SAHS & NDOH Hypertension Management Lecture Series

Back to Basics in Hypertension Management

Southern African Hypertension Society

SAHS

Know your blood pressure by

Special Populations & Compelling Indications In The Treatment of HT e.g Diabetics, Stroke, Pregnancy, Athletes etc.

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Prepared by Prof Nash Ranjith

Hypertension Guidelines – Special Populations

BASIS OF INITIAL THERAPY: FIVE MAJOR CLASSES OF DRUGS ARE INDICATED

ESH GUIDELINES 2018

ACEI, ARBs, BB, CCBs, diuretics : **thiazides and thiazide-like** (chlortalidone and indapamide) are indicated as the basis of antihypertensive treatment strategies

have demonstrated effective reduction of BP and CV events in RCTs

Combination treatment for most hypertensive patients, as initial therapy.

Preferred combinations :

- RAS blocker (either an ACE inhibitor or an ARB) with a CCB or diuretic.
- Other combinations of the five major classes can be used.

CANADA 2017

Thiazide/thiazide-like diuretics (with longer-acting diuretics preferred), b-blockers, ACE inhibitors, ARBs, or long-acting CCB.

AMERICAN GUIDELINES 2017

8.1.6. Choice of Initial Medication

Recommendation for Choice of Initial Medication

References that support the recommendation are summarized in Online Data Supplement 27 and Systematic Review Report.

COR	LOE	Recommendation
I	A[R]	1. For initiation of antihypertensive drug therapy, first-line agents include thiazide diuretics, CCBs, and ACE inhibitors or ARBs. (1, 2)

Chlorthalidone, is not available in South Africa

LATIN AMERICA 2017

Initiate with MONOTHERAPY:

I. DIURETICS (Thiazides, Chlorthalidone, Indapamide)
II. ACEIs
III. ARBs
IV. CCBs
V. BETA-BLOCKERS

- FIXED DOSE COMBINATION: MAY ALSO BE PRESCRIBED AS 1ST LINE

Summary Highlighting the Major Consensus Findings and Discrepancies between Guidelines

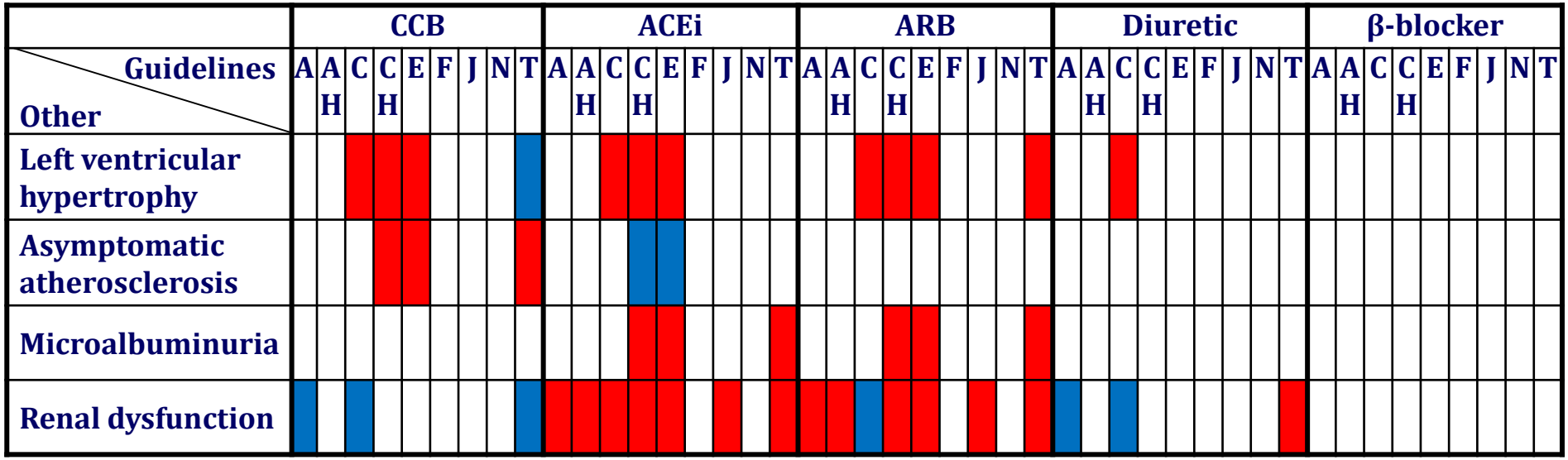
Treatment Recommendations for Specific Patient Groups	
Consensus Opinion*	**Discrepancies**
Specific treatment recommendations are required for patients with associated comorbidities **Treatment of black patients should be initiated with CCB or thiazide-like diuretic** **β-blockers should be prescribed for patients with a history of myocardial infarction, heart failure or angina pectoris**	–

*Consensus recommendations are those that are presented in the majority of the guidelines, with no conflicting advice presented in the other guidelines (although the subject may not be discussed)

ACC/AHA, American College of Cardiology/ American Hypertension Association; ASH/ISH, American Society of Hypertension/International Society of Hypertension; ESH/ESC, European Society of Hypertension/European Society of Cardiology; JNC 8, Eighth Joint National Committee; NICE, National Institute for Clinical Excellence (UK), ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker, BP blood pressure; CCB, calcium channel blocker; SPC, single pill combination

Adapted from Kjeldsen S et al. *Drugs* 2014; 74:2033-2051

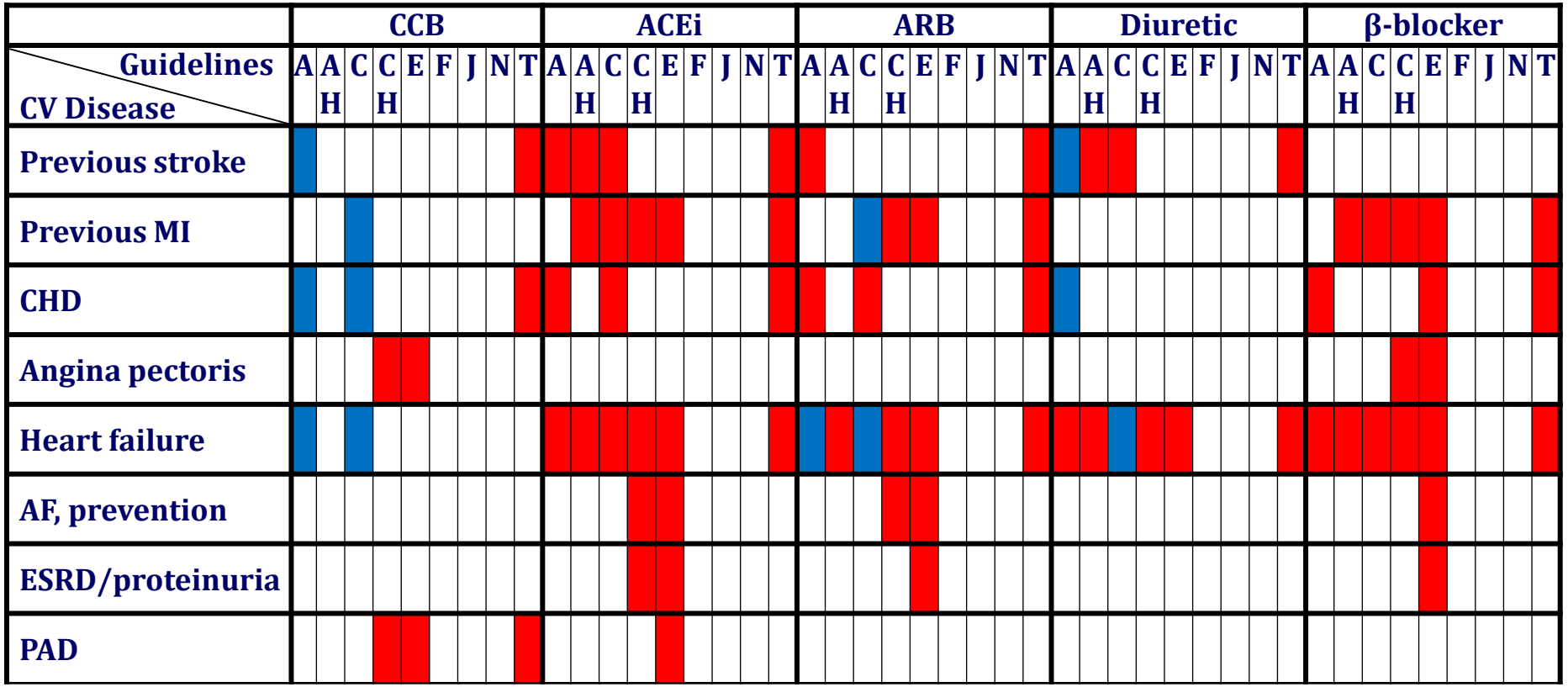
Recommended Therapies Specified by Each Guidelines for Specific Populations: Condition



Red squares refer to initial therapy recommendations
Blue squares refer to 2nd line therapy recommendations

Guidelines: A, ASH/ISH; AH, AHA/ACC/CDC; C, CHEP; CH, China; E, ESH/ESC; F, France; J, JNC8; N, NICE; T, Taiwan. ASH/ISH, 2014 American Society of Hypertension/ International Society of Hypertension; AHA/ACC/CDC, 2014 American Hypertension Association/American College of Cardiology/Centers for Disease Control and Prevention; CHEP, 2014 Canadian hypertension education program Recommendations, China, 2010 Guidelines; ESH/ESC, 2013 European Society of Hypertension/ European Society of Cardiology Guidelines; JNC 8, Eighth Joint National Committee; NICE, National Institute for Clinical Excellence (UK) [CG127, last updated 2016]; Taiwan, 2010 Guidelines;
ACEi, angiotensin converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; ESRD, end-stage renal disease; ISH, isolated systolic hypertension.
Kjeldsen S et al. *Drugs* 2014; 74:2033-2051

Recommended Therapies Specified by Each Guidelines for Specific Populations: CV Disease



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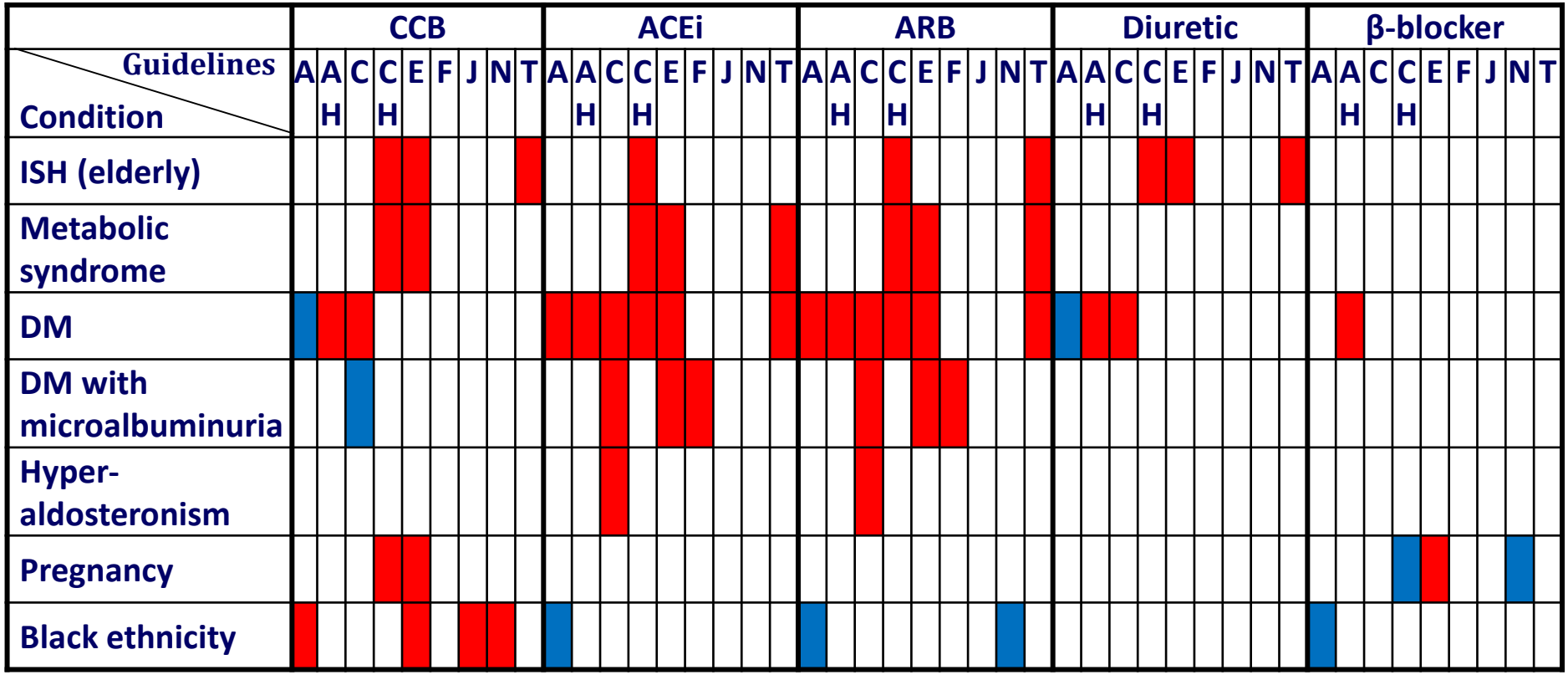
Kjeldsen S et al. *Drugs* 2014; 74:2033-2051

