Spedali Civili di Brescia – University of Brescia, Italy

Linee Guida ESC/ESH 2018 per il trattamento della ipertensione

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Potential conflict of interest

Honoraria for lectures and/or participation in Scientific boards from:

Servier, Menarini, Recordati, Malesci, Guidotti, Ferrer, Pfizer, DOC Gen.,Novartis, Sanofi

2018 ESC/ESH Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH)

Authors/Task Force Members: Bryan Williams* (ESC Chairperson) (UK), Giuseppe Mancia*(ESH Chairperson) (Italy), Ileana Desormais (France), Wilko Spiering (The Netherlands), Enrico Agabiti Rosei (Italy), Michel Azizi (France), Michel Burnier (Switzerland), Denis L. Clement (Belgium), Antonio Coca (Spain), Giovanni de Simone (Italy), Anna Dominiczak (UK), Thomas Kahan (Sweden), Felix Mahfoud (Germany), Josep Redon (Spain), Luis Ruilope (Spain), Alberto Zanchetti †, Mary Kerins (Ireland), Sverre E. Kjeldsen (Norway), Reinhold Kreutz (Germany), Stephane Laurent (France), Gregory Y. H. Lip (UK), Richard Mcmanus (UK), Krzysztof Narkiewicz (Poland), Frank Ruschitzka (Switzerland), Roland E. Schmieder (Germany), Evgeny Shlyakhto (Russia), Costas Tsioufis (Greece), Victor Aboyans (France).

Specific aims of 2018 ESC/ESH Guidelines

To produce pragmatic recommendations to make correct diagnosis and Treatment of HTN, thus improving the poor rates of BP control

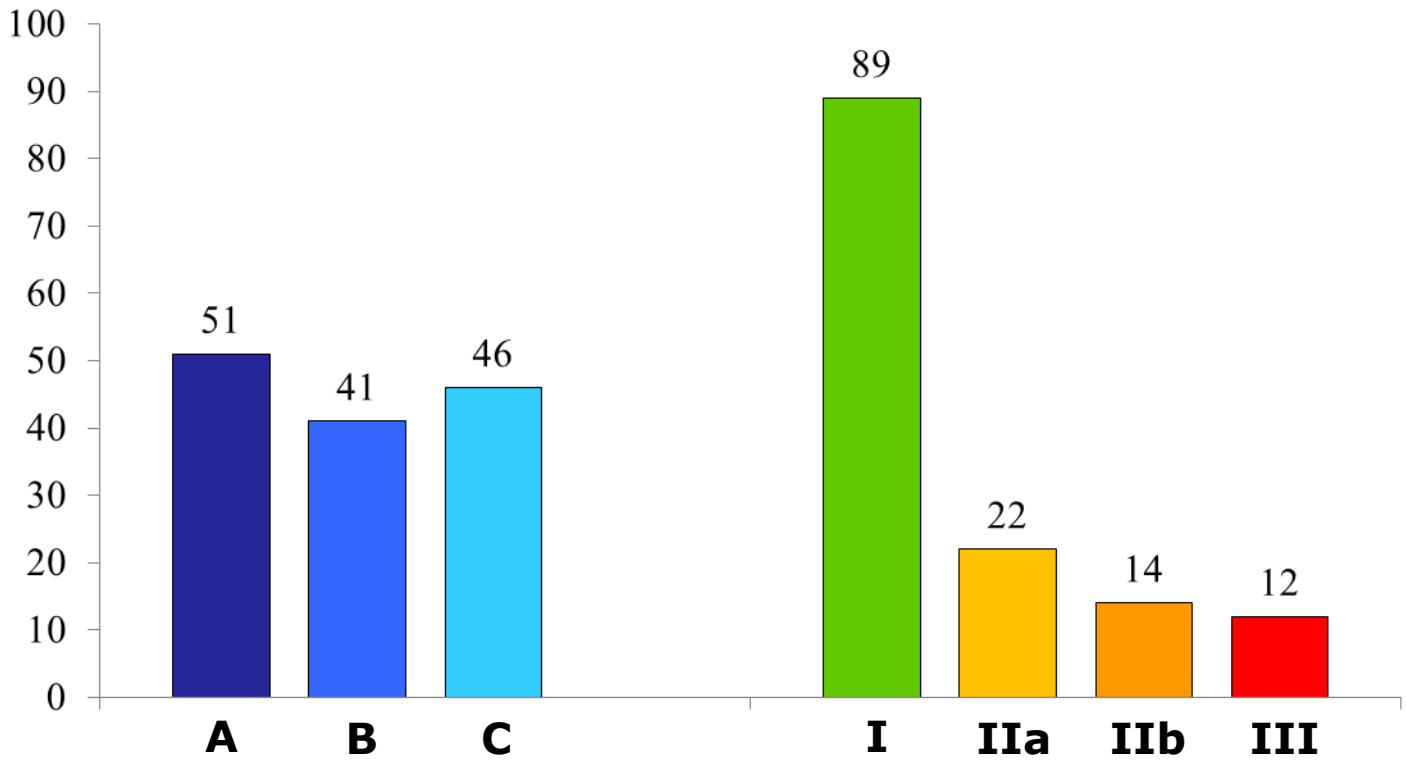
Based on data from:

a) RCT
b) Well conducted metaanalyses of RCT
c) Observational or registry-based studies for many important questions not addressed by RCT

