Guidelines for the Management of Hypertension in Nigeria 2020

Solomon Kadiri, #Fatiu Arogundade, Ayodeji Arije, Ayodele Omotoso, Basden Onwubere, Ademola Aderibigbe, Ambrose Isah, Amam Mbakwem, Babatunde Salako, Simeon Isezuo, Shamsudeen Ogun, Mahmoud Sani, Ifeoma Ulasi, Oluranti Familoni, Anthonia Ogbera, Okechukwu Ogah, Adebowale Ademola, Abimbola Opadeyi, Adanze Asinobi, for The Nigerian Hypertension Society Guidelines Committee

** Department of Medicine, University College Hospital, Ibadan*
 # Department of Medicine, Obafemi Awolowo University Teaching Hospital, Ile-Ife, Osun State
The Nigerian Hypertension Society Guidelines Committee

ABSTRACT

Background

Hypertension, defined as blood pressure ≥ 140/90 mmHg, has assumed greater public health importance in Nigeria in the last 2 decades. Many reports put the adult prevalence rates at 20-40%, with some major ones specifically reporting 27.8% and 28.9%. Low detection and reporting rates, inadequate investigation and treatment rates all combine to increase the burden. The guidelines provide updated information.

Recommendations

The traditional risk factors, with the addition of high income and education status, are highlighted. Recommendations regarding the use of devices and the setting, including home and ambulatory, in the measurement of the blood pressure, are updated. The importance of total cardiovascular risk assessment and risk stratification, employed in initiating and guiding therapy, is emphasized.

Lifestyle modifications are prescribed for all; they are described with estimates of BP responses and with a greater reference to local conditions. Attention is drawn to the early use of medicine therapy in those with high CV risk and multi-medicine therapy in those with BP ≥ 160/100 mmHg. The use of single pill combinations, wherever feasible, is recommended, and the prediction is made of most patients eventually requiring multi-medicine therapy.

Considerations of cost, availability, tolerance and patient-specific factors influence the choice of medicines, and although any of the several medicine classes could be used for initial therapy, thiazide and thiazide-like diuretics and calcium channel blockers are recommended for single or dual-medicine therapy. Alternatively, any of these and any of angiotensin converting enzyme inhibitor, angiotensin receptor blocker, centrally acting agent, beta-blocker or alpha-blocker could be used for combination therapy. Effective and recommended combinations and a list of the commonly available medicines in Nigeria are listed. Aspirin for secondary prevention and statin therapy should be used as required. The goal of treatment is commonly <140/90 mmHg, but could be lower in patients with diabetes, chronic kidney disease. Patient counselling, follow-up and treatment monitoring are emphasised.

Outlines of treatment in special groups or situations including diabetes, chronic kidney disease, haemoglobinopathies, HIV-infection, paediatric patients, patients with sexual dysfunction, resistant hypertension, hypertension emergency, community control and prevention are provided.

Keywords: *Hypertension, Nigeria, guidelines, management*

CHAPTER ONE

INTRODUCTION AND EPIDEMIOLOGY

1.1 Introduction

Hypertension is the commonest non-communicable disease (NCD) in Nigeria. Although the NCD Survey of the Federal Ministry of Health and Social Services published in 1997 remains the largest survey reporting hypertension prevalence in Nigeria, several other reports, including meta-analyses have since appeared providing updated prevalence rates.[1-3] Thus, current prevalence rates in adults would range broadly from 20-40%, using the 140/90 mmHg cut-off.[2,3] Additionally, the age standardized prevalence rates and the associated morbidity are higher in Africa, Nigeria included, than in many other regions of the world.[4,5]

The situation is further compounded by issues related to the increasing proportion of the aged in the population, rising diabetes rate and the worsening economic situation. With the rapid increase in information and resources for managing hypertension becoming available in the world, there is a need to rationalize management options and plans to serve health workers in severely underserved areas. Unfortunately, the situation still exists in Nigeria where wide disparities between hypertension guidelines recommendations and actual care persist.[6] Towards correcting that inadequacy, these guidelines address issues relating to the occurrence, diagnosis, investigation and treatment of hypertension at the personal level, and also management at the community level, in a more practical manner.

Much of this presentation is conceptually fashioned after the existing major guidelines and the current Nigerian guidelines with an appropriate addition of locally derived data.[7]

1.2 Prevalence of Hypertension in Nigeria

The World Health Organisation estimated the prevalence of hypertension (BP>140/90mmHg) in Nigerian adults over the age of 18 at 27.8%, comprising 28.1% and 27.5% in men and women respectively, against a background of 22% world prevalence.[4] By comparison, in another report describing another age set of over 25, the prevalence rates were put at 40% worldwide and 46% in Africa.[5]

More specifically, in a recent meta-analysis of twenty-seven studies involving 27,122 participants in Nigeria aged over 15, the pooled estimate of hypertension prevalence was 28.9% in both sexes, 29.5% and 25% in men and women respectively. This analysis also revealed a mean SBP of 128.6mmHg, mean DBP of 79.4 mmHg, and hypertension prevalence of 30.6% and 26.4% in urban and rural areas respectively.[2] The Non-Communicable Diseases Survey of the Federal Ministry of Health and Social Services 1997, which remains the largest survey of hypertension in Nigeria, used a cut-off of 160/95mmHg and reported a national prevalence of 11.2% (11.1% in men and 11.2% in women).[1]

The majority of the publications reviewed showed a rise in BP with age, male/female and urban/rural prevalence gradients, and a trend of rising prevalence rates in the four decades up to 2010.[2, 3, 8] Although ethnic and regional variations in the prevalence of hypertension have been reported, the disparities in the methodologies employed in the studies render comparisons difficult.[8]

1.3 Burden of Hypertension

Hypertension is the leading cause of death and disability adjusted life-years worldwide, accounting for 9.4 million deaths annually and 7% of disease burden.[9] Reports from diverse sources also show that countries in the African sub-region suffer disproportionately from this burden, as reflected in age-standardised death rates which are higher than those in many other parts of the world.[10, 11]

With a hypertension prevalence of around 30%, Nigeria, with its large population, contributes a large proportion to the overall burden of hypertension in the region. The number of Nigerians aged 20 years and above with hypertension was estimated at 20.8 million for the year 2010, and has been projected to rise to 39.1 million by the year 2030.[2]

Concomitant with this situation are the low awareness rates of 15-30%, treatment rates around 20% and control rates around 10%, which might relate to peoples' attitudes and lack of resources.[2, 8]

The sheer numbers affected and the relatively high cost of investigations and medicines constitute a financial burden. The direct cost of hypertension management is huge for a country where the majority of the patients may spend over 10% of their income on medications.[12]

1.4 Aetiology

In about 90% of cases, there is no identified organ cause for the hypertension described as primary hypertension, and in the other 10% there are identifiable causes for the hypertension, referred to as secondary hypertension.[13] However, hypertension is often not well investigated in the country due to a dearth, high costs of diagnostic laboratory investigations, and a low index of suspicion. Secondary hypertension is therefore underdiagnosed in the country and, consequently, there is a paucity of data on its aetiology in Nigeria.

Nonetheless, extrapolation from information emanating from developed countries suggest that a substantial number of cases in the country could be due to secondary hypertension.

The proper diagnosis and treatment of secondary hypertension could actually lead to a decrease in the burden of hypertension in the country.

1.5 Risk Factors for Hypertension

Risk factors for the development of primary hypertension include:

- Heredity
- High salt intake
- Obesity
- Physical inactivity
- Excessive alcohol intake
- Low potassium diet
- Low vegetables or fresh fruits content in the diet
- High saturated fats content in the diet.
- Low birth weight
- Obstructive sleep apnoea (sometimes classified under secondary hypertension)

Some reports have identified additional risk factors in Nigerians, and these include high and low (excluding middle) socio-economic status, high educational level and income.[1]

Other factors that may influence the development of hypertension include stress, though the evidence for this association is weak.[14]

CHAPTER TWO

DETECTION OF HYPERTENSION

2.1 Definition of Hypertension

Hypertension is defined as persistently elevated systolic and or diastolic blood pressure equal to or greater than SBP 140mmHg and DBP 90mmHg in an adult. This ordinarily refers to clinic or office values, and the cut-off varies according to the setting (Table 2.1).

