



MINISTRY OF HEALTH

**CLINICAL PRACTICE
GUIDELINES**

**Arterial Hypertension
in adult**

**A continuum of care for Hypertensive Patients both
with and without complications at NCD clinics/RHs**

**Bureau for NCD Prevention & Control
DEPARTMENT OF PREVENTIVE MEDICINE**

2015

Table of Content

Forward	2
Acknowledgements	3
I-Measurement & definition of blood pressure	4
II-Causes of Hypertension	5
1-Primary Hypertension	5
2-Secondary hypertension	5
III-Factors influencing prognosis	5
1-Risk factors for Cardiovascular disease	5
2-Target organ damage	5
3-Associated clinical conditions	5
IV-Recommendations for Management of Hypertension	6
1-Thresholds and Targets for Blood Pressure Lowering	6
2-Recommendation for antihypertensive treatment	7
3-Initial Therapy	9
4-Lifestyle modification	9
5-Recommended protocol	10
V-Investigation	10
ANNEXE 1: Possible combinations of classes of antihypertensive	12
ANNEXE 2: Hypertension Guideline Management Algorithm.....	13
ANNEXE 3: Strategies to dose Antihypertensive Drugs	14
ANNEXE 4: Measure serum creatinine annually and estimate GFR only if stable creatinine	15

Forward

Cardiovascular disease (CVD) is responsible for one third of global deaths and is a leading and increasing contributor to the global disease. Importantly, CVD is eminently preventable. In order to achieve significant reductions in the avoidable CVD burden, a combination of population – based and high risk strategies is necessary.

Hypertension is already a highly prevalent risk factor for CVD throughout the industrial world. It is becoming an increasingly common health problem worldwide because of increasing longevity and prevalence of contributing factors such as obesity, physical inactivity and unhealthy diet. Treating hypertension has been associated with about a 40% reduction in the risk of stroke and about a 15% reduction in the risk of myocardial infarction. Although the treatment of hypertension has been shown to prevent and to extend and enhance life, hypertension remains inadequately managed everywhere.

This Clinical Practice Guidelines for the management of arterial hypertension in adult is intended for health professionals who are working to provide a continuum of care for hypertension patients both with and without complications at NCD clinics and RHs. Its main objective is to guide them in the appropriate process of the management of the most common health problems of hypertensive Cambodian encountered at the referral hospital including unhealthy diet, smoking, physical inactivity and particularly dyslipidemia management.

I strongly believe that our guidelines provide for appropriate and affordable needs within our country according to our limited resources and the suggested treatment will benefit health professional while prescribing patients with hypertension. I have no doubt that these guidelines will play a prominent role in reaching a recognized process of care and our own appropriate treatment goals for high blood pressure at NCD clinics.

Finally, I would like to acknowledge those individuals who contributed to reviewing this guidelines, and to take this opportunity to express my gratitude for their generous contributions.

Phnom Penh,

2015

MINISTER OF HEALTH

ACKNOWLEDGEMENTS

Development of clinical practice guidelines for the management of arterial hypertension in adult with the participation of Technical advisory committee for Diabetes Health Care Services in provincial Cambodia, Central Hospital Physicians, provincial NCD clinic physicians and health workers from NGO, with the support of “International Development Cooperation Center of Jesus University ”

