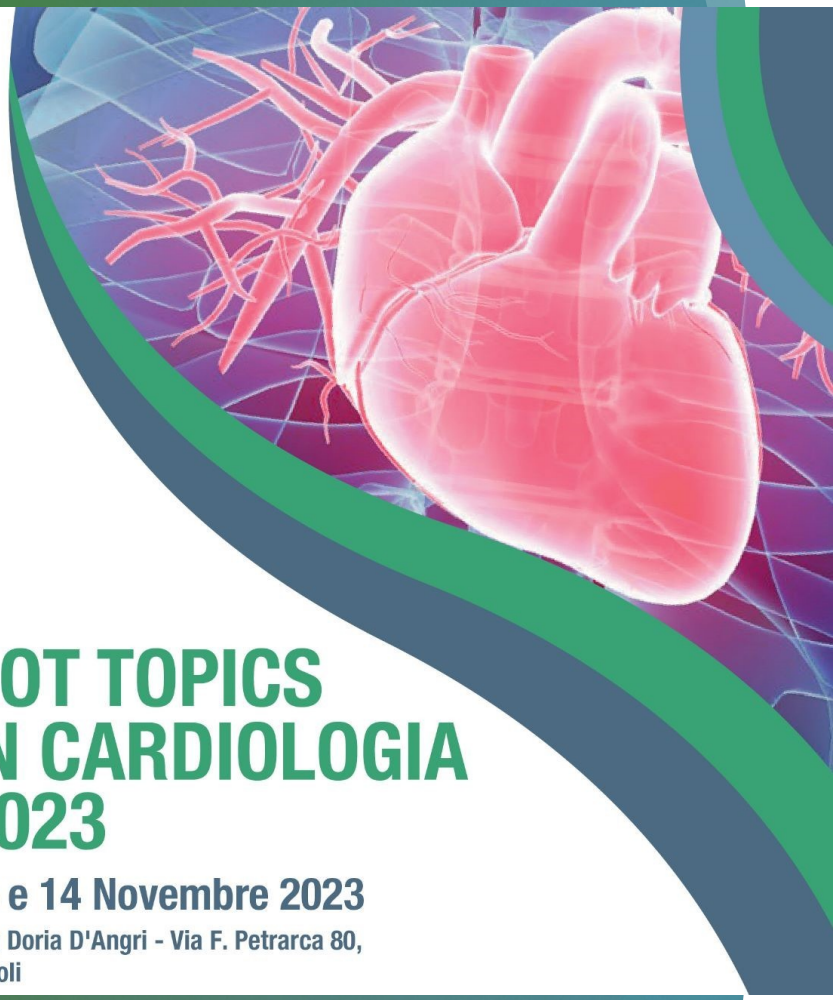


HOT TOPICS
IN CARDIOLOGIA
2023

13 e 14 Novembre 2023

Villa Doria D'Angri - Via F. Petrarca 80,
Napoli

La terapia antiipertensiva oggi alla luce delle nuove Linee Guida ESH

NICOLA DE LUCA

DPTU SCIENZE BIOMEDICHE AVANZATE

Università degli Studi “Federico II” - Napoli

ESC European Society of Cardiology

European Heart Journal (2018) **39**, 3021–3104
doi:10.1093/eurheartj/ehy339

ESC/ESH GUIDELINES

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), 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† (Italy), 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), and Ileana Desormais (France)

2018 ESC/ESH GUIDELINES
FOR THE MANAGEMENT OF ARTERIAL HYPERTENSION

BP treatment targets

Williams B, Mancia G et al, J Hypertens 2018 and Eur Heart J 2018
(doi:10.1093/eurheartj/ehy339)

ESC European Society of Cardiology

ESH European Society of Hypertension

2018 ESC/ESH GUIDELINES
FOR THE MANAGEMENT OF ARTERIAL HYPERTENSION

SBP targets in some hypertensive subgroups

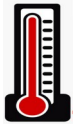
			Class / level
Age < 65 years	120 to <130 mmHg	(recommended)	IA
Age ≥ 65 years	130 to <140 mmHg	(recommended)	IA*
Diabetes	130 mmHg or lower**	(recommended)	IA
CAD	130 mmHg or lower	(recommended)	IA
CKD	130 to <140 mmHg	(recommended)	IA
Post-stroke/TIA	120 to <130 mmHg	(to be considered)	IIaB

*Close monitoring of adverse events / ** if tolerated

ESC European Society of Cardiology

Williams B, Mancia G et al, J Hypertens 2018 and Eur Heart J 2018 (doi:10.1093/eurheartj/ehy339)

ESH European Society of Hypertension



OFFICE BP TREATMENT TARGET RANGE

Age group	Office BP treatment target range (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 (mmHg)	< 80 to 70	< 80 to 70	< 80 to 70	< 80 to 70	< 80 to 70	

Williams B, Mancia G et al. J Hypertens. 2018 and Eur Heart J 2018 (doi:10.1093/eurheartj/ehy339)

ESC European Society of Cardiology

ESH European Society of Hypertension

ESC European Society of Cardiology

European Heart Journal (2021) **42**, 3227–3337
doi:10.1093/eurheartj/ehab484

ESC GUIDELINES

2021 ESC Guidelines on cardiovascular disease prevention in clinical practice

Age group	Office SBP treatment target ranges (mmHg)				
	Hypertension	+ DM	+ CKD	+ CAD	+ Stroke/TIA
18 – 69 years	120–130	120–130	<140–130	120–130	120–130
	Lower SBP acceptable if tolerated				
≥70 years	**<140 mmHg, down to 130 mmHg if tolerated**				
	Lower SBP acceptable if tolerated				
DBP treatment target (mmHg)	<80 for all treated patients				

CAD = coronary artery disease; CKD = chronic kidney disease; DBP = diastolic blood pressure; DM = diabetes mellitus; SBP = systolic blood pressure; TIA = transient ischaemic attack.

2023 ESH Guidelines for the management of arterial hypertension

The Task Force for the management of arterial hypertension of the European Society of Hypertension

Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA)

Authors/Task Force Members: Giuseppe Mancia (Chairperson)[a,*], Reinhold Kreutz (Co-Chair)[b,*], Mattias Brunström[c], Michel Burnier[d], Guido Grassi[e], Andrzej Januszewicz[f], Maria Lorenza Muiesan[g], Konstantinos Tsioufis[h], Enrico Agabiti-Rosei[i], Engi Abd Elhady Algharably[b], Michel Azizi[j,k], Athanase Benetos[l], Claudio Borghi[m], Jana Brguljan Hitij[n], Renata Cifkova[o,p], Antonio Coca[q], Veronique Cornelissen[r], J. Kennedy Cruickshank[s], Pedro G. Cunha[t,u], A.H. Jan Danser[v], Rosa Maria de Pinho[w], Christian Delles[x], Anna F. Dominiczak[y], Maria Dorobantu[z], Michalis Doumas[aa], María S. Fernández-Alfonso[bb,cc], Jean-Michel Halimi[dd,ee,ff], Zoltán Járai[gg], Bojan Jelakovic[hh], Jens Jordan[ii,jj], Tatiana Kuznetsova[kk], Stephane Laurent[ll], Dragan Lovic[mm], Empar Lurbe[nn,oo,pp], Felix Mahfoud[qq,rr], Athanasios Manolis[ss], Marius Miglinas[tt,uu], Krzystof Narkiewicz[vv], Teemu Niiranen[ww,xx], Paolo Palatini[yy], Gianfranco Parati[zz,aaa], Atul Pathak[bbb], Alexandre Persu[ccc], Jorge Polonia[ddd], Josep Redon[oo,eee,fff], Pantelis Sarafidis[ggg], Roland Schmieder[hhh], Bart Spronck[iii], Stella Stabouli[jjj], George Stergiou[kkk], Stefano Taddei[lll], Costas Thomopoulos[mmm], Maciej Tomaszewski[nnn,ooo], Philippe Van de Borne[ppp], Christoph Wanner[qqq], Thomas Weber[rrr], Bryan Williams[sss], Zhen-Yu Zhang[ttt], and Sverre E. Kjeldsen[uuu]

WHAT IS NEW AND WHAT HAS CHANGED

IN THE **2023** EUROPEAN SOCIETY OF HYPERTENSION ARTERIAL HYPERTENSION GUIDELINES?

