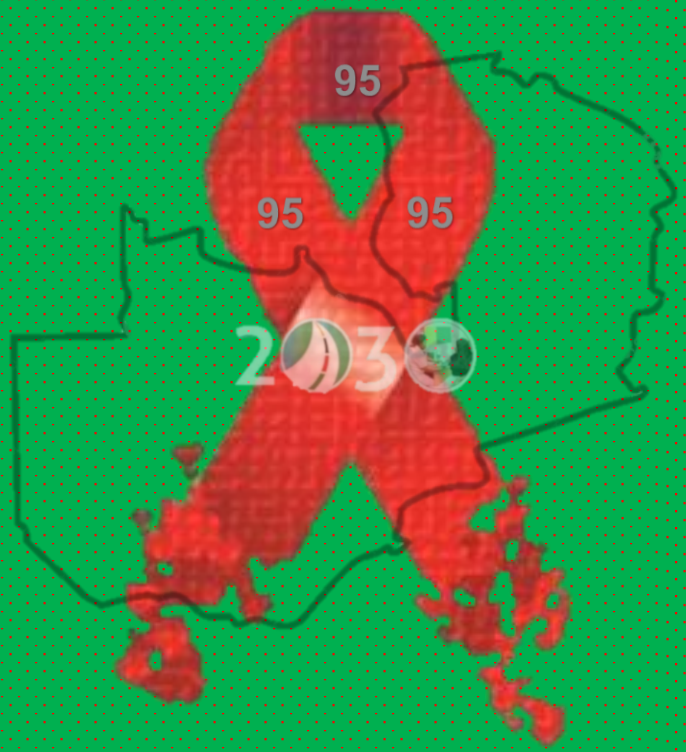
ZAMBIA CONSOLIDATED GUIDELINES

for Treatment and Prevention of HIV Infection



2022

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Republic of Zambia
Ministry of Health

Zambia Consolidated Guidelines

for Treatment and Prevention of HIV Infection

ZCGs May 2022 Version

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACRONYMS

3TC	Lamivudine
ABC	Abacavir
AIDS	Acquired Immunodeficiency Syndrome
ALT	Alanine Aminotransferase
AFB	Acid Fast Bacilli
ANC	Antenatal Care
ART	Antiretroviral Therapy
ARV	Antiretroviral
AST	Aspartate Aminotransferase
ATC	Advanced Treatment Centre
ATT	Anti-Tuberculosis Treatment
ATV	Atazanavir
AZT	Azidothymidine (Also Known as Zidovudine, or ZDV)
Bdq	Bedaquiline
BD	Twice Daily
BMI	Body Mass Index
ART	Antiretroviral Therapy
CD4	T-Lymphocyte Bearing CD4 Receptor
CD4 %	CD4 Percentage
CDC	Centers for Disease Control and Prevention
Cfz	Clofazimine
CNS	Central Nervous System
CPT	Co-trimoxazole Preventive Therapy
Cm	Capreomycin
CRAG	Cryptococcal Antigen
CrCl	Creatinine Clearance
CTX	Co-trimoxazole
Cs	Cycloserine
CSF	Cerebrospinal Fluid
d4T	Stavudine
DBS	Dried Blood Spot
Dlm	Delamanid
DMPA	Depot Medroxyprogesterone Acetate
DNA	Deoxyribonucleic Acid
DOTS	Directly Observed Therapy, Short Course
DRS	Drug Resistance Surveillance
DR TB	Drug Resistant Tuberculosis
H	Isoniazid
H^{HD}	Isoniazid High Dose
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HTS	HIV Testing Services
Km	Kanamycin
Lfx	Levofloxacin
INH	Isoniazid
INSTIs	Integrase Strand Transfer Inhibitors
IPT	Isoniazid Preventive Therapy
IRIS	Immune Reconstitution Inflammatory Syndrome
L&D	Labour and Delivery
LEEP	Loop Electrosurgical Excision Procedure
LPV	Lopinavir
MDR TB	Multidrug – Resistant Tuberculosis
MNCH	Maternal, Newborn, and Child Health
MOH	Ministry of Health
MTCT	Mother-to-Child Transmission (of HIV)
NAT	Nucleic Acid Test
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NUPN	National Unique Patient Number
NVP	Nevirapine
OD	Once Daily
OI	Opportunistic Infection
Ofx	Ofloxacin
PAS	Para – Aminosalicyclic Acid
PCP	Pneumocystis Pneumonia
PCR	Polymerase Chain Reaction
PEP	Post-Exposure Prophylaxis
PHDP	Positive Health Dignity and Prevention
PI	Protease Inhibitor
PLHIV	People Living With HIV
PO	Per os (Orally)
PNC	Postnatal Care
PrEP	Pre-Exposure Prophylaxis
QI	Quality Improvement

DRV	Darunavir
DST	Drug Susceptibility Testing
DTG	Dolutegravir
E	Ethambutol
EFV	Efavirenz
EHR	Electronic Health Record
EMTCT	Elimination of Mother-to-Child Transmission (of HIV)
EPI	Expanded Program for Immunization
ETR	Etravirine
ETV	Entecavir
FDC	Fixed-Dose Combination
FP	Family Planning
FTC	Emtricitabine
GRZ	Government of Republic of Zambia
Hb	Haemoglobin
HBeAg	Hepatitis B E-Antigen
HBsAg	Hepatitis B Virus Surface Antigen
HBV	Hepatitis B Virus
HCW	Health care Worker
FQ	Fluoroquinolone
R	Rifampicin
RR	Rifampicin Resistance
RoC	Recipient of Care
-r	Ritonavir (Low-Dose)
RNA	Ribonucleic Acid
R	Rifampicin
RAL	Raltegravir
sd-NVP	Single-Dose Nevirapine
TAF	Tenofovir alafenamide
FBC	Full Blood Count
TAT	Toxoplasmosis Antigen Test
TB	Tuberculosis
TDF	Tenofovir Disoproxil Fumarate
UNAIDS	Joint United Nations Programme on HIV/ AIDS
UNICEF	United Nations Children's Fund
VIA	Visual Inspection with Acetic Acid
XDR - TB	Extensively Drug – Resistant Tuberculosis
XTC	Lamivudine or Emtricitabine
FTC	Emtricitabine
Z	Pyrazinamide

FOREWORD

Zambia has been making remarkable progress in tackling the HIV epidemic. With more than 1,190,000 People Living with HIV on Antiretroviral therapy, we continue to improve in implementing strategies and interventions that are inclusive and leave no one behind. The END AIDS by 2030 target have ensured that the AIDS response is comprehensive and targets all underserved populations.

Despite this, each year, over 40,000 people are newly infected with HIV and the reduction of new HIV infections in the past 10 years has been slow. At this point in the HIV response, it is imperative that we accelerate our efforts in closing the tap of new HIV infections whilst sustaining the achieved goals. Preventing new HIV infections is central to ending the AIDS epidemic and eliminating HIV in the Zambian population.

It is along these lines that the 2022 ZAMBIA CONSOLIDATED GUIDELINES for Treatment and Prevention of HIV Infection have been formulated. These guidelines will foster efforts to reduce new HIV infections and HIV related deaths in Zambia. The interventions and clinical practice being steered by these guidelines will propel Zambia to HIV Epidemic Control. National efforts will focus on prevention and treatment interventions that are beneficial to the public at large, cost efficient and provide the most efficacious solutions.

The Zambian Government through Ministry of Health and its partners will work hard to provide all necessary commodities, drugs, laboratory consumables and reagents that will guarantee patients the highest quality of care at all levels of health provision. In addition, we will support implementation of differentiated service delivery in order to ensure retention of patients on ART. Other models of care with established benefits will be taken to scale in all applicable communities.

The Ministry of Health will continue to adopt better tolerated regimens which will make it easier for all populations including children to remain on ART and have better outcomes. TafED is one such combination suitable for children, elderly patients and patients with renal insufficiency. The 2022 guidelines have better clarified the use of newer ARVs in children and prevention of HIV acquisition. More Zambians will now be able to access these drugs in the prevention of HIV. Health care providers are extremely encouraged to promote the prevention of infections and promote non-discriminatory care to Zambians.

These guidelines will continue to be a reference on the best clinical practices in the prevention, treatment and management of HIV infection in Zambia. All communities are urged to know their HIV epidemic and to own the program responses. Health facility staff and community health workers must synergize efforts and meet patient expectations.

Hon. Sylvia T. Masebo, MP
MINISTER OF HEALTH

ACKNOWLEDGEMENTS

The Ministry of Health is proud to update the Zambia Consolidated Guidelines for Treatment and Prevention of HIV to ensure that our recipients of care have access to the latest and quality HIV care. We have employed a multi-disciplinary approach involving a wide range of stakeholders in the updating process of these guidelines. This is not only to safeguard our recipients of care but also to ensure that these guidelines are sound in all aspects including the technical, ethical, social and health systems domains. 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. These include but not limited to:

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INTRODUCTION

In July 2021, the World Health Organization released the updated Consolidated Guidelines for HIV prevention, testing, treatment, service delivery and monitoring. In the same line, Zambia through the Ministry of Health has updated its Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection. This version of the Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection provides simplified guidance on the country's transition plan, the continued approach that positively affects the continuum of HIV care, while adding to innovative methods that will reduce transmission rates and increase life span for those on treatment. This is all to further accelerate efforts to meet the ambitious END AIDS by 2030 target through achieving the 95-95-95 targets, thereby achieving major reductions in the number of newly HIV infected people and the number of people dying from HIV-related causes.

Besides the recommendation to provide lifelong antiretroviral therapy to all HIV infected populations regardless of CD4 cell count and WHO clinical staging, these guidelines present several recommendations, including Universal routine HIV Testing, counselling, and treatment in all public and private health facilities in Zambia. This approach gives a window to provide prioritized HIV testing and immediate treatment and care to all of those at substantial risk of HIV acquisition and those who never had an HIV test done recently. Furthermore, newly diagnosed HIV positive individuals will have their sample tested for HIV recency to determine whether they were recently infected or have long-term HIV infection. This will accelerate our strides towards achieving HIV epidemic control. Additionally, these guidelines provide the use of better and safer antiretroviral agents such as Darunavir-ritonavir (DRV-r) dosed as 800mg/100mg as part of Second-Line HIV treatment whilst emphasizing the use of newer agents like Dolutegravir (DTG) for all populations including children. The guidelines also emphasize and transitioning of recipients of care to DTG-based regimen WITHOUT a need for a viral load test. The legacy Efavirenz-400mg (EFV) based regimens are no longer preferred in these guidelines in view of the high resistance rate in Zambia.

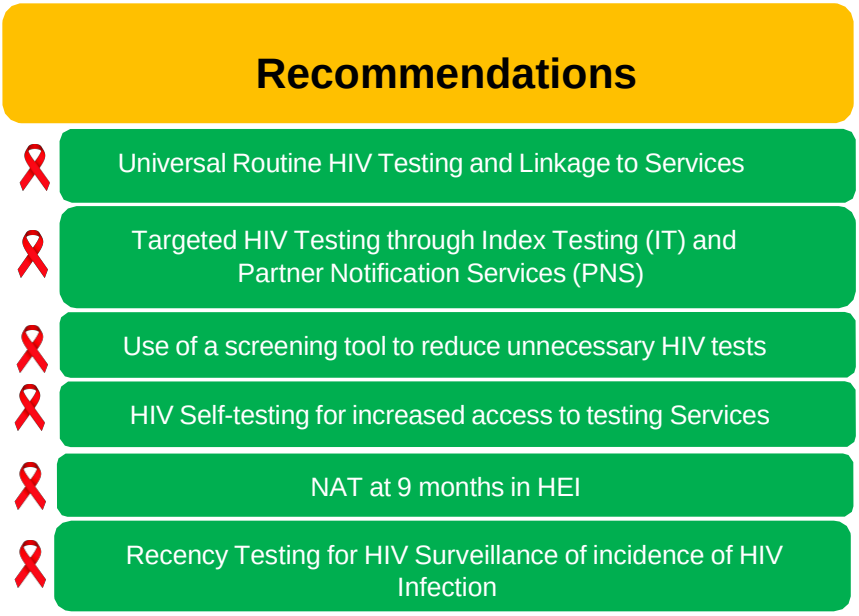
Our 2022 Consolidated Guidelines have also adopted the use of Dolutegravir for children aged 4 weeks and above and weighing 3kg and above 3kg. A fixed dose combination of Tenofovir alafenamide, Emtricitabine and Dolutegravir (TafED) is recommended to treat HIV positive children aged 6 years and above and weighing 25kg or more. To manage our patients better, these guidelines also recommend resistance testing in those with unsuppressed viral load after Enhanced Adherence Counselling (EAC) in those failing PIs and DTG-based regimen and the use of baseline viral load testing. Separate sections of COVID-19 and HIV, Sexually Transmitted Infections (STIs) and HIV and migrant populations have been included.

Importantly, these guidelines also highlight the management of patients failing Second-Line ART, who should be managed at higher-level health facilities called Advanced Treatment Centres (ATCs). All the recommendations have been adopted because of their anticipated public health impact.

Several significant recommendations from the previous guidelines remain a priority, namely providing lifelong ART regardless of CD4 cell count and WHO clinical staging, to all populations, and viral load testing as the preferred means of monitoring people on ART. Newer developments aim to complement and improve the service delivery of HIV services to our population. Importantly, the guidelines emphasize the need for differentiated approaches to care for people who are on ART, such as reducing the frequency of clinic visits and community ART distribution. Deliberate efforts to include the UNAIDS identified 12 populations that have been left behind in the HIV response including: People Living with HIV, adolescent girls and young women, prisoners, migrants, people who inject drugs, sex workers, gay men and other men who have sex with men, transgender people, children, and pregnant women living with HIV, displaced persons, persons with disabilities, migrants and people aged 50 years and older. Such efficiencies are essential for countries like Zambia with a high burden of HIV infection are to manage their growing numbers of people receiving ART and reduce the burden on people receiving treatment and on health facilities.

There will be continued concerted efforts required toward implementing these guidelines at district and health facility levels. The 2022 Zambia Consolidated Guidelines on HIV are an important step in supporting the goals of universal access to ARV drugs for preventing and treating HIV, and ultimately ending the HIV epidemic as a major public health threat by 2030.

HIV TESTING SERVICES



HIV testing services include the full range of services that should be provided together with HIV testing which include counselling (pre-test information and post-test counselling); linkage to appropriate HIV prevention, treatment and care services, and other clinical and support services; and coordination with laboratory services to support quality assurance and the delivery of correct results.

HTS is primarily conducted by trained and certified healthcare workers as well as supervised lay providers that can conduct safe and effective HIV testing using recommended test kits. HTS begins with assessing the risk of HIV infection using the HIV screening tool.

HTS should be done at all health service delivery points (see Table 1) within the facility, as well as in the community, as an efficient and effective way to identify people living with HIV (PLHIV), including the priority and key populations. Facility based HTS will largely focus on PITC using the HIV Screening Tool (for those 15 years and above) at all Service Delivery Points. Community-based testing largely centred on hotspot testing, social network, and Index testing. Hotspot testing is targeted at specific populations or places sharing similar characteristics putting them at risk of HIV acquisition or known to have high yields of HIV positive tests. Mapping of hotspots is based on trends in specific areas and could change (there is need to revisit such mapping every 6 months or as need arises).

HIV Repeat and Re-testing

Repeat Testing – Refers to a situation where additional testing is performed for an individual immediately after a first test during the same testing visit due to inconclusive or discordant results. This may include a repeat testing using Determine-Bioline algorithm if client reports positive HIV Self-Test (HIV-ST) or repeat HIV testing if HIV test result is indeterminate or discordant.

The same assays are used and, where possible, the same specimen.

Re-testing – Refers to a situation where additional testing is performed for an individual after a defined period of time for explicit reasons, such as a specific incident of possible HIV exposure within the past three months, or on-going risk of HIV exposure such as HIV negative persons with HIV-positive partner, sharing injecting equipment or having sex with a person of unknown status, or indeed re-test if on PrEP.

Re-testing is always performed on a new specimen and may or may not use the same assays (tests) as the one at the initial test visit.

UNIVERSAL ROUTINE HIV TESTING

Universal Routine HIV Testing Services is a policy statement by the Zambian Government that directs all health facilities, including public and private health facilities (Universal) to offer HTS whenever health services are provided (Routine). It is an opportunity to screen all clients to determine their HIV risk using the HIV Screening tool (for those aged 15 years and above) and provide immediate treatment and care to all HIV infected individuals through the "test and treat" strategy. Conversely, clients who test negative for HIV are linked to combination HIV prevention services.

Healthcare workers are therefore required to offer HTS to all individuals presenting to health facilities through the various entry points such as inpatient and outpatient departments, Children's malnutrition units, STI clinics, TB clinics, maternal and child health, community services and others. HTS should also be offered to the caregivers and other family members of people living with HIV (PLHIV). Universal routine HIV testing services should be offered with the following considerations:

1. Provide information in a confidential manner - those who opt out should continue to be counselled and offered an HIV test at each interaction with healthcare providers, including the opportunity to self-test.
2. Administer the HIV Screening tool (for individuals aged 15 years and above) to determine eligibility for an HIV test
3. If eligible, provide counselling on the benefits of HIV testing and other services available for HIV negative and positive individuals
4. Provide correct results following the HIV testing algorithms
5. Elicit contacts (sexual, biological children, and needle sharing partners) for index testing purposes from HIV positive individuals
6. Provide linkage to preventive, treatment and care services by issuance of a National Unique Patient Identification Number (NUPIN), regardless of the test result

National HIV Testing Screening Approaches

The National HIV testing Screening Tools are algorithms with a set of questions that help to prevent unnecessary retesting for HIV to avoid wastage of HIV test kits. The Screening Tools must exclude all individuals known to be HIV positive from HIV testing. Repeat testing in HIV clients should only be considered when there is need to verify an HIV-positive diagnosis. Further, repeat testing could also be done if there is no reliable record of previous HTS results or the client has had a recent exposure to HIV. Silent transfer patients (are positive patients that do not present as known positives at another facility) should be screened and identified to receive appropriate services. Additionally, screening tools may in selected populations, also identify individuals at high risk of being HIV infected and subsequently will need to have an HIV test done. The following are the elements of an HIV test screening tool in various populations.

Elements of an HIV Screening Tool for Adults and Key Populations

1. Determining Testing History: All Known HIV positive individuals should not have a repeat HIV test but must be linked to care and advised to be adherent to treatment and ensure they are virologically suppressed. All Key populations (individuals with high-risk of HIV acquisition) must have an HIV test every 3 months and all other sexually active individuals must have an HIV test every 12 months
2. The screening tool should also screen for silent transfer clients. This is referred to as screening for known positives.
3. Screening for symptoms suggestive of HIV
4. Screening for high-risk HIV exposure: Screening for HIV symptoms and its associated illnesses as well as STIs, and a screening for recent HIV exposure either sexually or through body fluid contacts must be used to determine who will need an HIV test. ALL individuals with symptoms suggestive of HIV or recent probable exposure to HIV must be tested for HIV
5. ALL pregnant and breastfeeding women must receive an HIV test every 3 months regardless of risk or exposure

Elements of an HIV Screening Tool for Children

1. Testing History: All known HIV positive children should NOT be tested for HIV again
2. HIV negative children with a documented result with no known HIV risk should NOT have an HIV test done
3. The screening tool should also screen for silent transfer clients. This is referred to as screening for known positives
4. All children will be eligible for HIV testing if they have never had HIV test before and have risk for HIV acquisition
5. Risk for HIV in children include children whose biological mother is HIV-positive, HIV status unknown both Parents are deceased, or has history of sexual assault or exposure to HIV infected body fluids
6. Screening for symptoms suggestive of HIV should not be used to withhold testing of a child who is eligible for testing
7. An age-appropriate HIV test must be done for children

A Clinician can override the HIV Screening Tool based on clinical presentation of the patient

HIV SELF-TESTING (HIV-ST)

HIV-ST is a process in which a person collects their own oral fluid or blood and then performs an HIV rapid test and interprets the result - often in a private setting either alone or with someone he or she trusts. It is targeted particularly among populations at ongoing high risk of HIV acquisition, who may be less likely to access testing or test less frequently, e.g., men, adolescents, Key Populations and sero-discordant couples. The test can be Assisted or Unassisted HIV-ST.

Assisted HIV-ST refers to trained providers or peers, giving individuals a personal demonstration before or during HIV-ST on how to perform the test and interpret the results.
Unassisted HIV-ST refers to when individuals test themselves for HIV and only use an HIV-ST kit with manufacturer-provided instructions for use.

An HIV self-test is a screening test, which requires further testing and confirmation for any reactive result. Healthcare providers should ensure that users receive clear information on:

1. How to perform the test and interpret the result correctly
2. Where to access HTS and further support services
3. How to safely dispose of the used test-kits
4. The ethical and legal obligations (no one should test a third party without their consent)

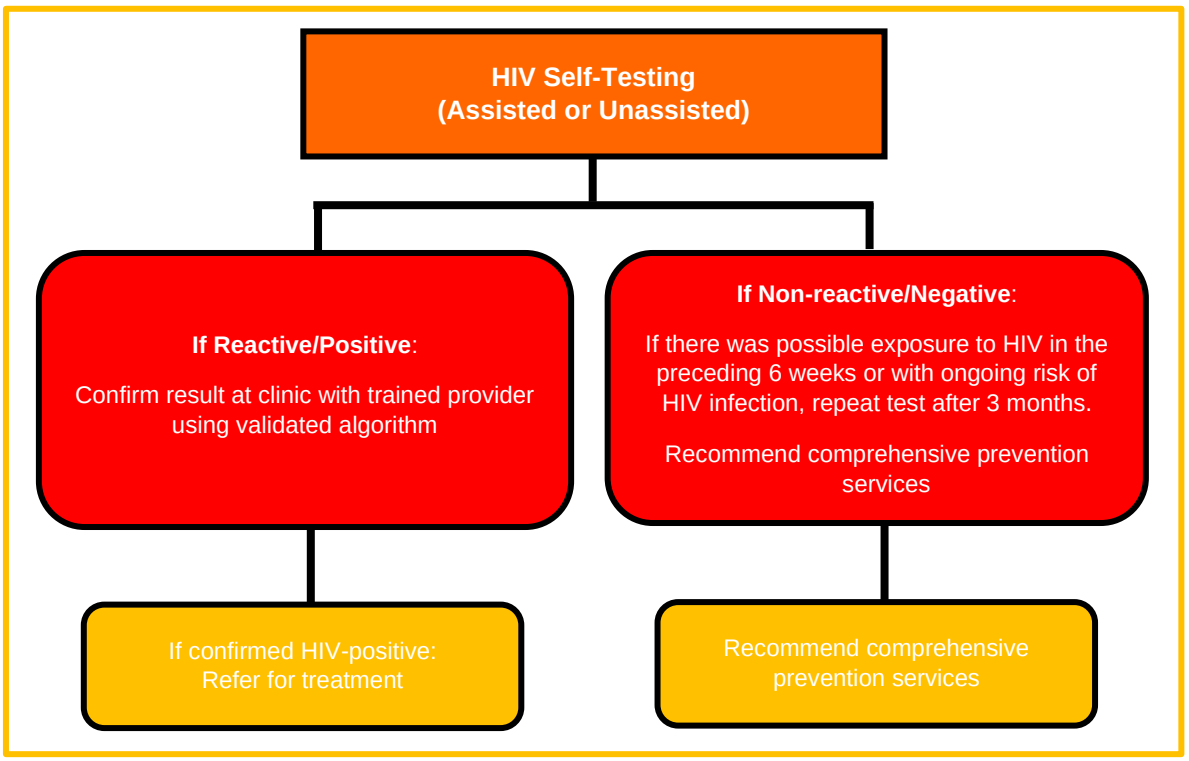
HIV-ST is not to be used as a pre-entry to a Determine test. It should not be used as a screening test either in the community or at the facility for the purpose of either to increase the positive tests yields or to identify those who require a Determine test. Healthcare providers should never use the self-test as a replacement for the Determine test when not available.

The use of HIV-ST in known HIV Positive individuals is not recommended.

Monitoring and Programming of HIV Self-Test

The monitoring of the effectiveness of the self-testing program is by assessing the number of HIV Self-Test kits that have been distributed to the individuals since the HIV Self-Test is meant to be an opportunity for individuals to know their HIV status

FIGURE 1: HIV SELF-TESTING ALGORITHM



Index Testing and Partner Notification Services

Index Testing is a focused HTS approach in which contacts (sexual networks, needle sharing partners and biological children of WLHIV, less than 19 years of age) who have been exposed to HIV infection are offered HIV Testing. An index client is identified as a newly diagnosed HIV positive client or a PLWHIV who has been identified. Contacts are elicited from the index client who could be a sexual partner, biological children from the female index clients and needle or blade sharing individuals.

The process starts with the Index clients sharing information on their partners, and if the client is female, all biological children under the age of 19 years. Contacts are then followed up and informed of their HIV exposure and offered HIV testing services. Those who test positive are immediately linked to care and they become new Index clients who will in turn give information on their sexual partners. If female, biological children under the age of 19 years, needle or blade sharing partners are elicited and the process starts all over again.

All HIV testing in this setting is done using a serological test, also known as antibody test, and HIV negative clients are offered a re-test after 3 months to account for the window period. Beyond the window period, they should be offered the test according to National HTS Guidelines.

HIV Partner Notification Services (PNS)

HIV Partner Notification is a voluntary process where trained healthcare providers (including lay providers) ask index clients (people diagnosed with HIV) about their sexual or drug injecting partners. With their consent, HIV testing is offered to these partners who may have been exposed to HIV preferably within the past 12 months.

Partner notification is provided using passive or assisted approaches. (It is recommended to use the best approach for each index client at that time).

Passive HIV Partner Notification Services is where HIV-positive clients are encouraged by healthcare workers to disclose their status to their sexual/drug injecting partners by themselves, and to suggest HTS to the partner(s) given their potential exposure to HIV infection. Being at the discretion of the index client to encourage their contacts to test, this approach is less effective.

Assisted HIV Partner Notification Services is where consenting HIV-positive clients are assisted by healthcare providers to disclose their status or to anonymously notify their sexual/drug injecting partner(s) of their potential exposure to HIV infection. The provider then offers testing to these partner(s).

Assisted partner notification is done using provider contract or dual referral approaches.

Provider Contract Referral is where HIV-positive clients enter into a contract with a trained provider and agree to disclose their status (and the potential HIV exposure to their partners) by themselves and to refer their partner(s) to HTS within 14 days. If the partner(s) of the HIV-positive individual do not access HTS or contact the healthcare provider within the two weeks, then the trained provider will contact the partner(s) directly and offer voluntary HTS.

Provider Referral is when the healthcare provider confidentially contacts the person's partner(s) directly and offers the partner(s) voluntary HTS.

Dual Referral is when a healthcare provider accompanies and provides support to HIV-positive clients when they disclose their status and the potential exposure to HIV infection to their partner(s). The trained provider also offers HTS to the partner(s).

In partner and family-based index testing, it is important to ensure that sexual partners and children under the age of 19 years are also offered an opportunity to test for HIV.

Assessment for Intimate Partner Violence (IPV) should be conducted during index testing and PMTCT/ART visits to avert Gender Based Violence. Where it occurs, it should be properly documented in the appropriate data collecting tools and survivor referred to appropriate services.

Family-based Index Testing is where a female index client is educated on the importance of having her biological children less than 19 years of age with unknown status tested for HIV. Just as in Partner Notification, family-based index testing uses approaches that will benefit the client. Some of these options include:

Contract Referral is where a female index client agrees with the healthcare provider within a specified time (14 days) to bring her biological children with unknown status to be tested for HIV. If the female index client does not bring the children to the facility within the agreed time frame, the healthcare provider will then follow her and offer HIV testing at the community and refer any positive child to the facility for ART initiation.

Community-based is where a healthcare provider visits the female index client and her biological children at home and provide HIV testing to children with an unknown HIV status.

Facility-based is where the index client agrees to bring her children to the health facility for HIV testing.

In partner and family-based index testing, it is critically important to ensure that sexual partners and children under the age of 15 years are also offered an opportunity to test for HIV.

How to assess for Intimate Partner Violence (IPV)

Assessment for IPV should be conducted during index testing and PMTCT/ART visits to avert Gender-Based Violence. Where it occurs, it should be properly documented in the appropriate data collecting tools and survivors referred to appropriate services.

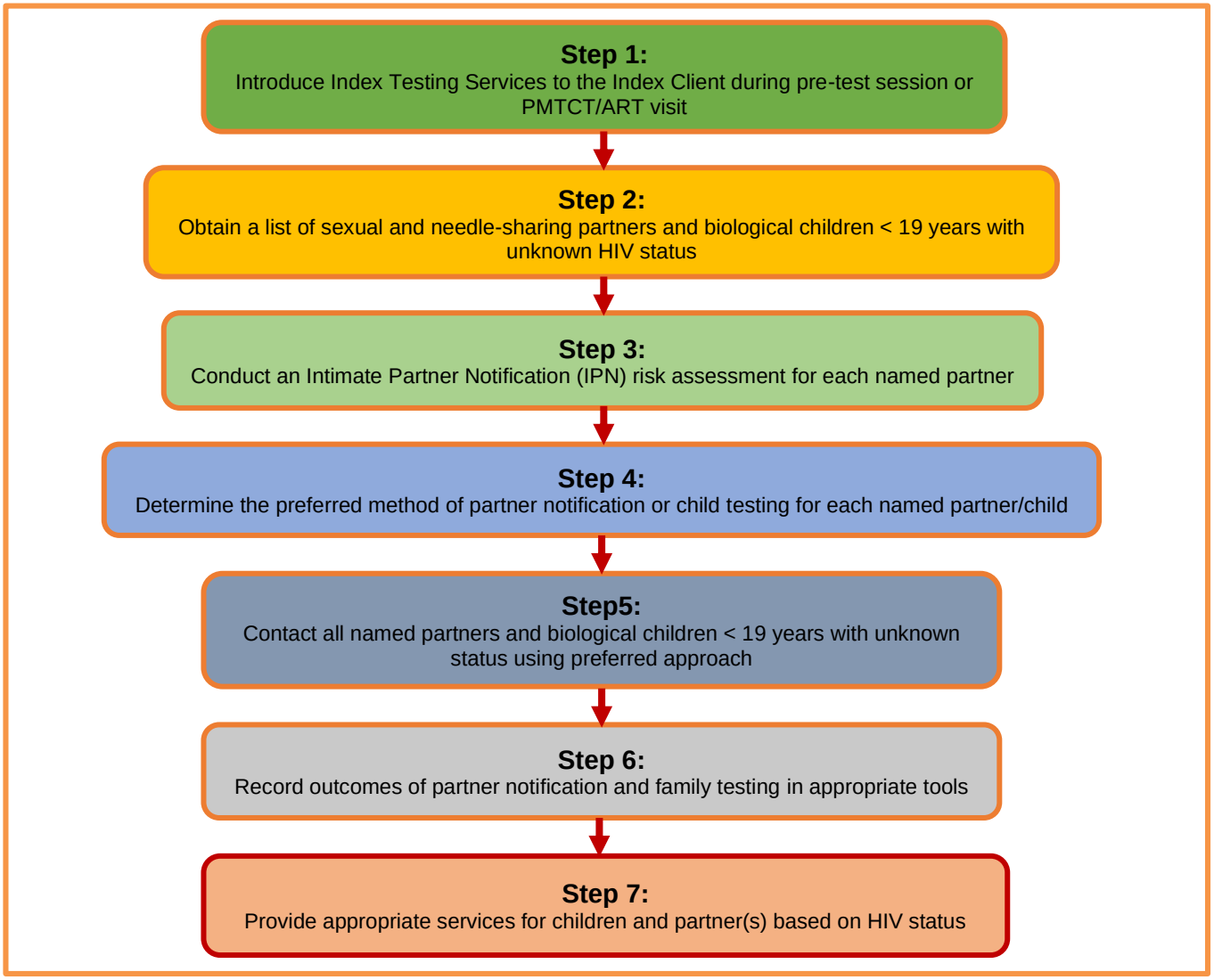
Healthcare providers are ethically mandated to do no harm. To protect the safety of the index client, partners who pose a risk of Intimate Partner Violence (IPV) may need to be excluded from Partner Notification Services.

Each named partner should be screened for IPV using the 3 screening questions which include:

1. Has [partner's name] ever hit, kicked, slapped, or otherwise physically hurt you?
2. Has [partner's name] ever threatened to hurt you?
3. Has [partner's name] ever forced you to do something sexually that made you feel uncomfortable?

Index Testing should not be done for that contact if a client answers YES to any of the above questions

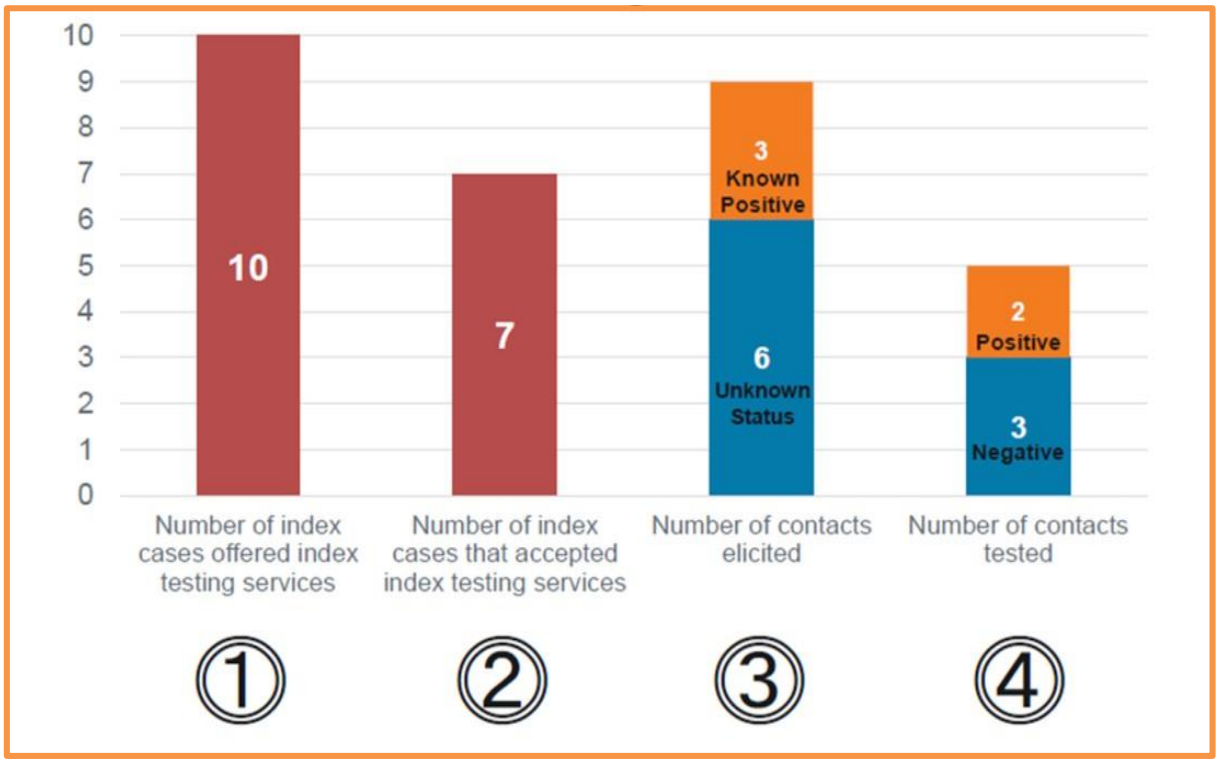
FIGURE 2: INDEX TESTING AND PARTNER NOTIFICATION



Monitoring and Programming of Index Testing

The Index Testing Cascade is used to monitor the extent (scalability) and quality (fidelity) of the implementation of Index Testing. Figure 3 below shows the Index Testing Cascade:

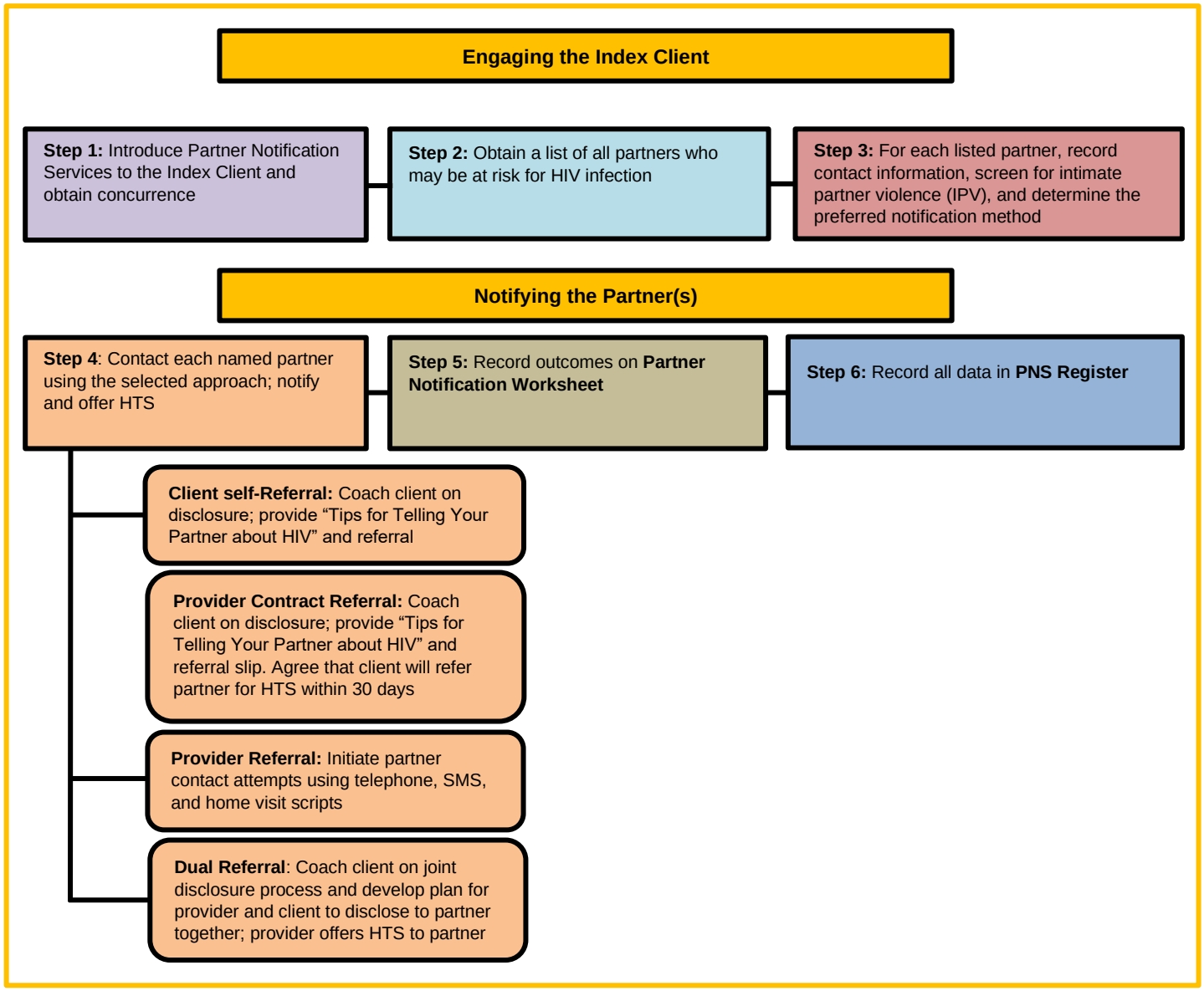
FIGURE 3: INDEX TESTING CASCADE



The following indicators could be measured from the Index Testing Cascade:

- Number of index clients offered index testing services
- Number of index clients who accept index testing services
- Number of partners/children listed by index clients
- Number of partners successfully contacted
- Number of partners/children known to be HIV-positive at the time of contact
- Number of partners/children diagnosed with HIV
- Number of HIV-positive partners/children linked to HIV treatment
- Number of HIV-negative partners linked to combination HIV prevention services (condoms, PrEP, VMMC)

FIGURE 4: PARTNER NOTIFICATION SERVICES ALGORITHM



Early Infant Diagnosis

For children <24 months old who are breastfeeding, the mother should be tested first. If she is HIV-positive, perform a Nucleic Acid Test (NAT) which can be done on the HIV-exposed infant (HEI), regardless of age. NAT can be performed on either a Dried Blood Spot (DBS) which is sent to the laboratory or fresh blood sample using a Point-of-care machine (POC). The advantage of POC technologies is that they are available at the point of service delivery and offer same-day results. Infants who have HIV detectable by NAT at birth are likely to have been infected in-utero. These infants will progress to disease rapidly, and, in the absence of treatment, will experience high mortality in the first few months of life. Infants infected at or around delivery may not have the virus detectable by NAT for several days to weeks. The ability of NAT to detect the virus in the blood may be affected by ARV drugs taken by the mother or infant for postnatal prophylaxis, resulting in false-negative results. This includes drugs present in breast milk as a result of maternal ART during breastfeeding.

The rationale behind this recommendation is that infants who are first identified as HIV-exposed postpartum have a high cumulative risk of already having acquired HIV by the time prophylaxis is initiated; thus, NAT should be performed around the time of initiating prophylaxis, which would be at birth. This will help to minimize the risk of development of resistance because of extended prophylaxis in infected infants and help to promote linkage to timely initiation of ART.

Linkage to HIV Treatment and Support Services

Linkage to care is a process of actions and activities that support people testing for HIV and those diagnosed with HIV to engage with prevention, treatment, and care services as appropriate for their HIV status. Linkage to care and treatment is the period beginning with HIV diagnosis and ends with a person being initiated on ART.

For clients who test HIV negative, it is necessary to link them to prevention services including condoms, VMMC, PrEP, and others depending on their individual risk factors. Linkage to treatment is a vital bridge between diagnosis and treatment initiation. All identified positives should be linked to care, treatment and supportive services

Quality Assurance/Improvement

Quality Assurance:

Overview: Quality Assurance for HIV testing

Quality assurance (QA) is a part of quality management focused on providing confidence that quality requirements will be fulfilled. Quality assurance implemented through quality management systems is essential for any testing service, ranging from HIV testing conducted in laboratories and health facilities to community-based settings, including Rapid Diagnostic Tests (RDTs) performed by lay providers.

Quality assurance is an ongoing set of activities that help to ensure that the **test** results provided are as accurate and reliable as possible for all persons being **tested.** It is the ethical responsibility of all people conducting HIV testing (including lay providers) and all programs or facilities offering HTS to conduct testing according to quality management system principles to ensure the highest level of quality and accuracy.

The Ministry of Health recommends all testing sites and testers must be certified every 2 year for HIV testing.

FACILITY CONFIRMATION USING NAT

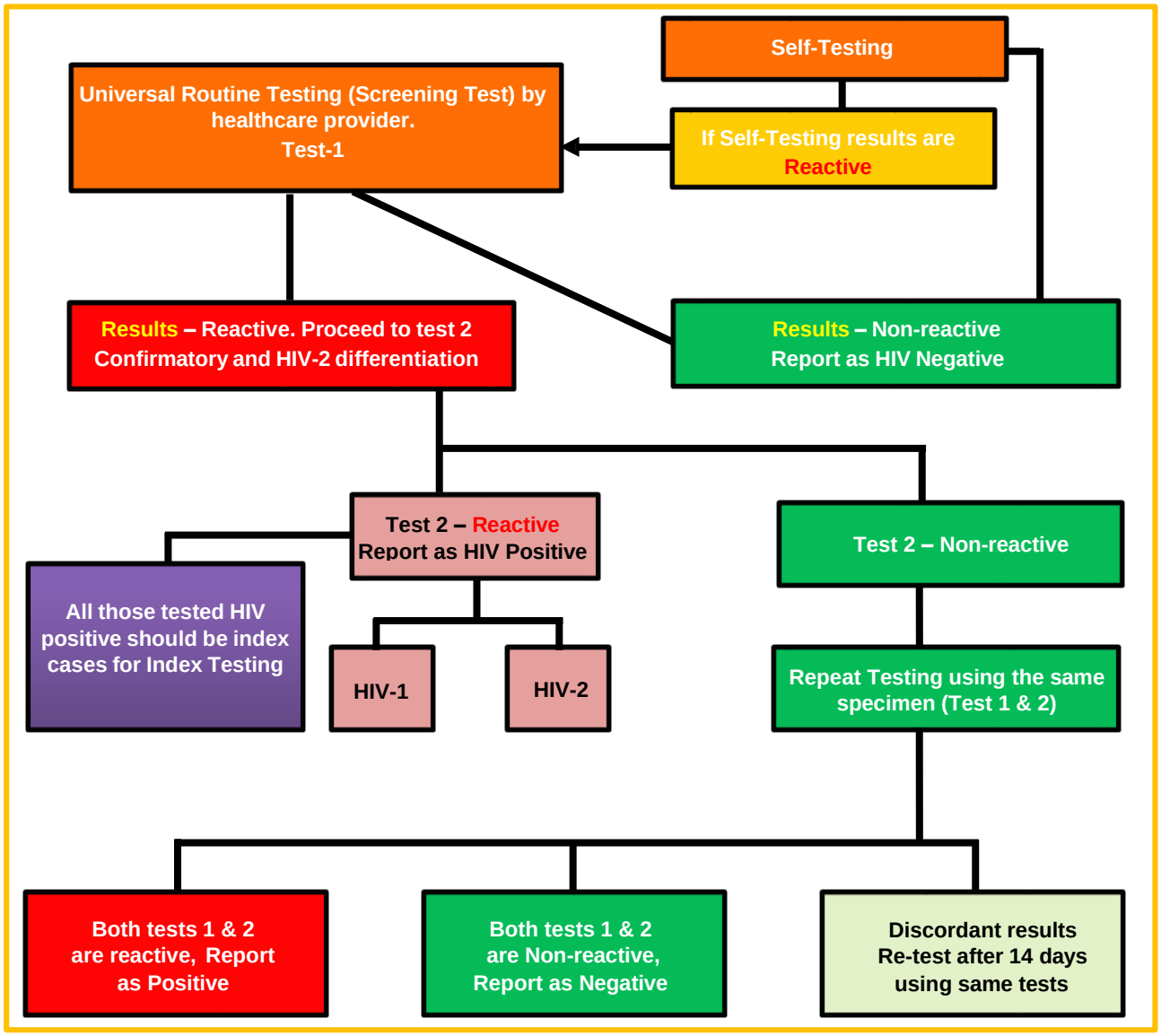
1. **Early Infant Diagnosis using NAT**
    a. If NAT 1 is positive, initiate ARV and collect NAT 2 to verify the HIV positive status
    b. If NAT 2 is positive, continue with ART for live and no need for an extra NAT
    c. If NAT 1 is positive and NAT 2 negative, these are called discordant or indeterminate results. Do not report as positive nor initiate ART but maintain prophylaxis per national protocol. Together with clinical information, these should be reviewed by a team of laboratories, paediatricians, complex case experts (if possible), and caregivers. Infants should be actively tracked to ensure follow-up and retention
2. **Retesting for verification of HIV positive status** before or at the point ART initiation is only done for persons who have already been diagnosed HIV- positive as per the national HIV testing guidelines
    a. All clients diagnosed HIV-positive by Community Based Volunteers (CBV) or lay counsellors at community and facility level should be retested by a **certified** lab personnel or other HCW (at the nearest facility). This is for verification of HIV status before or at the point of ART initiation. This should use a new specimen and preferably a second operator using the same national HIV testing protocol
    b. Retesting for verification is primarily done as a quality assurance activity to avoid misdiagnosis and to ensure those initiated on ART and treatment services are indeed HIV positive. Thus, HIV testing conducted to verify status should not be counted under new HIV positives (HTS_TST), since their initial HIV diagnosis will have already been counted at the point of the initial receipt of the HIV diagnosis (as per the national HIV testing guidelines)
3. All testing sites should participate in HIV proficiency testing at least twice per year. For all people conducting HIV testing, including lay providers, every 10th sample (10%) should be sent for External Quality Assurance test at the nearest laboratory
4. All testers and testing sites (conducting HIV tests) should be certified to ensure competence and quality in the services rendered

TABLE 1: TIMING OF HIV TESTING SERVICES FOR SPECIFIC POPULATIONS

Specific	Whom to test	When to test	Type of HIV testing
Pregnant women, breastfeeding women (and their sexual partners)	All	During antenatal care (ANC): at first ANC visit and retest every 3 months if negative In labour and delivery (L&D): test if last test >6 weeks ago During postnatal care (PNC): test at first contact if unknown status. Serological test at 6 weeks if negative. If breastfeeding: retest every 3 months if negative until cessation of breastfeeding Partner testing: same time points	Serological test
(0 to <10 years old)	Well, never-breastfed HIV Exposed Infant (HEI)	At birth/first week of life or at first contact	NAT*
		6 weeks old	
		24 months old	Serological test
	Well, breastfed HEI	At birth/first week of life or at first contact	NAT*
		6 weeks old	
		6 months old	
		9 months old	NAT
		12 months old	Serological test, if positive, follow up with NAT. If negative, follow up with serological test at 18 months
		18 months old	Serological test; if positive, follow up with NAT. If negative, follow up with serological test at 24 months
		24 months old	Serological test; if positive, follow up with NAT
	Infant or child who has completely stopped breastfeeding	≥6 weeks after breastfeeding cessation in children <24months old	Serological test; if positive, follow up with NAT
		>24 months old	Serological test
	Asymptomatic infant with unknown HIV exposure	At first contact	Maternal serological test and/or infant serological test; follow up with NAT for positive serological child ≤24 months old
	Infant or child symptomatic for HIV infection	Immediately regardless of age	Serological test; follow up with NAT for positive serological child ≤24 months old
	Positive serological child <24 months old	At first contact	NAT
	All infants and children with unknown HIV status admitted for inpatient care, attending malnutrition clinic, outpatient care or immunization clinics	Administer Paediatric Screening Tool and test appropriately	Age-appropriate tests
Adolescents (10 – 19 years) and adults	All sexually active persons with their partners and any person of unknown HIV status	Administer the HIV Screening Tool at first contact, if negative repeat test at 3 months and appropriate intervals depending on risk assessment	Serological test

* **Where there is no POC NAT a DBS should be sent for HIV DNA PCR.** Where NAT is positive, a repeat test should be done to rule out false-positive results. ART should be initiated without waiting for the receipt of the second test result because of the high risk of mortality within utero infection; if the second specimen tests negative, a third NAT should be performed before interrupting ART. Although plasma remains the gold standard sample for NAT, DBS will be the preferred mode of sample transportation for both DNA and RNA testing

FIGURE 5: HIV SEROLOGICAL TESTING ALGORITHM



HIV testing for those ≤24 months, NAT is gold standard. Although plasma remains the gold standard sample for NAT, DBS will be the preferred mode of sample transportation for both DNA and RNA testing

Index patient refers to the client being tested and identified HIV positive, whether child, adolescent or adult

Determine is used as a screening test and Bioline as confirmatory test (discriminates between HIV-1 and HIV-2)

If discordant result and POC available, you may perform a NAT

RAPID TEST FOR RECENT INFECTION

Background

HIV Epidemic Control is defined as limiting the annual number of new HIV infections in a country to less than the number of deaths among people living with HIV. As the national HIV program is implementing interventions to reduce new HIV infections, there is a need to track and distinguish a recent HIV infection (acquired within the last 12 months) from a long-term infection also quickly and easily. This information with other surveillance data can be used to estimate national and sub-national HIV incidence.

What Recency Testing is

This is HIV testing that can diagnose HIV infection and distinguish recent from long-term infection. These tests can be performed using a laboratory-based test (which takes several days to get a result) or the newer Rapid Test Recency Infection (RTRI) tests. These tests only work for HIV-1 infection and work on the same principle of using limiting antibody to distinguish recent or long-term HIV infections. However, with RTRI results can be available within 20 minutes. RTRI have been evaluated and can characterize recent HIV infection as having been acquired within the past 12 months.

Purpose of Recency Testing

Recently (or newly acquired) HIV infections frequently characteristically result in infected persons having high viral loads, immature, and weak immune responses. These individuals commonly have continued high risk behaviour and on-going transmission. This strategy will help identify new clusters of transmissions, inform and maximize the efficiency of testing contacts, reach communities and networks eluding notice now, and provide useful information to clients that can help them to be better involved in their care.

There are interventions that can interrupt transmission, which include index testing with successful contact tracing (as contacts are recent) and targeted testing based in regions or catchments were on-going transmission can be mapped. Provision of intensified HTS and same day ART (SDART) services can quickly curb new infections.

How will Recency Testing be done

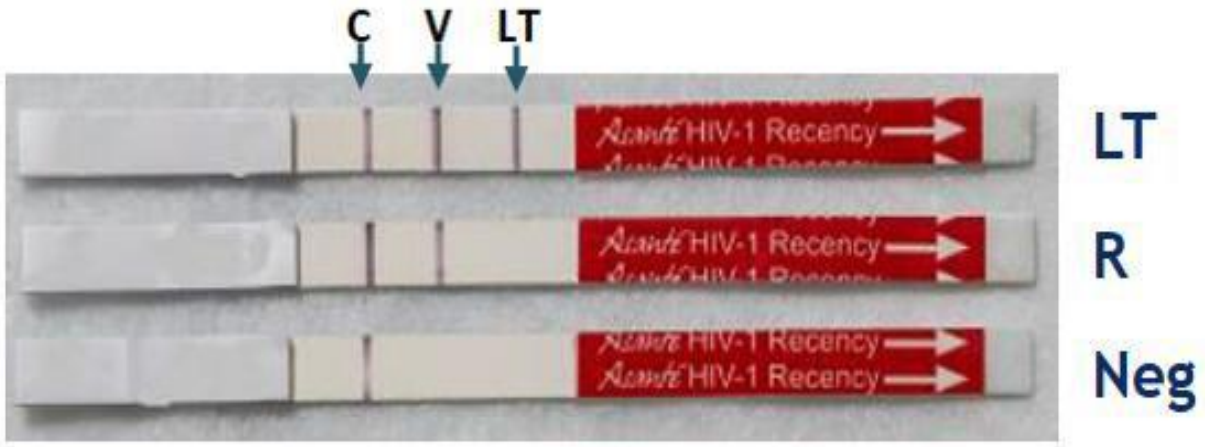
Recency testing will be performed on patients whose HIV tests are positive using the routine HIV testing algorithm. To avoid false recent results, a recent infection testing algorithm with viral load testing is used. This algorithm combines laboratory tests and clinical information to correct classify an HIV infection as recent or long-term. Patients who are on ART, elite controllers, those infected with HIV-2 or certain subtypes (e.g., clade D) may show a false positive recency test result. To control for this, a clear clinical and lab history can assist in avoiding these errors.

Persons who test recent on the RTRI should have a blood specimen tested for viral load. while those who test negative on RTRI, should have RTRI test repeated. If the result for the repeat RTRI is still negative, ensure to follow the existing Zambia HIV serological testing algorithm (refer to Figure 5). Those who test recent on the RTRI and have a viral load ≥1,000 copies/mL are considered as a confirmed recent case. It is important to note that elite controllers (these are people living with HIV who can maintain undetectable viral load for at least 12 months without being on ART), who represent less than 0.5% (1/200) of people living with HIV could have a positive recency test result with suppressed viral load.

In Zambia, HIV Recency testing has been introduced using an antibody test (Asanté™) on a surveillance basis while awaiting rapid tests for clinical use. Because HIV care and treatment will not be affected by the result of the recent infection test, and RTRIs (such as the Asanté™ test) are not yet certified for diagnostic purposes, recent infection test results will not be returned to recipients of care.

How will Recency data should be utilized

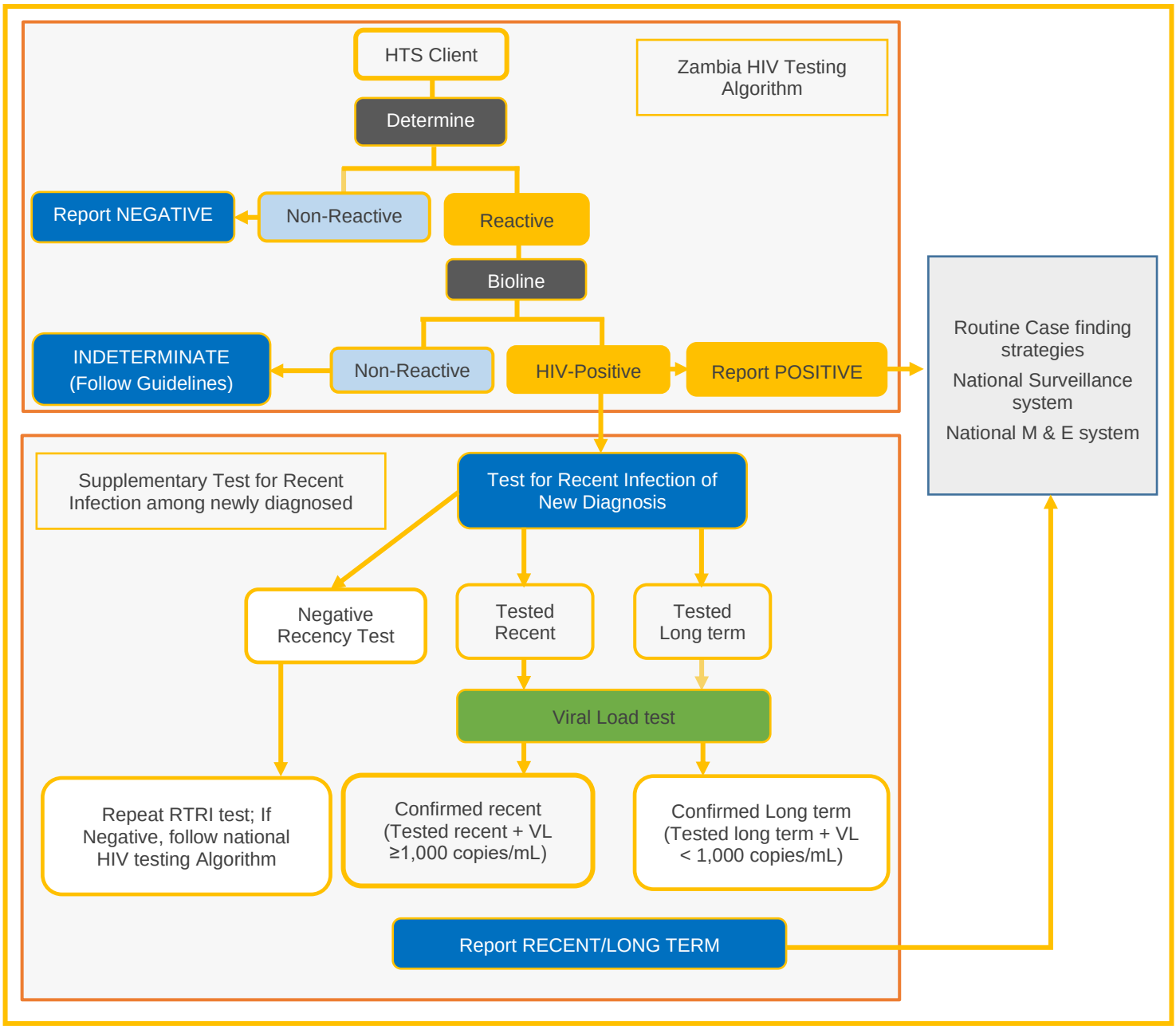
Recent infection test results will be entered into the existing national surveillance, M & E, and laboratory systems. The data will be analysed, summary reports and appropriate feedback will be shared with designated officials at district, provincial, and national levels on a routine basis. The data will inform the program about clusters of populations and geographies associated with recent infection that will guide case identification strategies such as social networking, index testing and contact tracing. This data will additionally inform targeted HIV prevention interventions such as PrEP, VMMC, Condom Distribution and SBCC strategies. The data will also help identify clusters of known HIV positive individuals virally suppressed or un-suppressed and likely to be on ART that could benefit from treatment interventions such as Adherence counselling, treatment re-engagement, EAC and improved clinical management.



Key:

LT – Long term line; R – Reactive; Neg – Negative; C – Control line; V – Verification line

FIGURE 6: RECENT INFECTION ALGORITHM (RITA) WITH VIRAL LOAD TESTING IN ROUTINE HIV TESTING



Summary/Key Points

- HIV testing services (HTS) include HIV testing, pre-test information, post-test counselling, linkage to appropriate HIV prevention, treatment, care, other clinical services, and coordination with laboratory services to support quality assurance (QA) and delivery of accurate results
- HTS should be done at all service delivery points within the facility, as well as in the community, as an efficient and effective way to identify people with HIV
- HIV testing is the gateway to HIV prevention, treatment, care, and other support and clinical services, and Universal HIV Testing, Counselling and Treatment (HTCT) should be offered to all clients and in all service points
- HIV testing is primarily conducted by healthcare workers. Lay providers who are trained, certified by MoH, and supervised can conduct safe and effective HIV testing using recommended diagnostic tests
- All mothers of breastfeeding children ≤ 24 months old should be tested every 3 months. If she tests HIV positive, a Nucleic Acid Test (NAT) should be performed on the HIV-Exposed Infant (HEI). Where NAT is positive, a confirmatory NAT test should be done to rule out false-positive results

- ART should be initiated without waiting for the receipt of the second test result because of the high risk of mortality with in-utero infection; if the second specimen tests negative, a third NAT should be performed before interrupting ART
- Where NAT is negative in a never breastfed HEI, a repeat test should be done at 6 weeks
- Where NAT is negative and HEI is still breastfeeding, NAT retest should be done at 6 weeks, 6 months, and 9 months then do serological test at 12 months, 18 and 24 months
- Community-based testing embraces Index Testing and Hot Spot Testing, where index-patient leads to early diagnosis of HIV infection and prompt linkage to care and treatment
- Recency Testing will help identify new clusters of transmissions, inform and maximize the efficiency of testing contacts and fast track immediate ART

PREVENTION

Recommendations

- Linkage of HIV Negative Persons to HIV Prevention Services
- PrEP to be used as preventive measure of HIV transmission in combination with other methods in all people at substantial risk of HIV acquisition
- Long-Acting Injectable Cabotegravir for HIV Prevention
- Correct and Consistent Condom Use
- Adherence and Retention to Care Support for those on PrEP
- Offer PrEP to all HIV Negative Persons (including PBFW) in Serodiscordant relationships or at substantial risk of HIV acquisition
- Comprehensive, Age Appropriate and Gender-Sensitive Social and Behavior Change Communication
- Effective Prevention and Management of Sexual and Gender-Based Violence (SGBV)
- VMMC Services to be Offered to all Males (with Priority given to those aged 15-24 years) as Entry Point to Access other HIV Prevention Services
- Screening and Management of STIs at all HIV Prevention Entry Points
- Implementation Considerations for Priority Populations

HIV prevention is the cornerstone of HIV epidemic control. Abstinence from risky sexual activities is the bedrock of HIV prevention. High risk sexual activities include multiple sexual partners, transactional sex, sexual intercourse without a condom and sexual activities among key populations such as transgender population and men who have sex with men. HIV Prevention programs should be targeted towards high-risk groups especially adolescent girls, young women, and young men with preventative modalities such as condom distribution, VMMC, and ARV based Prevention such as PrEP, PEP, PMTCT and ART.