Dr Prak Piseth Raingsey	Director, Preventive Medicine Department	TAC* head
Dr Seng Serey	Diabetologist, Preah Kossomak hosp	TAC member
Dr Touch Khun	Diabetologist, Preah Kossomak hosp	TAC member
Pouv Sothearin	Peer head, MoPoTsyo NGO	TAC member
Dr Bun Soheat	MoPoTsyo NGO	
Ph Huot Seng Thong	Vice director, DDF/MOH	
Ph Va Sokea	Vice director, CMS/MOH	
Dr Ngeth Sovann	Vice director, Preventive medicine Dpt	
Dr Sum Satha	Endocrinologist, Calmette hosp	
Dr Theng Youdaline	Cardiologist, Calmette hosp	
Dr Prok Vichetra	Internist & cardiologist, Calmette hosp	
Dr Sorng Sopheak	Cardiologist, Calmette hosp	
Dr Lim Vadhana	Nephrologist, Calmette hosp	
Dr Suy Sovannara	Cardiologist, khmero-Russia friendship hosp	
Dr Thel Sophea	Endocrinologist, Khmero-Russia friendship hosp	
Dr Mao Si Vanna	Pursat provincial hosp	NCD clinic
Dr Hean Ravy	Kg Cham provincial hosp	NCD clinic
Dr Mang Sokhom	Prey Veng provincial hosp	NCD clinic

Secretariat:

Dr Chhun Loun	Chief of NCD bureau, PMD	TAC member
Dr Sok Kong	Vice NCD bureau chief, PMD	TAC member
Kim mi Yeon	Mid manager, IDCC**, Jesus university	
Park Hyun Ah	R.Nurse, IDCC, Jesus university	
Jung Yulha	Social worker, IDCC, Jesus university	
Dr Thach Varoeun	Medical coordinator, IDCC, Jesus university	

*TAC: Technical advisory committee for diabetes health care services in provincial Cambodia

**IDCC: International development cooperation center

Guideline for the Management of Arterial Hypertension in Adults

Hypertension is the common condition seen in primary care and remains one of the most important preventable contributors to diseases and death. It plays a major etiologic role in the development of cerebrovascular disease, ischemic heart disease, cardiac and renal failure. In addition hypertension often coexists with other cardiovascular risk factors, such as tobacco use, diabetes, hyperlipidemia and obesity, which compound the cardiovascular attributable to hypertension.

I-Measurement & definition of blood pressure

Measure after patient has been sitting for at least 5 minutes with arm at heart level.

No coffee for at least 30 mn.

Use a mercury sphygmomanometer or validated meter in good working order and an appropriately sized cuff.

Record all values in patient notes and on patient's own record card.

Definition of Hypertension

- Systolic Blood Pressure ≥ 140
and/or
- Diastolic Blood Pressure ≥ 90

WHO/ISH classification of hypertension

Blood Pressure	Grade 1	Grade 2	Grade 3
SBP (mm Hg)	140-159	160-179	≥ 180
DBP (mm Hg)	90-99	100-109	≥ 110

Remark: Another Definitions and classification of Blood Pressure levels (mm Hg)^a

Category	Systolic		Diastolic
Optimal	< 120	and	< 80
Normal	120-129	and/or	80-84
High normal	130-139	and/or	85-89
Grade 1 Hypertension	140-159	and/or	90-99
Grade 2 Hypertension	160-179	and/or	100-109
Grade 3 Hypertension	≥ 180	and/or	≥ 110
Isolated systolic Hypertension	≥ 140	and	< 90

^aThe blood pressure (BP) category is defined by the highest level of BP, whether systolic or diastolic.

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

II-Causes of Hypertension

1- Primary Hypertension

- About 95% of adults with high blood pressure have primary hypertension (sometimes called essential hypertension).
- The cause of primary hypertension is not known, although genetic and environmental factors that affect blood pressure regulation are now being studied.
- Environmental factors include excess intake of salt, obesity, and perhaps sedentary lifestyle.
- Some genetically related factors could include inappropriately high activity of the renin-angiotensin aldosterone system and the sympathetic nervous system and susceptibility to the effects of dietary salt on blood pressure.
- Another common cause of hypertension is stiffening of the aorta with increasing age. This causes hypertension referred to as isolated or predominant systolic hypertension characterized by high systolic pressures (often with normal diastolic pressures), which are found primarily in elderly people.

2- Secondary hypertension

- This pertains to the relatively small number of cases, about 5% of all hypertension, where the cause of the high blood pressure can be identified and sometimes treated.
- The main types of secondary hypertension are chronic kidney disease, renal artery stenosis, excessive aldosterone secretion, pheochromocytoma, and sleep apnea.

