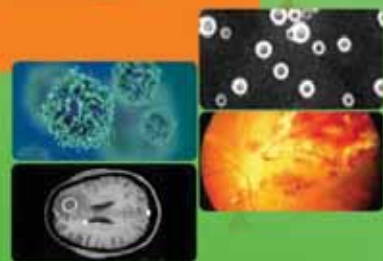




Republic of Zambia  
Ministry of Health

# ZAMBIA GUIDELINES

## *for* MANAGEMENT OF ADVANCED HIV DISEASE



February 2021

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# GUIDELINES FOR MANAGEMENT OF ADVANCED HIV DISEASE IN ZAMBIA

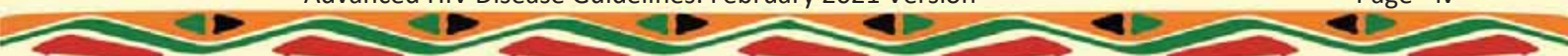
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## Acronyms

3TC	Lamivudine	FQ	Fluoroquinolone
ABC	Abacavir	H	Isoniazid
AIDS	Acquired Immunodeficiency Syndrome	H <sup>HD</sup>	Isoniazid High Dose
AHD	Advanced HIV Disease	HIV	Human Immunodeficiency Virus
ALT	Alanine Aminotransferase	HPV	Human Papilloma Virus
AFB	Acid Fast Bacilli	HTS	HIV Testing Services
ANC	Antenatal Care	Km	Kanamycin
ART	Antiretroviral Therapy	LFX	Levofloxacin
ARV	Antiretroviral	INH	Isoniazid
AST	Aspartate Aminotransferase	INSTIs	Integrase Strand Transfer Inhibitors
ATC	Advanced Treatment Centre	IPT	Isoniazid Preventive Therapy
ATT	Anti-Tuberculosis Treatment	IRIS	Immune Reconstitution Inflammatory Syndrome
ATV	Atazanavir	L&D	Labour and Delivery
AZT	Azidothymidine (Also Known as Zidovudine, or ZDV)	LAM	Lipoarabinomanon
Bdq	Bedaquiline	LEEP	Loop Electrosurgical Excision Procedure
BD	Twice Daily	LPV	Lopinavir
BMI	Body Mass Index	MDR TB	Multidrug – Resistant Tuberculosis
ART	Antiretroviral Therapy	MNCH	Maternal, Newborn, and Child Health
CD4	T-Lymphocyte Bearing CD4 Receptor	MOH	Ministry of Health
CD4 %	CD4 Percentage	MTCT	Mother-to-Child Transmission (of HIV)
CDC	Centers for Disease Control and Prevention	NAT	Nucleic Acid Test
Cfz	Clofazimine	NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
CNS	Central Nervous System	NRTI	Nucleoside Reverse Transcriptase Inhibitor
CPT	Co-trimoxazole Preventive Therapy	NUPN	National Unique Patient Number
Cm	Capreomycin	NVP	Nevirapine
CMV	Cytomegalovirus	OD	Once Daily
CRAG	Cryptococcal Antigen	OI	Opportunistic Infection
CrCl	Creatinine Clearance	Ofx	Ofloxacin
CTX	Co-trimoxazole	PAS	Para – Aminosalicyclic Acid
Cs	Cycloserine	PCP	Pneumocystis Pneumonia
CSF	Cerebrospinal Fluid	PCR	Polymerase Chain Reaction
DBS	Dried Blood Spot	PEP	Post-Exposure Prophylaxis
Dlm	Delemanid	PHDP	Positive Health Dignity and Prevention
DMPA	Depot Medroxyprogesterone Acetate	PI	Protease Inhibitor
DNA	Deoxyribonucleic Acid	PLHIV	People Living With HIV
DOTS	Directly Observed Therapy, Short Course	PO	Per os (Orally)
DR TB	Drug Resistant Tuberculosis	PrEP	Pre-Exposure Prophylaxis

## FOREWORD



On December 1<sup>st</sup>, 2020, World AIDS Day, Zambia was officially recognized to have achieved the UNAIDS fast track epidemic control 90-90-90 targets. Achieving these targets means that over 90% of Zambians infected with HIV now know their HIV status, over 90% of these are on life saving antiretroviral therapy and over 90 of those on antiretroviral therapy are virologically suppressed. Antiretroviral therapy coverage has increased with over 1,100,000 people on antiretroviral therapy in Zambia. These gains keep Zambia well posed to achieve the target to end AIDS by 2030.

Despite the increase in the coverage of antiretroviral therapy and high virologic suppression rates in Zambia, mortality due to HIV remains the number one cause of death in Zambia. From its peak of about 80,000 HIV related deaths in 2004, the annual HIV related deaths have fallen by 60% to around 18,000 in 2020. Unfortunately, this number remains high and way above the target to reduce annual HIV associated mortality to less than 5,000 by 2020 as espoused in the Zambia National HIV Strategic Framework 2017-2020 (NHSF 2020-2021). There can never be true epidemic control of HIV without an impactful absolute reduction in individuals dying from HIV/AIDS.

Most of the HIV associated deaths occur in HIV infected individuals who have advanced HIV Disease defined as the presence of a CD4 cell count below 200 cells/mm<sup>3</sup>, denoting severe immunosuppression or AIDS, or the presence of World Health Organisation Stage III or IV condition. Typically, Individuals with Advanced HIV Disease are those who present late for treatment after living with untreated HIV infection for many years, those who have fallen out of care or those whose antiretroviral treatment is no longer efficacious due drug resistance. Tuberculosis, Cryptococcal meningitis and severe bacterial infections are the leading cause of death among those with advanced HIV Diseases. Further, non-communicable diseases such as cancers and cardiovascular diseases are more common, more severe and presents at a younger age in HIV infections and are emerging as an important cause of death among PLHIV.

Going forward, the Ministry of Health intend to reduce HIV associated mortality and eradicate AIDS in Zambia. Consequently, these Zambian Guidelines for Advanced HIV Disease Management have been developed. These guidelines are a concise and instructive guide on the provision of person-centred services to individuals with Advanced HIV Disease. They will include instruction on screening of advanced HIV Disease, and the screening and management of specific AIDS defining conditions including NCDs and mental health conditions. They can be used as a standard operation procedure or just as a reference guide. I encourage clinical and non-clinical health workers to take advantage of this resource. Once implemented with fidelity, these guidelines will improve the identification and treatment of individual with advanced HIV Disease and subsequently will decrease HIV related mortality in Zambia.

**Dr. Jonas Chanda**  
**MINISTRY OF HEALTH**

## ACKNOWLEDGEMENTS



The Ministry of Health is proud to produce the *Zambian Guidelines for Management of Advanced HIV Disease*. This document will provide guidance on the use of innovative tools to screen, identify and provide prophylaxis or treatment to recipient of care with advanced HIV disease. It is anticipated that a resolute implementation of these guidelines will result into a reduction in HIV associated mortality.

We have employed a multi-disciplinary approach involving a wide range of stakeholders in developing these guidelines. To this effect, I would like to extend my sincere appreciation and thanks to the following organizations and individuals who have worked tirelessly to achieve this exceptional work. This include but not limited to:

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## Module 1: Introduction to the Management of Advanced HIV Disease

### Introduction

Zambia has made significant progress over the years in improving the coverage of Antiretroviral Therapy (ART) with over 1,100,000 on treatment as at the end of 2020. Despite this improvement, HIV associated mortality remains high estimated at 17,200 for the year 2020. This is against the national target to reduce mortality to less than 5,000 stated in the National AIDS Strategic Plan 2017-2021. Most of the individuals who die from HIV have Advanced HIV Diseases (AHD) and present with opportunistic infections. Approximately 13,000 HIV/TB coinfecting individuals died in 2018 in Zambia and it is estimated that around 5,000 Cryptococcal Meningitis cases occur each year in country. Those who die due to AHD include those initiating ART after a prolonged HIV infection period without ART, those falling out of care and those on non-effective ART due to HIV drug resistance. Other causes of mortality among HIV infected individuals include Non-Communicable Diseases (NCDs). This is compounded by mental health which causes both delays in commencement of care and attrition out of care.

The aim of these guidelines is to reduce the HIV associated mortality in Zambia by providing a prescriptive guidance in delivering a package of care for all HIV infected individuals presenting with AHD in the country. This package of care includes timely recognition of patients with AHD and opportunistic infections through screening. It also includes the provision of optimized prophylaxis, enhanced diagnosis and treatment for opportunistic infections. These guidelines further stipulate the mode of the provision of these AHD guidelines using the national health systems across the various levels of care including personal centered HIV services and the center of excellences for patients who present with complicated HIV related conditions. Guidance on mental health and NCDs in PLHIV is also provided.

### Burden of Advanced HIV Disease in Zambia

Recent estimates suggest that about 30–40% of people living with HIV starting ART in low- and middle-income have a CD4 cell count of  $< 200$  cells/mm<sup>3</sup>, and 20% have a CD4 cell count of  $< 100$  cells/mm<sup>3</sup>.

In some settings, up to half of the number of people present to care with AHD. This includes people who have temporarily interrupted ART and who return to care after a period off treatment, with a low CD4 cell count and new clinical symptoms. The ZAMPHIA 2016 estimated that 17.7% of people newly diagnosed HIV aged between 15 to 59 years old had a CD4 count of  $< 200$  cells/mm<sup>3</sup>.

People with AHD frequently have opportunistic infections such as Tuberculosis and Cryptococcal infections. TB remains the largest contributor to mortality in HIV infection. The morbidity due to OIs is attributed to late presentation, limited diagnostic facilities and inappropriate therapies in some cases.

### Definitions of Terms

#### Advanced HIV Disease

For adults and adolescents, and children older than five years, AHD is defined as CD4 cell count  $<200$  cells/mm<sup>3</sup> or WHO stage 3 or 4 event. All children younger than five years old with HIV are considered as having AHD.

A **seriously ill adult or adolescent**: RR  $\geq 30$  breaths per minute; HR  $\geq 120$  beats per minute; or unable to walk unaided. Other parameters including a **temperature  $\geq 39^{\circ}\text{C}$**  can also be considered. A **severely immunosuppressed** adult is defined as having a CD4 cell count **below 50 cells/mm<sup>3</sup>**.

#### Prophylaxis Therapy

It is the provision of therapy to avoid either the **first** occurrence of infections (primary prophylaxis) in individuals without the diseases or the **recurrence** (secondary prophylaxis or maintenance) in individuals who have previously suffered from the disease.

#### Pre-emptive Therapy

It is an alternative strategy to prophylaxis that aims to prevent progression to disease **after** infection has occurred. For example, the term pre-emptive therapy is used to describe treating people who are positive for Cryptococcal antigen since, by the time Cryptococcal antigen is positive in the blood, disease and dissemination are considered significant even if they are not clinically apparent.

#### Presumptive Treatment

This is also referred to as empirical treatment and refers to treatment that is initiated based **exclusively on clinical suspicion** and relying on **clinical judgement**. Presumptive treatment is generally reserved for severely ill people in settings where laboratory investigations are not available. There are two broad approaches: (1) treatment without laboratory diagnosis based on the opinion of an experienced clinician after considering all the available information and (2) treatment based on a pre-specified clinical rule that aims to identify individuals at higher risk and does not require clinical judgement.

## Screening for Advanced HIV through CD4 Cell Count Testing

CD4 cell count testing is the gateway to the identification of PLHIV who have AHD. In Zambia, screening for AHD using a CD4 count should be done at initiation of therapy, then repeated at six months, twelve months and then annually if it is  $\leq 350$  cells/mm<sup>3</sup>. This also applies to patients returning to care after disengaging therapy and those being switched to the next line of therapy after treatment failure. Monitoring of CD4 cell count is discontinued after 2 consecutive CD4 cell count test results  $> 350$  cells/mm<sup>3</sup>. CD4 count testing is resumed when a patient in care develops a WHO stage 3 or 4 condition or when the HIV viral load rises to  $> 1000$  copies/mL. CD4% should be done every 6 months for children below 5 years. Take note that CD4 count must not be used to diagnose treatment failure. However, it is still being used to assess risk of opportunistic infections and determine eligibility for Co-trimoxazole prophylaxis. All PLHIV with advanced HIV disease, pregnant and children less 5 years old are eligible for CTX prophylaxis regardless of CD4 count. *For implementation purpose, all HIV infected individual presenting with an illness requiring admission to a health facility must have a CD4 cell count done.*

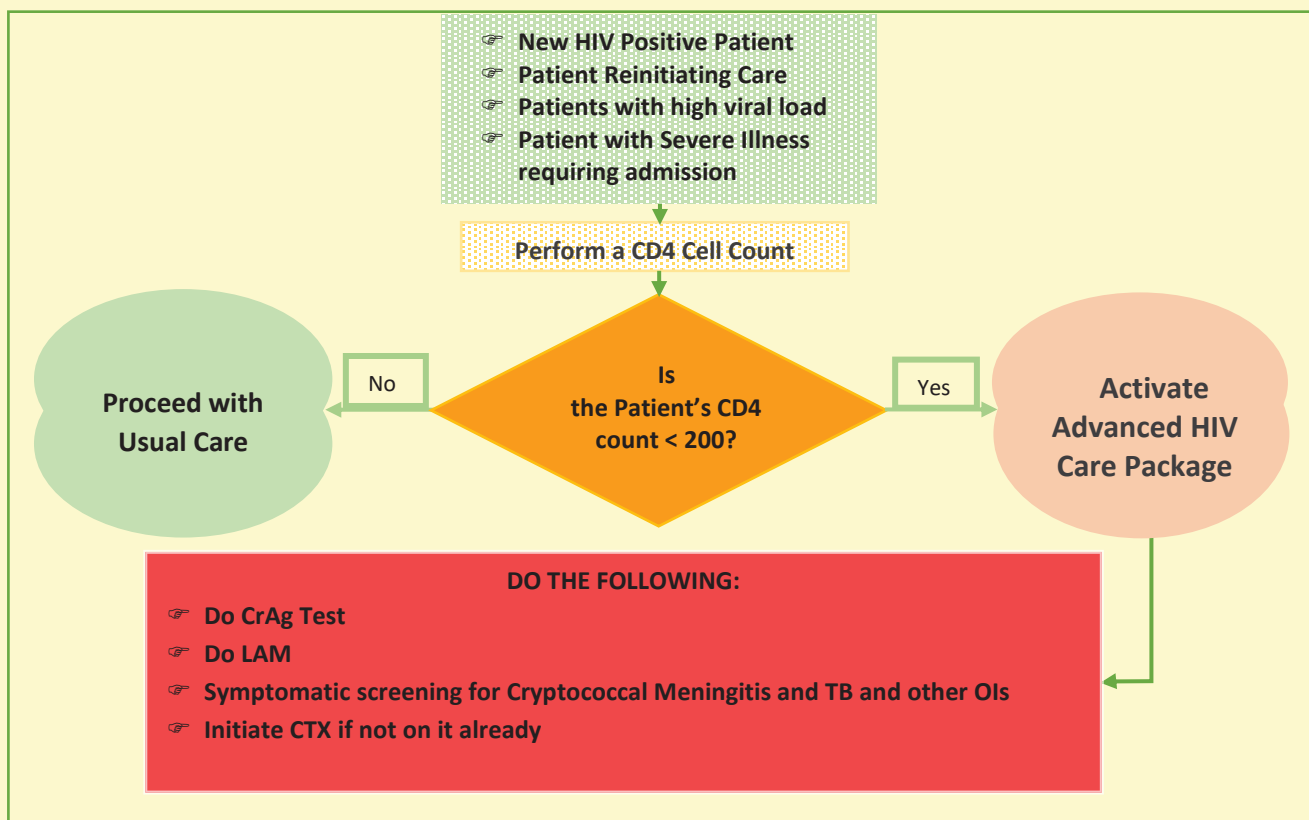


Figure 1.1: CD4 Cell Count Screening: A Gateway for Advanced HIV Disease Care

## Rapid ART Initiation in Advanced HIV Disease

Rapid initiation of ART is beneficial for individuals with AHD. Rapid initiation is defined as initiation of ART within seven days from the day of HIV diagnosis. People with advanced HIV disease should be given priority for assessment and initiation of ART. Same day ART initiation is defined as ART initiated on the day of HIV diagnosis. While the need to screen, identify and treat opportunistic infection is of a greater priority in AHD, ART must be initiated as soon as possible, preferably within two weeks as soon as they tolerate OI treatment. Special circumstances are in the case of Cryptococcal Meningitis and Meningeal Tuberculosis where the initiation of ART must be delayed for 8-10 weeks.

## Screening for Opportunistic Infections in Advanced HIV Care

Screening is the assessment for the identification of a disease prior in individual who are not presenting complaints for that particular condition. Screening can be done *symptomatically* or by using a *laboratory test*. Screening is appropriate for those conditions which are common and treatment in the asymptomatic stage is available and beneficial. Therefore, all patients with AHD must be screened for Cryptococcal meningitis and Tuberculosis because treatment in the asymptomatic stage for these conditions is beneficial. Cryptococcal meningitis accounts for about 15% of all AIDS-related deaths, three quarters of which occur in SSA (*WHO AHD guidelines 2018*). Treatment of asymptomatic Cryptococcal antigenaemia reduces progression to Cryptococcal meningitis with a 28% reduction in mortality among people presenting with AHD (*REMSTART 2015*). Additionally, enhanced prophylaxis for TB and Cryptococcal disease reduced incidence and hospitalizations with no increase in adverse events (*Reality study*). Early screening and treatment of OIs also resulted in improved ART adherence (*Remstart study*).

## Prophylaxis in Advanced HIV Disease

Prophylaxis is the use of drugs to prevent the occurrence or re-occurrence of a disease. Cotrimoxazole (CTX) prophylaxis has been shown to prevent bacterial infections, PCP and parasitic infections such as Malaria and Cyto-isosporiosis. CTX has mortality benefit and must be provided in all patients with AHD and those with a CD4 cell count below 350 cell/mm<sup>3</sup>. This is different from preemptive treatment in Cryptococcal Meningitis which is the treatment of positive serum CrAg test in an individual without symptoms of Cryptococcal Meningitis to prevent progression to Cryptococcal Meningitis. In Latent TB, Tuberculosis Prophylactic Treatment (TPT) treats inactive TB to prevent later activation. There is insufficient evidence for routine use of other antibiotics besides CTX for prophylaxis against bacterial infections in AHD.



## Advanced HIV Disease Package of Care

A package of care is a collection of services that must be provided as a minimum standard of care. For individuals with AHD, the Ministry of Health recommends a package of care that includes screening and prophylactic services that targets at Tuberculosis, Cryptococcal Meningitis and severe bacterial infections. Rapid initiation of ART is part of this package.

***In symptomatic patients, the Package of Care can still be activated even when a CD4 cell count is unknown or unavailable***

**Table 1.1: Components of the Package of Care**

	Intervention	CD4 Cell count	Adults	Adolescents	Children
Screening and Diagnosis	<ul style="list-style-type: none"> <li>LF-LAM for TB screening in AHD</li> <li><b>Chest-X-ray for TB in AHD where available</b></li> </ul>	≤200 cells/mm <sup>3</sup> or at any CD4 count if seriously ill people living with HIV who are seriously ill (respiratory rate >30 breaths per minute, temperature >39°C, heart rate >120 beats per minute and/or unable to walk unaided) regardless of CD4 cell count or with unknown CD4 cell count	Yes	Yes	Yes
	Sputum Xpert® MTB/RIF as the first test for TB diagnosis among symptomatic people  Chest-X-ray for all TB symptomatic AHD (refer for CXR if not available)	Any	Yes	Yes	Yes
	Cryptococcal antigen screening	The routine use of serum or plasma Cryptococcal antigen screening among ART-naive adults before ART initiation (or re-initiation) among people with a CD4 cell count of less than 200 cells/mm <sup>3</sup>	Yes	Yes	No
Prophylaxis	Co-trimoxazole prophylaxis	≤350 cells/mm <sup>3</sup> or clinical stage 2, 3 or 4 and all pregnant women	Yes	Yes	Yes, all children under 5 years
	TB preventive treatment	Any	Yes,	Yes	Yes
	Fluconazole pre-emptive therapy for Cryptococcal antigen – positive people without evidence of meningitis	<200 cells/mm <sup>3</sup>	Yes	Yes	NA
ART Initiation	Rapid ART initiation	Any	Yes	Yes	Yes
	<b>Defer ART</b> initiation if clinical symptoms suggest TB or Cryptococcal Meningitis	start ART within two weeks of ATT for TB (or as soon as tolerated) and at least 6 weeks after starting treatment for Cryptococcal Meningitis	Yes	Yes	Yes
Adherence	Tailored counselling to ensure optimal adherence to the advanced disease package, including home visits if feasible	<200 cells/mm <sup>3</sup> or WHO Clinical stage 3 or 4	Yes	Yes	Yes

## Advanced HIV Disease Service Provision in Zambia

Access to AHD services must be universal in Zambia in keeping with the principles of universal health coverage. All health facilities that provide ART must have the capacity to identify AHD through CD4 cell count testing. The process of providing the AHD services must be systematic, deliberate and methodical so that all patients receive the minimum quality of care without anyone being missed. This process must be aided by continuous training, facility data use, use of standard operating procedures and an effective logistical supply system. **A prompt referral to a facility with adequate capacity to treat a particular condition is recommended.**

**Table 1.2: Service Delivery Packages for Different Levels of Health Care in Zambia**

level	Minimum Laboratory Services	Treatment Services
Regional/Specialist Hospital	<ul style="list-style-type: none"> <li>• Molecular tests for AHD associated organisms.</li> <li>• Histology for AHD associated organisms.</li> <li>• Full microbiology testing</li> <li>• Parasitology services for selected AHD organism</li> <li>• CSF Testing</li> <li>• Xpert® MTB/RIF</li> <li>• Urine LF-LAM</li> <li>• Serum CrAg</li> <li>• CD4 cell count testing</li> </ul>	<ul style="list-style-type: none"> <li>• TPT</li> <li>• Co-trimoxazole prophylaxis</li> <li>• Pre-emptive Fluconazole treatment</li> <li>• Secondary Fluconazole prophylaxis</li> <li>• Active Pulmonary tuberculosis</li> <li>• Cryptococcal Meningitis treatment</li> <li>• Extra pulmonary TB Treatment</li> <li>• PCP treatment</li> <li>• Severe bacterial infections</li> <li>• Organ and Disseminated Viral infections</li> <li>• Other invasive fungal infections</li> <li>• GIT parasitic infections</li> </ul>
First level and District Hospital	<ul style="list-style-type: none"> <li>• Full microbiology</li> <li>• Parasitology services for selected AHD organism</li> <li>• CSF Testing</li> <li>• Xpert® MTB/RIF</li> <li>• Urine LF-LAM</li> <li>• Serum CrAg</li> <li>• CD4 cell count testing</li> </ul>	<ul style="list-style-type: none"> <li>• TPT</li> <li>• Co-trimoxazole prophylaxis</li> <li>• Pre-emptive Fluconazole treatment</li> <li>• Secondary Fluconazole prophylaxis</li> <li>• Active Pulmonary tuberculosis</li> <li>• Cryptococcal Meningitis treatment</li> <li>• Extra pulmonary TB Treatment</li> <li>• PCP treatment</li> <li>• Severe bacterial infections</li> </ul>
Zonal Clinic	<ul style="list-style-type: none"> <li>• Serum CrAg</li> <li>• Urine LF-LAM</li> <li>• CD4 cell count testing</li> </ul>	<ul style="list-style-type: none"> <li>• TPT</li> <li>• Co-trimoxazole prophylaxis</li> <li>• Pre-emptive Fluconazole treatment</li> <li>• Secondary Fluconazole prophylaxis</li> <li>• Active Pulmonary tuberculosis</li> </ul>
Health Centre	<ul style="list-style-type: none"> <li>• CD4 cell count testing</li> </ul>	<ul style="list-style-type: none"> <li>• Co-trimoxazole prophylaxis</li> </ul>

All recipients of care identified to have AHD must receive full clinical evaluation as shown in figure 1.2 below.

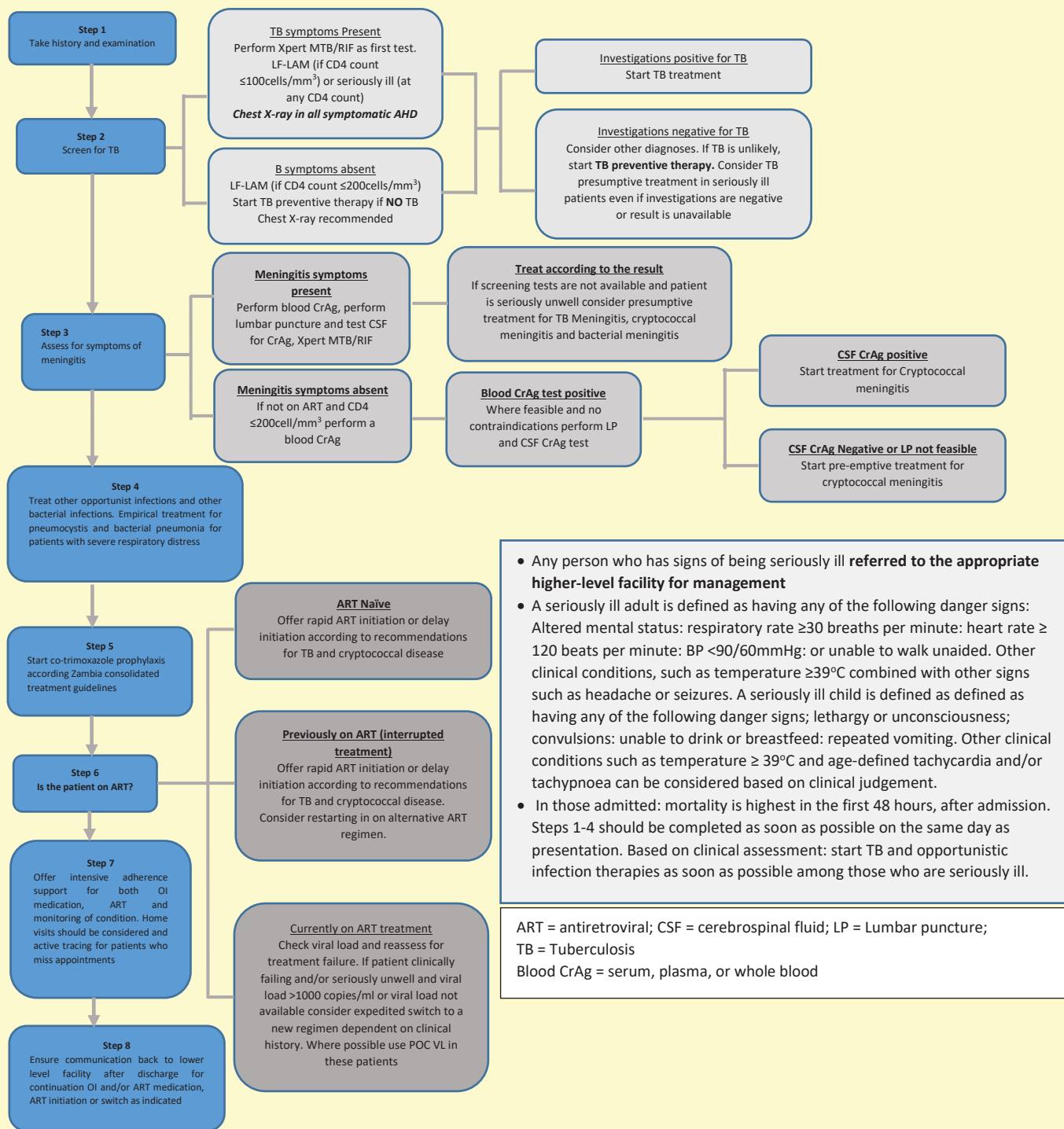


Figure 1.2: Algorithm for providing Package of Care in Advanced HIV Disease at Health Facility

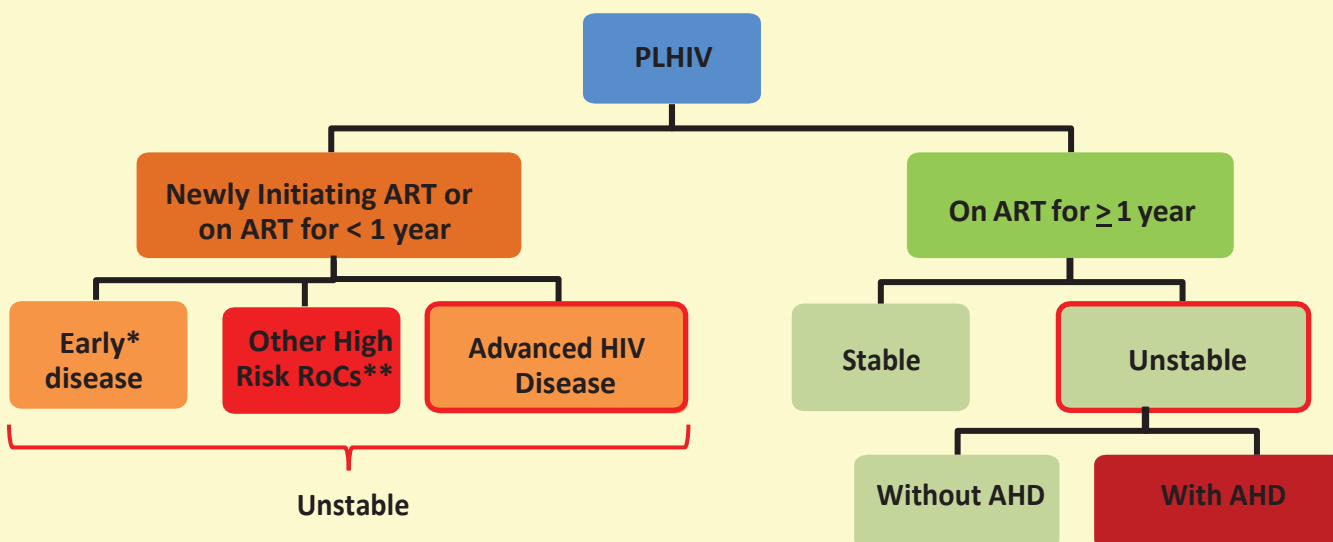
## Module 2: Differentiated Service Delivery (DSD) for Advanced HIV Disease

Individuals with AHD require patient centered care to improve outcomes. Often, AHD is found in individuals who are either just being initiated in HIV care or are returning after falling out of care. In both scenarios, this is a critical and fragile period in the journey of RoC and patient centered care to meet their special needs is paramount. These needs include medical related needs such as access to specialist doctors, specialized laboratory services and medicines. They may also need supportive care such as frequent clinician’s reviews, psychosocial support and community-based services.