Cut-off levels will be lower in paediatric patients (Refer to chapter 4 – Hypertension in Children).

White coat hypertension refers to the condition when clinic (office) BP is elevated whereas BP outside the clinic is normal. In masked hypertension, the clinic BP is normal and that outside the clinic is elevated. There is evidence that both conditions are associated with increased cardiovascular risk, and should be followed up.[15]

Blood pressure levels are continuously related to the risk of cardiovascular disease.[16]

2.2 Measurement of Blood Pressure

Hypertension control begins with detection, and requires surveillance. Therefore, health care workers are advised to measure the BP at each contact with the patient. The diagnosis of hypertension and decisions on management should be based on several BP measurements taken over one-two weeks, unless the BP is markedly increased or there are signs of organ damage. Repeated BP measurements will determine whether initial elevations persisted and require management, or have returned to normal and need only periodic measurements.

Table 2.1: Hypertension cut-off points for different settings

	SBP (mmHg)	DBP (mmHg)
Office or Clinic	140	90
24-Hour	125-130	80
Day	130-135	85
Night	120	70
Home	130-135	85

Blood pressure should be measured under optimal conditions and the following techniques are recommended:

- The subject should not have smoked or ingested caffeine or other stimulants or food in the 30 minutes before the measurement, which should begin after at least 5 minutes of rest in a quiet and calm environment.
- The urinary bladder should be emptied and the subject should be seated, feet on the floor, with the arm bared and supported at heart level.
- The BP should be measured in both arms at the first visit, and subsequently in the arm that gave the higher reading.
- Measurement should be taken with a validated electronic device or aneroid manometer, hybrid device or mercury sphygmomanometer.
- The appropriate cuff size should be used, and this generally requires that the bladder should cover two-thirds of the circumference of the arm. The following is given as a guide. (Table 2.2)

Table 2.2: Mid–arm circumference and recommended cuff bladder size

Mid-Arm Circumference (cm)	Cuû Bladder Size (cm)
<22	9 x 18
22 – 26	12 x 22
27 – 34	16 x 30
35 – 44	16 x 36
>44	16 x 42

Adapted from AHA recommendations [17]

- The cuff is rapidly inflated to a point 20mmHg above the pulse obliteration pressure, quickly deflated, then re-inflated to the same top point and slowly deflated to measure the BP.
- The first appearance (phase I) of repeated sounds and the disappearance of the sounds (phase V) correspond to the systolic and diastolic points respectively. In hyperdynamic states, the muffling of the sounds (phase IV) and phase V should be indicated.
- Readings should be recorded to the nearest 2mmHg and the pulse rate should be recorded.
- Two or more readings separated by an interval of 2 minutes should be averaged and if the first two readings differ by more than 10mmHg, additional readings should be obtained.
- BP and pulse rate should also be taken after 1 minute in the standing position, especially in the elderly, diabetics and those taking anti-hypertensive medications.
- Subjects should be told their BP readings and adequately advised on the implications of the readings.

2.2.1 Home and Ambulatory Blood Pressure Monitoring

Home Blood Pressure monitoring (HBPM) is recommended for all patients and is necessary in the following situations:

- Unusual variability of BP
- White coat hypertension
- Masked Hypertension
- Unresponsiveness to treatment

Ambulatory Blood Pressure Measurement (ABPM) may be indicated in the further assessment of the patient in some of these situations and has been shown to be a better indicator of Cardiovascular risk and mortality.[15] However, the equipment required for ABPM is generally more expensive and may not be readily available.

There are a number of validated electronic and aneroid devices which can be used for upper arm home measurements. They may need to be calibrated and checked for accuracy from time to time. Devices that measure BP below the elbow, such as wrist and finger devices, are likely to give inaccurate readings and are not recommended.

2.3 Classification of Blood Pressure

The following classification is recommended.

Table 2.3: Classification of blood pressure levels

Category	**SBP (mmHg)**	**DBP** (mmHg)
Optimal BP	<120	<80
Normal BP	<130	<85
High-Normal BP	130-139	85-89
Grade 1 Hypertension	140-159	90-99
Grade 2 Hypertension	160-179	100-109
Grade 3 Hypertension	≥180	≥110
Isolated systolic hypertension	≥140	<90

Source: adapted from the WHO/ISH statement 2003.[18]

When the SBP and DBP fall into different categories, the higher category should apply.

CHAPTER THREE

MANAGEMENT OF HYPERTENSION

3.1 Assessment of the Patient

The assessment should be conducted with the following aims:

- To confirm a persistent elevation of BP.
- To identify secondary causes of the hypertension.
- To determine the presence of hypertension mediated organ damage (HMOD) and quantify its extent.
- To search for other cardiovascular risk factors and clinical conditions which may influence the treatment and prognosis.

Table 3.1: Factors influencing prognosis in hypertension

Risk factors for cardiovascular disease	Hypertension mediated organ damage (HMOD)	Complications
• Men > 55years • Smoking • Family history of premature cardiovascular disease • Obesity • Total cholesterol>200mg/dl • Reduced HDL-cholesterol • Raised LDL-cholesterol • Elevated uric acid • Diabetes	• ECG or ECHO LVH • Microalbuminuria • eGFR 30-59 ml/min • Radiological or ultrasound evidence of atherpsclerotic plaques • Retinal Hemorrhages and exudates	• Stroke • Transient ischemic attack • Heart failure • Angina • Myocardial infarction • Coronary revascularization • Macroalburminuria • eGFR<30ml/min • Peripheral arterial disease

Source: Adapted from 2018 ESH/ESC Hypertension Guidelines [22]

The assessment should include:

- Clinical and family history – Information about age, gender, alcohol consumption, tobacco smoke, use of recreational and other medicines, dietary history as regards intake of salt, fruits and vegetables, physical activity and current or previous use of antihypertensive medicines should be obtained. Others include personal and family history of cardiovascular disease (stroke, heart failure, heart attack, sudden death) kidney disease and diabetes.
- Physical examination – weight and height to determine the Body Mass Index (BMI), waist and hip circumference, cardiovascular and other system examinations; and evidence of peripheral vascular disease, heart disease, stroke and kidney disease; fundoscopy.
- Laboratory investigations:
  - Haemoglobin and/or haematocrit.
  - Urinalysis for protein, blood and glucose.
  - Microscopic examination of the urine.
  - Serum potassium, sodium, creatinine with estimation of GFR.
  - Fasting plasma glucose; repeat if the test is abnormal and the patient is not a known diabetic.
  - Serum lipid profile.
  - Serum Uric acid.
  - Chest X ray.
  - 12 lead electrocardiogram.

Further investigations will be dictated by the clinical findings and the results from these initial tests. For resistant and complicated hypertension, investigations for cerebral, cardiac, renal and vascular damage including echocardiography, renal ultrasonography, carotid Doppler should be carried out.

Body weight and Body mass index should be assessed at every visit. Waist circumference should be assessed at first visit and yearly.

Urinalysis, serum creatinine, potassium, fasting blood glucose, fasting lipid profile and ECG should be carried out every year if the previous results were normal, and more frequently if there were abnormal results.

Reports show that over a third of hypertensive patients in Nigeria have Hypertension Mediated Organ damage (HMOD) at diagnosis, the most frequent being left ventricular hypertrophy.[19,20]

3.2 Assessment of Cardiovascular Risk

Decisions on the management of patients should not be based on their BP alone, but also on the consideration of cardiovascular risk assessment.[21]

An assessment of patients' global cardiovascular risk should be made using prediction charts or programmes, with particular regard given to identifying patients with predicted high risk.

Patients with diabetes, chronic kidney disease (CKD), HMOD and complications fall in the high risk category (Tables 3.1 and 3.2) and are considered along with patients with predicted high risk. This stratification allows for prioritization of options, and choice of initial therapy.