III-Factors influencing prognosis

1- Risk factors for Cardiovascular disease

Levels of systolic and diastolic blood pressure (Hypertension* grade 1-3)

- Age
 - Male aged > 55 years
 - Female aged > 65 years
- Smoking
- Dyslipidemia*
 - Total cholesterol > 6.1 mmol/L (240 mg/dL) or LDL-cholesterol > 4.0 mmol/L (160 mg/dL)
 - HDL-cholesterol < 1.0 mmol/L (< 40 mg/dL) in men, < 1.2 mmol/L (< 45 mg/dL) in women
 - Triglyceride > 1.70 mmol/L (150 mg/dL)
- History of cardiovascular disease in first-degree relatives before age 50 years
- Obesity*
- Physical inactivity

2- Target organ damage

- Left ventricular hypertrophy (electrocardiogram or echocardiogram)
- Microalbuminuria [20-300 mg/day],
- Radiological or ultrasound evidence of extensive atherosclerotic plaque (aorta, carotid, coronary, iliac and femoral arteries)
- Hypertensive retinopathy grade III or IV)

3- Associated clinical conditions

- Diabetes*

- Cerebrovascular disease(ischemic stroke, cerebral hemorrhage, transient ischemic attack)
- Heart disease(myocardial infarction, angina, coronary revascularization, congestive heart failure)
- Renal disease
 - a. Plasma creatinine concentration:
 - . females > 1.4mg/dl (120 μmol/l)
 - . males > 1.5mg/dl (133 μmol/l)
 - b. Albuminuria > 300 mg/day
- peripheral vascular disease

NB: * components of metabolic syndrome

Decisions about the management of hypertensive patients should not only take the blood pressure levels into account, but also the presence of other cardiovascular risk factors, target organ damage and associated clinical conditions.

Table: WHO/ISH stratification of risk to Quantify Prognosis

Other risk factors, asymptomatic organ damage or disease	Blood Pressure (mm Hg)		
	Grade 1 SBP 140-159 or DBP 90-99	Grade 2 SBP 160-179 or DBP 100-109	Grade 3 SBP ≥ 180 or DBP ≥ 110
I No risk factors	Low	Medium	High
II 1-2 risk factors	Medium	Medium	High
III ≥ 3 risk factors or TOD or ACC	High	High	High

ACC, associated clinical condition; DBP, diastolic blood pressure; SBP, systolic blood pressure; TOD, target organ damage.

IV-Recommendations for Management of Hypertension

1-Thresholds and Targets for Blood Pressure Lowering

There is strong evidence to support treating hypertensive persons aged 60 years or older to a blood pressure goal less than 150/90 mm Hg and hypertensive persons 30 through 59 years of age to a diastolic goal of less than 90 mm Hg; however, there is insufficient evidence in hypertensive persons younger than 60 years for a systolic goal, or in those younger than 30 years for a diastolic goal, so the panel recommends a blood pressure of less than 140/90 mm Hg for those groups based on expert opinion. The same thresholds and goals are recommended for hypertensive adults with diabetes or non diabetic chronic kidney disease (CDK) as for general hypertensive population younger than 60 years.

There is moderate evidence to support initiating drug treatment with an angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, calcium channel blocker, or thiazide-type diuretic in the nonblack hypertensive population, including those with diabetes. In the black hypertensive population, including those with diabetes, a calcium channel blocker or thiazide-type diuretic is recommended as initial therapy. There is moderate evidence to support initial or add-on antihypertensive therapy with an angiotensin-convertin inhibitor or angiotensin receptor blocker in persons with chronic kidney disease to improve kidney outcome.

Although this guideline provides evidence-based recommendations for the management of high blood pressure and should meet the clinical needs of most patients, these

recommendations are not a substitute for clinical management, and decisions about care must be carefully consider and incorporate the clinical characteristics and circumstances of each individual patient.