### Defining High-Risk Patients (Recipients of Care)

**Table 2.1: Defining High-Risk Recipients of Care**

Advanced HIV Disease	Unstable
Adults, adolescents, and children older than the age of five years: CD4 <200 cells/mm <sup>3</sup> or WHO stage III/IV	On ART for >1 year and any of the following: <ul style="list-style-type: none"> <li>• Not virally suppressed*</li> <li>• CD4 &lt;200 cells/mm<sup>3</sup></li> <li>• Adverse drug reaction requiring ongoing monitoring.</li> <li>• Pregnant and breastfeeding women</li> <li>• Active OI, including TB.</li> <li>• Non-adherent with ART**</li> <li>• Substance abuse and mental illness</li> <li>• Comorbid condition(s) requiring frequent follow-up</li> </ul>
<b>Children ages younger than five years:</b> All children ages younger than five years with HIV are considered as having advanced HIV disease	
<small>*Not virally suppressed = most recent VL&gt;1,000 and/or no VL in the past six months                      **Non-adherent = two or more missed doses a month for patients on once-daily regimens, four or more missed doses a month for patients on twice-daily regimens; and/or misses drug pickups</small>	



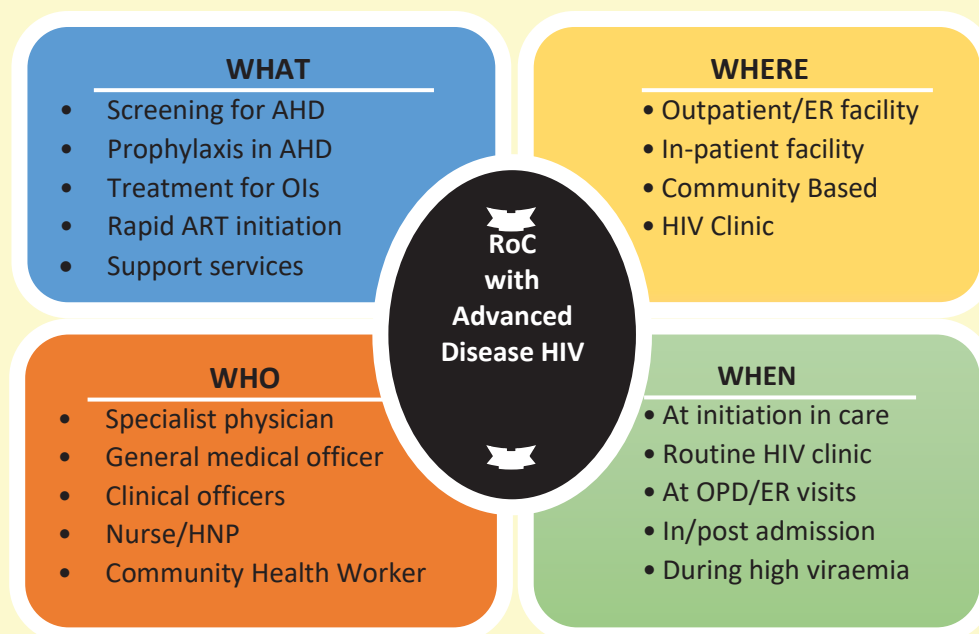
\*Early disease refers to adults with CD4 Cell count > 200 cell/mm<sup>3</sup> and without WHO Stage III/IV conditions

\*\* Other High-risk individuals include those that have a high likelihood of poor outcomes such as Adolescents, PBFW, KPs mental illness and Alcoholics Adopted from the ICAP Approach to Differentiated Care, 2017

**Figure 2.1: Overview of Patient Classification for Differentiated Care**

## Choosing DSD Models for Advanced HIV Disease

The What, Where, Who and When approach can help in developing and choosing DSD models for AHD. Figure 2.2 shows a schema on developing and choosing DSD models for AHD.



**Figure 2.2: Schema on Developing and Choosing DSD Models for AHD**

DSD models for AHD can be offered in the facility or the community depending on the characteristics of the RoC and the service to be provided. Since most patients with AHD are at risk of acute illness and subsequent death, referral services and frequent linkage to facility-based services is encouraged whenever community-based services are being given.

**Table 2.2: Key Considerations for Service Delivery for People who Present with AHD**

Patients who Present with Advanced HIV Disease (WHO Stage 3 or 4, or CD4+ count <200 cells/mm <sup>3</sup> )	
Location of Service	<ul style="list-style-type: none"> <li>☞ Management at any ART service delivery point; all facility levels</li> <li>☞ Initial management and ART initiation by trained and experienced HCW</li> <li>☞ Consultation with MDT, TWG, mentors, and senior clinicians as needed (including telephone consultation, HIV information hotline)</li> <li>☞ Referral to a higher-level facility, when feasible and if consultation is not adequate to stabilize the patient</li> </ul>
Focus of Treatment Preparation Counseling	<ul style="list-style-type: none"> <li>☞ ART is required to prevent further damage to the immune system</li> <li>☞ Starting ART soon will decrease risk of disease progression, including wasting and OIs</li> <li>☞ ART is the most important treatment to restore health</li> </ul>
Frequency of Follow-up	<ul style="list-style-type: none"> <li>☞ Weekly follow-up until ART initiation, and then at week two and four after ART initiation, and then monthly until confirmed viral suppression.</li> <li>☞ More frequent visits or in-patient hospitalization may be required to stabilize acute medical conditions and address psychosocial and other concerns</li> </ul>

### Recommendations

Rapid ART initiation should be offered to all people living with HIV following a confirmed HIV diagnosis and clinical assessment. ART initiation should be offered on the same day to people who are ready to start provided there are no contraindications

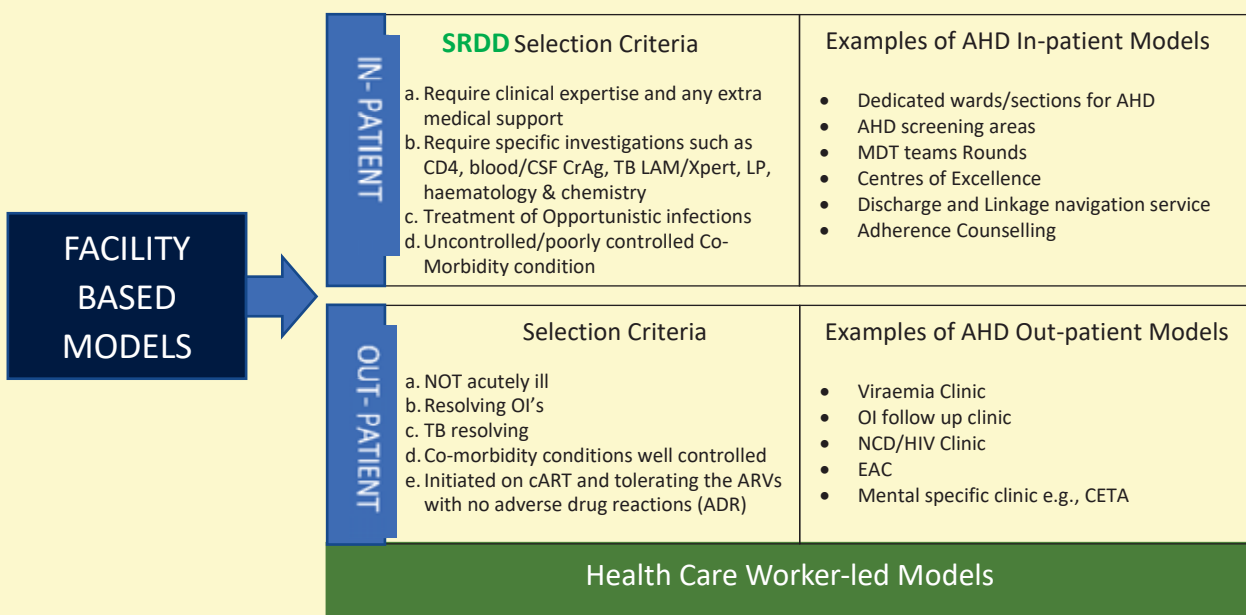


Figure 2.3: Selecting facility DSD Models for AHD

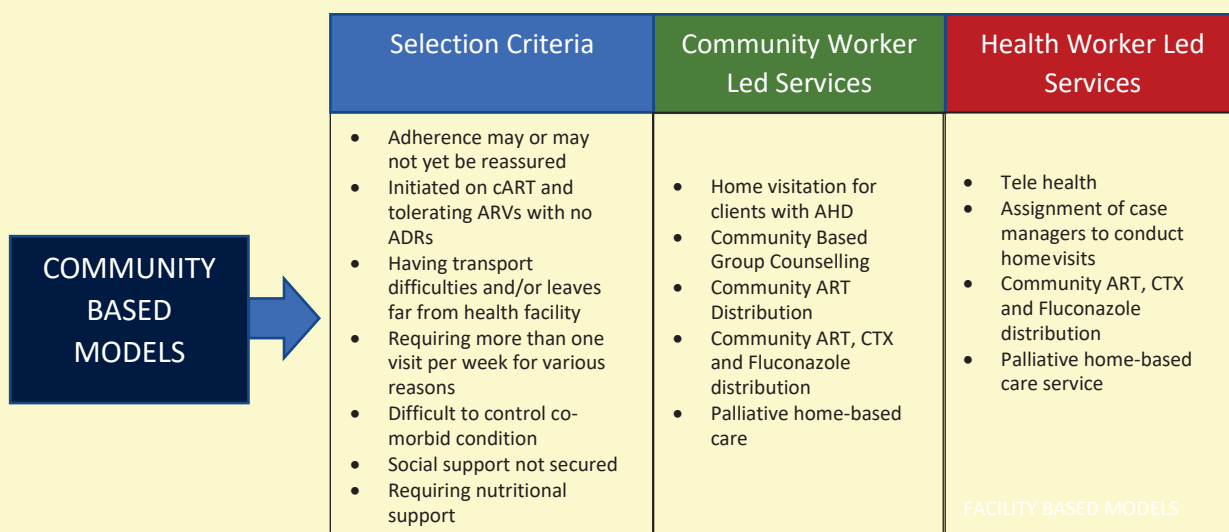


Figure 2.4: Selecting Community DSD Models for AHD

## Management of Co-Morbid Chronic Conditions

### Integrating HIV and NCD Services

PLHIV are at higher risk of CVD than the general population. This is due to the hyper-inflammatory state due to HIV viral replication as well as the increased risk of hyperlipidemia and diabetes associated with some antiretroviral (ARV) drugs. HIV and NCD care services must be integrated and synchronized in the form of: **Clinic visit appointments; Multi-month prescription, and Community-based services.**

### Differentiating Services: Identifying the “How”

**Table 2.3: Guidance for Providing Services for Patients Presenting with AHD in the Facility**

When	What	By Whom	Where
<b>First Visit (Time 0)</b>	<i>Clinical visit:</i> Confirm HIV diagnosis; CD4 test (baseline); WHO Staging. Screen for CrAg and TB Adherence support and counseling <i>Drug:</i> ART and CTX initiation	Clinician Adherence Counselor <sup>+</sup>	HIV Clinic OPD, ER In Patient
<b>Week 2</b>	<i>Clinical visit:</i> Management of OIs, monitor side effects/toxicity Adherence assessment, support and counseling. <i>Drug:</i> ART and CTX refill for one month	Clinician <sup>+</sup>	HIV Clinic
<b>Month 1-2</b>	<i>Clinical visit:</i> Monitor side effects/toxicity; manage OIs; initiate IPT Adherence assessment, support and counseling. <i>Drug:</i> ART, INH, and CTX refill for one month	Clinician <sup>+</sup>	HIV Clinic
<b>Month 3</b>	<i>Clinical visit:</i> Monitor side effects/toxicity Adherence assessment, support and counseling <i>Drug:</i> ART, INH, and CTX refill for one month	Clinician <sup>+</sup>	HIV Clinic
<b>Month 4-5</b>	<i>Clinical visit:</i> Monitor side effects/toxicity Adherence assessment, support and counseling <i>Drug:</i> ART, INH, and CTX refill for one month	Clinician <sup>+</sup>	HIV Clinic
<b>Month 6 Milestone Visit</b>	<i>Clinical visit:</i> Monitor side effects/toxicity <i>Lab:</i> VL sample collection Adherence assessment, support and counseling <i>Drug:</i> ART, INH, and CTX refill for one month	Clinician <sup>+</sup>	HIV Clinic
<b>Month 7</b>	<i>Clinical visit:</i> VL results delivered to patient; monitor clinical symptoms via symptom checklist and check for side effects/toxicity. Adherence assessment, support and counseling Stepped up counseling and support as needed, based on VL results. <i>Drug:</i> INH refill for one month, ART and CTX refill for three months	Clinician <sup>+</sup>	HIV Clinic
<b>Month 8-11</b>	<b>VL&gt;1000 copies/mL</b> <i>Clinical visit:</i> Monitor side effects/toxicity Adherence support; Stepped up counseling <i>Drug:</i> ART and CTX refill for one month. <i>Lab:</i> Repeat VL between M9 and M11 after good adherence has been achieved	Clinician <sup>+</sup>	HIV Clinic
	<b>VL&lt;1000 copies/mL</b> <i>Clinical Visit:</i> Monitor side effects/toxicity Adherence assessment, support and counseling <i>Drug:</i> ART and CTX refill for three months	Clinician <sup>+</sup>	HIV Clinic
<b>Month 12 Milestone Visit</b>	<i>Clinical visit:</i> Monitorside effects/toxicity <i>Lab:</i> Second VL sample collection Adherence counseling and support <i>Drug:</i> ART and CTX refill for one month Reclassify patients as stable vs. unstable based on clinical evolution and VL results	Clinician <sup>+</sup>	HIV Clinic

<sup>+</sup> Clinician includes physicians, nurses, clinical officers and medical technicians

\* At every contact with patients, HCW (clinician, nurse or lay counselor) should assess the patient and reclassify him/her as “early” or “advanced” disease and refer to the appropriate follow-up if indicated

## Module 3: Cryptococcal Meningitis in Advanced HIV Disease

### Introduction

Cryptococcal meningitis (CM), is a chronic meningitis arbitrary presenting insidiously over 4 weeks period. It is caused by *Cryptococcus neoformans* and it is responsible for about 15% of mortality among patients with advanced HIV disease. An estimated 5,000 cases of Cryptococcal meningitis occur annually in Zambia.

### Risk Factors and Clinical Features

It usually occurs at CD4 counts < 100 cells/mm<sup>3</sup> but can occur at higher CD4 counts. The disease usually progresses slowly and develops over weeks. Although the route of entry is airborne, initial presentation of infection does not usually include pulmonary complaints.

Symptoms	Signs
Headache (severe)	Cranial nerve palsies
Fever	Increased plantar reflexes
Lethargy	Rash similar to Molluscum contagiosum
Memory loss	Meningism
	Coma

### Screening for Cryptococcal Disease

Screening for Cryptococcal antigen is the optimal approach for guiding resources in a public health approach and is the preferred approach for prevention of progression to disease when managing people presenting with AHD. Where CrAg test is not available, Fluconazole prophylaxis must be given to all HIV positive individuals with a CD4 cell count < 100 cells/mm<sup>3</sup>.

#### WHO to Screen

HIV + adults and adolescents above 10 years with CD4 < 200 cells/mm<sup>3</sup> who are:

- Initiating ART for the first time
- Switching after ART failure
- Re-entering into care after prior disengagement
- High viral load

#### How to Screen

Rapid blood, plasma or serum CrAg test

### Diagnostic

A lumbar puncture is recommended for all symptomatic patients with a new positive blood CrAg screening result. Lumbar puncture (LP), recording opening pressure, if feasible (opening pressure often high).



The following features maybe present

- ↑ WBC (or none)
- ↑ Protein (mildly elevated)
- ↓ Glucose (mildly low)
- Positive India ink or CrAg is very sensitive and very specific
- Cryptococcal culture

Where a lumbar puncture is contraindicated, treatment for cryptococcal meningitis can be commenced based on serum CrAg and compatible symptoms in HIV infected individuals with a CD 4 cell count < 100 cells/mm<sup>3</sup>. Where a lumbar puncture is contraindicated and CrAg test is not available, the patients should be referred to a facility with a CrAg test and quick results.

*Patients with prior CM do not need to routinely be screened. CSF and blood specimens may remain CrAg + for months to years after a CM diagnosis and successful treatment. If these tests are positive in the absence of symptoms and signs, this is not an indication of relapse. A CSF culture on sabouraud media can be done in those who have previous CM and symptomatic, but CSF India ink is negative.*

	Relapse	Persistent	IRIS
Symptoms	+	+	+
Signs	+	+	+
Serum CrAg	+	+	+/-
Culture	+*	+	-

\* becomes positive after successful treatment after 28 days of induction treatment

## Managing Raised Intracranial Pressure

PLHIV with suspected cryptococcal meningitis should have an initial lumbar puncture and an early repeat lumbar puncture with measurement of CSF opening pressure to assess for raised intracranial pressure regardless of the presence of symptoms or signs of raised intracranial pressure.

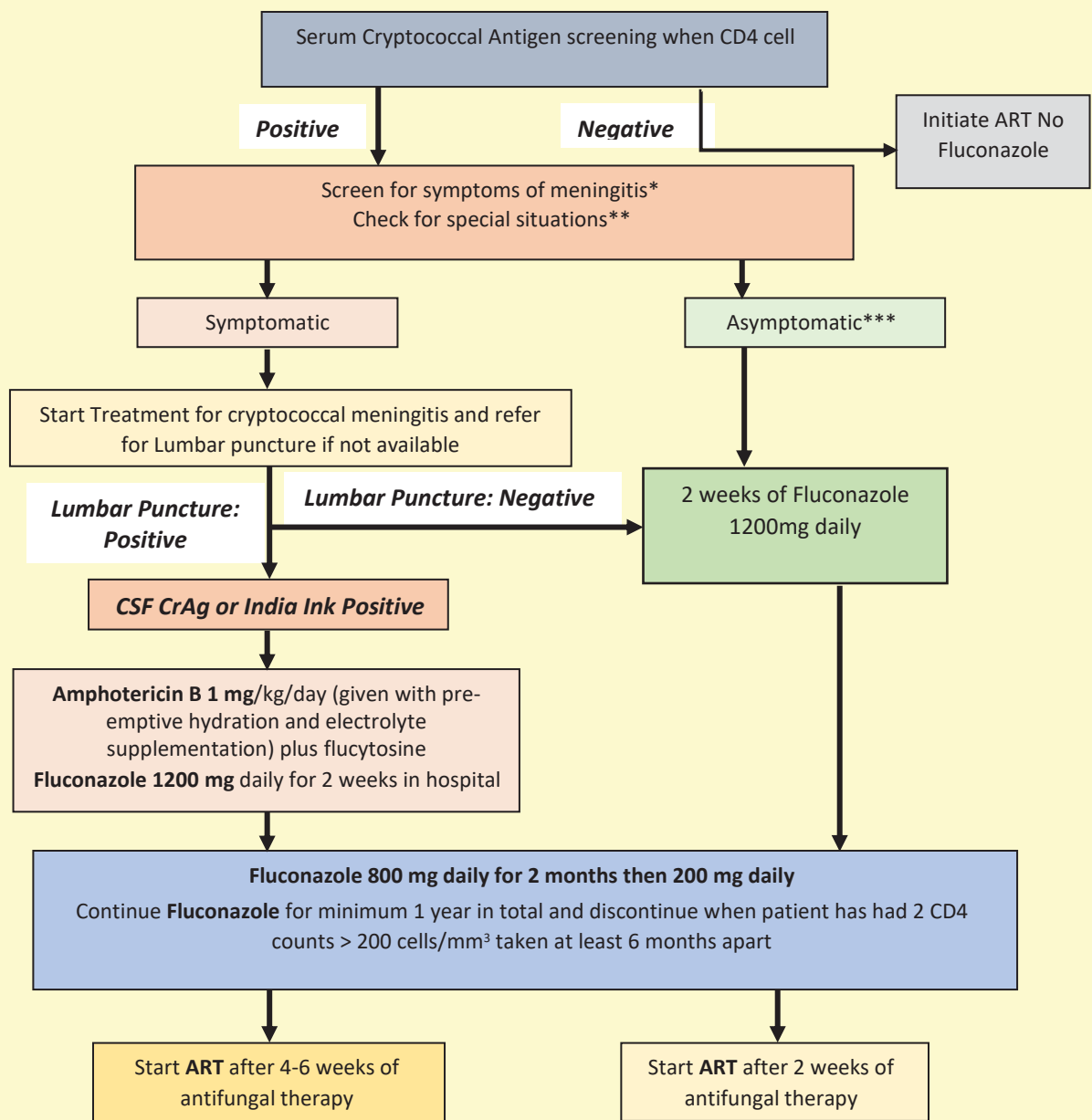
### Managing raised Intracranial Pressure

- Therapeutic lumbar puncture: relieve pressure by draining a volume sufficient to reduce the CSF pressure to < 20 cm H<sub>2</sub>O or halving the baseline pressure if the baseline pressure was too high.
- The persistence or recurrence of symptoms or signs of raised intracranial pressure should determine the frequency of repeat therapeutic lumbar puncture. For people with persistent symptoms of raised intracranial pressure, repeat daily therapeutic lumbar puncture.

### Treatment:

#### 1. Pre-emptive Management of Positive Cryptococcal Antigenemia

Studies show that 40-70% of people with Cryptococcal antigenemia are lost to follow up or die within the first year of ART. In these patients, Fluconazole prophylaxis reduces mortalities by 70%.



*\*Symptomatic for meningitis if either headache or confusion is present; \*\*Special situations include prior Cryptococcal Meningitis, pregnancy or breastfeeding mother; \*\*\*A lumbar puncture should be considered unless contraindicated.*

**Figure 3.1: Algorithm for Screening and Managing Cryptococcal Meningitis**

2. The antifungal treatment of HIV-associated Cryptococcal Meningitis disease is divided into three phases; **Induction, Consolidation and Maintenance.**

**Table 3.1: Antifungal Treatment of HIV-associated Diseases**

Phase	Duration	Treatment	Remarks
Induction	Option 1 7 day ( <i>Recommended</i> )	Preferred: Amphotericin B Deoxycholate 0.7-1mg/kg IV x 7 days and Flucytosine 25mg/Kg PO QID 7 day followed by 1 week of Fluconazole (1200mg/day for adults, 12mg/kg/day for children and adolescents, up to a maximum dose of 800mg daily)	- Hydration of the patient - Caution when using with Tenofovir (TDF) due to potential overlapping renal toxicities
	Option 2 2 weeks	Alternative; Amphotericin B deoxycholate 0.7 – 1mg/kg/day IV x 14 days with Fluconazole* 1200 mg – 800mg PO or IV daily x 14 days	
	Option 3 2 weeks	Alternative: Fluconazole (1200mg daily for adults, 12mg/kg/day for children and adolescents) x 14day + Flucytosine (25mg/kg/day, QID) x 14 days	- Consider in patients with renal dysfunction
Consolidation	8 weeks	Fluconazole 400mg – 800mg PO OD; 12mg/kg for children	- Fluconazole increases risk of hepatotoxicity
Maintenance	At least for 12 months or until CD4 > 200 cells/mm <sup>3</sup> for 6 months on two occasions with a suppressed viral load	Fluconazole 200mg PO OD (for children 6mg/kg)	

*Note for children use weight-based dosing.*

\*caution on use of Fluconazole in the 1<sup>st</sup> trimester. If patients on Fluconazole already and falls pregnant, seek expert opinion.

**Table 3.2: Minimum Package for Preventing, Monitoring and Managing Amphotericin B Toxicity**

Pre-emptive hydration and electrolyte supplementation for patients on Amphotericin B	
<b>Adults and adolescents</b>	One litre of Normal Saline solution with 20mEq of Potassium Chloride (KCl) over two hours before each controlled infusion of Amphotericin B and one to two 8mEq KCl tablets orally twice daily. An additional 8-mEq KCl tablet twice daily may be added during the second week. If available, Magnesium supplementation should also be provided (two 250mg tablets of Magnesium Trisilicate or Glycerophosphate twice daily, or Magnesium Chloride 4mEq twice daily).
Monitoring (adults, adolescents and children)	
<b>Serum Potassium</b>	Baseline and 2–3 times weekly
<b>Serum Creatinine</b>	Baseline and 2–3 times weekly
<b>Haemoglobin</b>	Baseline and weekly
Management (adults, adolescents and children)	
<b>Hypokalaemia</b>	If potassium is <3.3mol/L, increase Potassium supplementation to 40mEq KCL <b>SLOWLY</b> by intravenous infusion and/or 2 tabs 600mg Slow K TDS
<b>Elevated creatinine</b>	If creatinine increases by $\geq 2$ fold from the baseline value, increase pre-hydration to 1 L every eight hours and consider temporarily omitting a dose of Amphotericin B. Alternatively, switch to Flucytosine and Fluconazole combination if available
<b>Severe anaemia</b>	Transfusion should be undertaken for severe Amphotericin B-related anaemia

### Tips on the use of Flucytosine in Cryptococcal Meningitis

- Flucytosine is a pyrimidine analogue antifungal which converted to Fluorouracil inside the fungus and inhibits fungal protein synthesis
- Flucytosine and Amphotericin B combination improves fungal clearance rates compared to Amphotericin B alone or with Fluconazole

Side effects of Flucytosine include:

- Bone marrow suppression
- Psychosis
- Anaphylaxis
- Nausea, anorexia and diarrhoea

**Monitoring Treatment Response**

- Clinical response (including resolution of fever, headache and symptoms or signs of raised intracranial pressure) should be assessed daily during the initial two weeks of induction therapy
- Among people with evidence of a sustained clinical response, routine follow up lumbar puncture after completing induction treatment to assess antifungal treatment response (CSF fungal culture and CSF Cryptococcal antigen) or serum or plasma Cryptococcal antigen is **NOT** advised
- Persistent or recurrent symptoms beyond two weeks can be due to failure of fungal clearance, persistence increased intracranial pressure or paradoxical immune reconstitution inflammatory syndrome. Repeat lumbar puncture with measurement of CSF pressure and fungal culture is advise. CT Scan brain imaging can be done where available. Inadequate dosage or administration of Amphotericin B is the commonest cause of delayed CSF fungal clearance

**Prevention and Management of Cryptococcal Meningitis Relapse**

Cryptococcal meningitis relapse is commonly due poor adherence to the secondary prophylaxis with Fluconazole in the consolidation/maintenance phase. The standard induction therapy must be recommenced if the patient's is symptomatic and CSF India ink is positive.

To prevent relapse, a proactive referral and linkage to out-patient services for continual of secondary prophylaxis is recommended. Specific DSD models for this purpose are encouraged (see diagnosis of relapse above)

**Adjuvant Therapies**

- Initiation of ART: These patients should be initiated on **cART at least 6 weeks of starting Cryptococcal Meningitis treatment.** (Early cART initiation increases the risk of IRIS which in turn increases mortality)
- Steroids are contraindicated in Cryptococcal Meningitis treatment (*can be used with expert advice if Cryptococcal Meningitis IRIS is suspected*).
- Measure intracranial pressure using a manometer
- *Serial lumbar punctures in patients who have raised intracranial pressure suggested by symptoms such as reduced levels of conscious, convulsions, papilloedema, persistent headaches, or on fundoscopy or imaging*

**Important points**

1. Lumbar puncture should be done at a facility with skilled personnel and with appropriate resuscitative capacity such as Zonal clinics, First level hospital or higher.
2. The maintenance phase of CM treatment with Fluconazole should be discontinued as follows in children:
  - o Children < 2 years: continue until 2 years old
  - o Children 2-5 years old: continue for a minimum 1 year and discontinue when CD4 > 750 cells/mm<sup>3</sup>
  - o > 5 years old: continue for minimum of 1 year and discontinue has had two CD4 counts greater than 200 cells/mm<sup>3</sup> taken at least 6 months apart and the suppressed viral load

**Table 3.3: Differential diagnosis of Chronic Meningitis**

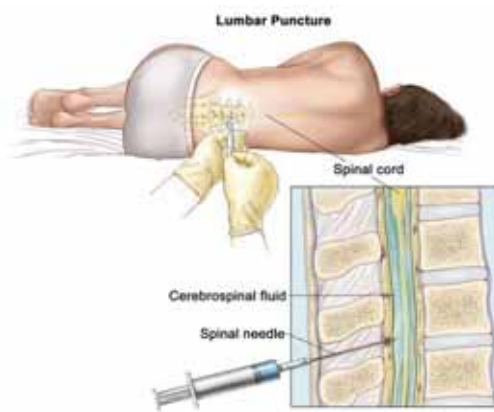
	Cryptococcal Meningitis	TBM
Clinical pearl	<ul style="list-style-type: none"> <li>• HIV naïve or failing ART with severe immunosuppression</li> <li>• Typically presenting with persistent headache</li> <li>• Occasionally skin manifestations of cryptococcus may be present</li> </ul>	Can affect an HIV + patient. Other symptoms of TB like lymphadenopathy or pulmonary involvement may be present. CXR fibro-cavitary picture
CSF	CrAg (+) Protein moderately raised Gene Xpert (-) Culture (+)	CrAg (-) Protein very high Gene Xpert (+/-) TB culture (+ but takes over 6 weeks)

**Collection of Cerebrospinal fluid through a Lumbar Puncture**

Contraindications of a Lumbar Puncture in cryptococcal meningitis include:

- Focal neurological signs (excluding isolated CN VI or VII palsy)
- Prolonged seizures
- Coagulation disorders
- Localized infections on the LP site
- Cardiopulmonary insufficiency

*(Note that LP is therapeutic for increased ICP in Cryptococcal Meningitis)*



## Module 4: Tuberculosis in Advanced HIV Disease

Under this topic, only TB in AHD is addressed. For other patient categories, please refer to the 2020 Zambia Consolidated Guidelines for the management of HIV and the 2017 National Tuberculosis and Leprosy Control Program TB MANUAL.