1. Modified and simplified criteria for evidence grading recommendations
2. Pathophysiological background of primary hypertension
3. Clinical BP measurements by different methods and in different settings and clinical conditions
4. Thorough description of office, ambulatory and home BP measurements and value in different demographic and clinical conditions
5. Upgrading of out-of-office BP measurements in hypertension management
6. New HMOD measurements and their clinical value in hypertension work-up
7. New CV risk factors and update on CV risk assessment
8. Update and comprehensive summary of secondary forms of hypertension
9. Update on lifestyle interventions

WHAT IS NEW AND WHAT HAS CHANGED

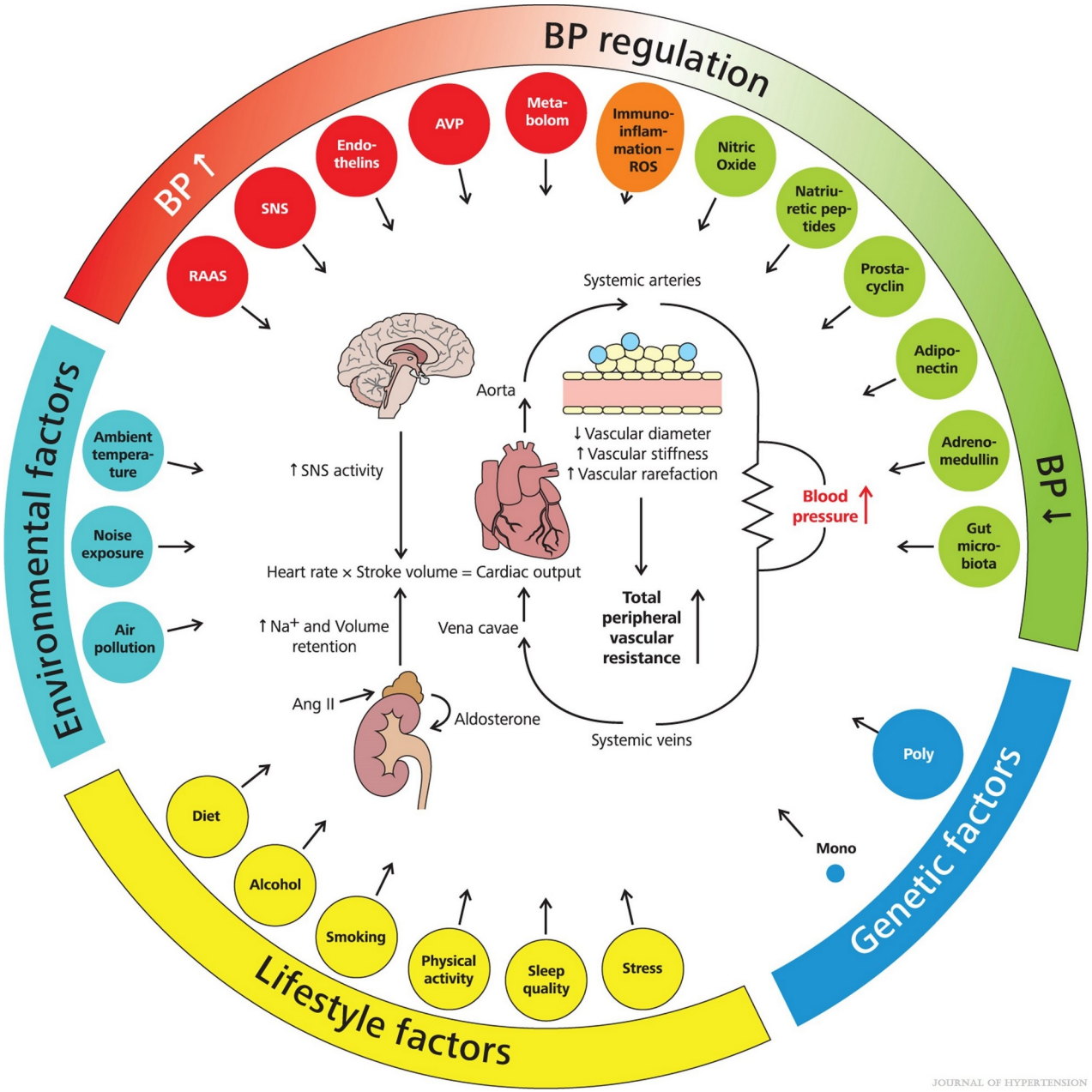
IN THE **2023** EUROPEAN SOCIETY OF HYPERTENSION ARTERIAL HYPERTENSION GUIDELINES?

11. Confirmation of preferred use of RAS blockers, CCBs and Thiazide/Thiazide-like diuretics, and their various combinations for BP-lowering treatment. Inclusion of BBs among the major antihypertensive drugs
12. Update on available combination-based drug treatment strategies, including the quadpill and the polypill Emphasis and update on the diagnosis and management of true resistant hypertension
13. Update on use and position of renal denervation for antihypertensive treatment
14. Impact of hypertension and its treatment on cognitive dysfunction and dementia
15. Management of hypertension in older people according to the frailty and functional level
16. Update on treatment of hypertension in HFrEF and HFpEF
17. New diagnostic approaches to diagnosis and treatment in hypertensive patients with AF
18. Update on treatment in CKD, including kidney transplantation
19. Update and novel treatment approaches to patients with type 2 diabetes

WHAT IS NEW AND WHAT HAS CHANGED IN THE 2023 EUROPEAN SOCIETY OF HYPERTENSION ARTERIAL HYPERTENSION GUIDELINES?

1. Modified and simplified criteria for evidence grading recommendations
2. Pathophysiological background of primary hypertension

Mechanisms involved in BP regulation and the pathophysiology of hypertension.

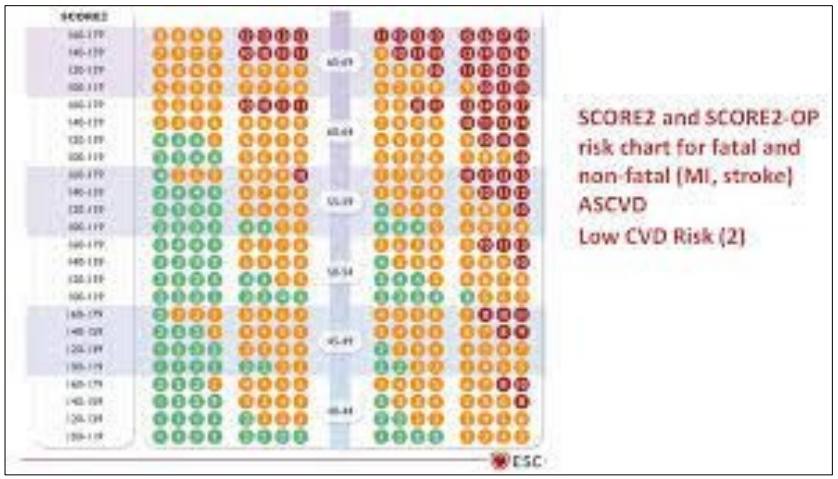


JOURNAL OF HYPERTENSION
Journal of Hypertension41(12):1874-2071, December

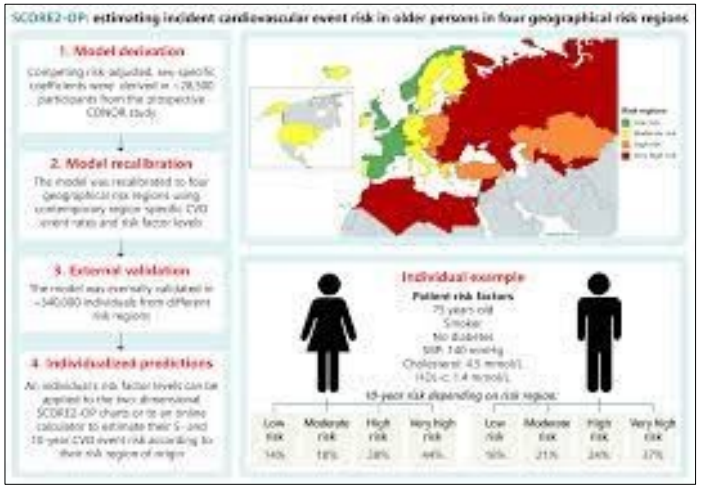
WHAT IS NEW AND WHAT HAS CHANGED IN THE 2023 EUROPEAN SOCIETY OF HYPERTENSION ARTERIAL HYPERTENSION GUIDELINES?

1. Modified and simplified criteria for evidence grading recommendations

CardioVascular assessment



SCORE2 and SCORE2-OP risk chart for fatal and non-fatal (MI, stroke) ASCVD
Low CVD Risk (2)



Recommendations and statements	CoR	LoE
CV risk assessment with the SCORE2 and SCOR2-OP system is recommended for hypertensive patients who are not already at high or very high risk due to established CVD or CKD, long-lasting or complicated diabetes, severe HMOD (e.g. LVH) or a markedly elevated single risk factor (e.g. cholesterol, albuminuria).	I	B

Journal of Hypertension41(12):1874-2071, December

Cardiovascular risk according to grade and stage of hypertension.

