TASKPEN CLINICAL GUIDELINES:

Protocols for the Integrated Management of Cardiometabolic conditions in Adult PLHIV

Treatment Guidelines for Hypertension, Diabetes, Dyslipidemias and Obesity in Zambia

THE UNIVERSITY OF ZAMBIA
SERVICE AND EXCELLENCE

NIH
National Institutes of Health

CIDRZ
for a healthy Zambia

Acronyms and Abbreviations

ART	Antiretroviral Treatment
BMI	Body Mass Index
BP	Blood Pressure
CAD	Coronary Artery Disease
CD4 count	Cluster of differentiation 4
CVD	Cardiovascular Diseases
CXR	Chest X-Ray
DASH	Dietary approaches to stop Hypertension
DBP	Diastolic Blood Pressure
GDM	Gestational Diabetes Mellitus
HbA1c	Glycosylated Haemoglobin A1c
HDL	High-density lipoprotein
HIV	Human Immunodeficiency Virus
HMOD	Hypertensive-mediated end-organ damage
HTN	Hypertension
LMICs	Low and Middle Income Countries
LDL	Low density lipoprotein
NCDs	Non-communicable diseases
OGTT	Oral Glucose Tolerance Test
PIH	Pregnancy Induced Hypertension
PE	Pre-Eclampsia
PLHIV	People living with HIV
RBG	Random Blood Glucose
RFTs	Renal Function Tests
SBP	Systolic Blood Pressure
SPE	Severe Pre-Eclampsia
WHO	World Health Organisation
VL	Viral Load

Foreword

Non-communicable diseases (NCDs)—and cardiovascular disease in particular—have become the leading cause of death worldwide, and disproportionately afflict low- and middle-income countries. This has been attributed, in part, to the rapid levels of urbanization in geographical locations such as sub-Saharan Africa, an area that until recent decades faced a burden of disease mostly from infectious causes.

The upsurge in the incidence and prevalence of NCDs to epidemic levels has impacted negatively on the productivity, quality of life, quality of care and healthcare-related expenditures in sub-Saharan Africa. Infectious diseases that were among the top causes of death in 2000, particularly HIV/AIDS, have fallen on the list. In contrast, diabetes mellitus has entered the top ten causes of death following a significant increase since 2000. The manifestation of this NCD "epidemic" in Zambia and much of sub-Saharan Africa has largely been insidious and threatens to erode the significant health care gains achieved over recent years.

The most important modifiable predictors of cardiovascular events in PLHIV are:

- Elevated SBP
- Diabetes
- High total cholesterol
- Low density lipoprotein
- Smoking
- Unhealthy alcohol use
- Low CD4 count
- Unsuppressed HIV viral load

Unhealthy diets, obesity, and sedentary lifestyles also contribute to CVD by promoting these predictors.

Successful management of hypertension, diabetes mellitus and dyslipidemia is among the most important challenges facing clinicians today and continues to hamper/impede reduction in major adverse cardiovascular events.

This guideline, developed through a consultative, participatory and transparent process with partners and stakeholders, serves as a timely intervention to address NCDs among people living with HIV. It also underscores the need to focus additional clinical resources toward the integrated management of multi-faceted NCDs that continue to confront patients and frontline non-physician healthcare workers on a daily basis.

Although these guidelines are primarily envisioned to provide pragmatic and standardized recommendations for integrated treatment and care of cardio-metabolic conditions in PLHIV, every opportunity has been made to highlight the need to promote preventive lifestyle modifications, as well as rehabilitative and palliative measures when they are appropriate to the overall management of PLHIV.

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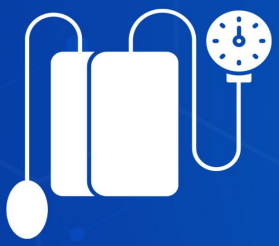


Hypertension

1.0 Hypertension

WHO defines hypertension, also known as high or raised blood pressure, as a condition in which the blood vessels have persistently raised pressure. Blood pressure refers to the force exerted by the blood pushing against the walls of the blood vessels. The force is generated by the pumping action of the heart and the compliance of the blood vessels. The higher the pressure, the harder the heart has to pump.

Hypertension is a chronic condition and its complications are the leading cause of death worldwide. People living with HIV (PLHIV) are also at risk of hypertension and its complications. Complications of hypertension include stroke, dementia, damage to the eye (retinopathy), coronary artery disease including myocardial infarction (heart attack), hypertensive heart disease, heart failure, damage to blood vessels (peripheral vascular disease) and kidney disease (nephropathy). These are often collectively referred to as hypertension-mediated end-organ damage (HMOD).

Hypertension may be classified as:

- Primary/Essential – wherein no identifiable cause can be ascertained
- Secondary – wherein an identifiable cause/ underlying condition is evident (e.g. Kidney disease, Endocrine disease)

Hypertension is largely ASYMPTOMATIC. However, some patients may present with one or more of the following symptoms:

- Headache
- Awareness of one's heart beat (palpitations)
- Visual disturbances
- Fatigue/tiredness
- Nausea
- Vomiting
- Dizziness

The above list is neither exhaustive nor exclusive.

When to measure Blood Pressure

All clients who attend the clinic must have their blood pressure measured at each visit.

Measurement of Blood Pressure

It is important to measure the blood pressure correctly and accurately using a blood pressure machine or a stethoscope and blood pressure cuff known as a sphygmomanometer. Both systolic and diastolic pressures should be measured and documented.

What equipment is needed to measure Blood Pressure?

There are different types of blood pressure machines namely:

1.

2.

3.

1. **Conventional Mercury Sphygmomanometer** (gold standard)
2. **Aneroid Sphygmomanometer**
3. **Digital electronic device** (preferably WHO-validated automated machines)

To avoid a falsely raised BP, follow these steps:

Patient should be seated in relaxed position at rest for at least 5 minutes and seated:

- with the back supported,
- with the legs uncrossed,
- with the feet flat on the floor,

Ideally, the patient should also:

- have an empty urinary bladder,
- not be talking on the phone,
- and not have smoked, exercised, or ingested caffeine-containing beverages or food in the previous 30 minutes

Use the appropriate cuff size (standard cuff 12-13cm wide and 35cm long). Use a larger cuff for arm circumference > 32cm or a smaller cuff for smaller arms <22cm female; < 23cm male. When the ordinary cuff is too loose when fitted correctly, for instance in severely undernourished adults, consider using a paediatric cuff.

Using the markings (arrows) on the cuff to ensure correct positioning on the arm:

- Apply the cuff 2cm above the elbow
- Ensure the cuff is at the level of the heart; hold the arm slightly elevated, or rest it on a table, if necessary

Measure blood pressure in both arms (if possible)

- The left arm is preferred
- The arm should be supported on a table or arm rest; not held by patient

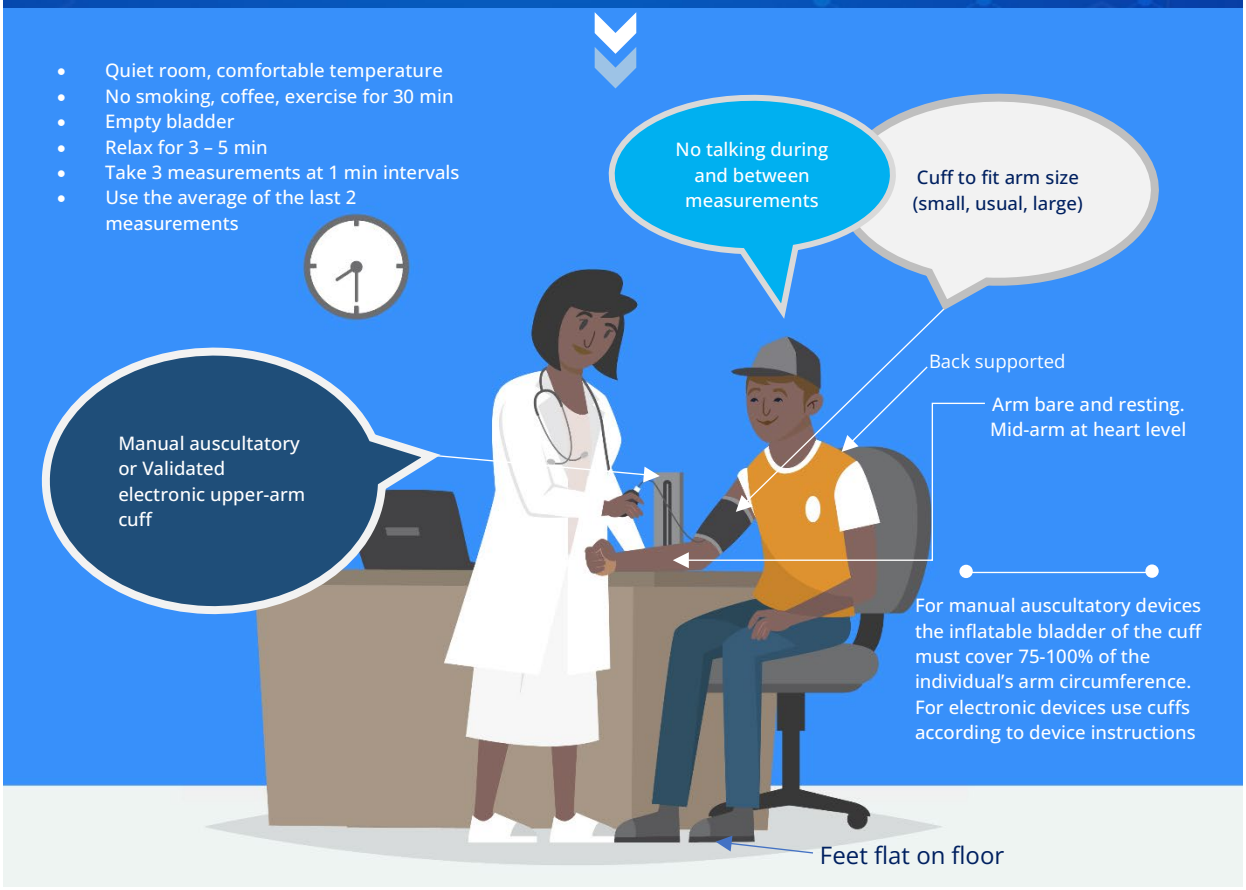
If the first BP reading is higher than 140/90, repeat it again after 1-2 minutes and take the average of the second and third readings

When using a mercury sphygmomanometer, record Phase I (hearing of the first sound) as the systolic blood pressure (SBP) and Phase V (disappearance of the sound) as the diastolic blood pressure (DBP)

If using a digital machine, the rhythm of the radial pulse (whether it is regular or irregular) should also be assessed by palpation

For patients with an irregular pulse (without prior diagnosis), alert physician or refer to next level of care after BP measurement

Figure 1: Ideal positioning and conditions for accurate blood measurement



Making a diagnosis of Hypertension

- A diagnosis of Hypertension is made when there are 2 consecutive readings of systolic blood pressure ≥140mmHg and/or diastolic blood pressure ≥90mmHg on two visits 1 – 4 weeks apart or **on two separate measurements taken 1 hour apart.**
- Hypertension may also be diagnosed in the setting of a single BP reading with systolic blood pressure ≥ 160mmHg or diastolic blood pressure ≥100mmHg.

Table 1 below illustrates the classification of hypertension according to the World Health Organisation (WHO).

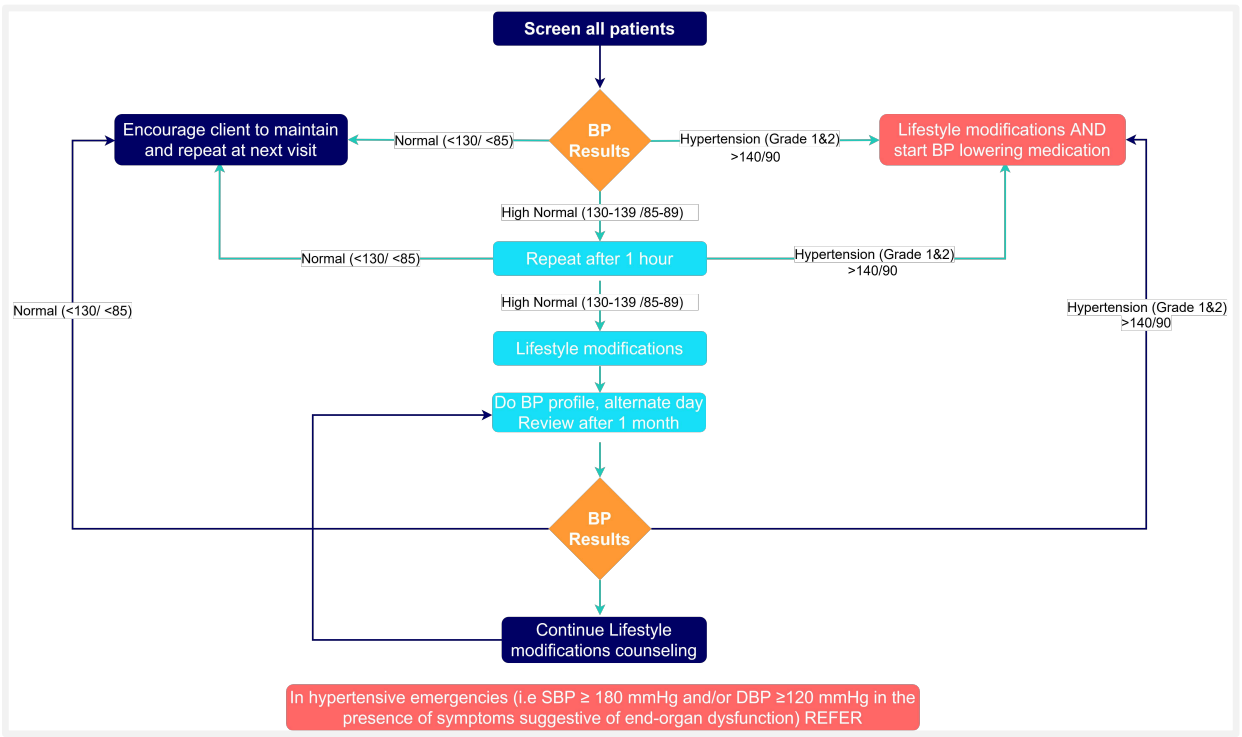
Table 1: Classification of Hypertension (WHO)

Category	Systolic BP (mmHg)		Diastolic BP (mmHg)
Normal BP	< 130	and	< 85
High-normal BP	130 - 139	and/or	85 – 89
Grade 1 hypertension	140 - 159	and/or	90 – 99
Grade 2 hypertension	≥ 160	and/or	≥ 100

If the SBP and DBP readings fall into different categories, the higher category should be used to classify the hypertension (e.g. a BP of 130/100mmHg should be classified as grade 2 hypertension).

All clients must be screened for Hypertension and the screening algorithm shown in Figure 2 can be used to institute appropriate management.

Figure 2: Initial approach to screen and treat high blood pressure



Patients with Heart Failure must be referred to next level of care

For clients whose blood pressure reading is >130/85mmHg but <140/90mmHg, emphasis on lifestyle modification should be made and home BP measurements should be encouraged. BP control should be evaluated at every subsequent visit.

If BP is >140/90mmHg, screen the patient for comorbidities (i.e., kidney disease, diabetes mellitus, heart disease, history of stroke, history of myocardial infarction, dyslipidemia). Document comorbidities present. For all patients in this category, initiate pharmacological treatment *immediately* and continue counselling on lifestyle modification.

Lifestyle modifications are an integral component of managing hypertensive patients. Despite being on pharmacological treatment, lifestyle modifications should be discussed at each visit. Lifestyle modifications are described below under the section on treatment.

Physical Examination of a Hypertensive Patient

The following must be checked in a patient with Hypertension at each visit:

1. Body Mass Index (BMI) – Weight (kg) /Height^2 (m)

Table 2: BMI Chart

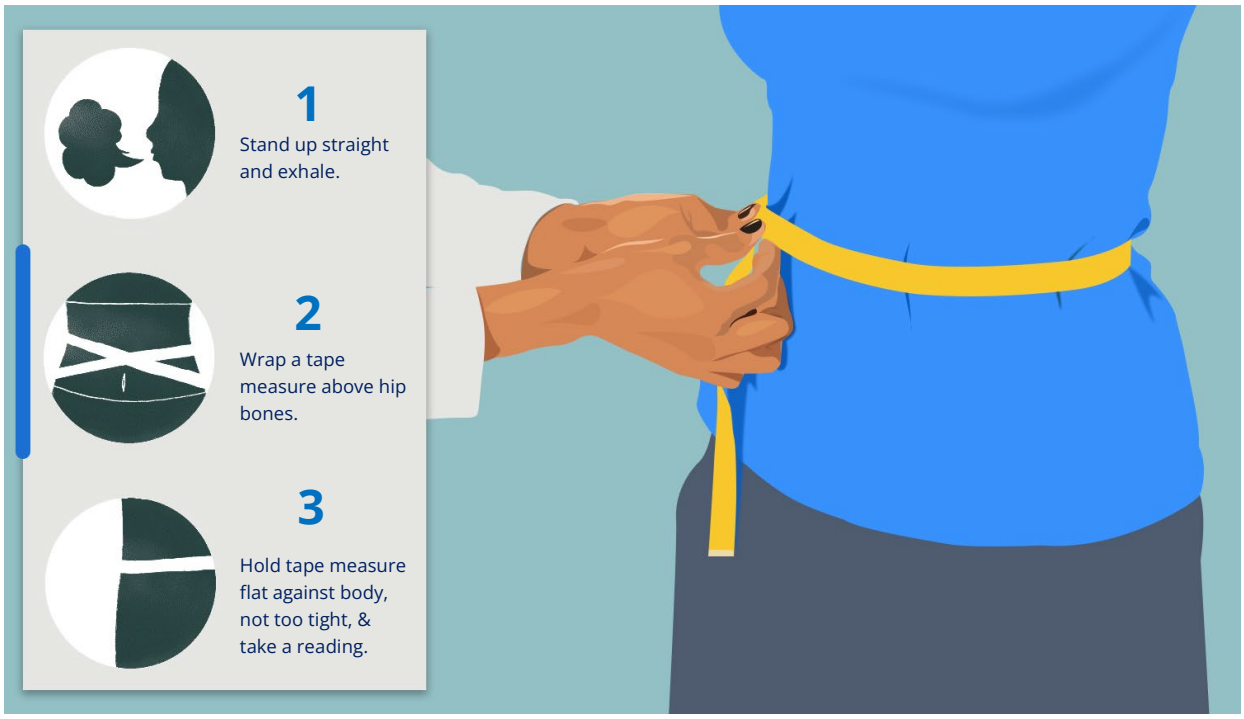
BMI	Classification
< 18.5	Underweight
18.5 – 24.9	Normal
25 - 29.9	Overweight
30 – 34.9	Obese
35 – 39.9	Severely Obese
≥ 40	Morbidly Obese

2. Waist circumference

Table 3: Waist Circumference chart

Health Risk	Women	Men
Normal	< 80cm	< 94cm
High risk	80 – 88cm	94 – 102cm
Very High risk	> 88cm	> 102 cm

Figure 3: How to measure waist circumference



3. Pulse rate and rhythm; look out for arrhythmias (irregular pulse).
   The normal heart rate in adults should be between 60 and 100 beats per minute at rest
4. Signs of Heart Failure (shortness of breath, difficulties in breathing while lying down, getting tired easily, limb swelling, abdominal distension)
5. Check distal pulses for diminished/ absent pulses that may indicate impaired flow
6. Discuss barriers to medication adherence such as drug stockouts, infrequent refills, side effects, and travel costs to the clinic

Investigations

It is also important that hypertensive patients are evaluated for hypertension- mediated end-organ damage by obtaining the following studies:

- Urinalysis, albumin to creatinine ratio (ACR) and Renal function tests (urea and creatinine)
- Dyslipidemia (Cholesterol, LDL, HDL, triglycerides)
- Random or fasting blood sugar to screen for Diabetes Mellitus
- Eye examination for visual impairment, if symptomatic
- ECG if patient has chest pain, suspected arrhythmia or heart failure symptoms

The table below lists recommended investigations and the frequency with which they may be ordered.

