Royal Government of Bhutan
Ministry of Health

National Guideline on Treatment & Management of HIV & AIDS

"Treat All"

Revised Version 2024

World Health Organization
Bhutan

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Contents

Acronyms and Abbreviations

ABC	Abacavir	EFV	Efavirenz
AHI	Acute HIV Infection	EID	Early Infant Diagnosis
AIDS	Acquired Immunodeficiency Syndrome	ELISA	Enzyme Linked Immunoassay
ANC	Antenatal Clinic	FNAC	Fine Needle Aspiration Cytology
ART	Antiretroviral Therapy	GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
AZT	Zidovudine	GI	Gastro-Intestine
PHC	Primary Health Care	HBV	Hepatitis B Virus
CDC	Centre for Disease Control	HCT	HIV Counseling and Testing
CPT	Clotrimazole Prophylaxis Therapy	HCV	*Hepatitis C* Virus
CM	Cryptococcal Meningitis	HCW	Health Care Worker
CMV	*Cytomegalovirus*	HISC	Health Information Service Centre
CrAg	Cryptococcal Antigen	HIV	Human Immunodeficiency Virus
CNS	Central Nervous System	HSV	*Herpes simplex* virus
CSF	CerebroSpinal Fluid	IDU	Injecting Drug Users
CST	Care, Support and Treatment	IR	Initial Reactive
DoPH	Department of Public Health	IRS	Immune Reconstitution Syndrome
DOTS	Directly Observed Treatment Short Course	JDWNRH	Jigme Dorji Wangchuck National Referral Hospital
DNA	Deoxyribonucleic Acid	KS	Kaposi Sarcoma
DTG	Dolutegravir	LDH	Lactate Dehydrogenase
EBV	*Epstein-barr* Virus	LIP	Lymphoid Interstitial Pneumonia

MAC	*Mycobacterium avium complex*	NAAT	Nucleic Acid Amplification Test
MCH	Maternal Child Health	NSP	Needle Syringe Program
MDG	Millennium Development Go	OI	Opportunistic infection
MoH	Ministry of Health	pALD	Pediatric Abacavir/ Lamivudine/ Dolutegravir fixed dose combination
MRI	Magnetic Resonance Image	RCDC	Royal Centers for Disease Control
MSM	Men who have Sex with Men	TB	Tuberculosis
MSTF	Multi Sectoral Task Force	TPT	TB Preventive Therapy
MTCT	Mother To Child Transmission	WHO	World Health Organization
NACP	National HIV/AIDs, STI Control Programme		

Foreword

As we address the multifaceted challenges posed by HIV, it is with great pride and dedication that we present this updated guideline. The treatment and management strategies in the field of HIV have evolved since the last guidelines. This present effort is a testament to our unwavering commitment to improving the lives of those affected and to achieving global health goals.

This guideline represents the culmination of rigorous research, collaboration, and the invaluable input of healthcare professionals, researchers, and policymakers. It serves as a comprehensive resource, offering evidence-based recommendations that reflect the latest advancements and best practices in the field particularly designed to suit our local context and available resources.

Key highlights include the adoption of Dolutegravir as the first-line antiretroviral therapy (ART) for adults and children, aligning with recent WHO recommendations. This decision underscores our commitment to optimizing treatment outcomes and enhancing patient care. Additionally, the guideline provides updated protocols for monitoring CD4 counts, viral loads, and the management of HIV-co infections, ensuring holistic and effective care.

Furthermore, in recognition of the importance of prevention, care, support and treatment, this book also includes high-quality HIV testing services accessible to key and vulnerable populations as it is critical to increase access to prevention modalities such as PrEP, and to reduce onward transmission by initiating early treatment for those who test positive.

By aligning with WHO HIV testing guidelines and promoting the "Treat All" approach, we strive to ensure equitable access to quality healthcare for all individuals affected by HIV. Our collective efforts are guided by the ambitious UNAIDS 95-95-95 targets, aiming to achieve universal access to HIV prevention, treatment, and care. This book not only equips healthcare providers with essential tools and knowledge but also underscores our shared commitment to improving health outcomes and promoting the well-being of communities worldwide.

We extend our heartfelt gratitude to everyone who contributed to the development of this guideline. Your dedication and expertise have been instrumental in shaping this invaluable resource. Together, we continue to advance towards a future where HIV is no longer a barrier to health and well-being.

Pemba Wangchuk
Secretary
Ministry of Health

Acknowledgements

The National HIV/AIDS, STIs & Hepatitis Control Programme, Department of Public Health, Ministry of Health gratefully acknowledges the contributions of Technical Advisory Group (TAG) and many other individuals to the revision of this National Guideline on treatment and Management of HIV & AIDS. It was reviewed based on the new recommendations from the World Health Organization (WHO). We also would like to thank the World Health Organization (WHO) for the financial and technical support rendered to NACP. In particular, we acknowledge the support and contribution of the following officials:

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CHAPTER I

HIV COUNSELING AND TESTING (HCT)

Key Points

- Rapid HIV antibody testing facilities are available in all the district hospitals including some PHCs and the free-standing Health Information and Service Centers (HISCs) in six major towns of Thimphu, Phuentsholing, Samdrup Jongkhar, Gelephu, Kuenga Rabten in Trongsa and Lobesa in Punakha.

Introduction

People access HIV treatment, care and prevention through the gateway of HIV testing and counseling. It is estimated that globally about half of the people living with HIV do not know their HIV status. Those who do know are often tested late. Poor linkages from HIV testing and counseling and delays in initiation of ART results in poor health outcomes and ongoing HIV transmission. The overall HIV testing and counseling goal for the national programme is to intensify the HIV diagnosis facilities to detect as many cases as possible at the earlier stage of the infection and subsequently make linkage to the continuum of care.

Rapid HIV antibody testing facilities are available in all the district hospitals including some PHCs and the free-standing Health Information and Service Centers (HISCs) in six major towns of Thimphu, Phuentsholing, Samdrup Jongkhar, Gelephu, Kuenga Rabten in Trongsa and Lobesa in Punakha. The services are also available in integrated HISC set up in Samtse hospital. ELISA testing facilities are currently available only in the national and regional referral hospitals including some district hospitals in strategic locations. Trained counselors provide HCT services. They also carry out patient monitoring and follow-up for continuum of care as well as recording and reporting of the HIV data including monthly HCT reporting.

All forms of HIV testing and counseling will be voluntary, however the provider-initiated testing and counseling (PITC) are provided to the individual clients based on their existing health conditions such as for patients with tuberculosis (TB), sexually transmitted infections (STI) and antenatal clinic (ANC), patient undergoing invasive surgery and other medical conditions. Similarly, for the general population, the HIV testing is offered adhering to the five C's alongwith the pre/post test counseling as follows:

- *Consent* - HIV testing is initiated only after obtaining an informed consent.
- *Confidentiality* - HIV counseling and testing services are kept confidential
- *Counseling* - HIV counseling and testing services must be accompanied by pre-test information and post-test counseling.
- *Correct test* - HIV counseling and testing providers should strive to provide high-quality and quality assured testing services

- *Connection to care & treatment* - Connections to prevention, care and treatment services include the provision of a referral system for appropriate follow-up, including treatment, care and support services.

Pre-Test information:

- Basic information about the potential benefits of testing
- Basic information about HIV and its transmission
- Risk assessment and risk reduction plan

Post Test Counseling:

- Consider possible exposure in window period – including any risks, which may have occurred since pre-test counseling
- Reinforce information on transmission, safer sex and other practices
- Explanation of their result
- Emphasize the client's requirement of subsequent testing with appointment if necessary
- Partner notification if positive
- Providing continuum of counseling and psychosocial support
- Referral if required

Refer to counseling and testing guidelines for detail.

Table 1: The different levels of HIV testing facilities

Health Facility Level	HIV Testing Services	Human Resource	Remarks
Royal Centre for Disease Control (RCDC)	• Rapid diagnostic test • Enzyme-linked Immunoassay (ELISA) (4th Gen.Ag-Ab/ latest Assays) • NAAT	Laboratory Specialists, Laboratory Technologists, Laboratory Technicians	HIV confirmation is decentralized to three Regional Referral Hospitals and Phuentsholing Hospital

National/Regional Referral Hospital	● Rapid diagnostic test ● Enzyme-linked Immunoassay (ELISA) ● HIV Viral Load Testing by Gene Xpert ● NAAT for Early Infant diagnosis (EID) and Viral Load ● CD4 count	Laboratory Technologists, Laboratory Technicians	GeneXpert facility available in JDWNRH, ERRH, CRRH, Phuntsholing, Samtse, Samdrup Jongkhar, Nganglam, Trashigang and Wangduephodrang Hospitals
District/General Hospital	● Rapid diagnostic test ● NAAT for Early Infant diagnosis (EID) and Viral Load	Laboratory Technologists, Laboratory Technicians	NAAT, ELISA and CD4 count testing available hospitals located in strategic areas.
Ten Bedded Hospitals	● Rapid diagnostic test	Laboratory Technicians	
Primary Health Care	● Rapid diagnostic test	Trained counselor	
Health Information and Service Center (HISC)	● Rapid diagnostic test	Trained counselor	
Private Diagnostic Lab	● Rapid diagnostic test	Laboratory Technicians	

Testing algorithm

HIV testing and confirmation procedures will be as per the National Guideline. All testing centers will use the standard operating procedures (SOP) for initial screening (A1) at their facilities using RDTs or ELISA wherever feasible. The test will be repeated for all the initial reactive (IR) tests. If the repeat test is reactive the samples will be sent to the Public Health Laboratory for a confirmatory test. Tests A2 and A3 are carried out at the confirmatory centers as detailed in the fig.1.

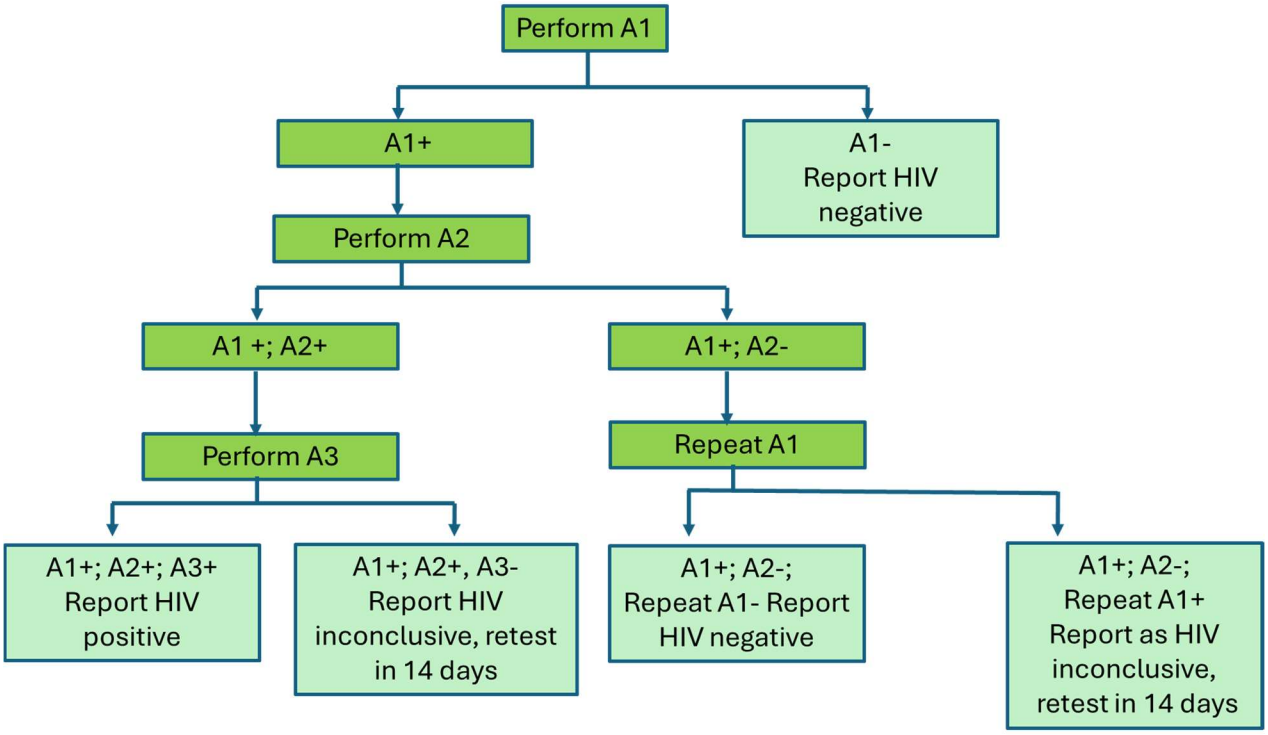

Figure 1: National testing algorithm

Test Stage/Kit

A1: Rapid/ELISA at primary testing center
A2: ELISA (HIV 1/2 Ab/Ag combo) at confirmatory test center
A3: Gelatin particle agglutination test (GPA) / Western Blot Assay/ NAAT/ any other confirmatory test available

Summary of testing approaches for infants

Any infant born to infected mothers should be tested for HIV as in the following table:

Table 2: Summary of testing approaches for neonates and infants

Category	Test Provided	Testing Period/Frequency	Service Availability	Action
Healthy, HIV exposed neonates	NAAT	• At birth • Repeat after 4- 6 weeks if negative	JDWNRH	Start ART Immediately

Healthy, HIV exposed infant	NAAT/Serological test (Rapid/ELISA)	9 months and above	ELISA and NAAT in selective hospitals and Rapid in all health facilities	Repeat at 18 months if positive If negative, repeat once after one month and then only declare Negative
Healthy, HIV exposed baby	NAAT/Serological test (Rapid/ELISA)	18 months	ELISA and NAAT in selective hospitals and Rapid in all health facilities	For confirmation of HIV status

NAAT and EID

All HIV exposed neonates, and all infants with unknown or uncertain HIV status, should have a NAAT performed immediately at 6 weeks of age or at the earliest opportunity thereafter. All infants with an initial positive NAAT should be started on ART without delay and a second specimen should be collected to confirm the initial positive test result.

Serological tests should be done for all HIV-exposed infants and children aged 9 to 18 months. Only those with reactive serological assays should undergo NAAT to confirm HIV infection and determine the need for ART.

Quality control of HIV testing

Quality control is an essential part of HIV laboratory diagnosis. It is a way to ensure reliability of the test results. Laboratories of all health centers, HISCs and private diagnostic centers that perform HIV tests will be required to mandatorily participate in National External Quality Assessment Scheme (NEQAS) organized by RCDC. The NEQAS panel for HIV/STI serology will be sent at least once in a year to all participating laboratories and the findings used for identifying errors and gaps in their testing methods and knowledge.

RCDC, as the coordinator for NEQAS participates in the External Quality Assessment Scheme (EQAS) provided by an internationally recognized institute

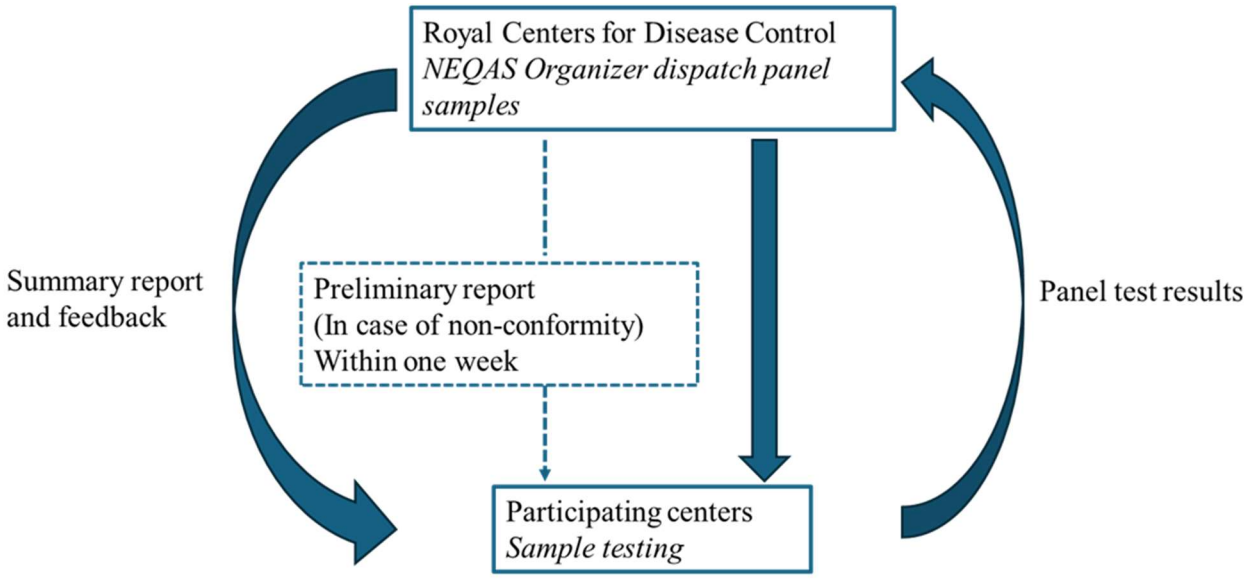

Figure 2: Flow process of NEQAS for HIV/STI serology

HIV Self-Testing (HIVST)

HIVST is usually provided for the population at high risk. The service is available to the public through district hospitals and HISCs who also provide pre-test information. The reactive results are submitted to the health-care worker who will carry out necessary counseling and further confirmation as stated in figure 3 below.

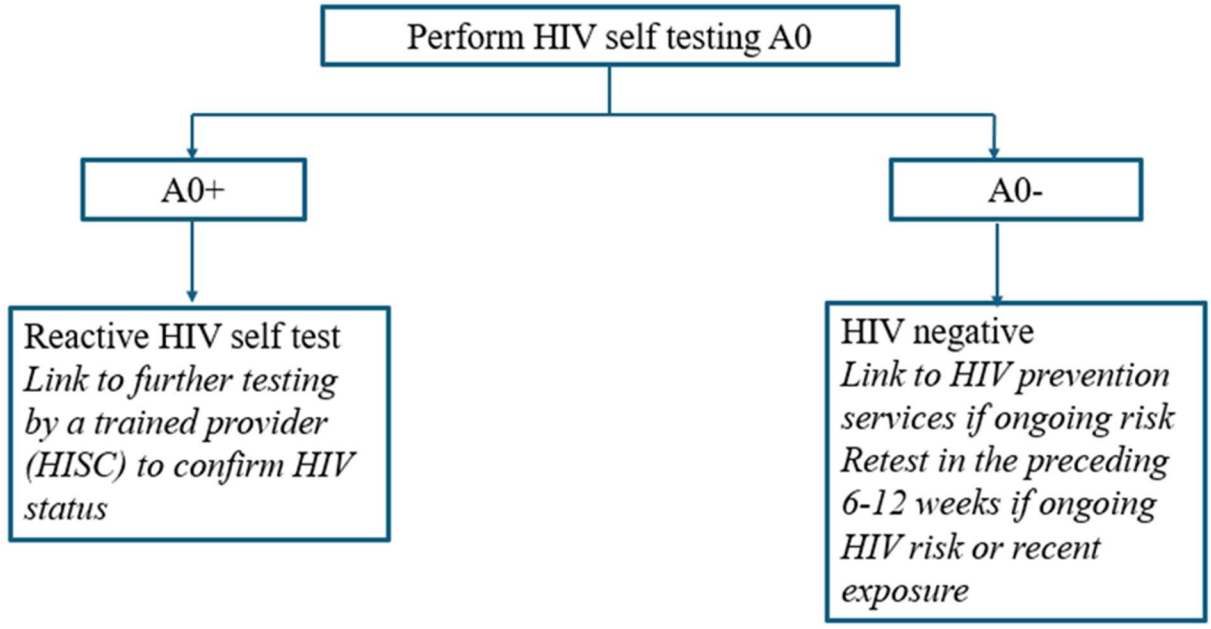

Figure 3: Flow process for HIV self testing and reporting

CHAPTER II

ANTIRETROVIRAL THERAPY (ART)

Key Points

- 2 NRTIs remain the integral component of ART with an integrase inhibitor.
- Combination of Lamivudine, Tenofovir and Dolutegravir is the preferred first line ART regimen for adults and adolescents.

The primary aim of ART is to prevent the mortality and morbidity associated with chronic HIV infection. This goal is best accomplished by using effective ART to maximally inhibit HIV replication, so that plasma HIV RNA levels (viral load) remains suppressed or undetectable. A further aim of treatment is the reduction in sexual transmission of HIV and to prevent mother-to-child transmission (PMTCT).

Table 3: Goals of Therapy

Clinical Goals	Prolongation of life and improvement in the quality of life and absence of symptoms and concurrent infection
Virological Goals	Decline in viral load to < 50 copies/mL within 6 months of commencing ART, and sustained thereafter
Immunological Goals	CD4 >200 cells/mm^3 within 6 months of commencing ART
Therapeutic Goals	Rationalize the sequencing of drugs to achieve clinical, virological and immunological goals while maintaining treatment options, limiting drug toxicity and facilitating adherence.
Epidemiologic Goals	Reduce transmission of HIV.

Prerequisites for Starting ART

The following services are essential for starting ART:

a. Access to HIV voluntary counseling and testing and follow up counseling services. This also includes psychological support.
b. A well-equipped medical Centre for diagnosis and management of opportunistic infections.
c. Reliable laboratory services capable of carrying out investigations such as CBC, biochemistries, CD4 counts, culture facilities and viral load estimations.

d. Drugs: reliable, affordable and sustained supply of antiretroviral drugs and drugs for prophylaxis and treatment of opportunistic infections (OIs)

Clinical evaluation of the patient prior to treatment initiation

- Complete history and physical examination
- Detailed clinical examination of the patient should aim to assess the clinical staging of the HIV infection (*see WHO clinical staging table 4*)
- Conduct routine laboratory investigations: CD4+ T lymphocyte count and viral load.
- Identify past and current HIV related illnesses that would require treatment
- Identify coexisting medical conditions which may influence the choice of therapy

Table 4: WHO Clinical Staging

STAGE	SIGNS AND SYMPTOMS
Stage 1	Acute retroviral syndrome, asymptomatic HIV infection and Persistent Generalized Lymphadenopathy (PGL-lymphadenopathy of at least two sites excluding inguinal lymph nodes) for longer than 6 months.
Stage 2	Symptomatic but ambulatory, mild HIV related diseases, e.g. mucocutaneous lesions, herpes zoster, pruritic papular eruptions, fungal nail infections, seborrheic dermatitis, angular cheilitis and recurrent respiratory tract infections.
Stage 3	Bedridden < 50% of daytime, HIV related conditions, e.g. diarrhea more than one-month, unexplained weight loss of 10%, fever more than 1 month, oral candidiasis, Oral Hairy Leukoplakia (OHL)
Stage 4	Bedridden for more than 50% of daytime in prior month, AIDS, e.g. PCP, Toxoplasmosis, Lymphoma, extra-pulmonary TB, esophageal candidiasis, Cryptococcus meningitis, salmonellosis, bacterial, septicaemia pneumonia, etc.

History

Medical history should include the following questions:

- When and where the diagnosis of HIV was made
- Source and route of infection (e.g. IDU, homosexual, heterosexual, etc.)
- Current and past signs and symptoms of HIV
- Past medical treatment of established diseases
- Treatment and/or contact with tuberculosis
- History of Sexually Transmitted Infections (STIs),
- Previous ART received, if any

- Pregnancy and Oral Contraceptive Pills (OCP) used
- Sexual history and social habits

Physical Examinations

- Weight of the patient
- Skin: look for herpes, Kaposi Sarcoma (KS), pruritic papular eruptions, dermatitis, etc.
- Lymphadenopathy
- Oropharyngeal mucosa: look for oral candidiasis, herpes simplex, oral hairy leukoplakia (OHL), KS
- Cardiovascular system and respiratory system - look for signs of PTB, PCP, etc.
- Abdomen: look for hepatosplenomegaly/ascites
- Central nervous system: assess the mental status and look for any localizing signs
- Eyes/fundus examination- rule out CMV retinitis
- Genital/gynecological examination - for HSV type 2, ulcers, warts

Table 5: Laboratory Examinations

Important	Supplementary
Routine ● Complete blood count ● Biochemistry - Eg RFT/Electrolytes, LFT, Blood sugar, Lipid Profile ● Chest X-ray ● Sputum GeneXpert and MTB culture **Specific** ● HIV serology (ELISA) and HIV RNA (viral load) ● CD4+T lymphocyte count and CD4 percentage ● Hepatitis B and C ● STI profile ● Pregnancy test	● Culture facilities: blood, urine, sputum and fungal culture ● HPV/PAP smear ● Urinary LAM ● Serum /CSF cryptococcal antigen ● Lumbar Puncture if indicated ● MRI of brain if indicated

Standardized eligibility for starting ART

When to start ART in People Living with HIV
ART should be initiated as soon as possible in all people living with HIV including children, regardless of WHO Clinical Stage and at any CD4 cell count.

****** Timing of initiation of ART in special situation (refer chapter XII OIs for details)**

Timing for ART for PLHIV + TB coinfection
ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 cell count, among people living with HIV. For TB meningitis defer ART by at least 4 weeks of initiation of ATT.
Timing for ART PLHIV cryptococcal meningitis
Immediate ART initiation is not recommended for adults, adolescents and children living with HIV who have cryptococcal meningitis because of the risk of increased mortality and should be deferred by 4–6 weeks from the initiation of antifungal treatment

What ART to start with?

2 NRTIs remain the integral component of ART with an integrase inhibitor, NNRTI or Ritonavir boosted Lopinavir. Combination of Lamivudine, Tenofovir and Dolutegravir is the preferred first line ART regimen for adults and adolescents.