Table: Threshold and Blood Pressure Goal recommendation

Hypertensive Patient	Initiate pharmacologic treatment	BP goal
≥ 60 years*	SBP ≥ 150 mm Hg or DBP ≥ 90 mm Hg	SBP < 150 mm Hg and DBP < 90 mm Hg
< 60 years		
18-59 years	SBP ≥ 140 mm Hg	SBP < 140 mm Hg
	DBP ≥ 90 mm Hg	DBP < 90 mm Hg
≥ 18 years with		
CKD or/and Diabetes	SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg	SBP < 140 mm Hg and DBP < 90 mm Hg

*In the general population aged ≥60 years, if pharmacologic treatment for high BP results in lower achieved SBP (eg, <140mm Hg) and treatment is well tolerated and without adverse effects on health and quality of life, treatment does not need to be adjusted (expert opinion-grade E).

2- Recommendation for antihypertensive treatment

Recommendation 1

In the general nonblack population, including those with diabetes, initial antihypertensive treatment should include a thiazide-type diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme inhibitor(ACEI), or angiotensin receptor blocker (ARB). (moderate recommendation- Grade B).

Recommendation 2

In the general black population, including those with diabetes, initial hypertensive treatment should include a thiazidique-type diuretic or CCB. (for general black population: moderate recommendation-Grade B; for black patients with diabetes: weak recommendation-Grade C).

Recommendation 3

In the population aged ≥ 18 years with CKD, initial (or add-on) antihypertensive treatment should include an ACEI or ARB to improve kidney outcomes. This applies to all CKD patients with hypertension regardless of race or diabetes status. (moderate recommendation-Grade B).

Recommendation 4

The main objective of hypertension treatment is to attain and maintain goal BP. If goal BP is not reached within a month of treatment, increase the dose of initial drug or add a second drug from one of the classes in recommendation 1 (thiazide-type diuretic, CCB, ACEI, or ARB). The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. Do not use ACEI and ARB together in the same patient. If goal BP cannot be reached using only the drugs in the recommendation 1

because of contraindication or the need to use more than 3 drugs to reach goal BP, antihypertensive drug from other classes can be used. Referral to a hypertension specialist

may be indicated for patients in whom goal BP cannot be attained using the above strategy or for the management of complicated patients for whom additional clinical consultation is needed. (expert opinion-Grade E)

Note: the following important points should be noted:

- a- Many people will require treatment with more than one antihypertensive drug to achieve BP control. While this recommendation applies only to the choice of the initial antihypertensive drug, the panel suggests that any of these 4 classes would be good choices as add-on agents (recommendation 1).
- b- This recommendation is specific for thiazidique-type diuretics, which include thiazide diuretics, chlorthalidone, and indapamide; it does not include loop or potassium-sparing diuretics
- c- It is important that medications be dosed adequately to achieve results similar to those seen in the RCTs (table below).
- d- RCTs that were limited to specific non hypertensive populations, such as those with coronary artery disease or heart failure, were not reviewed for this recommendation. Therefore, recommendation 1 should be applied with caution to these populations.

Recommendations for those with CKD are addressed in recommendation 3.

Table: Evidence-based dosing for Antihypertensive Drugs

Antihypertensive Medication	Initial Daily dose, mg	Target dose In RTCs reviewed, mg	No of Doses/d
ACE inhibitors			
Captopril	50	150-200	2
Enalapril	5	20	1-2
Lisinopril	10	40	1
Angiotensin receptor blockers			
Eprosartan	400	600-800	1-2
Candesartan	4	12-32	1
Losartan	50	100	1-2
Valsartan	40-80	160-320	1
Irbesartan	75	300	1
β-Blockers			
Atenolol	25-50	100	1
Metoprolol	50	100-200	1-2
Calcium channel blocker			
Amlodipine	2.5	10	1
Diltiazemextended release	120-180	360	1
Nitrendipine	10	20	1-2
Thiazide-type diuretic			
Bendroflumethiazide	5	10	1
Chlorthalidone	12.5	12.5-25	1
Hydrochlorothiazide	12.5-25	25-100 ^a	1-2
Indapamide	1.25	1.25-2.5	1

^a current recommended evidence-baseddose that balance efficacy and safety is 25-50 mg daily.