HIV PREVENTION AMONG ADOLESCENT AND YOUNG PEOPLE

Data has shown that new HIV infection are highest among the 18-24 years old, and females are more than ten times more affected than males. Therefore, HIV prevention services must be focused and prioritized for this sub-population. Key factors associated with high HIV incidence among adolescents include low levels of comprehensive knowledge of HIV (38% for 15–19-year-olds), early sexual debut (17% of women sexually active at 15 years old), high levels of teen pregnancies, high school dropout for girls and low condom use (only 33.7% of 15-24 year olds use condoms with a non-regular partner). The following strategies could be considered:

a) Social network testing and preventive messaging
b) PrEP should be promoted for older adolescents and young people
c) DREAMS (Determined, Resilient, Empowered, AIDS-free, Mentored and Safe) and DREAMS-like interventions must be promoted
d) Collaborations with other entities such as Schools to promote HIV preventive messaging
e) Fostering linkage to OVCs and other empowerment programmes for adolescents and young people to keep them off harmful activities

CONDOM AND LUBRICANT PROGRAMMING

Condom and lubricant programming are highly effective in preventing sexual transmission of HIV. The consistent and correct use of the male condom significantly reduces HIV during vaginal (80%) and anal sex (70%). Female condoms can provide protection by approximately 97%, making them among the most effective prevention technology available today, exceeding consistent use of antiretroviral therapy (ART) in reducing HIV transmission (86–96%) and pre-exposure prophylaxis (up to 92%).
The goal of condom programming is to ensure that sexually active persons at risk of HIV/STIs are motivated to use condoms, have easy access to quality condoms, and can use them consistently and correctly.

Male and female condoms play a central role in halting the rising rates of STIs and HIV and including unwanted pregnancies. For people who are not practicing monogamous sex with an uninfected partner, condoms remain the best tool for reducing the risk of acquiring STIs (if uninfected) or transmitting these infections (if infected).

PRE-EXPOSURE PROPHYLAXIS (PREP)

What is PrEP?

Pre-exposure prophylaxis, or PrEP is a daily course of antiretroviral drugs (ARVs) taken by HIV-negative people to protect themselves from HIV infection. Trials of oral PrEP have shown that, when taken consistently and correctly, PrEP is very effective and reduces the chances of HIV infection. When someone is exposed to HIV through sex or injection drug use, these medicines can work to keep the virus from establishing a permanent infection. The effectiveness of PrEP is closely linked to adherence. It is important that any programme offering PrEP provides it as part of a combination package of prevention initiatives based on an individual's circumstances with support and advice on the importance of PrEP adherence.

PrEP involves the use of antiretroviral (ARV) drugs before HIV exposure by people who are not infected with HIV to block the acquisition of HIV. Twelve trials on the effectiveness of oral PrEP have been conducted among sero-discordant couples, heterosexual men, women, men who have sex with men, people who inject drugs, transgender men and women. Where adherence has been high, significant levels of efficacy have been achieved, showing the value of this intervention as part of combination prevention approaches. Oral PrEP containing Tenofovir Disoproxil Fumarate (TDF) or alternatively Tenofovir alafenamide (TAF) with either Emtricitabine (FTC) or Lamivudine (3TC) should be offered as an additional prevention choice for people at substantial risk of HIV acquisition as part of combination HIV prevention approaches.

Considerations for PrEP

- The combination of TDF or TAF + XTC (Emtricitabine or Lamivudine) is active against Hepatitis B infection thus discontinuation of TDF + XTC requires close monitoring in those infected with Hepatitis B due to the concern for rebound viremia
- In case of renal insufficiency, with CrCl between 30 – 50 mL/min, TAF + FTC can be used. However, note that TAF is not currently recommended for use in patients on Rifampicin-based TB treatment
- Persons with osteopenia/osteomalacia/osteoporosis may be at risk of bone loss associated with TDF. Therefore, TAF would be recommended in such populations
- TDF should not be co-administered with other nephrotoxic drugs, e.g., aminoglycosides
- Standard hormonal contraception does not affect PrEP effectiveness, nor does PrEP affect contraceptive effectiveness
- PrEP clients must be routinely tested for HIV infection, and ART offered immediately if the PrEP user seroconverts
- PrEP alone is not 100% effective at preventing HIV and clients need to be counselled that it should be used in combination with other HIV prevention methods as well

Who should take PrEP?

Eligibility Criteria

- All HIV negative clients with a perceived risk of HIV acquisition willing to be adherent
- No suspicion of acute HIV infection
- Able to attend regular 3-months reviews and HIV testing
- Able to concomitantly apply other prevention methods such as barriers to prevent the transmission of other STIs
- Willing to stop taking PrEP when no longer eligible

And: at **substantial risk for HIV infection**, defined as engaging in one or more of the following activities within the **last six months:**

- Vaginal/anal intercourse without condoms with more than one partner
- Sexually active with a partner who is known to be HIV positive or at substantial risk of being HIV positive
- Sexually active with an HIV-positive partner who is not on effective treatment (defined as on ART for < 6 months or not virally suppressed)
- History of STI (based on lab test, syndromic STI treatment, self-report
- History of Post-Exposure Prophylaxis (PEP) use
- Sharing injection material or equipment

Screening for PrEP

Substantial Risk for HIV Infection (based on history in the past 6 months)

- Client who is sexually active in a high prevalence population (either in the general population or key population group) and reports being at substantial risk of HIV, as defined by the criteria above.

Screening for Substantial Risk

- Screening questions should be **framed in terms of people's behaviour** rather than their sexual identity and should **refer to a defined time (6 months)**
- It is important for PrEP providers to be **sensitive, inclusive, non-judgmental, and supportive**
- Be careful not to develop a screening process that might discourage PrEP use

PrEP may also be considered for key populations (as defined by the 2017 NASF) or by persons self-selected as high-risk for HIV acquisition. Such persons should meet the eligibility criteria stated above.

Screening For IPV

Assessment for IPV should be conducted during the screening process prior to initiation on PrEP to avert Gender-Based Violence. Where there are indications of GBV, it should be properly documented in the appropriate data collecting tools **and survivors referred to appropriate services.**

Healthcare providers are ethically mandated to do no harm. To protect the safety of the clients on PrEP, partners who pose a risk of IPV may need to be excluded from initiation on PrEP.

Every client on PrEP should be screened for IPV using the 3 screening questions which include:

1. Has [partner's name] ever hit, kicked, slapped, or otherwise physically hurt you?
2. Has [partner's name] ever threatened to hurt you?
3. Has [partner's name] ever forced you to do something sexually that made you feel uncomfortable?

PrEP initiation should not be considered if a client answers YES to any of the above questions

Contraindications to PrEP:

Acute HIV Infection (AHI)

Acute HIV infection (AHI) is the early phase of HIV disease that is characterized by an initial burst of viremia. AHI infection develops within two to four weeks after someone is infected with HIV. Approximately 40% to 90% of patients with AHI will experience "flu-like" symptoms. These symptoms are not specific to HIV, as they occur in many other viral infections. Remember that some patients with AHI can be asymptomatic. Do NOT start PrEP in clients with suspected AHI.

Chronic HIV Infection

Anyone with a diagnosis of HIV should not take PrEP as this may lead to sub-optimal treatment of HIV and ARV resistance.

Acute or chronic kidney disease

TDF may worsen pre-existing kidney disease. Thus, PrEP clients should be screened with Creatinine Clearance and those with CrCl < 50 mL/min should not go on TDF-based PrEP.

Bone Mineral Disease

Clients with osteopenia or osteomalacia should similarly not be placed on a TDF-based PrEP regimen as TDF may worsen bone loss.

PrEP INITIATION

HIV testing is required before PrEP is offered

- Repeat HIV testing at 1-month post initiation and every 3 months is mandatory while a client is on PrEP
- The frequent HIV testing during PrEP use should also ideally become an opportunity for STI screening and management
- Those who seroconvert while on PrEP should be immediately switched to a standard first line regimen
- PrEP should be provided as part of the combination prevention package (condom use, HTS, family planning, STI screening, etc.)

Lab Tests before PrEP

- HIV test (only HIV-negative partners should be on PrEP)
- Creatinine (or urinalysis if creatinine not available)
- ALT
- RPR/RST
- Hepatitis B (those with positive results should be on lifelong TDF + XTC to treat HBV)

ARV regimen to be used for oral PrEP

- Tenofovir Disoproxil Fumarate in combination with Emtricitabine (TDF + FTC) is preferred for PrEP
- However, if Emtricitabine is not available, Lamivudine in combination with Tenofovir (TDF + 3TC) may be used for PrEP
- Tenofovir alafenamide in combination with Emtricitabine (TAF + FTC) can be used as an alternative in patients with renal insufficiency (CrCl between 30 – 50 mL/min) or where Creatinine is not available. However, it is not currently recommended for patients on Rifampicin-based TB treatment

Recommendations

- PrEP should be taken for a minimum of 7 days in men, and 21 days in women to achieve maximal protection from HIV acquisition before engaging in high-risk sexual exposure and must be continued as long as risky exposure persists or one remains negative

PrEP Follow-Up

Clinical Monitoring while on PrEP

- Clients should be seen at month 1, 3, 6, 9, 12 and every 3 months thereafter while on PrEP
- At each visit, the clinician should assess for side effects of PrEP, screen for IPV, STIs and check adherence
- Clinician should also assess if clients remain at risk and still has an indication to continue PrEP

Lab Monitoring while on PrEP

- Creatinine at 1 month, 2 months, every 3 months for first 12 months then annually thereafter
- ALT every 3 months for first 12 months then annually thereafter
- Repeat HIV testing is recommended while PrEP is taken at one month and every 3 months
- Necessary lab tests (e.g., STIs) as per indication
- Pregnancy test

PrEP considerations for Pregnant and Breastfeeding Women

Pregnant and breastfeeding women, often remain at substantial and increased risk of HIV acquisition during pregnancy and breastfeeding. Biological factors increase susceptibility, and social and behavioural factors may increase exposure to HIV infection. Pregnant and breastfeeding women who acquire HIV at this time have a greater risk of transmitting HIV to their infant than women who became infected with HIV before pregnancy.

PrEP is safe for use during pregnancy and breastfeeding for HIV-negative women who are receiving PrEP and remain at risk of HIV acquisition. The guidelines conclude that in such situations the benefits of preventing HIV acquisition in the mother, and the accompanying reduced risk of mother-to-child HIV transmission outweigh any potential risks of PrEP, including any risks of foetal and infant exposure to TDF and XTC in PrEP regimens. Active toxicity surveillance for ARV use during pregnancy and breastfeeding is highly recommended though.

Indications for PrEP in Pregnant and Breastfeeding Women

- A woman taking PrEP who subsequently becomes pregnant and remains at substantial risk of HIV infection
- A pregnant or breastfeeding HIV-negative woman who is perceived or perceives herself to be at substantial risk of HIV acquisition
- A pregnant or breastfeeding HIV-negative woman whose partner is HIV-positive
- An HIV-negative woman who is trying to conceive if her partner is HIV-positive

In such cases, PrEP combined with screening for acute infection, adherence counselling, safety monitoring and HIV retesting every three months, in addition to other existing HIV prevention options, including condoms, should be offered.

Key messages

1. **PrEP is safe during pregnancy and breastfeeding:** The ARVs used for PrEP, TDF or TAF + XTC, are frequently used in combination with other ARVs for HIV treatment and are safe in this population
2. TAF + FTC can be used in patients with CrCl between 30 and 50mL/min, though TAF is not currently recommended for use in patients with TB. Evidence not sufficient/conclusive for use of TAF in such patients on Rifampicin-based ATT
3. **PrEP should be provided as part of a comprehensive package:** PrEP is part of a package of combination HIV prevention and other services that includes HIV testing services, assisted partner notification, provision of male and female condoms and lubricants, contraception choices and screening and treatment of STIs
4. **Adherence matters:** Women must understand the benefits of PrEP and will benefit from advice and support. Adolescents may need special support for adherence
5. **Disclosure can have benefits:** Some women may find disclosure of their PrEP use to their partners helpful in supporting their own adherence
6. **Recognize "seasons of risk":** A woman's risk may vary over time as circumstances change. Women should be supported to start and to stop PrEP if their HIV risk changes. Risk for HIV acquisition is not constant
7. **Hormonal contraception:** PrEP can be used with hormonal contraception. Recommended PrEP regimens do not appear to alter the effectiveness of hormonal contraception
8. **PrEP is not for everyone:** It is a choice, and women should be making an informed decision based on their risk for HIV. All women should be counselled on the range of HIV prevention modalities that they can choose from to minimize the risk of HIV acquisition during pregnancy
9. **Ongoing surveillance is necessary:** Active surveillance of pregnant and breastfeeding women receiving PrEP is needed to identify and record adverse pregnancy and infant outcomes. Clients on PrEP need to be followed up at the clinic for routine monitoring

TABLE 2: PREP FOLLOW-UP

Activity	Timing of Visit
Confirmation of HIV-negative status	Initial visit, month 1, and then every 3 months
Adherence Counselling	Every visit
Side effects	Every visit
Creatinine Clearance Test	Initial visit, month 1, 2, then every 3 months for the first year, then annually
ALT	Every 3 months for first year, then annually
STI Screening	Every visit
PrEP Drug Dispensation	Initial visit, month 1, and then every 3 months
IPV Screening	Every visit
Behavioural sexual risk reduction counselling	Every visit

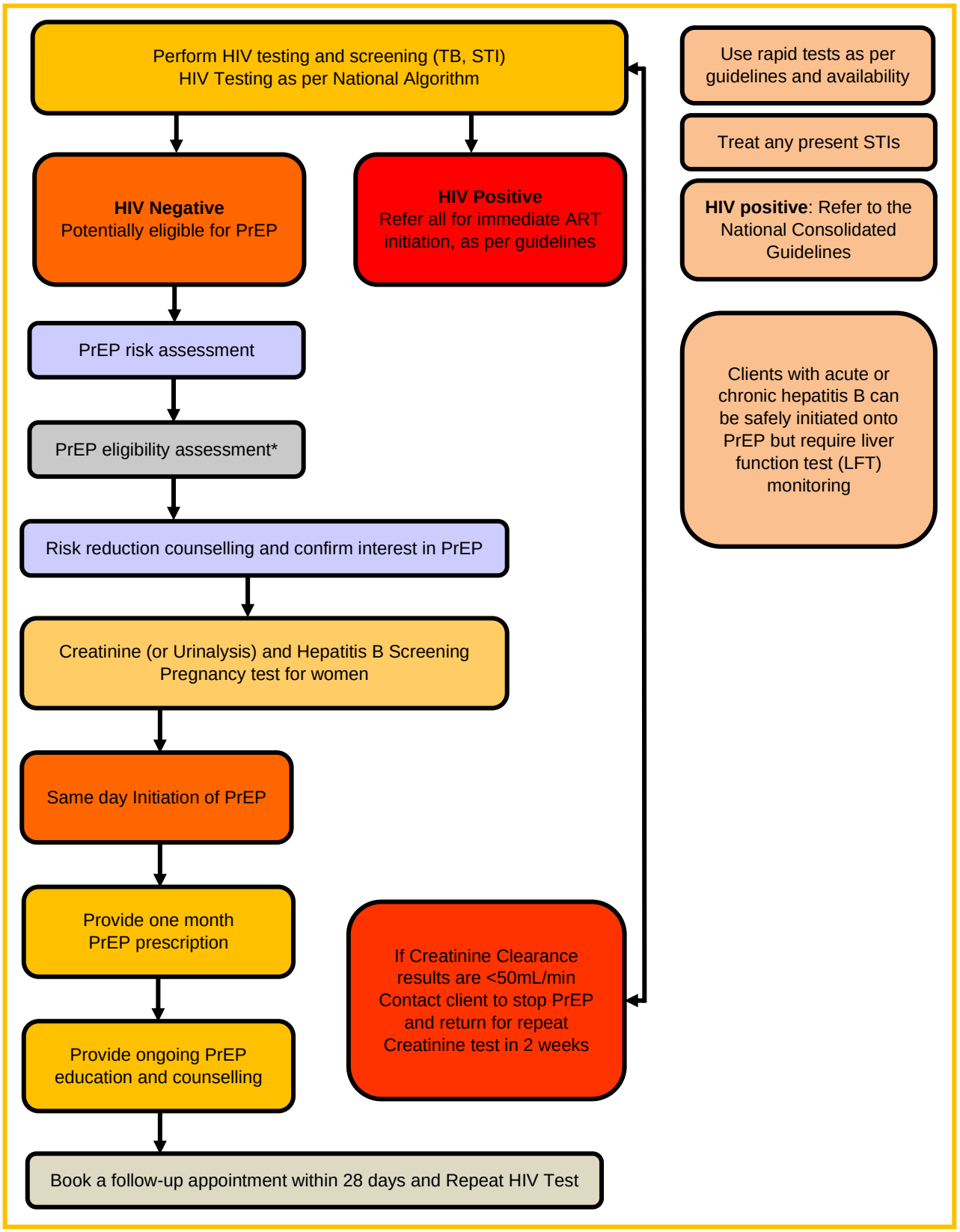
Adherence Support on PrEP

- Support for adherence should include information that PrEP is highly effective when used with strict adherence
- PrEP users should be advised that **PrEP only becomes effective after 7 days (21 days in women)** and must be continued if risky exposure persists and one remains negative
- Brief client-centred counselling that links daily medication use with a daily habit (such as waking up, going to sleep, or a regular meal) may be helpful
- Special programs to facilitate adherence among groups—such as young people and women—may be needed
- Support groups for PrEP users, including social media groups (for example, https://www.facebook.com/groups/PrEPFacts) may be helpful for peer-to-peer sharing of experience and challenges
- People who start PrEP may report side effects in the first few weeks of use. These side effects may include nausea, abdominal cramping, or headache, are typically mild and self-limiting, and do not require discontinuation of PrEP. People starting PrEP who are advised of this start-up syndrome may be more adherent

When to Stop PrEP

- PrEP can be discontinued if a person taking PrEP is no longer at risk and when this situation is likely to be sustained (i.e., no longer engaging in any high-risk behaviours as defined above)
- PrEP should be discontinued after 4 weeks of elimination of the risky exposure
- Significant side effects or if the Creatinine Clearance decreases to <50mL/min for recipients of care on TDF-based PrEP regimen (and TAF-based regimen is not available)
- If in a sero-discordant relationship, the HIV positive partner has been on ART for more than 6 months, is known to be virally suppressed, and there are no other partners, then the HIV negative partner on PrEP may discontinue therapy. However, for pregnant or breastfeeding women, PrEP should be continued

FIGURE 7: PREP FLOW CHART



*For PrEP eligibility assessment, refer to eligibility criteria on page 20

LONG-ACTING INJECTABLE CABOTEGRAVIR FOR HIV PREVENTION

PROPHYLAXIS

Long-acting injectable cabotegravir (CAB-LA) is an integrase strand-transfer inhibitor (INSTI). It is given at a dose of 600 mg, intramuscularly, four weeks apart for the first two injections and every eight weeks thereafter for HIV pre-exposure prophylaxis (PrEP). Potential barriers to the uptake and effective use of oral PrEP, such as not wanting to take an oral pill regularly, may be overcome with a long-acting injectable option. Offering additional PrEP choices has the potential to increase uptake and effective use of PrEP, and HIV prevention overall, as it allows people to choose a method that they prefer.

Studies have shown that CAB-LA is superior to oral PrEP. A meta-analysis of the blinded phase of the two efficacy studies found a 79% reduction in risk of HIV acquisition among study participants receiving CAB-LA when compared with participants receiving TDF/ FTC as oral PrEP.

In Zambia, CAB-LA should be offered as an additional prevention choice for people at substantial risk of HIV infection, as part of combination prevention approaches.

Even though Zambia has a generalized HIV epidemic, there are population and places which have a disproportionately higher incidence of HIV and these should be prioritized for CAB-LA. These include adolescent girls and young women, key population such as FSW, MSMs and migrant populations.

As with oral PrEP, HIV testing using routine national standard testing algorithm is required before offering CAB-LA and should also be done before each injection while using CAB-LA and, ideally, regularly after CAB-LA discontinuation.

CAB-LA, should be provided in combination with other effective and well established prevention approaches and integrated with other health services. This may include the provision of condoms, post-exposure prophylaxis (PEP) for HIV, testing and treatment of STIs and viral hepatitis, sexual and reproductive health services, mental health support, services that prevent and protect against gender-based violence, and harm reduction services for people who use drugs.

ADHERENCE to the 2 monthly injection of CAB-LA is important as incident infections could occur in those who delay/miss the injections. However, like oral PrEP, it may be stopped if an individual is no longer at risk or decides to use an alternative PrEP product or HIV prevention strategy. Other modes of HIV prevention such as oral PrEP are advised in individuals who stop CAB-LA but still remain with a substantial risk of HIV acquisition.

Clients may benefit from tailored interventions to support adherence to the injection schedule, especially when receiving a new product and for certain populations, such as younger PrEP users. Support groups for PrEP users, including social media groups, may be helpful for peer-to-peer sharing of experiences and challenges

While CAB-LA is generally safe, side effects have been observed among people receiving CAB-LA. Injection site reactions (particularly pain and tenderness) have been commonly reported among people who received CAB-LA. Other side effects reported include headache, diarrhoea, nausea and fatigue. Clients should be counselled on the occurrence of possible side effects and informed that they do not indicate a more serious underlying condition.

HIVDr, Baseline HIVDR on those positive on CAB-La or given DTG sparing regimens.

CAB-LA and Pregnancy: There is not evidence on the safety of CAB-LA in pregnancy. Women who fall pregnant while on CAB-LA should continue on it. Women who are pregnant or breastfeeding should be offered alternative PrEP. Contraceptive are not a requirement for wmen of child beraing age to be initiated on CBA-LA.

Indications Age and weight
Issues or Choice,,,

Priority groups; AGYW
Hot spots
Key populations
Contraindication: HBV infection, Hepatoxicity,
DSDs for CAB-LA

POST-EXPOSURE PROPHYLAXIS (PEP)

Post-Exposure Prophylaxis (PEP) is the use of ART to prevent HIV transmission. Non-occupational exposure to HIV in children and adolescents is mostly attributed to sexual abuse. In adults, exposure to HIV is mostly associated with occupational injuries. The risk of acquiring HIV infection after occupational exposure to HIV-infected blood is low (1:300 after percutaneous exposure to <1:1000 after mucocutaneous exposure).

There is no risk of transmission when the skin is intact. Factors associated with an increased risk include deep injury, visible blood on the device that caused the injury, injury with a large bore needle from artery or vein, and unsuppressed HIV viral load in source patient. Body fluids and materials that pose a risk of HIV transmission are amniotic fluid, cerebrospinal fluid, human breast milk, pericardial fluid, peritoneal fluid, pleural fluid, saliva in association with dentistry, synovial fluid, unfixed human tissues and organs, vaginal secretions, semen, any other visibly blood-stained fluid, and fluid from burns or skin lesions. Other blood-borne infections are Hepatitis B and Hepatitis C viruses which pose a heightened risk of HIV infection. Thus, all HCWs should receive HBV vaccination.

Management of occupational exposure to infectious substances includes the following steps:

Immediately after exposure:

- Clean the site: wash skin wounds with soap and running water. DO NOT squeeze, allow wound to freely bleed. If the exposed area is an eye or mucous membrane, flush with copious amounts of clean water. DO NOT USE BLEACH or other caustic agents/disinfectants to clean the skin
- Contact your In-Charge or supervisor
- Consult the trained healthcare provider, who will do the following:
  - Determine the need for post-exposure prophylaxis (PEP) based on the risk of transmission and risks and benefits of taking (or not taking) ART

TABLE 3: POST EXPOSURE PROPHYLAXIS RECOMMENDATIONS BY RISK CATEGORY

Risk category	ART	Duration
No risk: intact skin	Not recommended	
Medium risk: invasive injury, no blood visible on needle	Preferred: TDF or TAF + XTC + DTG Alternative: TDF or TAF + XTC + DRV-r TDF or TAF + XTC + LPV-r TDF or TAF + XTC + ATV-r AZT + 3TC + LPV-r (children < 20kg) AZT + 3TC + DTG (children ≥ 3kg, where available) TAF + FTC + DTG (children ≥ 25kg)	28 days
High risk: large volume of blood/fluid, known HIV-infected patient, large bore needle, deep extensive injury		
Penetrative sexual abuse		

Clients on PEP should have an HIV test before starting PEP, 6 weeks and at 3 months. While on PEP, the client should be reviewed and offered appropriate laboratory investigations

PEP registers/M&E (separate PEP and PrEP)

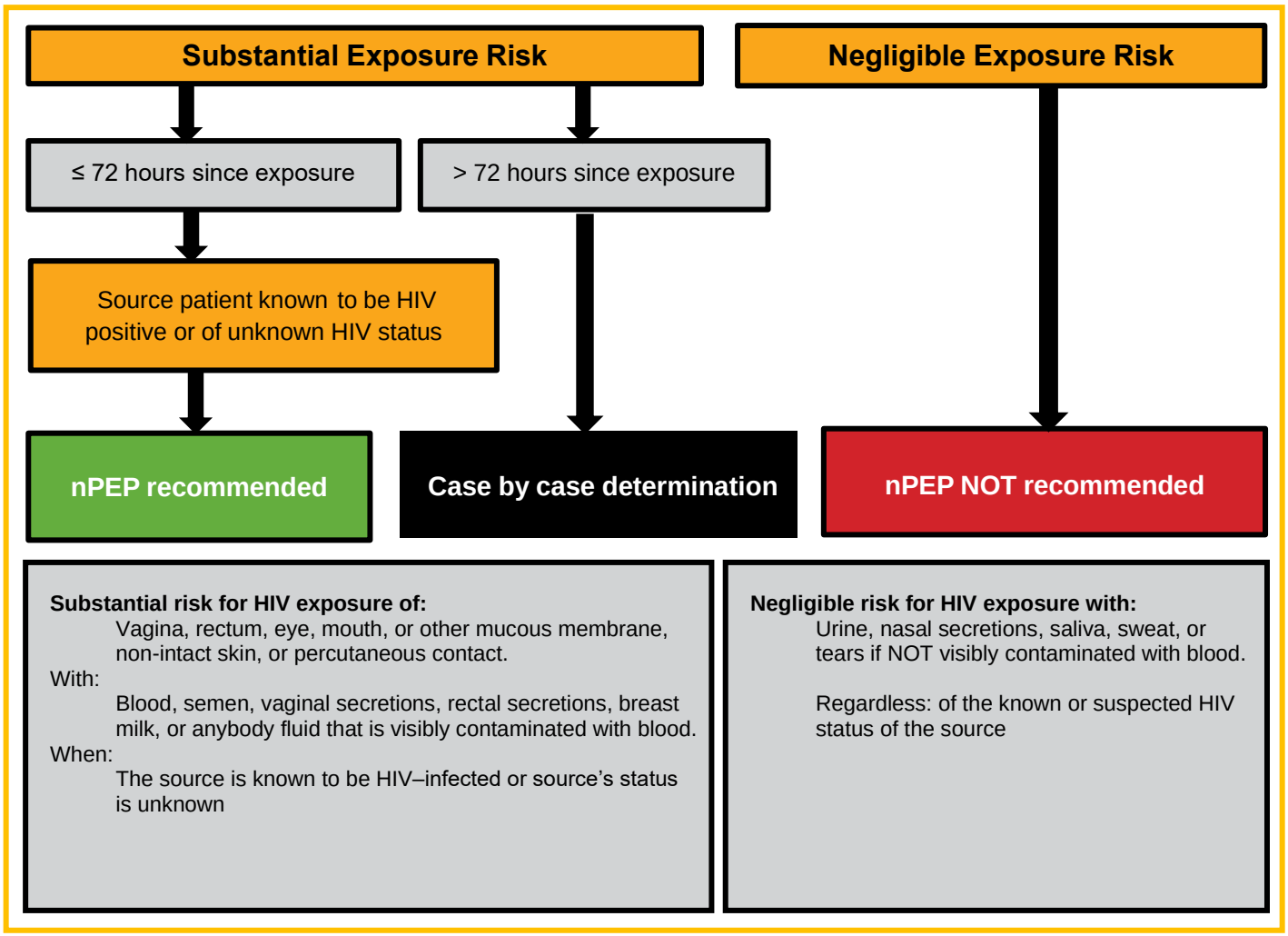
Management of non-occupational exposure to infectious substances should be managed as shown in Figure 8 below:

Non-Occupational Post Exposure Prophylaxis (nPEP) is the provision of ARVs to individuals with significant exposure to HIV within 72 hours. This should be given especially to individuals who have been sexually assaulted where the HIV status of the assailant is unknown or in any other circumstance where there is significant exposure to HIV contaminated body fluid.

Clients who come for non-Occupational PEP should be evaluated for substantial risk behaviour for HIV acquisition. Those with substantial risk or repeated requests for non-Occupational PEP must be counselled for PrEP.

The drugs for nPEP are the same as those for PEP due to occupational exposure as shown above.

FIGURE 8: ALGORITHM FOR EVALUATION AND TREATMENT OF POSSIBLE NON-OCCUPATIONAL HIV EXPOSURE



PREVENTION OF MOTHER TO CHILD TRANSMISSION OF HIV (PMTCT)

Recommendations

- Elimination of Mother-To-Child Transmission of HIV, Syphilis and Hepatitis B Virus (HBV) – Triple EMTCT
- Viral Load Monitoring in HIV Infected Pregnant and Breastfeeding Women: Every 3 months
- PrEP for Pregnancy and Breastfeeding Women
- Extended ARV Prophylaxis in HIV Exposed Infants = AZT/3TC + NVP for at least 12 weeks

Introduction

Globally mother to child transmission of HIV is a significant contributor (9%) of paediatric HIV infections. In Africa more than 95% of paediatric HIV infections is due to mother to child transmission of HIV. The Government of the Republic of Zambia (GRZ) through the Ministry of Health (MOH) has joined the global community in the elimination of mother to child transmission (MTCT) of HIV, Syphilis, and Hepatitis B virus (HBV) as a public health priority1. In this regard the goal of MOH through the Prevention of Mother to Child Transmission (PMTCT) of HIV programme is to eliminate MTCT of HIV, Syphilis and HBV (Triple EMTCT).

The similarity of the critical interventions necessary to prevent transmission adds to the feasibility and benefit of an integrated approach to EMTCT of all three infections. The WHO 2016–2021 three global health sector strategies (GHSS) on HIV, sexually transmitted infections (STIs) and viral hepatitis call for Member States and WHO to work together towards the goals of zero new HIV infections in infants and young children by 2030, elimination of Congenital Syphilis (CS) and viral hepatitis as public health threats by 2030 and ≤0.1% prevalence of hepatitis B surface antigen (HBsAg) among children ≤5 years of age.

The implementation of the PMTCT programme follows the WHO four pillars /prongs as indicated in Figure 9 below.

FIGURE 9: THE FOUR PILLARS/PRONGS OF EMTCT

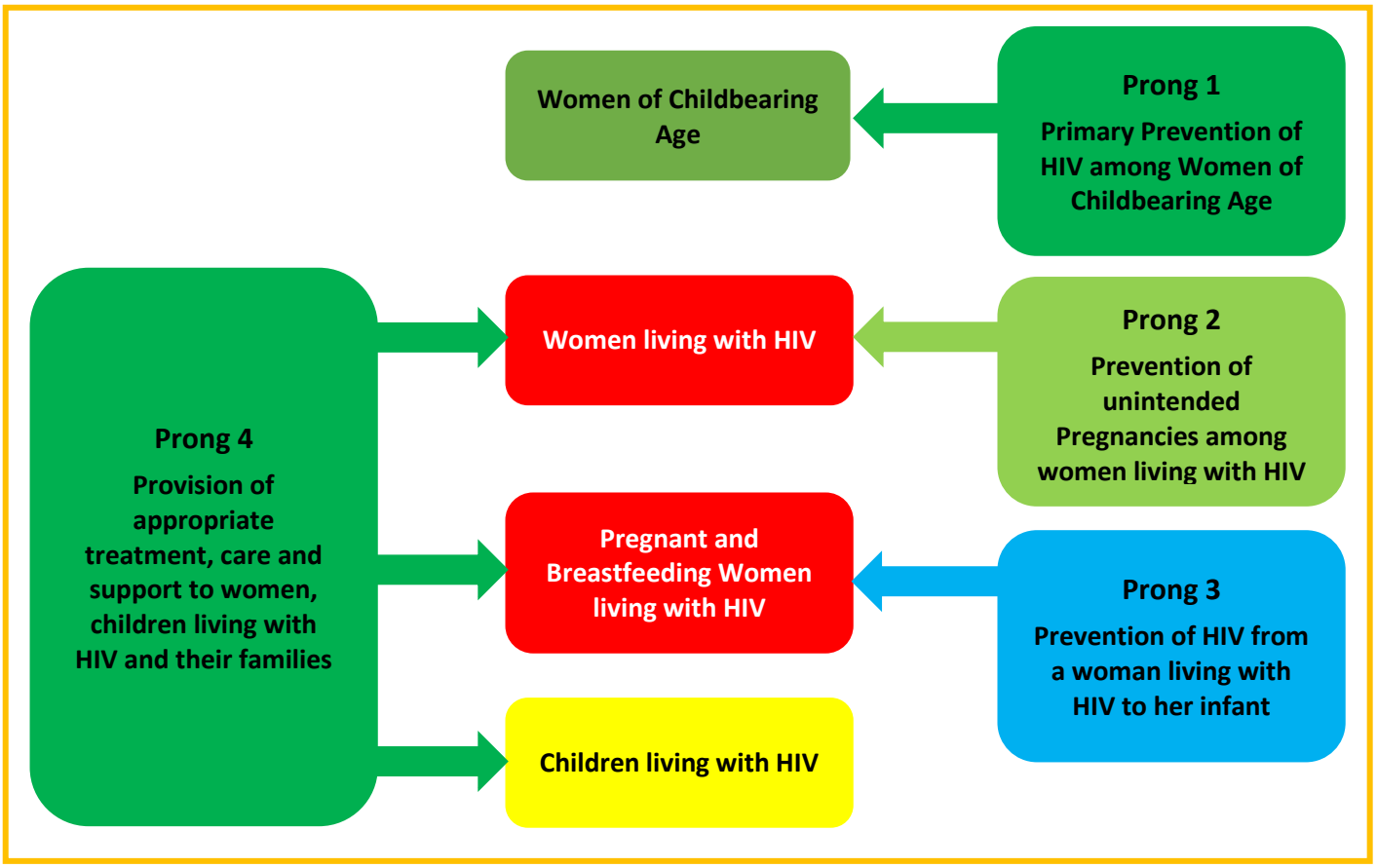


TABLE 4: PRE-PREGNANCY AND ADOLESCENTS

Specific Population	Description	Child-bearing Female with Negative HIV Test Result	Child-bearing Female with Positive HIV Test Result
Pre-Pregnancy/Adolescents	Family Planning/Contraception	Counsel on family planning and offer dual method of contraception with either of the following: progestogen-only contraceptive methods without restriction copper-bearing intrauterine devices (Cu-IUDs) and LNG-IUDs without restriction combined hormonal contraceptive methods without restriction	Counsel on family planning and offer dual method of contraception with either of the following: progestogen-only contraceptive methods without restriction copper-bearing intrauterine devices (Cu-IUDs) and LNG-IUDs without restriction combined hormonal contraceptive methods without restriction
	Co-morbidity	Screen for Hep B and Syphilis: If positive treat client plus partner	Screen for Hep B, Syphilis and OIs, if positive treat client plus partner
	HIV Prevention	Counsel client and partner on HIV combination prevention Provide condoms or information on where to access condoms, including female condoms Refer to youth friendly services for more comprehensive sexual information, including HIV prevention Retest for HIV every 3 months	Counsel and continue/Initiate ART Positive health dignity and prevention (PHDP)
		Counsel and Initiate PrEP if eligible	Provide condoms or information on where to access condoms, including female condoms

TABLE 5: PREGNANCY

Specific Population	Description	Child-bearing Female with Negative HIV Test Result*	Child-bearing Female with Positive HIV Test Result*
Pregnancy	1st Trimester	Screen for Hep B and Syphilis. If positive treat client plus partner	Counsel and continue/Initiate ART
		Counsel and Initiate PrEP if eligible (see page 21 for eligibility criteria)	Screen for Hep B, Syphilis and OIs If positive treat client plus partner
			At ANC1, for known positives on ART, check if VL was done: if >3 months retest, and thereafter every 3 months For those who initiate ART in ANC do VL at 3 months, thereafter, retest every 3 months
		Counsel client and partner on HIV combination prevention Provide condoms or information on where to access condoms, including female condoms Refer to youth friendly services for more comprehensive sexual information, including HIV prevention Retest for HIV every 3 months	Provide condoms or information on where to access condoms, including female condoms
	2nd Trimester	Screen for Hep B and Syphilis. If positive treat client plus partner	Counsel and continue/Initiate ART
		Counsel and initiate PrEP if eligible	Screen for Hep B, Syphilis and OIs, if positive treat client plus partner
		Counsel client and partner on HIV combination prevention Provide condoms or information on where to access condoms, including female condoms Refer to youth friendly services for more comprehensive sexual information, including HIV prevention Retest for HIV every 3 months	At ANC1, for known positives on ART, check if VL was done: if >3 months retest, and thereafter every 3 months For those who initiate ART in ANC do VL at 3 months, thereafter, retest every 3 months
			Provide condoms or information on where to access condoms, including female condoms
	3rd Trimester	Screen for Hep B and Syphilis. If positive treat client plus partner	Counsel and continue/Initiate ART
		Counsel and Initiate PrEP if eligible	Screen for Hep B, Syphilis and OIs, if positive treat client plus partner
			Check if VL was done/do if not done and if >3 months repeat Repeat viral load 1- 4 weeks before delivery
		Counsel client and partner on HIV combination prevention Provide condoms or information on where to access condoms, including female condoms Refer to youth friendly services for more comprehensive sexual information, including HIV prevention Retest for HIV every 3 months	Provide condoms or information on where to access condoms, including female condoms
	Labour and delivery	Do HIV test if done >6 weeks	Counsel and continue/Initiate ART

ANC1 = First antenatal visit; OIs = Opportunistic Infections

*Duo HIV/Syphilis Test kits should be used to test for both HIV and Syphilis in pregnant women and their sexual partners.

TABLE 6: INFANTS AND CHILDREN

Specific Population	Description	Child-bearing Female with Negative HIV Test Result	Child-bearing Female with Positive HIV Test Result		
Children	**Birth**	• Do HIV test if done >6 weeks • Counsel and Initiate PrEP if eligible • Counsel client and partner on HIV combination prevention	**HIV Exposed Infant/Child** 1. Send DBS or fresh blood for NAT 2. Send blood for Syphilis (RPR) where indicated 3. Scheduled immunization		**Mother** • Adherence Counselling and continue/Initiate ART • Infant Feeding Counselling
			Positive NAT • Term infants; Initiate treatment AZT+3TC+NVP until 4 weeks old and weight ≥3kgs. Thereafter change to the ABC+3TC+DTG • Preterm infants; Initiate treatment AZT+3TC+NVP until 40+4weeks old and weight ≥3kgs. Thereafter change to the ABC+3TC+DTG • Send fresh DBS or blood for confirmatory NAT • Treat for congenital Syphilis as in Negative NAT infants	**Negative NAT** • Initiate AZT+3TC+NVP prophylaxis for 12 weeks Treat for Congenital Syphilis if • Infant has clinical symptoms of congenital Syphilis • Infant has tested positive for Syphilis • Mother has Syphilis but: was not treated, or inadequately treated (less than 30 days before delivery), or treated with non-penicillin drugs during pregnancy	
	6 weeks	• Do HIV test if done >6 weeks • Counsel and Initiate PrEP if eligible • Counsel client and partner on HIV combination prevention • Provide condoms or information on where to access condoms, including female condoms • Refer to youth friendly services for more comprehensive sexual information, including HIV prevention	**Positive NAT** • Start Co-trimoxazole • Continue ART • Scheduled immunization • Newly diagnosed and weight ≥3kgs initiate on ABC+3TC+DTG • Continue adherence counselling	**Negative NAT** • Start Co-trimoxazole • Send DBS or fresh blood for NAT • Continue AZT+3TC+NVP prophylaxis • BUT if never breastfed, stop the AZT+3TC+NVP prophylaxis • Scheduled immunization	• Adherence Counselling and continue/Initiate ART • Infant Feeding Counselling
	10 weeks	• Do HIV test if done >6 weeks • Counsel and Initiate PrEP if eligible • Counsel client and partner on HIV combination prevention • Provide condoms or information on where to access condoms, including female condoms • Refer to youth friendly services for more comprehensive sexual information, including HIV prevention	**Positive NAT** • Continue Co-trimoxazole. • Continue ART • Continue adherence counselling • Scheduled immunization • Initiate any newly diagnosed to ABC+3TC+DTG	**Negative NAT** • Continue Co-trimoxazole • Continue AZT+3TC+NVP • Scheduled immunization	• Viral Load Testing in the mother • Adherence Counselling and continue/Initiate ART • Infant Feeding Counselling
	14 weeks	• Do HIV test if done >6 weeks • Counsel and Initiate PrEP if eligible • Counsel client and partner on HIV combination prevention • Provide condoms or information on where to access condoms, including female condoms • Refer to youth friendly services for more comprehensive sexual information, including HIV prevention	**Positive NAT** • Continue Co-trimoxazole. • Continue ART • Continue adherence counselling • Scheduled immunization Initiate any newly diagnosed to ABC+3TC+DTG	**Negative NAT** • If mother virally suppressed stop AZT+3TC+NVP • Mother not virally suppressed continue AZT+3TC+NVP Scheduled immunization	• If mother virally suppressed continue same regimen • Mother not virally take action to ensure mother is on more efficacious regimen

Specific Population	Description	Child-bearing Female with Negative HIV Test Result	Child-bearing Female with Positive HIV Test Result		
			HIV Exposed Infant/Child		Mother
			Positive NAT	Negative NAT	
	6 months	• Do HIV test if done >6 weeks • Counsel and Initiate PrEP if eligible • Counsel client and partner on HIV combination prevention • Provide condoms or information on where to access condoms, including female condoms • Refer to youth friendly services for more comprehensive sexual information, including HIV prevention	• Continue Co-trimoxazole. • Continue ART • Continue adherence counselling • Scheduled immunization • Initiate any newly diagnosed to ABC+3TC+DTG	• Send DBS or fresh blood for NAT • At next child visit, Stop AZT+3TC+NVP prophylaxis if mother suppressed. • Continue AZT+3TC+NVP if mother not suppressed • If NAT positive start ABC+3TC+DTG • Scheduled immunization	• Viral load • Adherence counselling • Continue ART • Review in 2-4 weeks with results of viral load [within or at time of next child visit]
	9 months	• Do HIV test if done >6 weeks • Counsel and Initiate PrEP if eligible • Counsel client and partner on HIV combination prevention • Provide condoms or information on where to access condoms, including female condoms • Refer to youth friendly services for more comprehensive sexual information, including HIV prevention	• Continue Co-trimoxazole. • Continue ART • Continue adherence counselling • Scheduled immunization • Initiate any newly diagnosed to ABC+3TC+DTG	• Send DBS or fresh blood for NAT • At next child visit, Stop AZT+3TC+NVP prophylaxis if mother suppressed. • Continue AZT+3TC+NVP if mother not suppressed • If NAT positive start ABC+3TC+DTG • Scheduled immunization	• Viral load • Adherence counselling • Continue ART • Review in 2-4 weeks with results of viral load [within or at time of next child visit]
	12 months	• Do HIV test if done >6 weeks • Counsel and Initiate PrEP if eligible • Counsel client and partner on HIV combination prevention • Provide condoms or information on where to access condoms, including female condoms • Refer to youth friendly services for more comprehensive sexual information, including HIV prevention	• Continue Co-trimoxazole • Continue ART • Continue adherence counselling • Scheduled immunization • Initiate any newly diagnosed to ABC+3TC+DTG	• Do serology test if positive send DBS or fresh blood for NAT • At next child visit, Stop AZT+3TC+NVP prophylaxis if mother suppressed. • Continue AZT+3TC+NVP if mother not suppressed • If NAT positive start ABC+3TC+DTG • Scheduled immunization	• Viral load • Adherence counselling • Continue ART • Review in 2-4 weeks with results of viral load. [within or at time of next child visit]
	18 months	• Do HIV test if done >6 weeks • Counsel and Initiate PrEP if eligible • Counsel client and partner on HIV combination prevention • Provide condoms or information on where to access condoms, including female condoms • Refer to youth friendly services for more comprehensive sexual information, including HIV prevention	• Continue Co-trimoxazole. • Continue ART • Continue adherence counselling • Scheduled immunization • Initiate any newly diagnosed to ABC+3TC+DTG	• Do serology test if positive send DBS or fresh blood for NAT • At next child visit, Stop AZT+3TC+NVP prophylaxis if mother suppressed. • Continue AZT+3TC+NVP if mother not suppressed • If NAT positive start ABC+3TC+DTG • Scheduled immunization	• Viral load • Adherence counselling • Continue ART • Review in 2-4 weeks with results of viral load. [within or at time of next child visit]
	24 months	• Do HIV test if done >6 weeks • Counsel and Initiate PrEP if eligible • Counsel client and partner on HIV combination prevention • Provide condoms or information on where to access condoms, including female condoms • Refer to youth friendly services for more comprehensive sexual information, including HIV prevention	• Continue Co-trimoxazole. • Continue ART • Continue adherence counselling • Scheduled immunization • Initiate any newly diagnosed to ABC+3TC+DTG	• Do serology test if positive send DBS or fresh blood for NAT • At next child visit, Stop AZT+3TC+NVP prophylaxis if mother suppressed • Continue AZT+3TC+NVP if mother not suppressed • If NAT positive start ABC+3TC+DTG • Scheduled immunization	• Viral load • Adherence counselling • Continue ART • Review in 2-4 weeks with results of viral load. [within or at time of next child visit]

INFANT PROPHYLAXIS DOSING

Management of an HIV-Exposed Infant (HEI) and Extended Prophylaxis

- All HEI should receive prophylaxis for at least 12 weeks with AZT + 3TC plus NVP to be stopped when there is a documented suppressed Viral Load in the mother at 3 months postnatally. See Tables 7 and 8 for the weight-based dosing
- In a situation where the Viral Load of the mother is unsuppressed (or the mother not on ART), the prophylaxis should be documented while closely monitoring for side effects in the baby. This prophylaxis should be extended until the mother is suppressed or one-week post-breastfeeding cessation
- Where the mother refuses to be on treatment, continued counselling should be done, and ART initiated as soon as possible while the baby is on extended prophylaxis

TABLE 7: SIMPLIFIED INFANT PROPHYLAXIS DOSING

Weight Band	NVP 10mg/mL	AZT/3TC 60/30mg tablet dissolved in 6mL of water (10mg/5mg/mL)
Birth weight < 2kg	0.8mL OD	0.8mL BD
Birth weight 2 – 2.499kg	1mL OD	1mL BD
Birth weight > 2.5kg	1.5mL OD	1.5mL BD
6 weeks to < 6 months old	2mL OD	Use treatment dose based on infant's weight (Table 8)
6 months to 9 months old	3mL OD	Use treatment dose based on infant's weight (Table 8)
9 months old to 1 week after cessation of breastfeeding	4mL OD	Use treatment dose based on infant's weight (Table 8)

TABLE 8: SIMPLIFIED DOSING CHART FOR AZT/3TC PROPHYLAXIS

Weight Band	Strength of AZT/3TC Tablet	AZT/3TC Dosage for Prophylaxis
3 – 5.9kg	60/30mg	1 tablet BD
6 – 9.9kg	60/30mg	1.5 tablets BD
10 – 13.9kg	60/30mg	2 tablets BD
14 – 19.9kg	60/30mg	2.5 tablets BD

NOTE:

- AZT/3TC is a dispersible tablet containing AZT = 60mg and 3TC = 30mg:
  - Dissolve 1 dispersible tablet into 6mL of water; 1mL of the suspension will contain 10mg of AZT and 5mg of 3TC
  - Take NOTE that the suspension made should be kept in a cool place! Daily reconstitution is recommended to assure stability of the suspension
    - Shake the suspension before use
- Care givers should be educated by the pharmacists and clinicians on how to reconstitute the AZT/3TC dispersible tablets. Care givers should demonstrate to the pharmacists on how they are reconstituting these formulations
- Care givers should demonstrate to the pharmacist on how they are reconstituting these formulations
- Infants weighing <2kg should receive 2mg/kg NVP once daily and 2mg/kg once daily calculated based on the AZT in the AZT/3TC
- For complicated cases e.g., severe AZT induced anaemia, consult a medical officer with appropriate training or call 7040

TABLE 9: PROCESS AND IMPACT INDICATORS FOR HIV, SYPHILIS AND HEPATITIS B VIRUS TRIPLE EMTCT

Elimination targets	HIV EMTCT	Syphilis EMTCT	HBV EMTCT
2030 WHO GHSS and UNGA political declaration aspirational targets	Zero new infections among infants and young children and achievement of the 95-95-95 targets	≤50 cases of Congenital Syphilis per 100,000 live births in 80% of countries	95% reduction in incidence of chronic HBV infections
Impact Indicators	Case Rate of MTCT of ≤50 per 100,000 live births	Case Rate of ≤50 per 100,000 live births	≤0.1% prevalence* HBsAg in children ≤5 years old
	MTCT Rate of HIV of <5% in a breastfeeding population (<2% in a non-breastfeeding)	None	Additional target ≤2% MTCT rate (for countries using targeted timely HepB-BD)
Process Indicators	Population-level ANC-1 Coverage (at least one visit) of ≥95%		Countries with universal timely HepB-BD ▸ ≥90% HepB3 vaccine coverage ▸ ≥90% HepB-BD coverage
	Coverage of HIV testing of pregnant women of ≥95%	Coverage of Syphilis testing of pregnant women of ≥95% among those who attended at least one ANC visit	Countries with targeted timely HepB-BD or without universal timely HepB-BD ▸ ≥90% HepB3 vaccine coverage ▸ ≥90% HepB-BD coverage ▸ ≥90% coverage of maternal HBsAg testing ▸ ≥90% coverage with antivirals for eligible HBsAg-positive pregnant women
	ART coverage of HIV infected pregnant women of ≥95%	Adequate treatment of syphilis seropositive pregnant women of ≥95%	

HBV=hepatitis B virus; GHSS=global health sector strategy; CS=congenital syphilis; EMTCT=elimination of mother-to-child transmission; MTCT=mother-to-child transmission; ANC=antenatal care; ART=antiretroviral therapy; HepB3=three doses of hepatitis B vaccine (infant vaccination); HepB-BD=hepatitis B birth dose vaccine; HBsAg=hepatitis B surface antigen; UNGA=United Nations General Assembly

HIV TESTING AMONG PREGNANT WOMEN AND PARTNER(S)

Testing of HIV in pregnant women follows the same guidance as testing in the general population as explained above. HIV can be transmitted from mother to child during pregnancy, delivery, and breastfeeding. Without intervention, the estimated mother-to-child transmission (MTCT) rate of HIV is 15 – 45 %. MTCT contributes significantly to new infections as globally 9% of new infections is contributed by MTCT (WHO 2017, Guidance on EMTCT). In Africa MTCT is responsible for more than 95% of paediatric HIV infections. Transmission of HIV from mother-to-child is more likely in the presence of other co-infection such as Syphilis. A pregnant woman with Syphilis and HIV is 2.5 times more likely to transmit HIV to her child than a woman who is uninfected with Syphilis. (Mwapasa et al, 2007) Beyond its impact on HIV risk, Syphilis infection in pregnancy results in an adverse event in one out of every two pregnancies if left untreated. Statistics on adverse outcome due to maternal Syphilis indicate 21% of pregnancies present in stillbirth, 9% result in a neonatal death, 16% result in disability due to congenital Syphilis, and 6% result in a low birth weight. Syphilis screening and treatment among pregnant women and partners is an essential component of any elimination of mother-to-child transmission (EMTCT) of HIV strategy. This is the reason the government through MoH and specifically the prevention of mother to child transmission of HIV (PMTCT) in 2018 embarked on the implementation of the Elimination of Mother to Child transmission of HIV and Syphilis, referred to as dual EMTCT. An integrated and harmonised dual EMTCT approach serves to improve a broad range of maternal and child health outcomes as the two diseases are not only both vertically transmitted but also cause perinatal morbidity and mortality. An integrated approach is necessary to improve efficiency and quality of MCH services, offer women more comprehensive primary care, and ultimately reduce preventable adverse birth outcomes.

The monitoring of progress towards achieving the goal of EMTCT is through the process indicators for which the target is 95%. for each disease. This is outlined in the table above

The programme reviewed the performance of the duo EMTCT of HIV and Syphilis in the last three years (2019-2021) by looking at the process indicators and the results are summarized in the table below.

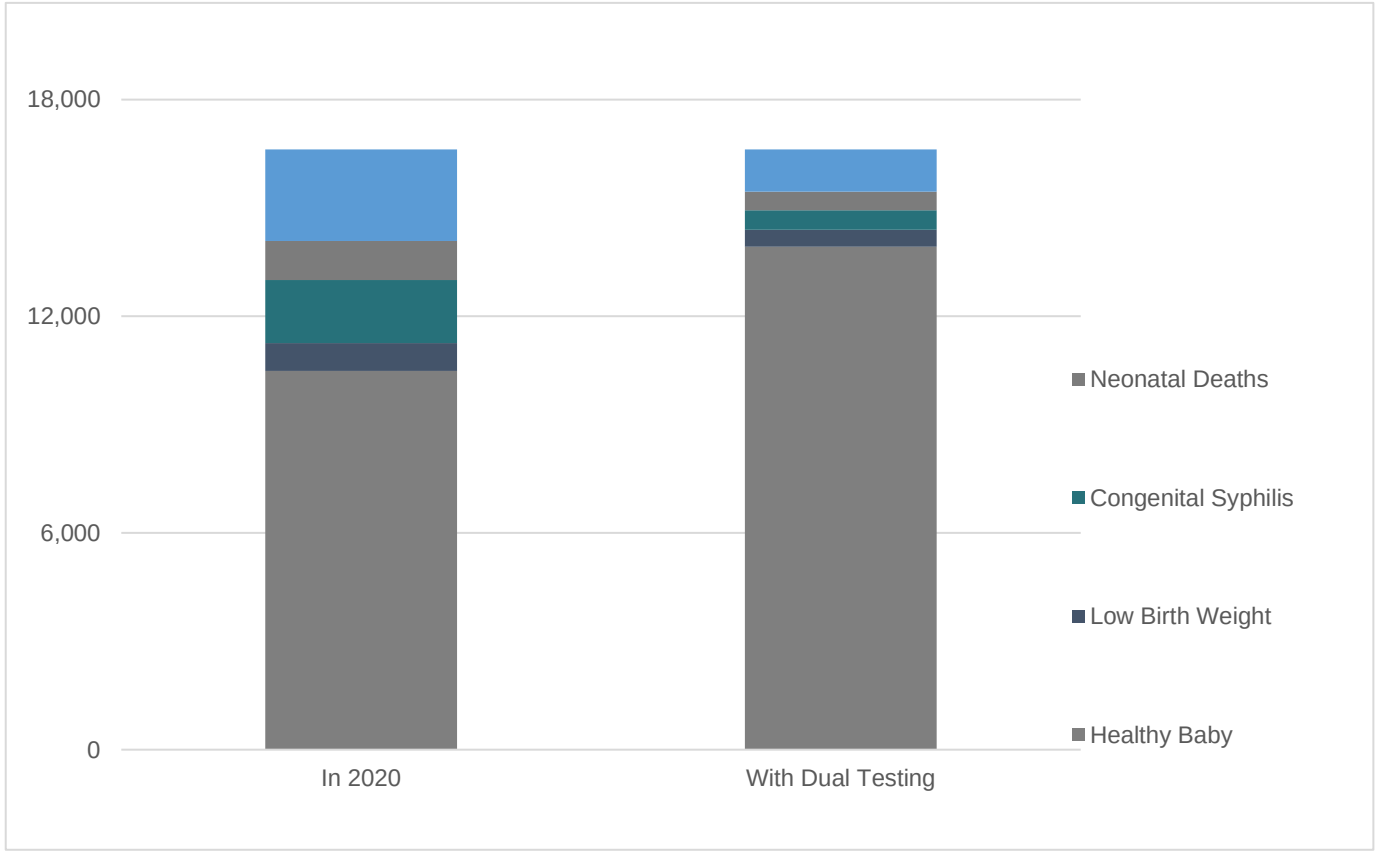
TABLE 10: PROCESS INDICATORS FOR 2020 AND 2021

	Target		
Process Indicators	Achieved %		
	2019	2020	2021
HIV Testing Coverage for Pregnant Women	94	87	83
Syphilis testing coverage for pregnant women	54	48	44

The data showed that Syphilis indicators were lagging compared to HIV. The difference in the indicators between the two diseases is attributed to inconsistent availability of Syphilis testing commodities at the point of service delivery.

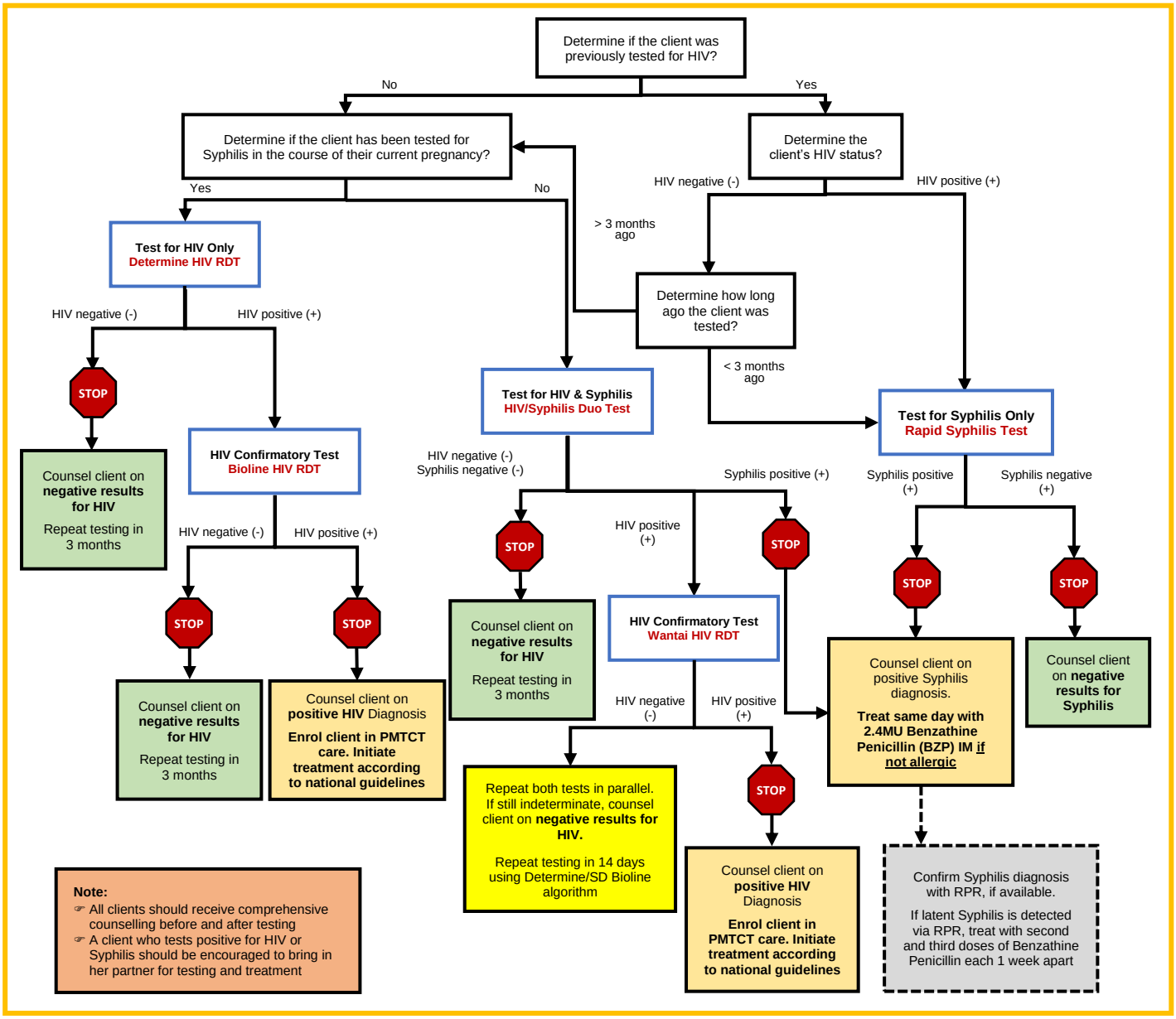
In view of the above picture, the PMTCT programme has developed HIV/Syphilis dual testing algorithm to be used in ANC settings for testing of pregnant women and their sexual partners for HIV and Syphilis (Figure 11). The adopting of HIV/Syphilis duo testing and strengthening of Syphilis treatment would ensure that at least 200,000 women are tested every year and 3,000 lives of the newborn babies would be saved.

FIGURE 10: PROJECTED REDUCTION IN ADVERSE BIRTH OUTCOMES IF DUO TESTING WERE ADOPTED



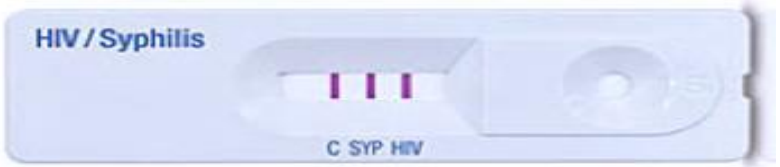
Source: Estimated based on Spectrum STI modelled prevalence and GRZ reported data on screening and treatment coverage for HIV and Syphilis

FIGURE 11: DUO HIV/SYPHILIS ALGORITHM FOR PREGNANT AND MALE PARTNERS



The SD Bioline HIV/Syphilis Duo (Figure 12) has been evaluated and adopted for use as a screening test for both HIV and Syphilis. Additional HIV/Syphilis dual tests that have been prequalified by the World Health Organization may also be adopted for use, including the Premier First Response HIV/Syphilis Combo and the SD Biosensor Standard Q Combo. The Wantai rapid HIV test kits will be used for confirming HIV if the SD Bioline is positive for HIV. Zambia adopted and introduced the HIV/Syphilis dual test in 2021.