Table 4: Investigations in patients with Hypertension

First visit and six monthly* (if normal)	As indicated
FBC	ECG
Blood glucose (RBS, FBS if raised RBS reading)	ECHO
Serum Urea and Creatinine	CXR
Random Total Cholesterol (TC, TG, LDL-C, HDL*)	Electrolytes (potassium, sodium, etc.)
Urinalysis (blood, protein, glucose), UAlbumin: Creatinine Ratio (ACR)	

*If random profile is deranged, do a fasting profile

Treatment

LIFESTYLE MODIFICATIONS (Nonpharmacological Treatment) for high normal or true hypertension

This involves counselling and instituting lifestyle modifications. Further still, this must be continually discussed with clients at every visit, even those that are already on pharmacological treatment for hypertension.

Counselling should include empathic, client-centered discussions about:

- Diet modification
- Smoking and alcohol use
- The meaning and consequences of hypertension
- Patient needs and supports to ensure good adherence to therapy
- Myths regarding water therapy and other homeopathic remedies
- The use of conventional evidence-backed therapies
- Myths about drug therapy not perpetuating further treatment
- Dangers of intermittent adherence to treatment

Recommended for all patients:

Figure 4: Lifestyle Modifications guide

LIFESTYLE CHANGES THAT LOWER BLOOD PRESSURE

Adapted from ZAHESFO guidelines

- Stop all tobacco use and avoid passive tobacco smoke
- Eat a heart healthy diet (see table below)
- Eat a low sodium diet (No more than 1 teaspoon [6g] of table salt in a day including from salted snacks; No added salt at the table);
- Reduce consumption of saturated fats. Saturated fats are found in foods such as butter, palm oil, cheeses, chicken skins, sausage and most fried foods.
- Do stress-reducing activities such as mindful breathing exercises
- Avoid 'unhealthy' alcohol consumption. Unhealthy is more than 14 units per week (spread evenly) for both male and female
- Maintain optimal weight (refer to Table 2)
- Regular physical activity equivalent of brisk walk, 30 minutes daily for at least 5 days per week

Table 5: Alcohol recommendations (NICE)

Gender	Units/ week	Beer (4%)	Wine (12%)	Spirits (40%)
Male/Female	14	6 Pints	7 Glasses (175mls)	14 Glasses (25mls)

1 Unit = Strength (Alcohol by Volume) x Volume (ml) ÷ 1000

- **One unit of alcohol is equivalent to:**
- Half a pint of beer containing 3-4 percent alcohol by volume **(Pint500mls)**
- A small measure (25mls) of spirit containing 40 percent alcohol by volume
- Two-thirds of a125ml glass of average-strength (12%) **wine**; half a 175ml glass of average-strength (12%) **wine**; a third of a 250ml glass of average strength (12%) **wine**.
- In Zambia, a packet of Chibuku is equivalent to 2-3 pints of beer
- In Zambia, a 200 ml bottle of Kachasu is equivalent to 8 glasses of spirits

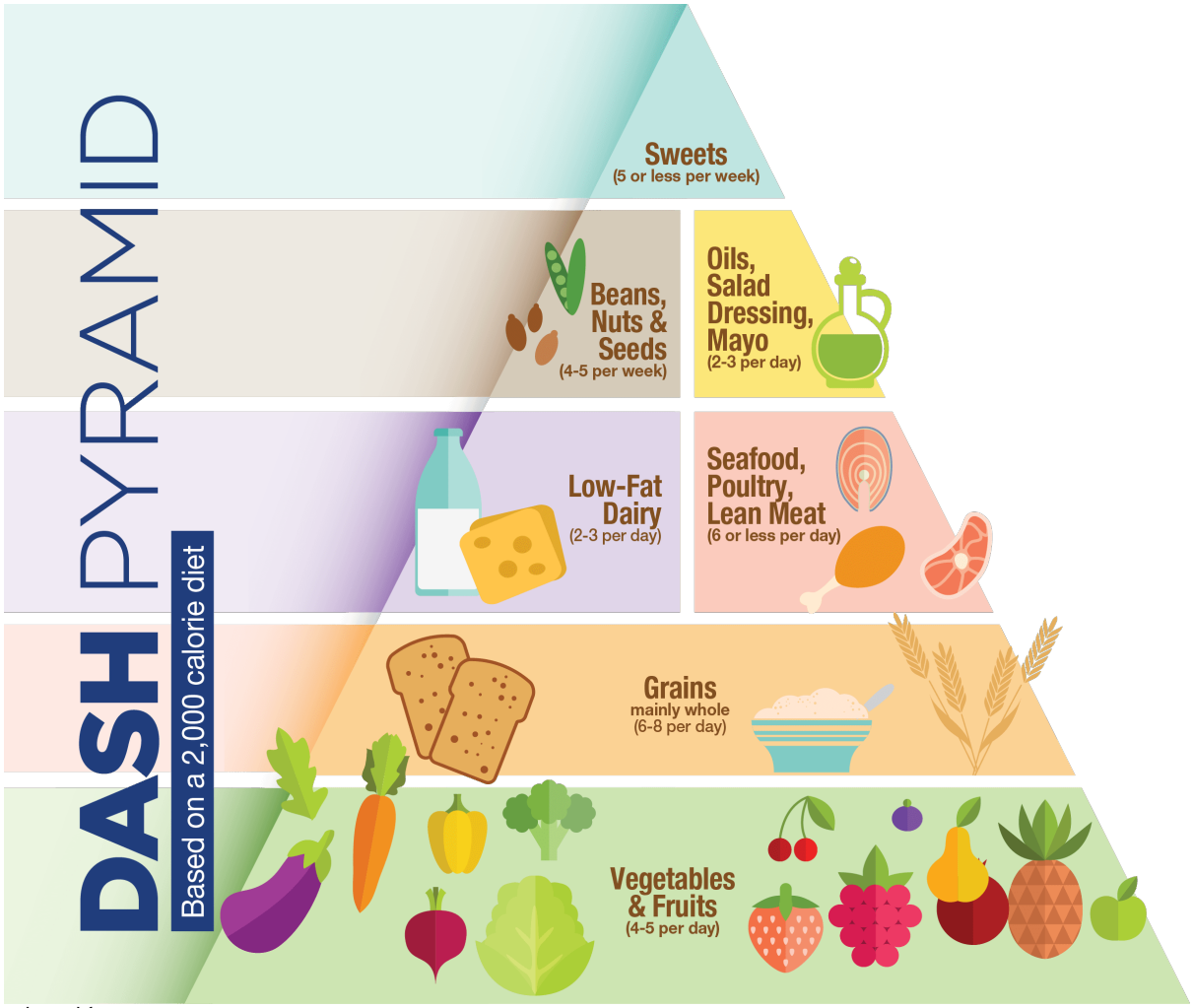
The table below outlines dietary changes hypertensive patients need to adjust to under lifestyle modifications.

Table 6: DASH Diet (i.e. Heart healthy diet) consider referral and input from nutritionist.

Avoid these	Encourage these
Total and saturated fat and trans fats (chicken skin, deep-fried foods, or "fast foods")	Lean protein (e.g. baked fish and chicken), fibre, whole grains, nuts
Fat dairy foods (cheese)	Fresh fruits and plenty vegetables (Eat ≥5 servings per day)
Red meats – limit to once per week	Potassium (bananas), calcium (dark green/ leafy vegetables), magnesium (spinach)
Sweets and sugared beverages (avoid cakes, sweets, and juices)	
Limit salt intake (No more than 1 teaspoon of salt in a day including snacks; No added salt at the table)	

For more information on foods and portion see Appendix

Figure 5: DASH Pyramid



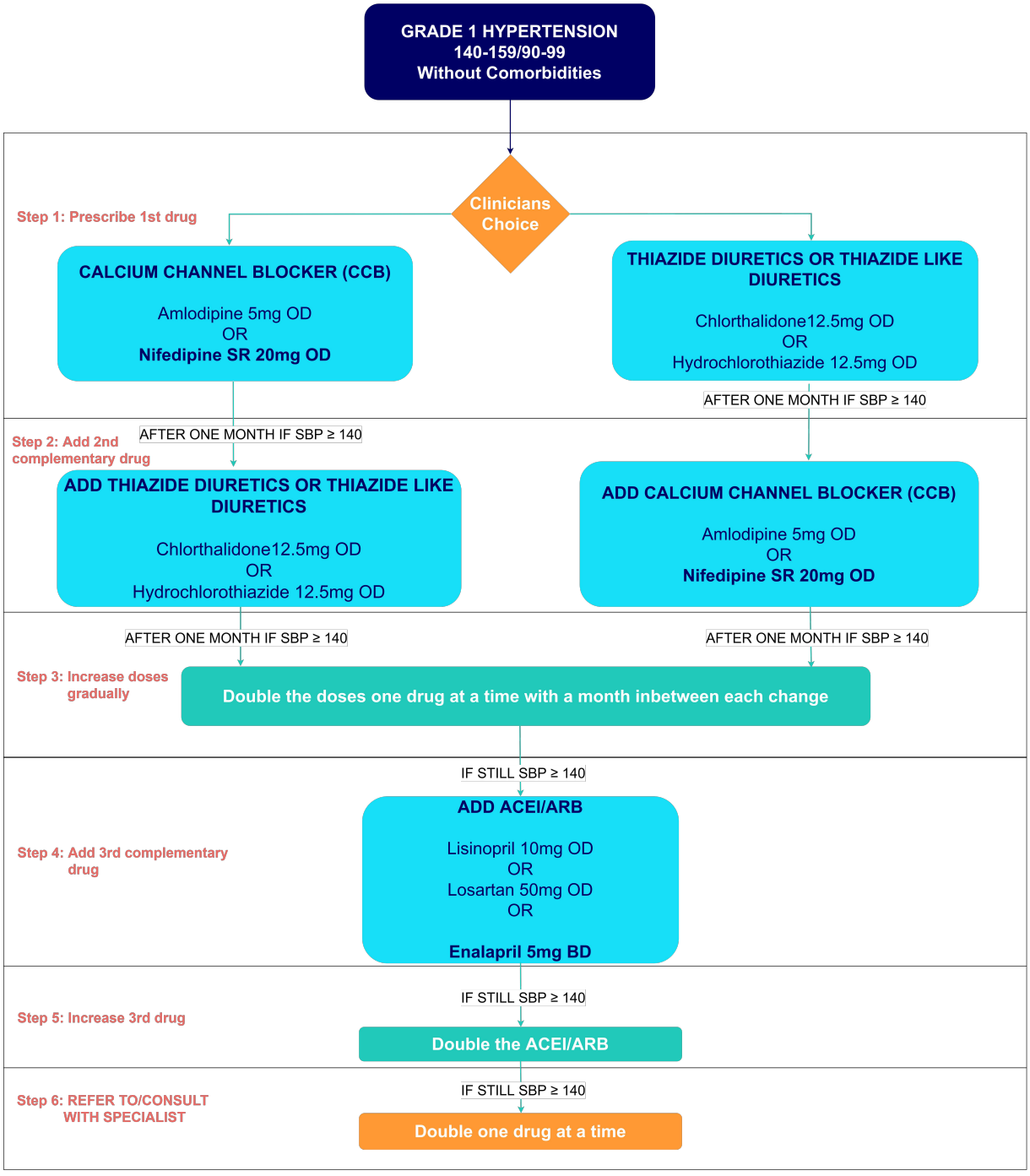
Adapted from SOMOs community care

Pharmacological Treatment of Hypertension

Guiding Principles

1. Stage 1 hypertension should be treated with monotherapy (1 agent)
2. Stage 2 hypertension should be treated with combination therapy (at least 2 complementary [i.e., different classes] agents)
3. Start with lowest dose, as it will have the fewest side effects.
4. Where combination therapy is indicated, single pill formulation are preferred to improve adherence.
5. In stage 1 hypertension, if BP remains elevated despite initial treatment, it is more effective and creates less side effects to add a second complementary drug (i.e., different class) before you increase the dose. Complementarity works well because hypertension is often caused by multiple overlapping mechanisms.
6. Use recommended agents for patients in specific scenarios (e.g. ACEI/ARBs for patients with kidney disease and/or who have diabetes)
7. When possible, use long acting medications (OD preferred over BD or TD) that are taken once a day to encourage good adherence
8. Strongly consider availability at your pharmacy and cost when prescribing

Figure 6: Stepped Care Approach for the Management of Stage 1 Hypertension in Adults ≥ 18 years without comorbidities in Zambia (i.e. kidney disease, coronary artery disease, and diabetes NOT PRESENT)



Note: Drug dosages indicated are initiation doses and may be titrated as needed

Repeat Renal function tests at least every three months OR at shorter intervals where indicated

Where single formulation Hydrochlorothiazide 12.5mg, Hydrochlorothiazide-amiloride can be used in its place as 1 tab.

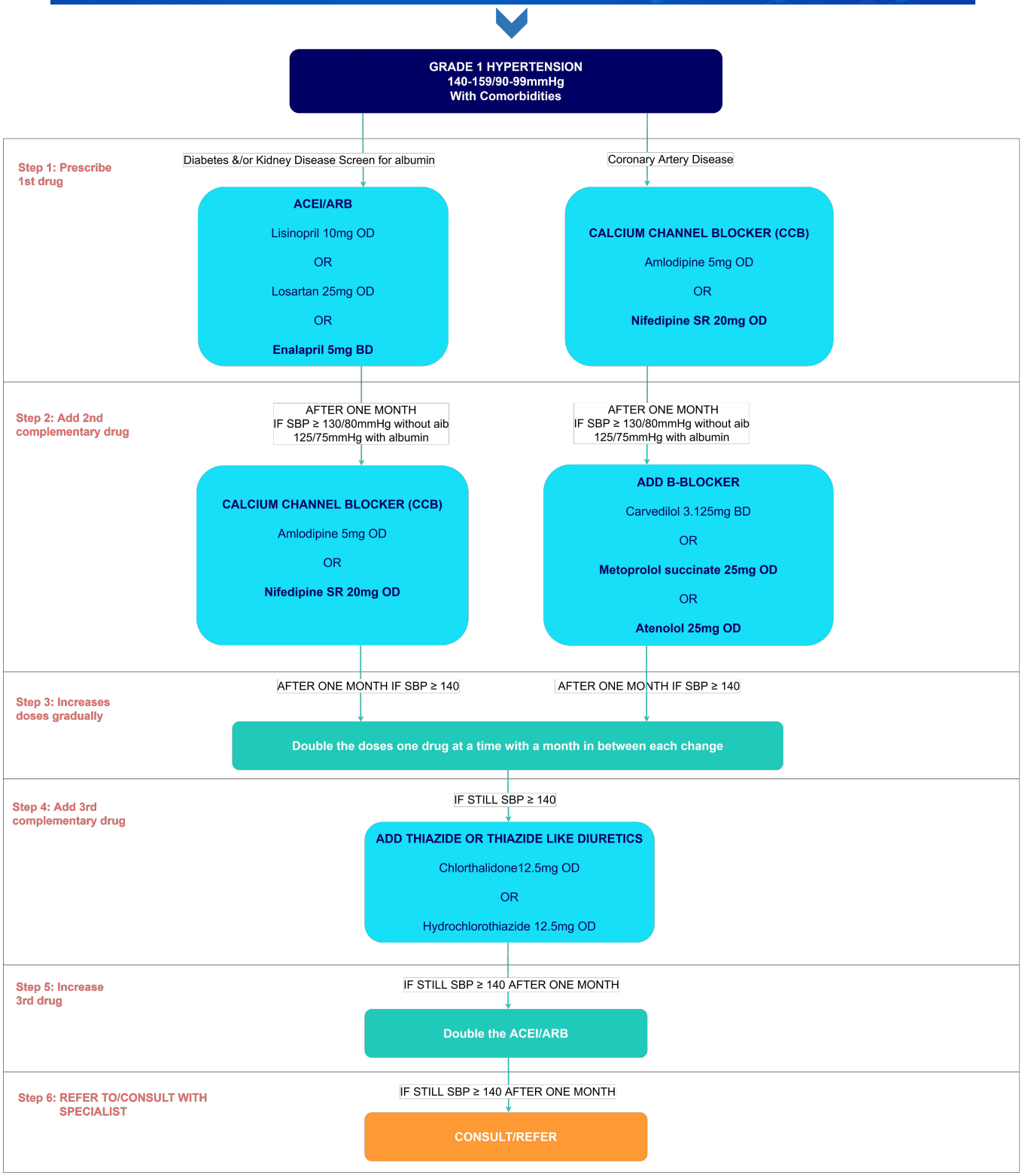
Comorbidities

The management of Hypertension may be altered in the setting of certain comorbidities. These include:

- Chronic Kidney Disease
- Diabetes Mellitus
- Stable Coronary Artery Disease (i.e. stable angina – chest pain brought on with exercise and relieved by rest). Suspected heart attack/ myocardial infarction should be referred emergently.

The algorithm in figure 7 gives recommended agents for specific comorbidities.