Table 3.2: Risk stratification

Other risk and disease history	Hypertension		
	Grade 1	Grade 2	Grade 3
No other risk factors	Low Risk	Medium Risk	High Risk
1-2 risk factors	Medium	Medium Risk	High Risk
3 or more risk factors/predicted high risk/hypertension-mediated organ damage or complications	High Risk	High Risk	High Risk

3.3 Treatment of Hypertension

Randomized trials have provided clear evidence for a lower incidence of major cardiovascular events after lowering of blood pressure in hypertension. Effective treatment of hypertension has been associated with reduction in cardiovascular risk, 20% reduction in all major cardiovascular events, 10-15% reduction in all- cause mortality, over 40% reduction in heart failure, 35% reduction in stroke and 20% reduction in coronary events.[23, 24]

Some reports suggest that this benefit can be conferred independently of the medicine type used for therapy, but others suggest the greater effectiveness of specific medicine classes in certain situations.[23]

Lifestyle modifications and medicine therapy are employed in the treatment of hypertension as shown in Fig. 3.1.

3.3.1 Overall Strategy

- The level of cardiovascular risk should be determined.
- Lifestyle measures should be offered to all patients.
- The decision to initiate medicine therapy is made according to guidelines in Fig. 3.1 and in consultation with the patient.
- Patients with grades 2 and 3 hypertension should receive lifestyle modification and medicine therapy on diagnosis. Initial medicine therapy should consist of two medicines from different classes, preferably in a pill combination.
- Patients with grade 1 hypertension and medium-high Cardiovascular risk should receive lifestyle modification and medicine therapy on diagnosis. Others should be given lifestyle modification, observed and reassessed after three months.
- Patients with high normal BP and high Cardiovascular risk should be given lifestyle modifications and may be given a single medicine in addition.[25]

3.3.2 Lifestyle Modifications

Lifestyle modifications prevent the development of hypertension in some persons, lead to modest reductions in blood pressure in persons with hypertension and, even when they are themselves inadequate in controlling hypertension, may reduce the number and dosage of medications needed to

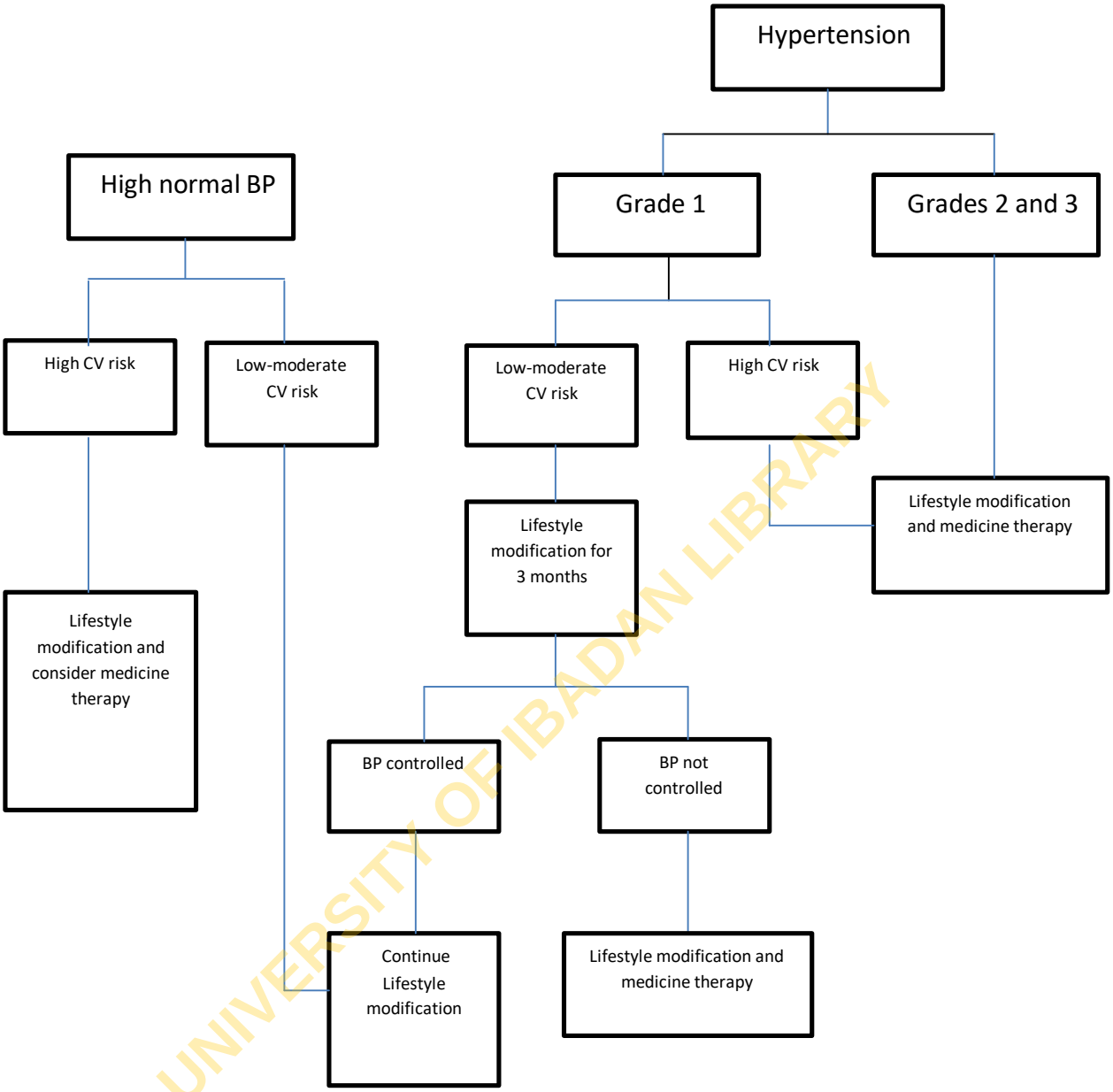

Figure 3.1: Management strategy

achieve control. Small reductions in blood pressure have been shown to result in reduction of cardiovascular risk, but lifestyle modifications alone, are insufficient in high-risk patients.

The risk factors addressed by these modifications are commonly present in persons with hypertension in Nigeria and elsewhere.[26] Information on lifestyle modifications should therefore be given to all patients when BP measurement is performed, and appropriate measures instituted as applicable.

Lifestyle modifications that have been shown to reduce BP include [27]:

- Reduction in salt intake
- Weight reduction
- Physical activity
- Moderation of alcohol intake
- Increased dietary potassium intake
- Consumption of diet with increased fresh fruits and vegetables, and reduced saturated fat.

Lifestyle measures are less expensive than medicine therapy; are without adverse effects and they improve the sense of well-being of the patient.

3.3.3 Reduction in Salt Intake

There is clear, epidemiological evidence linking salt intake with blood pressure, and this association is more marked in predisposed, salt-sensitive, individuals, who include the greater proportion of blacks, the elderly and the obese.[28, 29] Salt sensitivity and increased salt taste threshold have been found to be associated with hypertension in Nigerians.[30]

- Reduction in salt intake below one level teaspoon of salt (6 grams of salt /2400mg of sodium /100mmol of sodium)/day is effective in reducing BP, and this effect is enhanced by potassium supplementation. Reductions in SBP of up to 5mmHg may be expected from sodium restriction.
- There is local evidence that salt restriction is feasible and could, with adherence, produce the expected results in as little as a few weeks.[31]
- Reduction of salt intake generally requires that little or no salt be added to cooking, and that table salt, salt-rich foods, preserved and processed foods, and salt-based additives be eliminated. Salt content is listed as sodium on food labels, which patients should be encouraged to read. Patients should be informed that the food taste may be bland initially, but that taste adaptation to reduced sodium intake occurs with time. The use of commercially available alternatives to salt, such as low sodium containing salts, should be encouraged and the services of a dietitian should be obtained for optimal results.

3.3.4 Weight Reduction

Weight reduction leads to reduction in blood pressure in a large proportion of overweight and obese hypertensive individuals and also improves the efficacy of antihypertensive medications.[32] Additionally, the BP lowering effect is enhanced by other lifestyle measures. Other benefits of weight reduction include the reduction of other cardiovascular risk factors such as diabetes and dyslipidaemia.