FIGURE 12: SD BIOLINE HIV/SYPHILIS TEST STRIP



The following is the summary on the use of duo test kits in testing the Pregnant Women and their Partners for HIV and Syphilis:
The HIV/Syphilis duo test is to be used when a pregnant woman has:

- An unknown HIV status or is eligible for HIV retesting, and
- Not been tested for Syphilis in the course of their current pregnancy

A Syphilis-only rapid diagnostic test is to be used when

- A pregnant woman is known HIV +ve client
- A pregnant woman is HIV -ve and not eligible for retesting (tested <3 months before)
- An HIV-only rapid diagnostic test (according to the algorithm for the general population) is to be used when a pregnant woman
- Was previously tested for syphilis in the course of their current pregnancy
- Is in the postnatal period

Note: For a pregnant woman who is first screened via the HIV/Syphilis duo test, the additional test used for confirmation of HIV status is the Wantai, rather than the SD Bioline, and so the type of HIV (Type 1 or Type 2 or both) will not be detected. All HIV +ve pregnant women should be initiated on the same ARVs regardless of HIV type and so knowledge of the type is not required for appropriate management of the woman's HIV.

A pregnant woman who is found to be negative for HIV and syphilis should be counselled on safe sex practices to reduce the risk of contracting HIV and Syphilis. She should be scheduled for HIV retesting in 3 months, and she should be offered PrEP counselling and services. A woman who is found to be positive for HIV must be immediately enrolled in PMTCT, initiated on ARVs, and counselled in index testing so that her partner(s) and any children under 19 years old can be tested for HIV. A woman who is found positive for syphilis must be immediately treated (during the same appointment) with 2.4MU Benzathine Penicillin IM (unless she is allergic in which case a second line treatment can be provided) and counselled to bring her partner(s) in for syphilis testing. Timely treatment of maternal Syphilis is critical to preventing mother to child transmission of Syphilis. Confirmatory testing for Syphilis should only be initiated after the first dose of 2.4MU Benzathine Penicillin, or second line treatment in case of allergy, has been provided. A Rapid Plasma Reagin (RPR) should be done to determine the stage of the disease using the titre results.

If the RPR titre results is:

- $<1.8 \rightarrow$ early Syphilis
- $\geq 1.8 \rightarrow$ latent Syphilis
- $\leq 1.4 \rightarrow$ previously treated Syphilis

If it is early Syphilis, then the single dose of Benzathine Penicillin 2.4MU given is sufficient. If it is latent Syphilis, then the woman should be requested to return to the facility for two additional dosages of Benzathine Penicillin that should be given over two consecutive weeks (1x week). The various treatment options for Syphilis in Pregnant women/their partners are summarized below:

TABLE 11: RECOMMENDED SYPHILIS TREATMENT FOR PREGNANT WOMEN

	Early Syphilis (< 2 years after infection)	Late Syphilis (≥ 2 years after the infection)
First-Line	Benzathine Penicillin G 2.4MU injection one time	Benzathine Penicillin G 2.4MU injection Three times (once per week)
Second-Line It should only be used when a woman says is allergic to penicillin	Ceftriaxone 1g IM; Daily for 10-14 days Erythromycin (does not cross the placenta) 500mg orally; 4 X per day for 14 days Azithromycin (does not cross the placenta) 2g oral; one time	Erythromycin (does not cross the placenta) 500mg orally; 4 X per day for 30 days

Benzathine Penicillin should only be used to treat Syphilis. IT DOES NOT WORK EFFECTIVELY AGAINST OTHER STIs

Congenital Syphilis

Treat newborns for Congenital Syphilis if any of the following occur:

- Infant has clinical symptoms of congenital Syphilis
- The infant has tested positive for Syphilis
- Mother has Syphilis but was
- Not treated
- Inadequately treated (less than 30 days before delivery
- Treated with non-penicillin drugs

Recommended treatment for newborns

- Aqueous Benzyl Penicillin 100,000 – 150,000 U/kg/day intravenously for 10-15 days every 8-12 hours
- Procaine Penicillin 50,000 U/kg/day single dose IM for 10-15 days

Transition to Triple Elimination: HIV/Syphilis/Hepatitis B Virus from 2022 dual EMTCT will be transitioned to triple EMTCT

References
WHO, (2021), Global Guidance on Criteria and Processes for Validation: ELIMINATION OF MOTHER TO CHILD TRANSMISSION OF HIV, SYPHILIS AND HEPATITIS B VIRUS
Mwapasa V, et al (2006) Maternal Syphilis infection is associated with increased risk of mother-to-child transmission of HIV in Malawi. AIDS 20 (14) 1869-77)
WHO (2017) Global Guidance on Criteria and Processes for Validation. ELIMINATION OF MOTHER TO CHILD TRANSMISSION OF HIV AND SYPHILLIS
WHO (2021) Global Guidance on Criteria and Processes for Validation. ELIMINATION OF MOTHER TO CHILD TRANSMISSION OF HIV, SYPHILLISAND HEPATITIS B VIRUS

MANAGEMENT OF HIV-INFECTED POPULATIONS

Recommendations

- Treat ALL regardless of CD4 count or WHO Clinical Stage
- DTG based regimen as standard First-Line in all adult populations
- pDTG for Children ≥ 4 weeks and ≥ 3kg
  TafED for Children ≥ 25kg
  TLD in Children ≥ 30kg
- Genotype Test after treatment failure
- Darunavir-r in Second-Line ART

TREATMENT OF HIV INFECTED POPULATIONS

TABLE 12: ARV PRESCRIBERS AND CORRESPONDING REGIMENS FOR ART INITIATION

Cadre with specific training	Initiation of ART
Nurse/Midwife (registered, enrolled) certified with Integrated HIV Care Training*	1st line
Nurse Prescribers with Integrated HIV Care Training*	1st line, 2nd line**
Clinical Officers with Integrated HIV Care Training*	1st line, 2nd line**
Medical Licentiates with Integrated HIV Care Training*	1st line, 2nd line
Medical Officers with Integrated HIV Care Training*	1st line, 2nd line
Medical Specialists with relevant training and experience†	1st line, 2nd line, 3rd line

*Providers with Integrated HIV Care Training should satisfy requirements of competency-based training in the use of ART for treatment and prevention of HIV
**Initiation on Second-Line should only be done in consultation with a medical officer with appropriate training
†Relevant training and experience refer to management of advanced and complicated HIV, including Second-Line treatment failure

To improve ART initiation and adherence, counselling must be done so that the individual (or caregiver) understands its benefits. The benefits of starting ART earlier include:

- Reduced rates of HIV-related morbidity and mortality
- Reduced MTCT (in pregnant and breastfeeding women)
- Potential reductions in the incidence and severity of chronic conditions (e.g., renal disease, liver disease, certain cancers, and neurocognitive disorders)
- Reduction in infectious complications (e.g., TB)
- Reduced sexual transmission
- High levels of adherence to ART are needed to attain these objectives

FIGURE 13: FLOW DIAGRAM FOR HIV CARE AND TREATMENT FROM HIV TESTING TO ART INITIATION

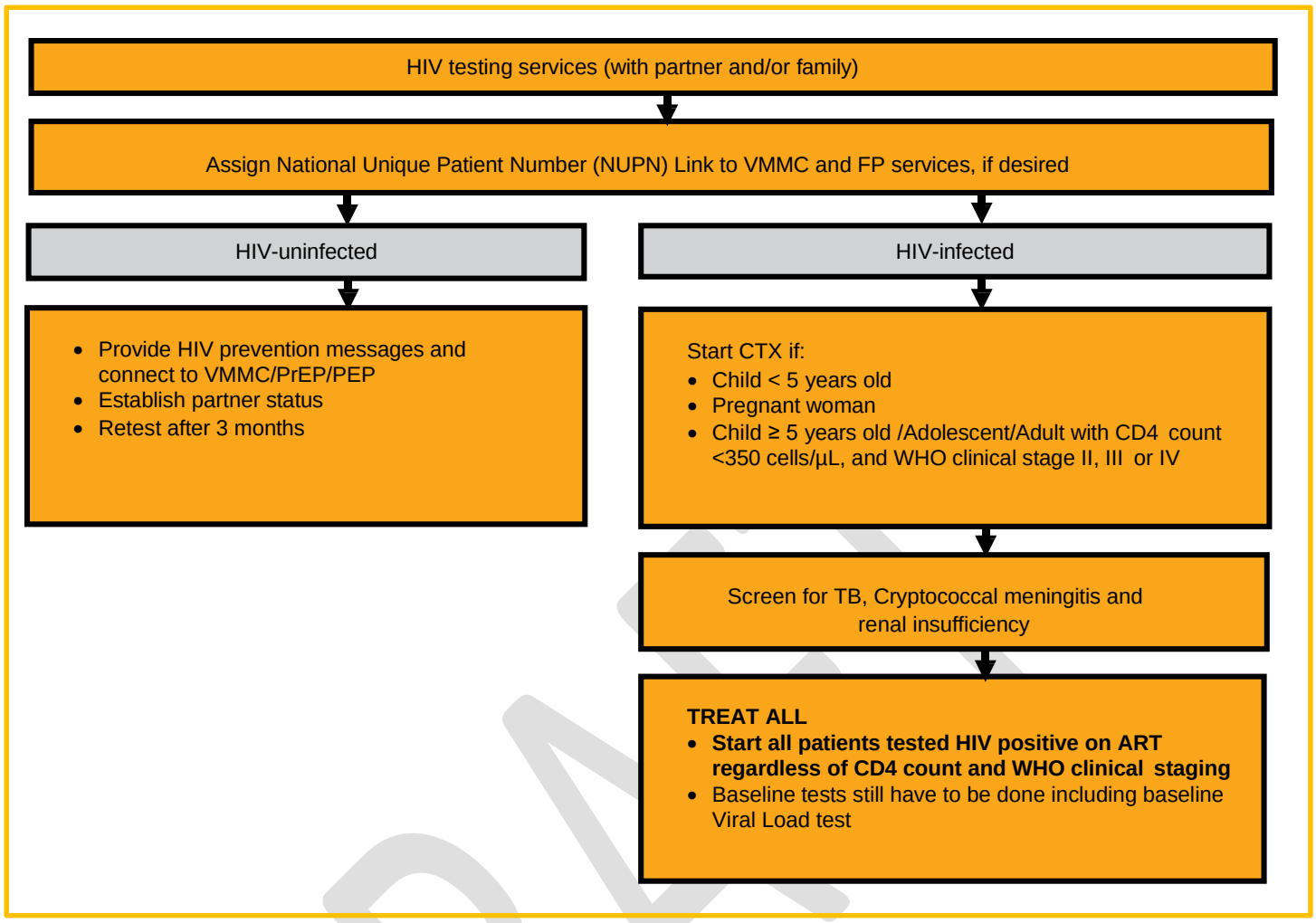


TABLE 13: WHO CLINICAL STAGING OF HIV DISEASE BY SPECIFIC POPULATIONS

Children (0 to <10 years old)	Adolescents (15 to 19 years old)
	Pregnant & Breastfeeding Women
Adolescents (10 to 15 years old)	Adults
Clinical Stage 1	
• Asymptomatic • Persistent generalized lymphadenopathy	• Asymptomatic • Persistent generalized lymphadenopathy
Clinical Stage 2	
• Unexplained persistent hepatosplenomegaly • Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) • Herpes zoster • Lineal gingival erythema • Recurrent oral ulceration • Papular pruritic eruption • Fungal nail infections • Extensive wart virus infection • Extensive molluscum contagiosum • Unexplained persistent parotid enlargement	• Moderate unexplained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis) • Herpes zoster, Angular cheilitis • Recurrent oral ulceration • Papular pruritic eruption • Fungal nail infections • Seborrheic dermatitis
Clinical Stage 3	
• Unexplained moderate malnutrition not adequately responding to standard therapy • Unexplained persistent diarrhoea (14 days or more) • Unexplained persistent fever (above 37.5°C, intermittent or constant, for >1 month) • Persistent oral candidiasis (after 6 weeks old) • Oral hairy leukoplakia • Lymph node tuberculosis • Pulmonary tuberculosis • Severe recurrent bacterial pneumonia • Acute necrotizing ulcerative gingivitis or periodontitis, unexplained anaemia (<8g/dL), neutropenia (<0.5 x 10^9/L) or chronic thrombocytopaenia (<50 x 10^9/L) • Symptomatic lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease, including bronchiectasis	• Unexplained severe weight loss (>10% of presumed or measured body weight) • Unexplained chronic diarrhoea for longer than 1 month • Unexplained persistent fever (intermittent or constant for >1 month) • Persistent oral candidiasis • Oral hairy leucoplakia • Pulmonary tuberculosis • Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia) • Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis • Unexplained anaemia (<8g/dL), neutropenia (<0.5 x 10^9/L) and/or chronic thrombocytopaenia (<50 x 10^9/L)

Children (0 to <10 years old)	Adolescents (15 to 19 years old)
	Pregnant & Breastfeeding Women
Adolescents (10 to 15 years old)	Adults
Clinical Stage 4	
• Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy • Pneumocystis jirovecii pneumonia • Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) • Chronic herpes simplex infection (or labial or cutaneous of more than 1 month's duration or visceral at any site) Oesophageal candidiasis (or candidiasis of trachea, bronchi, or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs with onset at > 1 month old) • Central nervous system toxoplasmosis (after the neonatal period) • HIV encephalopathy • Extrapulmonary cryptococcosis, including meningitis • Disseminated non-tuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis (with diarrhoea) • Chronic isosporiasis • Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis) • Cerebral or B-cell non-Hodgkin lymphoma • HIV-associated nephropathy or cardiomyopathy	• HIV wasting syndrome • Pneumocystis (jirovecii) pneumonia • Recurrent severe bacterial pneumonia • Chronic herpes simplex infection (or labial, genital or anorectal of more than 1 month's duration or visceral at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi, or lungs) • Extrapulmonary tuberculosis • Kaposi sarcoma • Cytomegalovirus infection (retinitis or infection of other organs) • Central nervous system toxoplasmosis HIV encephalopathy • Extrapulmonary cryptococcosis, including meningitis • Disseminated non-tuberculous mycobacterial infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis • Chronic isosporiasis • Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis) • Lymphoma (cerebral or B-cell non-Hodgkin) • Symptomatic HIV-associated nephropathy or cardiomyopathy • Recurrent septicaemia (including non-typhoidal Salmonella) • Invasive cervical carcinoma • Atypical disseminated leishmaniasis

TABLE 14: ELIGIBILITY CRITERIA FOR ART INITIATION IN CHILDREN, ADOLESCENTS, PREGNANT AND BREASTFEEDING WOMEN AND ADULTS

Specific populations	Description
Pregnant & Breastfeeding Women	Treat irrespective of WHO clinical stage or CD4 count
Children (0 to <10 years old)	
Adolescents (10 to ≤19 years old)	
Adults	

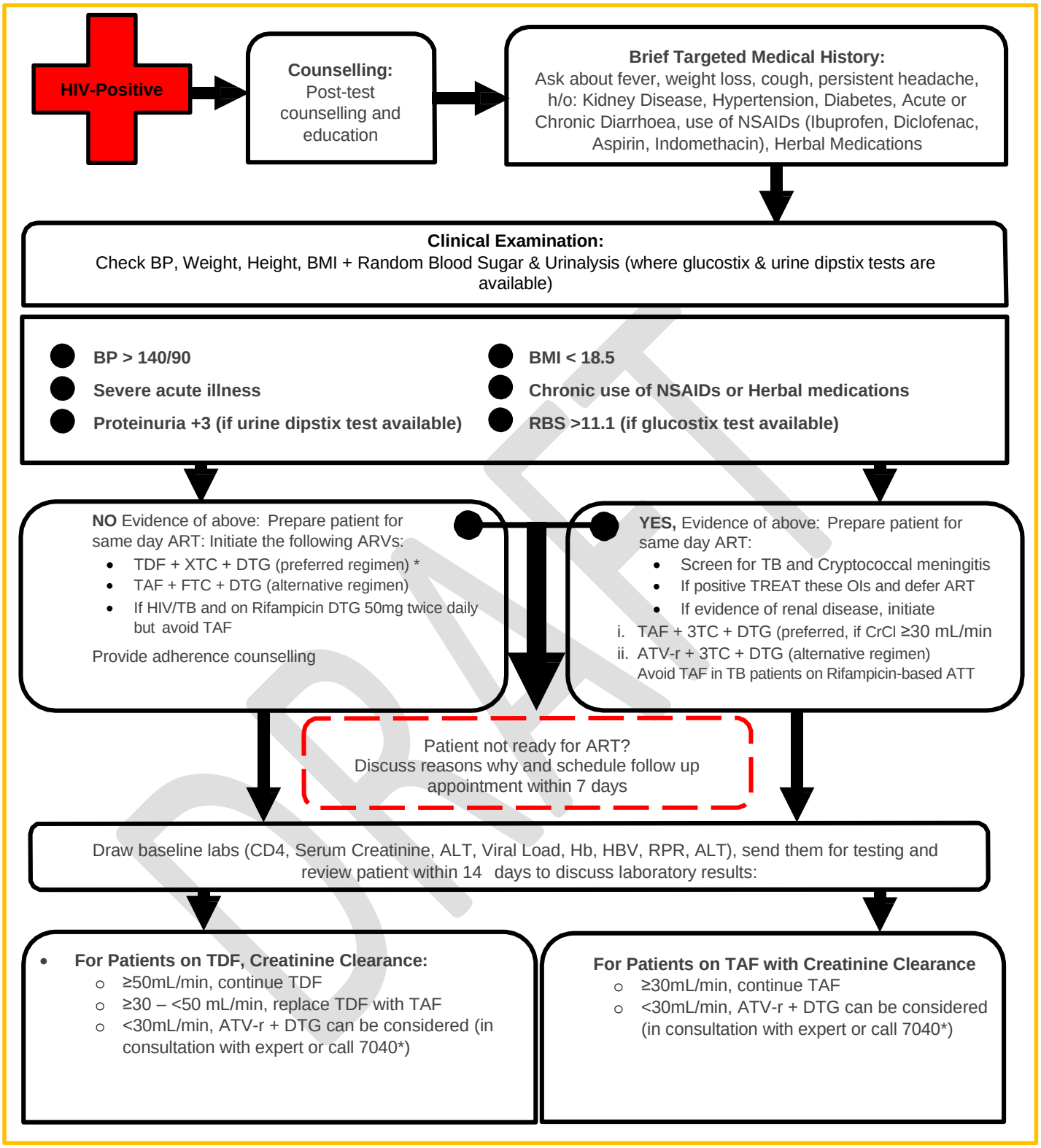
Under these new guidelines: Treat ALL, the assessment through WHO Clinical Staging (Table 13) guides the evaluation and management of HIV; however, initiating ART does not require a CD4 count

TABLE 15: PRE-INITIATION TASKS

Timeline/Specific populations		Clinical tasks	Laboratory tests*
Visit 1 Enrolment/ Initiate ART based on patient readiness	**Children**	• Complete history & examination • Screen for TB and other Opportunistic Infections (OIs) • Adherence counselling and PHDP† messages, including the caregiver: sessions 1 & 2 • WHO clinical assessment • Initiate CTX for child ≥ 6 weeks to ≤ 5 years old Initiate CTX for child ≥ 5 years if CD4 <350 cells/μL or WCS II, III or IV • Initiate TPT if TB screening is Negative • HPV vaccine for girl <10 years old	• Creatinine (calculate CrCl) ** • ALT • Hb/FBC** • Blood glucose • CD4 ** • Baseline Viral load • HBsAg (if not vaccinated) • Pregnancy test (Adolescent or woman of reproductive age) • Syphilis test (adolescent or adult) • Cholesterol, and triglycerides (especially if starting PI) • HPV test or visual inspection with acetic acid (VIA) in a sexually active adolescent or woman
	Adolescents **Adults**	• Complete history & examination Screen for TB and other OIs WHO clinical assessment • Initiate CTX if eligible (CD4 <350 cells/μL or WCS II, III or IV, or pregnancy) • Initiate TPT if TB screening is Negative if not initiated • Adherence counselling and PHDP† messages • Urinalysis	
Visit 2 **1-2 weeks later** **Initiate ART if not initiated at visit 1**	**Children**	• Targeted history and examination • Screen for TB, Cryptococcus, and PCP • Review CTX adherence (if already started) • Initiate CTX (if eligible and not initiated at enrolment) • Initiate TPT if TB screening is Negative if not initiated • Review laboratory test results • Initiate ART if not initiated at visit 1 • Adherence counselling and PHDP† messages, including the caregiver	• Urinalysis • Sputum AFB smear/GeneXpert MTB RIF in individuals with a positive screening • Serum CrAg for adolescents and adults with CD4 count <200 cells/μL or WCS III or IV • Urine LAM for children >5 years and adults with CD4 count <200 cells/μL
	Adolescents **Adults**		
Visit 3 **2-4 weeks from enrolment** **Initiate ART if not initiated at visits 1 and 2**	**Children**	• Targeted history and examination • Screen for TB and other OIs • Review CTX adherence • Initiate TPT if TB screening is Negative if not initiated • Initiate ART if not yet started in the last two visits Adherence counselling and PHDP† messages	• Urinalysis • Sputum AFB smear/GeneXpert MTB RIF in individuals with a positive screening • Serum CrAg for adolescents and adults with CD4 count <200 cells/μL • Urine LAM for children >5 years and adults with CD4 • count <200 cells/μL
	Adolescents		
	Adults		

† Positive Health Dignity and Prevention (PHDP) includes risk reduction, ART adherence, correct condom use, family planning, STI screening, and partner HIV testing

FIGURE 14: SAME DAY ART INITIATION ALGORITHM IN ADULTS



*For 3TC dose adjustment, refer to appendix 1
*For same day ART initiation, where Creatinine is not available, TAF is preferred over TDF

First-Line ART

Providing optimized, fixed-dose ART regimens in all populations have consistently demonstrated that there are better clinical and laboratory outcomes if HIV treatment is initiated early. Reduce the time between HIV diagnosis and ART initiation. This is based on an assessment of the person's readiness, and it is preferred that initiation is done immediately or within 7 day.

Table 16: Preferred First-Line ART and Alternative Regimens by Specific Populations

Specific Populations	Description	Preferred 1st line ART	Alternative Regimen
Children (0-4 weeks)	All	AZT + 3TC + NVP	Get Expert Opinion or call 7040 for advice
Children (≥4weeks), adolescents and adults	3 – 24.9kg	ABC + 3TC + pDTG*	ABC + 3TC + LPV-r
	≥ 25kg	TAF + FTC + DTG	ABC + 3TC + DTG
	≥ 30kg	TDF + XTC + DTG TAF + FTC + DTG	TDF + 3TC + DRV-r ABC + 3TC + DTG TDF + 3TC + LPV-r TDF+ 3TC + EFV
Children, adolescents and adults Co-infected with TB	3 – 29.9kg	ABC + 3TC + DTG	ABC + 3TC + AZT ABC + 3TC + LPV-r
	≥ 30kg	TDF + XTC + DTG Increase the frequency of DTG to 50mg twice daily if on Rifampicin-based ATT	ABC + 3TC + DTG TDF + XTC + LPV-r

*DTG 10mg is available for children weighing 3 – 19.9kg and for children and adults weighing ≥20kg, 50mg is available. Note that DTG is dosed once daily

Phasing out of EFV/NVP due to High Resistance Rate

The Zambia HIVDR survey of 2019 showed that baseline resistance to NNRTIs is at 16.2%. For this reason, it is recommended that EFV and NVP must be phased out of use by observing the following:

- New patients should NOT be initiated on EFV based regimen
- All existing patients on EFV based regimen should be transitioned to DTG based regimen WITHOUT requiring a viral load test
- Existing patients who have side effects to DTG or are unwilling to be transitioned to DTG can use EFV based regimen as exceptional circumstances

Newer Antiretroviral Agents and Their Use

1. Dolutegravir (DTG)

a. Dolutegravir (DTG) is a newer Integrase Inhibitor with a higher genetic barrier to resistance than Raltegravir (RAL) and Elvitegravir (EVG) and NNRTIs

b. DTG is associated with the following mutations: F121Y, E138A/K, G140S/A, **Q148 H/K/R**, N155H, R263K.

c. Cross-resistance studies with RAL and EVG-resistant viruses indicate that G140S and **Q148 H/K/R in combination with** L74I/M, E92Q, T97A, E138A/K, G140A, or **N155H** are associated with 5-fold to 20-fold reduced DTG susceptibility and reduced virologic suppression in patients

d. DTG 10mg tablet is available for children weighing 3 – 19.9kg. It is available as scored dispersible tablets. Paediatric DTG (pDTG) can be dispersed in water or swallowed whole

e. DTG 50mg is dosed once daily in adults and children weighing ≥20kg

f. For patients on Rifampicin or those with Integrase mutations, DTG should be given TWICE DAILY

g. It has no food restrictions and has few drugs interactions

h. It has drug interactions with UDP glucuronyl transferase inducers like Rifampicin, which leads to decreased plasma DTG levels

i. It also has decreased absorption with aluminium, calcium or magnesium containing antacids and Iron and Zinc containing preparations, so DTG should be given 2 hours before or 6 hours after the antacids
j. DTG has the potential to interact with the carbamazepine, phenytoin and phenobarbitone but not with Sodium Valproate, Lamotrigine and Levetiracetam, the viral load should be closely monitored
k. There is also reported increase in serum Creatinine with no true effect on the glomerular filtration rate (GFR)

Practical hints on the use of DTG

- It should be used in the following populations:
  - Adults and adolescents with HIV-1 or HIV-2 or HIV-1/HIV-2 mixed infection who are being initiated on ART as part of combination ART as
    - TDF (or TAF) + XTC + DTG
  - Adults and adolescents with HIV-1 regardless of the viral load on NNRTI based First-Line as
    - TDF + XTC + EFV to TDF (or TAF) + XTC + DTG
    - ABC + 3TC + EFV to ABC (or TAF) + XTC + DTG
  - Children and adolescents with HIV-2 or HIV-1/HIV-2 mixed infection on PI based First-Line as
    - TDF + XTC + LPV-r to TDF (or TAF) + XTC + DTG
    - ABC + 3TC + LPV-r to ABC (or TAF) + XTC + DTG
    - In HIV/TB infected populations on Rifampicin increase the frequency of DTG to 50mg twice daily instead of the usual 50mg once daily
    - At the end of the TB treatment, continue giving DTG twice daily for two weeks before reverting to the initial once daily dosing of DTG
    - However, where the single 50mg tablet is not available the following switch should be done:
      - TDF + XTC + EFV to TDF + XTC + LPV-r
        - the dose of LPV-r should be doubled
- DTG significantly increases Metformin plasma levels, which can be partially explained by Organic Cation Transporter-2 inhibition. It is recommended that dose adjustments of Metformin be considered to maintain optimal glycaemic control when patients are starting/stopping DTG while taking Metformin
  - In patients taking DTG who are starting Metformin, begin with low Metformin dose and titrate up carefully. Recommended dose limit of Metformin 1,000mg daily. If patient is already on Metformin and initiating DTG, monitor glucose, haemoglobin a1c, and Metformin adverse effects and adjust dose as necessary.

2. Tenofovir alafenamide (TAF)

Tenofovir alafenamide is a phosphonoamidate prodrug of the nucleotide analogue Tenofovir (TFV) which belongs to a class of Nucleotide reverse transcriptase inhibitors. It is predominantly metabolized intracellularly to Tenofovir which undergoes subsequent phosphorylation to yield the active Tenofovir diphosphate (TFV-DP) metabolite which inhibits the activity of HIV reverse transcriptase by competing with natural substrates and causing DNA chain termination after being incorporated into viral DNA

a. TAF is dosed as 25mg once daily (when used without pharmaco-enhancers)
b. TAF has also demonstrated **IN VITRO** and **IN VIVO** activity against HBV
c. The median terminal half-life of TAF is 0.51 hours and the active metabolite, TFV-DP, has an intracellular half-life of 150 to 180 hours
d. TAF is intracellularly metabolized in hepatocytes, peripheral blood mononuclear cells (PBMCs) and macrophages and less than 1% of the dose is excreted in the urine and 31.7% excreted in faeces
e. TAF has been associated with K65R and the K70E substitutions which lead to reduced susceptibility to Abacavir, Didanosine, Emtricitabine, Lamivudine, and TDF. HIV-1 containing multiple thymidine analogue mutations (TAMs) (M41L, D67N, K70R, L210W, T215F/Y, K219Q/E/N/R) lead to resistance to TAF. In addition, multi-nucleoside resistant virus with a T69S double insertion mutation or with a Q151M mutation complex including K65R exhibit **IN VITRO** resistance to TAF
f. Adverse events include diarrhoea, fatigue, nausea, and rash
g. TAF is associated with significantly less increase in proximal tubular proteinuria and less reduction in estimated glomerular filtration rate (eGFR) when compared to TDF
h. TAF is associated with significantly less change in spine and hip bone mineral density (BMD) compared to TDF
i. There is insufficient safety and efficacy data on the use of TAF in people with HIV/TB co-infection on Rifampicin-based ATT

Practical hints on use of TAF

- It should be used in the following populations:
  - Adults and adolescents with HIV-1 or HIV-2 or HIV-1/HIV-2 mixed infection who are being initiated on ART as part of combination ART as
    - TAF + FTC + DTG
  - Adults and adolescents with HIV-1 on NNRTI based First-Line as
    - TDF + XTC + EFV to TAF + FTC + DTG
    - ABC + 3TC + EFV to TAF + FTC + DTG
  - Adults and adolescents with HIV-2 or HIV-1/HIV-2 mixed infection on PI based First-Line as
    - TDF + XTC + LPV-r to TAF + FTC + DTG
    - ABC + 3TC + LPV-r to TAF + FTC + DTG
- It is not yet recommended for use in HIV/TB infected populations on Rifampicin-based ATT
  - It is therefore recommended that such patients are on TDF or ABC containing regimen instead of TAF containing regimen
- TAF can be a used in HIV infected pregnant women at any gestation age

For programmatic purposes, TAF will be prioritized for the following populations (if eligible):

- Women 45 years and above
- Men 50 years and above
- Creatinine clearance ≥30 mL/min
- Children 25kg and above
- All those initiated on TAF must continue with TAF unless a contraindication arises

FIGURE 15: ALGORITHM FOR SELECTING DTG IN PATIENTS INITIATING ART

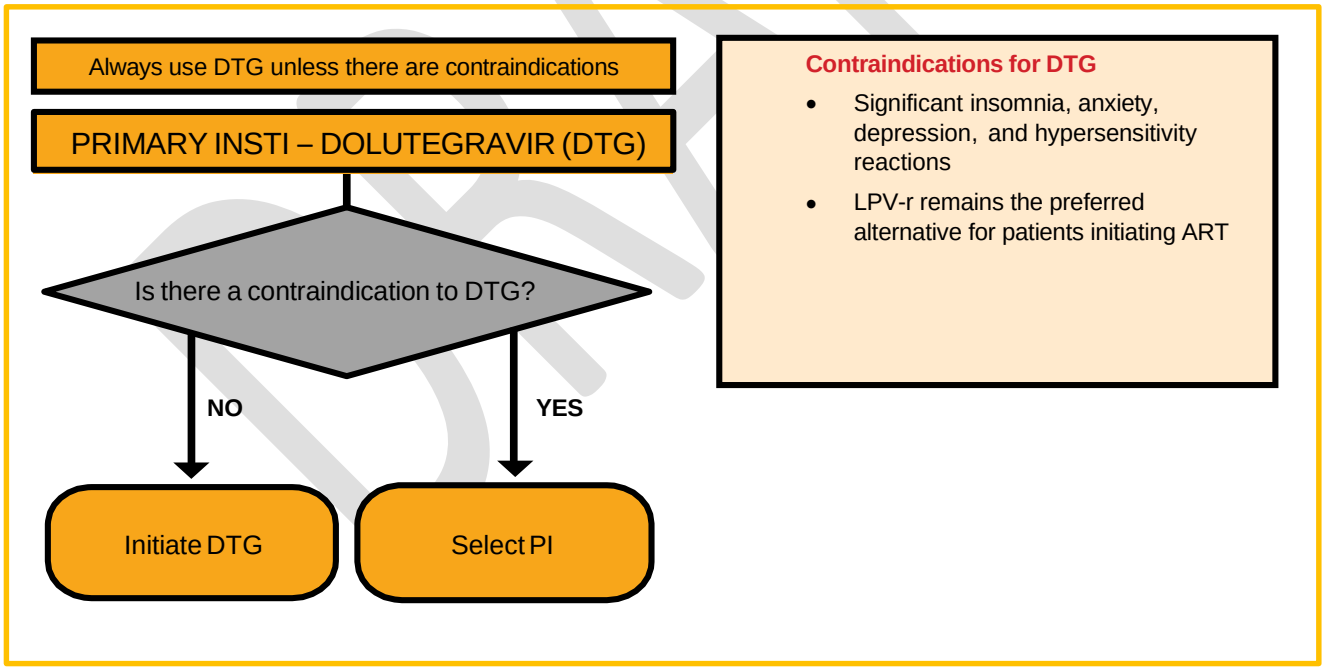
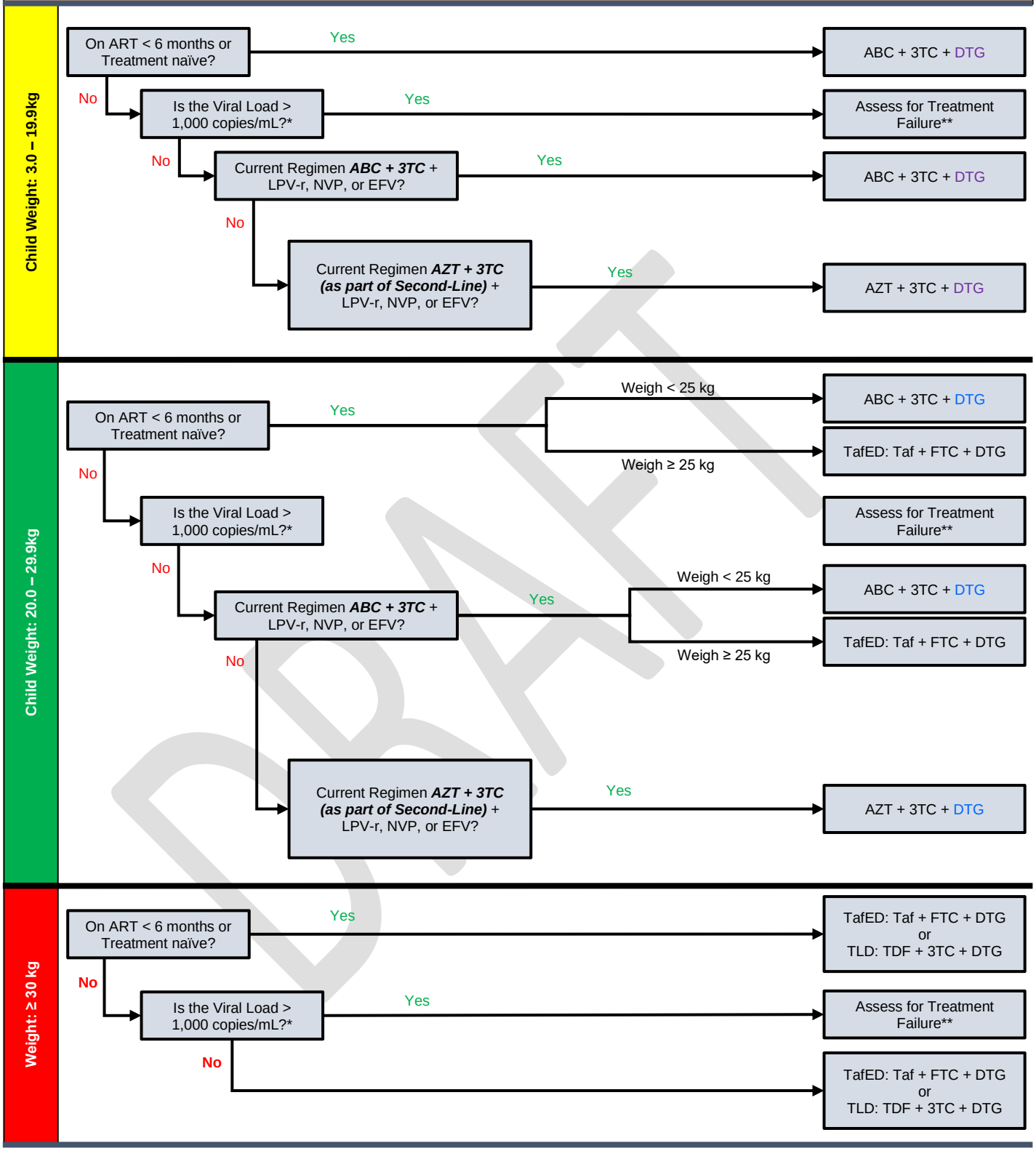


FIGURE 16: DTG PRESCRIBING ALGORITHM FOR ADOLESCENTS AND CHILDREN

For children aged < 4 weeks or who weigh <3 kg, use AZT, 3TC & NVP.
Use MoH dosing charts for precise dosing instructions for each paediatric formulation.



*If there is no valid VL on file, previous untraced results should be followed up and those eligible for VL test should have it performed
Absence of a valid VL should not stop transition! Assess previous adherence history and consider previous suppressed VL results before transitioning

**When assessing treatment failure, start with adherence assessment using well-structured EAC sessions with VL collected after 3 months of optimized EAC. Unsuppressed VL after EAC should result in regimen switch e.g., ABC + 3TC + LPV-r to AZT + 3TC + DTG

Children with TB: For children with TB taking Rifampicin, DTG should be double dosed. This means it should be dosed twice daily. For children on DTG 10mg or DTG 50mg, this should be taken once in the morning and once in the evening. For children on TLD, this should be taken as 1 pill of TLD then 1 pill of DTG 50 mg after 12 hours. **At the end of TB treatment, continue giving the DTG twice daily for two weeks before going back to the initial dosing.**

Darunavir-ritonavir (DRV-r)

j. Darunavir-ritonavir is a boosted protease inhibitor with efficacy and tolerability superior to Lopinavir-ritonavir and Atazanavir-ritonavir. Until recently widespread adoption of DRV-r has been hampered by the lack of an affordable generic fixed dose combination
k. DRV-r has virologic outcomes comparable to ATV-r and RAL, and a lower rate of discontinuation compared to ATV-r
l. DRV-r leads to higher viral suppression and fewer discontinuations compared to LPV-r
m. DRV-r can continue to be used in Third-Line (after failure of a PI) with increased dose given high barrier to resistance
n. The recommended oral dose for adult patients is as follows:
    1. Adult PI treatment-naïve patients: two 400/50mg tablets taken once daily (800/100mg once daily)
    2. Adult PI treatment-experienced patients including Third-line patients: DRV 600mg taken with ritonavir 100mg twice daily
    3. Pregnant patients: DRV 600mg taken with ritonavir 100mg twice daily except where viral load is already undetectable, and the increased dose would be detrimental to adherence or is not available
o. DRV-r must be administered with food to achieve the desired antiviral effect
p. Adverse events include diarrhoea, nausea, rash, headache, abdominal pain and vomiting
q. Discontinue DRV-r immediately if signs or symptoms of severe skin reactions develop (including but not limited to severe rash or rash accompanied with fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, hepatitis and/or eosinophilia)
r. Patients suspected of or with underlying liver disease should be monitored for elevation of liver enzymes during first several months of treatment
s. Precaution should be taken when DRV-r is co-administered with drugs dependent on CYP 3A enzyme system for clearance e.g., in TB treatment (Rifampicin, Rifapentine), Antibiotics (e.g., Clarithromycin), Antifungals (e.g., Fluconazole), Anti-epileptics (e.g., Phenytoin)
t. The combination of DRV-r and Artemether/Lumefantrine can be used without dose adjustments; however, the combination should be used with caution as increased lumefantrine exposure may increase the risk of QT prolongation
u. Effective alternative (non-hormonal) contraceptive method or a barrier method of contraception is recommended
    1. For co-administration with Drospirenone, clinical monitoring is recommended due to the potential for hyperkalaemia
    2. No data are available to make recommendations on co-administration with other hormonal contraceptives

Practical hints on use of DRV-r

- It is recommended for use by patients failing First-Line DTG-based regimens
- DRV-r may be given in combination with DTG
- DRV-r can be used after ATV-r or LPV-r (and even DRV-r) failure when administered at the higher 600/100mg twice daily dose
- DRV-r should **NOT** be used in HIV/TB infected populations when TB treatment includes Rifampicin
    - It is therefore recommended that such patients receive an LPV-r containing regimen instead of a DRV-r containing regimen during TB treatment when Rifampicin is used
    - DRV-r may be used in TB treatment with Rifabutin, or in drug-resistant TB patients where Rifampicin is not part of the regimen

3. Long Acting Injectable ARVs

Cabotegravir and Rilpivirine 4 weekly and 8 weekly injections have be approved by the FDA and European Medical Agency for use for treatment is ART naive individuals. Approval from the WHO is pending. Despite the superiority of these long acting injectable, implementation questions and barriers do exist. Some of the considerations that could be barriers are outlined in the table below. The Zambia national HIV programme will systematically roll out these commodities as they became available. Implementation guidelines will be given as separate updates.

SCREENING FOR ADVANCED HIV DISEASE

Definition of Advanced HIV Disease

HIV associated mortality remains high in Zambia estimated at 17,200 for the year 2020. Most of the individuals who die from HIV have Advanced HIV Diseases (AHD) and present with opportunistic infections. For adults and adolescents, and children older than five years, AHD is defined as CD4 cell count <200 cells/mm^3 or WHO stage 3 or 4 event. All children younger than five years old with HIV are considered as having AHD.

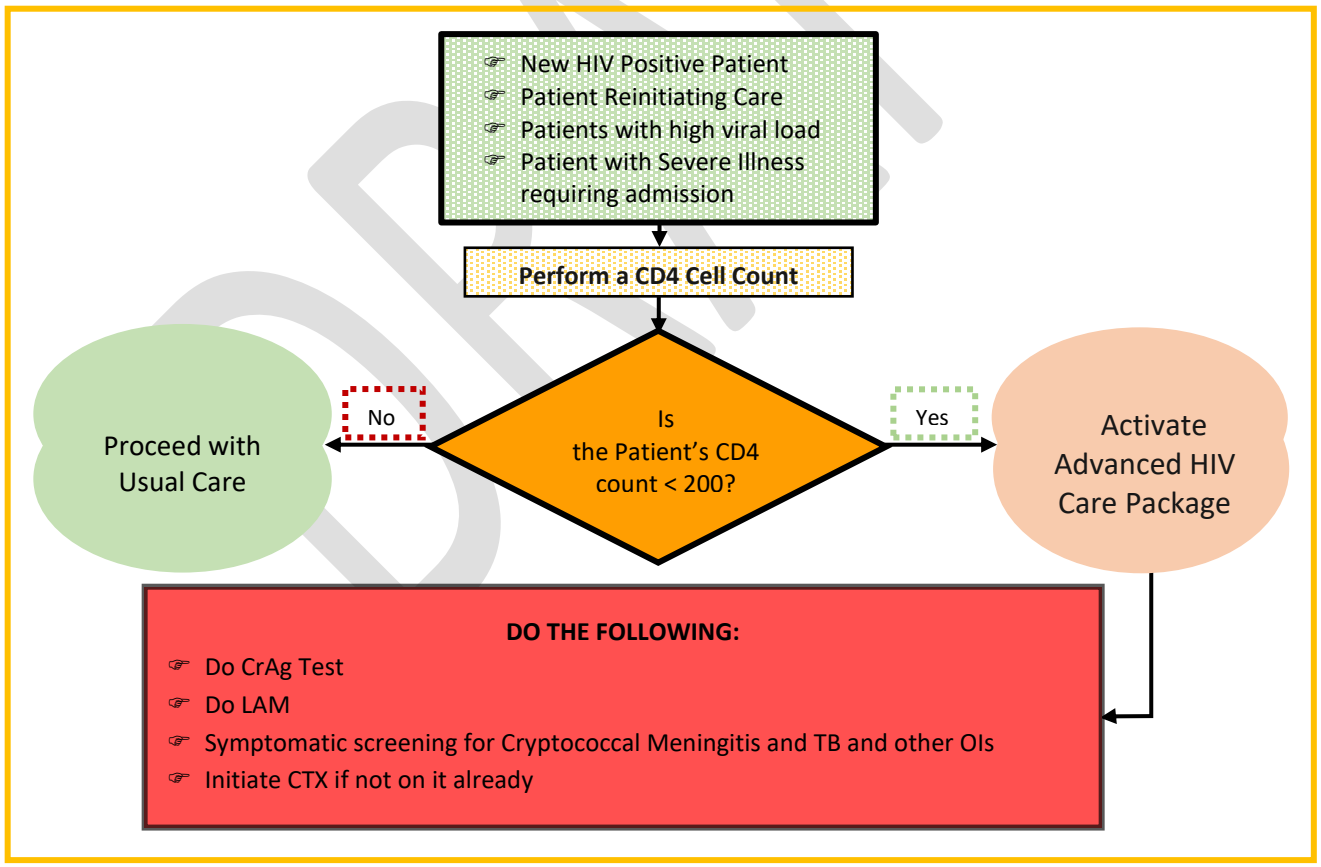
Although children younger than five years are defined as having advanced disease at presentation, those who have been receiving antiretroviral therapy for more than one year and who are stable should not be considered to have advanced disease and should be eligible for multi-month dispensing.

Screening for Advanced HIV Disease

To reduce HIV associated mortality, it is recommended that the following categories of HIV+ patients are reflexively screened for advanced HIV disease using a CD4 cell count test or WHO Clinical Staging where the CD4 cell count test is not available. These include:

- Those newly diagnosed with HIV
- Those reinitiating into care following treatment interruption
- Those with a high viral load
- Those hospitalized with a serious illness defined as respiratory rate ≥30 breaths per minute; Heart Rate ≥120 beats per minute, temperature ≥39°C, or unable to walk unaided

FIGURE 17: CD4 CELL COUNT SCREENING: A GATEWAY FOR ADVANCED HIV DISEASE CARE



THE ADVANCED HIV DISEASE PACKAGE OF CARE

All patients that screen positive for advanced HIV disease must be offered the 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 for opportunistic infections especially Tuberculosis and Cryptococcal infection
- Prophylactic services against Tuberculosis, Cryptococcal infection and severe bacterial infections
- Rapid initiation of ART (within 7 days)
- Adherence Counselling

PACKAGE OF CARE FOR PEOPLE WITH AHD

	Intervention	CD4 Cell Count	Adults	Adolescents	Children
Diagnosis	Sputum Xpert MTB/RIF as the first test for TB diagnosis among symptomatic people	Any	Yes	Yes	Yes
	LF-LAM for TB diagnosis among people with symptoms and signs of TB	≤200 cells/mm^3 or at any CD4 count if seriously ill	Yes	Yes	Yes (limited data for children)
	Cryptococcal antigen screening	≤200 cells/mm^3	Yes	Yes	No
Prophylaxis and Pre-emptive Treatment	Co-trimoxazole prophylaxis	≤350 cells/mm^3 or clinical stage 3 or 4	Yes	Yes	Yes (regardless of CD4 for under 5)
	TB preventive treatment	Any	Yes	Yes	Yes
	Fluconazole pre-emptive therapy for cryptococcal antigen–positive people without evidence of meningitis	<200 cells/mm^3	Yes	Yes	Not applicable (Screening not advised)
ART initiation	Rapid ART initiation	Any	Yes	Yes	Yes
	Defer initiation if clinical symptoms suggest TB or cryptococcal meningitis	Any	Yes	Yes	Yes
Individualised Adherence Support	Tailored counselling to ensure optimal adherence to the AHD package, including home visits if feasible	<200 cells/mm^3	Yes	Yes	Yes

HIV-2 Treatment

Clinicians should:

- Use the preferred standard First-Line regimen TDF (or TAF) + XTC + DTG
  - o If unable to tolerate DTG, substitute with a Lopinavir-ritonavir when prescribing ART for HIV-2 mono-infected or HIV-1/ HIV-2 co-infected individuals
- Not prescribe NNRTIs (NVP, EFV or RPV) or the PI Atazanavir-ritonavir as part of an ART regimen against HIV-2 mono-infection
- Consult with a provider with the ATCs in the management of HIV-2 where there are doubts before initiating ART in HIV-2-infected patients
- Educate patients with confirmed HIV-2 infection about the types of drugs that can be used to treat it

No randomized clinical trials have been conducted to determine when to initiate ART in the setting of HIV-2 infection, and the best choices of therapy for HIV-2 infection remain under study. Because the optimal treatment strategy for HIV-2 infection has not been defined, the recommendations provided in this section are based on this committee's expert opinion with supporting evidence highlighted in Table 17 below.

Although HIV-2 is generally less aggressive, and progression to AIDS is less frequent, HIV-2 responds less predictably to ART when progression occurs, and response is more difficult to monitor. The standard methods and interpretation protocols that are used to monitor ART for HIV-1-infected patients may not apply for HIV-2-infected patients. Some ART regimens that are appropriate for HIV-1 infection may not be as effective for HIV-2. The following factors should be considered:

- Most HIV-2-infected patients are long-term non-progressors
- HIV-2 may confer more rapid resistance to ART agents because of wild-type genetic sequence that results in a significant increase in resistance to ART agents compared with HIV-1
- Pathways for the development of drug mutations may differ between HIV-1 and HIV-2

Table 17: Preferred First-Line ART And Alternative Regimens For HIV-2

Specific Populations	Description	Preferred 1st line ART	Alternative regimen
HIV-1 / HIV-2 co-infected	Adolescents and adults	TDF (or TAF[a]) + XTC + DTG[b]	TDF (or TAF[a]) + XTC + LPV-r [c] or TDF (or TAF[a]) + XTC + DRV-r or ABC + 3TC + LPV-r or ABC + 3TC + DRV-r or ABC + 3TC + DTG [d]
HIV-1 / HIV-2 co-infected	Children	ABC + 3TC + DTG*	ABC + 3TC + LPV-r or ABC + 3TC + DRV-r

a. TAF should be avoided in HIV/TB patients on Rifampicin-based ATT. Evidence not sufficient/conclusive for use of TAF in such patients
b. DTG is active against HIV-1 and 2
c. LVP-r and DRV-r are active against HIV-2
d. DRV-r can be given to children aged ≥3 years

TABLE 18: EFFICACY OF ANTIRETROVIRAL THERAPY AGAINST HIV-2 INFECTION

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
• Although most in vitro studies have shown that similar concentrations of NRTIs are needed to block both HIV-1 and HIV-2 replication, data suggest that some NRTIs may not be as effective against HIV-2   o for example, HIV-1 more readily incorporates Zidovudine and is more susceptible to Zidovudine than HIV-2, and there is a lower barrier to resistance with HIV-2 than with HIV-1 • Genotypic analysis of HIV-2-infected patients on ART has shown that many of the same amino acid substitutions that are associated with NRTI resistance in HIV-1 may be implicated in HIV-2. Some resistance mutations (*K65R, Q151M, and M184V*) in combination can confer class-wide NRTI resistance and cause rapid virologic failure
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
• NNRTIs block HIV-1 reverse transcription through a specific binding site that is not present in HIV-2; this class of drugs will not be effective against HIV-2 • HIV-2 appears to be intrinsically resistant to NNRTIs; the *Y188L* polymorphism appears naturally in all HIV-2 isolates. Reversion to *Y188* restores the reverse transcriptase sensitivity to some NNRTIs, including Efavirenz • In general, NNRTIs inhibit HIV-2 at effective concentrations that are at least 50-fold higher than those that inhibit HIV-1, making the use of these drugs for HIV-2 infection problematic • Etravirine appears to have limited activity against HIV-2, but this may not be clinically relevant because the mean 50% effective concentration in MT4 cells is 2500-fold higher than that observed for HIV-1
Protease Inhibitors (PIs)
• HIV-2 expresses natural polymorphisms in the protease that may be implicated in emergent drug resistance and accelerate time to development of PI resistance • One study noted that the pathways for HIV-2 protease drug resistance may differ from those for HIV-1 • Saquinavir, Lopinavir, and Darunavir have shown comparable activity against HIV-1 and HIV-2 • Atazanavir has lower and variable activity against HIV-2 in comparison with HIV-1. It should not be prescribed for HIV-2 and in HIV/TB patients on Rifampicin-based treatment • Lopinavir dose should be doubled for HIV/TB patients on Rifampicin-based treatment
Integrase Strand Transfer Inhibitors (INSTIs)
• Dolutegravir is safe for use in HIV-2 • The integrase inhibitors Raltegravir and Elvitegravir have demonstrated activity in vitro. Clinical response to Raltegravir was reported in a patient with highly treatment-experienced HIV-2 infection but the emergence of mutations was reported in another patient
CCR5 co-receptor antagonists
• The activity of Maraviroc has been limited to patients with CCR5-tropic viruses. • Primary HIV-2 isolates can utilize a broad range of co-receptors, including CXCR4, CCR5, CCT-5, GPR15, and CXCR6. This limits the therapeutic utility of Maraviroc in HIV-2 infection
Fusion inhibitors
• HIV-2 is intrinsically resistant to the fusion inhibitor Enfuvirtide

MONITORING HIV-INFECTED POPULATIONS ON ART

Recommendations

- Baseline Viral Load Testing for ALL Populations
- TLD Transition – Transition ALL regardless of Viral Load
- Viral Load Monitoring in HIV Infected Pregnant and Breastfeeding Women: Every 3 months
- Viral Load Monitoring for ALL populations on ART
- Genotype Test after Treatment Failure

CLINICAL AND LABORATORY MONITORING

Monitoring consists of two components: Clinical and Laboratory

- Clinical monitoring includes history and examination, as well as evaluation of adherence, side effects and relevant drug toxicities
- Laboratory tests need to be conducted routinely and as needed (Table 19). It includes CD4 count, viral load and toxicity monitoring

The purpose of monitoring includes:

- Evaluation of treatment response and diagnose treatment failure early
- Evaluation of adherence
- Screening for Pulmonary tuberculosis
- Detection of toxicity to ARV drugs

Viral load is recommended as the preferred monitoring approach to determine the performance of ART in an individual (Figure 20).

SPECIAL NOTES ON BASELINE VIRAL LOAD FOR ALL POPULATIONS

Introduction

The ministry of health has made significant progress towards reaching the epidemic control of HIV with now about 1,200,000 individuals on antiretroviral therapy. With this many people on ART, the HIV programme has prioritized retention and tracking of missed appointments. Programme data shows that up to 30% of those identified as new HIV infections may be individuals already on treatment termed as silent transfers. Further, the positive predictive value of HIV test is thought to reduce as the prevalence of unidentified cases reduce in the community.

It is along these lines that MoH has introduced the baseline viral load testing for all newly identified HIV positive individuals at the entry of care or prior to lifelong ART initiation.

Rationale for Baseline Viral Load Testing

In ascertaining of a Positive HIV Diagnosis

To ensure the quality of the tracking of HIV infected individuals and as an interim measure of HIV testing quality assurance. The baseline VL test shall be collected as part of the initial safety laboratory tests with clear documentation on the requisition form. All HIV positive patients must be initiated on ART as part of the “test and treat” guidelines without waiting for the VL results. The VL testing laboratories will follow standardized procedures on the undetectable VL results. These may be classified as either silent transfers or incorrect HIV diagnosis

For Basis of Future Monitoring

The baseline VL result should be documented as such in appropriate register or the SmartCare system. The result may help for future monitoring of treatment response.

Studies have shown that baseline viral loads exceeding 100,000 copies/mL had lower rates of VL suppression at month one even among people receiving DTG-based regimens. Similarly, children with viral loads exceeding 100,000 copies/mL had poor suppression rates one and three months after initiating ART. (Adapted from: 2021 WHO HIV Guidelines, page 152)

Interpretations of Baseline Viral Load Results

- **Detected Viral Load**: this confirms the HIV infection
- **Viral load >1,000 copies/mL**: This might indicate one of the following scenarios:
    - The patient has not been previously on ART
    - The patient might have been on treatment in a different facility, defaulted or stopped medication. He now presents to another facility as a newly identified HIV positive
- **Viral load 20 to <1,000 copies/mL**: this might indicate any of the following:
    - The patient can be a silent transfer from one facility to another
    - The patient has been self-medicating secretly (e.g., HCWs)
- **Undetected Viral Load**:
    - This might indicate any of the following:
        - Silent transfer
        - False positive is one of the possibilities
        - The patient may be an HIV type 1 (HIV-1) elite controller also called long-term non-progressor. Elite controllers represent a rare group (<0.5%) of individuals with an ability to maintain an undetectable HIV-1 viral load overtime in the absence of previous or ongoing antiretroviral therapy and maintain CD4 count in the normal range

Action to be Taken in Different Scenarios

a. If HIV status is confirmed to be positive, continue with lifelong ART
b. If HIV status is yet to be confirmed, continue with ART until the final HIV status is determined
    - If HIV status is confirmed as positive, continue with lifelong ART
    - If HIV status is confirmed as negative, counsel patient that his/her status is likely negative. Ensure linkage to prevention services and discontinue ART. The patient should be monitored closely (with appropriate HIV tests) for possible viral rebound

Managing HIV Discordant Results and Treatment Interruption in HIV Exposed Infants

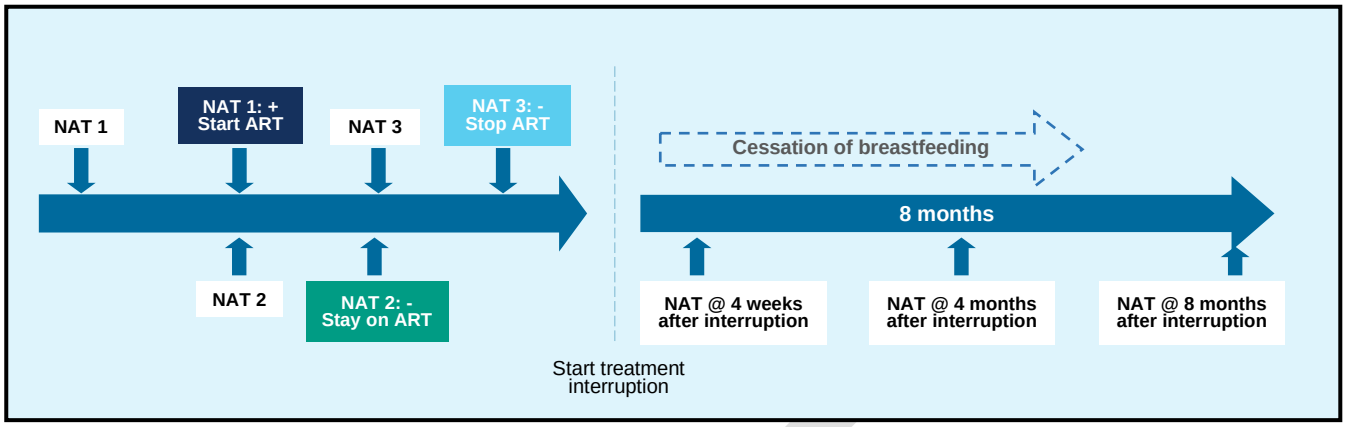
Several factors should be considered when assessing HIV Exposed Infants (HEI) for ART interruption after discordant test results (positive then a negative result) are followed by a third test with a negative result:

- The infant ought to have no clinical signs or symptoms suggesting HIV infection
- A follow-up plan should be agreed on with the family, caregiver(s) and health-care staff
- The tracking information (phone, address, etc.) of the family and caregiver(s) should be collected and confirmed

The following factors should be considered when following up any infant undergoing treatment interruption:

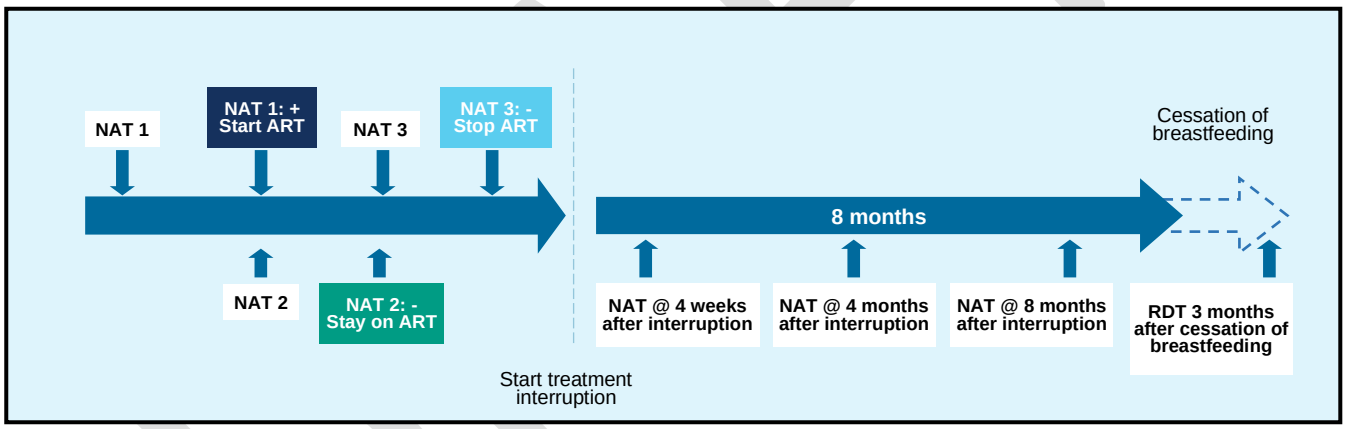
- Active follow-up is needed to ensure that a potentially infected infant is retained in care and reinitiates treatment when viral rebound occurs
- Viral rebound among infants living with HIV starting treatment early is expected to happen within eight months of interruption in >99% of cases
- Infants who develop signs and symptoms indicating HIV infection should undergo immediate- testing
- Breastfeeding and continued risk of transmission require follow-up and appropriate testing throughout the period of risk until final diagnosis
- There is value in minimizing follow-up testing by leveraging existing opportunities for infant testing (based on the national infant testing schedule and immunization or well-child appointment schedules) until final diagnosis is ascertained

Figure 18: Cessation Of Breast-Feeding Occurs Before Completion Of Follow Up Post ART Interruption



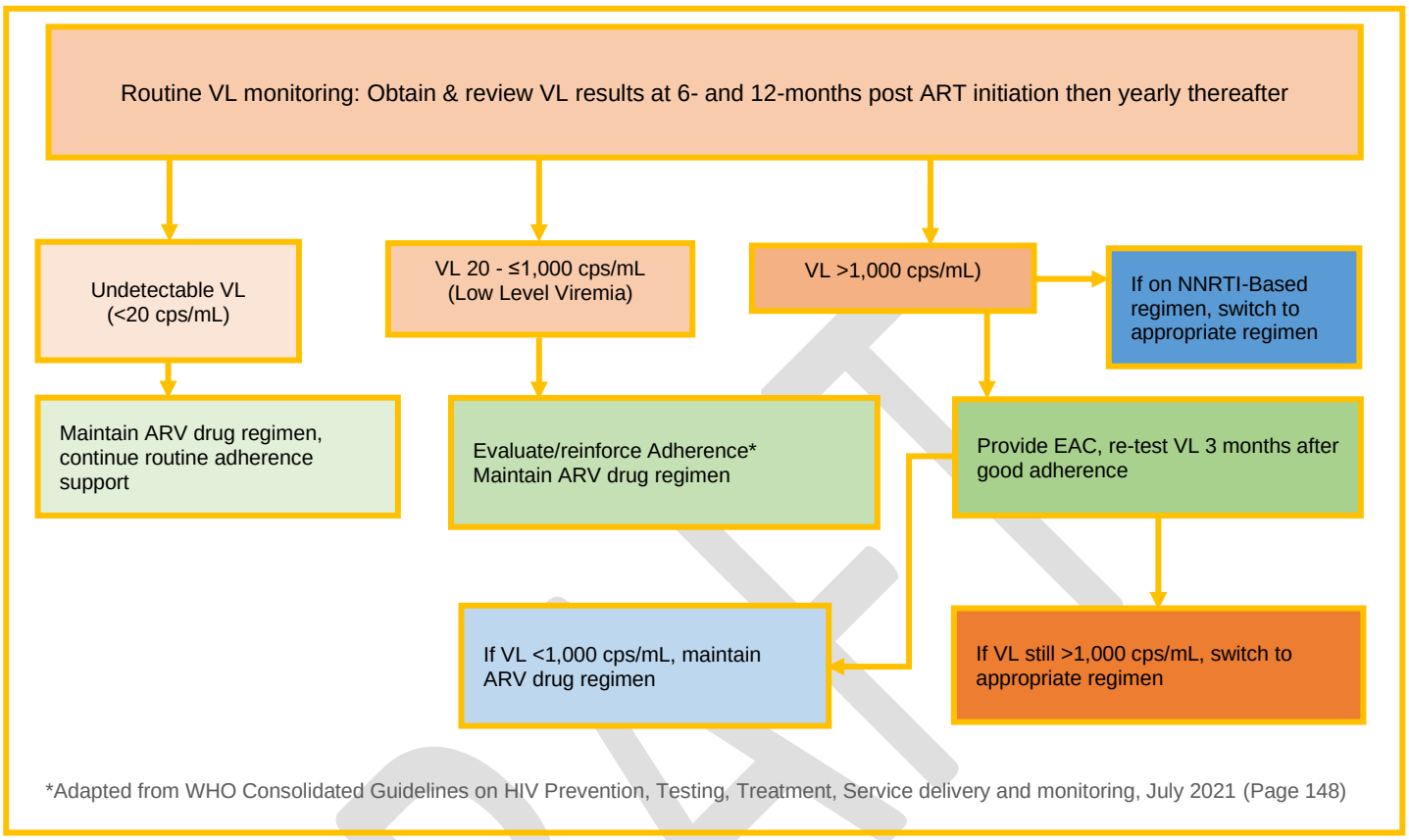
Source : https://apps.who.int/iris/bitstream/handle/10665/273155/WHO-CDS-HIV-18.17-eng.pdf, page 19

Figure 19: Cessation Of Breast-Feeding Occurs After Completion Of Follow Up Post ART Interruption



Source : https://apps.who.int/iris/bitstream/handle/10665/273155/WHO-CDS-HIV-18.17-eng.pdf, page 19

FIGURE 20: TREATMENT MONITORING ALGORITHM FOR PATIENTS ON ART



*Adapted from WHO Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service delivery and monitoring, July 2021 (Page 148)

**Follow normal VL monitoring algorithm. The clinical management of low-level viremia (LLV) remains unclear. LLV ≥ 200 is associated with virologic failure. Persistent viremia ≥ 200 may require more intensive monitoring because of increased risk for virologic failure. (adapted from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6774874/)

OPTIMIZED VIRAL TESTING IN PREGNANT AND BREASTFEEDING WOMEN

To accelerate the progress towards elimination of mother to child transmission of HIV, Viral Load monitoring in Pregnant and Breastfeeding Women (PBFW) should be more stringent. Viral Load monitoring in PBFW should be done every 3 months (Figure 21).

