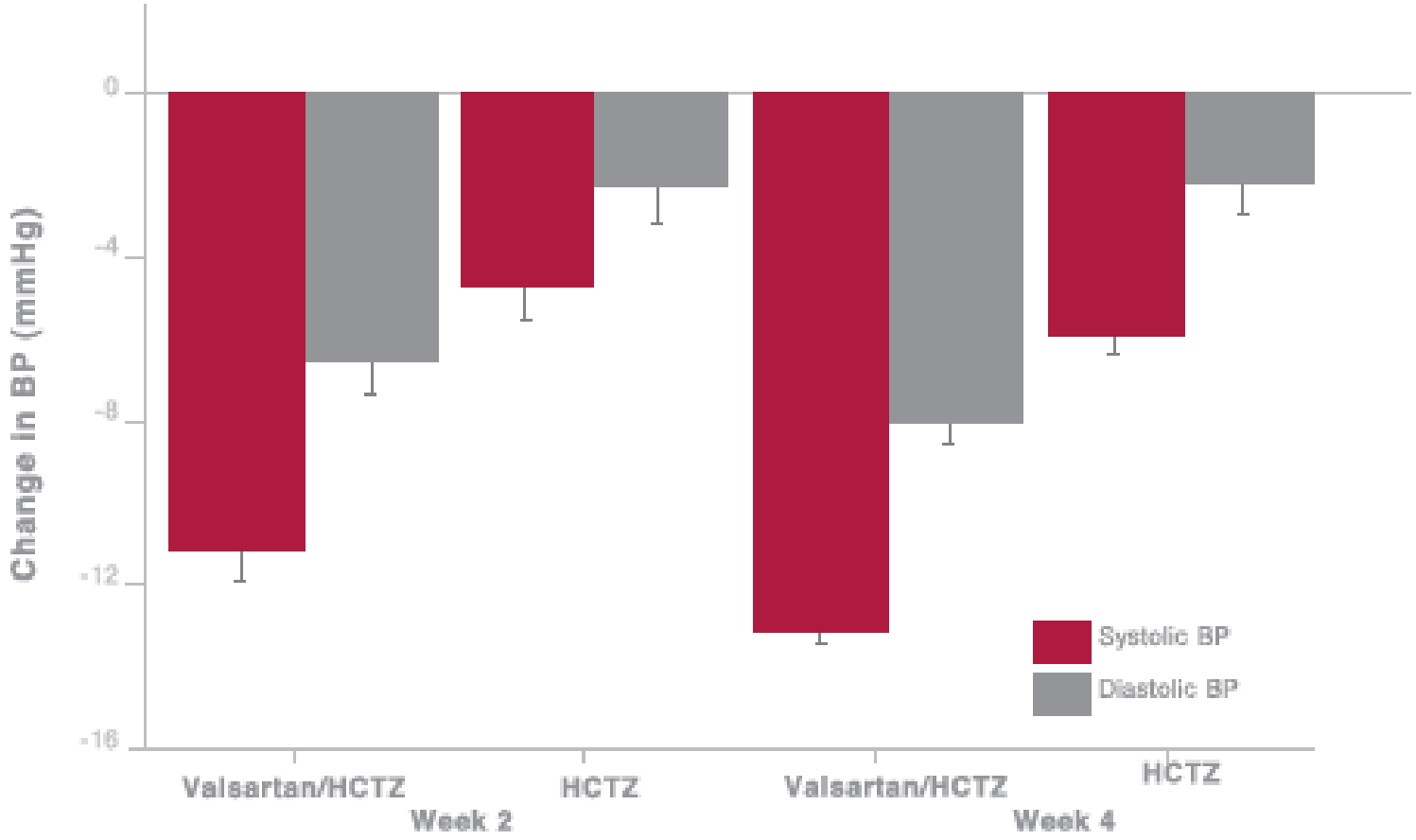
The primary end point:

% patients achieving clinic BP<140/90mmHg

J Clin Hypertens (Greenwich). 2008;10(6):450-8.