Graded as class of recommendation and level of evidence

Level of evidence

Classes of recommendations



Agenda

- Screening and diagnosis of HTN
- CV risk assessment and HMOD detection
- Thresholds and targets of treatment
- Start of treatment with two drugs in most patients (SPC strategy) and simplified drug-treatment algorithm

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BP measurement

Wider use of out-of-office BP measurement with ABPM and/or HBPM (especially HBPM), as an option to confirm the diagnosis of hypertension, detect white coat and masked hypertension and monitor BP control

BP measurement - 2

Recommendations	Class	Level
It is recommended to base the diagnosis of hypertension on:		
• Repeated office BP measurements on more than one visit, except when hypertension is severe (e.g. grade 3 and especially in high-risk patients). At each visit, three BP measurements should be recorded, 1–2 min apart, and additional measurements should be performed if the first two readings differ by > 10 mmHg. The patient's BP is the average of the last two BP readings.	I	C
Or •Out-of-office BP measurement with ABPM and/or HBPM, provided that these measurements are logistically and economically feasible.	I	C
Out-of-office BP (i.e. ABPM or HBPM) is specifically recommended for a number of clinical indications, such as identifying white-coat and masked hypertension, quantifying the effects of treatment, and identifying possible causes of side-effects (e.g. symptomatic hypotension).	I	A
It is recommended that all hypertensive patients undergo pulse palpation at rest to determine heart rate and search for arrhythmias such as AF.	I	C
Other BP measures and indices (pulse pressure, BP variability, exercise BP, central BP) may be considered but are not often used for routine clinical use at present. They may provide useful additional information in some circumstances and are valuable tools for research.	IIb	C

Clinical indications for HBPM or ABPM

Conditions in which white-coat hypertension is more common, e.g. • Grade I hypertension on office BP measurement • Marked office BP elevation without HMOD
Conditions in which masked hypertension is more common, e.g. • High-normal office BP • Normal office BP in individuals with HMOD or at high total CV risk
Postural and post-prandial hypotension in untreated and treated patients
Evaluation of resistant hypertension
Evaluation of BP control, especially in treated higher-risk patients
Exaggerated BP response to exercise
When there is considerable variability in the office BP
Evaluating symptoms consistent with hypotension during treatment
Specific indications for ABPM rather than HBPM: • Assessment of nocturnal BP values and dipping status (e.g. suspicion of nocturnal hypertension, such as in sleep apnoea, CKD, diabetes, endocrine hypertension, or autonomic dysfunction)

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Comparison of ABPM and HBPM

ABPM	HBPM
Advantages • Can identify white-coat and masked hypertension • **Stronger prognostic evidence** • **Night-time readings** • **Measurement in real-life settings** • Additional prognostic BP phenotypes • **Abundant information from a single measurement session, including short-term BP variability**	**Advantages** • Can identify white-coat and masked hypertension • **Cheap and widely available** • Measurement in a home setting, which may be more relaxed than the doctor's office • **Patient engagement in BP measurement** • **Easily repeated and used over longer periods to assess day-to-day BP variability**
Disadvantages • Expensive and sometimes limited availability • Can be uncomfortable	**Disadvantages** • Only static BP is available • Potential for measurement error • No nocturnal readings

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Additional CV risk factors frequently cluster with hypertension

Clustering of risk factors has a multiplicative effect on CV risk

Formal CV risk assessment is recommeded using the SCORE system

It is important to recognize that CV risk estimated by the SCORE system is increased by other risk modifiers and ,in particular, by the presence of HMOD (especially LVH, CKD and advanced retinopathy) which, therefore, should be screened for in hypertensive patients

10-year CV risk categories (SCORE system)

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, 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, 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, that may be moderate risk) **Hypertensive LVH** **Moderate CKD eGFR 30–59 mL/min/1.73 m^2)** **A calculated 10-year SCORE of 5–10%**
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%**

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Hypertension and CV risk assessment

Recommendation	Class	Level
CV risk assessment with the SCORE system is recommended for hypertensive patients who are not already at high or very high risk due to established CV or renal disease or diabetes or a markedly elevated single risk factor (e.g. cholesterol), or hypertensive LVH.	I	B