Table 6 shows the first line ART regimen in different categories of population including children:

Table 6: ART regimen for various categories of population

Populations	Preferred first line regimen	Alternative first line regimen	Special circumstances
Adults and adolescents	TDF 300 mg + 3TC 300 mg + DTG 50mg (FDC)	TAF+ 3TC + DTG ABC + 3TC + DTG TDF + 3TC + PI/r	TAF+ 3TC + DTG (When TDF cannot be given) ABC + 3TC + DTG (When TAF cannot be given)

Pregnant women	TDF+3TC+DTG is recommended throughout pregnancy		
Children	ABC 60 mg + 3TC 30mg + DTG 5mg (FDC) For children weighing more than 6 kg and are at least 4 weeks old.	ABC+3TC+ NVP AZT+3TC+NVP	AZT+3TC+LPV/r ABC+3TC+LPV
Neonates	AZT+3TC+NVP For children weighing less than 6 kg and are less than 4 weeks old		

Table 7: Dosage of Antiretroviral Agents in both adult and pediatric population

Drugs	Adults	Pediatrics	*Side Effects*
Dolutegravir (DTG)	50mg OD	• 3 - <6kg (<6 months): 5 mg q24h • 3 - <6kg (>6 months): 10 mg q24h • 6 - <10kg: 15 mg q24h • 10-<14kg: 20 mg q24h • 14-<20kg: 25 mg q24h • >20kg: 50 mg q24h	Increased cholesterol, sleep disorders, weight gain
Lamivudine (3TC)	300 mg od	• Neonates: 2 mg/kg po q12hr • ≥ 1 month: 4 mg/kg po q12hr • ≥ 3 months: 5 mg/kg po q12hr	Minimal.
Tenofovir (TDF)	300 mg od	Recommended in child age ≥ 2 years and >10kg: • 8 mg/kg po once a day and not to exceed 300 mg per day	Fanconi syndrome +/- renal failure (rare), HBV flare

TDF 300 mg + 3TC 300 mg + DTG 50mg	1 tablet once daily	Available for adults only	
Abacavir (ABC)	300 mg bid or 600 mg od	• ≥ 3 months: 8 mg/kg po q12hr • 3 to <6kg: 60mg bd • 6-<10kg:80mg Bd • 10-<14kg :120mg bd • 14 kg to <20kg :150 mg bd • ≥20kg to <25kg: 150mg AM and 300mg PM • >25kg: 300mg Bd	*Severe hypersensitivity reaction*
(pALD) (Fixed dose combination) ABC 60mg+ 3TC 30mg+DTG 5mg		**Weight Based:** 1. **3 to 5.9 kg: use separate products, 1 tablet (ABC 120mg+ 3TC 60mg) + ½ tablet (DTG 10mg) per day** 2. **For weight above 6 kg, use: (ABC 60mg+ 3TC 30mg+DTG 5mg)** • 6 to 9.9kg: 3 tablets per day • 10 to 13.9kg:4 tablets per day • 14 to 19.9kg:5 tablets per day • 20 to 24.9kg:6 tablets per day	
Zidovudine (AZT)	300 mg bid	**Weight Based:** • Birth to 4 weeks: 4 mg/kg po q12hr • >4 weeks: 12 mg/kg po q12hr	*Anemia, neutropenia,* headache, asthenia, GI intolerance, lactic acidosis

Nevirapine		**Neonates <4 weeks of age (weight based)** ● 2- <3 kg: 15mg bd ● 3- 4 kg: 20mg bd ● 4 - <5 kg: 25mg bd **Infants >4 weeks (weight based)** ● 3-5.9kg: 50mg Bd ● 6-9.9kg: 80mg Bd ● 10-13.9kg: 100mg bd ● 14-19.9kg: 130 mg bd ● 20-24.9kg: 150 mg bd ● >25kg: 200 mg bd or 400 mg OD	
Efavirenz (EFV)	600mg OD	**Weight Based:** ● 3.5 - <5kg: 100 mg q24h ● 5 - <7.5kg: 150 mg q24h ● 7.5 - <15kg: 200 mg q24h ● 15 - <20kg: 250 mg q24h ● 20 - <25kg: 300 mg q24h ● 25 - <32.5kg: 350mg q24h ● 32.5 - <40 kg: 400 mg q24h ● ≥ 40kg: 600 mg q24h	*Dizziness, somnolence, abnormal dreams*, rash, increased ALT/AST, lipoatrophy, hypercholesterolemia
Lopinavir/Ritonavir (LPV/r)	400 mg/100 mg bid	**Weight Based:** ● 7 - <15kg: 12mg/kg/dose q12 h based on lopinavir component ● 15 – 40 kg: 10mg/kg/dose q12h based on lopinavir component ● >40kg: same as adults	

What ART regimen to switch to (second - line ART)

***For switching to second line ART- to consult and discuss with TAG members.**

Table 8: Summary of preferred second line ART regimen

Population	Failing First Line Regimen	Preferred Second Line Regimen	Alternative Second Line Regimen
Adults and adolescents	TDF + 3TC + DTG	AZT + 3TC + LPV/r	AZT + 3TC + DRV/r
	TDF + 3TC + EFV	AZT + 3TC + DTG	AZT + 3TC + ATV/r
	AZT + 3TC + EFV	TDF + 3TC + DTG	TDF + 3TC (or FTC) + ATV/r
Children and infants	ABC+3TC+DTG	ABC (or AZT) + 3TC +LPV/r	
	ABC + 3TC + NVP	ABC (or AZT) + 3TC + DTG	
	ABC (or AZT + 3TC + EFV	ABC (or AZT) + 3TC + DTG	AZT (or ABC) +3TC + LPV/r (or ATV/r)
	ABC (or AZT) + 3TC + LPV/r	ABC+3TC+DTG	

CHAPTER III

MONITORING ANTIRETROVIRAL THERAPY

Key Points

- Viral load is recommended as the preferred monitoring approach to diagnose and confirm treatment failure
- Routine viral load monitoring should be carried out at 3, 6 and 12 months and yearly, once the patient is established on ART.
- In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped for individuals who are established on ART.

Clinical assessment and laboratory tests play a key role in assessing individuals before ART is initiated and then monitoring their treatment response and possible toxicity of ART.

Clinical Monitoring

Enquiry should be made about (*the acronym ABCD*):

A - Appetite
B - Body weight
C - Complaints related to ART and OIs
D - Disease progression

Furthermore, at every visit, the patients should be screened for tuberculosis by asking history of:

- cough,
- fever,
- night sweats, and
- weight loss

Table 9: Recommended and desirable laboratory tests at HIV diagnosis and monitoring on ART

Phase of HIV management	Recommended	Desirable
HIV diagnosis	HIV serology CD4 cell count TB screening	• HBV (HBsAg) serology • HCV serology • Screening for sexually transmitted infections • Assessment for major non communicable chronic diseases (hypertension, diabetes mellitus, dyslipidemias and ischaemic heart disease)
Pre ART	CD4 cell count and Viral load	
ART initiation	CD4 count and Viral load (if not done before ART initiation)	• Haemoglobin test for AZT • Pregnancy test • Blood pressure measurement • Urine dipstick for glycosuria and estimated glomerular filtration rate (eGFR) and serum creatinine for TDF
Receiving ART	HIV viral load *(refer to figure 4)*	• Urine dipstick for glycosuria and serum creatinine for TDF
Treatment failure	HIV viral load Drug resistance testing (in case of virological failure)	• HBV (HBsAg) serology (before switching ART regimen if this testing was not done or if the result was negative at baseline)

Table10: WHO definitions of clinical, immunological and virological failure for the decision to switch ART regimens

Failure	Definitions	Comment
Clinical Failure	**Adults and adolescents** New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 conditions) 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.
Immunological failure	Adults and adolescents CD4 count at 250 cells/mm^3 following clinical failure or Persistent CD4 cell count below 100 cells/mm3.	Without concomitant or recent infection to cause a transient decline in the CD4 cell count. Current WHO clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure. There is currently no proposed alternative definition of treatment failure and no validated alternative definition of immunological failure.

	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	
Virological Failure	Viral load above 1000 copies/mL based on two consecutive viral load measurements three months apart, with adherence support following the first viral load test. Switch ART 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 > 50 to < 1000 copies, maintain ARV regimen, enhance adherence counseling and repeat viral load testing after three months. Consider switch after second viral load >50 to < 1000 copies/mL if people are on NNRTI-based ART

Viral Load Testing

HIV viral load (VL) monitoring is key to the success of ART. Decisions to change ART are made on the basis of virological failure, rather than on clinical or immunological failure alone, have been shown to result in better patient outcomes. If the VL is undetectable, then the virus cannot mutate and develop resistance. A sustained VL < 50 copies/mL is associated with the most durable benefit. A suppressed VL also prevents transmission of HIV to contacts: Undetectable = Untransmittable (U=U).

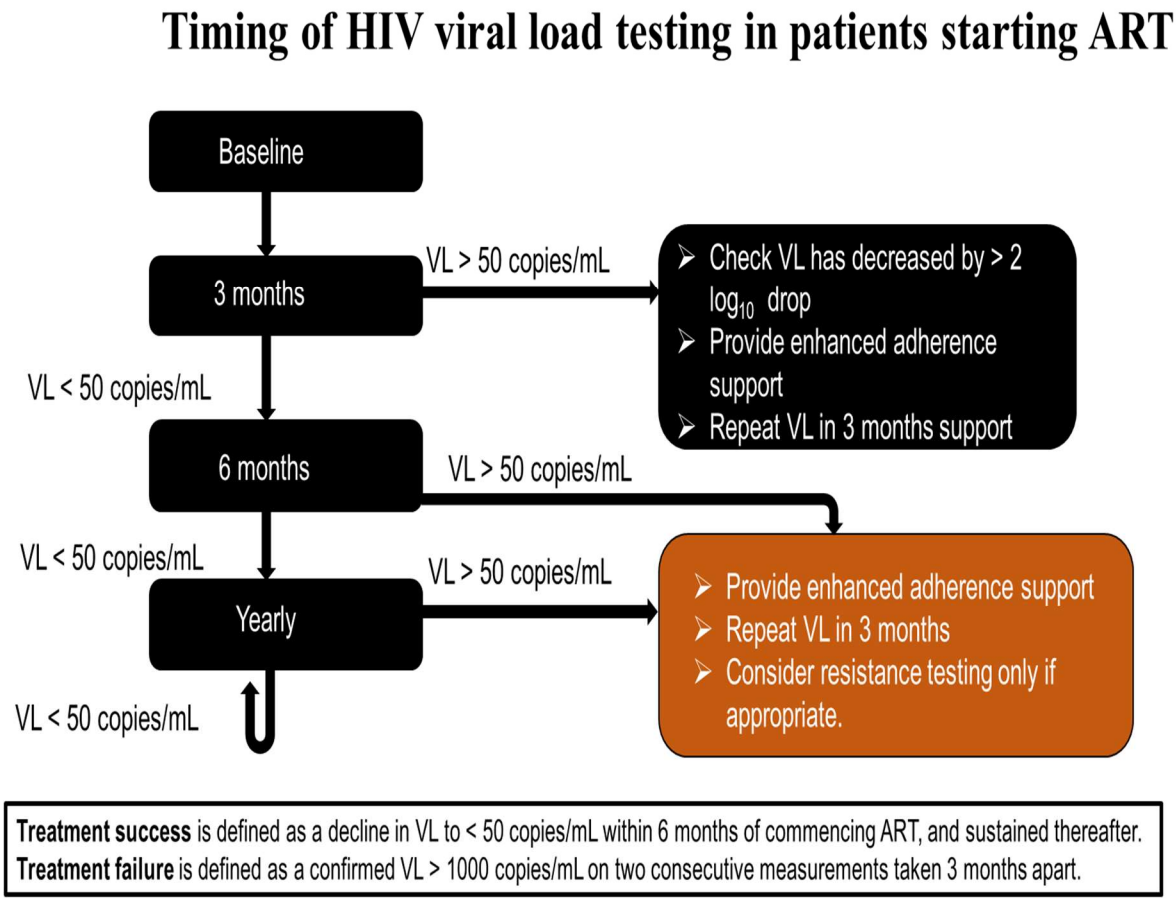

Figure 4. Monitoring of HIV viral load testing in patients starting ART

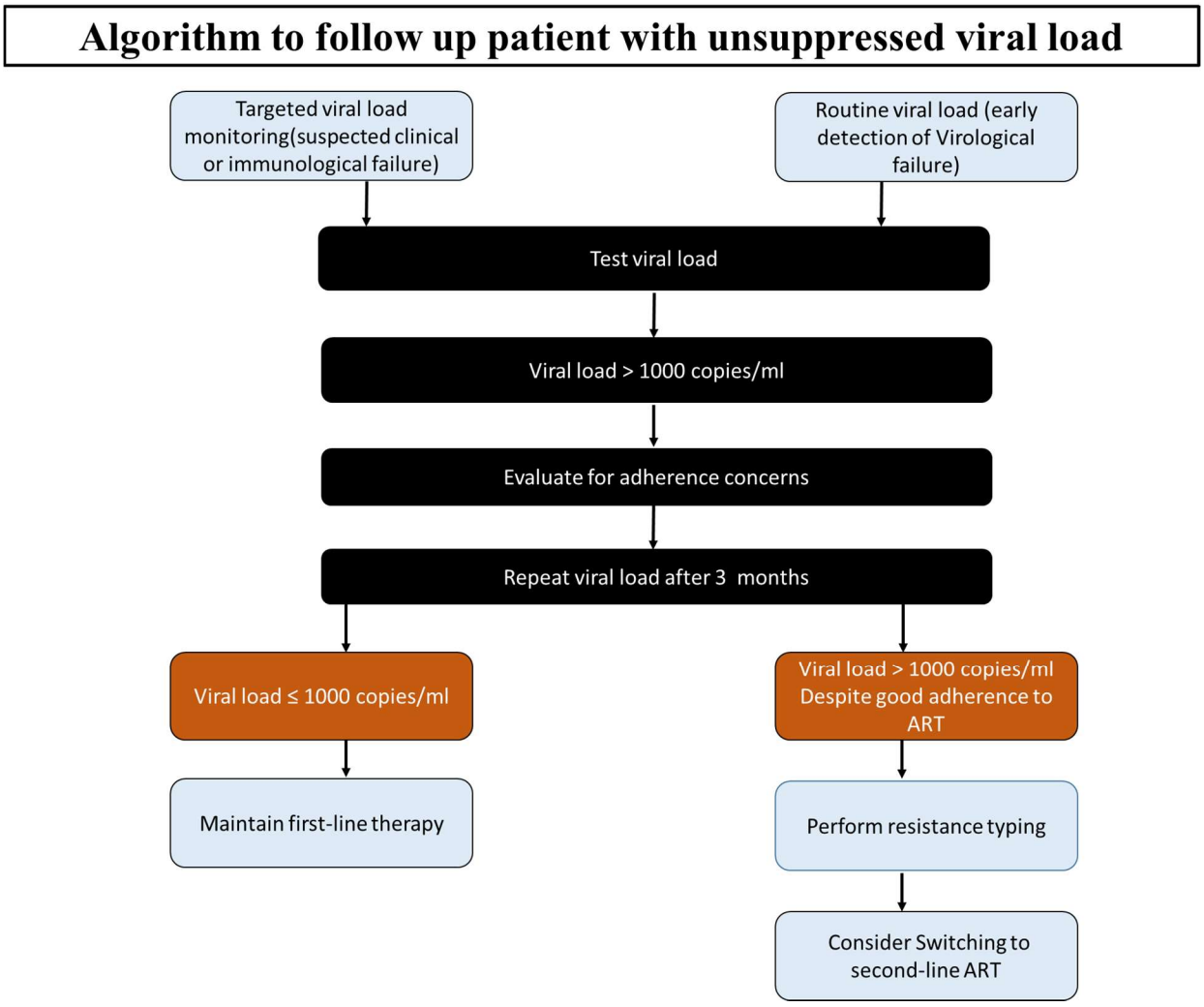

Figure 5: Algorithm for Viral load testing

Timing of CD4 testing in patients

CD4+ count monitoring can be stopped when CD4 count is >200 cells/UL and the VL is suppressed

Repeat CD4+ to guide management if there is

1. Virological failure or clinical failure
2. If the viral load rebounds above 1000 copies/ml due to adherence challenges
3. If patients return to care after interruption

*** Refer chapter IV, Table 11 for monitoring of toxicities associated with the ART**

CHAPTER IV

PHARMACOLOGY OF ANTIRETROVIRALS

KEY POINTS

- DTG is the preferred INSTI because it has a high barrier to resistance, is well tolerated, is available in a FDC formulation, and can be taken once daily

Substantial advances have been made in antiretroviral therapy since the introduction of the first agent, Zidovudine, in 1987. Greater knowledge of viral dynamics through the use of viral load and resistance testing has made it clear that combination therapy with potent agents will reduce viral replication to the lowest possible level and decrease the likelihood of emergence of resistance. Thus, administration of combination antiretroviral therapy, typically comprising at least three antiretroviral agents, has become the standard of care.

Six classes of antiretroviral agents are currently available for use: nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), fusion inhibitors, CCR5 receptor antagonists, and integrase inhibitors.

Combinations of three antiretrovirals, typically two reverse transcriptase inhibitors plus either a non-nucleoside reverse transcriptase inhibitor, boosted protease inhibitor or an integrase inhibitor is referred to as ***highly active antiretroviral therapy*** (***HAART***). These drug regimens have produced sustained reductions in viral load often to levels below the limit of detection, and have been associated with improvements in CD4 cell counts, immune function, and clinical well-being.

1. Nucleoside reverse transcriptase inhibitors (NRTIs)

Nucleoside Reverse Transcriptase Inhibitors targets the HIV enzyme reverse transcriptase. Acting as alternative substrates, they compete with physiological nucleosides which in turn get incorporated into viral DNA.

NRTIs are easy to take, do not have significant interaction with food and once daily dosing is sufficient for most of these drugs. Overall tolerability is good. Lamivudine, zidovudine and tenofovir are the NRTIs available in Bhutan for the treatment of HIV infection.

Lamivudine (3TC)

(Available as 150mg tablets and 10mg/mL syrups.)

Lamivudine is well-tolerated and recommended as a part of the first line regimen. It is considered the safest of NRTIs. Use in pregnancy is extensive and well established.

Dose

1. **Adults:**
   - Usual dose: 150 mg every 12 hourly or 300 mg every 24 hourly
   - Dose adjustment in renal impairment:

Creatinine clearance	Dosage
30-49mL/min	150mg every 24 hours
15-29mL/min	150mg first dose then 100mg every 24 hours
5-14mL/min	150mg first dose then 50mg every 24 hours
<5mL/min	50mg first dose then 25mg every 24 hours

2. **Children:**

Neonates	2 mg/kg po every 12 hourly
≥ 1 month	4 mg/kg po every 12 hourly
≥ 3 months	5 mg/kg po every 12 hourly

Side Effects

- Side effects are minimal
- Common side effects include headache, nausea, vomiting, diarrhea, abdominal pain, fever, cough and nasal signs and symptoms.
- Class related side effects of lactic acidosis and steatosis are listed but not clear if it can be attributed to 3TC therapy.

Drug Interactions

Drug	Interaction
Emtricitabine	therapeutic duplication
Sorbitol (sweetening agent)	reduces the effects of lamivudine
Food	can be taken with or without food

Zidovudine (AZT)

(Available as 300mg tablets and 10 mg/mL syrup)

Zidovudine was the first medication to be FDA approved for the treatment of human immunodeficiency virus type 1 (HIV-1). AZT is recommended for use only where both tenofovir and ABC are unavailable or contraindicated. In these instances, AZT can be used, provided that the hemoglobin (Hb) is > 8 g/dL. AZT can cause neutropenia and anemia; platelet counts generally rise with the use of the drug. It is also used as a monotherapy to prevent vertical transmission from mother to child.

Dose:

Patient group	Dose
Adults	300 mg 12 hourly
birth to 4 weeks	4 mg/kg po every 12 hourly
> 4 weeks	12 mg/kg po every 12 hourly

Drug interaction:

Drug	Interaction
Ganciclovir/Valganciclovir	Increase the toxicity of zidovudine
Clarithromycin	Reduces absorption of zidovudine*
Doxorubicin	Increase risk of adverse reaction to AZT
Valproic acid	Increase risk of adverse reaction to AZT
Food	Can be taken with or without food

* *Administer at least 2 hours apart.*

Side Effects

More common: Hematologic toxicity, including neutropenia and anemia, particularly in patients with advanced HIV disease. Headache, malaise, nausea, vomiting, and anorexia.

Less common (more severe): Myopathy (associated with prolonged use), myositis, and elevated liver enzymes. Cases of lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported.

Tenofovir disoproxil fumarate (TDF)

(Available as 300mg capsules)

Tenofovir is available in two oral prodrug forms: tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF). Both are converted to the pharmacologically active form, tenofovir diphosphate, intracellularly. It forms the mainstay of triple regimen in patients with HBV coinfection owing to its established efficacy against HBV. Of the two forms of tenofovir, TDF is recommended as the drug for use with 3TC in most instances, as it is more widely available as a FDC, and is generally well-tolerated. TDF should not be used if the estimated glomerular filtration rate (eGFR) is < 50 mL/min. TAF can be given down to a minimum eGFR of 30 mL/min. However, if given as a separate tablet, TAF can be given down to an eGFR of 15 mL/min, as well as to patients on chronic haemodialysis.

Dose

1.Adult

- Usual dose: 300 mg every 24 hourly to be taken with food
- Dose adjustment is required in case of renal impairment as follows:

Creatinine clearance	Dosage
≥50 mL/min	dose adjustment not necessary
30-49 mL/min	300mg every 48 hours
10-29 mL/min	300mg every 72-96 hours
Haemodialysis	300mg every 7 days or after a total of ≈12 hours of dialysis

2.Children

- Weighing > 35 kg, provide adult dose

Side Effects

The most common side effects associated with Tenofovir include nausea, vomiting, diarrhea, and asthenia. Less frequent side effects include hepatotoxicity, abdominal pain, peripheral neuropathy, myalgia and skin rashes. Hypophosphatemia is also common. Nephritis, nephrogenic diabetes insipidus, renal impairment, acute renal failure, and effects on the renal proximal tubules, including Fanconi syndrome is a concern. There have also been reports of raised liver enzymes, hepatitis, hypertriglyceridemia, hyperglycaemia and neutropenia.

Drug interactions

Drug	Interaction
Aspirin	increase nephrotoxic effects of tenofovir
Amphotericin B	increase nephrotoxic effects of tenofovir
Dabigatran	increases the concentration of dabigatran
Food	should be taken with food

Abacavir (ABC)

(Available as 300mg Tablet and 20mg/mL solution)

Abacavir is a nucleoside reverse transcriptase inhibitor used in combination with other medications as part of highly active antiretroviral therapy (HAART). Abacavir (ABC) does not require dose adjustment in renal failure and is especially useful in patients with chronic renal failure, in whom tenofovir is nephrotoxic and zidovudine (AZT) could aggravate the anemia of renal failure.

Dose

1. **Adults**:
   - Usual dose: 300 mg every 12 hourly; 600 mg every 24 hours.
   - Dose adjustment is required with hepatic impairment as follows:
     - Mild (Child-Pugh score 5 or 6): 200mg every 12 ho

2. **Children:**
   - ≥ 3 months: 8 mg/kg every 12 hourly

Weight band	Dosage
3 - <6kgs	60 mg every 12 hours
6 - <10kgs	80mg every 12 hours
10 - <14kgs	120mg every 12 hours
14 - <20kgs	150 mg every 12 hours
≥20 - <25kgs	150mg AM and 300mg PM
≥25kgs	300 mg every 12 hours

Side Effects
Common side effects include: nausea and vomiting, headache, diarrhea, reduced appetite, fever and chills, ear, nose or throat infections.

Serious side effects include: severe upper stomach pain, nausea, vomiting, loss of appetite; dark urine, clay-coloured stools, or jaundice, lactic acidosis, increased risk of cardiovascular disease.

Note: *Should only be prescribed if HLA B*5701 negative to reduce risk of hypersensitivity (5% incidence in unscreened populations). Patients must NEVER be re-challenged if abacavir withdrawn due to suspected hypersensitivity. Rechallenge is not recommended.*

Drug interaction

Drug	Interaction
Ganciclovir/valganciclovir	Increased risk of hematologic toxicity
Ribavirin	increase toxicity of abacavir, increased risk of lactic acidosis
Alcohol	increases the concentration of abacavir
Rifampicin	may reduce the concentration of abacavir
Food	Can be taken with or without food

2. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) work by binding irreversibly to HIV's reverse transcriptase enzyme, which causes a conformational change in the enzyme's active site and impairs its functioning. The two NNRTIs currently available in Bhutan i.e., efavirenz (EFV) and nevirapine (NVP). Although the prevalence of NNRTI resistance is higher than PI resistance in antiretroviral naïve patients, it has been reported that patients receiving NNRTIs show a higher rate of adherence than patients receiving PIs. The simple dosing and the overall good tolerability are some of the advantages.

Nevirapine (NVP)
(Available as 200mg tablets and 10 mg/mL syrup)
Nevirapine is one of the most commonly used NNRTI as a component of ART. It is also used for PMTCT.

Dose

1.Adult:

The 14-day lead-in period with nevirapine (200 mg once daily) must be strictly followed; it has been demonstrated to reduce the frequency of rash; then increased to 200 mg twice daily if there is no rash. If a rash is seen, the dose should not be increased until the rash resolves.

2.Child:

Neonates < 4 weeks of age:

Weight band	Dose
2 - < 3 kg	15mg every 12 hours
3 - < 4 kg	20mg every 12 hours
4 - < 5kg	25mg every 12 hours

Infants >4 weeks of age:

Weight band	Dose
3 - 5.9kg	50mg every 12 hours
6 - 9.9kg	80mg every 12 hours
10 - 13.9kg	100mg every 12 hours
14 - 19.9kg	130 mg every 12 hours
20 - 24.9kg	150 mg every 12 hours
>25kg	200mg every 12 hours/400mg every 24 hours

Side effects

The most common adverse reaction is rash. In adults the incidence of rash is 15% while in the pediatric patients the incidence of rash is about 21%.

Rashes usually occur within the first 6 weeks of starting therapy. Severe and life-threatening skin reactions including Stevens-Johnson syndrome and, more rarely, toxic epidermal necrolysis have been reported. Severe hepatotoxicity, including hepatitis and hepatic necrosis, has occurred and

may be more prevalent in women and patients with high CD4 cell counts at the start of treatment. Other common adverse effects include nausea, vomiting, diarrhea, abdominal pain, fatigue, drowsiness, and headache.

Drug Interactions

Drug	Interaction
Ketoconazole	Decreased concentration of ketoconazole
Oral contraception	Decreased effectiveness of OCPs
Rifampicin	Reduced concentration of nevirapine
Food	Can be taken with or without food

Caution

- *Severe, life-threatening, and in some cases fatal hepatotoxicity, particularly in the first 18 weeks, has been reported in patients treated with nevirapine.*
- *Severe, life-threatening skin reactions, including fatal cases, have occurred in patients treated with nevirapine.*
- *Patients must be monitored intensively during the first 18 weeks of therapy with nevirapine to detect potentially life-threatening hepatotoxicity or skin reactions.*
- *Therapy should be interrupted in patients who develop moderate to severe liver functions test results.*
- *Therapy should be reinstated with a 14 day once daily dosing when liver function returns to normal.*
- *If liver function worsens, nevirapine should be discontinued.*

Efavirenz (EFV)

(Available as 600mg tablets)

Efavirenz is used as an alternative to Nevirapine when Nevirapine is not tolerated or contraindicated and vice versa.

Dose

As capsules

- Adult and child 40 kg and over – 600 mg OD
- Children (based on body weight):

Body weight	Dosage
3.5 - <5kg	100 mg every 24 hours
5 - < 7.5kg	150 mg every 24 hours
7.5 - <15kg	200 mg every 24 hours
15 – <20kg	250 mg every 24 hours
20 – <25kg	300 mg every 24 hours
25 - <32.5kg	350 mg every 24 hours
32.5 – <40 kg	400 mg every 24 hours
≥40kg	600 mg every 24 hours

Dose should preferably be taken at bedtime to reduce occurrence of CNS side effects.

Side Effects

The most common adverse effects associated with efavirenz are skin rashes and CNS disturbances. CNS symptoms include dizziness, headache, insomnia or somnolence, impaired concentration, abnormal dreaming, and convulsions. Symptoms resembling psychoses and severe acute depression have also been reported. Other adverse effects include nausea and vomiting, diarrhea, fatigue, and pancreatitis. Raised liver enzyme values have been noted, particularly in patients with viral hepatitis. Raised serum-cholesterol and triglyceride concentrations have been reported.

Precautions

- Efavirenz is contraindicated in patients with previously demonstrated clinically significant hypersensitivity (e.g., Stevens-Johnson syndrome, erythema multiforme, or toxic skin eruptions).
- Efavirenz is contra-indicated in patients with severe hepatic impairment, and should be used with caution, and liver enzyme values monitored, in patients with mild to moderate liver disease.
- Caution should be exercised in patients with a history of seizures or psychiatric disorders.
- Monitoring of plasma-cholesterol concentrations may be considered during Efavirenz treatment.