Hypertension disease staging	Other risk factors, HMOD, CVD or CKD	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 DBP ≥ 110
Stage 1	No other risk factors[a]	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	HMOD, CKD grade 3, or diabetes mellitus	Moderate to high risk	High risk	High risk	Very high risk
Stage 3	Established CVD or CKD grade ≥4	Very high risk	Very high risk	Very high risk	Very high risk

	<50 years	60–69 years	≥70 years
	<2.5%	<5%	<7.5%
	2.5 to <7.5%	5 to <10%	7.5 to <15%
	≥7.5%	≥10%	≥15%

Complementary risk estimation in Stage 1 with SCORE2/SCOR2-OP

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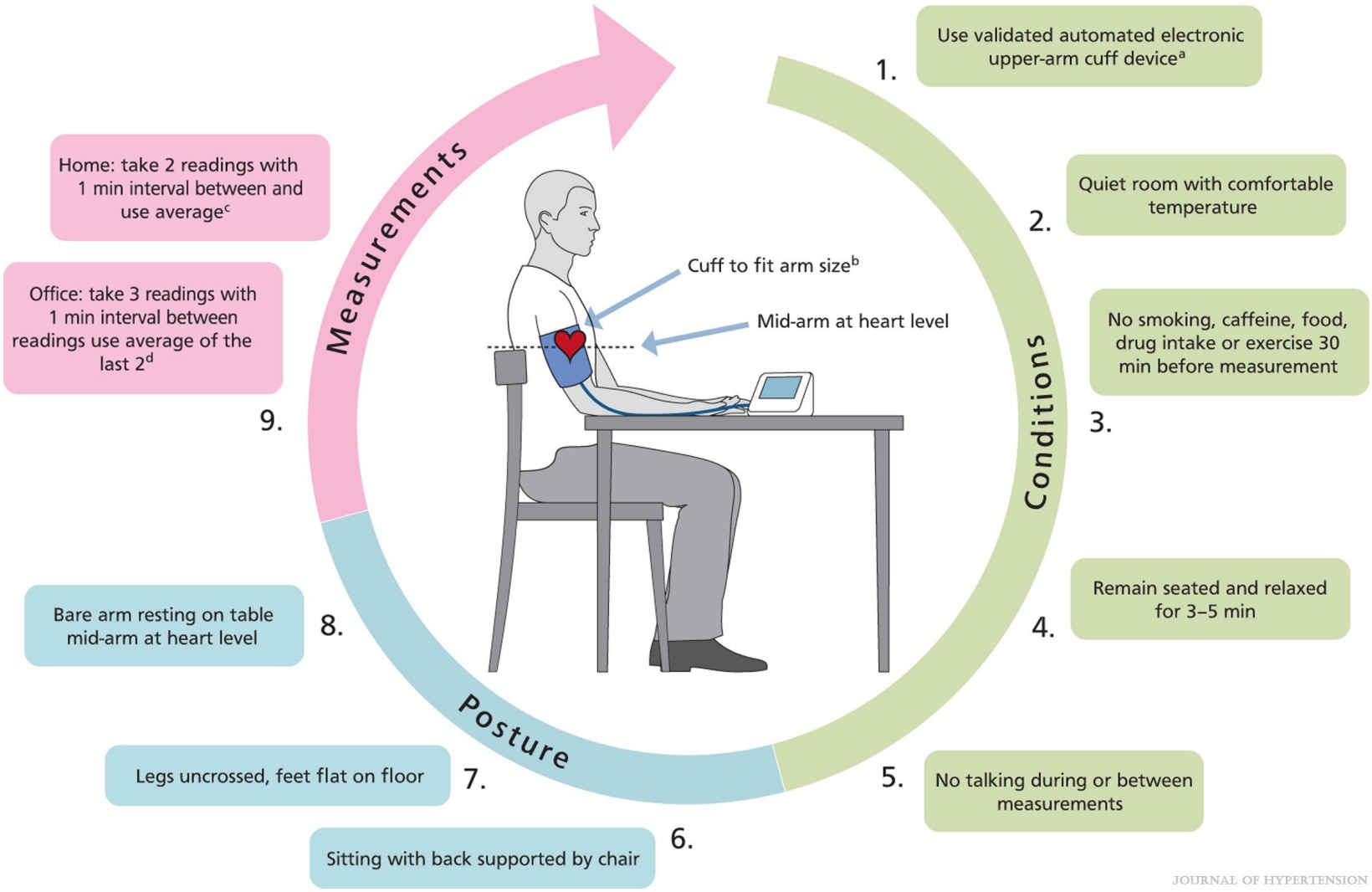
Recommendations for BP measurements in the office and at home.



Blood pressure measurments

Recommendations and statements	CoR	LoE
Automatic electronic, upper-arm cuff devices are recommended for office and out-of-office BP measurement (home and ambulatory).	I	B
Hybrid manual auscultatory devices with LCD or LED display, or digital countdown, or shock-resistant aneroid devices can be used for office BP measurement if automated devices are not available.	I	B
Only properly validated devices should be used. www.stridebp.org	I	B
Cuffless BP devices should not be used for the evaluation or management of hypertension in clinical practice.	III	C

JOURNAL OF HYPERTENSION

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6. New HMOD measurements
6. and their clinical value in hypertension work-up

WHAT IS NEW AND WHAT HAS CHANGED IN THE 2023 EUROPEAN SOCIETY OF HYPERTENSION ARTERIAL HYPERTENSION GUIDELINES?

Class of Recommendation		Level of Evidence		
	Definition		Definition	Interpretation
I	Evidence or general agreement that a treatment/test/procedure is beneficial, useful or effective AND that potential benefits clearly outweigh potential risk	A	- RCT or meta-analysis of RCTs with CVD outcomes - Single trial enough if sufficient power and without important limitations [a]	Strong evidence. Evidence of high certainty. Unlikely that future studies will change the effect estimate substantially
II	Conflicting evidence or opinion about the benefit, usefulness and effectiveness of a treatment/test/procedure OR uncertainty about benefit-risk balance	B	- RCT with surrogate measures (BP, HMOD) - Observational studies with CVD outcomes and no major limitations[a] - Meta-analyses including the above study types	Moderate evidence. Evidence with some uncertainty. Future studies may modify, at least the magnitude of, the effect estimate
III	Evidence or general agreement that a treatment/test/procedure is not beneficial, useful or effective OR that potential risks outweigh the potential benefit	C	- Observational studies of surrogate measures - Any study type may be downgraded to level C due to limitations[a] - Expert opinion (EO)	Weak evidence. Evidence of low certainty. Future studies may change the effect estimate substantially.

JOURNAL OF HYPERTENSION

Class of recommendation (CoR) and level of evidence (LoE).

BP, blood pressure, CVD, cardiovascular disease, HMOD, hypertension mediated organ damage,

RCT, randomized controlled trial.

aLimitations affecting the level of evidence include (but may not be limited to) high risk of bias, inability to account for important confounding factors in observational studies, questionable external validity and uncertain effect estimates (confidence intervals including negligible effect).

Characteristics of the most frequent markers of HMOD in hypertension.

Marker of HMOD	Sensitivity to changes	Reproducibility and operator independence	Time to changes	Prognostic value of changes
LVH by ECG	Low	High	Moderate (> 6 months)	Yes
LVH by echocardiogram	Moderate	Moderate	Moderate (> 6 months)	Yes
LVH by MRI	High	High	Moderate (> 6 months)	No data
eGFR	Moderate	High	Moderate (> 6 months)	Yes
UACR	High	Moderate	Fast (weeks to months)	Yes
RRI	Low	High	Slow (>12 months)	Yes
Carotid IMT	Very low	Low	Slow (> 12 months)	Limited data
PWV	High	Low	Fast (weeks to months)	Limited data
ABI	Low	Moderate	Slow (> 12 months)	Limited data
Retina Microvasculature[a]	High	High	Moderate (> 6 months)	No data

A Using modern adaptive optics technology.

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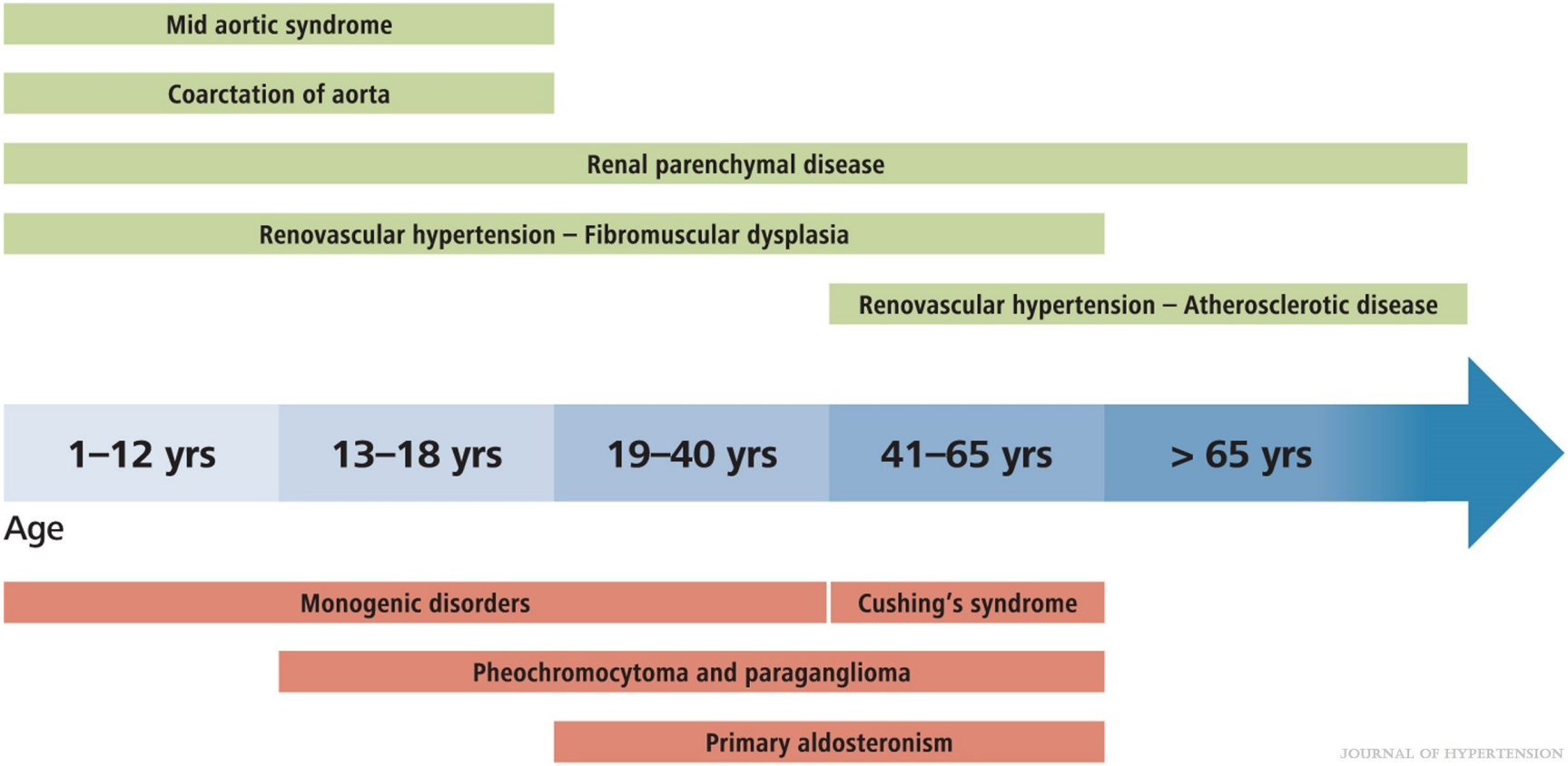
Incidence of selected forms of secondary hypertension according to age.