- Recommended approaches to weight reduction are reduction in calorie intake, increased physical activity, accompanied by counselling, but medications and surgery may be required in some cases.
- The reduction in BP usually occurs early in the course of treatment, with as little as a 5Kg reduction in weight. SBP decrease of about 5mmHg should be expected and that should be the initial target; further losses may be prescribed if necessary, although the responses may be diminished.
- The aim should be to reduce the BMI to below 27, and ideally to keep it between 20 and 25, reduce the waist/hip ratio to below 0.9 and 0.85 in men and women respectively, and reduce the waist circumference (WC) to below 100cm and 85cm in men and women respectively. Achievement of these targets is recommended for non-hypertensive individuals to prevent hypertension, and for hypertensive patients to reduce BP. Targeting the BMI and WC perhaps provides more reliable results in this regard.[33]

3.3.5 Increased Physical Activity

Regular physical activity at a certain level reduces blood pressure and in addition, reduces the incidence of type 2 diabetes.[34] Some forms of exercise may be more effective than others, and SBP reductions of up to 10 mmHg may be expected.[35]

- Recommended forms of exercise include brisk walking, jogging, cycling and swimming for 30 minutes daily on most days of the week but where these are not feasible, patients should be encouraged to increase their physical work level at home and in the workplace.
- Patients should be advised to employ appropriate technology based on their settings, environment and circumstances. They could walk/jog on the streets or compound, climb stairs, or use a treadmill or bicycles. Exercise should be graded, and unaccustomed exercise avoided.

3.3.6 Moderation of Alcohol Intake

Although there is a continuous relationship between alcohol consumption and the blood pressure, and heavy drinking is associated with an increased incidence of stroke, the consumption of small amounts raises the ratio of HDL/LDL cholesterol and lowers cardiovascular risk.[36]

- Moderation of alcohol intake lowers the blood pressure, so a reduction of intake to 20-30g ethanol/day in men and 10-15g/day in women is recommended. These are the amounts contained in approximately one bottle and half a bottle respectively, of most beers available in Nigeria. The equivalent amounts of alcohol contained in most beers, table wines and spirits are in volume ratios of approximately 1, 1/3- 1/2, 1/9-1/8 respectively.
- The total alcohol consumption should not be more than 140g per week for men and 80g per week for women. Hidden or unrecognized sources of alcohol, which include some herbal preparations and some bitters, should be pointed out.
- In patients with heart muscle disease, the consumption of alcohol should be appropriately reduced or eliminated because of the depressant effect on the myocardium.
- The blood pressure may rise transiently following withdrawal from heavy drinking.

3.3.7 Other Dietary Changes and Recommendations

The consumption of a diet rich in fresh fruits and vegetables and low in saturated fats as obtains in the DASH or Mediterranean diet lowers blood pressure, lipids and glucose levels.[37, 38] Other beneficial accompaniments of the consumption of this diet include increased potassium and calcium intake.

- It is recommended that hypertensive individuals take at least one fruit per day (taken with the flesh) and also take fresh or partially cooked vegetables daily. They should also be advised to take fish at least two times in a week. With regard to egg consumption, not more than four eggs / week is recommended, as generally contained in the DASH diet.
- Hypertensive individuals should be advised to avoid animal fat and dairy products such as cheese, butter, fried lard from cow (e.g manshanu), fried meat and 'suya'. Reduction in intake of groundnut and palm oil is also recommended. In general, food should not be prepared by means that increase its oil content such as frying or deep-frying, and as much as practicable, food should be boiled, baked or grilled rather than fried.
- The BP lowering effect of the consumption of this diet is enhanced by combination with other lifestyle measures.
- Less consistent BP lowering results have been obtained from other lifestyle measures such as stress reduction and reduction in consumption of caffeine containing drinks such as coffee, energy drinks and kolanuts.

3.3.8 Additional Therapeutic Measures

Smoking may cause acute rises in BP but it has no recognised chronic effect.[39] It is however a very powerful cardiovascular risk factor, and quitting smoking is perhaps the single most important lifestyle measure for prevention of cardiovascular disease.[9]

- Hypertensive individuals should avoid the use of all tobacco products including snuff, as the cardiovascular disease protection derivable from blood pressure reduction may be lost if smoking is not stopped. Smokers may be offered nicotine replacement therapy or other medicine therapy where necessary.
- Management of lipid abnormalities is recommended and when dietary measures fail to achieve this, medicine therapy with a statin should be instituted.

3.4 Assessment and Follow-Up

The impact of lifestyle modifications should be periodically assessed, and when lifestyle modifications fail to produce the required reductions in Blood Pressure (as shown in Fig. 3.1) medicine therapy should be instituted.

3.5 Pharmacologic Treatment

There are general principles which govern the use of antihypertensive agents and these include:

- The use of low doses of medicines to initiate therapy thereby minimizing adverse effects and, in some patients, control may be achieved.
- The use of long acting medicines which provide 24- hour protection in a single dose. This minimizes blood pressure variability and also ensures greater patient adherence with treatment.
- The use of two or more medicines from different classes for initial therapy if the blood pressure is 20/10 mmHg above the goal level.[40, 41]

- The use of appropriate medicine combinations from different classes to maximize antihypertensive efficacy, minimize adverse effects of individual medicines, and neutralize those of others.
- Different medicines within the same class show little differences in efficacy.
- Most patients would eventually require two or more medicines to achieve control.[40, 41]
- The use of single pill combinations containing two or three medicines in a single formulation aids adherence, and should be employed for therapy in suitable cases.[40, 42]
- The choice of medicines which provide additional benefits in patients with co-morbidities.
- Cost considerations influence affordability and, consequently, adherence to treatment.

3.5.1 Choice of Medications

Diuretics, calcium channel blockers (CCBs), angiotensin converting enzyme inhibitors (ACEI), angiotensin-II receptor blockers (ARB) and beta-blockers have been shown in large trials to reduce cardiovascular events, and are arguably employable.[43]

The use of diuretics and CCBs is especially effective in Blacks.[44] This is related to the associated low renin state, which is found in a large proportion of Nigerians, and indeed Blacks and the elderly. A recent report confirmed the value of CCBs, and diuretics, in combinations, in the treatment of hypertension in Nigerians.[45] Another, a multi- centre study which included Nigerian participants, showed the efficacy of a CCB and an ARB in a combination pill.[46]

Alternatively, and depending on such considerations as the clinical setting, availability and affordability, any of the ACEl, ARB, alpha-blockers, beta-blockers, direct vasodilators and centrally-acting agents may be used for therapy.

Beta-blockers, ACEIs and ARBs are less effective in Blacks and these, as well as alpha blockers, may not be adequate for monotherapy in Nigerians.

Patients on once daily medication should be advised to take the medicines, except diuretics, in the evening.[47]

3.5.2 Recommended Approach

- For single medicine therapy, a low dose thiazide or thiazide-like diuretic (or in combination with amiloride or triamterene), or a CCB is recommended unless there are contraindications or compelling indications for the use of other medicines, as shown in Tables 3.3 and 3.4.
- If the BP is not controlled on diuretic or CCB therapy, or when initial therapy requires the use of two medicines, the combination of diuretic and CCB could be used, or another medicine selected from ACEI, ARB, beta-blocker, alpha-blocker or centrally acting agent should be added to the diuretic or CCB.
- A third medicine, from a class other than the two, should be added as required.
- Effective and recommended medicine combinations include:
  - Diuretic + CCB
  - Diuretic + ARB
  - Diuretic + ACEI
  - Diuretic + centrally acting medicine
  - Diuretic + ß- blocker
  - CCB +ß-blocker
  - CCB + ACEI
  - CCB + ARB
  - CCB + ß-blocker + ACEI/ARB
  - Diuretic + CCB + ACEI/ARB
  - Diuretic + CCB + centrally acting medicine
- Diuretic + ß-blockers should be used with caution because of the risk of new-onset diabetes.
- The combination of ACEI and ARB is not recommended because of the risk of lowering the GFR.
- The combination of thiazides with methyldopa and the use of reserpine-containing fixed dose combinations have endured and been found to be efficacious and cost effective. However, the introduction and availability of generic formulations of CCB, ACEI and ARBs has made these medicines more affordable.
- A list of commonly available medicines in Nigeria is shown in appendix 1.