Valzodec-HCT®

Val-DICTATE Trial

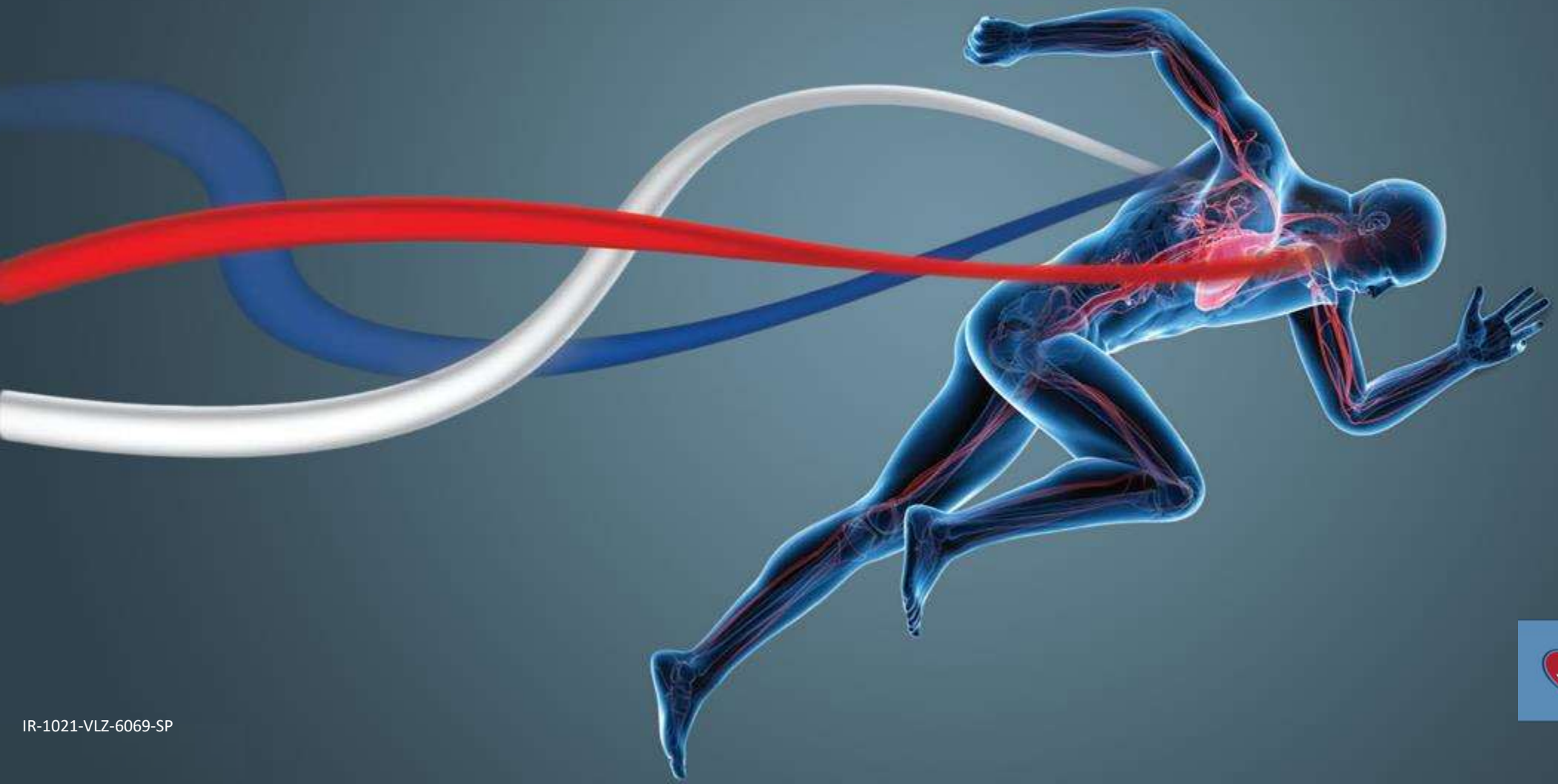


ARB/Diuretic combination more effective in lowering BP & achieving BP goals than increasing the dose of the diuretic

J Clin Hypertens (Greenwich). 2008;10(6):450-8.