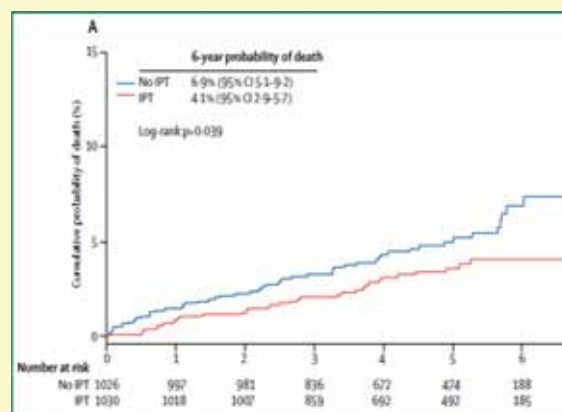
### Mycobacterium Tuberculosis (TB) in AHD: General Overview

Tuberculosis is the leading cause of mortality in HIV infected individuals accounting for 30% of all HIV related mortalities. Extrapulmonary and disseminated forms of TB are more common in AHD than in non-immunosuppressed individuals. In AHD, TB symptoms may be non-specific and include general unwellness, anaemia and weight loss **without** fever or night sweats. **The sensitivity of classic TB symptoms is lower in people with HIV and the diagnosis is usually depended on high index of suspicion, screening and occasionally can be presumptive.**

### Prevention of TB Through the use of TB Prophylactic Therapy

HIV infected individuals are 10 times more likely to progress to active Tuberculosis. TB Prophylactic Therapy reduces mortality by 39% at 78 months of follow-up. ALL HIV infected individuals must receive TPT after symptomatically excluding active tuberculosis. TPT is give every three years and only symptomatic screen for exclusion of active TB is required. A negative sputum, Chest x-ray, Mantoux or IGRA test are not a requirement for commencing TPT. However, TPT must not be given in individuals with signs of active tuberculosis.

(Please refer to the TPT Guidelines for more information on TPT in Zambia)



Sources: 1. Gupta, PLoS One 2012. 2. Ayele, PLoS One 2015; 3. TEMPRANO ANRS 12136 Study group, NEJM 2015; 4. Akolo, Cochrane Database 2010; 5. Golub, CID 2015; 6. Rangaka, Lancet 2014; 7. Azadi; IJTL 2014; 8. Hausler, WHO Bulletin 2006; 9. Shrestha, IJTL 2007; Graph: Badje, Lancet Global Health 2017

**Table 4.1: TPT Regimens in Zambia**

Regimen	Duration	Dosage	Comments
Isoniazid and Pyridoxine	6 months	300mg Isoniazid 50mg Pyridoxine	Watch out for rash, hepatitis, and peripheral neuropathy
Isoniazid and Rifampicin	3 months	300mg Isoniazid and 300mg Rifampicin	Watch out for rash, hepatitis, and peripheral neuropathy
Rifapentine and High dose Isoniazid	3 months	Isoniazid 15mg/kg weekly Rifapentine weight based weekly (900mg in <50kg)	Watch out for rash, hepatitis and peripheral neuropathy, body fluids discoloration

## Screening and Diagnosis of Tuberculosis in Advanced HIV Disease

All adults and adolescents with AHD must be screened using a **LAM test** (< CD4 cell count <200 cells/mm<sup>3</sup>) **and Chest X-ray** in addition to symptomatic screening. ALL HIV infected persons must have a symptomatic screening for TB at all clinical contacts using the 4 symptoms screen. Those that have a positive symptomatic screen must have a diagnostic test using a Gene Xpert.

An Xpert MTB/RIF test is recommended as the preferred initial microbiological test for suspected tuberculosis in patients with AHD. It can also be used as an add-on test where smear microscopy is negative. It should be noted that in persons with HIV infection, sputum microscopy is less sensitive than in persons without HIV infection. In individuals with suggestive symptoms but both Xpert and smear are negative, treatment for tuberculosis can still be commenced and sputum samples sent for AFB culture.

### Lateral Flow Urine Lipoarabinomannan (LF-LAM)

Lipoarabinomannan (LAM) is an *M. tuberculosis* cell wall polysaccharide that can be detected in the urine of TB patients. The LAM test is a bedside point of care test for rapid screening and diagnosis of tuberculosis. It is recommended for use in HIV infected with symptoms and signs of TB or seriously ill; or irrespective of signs and symptoms in **inpatients** with CD4 cell count < 200 cells/mm<sup>3</sup> or outpatient with CD4 cell count < 100 cells/mm<sup>3</sup>.

The diagnostic utility of LAM is limited by a low sensitivity (37 to 56%) but has the advantages of being available as a true point of care test that can be performed on urine. Specificity is up to 95%. In addition, LAM has higher sensitivity in patients with worse prognoses, who are therefore a high priority to identify active TB. LAM should be combined with other diagnostic strategies to improve diagnostic yield.



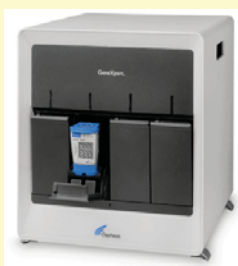
**Table 4.2. Diagnostic Tests for Tuberculosis**

Test	Comment
<b>The Xpert MTB/RIF Assay</b>	Frontline diagnostic test. If not available, refer samples of priority patients
<b>Sputum smear and culture</b>	First line test where Xpert MTB/RIF is not available. Smear-negative results common in AHD even in the presence of active TB
<b>Chest radiograph</b>	Should always be done regardless of form of TB being investigated
<b>Lipoarabinomannan (LAM)</b>	Urine based test. Recommended in HIV with CD4 <200 cells/mm <sup>3</sup> counts or who are seriously ill without a known CD4 count
<b>Line Probe Assay (LPA)</b>	<b>Diagnostic test based on DNA isolation and amplification of MTB.</b> 1 <sup>st</sup> line LPA is recommended for the rapid detection of resistance to Rifampicin and Isoniazid. 2 <sup>nd</sup> line LPA is recommended for patients with confirmed rifampicin resistance (RR-TB) or multi drug resistant tuberculosis (MDR-TB)
<b>Culture and Drug susceptibility testing (DST)</b>	<b>Recommended for suspected DRTB</b> (retreatment cases, Treatment failure, Xpert MTB RIF Resistant)

## Treatment of Tuberculosis in Advanced HIV Disease

**Principles of therapy must always be maintained as guided in the TB Manual.** Drugs used in management of DS-TB are Isoniazid (H), Rifampin (R), Ethambutol (E), and Pyrazinamide (Z)

- 2 months of RHEZ intensive phase
- 4 months of RH continuation phase



*Gene Xpert is the first line test for the diagnosis of TB individuals with advanced*

If rapid DST results indicate resistance to Rifampin, with or without resistance to other drugs, an initial DRTB regimen should be prescribed (refer to DRTB TREATMENT GUIDELINES)

### *Common Differential Diagnosis of PTB in AHD*

- Bacterial pneumonia
- PCP (CD4 usually < 200)
- Non-Tuberculous Mycobacteria (MAC)
- Cryptococcosis or other fungal pneumonia (CD4 usually < 100)
- Cytomegalovirus (CD4 usually <50)
- Kaposi's sarcoma (usually occurs with CD4 < 100)
- Lymphoma (CD4 usually < 100)
- Lung cancer
- Congestive Cardiac Failure

**Initiation of antiretroviral therapy (ART) in patients co-infected with TB/HIV**

Management of HIV/TB co-infection requires that both infections be addressed. For patients already on cART, TB therapy must be started immediately. Assess for cART treatment failure, and modify of cART must be done if indicated

**In cART naïve patients (and defaulters), TB treatment should be initiated first followed by cART as soon as possible within the first two weeks of treatment**

***Drug-Drug Interactions in the Treatment of HIV-Related TB***

Management of HIV/TB co-infection is complex because of:

- The adherence demands of multidrug therapies for two infections causing high pill burden.
- Drug-drug interactions between the Rifamycins and many antiretroviral drugs like Dolutegravir
- Overlapping side effect profiles of anti-TB and antiretroviral drugs
- Development of Immune Reconstitution Inflammatory Syndrome (IRIS) since rates of IRIS are primarily higher in those with lower CD4 cell counts. Steroids, like Prednisolone 40-60mg P.O once a day for 4 weeks can be used in TB associated IRIS.

The Rifamycins (Rifampin, Rifabutin, and Rifapentine) are key to the effective treatment of drug-sensitive TB. However, they have significant clinical interactions with a number of antiretroviral drugs (INSTI, PIs and NNRTIs).

**Choice of Drugs when Co-administering ATT and cART**

1. If on ATV-r, switch to LPV-r and double the dose of LPV-r
2. If on LPV-r, double the LPV-r dose or super-boost with ritonavir to LPV: RTV ratio of 1:1.  
\*increase LPV-r dose from 2 tablets BD to 3 tablets BD for 2 weeks and then to 4 tablets BD for the remainder of TB treatment period
3. If on DTG, switch to EFV (if on first line) or provide twice daily DTG 50 mg where available. DTG single formulation is available
4. Where Rifabutin is available, switch Rifampicin to Rifabutin and continue cART on usual dosages
5. Where the protease Inhibitor cannot be changed, dose changed or super-boosted and Rifabutin is unavailable, Rifampicin can be replaced with other bactericidal anti-tuberculous drugs such as Moxifloxacin, Linezolid or Carbapenems
6. If on TafED, switch to TLD and add an extra DTG 50mg separate dose or Switch to TLE.  
(Note that there is still not evidence for the use of TafED with Rifamycins)

## Monitoring of TB Treatment in Critical Ill Patients

Individuals with AHD and TB are often very ill requiring admission. These patients typically have disseminated TB with mycobacteraemia and could progress to sepsis and multiple organ failure. They are also prone to adverse drug reactions due to polypharmacy. Monitoring for the following parameters that contribute to high mortality is recommended.

**Table 4.3: Parameters to Monitor in Admitted TB Patients**

Parameters to monitor in admitted TB patients	Comments
Hypoglycaemia	Daily RBS and 4 hourly RBS in critically ill. Hypoglycaemia is due to adrenal insufficiency, liver failure, renal failure, sepsis, or starvation
Hypotension (shock)	4 hourly BP monitoring: Minimal fluid support, inotropic support, and Hydrocortisone for mineralocorticoid support. Shock (low BP) is due to septic shock, adrenal insufficiency, or hypovolaemia
Acute Liver Injury (ALI)	Weekly ALT/AST: ALI is due to ATT, hypotension, or direct injury by the mycobacteria (granulomatous hepatitis). Modify ATT to liver friendly regimen ( <i>Consult ID specialist or physician</i> )
Acute Renal Injury (ARI)	Monitor creatinine, urea, and electrolytes every at least every 72 hours. ARI is due to sepsis, ART ( <i>tenofovir</i> ) or hypotension. Adjust Ethambutol dose and discontinue all other nephrotoxic drugs and monitor other electrolytes. ( <i>Consult nephrologist for possibility of renal replacement therapy</i> )

## Extrapulmonary Tuberculosis

Extrapulmonary and disseminated TB are more common in AHD. TB must be considered in disease processes involving any site in the body, but especially those related to Central Nervous System (CNS) or meningeal symptoms in which early TB treatment is essential to improve outcomes. Disseminated TB is the presence of pulmonary TB with the occurrence of TB in other organs. Disseminated TB usually involves the presence of *mycobacteria* in blood (mycobacteraemia). A miliary chest X-ray picture is a sign of disseminated TB and should warrant a search of TB in other organs.

Symptoms will depend on the anatomic site of TB infection and are listed in the table below.

**Table 4.4: Type of Extra-pulmonary TB and Symptoms**

Type of Extra pulmonary TB	Symptoms
Pleural effusion	Shortness of breath, chest pain
Pericardial effusion	Tiredness, chest pains, shortness of breath, signs of cardiac tamponade that include <i>raised jugular venous pressure, enlarged liver, low volume pulse, ankle swelling</i> etc
TB meningitis	Headaches, neck stiffness, altered consciousness-lethargy, seizures, confusion, coma, neurological deficits/localising signs.
TB adenitis	Note that 50% of adenitis in Zambia is caused by TB)
TB abdomen	Abdominal distension, ascites, palpable masses, organomegaly and diarrhoea
Bone and joint TB especially spinal TB	Backache, joint swellings and pain, spontaneous fractures, neurological deficit e.g., paraplegia
Adrenal and Urogenital TB	Hypoglycaemia, hypotension, dysuria, lower abdominal and back pain and fever

### Diagnosis of Extrapulmonary Tuberculosis

Initial testing is directed at the anatomic site of symptoms or signs (e.g., lungs, lymph nodes, urine, cerebrospinal fluid). Evaluation of suspected TB should always include a chest radiograph, regardless of the presence of pulmonary symptoms or signs. Sputum Xpert and/or microscopy must be evaluated for any form of TB.

- Aspiration of sites (pleura, lymph nodes, pericardium, and abdomen) for Xpert MTB/RIF or ZN stain and MCS
- Tissue biopsy for histopathology, smear, and culture (may use Xpert MTB/RIF)

### Treatment of Extrapulmonary Tuberculosis

- Antituberculosis drugs may be given for a longer duration (12 months for TBM and bone TB)
- Steroids are indicated in certain types of EPTB (Pericarditis, meningitis, Large pleural effusions due to TB)

## TB Meningitis

Worldwide, TB is the most common cause of brain infection in HIV patients and is more common in patients with lower CD4 counts. TB of the brain can present as basilar meningitis, cerebritis or as a tuberculoma. A high index of suspicion is required to diagnosed TB meningitis.

### Presentation

TB Meningitis (TBM) may present with headache, weakness, increased reflexes, poor hearing, poor vision, confusion, and fever and weight loss. Tuberculomas are mass lesions of TB in the brain and thus have a presentation consistent with other brain mass/space occupying lesions (headache; seizures; stroke; fever; confusion localising signs). If considering TB in the brain, also consider TB in other places (lung, lymph nodes, bone marrow). Conversely, look for TB meningitis in disseminated TB.

Symptoms are usually present for weeks to months to even a year prior presentation to a clinician.

### Diagnosis

Lumbar puncture should be performed if TBM is suspected. An Xpert MTB/RIF test on cerebrospinal fluid is recommended as the preferred initial microbiological test in persons suspected of having tuberculous meningitis because of the need for a rapid diagnosis. CSF AFB smear and CSF AFB culture can also be done and typically require about 10 ml of CSF. LP CSF results in TBM are typically as shown in Table 4.5. ***The presence of CSF high protein, CSF lymphocytosis, or abnormal Chest X-ray findings would warrant presumptive treatment for TBM in the presence of CNS symptoms in AHD.***

**Table 4.5: CSF Results in Tuberculosis Meningitis**

Parameter	Findings
Appearance	Turbid, fibrin clots (spider web clots)
Opening Pressure	Normal or raised (> 20 cm H <sub>2</sub> O)
Cell Count	High (100 – 500 cells/mm <sup>3</sup> , with lymphocyte predominance - > 70%)
Protein	Raised (0.1 – 0.5 g/dL)
Glucose	Low or Normal (< 2/3 of serum Glucose)

### Differential Diagnosis of TB Meningitis

- Cryptococcal meningitis
- CNS lymphoma
- Toxoplasmosis
- Neurosyphilis
- Bacterial Meningitis

### Treatment

- Adults: Drug susceptible; (2RHZE/10RH)
- Drug Resistant; refer to NTLP guidelines
- Children Drug susceptible (2REZH/10RH)
- Steroids indicated for all cases of TBM, as they lower death from TBM by 30%
  - Very sick: Inpatient, Dexamethasone 8 mg IM TDS
  - Less sick: Outpatient, Prednisolone 30 mg PO BD; Taper slowly over 4-8 weeks

#### Complications of TB Meningitis

*Where available, a CT scan and fundoscopy must be done to identify the following complications of TBM:*

- *Increase Intracranial pressure: Serial LP to reduce the pressure*
- *Hydrocephalus: Ventriculo-peritoneal shunts should be insert by neurosurgeons*
- *Tuberculoma with mass effect: Neurosurgical consult for excision*

### TB Pericarditis

#### Presentation

Mycobacterium spreads from the lungs to the pericardial sac and can have similar constitutional symptoms to PTB. On physical exam the patient may have pericardial friction rub and there may be evidence of heart failure. If the fluid accumulates quickly, you may find pulsus paradoxus which is a sign of cardiac tamponade. Chest X-ray will show an enlarged heart due to the fluid around it with a straight heart border. Echocardiography if available may show fluid or fibrinous strands.

An Xpert MTB/RIF test on pericardial fluid would assist with the diagnosis. The fluid will typically show an exudate picture and the Adenosine Deaminase test (ADA) will be positive. Long term complications of TB pericarditis include calcification of the pericardium and possible restrictive pericarditis.

**Treatment for TB Pericarditis**

- Adults: usual regimen (2RHZE/7-10RH)
- Children: category (2RHZE/7RH) plus steroids 2mg/kg tapered slowly over 4 to 8 weeks
- Steroids:
  - Very sick: Inpatient, Dexamethasone 8mg IM TDS
  - Less sick: Outpatient, Prednisolone 30mg po BD
  - Taper slowly over 4-8 weeks

**Spinal TB**

The most well recognized TB of the bone is Pott's disease or spinal TB, but TB can occur in other bones as well. Pott's disease is more common in HIV negative young men and predominantly involves the thoracolumbar spine. Cervical disease is however rare.

Back pain is the most common symptom, but disease can progress to cord compression resulting in weakness, hyper-reflexia and incontinence. Abscess may develop.

Patient may develop a "Gibbus deformity" (see Figure 4.1) which is a hump on the back that occurs due to collapse of the vertebrae from infection. Tissue biopsy for Xpert, AFB smear and Culture can aid in the diagnosis. Spine X-rays typically will show sparing of the vertebral edges. Surgery is not usually indicated unless more than one vertebra is involved, or neurological signs are present.

**Treatment**

- Adults: 2HRZE/10RH
- Children: 2HRZE/10RH

For bone in adults can use: 2HRZE/7 to 10 months RH depending on response.

- Steroids not indicated
- Consult surgeons/orthopaedic surgeons if:
  - a) More than 2 vertebrae involved
  - b) High angulation
  - c) Worsening of neurological signs



**Figure 4.1: Gibbus Deformity**

## TB Abdomen

TB of the abdomen can present as peritonitis with ascites, TB of the intestines with diarrhoea, or in abdominal lymph nodes with abdominal masses. Severe wasting may be seen in these patients and most will have ascites on exam.

### Diagnosis

Diagnosis is difficult but if clinical suspicion is high, a paracentesis can be performed. Paracentesis results may appear as shown in Table 4.6. Exploratory surgery can be performed and may reveal granulomas on the peritoneum that are diagnostic of abdominal TB. The Serum: Ascitic Albumin ratio (SAAG) will be  $> 1.1\text{mg/dL}$  indicating a non-portal hypertension ascites. ADA will be positive. Abdominal lymphadenopathy on abdominal Ultrasound Scan is very suggestive of TB abdomen.

**Table 4.6: Paracentesis Results in TB Abdomen**

Parameter	TB Abdomen typical finding
Protein	$> 0.3\text{g/L}$
WBC	$> 1000\text{WBC}$ per microlitre
AFB	M. tuberculosis seen sometimes
Gene Xpert	MTB/RIF Assay
Adenosine Deaminase (ADA)	Positive

### Treatment

TB treatment can be initiated empirically if the clinical picture is consistent with TB use the standard regimen - 2RHZE/6RH.

Surgical consultation may be required if there are signs of bowel obstruction or peritonitis.

## TB Lymphadenitis

### Presentation

TB lymphadenitis may occur in a single or multiple lymph nodes. The mycobacteria may infect lymph nodes that drain the lung or may infect the lymph nodes through the blood. Fever, weight loss, and cough are again common in this form of TB infection. The nodes can be hard or soft, matted and vary in size. Some nodes may be purulent.



## Diagnosis

Look for TB in other places with particular attention to the lung.

If the node is fluctuant, a fine needle aspiration can be performed and sent for Gene Xpert/MTB Rif or stained for AFB. If purulent material is draining, the material can be sent for Gene Xpert or a glass slide can be pressed to the lesion and sent for AFB stain.

### Treatment and Prognosis

- Standard regimen - 2RHZE/4RH
- Nodal TB alone is a mild disease with a good prognosis.
- Be careful to look elsewhere (brain, lung)
- Be aware that “paradoxical worsening” may occur, and the lymph node may enlarge before healing. This is a form of immune reconstitution in the presence or absence of HIV or ART.

## Pleural TB

Pleural TB is the leading form of extra-pulmonary TB in AHD. TB infects the sac around the lung. The sac is filled with exudative fluid which is commonly one-sided (unilateral). Symptoms include fever, cough, and shortness of breath. On examination, there may be dullness to percussion. Pleural TB has low mortality rate unless patients present late. Pleural fluid must be obtained to identify an exudative fluid using the Light’s criteria as the first diagnostic step.

## Diagnosis

- Any patient with pleural effusion in AHD should be investigated for TB
- Sputum Xpert and AFB smear
- Look for TB elsewhere (lymph node, brain)
- Diagnostic thoracentesis and fluid for M/C/S, albumin, LDH, Xpert, Adenosine deaminase
- Pleural biopsy is technically difficult and usually not necessary

### Treatment

- Standard regimen 2HRZE/4RH
- Empirical TB therapy may be warranted in any patient with undiagnosed pleural effusion
- Therapeutic drainage (by thoracentesis or chest tube) is usually not necessary unless patient is breathless at rest

### Differential Diagnosis Pleural TB

- Empyema: usually very sick
- Kaposi’s sarcoma
- Bacterial pneumonia with parapneumonic effusion
- Heart failure and renal failure
- Lymphoma
- Breast and Lung cancer
- Mesothelioma

## Tuberculosis in Children

All Children Living with HIV under 5 years old are considered to have AHD. Making a diagnosis of Tuberculosis is challenging and requires a bit more effort due to the insidious nature usually heralded by failure to thrive. Due to the high incidence of other pneumonias in HIV-infected children, the picture is further complicated, and the diagnosis becomes even more unclear. Transmission of TB to a child indicates recent exposure from a close contact. HIV/TB Co-infected children will experience rapid progression from TB exposure and infection to active disease. Extra pulmonary TB is seen more often in the TB/HIV co-infected children. Fatality rates are also higher in this population. Confirming TB in children requires careful and thorough assessment of all the evidence derived from a careful history, clinical examination, and relevant investigations, including chest x-ray. Sputum for gene-Xpert and AFB smear is very difficult to obtain in children under 6 to 8 years; often a gastric lavage or aspirate for gene-Xpert or AFB may substitute. Stool can be used for gene-Xpert in situations where respiratory specimens cannot be obtained.

### **Risk factors of TB in children**

- Contact with TB patient
- Children aged less than 5 years
- Malnutrition
- HIV positive status
- Recent measles disease
- Other immune deficiency conditions such as diabetes, cancer, steroids use.

Bacteriologic confirmation of TB should be sought whenever possible. However, most children will be negative for mycobacterial confirmation before commencement of therapy.

**Table 4.7: Assessment of a Child with Respiratory Symptoms**

Symptoms	Signs
Current cough	Hilar adenopathy
Difficult breathing, fast breathing, chest indrawing and respiratory distress	Thin or wasted
Anorexia, poor weight gain, weight loss, weight faltering and failure to thrive	Temperature: normal or elevated
Reduced activity and irritability or lethargy	Lymph nodes: enlarged, painless (may be matted or with discharging sinus)
Fever for at least 2 weeks without other obvious cause and not improving with antibiotics/antimalarials (consider *TB even if the fever is of less than 2 weeks)	Pallor

**Physical Examination**

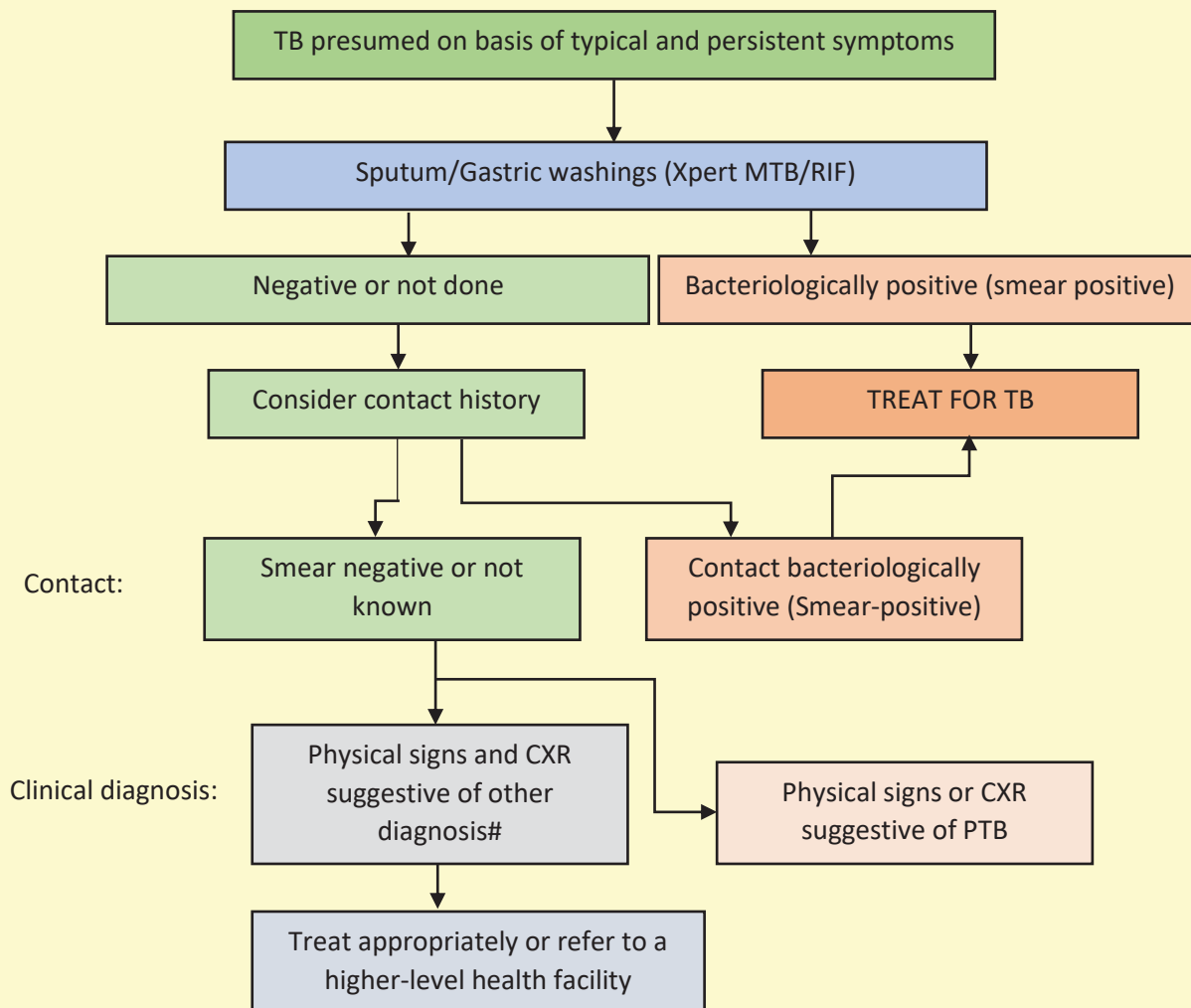
Abdomen.

- Distension
- Ascites
- Masses

Joints:

- Swelling/effusion
- Angulation of the spine [gibbus deformity]

## TB Diagnosis in Children



**Figure 4.2: Approach to TB Diagnosis in HIV-infected Child**

### Atypical clinical presentations of PTB

- Acute severe pneumonia
- Presents with fast breathing and chest in-drawing
- Occurs especially in infants and HIV-infected children
- Presume PTB if poor response to antibiotic therapy
- Wheezing. Asymmetrical and persistent wheeze can be caused by airway compression due to enlarged tuberculous hilar lymph nodes

### Differential Diagnosis of Respiratory Symptoms in Children

- Bacterial Pneumonia
- PTB
- PCP
- LIP
- Pertussis (Whooping cough)
- Aspirated foreign body
- Severe gastro-oesophageal reflux
- Bronchiectasis

	Intensive phase	Continuation phase	Use of Pyridoxine
All DSTB	2 (HRZE)	4 (HR)	Supplemental Pyridoxine 5-10mg/kg/day
TB forms meningitis, osteoarticular, pericardial, Spinal TB, other severe forms of TB (corticosteroids indicated)	2 (HRZE)	10 (HR)	Malnourished children HIV infected children Breastfeeding children Nutritional support

*Prednisolone 2mg/kg daily, increased to 4 mg/kg daily in the case of the most seriously ill children, with a maximum dosage of 60 mg/day for 4 weeks may be used. Taper over 1–2 weeks.*

Severe malnutrition is associated with increased mortality in TB patients - children and adults - and a child’s nutritional status should be assessed regularly during treatment.

### Decisions regarding ART

- Choice of ARVs
- Risks of ARV-ATT interactions
- Timing of ART initiation: start cART 2 weeks after ATT initiation
- Monitoring

*Please see the ZCGs 2020 for ART regimens in HIV/TB co-infected children*

*CTX must be given to Adults and Adolescents with <350 cells/mm<sup>3</sup> or WHO Stage II/III/IV, Pregnant and breast-feeding women and Children < 5 years old among PLHIV*

## Module 5: Severe Bacterial Infections in Advanced HIV Disease

People with AHD frequently are severely immunosuppressed and are susceptible to severe bacterial infections including bloodstream, respiratory, central nervous system, and gastrointestinal infections. Severe bacterial infections are estimated to cause more than one third of the hospitalizations among adults and children living with HIV worldwide. This is compounded by the background high prevalence of bacterial infections in LMIC like Zambia. Increasing resistance to antimicrobial drugs can complicate the treatment of people with severe bacterial infections.

### Prophylaxis for Severe Bacteria Infection in Advanced HIV disease

Co-trimoxazole (Trimethoprim-Sulfamethoxazole) prophylaxis provides protection against some but not all severe bacterial infections. Routine prophylaxis with antibiotics is not recommended.

### Diagnosis and treatment of Invasive Bacteria Infection

The diagnosis of Invasive Severe Bacteria Infections requires the isolation of the organism on microscopy or culture. Drug susceptibility patterns will aid optimal antibiotic selection. Where culture and sensitivity testing are not feasible, empiric treatment targeting suspected organisms, provided there is evidence of the presence of an infection, is recommended. *Remember that irrational use of antimicrobials promotes drugs resistance and unnecessary toxicity.*

### Bacterial Meningitis in Advanced HIV Disease

Bacterial Meningitis is a serious infection of the meninges with very high mortality. Bacterial meningitis presents acutely with short duration of illness (within 10 days) with headache, fever, neckaches, photophobia, altered mental status or seizures.