3- Initial Therapy

The WHO/ISH agreed that the aggregate trial data suggest the morbidity/mortality benefits of antihypertensive treatment derive largely from blood pressure reduction. At the same time, strong evidence that specific agents benefit patients with compelling indications is cited as the basis for recommending certain classes of drugs in such patients.

Table: Goal BP and initial drug therapy for adults with Hypertension

Population	Goal BP, mm Hg	Initial drug treatment options
General \geq 60y	< 150/90	thiazide-type diuretic, ACEI, ARB or CCB
Diabetes	< 140/90	Thiazide-type diuretic, ACEI, ARB or CCB
CKD	< 140/90	ACEI or ARB

Table: Compelling indications for specific Antihypertensive Drugs

Compelling Indication	Preferred Drug	Primary Endpoint
Elderly with isolated systolic hypertension	Diuretic	Stroke
	DHCCB	Stroke
Renal disease		
Diabetic nephropathy type 1	ACE inhibitor	Progression of renal failure
Diabetic nephropathy type 2	ARB	Progression of renal failure
Nondiabetic nephropathy	ACE inhibitor	Progression of renal failure
Cardiacdisease		
Post MI	ACE inhibitor	Mortality
Left ventricular dysfunction	Beta-blocker	Mortality
	ACE inhibitor	Heart failure
	ACE inhibitor	Mortality
CHF (diuretic most always included)	Beta-blocker	Mortality
	Spironolactone	Mortality
Left ventricular hypertrophy	ARB	Cardiovascular morbidity and mortality.
Carebrovascular disease	ACEI + diuretic	Recurrent stroke
	Diuretic	Recurrent stroke

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CHF, congestive heart failure;

DHCCB, dihydropyridine calcium channel blocker; MI, myocardial infarction

4- Lifestyle modification

Lifestyle modifications can help prevent or delay the onset of hypertension and reduce blood pressure in already hypertensive patients. In addition to preventing or reducing high blood pressure, these modifications reduce the risk of other cardiovascular diseases.

- Weight loss in the overweight
- Increased physical activity

- Smoking cessation
- Moderation of alcohol intake
- Dietary changes:
 - more fruit, vegetables
 - low saturated fat
- Reduction of dietary sodium and increased dietary potassium

5- Recommended protocol

In order to improve rational drug use for outpatient consultation at NCD clinic and maintain appropriate supply from CMS and due to limited resources the ministry of health recommends:

For patients without compelling indications:

- a. Initial medication should be
 - Thiazide type diuretic for patient aged > 55 years
 - ACE inhibitor for patient aged < 55 years

*** If target blood pressure not met, the following combination should be considered:

 - ⇒ THIA + CCB
 - ⇒ ACEI + CCB or
 - ⇒ ACEI + THIA or
- b. Therapy with 2 drugs simultaneously should be considered in patient with
 - SBP >160 mm Hg and/or DBP >100 mm Hg or
 - If SBP >20 mm Hg above the goal and/or DBP >10 mm Hg above the goal.
- c. If the goal of the blood pressure can not be reached under two drug therapy, the third medication should be added. For more detail please see the algorithm and strategies to dose antihypertensive drug tables.

For high risk patients:

In high risk patients with large benefits from the treatment, specific antihypertensive drugs shown in the table above maybe cost-effective.