It is recommended that a viral load result should be available within 4 weeks before the Estimated Date of Delivery (EDD). It is also emphasized that in HEIs who have taken prophylaxis for at least 12 weeks, there should be a current suppressed viral load result before stopping the HIV prophylaxis

FIGURE 21: VIRAL LOAD MONITORING IN PREGNANT AND BREASTFEEDING WOMEN ON ART

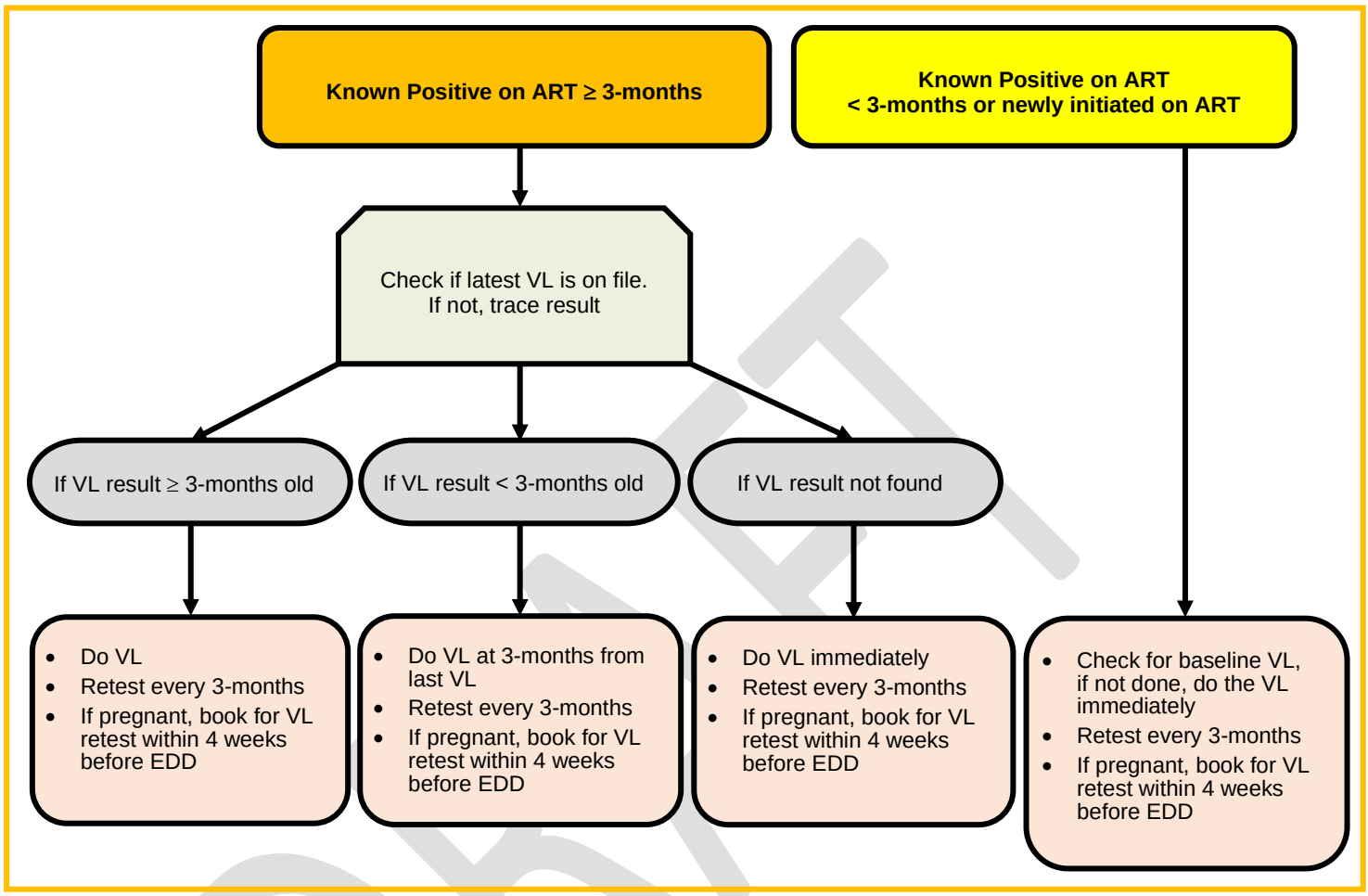


TABLE 19: CLINICAL AND LABORATORY MONITORING – GENERAL ART POPULATION

Timeline	Clinical tasks	Laboratory tests
Enrolment and ART initiation (Baseline period)	• History and examination • Screen for TB • Screen for Cryptococcus for those with AHD • Adherence counselling • PHDP† messages • Initiate ART after adherence counselling • If no signs and symptoms of active TB disease, initiate TPT (i.e., after ruling out TB)	• Serum Creatinine • ALT • Hb or FBC • CD4 count • Baseline Viral Load CrAg Tests for those with CD4 cell count <200 cells/μL or WCS III/IV Urine-LAM CrAg Tests for those with CD4 count <200 cells/μL or WCS III/IV • HBsAg • Syphilis test • Urinalysis for protein and glucose, RBCs • Blood glucose • Cholesterol, and triglycerides (especially if starting PI)
Week 2 post-initiation	• Targeted history & examination • Screen for TB, Cryptococcus (for those with AHD) • Review adherence, side effects, toxicity • Review laboratory tests • Adherence counselling	• Serum Creatinine (if on TDF) • Urinalysis (if on TDF)
Week 4 post-initiation	• Targeted history & examination • Screen for TB, Cryptococcus • Review adherence, side effects, toxicity • Adherence counselling	• Serum Creatinine (if on TDF) • Urinalysis (if on TDF)
Week 12 post-initiation	• Review adherence, side effects, toxicity* • Adherence counselling • PHDP† messages Review laboratory tests • Refill ART with enough supply to next visit (maximum: 3 months of supply)	• Serum Creatinine (if on TDF) • Urinalysis (if on TDF)
6 months post-initiation	• Review adherence, side effects, toxicity* • Adherence counselling • PHDP† messages • Review laboratory tests • Refill ART with enough supply to next visit (maximum: 3 months of supply unless transferred to appropriate DSD models)	• Viral load • CD4 cell count * • Serum Creatinine (if on TDF) • Urinalysis (if on TDF) • Cholesterol, and triglycerides (especially if on PI)
12 months post-initiation and every 12 months	• Review adherence, side effects, toxicity* • Adherence counselling • PHDP† messages • Review laboratory tests	• Viral load • CD4 count * • Serum Creatinine (if on TDF) • Urinalysis (if on TDF) • Cholesterol, and triglycerides

	▸	Refill ART with enough supply to next visit (maximum: 3 months of supply unless transferred to appropriate DSD models)	(especially if on PI)

Those with CD4 cell count >350 cells/μL at baseline and at 6 months of ART with Suppressed viral load should NOT have subsequent repeat CD4 count monitoring as long as the viral load remains suppressed.

TABLE 20: CLINICAL AND LABORATORY MONITORING FOR HIV-INFECTED PREGNANT AND BREASTFEEDING WOMEN

Timeline	Clinical tasks	Laboratory tests
Day 0: Enrolment & ART initiation (Baseline period)	▸ History and examination ▸ If pregnant, focused ANC (FANC) ▸ Screen for TB, Cryptococcus ▸ Adherence counselling ▸ PHDP† messages ▸ Initiate ART after adherence counselling ▸ If no signs and symptoms of active TB disease, initiate TPT (i.e., after ruling out TB)	▸ Serum Creatinine ▸ ALT ▸ Hb or FBC ▸ CD4 count ▸ HBsAg ▸ Syphilis test ▸ Baseline Viral load test Urinalysis for protein and glucose, RBCs ▸ Cholesterol, and triglycerides (especially if starting PI)
Week 2 post-initiation	▸ Targeted history & examination	▸ Serum Creatinine ▸ Urinalysis
Week 4 post-initiation	▸ Screen for TB, Cryptococcus, and other OIs	▸ As needed
Subsequent visits to occur per: ▸ ANC if pregnant ▸ HEI schedule if postnatal and breastfeeding ▸ Adult ART schedule if postnatal and not breastfeeding	▸ If pregnant, ANC ▸ Review adherence, side effects, toxicity* ▸ Adherence counselling ▸ PHDP† messages Review laboratory tests ▸ Refill ART with enough supply to next visit (maximum: 3 months of supply)	▸ Viral load to be done every 3 months during pregnancy and breastfeeding period ▸ Serum Creatinine and urinalysis at every ANC visit ▸ Laboratory testing to occur per: ANC while pregnant except for viral load ▸ VL within 4 weeks before labour & delivery ▸ Cholesterol and triglycerides to be done at 6 months post ART initiation during pregnancy ▸ Follow adult ART schedule when postnatal except for viral load
First postnatal visit	▸ CD4 count to determine need for continuation of Co-trimoxazole	
24 months after delivery	▸ ART dispensed in MNCH until transferred ▸ Transfer to ART clinic for continuum of HIV care and treatment ▸ Earlier transfer or referral may be done for logistical reasons or complicated cases	

† Positive Health Dignity and Prevention (PHDP) includes risk reduction, ART adherence, correct condom use, family planning, STI screening, and partner HIV testing

* See Appendix 3 regarding WHO toxicity estimate

* Consider a woman who fails to initiate ART

Monitoring of Children on ART

In the monitoring of HIV-infected children, the following considerations should be made:

a. Successful outcomes are dependent on the caregiver and hence a holistic counselling with a family-centred approach
b. The weight of a growing child changes regularly and doses must therefore be adjusted accordingly. For this reason, all children below the age of 24 months must be reviewed monthly, and 3-monthly for those 24 months and above once stable on ART
c. Growth and developmental monitoring should be done at every visit

TABLE 21: CLINICAL AND LABORATORY MONITORING FOR HIV-INFECTED CHILDREN (<15 YEARS)

Timeline	Clinical tasks	Laboratory tests
Day 0: Enrolment & ART initiation (Baseline period)	› History and examination › Adherence counselling/treatment preparation › Assisted age-appropriate disclosure counselling › Review Immunization booklet (if eligible) › Review and update growth monitoring chart › Nutrition status assessment › Initiate ART and dispense two weeks' worth of medication › Demonstrate to the caregiver and/or the child how to take ARVs and any other prescribed drugs › Ensure patient/caregiver knows what to do in the event of new symptoms or problems › Screen for TB, Cryptococcus*** and other OIs › If no signs and symptoms of active TB disease, initiate TPT (i.e., after ruling out TB or any other contraindication to TPT)	› Serum Creatinine (or urinalysis for protein and glucose, RBCs) › ALT, AST › Hb or FBC, DC › CD4 count** or CD4% › RBS or FBS › HBsAg › Baseline Viral Load › Syphilis test › Cholesterol, and triglycerides (especially if starting PI) Serum CrAg screening for adolescents with advanced HIV disease
Week 2 post-initiation	› Targeted history and examination › Screen for TB, Cryptococcus*** and other OIs › Review adherence*, disclosure, side effects and toxicity › Assisted age-appropriate disclosure counselling › Review Immunization booklet (if eligible) › Review and update growth monitoring chart › Nutrition status assessment › Adjust ARVs doses if necessary	› Review baseline lab results and take appropriate action if necessary › Serum Creatinine (if on TDF) › Urinalysis (if on TDF)
Week 4 post-initiation	› Targeted history and examination › Screen for TB, Cryptococcus*** and other OIs › Review adherence*, side effects and toxicity › Assisted age-appropriate disclosure counselling › Review Immunization booklet (if eligible) › Review and update growth monitoring chart › Nutrition status assessment › Re-calculate ART dosing based on new weight	› As needed

Timeline	Clinical tasks	Laboratory tests
Week 8 post-initiation	Screen for TB, Cryptococcus*** and other OIs Review adherence*, side effects and toxicity Assisted age-appropriate disclosure counselling Review Immunization booklet (if eligible) Review and update growth monitoring chart Nutrition status assessment Re-calculate ART dosing based on new weight Targeted history and examination Screen for TB, Cryptococcus*** and other OIs Review adherence*, side effects and toxicity	Serum Creatinine (or urinalysis for protein and glucose, RBCs) ALT, AST Hb or FBC
Week 12 post-initiation	Targeted history and examination Screen for TB, Cryptococcus*** and other OIs Review adherence*, side effects and toxicity Assisted age-appropriate disclosure counselling Review Immunization booklet (if eligible) Review and update growth monitoring chart Nutrition status assessment Re-calculate ART dosing based on new weight	Serum Creatinine (if on TDF) Urinalysis (if on TDF) Serum CrAg screening for adolescents with advanced HIV disease
6 months post-initiation	Targeted history and examination Screen for TB, Cryptococcus*** and other OIs Review adherence*, side effects and toxicity Assisted age-appropriate disclosure counselling Review Immunization booklet (if eligible) Review and update growth monitoring chart Nutrition status assessment Re-calculate ART dosing based on new weight	Viral load CD4 count or CD4% Serum Creatinine (if on TDF) Cholesterol, and triglycerides (especially if starting PI) Serum CrAg screening for adolescents with advanced HIV disease
12 months post-initiation and every 12 months	Targeted history and examination Screen for TB, Cryptococcus*** and other OIs Review adherence*, side effects and toxicity Assisted age-appropriate disclosure counselling Review Immunization booklet (if eligible) Review and update growth monitoring chart Nutrition status assessment Re-calculate ART dosing based on new weight	Viral load CD4 count or CD4% Serum Creatinine (if on TDF) Cholesterol, and triglycerides (especially if starting PI) Serum CrAg screening for adolescents with advanced HIV disease

*During adherence assessment, always ask the patient and caregiver to demonstrate how he/she (patient) is taking ARVs and other drugs. Verify if patient is taking correct drug and dosage, not missing appointments, not taking other substances (e.g., herbal medications), not sharing Drugs with others.

**CD4 count/CD4% should be done every 6 months for children below 5 years

***Cryptococcal screening should only be done for children ≥10 years old

MONITORING DRUG SIDE EFFECTS AND TOXICITIES

Serious adverse reactions due to ART are uncommon. Therapy should only be switched in the presence of Grade 3 or 4 adverse drug reactions. Changing an ARV drug should only be done after careful review of adherence. The indication for changing needs to be addressed. A specific ARV drug may be changed (substitution) because of:

- Toxicity, such as anaemia, peripheral neuropathy, lipodystrophy, liver or renal abnormalities
- Intolerance or unresolved and prolonged side effects
- Poor adherence: change indicated only to simplify dosing schedule and to improve adherence
- Occurrence of active TB (refer to section on TB-HIV co-infection)
- Failure (clinical, immunologic, or virologic)

When patients are switched to alternative regimen (see Table 22 below) the goals are to achieve HIV viral suppression, avoid adverse events, and optimize adherence.

TABLE 22: COMMON ART TOXICITIES AND RECOMMENDED SUBSTITUTES (FOR ALL POPULATIONS)

ARV drug	Common associated toxicity	Recommended ARV substitute
ABC	Hypersensitivity reaction	TAF (if CrCl ≥ 30mL/min and weight ≥ 25kg), or TDF (if normal Creatinine Clearance or if child ≥ 30kg), or AZT (if child < 25kg)
ATV-r	Hyperbilirubinaemia,	Substitute LPV-r or DRV-r. If boosted PIs are contraindicated, consider substituting INSTIs (e.g., DTG)
AZT	Severe anaemia or neutropenia, severe gastrointestinal intolerance, lactic acidosis	Substitute TDF or ABC
DTG	Hepatotoxicity, hypersensitivity reactions	Substitute another therapeutic class: EFV or boosted PIs
	Insomnia, body weight gain or obesity**	Consider morning dose or substitute EFV or boosted PI Monitor body weight and promote anti-obesity measures (such as diet and physical exercise). If significant increase despite measures, consider substituting EFV or boosted PI
EFV	Persistent CNS toxicity (e.g., dizziness, insomnia and abnormal dreams) or mental symptoms (anxiety, depression and mental confusion) or convulsions	Substitute DTG or boosted PIs
	Hepatotoxicity, Severe skin and hypersensitivity reactions, gynaecomastia	For severe hepatotoxicity or hypersensitivity reactions, substitute another therapeutic class (INSTIs or boosted PIs)
LPV-r	Hepatotoxicity (common if underlying hepatic disease, coinfection with hepatitis B or C	Substitute another therapeutic class (INSTIs) or boosted PIs
	Pancreatitis (in Advanced HIV Disease, alcohol abuse)	
	Dyslipidemia (Cardiovascular risk factors such as obesity and diabetes)	
	Diarrhoea (Risk factors unknown)	
DRV-r	Hepatotoxicity, Severe skin and hypersensitivity reactions	Substitute with ATV-r or LPV-r. When it is used in third line ART, limited options are available For hypersensitivity reactions, substitute another therapeutic class
NVP (or EFV)	Rash, Stevens Johnson Syndrome, hepatitis	DTG, ATV-r or LPV-r
TAF	Dyslipidemia and Body weight gain (common in female sex, concomitant use of DTG)	Monitor body weight and promote anti-obesity measures (such as diet, physical exercise). If significant increase despite measures, consider substituting EFV or boosted PI
TDF	Chronic kidney disease and Acute kidney injury, Fanconi syndrome, Decreases in bone mineral density, Lactic acidosis or severe hepatomegaly with steatosis	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 TAF may be used if CrCl ≥30mL/min DTG/ATV-r is an option if HIV-1 RNA < 500,000 copies/mL, no HBV, and if there are no contraindications (in consultation with an HIV and/or renal expert) Refer to tertiary level of care if unable to monitor patients with CKD or if deterioration in CrCl falling below 30mL/min

*Hyperbilirubinaemia and icterus do not reflect hepatic disease and are not contraindications to continued therapy. Only substitute ATV-r if the condition is intolerable to the patient.
**For patients with weight gain, a patient centred approach must be taken considering a patient's concerns, the level of BMI (>30) and the proportion of change (>10%). A healthy lifestyle must be promoted. Consider monitoring for serum glucose level, BP and serum lipid level.

SAFETY MONITORING (PHARMACOVIGILANCE)

Pharmacovigilance (PV) relates to the science and activities relating to detecting, assessing, understanding, and preventing adverse effects or any other drug-related problems. Monitoring the safety of medicines is a critical component of Zambia's national patient monitoring system as knowledge of adverse drug reactions and drug interactions helps to generate much-needed safety data to help improve care and treatment outcomes for patients including people living with HIV. It is therefore essential for the review and update of treatment guidelines to include pharmacovigilance. An effective PV system can also reveal problems of irrational use of medicines, medication errors and drug quality issues.

Aims of Pharmacovigilance include:

- Identify signals of previously unidentified adverse reactions to medicines.
- Quickly identify events that are likely to affect adherence to treatment; determine their rates and the risk factors that make these events more likely.
- Estimate rates of events so that the safety of medicines can be compared and informed choices made
- Determine safety in pregnancy.
- Determine safety in children and
- Monitor for new specific toxicities

In Zambia, a cohort of HIV-infected patients on ART has been selected as the principal means of drug-related event monitoring (active pharmacovigilance). This cohort includes patients initiating DTG-based ART regimens and those transitioning from NNRTIs to DTG based ART. Patients will be enrolled as they access their ART services in the various clinics. Monitoring will commence from the time of enrolment for a specified period. The monitoring is prospective, free of selection bias, inceptional (each patient is monitored from the beginning of treatment), dynamic (new patients are added as the program proceeds) and longitudinal (where effects are studied over a known time). Monitoring will involve capturing demographic data and co-morbidities, assessing response to ART and drug-related toxicities.

As part of the process of cohort event monitoring, a pregnancy register will be established in which data will be entered for all women of childbearing age for pregnancy outcomes. Pregnant women who fail to attend the HIV/AIDS clinic for their scheduled visits, follow-up with antenatal clinics or birthing units will be done. See Appendix 8.

The database will be established with all the fields necessary for adequate case assessment, accurate analyses and possible follow-up.

Therefore, all healthcare workers, recipients of care/consumers, manufacturers/distributers and the public are encouraged to report safety issues such as adverse drug reactions, medication errors and quality problems. Everyone is encouraged to report as soon as possible even when not sure or does not have all the information. Reporting can be made using various tools which the Ministry of Health has put in place through the Zambia Medicines Regulatory Authority (ZAMRA). These reporting tools are:

1. Paper ADR report form which can be accessed from your pharmacy department
2. Mobile phone application *Med Safety* for android and IOS platforms, found on Play Store and iStore respectively
3. Electronic reporting form on the ZAMRA website; http://www.zamra.co.zm

NB. Paper ADR reporting forms should be submitted/sent/mailed as soon as possible to:

The National Pharmacovigilance Unit (NPVU)
Zambia Medicines Regulatory Authority
P.O Box 31890, Lusaka, Zambia
Email: pharmacy@zamra.co.zm
Tel: +260211220429

In the event one is unable to submit directly to NPVU at ZAMRA, forms can be submitted through the following reporting centres:

1) ZAMRA regional offices
2) Regional Pharmacovigilance centres
3) District Health Office
4) Provincial Health Office
5) Responsible officer/In-charge of the dispensary or community pharmacy
6) Posted at the nearest post office (Zambia Postal Services)

Where available, active pharmacovigilance or cohort event monitoring should be performed as guided

ZAMRA/NPVU/FORM/0001 version 00

ADVERSE DRUG REACTION, MEDICATION ERROR AND PRODUCT QUALITY PROBLEM REPORTING FORM

(Identities of reporter and patient will remain strictly confidential)

NATIONAL PHARMACOVIGILANCE UNIT (NPVU)

The Director General
The Zambia Medicines Regulatory Authority
Plot No. 6903, Tuleteka Rd, Off Makishi Rd,
P.O. Box 31890, Lusaka, Zambia.

Telephone: +260211220429
Telefax: +260211238458
Email: pharmacy@zamra.co.zm

PATIENT INFORMATION

Patient initials: ..... File No. ..... Age: ..... Weight (kg): .....

Sex: Male ☐ Female ☐ Date of birth: ..... /..... /..... Height (cm): .....

DETAILS OF ADVERSE DRUG REACTION OR PRODUCT QUALITY PROBLEM

I am reporting on: 1) an Adverse Drug Reaction ☐ Date of onset of reaction: ..... /..... /.....

2) a Product Quality Problem ☐ Category: medicine ☐ medical device ☐

Description of Adverse Drug Reaction or Product Quality Problem: .....

.....

.....

1. MEDICINES/ VACCINES/ MEDICAL DEVICES: *(✓) Tick against the **suspected** medicine/ vaccine*
Indicate all medicines the patient is taking

(✓)	Trade/ Generic Name & Batch Number	Dosage & dosing frequency	Route of administration	Start date (dd/mm/yy)	Stop date (dd/mm/yy)	Reasons for use

ADVERSE DRUG REACTION OUTCOME: ***(Tick all that apply)***

Outcome: ☐ Death ☐ Life threatening ☐ Disability ☐ Hospitalization ☐ Congenital abnormality

☐ Other *(specify):* .....

Recovered: ☐ Yes ☐ No If YES, date of recovery: ..... /..... /.....

Additional information *(e.g. Relevant medical history, medicines taken in the last 28 days, allergies, previous exposure, baseline test results/ lab data)*..... .....

.....

2. PRODUCT QUALITY PROBLEM

Trade Name	Batch Number	Registration Number	Dosage Form & Strength	Expiry Date (mm/yyyy)	Size/ Type of container

Product sample(s) have been submitted for evaluation: ☐ Yes ☐ No Number of submitted samples: ☐

DETAILS OF REPORTER

Name: ..... Profession: ..... Signature: ..... Date (dd/mm/yyyy):.....

Contact address: ..... Phone: ..... Email: .....

MANAGEMENT OF TREATMENT FAILURE

Monitoring people on ART is important to ensure successful treatment, identify adherence problems and determine whether ART regimens should be switched in case of treatment failure. Compared with clinical or immunological monitoring, viral load testing provides an early and more accurate indication of treatment failure and the need to switch from first line to second-line drugs, reducing the accumulation of drug resistance mutations and improving clinical outcomes. Measuring viral load also helps to discriminate between treatment failure and non-adherence, following enhanced adherence support. Further, viral load testing gives clients a measure of understanding, control and motivation to adhere to treatment and understand their HIV infection. Viral load testing has been strongly recommended as the preferred approach to monitor treatment among people living with HIV.

TABLE 23: DIFFERENT TYPES OF TREATMENT FAILURE (WHO DEFINITIONS)

Failure	Definition	Comments
Clinical failure	**Adults and adolescents** New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) after six months of effective Treatment **Children** New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical conditions except for TB) after six months of effective treatment	The condition must be differentiated from immune reconstitution inflammatory syndrome occurring after initiating ART. For adults, certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure
Immunologic failure	**Adults and adolescents** CD4 count at 250 cells/mm^3 following clinical failure or Persistent CD4 cell count below 100 cells/mm^3 **Children** *Younger than five years* Persistent CD4 cell count below 200 cells/mm^3 *Older than five years* Persistent CD4 cell count below 100 cells/mm^3	Without concomitant or recent infection to cause a transient decline in the CD4 cell count Current WHO clinical and immunologic criteria have low sensitivity and positive predictive value for identifying individuals with virologic failure. There is currently no proposed alternative definition of treatment failure and no validated alternative definition of immunologic failure
Virologic failure	Viral load >1,000 copies/mL based on two consecutive viral load measurements three months apart, with adherence support following the first viral load test. ART switch after first viral load >1,000 copies/mL for those receiving NNRTI-based regimens	An individual must be taking ART for six months before it can be determined that a regimen has failed Individuals with viral load >20 to <1,000 copies/mL, maintain ARV regimen, EAC may be considered and repeat viral load testing after three months

Genotype Test after HIV Treatment Failure

Genotype test informs the clinician on the type of HIV drug resistance mutations and helps them to select the appropriate drugs for therapy. Routine resistance testing is important for the surveillance of HIV drug resistance in the population. HIV genotype resistance test will only be done on patients failing DTG- or PI-based regimens who completed EAC with a repeat VL test which is >1,000 copies/mL. Genotype testing does not have to be done for patients failing NNRTIs.

The test must be performed only on patients who have evidence of being adherent to ART for at least 30 days. It should NOT be done on patients who are not currently taking ARVs even though the VL is high. Such patients should be subjected to EAC until there is evidence of being adherent to ART. Patients failing First-Line treatment must be switched to the standard Second Line according to the guidelines without waiting for the genotype results. The Second-Line regimen can be modified once the genotype results are out.

Genotype results are interpreted using a standard software (e.g., Stanford Database) and their use to modify the treatment must be done in consultation with an HIV specialist or physician/paediatrician experienced in the management of HIV drug resistance cases.

The test will be performed in centralized laboratories (UTH and ADCH). Therefore, all genotype test samples must be couriered using cold chain at -20°C using Nitrogen or dry ice. See Figure 23

When patients are switched to Second-Line ART regimens, the goals are to achieve HIV viral suppression resulting in reconstitution of the clinical and immunologic status, avoid adverse events, and optimize adherence. LPV-r is the primary recommended Second-Line PI (see Figure 22).

TABLE 24: RECOMMENDED SECOND-LINE ART REGIMENS BY SPECIFIC POPULATIONS

Specific populations	Description	1st line ART used	Preferred 2nd line ART	Alternative 2nd line ART
Children (0 – 4 weeks)	All	AZT + 3TC + NVP		
Children (≥4 weeks), Adolescents and Adults	3 – 24.9kg	ABC + 3TC + DTG	AZT + 3TC + LPV-r	AZT + 3TC + DRV-r[1]
		ABC + 3TC + LPV-r	AZT + 3TC + DTG	AZT + 3TC + DRV-r[1]
	≥25kg	TAF + FTC + DTG[3]	AZT + 3TC + LPV-r	AZT + 3TC + DRV-r[1]
	≥30kg	TDF + 3TC + DTG	AZT + 3TC + LPV-r	AZT + 3TC + DRV-r[1]
		TAF + FTC + DTG	AZT + 3TC + LPV-r	AZT + 3TC + DRV-r[1]
				AZT + 3TC + ATV-r
		TDF + XTC + EFV	TDF + 3TC + DTG[2]	AZT + 3TC + DRV-r[1]
			TAF + FTC + DTG[3]	AZT + 3TC + DTG
				AZT + 3TC + LPV-r
				AZT + 3TC + DRV-r[1]
				AZT + 3TC + ATV-r

1 Only use in children ≥ 3 years
2 Emerging evidence indicates the backbone of TDF + XTC can be maintained or recycled even if used in First-Line
3 Note that evidence not sufficient/conclusive for use of TAF in patients co-infected with TB on Rifampicin-based ATT, therefore avoid use in such patients

TABLE 25: SUMMARY OF PREFERRED SECOND-LINE ART REGIMENS FOR ADULTS AND ADOLESCENTS WITH TB AND HEPATITIS B CO-INFECTION

Specific Conditions	Description	1st line ART used	Preferred 2ndline ART	Alternative 2nd line ART
HIV and HBV Co-infection in Adolescents and Adults	All	TDF + XTC + EFV	TDF + 3TC + DTG	Consult expert opinion
		TDF + 3TC + DTG	AZT + 3TC + LPV-r + TDF*	
		TAF + FTC + DTG		
Children, Adolescents, and Adults Co-infected with TB	3 – 29.9 kg	ABC + 3TC + DTG	AZT + 3TC + LPV-r	
	≥30 kg	TDF + 3TC + DTG		

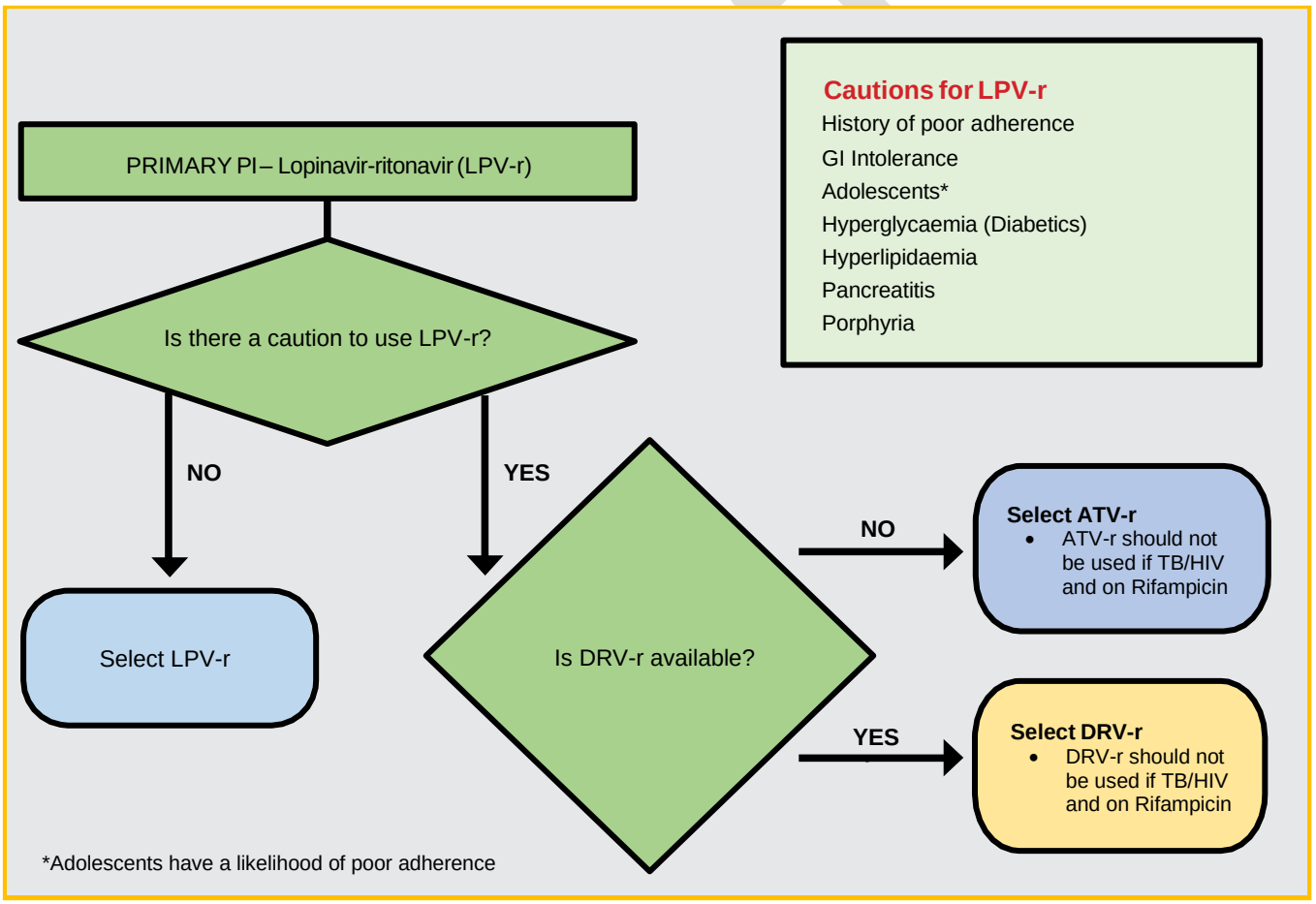
TDF + XTC should always be part of the combination in HBV/HIV co-infections. Since stand-alone TDF is currently not available, use TDF+XTC in consultation with expert or call 7040

TABLE 26: RECOMMENDED SECOND-LINE ART REGIMENS FOR HIV-2

Specific populations	Initial 1st line category	Failing 1st line ART	2nd line ART
HIV-1 / HIV-2 Co-infected	DTG - based First-Line regimen	TDF + XTC + DTG	AZT + 3TC + LPV-r AZT + 3TC + DRV-r[a]
		ABC + 3TC + DTG	
HIV-2 Mono-infected		TDF + XTC + DTG	AZT + 3TC + LPV-r AZT + 3TC + DRV-r
		ABC + 3TC + DTG	

[a] DO NOT substitute with Atazanavir in HIV-1/HIV-2 con-infection or HIV-2 mono-infection. Atazanavir is not active against HIV-2

FIGURE 22: ALGORITHM FOR CHOOSING A PI IN SECOND-LINE



CLINICAL GUIDANCE ON USE OF ATV-R

Administration

- ATV-r is given once a day (300/100mg)
- Do not split or crush ATV-r tablets

Patient Sensitization

- ATV-r is safe for use in pregnancy
- Ensure patients on ATV-r drink plenty of fluids to reduce the risk of kidney stones
- A common side effect associated with ATV-r is jaundice, which is benign, and in most cases should resolve in a few weeks
- Jaundice from unconjugated hyperbilirubinaemia is largely a cosmetic issue and not related to hepatitis or liver damage
- A liver function test, if available, should be conducted to help rule out other causes of jaundice
- If patient has symptomatic or profound jaundice, consult the UTH Advanced Treatment Centre

Contraindications

- **Do not use ATV-r** with Rifampicin-containing TB treatment. If patient is on ATV-r with no exposure to DTG in First-Line and they develop TB replace ATV-r with DTG 50mg twice daily (see Figure 22)
- Do not use ATV-r with proton pump inhibitors (Omeprazole, Pantoprazole, Lansoprazole)
- Substitute PPIs (Omeprazole) with H2 receptor blockers (e.g., Cimetidine). It should be taken 2-3 hours apart with ATV-r
- Do not start patients with pre-existing jaundice or suspected hepatitis on ATV-r

CLINICAL GUIDANCE ON TRANSITIONING OF PATIENTS ON ART FROM EFV-BASED TO DTG-BASED REGIMENS

Transitioning patients on First-Line ART

- Patients on TDF + XTC + EFV should be transitioned to TDF + XTC + DTG regardless of Viral load results
- Patients on TDF + XTC + LPV-r or TDF + XTC + ATV-r should be transitioned to TDF + XTC + DTG or TAF + FTC + DTG with a valid suppressed VL result
- Patients on ABC + 3TC + LPV-r with weight ≥ 30kg and CrCl ≥50 mL/min should be transitioned to TDF + 3TC + DTG with a valid suppressed VL result
- Patients on ABC + 3TC + LPV-r with weight ≥25kg and CrCl ≥30 mL/min should be transitioned to TAF + FTC + DTG with a valid suppressed VL result

PEOPLE RE-ENGAGING WITH CARE AFTER TREATMENT INTERRUPTION OR TREATMENT FAILURE

People re-engaging with care after treatment interruption with AHD should be offered comprehensive clinical assessment. The package should be given to people who are re-engaging with care after a period of ART interruption or when ART fails, and they have developed AHD. Such people are likely to benefit from the same set of interventions as ART-naive people with AHD

People interrupting treatment on a NNRTI–containing regimen are at risk of drug resistance and may require more intensive virological monitoring, and consideration should be given to restarting ART using DTG-containing regimen with a goal of re-establishing viral suppression

For people presenting with diagnosis consistent with clinical failure (defined as a new or recurrent clinical event indicating severe immunodeficiency), WHO recommends viral load testing. CD4 cell count testing is no longer recommended for ART monitoring for people receiving ART who are clinically stable where viral load monitoring is available. However, CD4 cell count testing should be specifically prompted for people with a viral load exceeding 1,000 copies/mL and for everyone whose clinical presentation suggests AHD regardless of ART exposure. For people with suspected treatment failure and AHD, CD4 cell count and viral load should be carried out in parallel.

People presenting with AHD because of treatment failure should also benefit from the advanced HIV disease package. If they are severely ill, an expedited switch to a more efficacious regimen should be considered.

When to stop ART

Patients may choose to postpone or stop therapy, and providers on a case-by-case basis, may select to defer or stop therapy on the basis of clinical and/or psychosocial factors.

The following are indications for stopping ART:

- Patient's inability to tolerate all available ARV medications
- Patient's request to stop after appropriate counselling
- Non-adherence despite repeated counselling: treatment should be stopped to avoid continued toxicity, continued evolution of drug resistance, and transmitting drug resistant HIV
- Unreliable caregiver
- For children, the caregiver is instrumental in ART adherence. Any factors that affect the capability for the caregiver to give medications consistently may be an indication to stop ART in an HIV-infected child
- Serious drug toxicity or interactions
- Intervening illness or surgery that precludes oral intake
- ARV non-availability

Treatment Failure with No Further Treatment Options

Continue the failing ART regimen unless there are intolerable toxicities or drug interactions. Even with treatment failure, the regimen is likely to have some residual antiviral activity. Stopping therapy in the setting of virologic failure can be associated with rapid falls in CD4 counts and development of OIs.

When to Consult or Refer to the Next Level

The following criteria are indications to consult or refer to the next level:

- Suspected hepatotoxicity not responding to standard management (e.g., TB/HIV co-infection treatment, ALT/AST >3-fold of upper limit of normal with symptoms and >5-fold upper limit of normal without symptoms)
- Second-Line treatment failure or inability to tolerate Second-Line therapy
- Complications on PI-based regimen
- Severe or life-threatening adverse reactions
- Inability to tolerate therapy despite change in regimen
- HIV-HBV co-infection with renal insufficiency

THIRD-LINE ART: SECOND-LINE TREATMENT FAILURE

Treatment failure is defined by a persistently detectable viral load >1,000 copies/mL. For adolescents and adults, failure is two consecutive viral load measurements within a three-month interval, with adherence support between measurements after at least six months of using triple combination ARV drugs. For children, viral load may still be detectable at 6-9 months after initiation and does not necessarily mean treatment failure. Viral blips or intermittent low-level viremia (20–1,000 copies/mL) can occur during effective treatment but have not been associated with an increased risk of treatment failure unless low-level viremia is sustained. A repeat blip should be assessed further at the ATC. Additionally, clinical and epidemiological studies show that the risk of HIV transmission and disease progression is very low when the viral load is lower than 1,000 copies/mL.

Provision of Third-Line ART occurs in very rare circumstances and is beyond the scope of most ART providers. All patients being considered for Third-Line ART should have:

- Confirmed Second-Line ART failure (defined by a persistently detectable viral load exceeding 1,000 copies/mL [i.e., two consecutive viral load measurements within a three-month interval with enhanced adherence support between measurements] after at least six months of using Second-Line ART)
- Genotype (resistance) testing (Figure 23) at an Advanced Treatment Centre (ATC) with a complete ART treatment history (i.e., all previous ARV drugs that the patient has taken with duration of use)
- Before starting Third-Line, establish the reason for treatment failure (e.g., poor adherence, suboptimal dosing, drug-drug interactions) and conduct intensive adherence counselling sessions until there is agreement between the patient, provider, and adherence counsellor that the patient is ready to commence Third-Line ART
- Use of treatment supporters for such patients is STRONGLY recommended

The most likely ARVs to be successful in patients who have followed National Guidelines are Integrase Strand Transfer Inhibitors (INSTIs) such as Dolutegravir or Raltegravir and Protease Inhibitors such as Darunavir with ritonavir (DRV-r) plus optimal Nucleoside background (e.g., TDF+XTC)

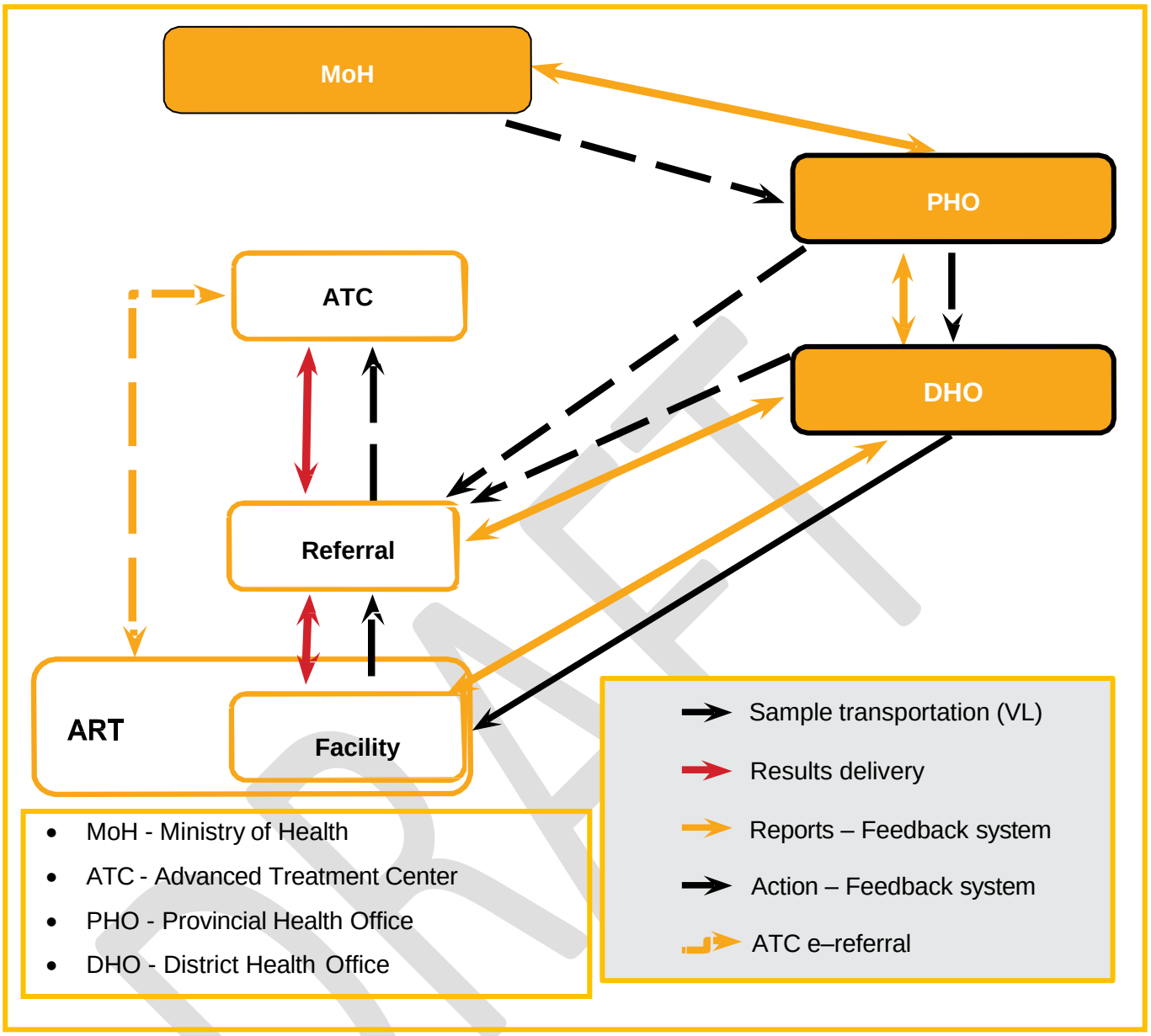
Other considerations with major constraints:

- Etravirine: especially if genotype is available at time of First-Line NNRTI failure, although in some patients NNRTI mutations persist even after non-exposure to NNRTIs in Second-Line
- Maraviroc: needs special tropism test before initiation, which is currently not available in Zambia

Before switching therapy in suspected treatment failure, HCWs need to rule out:

- Poor adherence: change therapy only after enhanced adherence counselling has been conducted
- Immune Reconstitution Inflammatory Syndrome (IRIS): treat underlying condition and continue ART if tolerated
- Untreated OIs: treat underlying condition and continue ART if tolerated
- Pharmacokinetics (e.g., Rifampicin reduces DTG, NVP or LPV-r blood levels): give DTG as BD, switch NVP to EFV or double the dose of LPV-r or switch Rifampicin to Rifabutin
    - Current infections causing transient decrease in CD4 count: treat infection, and if possible, repeat CD4 one month after resolution of illness to confirm immunologic failure

FIGURE 23: INFORMATION PATHWAYS FOR PATIENTS NEEDING ATC SERVICES



NUTRITIONAL CARE

Nutrition in HIV-Infected Children

Routine assessment is essential to identify malnutrition and growth faltering early. The following should be done for HIV-infected infants and children:

- Assess nutritional status, diet, and symptoms at every visit
- Laboratory monitoring includes total cholesterol, triglycerides, glucose, and Hb
- Assess WHO clinical stage, ask about history of recent diseases such as persistent diarrhoea or OIs (associated with increased nutritional needs), determine energy needs, and provide additional energy
- Measure weight and height at each visit and plot against national growth curves
    - Normal growth
    - Underweight (weight-for-age <3rd %)
    - Stunted (height-for-age <3rd %)
    - Wasted (weight-for-height <3rd %)
- If normal child growth, inform on healthy eating and avoidance of obesity
- If poor child growth
    - Full dietary assessment is needed
    - Assessment of drug adherence if the child is on ART
    - Mothers or caregivers should be asked about food availability and food types offered to the child, as well as who feeds the child, how much and how often children should be examined for signs of OIs or wasting
    - Provide appropriate clinical interventions (e.g., food support programs)
- If severe malnutrition
    - Stabilize the acute phase of malnutrition, like HIV-uninfected children with severe malnutrition and initiate ART soon after
    - Immediately initiate ART if unexplained malnutrition (e.g., not associated with untreated opportunistic infection [OI]) and does not respond to standard nutritional therapy
    - If unknown HIV status, test for HIV and consider ART initiation as needed
- If on ART, reassess frequently to adjust dose as needed. Recurrence of growth failure and severe malnutrition may indicate treatment failure, poor ART adherence, or OIs

Nutrition supplementation

- Give high-dose Vitamin A supplementation every 6 months for children 6 to < 60 months old
- Give Zinc supplementation for acute diarrhoea
- Mothers should exclusively breastfeed HIV-infected infants and young children for 6 months minimum and may continue up to 2 years old

Infant and Young Child Feeding

As a public health approach, all mothers should be encouraged to practice exclusive breastfeeding (EBF) for 6 months (Table 27). EBF is defined as giving a baby only breast milk and no other liquids or solids, not even water unless medically indicated. Thereafter, mothers should introduce nutritionally adequate complementary feeding while continuing breastfeeding up to at least 24 months old. Replacement feeding should only be considered if acceptable, feasible, affordable, sustainable, and safe (AFASS).

TABLE 27: INFANT AND YOUNG CHILD FEEDING OPTIONS

Maternal HIV status	Infant HIV status	Recommended Feeding	Timing of Complementary feeding	Recommended Timing of Complete Cessation of Breastfeeding*
Positive on ART	Negative or unknown	Exclusive breastfeeding (EBF) for 6 months Replacement feeding	After 6 months	At 12 months if food security assured Up to 2 years if food security not assured
Positive	Positive	EBF for 6 months		Up to 2 years
Negative or unknown	N/A	EBF for 6 months		Up to 2 years

*HIV-infected women should stop breastfeeding (at any time) gradually within one month

Nutrition in HIV Infected Adolescents, Breastfeeding Women and Adults

- Calculate the body mass index (BMI) = weight/height^2 to determine if the individual is underweight (<18.5kg/m^2), normal (18.5 to 24.9kg/m^2), overweight (25 to 29.9kg/m^2), or obese (≥30kg/m^2)
- If BMI <16kg/m^2 or anaemia (Hb <10g/dL) or has TB, refer for nutrition support programs. Observe closely for treatment complications, such as re-feeding syndrome, undiagnosed OIs, and IRIS
- If BMI >25kg/m^2, provide nutrition counselling, including dietary advice and need for physical exercise
- Table 28 lists some of the specific BMI-related ARV drug risks

TABLE 28: SPECIFIC BMI-RELATED ARV DRUG RISKS

BMI	ARV Drug	Associated Risks	Recommended Actions
<18kg/m^2	TDF	Tubular renal dysfunction Fanconi syndrome	Manage these patients with caution. Consult next level if necessary
>25kg/m^2	AZT	Lactic acidosis Severe hepatomegaly with steatosis	

IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME AND HIV

Immune Reconstitution Inflammatory Syndrome (IRIS) is an exaggerated inflammatory reaction from a re-invigorated immune system presenting as unmasking of previously sub-clinical opportunistic infections OR clinical deterioration of pre-existing opportunistic infections OR development of autoimmune disease.

- Onset: usually within 2-12 weeks after starting ART
- Frequency: 10% among all patients on ART, up to 25% when ART initiated with CD4 < 50 cells/µL
- Risk factors:
    - Initiating ART close to diagnosis of an opportunistic infection
    - Initiating ART when CD4 is less than 50 cells/µL
    - Rapid initial fall in HIV-1 RNA level in response to ART in patients with low CD4 counts
    - Commonly seen with TB, cryptococcal disease, Kaposi's sarcoma, and Mycobacterium Avium Complex infection
    - Patients initiated on DTG and with a low CD4 count have a higher risk of having IRIS

Management of IRIS

- Have high index of suspicion with early complications
- ART should be continued
- If ART continuation is impossible, temporarily interrupt the ART and restart same regimen after OI or IRIS is addressed
- Diagnose and treat OI or inflammatory condition
- Corticosteroid treatment in moderate to severe cases: Prednisolone 0.5-1.0mg/kg/day for 5-10 days

ART ADHERENCE

Recommendations

- Strengthening adherence support interventions at the Community Level
- Enhanced Adherence Counselling (EAC) for ALL patients with unsuppressed Viral Loads 6 months post-ART initiation

Adherence to ART is important to achieve the goals of ART including viral load suppression. Poor adherence to ART is the most important cause of unsuppressed viral load and treatment failure. Adherence assessment and messages must be given to patients during treatment preparation and at all visits whether in the community or at the health facility. This is because the readiness and willingness of patients to adhere to treatment changes over time.

ENHANCED ADHERENCE COUNSELLING (EAC)

Enhanced Adherence Counselling (EAC) is a structured counselling intervention conducted on high viral load or unsuppressed patients (VL ≥1,000 copies/mL) who have been on ART for at least 6 months with the aim of re-suppression (VL <1,000 copies/mL). EAC explores the patients' possible barriers to adherence and identifies together with the patient the way forward. In Patients Living with HIV (PLHIV), VL is a direct indicator of viral replication. Higher VL leads to greater fall in CD4 count. This increases the risk of morbidity, mortality, and transmission of HIV infection to others. Suppressing the VL in PLHIV to <1,000 copies/mL is critical for reducing morbidity, mortality and HIV transmission. The HPTN052 clinical trial has shown that viral suppression due to ART can reduce HIV transmission by up to 96%.

Poor adherence to ART is the most common reason for unsuppressed VL. Several studies have shown that about 30-60% of treatment failures are because of poor adherence. Unsuppressed patients can attain VL suppression after undergoing EAC with a trained healthcare provider. Several studies have shown that EAC leads to viral suppression in over 70% of patients with high initial VL. World Health Organization (WHO) recommends EAC to address this problem. Good adherence to ART is critical to achieving and sustaining VL suppression among PLHIV. Barriers to adherence are categorized as follows; cognitive, socio-economic, behavioural and psychological.

How to Conduct EAC Sessions

The provider will schedule EAC sessions, preferably every two weeks or monthly and spread over a determined period. The number and frequency of EAC sessions will be determined based on the provider's assessment and should be discussed with the patient's and/or treatment supporters. By case to case, less or more sessions might be required before the re-test viral load is done. These sessions should provide an opportunity to administer a client-centred approach to identify barriers and strategies to overcome them. It is encouraged to involve other key stakeholders during the EAC sessions such as treatment supporter (or buddy), Adherence Support Workers (ASWs), pharmacist, etc. It is important to obtain informed consent from the patient who should identify or choose the treatment supporter. It is recommended to provide EAC in a viremia clinic. A multidisciplinary team should be formed in each facility for the viremia clinic. Trained health care worker should take the lead in providing the first EAC session.