#### Diagnosis of Bacterial Meningitis

A lumbar puncture should be performed unless there is no contraindication. Features that favor bacterial meningitis in CSF include:

- CSF glucose concentration of <1.9 mmol/dL,
- Ratio of CSF to blood glucose of <0.23,
- CSF protein concentration of >220 mg/dL,
- CSF leukocyte count of >2000 leukocytes/mm<sup>3</sup>
- CSF neutrophil count of >1180 neutrophils/mm<sup>3</sup>

#### Bacterial causes of meningitis in HIV

- *S. pneumoniae* (Commonest)
- *H. influenzae* (if not immunised)
- *Non-typhoid Salmonella*

**Table 5.1: Treatment of Bacterial Meningitis in Adults with Advanced HIV Disease**

	Targeted Organisms	Recommended Antimicrobial	Alternative Therapies
Empirical Treatment in the absence of identified organism	- <i>S. pneumoniae</i> - <i>H. influenzae</i> - <i>Non-typhoidal Salmonella</i> - <i>E. coli</i>	High dose third generation cephalosporin e.g., Ceftriaxone 2g BD or Cefotaxime 2g TDS for 10-14 days	Penicillin G in combination with Fluoroquinolone or Chloramphenicol <b>Consider adding Ampicillin in &gt;50yrs and pregnant women</b>
Specific therapy	<i>S. pneumoniae</i>	High dose third generation cephalosporin: Ceftriaxone 2g BD IV or Cefotaxime 2g TDS x 10-14 days	Penicillin G in susceptible organisms. Consider adding Vancomycin if the risk of resistance is high
	<i>H. influenzae</i>	High dose third generation cephalosporin; Ceftriaxone 2g BD IV or Cefotaxime 2g TDS x 7 days	Chloramphenicol or Fluoroquinolone
	<i>L. monocytogenes</i> (Consider in elderly and pregnant women)	Ampicillin 2g IV 4-hourly ± Gentamycin for synergy Treatment is for 21 days and can be longer in immunosuppressed.	Carbapenems
	<i>Non-typhoidal Salmonella and E. coli</i>	High dose third generation cephalosporin as above for 10-14 days	Fluroquinolones, Cefepime or carbapenems

**NOTE:**

- Adjunct steroids are not routinely recommended in bacterial meningitis in LMIC
- Brain CT Scan with contrast is useful to prior to Lumbar Puncture to exclude intra-cranial mass effect and confirm the presence of meningitis or complications such as hydrocephalus

**Bacterial Pneumonia in Advanced HIV Disease**

Recurrent invasive bacterial pneumonia is common in AHD. This commonest causative organism is *S. pneumoniae*. However, other organisms can cause a pneumonia in immune-compromised individuals as part of the disseminated bacteraemia from different sites. The clinical presentation includes an illness of short duration (< 2weeks) with cough, fever, dyspnoea, and bronchial breathing sounds or crepitations on auscultation. The Chest X-ray showing a lobar consolidation can distinguish a typical community acquired pneumonia from other causes such as pulmonary tuberculosis. Sputum for Xpert and AFB smear must be done in all AHD being assessed for a pneumonia.

**Bacteraemia in Advanced HIV Disease**

Blood stream infection is a serious condition that must be treated with intravenous antibiotics. Patients are often very ill with a toxic look. The common sources of infection include the **urogenital tract**, the **abdominal cavity via bacterial translocation**, the **lungs**, and the **skin and soft tissue**. Gram negative rods are the commonest cause of blood stream infections in AHD. The diagnosis can be confirmed by blood culture and sensitivity.

**Table 5.2: Treatment of a Bacterial Pneumonia in AHD**

	Targeted Organisms	Recommended Antimicrobial	Alternative Therapies
Out-patient in a stable patient	- <i>S. pneumoniae</i> , <i>H. Influenza</i> , <i>Moraxella</i> , and atypical organisms ( <i>mycoplasma in particular</i> )	Azithromycin 500mg PO day 1 then 250mg daily day 2-5 OR  Amoxicillin-Clavulanic acid 1000/62.5 mg PO BD x 7 days OR  Doxycycline 100mg BD PO x 5-7 days	Penicillin G in combination with Fluoroquinolone or Chloramphenicol
In- patient ill patient	<i>S. pneumoniae</i> and atypical organisms	Penicillin G in combination with a macrolide or	Ceftriaxone 1g IV OD +Azithromycin 500mg IV/PO OD x 5-days  Respiratory fluoroquinolone such as levofloxacin 750mg IV/PO OD x 5-7 days
Concerns of Hospital acquired infections or in a critically ill patient in shock or in ICU	<i>Methicillin resistance S. aureus</i> , <i>Pseudomonas species</i> and drug resistance gram negatives	As above plus Vancomycin 15-20mg/kg IV 8-12-hourly for MRSA. Consider Cefepime 2g IV BD for resistant gram-negative organisms	Linezolid 600mg OD IV/PO and Carbapenems

**Table 5.3: Treatment of Blood Stream Infection on AHD**

Sources of the infection	Targeted Organisms	Recommended Antimicrobial	Alternative Therapies
Genital urinary	<i>E. coli</i> and other gram-negative rods	3 <sup>rd</sup> generation cephalosporin: Ceftriaxone 1g OD IV	Fluoroquinolone or Chloramphenicol
Intra-abdominal	Gram negative rods and anaerobes and pseudomonas	3 <sup>rd</sup> generation cephalosporin (Cefotaxime 2g TDS IV or Ceftriaxone 2g OD IV) OR Fluoroquinolone (Ciprofloxacin 400mg BD IV OR Levofloxacin 750mg IV OD) with Metronidazole 1g loading dose then 500mg TDS x 10-14 days	Piperacillin Tazobactam, Cefepime or Carbapenems
Respiratory	<i>S. pneumoniae</i> and gram-negative rods	3 <sup>rd</sup> generation cephalosporin Ceftriaxone 1g OD IV 10-14 days	Respiratory Fluoroquinolone
Source unclear	Non-typhoidal <i>Salmonella</i> , other gram-negative rods, <i>pseudomonas</i>	3 <sup>rd</sup> generation cephalosporin (Cefotaxime 2g TDS IV or Ceftriaxone 2g OD IV) OR Fluoroquinolone (Ciprofloxacin 400mg BD IV OR Levofloxacin 750mg IV OD) + Metronidazole 1g loading dose then 500mg TDS x 10-14 days. If suspected MRSA add Vancomycin	Piperacillin Tazobactam, Cefepime or Carbapenems

Bacterial etiology of blood stream infections

- Non-typhoidal *Salmonella*
- *Pseudomonas species*
- *Klebsiella species*
- *H. influenzae*
- *E. coli*



## Module 6: Other CNS Condition in Advanced HIV Disease

Central Nervous system disease is the leading cause of mortality in AHD. Apart from CNS Cryptococcus and Mycobacteria infection, other rare but lethal causes of CNS disease in AHD are toxoplasmosis and viruses such as CMV, EBV, VZV, HSV and JCV.

### AIDS-related Cytomegalovirus Neurologic Disease

HIV-infected patients become susceptible to CMV disease when the CD4+ T-cell count falls below 100 cells/mm<sup>3</sup> but can present at CD4 > 100 cells/mm<sup>3</sup> due to IRIS. Prior to the availability of highly active antiretroviral therapy (HAART), CMV neurologic disease occurred in up to 2 percent of patients with AIDS but has reduced with the advent of ART but still with debilitating or fatal outcomes.

#### CMV Retinitis

CMV retinitis can cause blurring or loss of central vision, scotomata ("blind spots"), floaters, or photopsia ("flashing lights") resulting into irreversible loss of vision if not treated early. A complaint of floaters or photopsia is the single most powerful symptomatic predictor of CMV retinitis in an AHD patient and should always be evaluated with dilated ophthalmoscopy. Fundoscopy is sufficient for diagnosis and is aided by PCR for intravitreal fluid.



*CMV retinitis on fundoscopy*

Goals of therapy are:

- Prevent further loss of vision.
- Prevent visual loss in the contralateral eye
- Increase overall immunity with ARVs

#### Treatment

- Induction: Ganciclovir 5 mg/kg IV BD x 14-21 days or Valganciclovir 900 mg PO BD x 21 days AND/OR IV Ganciclovir injections or intraocular implant (if available)
- Post treatment suppression: Valganciclovir 900mg PO OD until CD4 cell count >100 for 6 months
- If lesions progress or relapse, re-induce with same agent. Watch for IRIS

### CMV Encephalitis

Chiefly a disease of immunosuppressed individuals. The clinical picture is typically dominated by confusion and lethargy, and the course is relatively rapid with sub-acute progression to coma and death. All patients have AHD, and most have a diagnosis of another disease related to cytomegalovirus, most commonly retinitis. Nystagmus, ataxia, and unilateral or bilateral cranial nerve palsies usually involving oculomotor or facial nerves are the most characteristic neurologic signs. One or more of the characteristics focal neurologic findings are present in 50% of patients. Rarely patients develop evidence of encephalitis shortly after presenting with lower-extremity weakness from polyradiculopathy. Diagnosis is by CSF CMV PCR aided by brain imaging. Treatment is with Ganciclovir or Valganciclovir as above.

### CMV Polyradiculopathy

CMV polyradiculopathy usually presents with ascending lower extremity weakness with diminished reflexes that progress to areflexia. Urinary retention and faecal incontinence also occur early in the course of the disease give a caudal equina syndrome. Up to 78% of patients with CMV radiculopathy also report sensory abnormalities in their lower extremities.

CSF studies in these patients show a mild pleocytosis that is predominantly neutrophilic. Accompanying the elevated neutrophils is an elevated protein and low glucose (50% or less). Diagnosis of CMV is confirmed by CMV PCR in CSF and MRI Spine. Treating is with ganciclovir or Valganciclovir as above.

### Herpes Simplex

HSV-1 causes a necrotising encephalitis in adults typically presenting with subtle neurologic changes such as headache, meningism, vomiting, lethargy, and cerebellar symptoms, personality changes with fever. HSV-2 (STI) causes a meningitis. HSV CNS diseases is not particularly high in advanced HIV diseases but is a common differential. Consider HSV encephalitis in any individual presenting with rapid deterioration of mental status with fever and CSF showing an aseptic picture. Other parameters such as increased RBS in CSF could point to HSV encephalitis. Empiric treatment is reasonable is highly suspicious cases. Confirmatory diagnosis is by CSF Serology or PCR for HSV.

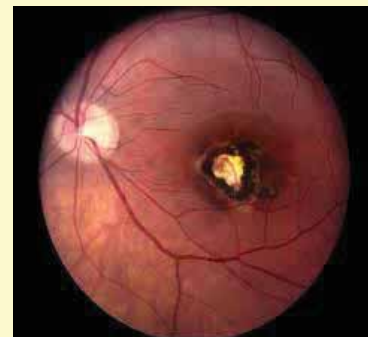
Treatment is with IV Acyclovir 30 mg/kg/day

## CNS Toxoplasmosis

CNS Toxoplasmosis in AHD is a reactivation of prior toxoplasmosis seropositivity. Patients with AIDS and  $< 100$  CD4 cells/mm<sup>3</sup>, who are toxoplasma seropositive, have an approximately 30 percent probability of developing reactivated toxoplasmosis if they are not receiving effective cotrimoxazole prophylaxis. CNS Toxoplasmosis gondii reactivation can present either as CNS cerebritis causing brain abscesses presenting with headache, fever, and seizures. It can also present as toxoplasmosis retinitis (see CMV retinitis). Definitive diagnosis is by brain biopsy, but clinical diagnosis can be made, and treatment commenced in a patient with CD4 cell count  $< 100$  cells/mm<sup>3</sup> with typical symptoms and:

- Is seropositive for T. gondii by IgG antibody or Antigen in blood or CSF
- Has not been receiving effective prophylaxis for toxoplasma
- Brain imaging demonstrates a typical radiographic appearance (e.g., multiple ring-enhancing lesions)

It is important to note other causes of ring enhancing lesions such as bacterial cerebral abscesses, CNS tuberculoma, Primary CNS lymphoma and Neurocysticercosis.



*Toxoplasmosis chorioretinitis on fundoscopy*

### Treatment for CNS Toxoplasmosis

First Line:

Seprin or Trimethoprim-Sulfamethoxazole (TMP-SMX) 10mg/kg (TMP component) for 6 weeks.

Second Line:

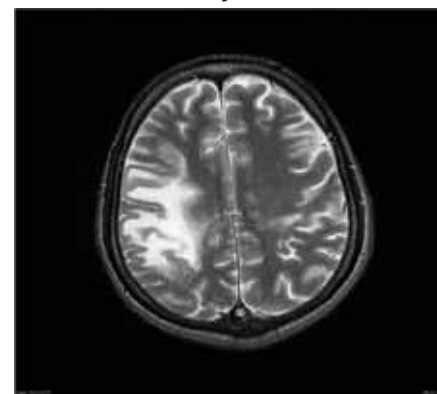
Pyrimethamine 75mg OD and Sulfadiazine 1000mg QID for 6 weeks

Remember to secondary prophylaxis with Seprin or Dapsone till is persistently above 200 cells/mm<sup>3</sup> and the images have resolve on MRI.

### Progressive Multifocal Leukoencephalopathy

Rare and usually fatal viral disease that is characterized by progressive damage or inflammation of the white matter of the brain at multiple locations. It occurs almost exclusively in people with severe immune deficiency CD4 cell count  $< 100$  cells/mm<sup>3</sup>. Progressive Multifocal Leukoencephalopathy (PML) is a demyelinating disease caused by a JC virus. It affects the white matter, which is mostly composed of axons from the outermost parts of the brain. Symptoms include weakness or paralysis, vision loss, impaired speech, and cognitive deterioration over time. Diagnosis is by isolation of JC virus in CSF. White matter disease on MRI Brain scan is very suggestive.

T-1 MRI for PML



ART is the mainstay treatment for progressive Multifocal Leukoencephalopathy

### HIV Associated Neuro-cognitive Disorder (HAND)

A brain disorder that occurs in people with AIDS that causes the loss of cognitive capacity, affecting the ability to function in a social or occupational setting. The exact mechanism by which HIV triggers the AIDS dementia complex has not been determined, but it may result from HIV infection of cells in the brain or from an inflammatory reaction to such an infection. Other names for ADC are HIV-associated dementia and HIV/AIDS encephalopathy. Common symptoms include decline in thinking, or “cognitive” functions such as memory, reasoning, judgment, concentration, and problem solving. Other common symptoms are changes in personality and behaviour, speech problems, and motor (movement) problems such as clumsiness and poor balance. When these symptoms are severe enough to interfere with everyday activity, a diagnosis of dementia may be warranted. AIDS dementia complex typically occurs as CD4+ count falls to less than 200 cells/mm<sup>3</sup>. It may be the first sign of AIDS. With the advent of cART, the frequency of ADC has declined from 30-60% of people infected with HIV to less than 20%. Neurosyphilis and other causes of dementia (especially in the elderly with NCD) must be considered as a possible differential diagnosis. Patients must not have other causes of dementia or confounding effect of substance abuse to meet the diagnosis criteria of HAND.

Treatment of HAND is by optimizing ART with high CNS penetration regimen

## Module 7: Pneumocystis Jiroveci Carinii and Other Respiratory Fungal Infections

An AIDS defining illness caused by a fungal infection. It mostly acquired through the respiratory tract in early childhood remaining latent until immunosuppression occurs. It can be spread from person to person through the air.

### Prophylaxis

Trimethoprim-Sulfamethoxazole is the recommended first line regimen for primary and secondary prophylaxis. The dosage is 960mg which is 1 table of double strength. This has added benefit of prevention of toxoplasmosis. Dapsone 100mg po daily can be used as an alternative in those that do not tolerate TMP-SMX.

### Clinical features

The symptoms are usually subtle with gradual progression over weeks. The ominous sign is hypoxia presenting as extreme tiredness with minimal exertion in the setting of fever and cough.

SYMPTOMS	SIGNS
Fever	High temperature (fever)
Non-productive cough	Tachypnea
Progressive dyspnea	Crackles, Ronchi (chest may be normal)
Chills	Oral thrush*
Chest pains	Reducing SpO <sub>2</sub> on exertions

Risk factors: for PCP

- Immunosuppression with CD4 < 200 cells/mm<sup>3</sup>
- No primary prophylaxis in those who are severely immunosuppressed

\*oral thrush usually found in patients with PJP.

### Investigations

Sputum induction or Bronchial alveolar lavage for microscopy and staining with conventional stains such as toluidine blue or Methenamine silver or Giemsa. Other labs may include the following:

- CD4 < 200 cells/mm<sup>3</sup>
- Elevated Lactate Dehydrogenase (LDH)

### Radiology:

Chest x ray shows bilateral symmetrical reticular (interstitial) or granular opacities. Rarely, it can present with:

- Pneumothorax
- Lobar
- Cysts
- Nodules

High resolution CT can show ground glass opacity and has a high sensitivity of >95%.

**Expert Tip**  
 Clinical and radiological presentation of PCP is very similar to COVID-19 Severe pneumonia. The duration of symptoms can distinguish the two since PCP is chronic and COVID-19 is acute. PJP has perihilar infiltrates on chest x ray while COVID-19 has peripheral infiltrates.

**Treatment**

Trimethoprim-Sulfamethoxazole (TMP-SMX) commonly known as Septrin is the recommended first line for mild, moderate and severe forms of PJP.

Dosing: 15mg of TMP in divided doses for 21 days. The adverse reactions are gastrointestinal intolerance, hepatotoxicity, increase in potassium (hyperkalemia) and Steven Johnson syndrome characterized by desquamating skin rash, fever.

Indications for steroids

Adjuvant steroids are for patients with moderate and severe PJP demonstrated by PO<sub>2</sub> less than 70 mmHg. The patients should be started on the steroids at the same time as the PJP therapy is started.

Dosing regimen for steroids: Prednisolone 40mg BD for 5/5 then 40mg for 5 days followed by 20 mg OD for remaining 11 days.

Secondary prophylaxis must always be given after treatment and can be discontinued after if CD4 > 350 cells/mm<sup>3</sup> and after receiving it for at least 2 years with a suppressed viral load.

## Other Common Fungal Pulmonary Infections in Advanced HIV Disease

Other rare fungal pulmonary fungal infections in AHD include: Histoplasmosis, Aspergillosis, Coccidioidomycosis and Blastomycosis. *Please note that Candida is not usually a cause of pneumonia even if the sputum test shows candida species and therefore must not be treated.*

**Pulmonary Histoplasmosis:** Histoplasmosis is the most common endemic mycosis in AIDS patients. Histoplasmosis generally occurs late during HIV infection, when CD4 lymphocyte counts are below 100 cells/mm<sup>3</sup>. It presents with pulmonary disease, but often progress to disseminated histoplasmosis, as a febrile and wasting illness. Diagnostic tests for disseminated *H. capsulatum* infection, including culture, serology, urine antigen testing, and direct microscopy; the diagnostic yield will depend on the stage of disease. Severe disease should be treated with Amphotericin B. Itraconazole can be used in mild localised disease. Fluconazole has limited activity and must only be used in localised disease when no alternative is available.

**Pulmonary Aspergillosis in AHD:** Although *Aspergillus* species are ubiquitous in nature, infection is uncommon, except in immunocompromised or immunosuppressed hosts. Pulmonary Aspergillosis in AHD will usually present as Invasive Pulmonary Aspergillosis which occurs in individuals with CD4 < 500 cells /mm<sup>3</sup> presenting as a pneumonia syndrome. It also commonly presents as an Aspergilloma where a fungal ball fills a post TB lung cavity. Diagnosis is by fungal culture of sputum or Antigen testing. Treatment of Invasive Pulmonary Aspergillosis is by Amphotericin B, Itraconazole, or Voriconazole (*Fluconazole has no activity against aspergillosis*). Treatment for Aspergilloma is surgery.

### **Blastomycosis in AHD**

Blastomycosis dermatitidis occurs in immunocompromised hosts including HIV infection in AHD and it commonly presents as pulmonary disease but may cause skin or disseminated disease. Definitive diagnosis requires growth of the organism from a clinical specimen. Unlike *Candida* and *Aspergillus* spp, colonization or contamination with *B. dermatitidis* does not occur. Treatment is by Itraconazole. Other treatment options for patients with blastomycosis include [Amphotericin B](#) or one of the azole drugs (usually [Itraconazole](#)). **Coccidioidomycosis** does rarely occur in HIV as an opportunistic infection and presents as pulmonary disease. Diagnosis is by isolation of the organism and treatment is by Itraconazole.

### Module 8: Gastro-Intestinal Tract Conditions in Advanced HIV Disease

With the progression of HIV infection, the gastrointestinal tract begins to be severely affected and atypical opportunistic infections occur. This causes diarrhoea, malabsorption and poor appetite which culminate into HIV wasting syndrome. The nutritional impact is grave, compounded by the background high catabolic state typical of HIV infection. Restoration of health in those severely malnourished is very difficult and mortality is high. Many complications occur due to micronutrients deficiencies including anaemia, neuropathy, and compromise skin integrity. Nutritional rehabilitation is cardinal, but clinician need to be wary of the refeeding syndrome.

#### Oral and Oesophageal Candidiasis

Oral candidiasis is a signal of treatment failure in those on ART. Oral candidiasis (thrush) can be described as pseudomembranous, atrophic, hyperplastic/hyperkeratotic, and angular cheilitis. Oral lesion caused by *Candida* are often painful. When the infection extends into the posterior oral cavity or into the oesophagus, painful swallowing (odynophagia) can occur. Physical examination typically reveals white plaques on the sides and roof (hard palate) of the mouth, and less frequently on the tongue.



Diagnosis is made by clinical inspection. White plaques can be scraped off, revealing an erythematous sore underneath.

**Oesophageal candidiasis** is a marker of AHD. It presents with dysphagia (difficulty swallowing, such as the sensation of food getting stuck) or odynophagia (painful swallowing) presenting with thrush visible on examination.

#### Treatment for Oral and Oesophageal Candida in HIV

##### Oral thrush:

- Nystatin 400,000 to 600,000 units QID for 7 days or Fluconazole 200mg PO OD x 7-14 days (for refractory cases that do not respond to Nystatin)

##### Oesophageal Candidiasis:

- Fluconazole 200mg PO OD x 14days



### HSV Oesophagitis

Patients with HSV oesophagitis usually present with oral blisters, oesophageal ulcers or gastric ulcers with odynophagia and dysphagia. Differential diagnosis includes aphthous ulcers and CMV oesophagitis. Diagnosis is by biopsy for histology and PCR.

#### Treatment for HSV Oesophagitis

- Mild cases Acyclovir 400-800mg 4-5x/day for 10-14 days
- Severe Cases where patient is unable to tolerate intake may require IV Acyclovir 5-10mg/kg TDS

### CMV Oesophagitis

CMV oesophagitis manifests similarly to HSV oesophagitis. It is more common than HSV oesophagitis. CMV oesophagitis should be considered in patients with oesophagitis who do not respond to a course of Fluconazole or Acyclovir. Diagnosis is definitively made by biopsy. Inclusion body is the characteristic finding on biopsy specimen. CMV is usually a systemic disease, other parts of the GI track can be involved, and patients should have an eye exam to evaluate for CMV retinitis.

#### Treatment for CMV Oesophagitis

- IV Ganciclovir 5mg/kg BD x 21-42 days (or until the symptoms disappear)  
(or Valganciclovir 900mg PO BD)
- Acyclovir is not helpful in treating oesophagitis caused by CMV

### Diarrhoea in Advanced HIV Disease

Diarrhoea is the occurrence of > 3 loose stools a day. It is common in HIV infected individuals with both advanced and no AHD.

**Table 8.1: Classification and Causes of Diarrhoea in AHD**

Acute Diarrhoea Disease ( $< 2$ weeks)	<ul style="list-style-type: none"> <li>• Bacterial: <i>E. coli</i>, <i>Salmonella</i>, <i>Shigella</i>, cholera, <i>Campylobacter</i>, <i>Clostridium difficile</i>, etc.</li> <li>• Viral: rotavirus, Norwalk virus, adenoviruses, hepatitis viruses, etc.</li> <li>• Protozoal: <i>Giardia lamblia</i>, <i>Entamoeba histolytica</i></li> <li>• Other: Medications, Food poisoning, Inflammatory Bowel Disease (IBD)</li> </ul>
Persistent Diarrhoea Disease ( $> 2$ weeks)	<ul style="list-style-type: none"> <li>• All acute causes plus:</li> <li>• Protozoal: <i>Cryptosporidium parvum</i>, <i>Cytospora (formerly isospora) belli</i>, <i>Microsporidia</i> spp., <i>Cyclospora cayetanensis</i></li> <li>• Mycobacterial: Mycobacterium Avium Complex (MAC)</li> <li>• Others: CMV, lymphoma, etc.</li> </ul>

### Bloody stool

The following organisms can cause bloody diarrhoea in AHD: Shigella, Salmonella, E. coli, Campylobacter, Amoeba histolytica and CMV.

#### **GIT Opportunistic infection in Advanced HIV Disease**

The following Organisms are opportunistic infections that affect the GIT in AHD: Cryptosporidia, Microsporidia, Cytoisospora, MAC, CMV and Tuberculosis. These should be evaluated whenever a patient with advanced HIV presents with diarrhoea

### **Empiric management**

#### **1. Children (< 5 years)**

- Assess the child with diarrhoea using IMCI (ASK, LOOK, FEEL); classify as no, some, or severe dehydration; and manage accordingly
- Give the child more fluids than usual using low osmolarity ORS, to prevent dehydration or IV fluids in those with severe dehydration or if shock appropriate treatment should be followed according to the standard SOPs
- Give supplemental Zinc (10mg < 6 months, 20mg > 6 months) to the child, every day for 10 to 14 days

Continue to feed the child to prevent malnutrition: **This is very important!**

Temporarily avoid or change consumption of lactose-containing foods if lactose intolerance present. Lactose intolerance is suspect when infants/young children predominantly on milk feeds continue to pass explosive, watery stools causing perianal erythematous excoriation very similar to perianal candidiasis. Special diets that are low in lactose or are lactose free may be indicated till the intestinal mucosa recovers.

#### **2. Children (>5 years) and adults**

Decisions on therapy are based on an assessment of diarrhoea severity and hydration status. Importance of maintaining hydration giving oral or intravenous (IV) rehydration, if indicated.

### Management of Acute Diarrhoeal Disease (ADD)

- Supportive treatment is critical: assess hydration status and rehydrate (orally or intravenously) as needed
- Stool for white blood cells, gram stain, Ova + Parasites (O+P) x 3 samples
- Treat specific pathogen if identified
  - Ciprofloxacin 500mg BD or Nalidixic Acid 500 mg QID should cover most bacterial pathogens
  - Metronidazole 400mg TDS X 10-14 days covers Giardia, Entamoeba, and C. difficile
  - Empirical treatment: Ciprofloxacin 500mg PO BD x 7days (Nalidixic Acid 500mg QID if no Ciprofloxacin) + Metronidazole 400mg PO TDS x 7 days can be considered

### Management of Persistent Diarrhoea Disease (PDD) in AHD

Individuals with AHD and persistent diarrhoea are often wasted due to malabsorption. In most cases, commencement of effective ART is the definitive treatment. However, the immediate treatment involves resuscitating the individual with oral or intravenous fluid, electrolyte correction and nutritional replacement. Ringer's lactate solution is a preferred fluid due to the hyperchloraemic dehydration that occurs in these patients.

Collect stool studies as listed above PLUS Stool for modified Ziehl-Neelsen (3 different samples on different days) to look for:

- Cryptosporidia
- Isospora
- Cyclospora

Stool for modified trichrome staining to look for Microsporidia can be collected but microsporidium is rare in Zambia.

If an agent is isolated, treat appropriately (see next details). If no agent isolated, consider empiric treatment. Note that you may need several stool and ova tests to isolate an organism.

#### Empiric Treatment of Persistent Diarrheal Disease

- Treat with Ciprofloxacin 500 mg BD and Metronidazole 400 mg TDS for 7-10 days (children; 7.5 mg/kg per dose TDS)

If no response:

- Co-trimoxazole 960mg QID x 10 days PLUS Metronidazole 800 mg TDS x 10 days (Children; 7.5mg/kg per dose TDS)
- This will treat Cyclospora, Cyclospora, most bacterial enteric pathogens, Giardia, and Entamoeba histolytica
- If patient responds, consider extending co-trimoxazole 960mg BD for 3 weeks more (to complete empiric treatment for Cyclospora)
- If no response, consider adding Albendazole 400mg BD x 3 weeks (treats Microsporidiosis)

Loperamide may be considered at any time for symptomatic relief.

### Cryptosporidiosis in AHD

*Cryptosporidium parvum* is a small and obligate intracellular protozoan. It is widely distributed in the environment and is most commonly transmitted by the faecal-oral route through ingestion of contaminated water, contact with soil or food that is contaminated with human or animal faeces, and during contact between infant and adult during diapering.

The course of infection can be acute and self-limiting, chronic severe but self-limiting, or fulminate and life threatening. HIV patients usually have a course of diarrhoea depending on their CD4 count at time of infection. If CD4 is more than 100 cells/mm<sup>3</sup>, diarrhoea can be self-limited, usually resolving in 2-8 weeks. Patients with advanced HIV (CD4 less than 100 cells/mm<sup>3</sup>) can present with severe diarrhoea, malnutrition, and marked dehydration. Rarely does fever occur with Cryptosporidiosis. It can also affect the biliary tract causing cholangiopathy. Diagnosis is made by modified ZN stain.

There is no specific proven effective treatment for cryptosporidiosis in HIV infection. The most important treatment is immune reconstitution with cART initiation. Symptoms can resolve as the CD4 counts start to increase. In fulminate cases, immediate initiation of cART is warranted. symptomatic treatment is important in managing patients with cryptosporidiosis. This includes anti-diarrheal agents such as Loperamide, bismuth salts, aggressive oral and intravenous rehydration, and electrolyte replacement.

For refractory cases, Nitazoxanide 500mg BD for 2-4 weeks may be considered.

### Cytoisporiasis in AHD

*Cytoispora belli* is a protozoon which can be transmitted by faecal-oral route like cryptosporidiosis. In immunocompetent patients, diarrhoea can be self-limited within 2-3 weeks. It is a common cause of diarrhoea in patients with CD4 less than 100 cells/mm<sup>3</sup>. Manifestation includes severe or persistent diarrhoea.

Diagnosis is made by modified ZN stain.

Once diagnosis is made, treatment can be initiated with Co-trimoxazole 960mg QID for 10 days than 960mg BD for 21 days.

In refractory causes, maintenance treatment may be required till immune reconstitution.

### Microsporidiosis in AHD

*Microsporidia* is another protozoan cause of diarrhoea in HIV patients. It is water-borne and occurs most often when the CD4 count is less than 100 cells/mm<sup>3</sup>. Manifestation includes profuse watery diarrhoea, weight loss, abdominal pain, and cramping. Rarely will the patient be feverish. Microsporidiosis also may result in encephalitis, ocular infection, sinusitis, myositis, and disseminated infection.

Diagnosis is made by modified trichrome stain.

Albendazole 400mg BD for 3 weeks is the treatment of choice for Microsporidiosis.