Figure 7: Stepped Care Approach for the Management of Stage 1 Hypertension in Adults ≥ 18 years without comorbidities (i.e. kidney disease, coronary artery disease, and diabetes NOT PRESENT)

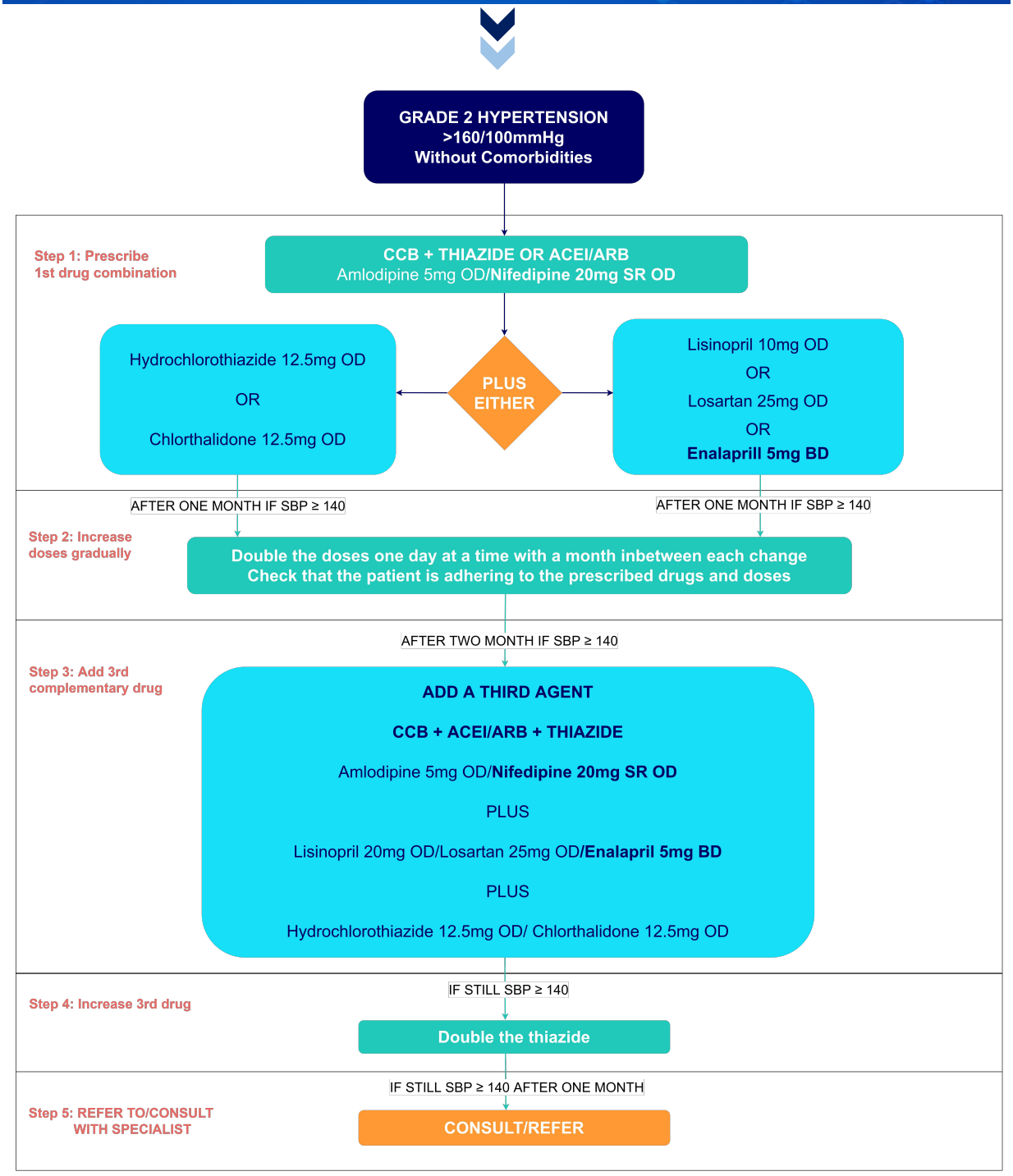


Repeat Renal function tests at least every three months OR at shorter intervals where indicated

Do not double the B Blocker if heart rate below 60 bpm

Where single formulation Hydrochlorothiazide 12.5mg, Hydrochlorothiazide-amiloride can be used in its place as 1 tab.

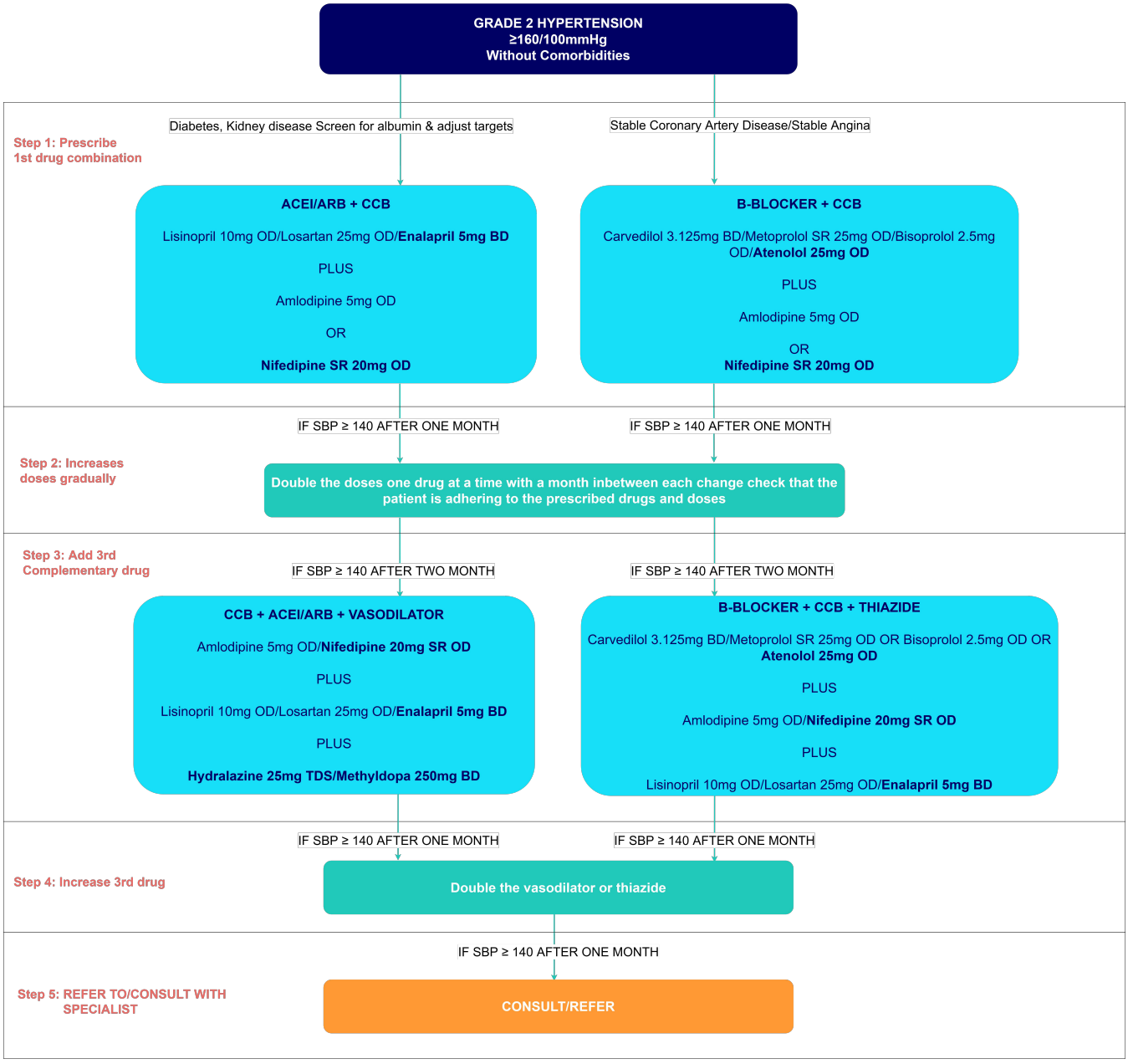
Figure 8: Stepped Care Approach for the Management of Stage 2 Hypertension in Adults ≥ 18 years without comorbidities (i.e. kidney disease, coronary artery disease, and diabetes NOT PRESENT)



Repeat Renal function tests at every visit OR at shorter intervals where indicated

Where single formulation Hydrochlorothiazide 12.5mg, Hydrochlorothiazide-amiloride can be used in its place as 1 tab.

Figure 9: Treatment Algorithm for the Management of Stage 2 Hypertension in Adults ≥ 18 years with comorbidities



Repeat Renal function tests at every visit OR at shorter intervals where indicated

Do not double the B Blocker if heart rate below 60 bpm

Where single formulation Hydrochlorothiazide 12.5mg, Hydrochlorothiazide-amiloride can be used in its place as 1 tab.

Table 7: Drug-Drug interactions with Antihypertensives

Antihypertensive	TDF/ TAF	AZT	3TC	FTC	EFV	NVP	DTG	LPV/ r	ATV/ r	DRV/r
Hydrochlorothiazide										
Amlodipine					↓	↓		↑	↑	↑
Enalapril					↓					
Bisoprolol*					↓			↑	↑	↑

*WHO Essential Medicines list includes atenolol, metoprolol, carvedilol as alternatives

	No interaction
	Potential Interaction with decreased level of sulfonyurea which may require dose adjustment of sulfonyureas
	Caution should be exercised as metformin levels are increased. Renal monitoring is recommended as PLHIV with renal insufficiency are at an increased risk of lactic acidosis due to increased metformin levels in DTG
↑	Increase in hypoglycaemic/antidiabetic agent
↓	Decrease in hypoglycemic/antidiabetic agent

Adapted from IAPAC guidelines

Table 8. Recommended blood pressure lowering agents for specific conditions

Compelling condition	Blood pressure lowering agent	Contraindications/ cautions	Evidence/ landmark trials
Diabetes mellitus	Angiotensin converting enzyme inhibitors (ACEi) Angiotensin II receptor blockers (ARB)	Obstructive lesions of the left ventricular outflow tract and arterial tree thereof. Including bilateral renal artery stenosis Pregnancy or child bearing potential without adequate contraception	Slows/ prevents progression to diabetic nephropathy and ESKD; Prevents and reduces albuminuria
Chronic Kidney Disease (CKD)	ACEi or ARB BP control typically requires combination therapy of a RAS blocker with either a Calcium channel blocker or a thiazide diuretic	Acute Kidney Injury and Acute on Chronic kidney Disease Hyperkalemia Pregnancy or child bearing potential without adequate contraception	RAS blockers are more effective at reducing albuminuria than other classes of BP lowering agents
	Loop diuretics	Pregnancy or child bearing potential without adequate contraception	Loop diuretics should replace thiazide/thiazide like diuretics when the eGFR falls below 30ml/min/1.73m^2
Coronary artery disease (CAD)/ Ischemic heart disease (IHD)	Beta blockers (Beta adrenergic receptor antagonists)	Hypotension Shock Heart block with symptomatic bradycardia Asthma Bronchospasm Uncontrolled heart failure (NYHA III/IV)	Antianginal e.g. Nebivolol Bisoprolol Metoprolol Carvedilol Atenolol
Heart failure with reduced ejection fraction (HFrEF)	Bisoprolol Metoprolol Carvedilol	As above	Improved long-term survival. US CARVEDILOL study, MERIT study, CIBIS study
	Angiotensin converting enzyme inhibitor or angiotensin receptor blocker		Improved long-term survival Myocardial reverse remodeling
	Calcium Channel Antagonists	Avoid in uncontrolled/ symptomatic Heart Failure	
Gout		Avoid use of thiazide diuretics	

Treatment Targets

The table below summarises key treatment targets for different age groups and comorbidities in the management of hypertension

Table 9: BP Targets by age, comorbidities

Age, Comorbidities	Target BP
18-55 years	<130 and <80 mmHg
56 – 79 years	<140 and <80 mmHg
80+ years	<140 and <90 mmHg
Any age with diabetes	<130 and <80 mmHg
Any age with CKD	<125 and <75 mmHg

Hypertensive Crisis

A hypertensive crisis is a medical emergency characterized by severely raised BP with or without end-organ injury. Hypertensive crises may be classified as hypertensive emergencies or hypertensive urgencies. Hypertensive emergencies are characterized by the presence of hypertensive mediated end organ damage (HMOD), whereas hypertensive urgencies are high BP without associated HMOD.

a. Hypertensive emergency

This is defined as BP ≥ 180/120mmHg with HMOD. Some examples of HMOD and their presenting symptoms include but are not limited to:

Table 10: Symptoms of Hypertensive EMERGENCY

HMOD	Symptoms
Pulmonary oedema	Difficulties in breathing, restlessness, cough, haemoptysis
Acute myocardial infarction/Heart Attack	Severe crushing chest pain radiating to left shoulder, inner aspect of left arm and jaw
Aortic dissection	Ripping pain in between the shoulder blades
Papilloedema	Blurred vision
Acute Kidney Injury (AKI)	Markedly reduced urine output or no urine at all, body swelling
Encephalopathy	Altered level of consciousness, confusion
Cerebral Vascular Accident (CVA)/ Stroke	Altered level of consciousness, loss of speech, weakness of limbs on one side of the body, numbness, facial weakness or droop (deviation of the mouth to one side of the face)

Early recognition and prompt referral are important in HMOD.

IMMEDIATELY REFER TO NEXT LEVEL OF CARE

b. Hypertensive urgency

This is defined as BP ≥ 180/120mmHg with no HMOD or no new deterioration of existing HMOD

Management

The short-term goal of management is to reduce the blood pressure to ≤160/≤100 mmHg. However, the pressure should not be lowered by more than 25 to 30 percent over the first 48 hours.

- Hydralazine oral 25mg (or IV 25mg) and re-assess in 30-60 minutes; if needed, ADD…
- Enalapril 5mg or lisinopril 20mg or other ACEi/ARB and re-assess in 1 hour; if needed, ADD…
- Amlodipine low dose 5mg

Other Conditions warranting referral

- Resistant hypertension
  - *Failure to control BP despite use of at least three blood pressure lowering agents of different (complementary) classes, one of which is a thiazide-like diuretic or when BP control is achieved but requires ≥ 4 agents.*

- Refractory Hypertension
  - *An elevated arterial blood pressure that remains above target levels despite the use of five (5) blood pressure lowering agents of different (complementary) classes, including a long-acting thiazide-type diuretic and a mineralocorticoid receptor antagonist*

- Heart Failure
- Hypertension in the young (< 35 years old)
- Suspected Secondary Hypertension (e.g. Thyroid gland disorders, Adrenal disorders, etc.)

Hypertensive disorders in Pregnancy

Key definitions

I. Chronic Hypertension (preexisting hypertension)

This is hypertension diagnosed

- before pregnancy or
- < 20 weeks gestational age or
- persistent after 12 weeks postnatal with BPs of ≥140/90mmHg taken on at least 2 occasions 4 hours apart. If the BP readings are severe (≥ 160/110mmHg) a diagnosis can be made 1 hour apart.

II. Gestational Hypertension

Gestational Hypertension encompasses Pregnancy Induced Hypertension (PIH) and Pre-eclampsia and is defined as: new onset of BP ≥ 140/90 mmHg at ≥ 20 weeks GA on at least two occasions at least 4 hours apart in a previously normotensive woman that resolves within 6 weeks postnatally.

A. Pregnancy induced Hypertension (PIH)

This is new onset of BP without proteinuria.

B. Pre-eclampsia

Raised BP ≥140/90 after 20 weeks gestational age on at least 2 occasions taken 4 hours apart in a previously normotensive woman with Proteinuria of ≥1+ OR end organ damage evidenced by one or more of the following:

- Low platelets (< $150x10^9$/L)
- Pulmonary oedema
- Visual disturbances
- Impaired liver function (elevated AST and ALT)
- Impaired serum creatinine

a) Mild Pre-eclampsia (now termed preeclampsia without severe features)

BP <160/110 mmHg with none of the severe symptoms such as headache, epigastric pain, visual disturbances or laboratory results showing low platelets, elevated liver enzymes, renal dysfunction

b) Severe Pre-eclampsia (now termed pre-eclampsia with severe features)

BP ≥ 160/110 mmHg and has one or more of the following severe features:

- Visual disturbance (i.e. scotomata, blurriness)
- Severe headache
- Epigastric and/or right upper quadrant pain
- Vomiting
- Liver tenderness
- Low platelets
- Elevated liver enzymes
- Elevated urea and creatinine
- HELLP syndrome (Haemolysis Elevated Liver enzymes Low Platelets)

c) Eclampsia

Generalized seizures in a patient with pre-eclampsia that cannot be attributed to any other causes.

d) Chronic hypertension with superimposed pre-eclampsia

New onset of proteinuria in a patient who previously had no proteinuria or an increase in proteinuria in a patient known to have proteinuria before pregnancy.

Treatment

The target BP is 135/85mmHg, reducing the BP below this target may lead to reduced utero-placental perfusion that may compromise the fetus.

I. Chronic Hypertension

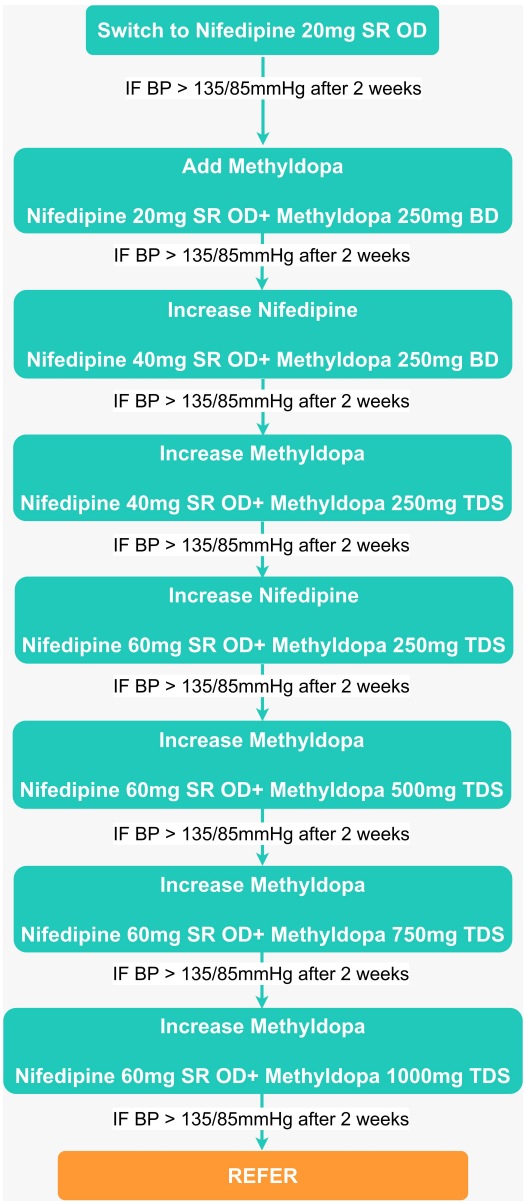
Care is best started preconception with revision of antihypertensives to stop any that are contraindicated in pregnancy such as thiazide diuretics, ACE inhibitors, ARBs and any others that are teratogenic.