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

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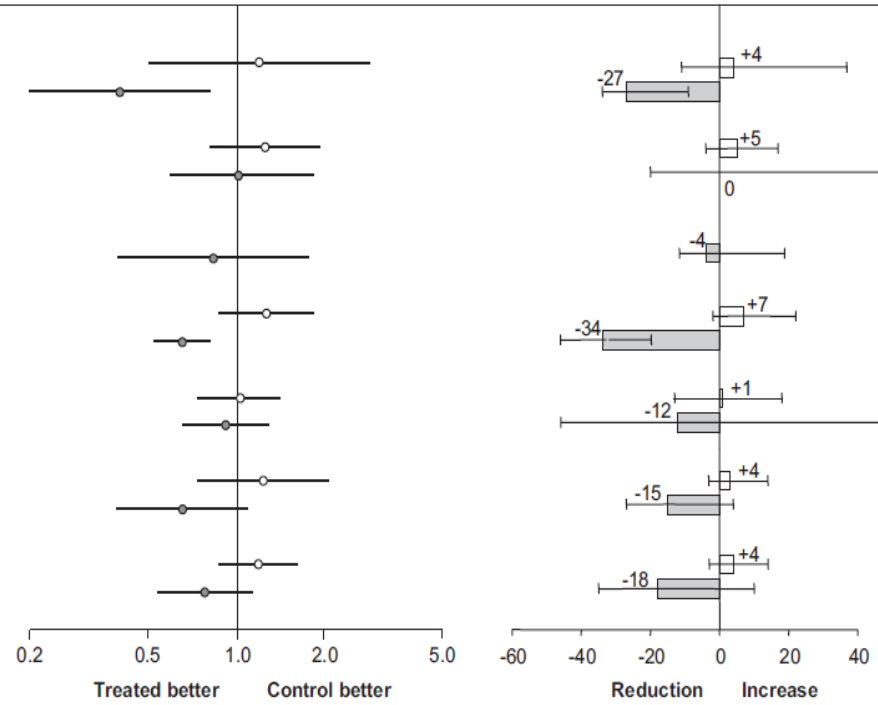
Initiation of hypertension treatment according to office BP

Recommendations	Class	Level
Prompt initiation of BP-lowering drug treatment is recommended in patients with grade 2 or 3 hypertension at any level of CV risk, simultaneous with the initiation of lifestyle changes.	I	A
In patients with grade 1 hypertension:		
• Lifestyle interventions are recommended to determine if this will normalize BP.	II	B
• In patients with grade 1 hypertension at low-moderate risk and without evidence of HMOD, BP-lowering drug treatment is recommended if the patient remains hypertensive after a period of lifestyle intervention.	I	A
• In patients with grade 1 hypertension and at high-risk or with evidence of HMOD, prompt initiation of drug treatment is recommended simultaneously with lifestyle interventions.	I	A
In fit older patients with hypertension (even if age > 80 years), BP-lowering drug treatment and lifestyle intervention are recommended when SBP is ≥ 160 mmHg.	I	A
BP-lowering drug treatment and lifestyle intervention are recommended in the fit older patients (> 65 years but not over 80 years) when SBP is in the grade 1 range (140–159 mmHg), provided that treatment is well tolerated.	I	A
Antihypertensive treatment may also be considered in frail older patients if tolerated.	IIb	B
Withdrawal of BP-lowering drug treatment on the basis of age, even when patients attain an age of ≥ 80 years, is not recommended, provided that treatment is well tolerated.	III	A
In patients with high-normal BP (130–139/85–89 mmHg):		
• Lifestyle changes are recommended.	I	A
• Drug treatment may be considered when their CV is very high due to established CVD, especially CAD.	IIb	A

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Effects of blood-pressure-lowering treatment on outcome incidence.12. Effects in individuals with high-normal and normal blood pressure: overview and meta-analyses of randomized trials

Outcome	CV risk	Trials (n)	Standardized RR (95% CI)	P-value homogeneity	Absolute Risk Reduction 1000 pts/5 years (95% CI)	P-value homogeneity
Stroke	L-M	4	1.20 (0.51-2.78)	0.006	+4	<0.001
	H-VH	8	0.40 (0.20-0.81)		-27	
CHD	L-M	4	1.25 (0.82-1.92)	0.089	+5	0.23
	H-VH	6	1.00 (0.60-1.84)		0	
HF	L-M	1	-	-	-4	-
	H-VH	5	0.82 (0.38-1.81)			
Stroke + CHD	L-M	3	1.27 (0.88-1.81)	<0.001	+7	<0.001
	H-VH	8	0.65 (0.52-0.80)		-34	
Stroke + CHD + HF	L-M	5	1.02 (0.73-1.39)	0.32	+1	0.11
	H-VH	6	0.91 (0.66-1.29)		-12	
CV Death	L-M	3	1.23 (0.74-2.06)	0.001	+4	<0.001
	H-VH	6	0.66 (0.40-1.09)		-15	
All Death	L-M	10	1.18 (0.88-1.60)	0.016	+4	<0.001
	H-VH	6	0.77 (0.54-1.13)		-18	



C. Thomopoulos et al, Journal of Hypertension 2017, 35:2150–2160

When to initiate antihypertensive treatment

- **Drug treatment in grade 1 hypertension at low-to-moderate CV risk**

1) **Metaanalyses:**

   a) **Thomopoulos et al., J Hypertens 2014, 32: 2285**

   b) **Brunstrom et al., JAMA Intern Med 2018, 178:28**

   c) **Gundstrom et al., Ann Intern Med 2015, 162:184**

2) **(HOPE)-3 trial**

When to initiate antihypertensive treatment

- **Drug treatment in older people with grade 1 hypertension**

  - **Chronological vs Biological age**
  - **Fit, independent vs physically and mentally frail patients**
  - **Several RCT included older patients at grade 1 hypertension**
  - **BP lowering drugs should not be withdrawn on the basis of age alone**