Recommended Therapies Specified by Each Guidelines for Specific Populations: Other



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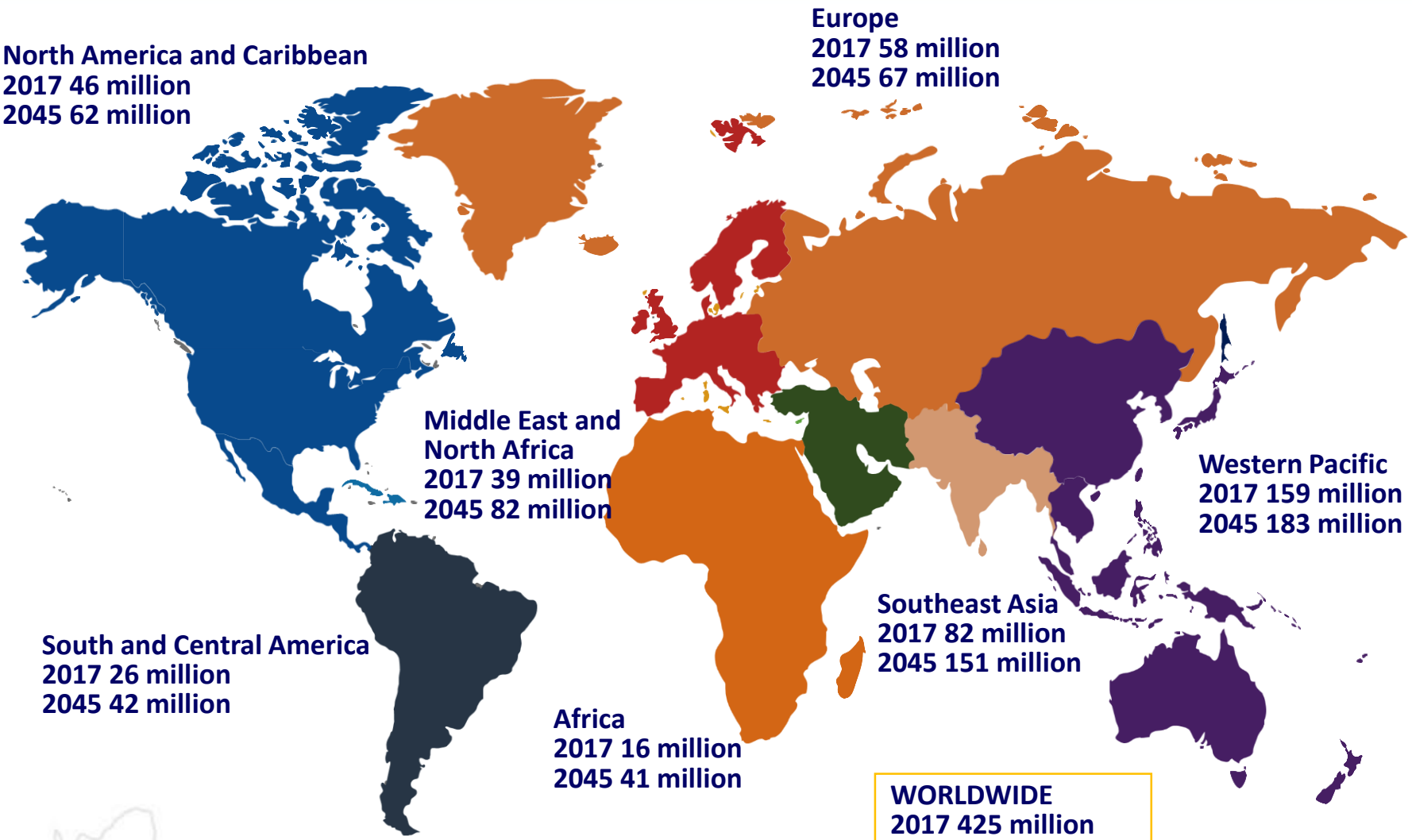
Kieldsen S et al. *Drugs* 2014; 74:2033-2051

Hypertension & Diabetes:

The Bad Companions

Estimated Number of People with Diabetes Worldwide



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Adapted from https://diabetesatlas.org/across-the-globe.html.

Excess Cardiovascular Risk In Diabetic Patients Is Attributable To Co-existent Hypertension

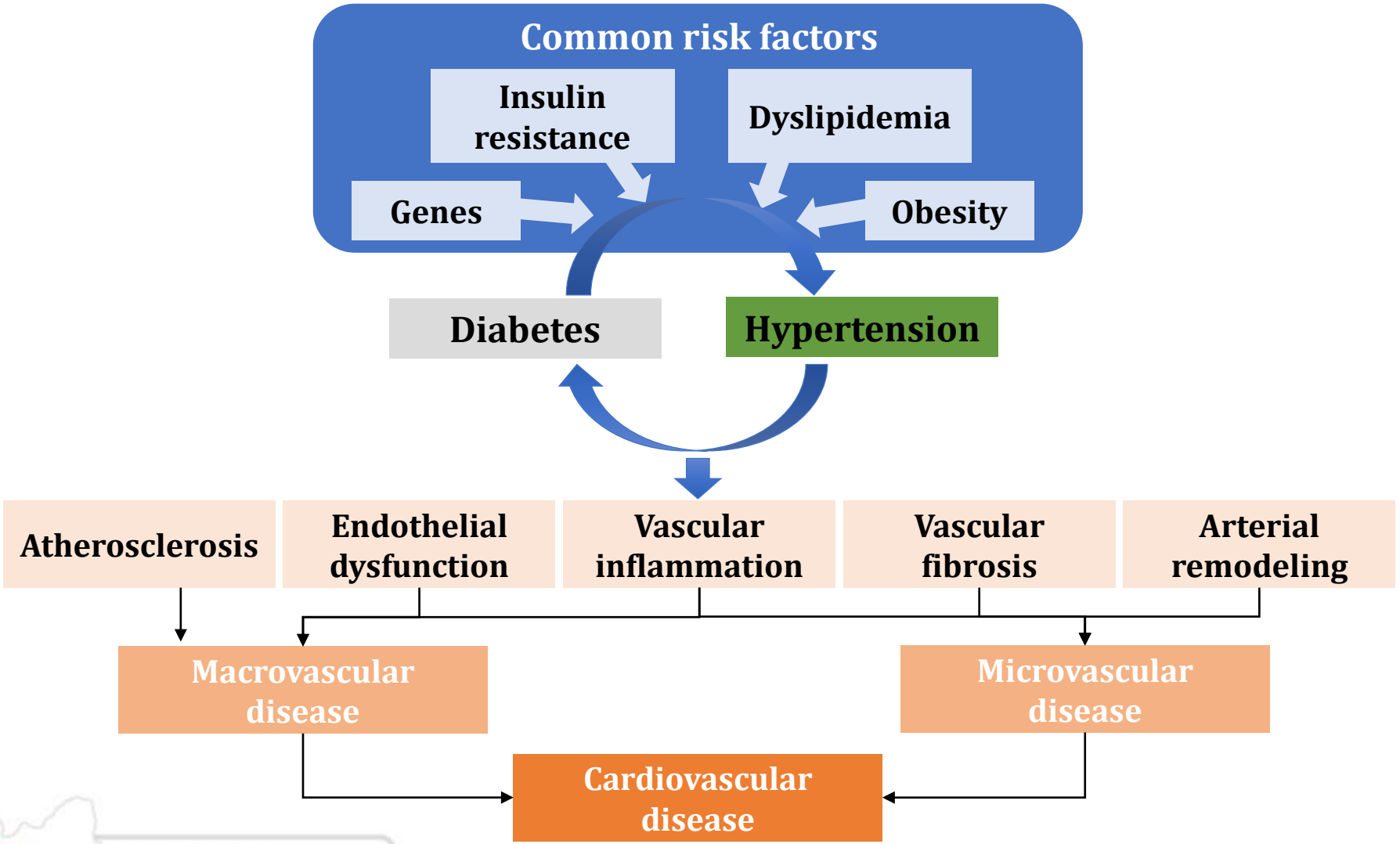
"Participants with hypertension at the time of diabetes diagnosis had higher rates of all-cause mortality and cardiovascular disease than did people with diabetes without hypertension"

All-cause mortality	**+72%**
Cardiovascular disease event	**+57%**

Know your blood pressure by

Ferrannini E, Cushman WC. *Lancet.* 2012;380(9841):601-610

Diabetes And Hypertension Predispose Patients To Cardiovascular Disease



Adapted from Petrie JR, et al. *Can J Cardiol* 2018;34(5):575-84.

Meta-analysis: Comparison of ACEi and ARBs on CV Outcomes in Hypertensive Patients with T2DM

	RCTs	n	OR	95% CI	*p*
ACEi					
All-cause mortality	5	1207	0.87	0.80-0.94	0.0008
CV death	5	1360	0.83	0.73-0.95	0.006
MI	4	321	0.77	0.66-0.90	0.0009
Stroke	5	549	0.88	0.78-0.99	0.04
Heart failure	4	318	0.65	0.47-0.90	0.01
CV events	5	1360	0.83	0.73-0.95	0.006
ARBs					
All-cause mortality	7	1384	1.06	0.97-1.15	0.17
CV death	7	524	1.02	0.78-1.33	0.88
MI	7	381	0.88	0.77-1.01	0.08
Stroke	7	515	0.96	0.84-1.09	0.50
Heart failure	5	422	0.81	0.61-1.07	0.14
CV events	8	1843	0.94	0.88-1.01	0.12

CV, cardiovascular; MI, myocardial infarction; OR, odds ratio; RCT, randomised controlled trial; T2DM, type 2 diabetes mellitus.
Adapted from Lv X, et al. *Medicine (Baltimore)* 2018;97(15):e0256.

Meta-analysis: Comparison of ACEi and ARBs on CV Outcomes in Hypertensive Patients with T2DM

Conclusions

ACEi showed a significant CV protection for all-cause mortality, CV death, and major CV events in patients with hypertension and T2DM

ARBs had no benefits on these outcomes except MI

In view of differential benefits on mortality and morbidity, ACEi appear preferable to ARBs for patients with hypertension and T2DM

CV, cardiovascular; MI, myocardial infarction; T2DM, type 2 diabetes mellitus.
Lv X, et al. *Medicine (Baltimore)* 2018;97(15):e0256.

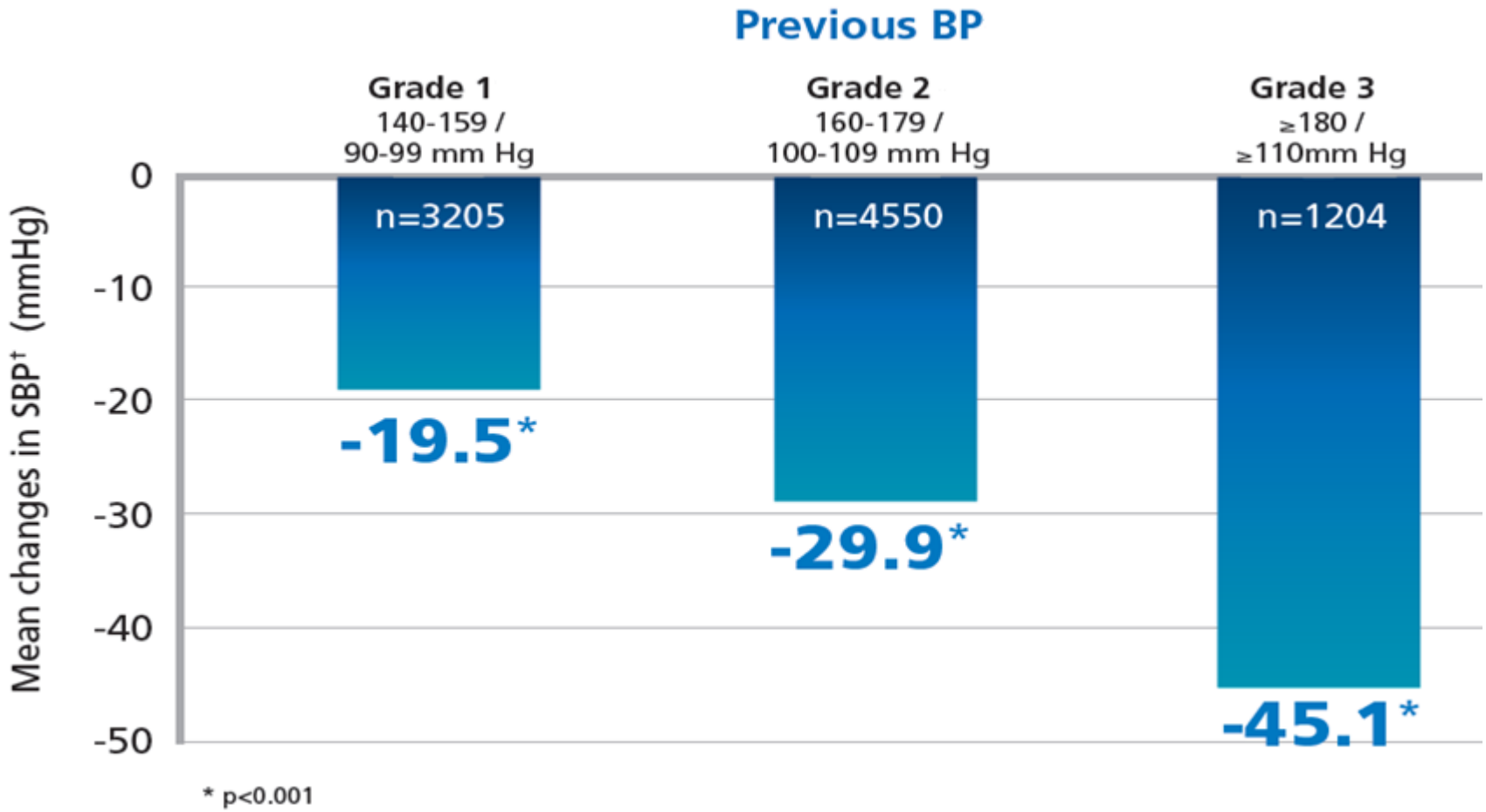
Renal and CV Protection in Antihypertensive Trials in Diabetic Patients