Preconception

Switch to Nifedipine 20mg SR OD (up to 60mg SR OD) and review after two weeks

AVOID SHORT ACTING AGENTS

Figure 10: Management of Chronic Hypertension Preconception – Consider and Ensure Early referral



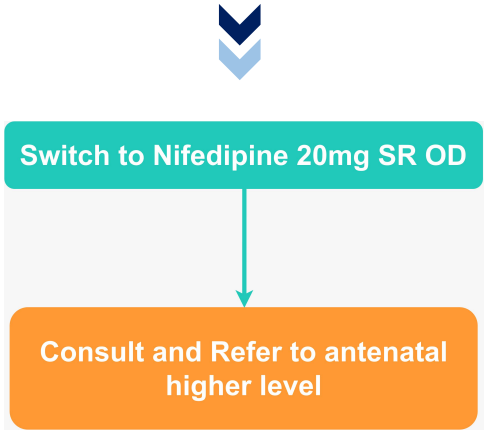
In Pregnancy

Start low dose aspirin at 75-150 mg once a day at 12 weeks gestation to prevent pre-eclampsia and stop at 34 weeks gestation (continued aspirin use beyond 34 weeks gestation may cause premature closure of the ductus arteriosus).

If the patient was not switched preconception then:
Switch to Nifedipine 20mg SR OD (up to 60mg SR OD) and review after two weeks (for a repeat BP reading).

AVOID SHORT ACTING AGENTS

Figure 11: Management of Chronic Hypertension in Pregnancy, earlier referral to antenatal higher level



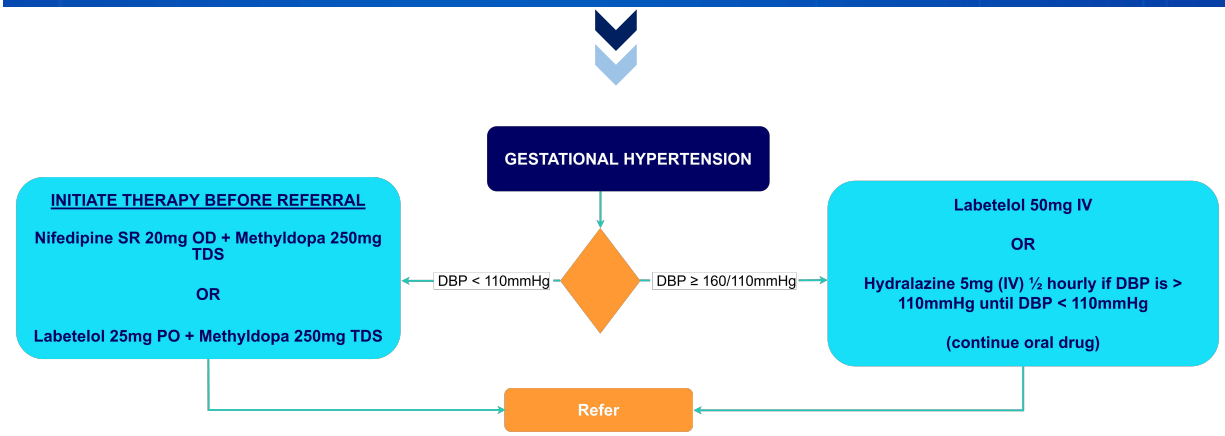
If patient cannot tolerate an agent, immediately switch to an alternative. Choices of BP lowering drugs in pregnancy may be restricted. For patients intolerant to Nifedipine, consider switch to oral labetalol 25mg.

Monitor renal function, and for signs and symptoms of pre-eclampsia/ eclampsia. Counsel on maintaining ideal weight, lifestyle modifications, and medication adherence and support.

II. Gestational Hypertension

Start Nifedipine or Labetalol and Methyldopa if DBP < 110mmHg, if BPs remain uncontrolled (> than the target of 135/85mmHg) or ≥160/110mmHg, refer to higher-level centre.

Figure 12: Management of Gestational Hypertension – Pregnancy Induced Hypertension – Refer EARLY



All patients with BP ≥160/110mmHg should be admitted and given prereferral intravenous blood pressure lowering therapy in addition to the oral agents.

- Hydralazine 5mg (IV) ½ hourly if DBP is greater/equal to 110mmHg until DBP less than 110mmHg.
- Labetalol is the desired first-line if available: give 20mg IV over 2mins then repeat after 10 minutes until target BP is reached to a maximum dose of 300mg.

Preeclampsia or Eclampsia

Refer immediately to higher centre but start antihypertensives and Magnesium sulfate ($MgSO_4$).

- For BP targets and doses of antihypertensives, please see above
- Use the Pritchard regimen for administration of $MgSO_4$:
  - Give loading dose of 14g as 4g IV diluted to 20% by using a 20 ml syringe:
    - Draw 4g of $MgSO_4$ 50% (8mL), then add 12mL water (or saline) for injection to the same syringe to make a 20% solution and administer the solution IV over 5-20 minutes.
    - Then give 5g of 50% solution IM mixed with 1ml of 2% lignocaine in a 20mL syringe into each gluteus/buttock (total 10g).
    - Then give a maintenance dose of 5g IM every 4 hours if the patient is still awaiting transport for referral
  - Give maintenance dose of $MgSO_4$: Give 5g of $MgSO_4$ as a 50% solution, together with 1mL of 2% lignocaine in the same syringe, by deep IM injection into alternate buttocks every 4 hours.
  - Before giving every does of $MgSO_4$, check that the RR > 12 breaths/minute and urine output is > 100ml/4hours or ≥30mL/hour over 4 hours and patellar reflexes are present. Hold or delay drug if any of these parameters are abnormal.
  - In case of RESPIRATORY ARREST, call for help, assist ventilation with mask and bag and give calcium gluconate 1g (10mL of 10% solution IV slowly).
  - If convulsions recur after 15 minutes, give 2g of $MgSO_4$ as a 20% solution by IV over 5 minutes

Investigations

Table 11: Laboratory investigations for Hypertensive disorders in pregnancy

At first presentation	At subsequent visits
FBC	Urinalysis
Renal Function Tests	FBC
Liver Function Tests	Renal function Tests
Obstetric Ultrasound	Liver Function Tests
Random Blood Sugar	
Lipid Profile	

Follow up

Antenatal visit intervals should be individualized for Chronic HTN and Gestational HTN without proteinuria, depending on the response to treatment.

All Pre-eclampsia and Eclampsia should be referred to an appropriate level of care.

Diabetes Mellitus

2.0

2.0 Diabetes Mellitus

WHO defines Diabetes as a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious damage to the heart, blood vessels, eyes, kidneys and nerves.

For PLHIV on ART, some anti-retroviral medications (i.e., ARVs) increase insulin resistance and, consequently, can contribute to increased risk for diabetes mellitus.

Prediabetes

This is defined as blood sugar levels that are higher than the normal range but not yet high enough to be diagnosed as diabetes (i.e. a glycosylated hemoglobin or "HbA1c," of 5.7%–6.4% or fasting blood sugar of 5.5–6.9mmol/L). Glycosylated hemoglobin (HbA1c) is a measure of the degree to which circulating red blood cells are coated with glucose molecules. It is expressed as a percentage and normally should be less than 5.5%. The higher level of glucose seen in diabetes correlates with a greater extent of red cell surface coating during its life span of 120 days. This is reflected as an HbA1c greater than 5.5%.

Prediabetes encompasses impaired glucose tolerance (IGT) or impaired fasting glucose (IFG). It is important to note that before a person develops type 2 diabetes, they almost always have "prediabetes" and this condition puts one at a higher risk for developing type 2 diabetes and cardiovascular disease. Prediabetes has no clear symptoms and therefore one may have it and not know it. Prediabetes is reversible with lifestyle modification. If a person is found to have prediabetes, they should be checked for type 2 diabetes every one to two years.

Classification of Diabetes Mellitus

Diabetes may be classified as shown in the table below:

Table 12: Classification of Diabetes Mellitus

Type	Description
Type 1 Diabetes	Resulting from an absolute lack of Insulin; onset is usually in childhood or early adulthood
Type 2 Diabetes	Results from insulin resistance or relative lack of insulin; commonly associated with being overweight or obese
Gestational diabetes mellitus	Diabetes first diagnosed in the second or third trimester of pregnancy that is not preexisting type 1 or type 2 and usually resolves after child delivery

For PLHIV, pre-diabetes and Type 2 Diabetes are the most common conditions encountered in the clinic. The following **risk factors** for Type 2 Diabetes can give a clue about when to suspect it in PLHIV:

- Overweight/ obesity (i.e., BMI ≥ 25 kg/m^2)
- Physical inactivity
- First-degree relative with diabetes (i.e., parent or sibling)
- History of gestational diabetes
- History of high blood pressure, dyslipidemia, or heart disease

Symptomatology

- Polyuria (Passing a lot of urine)
- Nocturia (Passing a lot of urine several times at night)
- Polydipsia (Excessive thirst)
- Polyphagia (Excessive eating, increased hunger/appetite)
- Loss of weight
- Fatigue
- Problems with the eyes or poor vision (double vision, blurred vision)

When and HOW to test

All adults attending the clinic should have a screening *Random* Blood Sugar (RBS; i.e., non-fasting or when fasting status is unknown) checked at every 3 or 6 monthly visits depending on their risk profile. In addition, any adult with one or more of the above symptoms should be tested.

Indications for screening every 3 months include one or more of the above **risk factors**. If the patient has none of the above risk factors and is <45 years old, screening can be done 6 monthly.

If RBS is greater than or equal to 11.1 mmol/L, this confirms diabetes.
If RBS is ≥7 but less than 11.1, further testing should be done for diabetes including: (a) a fasting blood sugar and (b) the HbA1C. These can be done the following day ideally.

If the RBS is <7, but the patient has symptoms or diabetes is suspected, a fasting blood sugar (FBS) and HbA1C should be done since RBS does not completely rule out the diagnosis of diabetes.

FBS should be ideally performed in the morning. HbA1C does not require fasting.

Making a Diagnosis

There are four (4) diagnostic tests which are recommended: fasting blood sugar, glucose tolerance testing, HbA1c and a random or post-prandial blood glucose.

WHO criteria for the diagnosis of diabetes are:

- Fasting plasma glucose ≥7.0 mmol/L (126 mg/dL)
- Random glucose ≥11.1 mmol/L (200 mg/dL)
- HbA1c ≥ 6.5%

Glucose tolerance testing is only required for borderline cases and for diagnosis of gestational diabetes.

Table 13: Diagnostic test for Diabetes Mellitus

	Fasting Blood Sugar	Random Blood Sugar	HbA1c
Normal	< 5.5mmol/L (126mg/dL)	< 7.7mmol/L* (200mg/dL)	4 – 5.7 %
Prediabetes	5.6 – 6.9 mmol/L (100 – 125mg/dL)	7.8 – 11.0mmol/l (140 – 199mg/dL)	5.7 – 6.4%
Diabetes	≥ 7mmol/L (126mg/dL)	≥ 11.1mmol/L (200mg/dL)	≥ 6.5%

* Not ideal for diagnosis but can be used when other tests are not available

Physical Examination of a Diabetic Patient

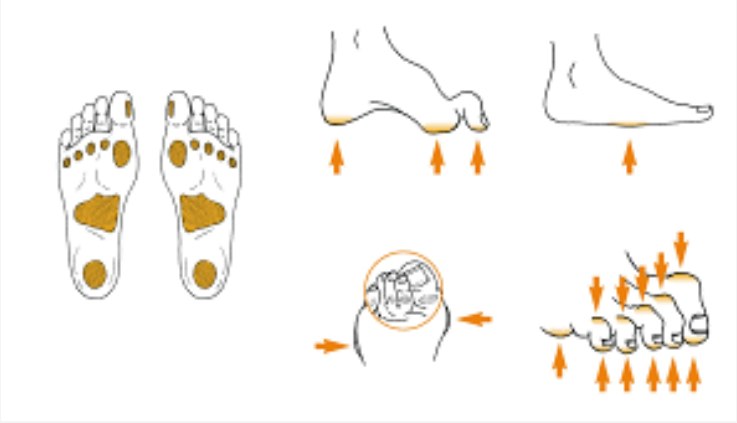
The following must be checked in a patient with Diabetes at each visit:

- Body Mass Index (BMI) - BMI (Weight kg/Height m^2)

Table 14: BMI chart

BMI	Classification
< 18.5	Underweight
18.5 – 24.9	Normal
25 – 29.9	Overweight
30 – 34.9	Obese
35 – 39.9	Severely Obese
≥ 40	Morbidly Obese

- Blood Pressure – target of 120–130/70-80 mmHg
- Peripheral pulses
- Heart exam for murmurs, gallops, or displaced point of maximum impulse
- Neurologic exam, including sensation, strength, and reflexes (for clinicians)
- Foot Inspection for skin break down or wounds:
  - In between toes
  - Pressure points



- Check the eyesight using a Snellen chart
- Urinalysis

Investigations

The table below (Table 15) lists and categorizes important laboratory investigations that must be done on patients with DM.

Table 15: Laboratory investigations for a patient with DM

First visit	At every visit	3-6 months	Every year	As indicated
Blood Sugar (FBS, RBS)	Blood Sugar (FBS, RBS)	HbA1c*	HbA1c*	ECG
Urinalysis	Urinalysis	Urinalysis		ECHO
FBC			FBC	
Serum Urea and Creatinine			Serum Urea and Creatinine	
Random Lipid Profile (TC, TG, LDL-C, HDL-C)		Fasting Lipid profile**	Random Lipid Profile (TC, TG, LDL-C, HDL-C)	

*HbA1c can be checked 3 monthly in patients whose therapy has changed or who are not meeting glucose control goals.
** If random lipid profile abnormal

Lifestyle modifications (Non-pharmacological Treatment)

Maintaining a healthy diet and regular exercise are essential components of the management of diabetes.

Lifestyle modifications must continually be discussed with clients at every visit, even for those that are already on drug treatment or therapy for hypertension. Weight loss through healthy diet changes and physical activity can improve many aspects of type 2 diabetes, including glucose control and high blood pressure.

Refer to Figure 4 and Table 5.

Diabetic diet

This is a diet that is low in fat, refined sugars/ carbohydrates, and calories but nutritious. Meals anchor on moderate amounts, eating at regular times and rich in fruits, vegetable and whole grains.

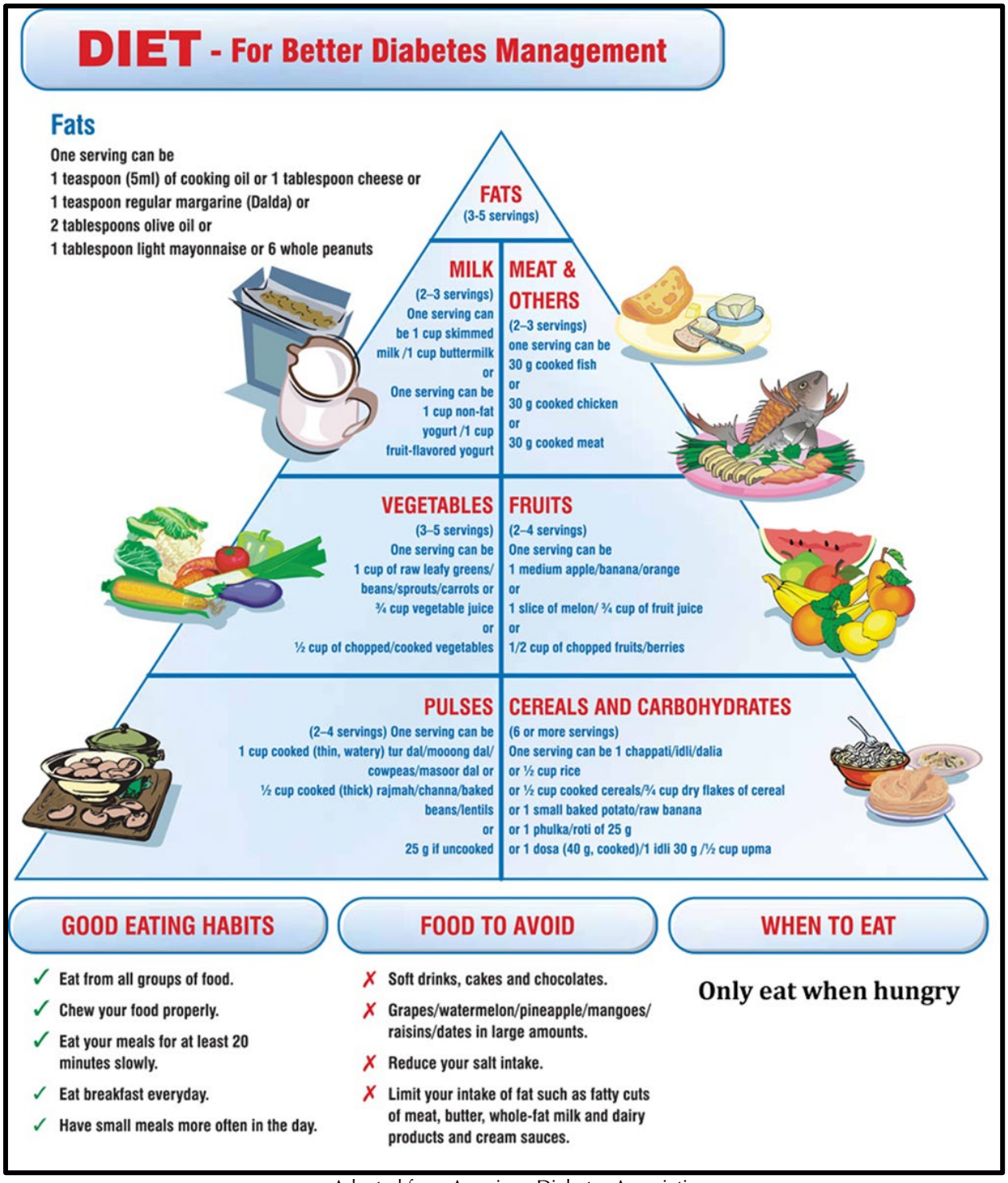
Recommended foods include:

- Roller meal nshima – Mugaiwa (not breakfast meal)
- Healthy carbohydrates (whole grains, beans/ legumes, low-fat dairy products like low-fat yogurt)
- Fibre-rich foods (vegetables, fruits, nuts, beans/ legumes, whole grains)
- Baked heart-healthy fish which are high in omega-3 fatty acids (like bream or salmon)
- Good fats (avocados, nuts, canola, olive and peanut oils)

The following foods must be avoided:

- Saturated fats (high-fat dairy products, animal proteins such as sausage, butter, bacon)
- Trans fats (found in processed snacks, baked goods)
- Cholesterol (high-fat dairy products and high fat animal proteins, egg yolks, liver)
- Sodium (aim for less than 2 teaspoons of salt a day in all foods)
- Refined carbohydrates (such as added sugar, sweets and candies, and sugary drinks)

Figure 13: Diabetic Diet



Adapted from American Diabetes Association

Pharmacological Management of Diabetes

There are three main drugs recommended for the management of Diabetes:

1st line:

Metformin is recommended as initial treatment

- **Contraindicated** in: chronic kidney disease, acute kidney injury, active tuberculosis, severe reduced liver function, acute cardiac insufficiency/ decompensated congestive heart failure, alcohol abuse, history of lactic acidosis
- **Metformin should be discontinued during acute illness** such as during pneumonia, severe infection, dehydration/ acute kidney injury, or myocardial infarction/ heart attack

2nd line:

Sulfonylures

- Gliclazide (second generation sulfonylurea) can be used as first-line if metformin is contraindicated or not tolerated.
- Glimepiride can also be used in addition to metformin.
- Glibenclamide
    - Not good for the elderly and has the risk of hypoglycaemia

3nd line:

Insulin

- Should be prescribed by a physician
- For patients with symptoms (e.g., weight loss)
- For patients with severe hyperglycaemia or poorly controlled hyperglycaemia despite oral agents
    - Fasting blood glucose13.9mmol/L [250 mg/dL]
    - Random blood sugar consistently > 16.7 mmol/L [300 mg/dL] HbA1c >9% [74.9 mmol/mol]
    - Not good for the elderly and has the risk of hypoglycaemia

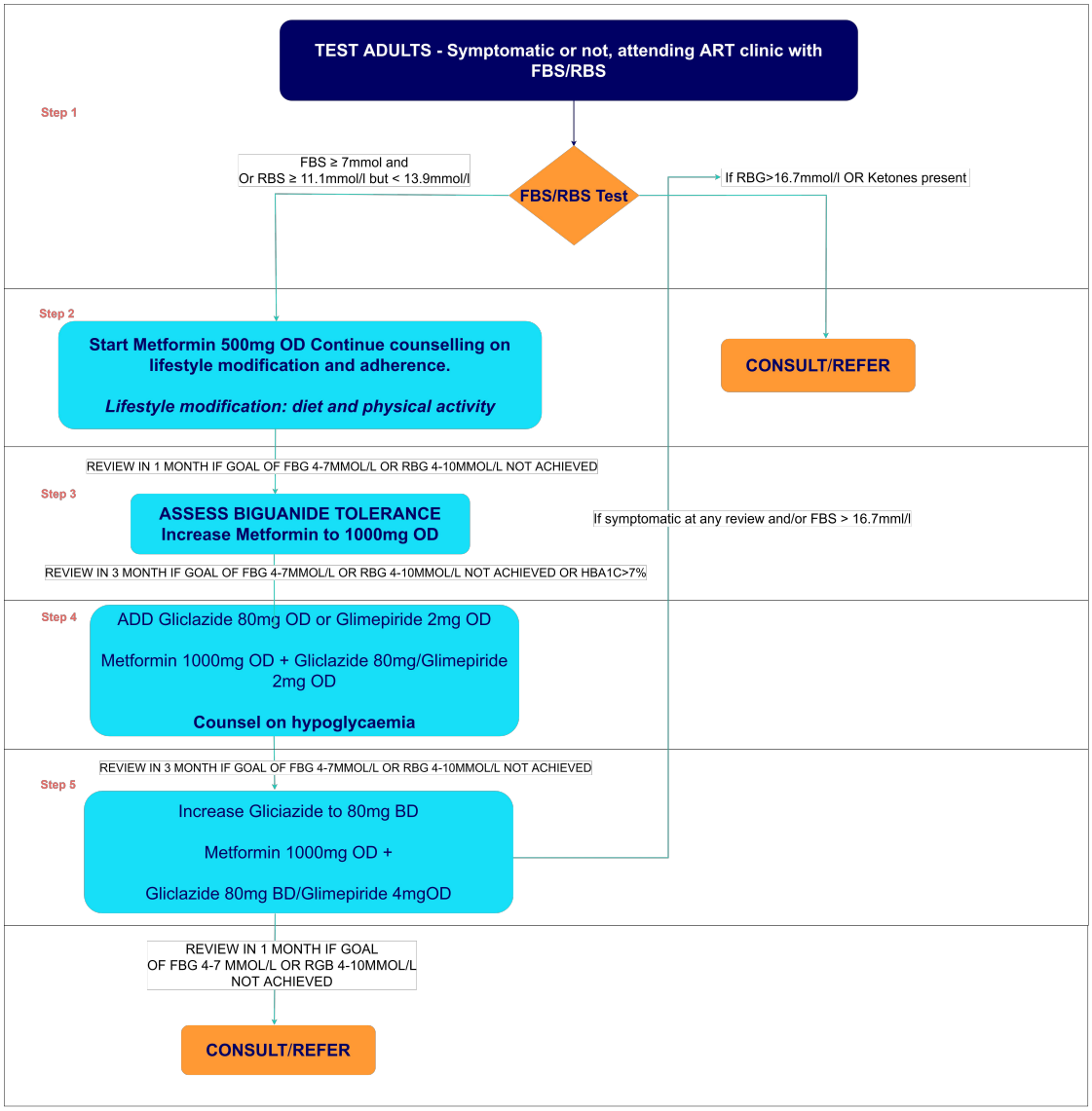
Practical management of diabetes

All patients with diabetes require advice about diet and lifestyle. Lifestyle changes (i.e., controlling weight, stopping smoking and alcohol consumption, and taking regular exercise), can prevent or delay the onset of type 2 diabetes in people with glucose intolerance. Good glycaemic control is unlikely to be achieved with insulin or oral therapy when diet is neglected, especially when the patient is also overweight. Regular exercise helps to control weight and reduces cardiovascular risk. Blood pressure control is vital using an angiotensin converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB).

Other practical recommendations:

- Provide counselling around lifestyle changes, including diet, physical activity and smoking cessation at every visit
- Initiate diabetes self-management education to reinforce treatment goals.
- Prescribe low-dose aspirin (81 mg) and statin (see section below) for diabetic patients with CVD.
- Measure blood pressure at every visit.
- Treat as per hypertension protocol if ≥130/80 mmHg.
- Measure weight and calculate BMI at every visit.
- Take HbA1c measurements every three to six months; every six months if stable on unchanging treatment.
- Arrange fasting lipid panel annually if available.
- Conduct foot exam for foot ulcers or peripheral neuropathy annually, or every visit if high-risk.
- Conduct annual urine protein dipstick (microalbuminuria dipstick or urine albumin to creatinine ratio) and serum creatinine measurement (GFR calculation) for CKD screening.
    - CKD is defined by GFR<60 ml/min/1.73 m^2 OR the presence of moderate or severe albuminuria (albumin-creatinine ratio ≥30 mg/mmol).
    - Refer for retinal exam every two years

Figure 14: Treatment Algorithm for Type 2 DM



DO NOT prescribe metformin over 1000mg OD in patients on dolutegravir (DTG)

For diabetic emergencies:

- Blood Glucose > 18mmol
- Unconscious diabetic patients on hypoglycemic agents and/or blood glucose < 2.8mmol
- Sever infection and/or foot ulcers
- Recent sudden deterioration in vision

Repeat Renal function two weeks after initiation

If Goals are not achieved, REFER for Cpeptide to be done

Treatment GOALS

FBS 4 to 7mmol/L

RBG 4 to 10mmol/L

HbA1c (3 monthly) 4 to 7%

Dolutegravir (DTG in "TLD") significantly increases Metformin plasma levels. It is recommended that dose adjustments of Metformin be considered to maintain optimal glycemic control when patients are starting/stopping DTG while taking Metformin.

- In patients taking DTG who are starting Metformin, begin with low Metformin dose (500 mg once daily) and titrate up carefully.
- **The recommended dose limit of Metformin in PLHIV on DTG is 1000 mg daily.** If patient is already on Metformin and initiating DTG, monitor glucose and HbA1c, and look out for Metformin adverse effects and adjust dose as necessary.
- Fasting lipid profile should be evaluated at baseline for all PLHIV, then annually if baseline screening is normal.

Table 16: Drug-Drug interactions

Oral hypoglycemic agents	TDF/ TAF	AZT	3TC	FTC	EFV	NVP	DTG	LPV/r	ATV/r	DRV/r
Metformin							↑			
Glibenclamide					↓	↓		↓	↓	↓
Glipizide					↓			↓	↓	↓
Gliquidone					↓			↓	↓	↓
Gliclazide					↓			↓	↓	↓
Glimepiride					↓			↓	↓	↓

	No interaction
	Potential Interaction with decreased level of sulfonyurea which may require dose adjustment of sulfonylureas
	Caution should be exercised as metformin levels are increased. Renal monitoring is recommended as PLHIV with renal insufficiency are at an increased risk of lactic acidosis due to increased metformin levels in DTG
↑	Increase in hypoglycaemic/antidiabetic agent
↓	Decrease in hypoglycemic/antidiabetic agent

Adapted from IAPAC guidelines

Late onset type 1 DM (LADA)

There are some forms of diabetes that may not fit into Type 1 or type 2. **Referral for physician evaluation** and measurement of C peptide is warranted in patients who are not achieving glycaemic control after three months of review and are adhering to drugs and lifestyle modification.

Monitoring of glycaemic control

Glycated haemoglobin (HbA1c) is recommended for monitoring glycaemic control. However, if not available the following options can be used:

- FBS (not less than 8 hours after a meal)
- Postprandial blood glucose (2 hours after a meal)
- Glucose profile with several 2 hours postprandial measurements over several days (N.B. Blood glucose done less than 2hrs after a meal will offer no clinically useful information)

Treatment Targets

Glycaemic control in diabetes is important for preventing complications and improving the quality of life for patients. The table below highlights the treatment targets for tests that can be used to monitor glycaemic control

Table 17: Treatment Targets in the management of DM

HbA1C	< 7%	3 – 6 monthly
FBS	< 7.0mmol/L	Every visit
Random Blood Sugar	< 11.1mmol/L	Every visit

Follow up

It should be noted that some patients may require more frequent monitoring and reviews accordingly to their clinical status. The guideline below should serve only as a checklist.

At each visit

- Review of self-monitoring results (glucose profile)
- Review current medications
- Review injection techniques (if taking insulin)
- Talk about targets and change where necessary
- Continued education, including lifestyle modification
- Review eating habits
- Measure weight and body mass index
- Measure blood pressure
- Test urine for protein
- Check condition of feet, pulses and neurologic exam
- Talk about any general or specific problems

Checked at least once a year

- Biochemical assessment of metabolic control (e.g. HbA1c)
- Measure plasma lipids (Total cholesterol)
- Measure visual acuity
- Refer for eye examinations (ophthalmoscope or retinal photo)
- Test blood for renal function (creatinine, eGFR)
- Refer to physician or kidney specialist for microalbuminuria or elevated creatinine

Control blood pressure

It is imperative that blood pressure is controlled in patients with diabetes to reduce the risk of CVD and other complications. This control usually requires dual therapy of thiazide diuretics and ACE inhibitors to get to a target BP of <130/80mmHg.

Control blood lipids

Dyslipidemia must be controlled to further reduce the risk of CVDs. This is fostered by a healthy lifestyle centering on diet and physical activity. In some cases, medication such as statins may be used for optimal care.

Table 18: Summary Table of Management Steps

STEP	KEY MESSAGE
LIFESTYLE MODIFICATION	⇒ Advise overweight patients to reduce weight ⇒ Advise all patients to practice regular daily physical activity
ORAL HYPOGLYCEMICS	⇒ Give metformin for type 2 not controlled by lifestyle modifications ⇒ Titrate metformin to target glucose levels (FBS <7mmol/l; HbA1c<7%) ⇒ Give a sulfonylurea to patients with contraindications to metformin or if metformin does not improve glycemic control
CARDIOVASCULAR CARE	⇒ Give antihypertensives for those with BP > 130/80mmHg ⇒ Give a statin to all with type 2 DM and dyslipidemia or known CVD ⇒ Stop smoking
FOOT CARE	⇒ Give advice on foot hygiene, nail cutting, treatment of calluses, appropriate protective footwear ♦ Avoid walking barefoot or without socks ♦ Wash feet in lukewarm water and dry well especially between toes ♦ Do not cut calluses or corns ♦ Look at your feet everyday and if you see a problem or an injury, go to your healthcare worker ⇒ Assess feet using simple methods (inspection, pin-prick sensation, and peripheral circulation assessment by palpation of pedal pulses)
EYE CARE	⇒ Check visual acuity annually ⇒ When available, use direct fundoscopy through dilated pupils to assess retinopathy ⇒ Referral is needed
REFERRAL	⇒ FBS >14mmol/l or HbA1c >9% despite maximal doses of metformin and sulfonylurea ⇒ Newly diagnosed DM and urine ketones ≥2+ ⇒ Severe infection and/or foot ulcers ⇒ Recent deterioration in vision ⇒ Gestational diabetes ⇒ BP ≥130/80mmHg despite treatment with 2 BP lowering agents
FOLLOW UP	⇒ At visit coinciding with HIV care

Adapted from IAPAC guidelines

Optimizing Medication Adherence

These steps must be reinforced at every visit and may be done by treatment supporters/ community health workers, nurse, pharmacy technician or pharmacist in addition to the clinician:

- Explain the diagnosis of diabetes.
- Inform patient of the complications of untreated diabetes.
- Discuss the possible symptoms of diabetes.
- Review with the patient the appropriate dose of all medications, particularly if there is a risk of hypoglycaemia (e.g., with sulfonylureas, insulin).
- Prescribe once-daily medications and longer-lasting supplies of medicine whenever possible (i.e., 3-month multi-month dispensing).
- Explain potential adverse effects of the medications and what to do if the patient experiences them.
- Explain how many times a day the patient should take the medication and at what time(s), and adopt the following simple steps to help them adhere to the guidelines:

    - Label and package the tablets.
    - Check the patient's understanding before the patient leaves the health facility.
    - Ask about who can be a treatment supporter at home or in their community

- Explain to the patient how important it is to:

    - Keep an adequate supply of medications safely at home.
    - Take the medicines regularly as advised, even if there are no symptoms.
    - Provide tools such as pill boxes and medication logs to help patients remember to take their medications.
    - Assess adherence and discuss barriers at every visit.
    - Reconcile clinician's medication list with patient's list, adjust dose, and eliminate unneeded medications.

Complications

All patients with diabetes are at risk for disabling long-term complications. It is important to prevent complications of Diabetes Mellitus. These complications, though not exhaustive, include:

1. Hypoglycaemia
2. Hyperglycaemic emergencies
3. Diabetic Foot
4. Diabetic Eye disease
5. Diabetic kidney disease
6. Diabetic Neuropathy
7. Coronary Heart Disease

1. Hypoglycaemia

Hypolglycaemia is abnormally low sugar defined as a blood glucose of <3.5 mmol/L. It is potentially life-threatening and patients with DM on blood glucose lowering treatment must be aware of symptoms and signs of hypoglycaemia and what measures to take. Symptoms and signs of hypoglycaemia include:

- Headache
- Hunger
- Irritability
- Anxiety
- Paresthesia
- Palpitations
- Sweating
- Trembling
- Confusion
- Seizures
- Coma

Management of hypoglycaemia

Self-management

Hypoglycaemia is a common symptom in diabetics taking medication and they should therefore be alert to it. It should be managed immediately by the ingestion of glucose (oral carbohydrate or a sugar sweetened soft drink or 1-2 teaspoons of sugar or 5-6 sweets) if the patient can swallow. This should be followed by a small meal. Patients are therefore advised to carry sweets or a snack on them at all times.

If the patient is unconscious and unable to eat or drink, **refer to a higher level**. If managing patient while awaiting referral, administer glucagon as an intramuscular injection 1mg. If glucagon is unavailable, give dextrose intravenously, which can be administered as 20 – 50ml of 50% dextrose over 1-3 minutes or 250ml of 10% dextrose as an infusion.

Risk factors for hypoglycaemia must be discussed with the patient and include (but are not limited to):

- skipping meals
- intense physical activity
- alcohol ingestion
- wrong dose of diabetes medication

2. Hyperglycaemic emergencies

Hyperglycaemic emergencies include Diabetic Ketoacidosis (DKA) and Hyperosmolar hyperglycaemic state (HHS) which are both life threatening complications of DM. DKA is uncommon in patients with type 2 diabetes mellitus but can occur. Symptoms and Signs of DKA and HHS include:

- Nausea
- Vomiting
- Abdominal pain
- In severe cases, Kussmauls breathing, which is deep rapid breathing (an indication that the body or organs have become too acidic).
- Dehydration
- Stupor or coma

Table 19: Biochemical characteristics of DKA and HHS

	DKA	HHS
Blood glucose level	≥ 13.9 mmol/L	≥ 33.3 mmol/L
Urine ketones	Positive	Negative (weakly positive)

Hyperglycaemic emergencies must urgently be **referred to the next level of care** and managed in a hospital setting with close monitoring and correction of dehydration and electrolyte imbalance and glycemic control with insulin. Infuse normal saline during transportation to the next level of care at a rate of 1L in first 2 hours then 1L 4 hourly thereafter.

What to do immediately:

I. Admit to Emergency room or Acute bay of the facility
II. Assess Airway, Breathing, and Circulation (ABC)
III. Establish IV access

Refer to Appendix for further management

3. Diabetic foot

This term refers to diabetic foot ulcer and diabetic foot infections. Patients with diabetes are at increased risk of foot ulceration, as well as infectious complications such as cellulitis, osteomyelitis, or gangrene. This is largely due to diabetic neuropathy which renders them insensitive to injury at high pressure points that in turn leads to ulcers from trauma or inappropriate foot wear. Compromised blood flow due to accelerated atherosclerosis leads to ischaemia, poor wound healing and may require amputation.

Other risk factors that contribute to the development of foot ulcers include poor glycaemic control, cigarette smoking, diabetic nephropathy and previous foot ulcerations or amputations.