Summary of office BP thresholds for treatment

Age group	Office SBP treatment threshold (mmHg)					Diastolic treatment threshold (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/TIA	
18–65 years	≥ 140	≥ 140	≥ 140	≥ 140	≥ 140	≥ 90
65–79 years	≥ 140	≥ 140	≥ 140	≥ 140	≥ 140	≥ 90
≥ 80 years	≥ 160	≥ 160	≥ 160	≥ 160	≥ 160	≥ 90
Diastolic treatment threshold (mmHg)	≥ 90	≥ 90	≥ 90	≥ 90	≥ 90	

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Office BP treatment targets in hypertensive patients

Recommendations	Class	Level
It is recommended that the first objective of treatment should be to lower BP to < 140/90 mmHg in all patients, and provided that the treatment is well tolerated, treated BP values should be targeted to 130/80 mmHg or lower, in most patients.	I	A
In patients < 65 years receiving BP-lowering drugs, it is recommended that SBP should be lowered to a BP range of 120 to < 130 mmHg in most patients.	I	A
In older patients (aged ≥ 65 years) receiving BP-lowering drugs:		
• It is recommended that SBP should be targeted to a BP range of 130 to < 140 mmHg.	I	A
• Close monitoring of adverse effects is recommended.	I	C
• These BP targets are recommended for patients at any level of CV risk and in patients with and without established CVD.	I	A

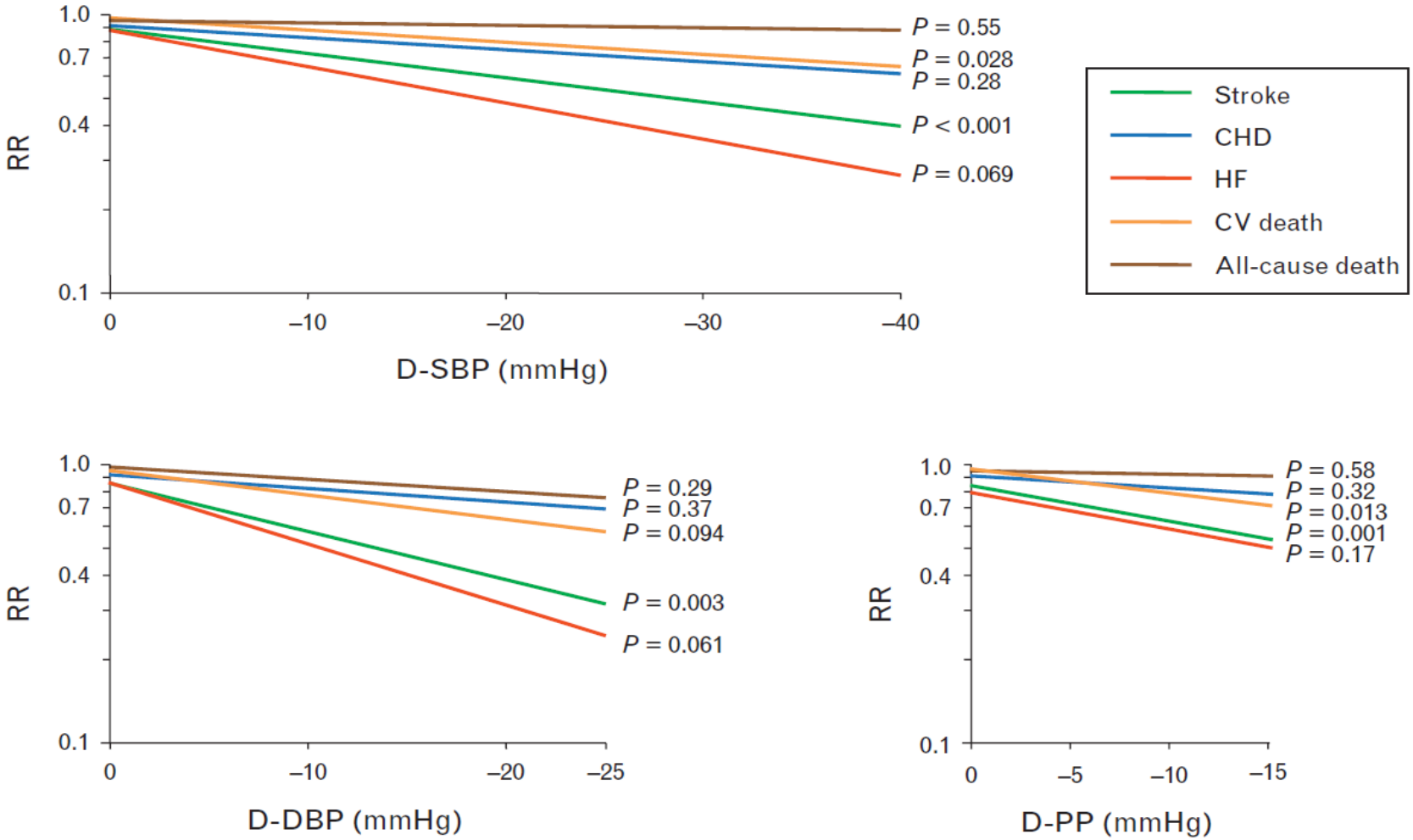
Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Office BP treatment target range