Valzodec-HCT®
Valsartan / Hydrochlorothiazide

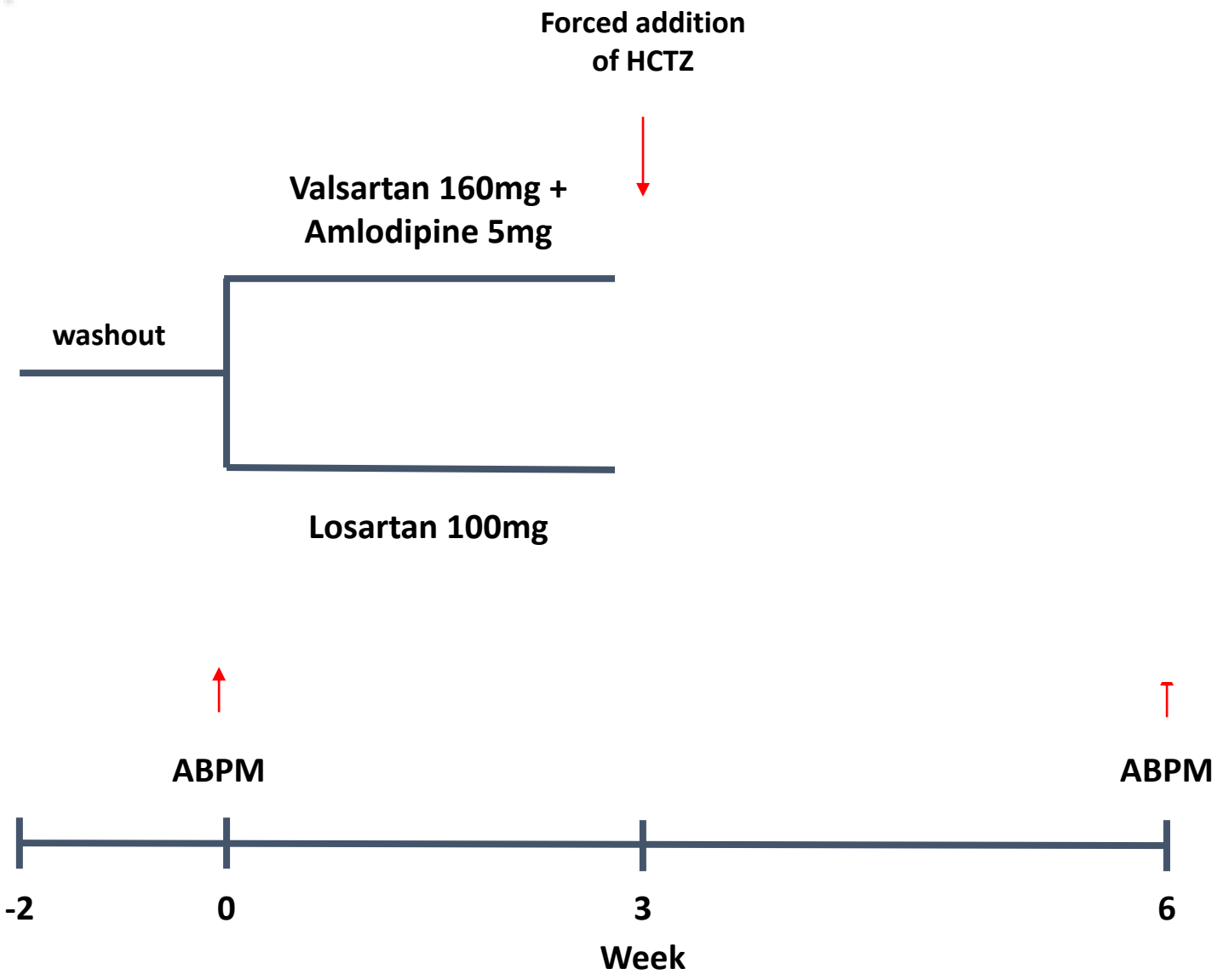
ARB/CCB/Diuretic Combination



Valzomix-HCT®
Amlodipine / Valsartan / Hydrochlorothiazide

IR-1021-VLZ-6069-SP

EXALT
ABPM sub study



Vasc Health Risk Manag. 2011; 7: 701–708.