### CMV Colitis in AHD

CMV colitis is the second most common manifestation of end organ CMV disease in HIV after CMV retinitis. It is associated with severe immunosuppression CD4 cell count < 50 cells/mm<sup>3</sup>. CMV colitis is associated with low-grade fever, weight loss, anorexia, malaise, and abdominal pain. Explosive watery diarrhoea is common but can be sporadic. Symptoms that suggest large bowel involvement include frequent small volume diarrhoea, tenesmus, and/or haematochezia. Extensive mucosal haemorrhage and perforation can be life-threatening complications. Diagnosis is by biopsy for histology and PCR.

#### Treatment

- Induction: Ganciclovir 5 mg/kg IV BD x 14-21 days or Valganciclovir 900 mg P.O BD x 21 days
- Post treatment suppression: Valganciclovir 900mg PO OD until CD4 cell count >100 for 6 months
- If lesions progress or relapse, re-induce with same agent. Watch for IRIS.

### Mycobacterium Avium Complex (MAC)

MAC includes the following organisms: *M. intracellulare*, *M. avium*, and *M. paratuberculosis*. It usually presents in patients with CD4 counts of less than 50. It can present as a pulmonary disease or systemic disease involving the GIT.

Systemic disease (fever, night sweats, weight loss, anorexia, diarrhoea, abdominal pain) is common and can persist for several weeks before patients seek medical care. Physical examination may reveal organomegaly.

Laboratory results may show anaemia, pancytopenia, elevated alkaline phosphatase, elevated LDH. Chest X-ray will show nodular or cavitary opacities for pulmonary disease. Abdominal ultrasound or CT scan may show lymphadenopathy. Diagnosis can be made by blood culture or can also be made by culture from bone marrow biopsy, liver biopsy, and lymph node biopsy. Bone marrow biopsy is preferred since usually the organism may be isolated faster than in other sites. A triad of 2 separate sputum samples, typical imaging, and absence of any other cause in a symptomatic patient is diagnostic for pulmonary disease. Like other Non-Tuberculous Mycobacteria (NTMs), MAC infection presents with a negative Xpert test in the presence of a positive sputum or tissue smear AFB.

### **Treatment of MAC**

Treatment for MAC should be for at least 18 months; specific regimens are listed below. Starting cART is also an important part to treat MAC.

HIV Patients who are co-infected with MAC may develop Immune Reconstitution Inflammatory Syndrome (IRIS) following initiation of cART. Immune reconstitution syndrome to MAC can present as fever, painful lymphadenitis, and abdominal pain 1-8 weeks after cART. It is reasonable to continue cART in most cases unless the immune reconstitution response is life-threatening.

*Preferred drugs:* Clarithromycin 500 mg BD or Azithromycin 600mg OD **Plus**  
Ethambutol 15mg/kg/day PO **Plus** Rifabutin 300mg OD

*Alternate:* Clarithromycin 500 mg BD or Azithromycin 600mg OD **Plus** Ethambutol  
15mg/kg/day PO **Plus** Ciprofloxacin, Levofloxacin, Moxifloxacin

IV aminoglycosides (Amikacin or Streptomycin) can be added as a fourth drug for cavitary disease

## Module 9: Kaposi's Sarcoma and other AIDS Related Malignancies

### Introduction

Individuals infected with HIV have a substantially higher risk of some types of cancer compared with uninfected people of the same age. The general term for these cancers is "HIV-associated cancers." Three of these cancers are known as "acquired immunodeficiency syndrome (AIDS)-defining cancers" or "AIDS-defining malignancies": Kaposi sarcoma, aggressive B-cell non-Hodgkin lymphoma, and cervical cancer.

In addition, individuals infected with HIV are at higher risk of several other types of cancer (collectively called "non-AIDS-defining cancers"). These other malignancies include colorectal carcinoma, Lung cancer, Hepatocellular carcinoma, oral/pharyngeal carcinoma, Bronchogenic carcinoma, and Hodgkin lymphoma.

### Kaposi's Sarcoma

Kaposi's sarcoma (KS) is a neoplasm that has been present in Zambia with its incidence markedly increasing in the HIV/AIDS era. It is the commonest HIV/AIDS-related neoplasms in Zambia. Human Herpes Virus type 8 (HHV-8) has been implicated in the aetiology of Kaposi's sarcoma.

It exists in four forms – classic, Africa endemic, secondary to iatrogenic immunosuppression, and HIV/AIDS related. HIV-associated Kaposi's sarcoma is more aggressive than the non-HIV-associated endemic Kaposi's sarcoma. Kaposi's sarcoma is an AIDS-defining condition (WHO Stage 4 disease). KS prognosis is poor in patients with advanced HIV infection or in individuals with systemic involvement.

### Signs and symptoms

The symptoms and signs of HIV-associated KS are system-dependent. Multiple systems are often involved.



*Kaposi's Sarcoma in HIV*





**Table 9.1: Location of the KS Lesion and Associated Clinical Features**

S/N	Location of lesions	Clinical features
	<b>Skin and mucous membranes</b>	<p><b>Oedema:</b> usually non-pitting but may occasionally be pitting, may or may not be painful, usually affects lower limbs, groin, external genitalia, periorbital, but may also affect other parts of the body such as upper limbs.</p> <p><b>Skin lesions:</b> Purplish, brown, or erythematous hyperpigmented macules, patches, papules, and/or nodules that may sometimes progress to ulcerative lesions.</p> <p><b>Mucous membrane lesions:</b> Erythematous or purplish macules, patches, papules, and/or plaques most commonly affecting the hard palate but may also occur anywhere in the mouth</p>
	<b>Lymphadenopathy</b>	Usually non-tender, firm, discrete, may be generalized. This may be the only presentation of Kaposi's sarcoma in younger children.
	<b>Respiratory</b>	Cough, Shortness of breath, Wheezing, Haemoptysis and Recurrent pleural effusions (usually haemorrhagic)
	<b>Gastrointestinal tract</b>	<p>Nonspecific abdominal pains</p> <p>Haematemesis (vomiting blood), melaena (black stools), Haematochezia (bloody stools)</p> <p>Abdominal distension/bowel obstruction, organomegaly, lymphadenopathy and ascites</p> <p>Persistent diarrhoea</p>
	<b>Cardiovascular</b>	Recurrent Pericardial effusions
	<b>Ocular</b>	<p>Subconjunctival haemorrhage</p> <p>Erythematous or purplish conjunctival growth</p>

**Diagnosis**

A probable diagnosis of KS is usually clinical. However, a biopsy is required for a definitive diagnosis.

**Treatment**

There is no universally agreed treatment that works well. However,

- For patients with mild mucocutaneous KS only, cART is the preferred treatment.
- Chemotherapy is indicated for severe cutaneous (e.g., with associated edema) KS, mucocutaneous KS that is not responding to ARVs, and disseminated KS (lymphatic involvement, pulmonary KS)
- IRIS due to KS does occur

The table below (Table 9.2) shows the chemotherapeutic options.

**Table 9.2: Chemotherapeutic Options for Kaposi's Sarcoma**

S/N	Treatment option	Remarks
1.	<p><b>3-drug combination chemotherapy:</b> Doxorubicin + Vincristine + Bleomycin</p> <ul style="list-style-type: none"> <li>• Doxorubicin 30mg/m<sup>2</sup> IV – usually 50 mg</li> <li>• Vincristine 1.4mg/m<sup>2</sup> IV – usually 2 mg</li> <li>• Bleomycin 10-20 IU/m<sup>2</sup> IV – usually 15 Units</li> </ul> <p>Given every 3-4 weeks for up to 6-8 cycles</p>	<p><b>Stop or switch the chemo if:</b></p> <ul style="list-style-type: none"> <li>• The disease is progressing despite chemotherapy.</li> <li>• The patient has had a maximal response and the disease is no longer shrinking.</li> <li>• There is only minimal disease left.</li> <li>• There is unacceptable toxicity.</li> <li>• The patient has had 450mg/m<sup>2</sup> of Doxorubicin over their lifetime</li> </ul>
2.	<p><b>2-drug combination therapy</b> Vincristine plus either Doxorubicin or Bleomycin (doses as listed above)</p>	For moderate disease, in very ill patients, or when all 3 drugs are not available
3.	<p><b>Single drug formulation with Liposomal Doxorubicin.</b> Give as single agent, at a dose of 20mg/m<sup>2</sup> once every 2-3 weeks</p>	<ul style="list-style-type: none"> <li>• Fewer toxicities</li> <li>• Equal or better response rates compared to standard 3-drug therapy.</li> <li>• More expensive</li> </ul>
4.	Paclitaxel given as a single agent at a dose 100mg/m <sup>2</sup> every 3 weeks (available as second line therapy in Zambia)	
5.	Single-agent chemotherapy using Vincristine, given weekly at 1.4mg/m <sup>2</sup> IV usually 2mg	<ul style="list-style-type: none"> <li>• Recommended for patients where Doxorubicin and Bleomycin are not available</li> </ul>

**Table 9.3: Response and Toxicities of Suggested Chemotherapy Agents**

	Therapy	Overall	Major toxicities	Remarks
	Vincristine	10-85%	Cellulitis and tissue necrosis with IV each extravasation; neurological symptoms (constipation, ileus, peripheral neuropathy)	Maximum weekly dose is 2 mg
	Vinblastine	25-30%	Myelosuppression	Reduce dose for < 3000/mm <sup>3</sup> or platelets
	Bleomycin, Vincristine	60-75%	Paresthesia (Vincristine); allergic reactions, pulmonary fibrosis (Bleomycin)	Maximum weekly dose of Vincristine is 2mg, maximum cumulative dose of bleomycin is 400 units
	Liposomal Doxorubicin	58-63%	Cardiomyopathy, myelosuppression	Not routinely available
	Adriamycin, Bleomycin, Vincristine	70-90%	Myelosuppression, cardiotoxicity, pulmonary fibrosis	Doxorubicin maximum dose not to exceed > 550mg/m <sup>2</sup>
	Paclitaxel	60-72%	Peripheral neuropathy, myelosuppression	Second line treatment

## Use of Chemotherapy in AIDS-related KS

### Cytopenias

These are frequent in patients with KS whether they are receiving cytotoxic chemotherapy or not. The cytopenias may be exacerbated by bone marrow suppressive drugs such as on Zidovudine or Trimethoprim-Sulfamethoxazole. Therefore, a complete blood count must be done prior to each cycle of chemotherapy.

Chemotherapy should not be administered if:

- Haemoglobin is  $< 8\text{g/dL}$
- absolute neutrophil count is  $< 1000/\text{mm}^3$
- platelets are  $< 75,000/\text{mm}^3$

If cytopenias occur, chemotherapy should be delayed until the counts return to above the listed thresholds.

### Drug Interactions

Use of cytotoxic chemotherapy with other drugs requires monitoring or avoidance of drug-drug interactions.

### Steroid Effects

KS lesions may progress with steroid therapy. Therefore, corticosteroids should be avoided in patients with HIV-related KS. They may be used in acute respiratory distress syndrome accompanying HIV-related opportunistic pulmonary infection, tuberculosis meningitis or pericarditis, or immune thrombocytopenic purpura, if necessary.

## HIV-related Lymphoma

Lymphomas are common in HIV infected individual and are associated with decreasing CD4 cell counts. Compared with lymphomas in the HIV-negative population, HIV-related Lymphoma (HRLs) are more likely to present with advanced stage disease, constitutional symptoms ("B" symptoms, i.e., fever, weight loss, night sweats), extra nodal involvement, or have disease involving unusual locations (e.g., body cavity, soft tissue). Because aggressive histology and extra nodal disease are common with HRLs, there is an increased risk for oncologic emergencies (e.g., tumour lysis syndrome, airway or gastrointestinal [GI] tract obstruction, involvement of the brain or meninges). Primary CNS Lymphoma (PCNSL) presents with an intracranial solitary lesion which may mimic CNS tuberculosis or Toxoplasmosis.

**Approach to a patient with a Lymphoma in AHD**

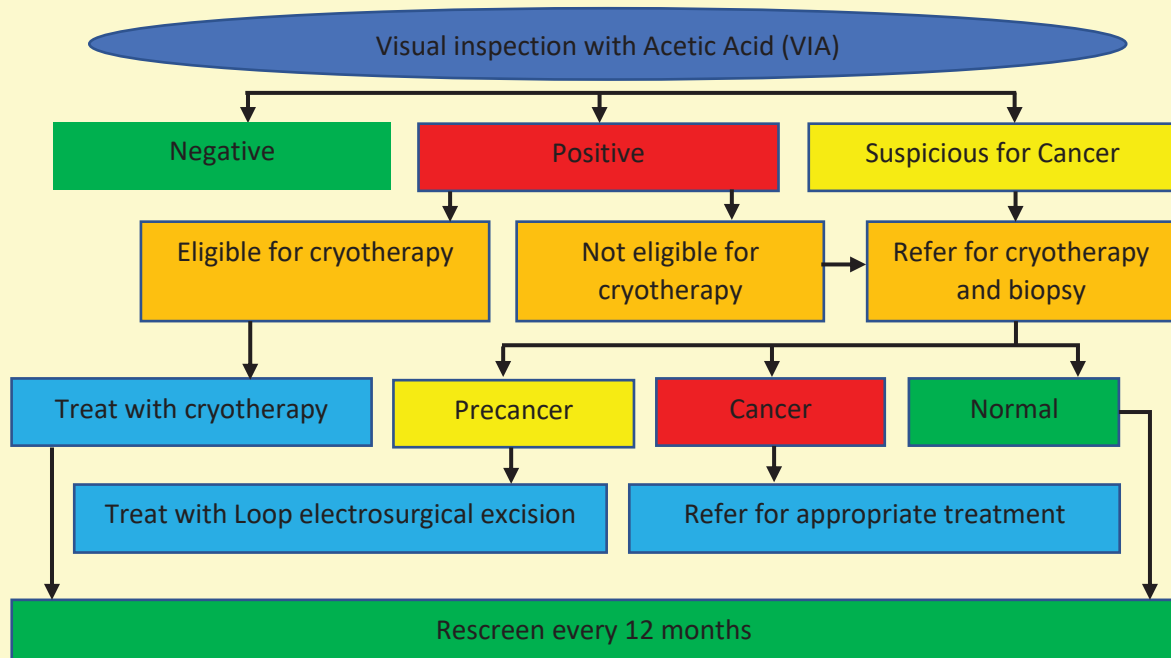
Diagnosis of a lymphoma is by biopsy. Since lymphoma can mimic other opportunistic infections, High index of suspicions is advised. Lymphomas must be considered as a differential whenever there is suboptimal response when to empiric or presumptive treatment for opportunistic infections. All masses and growth must have a biopsy done. Prompt referral to the cancer disease hospital for definitive treatment must be done.

**Types of HIV Related Lymphomas**

- (1) Lymphoma also occurring in immunocompetent patients
  - Burkitt and Burkitt-like lymphoma
  - Diffuse large B-cell lymphoma
    - Centroblastic
    - Immunoblastic (including primary CNS lymphoma)
  - Extra nodal marginal zone lymphoma of MALT type
  - Peripheral T-cell lymphoma
  - Classical Hodgkin lymphoma
- (2) Lymphoma occurring more specifically in HIV-positive patients
  - Primary effusion lymphoma
  - Plasmablastic lymphoma of the oral cavity type
- (3) Lymphoma also occurring in other immunodeficiency states
  - Polymorphic B-cell lymphoma (PTLD-like)

**Cervical Cancer and HIV**

Cervical cancer is the commonest cancer among women HIV-infected people in Zambia. Women with HIV infection have a higher risk of pre- and invasive cancers. Cervical cancer is curable if early diagnosis and treatment are instituted. All women regardless of age, should be screened for Cervical cancer with HPV test or Visual Inspection with Acetic Acid (VIA).



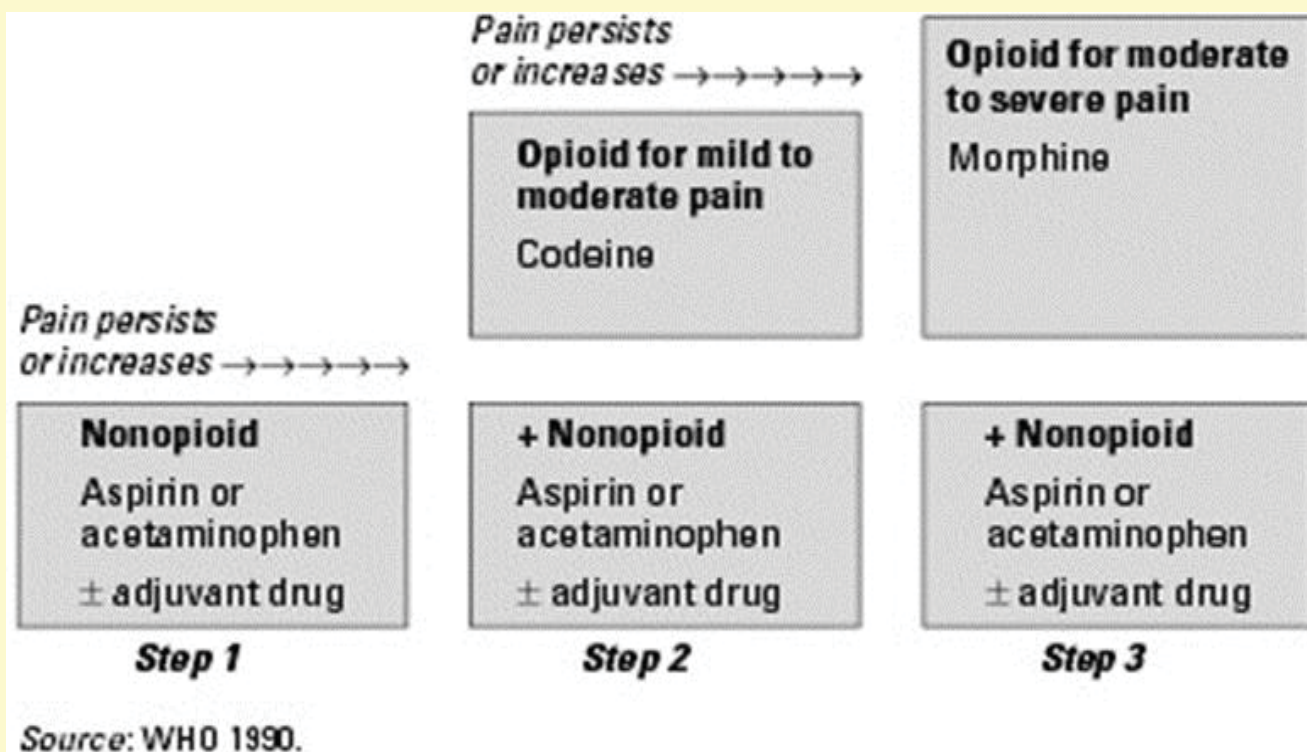
**Figure 9.1: Recommended Treatment Algorithm for Cervical Cancer**

*Adapted from ZCGs 2020*

## Palliative Care/Cancer and HIV

Healthcare workers also need to institute palliative care in patients with cancer. This involves care that is focused on symptom management and end-of-life care, making the patient feel as comfortable as possible. Effective pain control is important to encourage adherence. Various methods of pain relief include drugs, radiotherapy, and anesthetic, neurosurgical, and psychological approaches. However, drugs are a mainstay in pain management in Zambia. For effective pain control:

- Ensure that policies and regulations are put in place to allow ready access to opioids (Morphine, Tramadol, Codeine Phosphate) among the suffering patients
- Follow the step ladder approach
- Check specific drug-drug interactions with ARVs



## Module 10: Considerations for Specific Populations

The package of care should be provided to all patients presenting with AHD, unless specifically contra-indicated. The following section provides some additional considerations for specific populations.

### Children

WHO considers all children younger than five years to be eligible for the package for AHD. This is based on data which revealed that more than 80% of children younger than five years starting ART are WHO clinical stage 3 or 4 and/or have severe immunosuppression. The same definition of advanced HIV disease used for adults is applied to children five years and older.

The major causes of mortality and morbidity among children with AHD are:

- Tuberculosis
- Severe bacterial infections,
- Pneumocystis Jirovecii Pneumonia
- Malnutrition
- Cryptococcal disease, although relatively rare among children

To reduce morbidity and mortality among children living with HIV, WHO recommends an intervention summarized as **Screen, Treat, Optimize and Prevent AIDS (STOP AIDS)** in addition to the routine interventions such as deworming, immunisations, iron and vitamin A supplementation and growth monitoring.

A package of care consisting of screening, prophylaxis, treatment of current illness, rapid ART initiation and intensified adherence interventions should be offered to all children living with HIV presenting with advanced disease.

### Screen, Treat, Optimize and Prevent AIDS

#### Screen

**Screen for TB** using a clinical algorithm followed by X-ray when indicated and if available Use the following diagnostic tests to confirm TB as applicable.

- Rapid molecular diagnostic (Xpert® MTB/RIF or Ultra) on (induced) sputum, stool, gastric aspirate, or nasopharyngeal aspirate or other extrapulmonary samples if relevant
- Lateral flow urine lipoarabinomannan (LF-LAM) assayed

**Cryptococcal infection** screening among adolescents using Serum or plasma or blood cryptococcal antigen screening followed by lumbar puncture if positive or symptomatic.

## Malnutrition

- Weight-for-height
- Height-for-age
- Mid-upper arm circumference among children 2–5 years old

## Treat

Treat TB, severe pneumonia, severe bacterial infections, Cryptococcal Meningitis and severe acute malnutrition according to WHO guidelines.

Any child with active TB disease should start ART as soon as possible and within eight weeks after initiating TB treatment (other than TB meningitis), regardless of CD4 cell count and clinical stage.

Caution is needed in children living with HIV being treated for TB meningitis, as immediate ART is significantly associated with more severe adverse events when compared with initiation of ART 2 months after the start of TB treatment.

A seriously ill child is defined as having any of the following danger signs:

- Treat TB, severe pneumonia, severe bacterial infections, Cryptococcal Meningitis and severe acute malnutrition according to WHO guidelines
- Lethargy or unconsciousness
- Convulsions
- Unable to drink or breastfeed or repeated vomiting
- Other clinical conditions such as body temperature  $\geq 39^{\circ}\text{C}$  and age-defined tachycardia and/or tachypnoea can be considered based on clinical judgement



## Optimize

Rapid ART start – within seven days with optimal regimens

Antiretroviral therapy counselling

## Prevent AIDS

- ☞ Prevent Bacterial infections and Pneumocystis pneumonia – Co-trimoxazole prophylaxis
- ☞ TB preventive treatment
- ☞ Cryptococcal Meningitis among adolescents – Fluconazole pre-emptive therapy
- ☞ Vaccinations – Pneumococcal vaccine, Human papillomavirus, Measles, BCG
- ☞ Screening, diagnosis, and prevention components of the package of care for children and adolescents with AHD

**Table 10.1: Intervention Components of the Package of Care for Children and Adolescents with AHD**

Intervention	Component	< 5 years	5-9 years	10-19 years
Screening and diagnosis	Screen for TB using clinical algorithm followed by X-ray when indicated and if available. Xpert <sup>®</sup> MTB/RIF or Xpert <sup>®</sup> Ultra assay as the first test (Induced or expectorated) sputum, gastric aspirate, stool, or nasopharyngeal aspirate or other extrapulmonary specimens (induced or expectorated)	Yes	Yes	Yes
	LF-LAM assay	Yes	Yes	Yes
	Cryptococcal antigen screening (Specimen, plasma, or whole blood)	No	No	Yes
Prevention, prophylaxis, and pre-emptive treatment	Pneumococcal conjugate vaccine (catch-up)	Yes	No	No
	Co-trimoxazole	Yes	Yes	Yes
	TB Preventive Treatment	Yes	Yes	Yes
	Fluconazole pre-emptive therapy for Cryptococcal antigen-positive without evidence of meningitis	Not applicable	Not applicable	

*Adopted from WHO technical brief July 2020.*



## Adolescents

Adolescents generally face challenges in adhering to medication, and enhanced adherence counselling may be especially valuable. Simplify the cART regimen whenever possible.

## Pregnant and Breastfeeding Women

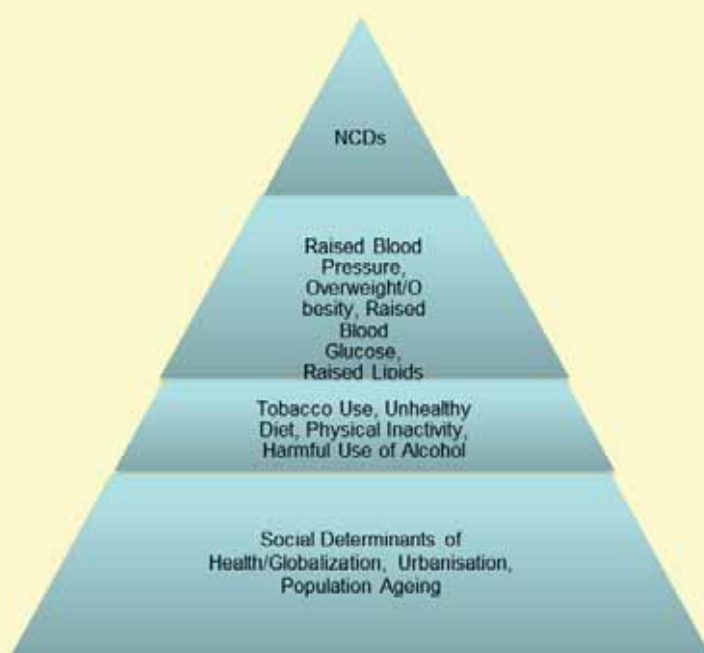
Pregnancy is an immunosuppressive state, and the presence of HIV infection may compound the predisposition to immunosuppression and subsequent death. The risk of death is even greater due to the background existing mortality risk due to obstetric causes. HIV infection does predispose to adverse maternal and foetal outcomes. A significant proportion of maternal mortalities in Zambia are due to HIV related conditions and opportunistic infections. Because some medicines for treatment or prophylaxis of OIs in advanced HIV disease, it is recommended that women of childbearing age who have advanced HIV disease are provided with effective contraception till the CD4 cell count is above 200cell/mm<sup>3</sup>. The following interventions are recommended in pregnancy and breastfeeding women to prevent AHD and subsequent maternal deaths and adverse foetal outcomes:

- Rapid initiation of ART with potent DTG based regimen in all HIV newly positive pregnant and breastfeeding women
- All pregnant and breastfeeding women must have viral load every 3 months and expedited switch to effective therapy when VL > 1000 copies/mL
- CD4 cell count screening must be done in HIV infected pregnant and breastfeeding women who are initiating treatment or presenting ill to a health facility or have an unsuppressed viral load
- LF-LAM and Serum CrAg screening must be done in all pregnant and breastfeeding women with AHD
- TPT with INH must be provided to all pregnant and breastfeeding women who screen negative for TB except in the first trimester of life
- Fluconazole pre-emptive therapy for cryptococcaemia must be provided in all pregnant and breastfeeding women who test positive for serum CrAg but are asymptomatic for Cryptococcal Meningitis

## Module 11: Non-Communicable Diseases and HIV

### Introduction

With the advent of ART, HIV-infection is set to transition from a once fatal disease to a chronic condition. Non-communicable Diseases (NCDs) are chronic diseases that are not caused by infections. NCDs are common in PLHIV due to the following reasons: HIV infection induces a chronic inflammatory state even when virally suppressed, the cohort of PLHIV is aging and some drugs used in the treatment of HIV cause NCDs including PIs, INSTI, NRTI (TFV). NCDs have a complex etiology with multiple risk factors and a prolonged latent period usually leading to a prolonged illness with resultant functional impairment, disability or death. Risk factors of NCDs can be modifiable (physical inactivity, tobacco use, unhealthy diet and harmful alcohol use) or non-modifiable (age, gender, race, family genetics).