Trial	Treatment	BP baseline, mmHg	SBP difference vs. control, mmHg	Reduction in renal outcomes	Reduction in mortality	
					CV	Total
IDNT (N = 1,148)	Irbesartan vs. placebo	159/87	-3.3	-20% (p = 0.02) Secondary prevention	No	No
RENAAL (N = 1,513)	Losartan vs. placebo	153/82	-2	-16% (p = 0.02) Secondary prevention	-	No
DIRECT (N = 5,231)	Candesartan vs. placebo	118/73	-3.3	-5.5% (p = 0.024) Secondary prevention	-	No
ROADMAP (N = 4,447)	Olmesartan vs. placebo	136/81	-3	Yes Primary prevention	No	No
TRANSCEND (N = 5,927)	Telmisartan vs. placebo	141/82	-4	No	No	No
ONTARGET (N = 17,118)	Telmisartan vs. ramipril	142/82	-2.4	No	No	No
ADVANCE (N = 11,140)	Perindopril/indapamide vs. placebo	145/81	-5.6	-21% (p < 0.0001) Primary and secondary prevention	-18% (p = 0.025)	-14% (p = 0.027)
ACCOMPLISH (N = 11,506)	Benazepril/amlodipine vs. benazepril/HCTZ	145/80	-1.1	-48% (p < 0.0001) Secondary prevention	No	No
ACCORD N = 4,733)	Intensive vs. standard	139/76	-14.2	Yes Secondary prevention	No	No

Know your blood pressure by

BP, blood pressure; CV, cardiovascular; SBP, systolic blood pressure.
Adapted from Garcia-Donaire JA, et al. *Blood Press* 2011;20:322-34.

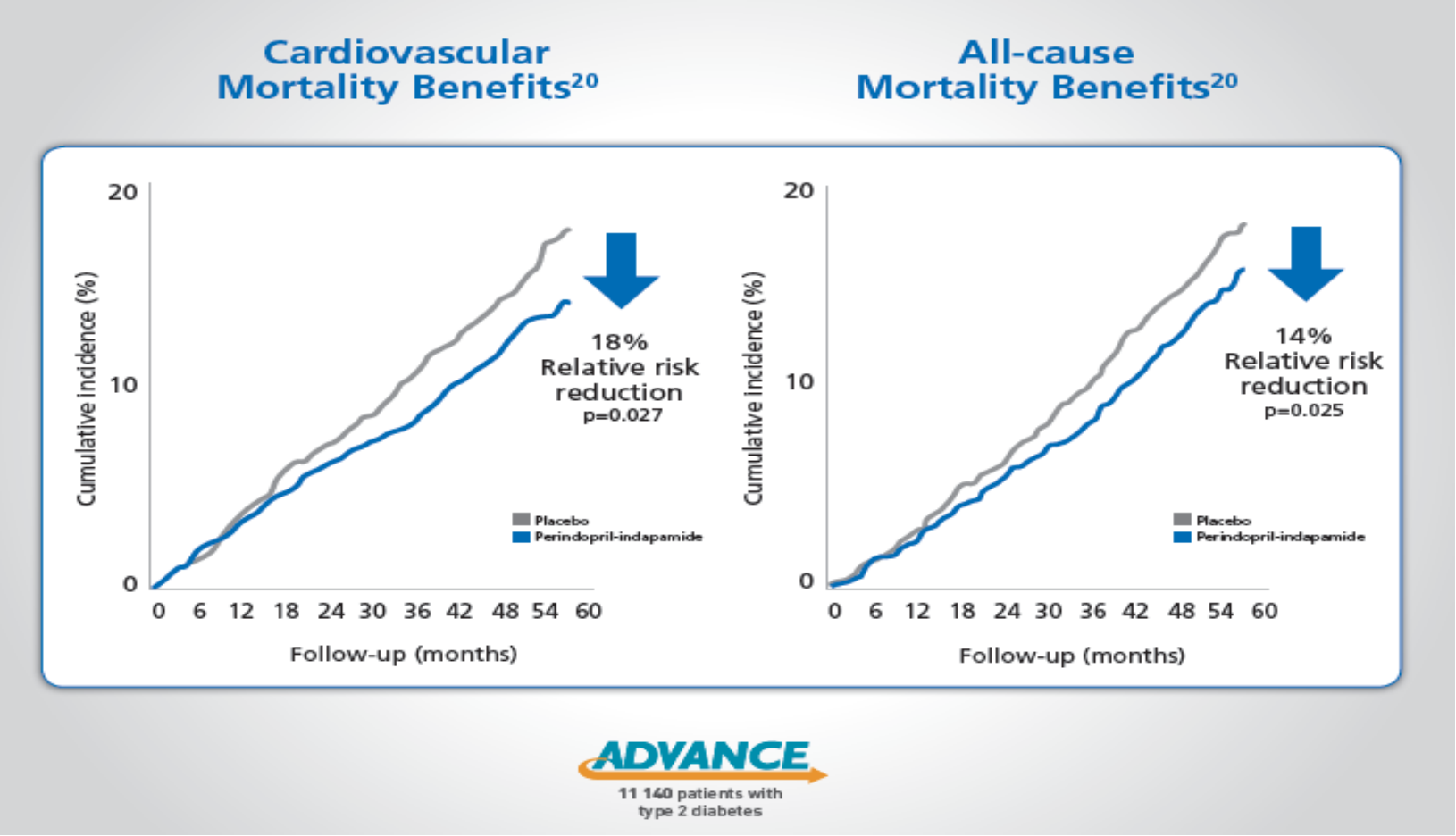
Significant BP Reduction with Perindopril & Indapamide



Know your blood pressure by

Farsang C et al; PICASSO investigators. *Adv in Therapy*. 2014;31:333-344.

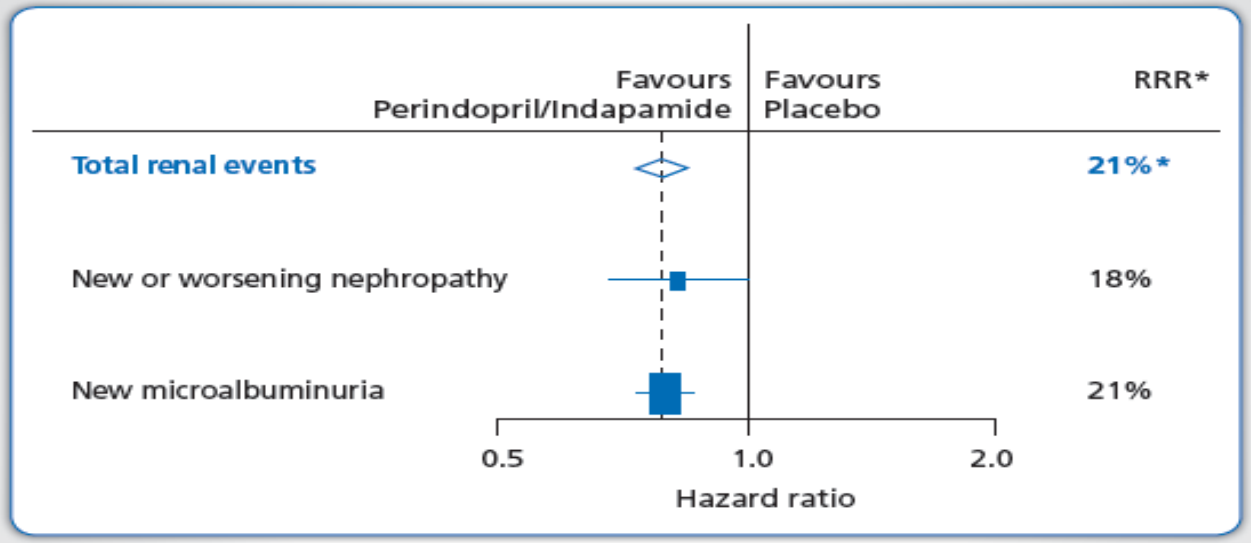
ADVANCE - Effect on Mortality



ADVANCE Collaborative Group. Lancet 2007;370:829-40

ADVANCE - Effect on Renal Events

Reduction Risk Total Renal events[20]



The combined benefits of reducing the risk of mortality AND providing renal protection distinguishes perindopril plus indapamide from other antihypertensives when reducing blood pressure in diabetics.[20,29]

ADVANCE
11 140 patients with type 2 diabetes

Know your blood pressure by

RRR* - Relative Risk Reduction

ADVANCE Collaborative Group. Lancet 2007;370:829-40

ESH/ESC Guidelines 2018
Office Blood Pressure Treatment Target Range

Age Group	Office SBP treatment target ranges (mmHg)					DBP Treatment range (mm Hg)
	HT	+ DM	+ 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
DBP treatment target range (mmHg)	<80 to 70	<80 to 70	<80 to 70	<80 to 70	<80 to 70	

SAHS Know your blood pressure by

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

Williams B, et al., *Eur Heart J* 2018;39:3021-104.

Definition of Chronic Kidney Disease

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health

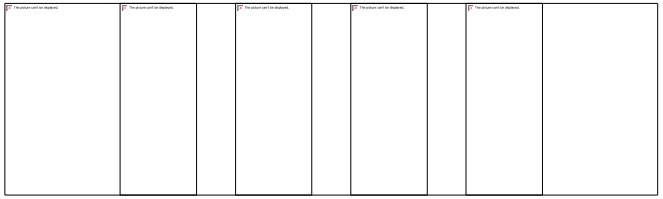
Criteria for CKD (either of the following present for >3 months):	
Markers of kidney damage (1 or more)	• Albuminuria (AER ≥ 30 mg/24 hours; ACR ≥ 30 mg/g (≥ 3 mg/mmol)) • Urine sediment abnormalities • Electrolyte and other abnormalities due to tubular disorders • Abnormalities detected by histology • Structural abnormalities detected by imaging • History of kidney transplantation
Decreased GFR	• GFR < 60 ml/min/1.73 m^2 (GFR categories G3a-G5)

GFR, glomerular filtration rate.
Adapted from *Kidney Int Suppl (2011)* 2013;3(1):19-62.

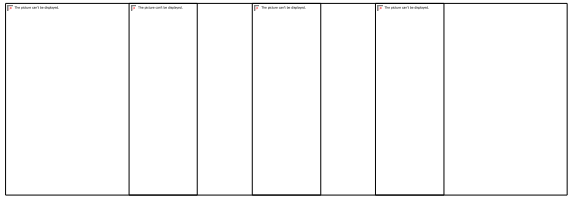
Alarming Increase in Chronic Kidney Disease (CKD) Prevalence

Population prevalence of CKD is > 10% and > 50% in high-risk subpopulations[1]

Ages 65-74

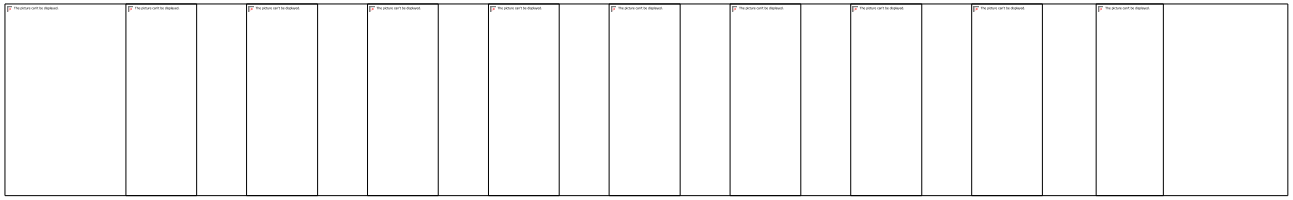


1 in 5 men



1 in 4 women

Ages 75+



Half of population

Due to increasing incidence of diabetes mellitus and hypertension in aging population[2]

Know your blood pressure by

Adapted from:
1. Eckardt KU, et al. *Lancet* 2013;382(9887):158-69.
2. Adapted from https://www.healthcare.siemens.se/news/chronic-kidney-disease.html.