Drug Interactions

Drug	Interaction
Amiodarone	Reduced effectiveness of amiodarone
Apixaban	Reduced clinical efficacy of apixaban
Atazanavir	Reduced exposure to atazanavir
Carbamazepine	Reduced clinical efficacy of carbamazepine
Chloroquine	Increased concentration of chloroquine
Food	Should be taken on an empty stomach

Note: *The absorption of a single dose of efavirenz increased when given with a high fat meal, relative to fasted conditions. This may lead to an increase in the frequency of adverse reactions.*

3. Protease Inhibitors (PIs)

They act by binding to the viral protease, in this way preventing the correct cleavage of viral proteins. Thus, they prevent HIV from being successfully assembled and released from the infected cells.

PI-based regimens using pharmacokinetic (PK) enhancement with RTV (also called PK boosting) increase concentration and prolong the half-lives of the PI. These regimens have demonstrated virologic potency, durability in treatment-naive patients, and a high barrier to resistance. All PIs require PK boosting with RTV to inhibit the CYP3A4 isoenzyme, which may lead to significant drug-drug interactions. This useful interaction between ritonavir and the other PIs simplifies daily regimens by reducing the frequency and number of pills to be taken every day, in many cases independent of food intake.

All PIs may be associated with cardiac conduction abnormalities (especially PR interval prolongation). This seldom results in clinically significant effects, but caution should be taken when co-prescribing other drugs that cause delayed cardiac conduction, such as macrolides. All PIs are, to some degree, associated with metabolic side-effects. Elevated triglycerides (TG) and elevated low-density lipoprotein cholesterol (LDL-C) are class effects, although these side-effects are more marked with LPV/r than with other PI combinations.

Lopinavir/Ritonavir (LPV/r)

(Available as 200/50mg tablets or (80mg+20mg)/mL oral solution)

LPV/r is a co-formulation of Lopinavir and Ritonavir, in which ritonavir acts as a pharmacokinetic booster.

Dose

- Adults: Lopinavir 400/ ritonavir 100 mg every 12 hours
- Children (based on the weight):

Body weight	Dosage
7 - <15kg	12mg/kg/dose every 12 hours based on lopinavir content
15 – <40kg	10mg/kg/dose every 12 hours based on lopinavir content
>40kg	Same as adults

Side Effects

Diarrhea in 15-25% nausea and abdominal pain, class side effects: insulin resistance, fat accumulation and hyperlipidemia, elevated transaminases.

Drug Interactions

Drug interactions with PIs are numerous and difficult to predict. Ritonavir is the most potent inhibitor of liver enzymes and is most likely to reduce hepatic metabolism.

Drug	Interaction	Remarks
Atorvastatin	Concentration of atorvastatin increased	use the lowest possible dose of 10mg/day
Clarithromycin	Concentration of clarithromycin increased	reduce dose of clarithromycin by 50%
Rifampicin	Concentration of Lopinavir decreased	Contraindicated
OCP	Concentration of OCP decreased	Use alternative contraception
Carbamazepine	Concentration of lopinavir decreased	Use alternative anticonvulsant
Food	Can be taken with or without food	

4. Integrase inhibitors (InSTI)

Integrase inhibitors are a class of antiretroviral drug designed to block the action of integrase, a viral enzyme that inserts the viral genome into the DNA of the host cell. Since integration is a vital step in retroviral replication, blocking it can halt further spread of the virus.

Dolutegravir (DTG)
(Available as 50mg tablets for adults, 10mg tablets for children)
Dose

- Adults:
    - 50mg every 24 hourly after meals

- Children (based on body weight):

Body weight	Dosage
3 - <6kg (younger than 6 months)	5mg every 24 hours
3 - <6kg (6 months or older)	10mg every 24 hours
6kg - <10kg	15mg every 24 hours
10kg - <14kg	20mg every 24 hours
14kg - <20kg	25mg every 24 hours
≥20kg	50mg every 24 hours

Side Effects
Weight gain, sleep disorders, increased cholesterol and triglycerides.

Drug Interactions

Drug	Interaction	Remarks
Rifampicin	Concentration of dolutegravir decreased	Increase DTG dose to 50mg 12 hourly
Metformin	Concentration of Metformin increased	Maximum metformin dose 500 mg 12 hourly
Antiepileptics e.g. carbamazepine, phenytoin, phenobarbitone	Concentration of DTG decreased	Avoid coadministration if possible. Alternative agents that do not interact with DTG include valproate, lamotrigine, levetiracetam, and topiramate. Remember that valproate is contra-indicated during pregnancy. Double DTG dose to 50 mg 12-hourly for carbamazepine, phenytoin, or phenobarbital if an alternative anticonvulsant cannot be used
Polyvalent cations (Mg^{2+}, Fe^{2+}, Ca^{2+}, Al^{3+}, Zn^{2+}) e.g. antacids, sucralfate, multivitamin and nutritional supplements	Concentration of DTG decreased	Calcium supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and calcium supplements can be taken at the same time if taken with food. It is safe to dissolve the DTG dispersible tablets in breast milk. Iron supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and iron supplements can be taken at the same time if taken with food. However, calcium and iron supplements must be taken at least 4 hours apart. Magnesium/aluminum containing antacids decrease DTG concentrations regardless of food intake and should be taken a minimum of 2 hours after or 6 hours before DTG
Food	Can be taken with or without food	

DRUGS FOR OPPORTUNISTIC INFECTIONS

Some of the drugs for the treatment of Opportunistic infections are not available on the Essential Drugs List. They are usually procured on Named Patient Basis (*Form II signed by the treating Specialist*) by the Pharmacy Department of the JDWNRH and delivered to the patients or the health centers wherever required. The drugs are expensive therefore they should be ordered only for use for the indication(s) as specified in this guideline.

Amphotericin B

(Powder for injection: 50mg vial)

Indications:

- *Esophageal and oral candidiasis resistant to azole derivative.*
- *Cryptococcal meningitis.*
- *Histoplasmosis and coccidioidomycosis.*
- *Aspergillosis and penicilliosis.*

Dose

- Esophageal and oral candidiasis: 0.5- 1mg/kg/day until symptoms resolve.
- Histoplasmosis and coccidioidomycosis: 0.5-1mg/kg/ day for at least 6 weeks.
- Penicilliosis: 0.6 - 1mg/kg/day for 7-14 days or until there is clinical resolution.

Side Effects

Common adverse effects which occur during or following intravenous infusion of amphotericin B include headache, nausea, vomiting, chills, fever, malaise, muscle and joint pains, anorexia, diarrhea, and gastrointestinal cramp. Hypertension, hypotension, cardiac arrhythmias including ventricular fibrillation and cardiac arrest, skin rashes, flushing, anaphylactoid reactions including bronchospasm and dyspnoea, blurred vision, tinnitus, hearing loss, vertigo, gastrointestinal bleeding, liver disorders, peripheral neuropathy, and convulsions have been reported occasionally. Partial reversible deterioration of renal function, progressive normochromic anemia and thrombocytopenia are less common.

Precautions: Concomitant administration of another nephrotoxic drug should be avoided.

Azithromycin

(Capsule:250mg, Powder for Oral Suspension: 200mg/ml)

Indications:

Treatment and prophylaxis of Mycobacterium avium complex (MAC) infection

Dose

• Treatment of MAC infection; 500mg once daily until the symptoms resolve
• Prophylaxis: 1.2g once a week indefinitely
• To be taken on an empty stomach one hour before food or two hours after.

Side Effects

Gastrointestinal disturbances such as abdominal discomfort and cramp, nausea, vomiting, and diarrhea are common but not as severe as erythromycin. Severe hypersensitivity reactions and photosensitivity occur rarely. Transient reductions in neutrophil counts have been seen in patients receiving azithromycin. Pain and inflammation may occur at the site of intravenous infusions.

Fluconazole

(150mg tablet)

Indications:

- Treatment and prophylaxis of cryptococcal meningitis: Following treatment with amphotericin B either for two weeks or until the condition improves fluconazole 800 mg oral or intravenous for 2 weeks followed by 400 mg once a day for 8 weeks and then reduced to 200 mg OD
- Treatment of oesophageal and resistant oropharyngeal candidiasis: 200mg initial loading dose followed by 100mg once a day until the symptoms resolve
- Vaginal candidiasis: 150mg stat
- Treatment and maintenance of coccidioidomycosis: 400mg orally in patients not tolerating amphotericin B

Side Effect

Gastrointestinal tract side effects such as abdominal pain, diarrhea, flatulence, nausea and vomiting, and taste disturbance are common. Other adverse effects include headache, dizziness, leucopenia, thrombocytopenia, hyperlipidemias, and raised liver enzyme values. Serious hepatotoxicity has been reported in patients with severe underlying disease such as AIDS or malignancy.
Drug Interactions Dose should be increased by half if co-administered with Rifampicin.

Ganciclovir

(Capsule 250mg, Powder for injection 500mg/vial)

Indications:

Treatment of cytomegalovirus end organ disease: 5mg/kg by slow IV infusion twice a day for two to three weeks or until the symptoms resolve.
Treatment and maintenance of CMV retinitis: 5mg/kg by slow IV infusion twice a day for two to three weeks followed by maintenance dose of 5mg/kg once a day.

Side Effects

The most common adverse effects of intravenous Ganciclovir are hematological and include neutropenia and thrombocytopenia; anemia also occurs. Other adverse effects occurring in patients given intravenous Ganciclovir include fever, rash, and abnormal liver function tests. Irritation or phlebitis may occur at the site of injection due to the high pH.

Table 11: Monitoring the toxicities associated with the antiretroviral agents available in Bhutan

ART Agent	Adverse Drug Reactions	Risk factors	Management
NRTIs			
ABC	ABC hypersensitivity reaction	Unknown	• Discontinue ABC and do not restart. • Give symptomatic treatment. • Re-exposure may lead to a severe and potentially life-threatening reaction
AZT	Anemia, neutropenia	• CD4 count < 200 cells/mm3; • Baseline anemia, neutropenia; • concurrent use of other drugs with similar ADR (cotrimoxazole, ganciclovir)	Substitute TDF or ABC Consider using low-dose AZT
	Lactic acidosis	• BMI>25(or body weight >75kg) • Prolonged exposure to NRTIs	• Discontinue ART and give supportive treatment. • After clinical resolution, resume ART, replacing the offending NRTI. • ABC, TDF and 3TC are less likely to cause this type of toxicity.

	Lipodystrophy	Low CD4 count	Substitute TDF or ABC
TDF	Chronic kidney disease Acute kidney injury and Fanconi syndrome	• Underlying renal disease; • age > 60 years; • BMI < 18.5 (or body weight < 50 kg); • Untreated diabetes; • untreated hypertension; • concomitant PI use or nephrotoxic drug	Discontinue TDF and give supportive treatment. After clinical resolution, resume ART, replacing the offending drug with another (AZT, ABC or TAF).
	Decreases in bone mineral density	History of osteomalacia (adults) and rickets (children) and pathological fracture Risk factors for osteoporosis or bone mineral density loss Vitamin D deficiency	
	Lactic acidosis or severe hepatomegaly with steatosis	Prolonged exposure to nucleoside analogues Obesity Liver disease	
NNRTIs			
NVP	Drug eruptions (mild to severe, including Stevens–Johnson syndrome or toxic epidermal necrolysis)	unknown	In mild cases, give antihistamines. Moderate rash, non-progressive and without mucosal involvement or systemic signs, consider a single NNRTI substitution (i.e. NVP with EFV). In moderate and severe cases, discontinue ART and give

	NVP>>EFV		supportive treatment. After resolution, resume ART with 3 NRTI or 2 NRTI + PI regimens
	Hepatotoxicity	More common if there is coinfection with hepatitis B or C	If ALT >5-fold from the baseline, discontinue ART and monitor. After resolution, replace the drug most likely to be associated with another one
EFV	CNS side effects	Pre-existing psychiatric disorder	For CNS symptoms, dosing at bedtime. EFV 400 mg/day is recommended or an INSTI (DTG) if EFV 400 mg is not effective at reducing symptoms
	Convulsions	History of seizure	
	Gynaecomastia	unknown	Switch from EFV to an alternative, and consult if gynecomastia does not improve
	Hepatotoxicity	Underlying hepatic disease Coinfection with hepatitis B or C Concomitant use of hepatotoxic drugs	For severe hepatotoxicity or hypersensitivity reactions, substitute another therapeutic class (INSTIs or boosted PIs)
PIs			
All PIs boosted with RTV	GI intolerance (LPV/r>DRV/r>ATV/r)	Unknown	Usually self-limited, no need to discontinue ART. Symptomatic treatment should be offered
	Dyslipidemia (LPV/r>DRV/r>ATV/r	Obesity; sedentary lifestyle; diet high in saturated fats and cholesterol	Consider replacing the suspected PI by drugs with a lower risk of metabolic toxicity
	ECG abnormalities	People with pre-existing conduction system disease	If LPV/r is used in the second line ART for adults, use ATV/r, DRV/r.

LPV/r	Hepatotoxicity	Underlying HBV and HCV coinfection, concomitant use of hepatotoxic drugs	Seek expert advice
INSTIs			
DTG	Insomnia, weight gain or obesity	Older than 60 years Low CD4 or high viral load Female African ethnicity Concomitant use of TAF	Consider morning dose or substitute EFV, 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
	Hepatotoxicity Hypersensitivity reactions	Coinfection with hepatitis B or C Liver disease	Substitute another therapeutic class: EFV or boosted PIs

CHAPTER V

PREVENTION OF MOTHER-TO-CHILD TRANSMISSION

Key points

- All HIV positive pregnant women should be started on ART irrespective of CD4 count.
- For TPT (TB prevention treatment) in pregnancy, Isoniazid 300 mg once daily for 6 months (6H) is recommended.

Rationale for PMTCT

The estimated number of perinatally acquired AIDS cases in the world had decreased dramatically over the last two decades. This is predominantly due to the implementation of prenatal HIV testing with antiviral therapy given to the pregnant woman and then to her neonate. A critical component of preventing perinatal HIV transmission is ensuring that a pregnant person with HIV receives ART that sustainably suppresses viral replication to an undetectable level as early as possible during pregnancy or, ideally, before conception.

However, more than 90% of the world's 2.5 million children living with HIV/AIDS were infected through MTCT. Without interventions, the rate of transmission is 25-45% in the developing countries. Combination of early diagnosis, effective ART, safer obstetric practice and no breast feeding, counseling and support can reduce the risk to less than 2%.

Table 12: Factors that can potentially increase the risk for MTCT at different stages of pregnancy.

Pregnancy/ postpartum stage	Factors	Risk of transmission*
Pregnancy	• High maternal viral load • Viral, Bacterial, or placental infection (e.g. Malaria) • Sexually transmitted infections (STIs) • Maternal malnutrition	5-10%
Labor & Delivery	• High Maternal viral load • Rupture of membranes more than 4 hours before labor begins • Invasive delivery procedures that increase contact with mother's infected blood or fetal scalp monitoring • Chorioamnionitis (from untreated STI or other infection)	10-20%
Breastfeeding	• High Maternal viral load (new or advanced HIV/AIDS) • Longer duration of breastfeeding. • Early mixed feeding (e.g. food or fluids in addition to breast milk) • Breast abscesses, nipple fissures, mastitis. • Poor maternal nutritional status • Oral disease in the baby (e.g. Thrush or sores)	10-20%

*Risks without any intervention

Effect of pregnancy on HIV-disease progression

All studies so far have not shown pregnancy to have any effect on the progression of HIV disease. Even repeated pregnancy does not have a significant effect on the clinical or immunological course of HIV viral infection.

Effect of HIV on pregnancy outcomes

Although maternal morbidity and mortality rates are not increased in sero-positive asymptomatic women. However, reported adverse fetal outcomes including preterm delivery, fetal growth restriction, and stillbirth were seen as more common among HIV-infected women compared with non-HIV infected women.

There are no studies that indicate an increase in the frequency of birth defects related to HIV infection. HIV is not an indication for termination of pregnancy.

Diagnosis/Testing

- All pregnant women attending ANC should be offered HIV testing and counseling preferably in the first trimester of pregnancy and if missed should be offered during the subsequent visits.
- Women who had not attended any ANC should be screened for HIV during labor or immediately after birth.
- ANC diagnosis of HIV should be linked with routine MCH service and with involvement of focal persons in each Hospital.
- Repeat HIV testing should be done in the third trimester preferably at 36 weeks.

Care during the antenatal period

- All pregnant women should have routine ANC care.
- Antenatal HIV care should be delivered by a multidisciplinary team.
- Screen for Tuberculosis.
- Rule out opportunistic infections.

Antiretroviral Therapy

- All HIV positive pregnant women should be started on ART irrespective of CD4 count. TDF+3TC+DTG is recommended as first-line ART (as in the general adult population).
- Women taking dolutegravir who are trying to conceive or in the first trimester of pregnancy should be recommended to take folic acid 5 mg once daily to reduce the risk of neural tube defect:
- Newly diagnosed, or known HIV positive women not on ART or on ART with HIV RNA >1,000 copies/mL at time of delivery:
    - If in labor, dosage: ZDV infusion at 2 mg/kg loading dose for 1 hour, followed by ZDV infusion 1 mg/kg for 2 hours until cord clamping.
    - In those who are undergoing a scheduled cesarean delivery, IV ZDV administration should begin at least 3 hours before the scheduled cesarean delivery. Dosage: 1-hour loading dose of ZDV at 2 mg/kg followed by a continuous IV ZDV infusion of 1 mg/kg for 2 hours.
    - If IV ZDV is not available, give a stat single fixed dose combination tablet of TDF, 3TC and DTG (TLD) and a stat single dose of NVP 200 mg >2 hours prior to delivery (Since NVP is not available through global fund, indent 1-2 doses in advance on from II basis).
    - For TPT in pregnancy, Isoniazid 300 mg once daily for 6 months (6H) is recommended, as 3 HR has not been studied in pregnant women. Testing for latent TB infection is not a prerequisite for initiating TPT.
    - Prophylaxis for opportunistic infection in HIV- ***refer chapter 12 on opportunistic infection.***

Monitoring

- CBC, RFT, LFT At booking and at 24-28 weeks or as when clinically indicated.
- Baseline Viral load:
    - At ANC booking
    - Thereafter 3 monthly. Increasing viral load on ART may need resistance testing
    - Baseline CD4 at ANC booking and thereafter every 3 months.

Management of Labor and delivery

Mode of delivery

- A decision regarding recommended mode of delivery should be made after review of plasma viral load results at 36 weeks.

- For women on ART with a viral load of <50 HIV RNA copies/mL at 36 weeks gestation, planned vaginal delivery should be supported. Cesarean deliveries for these women will be done for obstetrics indications only.

- In people with HIV RNA levels ≤ 50 copies/mL, if scheduled cesarean delivery or induction is indicated, it should be performed at the standard time for obstetric indications as per the OBGYN department protocol.

- In women with viral load more than 50 copies /ml prior to 38 weeks gestation shall be offered elective cesarean section before the onset of labor or rupture membrane at 38 completed weeks.

- In women with unknown plasma Viral Load, elective cesarean section will be offered at 38 completed weeks.
- All HIV positive mothers coming in labor and ruptured membranes can be allowed for vaginal delivery (Evidence is insufficient to determine whether cesarean delivery reduces the risk of perinatal HIV transmission for people who present in spontaneous labor or with ruptured membranes).
- The prescribed ART should be continued during labor or before scheduled cesarean delivery.

During vaginal delivery the following precautions should be done:

a. Avoid episiotomy as far as possible.
b. Reduce the number of internal examinations
c. Not to use fetal scalps monitoring.
d. Avoid prolonged labor.
e. Avoid instrumental delivery as far as possible.

Immediate newborn care consists of the following:

- Wipe the infant's mouth, eyes and nostrils with gauze when the head is delivered.
- Clamp cord immediately after birth, and avoid milking the cord. Cover the cord with a gloved hand or gauze before cutting.
- Use gentle suction only when meconium-stained liquid is present. Use either mechanical suction or bulb suction.
- All babies should be given a warm water bath with mild soap wearing protective gloves. Once the initial bath is given, then no need to wear gloves for handling the baby.
- Immunization at birth should be like at any other routine one including Vitamin K.

Infant prophylaxis

If available, the NAAT (nucleic acid amplification test) at birth (0–2 days) should be considered for early infant diagnosis. ***The detailed Infant diagnostic algorithm is covered in the pediatric chapter 6 and Algorithm figure 5.***

Neonates should be started on ART as soon as possible, ideally within the first 6-12 hours of delivery according to risk classification.

Table 13. Neonatal antiretroviral management according to risk of HIV infection in newborn

Level of Perinatal HIV Transmission Risk	Description	Neonatal ARV Management
Low Risk of Perinatal HIV Transmission	Mothers who received ART during pregnancy with sustained viral load ≤1000 copies per ml. OR	Four to six weeks of
	If viral load is not available but mother has received ART for four weeks or more prior to delivery.	prophylaxis with NVP 2 mg/kg once daily
Higher Risk of Perinatal HIV Transmission	Mothers who have not received ART or have received less than four weeks of ART at the time of delivery. OR	Dual prophylaxis with daily AZT and NVP for 6 weeks.
	With viral load >1000 copies/mL in the four	
	weeks before delivery. OR	
	Intrapartum or postpartum diagnosis of HIV.	
Newborn with HIV	Positive newborn HIV virologic test/NAT	Three-drug ARV regimen using treatment dose.

Table 14. Antiretroviral drug dosing for newborns

<table>
<tr><th>Drug</th><th colspan="2">Drug Doses by Gestational Age at Birth</th></tr>
<tr><td rowspan="9">ZDV</td><td colspan="2">≥35 Weeks Gestation at Birth to Age 4 Weeks:
• ZDV 4 mg/kg per dose orally twice daily
Age >4 Weeks:
• ZDV 12 mg/kg per dose orally twice daily;
only make this dose increase for infants with confirmed HIV infection</td></tr>
<tr><td colspan="2">Simplified Weight-Band Dosing for Newborns:
Aged ≥35 Weeks Gestation from Birth to 4 Weeks</td></tr>
<tr><td>Weight Band Volume of ZDV 10 mg/mL Oral Syrup Twice Daily</td><td>Weight Band Volume of ZDV 10 mg/mL Oral Syrup Twice Daily</td></tr>
<tr><td>2 to <3 kg</td><td>1 ml</td></tr>
<tr><td>3 to <4 kg</td><td>1.5 ml</td></tr>
<tr><td>4 to <5 kg</td><td>2 ml</td></tr>
<tr><td colspan="2">≥30 to <35 weeks Gestation at birth
Birth to age 2 weeks:
● ZDV 2 mg/kg per dose orally twice daily

Age 2 weeks to 6 weeks:
● ZDV 3 mg/kg per dose orally twice daily

Age >6 to 8 weeks:
● ZDV 12 mg/kg per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.</td></tr>
<tr><td colspan="2"><30 weeks gestation at birth
Birth to age 4 weeks:
● ZDV 2 mg/kg per dose orally twice daily

Age 4 to 8-10 weeks:
● ZDV 3 mg/kg per dose orally twice daily

Age >6 to 10 weeks:
ZDV 12 mg/kg per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.</td></tr>
</table>

3TC	≥32 Weeks Gestation at Birth Birth to Age 4 Weeks: • 3TC 2 mg/kg per dose orally twice daily Age >4 Weeks: • 3TC 4 mg/kg per dose orally twice daily
NPV	***≥37 Weeks Gestation at Birth*** Birth to Age 4 Weeks: • NVP 6 mg/kg per dose orally twice daily Age >4 Weeks: • NVP 200 mg/m2 of BSA per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.
	≥34 to<37 weeks gestation at birth Birth to Age 1 Week: • NVP 4 mg/kg per dose orally twice daily Age 1 to 4 Weeks: • NVP 6 mg/kg per dose orally twice daily Age >4 Weeks: • NVP 200 mg/m2 of BSA per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.
	≥32 to<34 weeks gestation at birth Birth to Age 2 weeks ● NVP 2 mg/kg per dose orally twice a day Age 2 to 4 Weeks ● NVP 4 mg/kg per dose orally twice a day Age 4 to 6 Weeks ● NVP 6 mg/kg per dose orally twice a day Age > 6 Weeks ● NVP 200 mg/m^2 BSA per dose orally twice daily; only make this dose increase for infants with confirmed HIV infection.

Feeding of the baby

- Breastfeeding is not recommended.
- The government supports supplementary feeding for two years for every baby after birth.
- The concerned focal person in each hospital should facilitate the procurement and supply of the infant formula for every baby.

Postpartum care

- Immediate postpartum care should be like routine care.
- Give breast milk suppression to the mother as follows:
  - Tab pyridoxine 100mg-once a day for 5 days.
  - Advice mothers to use firm bras for breast support.
  - Use Paracetamol for analgesia.
- Subsequent postnatal visits should be routine.
- educate the mothers to dispose of body secretions and fluids properly.
- All mothers on ART should continue for the same medication for life long. After six weeks they should be followed up in the CST(care and support) unit.

Sexual and Reproductive Health

- The use of appropriate contraceptive options to prevent unintended pregnancy and optimal interpregnancy intervals should also be discussed.
- Support the mother's choice of contraceptive method.
- HPV screening should begin at 25 years of age and if screening was not done in the past, it should be done at 6 weeks postpartum. If the initial HPV screening is negative, subsequent screening should be done every three years.
- If the person has not received HPV vaccination in the past, HPV vaccination should be given with 3 doses at 0,2 and 6 months.

CHAPTER VI

PEDIATRIC HIV/AIDS MANAGEMENT

Key Points

- HIV is diagnosed in infants and children under the age of 18 months using nucleic acid testing (NAAT) Refer to EID algorithm.
- DTG based HIV treatment is the preferred 1st line ART for children living with HIV weighing >3 kg and at least 4 weeks of age.
- Neonates should be started on ART as soon as possible, ideally within the first 6 - 12 hours of delivery according to risk classification (Refer to Table 13)
- For neonates with HIV, BCG vaccination should be delayed until ART has been started.
- In TB-HIV co-infection in children, early initiation of ART, within 2 weeks of TB drugs is recommended except for TB meningitis where ART should be deferred for a minimum of 4 weeks.
- All children born to HIV-infected mothers should receive Co-trimoxazole prophylaxis starting at 6 weeks after birth till HIV infection has been excluded by age appropriate HIV test.

Introduction

In the absence of any interventions, about a third of children born to HIV infected mothers will be born with HIV or infected through breastfeeding. Children born with HIV have very high mortality. They are over four times more likely to die by the age of two than children born without HIV. The clinical manifestations of HIV infection in children are different from those in adults. The immune system of young children, who are infected perinatally, is immature and hence dissemination throughout the various organs may occur very early. Organs such as the brain may be susceptible to the effects of the virus in a manner different from the ones observed in adults. Even the pattern of opportunistic infections in children is different from those in adults. Children tend to suffer from primary infection while adults are more likely to suffer from reactivation of infection as their immunity wanes in response to advanced HIV-infection. Therefore, it is important to start treatment and management of infants with HIV as early as possible.