3.5.3 Goal of Therapy

Target for blood pressure lowering should be <140/90mmHg for low to medium risk patients,

Table 3.3: Preferred anti-hypertensive medicines in specific situations

Situation Indication	Medicines
Cardiac disease	
• Left venticular hypertrophy	ACEI, ARB, diuretic, β-blocker.
• Heart failure	ACEI, ARB, β-blocker. * diuretic, MRA
• Ischaemic heart disease	β-blocker, ACEI, ARB.
• Left ventricular dysfunction	ACEI, ARB, diuretic
Stroke	CCB, diuretic, ACEI
Nephropathy	ACEO, ARB, diuretic
Diabetes mellitus	ACEI, ARB, low dose thiazide and thiazide-like diuretic, CCB
Elderly	Diuretic, CCB
Pregnancy	α-methyldopa, CCB (Nifedipine), labetalol, hydralazine

ACEI – Angiotensin converting enzyme inhibitor
CCB – Calcium channel blocker
ARB – Angiotensin – II blocker
MRA – Mineralocorticoid receptor antagonist (aldosterone anatagonists)

** Cautious use of these beta blockers in heart failure: Carvedilol, bisoprolol, metoprolol succinate, Nevibolol*

Table 3.4: Contraindication and caution for specific antihypertensive medicines

Medicine	Contraindications	Caution
Diuretic	Gout	Pregnancy, Glucose intolerance
CCB (Non-dihydropyridines)	2^0 and 3^0 heart block Heart Failure CCB	
CCB (dihydropyridines)		Nephropathy with proteinuria. Heart failure. Tachy arrhythmias
β-blocker	$2^0$and 3^0 heart block, Reactive airways disease, severe bradycardia <50/min. Peripheral vascular disease	Glucose intolerance, athletes, pregnancy, autonomic neuropathy
ACEI/ARB	Pregnancy, Hyperkalaemia, Bilateral renal artery stenosis	Women of child bearing age, GFR (<30 mis/min)
Centrally acting medicines		
• Methyldopa	Active Liver Disease	Liver disease Erectile dysfunction
• Reserpine		Elderly, Depression Erectile dysfunction

ACEI – Angiotensin converting enzyme inhibitor
ARB – Angiotensin receptor blocker
CCB – Calcium channel blocker

<130/80mmHg for those with diabetes or CKD with proteinuria, < 150/90 in those 80 years or older. Extra care should be taken with the latter category in view of the commonly associated frailty and likely intolerance to lowering BP.

However, since the effects of blood pressure increase are more marked in Blacks, it is wise to aim for a tighter control of BP in some Nigerian patients who should nevertheless be watched closely for adverse events.[48]

3.5.4 Additional Therapy

- The addition of antiplatelet therapy (e.g. low-dose aspirin) is useful in patients who have had a TIA, ischaemic stroke, ischaemic heart disease, peripheral arterial disease. Its use for primary prevention in high risk hypertensive patients should be weighed against the risk of bleeding.[49] Seventy-five to 150mg aspirin should be given but only after control of BP.
- The use of aspirin for primary prevention in low risk hypertensive patients is generally not recommended.[50]
- Statins should be given to patients who have had a TIA, ischaemic stroke, ischaemic heart disease, peripheral arterial disease and should be considered for primary prevention in other medium to high risk hypertensive patients with dyslipidaemia.[51]

3.6 Follow Up

- Patient counseling though very important has been reported to be inadequate in Nigeria. The need for therapy and adherence, and the expected adverse effects of medicines, should be explained to patients.
- Patients should normally be followed-up for life, with visit intervals ranging from one week to six months. Visit intervals will be short, one to four weeks, at initiation of therapy in all patients until BP control is achieved. In low risk patients and when the patient can be trusted to comply with therapy, intervals of six weeks to three months and up to six months follow- up sometimes appear to be adequate.
- Home monitoring of BP, using appropriate devices should be encouraged, and BP levels obtained at follow-up and at home perhaps predict prognosis more closely than clinic BP.
- The adverse effects of medicines should be sought, as they are not often volunteered. In addition, patients' medicines should be inspected or inquired into at every clinic visit for medication errors and adherence.
- Most patients will require increasing medications with time, but in a small proportion, the requirement may diminish. However, an attempt at complete withdrawal of therapy is not recommended.
- Continued monitoring of organ function should be carried out at least once a year, especially regarding the kidney, as renal impairment may develop in spite of apparently adequate control of blood pressure.
- Patients with low cardiovascular risk may be followed up in a primary care setting after control of Blood Pressure.
- Mobile phones should be used to assist communication between the care giver, especially at a primary care setting, and the patient. This would aid adherence to therapy.

CHAPTER FOUR

HYPERTENSION IN SPECIAL GROUPS

4.1 Hypertension with Diabetes

In this situation, consideration should be given to reducing BP, even in the high normal range. Most of the medicine classes have been shown to reduce cardiovascular events in diabetes, and therapy should be instituted with any of the thiazide or thiazide-like diuretics, CCB, ACEI or ARB.[52] Control of BP is more difficult than in many other situations and two-medicines therapy is often required at an early stage. An ACEI or ARB should be introduced especially in those with microalbuminuria or overt proteinuria to prevent, or slow the progression of nephropathy.[53] A lower target BP of <130/80mmHg is also recommended.

4.2 Hypertension with Renal Disease

Diuretic-based therapy is important in renal disease, but with reduction in GFR (<30ml/min), thiazide diuretics become less effective and loop diuretics are preferred. ACEI and ARB reduce proteinuria, are renoprotective, and form effective combinations with diuretics and CCBs. Target BP is < 130/80mmHg

particularly in patients with proteinuria, and there is often a need for more than one antihypertensive agent to achieve this. Monotherapy with dihydropyridine CCBs should be avoided in renal disease with proteinuria, as a worsening of the proteinuria and progression of the disease has been reported.[54] However, since there is often a need for more than one medicine, the combination with ARB or ACEI should be used as it attenuates the effect on proteinuria.

4.3 Hypertension in Pregnancy

This is defined as BP>140/90mmHg or an increase of >25/15mmHg from pre-pregnancy or first trimester levels. The recommended medicines for use are α-methyldopa, CCB (nifedipine), labetalol and hydralazine. These medicines are generally considered safe for the foetus and mother. The use of ACEI and ARB is contraindicated and diuretics should be avoided for adverse effects including foetal toxicity and placental insufficiency respectively. In preeclampsia, more urgent therapy is required with particular attention paid to the safety of the mother. Target BP of <140/90mmHg is recommended.

4.4 Hypertension and Haemoglobinopathies

Sickle cell disease is a common condition in blacks and BP values are generally lower than in those with haemoglobin AA.[55] Values above 130/80mmHg should be considered as elevated, because they are associated with cardiovascular and renal morbidity.[56]

Recommended treatment is with CCB and ACEI or ARB, as RAS blockade provides cardio-renal protection in sickle cell disease with proteinuria.[57]

4.5 Hypertension in HIV Infection

There is a high burden of hypertension in HIV infection, and several pathologic mechanisms are implicated. HAART therapy is often accompanied by unpredictability in the response to anti-hypertensives, which therefore requires close attention.[58]

4.6 Hypertension with Sexual Dysfunction

Sexual dysfunction is commoner in people with hypertension. This difference is accentuated by the use of certain medications including diuretics, beta-blockers and centrally acting agents in men but perhaps not in women.[59]

Sexual activity should be moderated in those with high cardiovascular risk and uncontrolled hypertension, and the treatment of erectile dysfunction should include switching to other medications and the use of medicines to aid erection.

4.7 Resistant Hypertension

Resistant hypertension is said to be present when control of BP is not achieved in spite of appropriate lifestyle methods and use of maximal doses of medicines from three different classes which must include a diuretic. Pseudo-hypertension, white coat hypertension and non-adherence to medications should be excluded in this situation. Reported frequency is in the order of 5-10%, and the presence should prompt the search for secondary causes of hypertension. Common causes include underlying secondary hypertension, advanced renal disease, obstructive sleep apnoea, uncontrolled lifestyle factors including obesity, excessive salt / alcohol consumption, and use of vasoactive substances and toxins. Therapy often requires the use of MRA, centrally acting medicines, direct acting vasodilators and alpha receptor blockers.