JOURNAL OF HYPERTENSION

INDICATION TO ANTIHYPERTENSIVE TREATMENT

Recommendations and statements	CoR	LoE
In patients 18 to 79 years, the recommended office threshold for initiation of drug treatment is 140 mmHg for SBP and/or 90 mmHg for DBP.	I	A
In patients ≥80 years, the recommended office SBP threshold for initiation of drug treatment is 160 mmHg.	I	B
However, in patients ≥80 years a lower SBP threshold in the range 140 – 159 mmHg may be considered.	II	C
The office SBP and DBP thresholds for initiation of drug treatment in frail patients should be individualized.	I	C
In adult patients with a history of CVD, predominantly CAD, drug treatment should be initiated in the high-normal BP range (SBP ≥130 or DBP ≥80 mmHg).	I	A

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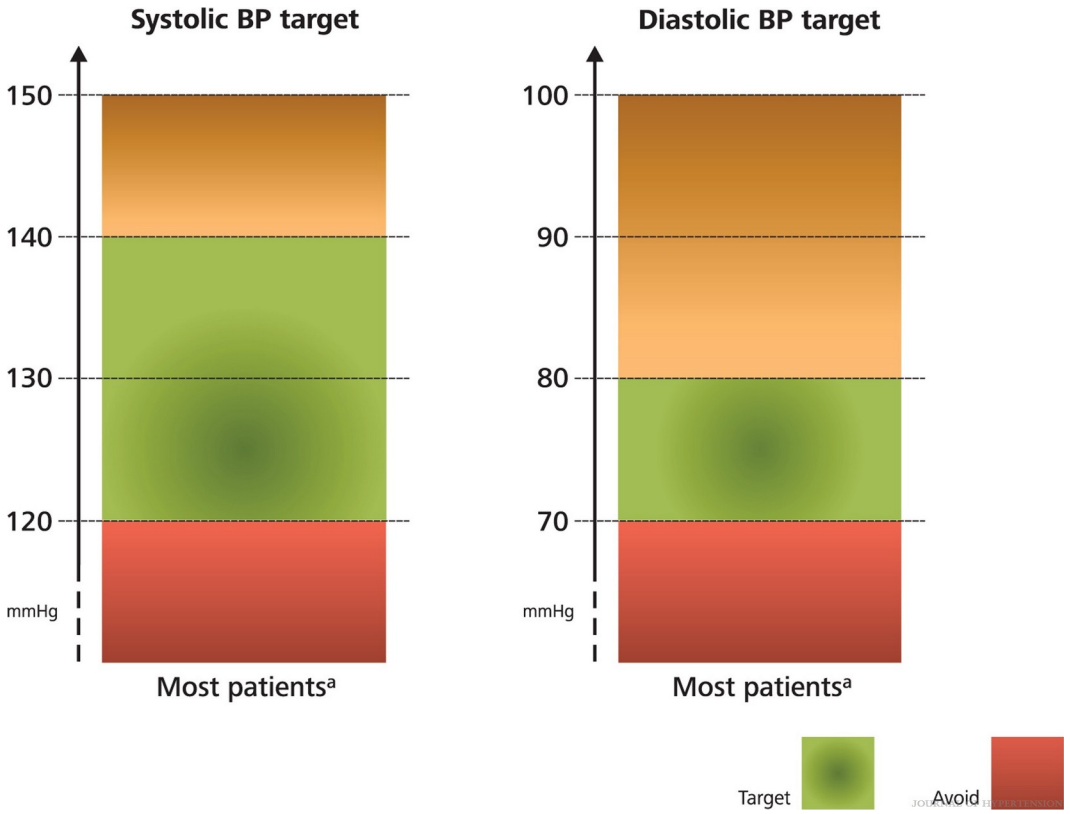
Journal of Hypertension41(12):1874-2071, December 2023.

doi: 10.1097/HJH.0000000000003480

TREATMENT GOALS



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doi: 10.1097/HJH.0000000000003480

Office BP targets in the general adult hypertensive population.aThe first objective of antihypertensive treatment should be to lower BP to <140/80 mmHg in most patients, because this accounts for the major portion of the protective effect of BP-lowering.aIf drug treatment is well tolerated, treated SBP values should be targeted to 130 mmHg or lower in most patients up to 79 years old.aDespite the smaller incremental benefit, an effort should be made to reach a BP range of 120–129/70–79 mmHg in patients up to 79 years old, but only if treatment is well tolerated. Evidence on the advantages of this lower BP target range is not available or unequivocal in a number of clinically important subgroups of patients (e.g. patients with LVH, CKD, or ISH). These issues are discussed in the sections on special conditions (see Sections 17 to 20).aIn patients at least 80 years old who are not frail, the first objective of antihypertensive treatment is to lower BP below 150 mmHg. However, a SBP target range between 130-139 mmHg may be considered, if well tolerated.aIn very frail patients, treatment targets should be individualized.

B.P. GOALS

Recommendations and statements	CoR	LoE
Patients 18 to 64 years old		
The goal is to lower office BP to <130/80mmHg.	I	A
Patients 65 to 79 years old		
The primary goal of treatment is to lower BP to <140/80mmHg.	I	A
However, lowering BP to below 130/80mmHg can be considered if treatment is well tolerated.	II	B
Patients 65 to 79 years old with ISH		
The primary goal of treatment is to lower SBP in the 140 to 150 mmHg range.	I	A
However, a reduction of office SBP in the 130 to 139 mmHg range should be considered if well tolerated, albeit cautiously if DBP is already below 70 mmHg.	I	B
Patients ≥80 years old		
Office SBP should be lowered to a SBP in the 140 to 150 mmHg range.	I	A
However, reduction of office SBP between 130 to 139 mmHg may be considered if well tolerated, albeit cautiously if DBP is already below 70 mmHg.	II	B
Additional safety recommendations		
In frail patients, the treatment target for office SBP and DBP should be individualized.	I	C
Do not actively aim to target office SBP below 120 mmHg or DBP below 70 mmHg during drug treatment.	III	C
However, in patients with low office DBP, i.e. below 70 mmHg, SBP should be still lowered, albeit cautiously, if on-treatment SBP is still well above target values.	II	C
Reduction of treatment can be consider in patient aged 80 years or older with a low SBP (< 120 mmHg) or in the presence of severe orthostatic hypotension or a high frailty level.	II	C