Age group	Office SBP treatment target ranges (mmHg)					Diastolic treatment target range (mmHg)
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/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	< 80 to 70
65–79 years	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	< 80 to 70
≥ 80 years	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	**Target to < 140 to 130** *if tolerated*	< 80 to 70
Diastolic treatment target range(mm Hg)	< 80 to 70	< 80 to 70	< 80 to 70	< 80 to 70	< 80 to 70	

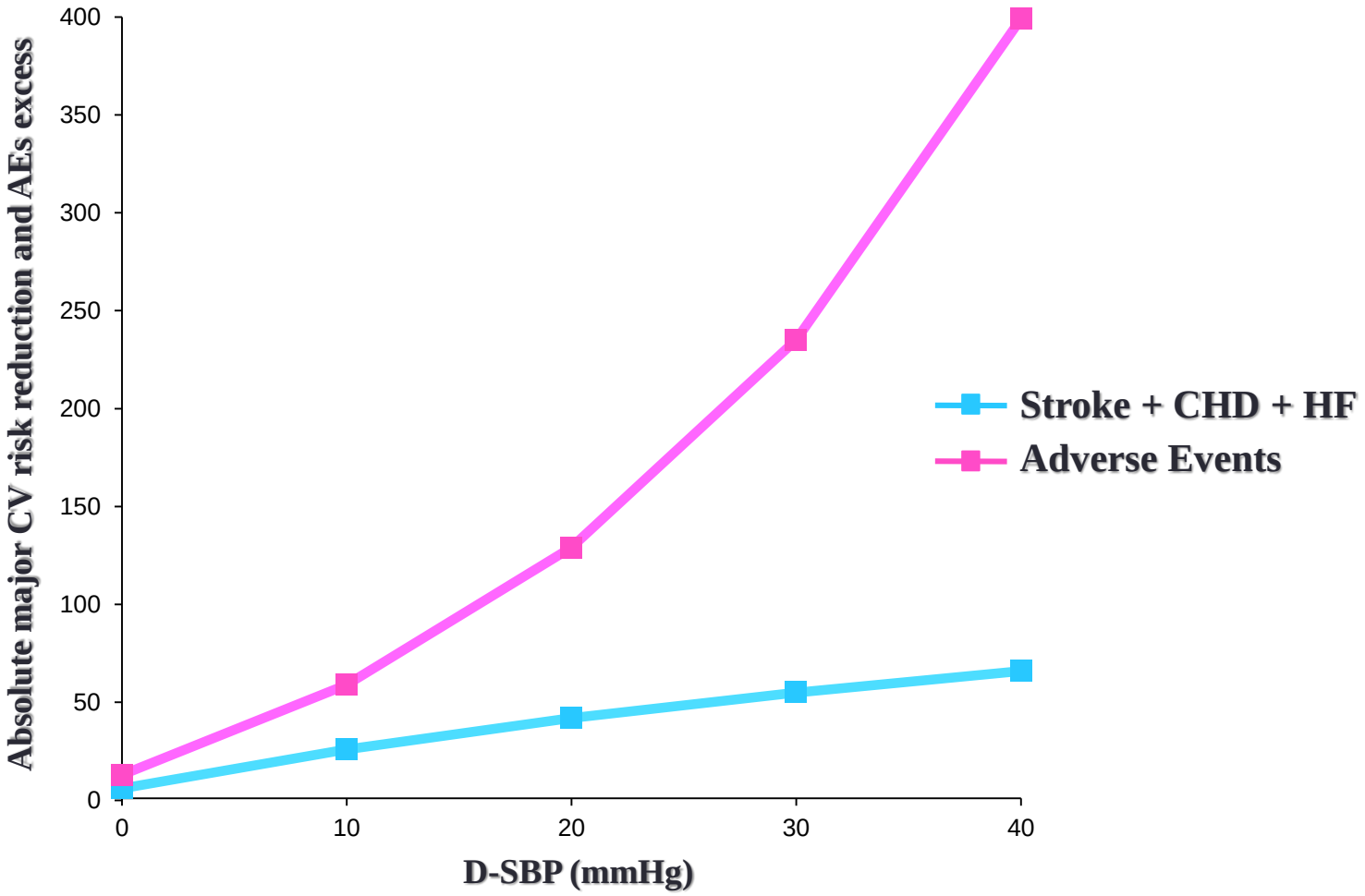
Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Relationships of outcome reductions to the extent of BP reductions
Meta regressions of risk ratios on absolute BP differences (active treatment group minus placebo or less active treatment group) in 47 trials of intentional BP lowering



C. Thomopoulos et al. Journal of Hypertension 2014, 32:2285–2295

Relationships of Numbers of Outcomes Prevented and Numbers of Excess in Treatment Discontinuations* to the Extent of SBP Reductions



* Attributed to treatment adverse events

J Hypertens 2016; 34: 1451-1463

Irrespective of the world region, economy and healthcare organization, BP control rates remain poor

In fact:

- **about 40% of hypertensive patients are treated**
- **Of these, only about 35% have BP < 140/90 mmHg**

Chow CK et al, JAMA 2013,

Consider

1. **Efficacy of pharmacological therapies**
2. **Physician or treatment inertia**
3. **Patient adherence to treatment**
4. **Insufficient use of combination treatment**
5. **Complexity of current treatment strategies**