4.8 Secondary Hypertension

This should be considered in the following settings:

- Young hypertensives (Age < 30 years)
- Childhood or longstanding history of kidney disease
- History of steroid use / substance abuse
- Features suggestive of endocrinopathies
- Abnormalities of peripheral arterial pulses
- Resistant hypertension
- Polycythaemia
- Unprovoked hypokalaemia
- Raised intracranial pressure

Treatment of the underlying cause would be essential in addition to treatment of the hypertension.

4.9 Hypertension Emergencies

These are conditions requiring rapid lowering of blood pressure over minutes to hours in order to prevent or halt acute or severe target organ damage. These conditions include:

- Hypertensive encephalopathy
- Acute left ventricular failure
- Acute myocardial infarction
- Dissecting aortic aneurysm
- Eclampsia

- Intracerebral haemorrhage
- Malignant hypertension

Treatment requires the use of parenteral medicines such as labetalol, á-methyldopa, hydralazine and reserpine which may be locally available. Others include intravenous sodium nitroprusside, diazoxide, nitrates and esmolol, although these are not commonly available in the country.

In intracerebral haemorrhage and malignant hypertension a slower reduction of BP over several hours may be required.

In malignant hypertension, incremental doses of oral agents including ACEI/ARB, beta-blocker and CCB can be used.

The use of sublingual nifedipine is not recommended due to the risk of sudden death.

4.10 Hypertension Urgency

This refers to conditions in which there are severe elevations of Blood Pressure without features of acute organ damage or immediate threat to life. In these situations, BP should be lowered to safe levels over days.

4.11 Hypertension in Children

Hypertension in children and adolescents is defined based on blood pressure normograms for age, gender and height. [60, 61] It is potentially associated with a high risk of morbidity and mortality. Measurement of BP in children requires the use of appropriately sized BP bladder cuffs. Oscillometric methods may be a useful non-invasive method of BP measurement in infants or in children who need continuous BP monitoring. Hypertension will however require confirmation with the mercury sphygmomanometer.[60, 61]

In the paediatric age group, hypertension is defined as SBP or DBP values consistently (three or more times) ≥95th percentile for age, gender and height. The classification of BP levels according to age and BP stages is shown in Table 4.1.

Hypertensive crisis describes an acute rise in BP that can cause rapid end-organ damage. The Blood Pressure in hypertensive crisis is usually well above the stage 2 HTN threshold and is usually greater than the 95th percentile + 30mmHg.

Hypertension emergency is symptomatic hypertension with signs of hypertensive encephalopathy such as seizures and altered sensorium.

Hypertensive urgency refers to severe hypertension with features such as headaches and vomiting but without altered sensorium.[60, 61]

Prevalence of hypertension in children ranges from 0.1-10% in Nigerian studies and increases with

Table 4.1: Classification of blood pressure in children and adolescents

	Age <13 yrs	Age ≥13 yrs
Normal BP	<90th percentile	<120/<80
Elevated BP	≥90th - <95th percentile OR 120/80 – <95th percentile (whichever is lower)	120/<80 – 129/<80
Stage 1 HTN	≥95th percentile – <95th percentile + 12 OR 130/80 – 139/89 (whichever is lower)	130/80 – 139/89
Stage 2 HTN	≥95th percentile + 12 OR ≥140/90 (whichever is lower)	≥140/90

Values are mmHg
Adapted from Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents[61]

age.[62-64] Causes of hypertension in children include acute glomerulonephritis, acute kidney injury, chronic kidney failure, renal artery stenosis, coarctation of the aorta, phaeochromocytoma, Cushing's disease, and exogenous use of steroids. Secondary Hypertension is more common than primary hypertension in children. The aetiology of secondary hypertension is frequently in the kidney, but it may also be caused by vascular or endocrine disorders. Primary hypertension is also increasingly diagnosed in children especially in obese children or those with family history of hypertension.[60]

Hypertension in children may be associated with features of kidney failure, heart failure, hypertensive encephalopathy, or other features of target organ damage such as retinopathy, left ventricular hypertrophy, and increased carotid intimal thickness.[65]

All children with confirmed hypertension should be referred to the Paediatrician. Treatment ranges from life-style changes, treatment of the underlying cause to pharmacologic interventions. Pharmacologic therapy includes the use of CCBs, ACE inhibitors, ARBs, beta- blockers, and diuretics. Severe symptomatic hypertension may need intravenous medications with the aim of gradual or graded reduction in Blood Pressure.

4.12 Community Programme for Blood Pressure Control

Community screening activities are important for population subgroups at high risk of developing cardiovascular disease, and with limited access to medical care. Community programmes may be an important strategy for primary prevention and early detection of hypertension, monitoring the progress of persons already receiving therapy, and promoting adherence by hypertensive persons already receiving therapy. Clinic attendance adherence needs to be effectively monitored.

Ideally, community and corporate programmes should be developed to include as many of the following as resources will allow:

- Incorporation of routine BP measurement into primary care and the increased role of nurses in diagnosis and treatment of hypertension.[66] This provides the additional benefit of sensitizing the client even when the BP is repeatedly found to be normal.
- Detection, education and referral for other cardiovascular risk factors.
- Multiple strategies to improve compliance to treatment.
- These include public, patients and professional education activities incorporating culturally sensitive approaches as well as environmental support, such as informative food labeling, heart healthy menus in restaurants and provision of trails for walking and cycling.
- Multiple centres providing reach to all segments of the population including all health care settings, schools, work sites, churches, mosques, community centers, supermarkets and pharmacies.
- Extensive use of media in promoting these activities.
- The use of religious institutions which appear to exert some influence in many communities.
- Cooperation and training of pharmacists who constitute an important source of information for patients.

When resources are inadequate for the provision of these comprehensive facilities, community programmes should be organised, beginning with modest activities which could be expanded when clinicians and other health care providers become involved. This cooperation occurs only if clinicians are aware of, and support the community programmes. Advisory board or community high blood pressure councils can facilitate cooperation among professionals, agencies, local health department, voluntary health agencies, hospitals, industries and other interested groups. These boards or councils can help in identifying community problems, resources, priorities, solutions, and methods of evaluating programme effectiveness. Such community involvement fosters a sense of commitment and acceptance of responsibility for the community's health problems and their solutions.

CHAPTER FIVE

PREVENTION OF HYPERTENSION

Various types of Hypertension prevention are recognized, namely primordial, primary, secondary and tertiary prevention.

5.1 Primordial Prevention

Primordial Prevention is achieved by avoiding those social, economic and cultural patterns of life that have been shown to contribute to the high incidence of the disease.

This can be achieved by promoting good ante-natal care, thus reducing the likelihood of low birth-weight.[67]

5.2 Primary Prevention

The objective is to reduce or modify risk factors already present 'in the individual and community, and forestall the development of overt disease.

This type of prevention can be accomplished by application of interventions to the general population (population- based strategy) with the objective of achieving a downward shift in the distribution of blood pressure. It can be complemented by special attempts to lower blood pressure in those who are likely to develop hypertension (targeted strategy). The latter include persons· with a family history of hypertension, high normal BP or one or more of the several risk factors for increased BP described earlier. The desired lifestyle changes are feasible. Achievement of the intervention goals has, however, been constrained by a number of societal barriers, including lack of satisfactory food substitutes, negative perceptions of a slim build and exercising, and the absence of a national campaign to promote the adoption of population-based and targeted intervention strategies necessary to prevent high blood pressure.

5.3 Secondary and Tertiary Prevention

These involve the management of the disease and its complications. Quite clearly, added benefits can be expected in the area of secondary prevention and control by the application of the foregoing, preventative, measures. There are important roles for primary care workers including community nurses in these aspects of prevention and control, even while recognising the contribution of all health workers.[67]

ACKNOWLEDGEMENTS

Pfizer Nig. Ltd. provided a grant for the project but was neither involved in the deliberations nor the determination of the contents of the guidelines.