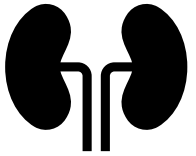
Cochrane Database Systematic Review: Drugs for Preventing Kidney Disease in People with Diabetes

Background

~ 60% of people with DM are affected by hypertension and require antihypertensive agents

These drugs help prevent the development of kidney disease

- **DM with normal blood pressure**
- **DM with high blood pressure**



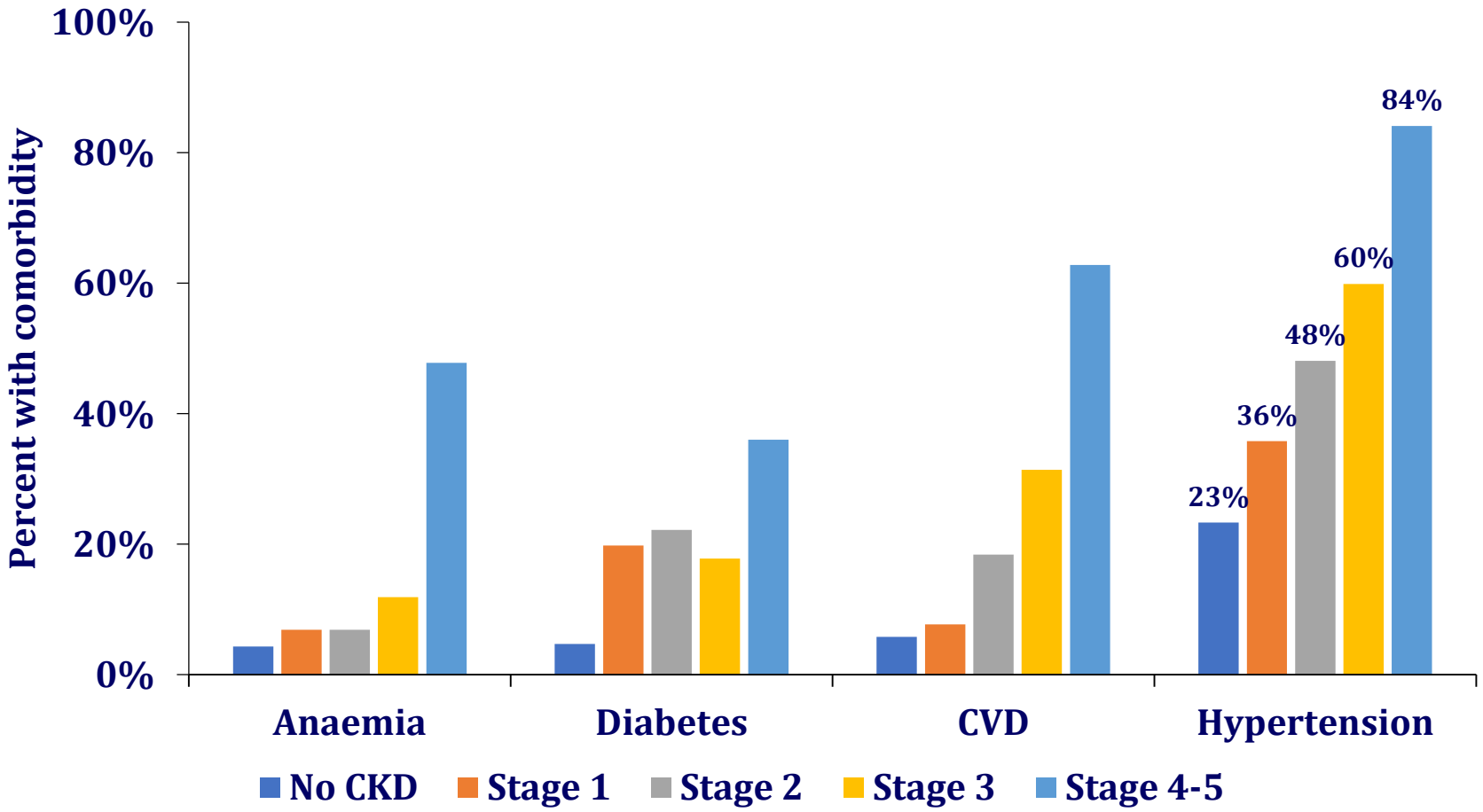
20-40% of people with diabetic kidney disease develop ESRD

- **Others die from heart disease or circulatory problems before ESRD develops**

Know your blood pressure by

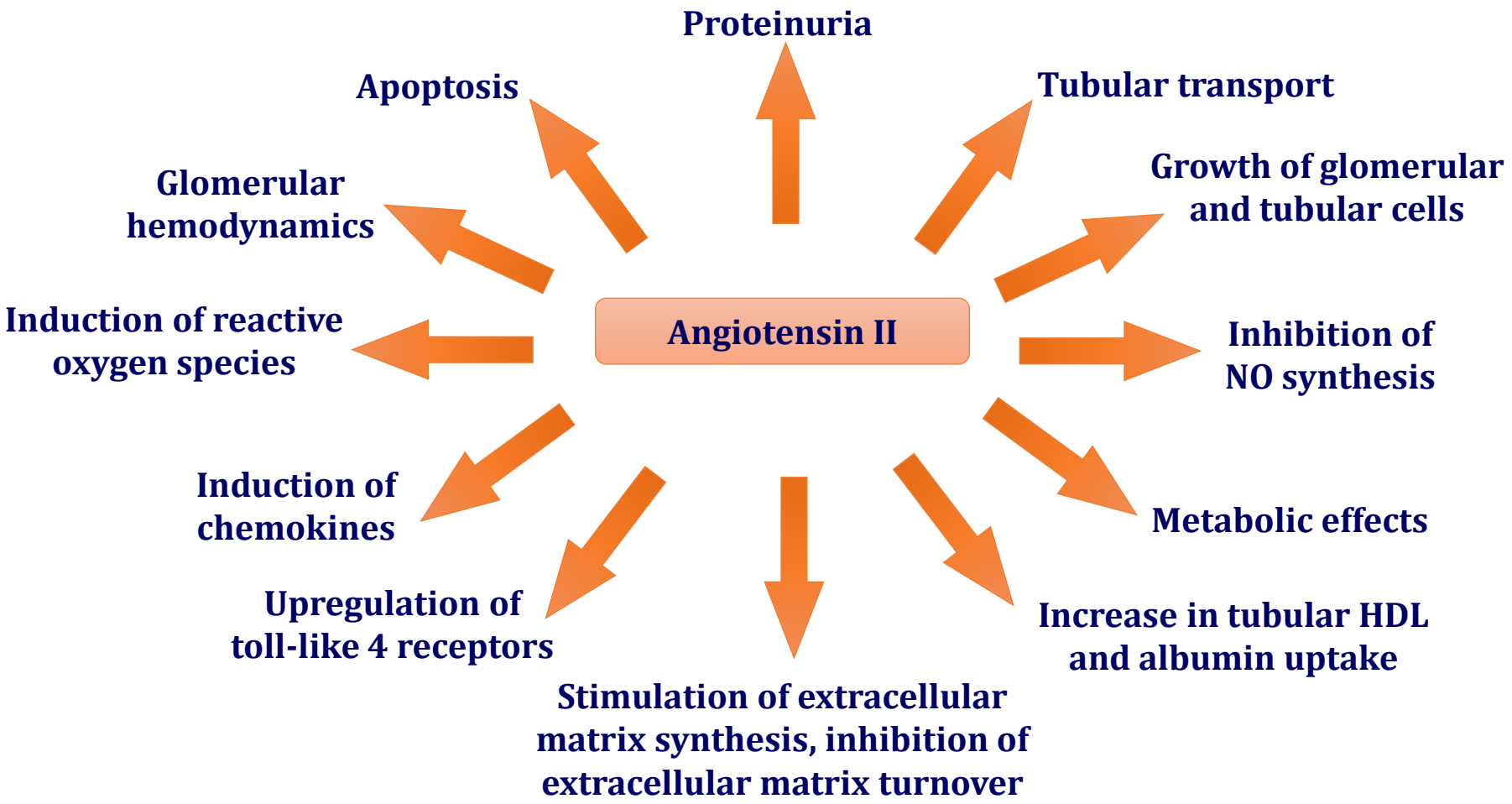
DM, diabetes mellitus; ESRD, end-stage renal disease.
Lv J, et al. *Cochrane Database Syst Rev* 2012;12:CD004136.

The Prevalence of Comorbidities Rises with CKD Stage, Especially Hypertension



CKD, chronic kidney disease; CVD, cardiovascular disease.
Adapted from U.S. Renal Data System (USRDS). 2009 ASRDS Annual Report Data. http://www.usrds.org/2009/pdf/V1_01_09.PDF.

Hyper-RAAS Activity: A Culprit in CKD



CKD, chronic kidney disease; HDL, high-density lipoprotein; NO, nitric oxide; RAAS, renin-angiotensin-aldosterone system.

Adapted from Rüster C, Wolf G *JASN* 2006;17:2985-91.

Effects of RAAS Inhibitors in Patients with Kidney Disease

RAAS system is one of the main causes of progression of kidney disease

Inhibition of RAAS can play protective roles in different stages of kidney disease via:

- **Reducing blood pressure**
- **Reducing proteinuria**
- **Decreasing the decline rate of renal function**
- **Preventing occurrence of peritoneal fibrosis**

There is a clear need for strategies to block the RAAS efficiently to reduce progression of kidney disease

RAAS, renin-angiotensin-aldosterone system.
Zhang F, et al. *Curr Hypertens Rep* 2017;19(9):72.

Meta-Analysis of RCTs: Effects of ACEi vs. ARBs on Proteinuria or Albuminuria in Primary Hypertension – Outcomes Summary

Studies included:

1. Sengul 2005
2. Tan 2010
3. Juarez 2013
4. Deyneli 2006
5. Lacourciere 2000
6. ONTARGET 2008
7. Zhu 2008
8. Scaglione 2005
9. Erik 2000
10. OGAQA 2007
11. Lun 2002
12. Tetsuya 2009
13. Aiguo 2004
14. Hong 2000
15. L-jie 2012
16. Honglin 2008
17. DETAILO 2004

Outcome	Studies, n	Participants, n	Effect size [95% CI]*
Albumin/creatine ratio (ACR)	7	17,109	0.15 [-1.88, 2.19]
Albumin excretion rate (AER)	10	842	0.09 [-0.18, 0.36]
Adverse reaction	13	18,327	1.53 [0.91, 2.58]
Systolic blood pressure	12	746	-0.5 [-1.58, 0.58]
Subgroup analysis – with diabetes	9	812	-0.26 [-0.69,0.17]
Subgroup analysis – without diabetes	7	399	0.16 [-0.18, 0.50]
Subgroup analysis – AER or AER < 30	3	16,842	0.81 [-2.50, 4.12]
Subgroup analysis – AER or AER < 300	7	718	-0.10 [-0.49, 0.30]
Subgroup analysis – AER or AER > 300	6	396	0.06 [-0.49, 0.62]

*No outcome measure showed statistically significant difference between ACEi and ARBs.

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Adapted from Xu R, et al. *Medicine (Baltimore)* 2015;94(39):e1560.

Meta-Analysis of RCTs: Effects of ACEi vs. ARBs on Proteinuria or Albuminuria in Primary Hypertension

Conclusions

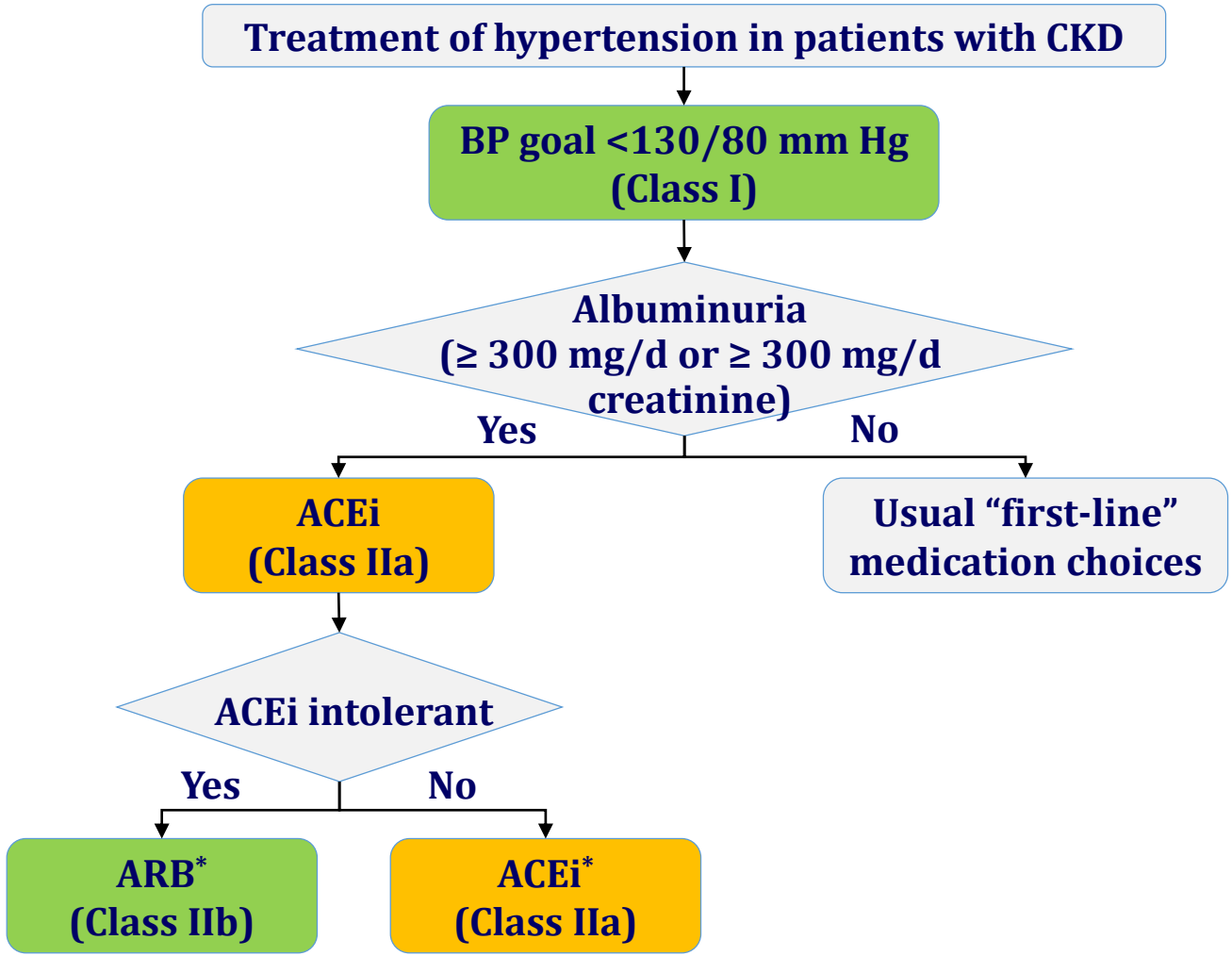
Based on a meta-analysis of 17 randomised controlled trials including 17,951 patients,