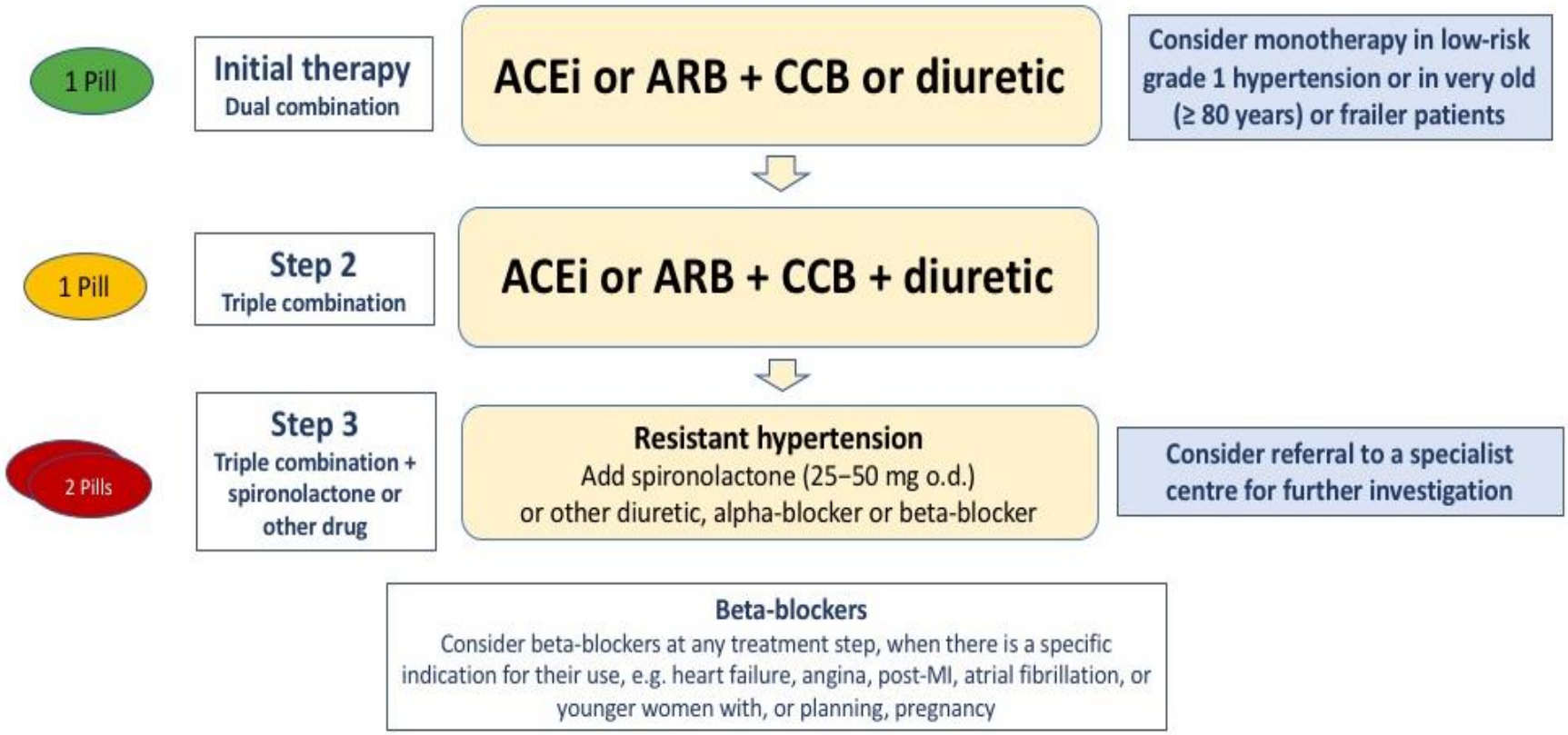
2018 ESH ESC Guidelines for the management of arterial hypertension

Drug treatment strategy for hypertension

Recommendations	Class	Level
Among all antihypertensive drugs, ACE inhibitors, ARBs, beta-blockers, CCBs, and diuretics (thiazides and thiazide-like such as chlortalidone and indapamide) have demonstrated effective reduction of BP and CV events in RCTs, and thus are indicated as the basis of antihypertensive treatment strategies.	I	A
Combination treatment is recommended for most hypertensive patients, as initial therapy. Preferred combinations should comprise a RAS blocker (either an ACE inhibitor or an ARB) with a CCB or diuretic. Other combinations of the five major classes can be used.	I	A
It is recommended that beta-blockers are combined with any of the other major drug classes when there are specific clinical situations, e.g. angina, post-myocardial infarction, heart failure, or heart-rate control.	I	A
It is recommended to initiate an antihypertensive treatment with a two-drug combination, preferably in a SPC. Exceptions are frail older patients and those at low risk and with grade 1 hypertension (particularly if SBP is < 150 mmHg).	I	B
It is recommended that if BP is not controlled with a two-drug combination, treatment should be increased to a three-drug combination, usually an RAS blocker + CCB + thiazide/thiazide-like diuretic, preferably as an SPC.	I	A
It is recommended that if BP is not controlled with a three-drug combination, treatment should be increased by the addition of spironolactone or, if not tolerated, other diuretics such as amiloride or higher doses of other diuretics, a beta-blocker, or an alpha-blocker.	I	B
The combination of two RAS blockers is not recommended.	III	A