REFERENCES

1. The National Expert Committee on NCD. Non- communicable diseases in Nigeria – final report of a national survey. Lagos: Fed Ministry Health Social Services. 1997
2. Adeloye D, Basquill C, Aderemi AV, Thompson JY, Obi FA. An estimate of the prevalence of hypertension in Nigeria: a systematic review and meta-analysis. J Hypertens 2015; 33:230-242.
3. Ogah OS, Okpechi I, Chukwuonye II, Akinyemi JO, Onwubere BJ, Falase AO *et al*. Blood pressure, prevalence of hypertension and hypertension related complications in Nigerian Africans: A review. World J Cardiol 2012; 4:327-340.
4. World Health Organization. Global status report on non-communicable diseases 2014. Geneva: WHO. 2014
5. World Health Organization. A global brief on hypertension: silent killer, global public health crisis. Geneva: WHO. 2013
6. Ale OK, Braimoh RW. Awareness of hypertension guidelines and the diagnosis and evaluation of hypertension by primary care physicians in Nigeria. Cardiovasc J Afr 2017; 28: 72-76
7. Nigerian Hypertension Society. Guidelines for the management of hypertension in Nigeria. Onwubere B & Kadiri S (eds) Second edition. Enugu: Ezu Books Ltd. 2005
8. Akinlua JT, Meakin R, Umar AM, Freemantle N. Current Prevalence Pattern of Hypertension in Nigeria: A Systematic Review. PLoS One 2015;10(10):e0140021.
9. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, *et al*. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990- 2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380:2224-2260.
10. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet 2005; 365:217- 223.
11. Abegunde DO1, Mathers CD, Adam T, Ortegon M, Strong K. The burden and costs of chronic diseases in low-income and

middle-income countries. Lancet 2007; 370: 1929-1938.
12. Ilesanmi OS, Ige OK, Adebiyi AO. The managed hypertensive: the costs of blood pressure control in a Nigerian town. Pan Afr Med J 2012;12:96. available online at: http://www.panafrican-med-journal.com/ content/article/12/96/full/
13. Rimoldi SF, Scherrer U, Messerli FH. Secondary arterial hypertension: when, who, and how to screen? Eur Heart J 2014; 35:1245-1254.
14. Nagele E, Jeitler K, Horvath K, Semlitsch T, Posch N, Herrmann KH, *et al.* Clinical effectiveness of stress- reduction techniques in patients with hypertension: systematic review and meta-analysis. J Hypertens 2014; 32:1936-1944.
15. Banegas JR, Ruilope LM, de la Sierra A, Vinyoles E, Gorostidi M, de la Cruz JJ, *et al.* Relationship between Clinic and Ambulatory Blood-Pressure Measurements and Mortality. N Engl J Med 2018; 378:1509-1520.
16. Rapsomaniki E, Timmis A, George J, Pujades- Rodriguez M, Shah AD, Denaxas S, *et al.* Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. Lancet 2014; 383:1899-1911.
17. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, *et al*. Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Circulation 2005; 111:697-716
18. World Health Organization/International Society of Hypertension Writing Group. 2003 World Health Organization/International Society of Hypertension statement on management of hypertension. J Hypertens 2003; 21:1983-1992.
19. Oladapo OO, Salako L, Sadiq L, Shoyinka K, Adedapo K, Falase AO. Target-organ damage and cardiovascular complications in hypertensive Nigerian Yoruba adults: a cross-sectional study. Cardiovasc J Afr 2012; 23: 379-384
20. Nelissen HE, Hendriks ME, Wit FW, Bolarinwa OA, Osagbemi GK, Bindraban NR, *et al.* Target organ damage among hypertensive adults in rural Nigeria: a cross-sectional study. J Hypertens 2014; 32:487-494.
21. Karmali KN, Lloyd-Jones DM. Global Risk Assessment to Guide Blood Pressure Management in Cardiovascular Disease Prevention. Hypertension 2017; 69:e2-e9.
22. TheTask Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. 2018 ESC/ESH Guidelines for the management of arterial hypertension. J. Hypertens 2018, 36:1953–2041
23. Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, *et al.* Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet 2016; 387:957-967.
24. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension. 1. Overview, meta-analyses, and meta-regression analyses of randomized trials. J Hypertens 2014; 32: 2285-2295.
25. Thomopoulos C, Parati G, Zanchetti A. Effects of blood-pressure-lowering treatment on outcome incidence. 12. Effects in individuals with high-normal and normal blood pressure: overview and meta- analyses of randomized trials. J Hypertens 2017; 35:2150-2160.
26. Oluyombo R, Akinwusi PO, Olamoyegun MO, Ayodele OE, Fawale MB, Okunola OO, et al. Clustering of cardiovascular risk factors in semi-urban communities in south-western Nigeria. Cardiovasc J Afr 2016; 27:322-327.
27. Whelton PK, He J, Appel LJ, Cutler JA, Havas S, Kotchen TA, *et al;* National High Blood Pressure Education Program Coordinating Committee. Primary prevention of hypertension: clinical and public health

advisory from The National High Blood Pressure Education Program. JAMA 2002; 288:1882-1888.
28. He FJ, MacGregor GA. A comprehensive review on salt and health and current experience of worldwide salt reduction programmes. J Hum Hypertens 2009; 23:363-384.
29. Suckling RJ, He FJ, Markandu ND, MacGregor GA. Modest Salt Reduction Lowers Blood Pressure and Albumin Excretion in Impaired Glucose Tolerance and Type 2 Diabetes Mellitus: A Randomized Double- Blind Trial. Hypertension 2016; 67:1189-1195.
30. Azinge EC, Sofola OA, Silva BO. Relationship between salt intake, salt-taste threshold and blood pressure in Nigerians. West Afr J Med 2011; 30:373-376.
31. Adeyemo AA, Prewitt TE, Luke A, Omotade OO, Rotimi CN, Brieger WR, *et al*. The feasibility of implementing a dietary sodium reduction intervention among free- living normotensive individuals in south west Nigeria. Ethn Dis 2002; 12:207-212.
32. Neter JE1, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension 2003; 42:878-884.
33. Ononamadu CJ, Ezekwesili CN, Onyeukwu OF, Umeoguaju UF, Ezeigwe OC, Ihegboro GO. Comparative analysis of anthropometric indices of obesity as correlates and potential predictors of risk for hypertension and prehypertension in a population in Nigeria. Cardiovasc J Afr 2017; 28:92-99.
34. Tuomilehto J, Lindstrom J, Eriksson JG, *et al.* Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001; 344:1343-1350.
35. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc 2013; 2(1):e004473. doi: 10.1161/ JAHA. 112. 004473.
36. O'Keefe JH, Bybee KA, Lavie CJ. Alcohol and cardiovascular health: the razor-sharp double-edged sword. J Am Coll Cardiol 2007; 50:1009-1014.
37. Appel LJ, Champagne CM, Harsha DW, Cooper LS, Obarzanek E, Elmer PJ, *et al;* Writing Group of the PREMIER Collaborative Research Group. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. JAMA 2003; 289:2083-2093.
38. Doménech M, Roman P, Lapetra J, García de la Corte FJ, Sala-Vila A, de la Torre R, *et al*. Mediterranean diet reduces 24-hour ambulatory blood pressure, blood glucose, and lipids: one-year randomized, clinical trial. Hypertension 2014; 64:69-76.
39. Yarlioglues M, Kaya MG, Ardic I, Calapkorur B, Dogdu O, Akpek M, *et al.* Acute effects of passive smoking on blood pressure and heart rate in healthy females. Blood Press Monit 2010;15: 251-256.
40. Gradman AH, Basile JN, Carter BL, Bakris GL; American Society of Hypertension Writing Group. Combination therapy in hypertension. J Clin Hypertens (Greenwich) 2011; 13:146-154
41. Mensah GA, Bakris G. Treatment and control of high blood pressure in adults. Cardiol Clin 2010; 28:609-622.
42. Gupta AK, Arshad S, Poulter NR. Compliance, safety, and effectiveness of fixed-dose combinations of antihypertensive agents: a meta-analysis. Hypertension 2010; 55: 399-407.
43. Thomopoulos C, Parati G, Zanchetti A. Effects of bloodpressure-lowering on outcome incidence in hypertension: 5. Head-to-head comparisons of various classes of antihypertensive drugs - overview and meta-analyses. J Hypertens 2015; 33:1321-1341.
44. Wright JT Jr1, Dunn JK, Cutler JA, Davis BR, Cushman WC, Ford CE, et al; ALLHAT Collaborative Research Group. Outcomes in hypertensive black and nonblack patients treated with chlorthalidone, amlodipine, and lisinopril. JAMA 2005; 293:1595-1608.
45. Ojji DB, Mayosi B, Francis V, Badri M, Cornelius V, Smythe W, *et al;* CREOLE Study Investigators. Comparison of Dual