Follow up consultations:

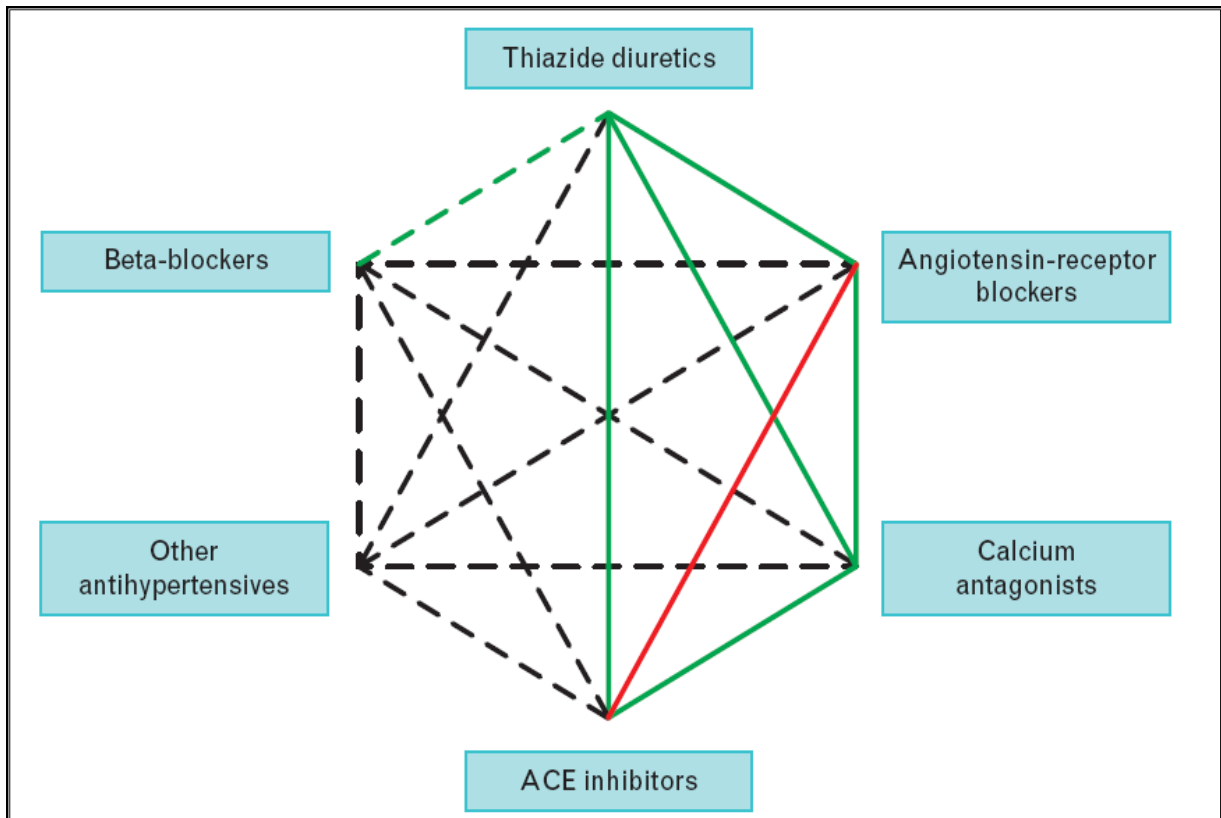
- a. Hypertensive Patients should be initially seen more frequently depending on control of blood pressure and possible side effects. This may need to be every 2 to 3 weeks if SBP and/or DBP goal not reached: adjust the first medication and/or add the second medication.
Then every 1 – 2 months
- b. Most patients should be seen every 2 months once stable (with on minimal medication, excellent control and understanding)

V-Investigation

Routine lab tests are recommended before beginning treatment of high blood pressure to determine organ or tissue damage or other risk factors. These lab tests include urinalysis, blood cell count, blood chemistry (potassium, sodium, creatinine, fasting glucose, total cholesterol and HDL cholesterol), and an ECG (electrocardiogram). Additional tests may be recommended based on your condition.