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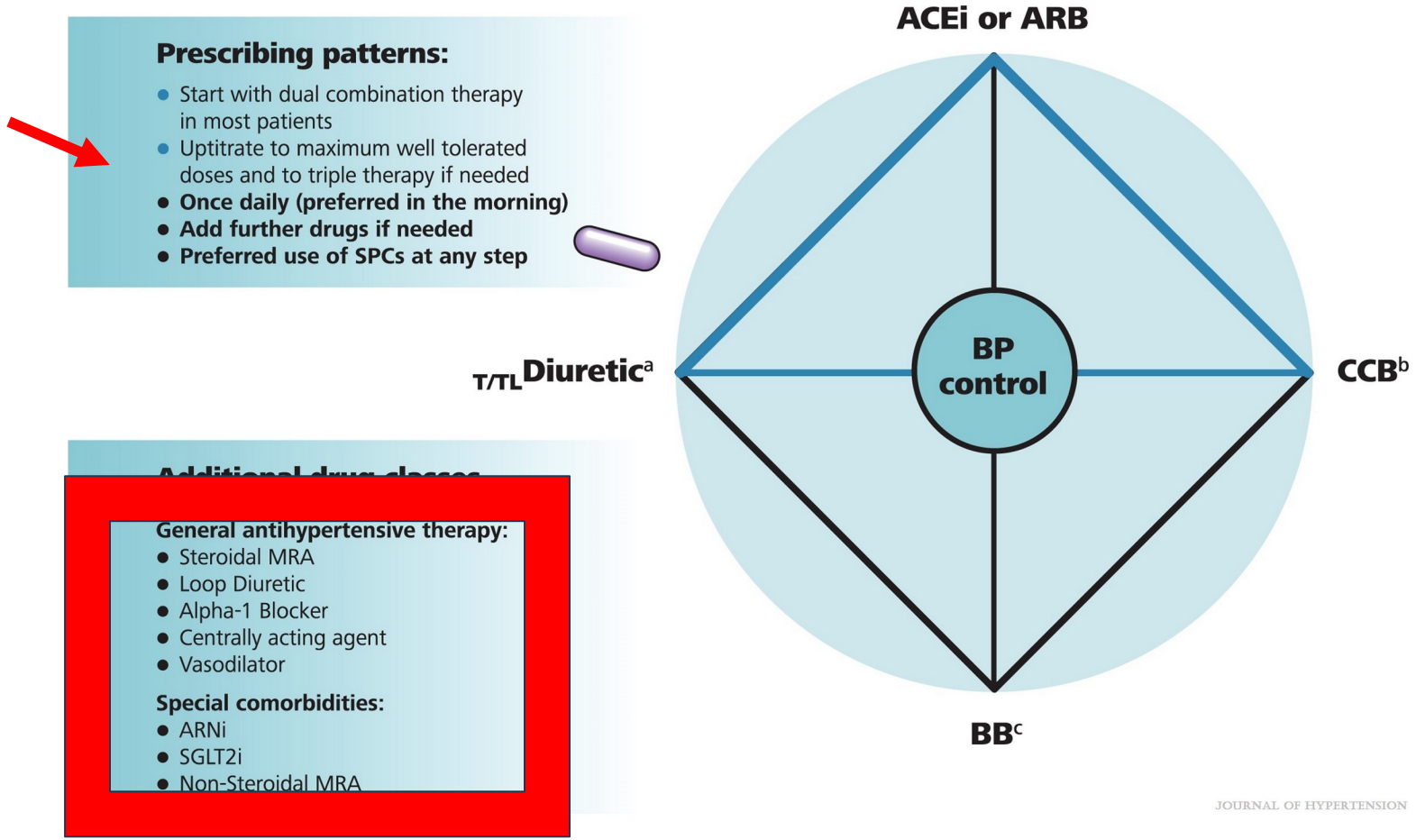
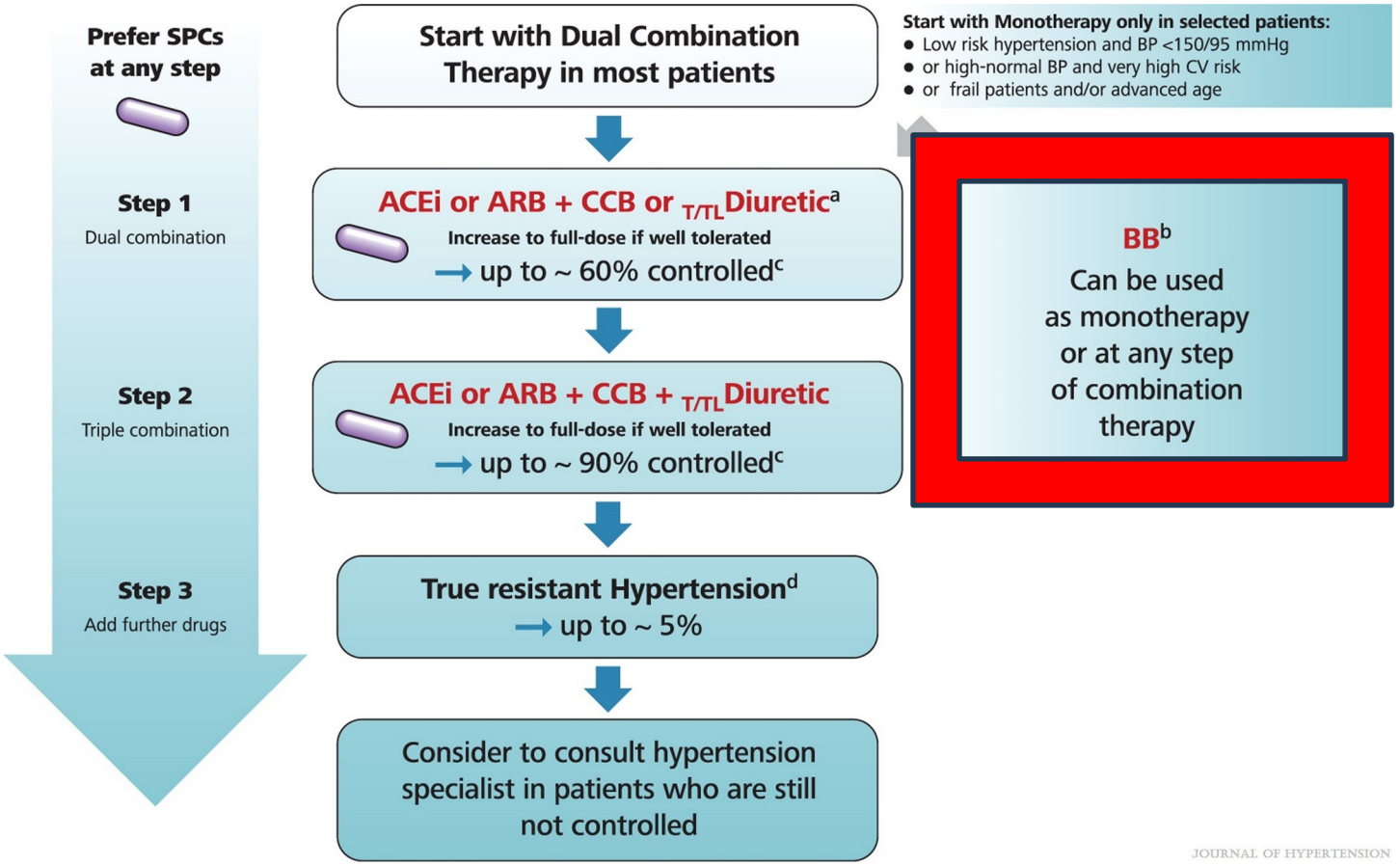
12. Update on available combination-based drug treatment strategies, including the quadpill and the polypill Emphasis and update on the diagnosis and management of true resistant hypertension
13. Update on use and position of renal denervation for antihypertensive treatment

Drug classes for BP-lowering therapy



(a) Use of Diuretics: Consider transition to Loop Diuretic if eGFR is between 30 to 45 ml/min/1.73 m2. If eGFR <30 ml/min/1.73 m2 use Loop Diuretic. (b) Non-DHP CCB should not be combined with BB. (c) BB should be used as guideline directed medical therapy in respective indications or considered in several other conditions (Table 16). Start with dual combination therapy including a RAS-blocker (either ACEi or ARB) plus a T/TLDiuretic or a CCB is recommended (thick blue lines). Triple therapy includes a combination of the three classes as indicated by the blue lines.

General BP-lowering strategy in patients with hypertension



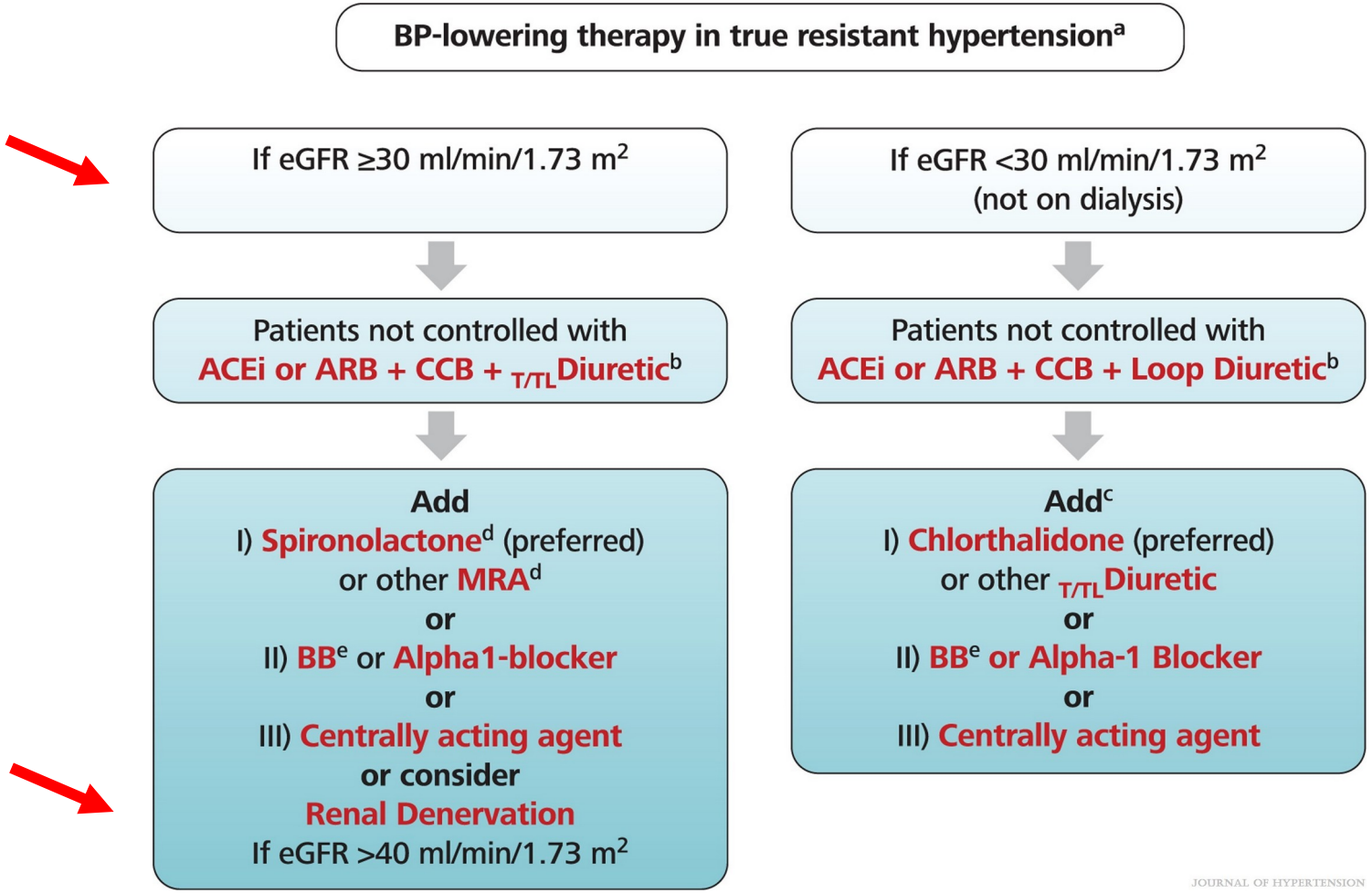
of Diuretics:–Consider transition to Loop Diuretic if eGFR is between 30 to 45 ml/min/1.73 m2–If eGFR <30 ml/min/1.73 m2 use Loop DiureticbBB should be used as guideline directed medical therapy in respective indications or considered in several other conditions (Table 16)cControlled below 140/90 mmHgd When SBP is ≥140mmHg or DBP is ≥90 mmHg provided that:–maximum recommended and tolerated doses of a three-drug combination comprising a RAS blocker (either an ACEi or an ARB), a CCB and a Thiazide/Thiazide-like diuretic were used–adequate BP control has been confirmed by ABPM or by HBPM if ABPM is not feasible–various causes of pseudo-resistant hypertension (especially poor medication adherence) and secondary hypertension have been excluded (see Section 12).