Key differences between adults and children

- Young children have immature immune systems, and if HIV-infected, are particularly susceptible to common childhood and opportunistic infections. They may experience a rapid progression of HIV disease if treatment is delayed.
- Maternal HIV antibodies can be passed to the child and last for up to 18 months, so HIV antibody testing does not reliably indicate HIV infection in children under 18 months of age. Positive HIV antibody testing in this time period can indicate exposure to HIV or HIV infection in the child and, where possible, should be followed up with a viral test.
- Children are at risk of acquiring HIV by breastfeeding from HIV-infected mothers. Negative HIV antibody testing in a child who stopped breastfeeding at least 6 weeks prior to the test usually indicates the child is not HIV-infected.
- In young children normal CD4 counts are higher, age-dependent, and more variable than in adults. For children under 5 years of age, it is best to use %CD4 rather than absolute count.
- ART drugs are handled differently in children's bodies, affecting the doses that are needed. ART medicine dosages must be adjusted as the child grows.
- It can be challenging to communicate effectively with children about their HIV status, about the care they need, and to support their adherence to ART. As children grow, the counseling they receive must evolve as well.

Diagnosis of HIV-infection in children

Tests for antibodies do not establish the presence of HIV infection in infants because of transplacental transfer of maternal HIV antibodies. These transferred maternal HIV antibodies can persist for as long as 18 months in children born to HIV-infected mothers. Therefore, all HIV exposed neonates, and all infants with unknown or uncertain HIV status, should have a NAAT test performed immediately and at 4-6 weeks of age or at the earliest opportunity thereafter. All infants with an initial positive NAAT test should be started on ART without delay and a second specimen should be collected to confirm the initial positive test result.

Although HIV antibody tests can be reliably used only after 18 months in a child to diagnose HIV, it can however be useful to exclude HIV infection in children. A negative HIV antibody test in a known HIV-exposed infant can be used for excluding HIV infection if there is no ongoing exposure. However, a child is suspected to have HIV infection if the child exhibits any clinical features as described in WHO clinical staging NAAT test will be done immediately and at 4 weeks. If these tests are not available, then HIV antibody testing is 9 months and 18 months of age.

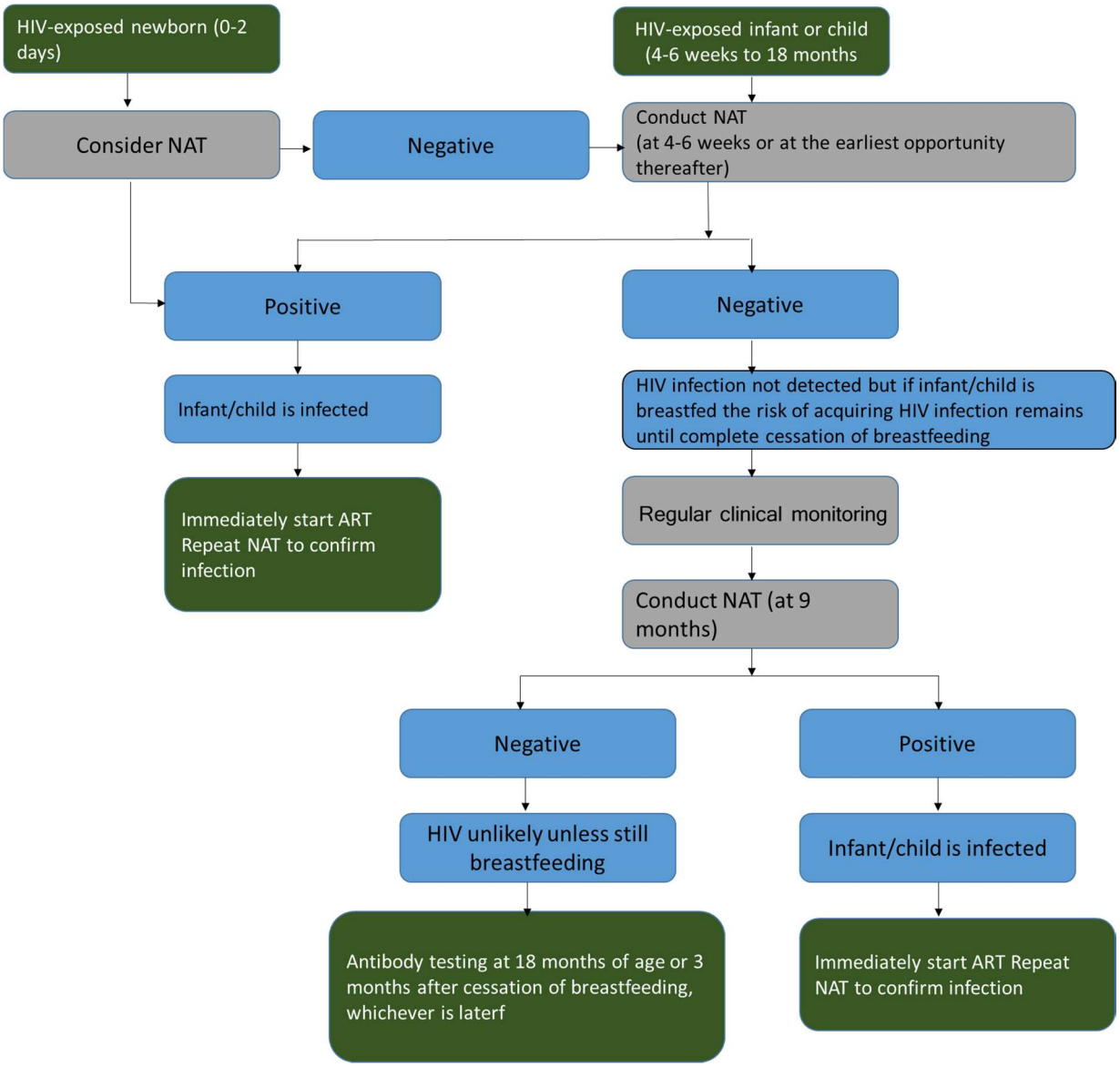

Figure 6: Flow chart showing infant diagnosis algorithm

Note:

- *Start ART without delay. At the same time, retest to confirm infection.*
- *As maternal treatment is scaled up and MTCT transmission rates decrease, false-positive results are expected to increase: retesting after a first positive NAT is hence important to avoid unnecessary treatment, particularly in settings with lower transmission rates.*
- *If the second test is negative, a third NAT should be performed before interrupting ART.*
- *For children who were never breastfed, additional testing following a negative NAT at 4–6 weeks is included in this algorithm to account for potential false-negative NAT results.*

Presumptive Diagnosis if EID is unavailable

If the child is <18 months and have symptoms and signs that are suggestive of HIV infection and there is no virologic testing available, it is possible to make a presumptive diagnosis by addressing the following issues:

A presumptive diagnosis of severe HIV disease should be made if:
The infant is confirmed HIV antibody positive; and
Diagnosis of any AIDS-indicator condition (s) can be made; or
The infant is symptomatic with two or more of the following:

- Oral thrush
- Severe pneumonia;
- Severe sepsis.

Other factors that support the diagnosis of severe HIV disease in an HIV sero-positive infant include: Recent HIV-related maternal death; or advanced HIV disease in the mother;

Signs or conditions that may indicate possible HIV infection:

HIV's clinical expression in children is highly variable. Many HIV-infected children develop severe HIV-related signs and symptoms in the first year of life. Other HIV-infected children remain asymptomatic or mildly symptomatic for more than a year and may survive for several years (rapid and slow progressors respectively)

Suspect HIV if any of the following symptoms, signs, and/or clinical events are present, as they are not common in children without HIV.

Recurrent infection: three or more severe episodes of a bacterial infection (such as pneumonia, meningitis, sepsis, cellulitis) in the past 12 months.

Oral candidiasis: After the neonatal period the presence of oral thrush is highly suggestive of HIV infection when it is occurring when there has been no antibiotic treatment, lasting over 30 days despite treatment, recurring, extending beyond the tongue, or presenting as oesophageal candidiasis.'

Chronic parotitis: unilateral or bilateral parotid swelling for >14 days, with or without associated pain or fever.

Generalized lymphadenopathy: enlarged lymph nodes in two or more extra-inguinal regions without any apparent underlying cause.

Hepatomegaly with no apparent cause: in the absence of concurrent viral infections such as cytomegalovirus (CMV).

Persistent and/or recurrent fever: fever (>38°C) lasting >7 days, or occurring more than once over a period of 7 days.

Neurological dysfunction: progressive neurological impairment, microcephaly, delay in achieving developmental milestones, hypertonia, or mental confusion.

Herpes zoster (shingles): painful rash with blisters confined to one dermatome on one side.

HIV dermatitis: erythematous papular rash. Typical skin rashes include extensive fungal infections of the skin, nails and scalp, and extensive molluscum contagiosum.

Chronic suppurative lung disease.

Signs or conditions very specific to HIV-infected children: Strongly suspect HIV-infection if the following conditions, which are very specific to HIV, are present: pneumocystis pneumonia (PCP), esophageal candidiasis, lymphoid interstitial pneumonia (LIP), and in girls, acquired recto-vaginal fistula.

Moderate or severe malnutrition: weight loss or a gradual but steady deterioration in weight gain from expected growth, as indicated on the child's growth card. Suspect HIV particularly in breastfed infants <6 months old who fail to thrive

Antiretroviral Therapy

When to start:
ART should be initiated immediately in all children infected with HIV, regardless of WHO clinical stage or at any CD4 cell count or percentage.

Table 15. Preferred and alternative first-line antiretroviral therapy regimens

Population	Preferred first-line regimen	Alternative first-line regimen
Children	ABC 60 mg + 3TC 30mg + DTG 5mg (FDC) For children weighing more than 6 kg and are at least 4 weeks old.	ABC + 3TC +NVP AZT + 3TC + NVP AZT + 3TC + LPV/r
Neonates	AZT+3TC+NVP For children weighing less than 6 kg and are less than 4 weeks old	

Note: *For dosage Refer Table 7. Dosage of Antiretroviral Agents in both adult and pediatric population (under Chapter II)*

Table 16. Preferred and alternative second-line antiretroviral therapy regimens

Population	Failing first-line regimen	Preferred second-line regimen	Alternative second-line regimen
Children and infants	ABC + 3TC + DTGa	ABC (or AZT) +3TC+ LPV/r	
	ABC + 3TC + NVP	ABC (or AZT) +3TC+DTG	
	ABC (or AZT) +3TC+EFV	ABC (or AZT)+3TC+DTG	AZT (or ABC) +3TC+LPV/r (or ATV/r)
	ABC (or AZT) +3TC+LPV/r	ABC+3TC+DTG	

Note: *For dosage Refer Table 7. Dosage of Antiretroviral Agents in both adult and pediatric population (Under Chapter II)*

WHO Pediatric Clinical Staging for HIV

In a child with diagnosed or highly suspected HIV infection, the clinical staging system helps to assess the degree of damage to the immune system, and to plan treatment and care options. The stages determine the likely prognosis of HIV and are a guide when to start, stop, or switch ARV therapy.

The clinical stages identify a progression sequence from least to most severe (number 1 through 4) - the higher clinical stage, the poorer the prognosis. For classification purposes, once a stage 3 clinical condition has occurred, the child's prognosis will likely remain in stage 3 and will not improve to stage 2, even once the original condition is resolved, or a new stage 2 clinical condition appears. Antiretroviral treatment with good adherence dramatically improves prognosis.

The clinical staging events can also be used to identify the response to ARV treatment if there is no easy or affordable access to viral load or CD4 testing.

CDC case definition: The CDC surveillance case definitions are used primarily for monitoring the HIV infection burden and planning for prevention and care in populations, **not** as the basis for clinical decisions in individual patients.

Table 17. CDC surveillance case definition HIV infection stage based on age-specific CD4+ T-lymphocyte count or CD4+ T-lymphocyte percentage of total lymphocytes

Stage	Age at time of CD4+ T-lymphocyte test*					
	<1 year		1 to 5 years		≥6 years	
	Cells/microL	Percent	Cells/microL	Percent	Cells/microL	Percent
0	NA	NA	NA	NA	NA	NA
1	≥1500	≥34	≥1000	≥30	≥500	≥26
2	750 to 1499	23 to 33	500 to 999	22 to 29	200 to 499	14 to 25
3 (AIDS)$^{\Delta}$	<750	<26	<500	<22	<200	<14
Unknown	NA	NA	NA	NA	NA	NA

OPPORTUNISTIC INFECTION IN CHILDREN

Table 18: Systemic manifestation of children with HIV

System	Manifestations
Neurological	• Loss of developmental milestone • Impaired growth or microcephaly
Cardiac	• Cardiomegaly • CCF • Cardiomyopathy • Cardiac Tamponade • Pericardial effusion • Conduction Disturbances and sudden death
Nephrology	• Proteinuria • Hematuria • Hypertension • RTA • Renal failure
Hematology	• Anemia • Thrombocytopenia • Neutropenia • Lymphopenia and Eosinophilia

Table 19: Diagnosis and Management

Opportunistic Infections	Clinical and lab manifestations	Diagnosis	Treatment
Pneumonia	Mild fever Hypoxia and degree of respiratory distress.	Chest X-ray	**For severe and very severe pneumonia:** ● Ampicillin or Crystalline Penicillin and Gentamicin as first line ● If this fails use ceftriaxone as 2nd line or Ciprofloxacin and Gentamicin. ● If bacterial pneumonia, response is fast within 3-5 days. Delayed responses only after 5-7 days would favor PCP.

Pneumocystis jiroveci pneumonia (PCP)	Dry cough, tachypnea, dyspnea, cyanosis	• Chest-X-ray: bilateral diffuse parenchymal infiltrates with "ground-glass" or reticulogranular appearance. • Associated with a high level of lactate dehydrogenase (LDH). • Microscopy of induced sputum by bronchoalveolar lavage (BAL): • GMS stain- stains cyst wall in brown or black • Wright stain: stains the trophozoites and intracystics porozoites in pale blue	• TMP/SMX 15-20 mg/kg/day of TMP in 3-4 divided doses for a 21-day course. • Steroids e.g. prednisolone can be used for severe acute PCP
Candidiasis	**Oral candidiasis:** Creamy white curd-like patches that can easily be scraped off with inflamed underlying mucosa. **Esophageal candidiasis:** 1. odynophagia, 2. dysphagia, and/or retrosternal pain.	**1. Oral candidiasis:** KOH preparation demonstrates budding yeast cells. **2. Esophageal candidiasis:** Barium swallow shows cobblestone appearance. **3. Endoscopy**: Small white raised plaques to elevated confluent plaques with hyperemia and extensive	**Oral candidiasis** • Clotrimazole oral 10 g or Nystatin 400,000 600,000 units 5 times daily 7–14 days. OR • Oral fluconazole 3-6 mg/kg once daily 7–14 days. **Esophageal candidiasis** • Oral fluconazole 3-6 mg/kg once daily 14–21 days.

Cryptococcosis	**1. Meningoencephalitis manifestation:** ● fever ● headache ● altered mental status, ● nuchal rigidity **2. Disseminated manifestation:** ● persistent fever with translucent umbilicated papules which may resemble molluscum	Elevated intracranial pressure and elevated CSF protein and mononuclear pleocytosis. India ink stains of CSF should show budding yeast. Cryptococcal antigen can be detected in CSF or serum by latex agglutination test. Wright stain of skin scraping shows budding yeast.	**1. Induction therapy:** Amphotericin B (0.7-1.5 mg/kg/day) plus flucytosine (25 mg/kg/dose four times daily) for 2 weeks. **2. Consolidation therapy:** Fluconazole 5–6 mg/kg/dose twice daily for 8 weeks. 3. **Maintenance therapy:** Fluconazole 3–6 mg/kg/day.

Herpes simplex	1. **HSV gingivostomatitis:** fever, irritability, superficial painful ulcers in the gingival, oral mucosa and perioral area. 2. **HSV encephalitis:** fever, alteration of consciousness, abnormal behavior.	HSV gingivostomatitis is diagnosed by clinical evaluation. HSV encephalitis is diagnosed by detection of HSV DNA in the CSF. HSV	**HSV gingivostomatitis**: Oral acyclovir 20 mg/kg/dose three times daily OR intravenous acyclovir 5-10mg/kg/dose three times daily for 7-14 days. **Disseminated HSV or encephalitis:** intravenous acyclovir 10mg/mg/dose or 500mg/m^2/dose three times daily for 21 days.
Herpes Zoster	1. **Primary varicella infection:** Generalized pruritic vesicular rash. 2. **Herpes zoster** Painful rash with fluid-filled blisters, dermato-maldistribution	Use clinical diagnosis. If clinical diagnosis is not clear then Giemsa staining (Tzanck preparation) of cell scrapings from lesions can be done, showing multinucleated giant cells suggestive of VZV (Note that this is also seen in HSV infection).	**Primary varicella infection:** intravenous acyclovir 10 mg/mg/dose or 500mg/m^2/dose three times daily for 7 days in children with moderate to **Severe immuno-suppression.** Oral formulation should be used only in a child with mild immunosuppression. **Herpes zoster:** Oral acyclovir 20 mg/kg/dose four times daily (max 800 mg/dose) for 7 days

Cytomegalovirus	**CMV retinitis:** Young HIV-infected children are frequently asymptomatic and discovered on routine examination. Older children present with floaters or loss of vision. **Extraocular CMV** disease: CMV colitis, CMV esophagitis, CMV pneumonitis, CMV hepatitis.	Diagnosis of CMV retinitis is based on clinical appearance with white and yellow retinal infiltrates and associated retinal hemorrhages. **Extraocular CMV disease:** recover of virus from tissues or histopathology demonstrates characteristic “owl’s eye” intranuclear inclusion bodies or positive staining with CMV monoclonal antibodies biopsy	Ganciclovir intravenous 5 mg/kg/dose twice daily for 14-21 days followed by lifelong maintenance therapy.

Mycobacterium **avium complex** **(MAC)**	Fever, night sweats, weight loss, fatigue, chronic diarrhea and abdominal pain. **Laboratory findings:** neutropenia, elevations in alkali alkaline phosphatase or lactate dehydrogenase.	**Definitive diagnosis: -** isolation of organism from blood or specimens from normally sterile sites. **Histology** macrophages-containing acid-fast bacilli is a suggestive finding	Treatment with at least 2 drugs: 1. Clarithromycin 7.5-15 mg/kg twice daily (max 500 mg/dose) plus, 2. Ethambutol 15-25 mg/kg/day once daily(max1g/dose). **Consider adding a third drug** e.g. Amikacin/ ciprofloxacin in severe cases. Duration of treatment: at least 12 months
Cryptosporidiosis	Subacute or chronic watery diarrhea often associated with cramps, nausea and vomiting	**Modified Kinyoun acid-fast stain of stool:** small oocyst (4–6 µm in diameter)	Effective ART is the only treatment that controls persistent cryptosporidiosis. Supportive care with hydration, correction of electrolyte abnormalities, and nutritional supplementation. Nitazoxanide is approved for treatment: ● Age 1-3 years: 100 mg twice daily ● Age 4–11 year:200 mg twice daily

Prognostic indicators

- In the underdeveloped countries the age at diagnosis and the type of clinical presentation are the only clinical factors related to prognosis.
- Infants who develop symptoms in the first year of life manifest the fastest progression of illness with the worst outcome.
- Similarly, the occurrence of opportunistic infections, progressive encephalopathy or hypogammaglobulinemia at any age often carries a poor prognosis.
- In contrast, generalized lymphadenopathy, hepatosplenomegaly, parotitisare associated with a more favorable outcome.
- ***Viral load*** is the most important prognostic marker of the risk of progression. But the availability and the cost are constraints. It is predicted that a favorable clinical outcome is most likely if virus replication is maximally suppressed before the immune system is irreversibly damaged.

Prophylaxis for HIV-infected Children

Cotrimoxazole Prophylaxis (CPT)

Table 20: Criteria for initiation and discontinuation of co-trimoxazole prophylaxis

Intervention	Indication to start	Indication to stop
Clotrimazole prophylaxis	1. **HIV exposed infants:** Co-trimoxazole prophylaxis starting at 6 weeks	• Until the risk of HIV transmission ends and HIV infection is excluded with age-appropriate test
	2. Children Less than 5 years and living with HIV: Initiate in all regardless of WHO clinical stage or CD_4 clinical stage 3 or 4) or CD4 cells count ≤350 cells/mm^3 **3. Children more than 5 years and living with HIV:** Initiate for everyone with severe or advanced HIV disease (WHO clinical stage 3 or 4) or CD4 cell count ≤350 cells/mm3	• In settings with high prevalence of malaria and/or severe bacterial infections: should be continued until adulthood. • In settings with low prevalence of both malaria and severe bacterial infections can be discontinued for those older than 5 years of age,who are clinically stable and or virally suppressed on ART for at least 6 months and with a CD4 count ≥350 cells/mm^3

Table 21: Dosing of Clotrimazole for prophylaxis

Weight / Age of child	Daily Dose
2.5- 4.9kg	100mg SMX/20mg TMP
5-13.9kg	200mg SMX/40mg TMP

TB Preventive Therapy in children (TPT)

Key Points

- An infant or child with HIV, without evidence of active TB, should receive INH preventive therapy for 6 months.
- INH dose: 10mgs/kg/ day to a maximum of 300 mgs per day with pyridoxine (5-10mg/day).

Vaccination

In general, HIV-exposed infants, children and adolescents with HIV should receive all vaccines under routine vaccination according to recommended national immunization schedules.

Table 22: HIV-specific guidance for selected vaccines from WHO vaccine position paper

Vaccines	Indication
BCG	1. Neonates born to women of known or unknown HIV status should be vaccinated. 2. For neonates living with HIV confirmed, BCG vaccination should be delayed until ART has been started
Measles	• In areas with a high incidence of both HIV infection and measles, an initial dose of measles containing vaccine may be offered as early as age six months
Pneumococcal conjugate vaccines	• Infants living with HIV and preterm neonates who have received their three primary vaccine doses before 12 months of age may benefit from a booster dose in the second year of life.

Infant Feeding/Replacement Feeding

Breastfeeding is associated with significant additional risk of HIV transmission from mother-to child. The risk of transmission is about 20-35% with breastfeeding up to six months. The risk further increases by 30-45% if breastfeeding is continued to 24 months. The Royal Government of Bhutan has thus decided to counsel all HIV positive mothers not to breastfeed and that the Government will supply infant formula for the first two years of life. All HIV infected mothers will be counseled for formula feeding and provided with formula milk support till one year of age.

Table 23: Approximate amount of formula needed per day

Age in months	Weight in kilos	Approximate amount of formula per 24 hours	Approximate number of feeds
1	3	450 ml	8*60 ml
2	4	600 ml	7*90 ml
3	5	750 ml	6*120 ml
4	5+	750 ml	6*120 ml
5	6	900 ml	6*150 ml
6	6+	900 ml	6*150 ml

In the first two months of life advise the mother to feed at least 8 times in 24 hours. Therefore, the number of feeds may be decreased to 6 times in 24 hours.

Commercial infant formula requirements

The amount of milk that needs to be given for each baby at various ages is given below. However, should the mother ask for more she may be given an extra one or two tins provided it is documented that her baby is growing well.

Table 24: Commercial infant formula requirements

Months	500g tins needed per month	450g time needed per month
1	4 tins	5 tins
2	6 tins	6 tins
3	7 tins	8 tins
4	7 tins	8 tins
5	8 tins	8 tins
6	8 tins	9 tins
7-8	7 tins	8 tins
9-11	6 tins	6 tins
12-24	6 tins	6 tins

Table 25: Monthly requirements of milk (approximately)

Age in months	Milk feeds per day	Cow's milk, water and sugar to make home prepared formula per day	Commercial formula needed per month
1	450	300 ml milk + 150 ml water + 30g sugar	4*500g tins
2	600	400 ml milk + 200 ml water + 40g sugar	6*500g tins
3	750	500 ml milk + 250 ml water + 45g sugar	7*500g tins
4	750	500 ml milk + 250 ml water + 45g sugar	7*500g tins
5	900	600 ml milk + 300 ml water + 56g sugar	8*500g tins
6	900	600 ml milk + 300 ml water + 56g sugar	8*500g tins
Total for 6 months		92 Liters of milk + 9 kg of sugar	40 * 500g (20 kg)

Up to 6 Months of Age

- Give formula feeds only
- Other foods or fluids are not necessary
- Prepare correct strength and amount just before use. Use milk within two hours and discard any left over
- Cup feeding is safer than bottle feeding
- Clean the cup and utensils with hot soapy water
- Give these amounts of formula 6 to 8 times per day *

6 months up to 12 months

- Give about 1-2 cups (500 ml) of full cream milk or infant formula per day
- Give milk with a cup, not a bottle
- If no milk is available, give 4-5 feeds per day
- Give 3 adequate servings of nutritious complementary foods plus one snack per day (to include protein,
- mashed fruit and vegetables). Each meal should be 3/4 cup*.
- If possible, give an additional animal-source food such as liver or meat.

12 months up to 2 years

- Give 3 adequate nutritious feeds plus 2 snacks per day (each meal should be 1 cup).
- If possible, give an additional animal-source food, such as liver or meat.
- Give fruit or vegetables twice every day
- Give about 2 cups (250 x 2=500 ml) of full cream milk or infant formula per day. If
- no milk is available, give 4-5 feeds per day.
- Feed actively with own plate and spoon

Wasting syndrome–Wasting is defined by meeting at least one of the following criteria in the absence of a concurrent illness other than HIV:

- Persistent weight loss greater than 10 percent of baseline
- Downward crossing of two or more major percentile lines on the pediatric weight-for-age chart
- Less than 5th percentile on weight-for-height chart on two consecutive measurements 30 or more days apart, plus chronic diarrhea or documented fever

Loss of lean body mass or wasting is a well-recognized AIDS-defining condition for children and adults. HIV infection per se, opportunistic infections, and increased metabolic demands all can lead to loss of weight and lean body mass. In children, wasting can severely impact normal growth and development. Wasting also is associated with a high risk for HIV disease progression and short-term mortality.

Nutrition

A child has increased energy needs associated with HIV infection, which requires a proactive approach to nutritional support after 6 weeks

- From the time of first infection, energy needs increase by about 10%
- In HIV-infected children with chronic conditions such as LIP, persistent diarrhoea, HIV-related malignancies, and during infections such as TB, energy needs can increase by about 25-30%
- During and following periods of severe malnutrition, energy requirements may increase by 50-100% in order to recover weight

CHAPTER VII

PRE-EXPOSURE PROPHYLAXIS (PrEP)

Key Points

- PrEP is use as antiretroviral medication to prevent HIV infection among people who could be exposed to HIV through unprotected sex or injection drug use
- In Bhutan oral PrEP (Tenofovir Disoproxil fumarate 300mg + Lamivudine 300mg) TDF/3TC tablets is recommended.

Pre exposure prophylaxis (PrEP)

PrEP is short for pre-exposure prophylaxis. It is the use of antiretroviral medication to prevent HIV infection among people who could be exposed to HIV through sex or injection drug use. All PrEP choices are effective HIV prevention options. In Bhutan oral PrEP (Tenofovir Disoproxil fumarate 300mg + Lamivudine 300mg) TDF/3TC tablets will be used.

Effective use is important to prevent HIV acquisition. PrEP does not offer prevention against other STIs or pregnancy. PrEP products are generally safe and well tolerated. Side-effects are typically mild and resolve on their own and can be treated symptomatically. Severe side-effects should be reported to the PrEP provider without delay. To start PrEP, you need to have a negative HIV test. PrEP use is one of the several ways of looking after our sexual health and it is important to note that PrEP only prevents you from getting HIV, not the other STIs, such as syphilis, gonorrhea and chlamydia. PrEP provides one with an opportunity to speak to a provider (doctor, nurse, outreach worker) about your other health needs, including mental health. Women who are pregnant or breastfeeding can safely use PrEP; it will not harm your baby. Regular follow-up is important to support effective PrEP use and to provide other services including HIV testing. The follow-up visit schedule will depend on the PrEP product chosen.