Conduct foot exam at every visit:

1) Check peripheral pulses (Dorsalis Pedis at the base of the big toe; Posterior Tibial behind medial malleolus)
2) Check for gangrene
3) Check for ulcers on the plantar (bottom) aspect of the foot
4) Conduct light touch test for tactile sensation using your fingers or a light piece of cotton wool or gauze swab. This should be done on the first, third and fifth toes for 1-2 seconds with the patients' eyes closed and responding by saying "yes" to when they feel the touch. When light touch is not sensed in two or more sites, there is loss of protective sensation (LOPS)
5) Check for joint, toe, or other tissue deformity
6) Check for callus
7) Check for Fungal Infections of the foot and toenail

At each visit, patients must be counselled to avoid foot complications. Encourage patients to:

- Inspect their feet daily by checking for cuts, blisters, swelling, nail colour changes, or skin colour changes
- Bathe feet daily and use lukewarm water and never hot water.
- Bathe feet gently using soft sponge or washcloth and ensure the feet are dry between the toes
- Moisturise the feet (not between the toes) to avoid dry and cracking skin
- Cut nails carefully and not too short. This is so that ingrown toenails are avoided.
- Seek medical attention early for corns and calluses. Do not try to cut them at home.
- Check your shoes for small stones or objects that may injure your feet without you feeling them.
- Wear appropriate shoes that are not too tight nor too loose.
- Do not walk barefoot
- Keep your diabetes under control
- Stop smoking (for cigarette smokers)
- Ensure your health care provider examines your feet regularly

A trained professional will need to provide treatment for pre-ulcerative lesions by:

- Removing calluses
- Draining and protection of blisters
- Treat ingrown and thickened toe nails
- Provide antifungal treatment for fungal infections—topical antifungal creams for skin infections of the foot (i.e., tinea pedis) or oral antifungal medications for severe toe nail infections (i.e., onychomycosis)

Active diabetic foot problems must be referred to higher level of care and managed in a multidisciplinary manner for the best outcome and prevention of amputations. Urgent referral must be instituted in the following cases:

- Infected ulcer
- Spreading infection
- Critical limb ischaemia
- Gangrene
- Suspicion of acute arthropathy
- Unexplained red swollen foot

4. Diabetic eye disease

Diabetic eye disease refers to retinopathy and other vision threatening conditions such as cataract and glaucoma. Diabetic retinopathy is the leading cause of blindness in adults worldwide. Patients with diabetic retinopathy may be asymptomatic in the early stages, but the condition will cause vision loss when advanced. Diagnosis often needs specialist services that examine the retina by ophthalmoscopy, slit lamp bio microscopy or retinal fundus photography.

Screening for diabetic retinopathy can be done by testing for visual acuity and, in advanced centres, by ophthalmoscopy and fundus photography.

Patients reporting vision loss at any visit who have not had a retinal examination in the past two years should be referred to an ophthalmologist.

Good control of blood sugar levels, blood pressure and dyslipidemia can slow the progression of diabetic retinopathy.

5. Diabetic kidney disease

Diabetic kidney disease is defined by albuminuria and/or a decreased estimated glomerular filtration rate (eGFR). Risk factors include poor glycaemic control, elevated blood pressure and/or genetic susceptibility.

Early signs include elevated blood pressure and proteinuria of trace or 1+ on urinalysis. Oedema will usually occur at late stages.

Diagnosis is made with:

- Presence of albuminuria in at least two urine samples, 1 to 3 months apart
- eGFR of <60mL/min per 1.73m^2 on at least 2 occasions, 1 to 3 months apart and/OR

Patients with diabetes must be screened at each visit with a urinalysis or a urine microalbumin: creatinine ratio to check for proteinuria.

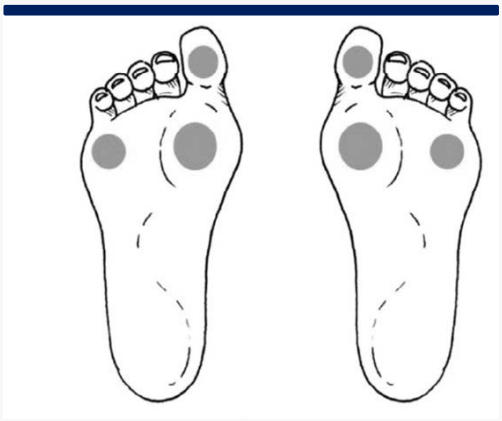
Delaying the onset and progression of diabetic kidney disease can be achieved by:

- Good glycaemic control (HbA1C < 7%)
- Maintaining BP at <130/80mmHg with an ACEi or ARB as the first-line anti-hypertensive agent for diabetics
- Modifying other major CVD risk factors (e.g., dyslipidemia, smoking cessation)

6. Diabetic neuropathy

Diabetic neuropathy is a group of conditions that result from nerve damage in patients with diabetes. These include:

- Peripheral neuropathy (sensory) which leads to loss of protective sensation and then, over time, foot ulcers from repeated soft tissue injury. Risk factors for this are duration of diabetes, poor glycaemic control and age. Symptoms include unsteadiness, loss of sensation, pain/ burning, tingling sensation and numbness. However, it can present without any symptoms. Diagnosis is made by the presence of two or more of sensory symptoms, decreased distal sensation in the feet/ legs and/or decreased or absent ankle reflexes



- Autonomic neuropathy may present as lack of awareness of hypoglycaemia, orthostatic hypotension, resting tachycardia, diarrhoea, constipation, fecal incontinence, erectile dysfunction, urinary incontinence and bladder dysfunction

Management of neuropathy centres around pain and glycemic control. Other causes of peripheral neuropathy must be excluded like from alcohol abuse, vitamin B12 deficiency, medications, renal disease, or HIV, to name a few.

Diabetes Mellitus in Pregnancy

Diabetes mellitus in pregnancy should be managed by obstetricians and physicians in a hospital setting. However, should such a patient present, immediate referral to a hospital for management with a multidisciplinary team after the acute problem is identified is warranted.

Diabetes in pregnancy is classified into

1. Pregestational (preexisting)
2. Gestational diabetes

Pregestational/preexisting diabetes mellitus

Type 1 or 2 diabetes diagnosed before pregnancy or diagnosed before the 20 weeks gestation.

Gestational Diabetes

The management of pregestational is divided into:

Preconception care

- Patient education and family planning to avoid unplanned pregnancy.
- Blood sugar control with the following targets:
  - FBS 5-7mmol/l;
  - RBS 4-7mmol/l and/or;
  - HbA1c <6.5%
- Foot care
- Adjustment and change of drugs to pregnancy friendly drugs:
  - Stop all oral drugs and substitute with insulin—n and to take 5mg Folic acid once a day. insulin remains the drug of choice for pregnant patients with diabetes.
  - For patients with type 2 diabetes on metformin monotherapy with good glycemic control, continue metformin through the first trimester and add insulin to achieve pregnancy glycemic goals as soon as pregnancy is confirmed.
  - Take 5mg Folic acid once a day to prevent neural tube defects (NTD)
- Stop Statins
- Stop and substitute ACE-is, ARBs if patient is hypertensive as these medications are teratogenic/ harmful to the fetus
- Encourage Lifestyle modifications
  - Continue known diabetic diet and weight control (BMI<27kg/m^2) and physical activity
- Early antenatal care – as soon as it is discovered that patient is pregnant

Prevention of complications

- Retinal assessment
- Renal assessment
- Early ultrasound scanning
- Patient education on delivery, analgesia and care for baby, changes in medication during and after delivery and contraception

Intrapartum care

- Blood sugar control (3 – 7mmol/L)
- Delivery in type 1 and 2 elective delivery by induction of labour or C-section if indicated between 37^{+0} and 38^{+6} gestational age.
- For gestational diabetes, deliver by 40^{+6} gestational age to avoid postdates.

Postpartum care

Emphasis is on blood sugar control

- Continue blood sugar monitoring as before pregnancy
- Interval postnatal care visits to be individualized
- Check sugar control 12 weeks postpartum using HbA1c and repeat as necessary.
- Review of medications, revert to the pre-pregnancy dosages.
- Lifestyle advice:
  - Weight control
  - Exercise
  - Dietary changes.
- Contraception

Gestational diabetes

Diagnosis of diabetes made during pregnancy after 20 weeks.
Always assess risk factors for gestational diabetes in the following women:

- BMI >30kg/m^2
- History of GDM in previous pregnancy
- History of macrosomic babies >4.0Kg
- Family history of diabetes
- Previous history of unexplained intrauterine fetal death
- Recurrent miscarriages

Diagnosis

- FBS of ≥5.6 mmol/l OR
- RBS of ≥7.8mmol/l 2 hours postprandial

Management

Lifestyle modification with nutritional therapy, physical activity and weight management

Pharmacological therapy if lifestyle modification does not achieve good glycemic control defined as FBS < 5.3mmol/l, 2 hours postprandial RBS of <6.7mmol/l 1 out of 3 or more times checked.

Start medication if a pregnant woman has a fasting blood sugar of > 7mmol/l. The options are insulin or oral antihyperglycemics such as Metformin and Glibenclamide or both.

Oral antihyperglycemic treatment

- Start Metformin 250mg BD
- Glibenclamide 5mg OD may be given when target is not achieved with Metformin or woman declines insulin.

Insulin treatment

- If glycemic control not achieved with metformin or patient presents with complications, refer as soon as possible.
- While awaiting referral, physician can give rapid-acting analogues (aspart and lispro), which are preferred to soluble insulin
  - Give Insulin 0.1U/kg SC short acting TDS with meals

Preexisting diabetes mellitus
Refer to a tertiary hospital for delivery and further management.

DYSLIPIDEMIA

3.0

3.0 DYSLIPIDEMIA

Dyslipidemia covers a broad spectrum of lipid abnormalities and has been well established as a CV risk factor. According to the WHO Global estimates of 2014, dyslipidemias contribute to one-third of ischemic heart disease and one-fifth of global cerebrovascular disease, equating to nearly 2.6 million deaths every year worldwide.

HIV-infected persons are at increased risk of cardiovascular disease and other non-communicable diseases, including cancers. This is in part because of the chronic immune activation that persists in HIV infection, even if a patient is on ART. Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population using the risk factors below:

- Older than 40 years
- Obesity
- Diabetes mellitus
- Known hypertension
- Kidney disease
- Waist circumference of >90 cm (women) and >110 cm (men)
- Family history of premature CVD or events
- Previous CV event like heart attack or stroke

HIV infection and some types of antiretroviral therapy (ART) can contribute to increased risk of cardiovascular disease in PLHIV. Depending on the ARVs used, ART may cause an increase in Low density lipoprotein cholesterol (LDL-C) and Triglycerides (TG), and, therefore, can increase Coronary Artery Disease (CAD) risk for PLHIV compared to comparable HIV-negative persons. Although lipoprotein metabolism is influenced to a lesser extent by newer integrase strand transfer inhibitors (INSTIs) and non-nucleoside reverse transcriptase inhibitors (NNRTIs), older protease inhibitors (PIs), like lopinavir-ritonavir, and some nucleoside reverse transcriptase inhibitors (NRTIs), like abacavir, may accelerate the onset of CAD-related events in persons with dyslipidemia and other cardiovascular risk factors.

Table 20: Dyslipidemia is defined by one or more of the following lipid levels:

Total Cholesterol (TC)	> 5.2 mmol/L
High density lipoprotein cholesterol (HDL-C)	< 1.0 mmol/L males <1.2 mmol/L females
Low density lipoprotein (LDL)	> 3.4 mmol/L
Triglycerides (TG)	> 1.7 mmol/L

The management of dyslipidemia has shifted away from treating dyslipidemia on its own and now focuses on managing dyslipidemia in the context of overall risk for CVD.

Measurement of Lipids

A standard lipid profile includes blood measurement of:

- Plasma or serum total cholesterol (TC)
- LDL-Cholesterol (LDL-C)
- HDL-Cholesterol (HDL-C)
- Triglycerides (TG)

Investigations

Table 21: Investigations in Dyslipidemia

First visit and 6 monthly	Subsequent visits	As indicated
Random lipid profile (TC, TG, LDL-C, HDL-C)	Blood Sugar (FBS, RBS)	ECG
Blood Sugar (FBS, RBS)	Urinalysis	ECHO
FBC		TSH
Urea and Creatinine		HbA1c
Urinalysis		
Liver enzymes (ALP, ALT)		

Risk Factors

Risk factors for dyslipidemias may be either modifiable or non-modifiable. Modifiable risks factors include:

- Smoking
- High saturated or trans fat diet
- Alcohol intake
- Physical inactivity
- Obesity

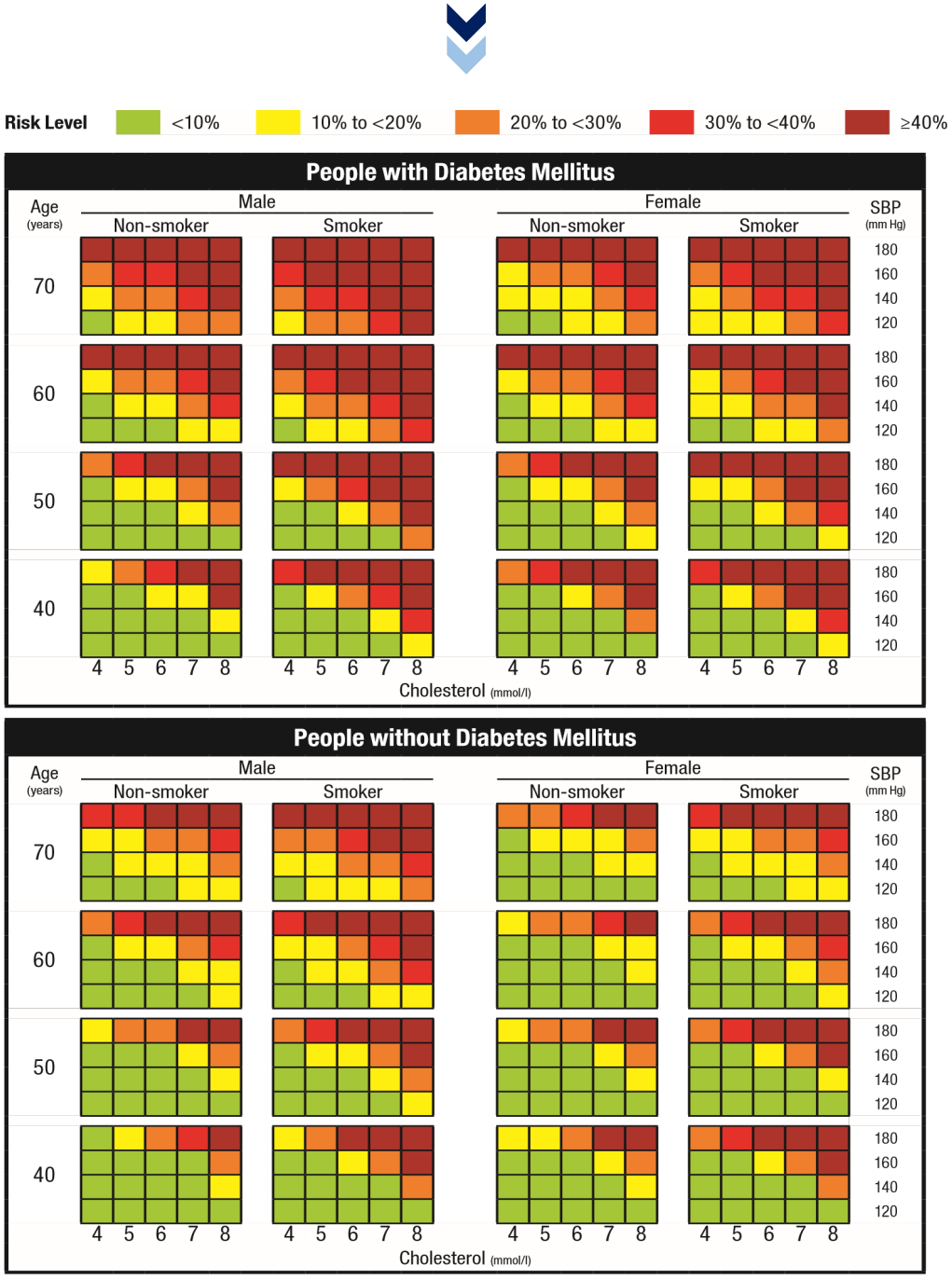
And non-modifiable risks include:

- Age (> 40 years, age is slightly lower than usual due to patients on ART being in a younger age group than those above 55 years)
- Genetic predisposition

Risk scoring

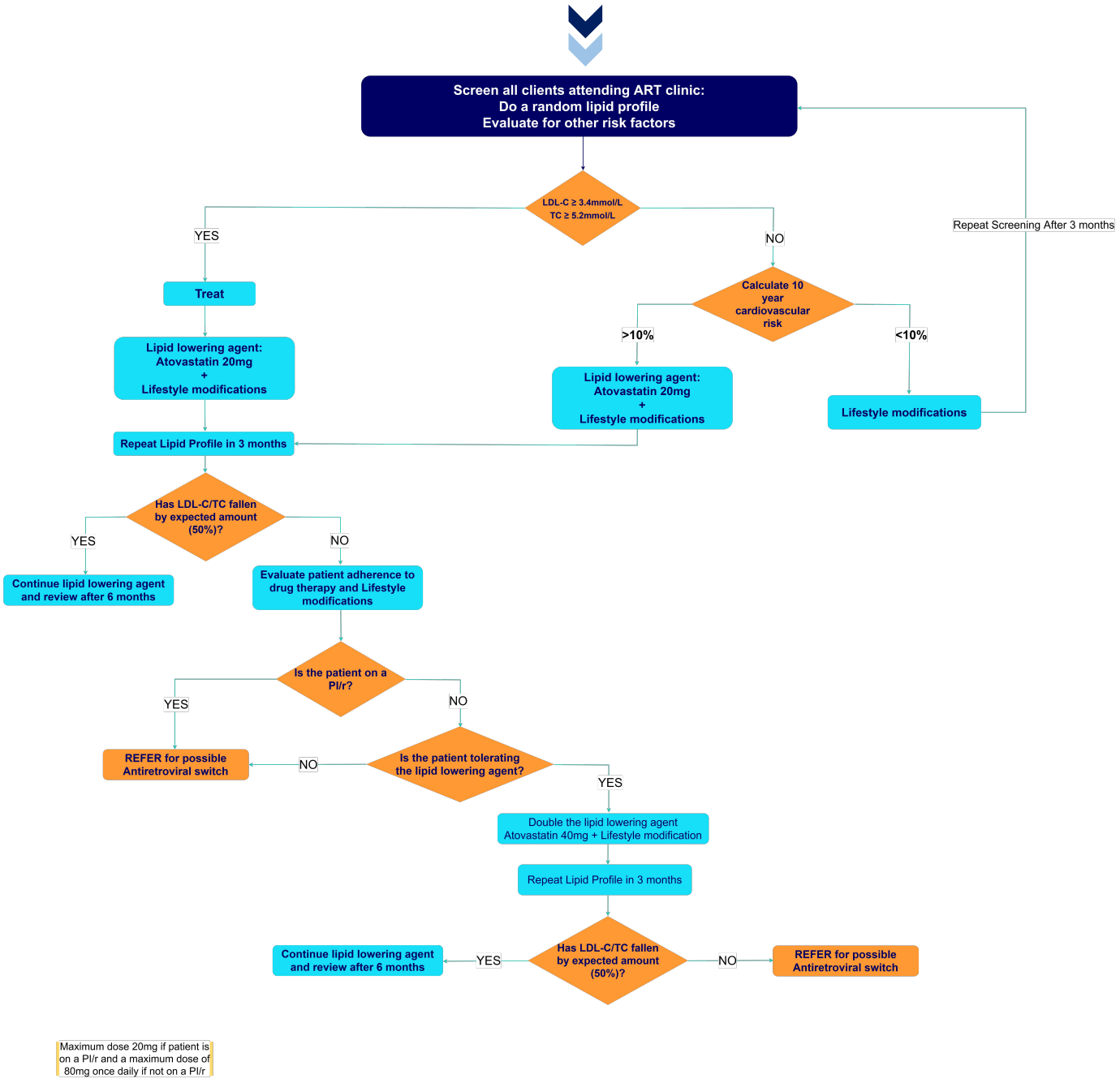
The WHO/ISH risk prediction chart can be used in settings where blood cholesterol can be measured. It provides an estimate of the 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, total blood cholesterol, smoking status and presence or absence of diabetes mellitus.

