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Oman Vision

وزارة الصحة
Ministry of Health

HIV Management in Oman

A guide for healthcare workers

Fourth Edition

June 2025

Center for Disease Control and Prevention
Department of Communicable Diseases
HIV/STI &Hepatitis Section

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Acknowledgement

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Message from the Ministry of Health

The fourth edition of HIV Management in Oman, a guide for healthcare workers, presents a significant step forward in Oman's national response to Human Immunodeficiency Virus (HIV) and our continued commitment to safeguarding the health and well-being of our nation.

The guide consolidates best evidence-based practices, global recommendations and the experiences of healthcare providers to ensure that all People Living with HIV or at risk of acquiring HIV are receiving a timely, effective and compassionate care.

The Ministry of Health in Oman has worked closely with national experts in developing this guide. The result is a comprehensive document that will support clinicians, health workers and program managers across all levels of the healthcare system. It aims to enhance the quality of HIV prevention, testing, treatment and support services, while promoting equity, confidentiality and respect for human dignity.

Oman has made remarkable progress in controlling the HIV epidemic. In 2022, the Sultanate became the first country in the Eastern Mediterranean Region to be validated by the World Health Organization for the elimination of mother-to-child transmission of both HIV and syphilis—a testament to our sustained investment in maternal and child health, robust surveillance systems and equitable access to healthcare services. However, we must remain vigilant. This guide is part of a broader national strategy to reduce new infections, eliminate stigma and discrimination and ensure that no one is left behind in our healthcare system.

As we continue to work toward the ambitious goals outlined in Oman Vision 2040, we reinforce our national values of inclusivity, sustainability and human dignity. Vision 2040 places health and well-being at the center of development, and this guide contributes directly to that vision by ensuring that individuals living with, affected by, or at risk of HIV receive the services they need with no stigmatization or discrimination.

Healthcare professionals in Oman are encouraged to use this guide as a cornerstone in their efforts to protect lives and promote wellness across the Sultanate of Oman.

Together, let us continue to uphold our responsibility to deliver quality healthcare to all people living with HIV, guided by knowledge, compassion and a commitment to public health excellence.

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Acronyms

ABC	Abacavir
ADI	Antibody differentiation immunoassay
Ag/Ab	Antigen/antibody
AIDS	Acquired immunodeficiency syndrome
Anti-HBc	Hepatitis B core antibody
Anti-HBs	Hepatitis B surface antibody
ART	Antiretroviral therapy
ARV	Antiretroviral
ATV	Atazanavir
AZT	Zidovudine
BIC	Bictegravir
BID	Twice daily
c	Cobicistat
CAB	Cabotegravir
CAB-LA	Long acting injectable cabotegravir
CBC	Complete blood count
CDC	Centers for Disease Control and Prevention
CD4	Cluster of differentiation 4
CLIAs	Chemiluminescent immunoassays
CMV	Cytomegalovirus
CNS	Central nervous system
CPHL	Central Public Health Laboratory
CrCl	Creatinine clearance
CYP	Cytochrome P450
DNA	Deoxyribonucleic acid
DOR	Doravirine
DRV	Darunavir
DTG	Dolutegravir
EDTA	Ethylenediaminetetraacetic acid
EFV	Efavirenz
EIA	Enzyme immunosorbent assay
ELISA	Enzyme-linked immunosorbent assay
ETR	Etravirine
FDA	Food and Drug Administration
FTC	Emtricitabine
HBeAg	Hepatitis B e antigen
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IGRA	Interferon-Gamma Release Assay
INSTI	Integrase strand transfer inhibitor

HAV	Hepatitis A virus
HCV	Hepatitis C virus
HDV	Hepatitis Delta Virus
HIV	Human immunodeficiency virus
HIV-1	Human immunodeficiency virus type 1
HIV-2	Human immunodeficiency virus type 2
HLA	Human leukocyte antigen
HSV	Herpes simplex virus
HTC	HIV testing and counseling
LA	Long-acting
LPV	Lopinavir
MENA	Middle East & North Africa
MVC	Maraviroc
Mg	Milligram
MOH	Ministry of Health
MSM	Men who have sex with men
NAATs	Nucleic Acid Amplification Tests
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside/nucleotide reverse transcriptase inhibitor
NVP	Nevirapine
OIs	Opportunistic infections
PCP	Pneumocystis carinii pneumonia
PCR	Polymerase chain reaction
PWID	People who inject drugs
PI	Protease inhibitor
PI/c	Cobicistat-boosted protease inhibitor
PI/r	Ritonavir-boosted protease inhibitor
PJP	Pneumocystis jirovecii pneumonia
PK	Pharmacokinetic
PLHIV	People living with HIV
PPI	Proton pump inhibitor
PR	Protease
PrEP	Pre-exposure prophylaxis
r	Ritonavir
RDTs	Rapid Diagnostic Tests
RAL	Raltegravir
RNA	Ribonucleic acid
RPR	Rapid plasma reagin
RPV	Rilpivirine
RTV	Ritonavir
STIs	Sexually transmitted infections
STR	Single-tablet regimen
TB	Tuberculosis