Eligibility criteria include:

- HIV-negative
- no suspicion of acute HIV infection
- substantial risk of HIV infection
- no contraindications to PrEP medicines (e.g. TDF/FTC)
- willingness to use PrEP as prescribed, including periodic HIV testing.

Process to follow:

1. Identify people who would benefit from PrEP
2. Prescribe oral PrEP (Tenofovir Disoproxil fumarate (TDF)300mg + Lamivudine (3TC)) 300mg tablets
3. Educate patients about the medications and the dosing regimen
4. Provide counseling on sexually transmissible infections (STIs) and their prevention
5. Provide medication-adherence support and counseling to help patients achieve and maintain protective levels of medication
6. Provide HIV risk-reduction support and offer harm reduction including referrals to help patients minimize their risk of acquiring HIV, viral hepatitis B and C and STIs.
7. Provide effective contraception to women who are taking PrEP and who do not wish to become pregnant
8. Monitor patients on a quarterly basis to screen for HIV infection, STIs and toxicity and to determine whether PrEP remains indicated

PrEP consist of following medication as per WHO:

- Oral tenofovir disoproxil fumarate (TDF) or co-formulated TDF/emtricitabine (TDF/FTC) or co-formulated TDF/lamivudine (TDF/3TC)

As per National ART guideline the drug used in Bhutan is:

- Co-formulated TDF/lamivudine (TDF/3TC)

The PrEP products do not protect against other STIs or pregnancy. However, PrEP services offer an opportunity to provide person-centered and comprehensive health services, addressing sexual and reproductive and other health needs of clients.

Indication:

HIV negative AND
Sexual partner with HIV who is not virally suppressed, OR
Sexually active in a high HIV incidence/prevalence population AND any of the following:

- Vaginal or anal sexual intercourse without condoms with more than one partner
- A sexual partner with one or more HIV risk factors
- A history of a sexually transmitted infections (STI)
- Use of post exposure prophylaxis (PEP)
- Requesting PrEP

Contraindications:

- HIV Positive
- Signs and symptoms of acute HIV infection, probable recent exposure
- Allergy or contraindications to any of the medicines used in PrEP

Risk of developing drug resistance is minimal, unless PrEP has been started in those with undiagnosed HIV infection.

Side effects of drugs: Most common side effects include;

- Gastrointestinal symptoms such as diarrhea, nausea, & abdominal cramps (mild and usually resolve after first month of taking PrEP)
- Elevated creatinine (reversible if PrEP is stopped)
- Asthenia
- Headache & dizziness

PrEP can be offered as:

1. **Daily Oral PrEP**: relevant focal people, irrespective of gender, sexual orientation, or sexual behavior.
2. **Event-Driven PrEP (ED-PrEP)**: recommended ONLY for men who have sex with men.

Table 26: Types of PrEP

For whom ED PrEP is appropriate	For whom ED-PrEP is NOT appropriate
A man who has sex with another man: Who would find ED-PrEP more effective AND, 1. Who has infrequent sex (for example, sex less than 2 times per week on average)? 2. Who is able to plan for sex at least 2 hours in advance, or who can delay sex for at least 2 hours?	1.Cisgender women or transgender women 2. Transgender men having vaginal/frontal sex 3. Men having vaginal or anal sex with women 4. People with chronic hepatitis B infection.

At this time there is evidence on safety and efficacy for ED-PrEP only for men who have sex with men. There is insufficient evidence for ED-PrEP for women, transgender women and men who have vaginal and/or anal sex with women.

Dosing schedule of ED- PrEP

Recommended dosing is "2+1+1".

This consists of the use of a double dose (two pills, which serves as the loading dose) of TDF/FTC (or TDF/3TC) between 2 and 24 hours in advance of sex; then, a third pill 24 hours after the first two pills, and a fourth pill 48 hours after the first two pills.

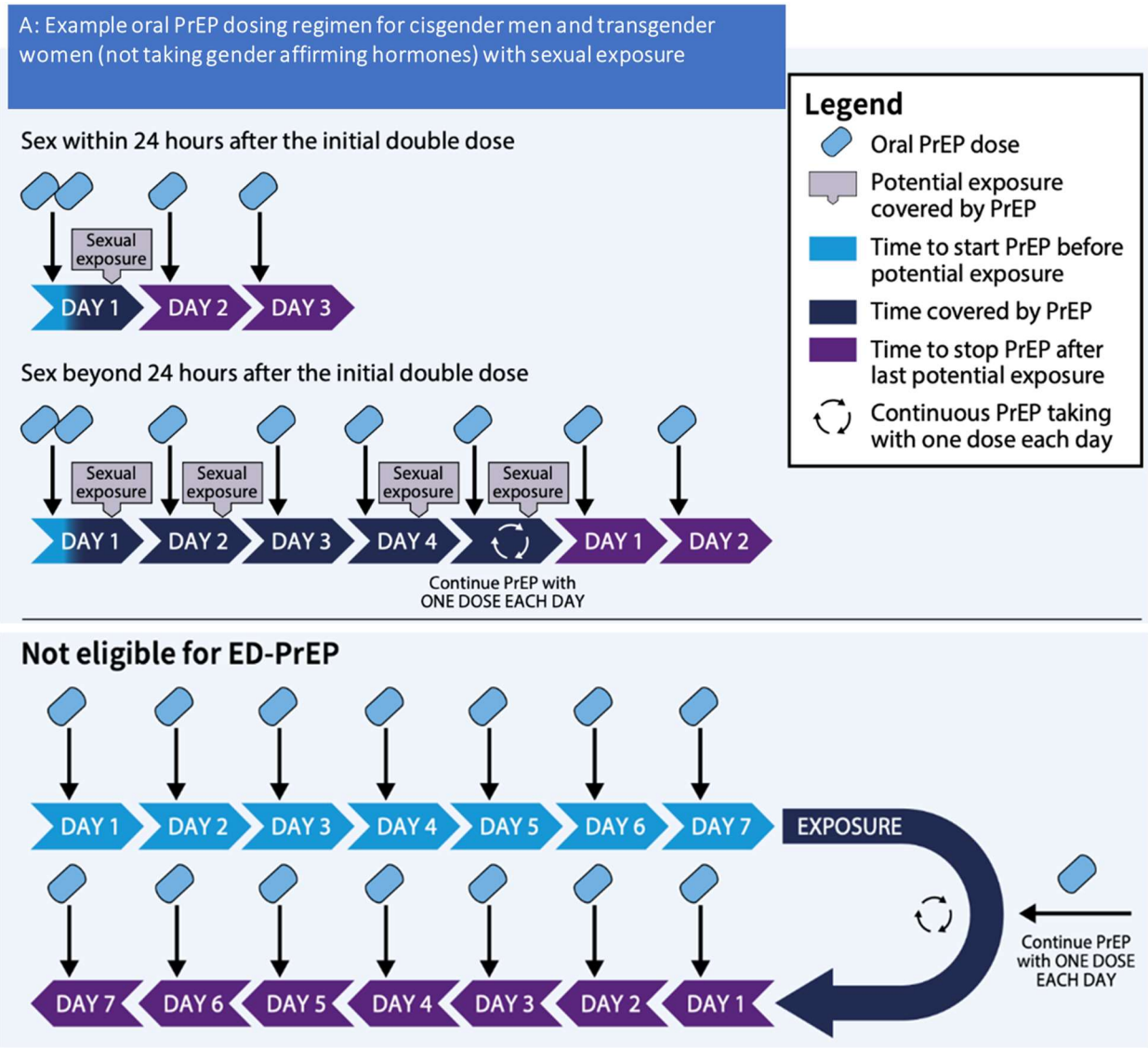

Figure 7: Dosing schedule of ED- PrEP

The 2+1+1 dosing describes ED-PrEP when an isolated act of sex is involved. If more sex acts take place over the following days, a single PrEP pill can be continued daily for as long as sex continues, with a single daily pill taken for each of two days after the last sex act.
It is important to understand how to safely start and stop ED-PrEP and how to shift back and forth between daily dosing and ED-PrEP.

Advantages of ED- PrEP

- Highly effective.
- Provides choice and convenience for men who have sex with men who may be at high HIV risk.
- Reduces pill burden.

How to offer PrEP in men who have sex with men?

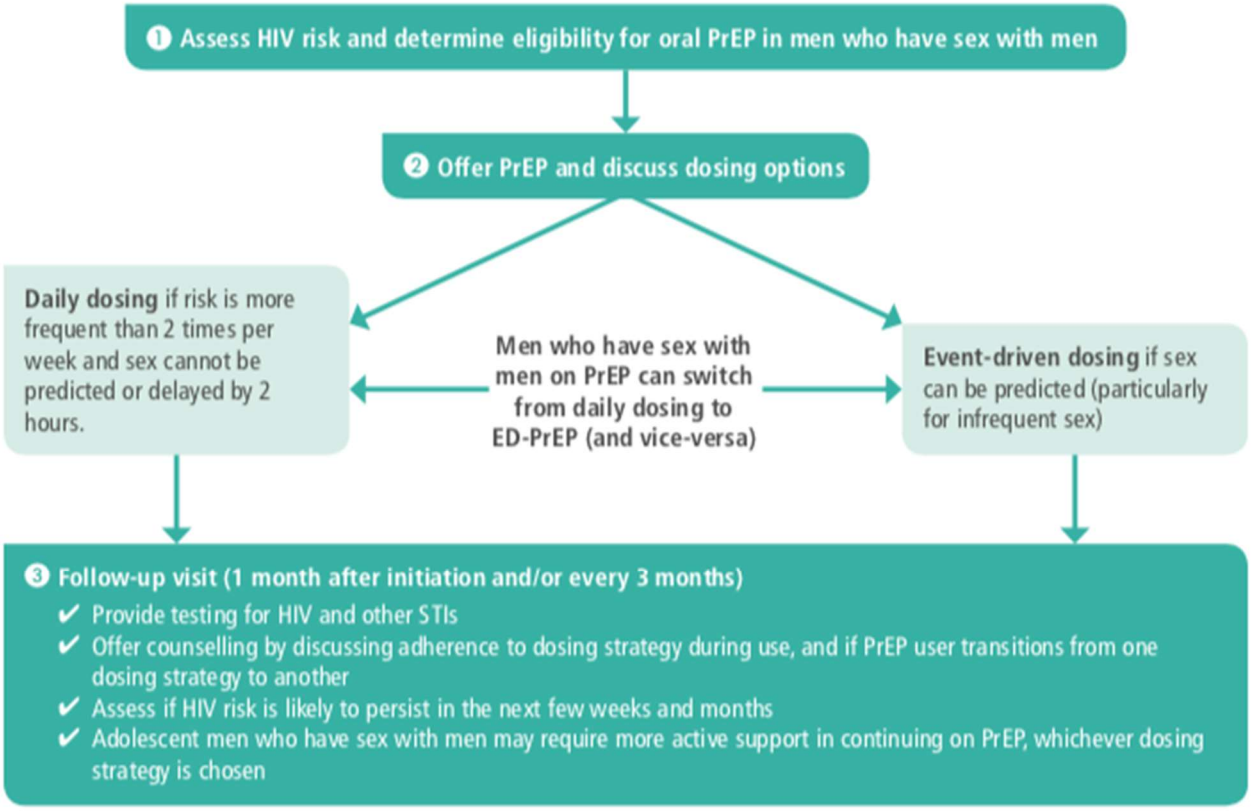

Figure 8: How to offer PrEP in MSM

Table 27: Procedures before starting PrEP

Investigation/ intervention	Rationale
HIV test	● To assess HIV infection status. ● If recent exposure (in the past 72 hours), consider PEP and re-test after 28 days. ● To complete a symptom checklist for possible acute HIV infection.
Serum creatinine (eGFR)	● **If eGFR is less than 60 ml/min, repeat serum creatinine in a new sample and if eGFR is above 60 ml/min, start PrEP.**
Hepatitis B surface antigen	● If negative, consider vaccination against hepatitis B. ● If positive, suggest further testing and assessment for hepatitis B treatment. ● Hepatitis B is not a contraindication for PrEP use.
Hepatitis C antibody	● Consider for MSM populations: If positive, consider referral for assessment and treatment for hepatitis C infection.
Rapid test for Syphilis.	● To diagnose and treat syphilis infection.
Other screening for sexually transmitted infection (syndromic or diagnostic testing)	● To screen and treat STI during each follow up visit.
Pregnancy testing	To guide antenatal care, contraceptive and safer conception counseling, and to assess risk of mother to child transmission. **Pregnancy is not a contraindication for PrEP use.**
Review vaccination history	Consider vaccination for hepatitis A, (e.g. MSM), human papillomavirus, Monkeypox virus
Counseling	● To assess whether the client is at substantial risk of HIV. ● To discuss prevention needs and provide condoms and lubricants. ● To discuss desire for PrEP and willingness to take PrEP. ● To develop a plan for effective PrEP use, sexual and reproductive health. ● To assess fertility intentions and offer contraception or safer conception counseling. ● To assess intimate partner violence and gender-based violence. ● To assess substance use and mental health issues.

Table 28: Follow up procedures

Intervention	Schedule Following Prep Initiation
Confirmation of HIV-negative status	At baseline before the initiation of Prep and thereafter every 3 months.
Address side-effects	Every visit.
Brief adherence counseling	Every visit.
Estimated creatinine clearance	At 0, after 3 months and thereafter every 6 months.
Hepatitis C antibody	Consider testing MSM every 12 months.
STI syndromic screening or testing:	**STI syndromic screening during each follow up (3,6,9, 12 months)** **STI testing** ● **Syphilis 6 monthly** using rapid tests for syphilis (TPHA test). If TPHA is positive, refer to the lab for confirmation. ● **Gonorrhea and Chlamydia 6 monthly, once the tests are made available.**
Provide screening for sexually transmitted infections (STI), condoms, contraception or safer conception services as needed. Provide counseling regarding effective PrEP use (adherence), prevention of STIs, recognition of symptoms of STIs, and issues related to mental health, intimate partner violence and substance use.	

Special situations:

- Exposure to HIV in past 72 hours: use PEP for 28 days, then start PrEP
- Acute retroviral syndrome: consider re-testing in one month before PrEP initiation
- Pregnancy and breastfeeding: PrEP can be offered and continued
- Adolescents may benefit more from frequent visits (monthly)
- If a client using PrEP tests positive for HIV, therapy for HIV infection can be started without a gap after PrEP is discontinued.

Counseling on taking PrEP:

- Make taking the tablets a daily habit, linked to something else that you do every day without fail.
- If you forget to take a tablet, take it as soon as you remember.
- Tablets can be taken any time of day, with food or without food.
- Can be taken with alcohol, but avoid excess alcohol.

- Start PrEP **seven consecutive days prior to exposure to HIV and** additional HIV prevention methods should be used during this time.

- Check for last potential HIV exposure in individuals wanting to stop taking PrEP. PrEP **should be continued for 7 days after the last potential HIV exposure** in those wanting to cycle off PrEP.
- No STI protection (other than HIV infection)
- PrEP does not affect the efficacy of hormonal contraceptives *and* hormonal contraceptives do not affect PrEP efficacy.

Note: WHO oral PrEP app is available on app store.

CHAPTER VIII

IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

Key points

- IRIS is an early complication in patients with advanced HIV disease occurring often within the 4- 8 weeks of ART
- Clinicians should include IRIS as part of the differential diagnosis when inflammatory signs or symptoms occur following recent initiation, re-initiation or a change in ART regimen
- IRIS is most frequently described in association with tuberculosis (TB) and cryptococcal meningitis (CM)
- ART is initiated within two weeks of diagnosis for most opportunistic infection, except in TB meningitis and cryptococcal meningitis, where it may have to be delayed up to 4 weeks
- ART should not be interrupted in patients with IRIS except in life-threatening cases

- Corticosteroids have been shown to reduce morbidity and improve symptoms in severe IRIS
- Steroid is contraindicated in Kaposi's sarcoma, Cryptococcal meningitis, Viral hepatitis and Herpes associated IRIS

Definition

Clinical deterioration following initiation of ART related to restored ability to mount an inflammatory response due to restoration of pathogen specific immunity. It can also occur following initiation, re-initiation or change to more potent ART. It usually occurs within the first 4 to 8 weeks after ART initiation

Incidence of IRIS in HIV patients on ART is around 25 to 30%.

IRIS can present as one of the two forms:

1. Paradoxical IRIS: worsening of a previously diagnosed disease after starting ART.

2. Unmasking IRIS: appearance of a previously undiagnosed disease after starting ART.

Diagnosis

The following criteria need to be met before the diagnosis of the IRIS in HIV positive patients:

1. The patient should be HIV-positive
2. Inflammatory signs or symptoms occur following recent initiation, re-initiation, or a change in ART regimen with associated increase in CD4 cell count and/or decrease in viral load
3. Clinical course NOT consistent with:
    - Expected course of previously diagnosed OI
    - Expected course of newly diagnosed OI
    - Drug toxicity or side effects.
4. Temporal association with the initiation of ART (4-8 weeks)

RISK FACTORS FOR IRIS

1. Starting ART treatment at a younger age or in male patients
2. CD4+T cell count less than 100 cells per microliter at the time of initiating ART
3. An accelerated rise in CD4 count following treatment with ART
4. Rapid HIV RNA viral suppression within 90 days of ART increases the risk of IRIS
5. Pre-existing latent opportunistic infection with a high antigenic burden increases the risk and severity of IRIS
6. Genetics also play a role in determining who is at an increased risk for IRIS, particularly in herpes and mycobacterial infections

Clinical features

Opportunistic pathogens such as *Mycobacterium*, fungi, viruses, parasites can cause latent or subacute infections in HIV/AIDS patients.

The clinical presentation depends on the underlying pathogen and organ/system involved and the severity of the inflammatory response.

Timing of ART Initiation in Patients with Recent OIs and Prevention of IRIS

Initiating ART

Initiate ART within 2 weeks of beginning treatment for active OIs, with exception for TB meningitis, CMV retinitis or cryptococcal infection in which ART may be delayed up to 4 weeks.

In patients with CD4 counts <100 cells/mm3 or known concomitant OIs who are initiating ART, clinicians should be vigilant for the signs and symptoms of IRIS.

For patients with HIV who have HBV or HCV co-infection, clinicians should measure transaminase levels before initiation of ART, at 6 and 12 weeks after initiation and at least every 6 months thereafter to monitor for IRIS.

Pulmonary TB

Patients with active TB and who are improving on TB therapy with a CD4+ count ≤ 100 cells/µl, upon starting ART can be initiated on prednisone 40 mg daily for 14 days followed by 20 mg daily for 14 days to prevent paradoxical TB-IRIS.

TB Meningitis
For patients with TB meningitis, timing of ART initiation should be delayed by 4 weeks

Cryptococcal Meningitis
ART-naive patients diagnosed with cryptococcal meningitis should be treated with standard antifungal therapy and delay ART initiation until the patient has completed at least 4 weeks.

CMV Retinitis
Clinicians should refer patients with HIV who have CD4 counts <100 cells/mm3 but without known or suspected CMV for a dilated ophthalmologic examination as soon as possible after initiating ART to assess for signs of CMV

Management of IRIS

The initiation of antimicrobial agents for the underlying opportunistic infection associated with the IRIS.
It is also highly recommended to continue ART unless there is evidence of severe ART-related toxicity or IRIS with central nervous system involvement.

Mild IRIS

NSAIDs can be used in cases of mild inflammation with pain or fever.
Abscesses need to be drained.

Inflamed and painful nodes should be excised.

Inhaled steroids to alleviate mild pulmonary inflammation that cause bronchospasm or cough.

Severe IRIS

Severe IRIS can cause decline in pulmonary capacity from TB or *Mycobacterium avium* complex (MAC) infection, neurologic complications from cryptococcal infection, or vision loss from CMV retinitis infection. Corticosteroid therapy to suppress inflammatory response is the most commonly used intervention in cases of severe IRIS.

1 to 2 mg/kg prednisone, the equivalent, for 1 to 2 weeks, followed by a period of tapering dose that is individualized or Prednisone 40 mg daily for 14 days, followed by 20 mg daily for 14 days.

Contraindications of Corticosteroid:

- Kaposi's sarcoma
- Cryptococcal meningitis in patients with HIV
- Viral hepatitis and herpes associated IRIS

Complications

1. TB-IRIS and Cryptococcus-IRIS can lead to death due to acute hypoxic respiratory failure and CNS complications.
2. Progressive multifocal leukoencephalopathy (PML) can be a potentially fatal demyelinating CNS disease due to the JC virus-associated IRIS.
3. Malignancies such as Kaposi sarcoma, Hodgkin lymphoma, non-Hodgkin lymphoma have been associated with the IRIS.
4. Permanent blindness in case of severe CMV keratitis.

CHAPTER IX

POST EXPOSURE PROPHYLAXIS (PEP)

Key points

- First dose of PEP should be offered immediately and no later than 72 hours post-exposure
- An HIV PEP regimen consisting of TDF+3TC+DTG is recommended for a duration of 28 days
- Site of a wound or needlestick injury should be cleaned with soap and water only and avoid squeezing the wound and use of surgical scrub brushes or other abrasive tools
- If the source of a high-risk exposure is not available for HIV testing, clinicians should recommend that the exposed individual complete the 28-day PEP regimen

This chapter covers consideration and initiation of antiretroviral (PEP) in occupational and non-occupational settings.

Definitions

PEP: The set of services that are provided to manage the specific aspects of exposure to HIV and help prevent HIV infection in a person exposed to the risk of getting infected by HIV.

Exposed person: The person who has been potentially at risk of acquiring HIV infection through exposure to blood or body fluids in his or her occupation or in another non-occupational situation.

Source person: The person who is (either identified or not identified as) the possible source of contamination through potentially infectious blood or body fluid.

EXPOSURE TO HIV IS A MEDICAL EMERGENCY: PEP should be initiated immediately but no later than 72 hours after an exposure.
Assessment of exposure, HIV and other baseline testing, and other related activities can proceed after the first dose of PEP is administered.

Risk of Infection Following an Exposure to HIV

A. Factors that increase the risk of transmission:

- Early and late-stage untreated HIV infection and a high level of HIV RNA in the blood
- Presence of genital or anorectal ulcers from sexually transmitted infections (STIs)
- Direct blood-to-blood exchange, such as syringe sharing during injection drug use

B. Factors that decrease the risk of HIV transmission:

- When the source of the exposure has a low or undetectable viral load
- Source person is on antiretroviral medications as pre-exposure prophylaxis (PrEP)
- Individuals do not sexually transmit HIV if they are taking antiretroviral therapy (ART) and have an undetectable viral load or HIV RNA <50 copies/mL.

Occupational exposure

- Break in the skin by a sharp object (including hollow-bore, solid-bore, and cutting needles or broken glassware) that has been in the source's blood vessel or is contaminated with blood, visibly bloody fluid, or other potentially infectious material.
- Bite from a patient with visible bleeding in the mouth that causes bleeding in the exposed individual.
- Splash of blood, visibly bloody fluid, or other potentially infectious material to the mouth, nose, or eyes.
- A non-intact skin (e.g. dermatitis, chapped skin, abrasion, or open wound) exposure to blood, visibly bloody fluid, or other potentially infectious material.

Table 29: Indications of PEP for Non-Occupational Exposure

Parenteral Exposure Risk	Sexual Exposure Risk	Exposure Risk in Children
Needle sharing during injections drug use Percutaneous (needlestick)	• Receptive penile-vaginal intercourse • Intsertive penile0vaginal intercourse • Anal intercourse • Oral sex: low	• Biting involving blood • Sexual abuse • Discarded needle

Exposures that DO NOT warrant PEP:

- Kissing, spitting, oral-to-oral contact in the absence of mucosal damage (e.g. mouth-to-mouth resuscitation)
- Human bites not involving blood
- Exposure to needles or sharps that have not been in contact with an individual with or at risk of HIV.

Management

A. Management of the Exposed Site

- The site of a wound or needlestick injury should be cleaned with soap and water only. It is best to avoid use of alcohol, hydrogen peroxide, povidone-iodine, or other chemical cleansers.
- Squeezing the wound may promote hyperemia and inflammation at the wound site, potentially increasing systemic exposure to HIV if present in the contaminating fluid.
- The use of surgical scrub brushes or other abrasive tools should be avoided
- Eyes and other exposed mucous membranes should be flushed immediately with water or isotonic saline

Table 30. Assessment of risk of infection

Definitely infectious	Potentially infectious	Non-infectious (unless visibly bloody)
Blood Semen Vaginal secretions Breast milk	CSF Synovial fluid Pleural effusion Amniotic fluid Peritoneal fluid	Saliva Tears Sweat Urine Feces

B. Antiretroviral Therapy

- **When should PEP be started?**
  - PEP should be initiated as soon as possible, preferably within 72 hours of exposure.