**Figure 11.1 Determinant of NCDs**

#### Examples of NCDs

- CVD Cardiovascular disease (e.g., Coronary heart disease, Stroke)
- Cancer
- Chronic respiratory disease
- Diabetes
- Mental disorders
- Chronic neurologic disorders (e.g., Alzheimer's, dementias)
- Arthritis/Musculoskeletal
- Mental Health
- Unintentional injuries (e.g., from traffic crashes)

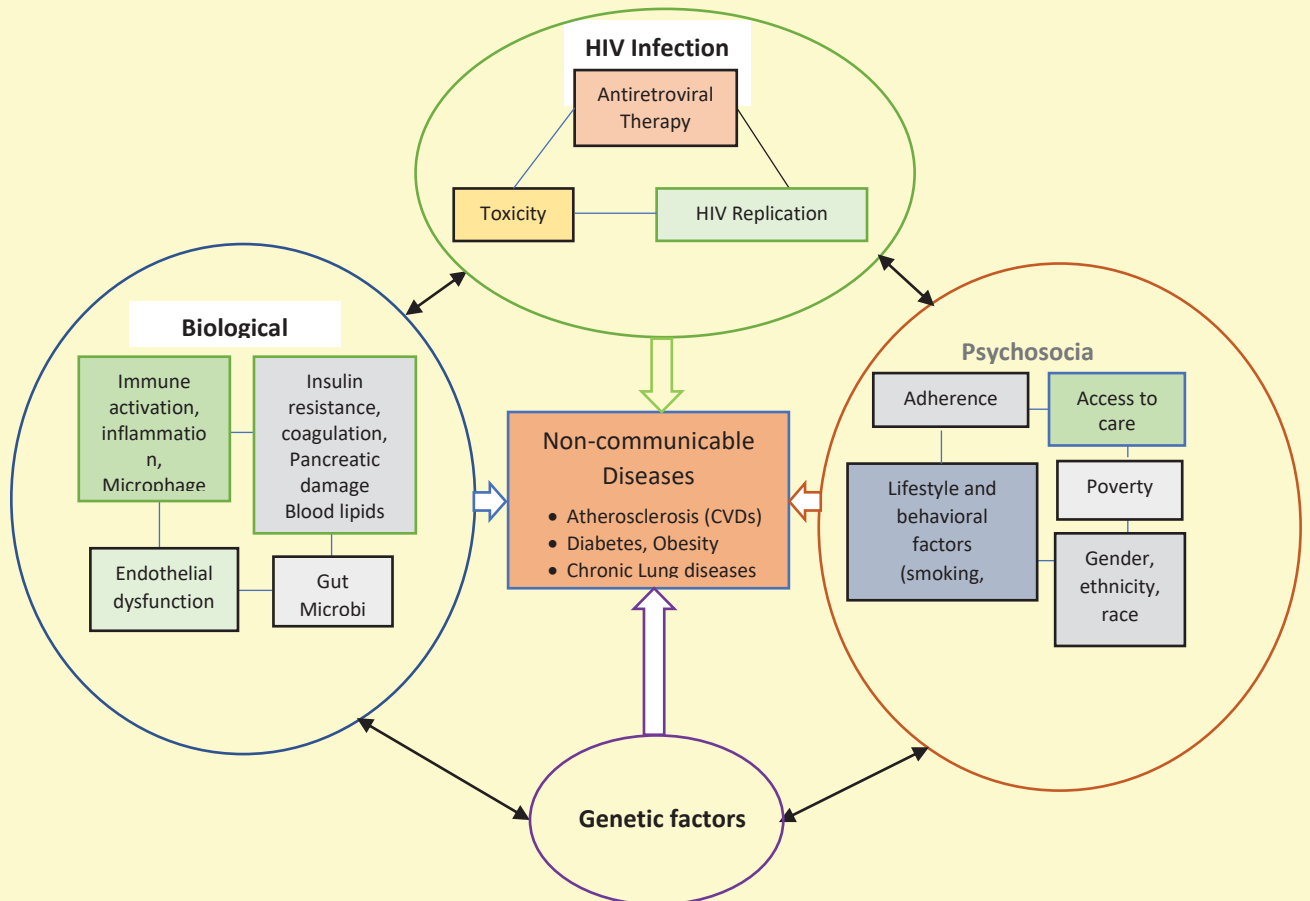
**Noncommunicable Diseases**  
**4 Diseases, 4 Modifiable Shared Risk Factors**

	Tobacco Use	Unhealthy diets	Physical Inactivity	Harmful Use of Alcohol
Cardio-vascular	✓	✓	✓	✓
Diabetes	✓	✓	✓	✓
Cancer	✓	✓	✓	✓
Chronic Respiratory	✓			

Noncommunicable Diseases World Health Organization

There are 4 important NCDs accounting for over 80% of all NCDs morbidity and mortality. These are due to an interaction of 4 modifiable risk factors. The risks factors lead to 4 leading metabolic risks namely;

1. Hypertension
2. Hyperlipidemia
3. Raises blood sugar
4. Obesity



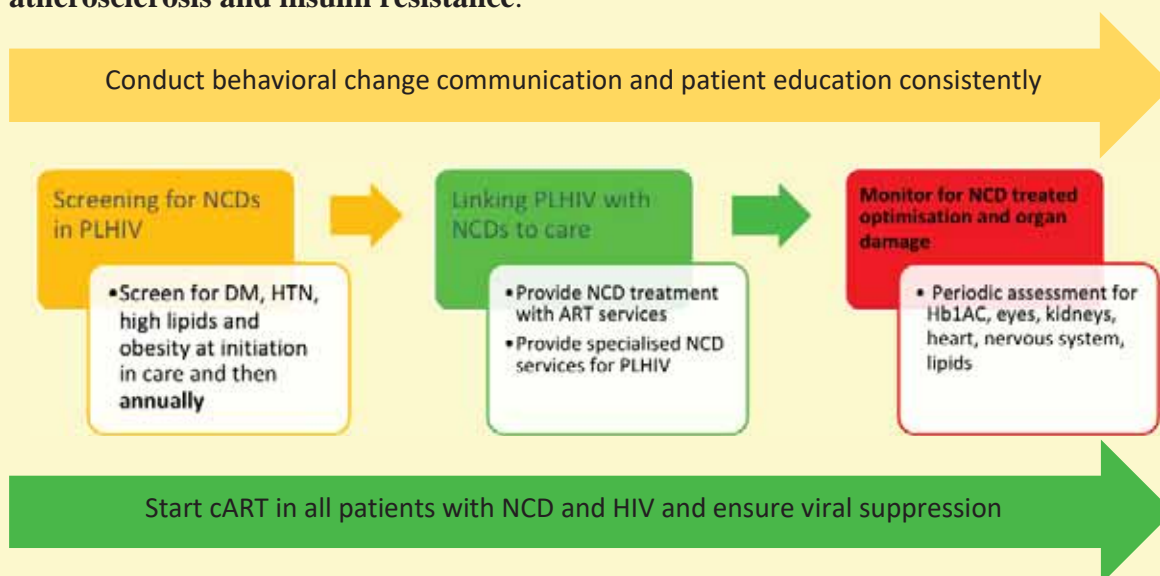
**Figure 11.2: Relationship between HIV and NCDs**

### Prevention of NCDs in PLHIV

Prevention of NCDs in PLHIV can be primary, secondary or tertiary. Primary prevention is the prevention of modifiable risk factors including smoking, inactivity, harmful use of alcohol and unhealth diets. This must be done at initiation to care and throughout the treatment journey at every contact between the RoC and the HCW. Health promotion intervention and messages are important for primary prevention. This include the provision of awareness that NCDs are higher among PHIV.

Antiretroviral Drugs toxicity and NCDs	
Lopinavir	Hyperlipadaemia, hyperglycaemia
Tenofovir	Renal dysfunction
Abacavir	Myocardial infarction
Atazanavir	Hyperlipidaemia
Dolutegravir	Weight gain, hyperglycaemia

Secondary preventions of NCDs in PLHIV involved prompt diagnosis of NCDs in PLHIV through screening, linkage to care for NCDs and monitoring for the effectiveness of therapy for NCDs. Secondary prevention must be targeted at screening, diagnosis and prompt treatment of the metabolic NCD risks including hypertension, raised blood sugar, hyperlipidaemias and obesity. All ART centers must screen PHIV for these four metabolic risks at entry into care and then annually. Those diagnosed with the conditions must be promptly linked to effective treatment and monitoring. Tertiary prevention involves the prevention of adverse outcomes by screening, diagnosis and prompt treatment of NCD conditions such as CVDs (IHD, HHD, Stroke) or diabetic nephropathy, eye diseases or neuropathy in those with diabetes. Prompt referral to specialised services is required. **ART and virologic suppression reduce the background inflammation thereby reducing atherosclerosis and insulin resistance.**



**Figure 11.3: Secondary Prevention of NCDs among PLHIV**

## HIV and NCD Integration Model

NCD services in PLHIV must be provided together with HIV services at the facility and community. Where there are special needs for individuals with NCDs among PLHIV, special models for services delivery must be provided to meet these needs. NCD services include screening, diagnosis and treatment for risk factors for NCDs, NCD cases and complications of NCDs. In Zambia, all PLHIV must be screened for modifiable primary risks including smoking, poor diet, inactivity and harmful alcohol use at initiation into care and annually. Appropriate tools and health promotion materials must be use. Once present, treatment for modifiable risk factors must be instituted and where treatment is not available referral to centers with these services must be made. Further, all PLHIV must be screened and be provided care for NCD related metabolic risk factors including Obesity, Hypertension, Diabetes Mellitus and Hyperlipidaemia at entry into care and annually. **NCD services must be provided wherever ART services are provided. Importantly, ALL ART services must have the capacity to treat for the metabolic risks including hypertension, diabetes mellitus, hyperlipidaemias and obesity.**

## NCD Models among PLHIV

Individuals with well controlled NCDs and HIV can be enrolled in DSD models for stables clients. Clients must be identified and screened before they are enrolled in a model. It is encouraged that these models must synchronize with the models for ART pickup and services. Those with uncontrolled NCDs such as advanced renal disease, advanced CVD and malignancies must also have specialized DSD models preferably involving specialist care. Attention to primary prevention of risk factors is still a cornerstone for services in the DSD models. Examples of models for the integration of NCDs and ART in Zambia include:

- Facility based model which incorporate both NCD and ART such as fast track drug refills, after-hours refills, weekend refills and other specialized support such as adherence counselling services.
- Integrating ART specific DSD models such as Multi-Month Dispensations (MMDs) 6 monthly refills and Community ART Dispensation (CAD) with the dispensation of medicines for NCD chronic diseases
- Community Health post which provides NCDs and ART care for PLHIV
- Community Adherence Groups which incorporate NCDs and ART

For patient in routine care, facilities are encouraged to setup systems and mobilise resources and inputs for NCD care at all points of Art services including counselling, triage, clinician consultations rooms, blood collection and pharmacy pick up points. All these points must be capacitated to act in the event of an NCD, or NCD risk factor case.

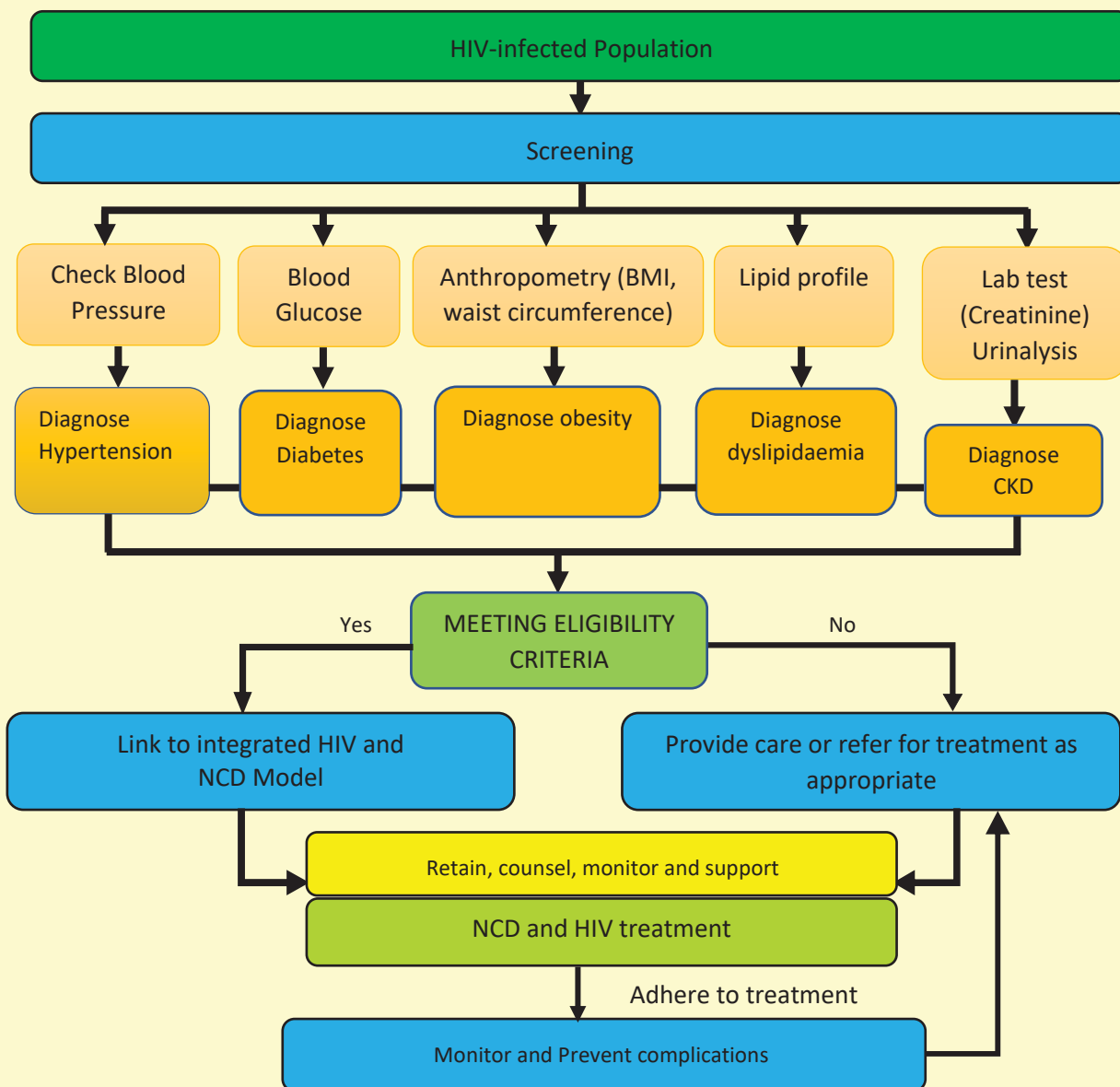


Figure 11.4: Algorithm for Integrated NCD and HIV Care

**Table 11.1: NCD Services in the ART Centre**

Service points	Registry	Triage	Counselling	Clinician Screening room	Blood Collection	Pharmacy
<b>NCD Service</b>	<ul style="list-style-type: none"> <li>• Synchronise NCD and ART appoints</li> <li>• Collate ART and NCD files</li> </ul>	<ul style="list-style-type: none"> <li>• Measure BP, RBS, height, BMI and those that need attention</li> </ul>	<ul style="list-style-type: none"> <li>• Always include lifestyle messages in the counselling include, smoking cessation, harmful use of alcohol, healthy diet, physical inactivity</li> </ul>	<ul style="list-style-type: none"> <li>• Check for signs and symptoms of NCDs, or their risks.</li> <li>• Monitoring for response in those with NCDs</li> <li>• Lifestyle counselling</li> </ul>	Collect blood samples for the NCD related monitoring	<ul style="list-style-type: none"> <li>• Commodity security for NCD conditions</li> <li>• Dispensation for NCD conditions</li> </ul>

## Approach to Common NCDs

### Cardiovascular Diseases (CVDs) and Risk Factors

Chronic immune activation that persists in HIV infection, even if on treatment, puts the HIV-infected population at a higher risk of CVDs. Furthermore, side effects of some ARVs and unhealthy lifestyle such as smoking, inactivity and poor diet also confounds the vicious cycle of NCDs. *See figure 11.2.*

CVDs are defined as the group of disorders of heart and blood vessels and include conditions such as coronary heart diseases, strokes, peripheral vascular diseases, cardiomyopathies among others. The common risk factors shared among most CVDs include obesity, Type 2 Diabetes Mellitus, age (>40 years), smoking, family history of CVDs, unhealthy eating habits and sedentary lifestyle. In children, CVDs are mainly as a result of rheumatic heart diseases and congenital heart diseases. General preventive measures are as shown below.

**Table 11.2: General Measures for the Prevention of CVDs**

Smoking cessation
Stoppage/reduction of alcohol consumption
Avoid high-saturated fatty meals (e.g., animal fat)
Limit salt intake (less than a teaspoon per day)
Increase intake of high-fiber and low- glycemic index foods
Avoid high sugar, sweets and sweetened beverages
Moderate intensity physical exercises (e.g., walking, bicycle rides, jogging, swimming for at least 30 minutes each time three times a week)

### Approach to Specific Common CVDs Risk Factors

Like the general population, assessment of CVDs in HIV-infected should incorporate identification and management of risk factors. The approach to CVDs risk is outlined in the tables from Tables 11.3 to 11.5

**Table 11.3: Obesity Screening, Diagnosis, and Initial Management for HIV-infected Individuals**

<b>Screening</b>
Check weight, waist-circumference, waist-hip ratio and BMI at every visit
<b>Diagnosis</b>
BMI $\geq 30\text{kg/m}^2$ , waist circumference $\geq 94$ cm for males and $\geq 80$ cm for females
<b>Management</b>
<ul style="list-style-type: none"> <li>☞ Check BMI at every visit</li> <li>☞ Active lifestyle with moderate-intensity physical activity (at least 30 minutes, 3 times a week)</li> <li>☞ Cut down consumption of fatty foods</li> <li>☞ Smoking cessation</li> <li>☞ Increase intake of whole grains, vegetables, fruit, and beans (nutritionists to be engaged in patient care)</li> <li>☞ Reduce/abstain from alcohol</li> <li>☞ Cut down sugar intake</li> <li>☞ Cut down salt intake to less than one teaspoon a day</li> <li>☞ Monthly self-weight monitoring should be done, if feasible, for patients on TAF/3TC/DTG</li> </ul>

**Remember to Link all stable clients to NCD and HIV DSD Model**

**Table 11.4: Dyslipidaemia Screening, Diagnosis, and Initial Management for HIV-infected Individuals**

<b>Screening</b>
Fasting lipid profile should be evaluated at baseline for all PLHIV, then annually if baseline screening is normal
<b>Diagnosis</b>
Dyslipidaemia is defined as high fasting total cholesterol ( $> 5.2\text{mmol/L}$ ), LDL ( $> 3.4\text{mmol/L}$ ) or triglycerides ( $> 2.2\text{mmol/L}$ )
<b>Management</b>
<ul style="list-style-type: none"> <li>☞ Lifestyle modifications for 3-6 months</li> <li>☞ If the patient is on an ARV known to cause or exacerbate Dyslipidaemia (primarily LPV-r) then consider a single-drug substitution to a more lipid-friendly drug (such as from LPV-r to ATV-r or DTG if naïve or RAL in children) as the treatment of choice before adding a lipid lowering drug</li> <li>☞ Check lipids 6 months after initiation of LPV-r based regimen in pregnant women.</li> <li>☞ If does not meet treatment target with lifestyle modifications, then add drugs:             <ul style="list-style-type: none"> <li>✓ Atorvastatin: starting dose of 10mg OD (maximum dose 20mg if patient is on a PI/r and a maximum dose of 80mg once daily if not on a PI/r)</li> <li>✓ Pitavastatin, Pravastatin and Rosuvastatin can be given as well if available.</li> <li>✓ Simvastatin and Lovastatin should be avoided in patients taking Protease Inhibitors.</li> <li>✓ Allow at least 3 months before repeating fasting lipids and titrating dose.</li> </ul> </li> </ul>
<b>Once targets achieved can monitor lipids every 6-12 months</b>

*Adapted from ZCGS 2018 with modifications*

**Link all stable clients in the NCD and HIV DSD Model**



**Table 11.5: Type 2 Diabetes Mellitus Screening, Diagnosis, and Initial Management for HIV-Infected Individuals**

<b>Screening</b>	
Blood glucose (fasting or random) should be evaluated at baseline for all PLHIV, then annually if baseline screening is normal; urine dipstick for protein and glucose can be used if blood glucose testing is not available	
<b>Diagnosis</b>	
Diabetes Mellitus is defined as fasting blood glucose (FBG) $\geq 7.0$ mmol/L, or random blood glucose $\geq 11.1$ mmol/L, or HbA1C $> 6.5\%$ while pre-diabetes is defined as FBG between $6.1 < 7.0$ mmol/L and random blood glucose between 6.8 to 11.2 hours after meals. <sup>2</sup> Abnormal results should be repeated to confirm the diagnosis	
<b>Management</b>	
<b>Monitoring Glycaemic Levels Goals</b>	
Test	Target
A1C	7.0% (53 mmol/mol)
Pre-prandial Capillary (FBS)	4.4–7.2 mmol/L
Peak Postprandial Capillary (RBS)	$< 10.0$ mmol/L
<ul style="list-style-type: none"> <li>☞ Monitor HbA1C (or FBS if HbA1C not available) every 3 months for patients with confirmed diagnosis of diabetes mellitus or pre-diabetes</li> <li>☞ Lifestyle modifications (weight loss, nutritional support to manage portion sizes and calculate glycaemic index of various foods to help with control of blood sugar) for 3-6 months</li> <li>☞ If does not meet treatment target with lifestyle modifications, then add drugs: Metformin</li> <li>☞ Obtain baseline Creatinine; do <b>NOT</b> use Metformin if Creatinine Clearance is than <math>&lt; 30</math> mL/min                             <ul style="list-style-type: none"> <li>✓ Start with low dose (500mg OD or BD) and titrate up every 1-2 weeks until reaches 1g BD (or maximum tolerated dose if less than 1g BD)</li> <li>✓ If does not meet treatment targets with Metformin for 3-6 months at maximum tolerated dose, then consider adding oral drugs from another class (such as glyburide) and/or specialist consultation</li> <li>✓ Maximum dose for Metformin should be 1g per day in patients on concomitant DTG based regimens, if DTG is withdrawn, consider dose increment to meet treatment targets or as tolerated</li> <li>✓ Some patients may require Insulin</li> </ul> </li> <li>☞ At every visit: A thorough history (to elicit features of hypoglycaemia, other cardiovascular disease risk factors, neuropathy, diabetic foot ulcers) and a physical exam (for BP, neuropathy, foot ulcers)</li> <li>☞ Annual ophthalmology examination for diabetic retinopathy</li> <li>☞ Annual urinalysis: start on an ACE-I/ARB if *proteinuria develops (even if BP normal)</li> </ul>	

Adapted from ZDGS 2018 with modifications

\*proteinuria – urine protein of 300mg/day or 1+ on urine dipstick

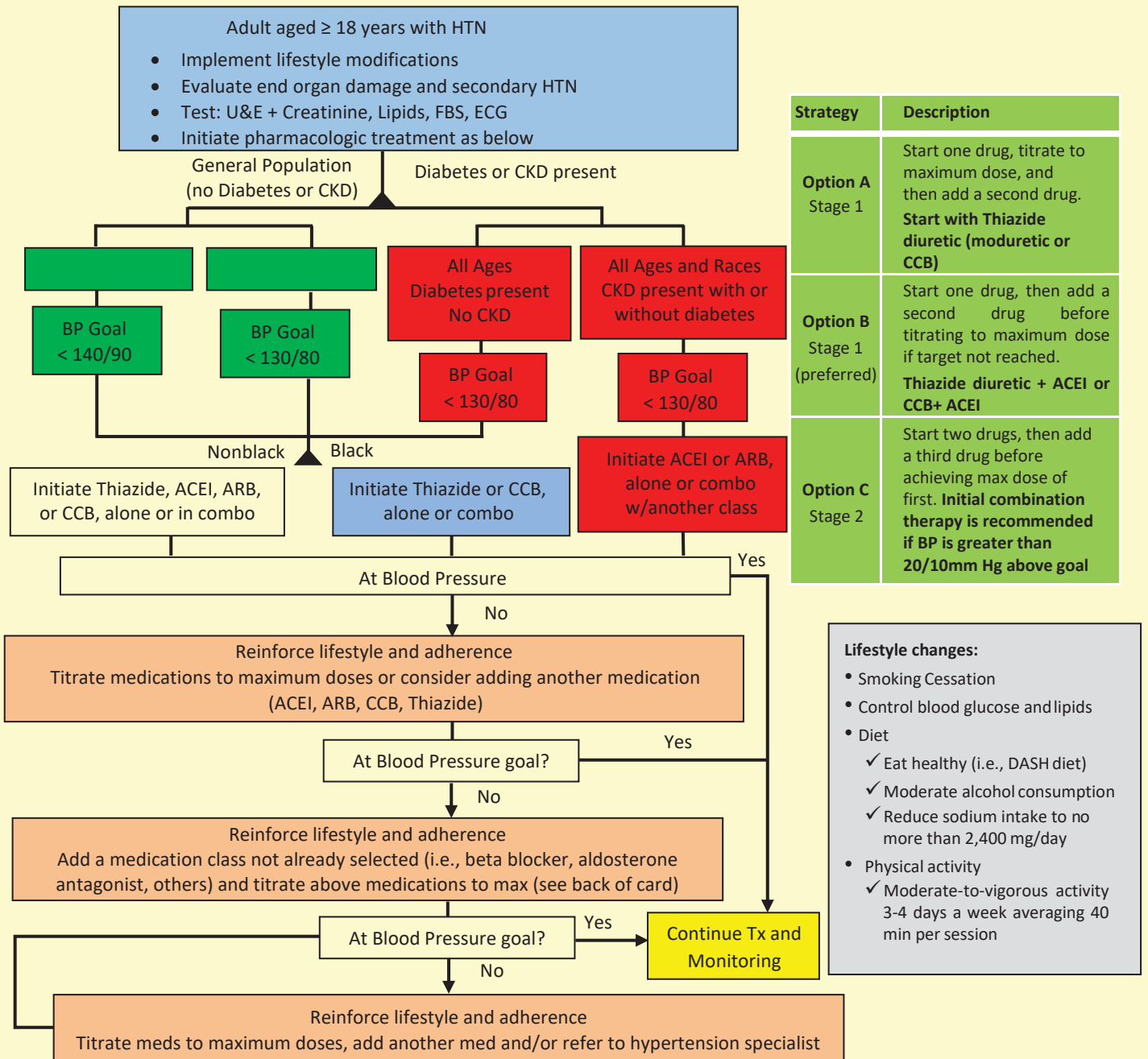
<sup>2</sup>International Diabetes Federation

**Link all stable clients in the NCD and HIV DSD Model**

**Approach to hypertension**

Hypertension is the leading cause of CVD in Zambia. It is defined as the occurrence of blood pressure reading above 139/89mmHg for two consecutive readings at separate visit.

Stage	Systolic (mmHg)	Diastolic (mmHg)	Management
Normal	<120	<80	Remeasure yearly in HIV
Prehypertension	120-139	85-89	Lifestyle changes
Stage 1	140-159	90-99	Pharmacological and lifestyle
Stage 2	160-179	100-109	Pharmacological and lifestyle



(Adapted from JNC8)

**Figure 11.5: Hypertension Guideline Algorithm**

**Table 11.6: Hypertension Treatment**

Compelling Indications		<p><b>Beta-1 Selective Beta-blockers</b> – possibly safer in patients with COPD, asthma, diabetes, and peripheral vascular disease:</p> <ul style="list-style-type: none"> <li>• Metoprolol</li> <li>• Bisoprolol</li> <li>• Betaxolol</li> <li>• Acebutolol</li> </ul>
Indication	Treatment Choice	
Heart Failure	ACEI/ARB + BB + Diuretic + Spironolactone	
Post – MI/Clinical CAD	ACEI/ARB AND BB	
CAD	ACEI, BB, diuretic, CCB	
Diabetes	ACEI/ARB, CCB, diuretic	
CKD	ACEI/ARB	
Recurrent Stroke Prevention	ACEI, diuretic	
Pregnancy	Labetalol (first line), Nifedipine, Methyldopa	
Drug Class	Agents of Choice	Comments
Diuretics	HCTZ 12.5-50mg, Moduretic (HCTZ 50mg+Amiloride 5mg), Chlorthalidone 12.5-25mg, Indapamide 1.25-2.5mg <i>K+ sparing</i> – Spironolactone 25-50mg, Amiloride 5-10mg, Triamterene 100mg Furosemide 20-80mg twice daily, Torsemide 10-40mg	Monitor for hypokalemia. Most SE are metabolic in nature. Most effective when combined with ACEI Stronger clinical evidence with Chlorthalidone. Spironolactone - gynecomastia and hyperkalemia Loop diuretics may be needed when GFR <40mL/min
ACEI/ARB	<i>ACEI</i> : Lisinopril 10mg -40mg, Enalapril 2.5mg - 40mg, Captopril 12.5-450mg, and Quinapril 10-40mg, <i>ARB</i> : Losartan 50-100mg, Telmisartan 20-80mg Candesartan 8-32mg, Valsartan 80-320mg, Olmesartan 20-40mg	SE: Cough (ACEI only), angioedema (more with ACEI), hyperkalemia Losartan lowers uric acid levels; candesartan may prevent migraine headaches
Beta-Blockers	Atenolol 25mg -100mg daily, Metoprolol succinate 50-100mg and Tartrate 50-100mg twice daily, Nebivolol 5-10mg, Propranolol 40-120mg twice daily, Carvedilol 6.25-25mg twice daily, Bisoprolol 5-10mg, Labetalol 100-300mg twice daily	Not first line agents – reserve for post-MI/CHF Cause fatigue and decreased heart rate Adversely affect glucose; mask hypoglycemic awareness
Calcium Channel Blockers	<i>Dihydropyridines</i> : Amlodipine 5-10mg, Nifedipine ER 30-90mg, <i>Non-dihydropyridines</i> : Diltiazem ER 180-360mg, Verapamil 80-120mg 3 times daily or ER 240-480mg	Cause edema; dihydropyridines may be safely combined with B-blocker. Non-dihydropyridines reduce heart rate and proteinuria
Vasodilators	Hydralazine 25-100mg twice daily, Minoxidil 5-10mg Terazosin 1-5mg, Doxazosin 1-4mg given at bed-time	Hydralazine and Minoxidil may cause reflex tachycardia and fluid retention – usually require diuretic + B-blocker. Alpha-blockers may cause orthostatic hypotension
Centrally acting Agents	Clonidine 0.1-0.2mg twice daily, Methyldopa 250-500mg twice daily Guanfacine 1-3mg	Clonidine available in weekly patch formulation for resistant hypertension

**Link all stable clients in the NCD and HIV DSD Model**

## Chronic Kidney Diseases in HIV-infected People

Causes of chronic kidney diseases (CKD) in HIV-infected are multifactorial ranging from drug toxicities such as TDF, pre-existing hypertension and/or diabetes as well as a possibility of direct HIV infection of glomerular endothelium and mesangial cells. Table 11.7 below provides a summary of approach to CKD in HIV-infected individual.

**Table 11.7: CKD Screening, Diagnosis and Initial Management**

Screening
Urinalysis (for protein) and serum creatinine should be evaluated at baseline for all
Diagnosis
Impaired renal function is defined as Creatinine Clearance (CrCl) < 50mL/min, or dipstick proteinuria ≥ 1+ (300mg/day) Abnormal results should be repeated to confirm diagnosis
Management
<ul style="list-style-type: none"> <li>☞ Address the cause of the renal impairment; additional investigations and/or specialist consultation may be required</li> <li>☞ Monitor creatinine levels and calculate CrCl every 3 months (or less if &lt; 30mL/min)</li> <li>☞ Follow national guidelines on creatinine monitoring for those who are newly diagnosed with HIV</li> <li>☞ Treat dehydration promptly and aggressively</li> <li>☞ If on TDF-containing regimen:               <ul style="list-style-type: none"> <li>✓ Substitute with another ARV, except for patients with HBV/HIV co-infection who need TDF to be maintained on adjusted doses or switch to Entecavir</li> <li>✓ TAF may be used if CrCl &gt; 30mL/min</li> <li>✓ DTG/ATV-r an option if HIV-1 RNA &lt; 500,000 copies/mL, no HBV, and if there are no contraindications</li> </ul> </li> <li>☞ Avoid nephrotoxic drugs (always check side effects of other concomitant drugs before administering dosage should be directed by CrCl)</li> <li>☞ Evaluate for and treat hypertension and diabetes</li> <li>☞ All NRTIs except ABC require dose adjustments for renal impairment, depending on the severity. NNRTIs, PIs, and Integrase Strand Transfer Inhibitors (INSTIs) do not require dose adjustments for impaired renal function</li> <li>☞ <b>Refer to tertiary level of care if unable to monitor patients with CKD or if deterioration in CrCl falling below 30mL/min</b></li> </ul>

**Link all stable clients in the NCD and HIV DSD Model**

## Module 12: Mental Health and HIV

### Introduction

HIV and Mental health have a bi-directional relationship: People with mental health are at high risk of HIV infections as they are often involved in high-risk activities such as unsafe sexual activities, alcohol abuse, IV drug use and are less likely to seek health related information and services. Likewise, HIV infected individuals are prone to mental health conditions including depression and anxiety disorders. From the traumatic event of the news of HIV infections to the daunting task of being on life-long ART, the burden of living with a major illness is compounded with socio-economic situations typical of HIV infections including stigma, a break in relationships, loss of employment due to illness and economic pressure of the disease. Further, some opportunistic conditions and side effects of drugs can present as mental health conditions in PLHIV.