ACEi and ARBs :

- **Reduced urine protein levels**
- **Improved blood pressure**
- **Similarly effective in reducing urinary protein excretion**

Xu R, et al. *Medicine (Baltimore)* 2015;94(39):e1560.

Recommendations for Treatment of HT in Patients with CKD 2017ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/ PCNA Guidelines



*CKD stage 3 or higher or stage 1 or 2 with albuminuria ≥ 300 mg/d or ≥ 300 mg/g creatinine.
Class I: strong; Class IIa: moderate; Class IIb: weak; BP, blood pressure; CKD, chronic kidney disease.
Adapted from Whelton PK, et al. *Hypertension* 2018;71(6):1269-324.

2018 ESC/ESH Guidelines: Drug Treatment Strategy for Hypertension and CKD

1 Pill — **Initial therapy**
Dual combination

ACEi or ARB + CCB or ACEi or ARB + diuretic (or loop diuretic)[b]

1 Pill — **Step 2**
Triple combination

ACEi or ARB + CCB + diuretic (or loop diuretic)[b]

2 Pills — **Step 3**
Triple combination + spironolactone[c] or other drug

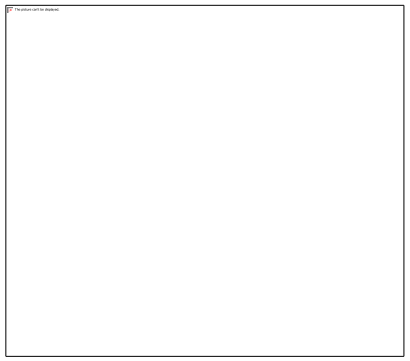
Resistant hypertension
Add spironolactone (25 to 50 mg once daily) or other diuretic, alpha-blocker or beta-blocker

Beta-blockers: Consider at any treatment step, when there is a specific indication for their use, e.g., heart failure, angina, post-MI, atrial fibrillation, or younger women with/planning pregnancy

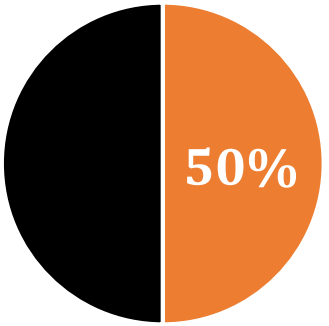
A reduction in eGFR and rise in serum creatinine is expected in patients with CKD[a] who receive BP-lowering therapy, especially in those treated with ACEi or ARB; a rise in serum creatinine of > 30% should prompt evaluation of the patient for possible renovascular disease

[a] CKD is defined as an eGFR < 60 mL/min/1.72 m^2 with or without proteinuria.
[b] Use loop diuretics when eGFR is < 30 mL/min/1.72 m^2, because thiazide/thiazide-like diuretics are much less effective/ineffective when eGFR is reduced to this level.
[c] Caution: risk of hyperkalaemia with spironolactone, especially when eGFR is < 45 mL/min/1.72 m^2 or baseline K+ ≥ 5.0 mmol/L.
BP, blood pressure; CCB, calcium channel blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MI, myocardial infarction.
Adapted from Williams B, et al. *J Hypertens* 2018;36(12):2284-309.

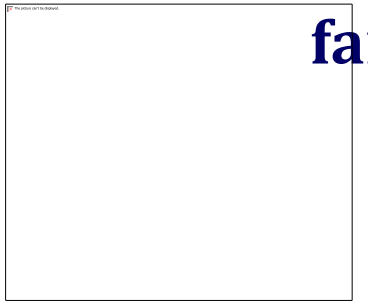
Heart Failure



Heart failure affects > 23 million people worldwide



~ 50% of people diagnosed with heart failure will die within 5 years



Heart failure ranks as the most frequent reason for hospitalisation in older people

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Xie W, et al. *Int J Cardiol* 2016;205:65-71.

2018 ESC/ESH Guidelines: Drug Treatment Strategy for Hypertension and HFrEF

Initial therapy

ACEi or ARB[a] + diuretic[b] (or loop diuretic) + beta-blocker

Step 2

ACEi or ARB[a] + diuretic (or loop diuretic) + beta-blocker + MRA[c]

When antihypertensive therapy is not required in HFrEF, treatment should be prescribed according to the ESC heart failure guidelines

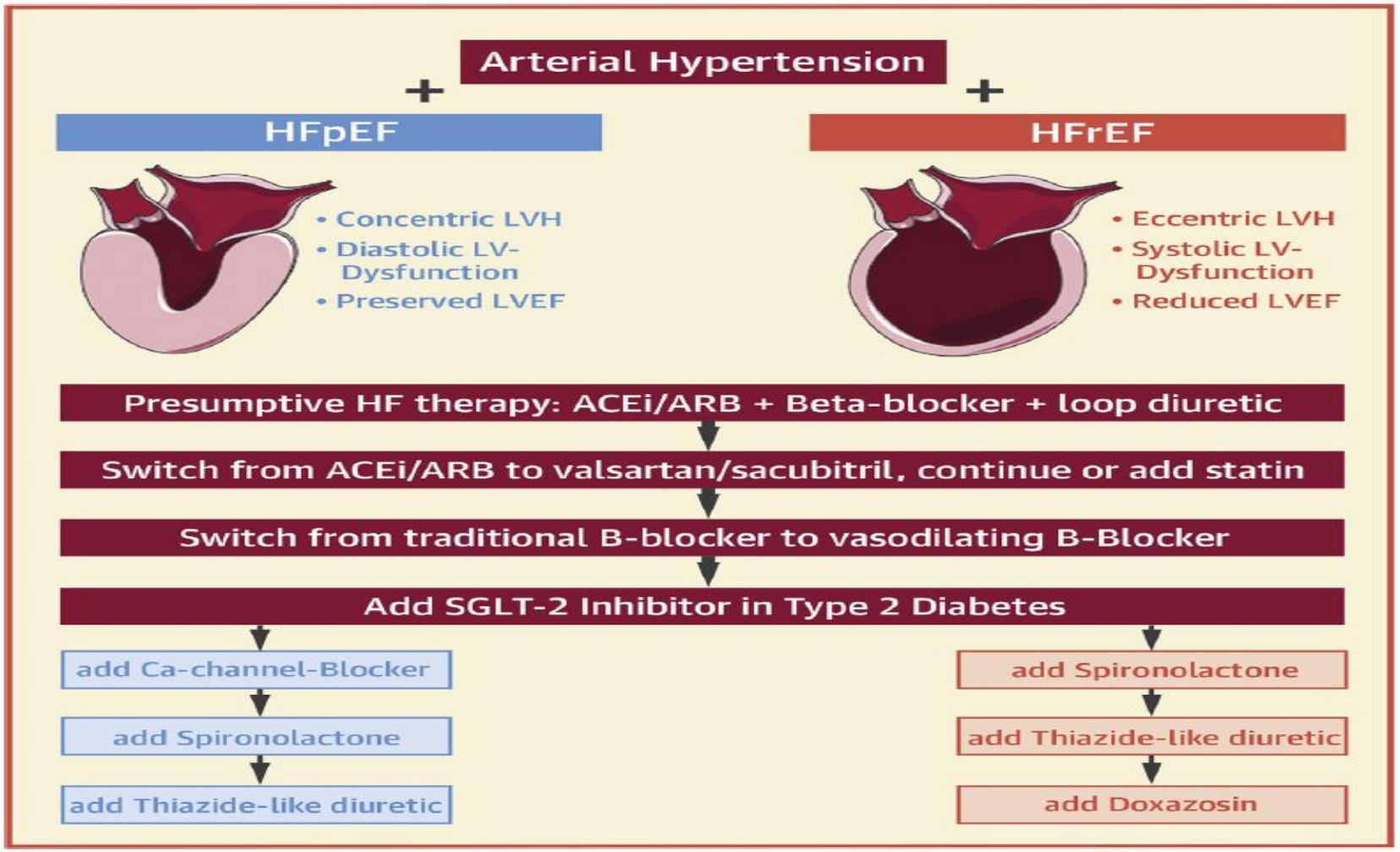
Do not use non-dihydropyridine CCBs (e.g., verapamil or diltiazem).
a Consider an angiotensin receptor/neprilysin inhibitor instead of ACEi or ARB per ESC Heart Failure Guidelines.
b Diuretic refers to thiazide/thiazide-like diuretic. Consider a loop diuretic as an alternative in patients with oedema.
c MRA (spironolactone or eplerenone).
CCB, calcium channel blocker; ESC, European Society of Cardiology; HFrEF, heart failure with reduced ejection fraction; MRA, mineralocorticoid receptor antagonist.
Adapted from Williams B, et al. *Eur Heart J* 2018;39:3021-104.

2018 ESC/ESH Guidelines: Therapeutic Strategies in Hypertensive Patients with HF or LVH

Recommendations	Class	Level
In hypertensive patients with heart failure (with reduced or preserved ejection fraction), BP-lowering treatment should be considered if BP is ≥140/90 mmHg	IIa	B
In patients with HFrEF, it is recommended that BP-lowering treatment comprises an ACEi or ARB, and a beta-blocker and diuretic and/or MRA if required	I	A
Dihydropyridine CCBs may be added if BP control is not achieved	IIb	C
In patients with HFpEF, BP treatment threshold and target values should be the same as for HFrEF	IIa	B
Because no specific drug has proven its superiority, all major agents can be used.	I	A
In all patients with LVH: It is recommended to treat with an RAS blocker in combination with a CCB or diuretic. SBP should be lowered to a range of 120–130 mmHg	I IIa	A B

BP, blood pressure; CCB, calcium channel blocker; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; LVH, left ventricular hypertrophy; MRA, mineralocorticoid receptor antagonist; RAS, renin-angiotensin system; SBP, systolic blood pressure.
Adapted from Williams B, et al. *Eur Heart J* 2018;39:3021-104.

Suggested Empirical Antihypertensive Strategy in HF Patients with Persisting Hypertension



Know your blood pressure by

Ca, calcium; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LV, left ventricular; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; SGLT2, sodium-glucose co-transporter 2 inhibitor.

Adapted from Messerli FH, et al. *J Am Coll Cardiol H.* 2017;5(8):543-51.