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Core drug-treatment strategy for uncomplicated hypertension

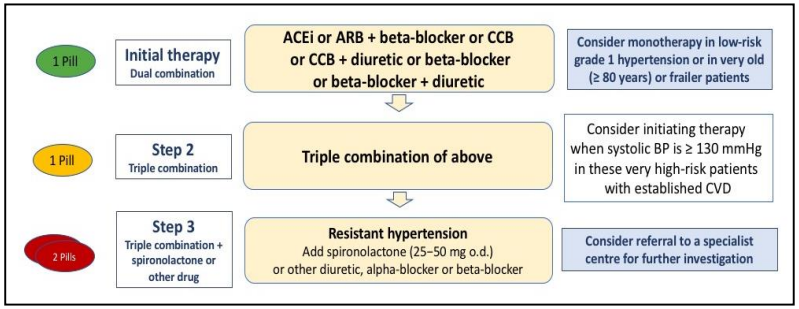


The core algorithm is also appropriate for most patients with HMOD, cerebrovascular disease, diabetes, or PAD

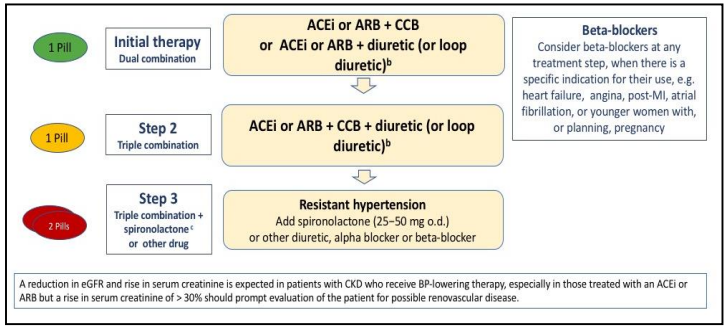
Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Drug-treatment strategies

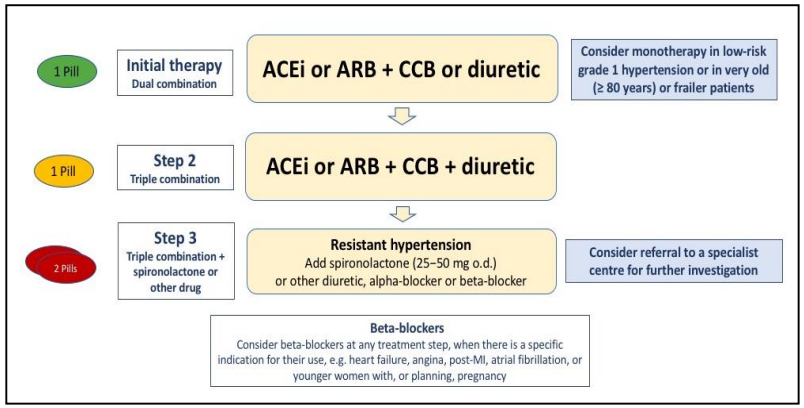
Hypertension and CAD



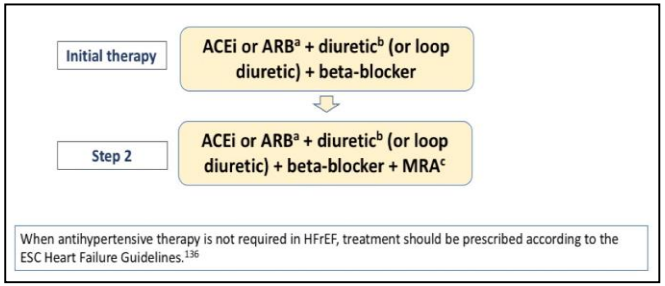
Hypertension and CKD



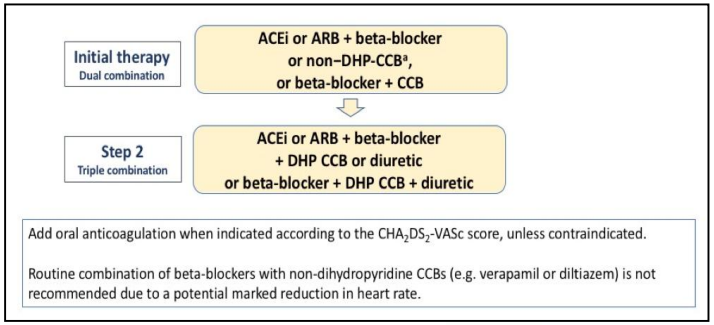
Core drug-treatment strategy for uncomplicated hypertension



Hypertension and HRrEF



Hypertension and AF



ESC European Society of Cardiology

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

European Society of Hypertension

Therapeutic strategies in hypertensive patients with acute stroke and cerebrovascular disease