Before the Session

The provider(s) must ensure that the following are in place:

- Viral load results
- EAC or high viral load register
- Index register
- Appointment or ART Tracking Register (where available)
- Patient File
- Conducive environment

During Subsequent Sessions

- Build rapport with patient: Introduce yourself, ensure patient is comfortable and reassure the patient on confidentiality.
- Show your appreciation to the patient for coming back to the facility
- Verify and confirm the contact details and viral load results for the patient
- Help patient identify and decide who in their social network may be available to provide immediate support
- Explain to the patient the meaning of "**good adherence**" and its' benefits such as reduction of viral load to undetectable levels and sustained for a longer period, restoration and preservation of immune system, reduction of risk of HIV related infection (also called Opportunistic Infections), improvement in the quality of life and "reduction" or elimination of HIV transmission's risk.
- Always verify the following:
    - Is your patient taking the correct drugs (ARVs)? And is he/she taking any other medication or herbal remedies? (Drug-drug interaction)
    - Is your patient taking the correct dose?
    - Is your patient taking ARVs in the correct frequency?
    - Is your patient taking ARVs at the same time throughout?
    - Is your patient skipping or maintaining appointments?
    - Is your patient sharing drugs (ARVs) with anyone? or
    - Does your patient have any specific challenges you need to know (e.g., alcohol abuse, disclosure, etc.)?
- EAC sessions should be focused on any adherence barriers or gaps identified
- Explain to the patient the meaning of undetected and/or suppressed viral load. Remember to discuss the concept of U=U (Undetectable = Untransmittable)
- Explain to the patient the meaning of high VL result and the negative impact of such a result
- Help patient cope with emotions arising
- Encourage and provide time for the patient to ask questions and discuss their concerns
- Make an active referral to community structures (Community Based Organizations) for psychosocial support
- Provide additional referrals for prevention, counselling, support and other services as appropriate (e.g., mental health services, family planning, ANC, nutritional and TB screening)

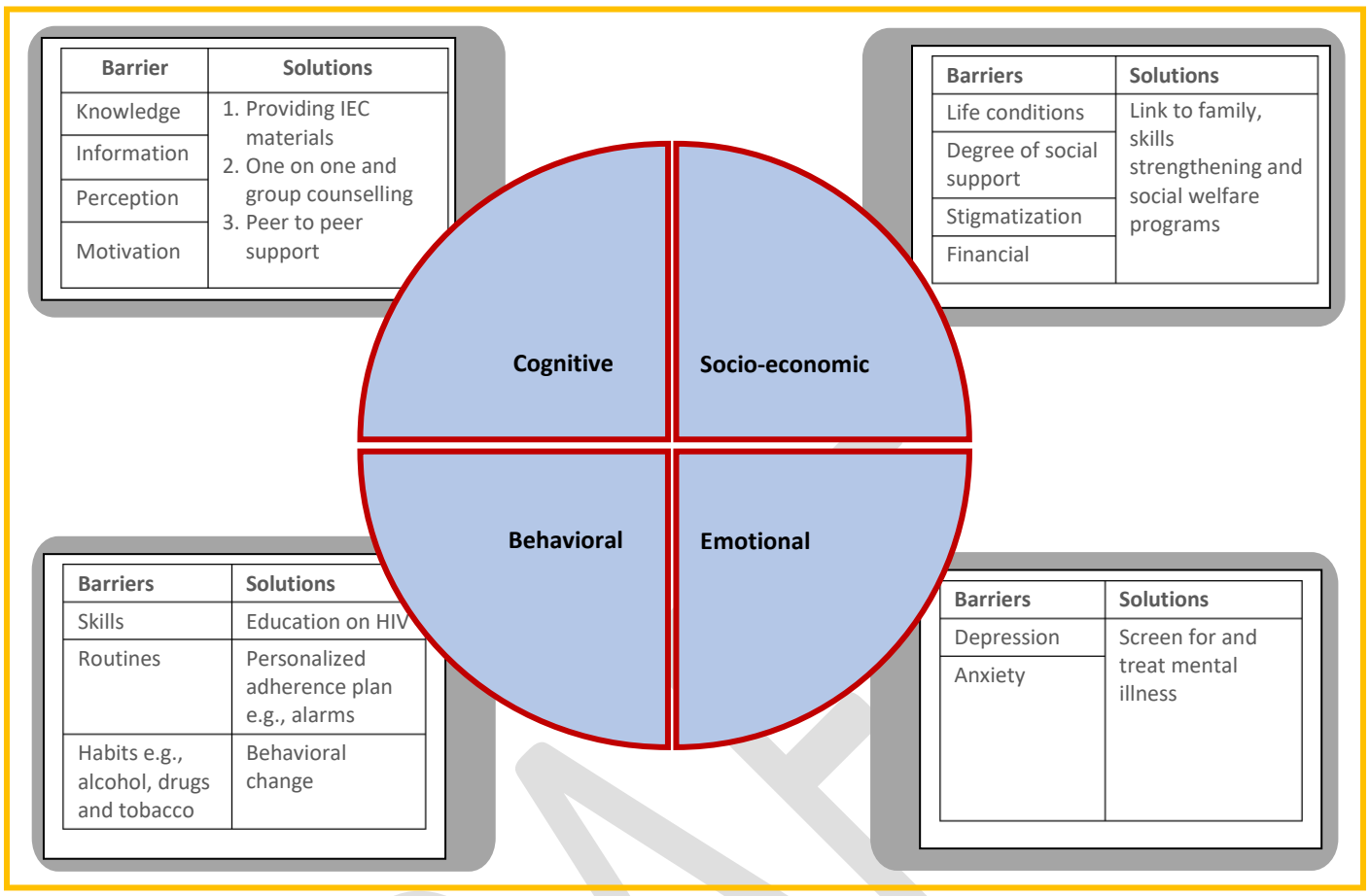
End of the Session

- Discuss any further questions or concerns that your patient may have
- Schedule follow-up visits suitable for both patient and healthcare provider
- Write the date of the follow-up visit in patient's appointment card
- Remind the patient that they shall be followed up through phone or home visit if they miss appointments and obtain consent for patient to be followed
- Provide relevant IEC materials
- Provide hope and encouragement to your patient
- The re-test VL should be done at 3 months AFTER good adherence which will be demonstrated by VL re-suppression

Undetectable = Untransmittable

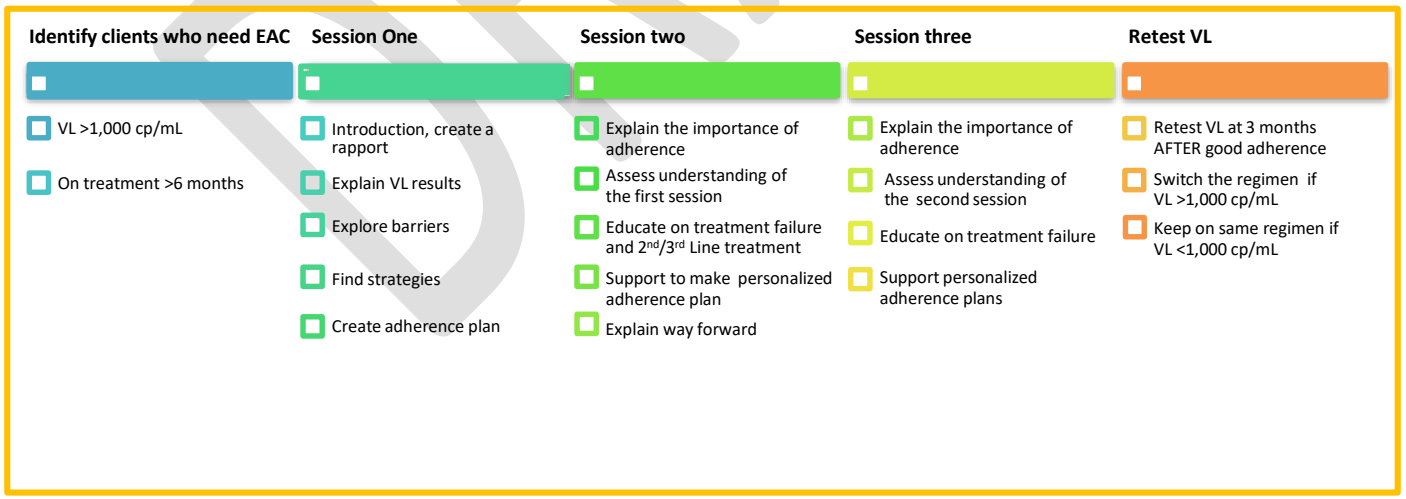
- Scientific evidence shows that an HIV positive individual who has an undetectable viral load is incapable of transmitting the virus. This evidence should be used as an incentive to encourage patients on treatment to adhere to the treatment so that they can reach the undetectable status
- In this regard, HIV discordant couples in need of conception could engage in condomless sex for the purposes of conception. However, the message of U=U must be applied with all other HIV preventative methods such as PrEP, Condoms and Abstinence

Figure 24: Barriers To Adherence



EAC must still be done on all recipients of care with a Viral Load >1,000 copies/mL. A minimum of 3 sessions must be given and a repeat Viral load must be done at the end with an appropriate intervention to the Viral Load test at the end.

Figure 25: Process Of Enhanced Adherence Counselling (EAC)



Summary of Key Points under ART Adherence

Provider-Related Strategies to Improve Adherence

- Establish trust and make sure the patient feels you are there to help manage and solve problems
  - Involve the patient in developing a plan for taking the drugs that is simple and works with the patient's daily activities
  - Educate about goals of therapy, side effects, what will happen if the patient does not take all the drugs
- Treat depression or substance abuse issues
- Treat and manage side-effects
- Monitor adherence at each visit
- Reinforce importance of adherence at each follow-up visit

Ensure patients identify treatment supporters with whom they are comfortable (e.g., family members, buddies) and encourage treatment supporters to attend counselling sessions and clinic visits

Structured treatment preparation before ART initiation (Table 15 and Figure 13) should be conducted for all patients for successful HIV treatment and care. Take note that ART can be initiated during any of these sessions (all patients should be fast-tracked after looking at safety and readiness):

- Session 1: Enrolment and Assessment, HIV education and ART initiation
- Session 2: ART support, preparation and ART initiation
- Session 3: ART education, preparation and ART initiation

Adherence assessment should be done by all members of the healthcare team using:

- Clinical and laboratory parameters
- Patient reports
- Pill counts
- Pharmacy pick-ups
- Other tools of adherence

CONTINUITY OF TREATMENT (RETENTION TO CARE)

Recommendations

- Lost to Follow-up now called "Interruption in Treatment (IIT) at 30 days
- Assignment of an appointment System Manager
- Immediate commencement of tracing of Missed appointment patients
- Screening for TB/OIs at Return to Care

Tracking and Keeping Patients in Care

Keeping patients in care is essential to achieve strong patient outcomes and prevent treatment resistance. Patients having an Interruption in Treatment (IIT), having Refused (Stopped) treatment, and picking up drugs late may lead to treatment failure, emergence of resistance, and the possibility of transmitting resistant virus. Health facilities should aim to do the following to minimize an IIT:

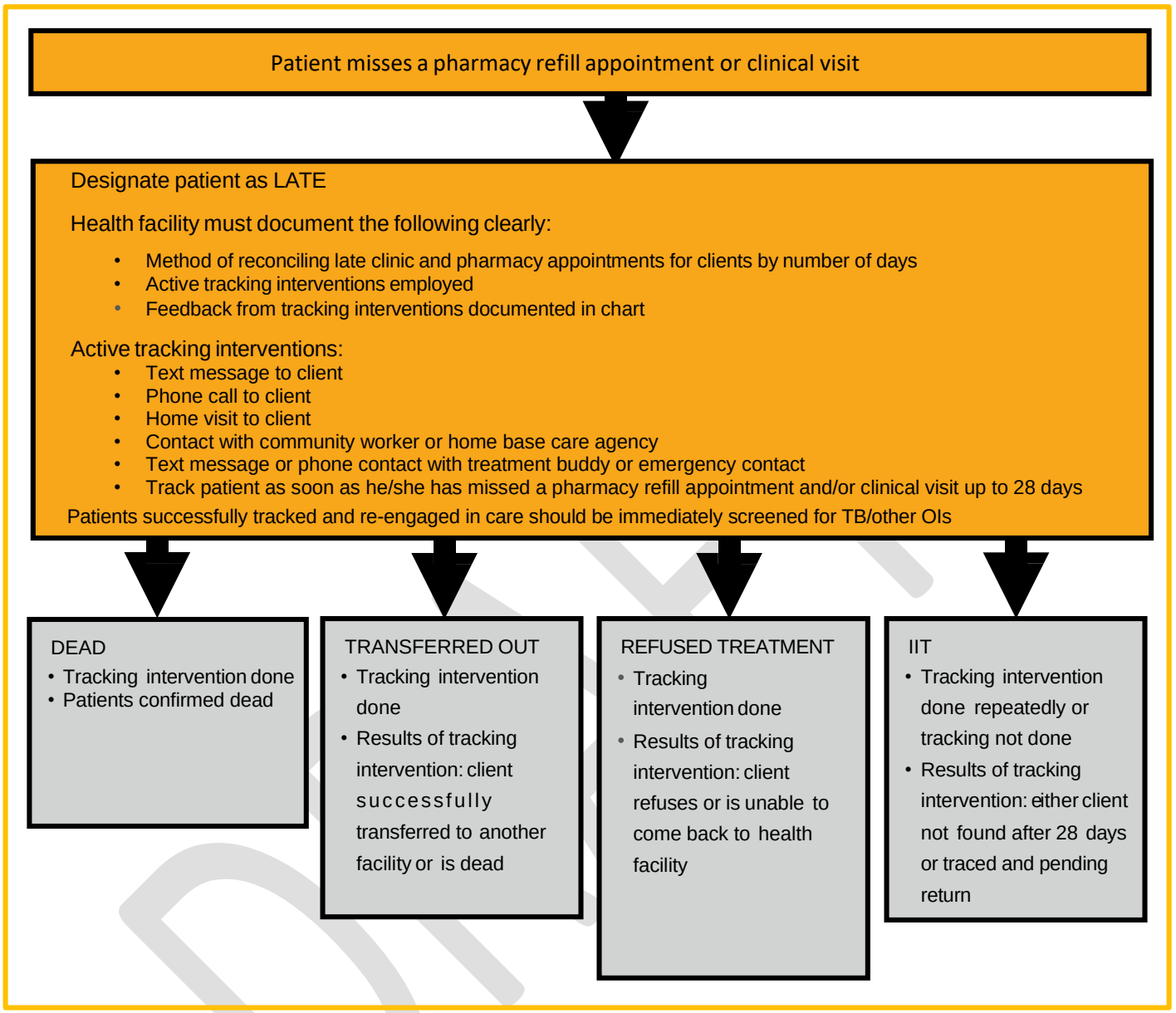
- Actively ensure patient appointments are kept including through structured facility appointment system and reminders
- Have a structured plan to track patients and prevent LTFU
- Monitor all missed clinic and pharmacy visits
- Create linkages with home-based care workers and volunteers
- Dedicate health facility staff to ensure patients who miss visits are contacted

Attrition

Attrition in an HIV program can occur as the following: Late, IIT, refused (Stopped) treatment, died, transferred out to another facility.

- Late: HIV-infected individual misses a scheduled pharmacy refill visits and/or clinical appointment
  - Take immediate action (e.g., CHW follow up, text message or mobile health [mHealth] follow up) within 24 hours and document findings. Every effort must be made to re-engage these patients in care
- IIT: HIV-infected individual (including PBFW and children) has not been traceable for ≥28 days after missed pharmacy refill visit despite exhausting all active tracking interventions (e.g., documented physical follow-up to home, phone calls to client and emergency contacts, text message recall, treatment buddy)
- Refused (Stopped) Treatment: HIV-infected individual has been located while late or IIT, but chooses not to return to care
- Died: the client was confirmed as dead by direct observation or by unambiguous report of family or close contact; it should not be presumed
- Transferred out to another facility: Patient was confirmed to be successfully transferred to another facility. It includes both silent transfers and down-referrals

FIGURE 26: ALGORITHM FOR ACTIVE INTERVENTIONS WHEN HIV-INFECTED CLIENTS ARE LATE AND DETERMINING THEIR ATTRITION STATUS



Structured Facility HIV Appointment System

A missed appointment is the first step of a patient's fall-out of care. Therefore, all ART centres must have a dedicated individual to manage the appointment system. Ideally, a list of scheduled appointments should be prepared a few days before the scheduled appointments and patients must be reminded to come for their appointments. Those who miss appointments should be tracked as soon as possible. Tracking methods should be comprised of 6 attempts using different modalities before a patient is said to be LTFU.

Each day that elapses after missed appointment could be a day without ART and increases the likelihood of resistance development and treatment failure. Scheduling patients for appointments and reviewing the list of patients expected on a given day is critical to tracking patients' missed appointments. All patients who are tracked must be documented in the community ART register or equivalent, including the outcome of the tracking process.

ADOLESCENTS AND HIV

Recommendations

- ALL facilities to have adolescent friendly spaces
- Adolescent led adolescent services
- Standardized Adolescent Transitioning to Adult Care
- Standardized HIV status Disclosure Processes

Adolescents 10-19 years old comprise one sixth of the world's population with almost 90% residing in low to middle income countries. Worldwide in 2018, 1.65 million adolescents were living with HIV and an estimated 190,000 were newly infected with HIV. The situation is especially dire for adolescent girls, who account for 74% of the adolescents acquiring HIV.

In Zambia nearly twice the proportion of males (17.1%) aged 15-24 years compared to females (9.5%) in the same age bracket reported having sexual intercourse before the age of 15 years. HIV prevalence among those aged 20-24 years is four times higher among females (8.3%) than among males (2.0%). The prevalence of VLS ranged from 30.7% among HIV-positive individuals aged 15-19 years to 79.0% among those aged 55-59 years. The disparity in HIV prevalence between males and females, particularly in those aged 15-24 years, suggests an increased focus on early testing and ART initiation for adolescent girls and young women as well as the need for preventative services.

Addressing the distinct and diverse needs of adolescents living with HIV to improve their HIV-related outcomes requires a comprehensive and integrated approach. There is thus a need to have policy direction on how to set priorities for, plan, implement, monitor and evaluate adolescent health programs, including HIV.

In addition to the routine services needed by adolescents, adolescents living with HIV need additional specific HIV-related services that support access to HIV prevention, testing, disclosure of their HIV status, linkage to treatment and care, retention, adherence and viral load testing. See Table 29 for the National Standards for Quality of Healthcare Services for adolescents.

TABLE 29: NATIONAL STANDARDS FOR QUALITY OF HEALTHCARE SERVICES FOR ADOLESCENTS

Standards	Description	Example of activities implemented to attain this standard
Adolescents' health literacy	The health facility implements systems to ensure that adolescents ▪ Are knowledgeable about their own health and ▪ Know where and when to obtain health services	Training of peer supporters and adolescents living with HIV in HIV prevention and sexual and reproductive health to address misinformation regarding HIV from social media, friend groups or others, incorrect knowledge regarding HIV by their caregivers, training of unsupportive (emotionally, financially, etc.) caregivers etc.
Community support	The health facility implements systems to ensure that parents, guardians and other community members and community organizations recognize the value of providing health services to adolescents and support such provision and the utilization of services by adolescents	▪ Adolescents living with HIV and their caregivers join clubs and are involved in both joint and separate activities ▪ Conducting sensitization and community dialogue sessions within schools, universities, and colleges to eliminate stigma and promote testing, community dialogues with traditional and religious leaders, engaging community and adolescents through sporting and traditional activities
Appropriate Package of services	▪ The health facility provides a package of information, counselling, diagnostic, treatment and care services that fulfils the needs of all adolescents ▪ Services are provided in the facility ▪ and through referral links and outreach	Facilities which provide routine adolescent care and treatment should be assessed and improved to ensure the inclusion of adolescent friendly considerations, such as: ▪ Separate clinic space whenever possible or separate waiting areas within adult or paediatric clinics ▪ Optimized clinic flows to ensure privacy and minimize wait time ▪ Flexible clinic hours (to ensure clients do not miss school, etc.) ▪ Non-judgmental providers ▪ Alternative service delivery settings, such as school and youth venues ▪ Greater assurances of confidentiality ▪ Provision of education to increase awareness of the need for, and decrease fear of testing, care and treatment ▪ Integrated services (e.g., SRH services, GBV care, nutrition services, trauma counselling, etc.)
Providers' competencies	▪ Health-care providers demonstrate the technical competence required to provide effective health services to adolescents ▪ Both health-care providers and support staff respect, protect and fulfil adolescents' rights to information, privacy, confidentiality, non-discrimination, non-judgmental attitude and respect	Training of health-care workers at service delivery points on providing adolescent-friendly health services within a comprehensive service package for peers, HCWs, and caregivers

Standards	Description	Example of activities implemented to attain this standard
Facility characteristics	The health facility has convenient operating hours, a welcoming and clean environment and maintains privacy and confidentiality. It has the equipment, medicines, supplies and technology needed to ensure effective service provision to adolescents	▪ Separate space for young people ▪ Special times when young people can receive services ▪ Convenient hours ▪ Convenient location ▪ Adequate space and privacy ▪ Comfortable, youth-friendly surroundings ▪ Availability of Peer Educators
Equity and non-discrimination	The health facility provides high-quality services to all adolescents regardless of age, sex, marital status, education level, ethnic origin, sexual orientation, sexual behaviour or other characteristics	▪ Services provided free of charge with no out-of-pocket expenses ▪ Client satisfaction survey done periodically to get feedback for improvement ▪ Involvement of multi-layered and multi-sectoral agencies, including social protection services and the district/provincial health team
Data and quality improvement	▪ The health facility collects, analyses and uses data on service utilization and quality of care, disaggregated by age and sex, to support quality improvement. ▪ Health facility personnel are supported in participating in continual quality improvement	▪ Develop and implement a monitoring and evaluation framework that clearly defines process and outcome indicators ▪ Develop and implement standard data collection tools at the facility level and a reporting template that capture age, sex and outcomes ▪ Adolescents need to be involved in the facility data reviews and should be active participants in QI teams ▪ Adolescent focused/led QI teams to routinely review disaggregated data and brainstorm for solutions with health facility staff and district teams
Adolescents' participation	Adolescents are involved in planning, monitoring and evaluating health services and in decisions regarding their own care and in certain appropriate aspects of service provision	▪ Implementation of youth advisory groups and processes for design, implementation and feedback on services ▪ Peer supporters taking part in relevant health team meetings such as case reviews and advocacy for adolescent-friendly health services ▪ Training peers to be self-health managers, to be self-motivated and be a source of positive peer pressure to others

Adolescent Considerations for HTS

The legal age for consent to HTS in Zambia is 16 years and above. For adolescents less than the legal age of consent, parental consent should be sought, and the adolescent should assent.

Assent refers to children's and adolescents' participation in decision-making on health care and research intervention(s) by giving an agreement. Assent is not regulated by law as is consent and is good practice in dealing with patients. It emphasizes that, in all cases, the child/adolescent has been adequately informed, and non-forced and non-rushed agreement of the adolescent has been obtained.

Where a guardian is not available to give consent for HIV testing, the adolescent may give consent if they fall under the following risk groups: Abused child, Married, Pregnant, high HIV-risk behaviours such as commercial sex work, engaging in sexual activity with multiple partners, or refusal to use condoms and Head of household.

NOTE: Special attention in terms HTS should be given to adolescents who are or have been; In prisons and other closed settings, in orphanages or boarding schools, children of chronically ill caregivers and Street or abandoned children.

Disclosure

Disclosure is an ongoing *process* of 1) informing the adolescent that she or he is HIV infected and helping him or her understand what that means and, 2) helping the Adolescents Living with HIV (ALHIV) to disclose her or his status to others. It is understood that this process may take place gradually over a period to ensure that the adolescent has an eventual full understanding of his/her diagnosis and feels empowered to take responsibility of his/her health.

Disclosure can be 1) **Partial disclosure** (usually done at age 5-10) done incrementally in age/developmentally appropriate language, or 2) **Full disclosure** (usually done at 10-14) resulting in full knowledge of HIV status, transmission and treatment and integration into a peer/adolescent model. The disclosure process can either be **Care giver initiated**, **HCW assisted,** or **Adolescent initiated**.

Benefits to disclosure may include prevention of onward transmission and support (psychosocial, financial, etc.), improved adherence and care giver relationships, and empowered adolescents.

Risks to disclosure may include violence from sexual partners, stigmatization, discrimination, abandonment, and or other legal consequences. HCWs should support psychosocial issues associated with disclosure using tools like HEADSS. Psychosocial challenges can be at the individual adolescent, family and community level. For additional information, consult the 2020 Zambia National Adolescent HIV Training Package (also see Table 30).

TABLE 30: STEP BY STEP GUIDE FOR CONVERSATION TO CHILDREN ON DISCLOSURE

VERY YOUNG (0-4 yrs old)	YOUNG CHILD [(PRE SCHOOL) 5-7 yrs old]	SCHOOL CHILD (8-11 yrs old)	SCHOOL CHILD (11-14 yrs old)
NO DISCLOSURE YET	**EARLY DISCLOSURE**	**PARTIAL DISCLOSURE**	**FULL DISCLOSURE**
DEVELOPMENTAL LEVEL • Depends on adults for all needs and information • Child needs comfort, support and most of all security **WHAT DO YOU EXPLAIN:** • Carry on consultation with child present • Child too young for direct information about HIV but explanations to caregiver about how HIV can affect the child remain important • Provide ideas to help caregiver support child taking medication • Congratulate child on taking medicines well • Address caregiver anxieties • Build relationship with the child through play /singing **AIM** BUILD UP CONFIDENCE of CHILD in HEALTH WORKERS and MEDICINE TAKING	**DEVELOPMENTAL LEVEL** • Can understand concrete based ideas e.g., new events in the present and past • Thinking is based in the present • Take the lead from confidence of caregiver interactions with health care workers • Beginning to link medicines and health **WHAT DO YOU EXPLAIN:** • Child needs to learn about illness but not HIV by name yet • Introduce ideas of good and bad by eating healthy food, keeping clean, exercising, looking after teeth, etc. • Medicines help to keep the body healthy and strong • Introduce infections as 'germs' that can hurt or damage the body/make you sick or hurt • Introduce (white) blood cells as the part of the body that look for and kill infections or germs • Some germs hide and you need to take medicines to help fight them **AIM** UNDERSTANDING that MEDICINES SUPPORT the body to KEEP WELL	**DEVELOPMENTAL LEVEL** • Able to hold on to ideas and apply them to new situations • Can understand past, present and future • Has social and moral awareness about right and wrong behaviour • Beginning to be more curious and take some control over their lives **WHAT DO YOU EXPLAIN:** • Explain that the germ concerned is a virus • Viruses are 'clever germs' which can damage white blood cells • If medicines are not taken correctly, the virus can get stronger and stop the medicines working (resistance) • Naming of virus as HIV may occur but not essential • Need to explain that information is private and should only be shared with those agreed with the caregiver(s) • Help the child identify who they can talk to about their health or HIV • Disclosure to symptomatic school age children is strongly encouraged **AIM** Naming of INFECTION as HIV	**DEVELOPMENTAL LEVEL** • More abstract thinking (understands future consequences of actions) • Increasingly making decisions on their own regarding identity, independence, school, career • Puberty /sexual development • Dependence on caregivers decreases • Importance of relationships with friends increases **WHAT DO YOU EXPLAIN:** • Check understanding of health, medicines, sexual development and HIV infection • Directly address young person during clinic consultations • Need to understand responsibility for not transmitting HIV i.e., abstinence and knowledge on HIV transmission, their rights i.e., confidentiality and self-dignity • Preparation for future, encourage direct involvement in discussions and decisions • Promote the benefit of attendance at adolescent support groups **AIM** FULL UNDERSTANDING of RIGHTS and RESPONSIBILITIES. ABILITY to NEGOTIATE own HEALTHCARE

TRANSITIONING FROM ADOLESCENT TO ADULT CARE

Transitioning is a multifaceted, active process that attends to the medical, psychosocial and academic or vocational needs of an adolescent as they move from adolescent to adult focused health services. Transitioning can be from adolescent to adult care setting or transitioning within the same facility, e.g., where an adolescent changes clinic day.

Challenges to Transition include worry and anxiety of adjusting to the increased responsibility and expectation in the adult care setting, fear of the loss of stable and long-term relationships with paediatric and adolescent healthcare team, lack of trained staff on the receiving side and poor communication between the two teams (referring and receiving teams).

Preparation for Transitioning

Transitioning to adult C&T is a process and requires prior planning and careful implementation. The adolescent should be involved in the planning of her or his transition as early as possible. For further guidance on readiness checklist and transition process timeline, refer to Appendices 9 and 10.

Evaluation after transition

The receiving team (adult care team) should assess the following: patient's self-involvement in their care (multiple missed appointments, discontinuation of medications and substance use or other behaviours), patient barriers, patient support needed and solutions, referrals for psychosocial/mentorship support.

MIGRANTS AND MOBILE POPULATIONS AND HIV

Recommendations

- Inclusion of Migrants and Mobile Populations (MMPs) in prevention and control of HIV/AIDS
- Strengthening Treatment Compliance among MMPs Migrants and Mobile Populations

The role of migrants and mobile populations (MMPs) in the spread and control of HIV/AIDS is increasingly being recognized and understood.[1] While migration does not automatically equal HIV/AIDS vulnerability, and not all MMPs are at increased risk of HIV/AIDS as a result of their mobility, in many contexts MMPs are exposed to a unique set of socio-cultural, economic and environmental factors that render them more vulnerable to HIV/AIDS including lack of access to health services, information and environments that are conducive to engaging in high-risk behaviour. A rise in migration globally poses a unique set of challenges in ensuring access to HIV/AIDS prevention, treatment, and care for mobile populations. Ongoing humanitarian emergencies resulting in human mobility continue to play a role in exacerbating the spread and impact of HIV/AIDS. There is need to have the health system pay particular attention to migration as social determinant to health, especially HIV.

Zambia has identified population mobility and labour migration as among the key drivers of the HIV epidemic, including migrants and mobile populations among the key populations (NAC, 2017). According to the 2018 ZDHS, the national HIV prevalence was 11.2 per cent (7.5% for males and 14.2% for females). Mobility and labour migration are listed among practices driving the epidemic in Zambia.[2] Migration for work or secure a livelihood is common in Zambia, with migrants often moving across provinces in search for employment. Regions where this is more common, such as Lusaka and Copperbelt sit alongside the main transport routes - in these areas, HIV prevalence is higher than in other regions.[2]

The large mobile groups in Zambia include long distance truck and public service vehicle drivers, sex workers, fishermen/women and fish traders, seasonal agricultural workers, cross border traders (especially young girls), miners, uniformed services personnel, prisoners, and refugees. The food crisis also results in population movements. It's also important to note that some migrants come from neighbouring countries while others come from regions where the nature of the HIV epidemic is different, use different prevention and treatment protocols etc. Some are returning migrants coming back to their country of origin and need to be integrated into the national HIV case management system.

There is need to address the HIV/AIDS vulnerability and risk faced by migrants and mobile people and to ensure universal access to HIV diagnostics, prevention, treatment care and support as well as to enhance understanding on the complex interaction of HIV/AIDS and migration and to counter myths and stigma towards migrants regarding their access to health services.

In relation to HTS, there is need to consider the fact that MMPs equally have an increased HIV risk and vulnerability which may be exacerbated by inadequate access to HIV prevention, treatment and care services and the fear of being stigmatized for seeking HIV-related information and support. Therefore, there is need for HTS to include the full range of services that should be provided together with HIV testing coupled with counselling (pre-test information and post-test counselling). These services should be all inclusive covering MMPs for the country to control the epidemic and health care works will need to be orientated on issues affecting migrant and mobile population to improve the attitude and practice in service provision particularly to these vulnerable populations.

References

HIV/AIDS and Population Mobility, IOM, July 2018

[2] *https://www.unaids.org/sites/default/files/country/documents/ZMB_narrative_report_2014.pdf*

Strengthening treatment compliance amongst migrants and mobile populations

More often ART guidelines provide only a menu for when to start treatment, what regimens to use, what clinical criteria to follow for treatment provision, and how to monitor treatment response. Migrants' populations, displaced people, mobile populations and those with a history of mobility are at a higher risk of infection, and are facing challenges in accessing care, and have a higher risk of poor adherence, treatment interruption, loss to follow-up and treatment failure. Specific emphasis is therefore deemed necessary not only due to the unique characteristics of these populations, but also due to their specific vulnerabilities and frequent exclusion from HIV/AIDS related services. Failure to provide HIV prevention and care to displaced persons not only undermines effective HIV prevention and care efforts, but it also undermines effective HIV prevention and care for host country populations.

These national guidelines highlight the importance of supporting health workers through the patient treatment process (from preparedness and initiation to adherence and treatment continuity) with detailed reference a patient's history of or intention.

Some overall principles to be taken in consideration are as follows:

- ART is a lifesaving intervention. As with all patients, regardless of migration or displacement status, ART should be initiated based on the national guidelines
- A history of displacement or the possibility of travel should not be a reason to deny or delay treatment, although there may be modifications to the treatment plan
- At follow-up, as with all patients, the focus should be on supporting the patient's ability to adhere to treatment
- Among those patients whose treatment has been interrupted, the focus should be on preventing treatment interruptions in the future and re-initiating treatment as quickly as possible

Travel away from home is a primary adherence challenge both for the general population and migrant and crisis-affected populations. Travel may be foreseen and predicted (e.g., seasonal migration, work-associated mobility, or travelling home for holidays) or unplanned (e.g., conflict and natural disasters that could lead to forced displacement). A treatment travel should be discussed and developed with the patient before and at treatment initiation. This plan should be reviewed and updated during every follow-up visit. The plan may include a combination of the following strategies:

- when possible, provide the patient with a health travel card in different languages with at least the following information: Name, regimen, last viral load and/or CD4 and date, concomitant medications and date. Health travel cards may be lost so patients should be aware of their basic medical history and be able to relate it verbally or store it on their mobile phones
- advise the patient to inform the clinic in case of any planned travel so that the following can be provided:
    - referral letter detailing the patient's condition and treatment history. Note that due to language differences, the healthcare worker at the destination site may not speak or read the referring site's language. Use generic names and terms (e.g., tenofovir, TB, cryptococcal meningitis) and internationally agreed upon abbreviations or acronyms (e.g., PMTCT for prevention of mother-to child transmission and HTC for HIV testing and counselling)
    - refill of 3 months if possible and perhaps even longer can be provided. Where longer refill times are not possible, consider providing an emergency supply of ART to be used in case of urgent travel (2–4 weeks will allow the patient sufficient time to make alternative plans for ART access). This emergency stock has to be rechecked routinely to examine the expiry date and is much less desirable than longer routine refills
    - a treatment map detailing alternative sites for ART refill depending on anticipated travel
- In case of unavoidable ART disruption, counsel the patient to:
    - seek continued care only through public or reputable programmes and to seek advice on safe interruption
    - avoid sharing ART and/or reducing or interrupting ART to extend the stock lifespan

Summary/Key Points

- Remember that migrants, emergency-affected and other mobile populations may be susceptible to discrimination, violence and abandonment, and other negative consequences upon disclosing their HIV positive status, therefore particular efforts may be needed to protect their privacy and safety
- There is need to identify key populations who are at increased risk for HIV acquisition and are bound to be stigmatized and discriminated against because of their behaviour, including Sex Workers (SWs), Men who have Sex with Men (MSM), transgender people (TG), People Who Inject Drugs (PWID)
- As with all patients, regardless of migration or displacement status, ART should be initiated based on the national guidelines
- Healthcare workers should be trained to provide non-stigmatized and non-judgmental services to MMPs and ensure that adequate referrals for care, treatment and support are offered

CO-MORBIDITIES

Recommendations

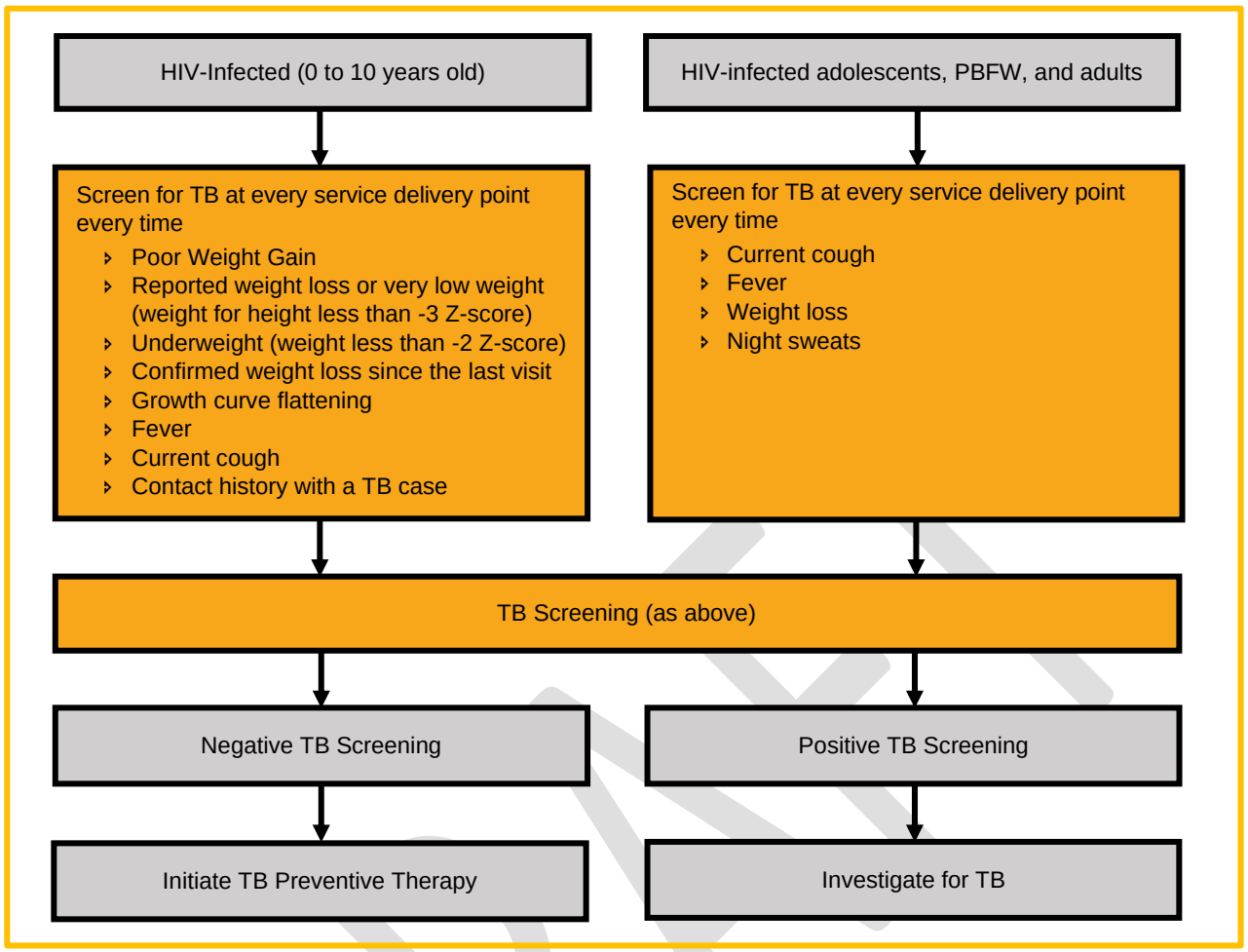
- ART should be started in all TB patients living with HIV regardless of CD4 count
- Xpert MTB/RIF is the preferred diagnostic test for HIV associated TB
- Oral-based DR-TB Treatment Regimen
- Bidirectional screening of patients with HIV and COVID-19
- Assessment and management of Cardiovascular Diseases (CVDs) in all HIV patients

TUBERCULOSIS AND HIV

There is a high incidence of TB among HIV-infected persons. According to the WHO TB REPORT, 2019, around 10 million people fell ill with TB in 2018 with about 10% of these co-infected with HIV. Consequently, given the high prevalence of co-infection, all HIV-infected individuals should be screened for TB and placed on TB treatment if found with TB. HIV-infected individuals with TB should begin anti-tuberculosis therapy (ATT) via directly observed therapy (DOTS) as per National TB Guidelines. Persons who screen negative for TB should be given Tuberculosis Preventive Therapy (TPT).

Screening for Active Tuberculosis

FIGURE 27: TB SCREENING ALGORITHM



Diagnostic Tools and Tests for TB

Tools and tests used for TB diagnosis provide either a definitive diagnosis (bacteriological confirmation of TB) or supportive information to aid diagnosis of tuberculosis.

Key Messages

- Xpert MTB/RIF is recommended as the initial diagnostic test in all presumptive TB patients
- While sputum is preferred, a stool sample for Xpert MTB/RIF can be used instead for children who are unable to give sputum
- Smear microscopy may continue being the initial test in settings where Xpert MTB/RIF is not yet available
- Smear microscopy --- and NOT Xpert MTB/RIF --- should be used for treatment monitoring
- All TB retreatment patients tested RIF negative on Xpert MTB/RIF should have FL LPA, Culture and DST
- All DR-TB and RIF positive on Xpert MTB/RIF patients should be tested with SL LPA, Culture and DST
- A negative laboratory test (i.e., smear, Xpert MTB/RIF, LPA and/or culture) in the setting of a TB-compatible clinical presentation does NOT definitively rule out TB. Such patients should be clinically evaluated for TB
- CRP and CAD have been introduced as supportive investigations for making a diagnosis of TB
- Urine LF-LAM should be done routinely for all patients with ADH
- Patients with strong clinical evidence of TB (especially PLHIV, Children, EPTB) should start TB treatment even if bacteriological tests are negative or not available (clinically diagnosed TB)

Bacteriological Tests for TB Diagnoses

Xpert MTB/RIF

Xpert MTB/RIF test* is a fully automated real time PCR based (molecular) test, disposable, cartridge-based nucleic acid amplification test

- Highly sensitive and specific, more sensitive than smear microscopy
- Rapid and simultaneous detection of tuberculosis and Rifampicin resistance (a reliable proxy for MDR-TB)
- Results are available within 2 hours
- Xpert MTB/RIF **should not** be used for following up of TB patients. Instead, use smear microscopy
- Collect one spot specimen (a minimum of 3-5 mL or 2-3 g for stool). Acceptable specimens include sputum, stool, gastric or lymph node aspirate, ascitic/pleural fluid, cerebrospinal fluid
- Submit the specimen as soon as possible for testing. Samples must be stored at 2-8°C for maximum of 5 days or at room temperature for a maximum of 3 days if testing cannot be done on the same day
- Xpert MTB/RIF is recommended as the first diagnostic test in all adults and children with signs and symptoms of TB where available (Figure 27)
- If not available, the samples from Priority* patients should be referred to facilities with GeneXpert machines (PLHIV, Children, EPTB, risk of DR-TB, HCW, miners, prisoners)

Limitations:

- Does not detect resistance to Isoniazid or other First- or Second-Line anti-tuberculosis medications
- Cannot be used for treatment monitoring (may remain positive even after treatment kills the bacteria because it detects TB DNA and not live bacteria)

XPERT MTB RIF MACHINE

XPERT MTB RIF CARTRIDGE

Reporting Xpert MTB RIF Results

Reporting Xpert positive results must also include the results from Rifampicin resistance testing
- MTB detected; RR positive (MTB detected with Rifampicin resistance detected)
- MTB detected; RR negative (MTB detected with no Rifampicin resistance detected)
- MTB detected; RRI (MTB detected Rifampicin resistance indeterminate)

Xpert Negative results must be reported:
- MTB not detected

In rare cases, where the only result that is available for Xpert MTB RIF is error, invalid or no result – this result should be captured as below and a repeat sample collected for testing:
- Err, Inv, No result

**Operational problems associated with this test include: the shelf-life of the cartridges is only 18 months, a very stable electricity supply is required, the machine needs to be calibrated annually, and the temperature ceiling is critical*

Smear Microscopy:

Smear microscopy is the first diagnostic test in facilities where Xpert MTB/RIF is not available.

- Smear microscopy is recommended to monitor treatment response (follow up). Results should be reported according to Tables 30 and 31
- Two spot specimens should be collected for smear microscopy at the time of request (at least 15 to 30 minutes apart). Should be used for treatment monitoring
- LED microscopy has a sensitivity gain of 10% over ZN and should be used in place of ZN
- The results of positive sputum examination should be recorded in red ink in the register for easy identification. Sputum results must be reported within 24 hours

Limitations:

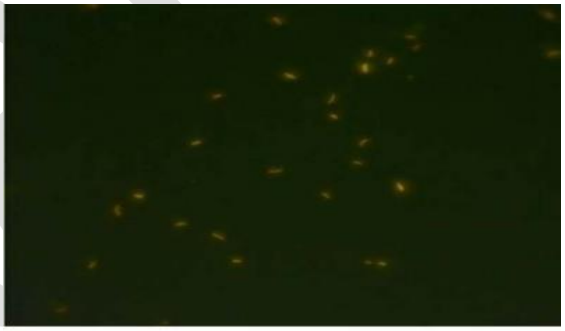
- It is often negative in PLHIV, children and EPTB samples and cannot detect Rifampicin resistance

Key Message

Sputum smear microscopy should only be used for diagnosis where Xpert MTB RIF is not accessible and in such an instance, ensure sample is sent for Xpert at the nearest centre

LED Microscope

Acid Fast Bacilli



The following WHO recommended method of reporting of smear microscopy results should be used:

Table 31: Reporting For Fluorescence Microscopy (FM) Results

200x	400x	Result Reported
No AFB in one length	No AFB in one length	No AFB Seen
1– 4 AFB in one length	1 – 2 AFB in one length	Report actual number*
5 – 49 AFB in one length	3 – 24 AFB in one length	Scanty Positive
3 – 24 in one field	1 – 6 AFB in one field	1+
25 – 250 AFB in one field	7 – 60 AFB in one field	2+
>250 AFB in one field	>60 AFB in one field	3+

**Confirmation required by another technician or prepare another smear, stain and read. Report as positive (actual number only if the result is confirmed by a second reader of a repeat smear)*

TABLE 32: REPORTING OF ZIEHL–NEELSEN (ZN) RESULTS

Number of bacilli seen in smear	Results	Result Reported
No AFB in 100 fields	Negative	No AFB Seen
1 – 9 AFB in 100 fields	Positive	Record exact number of bacilli
10 – 99 AFB in 100 fields	Positive	1+
1 – 10 AFB per field, check 50 fields	Positive	2+
>10 AFB per field, check 20 fields	Positive	3+

Line Probe Assay (LPA)

LPA is based on polymerase chain reaction (PCR) and the DNA strip technology. LPA does not eliminate the need for conventional culture and phenotypic drug susceptibility testing. LPA is available in Zambia at referral Mycobacterial culture laboratories. Line Probe Assay can be performed directly using a processed sputum sample or indirectly using DNA isolated and amplified from a culture of *Mycobacterium tuberculosis*.

- First-Line LPA is recommended for the rapid detection of resistance to Rifampicin and isoniazid in sputum specimens and cultures of *Mycobacterium tuberculosis*. It is recommended on DR–TB suspected patients with MTB detected and RIF negative on Xpert
- Second-Line Probe Assay (SL LPA) is recommended for patients with confirmed Rifampicin resistance (RR–TB) or multi-drug resistant tuberculosis (MDR-TB)

TABLE 33: INTERPRETATION OF RESULTS FOR LPA

Result	Interpretation
MTB complex detected	MTB was isolated from the specimen therefore, the patient has bacteriologically confirmed TB
MTB complex not detected	MTB was not isolated from the specimen
Rifampicin and Isoniazid susceptible	Patient has drug susceptible TB
Rifampicin and Isoniazid resistant	Patient has multi-drug resistant TB (MDR-TB)
Rifampicin resistant and Isoniazid susceptible	Patient has Rifampicin resistance (RR-TB)
Rifampicin susceptible and Isoniazid resistant	Patient has Isoniazid resistance

Mycobacterial Culture

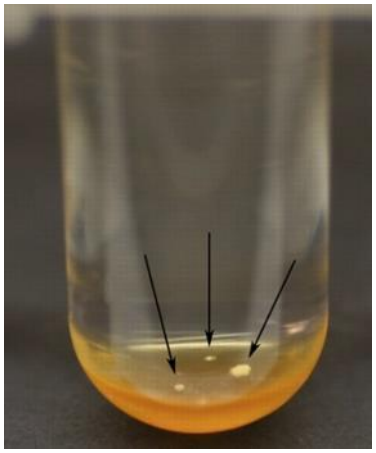
Culture is the gold standard for TB Diagnosis.

- Highly sensitive and specific method
- There are two culture methods available, namely solid and liquid. If liquid culture is used, sensitivity gain is +10% compared with Löwenstein-Jensen solid culture
- Refrigerate culture specimens at 2-8°C until ready for transport to the laboratory
- If a refrigerator is not available, specimens must be held in coolers with ice packs
- Specimens must be delivered as soon as possible, but no later than 48 hours from time of collection

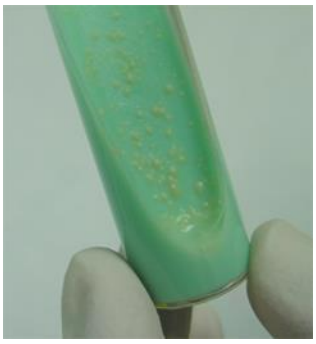
Limitations:

- Long turnaround time of the results (Liquid 21 days, Solid 48 days to inform a negative result)
- Expensive

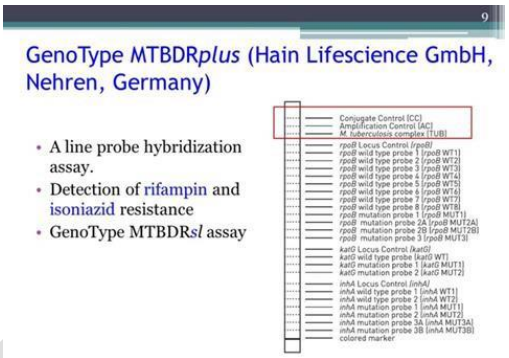
Positive Liquid Culture



Positive LJ Culture



Genotype Results (from LPA)



Culture is recommended for:

- All previously treated TB patients (loss to follow up, retreatment, failure)
- Smear-positive after 2 months of First-Line treatment
- Drug resistant TB contacts
- RR TB patients by Xpert MTB/RIF
- Patients who develop active PTB during or after IPT
- Healthcare worker, miners, prisoners
- Extra-pulmonary specimens
- Specimens from Children
- Diagnostic uncertainty

TABLE 34: INTERPRETATION OF RESULTS FOR CULTURE

Result	Meaning
Mycobacterium tuberculosis isolated	Positive
Mycobacterium tuberculosis not isolated	Negative
Contaminated	Specimen not properly handled (repeat specimen collection)
Not Done	The test was not performed due to many reasons such leaked specimen, mismatch information on the sample and request form and insufficient specimen, etc
Mycobacteria's other than Mycobacterium tuberculosis isolated (MOTT)	Non-Tuberculous Mycobacterium (NTM) which may or may not be clinically significant

Notes: A practical description of all the procedures for sputum smear microscopy, culture and DST and Xpert MTB/RIF is detailed in the relevant TB Laboratory Manuals

Phenotypic Drug Susceptibility Test (DST)

Phenotypic, culture methods are based on assessment of the ability of *M. tuberculosis* to grow in culture media (solid or liquid) containing a critical concentration of specific anti-TB agents (which indicates resistance) or conversely, its inability to grow in the same media (which indicates susceptibility).

- Phenotypic DST for First-Line agents (Isoniazid, Rifampicin, Ethambutol and Streptomycin), and selected Second-Line anti-TB drugs (Kanamycin, Amikacin, Ofloxacin, Levofloxacin) is generally reliable and reproducible
- Other anti-TB agents such as the later generation fluoroquinolones (Moxifloxacin and Gatifloxacin), Capreomycin, Thioamides, Cycloserine and Pyrazinamide are becoming increasingly important in the treatment of DR-TB and there is a need for their critical concentrations to be re-evaluated
- DST methods for new and repurposed drugs for the treatment of MDR-TB such as Bedaquiline, Delamanid, Linezolid, Clofazimine need validation

Lateral Flow Urine Lipoarabinomannan (LF-LAM)

- Tests based on the detection of LAM antigen in urine. LAM antigen is released from metabolically active or degenerating bacteria
- A positive result is diagnostic of active TB disease
- A negative result does not rule out TB
- Urine is easy to collect, and the test can be performed at bed side, and lacks the infection control risks associated with sputum collection
- In **in-patient settings**, it is recommended to use LF-LAM to assist the diagnosis of active TB in HIV-positive adults, adolescent and children with signs and symptoms of TB, or with advanced HIV or who are seriously ill or else irrespective of signs and symptoms of TB and a CD4 count < 200 cells/µL
- **In out-patient settings**. LF-LAM can be used to assist in the diagnosis of active TB in in HIV-positive adults, adolescents, and children: with signs and symptoms of TB or seriously ill; or else irrespective of signs and symptoms of TB and with a CD4 count of < 100 cells/µL
- In out-patient settings, LF-LAM should not be used to assist the diagnosis of active TB in HIV-positive adults, adolescents, and children without assessing TB symptoms; or without symptoms and unknown CD4 count; or else without TB symptoms and CD4 count ≥ 100 cells/µL
- The test is performed manually by applying 60 µL (2 drops) of urine to the Determine™ TB LAM Ag test strip and incubating at room temperature for 25 minutes
- The strip is then inspected by eye. The intensity of any visible band on the test strip is graded by comparing it with the intensities of the bands on a manufacturer-supplied reference card
- Whenever possible, a positive LF-LAM should be followed up with a confirmation test such as Xpert MTB/RIF, line probe assay or bacteriological culture and drug-susceptibility testing

TABLE 35: INTERPRETATION OF RESULTS FOR LF-LAM

Result	Meaning
Positive	MTB was detected from the specimen therefore the patient has bacteriologically confirmed TB
Negative	MTB was not detected from the specimen

Limitations:

- It is often negative in PLHIV, children and EPTB samples
- Does not provide information on drug susceptibility
- Cannot be used for treatment monitoring
- LAM cannot distinguish between Mycobacterium tuberculosis which causes TB and other types of mycobacteria (which could be harmless or could require different treatment

How to Classify a Patient Diagnosed with TB using Urine LAM

- A patient found as having TB using Urine LAM will be classified as having bacteriologically confirmed TB
- If the patient had presented with respiratory signs and symptoms this should be considered as a case of Pulmonary TB
- If there are no signs and symptoms and no findings to indicate pulmonary involvement, then the case should be considered as a case of Extra Pulmonary TB

Further Diagnostics Aids

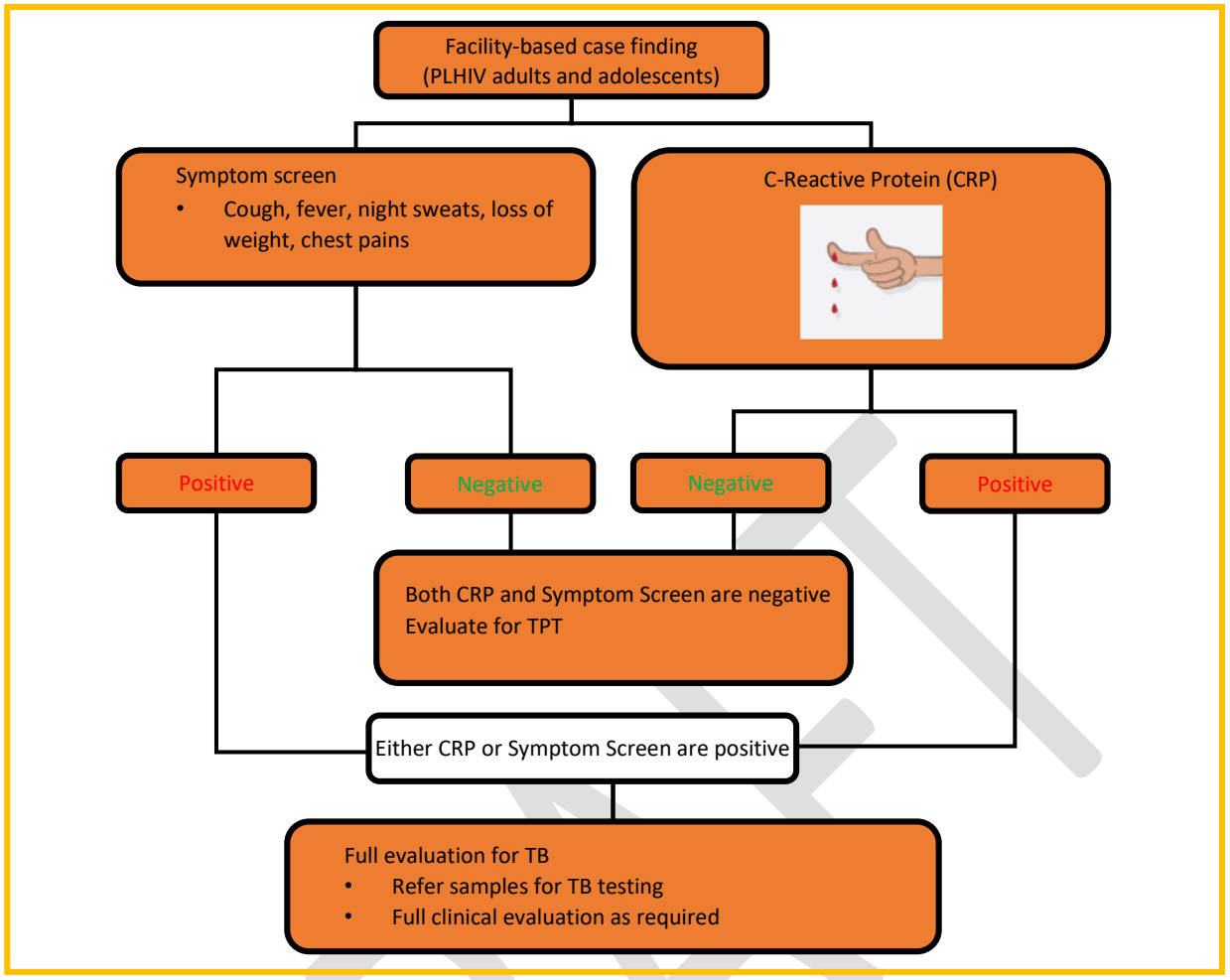
1. Computer Aided Diagnosis (CAD)

- Digital CXR machines may have artificial intelligence software often referred to as Computer Aided Diagnosis. CAD analyses CXR images and generates a continuous score between 0-100 (Note this score is not a percentage). CXR images are scored as normal or abnormal based on a set and agreed upon threshold
- All patients with an abnormal score are presumptive TB patients (Positive screen)
- An abnormal CAD score should not be interpreted as TB diagnosis
- For diagnosis of TB, an experienced clinician or radiologist should read and interpret the image
- Patients with CXR suggestive of TB must always submit sputum for evaluation of TB before start of treatment

2. C-Reactive Protein

- CRP is an acute phase protein and is a biomarker of conditions associated with inflammation. This tool should only be used for TB screening among adults and adolescents living with HIV
- It should be used in combination with symptom screening
- If either is positive, a person should be considered a presumptive TB patient
- The turnaround time from testing to result with many points of care CRP test kits is 3–5 min, allowing a quick clinical decision to refer a patient for diagnostic evaluation for TB disease or initiation of TPT
- An additional potential benefit of CRP is that it can alert clinicians to the presence of other diseases, such as bacterial pneumonia, bronchitis or other infectious or non-infectious conditions (e.g., lymphoma)

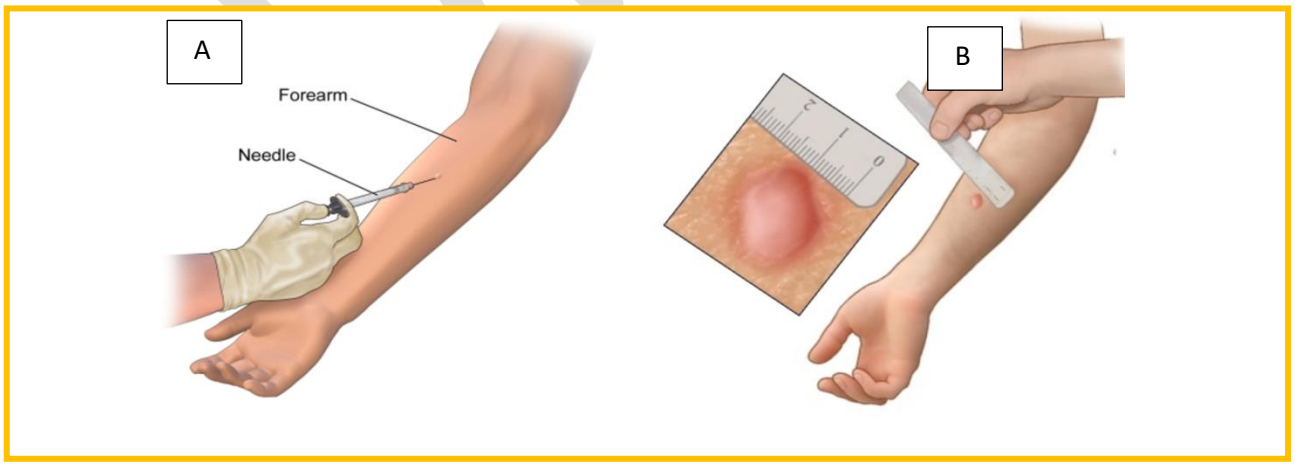
FIGURE 28: SCREENING ALGORITHM FOR TB USING C-REACTIVE PROTEIN AND SYMPTOM SCREENING



3. Tuberculin Skin Testing/Interferon Gamma Release Assay (TST/IGRA)

The Tuberculin Skin Test (TST) detects cell-mediated immunity to MTB through a delayed-type hypersensitivity reaction using a precipitate of heat-inactivated tubercle bacilli (purified protein derivative [PPD]–tuberculin). The TST has been the standard method of diagnosing LTBI in hypoendemic areas

Procedure for TST



#	Steps for TST
1	Bring PPD reagent to room temperature
2	Disinfect the site of injection and allow to dry
3	Draw up just over 0.1 mL of PPD by using 1 ml syringe. Remove excess PPD to make exactly 0.1 mL and remove air from the syringe if present
4	Using 27 g needle to inject the PPD intradermally to make the deposition wheel, in the diameter of 6 to 8 mm which will rise to the point of needle
5	Mark the area of injection with indicator
6	Read the result after 48-72 hours for induration

Interpretation of TST

1. Induration of diameter ≥5 mm is considered positive in:
   a. HIV-positive children
   b. Severely malnourished children (with clinical evidence of marasmus or kwashiorkor)
2. Induration of diameter ≥10 mm is considered positive in:
   a. All other children (whether they have received BCG vaccination)

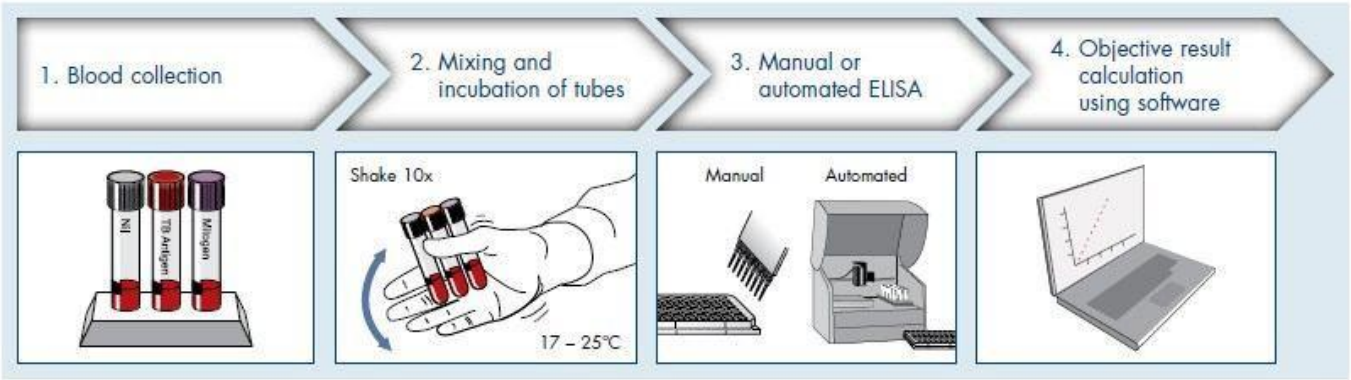
Causes of false negative TST

- Incorrect administration or interpretation of test
- Incorrect interpretation of test
- HIV infection
- Improper storage of tuberculin
- Viral infections (e.g., measles, varicella)
- Malnutrition
- Bacterial infections (e.g., typhoid, pertussis)
- Immunosuppressive medications (e.g., corticosteroids)
- Neonatal patient
- Diseases of lymphoid tissue (e.g., Hodgkin disease, lymphoma, leukaemia, sarcoidosis)
- Severe TB

Interferon-Gamma Release Assays (IGRA)

IGRAs are T cell–based assays that measure interferon gamma (IFN-γ) release by sensitized T cells in response to highly specific MTB antigens. Similar to TST in measuring T cell response but more specific for the antigens, particularly in the setting of BCG vaccination, and in excluding most nontuberculous mycobacteria.