Valzomix-HCT

EXALT
ABPM sub study

- ✓ **Randomized, double-blind, patients with Stage 2 hypertension**

Triple therapy ⇨ **ARB + CCB +HCTZ**

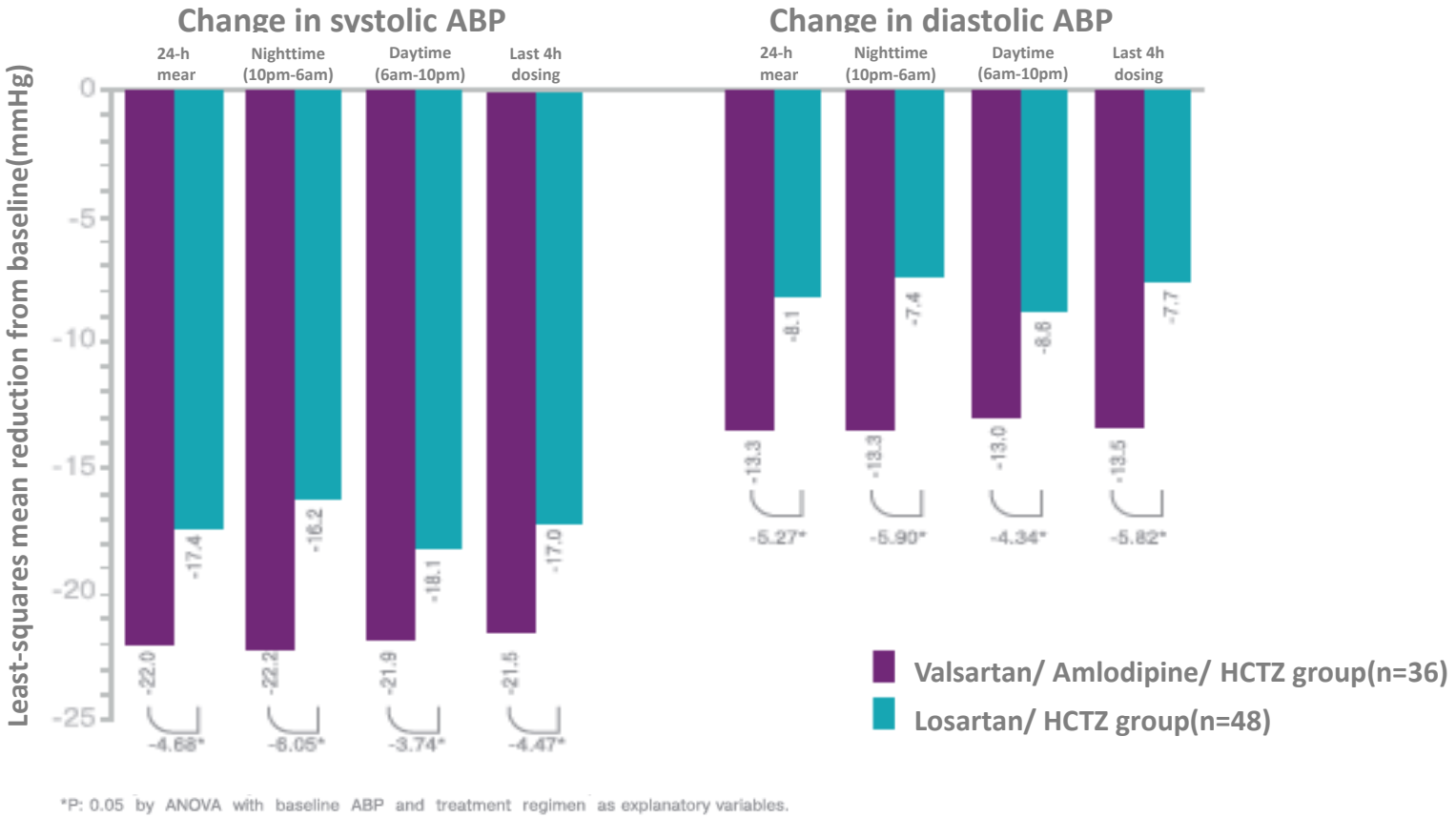
VS

Dual therapy ⇨ **ARB + HCTZ**

Valzomix-HCT

Vasc Health Risk Manag. 2011; 7: 701–708.

EXALT
ABPM sub study



*P: 0.05 by ANOVA with baseline ABP and treatment regimen as explanatory variables.

Initiating therapy of ARB/CCB with a diuretic is more effective than a maximal dose of an ARB with a diuretic

IR-1021-VLZ-6069-SP

Vasc Health Risk Manag. 2011; 7: 701–708.

Valzomix-HCT

Time of Administration

The Hygia Chronotherapy Trial

19 084 hypertensive patients

Daily dose of >_1 hypertension medications at **bedtime** (n = 9552)

Daily dose of >_1 hypertension medications **awakening** (n = 9532)

Whether bedtime in comparison to usual upon awakening hypertension therapy exerts better CVD risk reduction

6.3-year follow up

Eur Heart J. 2019;ehz754.