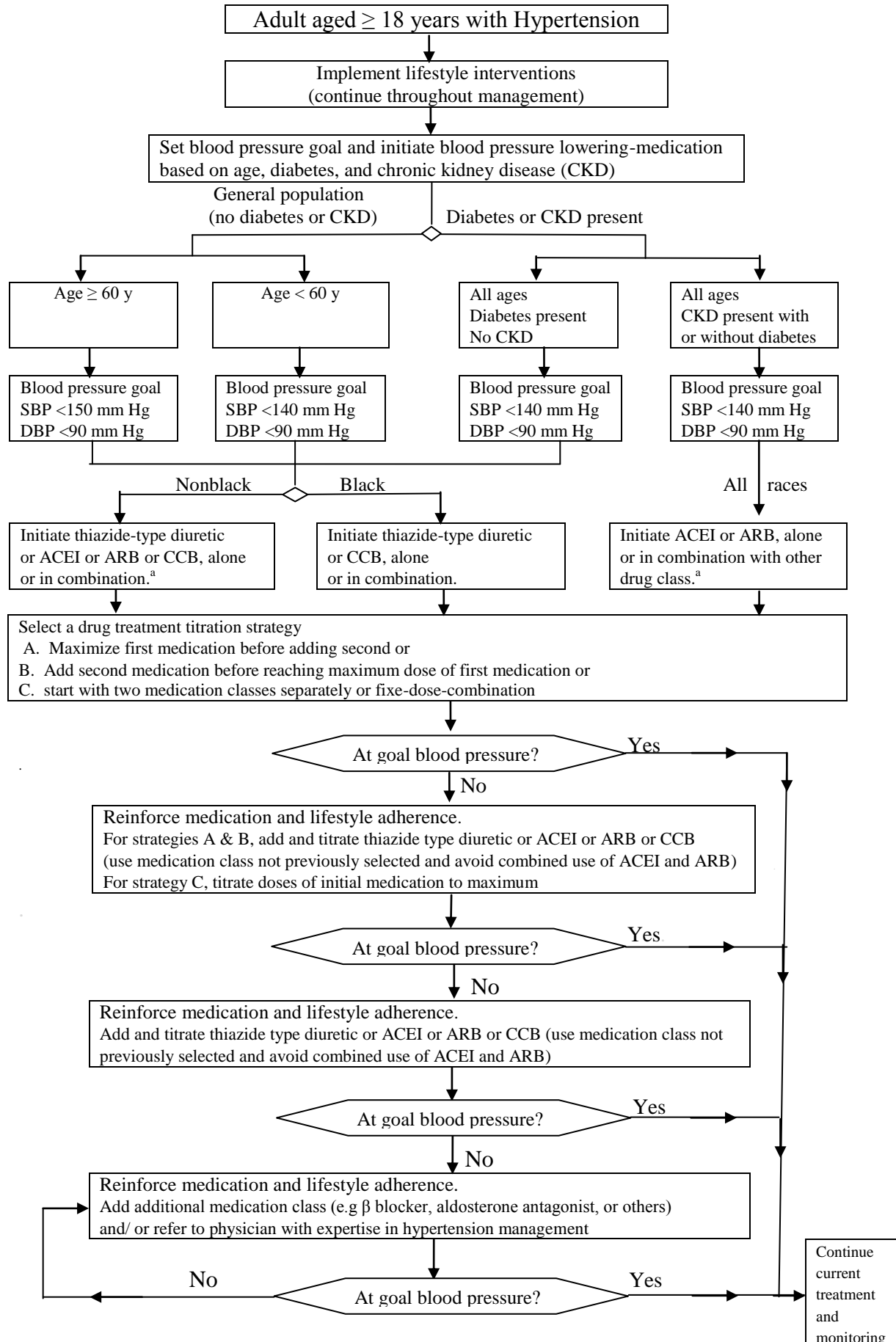
Test	Indicative of/ suggest	Frequency
Blood sample		
Electrolyte: potassium levels	High level ➡ renal disease	1/y
Blood glucose	Diabetes	1/y
Serum creatinine	High levels ➡ kidney disease	1/y
Lipids profile	HDL cholesterol + triglyceride LDL cholesterol ➡ starting statins ?	1/y
Hemoglobin/hematocrit	Hypertension and CVD Anemia associated with CKD	1/y
Urine sample	Albuminuria	1/y
ECG		1/y
Retinopathy		1/y
echocardiography		1/y
Transaminase		1/y