FIGURE 29: INTERFERON-GAMMA RELEASE ASSAY (IGRA) PROCEDURE



We recommend performing an interferon-γ release assay (IGRA) rather than a tuberculin skin test (TST) in individuals 5 years or older who meet the following criteria:

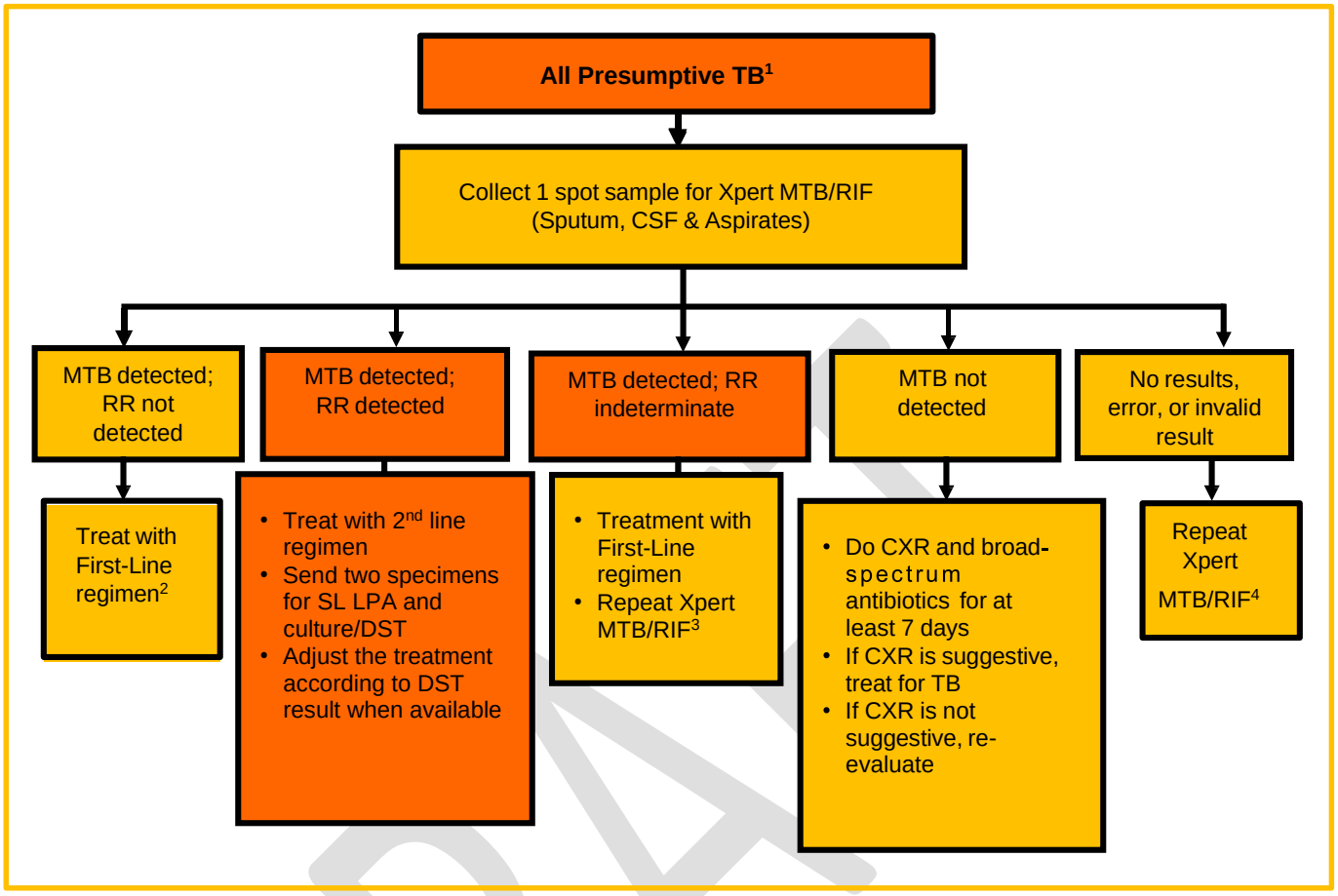
1. Are likely to be infected with MTB
2. Have a low or intermediate risk of disease progression,
3. It has been decided that testing for LTBI is warranted, and
4. Either have a history of BCG vaccination or are unlikely to return to have their TST read

Limitations of TST/IGRA

- The two test helps us to be certain about exposure to TB. They tell us about Latent TB infections but do not distinguish between active and latent TB
- Where available request for either test to support the clinical evaluation
- Whilst TST is less costly to perform, both require healthcare workers to be trained to correctly interpret the results to avoid inter-reader variability
- A positive test means the patient with TB symptoms has high likelihood of having active TB disease

Evaluating Patients for TB

FIGURE 30: ALGORITHM FOR EVALUATING PATIENTS FOR MTB RIF IN FACILITIES WITH ACCESS TO XPERT MTB RIF



[1] For PLHIV who have CD4 counts ≤100 cells/μL or are seriously ill with one or more danger signs, a urine LF-LAM assay may also be used if available

[2] Patients should be initiated on a First-Line regimen. A sample may be sent for First-Line LPA and culture/phenotypic DST if there is a risk of DR-TB:

- Previously treated TB patients: loss to follow up, retreatment, failure
- DR-TB contacts
- Smear positive at month 2 of First-Line treatment
- Healthcare worker
- Miners
- Prisoners

If patient has high risk of DR TB as a contact of a DR TB patient and patient is failing First-Line treatment, start Second-Line treatment while waiting DST results

[3] Treat the patient according to result of the repeat test. If the second Xpert MTB/RIF is negative, continue the First-Line TB treatment and send specimen for FL LPA, culture and phenotypic DST

Note that FL-LPA is recommended for use with smear-positive sputum samples only

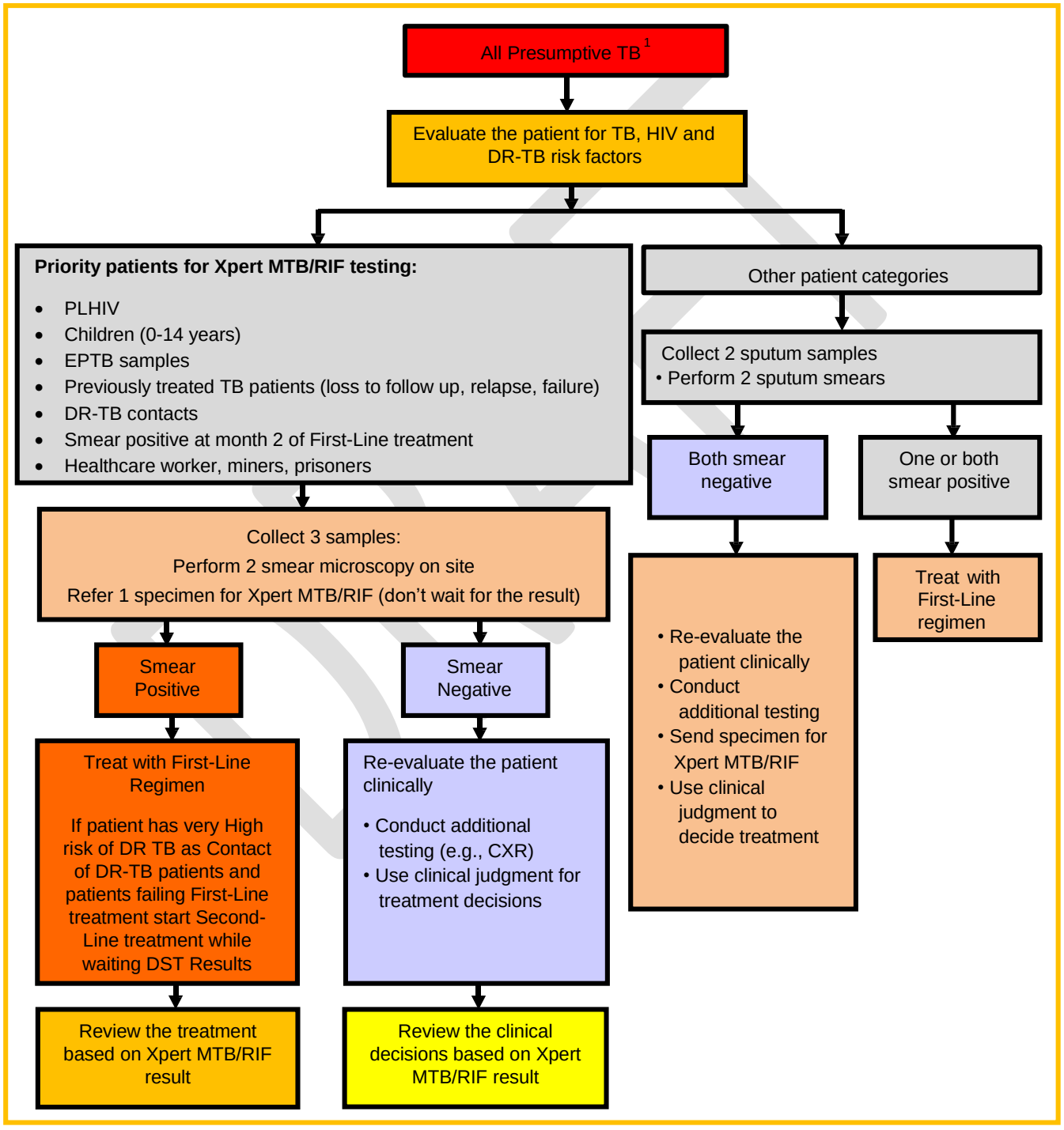
[4] Treat the patient according to result of the repeat test

Figure 31 is an interim algorithm in facilities where Xpert MTB/RIF is not yet available for all presumptive TB patients but is only available for priority populations, and smear microscopy is used for other patients.

HCW need to carefully assess the patients and ensure that all the priority patients (i.e., PLHIV, children, EPTB and patient with risk of DR-TB) collect and send samples to a facility where Xpert MTB/RIF is available.

HCW should decide the treatment of the patients without waiting for Xpert MTB/RIF results (as it can be delayed). Consider the possibility of clinically defined TB (i.e., no bacteriological confirmation). Use clinical judgement for treatment decisions. When the Xpert MTB/RIF result is available, treatment can be adjusted accordingly.

FIGURE 31: ALGORITHM OF SPUTUM SMEAR PLUS PRIORITY PATIENTS FOR XPERT MTB/RIF TESTING (FOR FACILITIES WITHOUT XPERT MTB/RIF ACCESS)



TUBERCULOSIS TREATMENT AND MANAGEMENT

Key Messages

- First-Line treatment (previously Category I) remains the same: 2 RHEZ/4 RH
- TB meningitis and Osteoarticular/spine TB are treated for 12 months (2RHEZ/10 RH)
- Category II treatment (2SRHEZ/1RHEZ/5RHE) should no longer be prescribed
- All previously treated patients should have their samples sent for Xpert MTB/RIF, First-Line LPA, Culture, and phenotypic DST to guide the treatment. Start First-Line treatment while awaiting the results.
- All DR TB contacts with a diagnosis of TB should start Second-Line treatment while awaiting the DST Results
- Patients failing First-Line treatment should start Second-Line treatment while awaiting the DST results
- Patients diagnosed with TB and are HIV infected should initiate ART within 2-3 weeks once TB treatment is tolerated. In cases of TB Meningitis, TB therapy should be delayed until after 8 weeks on TB therapy

Aims and Principles of TB Treatment

Early case finding and adequate treatment of tuberculosis using DOTS is the cornerstone of TB control.
The aims of treatment are:

- To cure patients and restore their quality of life and productivity
- To prevent further transmission of TB in the community
- To prevent relapse
- To prevent death from active TB or its late effects and complications
- To prevent the development of drug resistance – including MDR-TB and XDR-TB

The Principles of TB Treatment are:

- TB treatment involves use of correct doses of multiple drugs to ensure effectiveness of therapy
- Never add a single drug to a failing regimen
- At no time should monotherapy (use of a single anti-TB drug) be employed as treatment for active TB
- TB drugs should be taken daily for a specified period depending on the severity of the disease

Essential Anti-TB Medicines

The recommended essential First-Line anti-TB medicines are Rifampicin (R), Isoniazid (H), Ethambutol (E) and Pyrazinamide (Z). Fixed dose combination (FDC) is preferred over single drug formulation. The fixed dose combinations are 4FDC (RHZE) and 2FDC (RH). Drug dosage is based on weight. Monitoring the patient's weight is essential for proper dosing.

Key Messages

- TB medicines are available at no cost to the client
- It is essential that all facilities treating TB patients' stock single formulation drugs for use when necessary, especially in an event of side effects

The following table, shows the properties of anti-tuberculous drugs used as First-Line (Table 36):

TABLE 36: PROPERTIES OF FIRST-LINE TB DRUGS

Drug	Drug Property	Target Bacilli	Site of Action
Rifampicin	Bactericidal within 1 hour. High potency. Most effective sterilizing drug	All populations including dormant bacilli	Intracellular and extracellular
Isoniazid	Bactericidal after 24 hours. High potency: kills>90% bacilli in the first few days of treatment	Rapid and intermediate growing bacilli	Intracellular and extracellular
Ethambutol	Bacteriostatic. Low potency. Minimizes the emergence of drug resistance	All bacterial populations	Intracellular and extracellular
Pyrazinamide	Bactericidal with a low potency. Achieves its sterilizing action within 2-3 months	Slow growing bacilli	Intracellular bacilli in macrophages

Standardized First-Line Treatment

A standardized treatment regimen has been adopted comprising the 4FDCs (RHZE) and 2FDC (RH) for a period of 6-12 months depending on the severity and anatomical location of the disease

Intensive Phase

- Designed for the rapid killing of actively growing and semi-dormant bacilli
- Achieves a shorter duration of infectiousness
- The duration of the phase is two (2) months in new and retreatment cases

Continuation Phase

- Eliminates bacilli that are still multiplying and reduces the risk of failure and relapse
- The duration is for at least four (4) months in most cases and ten (10) * months if the patient has meningitis, Osteoarticular or spinal TB

*It is recommended to extend treatment to 12 months for TB meningitis because of the serious risk of disability and mortality and Osteoarticular /spinal TB because of difficulties of assessing response to treatment.

TABLE 37: RECOMMENDED REGIMENS

TB Disease Category	Recommended Regimen	
Treatment Phase	Intensive Phase	Continuation Phase
All forms of TB (non-severe)	2RHZE	4RH
TB Meningitis, Osteoarticular and Spinal TB (severe forms)	2RHZE	10RH

TABLE 38: DOSAGE RATES AND WEIGHT BANDS FOR DOSING OF ANTI-TB DRUGS

Drug	Daily Dosage in mg/kg (range)	Maximum Dose
Isoniazid (H)	10 mg/kg (7–15 mg)	300 mg/day
Rifampicin (R)	15 mg/kg (10–20 mg)	600 mg/day
Pyrazinamide (Z)	35 mg/kg (30–40 mg)	1500 mg/day
Ethambutol (E)	20 mg/kg (15–25 mg)	1200 mg/day

Weight band	Intensive Phase		Continuation Phase
	RHZ (75/50/150 mg)	E[a] (100 mg)	RH (75/50 mg)
	Number of tablets		
3–3.9 kg	0.75	0.75	0.75
4–7.9 kg	1	1	1
8–11.9 kg	2	2	2
12–15.9 kg	3	3	3
16–24.9 kg	4	4	4
>25 kg	Use adult dosages and formulations (RHZE 150/75/400/275, 2 tablets)		

[a] Ethambutol is provided as a separate 100 mg tablet

Body Weight (Kg)	Intensive Phase (RHZE 150/75/400/275)	Continuation Phase (RH 150/75)
25-37	2	2
38-54	3	3
55-70	4	4
Above 71	5	5

Key Message

Dosing for all patients including children should be according to weight and adjusted according to close weight monitoring

TB Treatment of New and Previously Treated Patients

- Treat all new TB patients (bacteriologically confirmed, clinically diagnosed and extra-pulmonary TB) with First-Line TB drugs except for the new patients who are confirmed DR-TB patients
- For patients with a known DR-TB contact, a Second-Line regimen based on the DST of the presumed index case should be started while awaiting DST results
- In previously treated patients, send samples for Xpert MTB/RIF, First-Line LPA, Culture and phenotypic DST. Start First-Line treatment while waiting for the results
- For patients failing First-Line regimen, send samples for Xpert MTB/RIF, First-Line LPA and culture. Start Second-Line regimen while waiting for the results. Adjust the therapy once DST results are available

Standard Indications of Steroids in the Treatment of Tuberculosis

- TB meningitis
- Constrictive TB pericarditis with suspected constrictive physiology
- TB IRIS
- Massive Pleural effusion
- Massive lymphadenopathy with pressure effects
- Severe hypersensitivity reactions to anti-TB drugs

Other Possible Indications for Steroids in the Treatment of Tuberculosis:

- Hypoadrenalism
- Renal tract TB (to prevent ureteric scarring)
- TB laryngitis with life threatening airway obstruction

The table below shows the recommended doses of adjuvant steroid therapy (Table 39):

TABLE 39: RECOMMENDED DOSES OF ADJUVANT STEROID THERAPY (DRUG OF CHOICE IS PREDNISOLONE)

Indication	Prednisolone (Dosage)
TB Meningitis	1-2mg/kg (max 60mg) for 2 weeks then tapers off by 10 mg in the daily dose each week over about 6 weeks
TB Pericarditis	1-2mg (max 60mg for 4 weeks then half for 4 weeks (max 30mg/day) then 15mg/day x 2 weeks, then 5 mg/kg x 1 week, then off
TB Pleural effusion (severe) /or IRIS	0.5 to 1mg (max 30mg) for 1-2 weeks then taper off over several weeks

Note: Steroids doses must not be stopped abruptly but must be tapered. If prednisolone is unavailable, equivalent doses of dexamethasone may be used as a substitute

Key Message

Steroids are immunosuppressant and may theoretically increase the risk of developing opportunistic infections in TB/HIV patients. However, used as indicated above, the overall benefit of steroid use outweighs the potential risk

TB Patients Monitoring and Follow-Up

- All TB patients must be seen at least once monthly by a healthcare provider for clinical review, assessment of side effects and dose adjustment according to weight
- All patients should have 1 sputum specimen (morning) taken for AFB smear at 2, 5 and 6 months. If sputum smear is positive at 2 months, proceed to continuation phase and send sputum specimens for Xpert MTB/RIF, First-Line LPA, culture and phenotypic DST
- Repeat smear microscopy at month 3. If sputum smear is still positive at month 3, send samples for Xpert MTB/RIF, First-Line LPA, culture and phenotypic DST (continue or adjust the treatment according to the results). Results should be available at these visits and must be recorded on the patient treatment card and registers

Key Messages

1. If a patient is found to have a drug resistant strain of TB at any time during the therapy, treatment is declared as failed and patient referred for DR-TB treatment and re-register as such
2. For previously treated TB patients, specimens for Xpert MTB/RIF, LPA, culture and phenotypic DST should be sent before starting treatment (DST should be performed for at least Rifampicin and Isoniazid, WHO 2017)

TABLE 40: SUMMARY OF SPUTUM MONITORING BY SMEAR IN FIRST-LINE TREATMENT

Treatment Phase	Months of Treatment	Sputum Smear Exam
Intensive Phase	1	
	2	If smear positive, send sample for LPA, culture and DST
Continuation Phase	3	If smear was positive at month 2, repeat smear at month 3. Send samples for culture, LPA and DST if still positive; ensure samples are received at the laboratory
	4	
	5	If smear positive, obtain samples for LPA, Culture and DST. If there is concern for MDR-TB, send sample for Xpert MTB/RIF to assess for Rifampicin resistance
	6	If smear negative, assign appropriate treatment outcome. If positive, obtain samples for LPA, Culture and DST

TABLE 41: HIV-TB CO-INFECTION CASE SCENARIOS AND RECOMMENDED MANAGEMENT FOR SUSCEPTIBLE TB

Scenario	TB management	Recommended ART
Pregnant, on ART and develops TB	Start ATT immediately	If on EFV-based ART, continue with same regimen; If on DTG-based, give DTG 50mg twice daily if single DTG tablet is available) Evaluate for failure and consider switching to 2nd line ART in consultation with next level
Pregnant, on ATT, and diagnosed with HIV	Continue ATT	Start ART immediately TDF + XTC + DTG* (add DTG 50mg to be given after 12 hours of TLD tablet daily if single DTG tablet is available)
Children 3 months to <3 years old with TB-HIV co-infection	Start ATT (RHEZ) immediately	ABC + 3TC + DTG
Newly diagnosed TB and HIV co-infection TB retreatment case and HIV co-infection	Start ATT immediately	Start ART as soon as ATT is tolerated (usually within 2-3 weeks) regardless of CD4 count or WHO Clinical Staging TDF + XTC + DTG* (DTG 50mg twice daily if single DTG tablet is available). ***If single tablet not available***, give: TDF + XTC + EFV-400mg
On ART and develops TB	Start ATT immediately	TDF + XTC + DTG* (DTG 50mg twice daily if single DTG tablet is available). If on ATV-r, switch ATV-r to DTG 50mg 12 hourly if DTG naïve. If DTG single tablet not available, give LPV-r and double the dose If on LPV-r, double dose of LPV-r Evaluate for failure and consider switching to 2nd line ART in consultation with next level
On ATT and diagnosed with HIV	Continue ATT	Start ART as soon as ATT is tolerated (usually within 2-3 weeks*), regardless of CD4 count or WHO clinical staging TDF + XTC + DTG (DTG 50mg twice daily if single DTG tablet is available)
On 2nd line ART with LPV-r and develops TB	Start ATT per guidelines immediately	Switch LPV-r to DTG 50mg 12 hourly ***If single tablet not available*** increase LPV-r from 2 tabs BD to 3 tabs BD for 2 weeks and then to 4 tabs BD for the remainder of TB treatment. If Rifabutin available (in place of Rifampicin), start at 150mg Monday/Wednesday/Friday

- Patients on TB treatment should be initiated on TDF + XTC + DTG. Take note that a 50mg DTG tablet in this case should be given 12 hours apart with the TDF + XTC + DTG fixed dose combination
- **REMEMBER to switch back to DTG 50mg once daily and LPV-r 2 tabs twice daily after TB treatment!**
- Patients on ART on TAF who develop TB, the TAF should be switched to ABC. If there is normal renal function or above 30kg, give switch to TDF
- HIV-positive TB patients with profound immunosuppression (e.g., CD4 counts less than 50 cells/µL) should receive ART within the first two weeks of initiating TB treatment
- TB meningitis patients with a new HIV diagnosis should have ART initiation delayed until after the first 8 weeks of ATT are completed, regardless of CD4 count
- If Rifabutin is available, use the same PI or DTG-based regimens as recommended for adults and adolescents.
- LPV-r and BDQ co-administration should be avoided
- Use LPV-r in First-Line or Second-Line ART if DTG not available or contraindicated

DRUG RESISTANT TB

Drug Resistant TB Patient Detection

The diagnosis and treatment of persons with drug resistant TB (DR-TB) starts with identification of a presumptive DR-TB patient.

Sputum samples from all presumptive TB patients should be sent for Xpert MTB/RIF rapid diagnostic testing, and a chest x-ray should be obtained for patients when the diagnosis of TB is uncertain.

Every effort should be undertaken to confirm the diagnosis of RR-TB/MDR-TB with Xpert MTB/RIF, especially for patients in the following risk categories:

- A close contact of a person diagnosed with DR-TB, especially if the person is not on treatment, is failing treatment, or has recently died from DR-TB disease
- Someone who has a history of TB treatment failure (either DS-TB or DR-TB), lost to follow up from DS-TB or DR-TB treatment, or could be considered to have early relapse from a previously treated case of DS-TB or DR-TB (successfully treated less than two years previously)
- HIV co-infected patients with severe immunosuppression: bacteriologic confirmation may be difficult, so a history of contacts and risk factors is important
- Persons recently from facilities with high rates of DR-TB: the risk of nosocomial infection is high for healthcare workers, miners, prisoners, and patients admitted for prolonged periods, especially in the absence of appropriate infection control measures
- DS-TB patients who remain smear positive ≥ 2 months on First-Line drug treatment, as this may indicate the presence of drug resistance

Diagnosis of Drug Resistant Tuberculosis

a) Clinical Presentation

- The clinical features of DR-TB are not different from those of drug susceptible TB (both pulmonary and extra-pulmonary TB)
- DR-TB is a bacteriological diagnosis. However, in patients where bacteriological confirmation is difficult, such as children, HIV positive patients, or those with extra-pulmonary TB, and who are also close contacts of known DR-TB patients, a clinical diagnosis of DR-TB can be made. Such cases should be discussed with the Clinical Expert Committee (CEC)

b) Bacteriologic Confirmation

Xpert MTB/RIF has been recommended as the primary diagnostic test in all adults and children with signs and symptoms of TB where available

- The diagnosis of DR-TB is done by Xpert MTB/RIF, line probe assay (First and Second-Line LPA), culture and phenotypic drug susceptibility testing (pDST)
- In facilities where Xpert MTB/RIF is not yet available, samples should be referred to the nearest facility where the test is available, especially for individuals with risk factors of DR-TB
- Only as a last resort should patients be started on empiric DS-TB treatment based on clinical history and positive smear microscopy results alone (e.g., severely ill patients in whom treatment initiation should not be delayed pending Xpert MTB/RIF, LPA, or culture/DST results
- Patients who require TB re-treatment based on history should NOT get the category II regimen (the standard DS-TB regimen plus streptomycin). Instead, patients should get drug susceptibility testing with rapid molecular testing (Xpert MTB/RIF, FL, and SL LPA) to inform the choice of treatment. WHO no longer recommends the use of the category II regimen
- For all patients with Rifampicin resistance detected on Xpert MTB/RIF, samples should be sent for SLLPA, culture and phenotypic DST; for those eligible, the shorter DR-TB treatment regimen should be started while awaiting results from LPA and/or culture/DST

- The turnaround time (specimen collection until receipt of results) for LPA and culture/DST results varies on when the test becomes positive and the type of media used (e.g., liquid or solid media for culture):
  - Line probe assay results should take between 3-14 days (turnaround time of LPA within the processing lab should be 48 hours):
  - Liquid culture (MGIT): positive results at 4-14 days, negative result by 42 days
  - Solid culture (LJ): positive results at 28-56 days, negative result by 60 days
  - Phenotypic DST results (from the date culture was positive): MGIT 14 days, LJ 30 days
- Phenotypic DST (pDST) is reliable and reproducible for Rifampicin, Isoniazid, Kanamycin, Amikacin, Ofloxacin, Levofloxacin
  - Moxifloxacin: there is a need for critical concentrations to be re-evaluated
  - Ethambutol, Streptomycin, Capreomycin, Ethionamide/Protionamide, Cycloserine, Pyrazinamide, para – Amino Salicylic Acid: pDST is not reliable
  - New and repurposed drugs Bedaquiline, Delamanid, Clofazimine, Linezolid: pDST needs validation and is not widely available outside of research settings

Causes of DR-TB

- Transmission from a patient with drug resistant TB
- Poor adherence to treatment by patients
- Use of anti-TB drugs of unproven quality (sale of such medications over the counter and on the black-market).
- Incorrect management of individual cases by clinicians
- Sub-optimal dosage
- Poor drug absorption
- Prolonged shortages of anti-TB drugs

Groups at Risk of DR-TB

- Contacts of DR-TB patients
- Patients previously treated for TB (Treatment failures, relapses, treatment after loss to follow up)
- Patients who are smear positive after 2 months of First-Line TB treatment
- TB patients who are close contacts of DR-TB cases.
- Healthcare workers
- Prisoners from facilities with high rates of DR-TB

Management of Presumptive DR-TB Patients

If a patient is presumed to have DR-TB, the following should be done:

- Collect sputum specimens for Xpert MTB RIF, LPA, culture and phenotypic DST
- Do not admit patient to a general ward (especially in high HIV settings as HIV positive individuals can easily get infected)

If hospital admission is necessary, the patient should be admitted to a special ward, which has good ventilation. At home advise patient to sleep in a well-ventilated room that is separate from others (if possible). If DR-TB is confirmed by the laboratory, the patient should be referred for treatment at a designated treatment facility under strict supervision.

Detection of DR-TB patients

Case detection for DR-TB is similar to that of TB. The basis for identification of DR-TB patient is bacteriological confirmation by either Xpert MTB/RIF, LPA, Culture and Phenotypic Drug Susceptibility Testing (DST) as well as previous history of treatment

NEW DRUG RESISTANT TUBERCULOSIS (DR-TB) TREATMENT REGIMEN

The National TB and Leprosy Program (NTLP) has updated the 2018 MDR-RR/TB guidelines based on the most recent available evidence from observational studies, individual patient data (IPD) metanalysis and clinical trials. Currently, there are two main treatment regimens recommended for use in Zambia. All are oral based regimens. The drugs are the same, with the only difference between the two being the duration of therapy based on patient characteristics

Use of second line injectable regimen is currently not recommended unless under specific circumstances after discussion with the National CEC

1. Shorter Regimen for RR/MDR-TB

The regimen is Bedaquiline + Levofloxacin/Moxifloxacin + Linezolid + Clofazimine given for 9-12 months

Eligibility criteria for fully oral shorter regimen

- Rifampicin resistant: resistance to at least rifampicin while awaiting LPA results
- Patient with uncomplicated form of MDR/RR-TB regardless of HIV status
- Children aged 6 and above with confirmed or clinically diagnosed RR/MDR-TB
- No prior exposure to second line TB drugs before
- No known resistance to any of the drugs on the regimen

Indications for transitioning from shorter to longer regimen:

1. Failure to culture convert by month 5
2. Remains symptomatic by month 5
3. Deterioration of the radiological picture
4. Unsuppressed viral load in the case of the TB/HIV co-infection (Why)

2. Standardized Longer Treatment Regimen (Fully All Oral Options)

1. 6 Bedaquiline, Levofloxacin, linezolid, Clofazimine /12 Levofloxacin, Linezolid, Clofazimine **(6Bdq-Levo-Lzd-Cfz/12Levo-Lzd-Cfz)***
2. 6 Bedaquiline, Levofloxacin/Moxifloxacin, Clofazimine. Cycloserine /12 Levofloxacin/Moxifloxacin, Clofazimine, Cycloserine
3. 6 Bedaquiline, Linezolid, Clofazimine, Cycloserine /12 Linezolid, Clofazimine, Cycloserine

***Preferred option for most patients**

Note: Decisions to start newly diagnosed patients on the standardized shorter MDR-TB regimen should be made after discussing with patient and based on clinical judgement

Modified Shorter Treatment Regimen Under Operation Research Conditions

The following patients should be started on all oral longer regimen:

- Any previous exposure to Second-Line treatment (more than 1 month) regardless of treatment outcome or pattern of resistance (e.g., MDR-TB, pre-XDR-TB, or XDR-TB)
- MDR/RR-TB in persons with presumed resistance to second line drugs, even if susceptibility is demonstrated on DST
- Persons with complicated EPTB: MDR/RR-TB meningitis, osteoarticular disease, abdominal, pericardial effusion, or miliary/disseminated
- Persons with extensive disease (i.e., bilateral, cavitary disease with significant fibrosis, or scarring/cavities in 3 or more lung zones)
- Any other situation in which the clinician, in consultation with the provincial or national Clinical Expert Committee (CEC), is uncertain of the patient's eligibility for the STR

Individualized Treatment Regimen

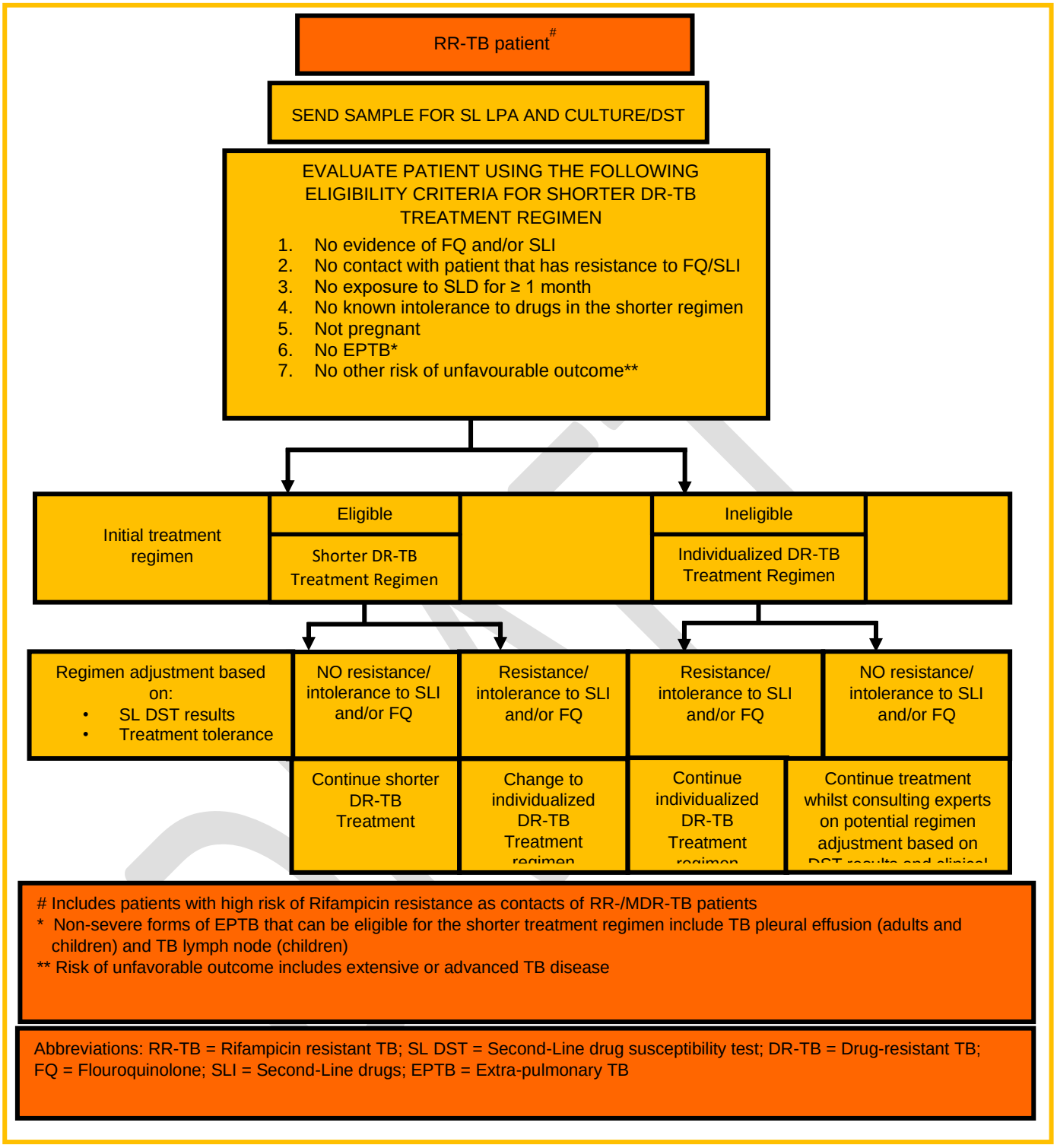
For patients who are not eligible for the Standardized Longer treatment regimen (all oral) or Shorter regimen, an individualized treatment regimen should be designed. The patients include pre-XDR-TB and XDR-TB patients.

Note: Individualized regimen should usually be designed to include at least five medicines considered to be effective.

IMPORTANT MASSAGES

- Every DR-TB patient should be followed very closely by each individual treatment centre and all records should be well documented in both paper and electronic registers
- Ensure a complete baseline assessment is done at the time of starting the patient on Second-Line drugs
- Follow up monthly smears, cultures and biochemistry tests is a must. When Amikacin is used audiometry tests at baseline and during treatment should be done
- Active monitoring and reporting of any adverse effects are the corner stone of good patient care practice
- The Provincial Clinical Expert Committee (CEC) should evaluate every DR-TB patient at treatment initiation and on monthly basis. Any change of the drug regimen should also be discussed
- Complicated cases should be brought to the attention of the National MDR-RR/TB Clinical Expert Committee
- Interim and final outcomes should be reported the National TB and Leprosy Program
- All DR-TB patients must be followed for at least 2 years post treatment

FIGURE 32: RR/DR TB PATIENT TRIAGE FLOW CHART



Dosage and administration

TABLE 42: WEIGHT-BASED DR-TB DRUGS IN ADULTS ≥ 30KG

Drugs	Daily dose	30–35kg	36–45kg	46–55kg	56–70kg	>70kg
Isoniazid- High dose (H^h)	10mg/kg Maximum 600mg/day	300mg	400mg	500mg	600mg	600 mg
Pyrazinamide (Z)	20–30mg/kg once daily	800mg	1,000mg	1,200mg	1,600mg	2,000mg
Ethambutol (E)	15–25mg/kg once daily	600mg	800mg	1,000mg	1,200mg	1,200mg
Capreomycin/Amikacin (Km/Cm/Am)	15–20mg/kg once daily	500mg	625mg	750mg	825mg	1,000mg
Levofloxacin (Lfx)	750–1000mg once daily	750mg	750mg	1,000mg	1,000mg	1,000mg
Moxifloxacin (Mfx)	400mg once daily	400mg	600mg	<50kg=600mg >50kg=800mg	800mg	800mg
Prothionamide (Pto)/ Ethionamide (Eto)	500–750mg/day in 2 divided doses	500mg	500mg	750mg	750mg	1,000mg
Cycloserine (Cs)/ Terizidone (Trd)	500–750mg/day in 2 divided doses	500mg	500mg	500mg	750mg	750mg
p-Aminosalicylic Acid (PAS)	8g/day in 2 divided doses	8g	8g	8g	8g	8–12g
Bedaquiline (Bdq)	400mg once daily for 2 weeks then 200mg 3 times per week					
Delamanid* (Dlm)	100mg twice daily (total daily dose = 200mg)					
Clofazimine (Cfz)	100mg twice daily for 2 first months, then reduce to 100mg daily					
Linezolid (Lzd)	600mg once daily	600mg	600mg	600mg	600mg	600mg
Amoxicillin/clavulanate (Amx/clv) 7/1	80mg/kg/day in 2 divided doses	2,600mg	2,600mg	2,600mg	2,600mg	2,600mg
Amoxicillin/clavulanate (Amx-clv) 8/1	80mg/kg/day in 2 divided doses	3,000mg	3,000mg	3,000mg	3,000mg	3,000mg
Imipenem/Cilastatin (Imp/cln)	1,000mg Imipenem/1000mg Cilastatin twice daily					
Meropenem (Mpm)	1,000mg three times daily (alternative dosing is 2,000mg twice daily)					

* Use of Delamanid in the shorter MDR-TB regimen under programmatic conditions is not recommended given the lack of data. However, it can be used when other options are not available and should be under Clinical Experts' guidance

* For children under the weight of 30kg, please consult the Clinical Expert Committee

Treatment Monitoring for MDR-TB/RR-TB Patients on Therapy

Adverse effects may occur with MDR-TB drugs and are dose dependent. However adverse effects can occur at normal dose. Patients should be monitored for adverse effects at each contact with a healthcare provider:

- Patients should be monitored closely for signs of treatment failure and adverse drug reactions (compare baseline and follow up examinations)
- Treatment can be monitored through clinical history; physical examination; psychosocial assessment; chest radiography; audiometry, bacteriological test (smear and culture); laboratory monitoring (haematology-FBC, Creatinine, Potassium, LFT, TSH); Pregnancy test, hepatitis B, C and HIV test (if positive CD4 and VL every 6 months) should be included when doing the baseline investigations
- Weight should be monitored monthly and drug dosages should be adjusted accordingly
- For patient under individualized regimen, additional monitoring is required: ECG (Dlm, Bdq), Serum Albumin (Dlm), and for Linezolid: vision test chards, Serum Amylase/Lipase and monthly haematology-FBC

For details on adverse effects monitoring and management, refer to the DR-TB manual

Important points:

- Patients on TB treatment should be initiated on TDF + XTC + DTG. Take note that a DTG 50mg tablet should be given 12-hours apart from the TLD
- **REMEMBER** to switch back to DTG 50mg once daily and LPV/r 2 tablets twice daily after completion of TB treatment
- **For** all patients on DTG-based regimens, they should be given their standard daily dose of DTG twice per day for the duration of their TB treatment plus for an additional two weeks after treatment cessation
- Patients on TAF-based ART who develop TB and on Rifampicin-based ATT should be switched to ABC if renal dysfunction still exists or TDF if eligible
- HIV-positive TB patients with profound immunosuppression should receive ART within the first two weeks of initiating TB treatment
- TB meningitis patients with a new HIV diagnosis should have ART initiation delayed until after the first eight weeks of ATT are completed, regardless of CD4 count
- All stable DR-TB patients should be reviewed monthly. Patients who are unstable should be reviewed frequently
- Evaluate patient's adherence to treatment at every visit and link all patients to a treatment supporter
- Perform Audiometry at baseline when using Amikacin and monthly for 6 months
- Conduct Active monitoring and reporting of any adverse effects
- Clinical Expert Committee (CEC) should review ALL complicated cases and patients that are failing treatment
- Report Interim and final outcomes to the National TB and Leprosy Programme
- Follow up all DR-TB patients for at least 2 years post treatment initially every 3 months in the first year and then every 6 months during the second year

TABLE 43: DR-TB TREATMENT MONITORING SCHEDULE FOR CONVENTIONAL DR-TB REGIMEN

Parameters	Month of Treatment																			
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Clinical evaluation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Sputum-smear	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Sputum-culture	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
DST	X				P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P	P
FBC/DC	X						X						X						X		X
LFTs	X			X			X			X			X			X			X		X
Na^{2+}, K^{2+}, U, Creatinine	X	X	X	X	X	X	X			X	I	I	I	I	I	I	I	I	I	I	I
TSH/free T-4	X			X			X			X			X			X			X		X
Pregnancy test	X																				
HIV test	X			X			X			X			X			X			X		
Audiometry	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
CXR	X						O						O								O

KEY: X = Required, O = Optional, P = If culture is positive, I = If indicated

COVID-19 AND HIV

At the height of the COVID-19 pandemic, researchers from the Ministry of Health and CDC were able to demonstrate that HIV infection was not independently associated with worse outcomes among patients hospitalized for COVID-19 in Zambia. However, among HIV-positive patients hospitalized for COVID-19, those with severe HIV disease were more likely to develop severe COVID-19 or to die of COVID-19 compared with those with controlled HIV disease. Ensuring that HIV-positive persons maintain disease control, including sustaining ART continuity and adherence, achieving viral suppression (<1,000 copies of HIV RNA per mL), and addressing underlying medical conditions, could reduce COVID-19–associated morbidity and mortality.

Special Considerations for PLHIV in the Context of COVID-19 in Outpatient Settings

a. Ensure recipient of care (RoC) is provided with 6 months' Multi-month Dispensing (6MMD)
b. Ensure VL is collected prior to providing 6MMD if the result is more than 6 months old
c. Ensure cervical cancer screening is provided to the client prior to dispensing 6MMD whenever eligible
d. Utilize DSD models such as buddy collection, home deliveries and spaced ART appointments to further reduce clinic congestion
e. Triage any RoC or HCWs who are unwell (flu-like/ respiratory symptoms) to be seen first and provide them with a face mask immediately upon arrival
f. Offer COVID-19 Vaccination and booster for all RoC visiting the facility

Special Considerations for PLHIV in the Context of COVID-19 in Inpatient Settings

a. All patients admitted for COVID-19 HIV
b. All those found to be HIV positive should have their CD4, VL and other markers of severity of HIV assessed
c. Consider PCP treatment with high-dose Sulfamethoxazole/Trimethoprim for RoC with AHD and severe COVID-19 infection
d. Screen for concomitant TB infection using the screening algorithms listed above (urine LF-LAM, CRP and TB GeneXpert) [ref Figure 30]
e. If TB screening is negative offer TPT especially where high dose steroids (e.g., Prednisolone 40mg daily) and interleukin 6 receptor blockers (e.g., Tocilizumab) were administered
f. Ensure the RoC maintains disease control, including sustaining ART continuity and adherence so as to achieve viral suppression (<1000 copies of HIV RNS per mL)
g. Once client has been stabilized and ready for discharge, offer COVID-19 vaccination and/or booster

As mentioned earlier, Tuberculosis is the most common cause of morbidity and mortality in people living with HIV. PLHIV have higher risk of progression to TB disease with an annual risk of 10% compared to HIV non-infected individuals who have 5-10% lifetime risk. PLHIV have a higher risk of TB relapse HIV-infected tuberculosis patients may present more frequently with extra-pulmonary tuberculosis and smear-negative tuberculosis.

Likewise, TB patients are an increased risk of contracting COVID-19 and conversely, post COVID-19 persons are at an increased risk of re-activating from latent to active TB. The COVID-19 infection and the high dose corticosteroid therapy used as part of the COVID-19 treatment contributes to this. As a result of the above a bidirectional TB and COVID-19 screening is warranted in all facilities offering HIV prevention and treatment services.

TABLE 44: RADIOLOGICAL FEATURES OF COVID-19 VS TUBERCULOSIS

COVID-19	Tuberculosis
Bilateral lower zone infiltrates (consolidation), & likely to be peripheral	May be unilateral, typically apical in HIV-Neg
Not observed	Miliary infiltrates in immunocompromised
No effusion	Effusion is a common feature
No evidence of Cavitation	Cavitation in immunocompetent
Ground glass on CT	Not a typical feature
No lymphadenopathy	Hilar Lymphadenopathy is typical
CXR may be normal	CXR may be normal
Rapid progression (within hours or days)	Slow progression weeks to months

Bi-directional TB Screening

This will be carried out in two settings. i.e., the chest clinic and the Post-Acute COVID-19 (PAC-19) clinic. Routine visits in the ART clinic are another opportunity to screen for both TB and COVID using the WHO standard screening questions for TB.

FIGURE 33: ALGORITHM FOR COVID-19 SCREENING IN TB CLINIC

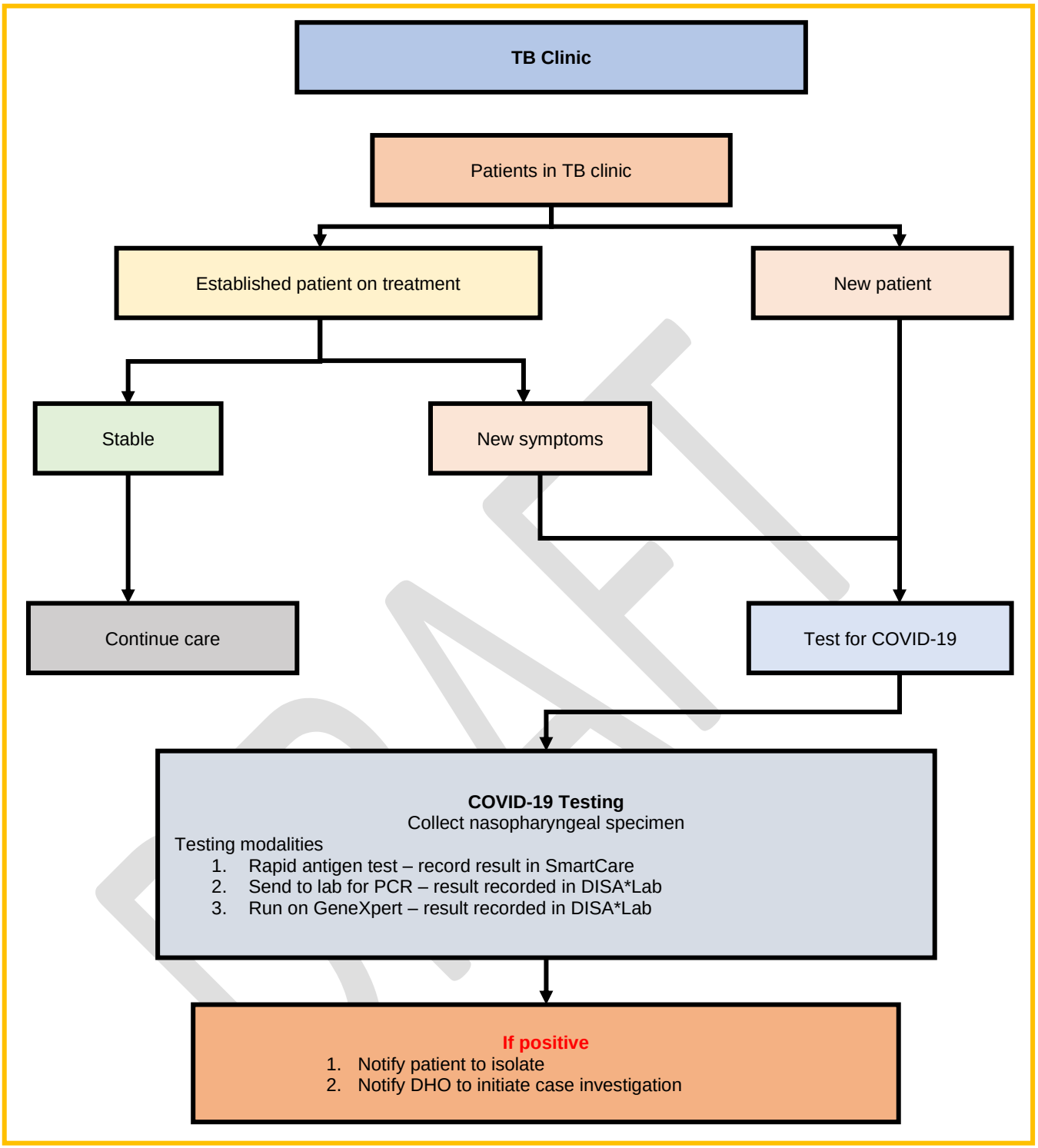
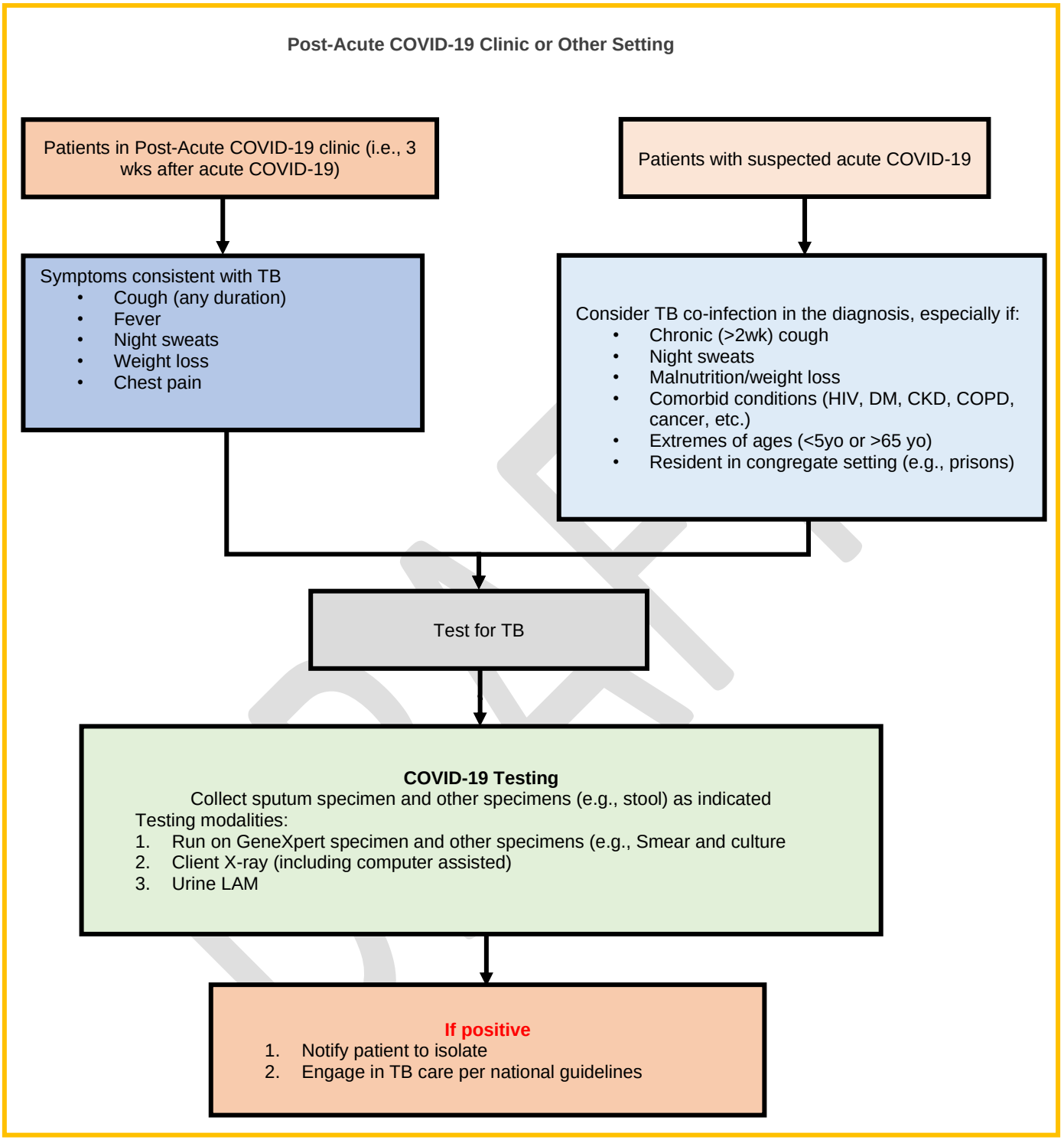


FIGURE 34: ALGORITHM FOR TB AND COVID-19 SCREENING



SEXUALLY TRANSMITTED INFECTIONS AND HIV

Screening and Management of Sexually Transmitted Infections

Sexually transmitted diseases are common among people living with HIV. They are also a risk factor for the acquisition of HIV. The risk of STI among even higher among key populations including FSW. The following recommendations should be done to address STIs in people living with HIV:

- Sexually transmitted infection and family planning services should be integrated within HIV care settings
- Assessment for high-risk sexual practises and symptomatic screening must be done on all clinical interaction
- Preventive strategies including condom distribution must be done for high-risk individuals
- Annual periodic serological testing for asymptomatic Syphilis infection can be offered in high-risk population
- HIV positive female sex workers and other high-risk individuals, in settings with limited clinical services, may have periodic presumptive treatment for asymptomatic sexually transmitted infections
- All pregnant women must be screened for Syphilis during the first antennal care visit

Recommendations for the Management of Symptomatic Sexually Transmitted Infections

Management of Urethral Discharge

- For people who present with urethral discharge from the penis, management is recommended to be based on the results of quality-assured molecular assays. However, in settings with limited or no molecular tests or laboratory capacity, same day syndromic treatment is advised. Management of Vaginal Discharge
- For people who present with vaginal discharge treatment for *N. gonorrhoeae* and/or *C. trachomatis* and/or *T. vaginalis* must be initiated on the same visit. Treatment should, as much as possible, be based on the results of quality-assured molecular **assays for** *N. gonorrhoeae* **and/or** *C. trachomatis* **and/or** *T. vaginalis*
- In settings in which treatment based on the results of molecular assay in the same visit is not feasible or that have limited or no molecular test, treatment based on testing with quality-assured rapid point-of-care tests or on syndromic treatment
- Bacterial vaginosis treatment must be instituted if vaginal discharge is present (for example, tenacious or thin) or based on the results of microscopy, if available
- Treatment for candidiasis should be instituted, where indicated, by type **of discharge** (such as curd-like with vaginal itching) or by the results of microscopy, if available

Management of Women with Lower Abdominal Pain

- For sexually active women who present with lower abdominal, asses for pelvic inflammatory disease and treating syndromically

Sexually active women with lower abdominal pain with either of the following features on clinical examination (bimanual palpation):

- Cervical motion tenderness; or
- Lower abdominal tenderness

The following is suggested

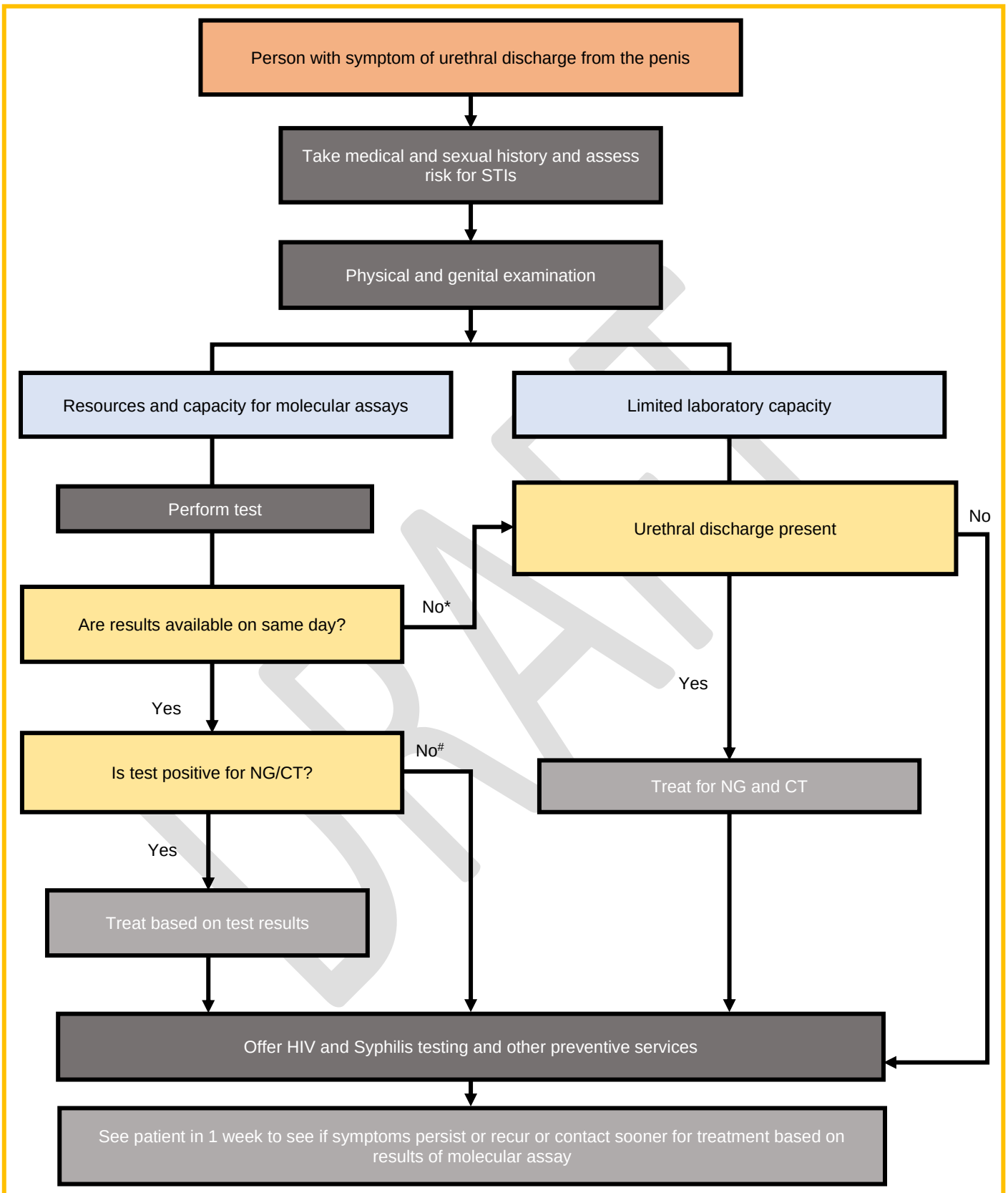
- Treat for pelvic inflammatory disease on the same visit.
- Test for infection with *N. gonorrhoeae* and *C. trachomatis* and, if available *Mycoplasma genitalium*, to support partner management when tests are available *(conditional recommendation, low-certainty evidence)*

Management of Genital Ulcer Disease, including Anorectal Ulcer

- For people who present with genital ulcers (including anorectal ulcers), it is recommended that treatment is based on quality-assured molecular assays of the ulcer
- However, in settings with limited or no molecular tests or laboratory capacity, syndromic same day treatment should be instituted

.