- **How long to continue?**
  - For four weeks (28 days) recommended
  - **If the source is not available:** When the source of a high-risk exposure is not available for HIV testing, clinicians should recommend that the exposed individual complete the 28-day PEP regimen

Three Drug Regimen; three drugs are preferred

- **Adult:**
  - Preferred regimen: TDF+3TC+DTG
  - Alternate regimen: TDF+3TC+LPV/r

- **Pediatric (<10 years)**
  1. **Preferred regimen:**
     - ABC + 3TC+ DTG
  2. **Alternate regimen**:
     -ABC+3TC +LPV/r

**** For details of dosing: refer Chapter 7 on pediatric HIV and AIDS management***

PEP after 72 hours:

- Clinicians should not provide PEP later than 72 hours after a potential exposure to HIV.
- If an individual presents for PEP past 72 hours post exposure, clinicians should perform baseline HIV testing and recommend serial HIV testing at 4- and 12-weeks post exposure

Other factors to be considered in an occupational exposure

- Source person: (a) presence of HBsAg(b) presence of HCV antibody
- Other risk factors:
  - HIV viral load
  - the length of exposure time: tenfold drop in infectivity every 9 hours with the initiation of PEP
  - Use of gloves
  - Hollow bore versus solid bore needle: large diameter needle is associated with increased risk

HIV PEP services would include the following as a core package

- Reporting incidence and possible referral capacity
- Risk assessment
- Counseling services for providing PEP
- Pre and post HIV test and counseling (for both the exposed person and the source person)
- Drug adherence and managing side effects
- Preventing the risk of transmission
- Initial testing of exposed individuals
- Testing of the source person when possible
- Providing PEP medications which includes the initial dose and the doses for 28 days (the full course)
- Support and follow up
- Appropriate record keeping and documentation

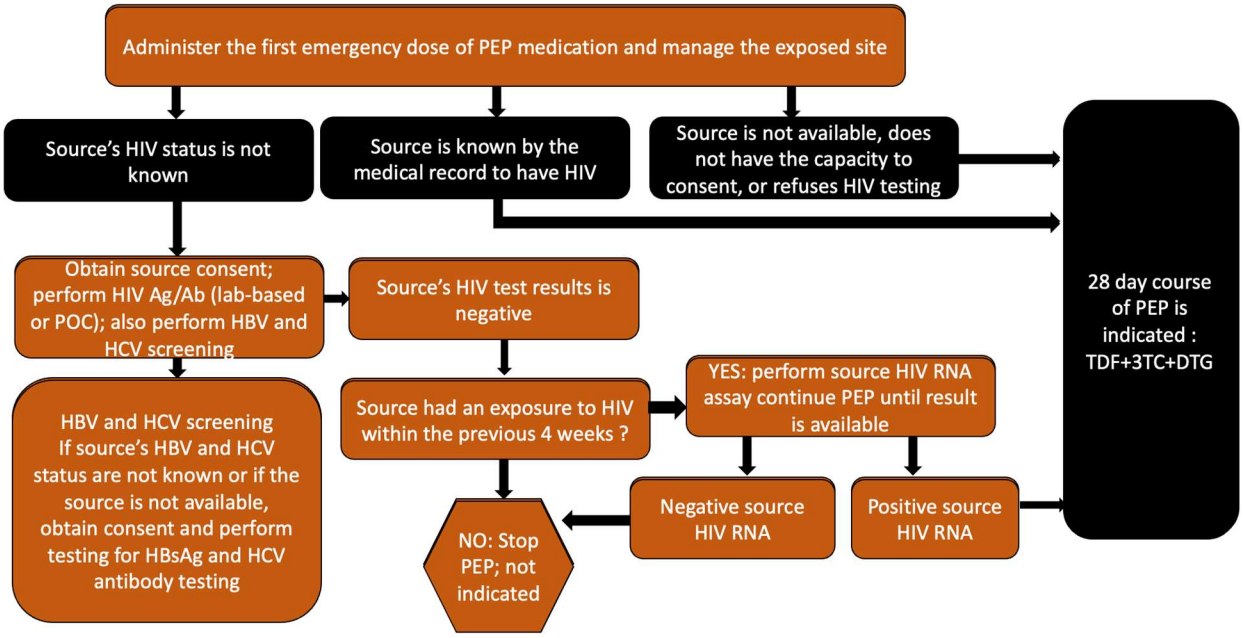

Figure 9: PEP and exposure management when reported within 72 hours

Table 31: Summary of clinical management of HIV post-exposure prophylaxis

Criteria	Recommendations
Eligibility for PEP	Exposure within 72 hours Exposure individual not known to be infected with HIV significant exposure The source of exposure is HIV infected or has unknown HIV status
Informed consent for post exposure prophylaxis	Information about risks and benefits Consent may be given verbally
Medicine	Preferred regimen: Adult: TDF+3TC+DTG Pediatric: ABC + 3TC+ DTG
Time of initiation	The initial dose given as soon as possible but no later than 72 hours after exposure
Duration of therapy	28 days

HIV testing with informed consent and pre- and post-test counseling according to protocols	Baseline HIV test in exposed person Follow-up HIV testing 3-6 months after exposure Rapid HIV test of the source person if feasible and based on informed consent and standard operating procedures
Additional Laboratory evaluations	Pregnancy testing Hemoglobin (for zidovudine-containing PEP regimens) Hepatitis B and C screening if available and based on the prevalence of the diseases
Counseling	For adherence; side effects; risk reduction; trauma or mental health problems; and social support and safety
Recor-keeping	Maintain accurate, confidential records

CHAPTER X

PROPHYLAXIS AND PREEMPTIVE THERAPY

Key points

- The three most essential forms of prophylaxis and pre-emptive treatment to consider are cotrimoxazole prophylaxis, TB preventive treatment and pre-emptive cryptococcal treatment for patients with a positive serum cryptococcal antigen (if cryptococcal meningitis has been ruled out).

TB Preventive therapy (TPT) in PLHIV

- Adults and adolescents living with HIV should be screened for active TB infection and TPT should be immediately started after ruling out active TB
- TST is not a requirement for initiating TPT in people living with HIV.
- TPT should be given regardless of the degree of immunosuppression, and also to those on ART, or previously treated for TB, pregnant women and children.

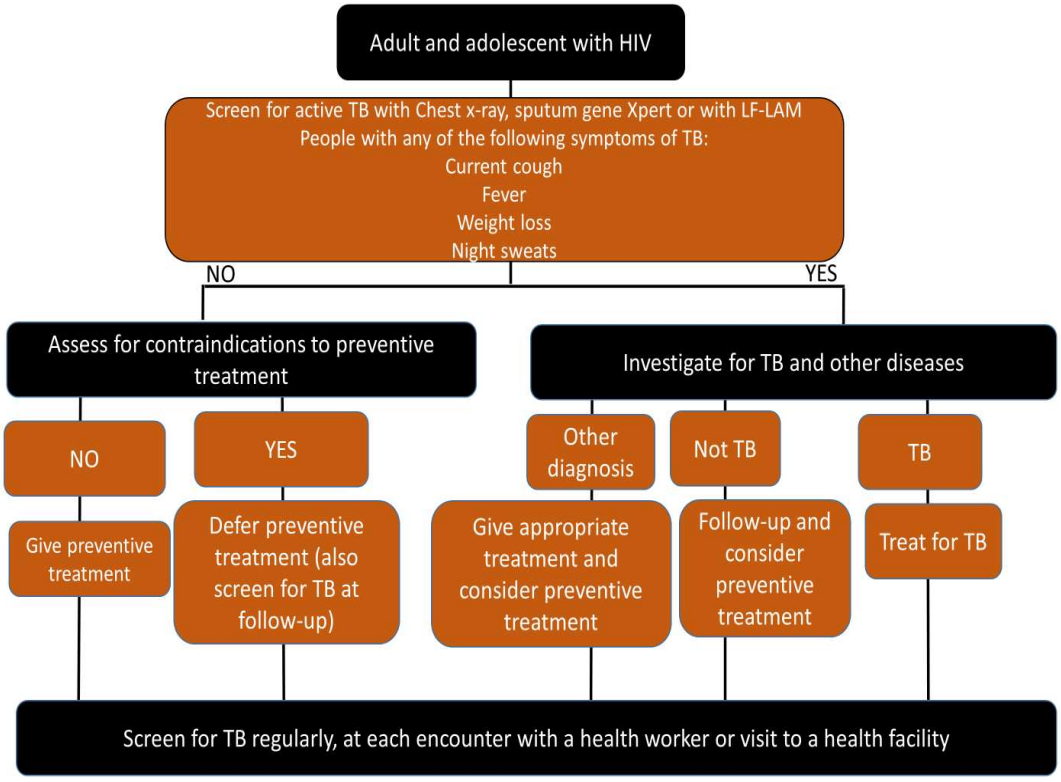

Figure 10: Algorithm for screening adults and adolescents living with HIV for active TB

Table 32: TB Preventive therapy (TPT) Regimen

Drug Regimen	Dose per kg body weight	Maximum Dose
3HP: Weekly Rifapentine plus Isoniazid for 3 months	Adults ≥ 30kg HP 3 tabs weekly for 12 weeks Individuals aged ≥ 14 years and weight 20-30 kg: HP 2 Tab weekly for 12 weeks	Rifapentine 900 mg Isoniazid 900 mg
Isoniazid, daily for 6 months	Adults, 5mg/kg	300mg

Prophylactic Pyridoxine should be given to individuals at high risk of peripheral neuropathy, such as those with malnutrition, chronic alcohol dependence, HIV infection, renal failure, diabetes or who are pregnant or breastfeeding when taking isoniazid containing regimens (Pyridoxine dose 25 mg).

If Pyridoxine is given, it should be given at least 12 hours apart along with anti -TB drugs.

Co-trimoxazole preventive therapy (CPT)

Routine co-trimoxazole prophylaxis should be given to all PLHIV with active TB disease regardless of CD4 count.

Table 33: Criteria for initiation and discontinuation of co-trimoxazole prophylaxis

Intervention	Indication to start		Indication to stop	
	Adults	Adolescents	Adults	Adolescents
Co-trimoxazole prophylaxis CPT- 2 single strength (960mg)	Severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and/or with a CD4 cell count **<350 cells/mm3**	Same as children-(Refer chapter VI Paediatric)	Clinically stable on ART, with evidence of immune recovery and viral suppression.	Same as children – (Refer chapter VI Paediatric)

Preemptive Fungal Therapy

Table 34: Criteria for initiation and discontinuation of preemptive fungal therapy

Intervention	Indication to start		Indication to stop	
	Adults	Adolescents	Adults	Adolescents
Preemptive antifungal therapy: **Fluconazole 800 mg/day for two weeks, then 400 mg/day for eight weeks and continued maintenance with Fluconazole 200 mg/day**	Blood cryptococcal antigen screening positive among people with CD4 counts <100 cells/mm3	Same as adult	If HIV viral load monitoring is not available: when people are stable and adherent to ART and receiving antifungal maintenance therapy for at least one year and have a CD4 count ≥200 cells/mm3 (two measurements six months apart) If viral load monitoring is available: when people are stable and adherent to ART and antifungal maintenance treatment for at least one year and have a CD4 cell count ≥100 cells/mm3 (two measurements six months apart) and a suppressed viral load	Same as adult

CHAPTER XI

CO-INFECTION

Key points

- In HIV/HBV coinfection the ART regime should include the NRTI backbone of TDF or TAF.

Hepatitis B co-infection

Hepatitis B virus infection is an important infection in HIV-infected individuals because of the influence of HIV on the natural history of HBV infection. HIV/HBV (HBV co-infection) increases the rate of progression to cirrhosis and liver cancer by four to five folds. The mortality of the patients with the above situation is approximately ten times higher than that of patients with either infection alone. There is accumulating evidence that ART greatly reduces progression to cirrhosis and death in individuals with co-infection.

Treatment

The aim of the HBV treatment is to suppress HBV viral replication and to achieve sustained disease amelioration. Initiate ART in all HIV infected individuals who are coinfected with HBV with severe chronic liver disease, regardless of WHO clinical stage and CD4 cell count. In the absence of a severe liver disease ART should be initiated as per the standard recommendations. The ART regimen should include the NRTI backbone of TDF or TAF. This treatment should be continued indefinitely.

Hepatitis C co-infection

HIV coinfection adversely affects the course of HCV infection, resulting in significantly accelerated progression of liver disease to cirrhosis, particularly those with CD4 cell count < 200 cells/mm^3. Unlike HIV and HBV, there is a chance of cure of HCV infection with specific therapy.

Treatment

- All patients with chronic Hepatitis C should be assessed and treated as per the National Viral Hepatitis Guideline.

CHAPTER XII

OPPORTUNISTIC INFECTIONS (OIS)

Key points

- For adults, adolescents and children > 5 years, advanced HIV disease is defined as a CD4 cell count <200 cells/mm3 or WHO clinical stage 3 or 4 at the time of presentation.
- The use of appropriate prophylaxis (primary or secondary) for OI is an essential part of HIV care.

OIs are the leading cause of morbidity and mortality in patients with advanced HIV disease. Therefore, it is important to identify primary opportunistic infection and to offer them the package of intervention including screening, treatment and/prophylaxis for major OI's. Most patients are diagnosed with HIV infections when they present with an opportunistic infection. Identification, prevention and treatment of OIs can significantly decrease morbidity and mortality. OIs can be a result of reactivation of previous infections as the immune system is weakened.

Types of OI Prophylaxis:

- **Primary:** to prevent even first occurrence of infection
- **Secondary:** to prevent a second occurrence of an infection that has already occurred at least once (prevention of recurrence).

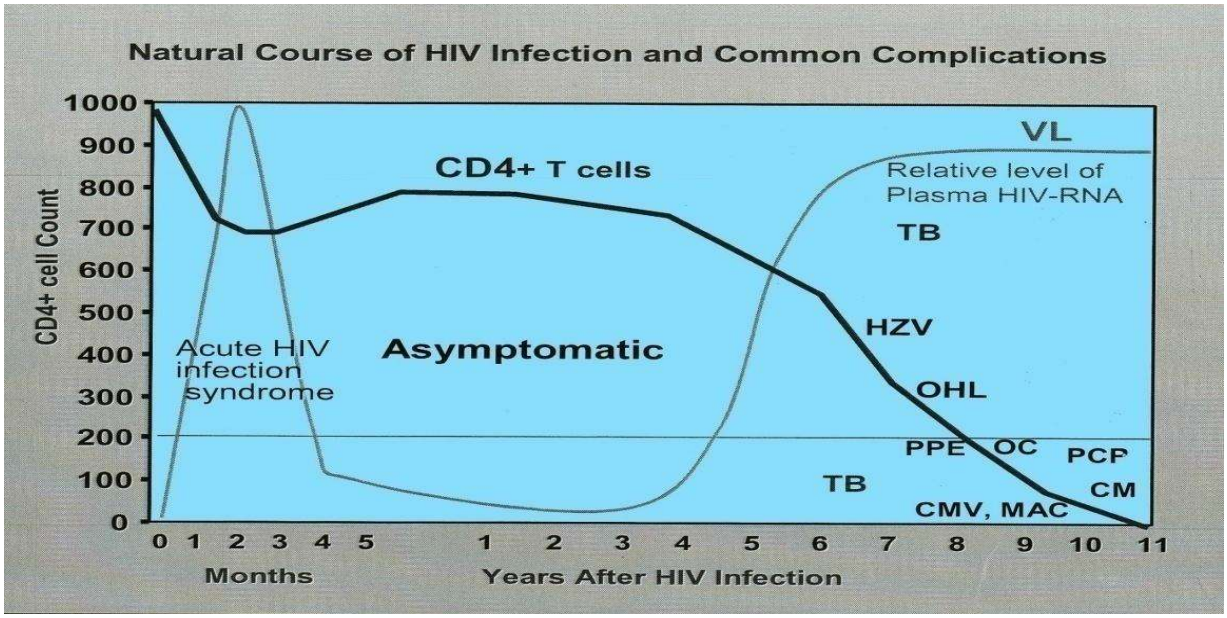

Figure 9: Natural course of HIV infection and common complications

Table 35: Spectrum of opportunistic infection associated with CD4 count cell counts

CD4 cells/mm^3	Opportunistic infections
200 – 500	Pneumococcal and other bacterial infections Pulmonary TB Herpes zoster Oral thrush
<200	PCP Extrapulmonary TB
<100	Toxoplasmosis Fungal Infections Cryptosporidiosis Esophageal candidiasis
<50	Disseminated CMV Disseminated Mycobacterium avium complex

Table 36: Diagnosis and Prophylaxis Components of package of care, intervention for Advanced HIV disease

Areas for the Package	Intervention	CD4 count	Adults	Adolescent	Children
Screening and 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	CD4 ≤200 cells/mm3 (inpatient) or ≤100 cells/mm3 (outpatient) or any CD4 count with symptoms or if seriously ill	Yes	Yes	Yes

	Cryptococcal antigen (CrAg) screening (in blood and CSF)	CD4 <100 cells/mm3. If serum cryptococcal antigen turns positive, to consider testing CSF for cryptococcal antigen and MRI brain	Yes	Yes	No
Prophylaxis and pre-emptive treatment	Co-trimoxazole	<350 cells/mm^3 or clinical stage3 or 4 Any CD4 count in setting with high malaria or severe bacterial infection	Yes	Yes	Yes
	TB preventive treatment	Any	Yes	Yes	Yes
	Fluconazole pre-emptive therapy for cryptococcal antigen positive people without evidence of meningitis	<100 cells/mm^3	Yes	Yes	Not applicable (screening not advised)
ART initiation	Rapid ART initiation	Any	Yes	Yes	Yes

	Defer ART initiation if clinical signs and symptoms are suggestive of TB meningitis or cryptococcal meningitis	Any	Yes	Yes	Yes
ART adherence support	Tailored counseling to ensure optimal adherence to the advanced disease package including home visits if feasible.	<200 cells/mm^3	Yes	Yes	Yes

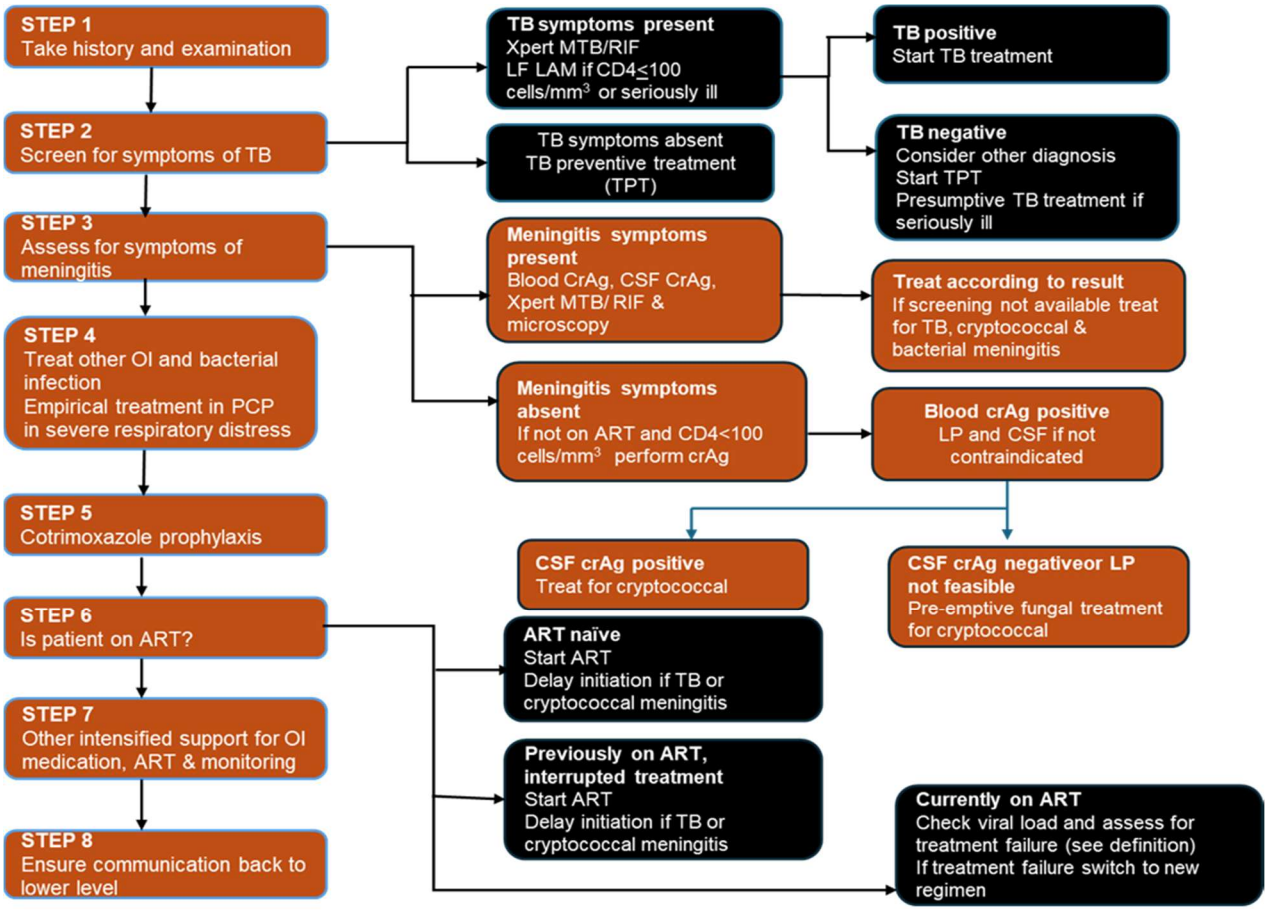

Figure 11: Algorithm for providing a package care for people with advanced HIV diagnosis

Mycobacterial infection: Tuberculosis

M. tuberculosis is especially frequent among HIV infected patients. Primary as well as reactivated disease occurs.

Impact of TB on HIV

- TB is the leading AIDS-related opportunistic infection.
- HIV disease progresses more rapidly in patients with TB, the level of plasma viraemia increases during active TB and successful treatment of tuberculosis brings back the plasma viraemia to the baseline.

Impact of HIV on Tuberculosis

- The lifetime risk of HIV infected patients developing TB is 50% as compared to HIV negative patients which is 5-10%.
- HIV increases not only the risk, but also the rate of progression of recent or latent *M. tuberculosis* infection to disease.
- Increases the incidence of extrapulmonary/disseminated TB.
- HIV increases the incidence of MDR-TB.
- In advanced AIDS, clinical and radiological features of tuberculosis can be atypical.
- TB-ART co-treatment involves higher pill burden and increased adverse drug reactions.

Diagnosis

- Chest X-ray: classic presentation with apical cavitary disease
- Sputum for GeneXpert/MTB/RIF for those who can produce sputum irrespective of the symptoms
- Culture for AFB (even if the smear is negative)
- LF-LAM is an immunocapture assay that detects lipoarabinomannan in urine. It is used as a test for active TB for people with advanced HIV disease with low CD4 counts:

Level of CD4 count for LF-LAM testing

- Inpatient CD4 ≤200 cells/mm3
- Outpatient CD4 ≤100 cells/mm3 or
- Any CD4 count with symptoms or if seriously ill

Table 37: When to start ART in patients with TB

	ART	Adjuvant Treatment
TB	• ART should be started **as soon as possible** within 2 weeks of initiating TB treatment, irrespective of CD4 count • If patients with HIV who are already on ART gets TB, continue ART and start anti-TB treatment at the earliest	In HIV-TB coinfection, start CPT- 2 single strength (960mg) at the time of initiation of ATT and continue till the completion of ATT, after which CPT should be considered according to CD4 count.
TB meningitis	• ART should be delayed at least 4 - 8 weeks after treatment for TB meningitis is initiated.	Corticosteroids therapy should be given during the initial 8 weeks of ATT.

Treatment of tuberculosis

The standard regimen is:

- 2HRZE+4HR

4FDC (Isoniazid 75mg+ Rifampicin 150 mg+ Pyrazinamide 400 mg + Ethambutol 275 mg)
2FDC (Isoniazid 75mg+ Rifampicin 150mg)

Treatment of TB meningitis

The treatment regimen of TB meningitis is the same as for immunocompetent host and the duration of the treatment should be 12 months

ART in DS- TB/HIV-Coinfection

In treatment of TB in HIV, the dose of dolutegravir should be doubled **DTG (50 mg BD)**

First line: 3TC+TDF + **DTG (50 mg BD)**
Alternative line: 3TC+TDF + EFV (600mg OD)
***Protease inhibitors are not recommended for Rifampicin based antitubercular regimen. Rifabutin is preferred over rifampicin.

MDR-TB/HIV Co-infection

- ART should be started promptly in all HIV-infected patients with MDR-TB regardless of CD4 cell count.
- Zidovudine has drug interaction MDR regimen (BpaLM regimen).
- The shorter regimen for MDR-TB is not recommended for treatment of extrapulmonary disease in PLHIV.
- Co trimoxazole Preventive Therapy (CPT) is the same as for DS-TB.

*****Refer National TB guideline, March 2024 – chapter 7 TB/HIV**

******TB-Preventive Treatment - refer chapter X (Prophylaxis and cotrimoxazole therapy).**

Mycobacterium avium complex (MAC)

- MAC is an acid-fast atypical mycobacterium
- MAC infection probably indicates an acute infection with organisms that are ubiquitous in the environment in both soil and water.
- The presumed portals of entry are the gastrointestinal and respiratory tracts.
- MAC infection is a late complication of HIV infection, occurring in patients with CD4 cells count of <50 cells/mm^3

Clinical Features

Fever, weight loss, night sweats, and diarrhoea with or without abdominal pain.
It is a disseminated disease with gastrointestinal, neurological, dermatological and respiratory manifestations.

Diagnosis

1. **Definitive:** Blood culture (positive in 90-95%)
2. **Probable:** By demonstrating the organisms in stool, bone marrow specimen, liver and skin biopsy.

Table 38: Treatment and Prophylaxis

	Drug	Dose	Duration
Treatment	Clarithromycin Plus Ethambutol **OR**	500 mg – BID P.O 15 mg/kg OD P.O	12 months, then secondary prophylaxis
	Azithromycin Plus Ethambutol	500 mg – OD P.O 15 mg/kg - OD P.O	12 months, the secondary prophylaxis
	In severe cases, consider adding a third drug Ciprofloxacin and/or Amikacin	500- 700 mg BD P.O 500 mg IV daily	First 2-3 months First 2-3 months
Primary Prophylaxis - CD4 count <50 cells /mm^3 in patients who are asymptomatic			
	Clarithromycin Or Azithromycin	500 mg BID P.O 1000-1250 mg P.O per week	Discontinuation in patients who have responded to ART with increase in CD4 count to > 100 cells/mm^3 for at least three months.
Secondary Prophylaxis -Disseminated MAC should receive lifelong secondary prophylaxis or maintenance therapy.			
	Clarithromycin Plus Ethambutol OR Azithromycin Plus Ethambutol	500 mg – BID P.O 15 mg/kg OD P.O	Discontinuation if sustained CD4 increase > 100 cells per mm^3 for ≥ 6 months in response to ART after 12 months of therapy for MAC is completed and if there are no symptoms or signs attributed to MAC.

Viral infection

Cytomegalovirus infection (CMV)

- CMV retinitis occurs frequently and accounts for 85% CMV disease in patients with AIDS.
- CMV pneumonitis, encephalitis, polyradiculopathy, dementia, oesophagitis and colitis are other manifestations.
- Usually occurs in patients with CD4<50 cells/mm^3.

Diagnosis

- Fundus examination by an experienced ophthalmologist
- CMV PCR - positive in vitreous and aqueous humor.

Treatment and Prophylaxis

Treatment can be local or systemic and is administered in two phases: induction and maintenance. This treatment should be carried out by an expert ophthalmologist in a specialized center.

Table 39: Treatment of CMV Co-Infection

Treatment
CMV retinitis Induction Therapy (Duration of therapy 2- 3 weeks, then secondary prophylaxis) ● Ganciclovir 5 mg/kg IV BID Or ● Foscarnet 90 mg IV BID Or ● Valganciclovir 900 mg BID ● If patients are not able to tolerate orally and retinal lesions are sight threatening – intravitreal Ganciclovir (by ophthalmologist) **CMV GI diseases** Induction Therapy (Duration of therapy 3 – 8 weeks and then secondary prophylaxis) ● Ganciclovir - 5 mg/kg IV BID Or ● Foscarnet 90 mg/kg IV BID ● If able to tolerate orally or milder disease – oral Valganciclovir 900 mg BID **CMV Encephalitis** Induction Therapy - Treat until symptoms resolved with clearance of CMV-DNA in CSF, then secondary prophylaxis ● Ganciclovir - 5 mg/kg IV BID plus ● Foscarnet 90 mg/kg IV BID
Prophylaxis/Maintenance
Primary – Not recommended **Secondary -** Valganciclovir 900 mg OD Discontinuation of maintenance therapy if ● Lesions have been treated for at least 3 months with consultation with ophthalmologist for CMV retinitis ● CD4 >100 cells/microL for at least 3 months

Herpes simplex infection

- Herpes simplex virus (HSV) type 1 and type 2 of this common virus affect humans.
- In advanced HIV lesions are likely to be persistent and atypical.
- Type 1 HSV produces mucosal lesions, predominantly of the head and neck, whilst type 2 is a sexually transmitted urogenital infection.
- The source of infection is a case of primary or active recurrent disease.
- Primary infection normally occurs as gingivitis in infancy. It may present as keratitis, viral paronychia, ('Whitlow'), vulvovaginitis, cervicitis or balanitis.
- Recurrent disease involving reactivation of HSV from latency in the dorsal root ganglion produces the classical 'cold sore' or herpes labialis. Prodromal hyperaesthesia is followed rapidly by vesiculation, postulation and crusting. Recurrence can be precipitated by UV rays, menstruation or fever of any cause. Type 2 (genital disease) is a common cause of recurrent, painful genital ulceration especially in females.