Cardiovascular Prevention

Recommendations and statements	CoR	LoE
Low-dose aspirin is not recommended for primary prevention in patients with hypertension.	III	A
Antiplatelet therapy is recommended for secondary prevention in hypertensive patients.	I	A
Use of a polypill containing low-dose aspirin can be considered in hypertensive patients for secondary prevention.	II	A

JOURNAL OF HYPERTENSION

BP-lowering strategy in true resistant hypertension according to renal function



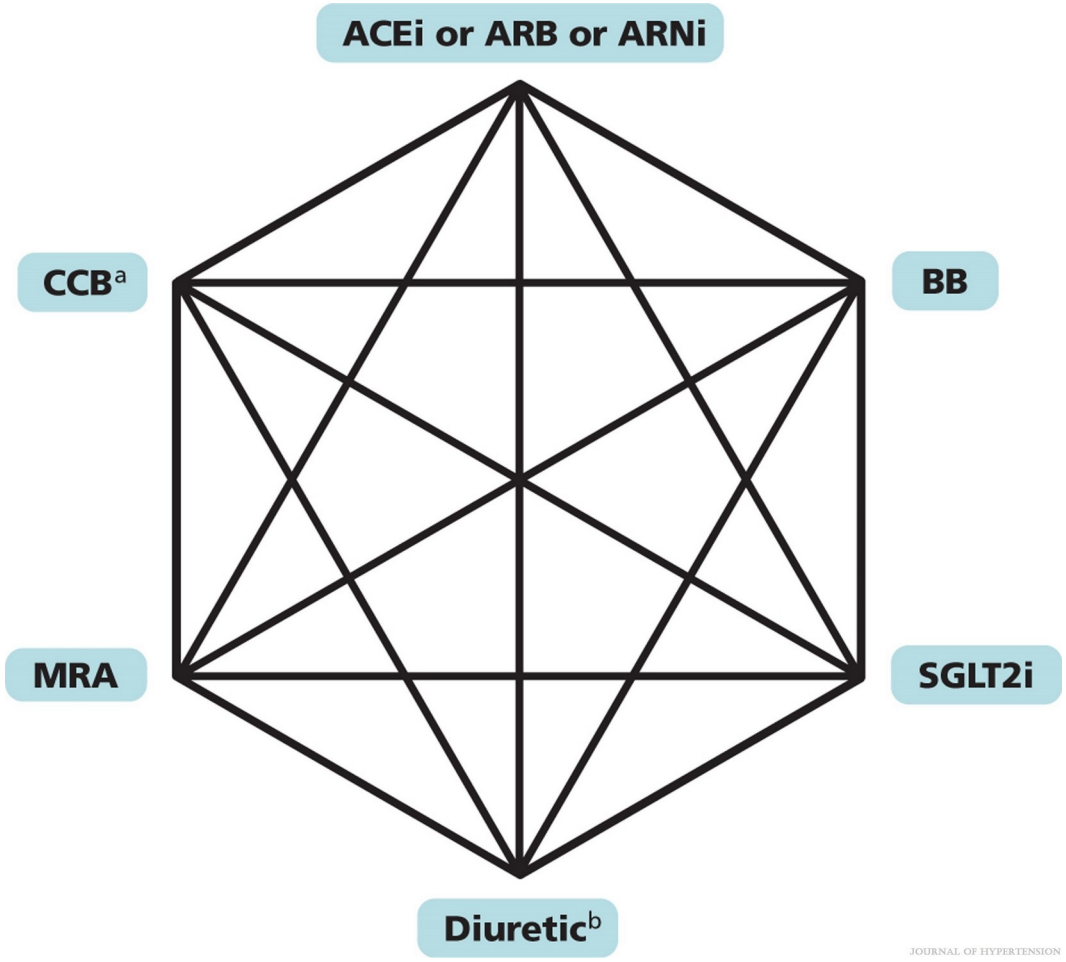
. (a) When SBP is ≥140mmHg or DBP is ≥90 mmHg provided that: maximum recommended and tolerated doses of a three-drug combination comprising a RAS blocker (either an ACEi or an ARB), a CCB and a T/TLDiuretic were used, adequate BP control has been confirmed by ABPM or by HBPM if ABPM is not feasible, various causes of pseudo-resistant hypertension (especially poor medication adherence) and secondary hypertension have been excluded (see Section 12). (b) Use of Diuretics: Use T/TLDiuretic if eGFR >45 ml/min/1.73 m2. Consider transition to Loop Diuretic if eGFR is between 30 to 45 ml/min/1.73 m2. Use loop Diuretic if eGFR <30 ml/min/1.73 m2. (c) MRA contraindicated. (d) Caution if eGFR <45 ml/min/1.73 m2 or serum potassium >4.5 mmol/l. (e) Should be used earlier at any step as guideline directed medical therapy in respective indications or considered in several other conditions (Table 16).

Renal Denervation

Recommendations and statements	CoR	LoE
RDN can be considered as a treatment option in patients with an eGFR >40 ml/min/1.73m^2 who have uncontrolled BP despite the use of antihypertensive drug combination therapy, or if drug treatment elicits serious side effects and poor quality of life.	II	B
RDN can be considered as an additional treatment option in patients with true resistant hypertension if eGFR is >40 ml/min/1.73m^2.	II	B
Selection of patients to whom RDN is offered should be done in a shared decision-making process after objective and complete patient's information.	I	C
RDN should only be performed in experienced specialized centers to guarantee appropriate selection of eligible patients and completeness of the denervation procedure.	I	C