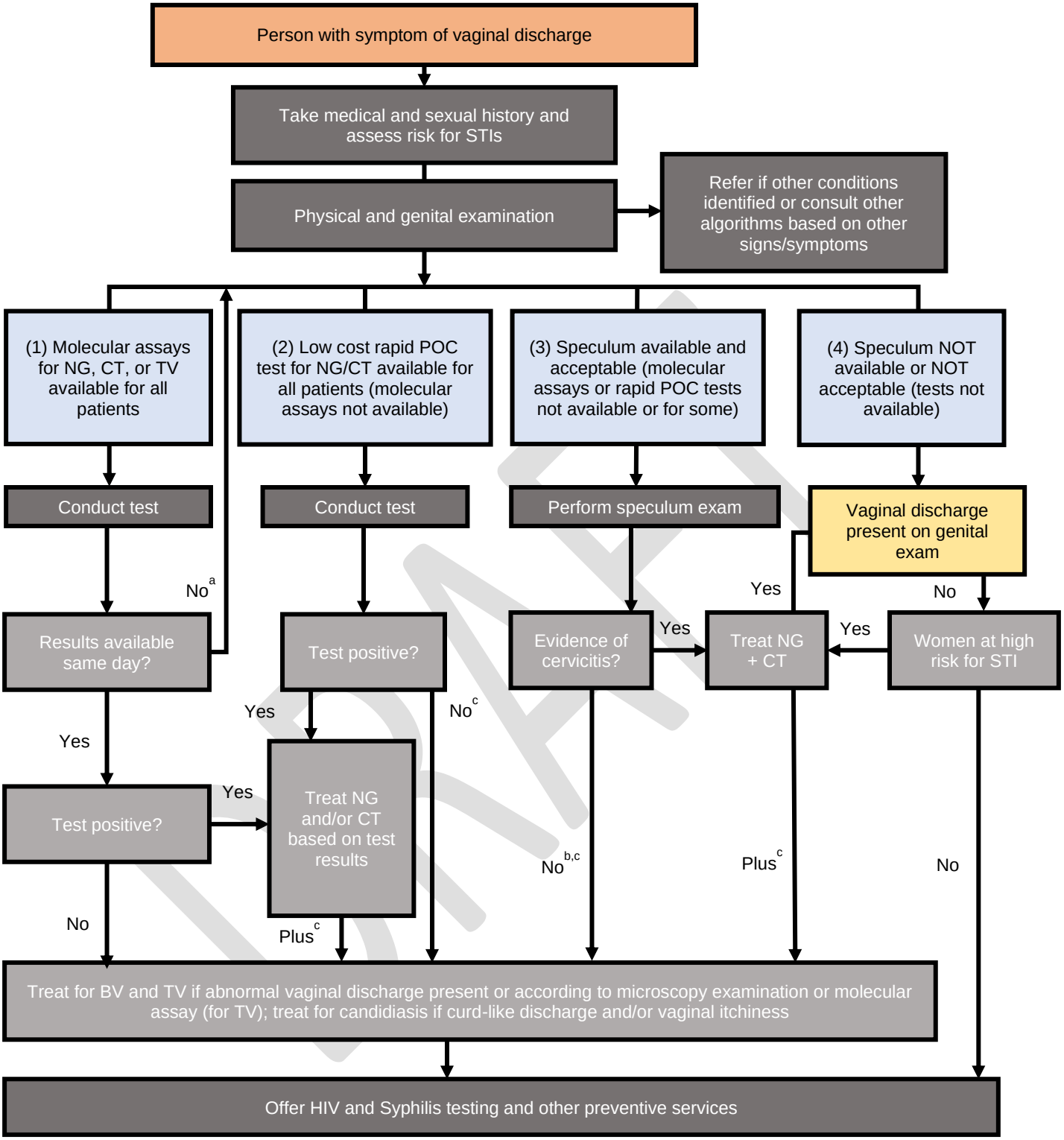
FIGURE 35: SYNDROMIC MANAGEMENT OF URETHRAL DISCHARGE SYNDROME



NG, N gonorrhoea; CT, C trachomatis
*If molecular assay was performed and results were not available on the same day, revise the syndromic treatment initially provided according to the test results when available
#If test is negative but urethral discharge is present, treat for non-gonococcal/non-chlamydial urethritis (such as *M. genitalum, T. vaginalis,* or *herpes simplex virus*)

Adopted from the 2021 WHO Guidelines for the Management of Symptomatic Sexually Transmitted Infections

FIGURE 36: SYNDROMIC MANAGEMENT OF VAGINAL DISCHARGE SYNDROME



NG, N. gonorrhoeae; CT, Chlamydia trachomatis; TV, Trichomonas vaginalis; BV, bacterial vaginosis

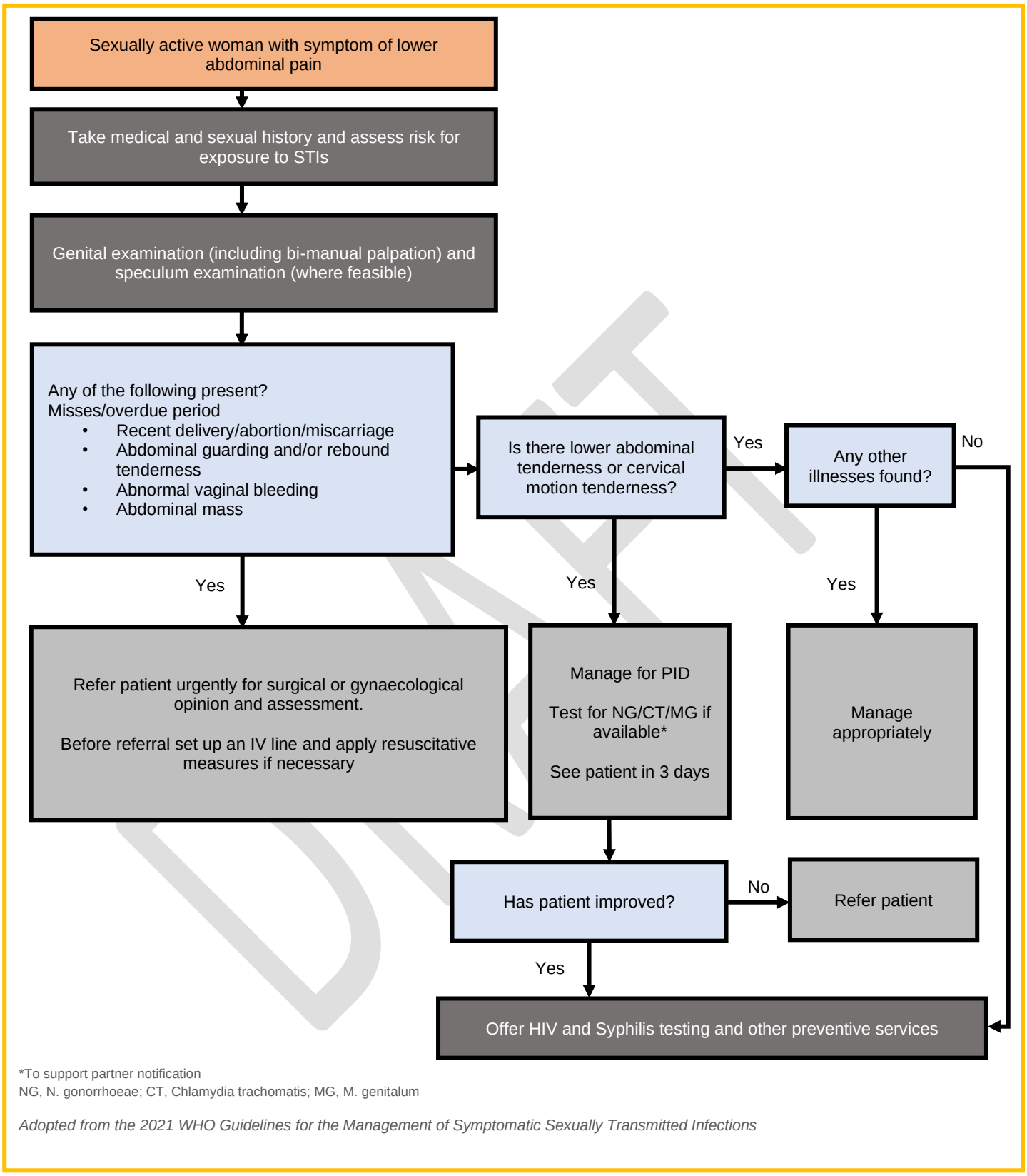
[a]If molecular assay was performed and results were not available on the same day, revise the syndromic treatment initially provided according to the test results when available

[b]Perform rapid point of care test or molecular assay if available to confirm NG/CT and treat if positive; if negative, do not treat and ask woman to recur

[c]If woman complains of recurrent or persistent discharge, refer to a centre with laboratory capacity

Adopted from the 2021 WHO Guidelines for the Management of Symptomatic Sexually Transmitted Infections

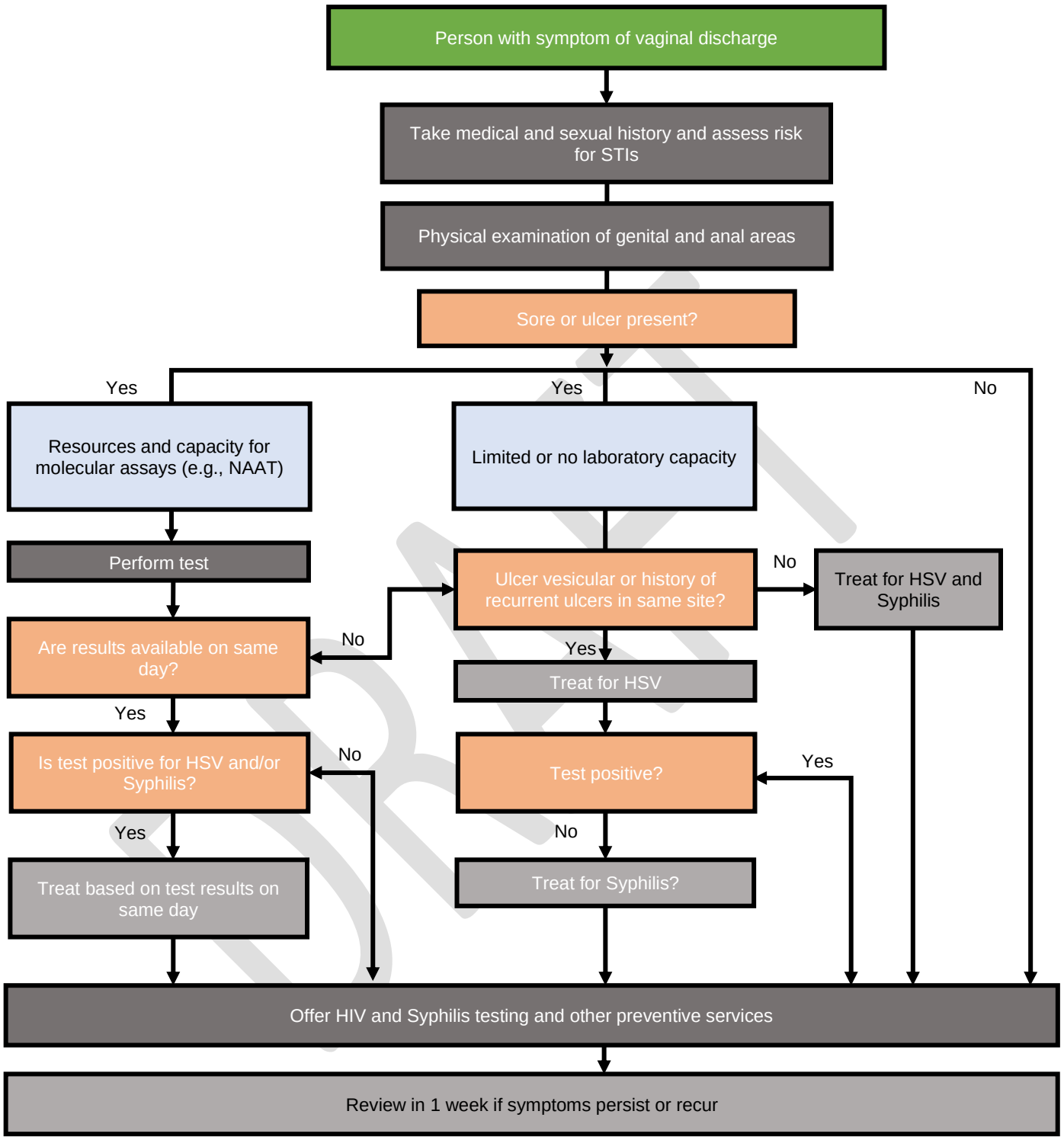
FIGURE 37: SYNDROMIC MANAGEMENT OF PELVIC PAIN



*To support partner notification
NG, N. gonorrhoeae; CT, Chlamydia trachomatis; MG, M. genitalum

Adopted from the 2021 WHO Guidelines for the Management of Symptomatic Sexually Transmitted Infections

FIGURE 38: SYNDROMIC MANAGEMENT OF GENITAL AND ANAL ULCERS



HSV, Herpes simplex virus
**If molecular assay were performed and results were not available on the same day, revise the syndromic treatment according to the test results when available*

Adopted from the 2021 WHO Guidelines for the Management of Symptomatic Sexually Transmitted Infections

TABLE 45: RECOMMENDED TREATMENT REGIMENS FOR SYNDROMIC TREATMENT OF STIS

STI Syndrome	First-Line Treatment	Alternative Treatment
Vaginal Discharge	Ceftriaxone 500mg IM stat PLUS Azithromycin 1g orally stat PLUS Metronidazole 2g orally stat	Cefixime 400mg orally stat Doxycycline 100mg BD orally for 7 days or Erythromycin 500mg QID in pregnant women for 14 days
Genital Ulcer	Benzathine Penicillin, 2.4 MU IM stat as a single injection split as 1.2 MU given in each buttock PLUS Azithromycin 1g, orally stat PLUS Acyclovir 400mg orally TDS for 7 days	In pregnant women: Give Erythromycin base/ stearate 500 mg orally QID for 14 days (when Erythromycin is used, the baby must be treated for Syphilis if the mother is positive for Syphilis)
Urethral Discharge	Ceftriaxone 500mg IM stat (to treat gonococcal infection) PLUS Azithromycin 1g orally stat (to treat chlamydial infections) PLUS Metronidazole 2g orally stat (to treat trichomonal infections)	Cefixime 400mg orally stat for GC PLUS Doxycycline* 100mg orally BD for 7 days, OR Erythromycin 500 mg orally QID for 7 days (for Chlamydia)
Inguinal Bubo	Azithromycin 1g orally stat and then 1g orally once weekly for 2 weeks (to treat both Chancroid and LGV) Aspirate bubo with a large bore needle through normal skin	Doxycycline 100mg orally BD for 14 days (to treat LGV) PLUS Ceftriaxone 500mg IM stat (to treat Chancroid)
Female Lower Abdominal Pain (PID)	Ceftriaxone 500mg IM stat (to treat gonococcal infection GC) PLUS Azithromycin 1g orally once weekly for 2 weeks OR Doxycycline* 100mg orally BID for 14 days PLUS Metronidazole** 400mg orally TDS for 7 to 14 days (to treat anaerobic bacteria)	Cefixime 400mg orally stat plus Erythromycin 500mg QID for 14 days
Genital Growth	Podophyllin 25% tincture (protect normal skin with Vaseline before application by health care provider) Benzathine Penicillin 2.4 MU IM weekly x 3 doses	Cauterization Trichloroacetic Acid Cryotherapy
Scrotal Swelling	Ceftriaxone 500mg IM stat PLUS Azithromycin 1g orally per week for 2 weeks	Cefixime 400mg orally stat Doxycycline 100mg BD x 14 days or Erythromycin 500mg QID x 14 days
Neonatal Conjunctivitis	Ceftriaxone 50mg/kg body weight (max. 125mg) IM single dose, (to treat gonococcal infection) PLUS Erythromycin syrup 50mg/kg body weight orally daily in 4 divided doses for 14 days (to treat chlamydial infection)	

Monkey Pox

Monkeypox (MPX) is a viral zoonotic disease that belongs to the Orthopoxvirus genus of the Poxviridae family. Human disease was first identified in 1970. In May 2022, multiple cases of monkeypox were identified in several non-endemic countries. On July 23, the WHO Director-General declared the escalating global monkeypox outbreak a Public Health Emergency of International Concern (PHEIC). In this, epidemic, MPX disproportionately affect people living with HIV in the western world and those immunosuppressed in the Global South.

Monkeypox can spread between people through close contact, skin-to-skin contact including sexual contact with a person with monkeypox, or contact with contaminated fomites (e.g., shared linens).

The incubation period of MPX is usually 6 to 13 days following exposure but can range from 5 to 21 days Although most people recover within weeks, severe complications and sequelae have been reported to be more common among those unvaccinated for smallpox compared with those vaccinated.

Clinical signs and symptoms: The initial phase of clinical illness typically lasts 1 to 5 days, during which time patients may experience fever, headache, back pain, muscle aches, lack of energy and lymphadenopathy. This is followed by a second phase, which typically occurs 1 to 3 days after fever subsides with the appearance of a rash The rash presents in sequential stages – macules, papules, vesicles, pustules, umbilication before crusting over and desquamating over a period of 2 to 3 weeks. The lesions range in size from 0.5 to 1 cm in diameter and from a few to several thousand in number. The eruption tends to be centrifugal, starting on the face and extending towards the palms and soles of the hands and feet, and can involve the oral mucous membranes, conjunctiva, cornea and/or genitalia Observations from current outbreaks in European and North American countries describe lesions starting in the genital area. Most reported deaths have occurred in young children and immunocompromised individuals, such as those with poorly controlled HIV.

Screening and Diagnosis:

All PLHIV meeting a **suspect** definition of MPX i.e, a triad of Fever , Lymphadenopathy, and typical rash, must be isolated and subjected to a test for MPX. Differential diagnosis for MPX include other infectious diseases or other conditions, including varicella zoster virus (VZV, chickenpox), herpes simplex virus (HSV), primary or secondary syphilis, disseminated gonococcal infection (DGI), foot and mouth disease, chancroid, lymphogranuloma venereum (LGV), granuloma inguinale, molluscum contagiosum, measles, scabies, rickettsia pox, chikungunya, zika virus, dengue fever, vasculitis and other bacterial skin and soft tissue infections.

Clinical Management

Most people with monkeypox recover fully within 2 to 4 weeks without the need for medical treatment. Treatment should therefore be symptomatic including pain relief and care for the rash. Antivirals (tecovirimat) where available may be used for people who are more likely to get severely ill, e.g immunosuppressed individuals. Life threating complications may occur including; superimposed bacterial infections on the skin lesions causing sepsis, pneumonia, corneal infection, severe dehydration and electrolyte abnormalities, retropharyngeal abscess and encephalitis.

Prevention and Control

Vaccination for people who have been exposed to monkeypox and people who may be more likely to get monkeypox is recommended. Approved vaccine include the 2 dose JYNNEOS vaccine and the single dose ACAM2000 vaccine. The following 3 steps are important the prevention of MPX:

1. Avoid close, skin-to-skin contact with people who have a rash that looks like monkeypox.
2. Avoid contact with objects and materials that a person with monkeypox has used.
3. Wash your hands often.

HEPATITIS B AND HIV

Screening and Management of Hepatitis B Virus (HBV) and HIV Co-Infection

- Patients with HIV-HBV co-infection experience twice the risk of mortality during ART compared to HIV-infected individuals who do not have HBV
- Everyone newly diagnosed with HIV should be screened for HBsAg and anti-HBs to identify those with chronic HB infection
- TDF (or TAF) and 3TC are active against HBV; however, using 3TC as the only HBV-active antiretroviral drug will lead to HBV drug resistance and is not recommended. ART regimens that contain TDF (or TAF) as the only HBV-active antiretroviral are okay because HBV resistance with TDF (or TAF) alone is very rare
- Hepatitis B surface antigen (HBsAg) should be done at baseline and in patients with unknown HBV status
- For children who have been fully vaccinated (i.e., 3 doses), do not screen for HBV unless there is strong clinical suspicion
- Start TDF-containing ART regardless of CD4 count in HIV/HBV co-infected patients
- Patients failing First-Line TDF (or TAF) + XTC treatment should continue the TDF (or TAF) in their 2nd line therapy (i.e., TDF (or TAF) + AZT + 3TC + LPV-r or ATV-r or DRV-r) to control their HBV infection
- For HBsAg positive patients with renal insufficiency (CrCl <50mL/min), consult or refer to next level
- For HBV-HIV co-infection in child <6 years old, consult or refer to the next level
- Children above 6 years old (≥ 25kg) can be on TAF-based regimen

HEPATITIS B MONO-INFECTION

Screening and Management of Hepatitis B Virus (HBV)

- Hepatitis B surface antigen (HBsAg) should be used for screening and diagnosis of active HBV infection; a negative HIV test is required to classify a person as having HBV mono-infection
- The ZAMPHIA 2016 study reported that 5.6% of adults were hepatitis B surface antigen positive; of these most were HIV-negative
- Other hepatitis B tests (like surface antibody or core antibody, core antibody, HBV antigen and HBV DNA viral load) can be used to know if the person has active infection
- Many cases of active HBV infection will not require immediate antiviral therapy but instead can be observed and followed up every 6-12 months
- APRI (AST-to-platelet ratio index) is the preferred non-invasive test (NIT) to assess for the presence of cirrhosis and can be calculated as follows:

$$\text{APRI} = \frac{\text{[AST Level / AST (Upper Limit of Normal)]}}{\text{Platelet Count } (10^9/\text{L})} \times 100$$

APRI Score Interpretation

AST aminotransferase to Platelet Ratio Index

- APRI score >2.0 in adults is highly suggestive of cirrhosis
- APRI score <1.0 can rule out the presence of cirrhosis
- APRI score 1.0-2.0 is a grey area

Eligibility Criteria for Antiviral Treatment

- The presence of cirrhosis is a treatment indication in all adults, adolescents, and children with chronic HBV infection regardless of ALT levels, HBeAg status, or HBV DNA levels
- Diagnosis of cirrhosis is based on APRI score >2.0 in adults
- Clinical signs of decompensated cirrhosis may include portal hypertension (ascites, variceal haemorrhage, and hepatic encephalopathy), coagulopathy, or liver insufficiency (jaundice). Other clinical features of advanced liver disease/cirrhosis may include hepatomegaly, splenomegaly, pruritis, fatigue, arthralgia, palmar erythema, and edema
- Treatment is recommended for adults who do not have clinical evidence of cirrhosis (or based on APRI score >2 in adults) but do have one of the following:
    - Persistently elevated ALT levels and evidence of high-level HBV replication (HBV DNA >20,000 IU/mL), regardless of HBeAg status
    - When HBV DNA testing (and/or HBeAg testing) is not available, treat when ALT is persistently elevated. Persistent means at least two elevated ALT levels over 6-12 months and newer HBV guidelines now define 'ALT elevation' as ALT >19 U/L for women and ALT>30 U/L for men
    - In HBV/HIV co-infected individuals, TDF based ART should be initiated regardless of CD4 count
- Remember in Zambia other common causes of ALT elevation are medications (such as ATT), liver infections (such as TB), and heavy alcohol consumption
- In treatment-eligible patients, measurement of Creatinine is recommended

Non-Eligible Patients

Antiviral therapy is not recommended or deferred in the following situations:

- No clinical evidence of cirrhosis
- APRI score ≤2.0 in adults
- Persistently normal ALT levels (i.e., ALT ≤20 in women and ≤30 in men)
- Low levels of HBV DNA replication (HBV DNA <2,000 IU/mL), regardless of HBeAg status

Continue monitoring in all persons with chronic HBV infection especially those who do not meet the above eligibility and non-eligibility criteria to determine if antiviral therapy may be indicated in the future to prevent progressive liver disease. Monitoring could be done every 3-6 months in those with ALT elevation and every 6-12 months in those with normal ALT.

First-Line Regimen

- In all adults, adolescents and children aged 10 years or older (≥ 30kg) the preferred drug is TDF+3TC
- In children aged 2 to <10 years, Entecavir is the preferred drug over Tenofovir
- The dosing should be as follows:
    - Tenofovir 300mg once daily
    - Tenofovir 300mg plus Lamivudine 300mg
    - Entecavir 0.5mg once daily (adult with compensated liver disease and lamivudine naive)
    - Entecavir 1mg once daily (adult with decompensated liver disease)
- Patients with CrCl <50mL/min should be referred to a higher level for further management
- Counselling patients that HBV treatment is potentially lifelong is important to set their expectation

Monitoring of Therapy in HBV

- There are several goals of HBV antiviral therapy, as follows:
  - Suppression of HBV viral load (i.e., HBV DNA below assay detection)
  - Normalization of the ALT
  - Conversion from HBeAg-positive to negative
  - Conversion from HBsAg-positive to HBsAg-negative
- Repeat ALT every 6 months is recommended during treatment
- Every 1-2 years HBsAg can be repeated; however, conversion to HBsAg-negative occurs at a rate of <5% per year during chronic infection
- Repeat Creatinine every 12 months is also recommended as TDF carries a small risk of renal toxicity
- Repeat an HIV antibody test every 12 months; if patient becomes HIV-positive during HBV treatment (i.e., HIV-HBV co-infection), ART should be initiated

When to Discontinue Therapy

- Discontinuation of HBV-active therapy can be associated with a fatal flare-up of hepatitis; therefore, counsel patients that after stopping they should return if they develop fever and jaundice or other signs of liver disease
- When there is evidence of conversion from HBeAg-positive to HBeAg-negative and after completion of at least one additional year of treatment AND the ALT is persistently normal
- When there is conversion to HBsAg loss and completion of at least one additional year of treatment and the ALT is persistently normal
- If HBV DNA testing is available, persistently undetectable HBV DNA in addition to the above criteria should also guide when to discontinue
- IMPORTANT NOTE: Relapse may occur after stopping therapy, especially in patients who were HBeAg-negative at the start of antiviral therapy. Therefore, after discontinuation, ongoing monitoring of ALT (every 6-12 months) is recommended. Restart therapy if there are signs of reactivation such as HBsAg or HBeAg become positive, ALT levels increase significantly, or HBV DNA becomes detectable again

General Measures to Reduce HBV Transmission

- HBsAg-positive persons should adopt correct and consistent condom use during sexual intercourse; not share razors, toothbrushes, or other personal care items; not donate blood, organs, or sperm; and follow standard universal precautions with open cuts or bleeding
- HBV vaccination of household and sexual contacts to HBsAg-positive individuals. Household members and sexual partners of persons with Chronic Hepatitis B should be vaccinated if they are negative for HBsAg
- Alcohol reduction to reduce disease progression
- Infants should receive all vaccines recommended through the Extended Program on Immunizations
- Infants born to HBsAg-positive mothers should have an HBV vaccine as soon as possible after birth if possible, which provides protection against mother to baby transmission

Measures to Reduce HBV Transmission in Hospital Settings

- Healthcare workers should be tested for HBsAg and vaccinated if they are negative for HBsAg
- Hand hygiene: including surgical hand preparation, hand washing, and use of gloves
- Safe handling and disposal of sharps and waste
- Safe cleaning of equipment
- Testing of donated blood
- Improved access to safe blood
- Training of health personnel

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CRYPTOCOCCAL DISEASE AND HIV INFECTION

Screening for Cryptococcal Disease

All HIV-infected patients with CD4 count < 100 cells/µL should be screened for Cryptococcal infection with symptomatic screening and Cryptococcal antigen (CrAg)

If CrAg is positive, and no symptoms suggestive of Cryptococcal Meningitis, prophylactic Fluconazole 800mg OD should be given for 14 days, then commence ART and continue Fluconazole 800mg OD for another 6-8 weeks, then maintenance Fluconazole 200mg OD till immune reconstitution

If symptoms of Cryptococcal Meningitis are positive and serum CrAg is positive, a Lumber Puncture (LP) must be done

Diagnosis of Cryptococcal Disease

- Prompt lumbar puncture with measurement of Cerebrospinal fluid (CSF) opening pressure and rapid CSF Cryptococcal antigen (CrAg) assay or rapid serum CrAg (either LA or LFA) is the preferred diagnostic approach

Treatment Options for Cryptococcal Disease

Phase	Duration	Treatment	Remarks
Induction	**Option 1** ***(Recommended) Single dose of Liposomal Amphotericin B***	High dose Liposomal Amphotericin B 10mg/kg on day 1 *plus* 14 days of Flucytosine 100mg/kg and Fluconazole 1200mg	▸ This has less nephrotoxicity and requires less monitoring
	Option 2 ***7 day of Amphotericin Deoxycholate***	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 (1,200mg/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 3 **2 weeks of** ***Amphotericin Deoxycholate***	Alternative: Amphotericin B deoxycholate 0.7 – 1mg/kg/day IV x 14 days with Fluconazole* 1,200 mg – 800mg PO or IV daily x 14 days	
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^3 for 6 months on two occasions with a suppressed viral load	Fluconazole 200mg PO OD (for children 6mg/kg)	

Non-communicable Diseases and HIV Infection

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

- Older than 40 years, obesity, diabetes mellitus, known hypertension, waist circumference of >90cm (women) and 110cm (men), family history of premature CVDs

Up to two thirds of premature deaths from the major NCDs are linked to four shared modifiable risk factors:

- Tobacco use, harmful use of alcohol, unhealthy diet, and physical inactivity

These risk factors result in a series of metabolic and physiological changes that eventually lead to NCDs. Broader social, economic, and environmental determinants of health and inequities associated with globalization and urbanization, alongside population ageing, are the underlying drivers of the behavioural risk factors, and thus the NCD epidemic.

In addition, it is important to note that certain ARVs are associated with metabolic issues. Because of this, it is important to continuously monitor metabolic and physiological changes in RoC.

Figure 39: Causal Links Between Underlying Drivers For NCDs, Behavioural Risk Factors, Metabolic /Physiologic Risk Factors And NCDs

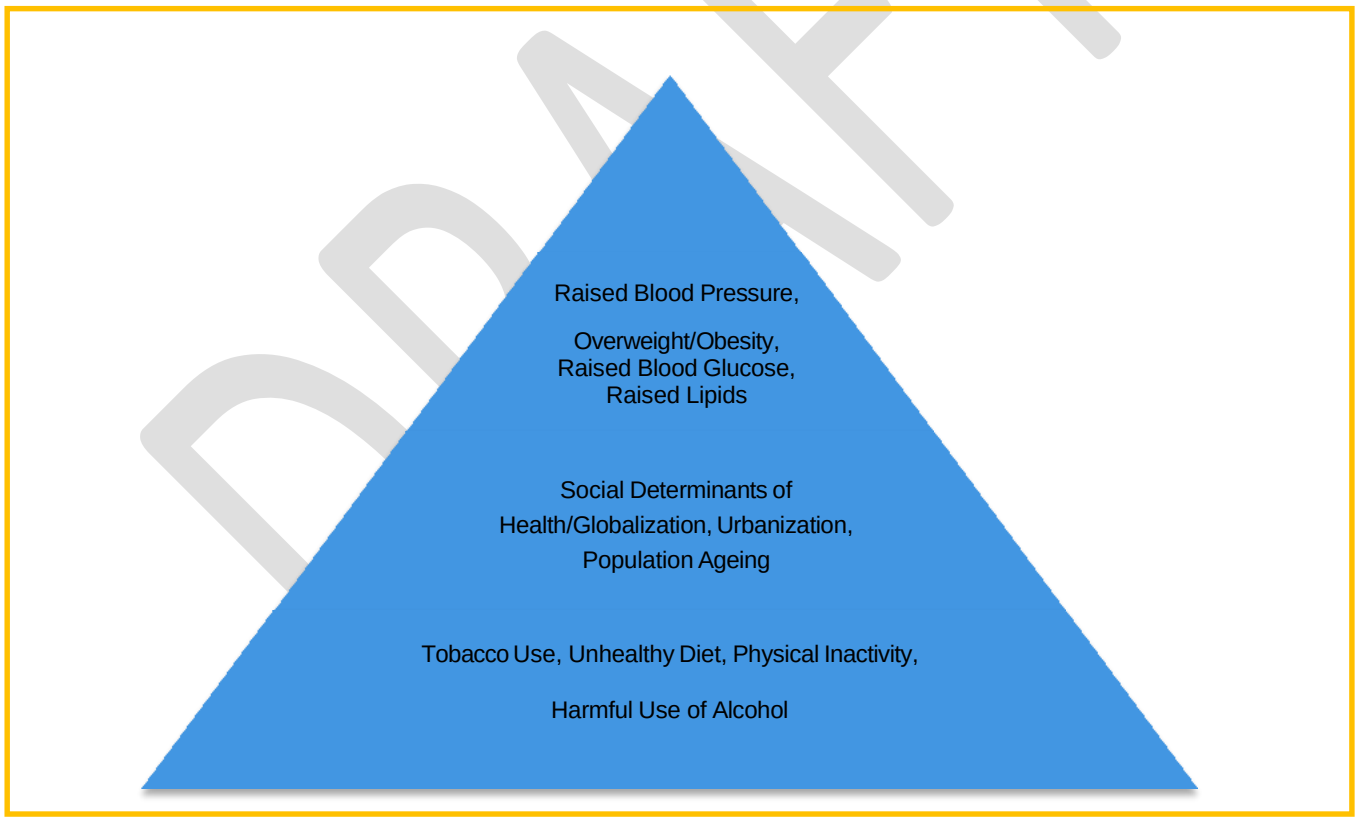


TABLE 46: LIFESTYLE MODIFICATIONS TO PREVENT AND MANAGE CVDS AMONG HIV-INFECTED INDIVIDUALS

Smoking Cessation

- Smoking cessation has multiple short-term and long-term benefits, including:
  - ✓ Skin does not age/wrinkle as quickly
  - ✓ Improved fitness and quicker recovery from common infections
  - ✓ Reduced risk of respiratory infections and chronic lung disease
  - ✓ Reduced risk of high blood pressure, diabetes, kidney disease, heart disease, and stroke
  - ✓ Improved infant outcomes (for pregnant women who smoke)
  - ✓ Reduced risk of cancers: lung, bladder, breast, mouth, throat, oesophagus
  - ✓ Evidence of better response to ART (better viral suppression)

Dietary Changes and Weight Loss

- ✓ Weight loss to maintain a healthy BMI (nutritionists to be engaged in patient care)
- ✓ Reduce/abstain from alcohol
- ✓ Cut down sugar intake
- ✓ Cut down red meat intake
- ✓ Cut down salt intake to less than one teaspoon a day
- ✓ Cut down consumption of fatty foods, fat for flavouring, and fried foods
- ✓ Increase intake of whole grains, vegetables, fruit, and beans (eating at least five servings of fruit and vegetables a day)
- ✓ Increase intake of fish

Physical Activity

- Active lifestyle with moderate-intensity physical activity
- It is recommended to have moderate-intensity physical activity for at least 30 minutes 3 – 5 times a week

TABLE 47: DYSLIPIDAEMIA SCREENING, DIAGNOSIS AND INITIAL MANAGEMENT FOR HIV-INFECTED INDIVIDUALS

Screening

- Fasting lipid profile should be evaluated at baseline for all PLHIV, then annually if baseline screening is normal

Diagnosis

- Dyslipidaemia is defined as high fasting total cholesterol (>5.2mmol/L), LDL (>3.4mmol/L) or triglycerides (>2.2mmol/L)

Management

- Lifestyle modifications for 3-6 months
- 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 DRV-r, ATV-r or DTG) as the treatment of choice before adding a lipid-lowering drug.
- If does not meet treatment target with lifestyle modifications, then add drugs:
  - ✓ 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). Note that There is a potential interaction between PIs and atorvastatin which can lead to increased atorvastatin levels and rhabdomyolysis
  - ✓ Allow at least 3 months before repeating fasting lipids and titrating dose
- Once targets achieved can monitor lipids every 6-12 months

TABLE 48: HYPERTENSION SCREENING, DIAGNOSIS AND INITIAL MANAGEMENT FOR HIV-INFECTED INDIVIDUALS

Screening
• BP should be measured and recorded at every visit
Diagnosis
• Hypertension requiring intervention is defined as BP ≥140/90mmHg on at least two different occasions ✓ It can also be diagnosed at the same visit if the BP is 180/110 or any BP associated with target organ damage
Management
If baseline BP is 140-159/90-99: • Lifestyle modifications for at least 6 months, along with monthly BP monitoring • If does not meet treatment target with lifestyle modifications, then add drugs: ✓ Introduce 1 drug at a time, and allow 2-3 weeks to achieve maximal effect before titrating up dosage; titrate to maximum dosage before adding an additional drug ✓ In PLHIV without kidney disease or diabetes, First-Line antihypertensive therapy is a thiazide diuretic such as Hydrochlorothiazide starting at 12.5mg OD (maximum dose 25mg OD) **OR** a calcium channel antagonist such as Amlodipine starting at 2.5mg OD (maximum 10mg OD) ✓ In PLHIV with kidney disease or diabetes the first antihypertensive should be an ACE-I or ARB such as Enalapril 2.5-10mg OD (maximum dose is 20mg BD); Losartan 50mg OD (maximum dose is 100mg OD) ✓ If inadequate response once dose has been titrated, an additional agent may be required (e.g., Hydrochlorothiazide starting at 12.5mg OD [maximum dose 25mg OD]) ✓ If inadequate response to two agents, consider consultation with or referral to a clinician experienced in the management of refractory hypertension. Note: Calcium-channel blockers have known drug interactions with PIs and NNRTIs and should be used with caution • If baseline BP ≥160/100mmHg: initiate lifestyle modifications and introduce anti-hypertensive medications concurrently • Target BP measurements ✓ Diabetic patients: <140/90 ✓ Non-Diabetic & Chronic Kidney Disease (CKD) patients: 140/90 ✓ Non-Diabetic & Non-CKD patients: <140/90 (<60 years); 150/90 (>60 years old)

ACE-I = Angiotensin Converting Enzyme Inhibitor; ARB = Angiotensin Receptor Blocker

TABLE 49: TYPE 2 DIABETES MELLITUS SCREENING, DIAGNOSIS AND INITIAL MANAGEMENT FOR HIV-INFECTED INDIVIDUALS

Screening

- 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

Diagnosis

- Diabetes Mellitus is defined as fasting blood sugar ≥7.0mmol/L, or random blood sugar ≥11.1mmol/L, or HbA1C >6.5%
- Abnormal results should be repeated to confirm the diagnosis

Management (treatment target is HbA1C ≤7.0% or FBS 4-7mmol/L)

- Monitor HbA1c (or FBS if HbA1c not available) every 3 months for patients with confirmed diagnosis of diabetes mellitus
- 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
- If does not meet treatment target with lifestyle modifications, then add drugs:
  - ✓ Metformin (the daily dose should be limited to 1000mg if patient is on DTG)
  - ✓ Obtain baseline Creatinine; DO NOT use Metformin if Creatinine Clearance <45mL/min
  - ✓ 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)
  - ✓ 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. Some patients may require Insulin
- 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)
- Additional routine screening for patients with diabetes:
  - ✓ Annual ophthalmology examination for diabetic retinopathy
  - ✓ Annual urinalysis: start on an ACE-I/ARB if proteinuria develops (even if BP normal)

ACE-I = Angiotensin Converting Enzyme Inhibitor; ARB = Angiotensin Receptor Blocker

TABLE 50: CHRONIC KIDNEY DISEASE SCREENING, DIAGNOSIS AND INITIAL MANAGEMENT FOR HIV-INFECTED INDIVIDUALS

- Urinalysis (for protein) and serum Creatinine should be evaluated at baseline for all PLHIV

Diagnosis

- Impaired renal function is defined as Creatinine Clearance < 50mL/min, or dipstick proteinuria ≥ 1
- Abnormal results should be repeated to confirm diagnosis

Management

- Management depends on the cause of the renal impairment; additional investigations and/or specialist consultation may be required
- Treat dehydration promptly and aggressively
- If on TDF-containing regimen, substitute with another ARV, with the exception of patients with HBV/HIV co-infection who need TDF to be maintained on adjusted doses or switch to Entecavir (see section on Hepatitis B/HIV co-infected)
- Avoid nephrotoxic drugs
- Evaluate for and treat hypertension
- 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

Mental Health and HIV Infection

Mental disorders are highly prevalent among people living with HIV (PLHIV), with major depressive disorder (MDD) occurring almost twice as frequently among this group than in the general population. Common Mental Disorders (CMDs) typically include depressive disorders, anxiety disorders, HIV-associated neurocognitive disorders, delirium disorders and substance use disorders. Adolescents are at a higher risk of mental health challenges. These disorders may increase an individual's risk for HIV infection through increased social vulnerability, altered risk behaviour, associated substance misuse and loss of control within sexual relationships. These may also have a substantial impact on HIV disease progression and ART adherence. Conversely, such disorders may also arise as a direct result of HIV neuro-invasion or psychosocial stressors, or due to complications of Antiretroviral Therapy (ART).

Despite their prevalence, mental disorders are often under-diagnosed or inadequately managed in PLHIV. The impact of untreated mental disorders on health outcomes is substantial. It is imperative that clinicians caring for HIV-positive individuals actively screen for, diagnose and manage mental disorders in this population, especially because patients rarely volunteer information about their mental state. Screening for depression may support adherence to ART, retention in care, suppression of viral loads and improve quality of life. Implementing treatment for depression among people living with HIV may require task sharing, building health-care worker capacity, national adaptation of screening tools and simplifying tools for use by non-specialized primary care providers.

All patients with mental disorders should be offered HIV testing, HIV-prevention/risk- reduction education and access to condoms. The presence of a mental disorder does not automatically equal incapacity to consent to HIV testing. Capacity to consent to HIV testing must therefore be assessed on an individual basis.

It is important to assess for suicide risk. Clinicians should always ask about suicidal ideation in patients with depressive symptoms. High risk is indicated by a clear plan for ending life, an identified lethal method, a previous suicide attempt, a lack of social support and severe (psychotic) depressive disorder.

For individuals with mental illness, integration of mental health care into existing health systems or linkage to the mental health services should be implemented in the settings in which health-care infrastructure and trained human resources are available. Adolescents in particular should be referred and offered mental services in adolescent-friendly spaces. Orphans and vulnerable children should be referred to organizations offering support services.

Cervical Cancer and HIV

Cervical cancer is preventable and is curable if diagnosed and treated early. All women regardless of age should be assessed for cervical cancer; women living with HIV have a higher risk of pre-cancer and invasive cancer (women with HIV are 4-5 times more likely to develop cervical cancer). Cervical cancer screening with HPV DNA test or Visual Inspection with Acetic acid (VIA) or cytology leads to early detection and management of cervical cancer.

Figure 40: Cervical Cancer Screening Algorithm With VIA (Screen And Treat Approach)

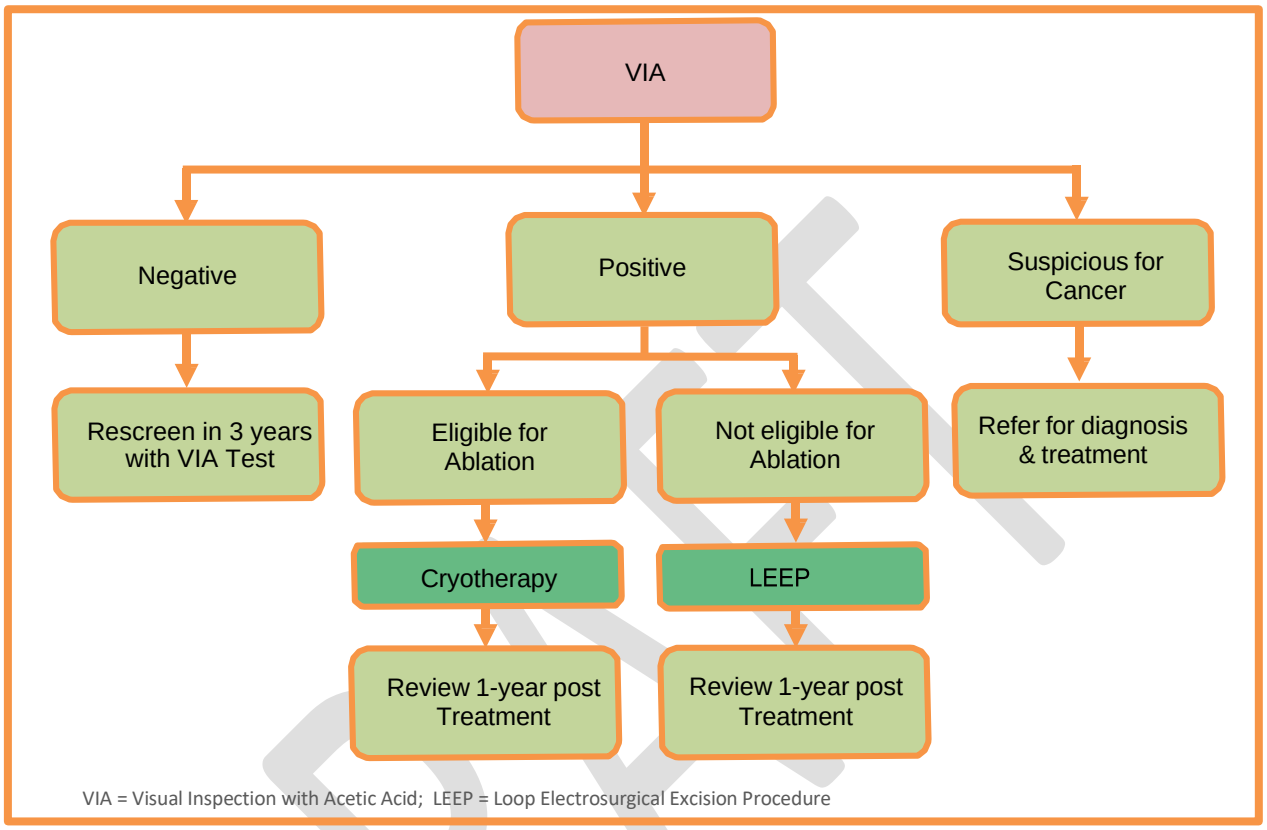


Figure 41: Cervical Cancer Screening Algorithm With HPV DNA Testing As A Primary Method And VIA Triage (Screen, Triage And Treat)

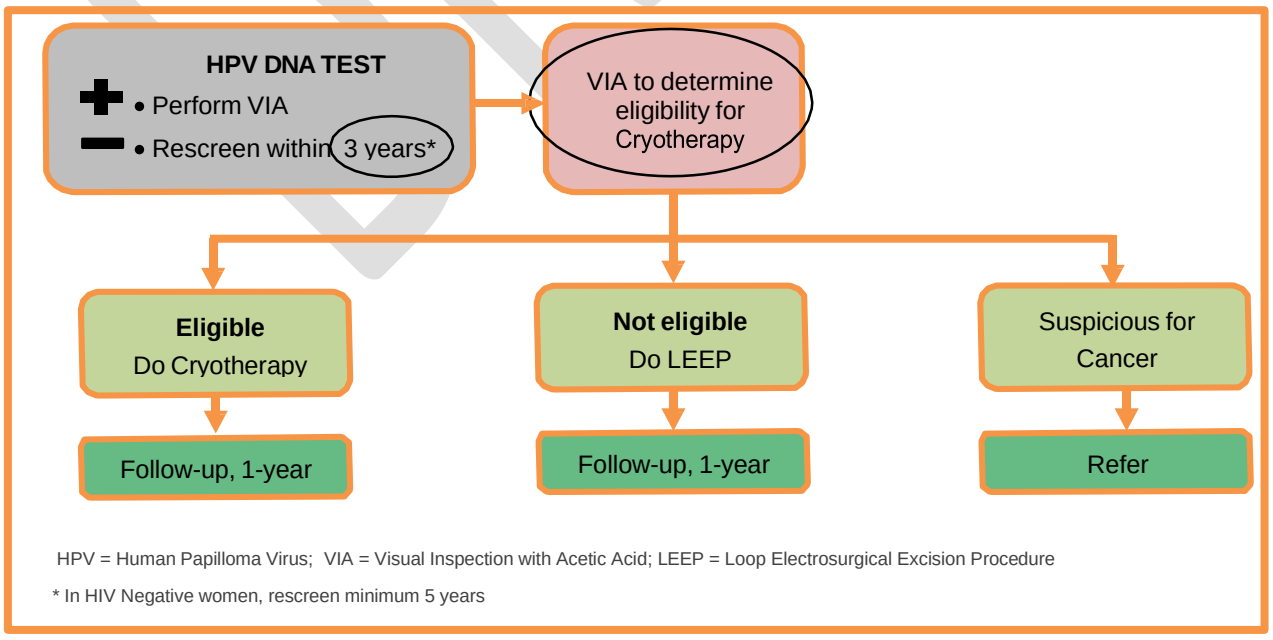
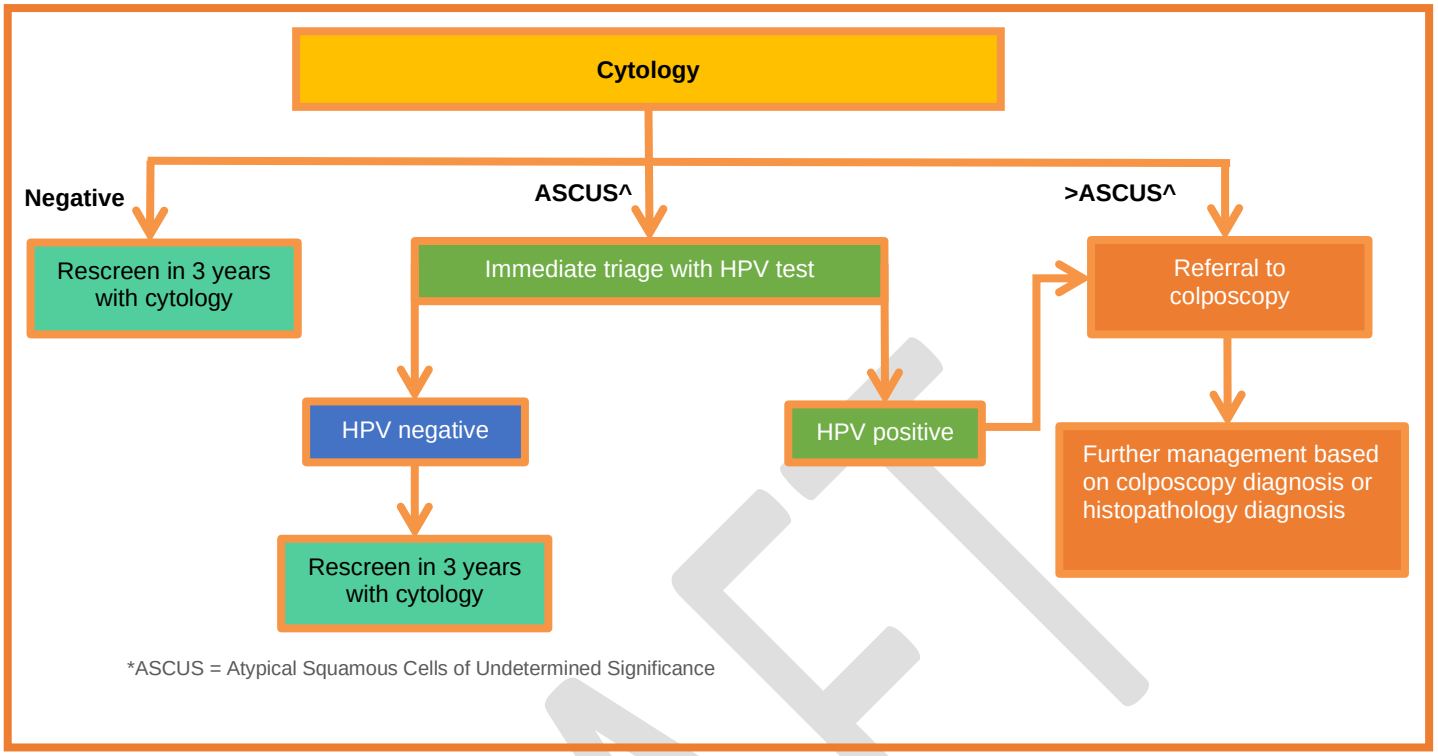


FIGURE 42: CERVICAL CANCER SCREENING ALGORITHM WITH PRIMARY CYTOLOGY SCREENING (CONVENTIONAL OR LIQUID-BASED)



TERMINAL ILLNESS/CANCER AND HIV

- Palliative care aims to relieve suffering in all stages of disease and is not limited to end-of-life care. The goals of palliative care include:
    - To improve the quality of life
    - To increase comfort
    - To promote open communication for effective decision making
    - To promote dignity
    - To provide a support system to the person who is ill and those close to them

In HIV-infected individuals, palliative care focuses on symptom management and end-of-life care. Throughout all stages of HIV disease, including when on ART, individuals may experience various forms of pain and other discomfort. HCWs should identify and treat the underlying cause, when possible, while controlling the pain. Effective management of side effects and possible overlapping ART-associated toxicities is important to support adherence

The care of the terminally ill child is a particular challenge in Zambia because there are few replicable models of planned terminal care, both institutional and community based. At the end of life, there are typically more symptoms that must be addressed, and the child may need to take multiple drugs to control and treat a variety of symptoms and conditions.

Terminal care preparation for children and their families is a long-term process and requires continuity of care through providers and services. Families must be involved in decisions about the best place for care and the preferred place of death in the child with end-stage HIV disease

TABLE 51: RECOMMENDED TESTS FOR HIV SCREENING AND MONITORING FOR CO-INFECTIONS AND NCDS

Phase of HIV Management	Desirable (*if feasible)
HIV Diagnosis	▸ Screening for TB, CM ▸ HBV or HCV serology ▸ Screening for STIs ▸ Hb or FBC ▸ Pregnancy test (woman of reproductive age) ▸ HPV test or visual inspection with acetic acid (VIA) in sexually active adolescent or woman) ▸ Syphilis test (adolescent or adult) ▸ NCDs risk factors: cholesterol, glucose, and triglycerides
ART Initiation	▸ Hb ▸ Pregnancy test (woman of reproductive age) ▸ BP measurement ▸ Serum Creatinine (for starting TDF) ▸ Baseline CD4
Suspected Treatment Failure	▸ Serum Creatinine for TDF ▸ HBV (HBsAg) serology (for HIV/HBV co-infected already using TDF and develop ART failure, TDF should be maintained regardless of selected Second-Line regimen) ▸ Pregnancy test (women of reproductive age) ▸ Review CTX adherence ▸ Initiate ART if eligible ▸ Adherence counselling and Positive Health Dignity and Prevention (PHDP) messages

* Reference 2016 WHO Guidelines

PROPHYLAXIS

TUBERCULOSIS PREVENTIVE THERAPY (TPT)

These guidelines focus on key interventions branded as the THREE I's (Intensive case finding, Isoniazid prophylaxis therapy and Infection control for TB) for HIV-TB activities that reduce TB-related morbidity and mortality in HIV-infected individuals. Another key intervention is the provision of ART.

Daily TPT can prevent TB in people who are at a high risk for developing TB, including HIV-infected individuals.

- Screen all patients for TB at any opportunity that presents (see Figure 27)
- Screen all pregnant and breastfeeding women, regardless of HIV status, for TB at every contact as it is part of Focused ANC
- Screen all children for TB at every contact
- Give TPT to the following:
    - HIV-infected children <12 months old with TB contact and after ruling out active TB
    - Newly HIV-infected pregnant and breastfeeding women, children ≥12 months old, adolescents, and adults after ruling out active TB
    - TPT should be given every 3 years in HIV-infected adults, adolescents and children ≥12 months old
- Do not give TPT to a patient who has any signs suggestive of active TB. This patient needs full investigation for TB and combination TB treatment if confirmed to avoid TB drug resistance
- Standard TB screening questions include:
    - Current cough: any duration, productive or non-productive
    - Unexplained weight loss (adults)
    - Failure to thrive and/or malnutrition (children)
    - Fever or night sweats
- Drugs for TPT
    - Daily Isoniazid with Pyridoxine (Vit B6) for 6 months
    - Daily Isoniazid with Rifampicin (RIFINA) for 3 months (DRV-r and ATV-r cannot be used with RIF)
    - Weekly High Dose Isoniazid (600 – 900mg) with Rifapentine (3HP) for 3 months (DTG does not require dose adjustment for 3HP)
- Contraindications and/or when to Stop TPT:
    - Suspected or confirmed active TB (start ATT)
    - Jaundice and/or icterus (yellow eyes) or active hepatitis
    - Known or suspected hypersensitivity to INH or severe skin rash
    - Confusion/convulsions
    - Dizziness
    - Low BMI <18kg/m^2
    - Peripheral neuropathy i.e., Severe numbness/burning pain and muscular weakness of legs and/or arms
    - Concomitant medication: Phenytoin, Carbamazepine, Warfarin, Theophylline, Selective Serotonin Re-uptake Inhibitor antidepressants (e.g., Fluoxetine, Paroxetine) oral Ketoconazole or Itraconazole
- How to give TPT
    - Educate patients on the side effects of TPT
    - In HIV-infected individuals, TPT should be dispensed for the same duration as ART to avoid multiple hospital visits
    - Side effects must be assessed at 1, 3 and 6 months after starting TPT preferably via telephone or any other appropriate modalities
    - Give concomitant Pyridoxine (Vitamin B6) 1 tablet 25-50mg once daily to prevent side effects of Isoniazid in all populations taking TPT
- Repeat TPT
    - In PLHIV, TPT should be given every 3 years as the protective effects wanes off with time

TABLE 52: DOSAGE FOR ISONIAZID PREVENTATIVE THERAPY, CO-TRIMOXAZOLE PROPHYLAXIS AND COMBINATION INH/CTX/VIT B6 DRUGS

Drug	Child tablet or oral suspension	Number of scoops or tablets by weight band					Adult tablet
		3 to < 6kg	6 to < 10kg	10 to < 14kg	14 to < 20kg	20 to < 25kg	≥ 25kg
Isoniazid (INH)	100mg	0.5	1	1.5	2	2.5	300mg (1 tablet)
Co-trimoxazole (CTX)	Suspension 200/40mg per mL	2.5 mL	5 mL	5 mL	10 mL	10 mL	–
	Tablet 100/80mg	1	2	2	4	4	–
	Tablet 400/80mg	NA*	1/2	1/2	1	1	400/80mg (2 tablets)
	Tablet 800/160mg	NA	NA	NA	1/2	1/2	800/160mg (1 tablet)
Pyridoxine (Vitamin B6)	Tablet 25mg	NA	NA	NA	1/2	1/2	25mg (1 tablet)
INH/CTX/Vit B6	Tablet 300/960/25mg	NA	NA	NA	1/2	1/2	300/960/25mg (1 tablet)

*NA = Not Applicable

CO-TRIMOXAZOLE PREVENTIVE THERAPY (CPT)

CPT prevents Pneumocystis Jirovecii Pneumonia (PCP), toxoplasmosis, isosporiasis, malaria, and other HIV- and non-HIV related diseases and prolongs survival. CPT can be safely taken with ART and/or ATT and in pregnancy (Tables 41 and 53). HIV-infected pregnant women on CPT should not be given Sulfadoxine-Pyrimethamine (SP; malaria prophylaxis in pregnancy)

All PLHIV with CD4 count < 350 cells/µL must be on CPT. CPT can be discontinued in adults after 2 consecutive CD4 counts that are > 350 cells/µL

All HIV infected pregnant women and children below 5 years old (but greater than 6 weeks old) must be on CPT

TABLE 53: CRITERIA FOR INITIATING, DISCONTINUING AND MONITORING CO-TRIMOXAZOLE PREVENTIVE THERAPY

Specific populations	Whom to Start	When to Start	When to Stop*
Pregnant & Breastfeeding Women	Pregnant women	Start as early as possible. Do not give SP. If SP taken, start CTX after 14 days	Continue throughout pregnancy
	Breastfeeding women	Continue if CD4 count <350 cells/µL or WCS II, II or IV	CD4 count ≥350 cells/µL for two consecutive values at least 6 months apart while on ART
Children (0 to <5 years old)	HIV-Exposed (e.g., breastfed) child	At 6 weeks old or first contact	Confirmed HIV-uninfected after full cessation of breastfeeding
	HIV-infected child ≤24 months old	Start regardless of WCS or CD4%	At 5 years old and CD4 count ≥350 cells/µL and Stage I
	HIV-infected child ≥24 months to <5 years old	WCS II, III and IV or CD4 level <25%	
	Presumptive HIV diagnosis <24 months old	Start (or continue) regardless of WCS or CD4%	Stop if confirmed HIV negative; if infected, stop at 5 years old and CD4 level ≥350 cells/µL and Stage I
Children (5 to <10 years old)	Child with a history of PCP	Start regardless of CD4 count or CD4%	At 5 years old and CD4 count ≥350 cells/µL and Stage I If 5 to <10 years old, stop based on adult criteria
Adolescents	HIV-infected children ≥5 years old, adolescents, and adults	CD4 count <350 cells/µL or WCS II, III or IV	CD4 count ≥350 cells/µL for two consecutive values at least 6 months apart while on ART
Adults			

Stop CTX if the person has Stevens-Johnson syndrome, severe liver disease, severe anaemia, severe pancytopaenia, or HIV negative status

CPT contraindications: severe allergy to sulfa drugs; severe liver disease, severe renal disease, and Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency and in these conditions DO NOT re-challenge

SP = Sulfadoxine/Pyrimethamine

WCS = WHO Clinical Staging

Common Chronic Co-morbidities and Non-communicable Diseases in Children

Children living with HIV, including those taking ART, are at risk of developing chronic multisystem comorbidities and concomitant disability. Common comorbidities include developmental delay and neurocognitive impairment, mental health disorders as well as certain organ system morbidities (chronic lung disease, heart disease and kidney disease) that are common among adolescents living with perinatally acquired HIV.

Growth

Although growth resumes after starting ART, children who have more profound stunting and begin ART in late childhood have a delayed growth spurt and are typically unable to reach their height potential. Age at initiating ART is also an important predictor of bone density.

Chronic Comorbidities

Cardiac, renal and metabolic comorbidity has been described in adolescents with late access to suboptimal ART regimens. This should decline as less-toxic ART regimens become more widely available. However, these new regimens may require specific monitoring of other potential comorbidities, such as DTG and potential weight gain. Surveillance is crucial, including conventional growth monitoring.

Neurodevelopmental Delay and Neurocognitive Disease

Children living with HIV who start ART after infancy can have subtle to severe neurocognitive deficits. The causes of neurocognitive impairment despite effective ART are likely to be multifactorial, including ongoing viral replication in the CNS and resulting neuroinflammation, irreversible CNS injury before ART and neurotoxic effects of ART, and could be compounded by socioeconomic and psychosocial factors. Children with neurocognitive impairment can appear asymptomatic, with deficits missed by routine testing. Screening tools and standardized definitions that are context-specific and have been culturally validated are scarce.

Children living with HIV face recurrent and cumulative psychosocial stressors that differ from other chronic childhood illnesses, such as stigma and discrimination, responsibility for the welfare of siblings or other family members who are ill, illness and the death of their parents and unstable guardianship. These stressors can hamper development of protective mechanisms and leave children mentally vulnerable and ill equipped for coping with challenges, most likely increasing the risk of mental health disorders. Mental health disorders affect an individual's adherence to ART and are associated with impaired quality of life but typically receive little attention compared with physical health concerns. Up to half of adult mental health problems begin during childhood and adolescence. This highlights the necessity to implement screening during adolescence. Promoting mental health and preventing mental health disorders and problems are being increasingly emphasized, with opportunities to integrate psychosocial support and mental health at key points, such as at the time HIV status is disclosed.

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MANAGING THE HIV PROGRAM

SERVICE DELIVERY

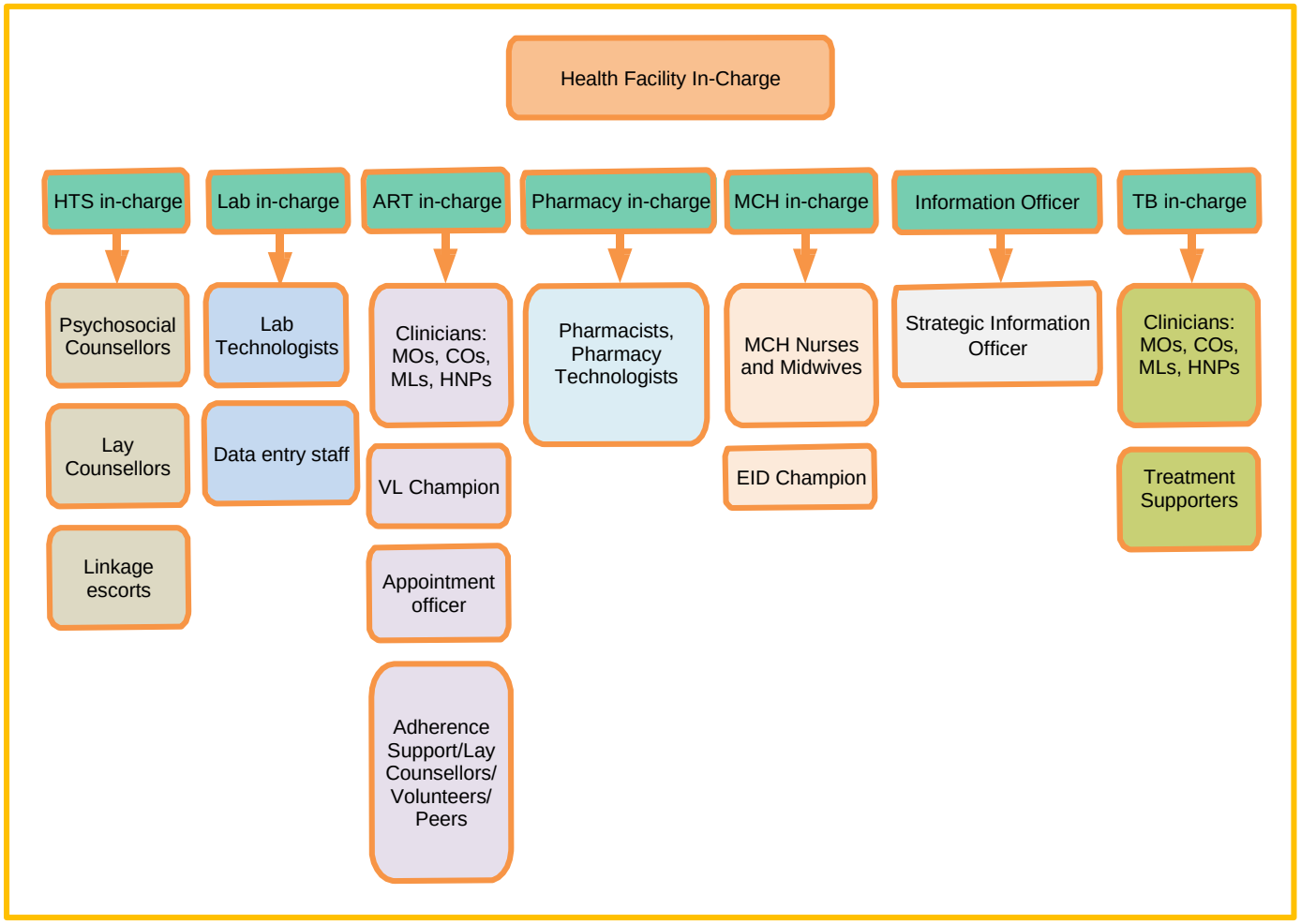
Recommendations

- Diversify interventions to ensure timely linkage to HIV Services
- Patient-centeredness to allow for delivery of care based on people's needs, preferences, clinical characteristics, and context
- Special considerations for Priority and Key Populations
- Task-shifting and investment in staff training and development
- Service delivery should be across the HIV continuum of care
- Establish effective systems for monitoring patients in care

The Ministry of Health recommends a comprehensive HIV service care delivery system which involves integration of HIV services with other services offered at the facility. This integrated model must work closely with the recipients of care resulting in services that are efficient and responsive to the needs of the community. These services should be accessible at all levels of care including in the community. These services must be delivered by trained cadres across the whole spectrum from community to the health facility. The ideal team consists of the following as shown in Figure 43.