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 <220mmHg	**III**	**A**
In patients with SBP ≥ 220mmHg, careful acute BP lowering with i.v. therapy, to <180mmHg 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 < 180/105mmHg for at least the first 24 hrs 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 hrs after the stroke onset.	**IIb**	**C**

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Therapeutic Strategies In Hypertensive Patients With Acute Stroke And Cerebrovascular Disease

Recommendations	Class	Level
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

Know your blood pressure by

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Blood Pressure Treatment Targets

Age Group [Years]	Office SBP Treatment Threshold [mmHg]					Diastolic Tx Threshold [mmHg]
	Hypertension	+ Diabetes	+ CKD	+ CAD	+ Stroke/TIA	
18 – 65	Target 130 or lower if tolerated Not <120	Target 130 or lower if tolerated Not <120	Target <140-130 if tolerated	Target 130 or lower if tolerated Not <120	Target 130 or lower if tolerated Not <120	<80-70
65 – 79	Target <140-130 if tolerated	Target <140-130 if tolerated	Target <140-130 if tolerated	Target <140-130 if tolerated	Target <140-130 if tolerated	<80-70
≥ 80	Target <140-130 if tolerated	Target <140-130 if tolerated	Target <140-130 if tolerated	Target <140-130 if tolerated	Target <140-130 if tolerated	<80-70
Diastolic Tx Threshold [mmHg]	<80-70	<80-70	<80-70	<80-70	<80-70	

The first objective of tx should be to lower BP to <140/90 mmHg in all patients

Old/Very old patients:

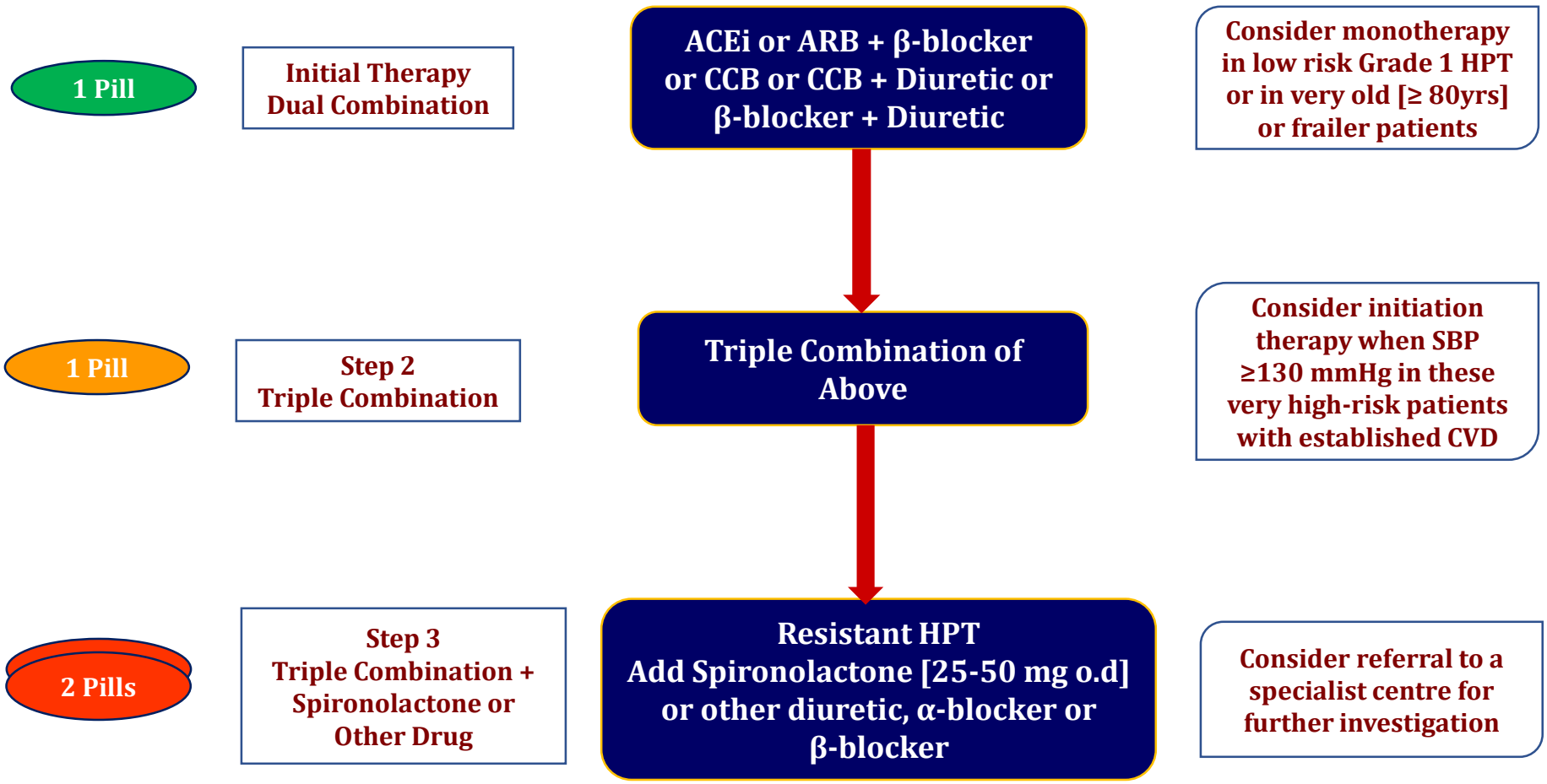
The new concept is to propose the less conservative blood pressure tx targets

Age <65 yrs	SBP 120 – 130 mmHg
Age >65 yrs	SBP 130 – 140 mmHg
Diabetes & CAD	SBP 130 or lower
CKD	SBP 130 – <140 mmHg
Post Stroke	SBP 120 - <130 mmHg [to be considered]

SAHS Know your blood pressure by

ESH CONGRESS Scientific Session: 2018 ESC/ESH Guidelines for the management of arterial hypertension

Hypertension & CAD



SAHS
Know your blood pressure by

ESH CONGRESS Scientific Session: 2018 ESC/ESH Guidelines for the management of arterial hypertension

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Post Stroke	SBP 120 - <130 mmHg [to be considered]

ESH CONGRESS Scientific Session: 2018 ESC/ESH Guidelines for the management of arterial hypertension

Hypertension & AF

Initial Therapy
Dual Combination

ACEi or ARB + β-blocker
or non DHP-CCB or CCB or
β-blocker + CCB

Step 2
Triple Combination

ACEi or ARB + β-blocker
+ DHP CCB or Diuretic or
β-blocker + DHP CCB + Diuretic

Add oral anticoagulation when indicated according to the CHA, DS, VASc score, unless contraindicated

Routine combination of β-blockers with non-DHP CCBs [e.g. verapamil or diltiazem] is not recommended due to a potential marked reduction in heart rate

Hypertension In Pregnancy

Major cause of maternal, foetal, and neonatal morbidity and mortality

Definition based on office BP values SPB ≥140 mmHg and/or DBP ≥90 mmHg

Hypertension in pregnancy classification

- **Mild – 140 – 159/90 – 109 mmHg**
- **Severe – ≥160/110 mmHg**

Hypertension In Pregnancy

Pre-existing hypertension - Precedes pregnancy or develops before 20 weeks of gestation and usually persists for more than 6 weeks post-partum and may be associated with proteinuria

Gestational hypertension – develops after 20 weeks of gestation and usually resolves within 6 weeks post-partum

Pre-existing hypertension plus superimposed gestational hypertension with proteinuria

Pre-eclampsia – gestational hypertension with significant proteinuria [>0.3 g / 24h or ≥30 mg/mmol albumin: creatinine ratio]. It is more frequent in the first pregnancy, in multiple pregnancy, in hydatidiform mole, in antiphospholipid syndrome, or with pre-existing hypertension, renal disease, , or diabetes

Management Of Hypertension In Pregnancy

Recommendations	Class	Level
In women with gestational hypertension or pre-existing hypertension Super imposed by gestational hypertension, or with hypertension and sub clinical organ damage or symptoms, initiation of drug treatment is recommended when SBP is ≥140 or DBP ≥90 mmHg.	I	C
In all other cases, initiation of drug treatment is recommended when SBP is ≥ 150mmHg or DBP is ≥ 95mmHg.	I	C
Methyldopa, labetalol, and CCBs are recommended as the drugs of choice for the treatment of hypertension in pregnancy.	I	B (Methyldopa)
	I	C (labetalol Or CCBs)
ACE inhibitors, ARBs, or direct renin inhibitors are not recommended during pregnancy.	III	C

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

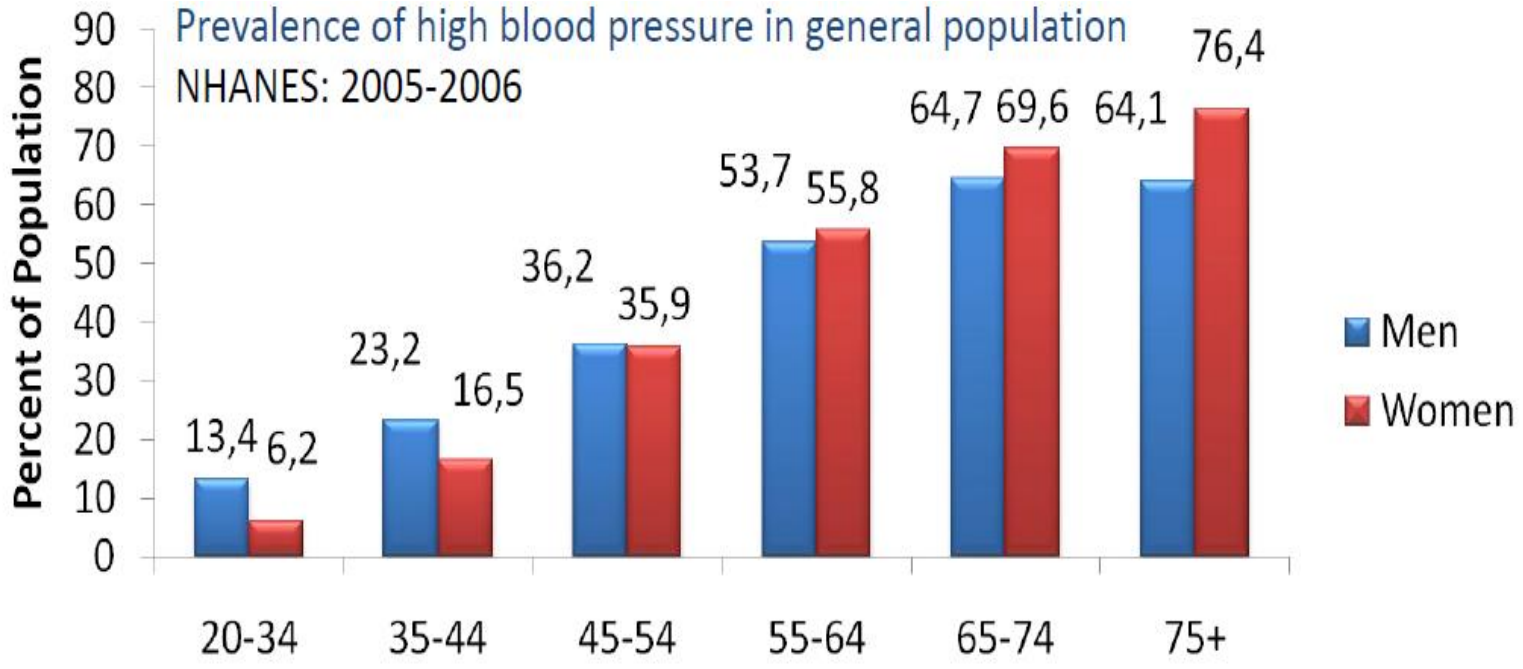
Management Of Hypertension In Pregnancy

Recommendations	Class	Level
SBP ≥ 170mmHg or DBP ≥ 110mmHg in a pregnant woman is an emergency, and admission to hospital is recommended.	I	C
In severe hypertension, drug treatment with i.v. labetalol or oral Methyldopa or nifedipine is recommended.	I	C
There commended treatment for hypertensive crisis is i.v. labetalol or nicardipine and magnesium.	I	C
In pre-eclampsia associated with pulmonary oedema, nitroglycerin given as an i.v. infusion is recommended.	I	C
In women with gestational hypertension or mild pre-eclampsia, delivery is recommended at 37 weeks.	I	B
It is recommended to expedite delivery in pre-eclampsia with adverse conditions such as visual disturbances or haemostatic disorders.	I	C

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Hypertension in Athletes: Epidemiology

...the overall prevalence of high blood pressure in athletes is approximately 50% lower than in the general population...