ANNEXE 1: Possible combinations of classes of antihypertensive drugs



- Green continuous lines: preferred combinations; Green dashed line: useful combination (with some limitations);
- Black dashed lines: possible but less well tested combinations;
- Red continuous line: not recommended combination

ANNEXE 2: Hypertension Guideline Management Algorithm



SBP indicates systolic blood pressure; DBP, diastolic blood pressure; ACEI, angiotensine-converting enzyme; ARB, angiotensine receptor blocker; and CCB, calcium channel blocker.

^aACEIs and ARBs should not be used in combination
^bIf blood pressure fails to be maintained at goal, reenter the algorithm where appropriate based on the current individual therapeutic plan

ANNEXE 3: Strategies to dose Antihypertensive Drugs

Strategy	Description	Details
A	Start one drug, titrate to maximum dose, and then add a second drug.	<p>If goal BP not achieved with initial drug, titrate the dose of the initial drug up to the maximum recommended dose to achieve goal BP.</p> <p>If goal BP is not achieved with the use of one drug despite titration to the maximum recommended dose, add the second drug (thiazide-type diuretic, CCB, ACEI, or ARB) and titrate up to the maximum recommended dose of the second drug to achieve goal BP.</p> <p>If goal BP is not achieved with 2 drugs, select a third drug from the list, avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose to achieve goal BP.</p>
B	Start one drug and then add a second drug before achieving maximum dose of the initial drug	<p>Start with one drug then add a second drug before achieving the maximum recommended dose of the initial drug, then titrate both drugs up to the maximum recommended dose of both to achieve goal BP.</p> <p>If goal BP is not achieved with 2 drugs, select the third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to maximum recommended dose to achieve goal BP.</p>
C	Begin with 2 drugs at the same time, either as 2 separate pills or as single pill combination	<p>Initiate therapy with 2 drugs simultaneously, either as 2 separate drugs or as a single pill combination.</p> <p>Some committee members recommend starting therapy with ≥ 2 drugs when SBP > 160 mm Hg and/or DBP > 100 mm Hg, or if SBP is > 20 mm Hg above goal and DBP is > 10 mm Hg above goal.</p> <p>If goal BP is not achieved with 2 drugs, select a third drug from the list (thiazide-type diuretic, CCB, ACEI, or ARB), avoiding the combined use of ACEI and ARB. Titrate the third drug up to the maximum recommended dose.</p>

ANNEXE 4: Measure serum creatinine annually and estimate GFR only if stable creatinine

Cockcroft and Gault:
$$\text{CrCl (ml/min)} = \frac{(140 - \text{age}) \times \text{body weight [kg]} \times K}{\text{Cr [micromol/l]}}$$

k = 1.23 (man); k = 1.04

not applicable with aging people, overweight, edema and pregnancy

Chronic renal failure classification

Stage	GFR (ml/mn)	
1	≥ 90	Normal or slightly reduced
2	≥ 60	Glomerular Filtration Rate
3	30-59	Moderate Chronic Renal Failure
4	15-29	Severe Chronic Renal Failure
5	< 15	End stage of Chronic Renal Failure

Online Glomerular Filtration Rate calculator

eGFR Calculator

Creatinine: micromol/l

Age: years

Sex: Male Female

Race: Black Other

estimated Glomerular Filtration Rate calculated by the abbreviated MDRD equation:
 $186 \times (\text{Creat} / 88.4)^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$