Figure 15: WHO/ISH prediction chart



Adapted from WHO ISH Prediction Charts

Figure 16: Management of Dyslipidemia



STEP 1

Lifestyle Changes/Modification

Therapeutic lifestyle changes (TLC) remains a critical component of health promotion and CVD risk reduction efforts both prior to and after commencement of lipid lowering therapies in all individuals. These measures should be promoted as a population-based strategy for prevention of CVD:

- Adhering to a healthy diet
- Regular exercise
- Avoidance of tobacco smoking
- Alcohol restriction
- Maintenance of an ideal weight

Refer to figure 4, 5 and table 6

STEP 2

Lipid Modifying Drugs

Most individuals at Low Risk (<10%) and Intermediate/Moderate Risk (10-20%) can be managed by lifestyle changes alone. Lipid modifying agents may be necessary to achieve target lipid levels in those at high and very high CVD risk and initiated simultaneously with lifestyle changes. In patients with comorbidities such as hypertension and diabetes, start a statin once dyslipidemia is detected.

Classes of Lipid modifying agents

Classes of Lipid modifying agents include:

- Statins
- Fibrates
- Niacin
- PSK 9
- Anion exchange resins
- Cholesterol Absorption Inhibitors

Statin therapy:

- Pravastatin has a good safety profile, has limited interaction with ART and is currently the longest used statin in these patients.
- Rosuvastatin is recommended if a greater reduction in LDL-C levels is needed.
- Lovastatin and Simvastatin are ***contraindicated*** in patients on a protease inhibitor (PI)
- Atorvastatin can be used at a lower dose especially in the presence of ART in combination with a booster in the form of cobicistat. This increases the effect of the atorvastatin.
- Statins are generally initiated at low dose in patients with HIV infection.
  - Atorvastatin: starting dose of 20mg OD
  - Pravastatin 40 mg OD
  - Rosuvastatin 10 mg OD

Allow at least 3 months before repeating fasting lipids and titrating the dose.

Monitoring for side effects is essential. Symptoms of muscle soreness or myopathy should prompt testing for elevated creatine kinase (CK) and liver enzymes, and should lead to holding of the statin until lab tests return or an alternative diagnosis is made.

Statin therapy is contraindicated in pregnancy and lactation. It should not be prescribed to women of reproductive age unless adequate contraception is taken. If pregnancy is planned, then statins should be discontinued.

If the patient is on an ARV known to cause or exacerbate dyslipidemia (primarily Lopinavir/ritonavir, LPV/r) then consider a single-drug substitution to a more lipid-friendly drug (such as from LPV/r to Darunavir/ritonavir or Atazanavir/ritonavir) as the treatment of choice before adding a lipid-lowering drug.

Once targets achieved can monitor lipids every 6-12 months.

Drug interactions

Integrase strand transfer inhibitors, like dolutegravir, are not known to have drug-drug interactions with statins (as shown in table 22).

Table 22: ARV-Statin interactions

Statin	TDF/TAF	AZT	3TC	FTC	EFV	NVP	DTG	LPV/r	ATV/r	DRV/r
Simvastatin					↓	↓				
Lovastatin					↓	↓				
Fluvastatin					↓				↑	
Pravastatin					↓				↑	↑
Atorvastatin					↓			↑	↑	↑
Pitavastatin									↑	

	No interaction
	Potential Interaction
	Contraindicated due to potential interaction for serious reactions such as risk of myopathy including rhabdomyolysis
↑	Potential decrease in statin drug level which may require an increased dose adjustment of statin
↓	Titrate dose of statin carefully and use lowest dose necessary

Adapted from IAPAC guidelines

Fibrate therapy

Elevated triglycerides are independently associated with cardiovascular risk. Fibrates, like fenofibrate, may be used initially to lower triglyceride levels in patients with significant cardiovascular risk and who have a triglyceride level >500 mg/dl. Fenofibrate (54 to 160 mg daily) is preferred because there is no significant interaction with ART.

Dyslipidemias in pregnancy

Statins are contraindicated in pregnancy and as such if a woman is intending to conceive or just discovered that she has conceived, ALL STATINS SHOULD BE SUSPENDED.

Care of women with known dyslipidemia should also be done in conjunction with their physicians.

Preconception Care

- Discuss the safety of pregnancy in the patient with their physician
- Advise optimisation of the dyslipidemia
- Lifestyle modification should be advised: weight management, physical activity, nutrition and to stop alcohol and smoking.

Dyslipidemia in pregnancy is associated with the following;

- Pre-eclampsia
- Preterm birth
- Gestational diabetes
- Off-spring are at a high risk of cardiovascular diseases

Management of Dyslipidemias in Pregnancy
Refer to next level of care

Risk factors for cardiovascular diseases

4.0

4.0 Risk factors for cardiovascular diseases

Tobacco use and smoking, unhealthy alcohol use, unhealthy diet and physical inactivity have been described as major risk factors for developing NCDs and in particular CVDs.

Tobacco Use and Smoking

WHO estimates that tobacco kills 8 million people each year with 7 million of these deaths attributable to direct tobacco use. Low and Middle income countries account for 80% of the world's tobacco use. MPOWER measures were developed to try and help reduce tobacco use and consists of:

Monitor tobacco use and prevention policies
Protect people from tobacco use
Offer help to quit tobacco use
Warn about dangers of tobacco
Enforce bans of tobacco advertising, promotion and sponsorship
Raise taxes on tobacco

At an individual level, smoking cessation is key to reducing cardiovascular risk and hence prolonging life.

Tobacco dependence can be assessed using the Fagerstrom Test for Nicotine Dependence and higher scores indicate higher dependence:

How to Score

1	How soon after waking up do you smoke?	Within 5minutes	3
		6 – 30 minutes	2
		31 – 60 minutes	1
		After 60 minutes	0
2	Do you find it difficult to refrain from smoking in places where it is forbidden? E.g. church,	Yes	1
		No	0
3	Which cigarettes would you hate most to give up?	The first one in the morning	1
		All others	0
4	How many cigarettes do you smoke in a day?	10 or less	0
		11 - 20	1
		21 - 30	2
		30 or more	3
5	Do you smoke more frequently during the first hours after waking up than during the rest of the day?	Yes	1
		No	0
6	Do you smoke if you are so ill that you are in bed most of the day?	Yes	1
		No	0

Scoring

0 - 2	Very low dependence
3-4	Low dependence
5	Medium dependence
6-7	High dependence
8- 10	Very high dependence

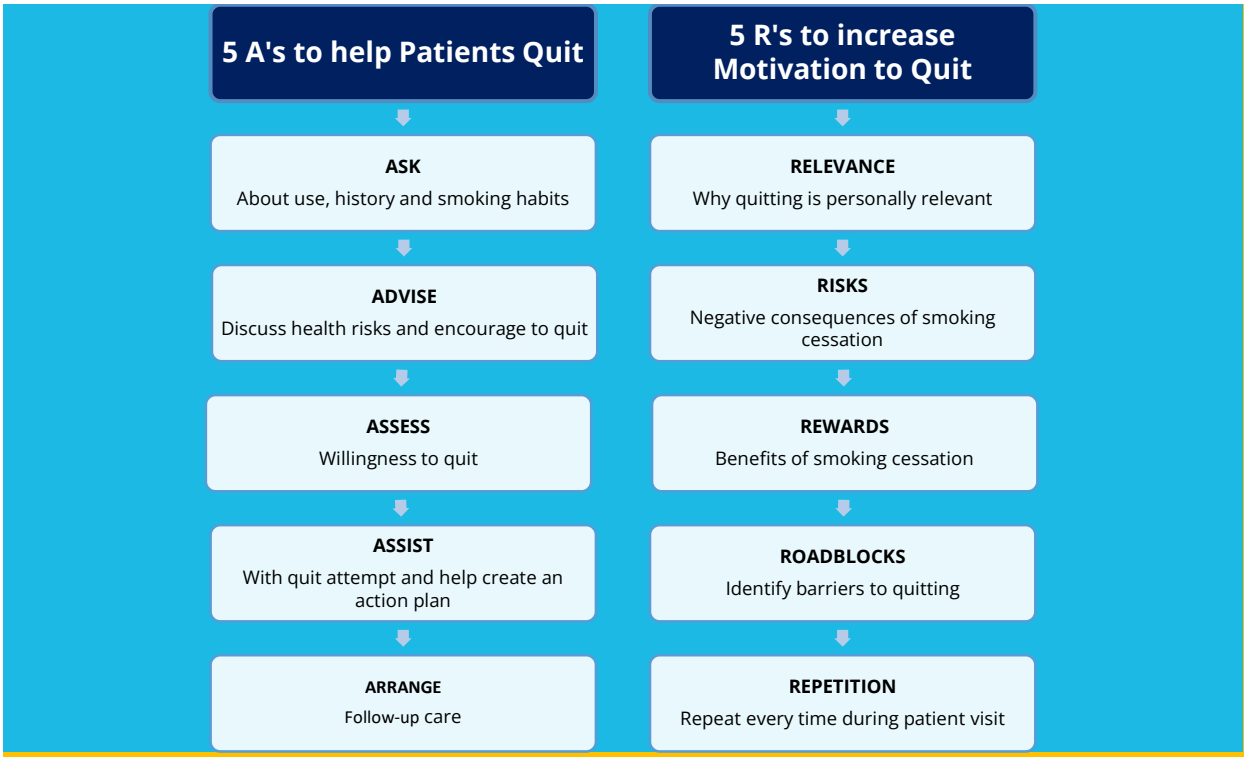
Once scored, this should be documented to track progress in smoking cessation.

It is also important for the health care worker or counsellor to identify barriers to quitting which may include withdrawals, stress, peer pressure, fear of gaining weight, etc.
Tobacco dependence cessation interventions can be categorized into:

1. Brief advice given by a healthcare professional
2. Behavioural support
3. Pharmacotherapy

1. Brief advice by a healthcare professional

The healthcare worker can use 5A's and 5R's in providing therapy.



2. Behavioural Support

Behavioural support aims to change thought processes and beliefs in the way a person may feel about tobacco use and will then trigger a change in behavior. This may be offered in the following ways:

a. Face to face support – individual counselling, group therapy
b. Telephone therapy
c. Self-help materials (booklets, brochures, contact information for further support)

Practical Counselling

a. Recognize danger situations– identify events, internal states or activities that increase risk of smoking relapse
b. Develop coping skills– identify and practice coping or problem solving skills
c. Provide basic information– about smoking and successful quitting

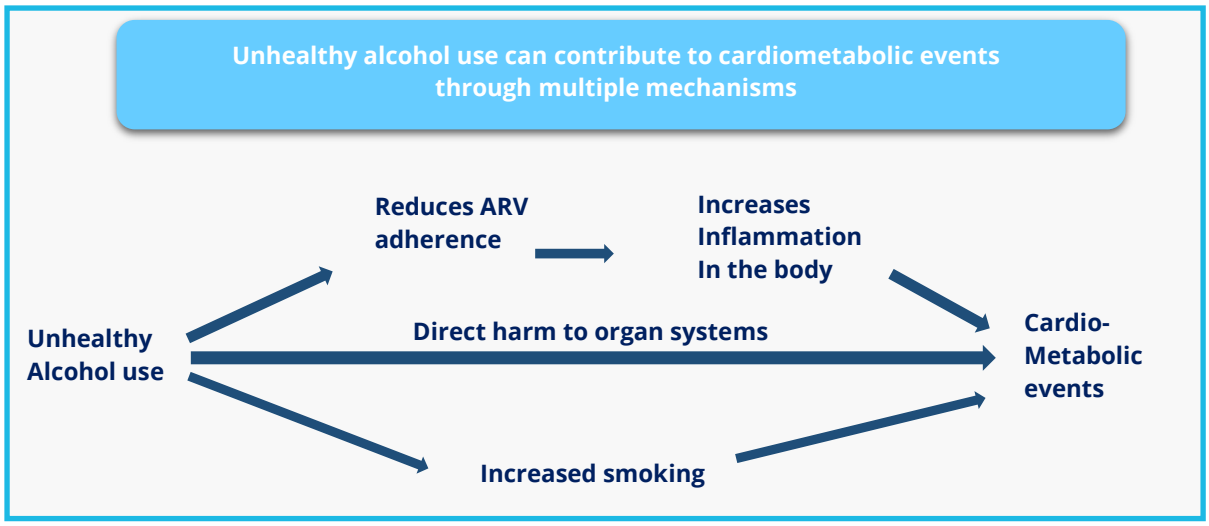
3. Pharmacological interventions

These may not be readily available but include nicotine replacement therapy (i.e., gums, patches, lozenges, inhalers, and/or sprays) and pharmacotherapy.

Unhealthy Alcohol Use

Unhealthy alcohol use is the third leading risk factor for poor health globally, and WHO has estimated that it causes 3 million deaths every year, representing 5.3% of all deaths, especially in the young. Alcohol misuse accounts for 5.1% of the global burden of disease as measured in disability-adjusted life years (DALYs).

Unhealthy alcohol use is especially bad for people living with HIV. It can promote the development of cardiometabolic events in multiple ways as shown on the next page.



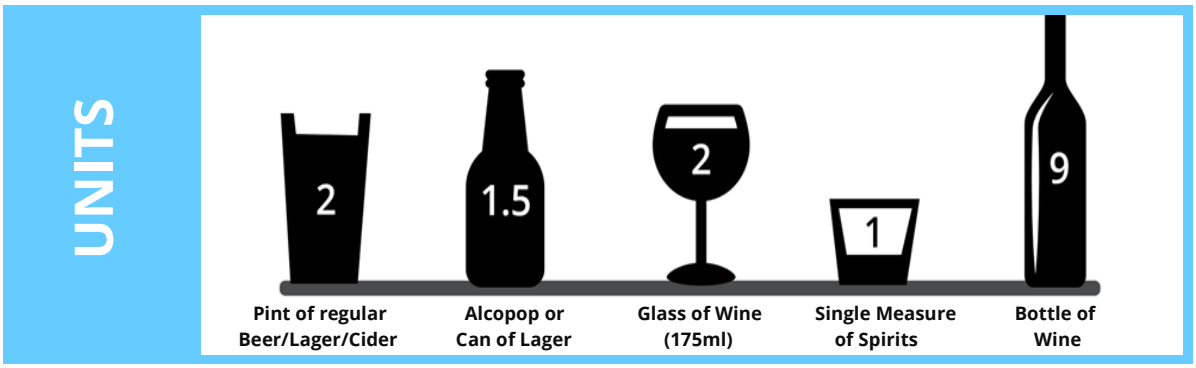
Therefore, screening for alcohol use among people with HIV is very important.

How to screen:

Screening can be done using the 3-question version of the Alcohol Users Disorders Identification test, called AUDIT-C. The 3-question version is faster than the full version of AUDIT to complete and yields similar information. Clients with unhealthy alcohol use must have their AUDIT-C Scores documented at each visit.

The 3 questions cover: (a) how often a person drank in past year, (b) when drinking, how many units (what is also called 'standard alcohol drinks') of alcohol were consumed, and (c) how often did binge (heavy episodic) drinking occur in past year.

For questions 2 and 3, it is important to learn what type of alcohol is being consumed, since beer has lower alcohol concentration than wine and spirits.



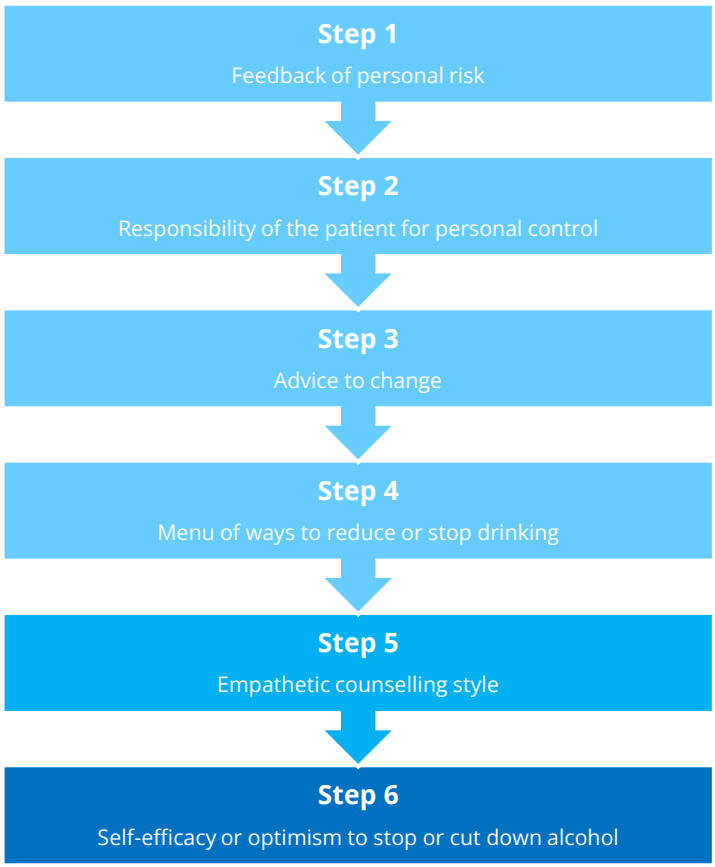
UDIT-C score of 3 or more points for women and 4 or more points for men is consistent with unhealthy alcohol use. Lower scores mean that the drinking is moderate and less harmful to the body.

Alcohol Users Disorders Identification Test (AUDIT)

Questions	Scoring System					Your Score
	0	1	2	3	4	
How often do you have a drink that contains alcohol	Never	Monthly or less	2 - 4 times Per month	2 – 3 times per week	4+ times per week	
How many standard alcoholic drinks do you have on a typical day when you are drinking?	1 - 2	3 -4	5 - 6	7 - 8	10+	
How often do you have 6 or more standard drinks on one occasion?	Never	Less than monthly	monthly	Weekly	Daily or almost daily	

Intervention for unhealthy alcohol use:

Regarding intervention, the FRAMES approach may be used to modify behavior by the counsellors or the clinicians.



The 5A's approach used in tobacco counselling can also be applied in alcohol counselling

Unhealthy Diet and Physical Inactivity

Unhealthy diets have been attributed as one the ten leading risk factors causing death and known to pose increase risk of cardiovascular disease. Diets high in sugars, saturated and trans fats, low fibre and high sugar drinks are considered unhealthy diets.