Recommendations	Class	Level
In patients with acute intracerebral haemorrhage:		
• Immediate BP lowering is not recommended for patients with SBP < 220 mmHg.	III	A
• In patients with SBP ≥ 220 mmHg, careful acute BP lowering with i.v. therapy, to < 180 mmHg should be considered.	IIa	B
In acute ischaemic stroke, routine BP lowering with antihypertensive therapy is not recommended, with the exceptions:	III	A
• In patients with acute ischaemic stroke who are eligible for i.v. thrombolysis, BP should be carefully lowered and maintained to < 180/105 mmHg for at least the first 24 h after thrombolysis.	IIa	B
• In patients with markedly elevated BP who do not receive fibrinolysis, drug therapy may be considered, based on clinical judgement, to reduce BP by 15% during the first 24 h after the stroke onset.	IIb	C
In hypertensive patients with an acute cerebrovascular event, antihypertensive treatment is recommended:		
• Immediately for TIA.	I	A
• After several days in ischaemic stroke.	I	A
In all hypertensive patients with ischaemic stroke or TIA, a 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

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Management of white-coat and masked hypertension

Management of white-coat hypertension		
Recommendations	**Class**	**Level**
In white-coat hypertensive patients, it is recommended to implement lifestyle changes aimed at reducing CV risk as well as a regular follow-up with periodic out-of-office BP monitoring.	I	C
In patients with white-coat hypertension:		
• Drug treatment may be considered in people with evidence of HMOD or in whom CV risk is high or very high.	IIb	C
• Routine drug treatment is not indicated.	III	C
Management of masked hypertension		
Recommendations		
In masked hypertension, lifestyle changes are recommended to reduce CV risk, with regular follow-up, including periodic out-of-office BP monitoring.	I	C
Antihypertensive drug treatment should be considered in masked hypertension to normalize the out-of-office BP based on the prognostic importance of out-of-office BP elevation.	IIa	C
Antihypertensive drug up-titration should be considered in treated patients whose out-of-office BP is not controlled (i.e. masked uncontrolled hypertension), because of the high CV risk of these patients.	IIa	C

Managing CV disease risk in hypertensive patients, beyond BP – Statins and Antiplatelet therapy

For hypertensive patients at **moderate CVD risk or higher or those with established CVD**, BP lowering alone will not optimally reduce their risk. These patients **would also benefit from statin therapy**, which further reduces the risk of a myocardial infarction by approximately one-third and stroke by approximately one-quarter **, even when BP is controlled**. **Similar benefits** have been seen in hypertensive patients at the **border between low and moderate risk**..

Antiplatelet therapy, especially low-dose aspirin, is recommended for secondary prevention in hypertensive patients, but is not recommended for primary prevention (i.e. in patients without CVD)

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

Device-based therapies for hypertension

Recommendation	Class	Level
Use of device-based therapies is not recommended for the treatment of hypertension, unless in the context of clinical studies and RCTs, until further evidence regarding their safety and efficacy becomes available.	III	B

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

New sections / recommendations

- When to suspect and how to screen for the causes of secondary hypertension
- Management of hypertension emergencies
- Updated recommendations on the management of BP in acute stroke
- Updated recommendations on the management of hypertension in women and pregnancy
- Hypertension in different ethnic groups
- The effects of altitude on BP
- Hypertension and chronic obstructive pulmonary disease
- Hypertension and AF and other arrhythmias
- Oral anticoagulant use in hypertension
- Hypertension and sexual dysfunction
- Hypertension and cancer therapies
- Perioperative management of hypertension
- Glucose-lowering drugs and BP
- Updated recommendations on CV risk assessment and management:
  (i) using the SCORE system to assess risk in patients without CVD;
  (ii) the importance of HMOD in modifying CV risk; and
  (iii) the use of statins and aspirin for CVD prevention.

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

New concepts - 1

BP measurement

Wider use of out-of-office BP measurement with ABPM and/or HBPM, especially HBPM, as an option to confirm the diagnosis of hypertension, detect white coat and masked hypertension and monitor BP control.

Less conservative treatment of BP in older and very old patients

Lower BP thresholds and treatment targets for older patients – with emphasis on considerations of biological rather than chronological age (i.e. the importance of frailty, independence, and the tolerability of treatment).
Recommendation that **treatment should never be denied or withdrawn on the basis of age,** provided that treatment is tolerated.

A SPC treatment strategy to improve BP control

Preferred use of two-drug combination therapy for the initial treatment of most people with hypertension.
A single-pill treatment strategy for hypertension with the preferred use SPC therapy for most patients.
Simplified drug-treatment algorithms with the preferred use of an ACE inhibitor or ARB combined with a CCB or/and a thiazide/thiazide-like diuretic as the core treatment strategy for most patients, with beta-blockers used for specific indications.

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018

New concepts - 2

New target ranges for BP in treated patients

Target BP ranges for treated patients to better identify the recommended BP target and **lower safety boundaries for treated BP**, according to a patient's age and specific comorbidities.

Detecting poor adherence to drug therapy

A strong emphasis on the **importance of evaluating treatment adherence** as a major cause of poor BP control.

A key role for nurses, pharmacists in the longer-term management of hypertension

The important role of nurses and pharmacists in the education, support, and follow-up of treated hypertensive patients is emphasized as part of the overall strategy to improve BP control.

Williams, Mancia et al., J Hypertens 2018 and Eur Heart J 2018