Following diagnosis and throughout the spectrum of care, HIV services should be tailored to respond to specific challenges or barriers faced by patients and aim to offer high quality care, client satisfaction and improved health outcomes. In order to ensure timely linkage to care and follow up for all people living with HIV, a package of differentiated interventions should be offered to clients.

FIGURE 43: HUMAN RESOURCE MANAGEMENT IN THE ART CLINIC



COs = Clinical Officers; EID = Early Infant Diagnosis; HNPs = Health Nurse Practitioners; MCH = Maternal and Child Health; MLs = Medical Licentiates; MOs = Medical Officers

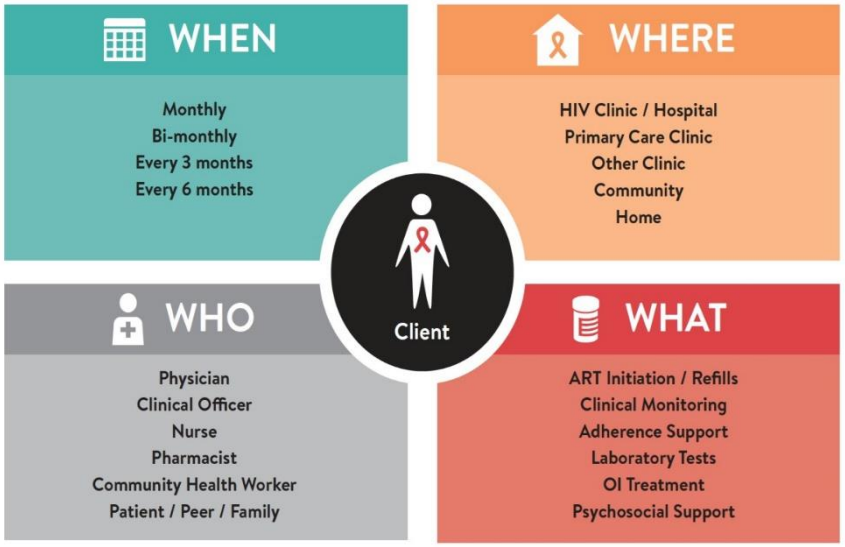
Following diagnosis and throughout the spectrum of care, HIV services should be tailored to respond to specific challenges or barriers faced by patients and aim to offer high quality care, client satisfaction and improved health outcomes. In order to ensure timely linkage to care and follow up for all people living with HIV, a package of differentiated interventions should be offered to clients.

Differentiated Service Delivery (DSD)

Differentiated Service Delivery (DSD) is "a client-centred approach that simplifies and adapts HIV services across the cascade in ways that both serve the needs of PLHIV better and reduce unnecessary burdens on the health system" (IAS, https://www.iasociety.org/Differentiated-Service-Delivery)

DSD models seek to adapt timing, location, nature, and content of clinical services to reduce burden and maximize effectiveness, while improving the efficiencies of the health system. By providing differentiated care, the health system can reallocate resources to those most in need. The building blocks of service delivery addressing the "**WHEN, WHERE, WHO**, and **WHAT"** of HIV DSD models (www.differentiatedcare.org).

FIGURE 44: BUILDING BLOCKS OF DIFFERENTIATED SERVICE DELIVERY



PRINCIPLES OF DIFFERENTIATED SERVICE DELIVERY

The principles of DSD are aimed at supporting the achievement of 90-90-90 targets while also improving the quality-of-care clients receive.

Implementation of DSD models should be guided by the following principles:

- Adequate and consistent supply of ARVs and health commodities
- Trained healthcare workers (HCWs) and community volunteers
- Monitoring and Evaluation (M&E) systems
- Adequate information and education
- Human rights and dignity
- Quality of care and good clinical practice
- People-Centred Health Services
- Controlled Flexibility
- Community engagement

Zambia offers DSD in 3 different areas:

1. HIV Testing and Prevention (see 2022 Zambia Differentiated Service Delivery Framework)
2. HIV Treatment and Care
3. Services for specific sub-populations

Differentiated HIV Testing and Prevention Services

These are HIV testing service-delivery models and approaches that are adapted to address specific barriers of a sub-group of individuals to enable them to know their HIV status. Differentiated HIV Testing Services (HTS) will facilitate early diagnosis of HIV-infected individuals with the aim to maximize yield, efficiency, and cost effectiveness of the country's HTS program. Specifically, differentiating HTS will result in:

- Focusing attention on those in need, based on available data
- Ensuring that service delivery addresses the needs and preferences of people in need of HTS (e.g., targeting the most at-risk and vulnerable populations), and the constraints of services providers
- Enhancing HTS integration with other health services
- Decentralizing HTS to primary healthcare facilities and in the community
- Encouraging and supporting task-shifting
- Ensuring improved linkage to treatment and prevention services

For further information on Differentiated HIV Testing and Prevention Services, please see the 2022 Zambia Differentiated Service Delivery Framework

Differentiated HIV Treatment and Care

DSD models aim at optimizing treatment outcome for ROC already in care or being initiated on treatment. After Information, Education, and Communication (IEC) material such as posters and brochures are shared, interested RoC should be given additional information on the model and have their questions answered by the HCW or CBV. Because factors like long waiting time, increased number of clinic visits and inability to travel to the clinic have been mentioned as contributors of RoC disengagement from HIV care, attractive DSD models should include the following:

- Less frequent clinical visits (twelve -months)
- Less frequent medication pick-up (three / six-months)
- Reduced waiting time

At a minimum, all facilities providing ART services should implement facility managed DSD models which are cost effective and easy to implement before considering other models. These include:

- Multi Month Scripts
- Fast Track Models

DSD for Specific Populations (children, adolescents, pregnant and breastfeeding women)

1. **Family based Approach**
   Important when considering care for children and their parents. Service provision models for children and their parents/caregivers should be aligned as this can improve the entire family case
2. **Integration of Services**
   Integration of HIV care with other services is a WHO recommendation to strengthen the continuum of treatment care. Integration has been highlighted as key to providing benefits to mothers and their infants, and combining adolescent HIV services with comprehensive services
3. **Leveraging and Encouraging Psychosocial Support**
   The importance of psychosocial support for all PLHIV, including support from communities and peers, is of particular significance to these special populations

DIFFERENTIATED SERVICE DELIVERY FOR HIV TREATMENT AND CARE

Eligibility Criteria for DSD for HIV Treatment and Care

The Zambia Differentiated Service Delivery Framework define a stable adult and adolescent >15 years as meeting all of the following criteria:

- On ART for at least 12 months
- No adverse drug reactions requiring regular monitoring
- No current illness requiring regular monitoring
- Not pregnant/breastfeeding
- Proven record of good adherence and evidence of treatment success
- Viral suppression < 1000 copies/mL within the last 12 months
- Controlled condition for those with non-communicable diseases

Note:

- All PLHIV in Zambia may be eligible for the DSD depending on their needs
- Children above 2 years who fit in the above criteria are also considered stable
- Stable clients are eligible for both facility and community-based models
- It is essential for clients to be made aware of all the models that are available at a particular facility

RoC at high risk (unstable) is defined as one with any one of the following:

- RoC on ART for < 12 months
- Any RoC presenting with advanced disease (WHO stage III or IV)
- Any RoC presenting with severe immunosuppression (CD4 count < 200 cells/µL)
- Any RoC not virally suppressed (VL > 1000 copies/mL)
- Adverse drug reactions requiring regular monitoring
- Non-adherence to ART
- Substance abuse
- Mental illness
- Any other uncontrolled chronic condition/comorbidity like NCDs

Note: *RoC who had not had a viral load measurement done must have a VL test ordered provided they meet other criteria for stable RoC prior to including them in DSD models.*

Benefits of DSD for Clients

- Availability of variety of models that meet individual client's needs
- Reduce distance to drug collection points
- Improved adherence
- Potentially reduces the HIV-related stigma
- Reduces the number of visits to the facility
- Saves client's time and resources spent travelling
- Improves retention in care
- Reduces waiting time for clients in the facility

Benefits of DSD for a Facility

- Facilitates provision of key services to clients
- Maximizes on available human resource
- Economizes on human resource, time and space at the health facility
- Allows for more time for healthcare workers to manage patients at high risk which will lead to improved quality of care
- Contributes to decongesting of facilities
- Reduced workload on healthcare providers on account of reduced patient volumes
- Reduced costs on healthcare system
- Helps the facility to analyse data and identify gaps in the continuum of care

TYPES OF DSD MODELS FOR TREATMENT AND CARE

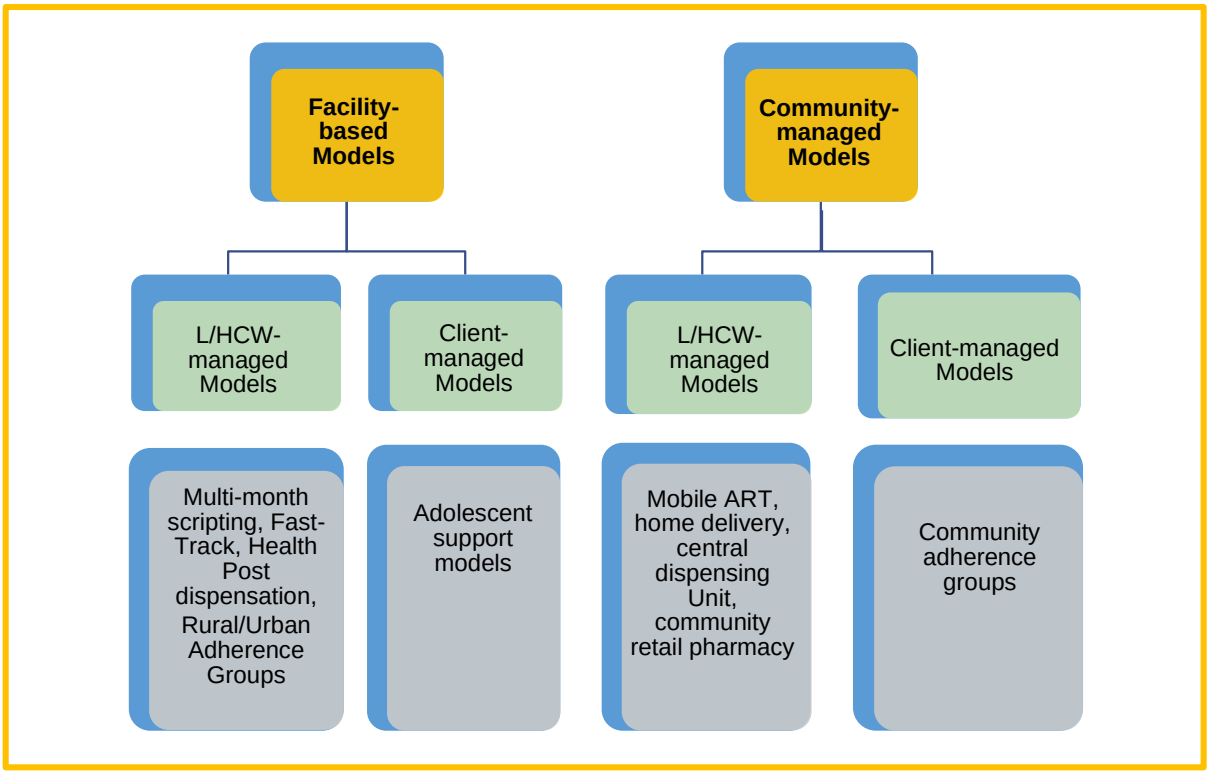
Approach of DSD model to be offered at any given facility should consider:

- Clinical characteristics of the client (stability, unstable, co-morbid/co-infections)
- Client preference
- Model available at the facility

DSD models can be categorized into two models (Zambia Differentiated Service Delivery Framework):

1. Facility Based Models: These are models that are managed at the Health Facility either by:
   a. Healthcare worker/Lay Healthcare worker
   b. Clients
2. Community Based Models: These are models that are managed in the Community either by:
   a. Healthcare worker/Lay Healthcare worker
   b. Clients

FIGURE 45: DIFFERENTIATED SERVICE DELIVERY MODELS FOR TREATMENT AND CARE



At a minimum, all facilities providing ART services should implement facility managed DSD models which are cost effective and easily implementable before considering other models. These include:

- Multi Month Scripts
- Fast Track Models

DIFFERENTIATED DELIVERY FOR SPECIFIC SUB-POPULATIONS

Despite health gains in HIV /AIDS response, gaps have been noted with specific sub populations living with HIV as they are underrepresented in the HIV care cascade. The HIV prevalence among the key populations and priority populations is substantially higher than it is among general population living with HIV. These populations have low access to treatment, face challenges in remaining on treatment, are faced with lack of adherence, stigma, low retention, and insecurity in accessing health services when compared to the general population living with HIV. WHO highlights that differentiated ART delivery can address inequalities in the access of specific sub populations to the HIV treatment services by developing ART delivery models that meet the specific need of the subpopulations and reach marginalized, criminalized, and stigmatized groups. DSD can also enable key communities to be more involved in HIV treatment and care. MOH recommends specific and separate models to target the three categories of the subpopulations.

Categories of Specific Sub-Populations

1. Unstable (High risk) RoC
2. Key Populations
    - Female Sex Workers (FSWs)
    - Prisoners/ Inmates
    - Men who have Sex with Men (MSM)
    - People Who Inject Drugs (PWID)
    - Lesbian, Gay, Bisexual, Transgender and Questioning, Queer (LGBTQ)
3. Priority Populations
    - Adolescents
    - Pregnant & Breast-feeding women
    - Children
    - Men (due to poor health seeking behaviour)
    - Persons with disabilities
    - Persons aged >50 years
    - Migrant and mobile populations

The eligibility criteria for the children and adolescent to be enrolled to a multi-month scripting/dispensation DSD model includes the following:

- Has been on optimal ART for more than 12 months with no dose or formulation changes for at least three months
- No intercurrent illness, malnutrition concerns or adverse drug reactions requiring intensified follow up
- Caregiver counselled and oriented on age-appropriate disclosure processes (full disclosure is not a requirement for MMD)
- Virally suppressed within the last 12 months
- If caregiver also infected, S/he is also virally suppressed
- Has consistently come to clinic appointments with motivated caregiver

Children 2-5 years

- Three-monthly ART refills (3MMD, including co-trimoxazole refill, disclosure process check-in) and clinical visits *(one visit for refills and clinical consultations, including weight and possible dosage adjustment)*

Children 5-10 years

- Three-monthly ART refills (3MMD, including co-trimoxazole refill, disclosure process check-in) and clinical visits *(one visit for refills and clinical consultations, including weight and possible dosage adjustment)*
- If the child weighs ≥20kg both ART refills and clinical visits can be spaced out to every 6 months (6MMD)

Children ≥10 years

- For children weighing more than 20kg, both ART refills and clinical visits can be spaced out to every 6 months (6MMD)

Note: Children at high risk may be enrolled into models for supporting viral load suppression and improving retention. Children who are virally unsuppressed can be enrolled in DSD models for unstable RoC. This includes direct observed therapy, viraemic ART specific clinics, and patient pairing. For further details, see 2022 Zambia Differentiated Service Delivery Framework.

TABLE 54: PACKAGES OF SERVICES OFFERED TO SPECIFIC SUBPOPULATIONS ACCESSING DSD

Building blocks/ Populations	Key populations Lesbians, MSM, FSW, Bisexual, Transgender, Injecting drug users and prisoners	Priority populations AGYW, Pregnant & Breast feeding, Children and migrants
What	▸ HIV Testing Services and Partner notification services (PNS) if tested HIV positive at facility and community level ▸ Psychosocial support ▸ Clinical, pharmacy (ART Refills/drug pickups) and laboratory services appointment and visits at facility and community level ▸ Adherence counselling ▸ Family planning – Condoms and oral contraceptive ▸ PrEP (If tested HIV negative) ▸ STI screening ▸ Reproductive Health Counselling ▸ GBV	▸ HIV Testing Services and Partner Notification Services (PNS) if tested HIV positive at facility and community level. ▸ Clinical, pharmacy (ART Refills/drug pickups) and laboratory services ▸ Psychosocial support ▸ Adherence counselling ▸ Family planning – Condoms and oral contraceptive ▸ PrEP (if tested HIV negative) ▸ STI screening ▸ Reproductive health Counselling ▸ GBV
Who	▸ Peer/Psychosocial counsellors ▸ Adherence counsellor Nurse, Pharmacy, Clinicians – (Li, CO, MO)	▸ Peer/Psychosocial counsellors ▸ Adherence counsellor ▸ Clinicians - (CO, MO, Li) Nurse and Pharmacy
When	▸ 3-monthly ▸ 6-monthly for Clinical/lab visits ▸ Those with special needs may require frequent visits ▸ Safe space – Patient's home, community, facility ▸ Facility – Health post, clinic, hospital	▸ 3-monthly ▸ 6-monthly for Clinical/lab visits ▸ Those with special needs may require frequent visits including children <24 months who need monthly visits ▸ Community ▸ Facility

TABLE 55: CATEGORIZATION OF SERVICES OFFERED AT DELIVERY POINTS

<table>
<tr><td colspan="2">HIV/AIDS Management
• At facility level are “high risk,” i.e., Pregnant and breastfeeding women, HEI, discordant couples, newly diagnosed/initiated patients
• Community services to focus on “stable” patients</td></tr>
<tr><td>Community structures such as: Community Adherence Groups (CAGs), Treatment Clubs, Private sector, Faith based groups, Health shops, etc</td><td>Facility: Health Centre, Level 1, Level 2, Level 3, and Level 4</td></tr>
<tr><td>Decentralization of Services</td><td>Diagnostic and Clinical Services</td></tr>
<tr><td>Retention in Care:</td><td>Health Centre:</td></tr>
<tr><td>› PMTCT sites should have functional community structure/groups affiliated with timely support and connection between health facility and community
› Interventions of mother-baby follow up through reminders for appointments, adherence support
› Community workers and message on identifying sick infants and sending to facilities
› Use of current interventions to follow up patients and infants (e.g., nutritional assessment)</td><td>› HIV testing at birth, 6 weeks, 6 months, 9 months, 12 months, 18 months, 24 months and across all populations (see Table 1)
› Triple prophylaxis depending on risk assessment
› Co-trimoxazole (CTX)
› Growth monitoring
› Immunization as per EPI schedule
› Clinical review and follow up
› Infant feeding counselling
› Ongoing HIV/AIDS counselling and screening
› Uptake of newly diagnosed cases and commence ARVs
› Treatment of OIs as per Standard Treatment Guidelines
› Palliative care (pain relief and management of common illnesses)</td></tr>
<tr><td rowspan="4">Task Shifting and Sharing:
› Less frequent clinical visits (3-6 months) being recommended for people stable on ART.
› The use of Community ART models for pick- up of ART, while initiation and monitoring at peripheral health facilities with maintenance at community level
› Trained and supervised community health workers can dispense ART between regular clinical vests</td><td>Level 1:</td></tr>
<tr><td>All the above and:
› Clinical review/examination
› FBC, CXR, HIV +/-CD4 count, U+E, Creatinine, urinalysis, treatment, and follow up management of OIs
› Infant feeding counselling If referred for further management
› Acceptance of referral back and joint management</td></tr>
<tr><td>Level 2:</td></tr>
<tr><td>All the above and:
› Management of severe symptoms and investigations
› Urine Protein Creatinine Ratio
› LFTs</td></tr>
<tr><td></td><td>Level 3:</td></tr>
<tr><td></td><td>› VL and genotype for treatment failures
› Metabolic complications management
› Research 3rd line management
› Triple prophylaxis depending on risk assessment
› Highly specialized research
› CTX prophylaxis
› Complicated cases:
▪ HIV plus co-morbidities</td></tr>
</table>

MONITORING AND EVALUATION

Recommendations

Use of data for decision making

Use of a single System for Monitoring and Evaluation (M & E)

Use of Electronic Health System

In order to efficiently and effectively monitor the provision of HIV Prevention, Care and Treatment services, there is need to ensure that Recipients of Care information is documented based on the services that may have been provided. This information is crucial for client management, programmatic planning and decision making. Ministry of Health has several HIV data collection tools developed and in use across the country. Data is collected either through paper or electronic Health Record System (EHR) depending on which system is available at the facility level or service delivery point. Health Facilities are urged to use only one system (Paper Based or EHR/SmartCare) and not both at the same time and electronic system (either E-Last, E-Fast or E-First) takes precedence over Paper Based System (usage of registers).

Monitoring and Evaluation Data Collection Tools

There are many data management tools used by facilities in recording comprehensive, family-centred HIV Prevention, Care and Treatment services. Some of the standard HIV data collection and patient care tools include:

Registers	ART Forms
HIV Testing Services (HTS) Register Antenatal Care Register Labour and Delivery Register Postnatal Care Register EID Register Baby-Mother Pair Register HIV Care and Treatment Activity Register HIV Care and Treatment Monthly Register Daily Activity Register (DAR for Pharmacy) PrEP Register PEP Register IPD Register OPD Register VMMC Register STI Register HIV Self Testing Distribution Register Facility/Laboratory Viral Load Register Integrated Family Planning Register	Adult Patient Locator Paediatric Patient Locator Adult Initial History, Physical and Initiation Paediatric Initial History, Physical and Initiation Adult Clinical Follow Up Paediatric Clinical Follow Up Short Visit Patient Status Form Stable on Care Missed Visits Referral Form HIV Care Summary Sheet Pharmacy Enhanced Adherence Form VL Requisition Form PMTCT Clinical Follow Up

All these tools have corresponding collation forms (activity and tally sheets). Wherever feasible, data regarding the continuum of HIV care and treatment should be entered into an Electronic Health Record (EHR) system (SmartCare). Use of standard tools is required by all health facilities to ensure a functioning supply chain system to avoid stock outs.

The recommended standard tools include:

- Report and Requisition (R&R) form
- Daily Activity Register
- Interval Monthly Summary Report
- Stock Control Cards
- Laboratory Usage report
- Report for Essential Medicines and Medical Supplies

HIV Diagnosis

The HIV testing services have been integrated into the general routine healthcare services. Various service delivery registers are designed to allow the recording of the HIV testing services at every designated service delivery point with all the HIV testing results recorded in the registers for the testing service provided. For instance, clients tested during OPD should be recorded in the OPD registers (with results entered).

HIV Care and Treatment

When providing HIV Care and Treatment, the first data collection tools to be used are the ART Forms. These forms will form the Recipient of Care (RoC)/Client/Patient File. The following are some of the forms to be filled in; 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 among others. The forms are in both electronic and paper forms.

After filling in 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, RoC/client/patient information is generated manually using paper documents that is forms, registers and Health Information Aggregation forms (HIA 2/3).

Upon provision of a service (daily), 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 purposes.

Electronic Health Record (EHR) System

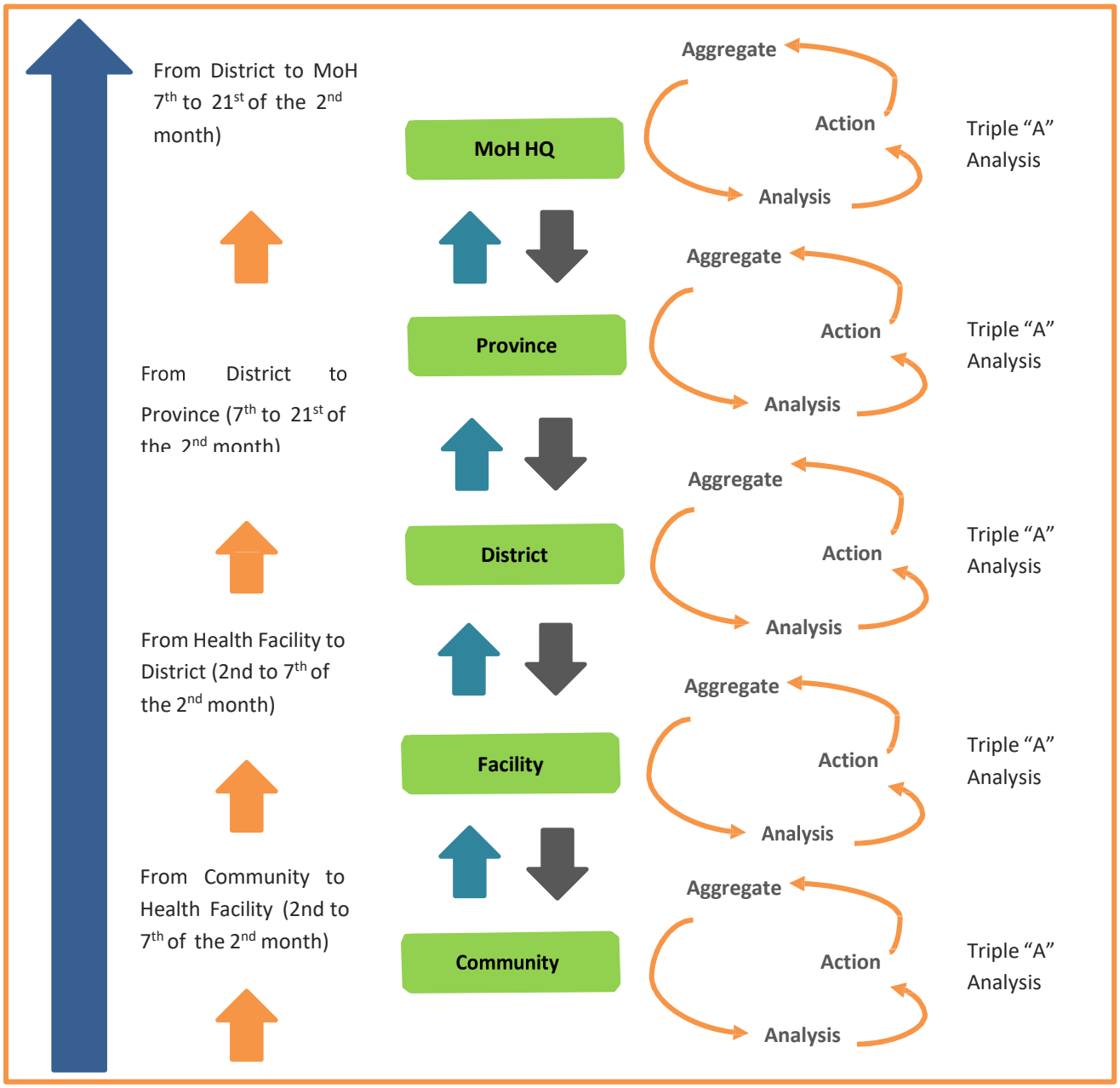
Under this system, RoC/client/patient information is entered in an EHR system (SmartCare). SmartCare is a fully integrated EHR system tracking the provision of continuity of care; it is a clinical management information system at the facility- and district-(management/administration) level and it is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

In relation to data entry, SmartCare uses different modes of implementation such as E-Last, E-Fast and E-First. E-last involves entering data after seeing all clients (transfer from Paper records to Electronic). E-fast operates like E-last except that for E-fast, the data entry for the services provided must be entered before RoC leaves a facility while E-first involves real -time data entry by provider(s). The EHR system is integrated into other systems such as the Case Based Surveillance (CBS) and active ART Pharmacovigilance systems to track the HIV epidemic.

At the end of each month, the facility should ensure that all the client information is entered and without leaving any backlog. Thereafter, various reports can be generated in SmartCare which may include the Health Aggregation Forms (HIA2/3), PEPFAR MER Reports, Daily Activity Register, ART Monthly Register, among others. Thereafter, Transport Data Base (TDB) must be sent to the district 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 46: HEALTH MANAGEMENT INFORMATION SYSTEM DATA FLOW GUIDELINE



SOME KEY FOR PROGRAMMATIC HIV INDICATORS

Key indicators tracked under the HIV Programme (Prevention, PMTCT, Treatment, and Cascade).

TABLE 56: SOME KEY MONITORED PROGRAMMATIC HIV INDICATORS

Measure Group	Indicator	Numerator	Denominator	Disaggregation	Source
Prevention	HIV Positivity (%)	Number of clients who tested positive for HIV	Number of clients who tested for HIV	Age, Sex	DHIS/HMIS
Prevention	Percentage (%) of clients newly diagnosed with recent HIV infections	Number of clients newly diagnosed with recent HIV infections	Number of clients newly diagnosed who had a recent HIV test	Sex, Age	LIS/Registers
Prevention	Percentage of People receiving PrEP	Number of People receiving PrEP	Number of People eligible to receiving PrEP	Age, Sex	DHIS/HMIS
Prevention	Percentage of People receiving PEP	Number of People receiving PEP	Number of People eligible to receiving PEP	Age, Sex	DHIS/HMIS
Prevention	HIV Prevalence	Number of People living with HIV	Total Population	Sex, Age	Spectrum/ZDHS/PHIA
Prevention	Estimated number of people living with HIV	--	--	Sex, Age	Spectrum
Prevention	VMMC coverage (%).	Number of males voluntarily circumcised.	Number of males targeted for circumcision.	Age	DHIS/HMIS/ VMMC
PMTCT	Percentage (%) of pregnant women who attended their first ANC contact	Number of pregnant women who attended their first ANC contact	Number of estimated pregnant women	-	DHIS/HMIS
PMTCT	Percentage (%) of pregnant women with known HIV status.	Number of pregnant women with known HIV status (Known positive at first ANC contact + Initial ANC HIV test)	Number of women who had their first ANC contact	-	DHIS/HMIS
PMTCT	Percentage (%) of women accessing antenatal care services who tested positive for Syphilis	Number of women accessing antenatal care services who tested positive for Syphilis	Number of women tested for Syphilis at first contact	-	DHIS/HMIS
PMTCT	Percentage (%) of HIV positive pregnant and breastfeeding women who received ARVs to reduce the risk of MTCT	Number of HIV positive pregnant and breastfeeding women who received ARVs to reduce the risk of MTCT	Number of HIV positive pregnant and breastfeeding women testing positive [including those with known HIV positive status]	-	DHIS/HMIS
PMTCT	Percentage (%) of infected HIV Exposed Infants who received an HIV test [PCR] within two months of birth	Number of infected HIV Exposed Infants who received HIV virological test for HIV within two months of birth	Number of HIV Exposed infants born from HIV Positive mothers	-	DHIS/HMIS
PMTCT	Percentage (%) of HIV Exposed Infants who received ART Prophylaxis within two months of birth	Number of HIV Exposed Infants who received ART Prophylaxis within two months of birth	Number of HIV Exposed infants born from HIV Positive mothers		DHIS/HMIS

Measure Group	Indicator	Numerator	Denominator	Disaggregation	Source
PMTCT	HIV Case Rate among HEI (%)	Maternal HIV Prevalence Rate * Mother to Child Transmission Rate* 10		-	DHIS/HMIS/ Spectrum/ZAMPHIA
PMTCT	PMCT final transmission rate	Number of children born of HIV positive mothers who were infected at within 24 months (it includes infected who are dead, lost to follow, defaulter and trans out, but exclude trans in who are infected)	Net cohort of HIV Exposed Children	-	DHIS/HMIS
Treatment	Percentage of HIV Positive clients who know their status and are currently receiving antiretroviral therapy	Number of clients currently on ART	Number of clients who Know their HIV status	Age, Sex	DHIS/SmartCare/ Spectrum
Treatment	Percentage (%) of clients diagnosed HIV positive linked to care	Number clients diagnosed HIV positive linked to care	Number people diagnosed with HIV	Age, Sex	DHIS/SmartCare
Treatment	Percentage (%) of clients diagnosed HIV positive initiated on ART	Number clients diagnosed HIV positive initiated on ART	Number people diagnosed with HIV	Age, Sex	DHIS/SmartCare
Treatment	Percentage (%) of clients currently on ART who are virally suppressed	Number of clients currently on ART who are virally suppressed	Number of currently on ART who are eligible of Viral Load test	Age, Sex	DHIS/DISA/SmartCare
Treatment	Percentage (%) of clients diagnosed with Advanced HIV Disease.	Number clients diagnosed with Advanced HIV Disease	Number of clients on ART	Age, Sex	DHIS/HMIS/SmartCare
Treatment	ART Coverage (%)	Number of clients actively on ART	Estimated number of clients living with HIV	Sex, Age	DHIS/HMIS/Spectrum
Treatment	ART Retention (%)	Number of clients actively on ART at the end of the reporting period	Net current on ART in given reporting period (Add number of clients actively on ART at the beginning of a period, Subtract Trans-Out but add Trans-In)	Age, Sex, period, cohort	DHIS/HMIS/SmartCare
Treatment	Percentage (%) HIV positive women assessing ART screened for cervical Cancer	Number HIV positive women assessing ART screened for Cervical Cancer	Number of HIV positive women assessing ART	Age	DHIS/HMIS
Treatment	Percentage (%) of clients eligible for TPT who received TPT	Number of clients eligible for TPT who received TPT	Number clients eligible for TPT	Sex, Age	DHIS/TB Reports

Treatment Cascade (95,95,95 Targets): ***For each of the 95–95–95 targets, the denominator is different. The first 95 value is the denominator for the second 95, and the second 95 value is the denominator for the third 95.***

First 95: People living with HIV who know their status. This is the first essential step before treatment can be initiated

Second 95: People living with HIV who know their status and are on HIV treatment. Linkages between testing and treatment

Third 95: People on HIV treatment who are virally suppressed

Quality Improvement

Quality Improvement (QI) is a process that aims to strengthen the quality of services provided at health facilities. The QI Technical Working Group (TWG) at MoH has identified five key QI indicators that will be tracked by all levels in the health sector. Of the five indicators, two are HIV-related:

- Percentage of exposed infants tested for HIV at 9 months old
- Percentage of all HIV positive clients retained on HIV care and treatment the last 12 months
    - Number of HIV testing sites scoring ≥80% in proficiency testing
    - Number of EID testing labs scoring ≥80% in proficiency testing
    - Number of viral load testing labs scoring ≥80% in proficiency testing
    - Number of labs enrolled in the CD4 External Quality Assurance (EQA) program scoring ≥80% in proficiency testing

Lifelong ART in pregnant and breastfeeding women also enhances maternal and child survival. For this reason, the following two QI indicators are also pertinent:

- Number of maternal deaths at the facility recorded in the last 1 month, 3 months (quarter), and 12 months
- Number of under-five children who died in the last 1 month, 3 months (quarter), and 12 months. (If possible, differentiate between early neonatal death, neonatal death, infant death, and under-five death)

Through structures that have been formed at all levels, the QI committees review these indicators regularly to identify performance gaps and root causes using the Performance Improvement Approach (PIA). This should be followed by implementation of appropriate interventions coupled with regular monitoring and evaluation to track progress.

These indicators will be reported through the Health Management Information System (HMIS), as well as tracked through the QI reporting structures from the health facility to the national level QI TWG. QI committees at any level should not be restricted to implement QI projects only related to the key indicators. Other areas of underperformance in health service delivery should be covered at the local level as identified with stakeholders, including clients and the community.

Mentoring and Supervision

Mentorship is a QI strategy that provides motivation to HCWs while building their knowledge and skills base. In collaboration with cooperating partners, MoH developed national guidelines and a mentorship training package. The multi- disciplinary Clinical Care Teams (CCT) at national, provincial, and district level spearhead mentorship and supervision of health facility staff. CCTs comprise clinicians, nurses, nutritionists, pharmacy, and laboratory staff and hold regular meetings to review HMIS reports, performance assessment reports, and any other source of information to identify performance gaps in health service delivery, including HIV care and treatment and PMTCT. Appropriate mentors are assigned from the CCT to conduct targeted, needs-based mentorship for QI. Request for specialized mentorship from higher level CCTs is encouraged. The multi-disciplinary approach achieves the following:

- Comprehensive coverage of clinical and support systems, including logistical and health information management
- Coordination, continuity, and availability of a pool of highly experienced mentors in the relevant fields
- Strengthened institutionalized, decentralized system of mentorship

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APPENDIX 1: DOSAGES OF ANTIRETROVIRALS FOR ADULTS, ADOLESCENTS AND CHILDREN

a) Dosages of Antiretrovirals for Adults and Adolescents

Drug	Normal Dose	Renal Dose
Abacavir (ABC)	Adult: 300mg BD PO Paediatrics: 8mg/kg BD PO	No adjustment
Atazanavir-r	Adult: 300/100mg OD PO Paediatrics: paediatric dosing by weight bands. No data for children <6 years old	No adjustment
Darunavir-r	Adult: 800/100mg OD PO (for PI naïve) Adult: 600/100mg BD PO (for PI experienced) Paediatrics: Not approved for children <3 years old DRV: 75/150mg tablets, RTV: 80mg/mL • ≥15kg - <30kg: 375/50mg BD • ≥30kg - <40kg: 450/60mg BD DRV: 600mg tablets, RTV: 100mg • ≥40kg: 600/100mg BD	No adjustment
Dolutegravir (DTG)	Adult: 50mg tablet • ≥20kg: 50mg OD PO Paediatrics: 10mg tablet • 3kg - 5.9kg: ½ tab OD • 6kg - 9.9kg: 1½ tabs OD • 10kg - 13.9kg: 2 tabs OD • 14kg - 19.9kg: 2½ tabs OD	No adjustment
Efavirenz (EFV)	Pregnant and/or breastfeeding: 400mg OD PO 600mg OD PO	No adjustment
Emtricitabine (FTC)	Adult: 200mg OD PO Paediatrics: 0-3 months old: 3 mg/kg/day (solution) 3 months-15years old (>33kg): 6mg/kg/day (solution; max 240mg daily) or capsule: 200mg OD (capsule)	Adult: CrCl 30-49: 200mg every 48 hours CrCl 15-29: 200mg every 72 hours CrCl <15: 200mg every 96 hours (Give after haemodialysis if on dialysis) Paediatrics: Reduce dose or increase dosing interval following adult recommendations in consultation with experienced clinician in renal dosing
Etravirine (ETR)	Adult: 200mg BD PO Paediatrics: Not approved for children <6 years old (approval under way for 2 months to 6 years old) • 16kg - <20kg: 100mg BD • 20kg - <25kg: 125mg BD • 25kg - <30kg: 150mg BD	No adjustment

Drug	Normal Dose	Renal Dose
Lamivudine (3TC	Adult: 150mg BD or 300mg OD PO Paediatrics: 2-4mg/kg BD PO	Adults: CrCl 30-49: 150mg OD PO CrCl 15-29: 150mg x 1 then 100mg OD PO CrCl 5-14: 150mg x 1 then 50mg OD PO CrCl <5: 50mg x 1 then 25mg OD (50 75mg OD still acceptable) Paediatrics: reduce dose or increase dosing interval following adult recommendations in consultation with experienced clinician in renal dosing
Lopinavir-r	Adult: 400/100mg BD PO Paediatrics: 10-13mg/kg BD PO for Lopinavir component	No dose adjustment, but use with caution in patients with CrCl <50 mL/min
Nevirapine (NVP)	Adult: 200mg OD PO x 14 days then 200mg BD PO Paediatrics: 4-7mg/kg BD PO	No dose adjustment, but give dose after dialysis
Tenofovir alafenamide (TAF)	Adult: 25mg OD PO Paediatrics: see Paediatric dosing by weight bands Not approved for adolescents less than 25kg	No adjustment
Tenofovir Disoproxil Fumarate (TDF)	Adult: 300mg OD PO Paediatrics: 8mg/kg OD PO Avoid in adolescents less than 30kg	Same for adults and paediatrics NOTE: Generally, avoid when CrCl <50 Only adjust dose when sure that the CKD is independent of the drug in consultation with experienced clinician in renal dosing CrCl 30-49: 300mg (8mg/kg) every 48 hours CrCl 10-29: 300mg (8mg/kg) twice weekly CrCl <10: consider 300mg (8mg/kg) OD PO (inadequate data) Haemodialysis: 300mg (8mg/kg) once weekly. To be given after dialysis CAPD: No data CAPD = Continuous Ambulatory Peritoneal Dialysis
Raltegravir (RAL)	Adult: 400mg BD PO (with Rifampicin 800mg BD PO) Paediatrics: see paediatric dosing by weight bands	No dose adjustment
Zidovudine (AZT)	Adult: 300mg BD PO Paediatrics: see paediatric dosing by weight bands	CrCl 30-49: 300 BD PO CrCl 10-29: 300 BD PO CrCl <10: 300mg OD PO in consultation with experienced clinician in renal dosing

b) Paediatric ARV Dosages by Weight Band

Dosing of AZT, 3TC and NVP in HIV Infected Babies younger than 4 weeks

Weight Band	NVP 10mg/mL	AZT/3TC 60/30mg tablet dissolved in 6ml of water (10mg/5mg/mL)
<2kg	0.8mL BD	0.8mL BD
2 to <3kg	1.5mL BD	1mL BD
3 to <4kg	2mL BD	1.5mL BD
4 to <5kg	3mL BD	2mL BD

Preferred Regimens			
Weight band	**Drug Strength**	**Number of tablets per dose**	**Drug Dose in mg**
3 – 5.9 kg	ABC/3TC 120/60mg tab DTG 10mg tab	ABC/3TC 1 tab OD + DTG 0.5 tab OD	ABC 120mg OD 3TC 60mg OD DTG 5 mg OD
6 – 9.9kg	ABC/3TC 120/60mg tab DTG 10mg tab	ABC/3TC 1.5 tabs OD + DTG 1.5 tabs OD	ABC 180mg OD 3TC 90mg OD DTG 15mg OD
10 – 13.9kg	ABC/3TC 120/60mg tab DTG 10mg tab	ABC/3TC 2 tabs OD + DTG 2 tabs OD	ABC 240mg OD 3TC 120mg OD DTG 20mg OD
14 – 19.9kg	ABC/3TC 120/60mg tab DTG 10mg tab	ABC/3TC 2.5 tabs OD + DTG 2.5 tabs OD	ABC 300mg OD 3TC 150mg OD DTG 25mg OD
20 – 24.9kg	ABC 300mg tab 3TC 150mg tab DTG 50mg tab	ABC 1.5 tabs OD + 3TC 1.5 tabs OD + DTG 1 tab OD	ABC 450mg OD 3TC 225mg OD DTG 50mg OD
20 – 24.9kg	ABC/3TC 120/60mg tab DTG 50mg tab	ABC /3TC 3 tabs OD + DTG 1 tab OD	ABC 360mg OD 3TC 180mg OD DTG 50mg OD
≥25kg	TAF/FTC/DTG 25/200/50mg tab	TAF + FTC + DTG 1 tab OD	TAF 25mg OD FTC 200mg OD DTG 50mg OD
≥30kg	TDF/3TC/DTG 300/300/50mg tab	TDF + 3TC + DTG 1 tab OD	TDF 300mg OD 3TC 300mg OD DTG 50mg OD
Alternative Regimens			
3 – 5.9 kg	For *alternative regimens* for children weighing 3 – 13.9kg, consult a medical officer with appropriate training or call **7040**		
6 – 9.9kg			
10 – 13.9kg			
14 – 19.9kg	AZT/3TC 60/30mg tab LPV-r 100/25mg tab	AZT/3TC 2.5 tabs BD + LPV-r 2 tabs BD	AZT 150mg BD 3TC 75mg BD LPV-r 200/50mg BD
20 – 24.9kg	AZT/3TC 300/150mg tab LPV-r 200/50mg tab	AZT/3TC 1 tab AM 0.5 tab PM + LPV-r 1 tab BD	AZT 300mg AM, 150mg PM 3TC 150mg AM, 75mg PM LPV-r 200/50mg BD
25 – 24.9kg	AZT/3TC 300/150mg tab LPV-r 200/50mg tab	AZT/3TC 1 tab BD + LPV-r 2 tabs AM 1 tab PM	AZT 300mg BD 3TC 150mg BD LPV-r 400/100mg AM, 200/50mg PM
≥35kg	AZT/3TC 300/150mg tab LPV-r 200/50mg tab	AZT/3TC 1 tab BD + LPV-r 2 tabs BD	AZT 300mg BD 3TC 150mg BD LPV-r 400/100mg BD

- Note that evidence not sufficient/conclusive for use of TAF in patients co-infected with TB and on Rifampicin-based ATT, therefore avoid use in such patients
- In TB/HIV co-infection, give DTG BD if Rifampicin-based ATT. Continue giving the DTG twice daily for two weeks before going back to the initial dosing
- DTG 10mg should be prescribed in children weighing ≥3kg and ≥ 4 weeks of age
- TDF + 3TC + DTG should only be used in children weighing ≥30kg as part of fixed dose combinations
- TAF + FTC + DTG should only be used in children weighing ≥25kg as part of fixed dose combinations
- For premature babies and children less than 3kg or less than 4 weeks of age, consult a medical officer with appropriate training or call 7040
- Use of TDF in children weighing < 30kg is not recommended

For complicated cases, consult a medical officer with appropriate training or call **7040**

APPENDIX 2: KEY DRUG-DRUG INTERACTION FOR ARVs

	ABC	AZT	TAF	TDF	3TC	FTC	d4T	ATV	DRV	LPV	RTV	EFV	ETR	NVP	DTG	RAL
Antibiotics (incl. anti-TB drugs)																
Rifampicin																
Rifabutin																
Bedaquiline																
Antimalarial drugs																
Amodiaquine																
Artemisinin																
Halofantrine																
Lumefantrine																
Antifungal																
Itraconazole																
Ketoconazole																
Antiretrovirals																
Efavirenz																
Etravirine																
Nevirapine																
Emtricitabine																
Zidovudine																
Lamivudine																
Stavudine																
Atazanavir																
Darunavir																
Lopinavir																
Abacavir																
Ritonavir																
Dolutegravir																
Gastrointestinal Agents																
Omeprazole																
Esomeprazole																
Lansoprazole																
Cardiovascular drugs																
Quinidine																
Simvastatin																
Amlodipine																
Enalapril																
Hydrochlorothiazide																
Anticonvulsants																
Carbamazepine																
Phenytoin																
Hypoglycaemic drugs																
Metformin																

COLOUR CODES FOR THE KEY DRUG–DRUG INTERACTIONS FOR ANTIRETROVIRAL DRUGS

	No clinically significant interaction or interaction unlikely based on knowledge of drug metabolism
	Potential interaction that may require close monitoring, alteration of drug dosage or timing of administration
	Interaction likely: do not use or use with caution
	No clear data, actual or theoretical, indicate whether an interaction will occur

APPENDIX 3: WHO TOXICITY ESTIMATES

Grade (Severity)	Characteristics	Management
1 - Mild	Transient or mild discomfort, no limitation in activity, no medical intervention needed	Does not require change in therapy Symptomatic treatment may be given
2 - Moderate	Limitation in activity, some assistance may be needed, no or minimal medical intervention or therapy required	Consult Continue ART if possible If no improvement, consider substitution with a drug in the same ARV class, but with a different toxicity profile
3 - Severe	Marked limitation in activity, some assistance usually required, medical intervention required, possible hospitalization	Refer or consult Substitute the offending drug without stopping therapy
4 - Life-threatening	Extreme limitation in activity, significant assistance required, significant medical intervention or therapy required, hospitalization or hospice care	Discontinue all ARV drugs, manage the medical event until patient is stable and toxicity has resolved

APPENDIX 4: CO-TRIMOXAZOLE DESENSITIZATION PROTOCOL FOR ADOLESCENTS AND ADULTS

Time Point	Dose for desensitization
Day 1	80mg SMX/16mg TMP (2mL of oral suspension)
Day 2	160mg SMX/32mg TMP (4mL of oral suspension)
Day 3	240mg SMX/48mg TMP (6mL of oral suspension)
Day 4	320mg SMX/64mg TMP (8mL of oral suspension)
Day 5	1 single-strength SMX/TMP tablet (400mg SMX/80mg TMP)
Day 6 onward	2 single-strength SMX/TMP tablets or one double strength tablet (800mg SMX + 160mg TMP)

Oral suspension is 40mg TMP/200mg SMX per 5mL of syrup

APPENDIX 5: POSITIVE HEALTH DIGNITY & PREVENTION (PHDP)

To have a significant effect on slowing the spread of the epidemic, prevention efforts must also be directed towards HIV-infected individuals who can transmit the virus.

Deliver consistent, targeted prevention messages and strategies during routine visits

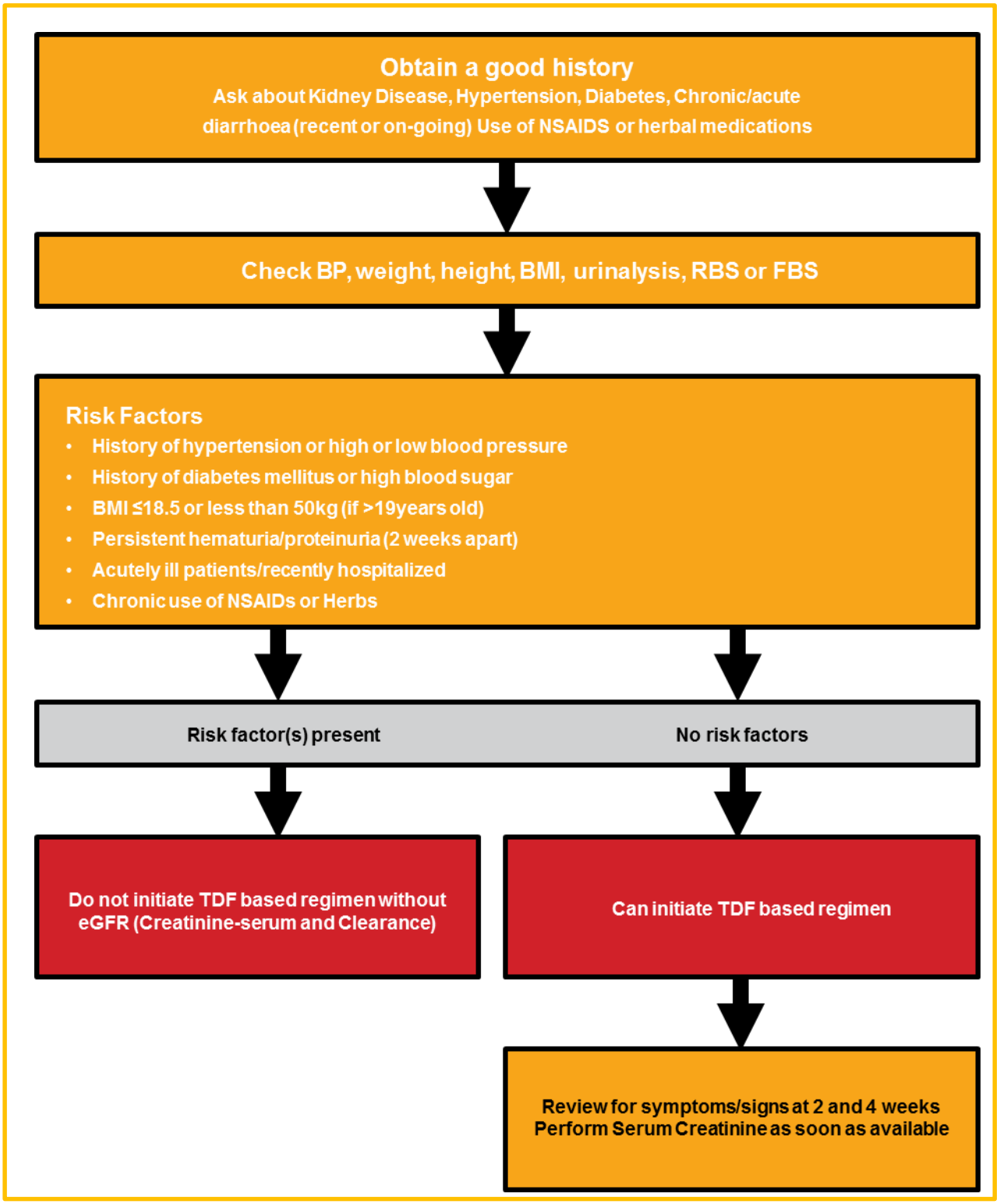
At every visit, assess for and counsel regarding:

- High risk sexual activity
- Partner's and children's HIV status
- Disclosure to partner/guardian/treatment supporter
- Signs and symptoms of STIs and cervical cancer
- Pregnancy status
- Adherence to ART and other medications
- Abuse of alcohol and other substances
- Positive living (nutrition, alcohol and smoking cessation)

Six (6) key steps for PHDP:

- Step 1: Give risk reduction messages to every patient at every visit
- Step 2: Assess adherence to ARVs
- Step 3: TB and STI screening and management
- Step 4: Family planning services and safer pregnancy counselling
- Step 5: Give patient condoms at every visit
- Step 6: Partner HIV testing

APPENDIX 6: RENAL INSUFFICIENCY SCREENING ALGORITHM (IN THE ABSENCE OF CREATININE TEST)



APPENDIX 7: FORMULAE FOR CALCULATING CREATININE CLEARANCE IN DIFFERENT PATIENT POPULATIONS

IN CHILDREN (10-18 YEARS) GLOMERULAR FILTRATION (SCHWARTZ)

Clinical Use: A simple estimate of Glomerular Filtration Rate in children derived from body length and serum Creatinine.

Formula:

$$\text{Creatinine Clearance} = \frac{(k \times \text{height})}{\text{Creatinine}}$$

Units:

- Creatinine: [mg/dL] mg/dL=88.4µmol/L
- Height: [cm]
- Constant as follows: 0.55 for adolescent girls and 0.7 for adolescent boys
- For pregnant women use serum Creatinine (should be less than 125µmol/L to use TDF

ADULTS (≥19 YEARS)

- **For Men:**

$$\text{CrCl} = \frac{[(140-\text{age})(\text{weight in kg})]}{0.815 \text{ x serum Creatinine } (\mu\text{mol/L})}$$

OR

$$\text{CrCl} = \frac{[(140-\text{age})(\text{weight in kg})]}{72 \text{ x serum Creatinine } (\text{mg/dL})}$$

- **For Women**

$$\text{CrCl} = \frac{[(140-\text{age})(\text{weight in kg})(0.85)]}{0.815 \text{ x serum Creatinine } (\mu\text{mol/L})}$$

OR

$$\text{CrCl} = \frac{[(140-\text{age})(\text{weight in kg})(0.85)]}{72 \text{ x serum Creatinine } (\text{mg/dL})}$$

APPENDIX 8: EVALUATING ADOLESCENTS' READINESS TO TRANSITION TO ADULT CARE AND TREATMENT

Tick	Transition Readiness Checklist to the Adult Clinic
	Ensure that the adolescent has been disclosed to of his/her HIV status
	Ensure that the adolescent understands that HIV is a chronic disease and must live with it positively
	Ensure that the adolescent is coming on his/her own for the follow-up, reschedule appointments and drug pickup
	Ensure that the adolescent knows the drugs s/he is taking and adhering to treatment
	Ensure that the adolescent has had three to four transition counselling sessions before being transitioned to the adult clinic
	Ensure that psychosocial issues have been addressed before being transitioned
	Ensure the patient has accepted his/her chronic illness and is oriented towards future goals and hopes including long term survival
	Ensure the patient has learned the skills needed to negotiate appointments and multiple providers in an adult practice setting (make, cancel and reschedule appointments)
	Patient has achieved personal and medical independence and is able to assume responsibility for his/her treatment and participating in decision making
	The referring provider is familiar with the new provider and practice setting and direct communication about individualized plan for the patient has taken place
	Mental health services have been transitioned at the same time as medical services
	Ensure that the psychosocial needs of the adolescent are met
	Ensure that the adolescent has been disclosed to of his/her HIV status
	Ensure that the adolescent understands that HIV is a chronic disease and must live with it positively
	Ensure that the adolescent is coming on his/her own for the follow-up, reschedule appointments and drug pick-up
	Ensure that the adolescent knows the drugs s/he is taking and adhering to treatment

APPENDIX 9: TIMELINE FOR ADOLESCENT TRANSITION TO ADULT CARE

Timeline for Adolescent Transition to Adult HIV/AIDS Care and Treatment Services			
10–12 years old	**13–15 years old**	**16–19 years old**	**19 years above**
▸ Encourage caregivers to fully disclose HIV infection status to the child ▸ Solicit direct conversation with the adolescent ▸ Increase one on one meetings and counselling sessions with the adolescent ▸ Explain medications and adherence ▸ Deal with early adherence issues and challenges ▸ Link to support groups ▸ Let adolescents understand that they will be moved to the next stage 13-15 years	▸ Assist adolescent with a calendar for appointments and medicines ▸ Ensure adolescent understands diagnosis, needed medications, adherence, health precautions, positive living, and positive prevention ▸ Let adolescents understand that they will be moved to the next stage 16-19 years	▸ Enforce responsibility in making and keeping appointments ▸ Provide ALHIV with copies of medical records and any other forms or documents required by the adult clinic ▸ Review medical history with the client ▸ Encourage questions about care plan and treatment regimen and possible changes ▸ Transfer medical records to new provider, highlight key issues ▸ Visit the adult clinic together with the adolescent client ▸ Where possible adolescents should be accompanied to the adult centre ▸ Let adolescents understand that they will be moved to the next stage >19 years	Provide health sessions to prepare older adolescents to adult life such as: ▸ Marriage and HIV ▸ STI messages ▸ Discordant couples ▸ Reinfections ▸ Drug resistance ▸ PMTCT messages ▸ Family planning information and messages

GLOSSARY

Antiretroviral Therapy (ART): Use of antiretroviral regimens consisting of a combination of at least three or more drugs from at least 2 classes

Body Mass Index (BMI): A measure of body fat based on one's weight in relation to height

Co-trimoxazole Preventive Therapy (CPT): Use of Co-trimoxazole to prevent opportunistic infections in susceptible Persons Living With HIV/AIDS (PLWHA)

Creatinine Clearance (CrCl): An estimation of millilitres of blood filtered by the kidneys per minute

Directly Observed Therapy short course (DOTs): refers to the WHO-recommended strategy for TB control and involves direct observation of patients taking TB medications. This is done to ensure that the patient takes the right medicines, in the right doses, at the right intervals

Focused Antenatal Care (FANC): A standard package of basic ANC services that all pregnant women should receive. FANC emphasizes the importance of developing a plan of care that meets each woman's individual needs

HIV Testing Services (HTS): Refers to the full range of services provided with HIV testing, including counselling; linkage to appropriate HIV prevention, treatment, and care, and other clinical services; and coordination with laboratory services to ensure delivery of accurate results

Isoniazid Preventive Therapy (IPT): Use of Isoniazid for prophylaxis to susceptible patients to offer protection against Mycobacterium TB

Immune Reconstitution Inflammatory Syndrome (IRIS): An exaggerated inflammatory reaction from a re-invigorated immune system

Integration: The two-way process of mutual adaptation between migrants and the societies in which they live, whereby migrants are incorporated into the social, economic, cultural, and political life of the receiving community

Internal migration: The movement of people within a State involving the establishment of a new temporary or permanent residence

International migration: The movement of persons away from their place of usual residence and across an international border to a country of which they are not nationals

Key populations: Groups who, due to specific higher risk behaviours, are at increased risk of HIV irrespective of the epidemic type or local context. They also often have legal and social issues related to their behaviours that increase their vulnerability to HIV

Labour migration: Movement of persons from one State to another, or within their own country of residence, for the purpose of employment. In line with the definition of migrant, labour migration is defined as covering both migrants moving within the country and across international borders

Migrant: An umbrella term, not defined under international law, reflecting the common lay understanding of a person who moves away from his or her place of usual residence, whether within a country or across an international border, temporarily or permanently, and for a variety of reasons

National Unique Patient Number (NUPN): A unique client identification number used in SmartCare patient records system

Nucleic Acid Test (NAT): Virologic testing technology used for early infant HIV diagnosis developed and validated for use at the point of care. This test detects both viral RNA and DNA

Polymerase Chain Reaction (PCR): A test done to detect HIV specific genetic material that indicates presence of HIV. In Zambia, using Dry Blood Spot (DBS) specimen, this test diagnoses HIV infection in children below 18 months of age

Positive Health Dignity and Prevention (PHDP): An HIV prevention strategy among PLWHA that focuses on risk reduction, ART adherence, correct condom use, family planning, STI screening, and partner HIV testing

Pre-exposure Prophylaxis (PrEP): An HIV prevention strategy where those at high risk of acquiring HIV are covered on prophylactic ARVs before exposure to the HIV virus

Post-exposure Prophylaxis (PEP): Short term antiretroviral treatment to reduce the likelihood of HIV infection after potential exposure to the virus

Repeat Testing: A situation where additional testing is performed for an individual immediately following a first test during the same testing visit due to inconclusive or discordant results

Re-testing: A situation where additional testing is performed for an individual after a defined period of time for explicit reasons, such as a specific incident of possible HIV exposure within the past three months, or on-going risk of HIV exposure such as HIV negative persons with HIV-positive partner, sharing injecting equipment or having sex with a person of unknown status

Severe Liver Disease: Progressive destruction of the liver parenchyma over a period greater than 6 months leading to fibrosis and cirrhosis

Treatment as Prevention (TasP): Refers to use of antiretroviral therapy in PLWHA to decrease the risk of HIV transmission to others

Treat All: WHO recommendation that all clients testing HIV positive should be initiated on ART irrespective of their WHO Clinical staging, CD4 or Viral load levels

Visual Inspection with Acetic acid (VIA): A cervical cancer screening method done using Acetic Acid