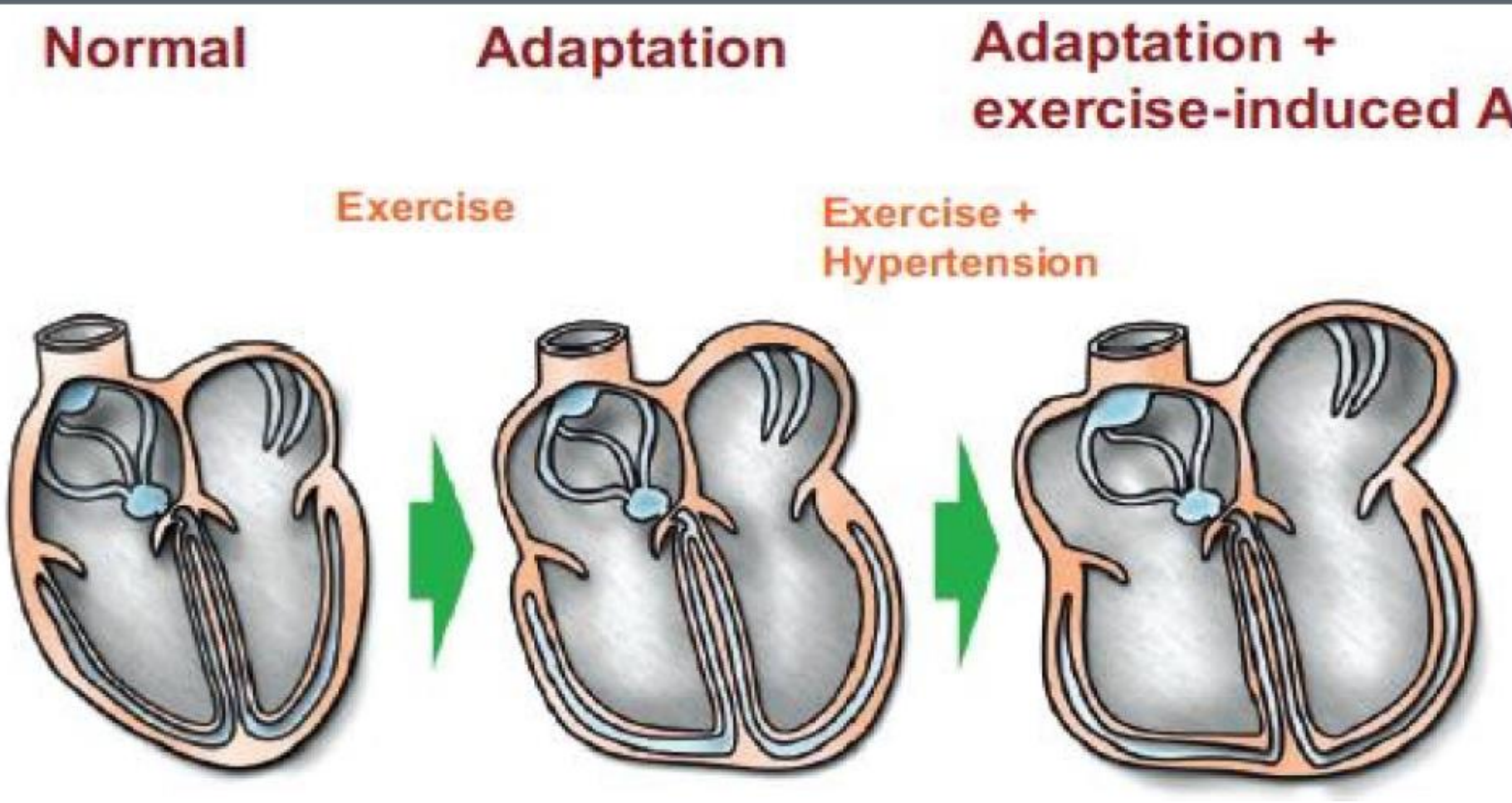


...so hypertension, though it may rarely be present in the young athlete, can occur frequently in the older sportsman!

Know your blood pressure by

Fagard RH, Cardiol Clin 2007

Aggravation of LVH

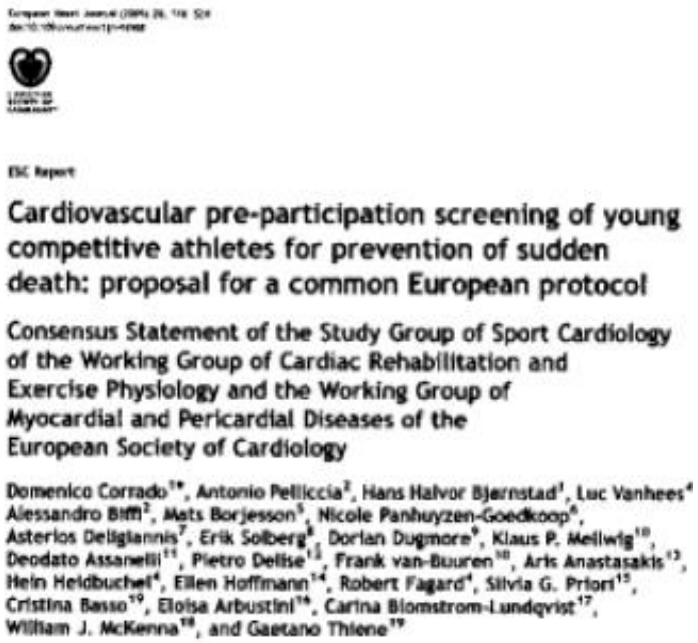


Know your blood pressure by

Leischik R, F1000Research 2014;3:105

Which Diagnostic Procedures are Indicated in Athletes with Hypertension?

ESC screening recommendations

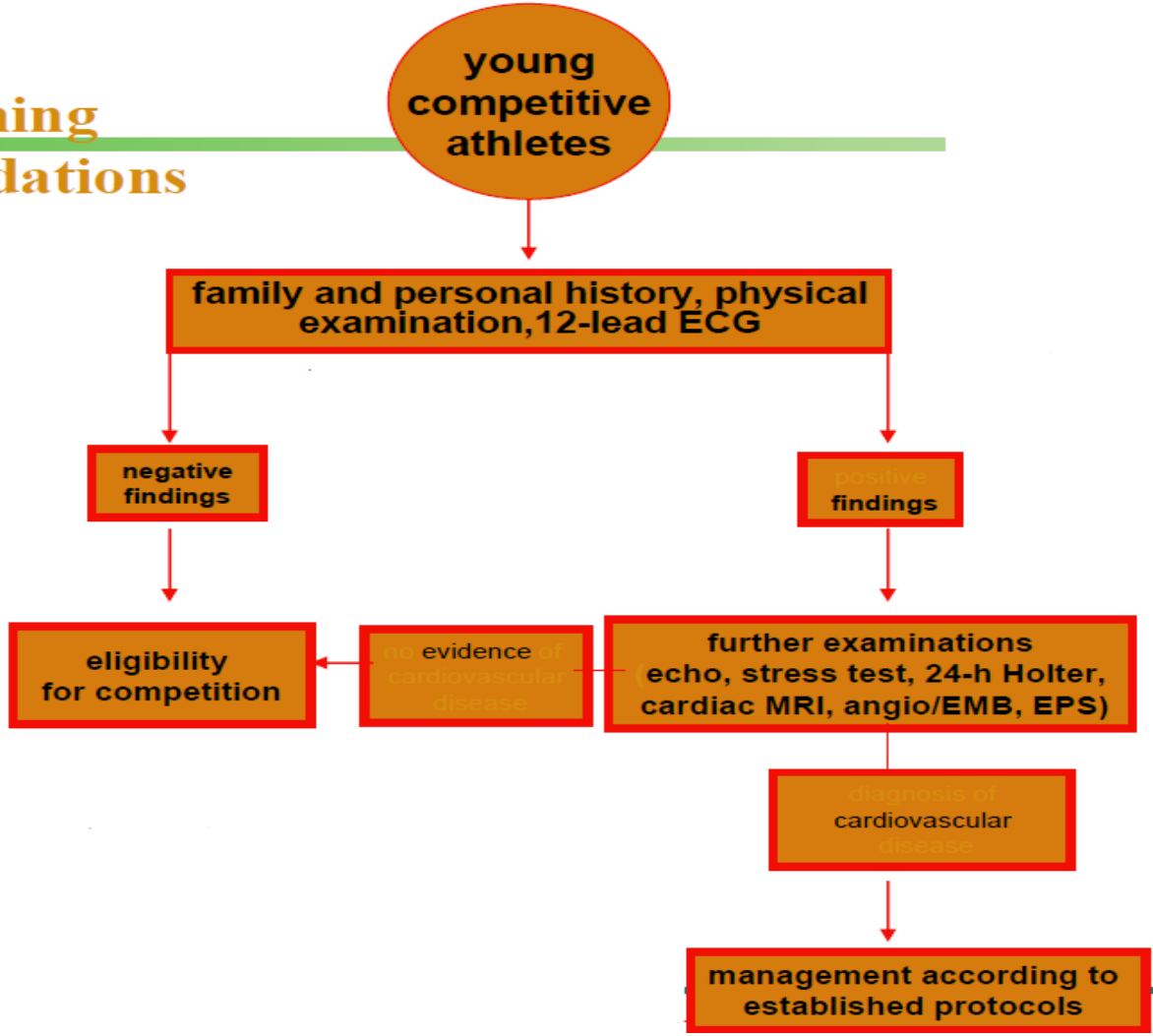


ESC Report

Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol

Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology

Domenico Corrado[1*], Antonio Pelliccia[2], Hans Halvor Bjørnstad[3], Luc Vanhees[4], Alessandro Biffi[2], Mats Borjesson[5], Nicole Panhuyzen-Goedkoop[6], Asterios Deligiannis[7], Erik Solberg[8], Dorian Dugmore[9], Klaus P. Mellwig[10], Deodato Assanelli[11], Pietro Delise[12], Frank van-Buuren[10], Aris Anastasakis[13], Hein Heidbuchel[4], Ellen Hoffmann[14], Robert Fagard[4], Silvia G. Priori[15], Cristina Basso[16], Eloisa Arbustini[16], Carina Blomstrom-Lundqvist[17], William J. McKenna[18], and Gaetano Thiene[16]



Corrado et al. EHJ 2005

Establishing BP Levels in Young Athletes or in Power Sports [Boxing, Wrestling, Weight Lifting]] Athletes is Not so Simple

Children & Adolescents

- Age-adjusted tables base upon gender & height percentile

Power Sport Athletes

- Measurement of forearm circumference

Appropriately sized cuff

- Good luck finding one

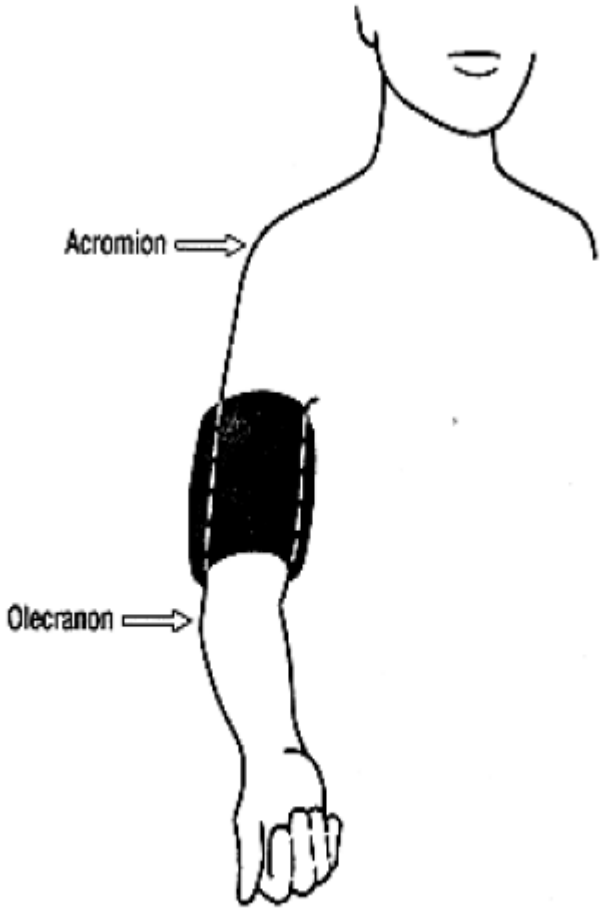


Fig 4. Determination of proper cuff size: step 2. The cuff bladder should cover 80% to 100% of the circumference of the arm.

Identify Secondary Causes of Hypertension

As usual, but paying particular attention to:

- **Oral contraceptive pills [commonly taken by female athletes]**
- **Caffeine, decongestants**
- **Herbs & dietary supplements used to increase energy or control weight [often contain "natural" substances such as guarana, mahuang, & ephedra, which are stimulants]**
- **Cocaine**
- **Anabolic steroids**
- **Growth hormone**
- **Erythropoietine**
- **Over-the-counter medications, including nonsteroidal anti-inflammatory drugs [NSAIDs]**

Performance – Enhancing Drugs: Androgenic – Anabolic Steroids

Synthetic derivatives of the male hormone testosterone increase strength of 5 – 20% & body weight [mainly lean mass] of 2 – 5 kg → used by body-builders, weight lifters; no effect on endurance performance

Cardiovascular Effects:

- **↑ Blood haemoglobin concentrations [↑ Epo]**
- **↑ Blood pressure**
- **↓ HDL – cholesterol levels**
- **Uncertain effect on cardiac structure & function**
- **Prothrombotic effect**
- **↑ Atherosclerosis**
- **Increased risks for CV events**

Effects underestimated because of the relatively low doses administered in studies lower than doses used by illicit steroid users

Performance – Enhancing Drugs: GH & Epo

Growth Hormone

- Increase muscle mass & decrease fat mass

Cardiovascular Effects:

- Hypertension
- Cardiac disease
- Diabetes mellitus

Erythropoietin

- Stimulates red blood cells production, ↑ blood viscosity
- Increases oxygen carrying capacity

Cardiovascular Effects

- Hypertension
- CV events

Which Diagnostic Procedures are Indicated in Athletes with Hypertension?

As usual:

Medical history & physical examination

Routine blood exams

ECG

Plus:

Echocardiography

Exercise testing

Know your blood pressure by

Mancia G et al. Guidelines on Hypertension, J Hypertens 2007

Pelliccia A et al. Eur Heart J 2005

Which Diagnostic Procedures are Indicated in Athletes with Hypertension?

Indications for exercise testing depends on the patient's risk profile

Demands of exercise (static or dynamic)	Risk category: Low or moderate	Risk category: High or very high[a]
Light (<40% of max)	No	No
Moderate (40%–59% of max)	No	Yes
High (≥60% of max)	Yes	Yes

Critical Issues:

Athletes are a population with a low probability of coronary heart disease & high prevalence of left ventricular hypertrophy → most positive tests on electrocardiography are falsely positive!