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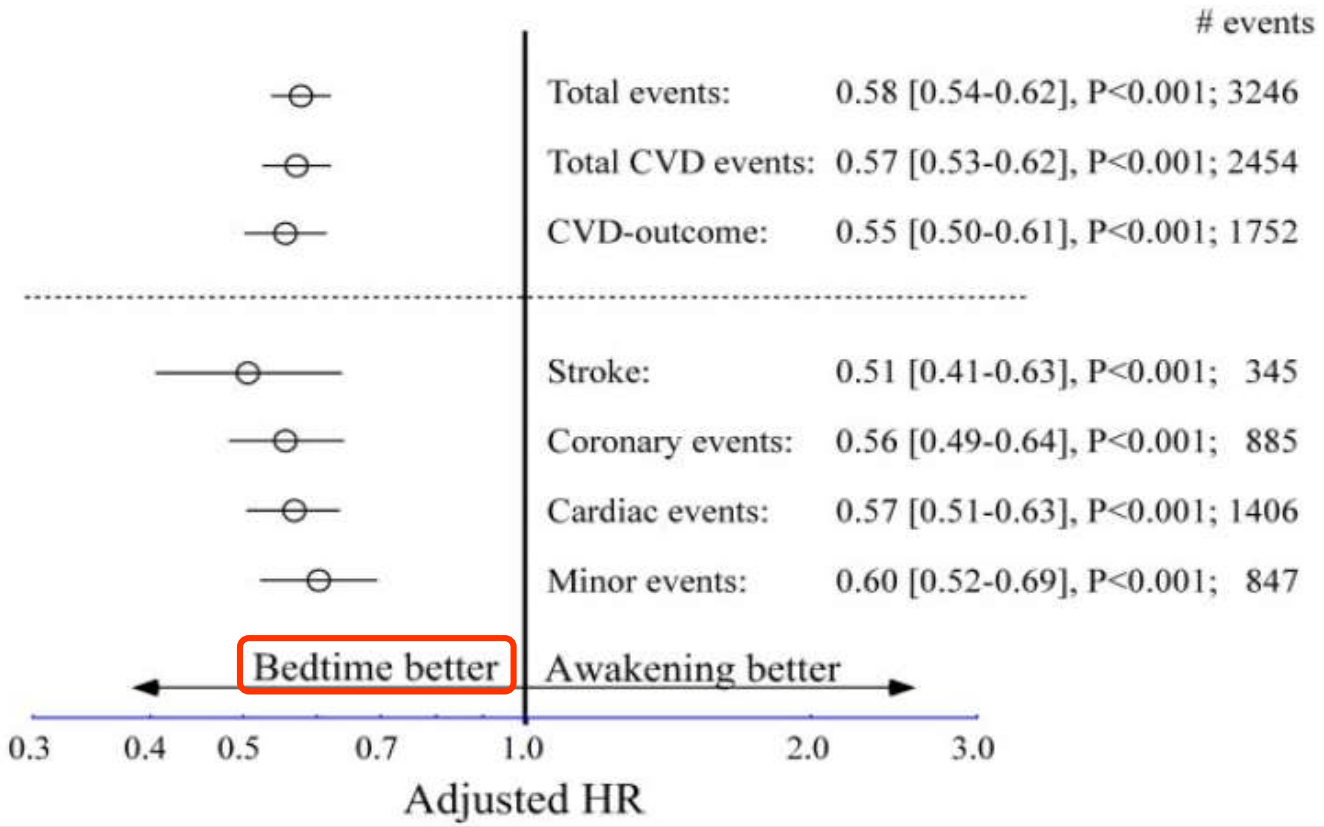
The Hygia Chronotherapy Trial



BP-lowering medications at bedtime results in improved ABP control and markedly diminished occurrence of major CVD events

IR-1021-VLZ-6069-SP
Eur Heart J. 2019;ehz754.

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Take home messages

Initiation of treatment with combination therapy is recommended by recent guidelines:

- ✓ **More efficacy, less titration steps**
- ✓ **Reducing polypharmacy – use of single pill combinations**
- ✓ **Once-daily dosing over multiple times per day dosing**
- ✓ **Increasing patient adherence**

Journal of human hypertension (2010) 24, 438-491

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Valzo family

Valzodec®
Valsartan

Valsartan

- 80
- 160

Valzodec-HCT®
Valsartan / Hydrochlorothiazide

Valsartan+Hydrochlorothiazide

- 80/12.5
- 160/12.5
- 160/25

Natamide® ER
Indapamide

- 1.5

Valzomix®
Amlodipine / Valsartan

Amlodipine+Valsartan

- 5/80
- 5/160
- 10/160

Valzomix-HCT®
Amlodipine / Valsartan / Hydrochlorothiazide

Amlodipine+Valsartan+ Hydrochlorothiazide

- 5/160/12.5
- 10/160/12.5

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