Therapies for Lowering Blood Pressure in Black Africans. N Engl J Med 2019; 380: 2429-2439.
46. M'Buyamba-Kabangu JR, Anisiuba BC, Ndiaye MB, Lemogoum D, Jacobs L, Ijoma CK, *et al*; Newer versus Older Antihypertensive Agents in African Hypertensive Patients Trial (NOAAH) Investigators. Efficacy of newer versus older antihypertensive drugs in black patients living in sub-Saharan Africa. J Hum Hypertens 2013; 27: 729-735.
47. Okeahialam B, Ohihoin E, Ajuluchukwu J. Chronotherapy in Nigerian hypertensives. Ther Adv Cardiovasc Dis 2011; 5:113-118.
48. SPRINT Research Group, Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, *et al.* A Randomized Trial of Intensive versus Standard Blood- Pressure Control. N Engl J Med 2015; 373:2103-2116.
49. Bibbins-Domingo K; U.S. Preventive Services Task Force. Aspirin Use for the Primary Prevention of Cardiovascular Disease and Colorectal Cancer: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med 2016; 164:836-845.
50. Marquis-Gravel G, Roe MT, Harrington RA, Muñoz D, Hernandez AF, Jones WS. Revisiting the Role of Aspirin for the Primary Prevention of Cardiovascular Disease. Circulation 2019; 140:1115-1124.
51. US Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, Curry SJ, Davidson KW, Epling JW, *et al.* Statin Use for the Primary Prevention of Cardiovascular Disease in Adults: US Preventive Services Task Force Recommendation Statement. JAMA 2016; 316:1997-2007.
52. Emdin CA, Rahimi K, Neal B, Callender T, Perkovic V, Patel A. Blood pressure lowering in type 2 diabetes: a systematic review and meta-analysis. JAMA 2015; 313:603-615
53. Thomopoulos C, Parati G, Zanchetti A. Effects of blood-pressure-lowering treatment on outcome incidence in hypertension: 10 - Should blood pressure management differ in hypertensive patients with and without diabetes mellitus? Overview and meta- analyses of randomized trials. J Hypertens 2017; 35: 922-944.
54. Wright JT, Bakris G, Greene T, Agodoa LY, Appel LJ, Charleston J, *et al.* Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease. Results from the AASK trial. JAMA 2002; 288: 2421-2431.
55. Aderibigbe A, Omotoso AB, Awobusuyi JO, Akande TM. Arterial blood pressure in adult Nigerian sickle cell anaemia patients. West Afr J Med 1999; 18:114- 118.
56. Gordeuk VR, Sachdev V, Taylor JG, Gladwin MT, Kato G, Castro OL. Relative systemic hypertension in patients with sickle cell disease is associated with risk of pulmonary hypertension and renal insufficiency. Am J Hematol 2008; 83:15-18.
57. Quinn CT, Saraf SL, Gordeuk VR, Fitzhugh CD, Creary SE, Bodas P. et al. Losartan for the nephropathy of sickle cell anemia: A phase-2, multicenter trial. Am J Hematol 2017; 92:E520-E528.
58. van Zoest RA, van den Born BH, Reiss P. Hypertension in people living with HIV. Curr Opin HIV AIDS 2017; 12: 513-522.
59. Thomas HN, Evans GW, Berlowitz DR, Chertow GM, Conroy MB, Foy CG, *et al*-SPRINT Study Group. Antihypertensive medications and sexual function in women: baseline data from the SBP intervention trial (SPRINT). J Hypertens. 2016; 34:1224-1231. doi: 10.1097/HJH.0000000000000911.
60. The National High Blood Pressure Education Program Working Group on high blood pressure in children and adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004; 114(2 Suppl.):555-576.
61. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, *et al.* Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Pediatrics 2017;140(3):e20171904
62. Odetunde I, Emeka E, Josephat M, Henrietta U, Oluwatoyin A, Osita U, *et al.* Elevated arterial blood pressure and body mass index

among Nigerian preschool children population. BMC Pediatrics 2014;14:64. doi: 10.1186/471-2431-14-64.
63. Ejike C, Ugwu CE, Ezeanyika L. Variations in the prevalence of point (pre)hypertension in a Nigerian school-going adolescent population living in a semi- urban and an urban area. BMC Pediatrics 2010;10:13. doi: 0.1186/471-2431-10-13.
64. Oyewole OO, Oritogun KS. Pre-hypertension and hypertension in adolescence: how much does it occur in a Nigerian community? West Afr J Med 2012; 31:71-75.
65. Flynn J. Evaluation and management of hypertension in childhood. Prog Pediatr Cardiol 2001;12:177-188.
66. Ibrahim MM, Damasceno A. Hypertension in developing countries. Lancet 2012; 380: 611-619
67. WHO. Global Nutrition Targets 2025: low birth weight policy brief (WHO/NMH/NHD/ 14.5). Geneva: World Health Organization. 2014.

APPENDIX 1

Antihypertensive medications commonly available in Nigeria

Antihypertensive agent	**Dose and dosage forms**
Diuretics	
Hydrochlorothiazide (HCT)	12.5mg, 25mg
Amiloride hydrochloride + HCT	Tablet 2.5mg+ 25mg
Bendrofluazide	Tablet 2.5mg, 5mg
Spironolactone	Tablet 25mg, 50mg
Indapamide	Tablet 1.25mg, 2.5mg
Calcium channel blockers	
Amlodipine	**Tablet:** 5 mg (besylate) 5mg, 10mg
Nifedipine retard	Tablet (slow release) 20mg
Nimodipine	Tablet 30mg
Beta blockers	
Atenolol	Tablet 25mg, 50mg, 100mg
Propranolol	Tablet (hydrochloride) 40mg, 80mg
Bisoprolol	Tablet 5mg, 10mg
Metoprolol	Tablet 25mg
ACE Inhibitors	
Lisinopril	Tablet 5mg, 10mg, 20mg
Ramipril	Tablet 5mg, 10mg
Captopril	Tablet 12.5mg, 25mg, 50mg
Enalapril	Tablet 5mg, 10mg
Angiotensin-II Receptor Blockers	
Valsartan	Tablet 40mg, 80mg, 160mg
Losartan	Tablet 25mg, 50mg
Telmisartan	Tablet 40mg, 80mg
Irbesartan	Tablet 75mg, 150mg, 300mg
Candesartan	Tablet 4mg, 8mg, 16mg
Alpha-blockers	
Doxazosin	Tablet 2mg, 4mg
Combined alpha and beta blockers	
Labetalol	Injection powder 5mg/ml in 20ml Ampoule Tablet (hydrochloride) 100mg, 200mg
Centrally acting agents	
Methyldopa	Tablet 250mg, 500mgI Injection 250mg
Peripheral adrenergic inhibitors	
Reserpine + dihydroergocristine + clopamide (in combination)	Tablet 100 µg + 500 µg + 5mg
Vasodilators	
Hydralazine	Tablet 50mg Injection powder (hydrochloride) 20mg ampoule
Fixed dose combinations	
Amiloride hydrochloride + HCT	Tablet 2.5mg + 25mg
Amlodipine + HCT	Tablet 5/10mg + 12.5/25mg
Lisinopril + HCT	Tablet 10/20mg + 12.5mg; 20mg + 25mg
Amlodipine + valsartan	Tablet 5/10mg + 80/160/320mg
Amlodipine + valsartan + HCT	Tablet 5/10mg + 80/160/320mg + 12.5/25mg
Losartan + HCT	Tablet 50/100mg + 12.5/25mg
Telmisartan + HCT	Tablet 40/80mg + 12.5mg
Indapamide + amlodipine	Tablet 1.5mg + 5/10mg
Indapamide + amlodipine + perindopril	Tablet 2.5mg + 5/10mg + 10mg
Perindopril + amlodipine	Tablet 5mg + 5mg
Ramipril + HCT	Tablet 2.5/5mg + 12.5mg
Reserpine + dihydroergocristine + clopamide	Tablet 100 µg + 500 µg + 5mg