Exaggerated blood pressure response to exercise → inconclusive evidence about its role. However, subjects with an excessive rise of blood pressure during exercise are more prone to develop hypertension & should be followed up more closely

Fagard RH, Cardiol Clin 2007

Sports Eligibility Depends on the Patients Risk Profile

Level of risk	Criteria for eligibility	Recommendations	Follow up
Low added risk	Well controlled BP	All sports	Yearly
Moderate added risk	Well controlled BP and risk factors	All sports, with the exclusion of high static / high dynamic sports (boxing, canoeing, cycling, triathlon, decathlon, speed skating)	Yearly
High added risk	Well controlled BP and risk factors	All sports, with the exclusion of high static sports (all above plus rock climbing, waterskiing,weight lifting, windsurfing, body building, wrestling, downhill skiing, snow boarding)	Yearly
Very high added risk	Well controlled BP and risk factors, no associated clinical conditions	Only low-moderate dynamic / low static sports (bowling, cricket, golf, riflery, table tennis, tennis, volleyball, baseball)	Yearly

Secondary hypertension of renal origin (particularly policystic kidney): avoid "collision" sports that could lead to kidney damage.

Choice of Pharmacological Therapy

No real compelling indications, but consider that:

Some antihypertensive drugs are considered doping substances & are banned by many sports associations

Some antihypertensive drugs have negative effect on exercise performance

Pharmacological Therapy: Diuretics

Used as doping substances: YES

- **Rapid weight loss: useful in boxing, wrestling, judo**
- **Excretion or dilution of illegal substances**

Adverse effects on sport performance: YES

- **Impair exercise performance & capacity in the first weeks of treatment through a reduction on plasma volume, but exercise tolerance appears to be restored during long-term treatment:**
- **[Loop >>>thiazide diuretics Hypovolemia, orthostatic hypotension, electrolyte imbalance [loss of potassium, magnesium]**
- **Muscle cramps, arrhythmias, and rhabdomyolysis in patients who are exercising intensely or competing in warm weather**

Indications

- **NO in elite athletes who are required to undergo drug testing**
- **2nd choice & low dosage in physically active patients with hypertension [association with potassium – sparing diuretics?] & salt – sensitive hypertensive athletes [i.e. blacks]**

Pharmacological Therapy: β-Blockers

Used as doping substances: YES

- **Anti-tremor, anxiolytic effect**
- **Precision sports: shooters, ski jumpers, archery, diving**

Adverse effects on sport performance: YES

- **Non cardio selective >>> cardio selective β-blockers**
- **↓ Inotropism & heart rate**
- **↑ Systemic vascular resistance [especially muscle & skin], ↓ cardiac output**
- **↓ Maximum oxygen uptake**
- **↓ Lipolysis & glycogenolysis → hypoglycaemia may occur after intense exercise**
- **Perception of greater exertion during exercise**
- **Possible bronchospasm**

Indications

NO in elite athletes of precision sports

Only if there is an underlying condition [e.g. CAD]

Combined alpha-beta blocker may be the best choice [less impairment of muscle blood flow & maximum oxygen uptake]

Pharmacological Therapy: RAS Blockers

Used as doping substances: NO

Adverse effects on sport performance: NO

- **↓ Systemic vascular resistance**
- **↑ Cardiac output**
- **No major effects on energy metabolism**
- **No impairment of maximum oxygen uptake**

Indications

- **First choice**
- **NO in female athletes in reproductive age**

Pharmacological Therapy: DHP Calcium-Channel Blockers

Used as doping substances: NO

Adverse effects on sport performance: NO

- **No major effects on energy metabolism, no impairment of maximum oxygen uptake, no deleterious effects on training or competition**
- **Potential competitive "steal" of muscle blood flow [because of vasodilatation] & earlier onset of the lactate threshold**

Indications:

- **First choice, especially in black athletes**

Secondary Hypertension

Hypertension due to an identifiable cause which may be treated with an intervention specific to the cause

A high index of suspicion and early detection of secondary causes of hypertension is important because interventions may be curative, especially in younger patients

Patients Characteristics That Should Raise The Suspicion Of Secondary Hypertension

Characteristic
Younger patients (< 40 years) with grade 2 hypertension or onset of any grade of hypertension in childhood
Acute worsening hypertension in patients with previously documented chronically stable normotension
Resistant hypertension
Severe (grade 3) hypertension or a hypertension emergency
Presence of extensive HMOD
Clinical or biochemical features suggestive of endocrine causes of hypertension or CKD
Clinical features suggestive of obstructive sleep apnoea
Symptoms suggestive of phaeochromocytoma or family history of phaeochromocytoma

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

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Common Causes Of Secondary Hypertension

Cause	Prevalence in Hypertensive Patients
Obstructive sleep apnoea	5–10%
Renal parenchymal disease	2–10%
Renovascular disease: Atherosclerotic renovascular disease Fibro muscular dysplasia	1–10%
Endocrine causes: Primary Aldosteronism Phaeochromocytoma Cushing's syndrome Thyroid disease (hyper-orhypothyroidism) Hyperpara thyroidism	5–15% <1% <1% 1–2% <1%
Other causes: Co-arctation of the aorta	<1%

Know your blood pressure by

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Incidence And Typical Causes Of Secondary Hypertension According To Age

Age group	Percent with Underlying cause	Typical causes
Young children (<12years)	70–85	Renal parenchymal disease Coarctation of the aorta Monogenic disorders
Adolescents (12–18years)	10–15	Renal parenchymal disease Coarctation of the aorta Monogenic disorders
Young adults (19–40years)	5–10	Renal parenchymal disease Fibromuscular disease(especially in women) Undiagnosed monogenic disorders
Middle-aged adults (41–65years)	5–15	Primary aldosteronism Obstructive sleep apnoea Cushing'ss yndrome Phaeochromocytoma Renal parenchymal disease Atherosclerotic renovascular disease
Older adults (>65years)	5–10	Atherosclerotic renovascular disease Renal parenchymal disease Thyroid disease

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Medications And Other Substances That May Increase BP

Medication/substance	
Oral contraceptive pill	Especially oestrogen containing; cause hypertension in 5% of women, usually mild but can be severe
Diet pills	For example, phenyl propanolamine and sibutramine
Nasal decongestants	For example, phenylephrine hydrochloride and naphazoline hydrochloride
Stimulant drugs	Amphetamine, cocaine, and ecstasy–these substances usually cause acute rather than chronic hypertension
Liquorice	Chronic excessive liquorice use mimics hyper aldosteronism by stimulating the Mineral ocorticoid receptor and inhibiting cortisol metabolism
Immuno suppressive Medications	Forexample,cyclosporinA(tacrolimushaslesseffectonBPandrapamycinhas almostnoeffectonBP),andsteroids(e.g.corticosteroids,hydrocortisone)
Anti angiogenic cancer Therapies	Antiangiogenic drugs, such as VEGF inhibitors (e.g. bevacizumab), tyrosine kinase Inhibitors (e.g.sunitinib), and sorafenib, have been reported to increase BP
Other drugs and substances that may raise BP	Anabolic steroids, erythropoietin, non-steroidalanti-inflammatory drugs, herbal Remedies (e.g.ephedra,mahuang)

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Rare Genetic Causes Of Secondary Hypertension

Condition	Pheno type	Mechanism and effect
Liddle syndrome	Hypokalaemia, metabolic alkalosis, low PRA or PRC , low PAC	Increased renal tubular ENaC activity–responds to treatment with amiloride
Apparent mineral ocorticoid Excess	Hypokalaemia, metabolic alkalosis, low PRA or PRC, low PAC	Decreased 11! - dehydrogenase Isoenzyme 2
Gordon syndrome	Hyperkalaemia ,metabolic acidosis, low PRA or PRC, low PAC	Over-activity of sodium chloride co-transporter
Geller Syndrome	Pregnancy-exacer bated hypertension; low PRA or PRC, low PAC	Agonist effect of progesterone on the mineral ocorticoid receptor
Glucocorticoid remediable Hypertension	Hypokalaemia, metabolic alkalosis, low PRC or PRA and increase PAC	Chimeric CYP 11! 1 to CYP11! 2 gene–response to treatment with glucocorticoids

Williams, Mancia et al., J Hypertens 2018;36:1953-2041 and Eur Heart J 2018;39:3021-3104

Take Home Messages

Office BP Treatment And Co-Morbidities

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 to130 *If tolerated*	Target to <140to130 *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	

SAHS Know your blood pressure by

AGE < 65 years: SBP 120 to <130 mm Hg

AGE > 65: SBP 130 to <140 mm Hg

should be avoided values of SBP <130 mm Hg

should not be targeted to SBP <120 mm Hg

Diabetes: SBP 130 or lower

CAD: SBP 130 or lower

CKD: SBP 130 to <140 mm Hg

Post stroke: SBP 120 to <130 mm Hg (to be considered)

New Concepts

SPC treatment strategy to improve BP control as initial therapy for most patients

SPC is the preferred strategy for 3-drug combination therapy when required

Conclusions

- Guidelines are required to be evidence-based and identify best practices through impartial evaluation of available data.
- Guidelines cannot cover all the subset of patients and should be integrated by the results of single studies or subset analysis.
- Flexible recommendations must consider a country's unique healthcare system to:
  - Enable their implementation across a range of clinical practices.
  - Facilitate patient specific personalization of treatment.
- Guidelines are intended to be recommendations, not prescriptive rules.

Know your blood pressure by

Kjeldsen S et al. *Drugs* 2014; 74:2033-2051 and expert opinion of the Scientific Steering Committee.

THANK YOU

"This is one of those new miracle drugs.
If you can afford it, it's a miracle."

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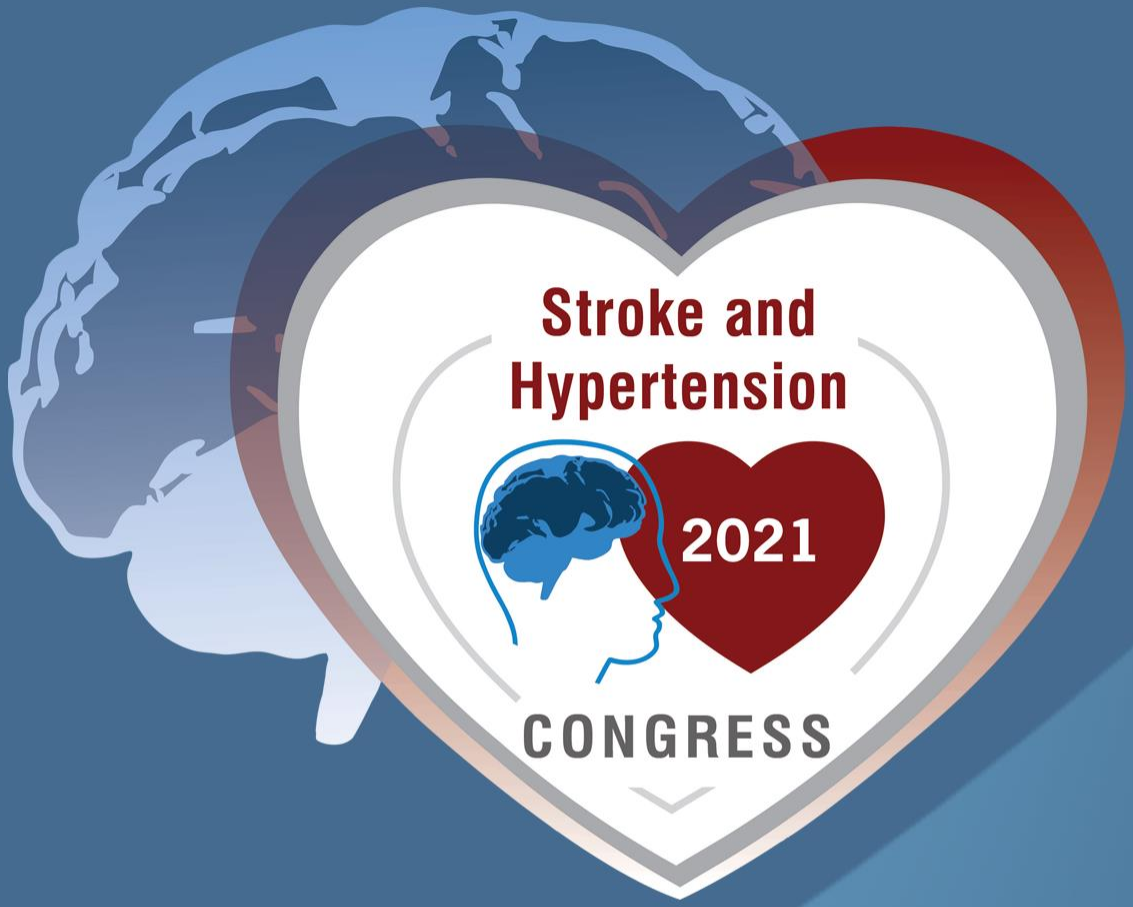
MAY MEASUREMENT MONTH
International Society of Hypertension



|SAVE THE DATE|

2021 - Gauteng

Become a SAHS member

www.hypertension.org.za