WHO recommends the following for a healthy diet:

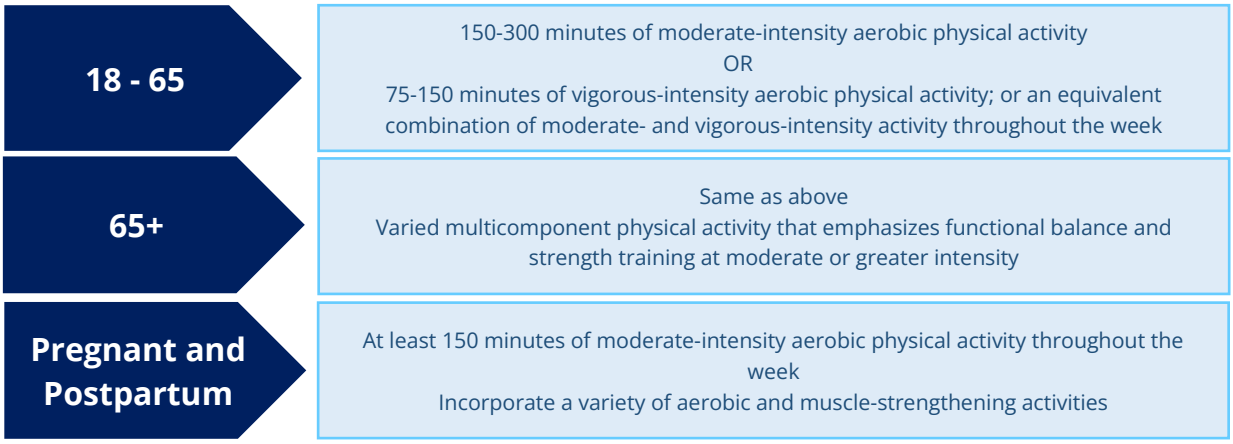
- Fruits, vegetables, legumes (e.g. lentils, beans), nuts and whole grains (e.g. unprocessed maize, millet, oats, wheat, brown rice)
- At least 5 portions of fruits and vegetables per day excluding sweet potatoes, cassava, starchy roots
- Less than 12 teaspoons of free sugars (sugars added to foods or drinks, honey, syrups, fruit juices and fruit juice concentrates)
- Unsaturated fats (found in fish, avocado, nuts, sunflower, soya, canola and olive oils) are preferable to saturated fats (found in fatty meat, butter, palm and coconut oil, cheese, cream) and trans-fats (found in baked and fried foods and prepackaged snacks and foods such as biscuits, spreads, cooking oils)
- Less than a teaspoon of salt per day

Physical Inactivity

Physical inactivity contributes to non-communicable diseases. Physical activity is described as bodily movement that requires energy expenditure. WHO estimates that 25% do not meet the global recommended levels of physical activity. People who are insufficiently active have an increased risk of death compared to those sufficiently active.

Activities can include walking, cycling, sports, active recreation and play. Regular physical activity has been proven to reduce noncommunicable disease and cardiovascular diseases

Figure 23: Recommended physical activity



5.0 Optimizing Integrated HIV Outcomes

HIV treatment optimization is a **process intended to enhance the long-term efficacy, adherence, tolerability, safety, convenience, and affordability of combination ART**. The ultimate goal of this process is to expand access to well tolerated and effective lifetime treatment to all those in need.

The fundamental principle of ART regimen optimization is first to maintain viral suppression without jeopardizing future treatment options and secondly, to select a regimen that fits with the patient in front of you and all of their unique characteristics like comorbidities, weight, age or other personal factors.

Adverse events, drug-drug or drug-food interactions, pill burden, pregnancy, cost, or the desire to simplify a regimen may prompt a regimen switch.

It is critical to review a patient's full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test results, before selecting a new antiretroviral therapy regimen.

Consultation with an HIV specialist is recommended when planning a regimen switch for a patient with a history of resistance to one or more drug classes or drug intolerance.

Close monitoring to assess tolerability, viral suppression, adherence, and safety is recommended during the first 3 months after a regimen switch.

Cardiometabolic effects of new antiretroviral drugs

New data on the cardiometabolic adverse reactions from new antiretrovirals shows that combinations including DTG and TAF or DTG alone were associated with substantial body weight gain and metabolic syndrome in some populations. This reaffirms the existing WHO recommendation on using TAF only in special situations and the expanded need for further research.
Body weight gain should be considered based on which regimen the person was on before switching to a DTG-based or TAF + DTG-based regimen. Recent trial data suggest that people who were obese at baseline continue to gain weight after starting or switching to a DTG-based or TAF + DTG-based regimen.

Key risk factors to be identified before treatment switch

Before switching/ initiating a new treatment regimen, it is important to screen and provide counselling to recipients of care found to have one or more of the following risk factors:

- Low CD4 cell count or high HIV viral load at baseline (before initiating a DTG-based regimen)
- Obesity at baseline (before initiating DTG-based regimens)
- Pre-existing diabetes mellitus
- Previous use of stavudine
- Elevated body mass index (>25) before initiation
- Hypertension
- Middle-aged (>40 years) or older (>50 years)
- Pre-existing dyslipidaemia, annual monitoring of lipid profile
- Pre-existing mental health conditions and ongoing treatment

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7.0 APPENDICES

Appendix 1: Drug formulary

Antihypertensives

Class	Drug	Side Effect	Monitoring	Contraindications
Thiazides	Bendrofluazide Hydrochlorothiazide Chlorthalidone Hydrochlorothiazide-amiloride	Hypokalaemia Hyperglycaemia Dyslipidemia Hyperuricemia Hyponatremia Erectile dysfunction	Serum Potassium Serum Sodium Blood Glucose Lipids Uric acid	
Calcium Channel Blocker	Nifedipine Amlodipine S-amlodipine	Headache Ankle oedema Tachycardia Excessive hypotension Constipation Headache Flushing Erectile Dysfunction	Pulse BP Pedal oedema	
ACE-I/ARBs	Enalapril Lisinopril Losartan Telmisartan	Cough Angioedema Renal function deterioration Risk of hyperkalemia especially in CKD	Renal function tests (urea, creatinine) Potassium	Pregnancy Advanced CKD Aortic Stenosis
Beta-blockers	Atenolol Carvedilol Bisoprolol Metoprolol	Bradycardia Dyslipidaemia Erectile dysfunction	Pulse rate Lipid profile	Acute Asthma Heart rate < 55bpm
MRAs	Spironolactone	Gynaecomastia Hyperkalemia	Potassium Breast examination	

Diabetes Medications

Class	Drugs	Side Effects	Monitoring	Contraindications
Biguanide	Metformin	Diarrhoea Cramps Nausea Vomiting Increased flatulence Low serum Vitamin B12 Myalgia and Weakness	Vitamin B12 (long term use)	CKD eGFR <30mL/minute/ 1.73m^2 Severe reduced liver function Acute cardiac insufficiency Respiratory insufficiency Alcohol abuse History of lactic acidosis
Sulfonylureas	Gliclazide Gliperimide Glibenclamide	Hypoglycaemia (marked with Glibenclamide) Nausea	Blood sugar BMI	Renal impairment (Glimepiride, Chlorpropamide) Severe liver disease

		Weight gain Vomiting Flatulence Diarrhoea/ Constipation Headache Parastheisas Skin reactions/rash		
Insulin	Actrapid Protaphane Actraphane	Hypoglycaemia Weight gain Headache Dyspepsia Diarrhoea	Blood Sugar BMI	Hypersensitivity

Lipid Modifying Drugs

Class	Drugs	Side Effects	Monitoring	Contraindications
Statins	Atorvastatin Rosuvastatin Simvastatin Pravastatin	Myopathy Increased liver enzymes Headache Arthralgia Diarrhoea	Liver Function Tests (enzymes)	Active or chronic liver disease
Fibrates	Fenofibrate (Antara)	Dyspepsia Diarrhoea Myopathy Increased liver enzymes Gallstone formation	Liver Function tests (enzymes) Abdominal Ultrasound	Severe hepatic disease Severe renal disease
PCSK 9	Alirocumab Evolocumab Inclisiran Praluent Repatha	Flu-like symptoms (nasopharyngitis) Nausea Myalgia Arthralgia Fatigue Injection site swelling/rash		Hypersensitivity
Niacin	Niacin Acipimox	Flushing Hyperglycaemia Hyperuricaemia (Gout) Nausea Vomiting Hepatotoxicity (rare)	Blood sugar Uric acid Liver Function tests	Chronic liver disease Severe Gout Pregnancy lactation
Cholesterol Absorption Inhibitors	Ezetimibe	Headache Abdominal Pain Diarrhoea		Lactation
Fatty acid compounds	Omega-3 acid ethyl esters omega-3 marine triglycerides	Nausea Belching		

Appendix 2: Calculation of creatinine clearance

$$\textit{Creatinine clearance (mL/min)} = \frac{\textit{(140 – age [years]) x weight [kg]}}{\textit{Serum creatinine [µmol/L]}} \quad \text{(Females)}$$

$$\frac{\textit{(140 – age [years]) x weight [kg] x 1.2}}{\textit{Serum creatinine [µmol/L]}} \quad \text{(Males)}$$

Appendix 3: DASH Diet Eating plan

Food Group	Servings (Per day unless otherwise stated)			Serving Sizes	Examples and Notes	Significance of Each Food Group to the DASH Eating Plan
	1,800 Calories	2,000 Calories	2,600 Calories			
Grains (Mainly whole grains)	6	6-8	10-11	1 slice bread 1 oz dry cereal + ½ cup cooked rice, pasta, or cereal ¼ bagel ½ English muffin	Whole wheat bread and rolls, whole wheat pasta, English muffins, pita bread, bagel, cereal, grits, oatmeal, brown rice, unsalted popcorn	Major sources of energy and fiber
Vegetables	3-4	4-5	5-6	1 cup raw leafy vegetable ½ cup cut-up raw or cooked vegetable ½ cup vegetable juice	Broccoli, carrots, collards, green beans, green peas, kale, lima beans, potatoes, spinach, squash, sweet potatoes, tomatoes	Rich sources of potassium, magnesium, and fiber
Fruits	4	4-5	5-6	1 medium fruit ¼ cup dried fruit ½ cup fresh, frozen, or canned fruit ½ cup fruit juice	Apples, apricots, bananas, dates, grapes, oranges, grapefruit, grapefruit juice, mangos, melons, peaches, pineapples, raisins, strawberries, tangerines	Important sources of potassium, magnesium, and fiber
Fat-free or Low-fat milk and dairy products	2-3	2-3	3	1 cup milk or yogurt 1 ½ oz cheese	Fat-free (skim) or low-fat (1%) milk or buttermilk; fat-free, low-fat, or reduced-fat cheese; fat-free or low-fat regular or frozen yogurt	Major sources of calcium and protein
Lean meats, poultry, fish	3-6	6 or less	6	1 oz cooked meats, poultry, or fish 1 egg	Select only lean meats; trim away visible fat; broil, roast or poach; remove skim from poultry	Major sources of protein and magnesium
Nuts, seeds, and legumes	3 per week	4-5 per week	1 per day	1/3 cup or 1 ½ oz nuts 2 tbsp peanut butter 2 tbsp or ½ oz seeds ½ cup cooked legumes (dry beans and peas)	Almonds, hazelnuts, mixed nuts, peanuts, walnuts, sunflower seeds, peanut butter, kidney beans, lentils, split peas	Rich sources of energy, magnesium, protein, and fiber
Fats and oils	2	2-3	3	1 tsp soft margarine 1 tsp vegetable oil 1 tbsp mayonnaise 2 tbsp salad dressing	Soft margarine, vegetable oil (such as canola, corn, olive, or safflower), low-fat mayonnaise, light salad dressing	Aim to consume 27 percent of calories as fat, including fat in or added to food
Sweets and added sugars	0	5 or less per week	≤ 2	1 tbsp sugar 1 tbsp jelly or jam ½ cup sorbet, gelatin 1 cup lemonade	Fruit-flavored gelatin, fruit punch, hard candy, jelly, maple syrup, sorbet, and ices, sugar	Sweets should be low in fat

DIABETIC DIET MEAL PLAN

Goals

⇒ To maintain or improve health through the appropriate and healthy food choices to control blood glucose levels close to normal as possible.
⇒ To maintain optimal nutrition status
⇒ Control signs and symptoms of hypo &hyperglycemia
⇒ To prevent diabetic complications. (nephropathy, retinopathy, neuropathy)

Dietary principles

- Avoid all refined carbohydrates due to their high glycemic index and low fiber content,
- Focus on complex carbohydrates
- Reduce on fast and fatty food as this is predisposing factor to high levels of cholesterol
- Reduce the intake of salt by not adding extra salt on the plate
- Avoid high sugar foods - ice cream, cakes, scones, biscuit as this may spike sugar levels
- Drink enough water to keep dehydrated (except in those with chronic kidney disease)

Breakfast 	▪ ½ *cup* Jungle Oats + low fat milk / fat free milk ▪ 2 bars Weetbix with fat free milk/ low fat milk ▪ 2 slice Brown bread add lettuce, onion cucumber / peanut butter if s/he willing or avocado ▪ ½ *cup* Brown rice ▪ 1 cup of porridge of millet with ground nuts or peanut ▪ Roller meal porridge with pounded groundnuts or fat free milk ▪ Tea without sugar or with cinnamon and lemon
Snack Options 	▪ Vegetable salads using lemon or vinegar ▪ Slice of brown bread with peanut butter ▪ Fruits: Strawberry or ½ a Green apple or ½ an Orange or a slice of watermelon or ½Blueberries ▪ 2 Cucumber per day ▪ Low fat natural yogurt ▪ An Avocado ▪ 1 cup Butternut ▪ A glass of fat free/ low fat milk ▪ A piece of unpeeled boiled sweet potato ▪ Vegetable salads without dressings ▪ A palm full of groundnuts ▪ ½ cob of fresh boiled or roasted maize ▪ 2 medium sized carrots
Lunch/Supper Options 	▪ Protein (Fish, Chicken without skin, Kapenta, Vosashila, beans and lean red meat once after 2weeks) ▪ Carbohydrates (1lump of millet / Roller meal Nshima or half cup brown rice or 2 boiled potatoes with skin. ▪ With any vegetables of your choice provided low salt and cooking oil, except cabbage due to its sugar content. ▪ Avoid all sweetened and carbonated drinks ▪ Avoid frying of any food ▪ Avoid skipping meals instead eat small meals but frequent 5 times per day ▪ Reduce on all fast and fat food e.g. butter, mayonnaise, full cream milk, and cream doughnut. vitumbuwa ▪ Avoid over ripe fruits due to its high level of fructose ▪ Drink more water approximately (35mls/ kg) per day to prevent dehydration ▪ 3 boiled eggs per week. * *Use vegetable oil for cooking e.g. ole, olive oil, soya oil* * *Boiling, roasting, grilling are the preferred methods of cooking*

Appendix 5: Locally adapted Six Food Group

Locally adapted Six Food Groups

Adapted from the Zambia Food Based Dietary Guidelines

Appendix 6: HMOD Management

Clinical scenario	Goal (BP) and duration	Preferred agent	Prereferral
Acute Ischaemic Stroke (AIS)	< 180/110mmHg or by 25% of SBP within the 1st hour	Labetolol or Nicardipine	
Haemorrhagic Stroke	< 140mmHg in the 1st hour	Labetolol or Nicardipine	
Aortic Dissection	< 120mmHg in the 1st hour; HR < 60bpm	Labetolol or Esmolol or Nicardipine or Nitroprusside	
Myocardial Infarction/Heart Attack		B-Blocker (Nebivolol/ Atenolol) + ACEI/ARB + Aspirin 300mg (chew) + Isosorbide dinitrate or mononitrate	B-Blocker (Metoprolol/ Atenolol) + ACEI/ARB + Aspirin 300mg (chew)
Pulmonary Oedema		Furosemide (IV) + Glyceryl trinitrate (GTN)IVI/Nitroprusside* + ACEI/ARB **alternative IV Labetelol*	Furosemide (IV) 80mg-120mg ACEI/ARB

Pulmonary Oedema → Furosemide (IV) + Glyceryl trinitrate (GTN) IVI/Nitroprusside* + ACEI/ARB
*alternative IV Labetelol

Myocardial Infarction → B-Blocker (Metoprolol/Nebivolol/Atenolol) + ACEI/ARB + Aspirin 300mg (chew) + Isosorbide dinitrate/mononitrate

CVA/Stroke → IV Nitroprusside/Labetelol + ACEI/ARB (Captopril) + Thiazide (HCTZ)

Adjuvant therapy: oxygen, morphine where there are no contraindications.

IMMEDIATELY REFER TO NEXT LEVEL OF CARE

Appendix 7: Management of DKA

FLUID:

Intravenous (IV) administration of 0.9% sodium chloride.

–1L in 30 min, then
–1L in 1h
– 1L in 2h
– 1L in 4h
– 1L in 8h

N.B. When blood glucose is between 10 – 15mmol/L, switch IV normal saline to D5 normal saline or 10% dextrose.

Fluid administration should be guided by the volume and haemodynamic status of the patient. Patients with CKD, Heart Failure and Valvular Heart Disease may be intolerant of large fluid volumes. Titrate therapy according to individual patient assessment.

If systolic blood pressure is below 80 mmHg, give 500 mL 0.9% sodium chloride over 15 min; if no response, give plasma expander

ELECTROLYTE REPLACEMENT
Add 20mmol Potassium Chloride (KCl)/L to the 3rd litre and every alternate litre. Ensure patient is passing urine.
Where Potassium results available: Give 20 mmol/h in infusion when K+ <3.5 mmol/L. Give 10 mmol/h when K+ = 3.5–5 mmol
Adjust KCl concentration depending on results of regular blood K+ measurement if available.

INSULIN:

Soluble insulin IV 0.1 IU/kg/h by infusion OR 20 units IM STAT followed by 6 units IM hourly.

1. Bedside glucose monitoring
   - Blood glucose
     - measure baseline and hourly initially
     - aim for fall of 3–6 mmol/L (55–110 mg/dL) per hour

2. Send Bloods to the Lab
   - Urea and electrolytes
     - do at baseline and hourly until 6 hours, then at 12 hours and 24 hours
   - Full blood count
   - Blood gases – at 0, 2 hours, 6 hours
   - Creatinine – at 0, 6, 12, 24 hours
   - Bicarbonate – at 0, 1, 2, 3, 6, 12, 24 hours.

If the pH is below 7.0 give 500 mL of sodium bicarbonate 1.26% plus 10 mmol KCl. Repeat if necessary to bring pH up to 7.0.

Once stable and able to eat and drink normally, transfer patient to four times daily subcutaneous insulin regimen (based on previous 24 hours' insulin consumption and trend in consumption).

Other semi-urgent procedures

- Blood and urine culture
- Cardiac enzymes
- CXR
- ECG (monitor if electrolyte problems or severe DKA)
- Catheterization if no urine passed after 3 hours of Hydration
- If unconscious – nasogastric tube
- Antibiotics if infection suspected
- Give subcutaneously (S.C.) prophylactic LMW heparin (0.5mg/kg body weight)


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