If left un-resolved, mental health are a poor predictor of ART outcome and result in high treatment interruption. This is even more important for the adolescent subpopulation where depression and suicidal tendencies are higher.

### Psychiatric Manifestations of HIV/AIDS

Psychiatric manifestations are due to direct effects of HIV virus on the brain very early in the illness or due to the side effects of the ARVs. the other prominent factors contributing to mental health problems secondary to HIV/AIDS are stigma secondary to contracting HIV, psychosocial stress related to the diagnosis of a life-threatening illness, denial, poor adherence, gender inequality and substance misuse.

Common mental health problems associated with HIV/AIDS are.

- Depression
- Anxiety Disorders
- Adjustment disorder
- Psychosis
- Delirium
- Mania
- Dementia

### Mental Health Consequences of HIV

Mental health conditions, which can:

- Undermine health-seeking behaviours, reduce adherence to treatment and lead to higher rates of mortality
- Lead to Development of HIV associated neurocognitive disorders (e.g., HIV-associated neurocognitive disorder, or HAND and HIV-Associated Dementia (HAD))

Some commonly prescribed antiretroviral (ARV) medications can also result in neuropsychiatric side effects.

- ARV side-effects can also include psychiatric symptoms
  - *Zidovudine* and *Abacavir* have been associated with mania and psychosis, while *Efavirenz* have been associated with mood changes and vivid dreams
  - Poor adherence to ART has been linked to *Efavirenz* use in some settings
  - Newer drugs like Dolutegravir have been linked to insomnia

## Mental Health and HIV Management Package

Mental Health and HIV management packages include integration of:

- Screening and care for mental health conditions in HIV service settings
- HIV/AIDS screening and care in Mental health services initiatives and programmes

**Table 12.1: Framework for Integration of Mental Healthcare and Support**

HIV Continuum of Care	Mental Health Issues	Related Interventions		
		Level 1 Psychiatric care and treatment	Level 2 Mental health services through primary health care/HIV clinics	Level 3 Community support programs/services
<b>PRE-ART PHASE</b>				
Counselling and testing	<ul style="list-style-type: none"> <li>• Lack of access to VCT in mental health populations</li> <li>• Emotional reactions to test results</li> <li>• Stigma and discrimination, non-disclosure</li> <li>• Risky sexual behaviour and risky drug and alcohol use</li> </ul>	Targeted HIV screening with mental health population	<ul style="list-style-type: none"> <li>• Post-test clubs</li> <li>• Screening and brief intervention to address mental health and substance use</li> </ul>	Stigma reduction programs Post-test peer support groups with focus on mental health/drug and alcohol use
Initiation of care	Anxiety and depression Social consequences of stigma (isolation, marginalization) Drug and alcohol use		<ul style="list-style-type: none"> <li>• Screening for depression.</li> <li>• Screening for drug and alcohol use; brief intervention and therapies for risky drug and alcohol use; treatment for abuse and dependence</li> </ul>	Community support and recovery groups

## GUIDELINES FOR MANAGEMENT OF ADVANCED HIV DISEASE IN ZAMBIA

<b>Retention in and maintenance of care</b>	<ul style="list-style-type: none"> <li>• Treatment adherence and drop out.</li> <li>• Risky behaviour</li> <li>• Co-occurrence of mental health and substance abuse problems</li> </ul>	Assessment and treatment of mental health and substance abuse problems (pharmacologic and psychotherapeutic interventions)	<ul style="list-style-type: none"> <li>• Adherence counselling</li> <li>• Psycho-educational approaches to reduce risk of transmission.</li> <li>• Screening and referral of mental health problems as needed.</li> <li>• Management of mild/moderate depression and anxiety disorders (see WHO mental health series)</li> <li>• Psychosocial support groups</li> </ul>	<ul style="list-style-type: none"> <li>• Community mental health services provided by nurses, community health workers.</li> </ul>
<b>ART PHASE</b>				
<b>A. Initiation of ART</b>	<ul style="list-style-type: none"> <li>• Access to ART</li> <li>• Stigma and discrimination</li> <li>• Drug and alcohol use/abuse</li> </ul>		<ul style="list-style-type: none"> <li>• Adherence counselling</li> <li>• Psychosocial support groups</li> <li>• Screening and brief intervention for hazardous drinking/drug use; treatment for abuse and dependence</li> </ul>	Peer/community support and recovery groups
<b>B. Maintenance on ART</b>	<ul style="list-style-type: none"> <li>• Treatment adherence and drop out.</li> <li>• Risky behaviour</li> <li>• Co-occurrence of mental health and substance abuse problems.</li> <li>• Side effects and neurocognitive changes.</li> </ul>	Assessment and treatment of mental health and substance abuse problems (pharmacologic and psychotherapeutic interventions) Assessment and management of side effects and neurocognitive changes	<ul style="list-style-type: none"> <li>• Adherence counselling</li> <li>• Psycho-educational approaches to reduce risk of transmission.</li> <li>• Screening and referral of mental health and substance abuse problems as needed.</li> <li>• Management of mild depression and anxiety disorders</li> <li>• Psychosocial support groups</li> </ul>	Community mental health services provided by nurses, community health workers. Peer/community support and recovery groups
<b>ADVANCED DISEASE/END-OF-LIFE PHASE</b>				
<b>C. Care for the caregivers</b>	<ul style="list-style-type: none"> <li>• Physical decline and increased symptoms</li> <li>• Depression and suicidal thoughts</li> <li>• Stigma and discrimination</li> </ul>	<ul style="list-style-type: none"> <li>• Management of major depression and suicidal risk</li> </ul>	<ul style="list-style-type: none"> <li>• Palliative care</li> <li>• Psychosocial and family support</li> </ul>	Home care and community-based care
<b>D. Deceased</b>	Burden of care on family members (typically women) Grief and loss		Grief counselling Management of mild/moderate depression and anxiety	Respite care Grief and bereavement support

*Source USAID 2009*

## Screening of HIV Patients

- All HIV patients should routinely be screened for common mental disorders (e.g., depression, anxiety, mania, alcohol and substance use, HIV-associated neurocognitive disorder, and delirium disorders)
- All HIV infected individuals must be screened for Intimate Personal Violence (IPV) before HIV testing and before initiation into care and at each visit. (*See 2020ZCG*)
- Certain patients may require more intensive screening, including:
  - those at their first ART assessment
  - those responding poorly to ART (detectable viral load (VL)/adherence issues)
  - those exhibiting worrying behaviour (looking anxious/depressed, expressing suicidal ideation or self-harm) or with history of alcohol misuse
  - Adolescents
- For individuals with mental illness, refer to a mental health provider or Tele consult with the mental health care specialist
- If an individual with mental illness appears to worsen after ART initiation, consider revising and switching to safer ART regimen
- Prior to HIV test and ART initiation, Patients should receive adequate emotional, psychological, and social support

## Management of Common Mental Disorders Co-morbid with HIV

### 1. Major Depressive Disorder (MDD) (moderate to severe depression)

Prior depression is a strong risk factor for the development of depression during the course of HIV/AIDS. Depression is a predictor of poor adherence to HIV treatment regimen. It increases the mortality in HIV/AIDS patients.

#### Screening:

Clinicians should always ask about suicidal ideation in patients with depressive symptoms using the available tools. Suicide screening and safety screening must be done. (*See Appendix 1*)

See also the ‘**SAD PERSONS**’ scale and Beck’s depression inventory scale.

See also the “**Mental state examination**”.

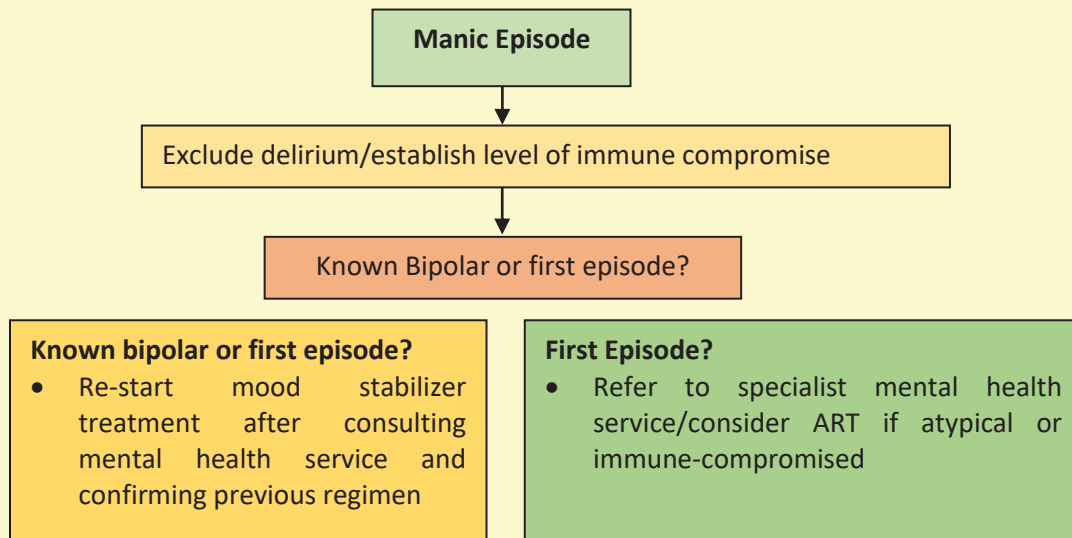
**Management:** adherence to the ARVs, anti-depressants (SSRI and SNRIs) and CBT

### 2. Mania:

Prevalence of manic episodes in HIV-infected patients is 10 times higher than in general population. Mania can result from HIV infection, opportunistic infections or due to ARVs.



Mania secondary to HIV/AIDS is seen in the later stages of HIV infections and it is difficult to treat. It is associated with impaired cognition and increased risk of dementia.



**Figure 12.1: Guidance on Management of Manic Episodes in HIV-infected Patients**

**Management:** adherence to ARVs, and mood stabilizers like; *Sodium Valproate*, *Sodium Divalproex* always consider drug interactions when prescribing in people on cART.

**\*NOTE:** *Carbamazepine* may be avoided due to its interactions with EFV and PIs\*  
**Alternative Agents:** *Gabapentin, Lamotrigine, Levetiracetam, Tiagabine, Topiramate*

**Hospitalization**

The patient requires hospitalization:

- If there is a high suicide risk
- In complex cases: the presence of psychosis and/or minimal social support and/or a poor response to out-patient treatment and/or a diagnostic dilemma
- In complex medical co-morbidity (to monitor antidepressant medication)
- In the event of severe psychomotor retardation or no eating/drinking

**Initiation of Antidepressant Treatment**

The initiation of antidepressant therapy in patients with CMDs is based on a stepwise approach as patients with HIV/AIDS are often more sensitive to side-effects of medication.

**Introducing an Antidepressant:** ‘Start low and go slow’\*

- Initiate *20mg Fluoxetine* (or similar) (SNRIs) at the lowest available dose and refer to psychosocial support services where available

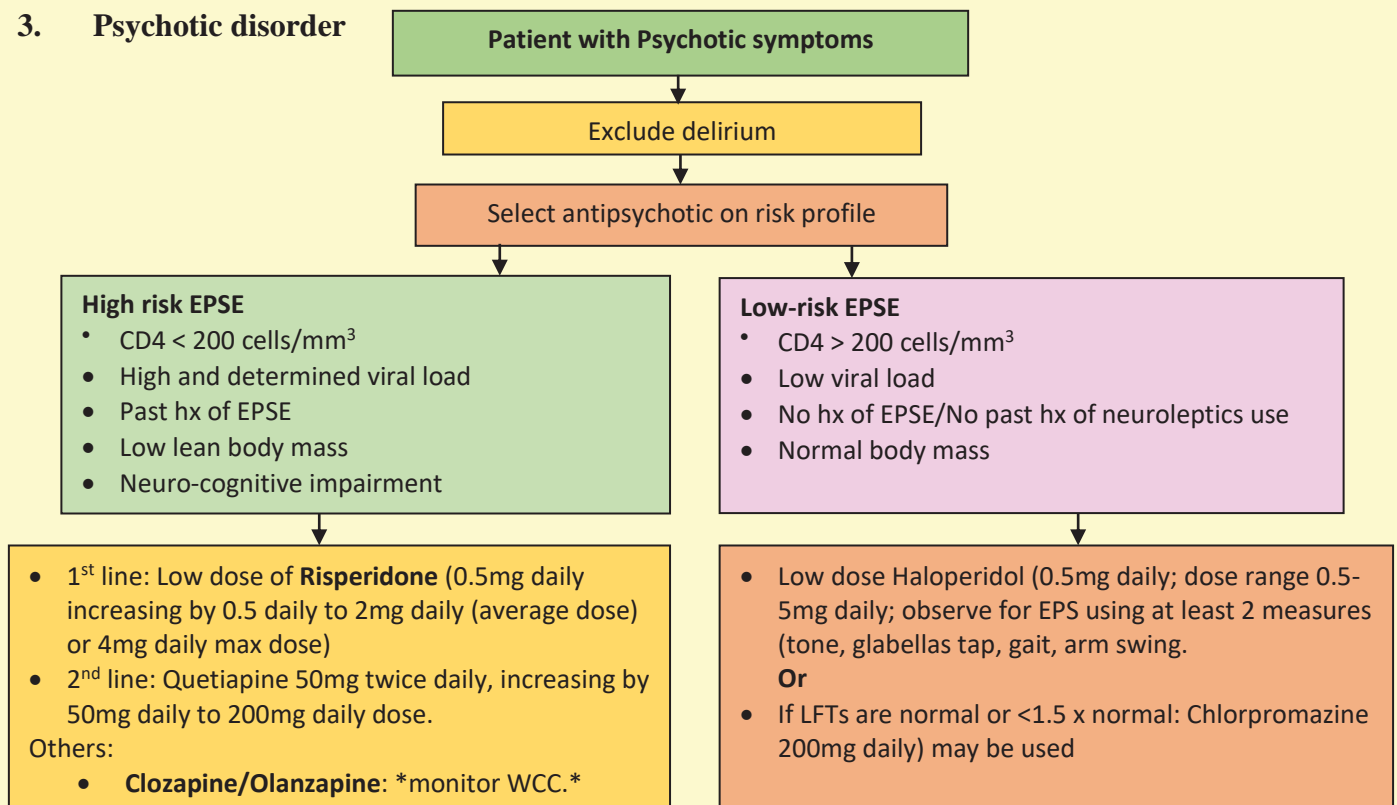
- Reassess at 2 - 4 weeks for side-effects (e.g., irritability, nausea, headache, disturbed sleep patterns); most side-effects settle within 2 weeks
- If after a total of 6 - 8 weeks there is no/minimal improvement, then increase the dose and reassess with the in 4 - 6 weeks
- If after reassessment there is still no improvement, then refer
- Fluoxetine and amitriptyline are the only antidepressants on the primary-level essential drugs list. Nurses are not currently permitted to prescribe – refer to a doctor
- If unsure at any point, then phone the referral centre for advice (Tele-consultation)
- If the depression worsens at any point, or if suicide risk increases, then refer the patient

**Psychotherapy**

If available, patients should be referred for psychological assessment and treatment.

- Evidence-based psychotherapy interventions for PLWHA and depression include:
  - Cognitive-Behavioural Therapy (CBT)
  - Interpersonal Therapy (IPT):
  - Group IPT (IPT-G)

**3. Psychotic disorder**

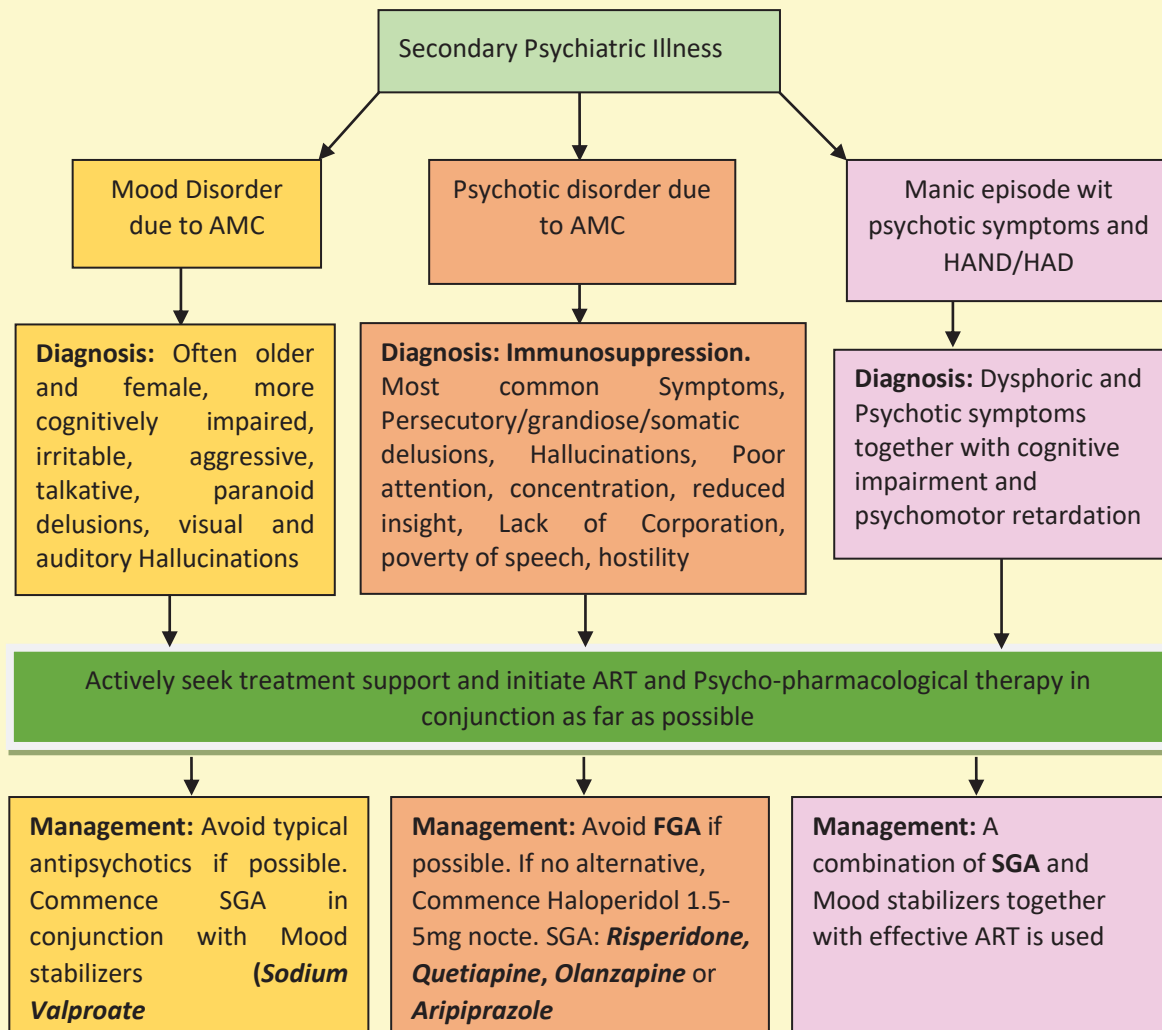


**Figure 12.2: Psychotic Disorders and their Management**

**Diagnosis of Severe Mental Disorders**

Secondary SMDs are the commonest mental disorders arising because of HIV infection. They are responsive to a combination of psychotropic medication and ART.

A careful approach will help diagnose these secondary SMDs resulting directly from HIV or an opportunistic infection.



**Figure 12.3: Diagnosis of Severe Secondary Mental Disorders**

**Non-Pharmacological Management**

- Counselling based therapies
  - Cognitive Behavioral Therapy (CBT)
  - Motivational interviewing therapy
  - Psychotherapy
  - Counselling (Adherence counselling)

### The use of CETA

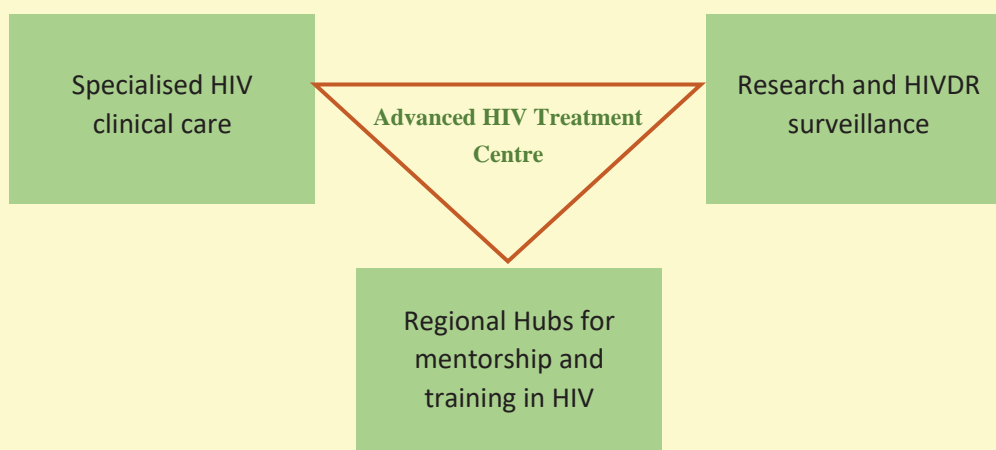
The Common Elements Treatment Approach (CETA) is a multi-problem, flexible, modular transdiagnostic treatment approach developed to address Co-morbid mental and behavioral health conditions with lay counsellor delivery in low and middle income countries (LMIC) ([www.cetaglobal.org](http://www.cetaglobal.org)) ([Murray et al., 2014](#)).

**Table 12.2: Common Elements Treatment Approach**

ELEMENT	COMMON NAME	DESCRIPTION
<b>Psychoeducation and Engagement</b>	Introduction and Encouraging Participation	<ul style="list-style-type: none"> <li>• Focus on obstacles to engagement.</li> <li>• Linking program to assisting with client's problems</li> <li>• Includes family when appropriate.</li> <li>• Program information (duration, content, expectations)</li> <li>• Normalization/validation of current symptoms/problems</li> </ul>
<b>Anxiety management strategies</b>	Relaxation	<ul style="list-style-type: none"> <li>• Strategies to improve physiological stress. Examples: deep breathing, meditation, muscle relaxation, and imagery. Others added by local cultures</li> </ul>
<b>Behavioral Activation</b>	Getting Active (GA)	<ul style="list-style-type: none"> <li>• Identifying and engaging in pleasurable, mood-boosting, or efficacy-increasing activities.</li> </ul>
<b>Cognitive Coping/Restructuring</b>	Thinking in a Different Way –Part I and Part II (TDW1 and TDW2)	<ul style="list-style-type: none"> <li>• Understand association between thoughts, feelings, and behaviour.</li> <li>• Learn to restructure thinking to be more accurate and/or helpful</li> </ul>
<b>Imaginal Gradual Exposure</b>	Talking about Trauma Memories (TDM)	<ul style="list-style-type: none"> <li>• Facing feared and avoided memories in detail.</li> <li>• Gradual desensitization/exposure</li> </ul>
<b>In Vivo Exposure</b>	Live Exposure	<ul style="list-style-type: none"> <li>• Facing innocuous triggers/reminders in the client's environment</li> <li>• Gradual desensitization/exposure</li> </ul>
<b>Suicide/Homicide/Danger Assessment and Planning</b>	safety	<ul style="list-style-type: none"> <li>• Assessing client risk for suicide, homicide, and domestic violence</li> <li>• Developing a focused plan with the client and client's family (when appropriate)</li> <li>• Additional referral/reporting when needed.</li> </ul>
<b>CBT for Substance Use and Relapse Prevention</b>	Substance Use Element (SU)	<ul style="list-style-type: none"> <li>• Utilizes motivation and CBT principles and activities to get client buy-in and alter behaviour patterns to change substance use/abuse behaviour</li> </ul>

## Module 13: Advanced HIV Treatment Centres

Advanced HIV Treatment Centres (ATCs) are centres of excellence where complicated HIV care, treatment and support services are offered to patients with HIV and complex needs. The functions of ATCs are mainly to provide care to persons with complicated HIV disease course, HIV drug resistance surveillance and research, and provision of training and mentorship to healthcare workers in management of HIV.



**Figure 13.1 Functions of ATC**

### Minimum Requirements for an ATC

The following requirements must be met to successfully set up an ATC.

**Table 13.1: Human Resource Requirements for an Advanced Treatment Centre**

Clinician	Pharmacy	Laboratory	Nurses	Support staff
Infectious Diseases Specialists Physician HIV Specialist Paediatricians  *with experience in treating ART experienced patients	Pharmacists  *Play a critical role and needs to have knowledge on HIV drug resistance	Laboratory scientists  *key in providing guidance in quality sample collection and referral	Trained HIV nurse practitioners	Data clerks/associates Counsellors

### Laboratory Requirements

- Viral Loading Testing capacity
- Resistance Testing (or able separate and process samples in readiness for transportation to resistance testing)
- Full Chemistry Panel

- Haematology Panel
- Storage facilities for Specimens

### **Pharmacy Requirements**

- Availability of drugs for third-line ART
- Minimum standards in place and adhered to

### **Data Requirements**

- Electronic Medical Records
- Secure back up

## Management of Patients with Complicated HIV

### **Assessment of Patients**

The Assessment and management of a patient who is experiencing failure of second line Antiretroviral Therapy (ART) is complex may require expert advice. Therefore, HIV clinicians need to be familiar with assessment to avoid either delayed referral for Third line treatment or unnecessary referrals in patients without true failure to Second line ART.

Evaluation of patients will include.

1. Adherence to therapy
2. Obtain a full drug history.
3. Drug-drug and drug-food interactions
4. Drug tolerability (which may also affect adherence)
5. HIV-1 RNA (viral load) and CD4+ cell counts over time.
6. Checking for prior and current resistance test results if available

### **Indications for Patient Referral to an ATC**

Patients presenting with the following are regarded as having complicated HIV and qualify for referral to an ATC:

1. HIV patients failing 2nd line treatment
2. Intolerance to ALL drugs in first- and second-line therapy
3. Complications on a PI or INSTI based regimen
4. Highly-treatment experienced individuals on complex regimens
5. Adolescents/young adults who started ART in infancy/childhood transitioning to adult care
6. Older patients previously treated with less potent early ARVs
7. Complex opportunistic infections requiring treatment at third level of care

8. Malignancies and Non-communicable disease i.e., Renal disease, Cardiovascular diseases
9. Severe or life-threatening adverse reactions
10. Patients transitioning from other countries with different first-and second line regimen

### **Prerequisites for Referral**

1. Ensure that the patient's adherence challenges have been addressed and documented. DOTs are encouraged where possible in patients with suspected second line treatment failure
2. Continue the current regimen the patient is taking
3. Prescribed referral form filled out by personnel who is certified to prescribe second line ART
4. Baseline investigations must be done (Viral load, CD4 count) as recommended in the guidelines
5. Order for HIV-1 genotyping while the patients is adherent on the failing regimen for at least a month
6. Ensure that an appointment is made and confirmed at ATC by directly contacting the specialists where feasible or the focal point person

### **Second Line Treatment Failure**

This defined as two detectable viral loads  $> 1000$  copies/mL at least three months apart, with evidence of good adherence in between, in a patient who has been on cART for a minimum duration of six months (Consider up to nine months for children less than five years old).

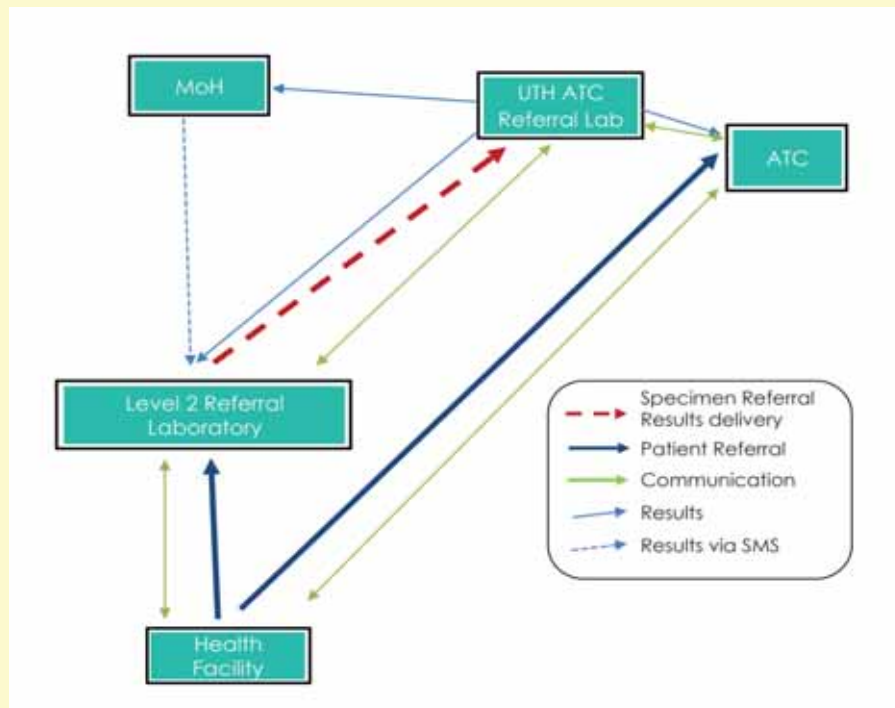
### **Drug Resistance Testing**

There are two types of HIV drug resistance testing namely, genotypic, and phenotypic testing. Genotypic testing detects specific mutations in the genome of a viral isolate that are associated with antiretroviral resistance, whilst phenotypic testing measures the ability of viruses to grow in various concentrations of antiretroviral drugs. Genotypic testing is preferred over phenotypic resistance testing for virologic failure/suboptimal response to First- or Second line ART, if resistance mutation patterns are known or not expected to be complex.