Diagnosis

- Multiple, painful grouped vesicles/pustules on an erythematous base is a reliable clinical finding.
- Differentiation from other vesico-papular or pustular lesions requires demonstration of the virus by PCR or culture from vesicular fluid.

Table 40: Treatment of HSV Co-Infection

Treatment
Mucocutaneous HSV infection • Primary infection (Duration of therapy 7- 10 days) Acyclovir (400-800 mg po TID Or Valacyclovir 1000 mg - BID If severe mucocutaneous lesion – Acyclovir 5mg/kg IV- TID and after lesions begin to regress, switch to oral treatment for 21-28 days or longer, until lesions have healed • Recurrent episodes (Duration of therapy 5- 10 days) Acyclovir 400 mg TID Or Valacyclovir 1gm BID

- Chronic suppressive therapy

Indications:

- For patients with severe recurrences, *or*
- Patients who want to minimize the frequency of recurrences, including pregnant women

To reduce the risk of genital ulcer disease in patients with CD4 counts<250 cells/mm^3 who are starting ART

Acyclovir 400-800 mg (BID or TID
or Valacyclovir 500 mg po bid

Duration of suppression therapy – depends on patient's clinical condition – once patient has achieved immune reconstitution on ART and number of HSV recurrences may have diminished and must be evaluated annually for ongoing need for suppression therapy

HSV Encephalitis

Acyclovir 10 mg/kg IV TID for 14-21 days

***HSV can become resistant to acyclovir, in which case foscarnet or Cidofovir, 5 mg/kg IV should be used.

Varicella Zoster Infection:

- May cause typical dermatological lesions or disseminated infection.
- It may also cause encephalitis, which is more common with ophthalmic distribution of facial nerves.
- It may be more commonly associated with complications such as pneumonia encephalitis than in non-HIV individuals.
- Multi-dermatomal lesions are more common in advanced HIV.

Table 41: Treatment of Varicella Zoster and Herpes Zoster Co-Infection

Treatment
Primary Varicella Infection (Chickenpox) (Duration of therapy 5-7 days) ● Valacyclovir 1g TID ● Or Acyclovir 800 mg 5 times daily **Herpes Zoster (Shingles)** (Duration of therapy 7-10 days, longer if lesions resolves slowly) ● Valacyclovir 1g TID ● Or Acyclovir 800 mg 5 times daily **Disseminated Herpes Zoster** ● Acyclovir 10 mg/kg IV every 8 hours until clinical improvement is evident switch to oral therapy (valacyclovir 1 g TID or acyclovir 800 mg PO 5 times daily to complete a 10 to 14 days course) when formation of new lesions has ceased and signs and symptoms of visceral VZV infection are improving.

Fungal Infections:

Pneumocystis jirovecii, previously known as Pneumocystis carinii pneumonia (PCP)

- *Pneumocystis jirovecii* is an opportunistic fungal pulmonary pathogen that is an important cause of pneumonia in an immuno-compromised host. Its natural habitat is the lungs.
- PCP occurs when CD4 count is below 200 cells/mm^3.
- Typical manifestation of PCP is a triad of dry cough, breathlessness on exertion and fever and low oxygen saturation on examination.
- Chest X-ray shows symmetrical pulmonary infiltrates. 10-20% of the patients show no radiological changes. Pleural effusion is not common.
- Lactate dehydrogenase is usually >500mg/dl.
- Sputum and broncheoalveolar lavage (BAL) may demonstrate the parasite.

Table 42: Treatment and Prophylaxis of PCP

Treatment	
Preferred Regimen Cotrimoxazole 80/400 mg (SS), PO, 6 tabs TID for 21 days or Trimethoprim 15 mg/kg P.O TID + Sulphamethoxazole 75 mg/kg P.O TID for 21 days **Steroid Therapy -** should be considered under following conditions and is beneficial if started within 72 hours of treatment.	
Conditions • If Pao2 <70 mmHg • If A-a gradient ≥35mm Hg	Prednisolone • 40 mg 12 hourly for five days • 20mg 12 hourly for 5 days • 20mg daily for 11 days
Alternative regimen For patients allergic to Sulfonamides Clindamycin 600-900 mg 6 hourly or 300-450 mg P.O. 6 hourly + Primaquine 15-30mg per day for 21 days.	
Prophylaxis (Primary and Secondary)	
Primary · CD4 <200 cells/mm^3 or CD4 percentage < 14% **Secondary** - Prior PCP infection **Preferred regimen:** · Cotrimoxazole 80/400 mg (SS), 2 tab daily **OR** · Dapsone 100mg daily or 50mg twice daily, if allergic to Cotrimoxazole ***Prophylaxis may be discontinued if the CD4 count is stable at ≥ 200 cells/mm^3 for more than 3 months in response to ART.***	

Candidiasis

- Candidiasis is common in HIV infected host
- Location of the infection can be oral, oesophageal or vaginal.
- Commonly seen in patients with CD4 <200 cells/mm^3.

Table 43: Treatment and Prophylaxis of Oropharyngeal Candidiasis

Treatment
Oropharyngeal Candidiasis: (Duration of Therapy: 7-14 Days) Fluconazole 150 mg PO once daily **Esophageal Candidiasis** (Duration of Therapy: 14- 21 Days) Fluconazole 150 mg (up to 400 mg) PO Or Voriconazole 200 mg BID **Prophylaxis -** not recommended

Cryptococcus neoformans

- Cryptococci are yeast-like fungi which are ubiquitous. The sources of infection are the bats and birds.
- It is the leading cause of meningitis in AIDS patients.
- It can present as acute primary illness or reactivation of previously dormant disease.

Clinical features

- Fever, headache, meningism (stiff neck in <25%), diplopia and mental status changes.
- It can also present as a pulmonary or cutaneous illness.
- Cryptococcus meningitis has a high mortality, the cause of death being raised intracranial pressure (ICP).

Screening

- Screening serum cryptococcal antigen is recommended before initiating or reinitiating ART for adults and adolescents living with HIV who have a CD4 cell count <100 cells/mm3.
- All people with HIV with CD4 <100 cell/mm3 with positive serum cryptococcal antigen should be tested for CSF cryptococcal antigen and undergo MRI brain.

Diagnosis

A) In settings with ready access to and no contraindication for lumbar puncture: if both access to a cryptococcal antigen assay and rapid results (less than 24 hours) are available:

i) Lumbar puncture with rapid CSF cryptococcal antigen assay is the preferred diagnostic approach.

ii) If access to a cryptococcal antigen assay is not available and/or rapid results are not available: Lumbar puncture with CSF India ink test examination is the preferred diagnostic approach.

B. In settings without immediate access to lumbar puncture or when lumbar puncture is clinically contraindicated

i) If both access to a cryptococcal antigen assay and rapid results (less than 24 hours) are available: rapid serum, plasma or whole-blood cryptococcal antigen assays are the preferred diagnostic approaches.

ii) If a cryptococcal antigen assay is not available and/or rapid access to results is not ensured:

- Prompt referral for further investigation and treatment as appropriate.

Table 44: Treatment and Prophylaxis of Cryptococcal Meningitis

Treatment
Cryptococcal Meningitis- Treatment consists of three phases: induction, consolidation and maintenance therapy. **Induction Regimen** (Duration of Therapy: 2 weeks, followed by Consolidation Therapy)– **Preferred regimen -** A single high dose (10 mg/kg) of liposomal amphotericin B with 14 days of flucytosine (100 mg/kg per day divided into four doses per day) and fluconazole (1200 mg/daily for adults; 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily) **Alternative Induction Regimens:** 1. If liposomal amphotericin B is not available: A seven-day course of amphotericin B deoxycholate (1 mg/kg per day) and flucytosine (100 mg/kg per day, divided into four doses per day) followed by seven days of fluconazole (1200 mg daily for adults and 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily). 2. If no amphotericin B formulations are available: 14 days of fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents) + flucytosine (100 mg/kg per day, divided into four doses per day). 3. If flucytosine is not available:

14 days of liposomal amphotericin (3–4 mg/kg per day) + fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily).

4. If liposomal amphotericin B and flucytosine are not available: 14 days of amphotericin B deoxycholate (1 mg/kg per day) + fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily).

Consolidation regimen - Fluconazole (400 - 800 mg daily for adults, 6–12 mg/kg/day for children and adolescents up to a maximum of 800 mg daily) for eight weeks following the induction phase.

Disseminated Cryptococcal Disease - Treatment of disseminated cryptococcal disease other than meningitis (diagnosed by a positive culture of Cryptococcus from blood) should be the same as for meningitis:

Induction regimen: Fluconazole 800 mg/day for two weeks followed by 400 mg/day for eight weeks followed by fluconazole 200-mg/day maintenance therapy.

Maintenance/Prophylaxis

Primary prophylaxis: CD4 cell count <100 cells/mm3

Secondary prophylaxis; Maintenance therapy after treating for cryptococcal meningitis and disseminated infection

Fluconazole (200 mg daily for adults, 6 mg/kg/day for adolescents and children) for a minimum of 1 year duration until immune reconstitution (CD4 >200 cells/mm3) and suppression of viral loads on ART.

Preemptive Fungal Therapy - refer chapter X (prophylaxis and preemptive fungal therapy)

Routine use of adjunctive corticosteroid therapy during the induction phase is not recommended in treating HIV-associated cryptococcal meningitis

Timing of ART
Immediate ART initiation is not recommended in cryptococcal meningitis because of the risk of increased mortality and should be deferred by **4–6 weeks** from the initiation of antifungal treatment.

Histoplasmosis

- Histoplasmosis is an airborne fungal infection.
- Suspect histoplasmosis in patients with fever, lymphadenopathy, hepatosplenomegaly and weight loss. It can also present as gram negative septicemia.

Diagnosis

- Blood and sputum culture are positive in 85% of the cases but it takes two to four weeks.
- Identification of the organism in the clinical specimens- discharges, FNAC.
- Pancytopenia develops due to bone marrow suppression.

Table 45: Treatment and Prophylaxis of Histoplasmosis Co-Infection

Treatment
Induction Therapy Severe to moderately severe histoplasmosis ● Liposomal amphotericin B, 3.0 mg/kg, for two weeks is recommended, then maintenance or secondary prophylaxis ● In settings in which liposomal amphotericin B is unavailable, deoxycholate amphotericin B, 0.7–1.0 mg/kg, is recommended for two weeks, then maintenance therapy Mild to moderate histoplasmosis ● Itraconazole 200 mg TID for three days and then 200 mg BID to continue as maintenance therapy **Histoplasma Meningitis (Duration of therapy: 4-6 weeks)** ● Liposomal amphotericin B 5 mg/kg IV daily
Maintenance Therapy/Secondary Prophylaxis
Itraconazole 200 mg twice daily for 12 months ****Less than 12 months of therapy can be considered when the person is clinically stable, receiving ART, has suppressed viral load and the immune status has improved*
Timing of ART - should be initiated as soon as possible among people with disseminated histoplasmosis for whom central nervous system involvement is not suspected or proven

Talaromycosis (formerly Penicilliosis)

- Talaromycosis is an invasive fungal infection caused by the dimorphic fungus *Talaromyces marneffei* (formerly *Penicillium marneffei*)
- It presents with fever, skin and mucosal lesion. Typical lesions are umbilicated papules with or without central necrosis. Can also present as ulcers, nodules or acne form lesions.
- Causes lymphadenopathy, hepatosplenomegaly, anemia and wasting seen in endemic areas Northern Thailand, Southern China with CD4 count <50 cells/mm3
- The diagnosis is established by the evidence of pathogenic culture, smear, or histopathology most frequent with right stain of skin scraping, node biopsy or marrow aspirate, smear show elliptical yeast, some with the characteristically clear central septation.

Table 46: Treatment of Talaromycosis Co-Infection

Treatment
Induction Therapy Liposomal amphotericin B 3-5 mg/kg/day IV for 2 weeks, followed by **Consolidation Therapy** Itraconazole 200 mg PO twice daily for 10 weeks, then secondary prophylaxis
Maintenance Therapy or Secondary Prophylaxis
• Itraconazole 200 mg PO daily • Stop if CD4 count >100 cells/mm3 for ≥6 months in response to ART

Protozoal infection:

Toxoplasma gondii

- Typically causes multiple CNS lesions and presents with encephalitis and focal neurological signs.
- The disease represents reactivation of previous infection and the serology workup is usually positive.

Often the diagnosis relies on response to empirical treatment as seen by clinical response and reduction in the size of the mass lesion.

Investigation

- MRI of the brain is the best radiographic technique for diagnosis.

Table 47: Treatment and Prophylaxis of Toxoplasma gondii Co-Infection

Treatment
Regimen (Duration of therapy - At least 6 weeks or longer duration if clinical or radiologic disease is extensive or response is incomplete at 6 weeks and then secondary prophylaxis) ● Trimethoprim (5mg/kg) and Sulphamethoxazole (25 mg/kg) P.O. BD **Alternative regimen** ● **Pyrimethamine** (Day 1: 200 mg OD, then, if ≥60 kg: 75 mg OD and < 60 kg: 50 mg OD) plus clindamycin 600 mg IV or PO QID **Other Considerations** ● Dexamethasone if there is evidence of cerebral oedema. ● Anticonvulsant in case of seizures, but not as prophylaxis in all patients.
Maintenance/Prophylaxis Therapy
Primary prophylaxis: Toxoplasma IgG positive with CD4 count <100 cells per mm^3 ● Drug of choice - Cotrimoxazole 480mg, 2 tabs **OD** **Discontinuation of primary prophylaxis:** ● CD4 count >200 cells/mm^3 for more than three months in response to ART **Secondary Prophylaxis** **Discontinuation of secondary prophylaxis** Successfully completed initial therapy, remain asymptomatic of signs and symptoms of toxoplasmosis, and CD4 count>200 cells/mm3 for > 6 months in response to ART ● Drug of choice - Cotrimoxazole 480 mg, 2 tabs BD

Other Protozoal infections:

- Cryptosporidium
- Cyclospora
- *Isospora belli*
- Microsporidia
- Strongyloides

Central nervous system manifestation of HIV/AIDS

CNS infection is common in HIV patients when CD4 count is <100 cells/mm^3. Neurologic complications of AIDS can occur as primary results of HIV, secondary neurologic complications and immunologic complications.

Primary Neurologic Complications of HIV

- Aseptic meningitis
- Chronic meningitis
- Encephalitis
- HIV-associated neurocognitive disorders (HAND), including HIV encephalopathy/AIDS dementia complex
- Polyneuropathy
- Myelopathy

Secondary Neurologic Complications

- Opportunistic infections.
- Secondary neoplasm.
- Vascular disease.

Immunologic Complications

- Acute Inflammatory Demyelinating Polyneuropathy (AIDP)
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- Mononeuritis multiplex

Gastrointestinal Manifestation in HIV/AIDS

Gastrointestinal manifestations used to be very common in patients with HIV/AIDS before the ART era but with the initiation of ART, the manifestations have become less common. HIV related GI disorders can present in many forms.

The GI manifestations include:

- Dysphagia due to oral lesions - thrush, hairy leukoplakia, and aphthous ulcers
- Esophagitis
- Diarrhea with or without abdominal pain
- Anorexia and vomiting
- Colitis
- Chronic diarrheal syndrome

Dysphagia/ Odynophagia

Causes: Candida, CMV, HSV, other fungal infections, TB infection, and drug induced oesophagitis.

Diarrhea

Diarrhea is still a common problem in the era of ART. It is caused by organisms like microsporidium, cryptosporidium, MAC, CMV, *E. histolytica*, *G. lamblia*, *Strongyloides*, *Salmonella, Shigella*, *C. jejuni*, Clostridium species. Idiopathic diarrhea is also common. Cryptosporidia, microsporidia, and Isospora belli are the most common opportunistic protozoa that infect the GI tract and cause diarrhea in HIV-infected patients.

Chronic diarrheal syndrome for which no etiologic agent other than HIV can be identified is known as AIDS enteropathy or HIV enteropathy. It is likely due to the direct result of HIV infection in the GI tract and improves with ART. Patients often have decreased or absent small-bowel lactase and malabsorption with accompanying weight loss.

Diagnosis

- Stool examination including culture and examination for parasites, fungi, protozoa and examination for Clostridium difficile toxin.
- In patients for whom this diagnostic evaluation is non revealing, a presumptive diagnosis of HIV enteropathy can be made if the diarrhea has persisted for >1 month.

Table 48: Treatment of Diarrhea

Treatment
• In acute diarrhea - Depends on suspected etiology • For chronic diarrhea - Depending on the suspected etiology, Cotrimoxazole, quinolones, or Metronidazole and Albendazole may be used. • The initiation of ART alone stops diarrhea in the majority of the cases.

Cutaneous Manifestations of HIV/AIDS

Cutaneous manifestations are very common in HIV/AIDS and have a very broad and diverse spectrum.

Cutaneous manifestation includes:

1. **Viral:** (Acute seroconversion syndrome) - Patients may present with fever, sore throat, cervical lymphadenopathy and erythematous maculopapular eruption. Mucosal involvement and sometimes involvement of palms and soles is seen.

- Exanthema of acute retroviral syndrome - maculopapular rashes seen in acute retroviral syndrome and is self-limiting.
- Chronic herpetic ulcers- usually present as painful orolabial or genital lesions and persist for more than a month.
- Reactivation herpes zoster (shingles) - vesicular eruptions along the nerve distribution can occur in normal CD4 counts.
- Infection with herpes simplex virus is associated with recurrent orolabial, genital, and perianal lesions as part of recurrent reactivation syndromes.
- Oral Hairy Leukoplakia (OHL) is caused by the Epstein Barr Virus (EBV), presents as white, frond-like lesions, generally along the lateral borders of the tongue and sometimes on the adjacent buccal mucosa. Despite its name, oral hairy leukoplakia is not considered a premalignant condition. Severe cases of oral hairy leukoplakia have been reported to respond to topical podophyllin or systemic therapy with anti-herpes agents.
- Molluscumcontagiosum: caused by pox virus. Multiple umbilicated pearly papules which can occur in any part of the body, except the palms and soles. Atypical lesions such as giant molluscum reported in advanced HIV.

2. **Fungal:** Tinea infection and onychomycosis are common in HIV.
    - **Proximal subungual onychomycosis** – is a fungal infection of the proximal nail bed is more specific to HIV.
    - **Oral candidiasis**- *see fungal infections*
    - **Talaromycosis (formerly Penicilliosis)**- *see fungal infections*

3. **Bacterial:**
    - Staphylococcus aureus infections – most common bacterial pathogen in patients with HIV.
    - Syphilis
    - Cutaneous tuberculosis
    - Staphylococcus Aureus infections
    - Impetigo
    - Folliculitis
    - Acne vulgaris

4. **Others:**
    - Eosinophilic pustular folliculitis is a rare form of folliculitis that is seen with increased frequency in patients with HIV infection. It presents as multiple, urticarial perifollicular papules that may coalesce into plaque-like lesions. Skin biopsy reveals an eosinophilic infiltrate of the hair follicle, which in certain cases has been associated with the presence of a mite. Patients typically have an elevated serum IgE level and may respond to treatment with topical anthelmintics.
    - Papular pruritic eruptions (PPE)-common finding in AIDS patients and is also a marker

of HIV infection. It occurs in patients with CD4 <50 cells/mm^3..

5. **Cutaneous drug eruptions**

   Most of the skin reactions are mild and not necessarily an indication to discontinue therapy but some patients may have particularly severe cutaneous reaction like **erythroderma, Stevens-Johnson syndrome, and toxic epidermal necrolysis,** as a reaction to drugs, particularly sulfa drugs, nonnucleoside reverse transcriptase inhibitors, abacavir, amprenavir, darunavir, fosamprenavir, and tipranavir.

Associated Neoplasms:

Kaposi's sarcoma (KS)

- Most closely associated with HIV infection and etiological agent is HHV-8.
- Skin lesions vary from small violaceous papules to plaques to large ulcerated nodules. Skin and mucosa are both affected.
- Lymph nodes are commonly affected with systemic involvement (the GI tract and lungs)

Treatment

Local therapy with liquid nitrogen or intra-lesional injection with alitretenoin or vinblastine has been used. Radiation may be useful as well. Systemic therapy involves chemotherapy (e.g. liposomal doxorubicin, paclitaxel, liposomal daunorubicin, thalidomide, retinoids), radiation, and interferon α.

Lymphoma

- Lymphomas commonly associated with AIDS are non-Hodgkin's lymphoma B cell type. Extra nodal involvement especially CNS, intestine and skin are common.
- EBV appears to be the associated virus in half the patients.

Cervical and peri-anal neoplasm

- Both HIV infected men and women are at high risk for human papillomavirus-related disease.
- Certain human papilloma virus subtypes, such as 16 & 18 are oncogenic.
- Cancer can also arise from peri-anal condyloma accuminata.
- HPV screening for PLHIV should begin at 25 years of age and if the initial HPV screening is negative, subsequent screening should be done every three years.
- If the person has not received HPV vaccination in the past, HPV vaccination should be given with 3 doses at 0,2 and 6 months.

CHAPTER XIII

ADHERENCE

Key Points

- Each patient commencing ART needs to be prepared for taking lifelong ART.
- Barriers to adherence and any misconceptions about HIV and ART must be identified.
- Patients must be educated about the importance of viral load suppression.

Definition

Adherence was defined for the first time as an *extent to which a patient's behavior coincides with medical/health advice*. Subsequently it was defined as *the extent to which the patients continue with an agreed mode of treatment*.

Adherence to ART has been correlated strongly with HIV viral suppression, reduced rates of resistance, an increase in survival, and improved quality of life. A low adherence is strongly associated with detectable viremia, progression to AIDS and death. Because HIV treatment is a lifelong endeavor, and because many patients will initiate therapy when they are generally in good health, feel well, and demonstrate no obvious signs or symptoms of HIV disease, adherence poses a special challenge and requires commitment from the patient and the health care team.

Some of the factors associated with poor adherence are:

- Lack of patient education
- Poor patient and clinician relationship
- Stigma and discrimination against the patient and their families
- Alcohol and substance abuse
- Mental depression/low mood
- Fear of disclosure
- Adverse events related to drugs
- Inability of the patient to identify their medications
- Being too ill

How to improve adherence?
The health worker must be prepared to assess the patient’s readiness to adhere, offer advice and monitor progress at every contact.

In order to improve adherence, health care provider must:

- share the benefits of ART
- give written instructions about the drugs prescribed in the manner that the patient understands
- explain the possible side effects about the medicines including what to do and who to contact if serious side-effects occur
- explain the importance of viral load monitoring on ART and viral load suppression
- reinforce regular follow up visits
- encourage and show hope
- seek peer support of peer educators on treatment known as "expert patient" and community treatment groups if any exists.

How to assess adherence?

Simplify regimens, dosing and food requirement, e.g.

- take every 12 hours, not as B.D.
- What time do you take the medicines normally?
- with meals or without meals
- Any dose missed or delayed in the last one to two weeks
- concomitant medication(s)
- Physical inspection of remaining drugs of the patient and reinforcing the ideal manner in which ART is to be administered.

CHAPTER XIV

MANAGEMENT OF PEOPLE LIVING WITH HIV/AIDS AT ALL LEVELS OF HEALTH FACILITY

Key Points

- All levels of the health care delivery systems in Bhutan including PHCs, 10 bedded hospitals, district hospitals and referral hospitals contribute to the management and treatment of people living with HIV/AIDS and work in close coordination in providing comprehensive care and support services

All levels of the health care delivery system in Bhutan can contribute to the management and treatment of people living with HIV/AIDS. The Primary Health Centres, 10 bedded hospitals, district hospitals and referral hospitals should work in close coordination in providing comprehensive care and support services

HIV care treatment team

The HIV care treatment team should take the lead role at the hospitals to ensure the continued support and care. The HIV positive people should be informed about the team and the responsibilities of each other. The team will be provided with 10 days of training on stigma and discrimination which was developed recently based on the findings of Community Led Monitoring (CLM). This helps in building the confidence among the people and reduces the stigma and minimizes discriminatory experiences in the health setting.

The membership of the teams should be left to the local decision to appoint most appropriate staff. The following are the components of the core team and their respective responsibilities at the hospital level:

1. Medical Officer (MO)

Responsibility: The Medical Officer will be overall in charge and delegate responsibilities to his/her subordinates and identify focal persons in the hospital. The trained medical officer can offer HIV tests to people who walk in as a client or patient. The MO is also responsible for reporting collective data to the national program.

2. Laboratory:

Responsibility: The laboratory will be responsible for doing tests and record keeping.

3. Pharmacy:

Responsibility: The Pharmacy will be responsible for antiretroviral treatment, ARV indenting and stock keeping, record keeping and reporting.

4. Ward In charges (Indoor)

Responsibility: The ward in charge will be responsible for care and support to the HIV positive people admitted, record keeping and reporting.

5. Community Health Unit

Responsibility: One of the active Health Assistant (HA) working in Community Health Unit (CHU) should be nominated as VCT Focal Person in every Hospital. He is responsible for providing pre-test/post-test counseling and testing to walk-in clients, follow up treatment, conduct advocacy and keep the records.

The following briefly outlines the scope of care and treatment at each level of health care system:

At Primary Health Centre

If found reactive, arrange to transfer the sample or refer the patient to the nearest hospital where the arrangement can be made for transferring the samples for confirmation.

a). Patient suspected with HIV/AIDS

If the patient is suspected with HIV/AIDS, perform a rapid test after proper counseling. If the testing facilities are not available and patient suspected suffering from HIV/AIDS based on sign and symptoms make arrangement for referral of patient to the hospital

b) Patient already diagnosed to have HIV infection but without signs of AIDS and not on ART

- Immediately refer the patient to the nearest hospital upon contacting the HCT focal person (patient need to put on ART)
- Provide routine treatment adherence counseling
- Follow up closely (at least three months) and advice on healthy living
- Counsel for safe sex practice and correct and consistent use of condoms

If there are any signs of drug interactions or toxicities, discuss with doctors and if severe refer to the nearest hospital.

- If a patient is co-infected with other opportunistic infections, refer the patient to the nearest health center upon contacting the concerned HCT focal person.
- Transfer the patient record to the district hospital (HCT focal person)

c) Patient is on ART and OI prophylaxis

- Visit or call the patient to the nearest PHC whenever necessary
- Ensure the patient's adherence to treatment
- Ensure the patient gets his/her regular medications
- Ensure that the patient takes the medications at the right interval
- Counsel and educate the patient about safe se
- Record and report to CST, JDWNRH as per the required schedule

Refer the patient to the District Hospital if there are signs of:

- Drug intolerance/toxicity
- Jaundice
- Losing weight despite treatment

At District Hospitals (DH) or hospitals:

a) Patient not on ART:

- Do laboratory examination including CD4 count and viral load
- Provide proper treatment literacy to the patient (to be executed by the HCT (focal)
- Continue to carry out contact tracing
- Voluntary counseling and testing (VCT) of the sexual partners/contacts

b) Patient already on ART

- Follow the PHC procedures
- Look for evidence of drug intolerance /toxicity
- Refer the patient for CD4 count whenever necessary.