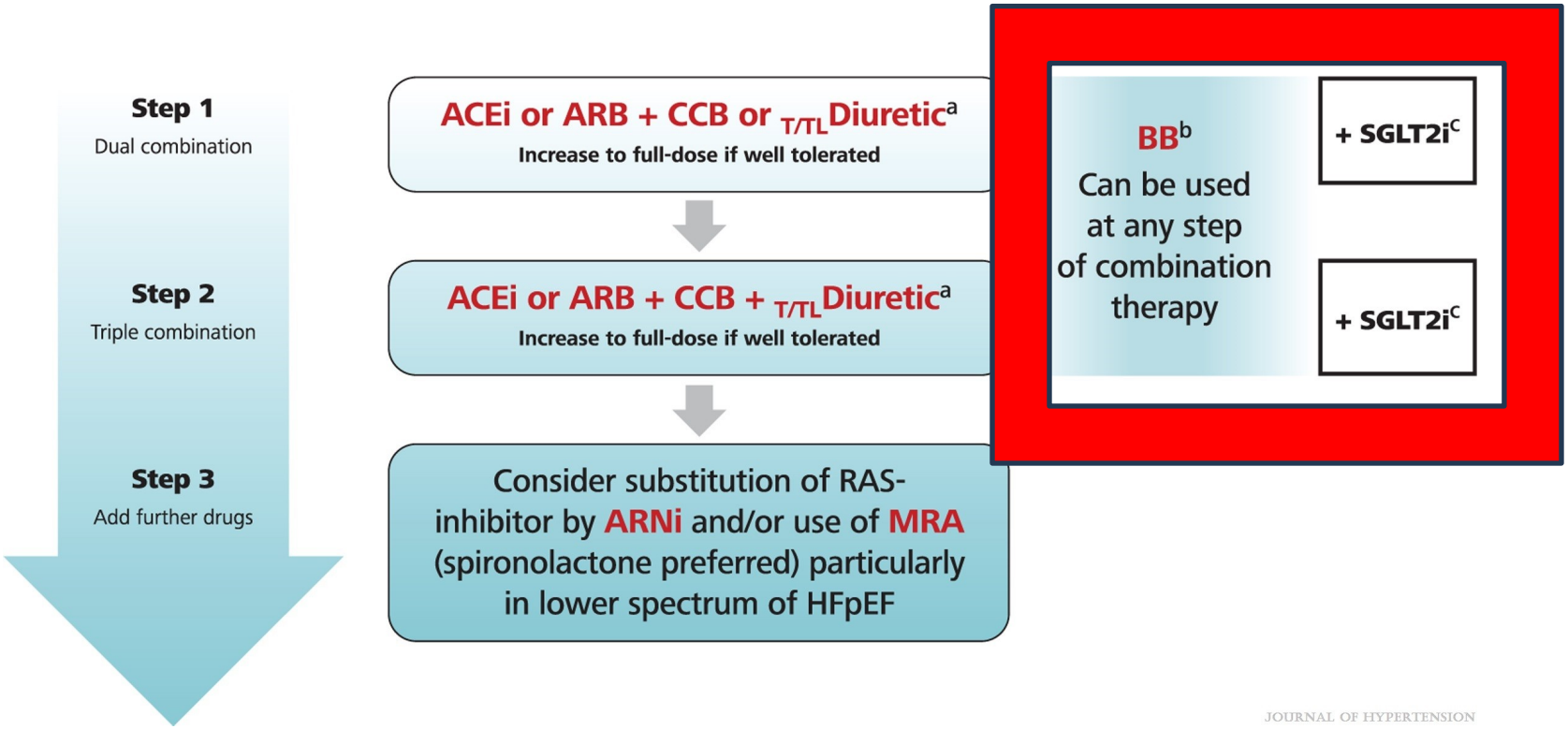
JOURNAL OF HYPERTENSION

1- BP-lowering drugs in hypertension and heart failure.



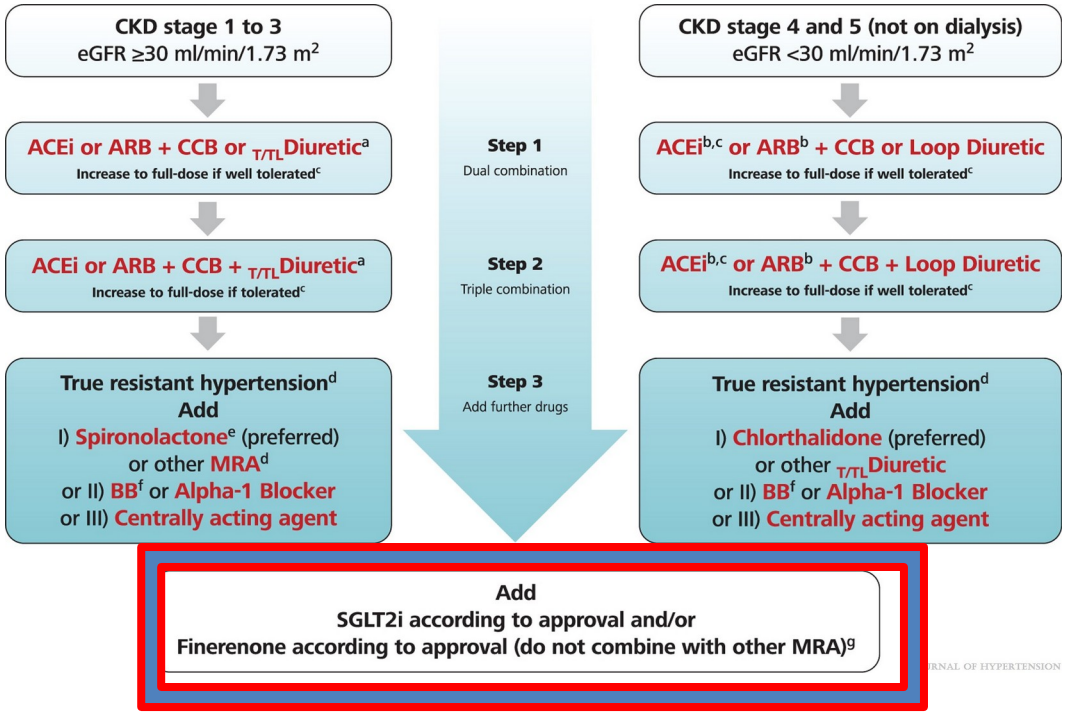
(a) Non-DHP CCB are not recommended in HFrEF and should not be combined with BB. (b) Use of Diuretics: Use T/TLDiuretic if eGFR >45 ml/min/1.73 m2. Consider transition to Loop Diuretic if eGFR is between 30 to 45 ml/min/1.73 m2. Use loop Diuretic if eGFR <30 ml/min/1.73 m2 or in patients with fluid retention/edema.

2 - BP-lowering therapy in hypertension and HFpEF.



(a) Use of Diuretics: Use T/TLDiuretic if eGFR >45 ml/min/1.73 m2. Consider transition to Loop Diuretic if eGFR is between 30 to 45 ml/min/1.73 m2. Use loop Diuretic if eGFR <30 ml/min/1.73 m2 or in patients with fluid retention/edema. (b) BB should be used as guideline directed medical therapy in respective indications or considered in several other conditions (Table 16) (c) Use SGLT2i according to approval.

3 - BP-lowering drugs in hypertension and CKD



2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA)

Mancia, Giuseppe; Kreutz, Reinhold; Brunström, Mattias; Burnier, Michel; Grassi, Guido; Januszewicz, Andrzej; Muiesan, Maria Lorenza; Tsioufis, Konstantinos; Agabiti-Rosei, Enrico; Algharably, Engi Abd Elhady; Azizi, Michel; Benetos, Athanase; Borghi, Claudio; Hitij, Jana Brguljan; Cifkova, Renata; Coca, Antonio; Cornelissen, Veronique; Cruickshank, J. Kennedy; Cunha, Pedro G.; Danser, A.H. Jan; Pinho, Rosa Maria de; Delles, Christian; Dominiczak, Anna F.; Dorobantu, Maria; Doumas, Michalis; Fernández-Alfonso, María S.; Halimi, Jean-Michel; Járai, Zoltán; Jelaković, Bojan; Jordan, Jens; Kuznetsova, Tatiana; Laurent, Stephane; Lovic, Dragan; Lurbe, Empar; Mahfoud, Felix; Manolis, Athanasios; Miglinas, Marius; Narkiewicz, Krzystof; Niiranen, Teemu; Palatini, Paolo; Parati, Gianfranco; Pathak, Atul; Persu, Alexandre; Polonia, Jorge; Redon, Josep; Sarafidis, Pantelis; Schmieder, Roland; Spronck, Bart; Stabouli, Stella; Stergiou, George; Taddei, Stefano; Thomopoulos, Costas; Tomaszewski, Maciej; Van de Borne, Philippe; Wanner, Christoph; Weber, Thomas; Williams, Bryan; Zhang, Zhen-Yu; Kjeldsen, Sverre E.

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BP-lowering therapy in patients with hypertension and chronic kidney disease. (a) Transition from T/TLDiuretic to Loop Diuretic should be individualized in patients with eGFR < 45 ml/min/1.73 m2. (b) Cautious start with low-dose. (c) Check for dose adjustment according to renal impairment for drugs with relevant renal excretion rate. (d) When SBP is ≥140mmHg or DBP is ≥90 mmHg provided that: maximum recommended and tolerated doses of a three-drug combination comprising a RAS blocker (either an ACEi or an ARB), a CCB and a T/TLDiuretic were used, adequate BP control has been confirmed by ABPM or by HBPM if ABPM is not feasible, various causes of pseudo-resistant hypertension (especially poor medication adherence) and secondary hypertension have been excluded (see Section 12). (e) Caution if eGFR <45 ml/min/1.73 m2 or serum potassium >4.5 mmol/l. (f) Should be used at any step as guideline directed medical therapy in respective indications or considered in several other conditions (Table 16). (g) SGLT2is and Finerenone should be used according to their approval for CKD treatment.