**Do NOT collect HIVDR genotype samples in patients who are NOT taking ART or those who have suppressed viral load**

## Referral of Specimens to the Specialized Laboratories for Resistance Testing

- All samples should be sent as plasma
- Cold chain should be maintained during transfer of plasma samples
- The specialized Labs will send the results to the referring facility with guidance from the ATC
- ATC should monitor for HIVDR among patients failing both first- and second-line failure



**Figure 13.2. Pathways for collection and transportation of HIVDR Samples**

### Specimen Type/Storage Type

- Plasma Treated with Anticoagulants Other Than Heparin Handling and Storage Conditions
- After collection of the specimen, plasma will have to be separated within 2 hours
- Whole blood will have to be spun at 1500 rpm for 15 minutes to separate the plasma
- Do not use powdered gloves, only nitrile or latex without powder gloves should be used. If only powdered gloves are available, then put gloves on and wash both sides of the gloves with clean water to get rid of the powder (powder from gloves inhibits the subsequent laboratory assay)



- 3 x 1 milliner aliquots of the separated plasma should be stored in clean RNase free 1.5ml tubes the separated plasma should be stored at -20°C or -40°C (samples should be stored for maximum of 1 month at Level 2 referral Lab) All specimens should bear the patient's index ID with facility code and patient number for ease of tracking

### **Limitations of Drug Resistance Testing**

- Relatively high cost
- Insensitivity for minor variants of the virus (<10-20%)
- Must be performed while the patient is taking antiretroviral regimen or within 4 weeks of treatment discontinuation and not when the patient has been off therapy for longer than 4 weeks
- Genotypic testing should not be ordered on patients whose VL <1000 copies/mL (check with local laboratory)
- Absence of resistance should be interpreted carefully in relation to the prior treatment history due to archiving of mutations

### **Potential Impact of Mutations**

- Thymidine analogues mutations develop progressive and that may impair future treatment options
- Mutations to 3TC, TDF and probably ABC remain stable over time and significantly decrease the virus' ability to replicate
- Theoretically increasing the time between virologic and clinical failure could substantially delay the need for expensive second- and third-line therapy, especially if treatment options are not compromised

### Selection of Drugs for Third Line ART

The selection of third line drugs will be an undertaking by Infectious disease/HIV specialist or physicians/paediatricians with experience and certified in managing complicated HIV cases based at ATCs. Clinicians initiating patients on third line outside ATCs should only do so in consultation with ATC specialists.

The following will guide selection of third line regimen.

**Table 13.2: Description of Second Line Treatment Failure and its Options**

	Description	Options
Group 1	Failing Second line (with DRM) to PI based regimen but not sensitised to DTG and RDM to NRTI and EFV	<b>DTG + DRV-r + ETR + TFV + 3TC (AZT + 3TC)</b>
Group 2	Failing Second line with PI based regimen and sensitised (RDM) to DTG and DRM to NRTI and EFV	<b>DRV-r + DOR (ETR) + TFV + 3TC (AZT + 3TC)</b>
Group 3	Failing Second line DTG (with DRM) based regimen but not yet sensitised to PIs and RDM to NRTI and EFV	<b>LPV-r (ATV-r) + DOR (ETR) + TFV + 3TC (AZT + 3TC)</b>

## Module 14: Programme Implementation, and Monitoring and Evaluation of Advanced HIV Disease

### Active Implementation of Advanced HIV Disease Services

Advanced HIV disease care services must follow active programme implementation processes which will include the establishment of facility and above facility level implementation teams and the programme improvement feedback cycles. The implementation teams at facility level will be responsible for the delivery of the package of care to all HIV infected individuals visiting the facility and will monitor the whole implementation of the program. Specifically, the team will be involved in the data usage to develop improvement cycles while paying a closer attention to AHD associated indicators especially HIV associated mortality rate at the facility. The oversight of AHD will be done by the national implementation task-team, a sub team of the HIV technical working group.

### Pharmaceutical Logistics Management System

Forecasting and quantification for AHD related medicines and laboratory reagents will be required to support the implementation of AHD services at facility level. This will require facilities to provide information on AHD related services obtained from updated registers and inventory control records for submission to the national ARV program on a quarterly basis. This information is needed for accurate forecasting and quantification. Medical Stores Limited will store and distribute drugs and laboratory reagents on behalf of MoH using the established mechanisms. Some of drugs including secondary generation PIs, liposomal Amphotericin B, Valganciclovir and Rifabutin will only be accessed at the ATCs. Pharmacists or pharmacy in-charge at ATC and ART facilities will be responsible for ensuring the outlined processes below are followed. Only pharmacists or pharmacy in charge at Advanced treatment centres will complete the Report and Requisition form (R&R) for 3rd line ART drugs for the ATCs and other ART treatment centres close to patients requiring 3rd line drugs. For example, stable patients on 3rd line from Chipata do not need to travel to Lusaka for drug refill. As a control measure to avoid inappropriate switches to this more expensive and complicated regimen, ATCs will coordinate the supply of 3rd line drugs to ART facilities closest to patients. For continued refills for stable patients who do not need to be seen at the ATCs, their closest ART site will generate a separate R&R with patient details specific for the requisition of 3rd line drugs and forward to the patient's ATC for refills.

The ATCs and ART sites will be required to maintain updated stock control cards as stipulated in the ARV logistics Standard Operating Procedures (SOPs). As per standard dispensing procedures, patients will be supplied third line drugs on prescription only. Details of dispensing transaction will be recorded in the Daily Activity Register (DAR) and the SmartCare pharmacy inventory control system.

### **Monitoring and Evaluation for Advanced HIV Disease**

Monitoring and evaluation for advanced for will be done within the main data reporting systems for HIV. However, local, or regional based dashboards are encouraged to help the data use and improvement cycle. Further, AHD specific indicators will need to be developed within the main M&E systems.

### **Advanced HIV Disease Data Collection Tools**

When providing Advanced HIV Care and Treatment, the first data collection tools to be used are the ART Forms. These forms will form the Recipient of care/Client/Patient File. The following are some of the forms to be filled include Patient Locator, Initial History and Physical, Clinical Follow Up, Short Visit, Patient Status Form, Stable on Care, Missed Visits, Referral Form, HIV Summary Sheet and Pharmacy. The forms are in both electronic and paper forms.

After filling of the ART forms, the various registers supporting Care and Treatment will be updated together with Tally Sheets, Activity Sheets and Summary Forms deepening on the system facility is using. For Paper based, the forms are used to update the registers while for electronic Systems, the registers are auto created and updated in the EHR system.

### **Paper-Based System**

Under this system, recipient of care/client/patient information is generated manually using paper documents that is forms, registers and Health Information Aggregation form 2/3.

Upon provision of a service (on a daily basis), a facility is expected to fill in the ART forms. In return, the ART forms should be used to create and update the various registers mentioned above. At the end of each month, a facility is expected to compile the Health Aggregation Form (HIA2/3) on HIV Testing, Care and Treatment from the registers and send the HIA forms to the District Health Office for entry in the District Health Information System (DHIS2). In some instances, data entry is done at facility level and are only expected to send HIA 2/3 to the DHO for verification supposes.

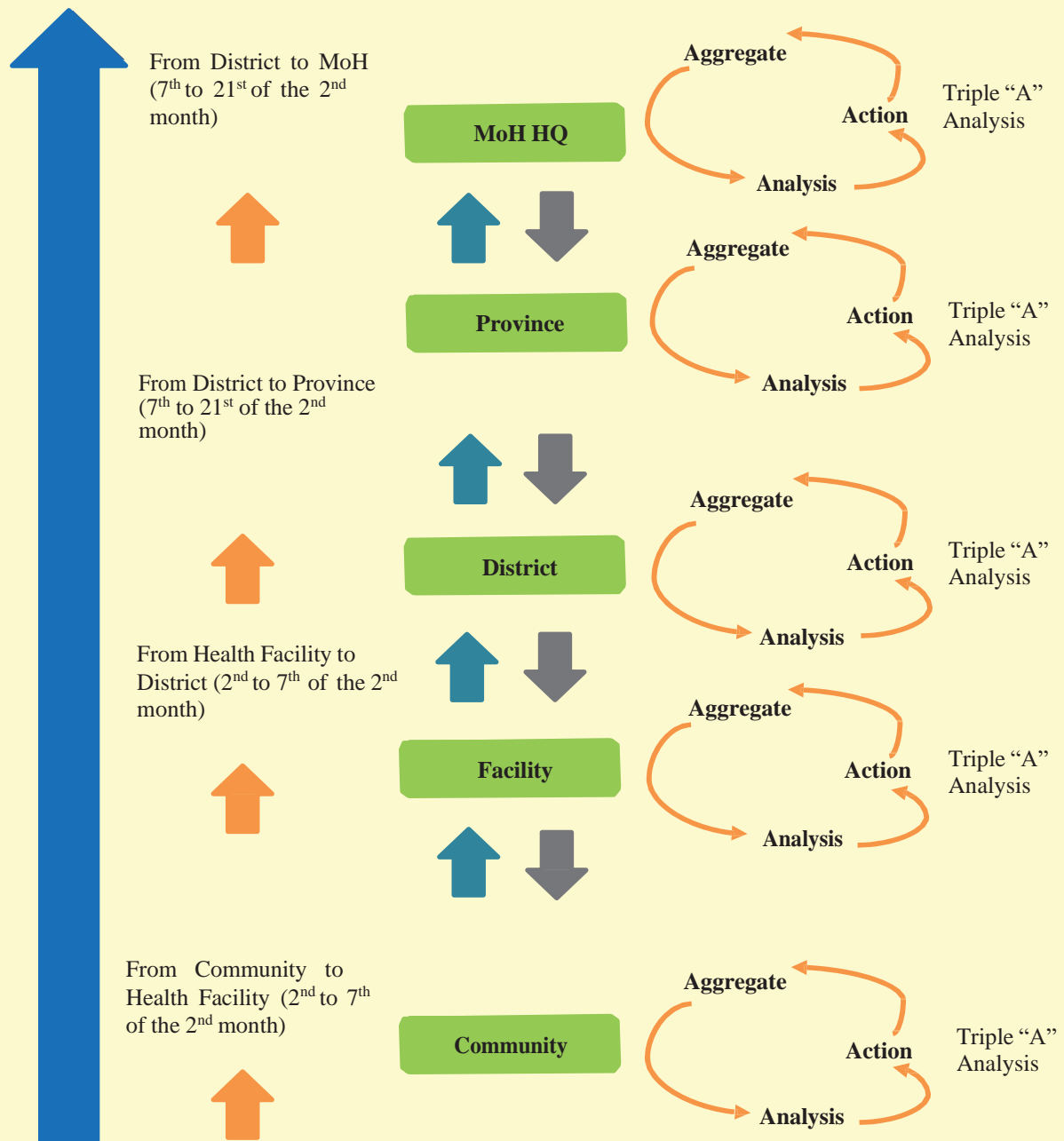
### **Electronic Health Record (EHR) System (SmartCare)**

Under this system, recipient of care/client/patient information is entered in an electronic system (SmartCare). SmartCare is a fully integrated electronic health record system tracking the provision of continuity of care; it is a clinical management information system at the facility and district (management/administration) level, and it is a key component in 'one National M&E system'.

In relation to data entry, SmartCare uses different modes of implementation such which are E-Last, E-Fast and E-First. E-last involves entering data after seeing all clients (transfer from Paper records to electronic) E-fast involves entering data just after seeing client while E-first involves real -time data entry by provider(s) as a service is being offered.

At the end of each month, the facility should ensure that all the information of the clients is entered and no backlog. Thereafter, various reports can be generated in SmartCare which may include the Health Aggregation Forms (HIA2/3), PEPFAR MER Reports, Daily Activity Register, HIV Care and Treatment Register among others. Thereafter, Transport Data Base (TDB) must be sent to the District Health Office for merging with other data from other facilities and for further submission to the province and national level for merging.

Below is the Data flow guideline from Community to National level:



**Figure 14.1: Health Management Information System (HMIS) Data Flow Guideline**

**Table 14.1: Advanced HIV Guidelines Indicator Matrix**

No.	Indicators	Indicator Definition	Numerator	Denominator	Data Source
1.	Number of patients eligible for CD4 cell count	Number of HIV patients who are initiating ART treatment, are presenting to care ill for treatments and those requiring a repeat CD4 cell count			SmartCare/Facility-based ART Registers
2.	Number of HIV positive clients screened for AHD with a CD4 count	Number of HIV positive clients screened for AHD with a CD4 count done	-	-	SmartCare/Facility-based ART Registers
3.	Number of individuals with AHD	HIV Positive individuals with CD4 cell count < 200 cells/mm <sup>3</sup> or WHO stage 3 or 4 and All HIV Positive Children under 5 years	-	-	SmartCare/Facility-based ART Registers
4.	Percentage of adults and children > 5 years old with AHD receiving ART	Number and percent of adults and children with AHD who are currently receiving combination antiretroviral therapy (ART) in accordance with a nationally approved treatment protocol during the reporting period	The number of adults and children with AHD who ever started ART minus those patients who are not currently on treatment prior to the end of the reporting period	Estimation of the number of people with AHD requiring (in need of and eligible for) ART. This estimation takes into consideration a variety of factors including, but not limited to, the current numbers of people with HIV, the current number of patients on ART, and the natural history of HIV from infection to enrolment on ART	SmartCare/DHIS2/Spectrum /Facility-based ART Registers
5.	Number of clients with AHD screened for Cryptococcus with a serum CrAg	Number of adults and children with AHD screened for Cryptococcus with a serum CrAg	-	-	SmartCare/Facility-based ART Registers
6.	Proportion of clients with AHD screened positive for a serum CrAg	Number of AHD clients screened positive for a serum CrAg compared to all clients screened with a serum CrAg	Number of AHD clients screened positive for a serum CrAg	Number of adults and children with AHD screened for Cryptococcus with a serum CrAg	SmartCare/Facility-based ART Registers
7.	Percentage of AHD clients screened positive for serum crag started on Pre-emptive Fluconazole therapy	Number and percentage of AHD clients (children and adults) screened positive for serum crag started on Pre-emptive Fluconazole therapy	Number of AHD clients (children and adults) screened positive for serum crag and started on Pre-emptive Fluconazole therapy	Number of AHD clients screened positive for a serum CrAg	SmartCare/Facility-based ART Registers

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<b>8.</b>	Proportion of AHD clients screened positive on CrAg and have symptoms for Cryptococcal Meningitis	Number of AHD clients screened positive on CrAg and are having symptoms compared to all those screened positive	Number of AHD clients screened positive on CrAg and are having symptoms for Cryptococcal Meningitis.	Number of AHD clients screened positive for a serum CrAg	SmartCare/Facility-based ART Registers/Patient Files
<b>9.</b>	Number of lumbar puncture done among AHD clients	Number of lumbar puncture performed among AHD clients	-	-	SmartCare/Facility-based ART Registers/Patient Files
<b>10.</b>	Proportion of probable Cryptococcal Meningitis with a lumbar puncture performed	Percentage of probable Cryptococcal meningitis with a lumbar puncture performed	Number of probable Cryptococcal Meningitis with a lumbar puncture performed	Proportion of probable Cryptococcal Meningitis cases.	SmartCare/Facility-based ART Registers/Patient Files
<b>11.</b>	Number of AHD clients treated for Cryptococcal meningitis	Number of AHD clients treated for Cryptococcal Meningitis	-	-	SmartCare/Facility-based ART Registers/Patient Files
<b>12.</b>	Proportion of Individuals with AHD tested for Cryptococcal Antigenemia	Proportion of Individuals with AHD tested for Cryptococcal Antigenemia.	Number of Individuals with AHD tested for Cryptococcal Antigenemia	Number of individuals with AHD	SmartCare/Facility-based ART Registers/Patient Files
<b>13.</b>	Number of AHD Clients with Cryptococcal Antigenemia	Number of Advanced HIV Disease Individuals coinfectd with Cryptococcal Antigenemia	-	-	SmartCare/Facility-based ART Registers/Patient Files
<b>14.</b>	Number of Individuals with AHD on Fluconazole pre-emptive therapy for Cryptococcal antigen	Individuals with AHD on Fluconazole pre-emptive therapy for Cryptococcal antigen	-	-	SmartCare/Facility-based ART Registers/Patient Files
<b>15.</b>	Number of AHD clients with Cryptococcal Meningitis	Individuals with AHD coinfectd with Cryptococcal Meningitis	-	-	SmartCare/Facility-based ART Registers/Patient Files
<b>16.</b>	Proportion of AHD clients screened with a urine LAM	Proportion of AHD clients screened with a urine LAM	Number of Advanced HIV Disease clients screened with a urine LAM	Number of clients with AHD	SmartCare/Facility-based ART Registers/Patient Files
<b>17.</b>	Proportion of AHD clients screened positive on urine LAM	Proportion of AHD clients screened positive on urine LAM	Number of Advanced HIV Disease clients screened positive on urine LAM	Number of AHD clients screened with a urine LAM.	SmartCare/Facility-based ART Registers/Patient Files





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<b>18.</b>	Proportion of Individuals with AHD with signs or symptoms of TB	Individuals with AHD with signs or symptoms of TB (current cough, fever, weight loss, night sweats)	Number of individuals with AHD	Number of Individuals with AHD with signs or symptoms of TB	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>19.</b>	Proportion of AHD clients symptomatically screened for TB	Proportion of AHD clients symptomatically screened for TB	Number of AHD clients symptomatically screened for TB	Number of Individuals with AHD with signs or symptoms of TB	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>20.</b>	Number of AHD clients screened negative symptomatically	Number of AHD clients screened negative symptomatically	-	-	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>21.</b>	Number of AHD started on TPT	Number of AHD started on TB Preventive Therapy (TPT)	-	-	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>22.</b>	Proportion of AHD clients screened positive with Gene Xpert started on TB Treatment	Proportion of AHD clients screened positive with Gene Xpert started on TB Treatment	Number of AHD clients screened positive with Gene Xpert started on TB Treatment	Number of AHD clients screened positive with Gene Xpert	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>23.</b>	Proportion of Individuals with AHD with confirmed TB	Individuals with AHD coinfecting with confirmed TB diagnosis	Number of Individuals with AHD with confirmed TB	Number of individuals with AHD	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>24.</b>	Proportion of Individuals with AHD with signs or symptoms of Extrapulmonary TB	Individuals with AHD with signs or symptoms of Extrapulmonary TB (enlarged lymph nodes)	Number of Individuals with AHD with signs or symptoms of Extrapulmonary TB	Number of individuals with AHD	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>25.</b>	Number of Individuals with AHD with confirmed Extrapulmonary TB	Individuals with AHD coinfecting with Extrapulmonary TB	-	-	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>26.</b>	Proportion of Individuals with AHD on IPT	Individuals with AHD taking TB Prophylaxis	Number of Individuals with AHD on IPT	Number of individuals with AHD	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>27.</b>	Proportion of AHD clients started on CTX	Proportion of AHD clients started on CTX	Number of AHD clients started on CTX	Number of individuals with AHD	SmartCare/Facility-based ART Registers/Patient Files/DHIS2



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<b>28.</b>	Proportion of women with AHD with Cervical Cancer	Women with AHD coinfecting with Cervical Cancer	Number of women with AHD with Cervical Cancer	Number of women with AHD	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>29.</b>	Proportion of individuals with AHD with Kaposi's Sarcoma	Individuals with AHD coinfecting with Kaposi's Sarcoma	Number of Individuals with AHD coinfecting with Kaposi's Sarcoma	Number of individuals with AHD	SmartCare/Facility-based ART Registers/Patient Files/DHIS2
<b>IMPACT INDICATORS</b>					
<b>30.</b>	Prevalence of AHD	The number of cases of AHD that are present in a particular population at a given time	Total Population	Number of individuals with AHD	ZAMPHIA/ZDHS
<b>31.</b>	Mortality due to AHD	Individuals who died due to AHD in a specific period	Total number of Individuals with AHD in a specific period	Number of individuals with AHD who died in a specific period	ZAMPHIA/ZDHS
<b>32.</b>	Mortality due to AHD and TB coinfection	Individuals who died due to AHD and TB coinfection	Total number of Individuals with AHD in a specific period	Number of individuals with AHD with TB who died in a specific period	ZAMPHIA/ZDHS
<b>33.</b>	Mortality due to AHD and Cryptococcal Meningitis	Individuals who died due to AHD and Cryptococcal Meningitis	Total number of Individuals with AHD in a specific period	Number of individuals with AHD with Cryptococcal Meningitis who died in a specific period	ZAMPHIA/ZDHS



## Appendix: CETA Mental Health Safety Plan

### PROCEDURES

#### Assessing for SUICIDE

All CETA providers must follow these steps when there is concern that the client has intentions or plans of killing him or herself. When assessing for suicidality risk levels, the CETA provider should ask the client the following questions:

1. “Do you plan or intend to hurt yourself in any accident either actively or passively?”
2. “Do you think that you would be better off dead or wish you were dead?”
3. “Do you think about hurting or injuring yourself or have mental images of harming yourself with at least some intent or awareness that you might die as a result?”
4. “Have you ever tried killing yourself?”

When the CETA provider asks Question 3,

- S/he tries to find out if the client has access to any means and tools to carry out the suicide act (E.g. medicine, a gun, rope, knife, poisonous chemicals). It is very important to know if a client who is thinking about suicide has immediate access to a way to commit suicide

When the CETA provider asks Question 4,

- S/he tries to find out if the client has ever tried killing themselves before; this indicates the highest suicidality risk. (Treat this client as an emergency) The CETA provider will ensure to purposely ask these questions in a direct way (use local language where appropriate) because suicide is a very serious, sometimes life/death situation

The CETA provider will then develop a safety plan if the client responds with a “yes” to any of the Four (4) questions.

If the client responds “yes” to ANY OF THE FOUR (4) QUESTIONS, the CETA provider should call one of the clinical supervisors while the client is still with them. The CETA provider should remind the client of the limits of confidentiality and tell them that you need to call your supervisor to help keep them safe.

- The CETA provider should talk with the supervisor about what the client reported and the specific safety concerns about this client AND go over the safety plan that was developed with the client.
- The CETA provider will check with the supervisor if there is anything else that needs to be added to the safety plan or done to keep the client safe?

- The CETA provider will also check if there is anything else that needs to be followed up on with the client quickly (before the next session or contact?)
- If it is recommended the suicidality risk-level is too high, the CETA provider may need to take the client to Clinical Officer Psychiatry at Mental Health and Psychiatry Unit

### **DEVELOPING A SAFETY PLAN FOR SUICIDE**

- The CETA provider will talk to the client about what s/he intends to do with the client (that is develop a safety plan for them)
- The CETA provider will normalize the clients feeling by saying “many people have thoughts of killing themselves”
- The CETA provider will then tell the client that there are many things that can be done to help the client feel better and also help the client stay safe.
- The CETA provider will then tell the client why it is important that they keep him or her safe. The CETA provider will explain to the client that the treatment the client is undergoing has helped many people with their feelings of sadness, anxiety, and wish to die

Possible step by step actions that the CETA providers can take:

#### 1. Telling a trusted family member

- The CETA provider will try to involve a family member or friend that the client trusts (such as parents, adult sibling, or another adult family member). This will ensure that another person knows the safety concerns of the client and also how to help the client stay safe
- The CETA provider will ensure the family member or friend being contacted or being called in the session is one the client trusts (and not a person who is hurting the client)
- The CETA provider should ensure that s/he meets with the client and the family member or friend that day or the next day as part of follow up. This is to develop a plan and safety support for the client

#### 2. With the client identify warning signs:

- The CETA provider should ask the client the following questions:
- What are some of the signs you have that trigger thoughts of killing yourself?
- How do you feel?
- What do you do?
- What are you thinking?
- What are the situations when you are most likely to think about killing yourself?

### 3. Help the client use their skills

- The CETA provider will encourage the client to use their skills, which could be things they already do and/or new things they have learned from counselling sessions
- The CETA provider will then ask the client the following questions:
  - i. When you start thinking or feeling or doing these things that trigger thoughts of suicide
  - ii. What are some of the things you do or think to help decrease the thoughts about wanting to die?
  - iii. Are there people you talk to or activities that you do to lessen the thoughts or distract yourself from the thoughts?
  - iv. Among these people you have mentioned or activities you have mentioned, which of these can you do more of or keep doing?
- The CETA provider should talk to the client about the skills s/he has learned in this or other programs they may have participated in. For example, CETA provider can ask the client “Are there things you have done in the past when you have felt this way that have helped you feel better?”
- The CETA provider shall make a list or review the skills the client has and can use to prevent or reduce the impact of suicidal thoughts. The CETA provider will thereafter ask the client the following questions:
  - “How will you know when the safety plan that we will develop should be used?”
  - “What can you do, on your own, if you [become suicidal again/ have urge to drink/hurt yourself, to help yourself not to act on thoughts or urges?”
  - “How likely is it that you would be able to do some of these things during a time of crisis?”
- If the client expresses doubt about use, ask “What might get in the way of you thinking of these activities or doing them if you think of them?”

### 4. Develop a contract for safety

- The CETA provider will develop a note together with the client that states that the client promises or gives their word that they will keep themselves safe and will not kill themselves for a short period of time (e.g. 24 hours). If they do feel like or think about killing themselves, the note will contain specific instructions of who to call or where they can go to stay safe

- “We want to make sure you are safe. I know this might be hard. Can you give me your word that you will keep yourself safe for a short period of time – just over the next day?”
5. Develop a safety watch
- If the client has someone, they are around often who is willing to help, the CETA provider can ask this person to “watch” the client. It is arranged that the client is never by him/herself, but is always surrounded by at least one family member or friend
  - This is set up for short periods of time (a few days)
  - “We want to help you keep yourself safe. Many times, we use family members to do this. Can you help me think of who in your family can be around you?”
  - “Can we work together to bring these family members in to agree to help be with you so that you stay safe?”

### **Plan for follow up**

- A plan for more frequent visits and/or follow ups should be put into place if a client expresses suicidal thoughts with a plan or there is real concern that the client will be unable to keep the contract for safety. This can take the form of brief check-ins over the phone or at the office. If a family member or friend whom the client trusts is identified, this adult can be included in these follow up visits and contacts
- Follow ups should take place more frequently right after the disclosure of suicidal thoughts (Three times a day for 3 days) and then slowly fade out as the concern for safety decreases

### **Assessing Risk of HOMICIDE/THREATENING VIOLENCE**

The CETA provider should ask the following questions:

- i. Have you ever tried to end someone’s life or hurt someone before?
- ii. Are you thinking of ending someone’s life or hurting someone?
- iii. Do you have a plan to end someone’s life or hurting that person?
- iv. Do you have access to that person? How do you intend to execute your plan?

If a client answers “YES” to any of the four (4) questions, immediately inform the clinical supervisors. The CETA provider will follow the steps below:

1. The CETA provider and the client will agree together that if the client has thoughts of killing anyone, the client will speak to the CETA provider personally before carrying out any plans to harm anyone.
  - a. The CETA provider will ask the client if s/he will be able to speak with the CETA provider if/when s/he has such thoughts

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2. If the client says "no" or "I don't know," to the questions 3 and 4, the CETA provider will ask the client the following questions:
  - a. The CETA provider will rephrase what the client is saying for example
  - b. "What I am hearing is that you are in a lot of pain right now and thinking of ending someone's life, so I want you to come with me right now to get some help to make you feel better. I will make sure you get there safely. Is there a family member or someone I can call to go with you?"
3. The CETA provider will arrange for the person to be accompanied to a Safe place, and will call her/his supervisor ahead to advise the supervisor of the situation
4. If the client refuses, the CETA provider will ask the client to wait at the location while the CETA provider calls the supervisor in another room to report that the person has threatened homicide/violence. The CETA provider will ask the supervisor what to do next. If the client has strong conviction of hurting or killing someone, the CETA provider should immediately notify the police officer on duty at the hospital police post

### **Assessing Risk of DOMESTIC VIOLENCE:**

To assess risk, the CETA provider will follow the study safety protocol and clearly ask the following three questions:

1. Is the perpetrator of domestic violence living with you?
2. In what ways has this person hurt you?
3. In what ways do you think this person could hurt you?

The CETA provider will talk to her/his supervisor while the client is still working with them.

The CETA provider and the client will decide or agree on a plan BEFORE the client leaves the session.

The CETA provider will work with the client and supervisor to develop an action plan. The action plan will follow the guidelines of the Zambian Anti-Gender Based Violence Act of 2011 which states:

“A police officer, labour inspector, social worker, counsellor, medical practitioner, legal practitioner, nurse, religious leader, traditional leader, teacher, employer or other person or institution with information concerning the commission of an act of gender based violence shall—

- a. inform a victim of the victim's rights and any basic support which may be available to assist the victim;
- b. obtain for the victim, or advise the victim how to obtain shelter, medical treatment, legal services, counselling or other service that may be required in the circumstances;

- c. advise the victim of the victim’s right to lodge a complaint against the respondent including remedies available to the victim under this Act.”

All CETA providers will provide adult victims of domestic violence with

- i. a copy of the full Zambian Anti-Gender Based Violence Act
- ii. a resource list that includes local the hospital police post, shelters, legal, medical and counselling services and contact information for other services that may be needed
- iii. assistance in reporting or lodging complaints against the perpetrator at the victim’s request

Find below a checklist to help review what the CETA provider must attend to. The action plan could include the following checklist:

- Has the CETA provider reported the incident to the child protection officer?
- Has the CETA provider reported the incident to the hospital police post?
- Has CETA provider notified the supervisor?
- Has CETA provider developed a safety plan with the client?

The child protection officer will have to report to the Child Protection Unit at the Ministry of Gender and Child Development. If necessary, the Child Protection officers will assist in getting the child to a temporary safe placement home until investigations are concluded.

**Assessing Risk for CHILD SEXUAL OR PHYSICAL ABUSE:**

To assess risk, the CETA provider should clearly ask the following four questions:

1. Is the abuse currently happening (i.e. within the past Two weeks or month)?
2. Do you know the person who is abusing you?
3. Does the abuser stay in the same house with you?
4. Is the abuser related to you?
5. Have you reported the abuse to anybody?
6. If you have reported the abuse, what has been done?

If the client answers “YES” to the first three questions, immediately the Ministry of Gender and Child Development on 09..... The CETA provider shall ensure to call their supervisor at the end of the session.

If the client says no to the first questions, ask for more information. For example:

- When was the last time the abuse happened?
- Where is the person who was abusing you currently staying?
- Does anyone in the home know about the abuse?





If you are not certain if this case should be reported to the Child Protection Unit please contact your clinical supervisors who will instruct you on who to contact (you may also need to contact the Social Welfare Office in cases where there is a question about reporting). Below are certain things to do during the session.

In addition to formulating a safety plan, use the following checklist to review what has been done:

- Have you informed your supervisor?
- Did you inform the child protection officer?
- Has the child protection officer reported to the Child Protection Unit under CDMCH who will get the child to safe temporary placement home until investigations are concluded? If child's life is proven to be in danger, we will work with CPU and the hospital police post in hopes of arresting and prosecuting the perpetrator. We will also follow up with CPU and the family to ensure the child remains in a safe environment
- If the Child Protection Officer doesn't succeed in getting in touch with the Child Protection Unit, the CETA provider will notify their supervisor who will get in touch with YWCA Project Coordinator for Abused children