At Regional/National Referral Hospital:

- Reconfirm the diagnosis
- Screen for OIs
- Carry out relevant investigations, including CD4 count/Viral load
- Patients are started on OI prophylaxis or ART depending on the CD4+T cell count.
- Review the patient after two weeks of starting ART for side effects
- Review the patient after four weeks of starting ART to monitor side effects and to reinforce adherence.
- After initiating ART, the patient can be sent back to the hospital with an instruction to send the blood sample for CD4 cell count and viral load every six months thereafter.

Care Support & Treatment Unit at JDWNRH
Roles and Responsibilities:

The care support & Treatment Unit at JDWNRH will serve as the nodal unit to coordinate care and treatment of PLHIV across the country. It is set up mainly to ensure better coordination as well as ensure continuous health services of the PLHIV. Its main responsibilities are:

1. Liaising with public health laboratory to ensure confirmatory test of reactive samples from districts are done timely and results communicated to the districts
2. Assign unique identification code for newly confirmed HIV positive and enter record in the database
3. Advice and guide delivery of positive results to the clients by the counselors in the fields
4. Ensure appropriate recording and reporting of HIV case details
5. Ensure timely and regular reporting on HIV case follow up to the CST by the districts
6. Ensure timely CD4 count and viral load are dome
7. Coordinate with the pharmacy unit, JDWNRH to ensure the patient is enroll to ART or ARV supplied to the health Center
8. Update and maintain PLHIV data in the database
9. Report the new HIV update to the national program every six monthly

Reference

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3. British HIV association. BHIVA guidelines on antiretroviral treatment for adults living with HIV-1. 2022. Available at: https://www.bhiva.org/file/63513a1745ea9/BHIVA-guidelines-on-antiretroviral-treatment-for-adults-living-with-HIV-1-2022.pdf

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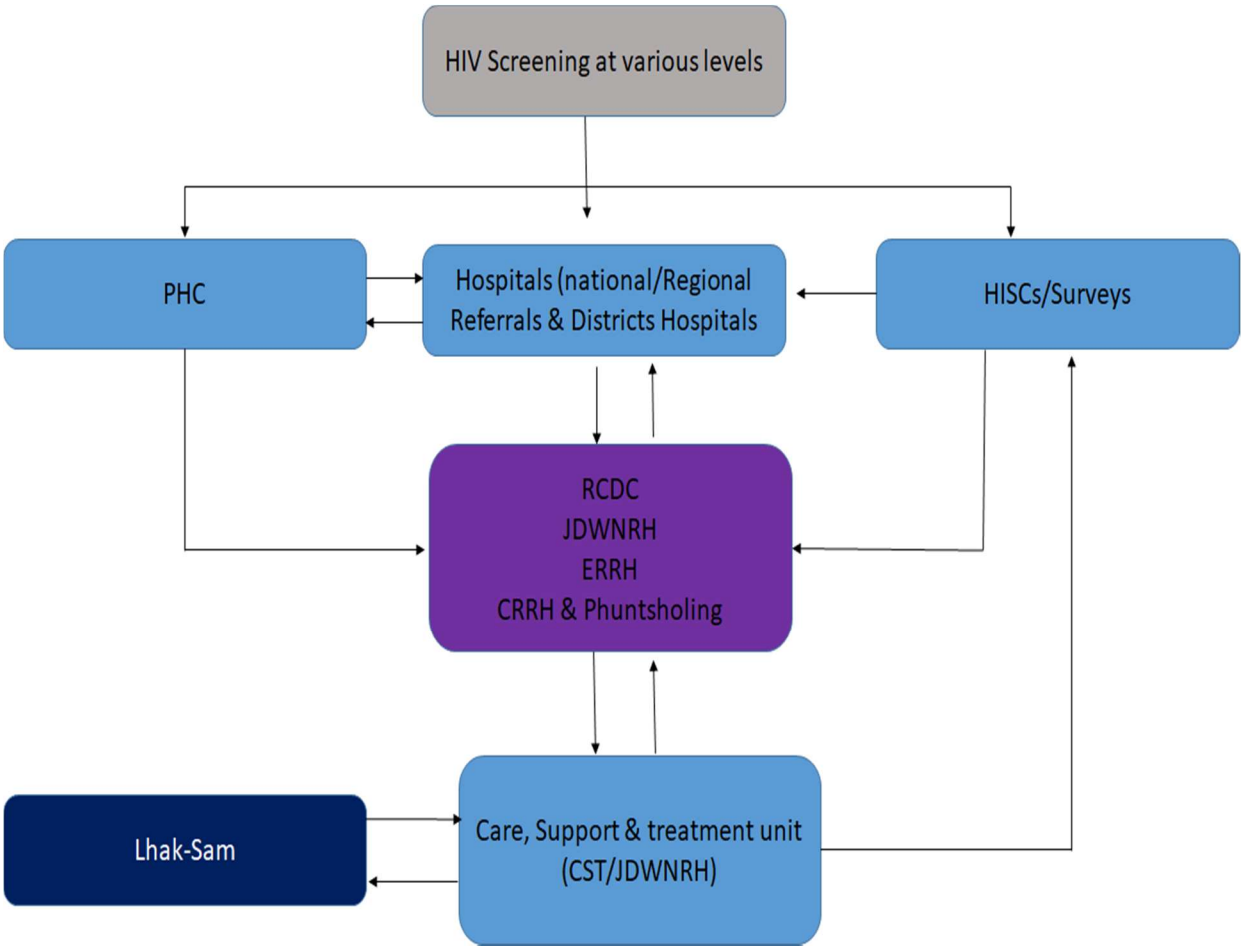
Annexures

Annex 1. Cascade of HIV care in Bhutan

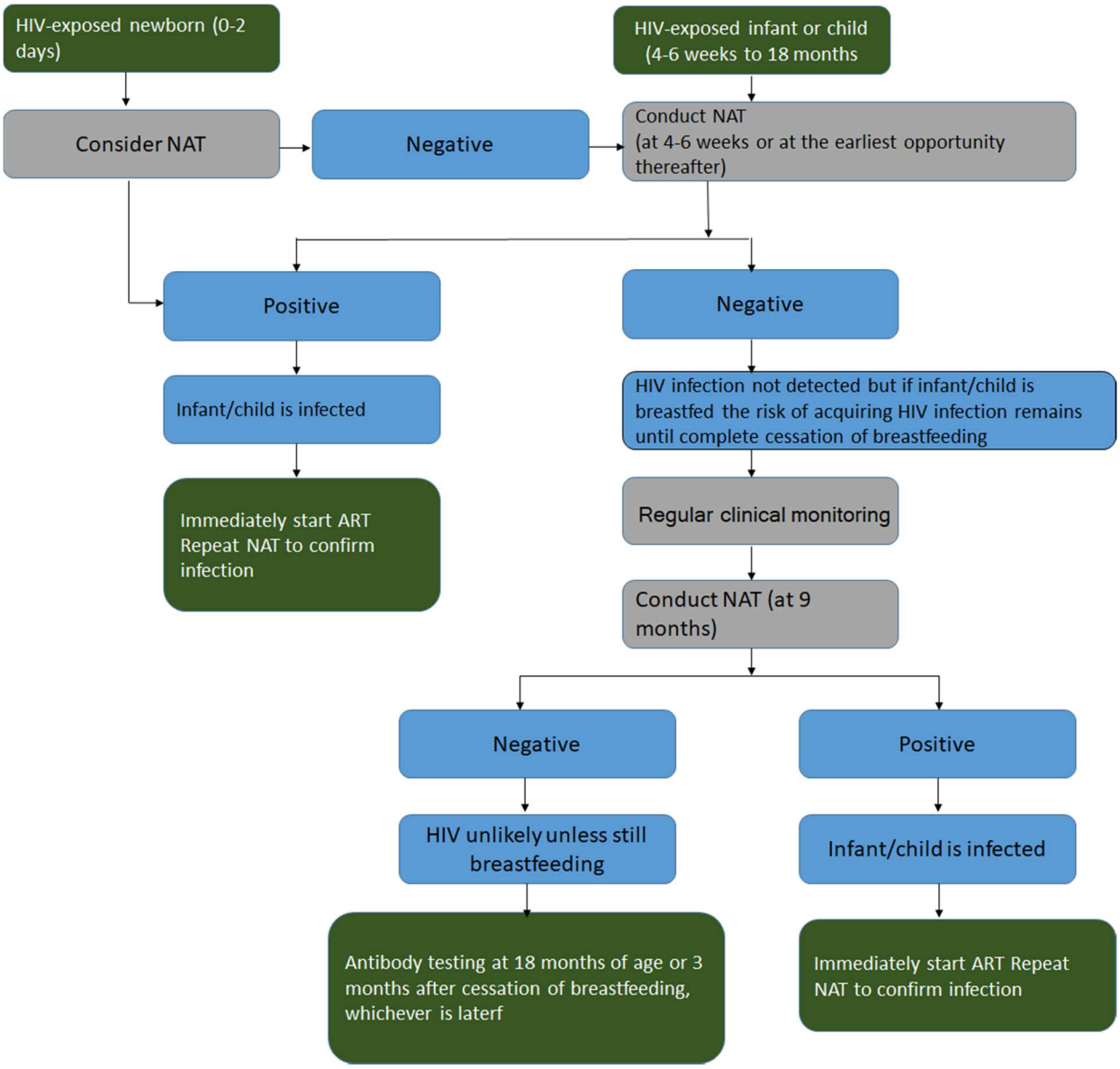


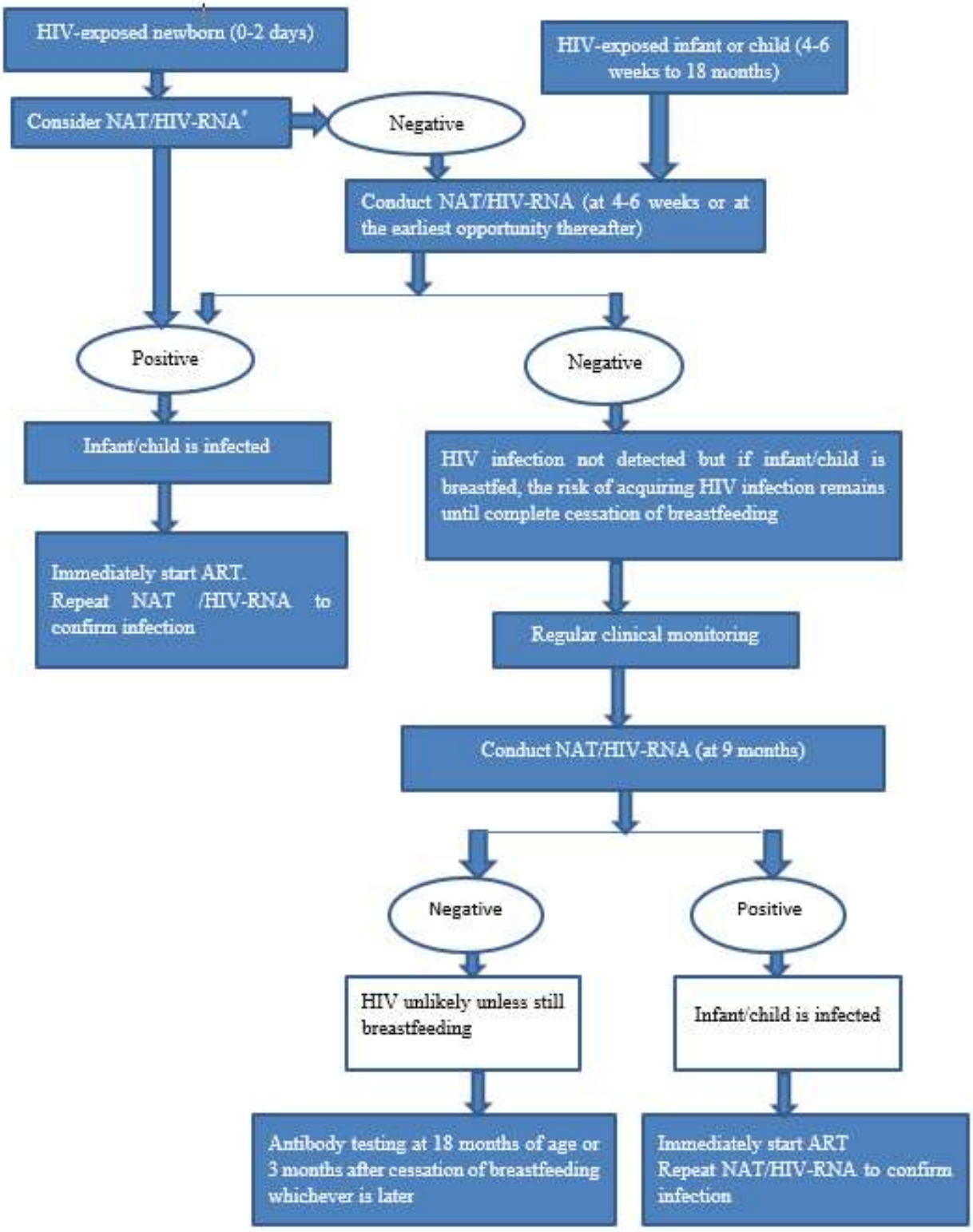
Annexure II: WHO clinical staging of HIV disease in adults, adolescents and children

Adults and adolescents	Children
Clinical Stage 1	
Asymptomatic Persistent generalized lymphadenopathy	Asymptomatic Persistent generalized lymphadenopathy
Clinical Stage 2	
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 infection Seborrheic dermatitis	Unexplained persistent hepatosplenomegaly Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) Herpes zoster Lineal ginigival erythema Recurrent oral ulceration Papular pruritic eruption Fungal nail infection Extensive wart virus infection Extensive molluscum contagiosum Unexplained persistent parotid enlargement
Clinical Stage 3	
Unexplained severe weight loss (>10% of presumed or measured body weight) Unexplained chronic diarrhea for more than 1 month Unexplained persistent fever (intermittent or consistent for longer than 1 month) Persistent oral candidiasis Oral hairy leukoplakia Pulmonary tuberculosis Severe bacterial infections (such as pneumonia, empyema, pyomyosistis, bone or joint infection, meningitis, bacteraemia) Acute necrotizing ulcerative stomatitis gingivitis or periodontitis Unexplained anaemia (<8g/dL), neutropenia ($0.5x10^9$/L) and/or chronic thrombocytopenia (<$50x10^9$/L)	Unexplained moderate malnutrition but not adequately responding to standard therapy Unexplained persistent diarrhea (14 days or more) Unexplained persistent fever (above 37.5°C, intermittent or consistent for longer than 1 month) Persistent oral candidiasis (after first 6 weeks of life) Oral hairy leukoplakia Lymph node tuberculosis Pulmonary tuberculosis Severe recurrent bacterial pneumonia Acute necrotizing ulcerative gingivitis or periodontitis

	Unexplained anaemia (<8g/dL), neutropenia ($0.5x10^9$/L) and/or chronic thrombocytopenia (<$50x10^9$/L) Symptomatic lymphoid intestinal pneumonitis Chronic HIV-associated lung disease including bronchiectasis
Clinical Stage 4	
HIV wasting syndrome Pneumocystis (jirovecii) Recurrent severe bacterial pneumonia Chronic herpes simplex infection (orolabial, 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 nontuberculous mycobacterial infection Progressive multifocal leukoencephalopathy Chronic cryptosporidiosis Chronic isosporiasis Disseminated mycosis (extrapulmonary Histoplamosis, coccidioidomycosis) Lymphoma (Cerebral or B-cell non-Hodgkin) Symptomatic HIV-associated nephropathy or cardiomyopathy Recurrent septicaemia (including nontyphoidal Salmonella) Invasive cervical carcinoma Atypical disseminated leishmaniasis	

Annexure III: Algorithm for Early Infant Diagnosis (WHO, 2018)





**if HIV DNA then the first test will be done at 2 weeks (not at birth).*

HIV Care and Follow up Form

1. Patient Identification

Patient ID Code

Name: _____ DOB: _____

Age: _____ Sex: [ ] Male [ ] Female [ ] Transwoman [ ] Transman

CID no._____

Nationality (please tick)

☐ Bhutanese
☐ Non-Bhutanese

Local Address: Village…….. Gewog…….. Dzongkhag…….

Permanent Address: Village…….. Gewog…….. Dzongkhag…….

Contact number: _____

Date confirmed HIV+ test: _____ Place: _____

2. Entry point (Reasons for HIV testing):

☐ HCT
☐ ANC
☐ TB
☐ MTCT
☐ STI
☐ Blood donor
☐ Clinical Symptoms,
☐ Medical screening
☐ Contact tracing,
☐ Screening for surgery/Medical procedures,
☐ Others Specify……..

3. Personal History:

Risk factors for HIV infection:

☐ Heterosexual
☐ MSM
☐ IDUs
☐ Blood Transfusion
☐ Mother-to-Child
☐ Others Specify……

4. Family History at the start:

a) Marital status:

☐ Single
☐ Married/Living
☐ Divorce/separate
☐ Widowed
☐ Others……

b) Family members/partners/children Status

Member	**Age/Sex**	**HIV status**	**ART status**	**Reg No**

5. Education level:

Education Level (*Please check)*	
No education	
Non-Formal Education (NFE)	
Primary (Cl PP-VI)	
Lower Secondary (Cl VII-VIII)	
Middle Secondary (Cl IX-X)	
Higher Secondary (Cl XI-XII)	

Tertiary (Degree & above)	
Monastic education	
Others…Specify…….	

6. Occupations:

Occupations *(Please check)*	
Civil servant	
Govt (GSP/ESP)	
Autonomous Agencies	
Non-Government Organizations	
Monks	
Gomchen/lay monks	
Nuns	
RBA	
RBP	
RBG	
Private security	
Farmer	
Tourism	
Private Organization	
Independent Business	
Truckers	
Taxi Drivers	
Public Transport Drivers	
Private Drivers	
Housewives/Home maker	
Maids/Maid/Domestic Helper	

Unemployed	
Sex workers	
Entertainment bars/Karaoke	
College student	
School student	
Vocational Trainee	
Institute Trainee	
Institute Trainee	
National Labours	
Migrant Workers	
Prisoners	
Migrant Workers	
Prisoner	
Other Specify	

7. Risk assessment						
7.a Presence of risk factors						
1. Did you ever have sexual contacts with a male?	Yes		No		Unknown	
2. Did you ever have sexual contacts with a female?	Yes		No		Unknown	
3. Did you ever have sexual contacts with a transgender person?	Yes		No		Unknown	
4. Did you ever inject any drugs not prescribed by a physician?	Yes		No		Unknown	
5. Did you ever receive blood or blood products transfusion or transplant?	Yes		No		Unknown	
6. Did you ever have any invasive surgical procedures?	Yes		No		Unknown	
7. Did you ever have intentional skin penetration (e.g. tattoo, scarring, traditional healer)?	Yes		No		Unknown	
7.b If heterosexual contact was reported:						
1. Did you ever had heterosexual contact with HIV-infected person?	Yes		No		Unknown	
2. Did you ever provide sexual services for money, gifts or any other kind of remuneration?	Yes		No		Unknown	
3. Did you ever have heterosexual contact with a person who injects drugs?	Yes		No		Unknown	
4. Did you ever had heterosexual contact with bisexual male?	Yes		No		Unknown	
5. Did you ever have heterosexual contact with sex worker or client of sex worker?	Yes		No		Unknown	

8. Baseline Laboratory Test Information				
Day	**Month**	**Year**	**Test**	**Count/Result**
			CBC	
			LFT	
			RFT	
			CD4	
			Viral Load	
			EID	
			RPR/TPHA	
			Hepatitis B	
			Hepatitis C	

9. Antiretroviral/prophylaxis treatment initiation Information

Treatment start Date……. Regimens…….

Place of initiation…….. Septran Prophylaxis Date: ……
TPT prophylaxis Date……

10. Tuberculosis treatment during HIV care		
Disease class (tick) Pulmonary TB [ ] Smear-positive [ ] Smear-negative [ ] Extrapulmonary [ ] Site:…… Past history of TB [ ]	**Regime**(tick) New treatment[ ] Retreatment[ ] MDR [ ] Date start TB Rx:…….	**TB registration** District:_____ Health Centre: _____ TB number: _____ Treatment outcome: Cure [ ] Rx completed [ ] Rx failure[ ] Died [ ] Default [ ] Transfer out [ ] Date:…….

11. Antiretroviral treatment follows up:

1. **Continue with the same drugs……Yes/No……**
2. **Switch to others……. If Yes regimens name……**

Reasons for switch/substitutes:	
Toxicity side effects,	
Change of new guidelines	
Drug out of stock,	
Clinical treatment failure,	
Immunological failures,	
Virologic failures	
Other Specify	

Opportunistic Infection:
Enter one or more codes –

- ☐ Tuberculosis (TB);
- ☐ Candidiasis (C);
- ☐ Diarrhea (D);
- ☐ Cryptococcal meningitis (M);
- ☐ Pneumocystis Carinii Pneumonia (PCP);
- ☐ Cytomegalovirus disease (CMV);
- ☐ Penicilloic (P);
- ☐ Herpes zoster (Z);
- ☐ Genital herpes (H);
- ☐ Toxoplasmosis (T);
- ☐ Other-specify

Drugs prescribed for prophylaxis of OIs……

Adherence:
>95% = < 3 doses missed in a period of 30 days;
80-95% = 3 to 12 doses missed in a period of 30 days;
< 80% = >12 doses missed in a period of 30 days

ART side effects *(Please check)*:

Skin Rashes	
Nausea	
Vomiting	
Diarrhea	
Neuropathy	
Jaundice	
Anemia	
Fatigue	
Headache	
Fever	
Hypersensitivity	
Depression	
Pancreatitis	
Lipodystrophy	
Other specify	

12. Reasons for stopping follow-up

Death Date of death: _____

Lost to follow-up (>3 months) Date last visit: _____

Transferred out Date: _____

New clinic: _____

ART Follow-up									
	Lab Results					Prophylaxis		TB screening	Next Visit
No.of ART Issued	LFT	RFT	CD4	CBC	VL	CPT	TPT		

Annexure 4: CD4 Count Request Form

Patient ID code:

Age/sex: _____

Name of Health Center: _____

Date / time of collection_____ Collected by: _____

Date / time of sample transfer_____

Contact No: _____

Email ID:_____

Received date / time_____

NOTE: Sample should reach the CD4 center within 48 hrs without ice pack.

Annexure VII: SAMPLE REFERRAL FORM

HIV Viral Load Testing

Name of the Health Center:…….

Dzongkhag/District: ……..

Sample No:	**Patient TP #:**	**Age/Sex:**
	Name:	**Lab. No:**

Collection date and time:……

Sample Referred by:

Name of Lab/HISC/VCT personnel:……

Contact #.....

Signature:……

Date:……

Note: Sample to be shipped to Serology section, Microbiology Unit, JDWNRH

Annexure IX: INDEX PATIENT INFORMATION FORM

Instructions: Complete this form while interviewing the HIV-positive index client who has verbally agreed to receive index partner testing or partner notification services.

***Complete one form per index client**
Date form completed (dd/mm/yyyy: _____ / _____ / _____
Name of person completing form: _____
Name of health facility or HIV testing site: _____

INFORMATION ABOUT THE INDEX CLIENT OR PATIENT

Index client's name (last, first, middle):_____
DOB: (dd/mm/yyyy):_____ Age: _____yrs

Gender:
♦ Male ♦ Female ♦ Transgender (Male to Female) ♦ Transgender (Female to Male)
Marital status:
♦ Single ♦ Engaged to be married ♦ Married/cohabiting-monogamous ♦ Divorced ♦ Widow/er ♦ Married-polygamous: # wives _____ # husbands_____

Client's

Contact number:_____

Alternate contact number (if available): _____

Present address:

- **Name of village/town_____**
- **District_____**

Permanent address

1. **Village_____**
2. **Gewog _____**
3. **District_____**

Date of HIV diagnosis: (dd/mm/yyyy): _____

Is the index client currently enrolled in an HIV treatment program?

♦ Yes ♦ No If yes, name of health facility _____

If yes, list the index client's TPN number: _____

For women: How many children age 18 or under does the index client have?
_____ # children age 18 and under.

Annexure X: PARTNER INFORMATION FORM
*Complete one form for each partner named by the index client.

Instructions: Ask the client to give you as much information as they can about each of the partners, they named on the partner elicitation form. Write "N/A" for any information not available. After completing a separate form for each contact, file all completed forms in the client's folder or medical chart. Be sure to observe measures to maintain confidentiality of this information.

Partner's name (last, first, middle): _____
Partner's nickname: _____
Partner's DOB (dd/mm/yyyy): _____ Partner's age: _____ yrs.
Partner's gender: ♦ Male ♦ Female ♦ Transgender Partner's physical description:
_____

Partner's address

Present address:

- Town/village:_____
- Districts:_____

Permanent address

- Village:_____
- Gewog:_____
- District:_____

How would you describe your relationship to this partner?

♦ My wife/husband/fiancée

♦ We live together but are not married

♦ My girlfriend/boyfriend

♦ Someone I had casual sex

♦ Someone who pays me or gives me things to have sex with her/him

♦ Someone I paid to have sex with

Do you currently live with this partner?

♦ Yes ♦ No ♦ Declines to answer

As far as you know, has this partner ever tested positive for HIV?

♦Yes ♦ No ♦ Don't know ♦ Declines to answer

If known HIV-positive partner: is this partner currently taking medications for HIV?

♦ Yes ♦ No ♦ Don't know ♦ Declines to answer

Annexure XII. INTIMATE PARTNER VIOLENCE SCREENING TOOL

SCREENING TOOL FOR INTIMATE PARTNER VIOLENCE Use this screening tool for all clients or patients who participate in Partner Notification (PN) services. Use one form for each partner identified by the client or patient. If the client or patient responds "yes" to any of these questions, consider options for PN that the index patient or client feels safe to use. Figure 3 on page 12 of this document illustrates a method to decide on PN methods based on the response to the intimate partner violence screening tool. Please state to the client or patient: Because your safety is very important to us, we ask all clients the following questions:

1. Has [partner's name] ever hit, kicked, slapped, or otherwise physically hurt you?

♦ Yes ♦ No

2. Has [partner's name] ever threatened to hurt you?

♦ Yes ♦ No

3. Has [partner's name] ever forced you to do something sexually that made you feel uncomfortable?

♦ Yes ♦ No

4. Has [partner's name] ever threatened you in other ways, such as divorce, desertion, lack of support, taking away access to your children, or other threats?

♦ Yes ♦ No

Annexure XIII. OPTIONS AND PLAN FOR PARTNER TESTING

DECIDE ON A PLAN FOR PARTNER TESTING

Instructions: Show the "Options for Getting Your Partner Tested" card to the index client or read this to them if there are any challenges with literacy. Review the three options. Ask the client which option they would prefer and record their chosen option below. If the client

chooses “contract referral,” record the date (30 days from today’s date) by which the partner should come for HIV testing services. s INDEX

CLIENT’S PLAN FOR NOTIFYING THIS PARTNER:

♦ Client Referral: Index client will notify partner.

♦ Provider Referral: Health care providers will notify the partner.

♦ Contract Referral: Both the index client and health care provider will notify the partner. The index client will first t y notifying the partner no later than _____/ _____ / _____ . After which the provider will contact the partner (with permission from the index client).

♦ No partner testing needed; partner is known positive.

♦ Partner testing is not recommended at this time due to safety concerns.

National HIV/AIDS & STIs Contorl Program
Department of Public Health
Ministry of Health

nacp@health.gov.bt

World Health Organization
Bhutan