4 - BP-lowering therapy in Diabetes

Recommendations and statements	CoR	LoE
BP should be monitored to detect hypertension in all patients with diabetes, because it is a frequent comorbidity associated with an increase CV risk and risk for kidney events.	I	A
Non-dipping or elevated night-time BP are frequent in type 2 diabetes and should be monitored by ABPM or HBPM.	I	B
Antihypertensive treatment in type 2 diabetes is recommended to protect against macrovascular and microvascular complications.	I	A
Immediate lifestyle interventions and antihypertensive drug treatment are recommended for people with type 2 diabetes when office SBP is ≥ 140 mmHg and DBP is ≥ 90 mmHg.	I	A
Drug treatment strategies in patients with type 2 diabetes should be the same as for patients without diabetes and the primary aim is to lower BP below <130/80 mmHg.	I	A
SGLT2is are recommended to reduce cardiac and kidney events in type 2 diabetes.	I	A
The non-steroidal MRA finerenone can be used, because of its nephroprotective and cardioprotective properties in patients with diabetic CKD and moderate to severe albuminuria.	I	A
There are only limited data on the potential benefits of combining SGLT2is and finerenone.	II	C

Hypertension induced by selected anticancer treatments

Drug class	Selected example drugs	Selected malignancies	Potential mechanisms	Hypertension incidences	Comments
VEGF inhibitors	Axitinib, Bevacizumab, Cabozantinib, Dasatinib, Lenvatinib, Nilotinib, Pazopanib, Ponatinib, Ramucirumab, Regorafenib, Sorafenib, Sunitinib, Tivozanib, Vandetanib	Renal, hepatocellular, thyroid, gastrointestinal stromal cancer	↑Endothelin-1 bioavailability ↓ NO bioavailability Oxidative stress Endothelial dysfunction Microvascular rarefication ↓Lymphangiogenesis Kidney injury	**20%-90%**	
Bruton TK inhibitors	Acalabrutinib, Ibrutinib	Chronic lymphocytic leukemia, mantle cell lymphoma	↓Heat shock protein ↓NO bioavailability	**71%**	Long-term effects
Platinum-based compounds	Carboplatin, Cisplatin, Oxaliplatin	Mesothelioma, testicular, bladder, gynaecological colorectal, and lung cancers	↓NO bioavailability Endothelial dysfunction Kidney injury	**53%**	Long-term effects
Alkylating compounds	Busulfan, Cyclophosphamide, Ifosfamide	Hematologic and solid organ malignancies	↓VEGF bioavailability and vascular/kidney toxicity (Cyclophosphomide)	**36% in adults 15%-58% in children**	Possible confounding by concomitant use of glucocorticoids; long-term effects
Calcineurin inhbitors	Cyclosporin, Tacrolimus	After stem cell transplantation	↑Vasoconstriction (↑RAS and Endothelin-1) ↓NO bioavailability ↑SNS	**30%–60%**	Long-term effects
Proteasome inhibitors	Bortezomib, Carfilzomib	Multiple myeloma	↓NO bioavailability Endothelial dysfunction	**10%-32%**	
BRAF/MEK inhibitors	Binimetinib, Cobimetinib, Dabrafenib, Encorafenib, Trametinib, Vemurafenib	Melanoma, colorectal cancer	CD47 upregulation ↓cGMP, ↓NO Endothelial dysfunction	**19.5%**	
RET kinase inhibitors	Pralsetinib, Selparcatinib, Vandetanib	Thyroid, non–small cell lung cancer	CD47 upregulation ↓cGMP, ↓NO Endothelial dysfunction	**21%-43%**	
PARP inhibitors	Niraparib, Olaparib[a]	Breast, ovarian cancer	Inhibition of dopamine, norepinephrine, and serotonin re-uptake	**19%**	
mTOR inhibitors	Everolimus, Sirolimus	Renal cell, breast, PNET cancer	↓VEGF bioavailability	**No data**	
Androgen synthesis inhibitors	Abiraterone	Metastatic prostate cancer Prostate cancer	Mineralocorticoid activity of accumulated steroid precursors	**26%**	
Androgen receptor blockers	Enzalutamide	Metastatic prostate cancer	Unknown	**11%**	

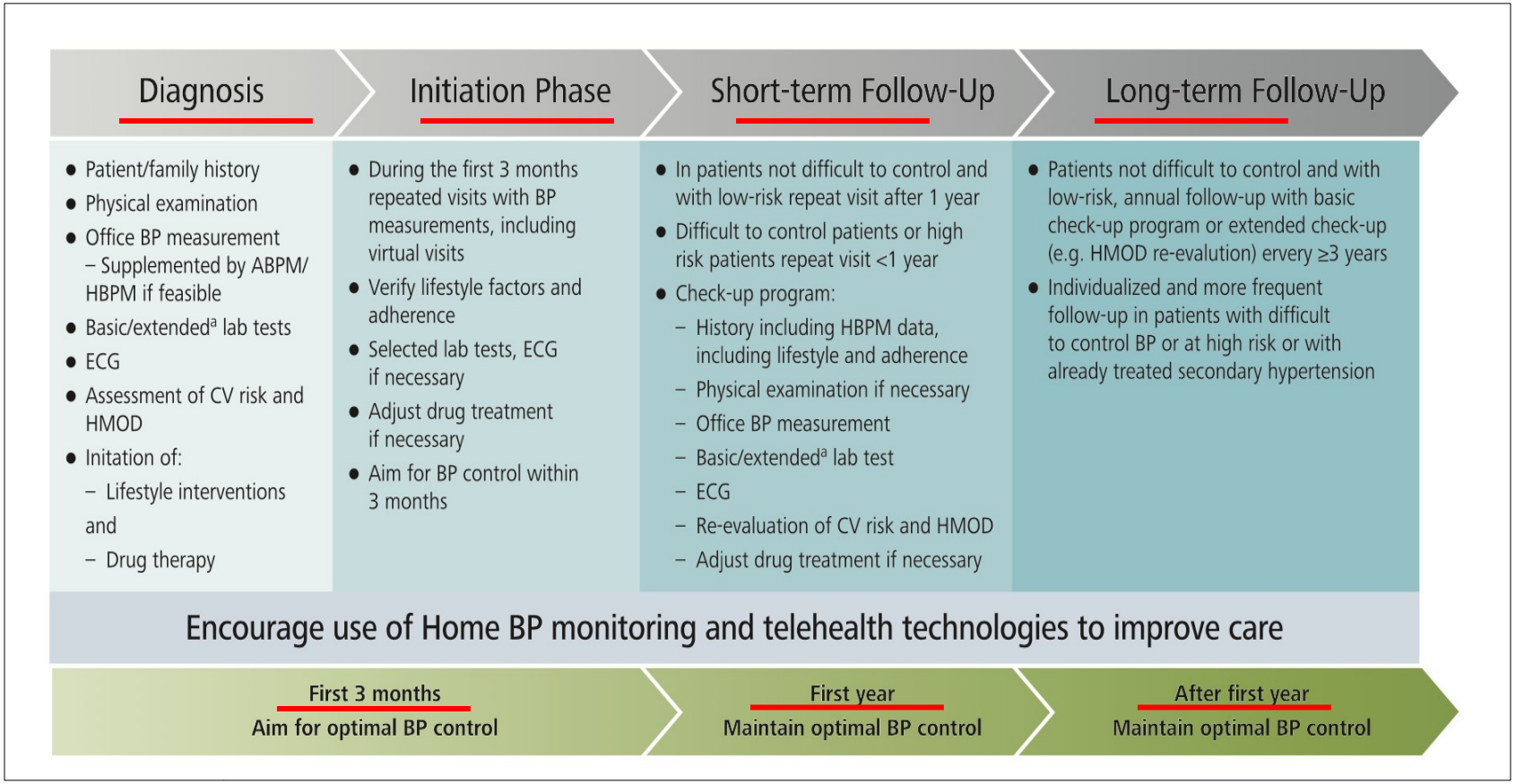
Data are obtained from Cohen *et al.* [1572] and van Dorst *et al.* [1571]. BRAF indicates v-raf murine sarcoma viral oncogene homolog B1; CD47, cluster of differentiation 47; cGMP, cyclic guanosine monophosphate; ET-1, endothelin-1; MEK, mitogen-activated protein kinase kinase; mTOR, mammalian target of rapamycin; NO, nitric oxide; PARP, poly ADP ribose polymerase; PNET, primitive neuroectodermal tumor; RET, rearranged during transfection; SNS, sympathetic nervous system; TK, tyrosine kinase; VEGF, vascular endothelial growth factor.

[a]Olaparib possible antihypertensive and cardioprotective effects

Managment of BP in Cancer patients

Recommendations	CoR	LoE
In patients with cancer, the same definition of hypertension, thresholds, targets, lifestyle interventions and drug treatment strategies are recommended as for the general hypertension population.	I	C
In patients with uncontrolled hypertension and BP values ≥180 mmHg for systolic and/or ≥110 mmHg for diastolic BP, it is not recommended to initiate anticancer therapy.	III	C
In patients with uncontrolled hypertension and BP values ≥180 mmHg for systolic and/or ≥110 mmHg for diastolic BP, measures to control BP and symptoms should be initiated by team-based multidisciplinary care to allow initiation of anticancer therapy as early as possible.	I	C
Thiazide/Thiazide-like diuretics may be used only if needed for BP control and in patients with fluid retention, because of their potential to cause unwanted effects in cancer patients including increases in serum calcium concentration in patients with bone metastasis, increased risk of cardiac arrhythmias due to prolonging the QT interval by inducing hypokalemia, increase the risk of hyponatremia, and potential worsening of hypovolemic states or dehydration.	II	C
Non-DHP CCBs should be avoided in cancer patients who are treated with anticancer drugs that are susceptible to pharmacokinetic interactions mediated by CYP3A4 and/or P-gp.	III	B
Hypertension induced by VEGF inhibitors may be treated with either RAS-inhibitors (ACEis or ARBs) or DHP-CCBs.	II	B
In severely ill cancer patients, treatment of hypertension should be individualized according to symptoms, co-morbidities and polypharmacy in a shared-decision making process.	I	C

IMPORTANCE OF FOLLOW-UP



Dalle linee guida…..

….alla pratica clinica

Terapie ben condotte riducono gli eventi, quindi i ricoveri...

quindi i costi

“…. Thanks

….for attention”