3TC	Lamivudine
TAF	Tenofovir alafenamide
TDF	Tenofovir disoproxil fumarate
VCT	Voluntary counseling and testing
VDRL	Venereal disease research laboratory
WB	Western blot
WHO	World Health Organization
ZDV	Zidovudine

1

Chapter 1: Introduction

Chapter 1: Introduction

1.1 Introduction

Human Immunodeficiency Virus (HIV) remains a significant public health concern globally, including in Oman. While the country has a relatively low prevalence of HIV, early detection, timely treatment, and comprehensive care are essential for controlling transmission and improving patient outcomes. Stigma and limited awareness among healthcare providers pose challenges to effective management, highlighting the need for clear, evidence-based guidelines.

1.2 Purpose of the guideline

This guideline has been developed to provide a standardized framework for healthcare workers in Oman, to manage and treat people living with HIV (PLHIV). By aligning with international best practices and national health priorities, the guideline aims to ensure consistent, high-quality care while addressing country-specific challenges and requirements. This updated 4th edition of the national HIV guidelines introduces several key revisions. Notably, it includes updated recommendations on first-line antiretroviral therapy (ART), highlighting the use of second-generation integrase inhibitors. It also revises the HIV viral load threshold for considering vaginal delivery, re-emphasizes the importance of intravenous zidovudine (AZT) during labour when indicated, and incorporates guidance on the use of pre-exposure prophylaxis (PrEP). Additionally, routine screening for anxiety and depression is now recommended as part of comprehensive HIV care.

1.3 Objectives and expected outcomes

The primary objectives of this guideline are:

- To enhance early detection and accurate diagnosis of HIV.
- To ensure timely initiation and adherence to antiretroviral therapy (ART).
- To improve the quality of life and health outcomes for PLHIV.
- To reduce HIV-related stigma and discrimination in the community and within healthcare settings.
- To support prevention strategies, including pre-exposure prophylaxis (PrEP).
- To strengthen healthcare workers' knowledge and capacity in HIV management.

Expected outcomes include improved patient retention in care, reduced HIV-related morbidity and mortality, and enhanced public health measures to curb transmission.

1.4 Scope

This guideline applies to all healthcare professionals involved in the diagnosis, treatment and care of individuals living with HIV in Oman. It is intended for use by a wide range of providers, including primary healthcare practitioners, non-HIV specialists in secondary and tertiary care, as well as dedicated HIV care teams—such as HIV/infectious disease physicians, pharmacists, clinical nurses, social workers, and counselors.

1.5 Structure

The guideline is structured into the following sections:

1. Epidemiology – Overview of HIV prevalence and epidemiology.
2. Screening and Diagnosis – Best practices for HIV testing and diagnosis.
3. Clinical Management – ART initiation, monitoring, and management of 7treatment failure.
4. Prevention Strategies – Prevention of mother-to-child transmission (PMTCT), PrEP, post-exposure prophylaxis (PEP), and prevention of opportunistic infections.
5. Psychosocial and Support Services – Addressing mental health, stigma, and patient support systems.

This guideline serves as a practical resource to ensure that all healthcare workers in Oman are equipped with the necessary knowledge and tools to provide optimal care for individuals living with HIV.

2

Chapter 2: Methods

2.1 Methods and procedures for guideline development

Chapter 2: Methods

2.1 Methods and procedures for guideline development

The development of these guidelines followed a structured and collaborative process to ensure alignment with national policies and international best practices. A Guidelines Writing Group was formed, comprising experts in adult infectious diseases, pediatric infectious diseases, obstetrics, public health, and laboratory medicine.The writing process began with an initial meeting in October 2024, where key objectives and content areas were identified.

- Draft chapters were developed by contributing authors from various specialties.
- Two senior experts edited the chapters to ensure coherence, accuracy, and consistency.
- To ensure a comprehensive and collaborative approach, the Guidelines Writing Group held multiple meetings at key stages of development.
- To maintain consensus and quality in guideline development, the following mechanisms were implemented to resolve disputes and differing opinions:
    - Expert Panel Discussions – In cases of conflicting recommendations, the writing group consulted a panel of senior experts to review evidence and provide a resolution.
    - Consensus-Based Decision-Making – Where multiple perspectives existed, decisions were made through structured discussions, ensuring alignment with national and international best practices.
    - Final Arbitration by the MOH – If consensus could not be reached, the MOH provided the final decision based on strategic healthcare priorities.
- Three reviewers from the MOH assessed the guidelines for alignment with national health policies and strategic directions.
- An external reviewer provided additional feedback to enhance clarity and applicability.
- By June 2025, the final version of the guidelines was completed and prepared for dissemination.

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Chapter 3: Responsibilities

3.1 Responsibilities of stakeholders

Chapter 3: Responsibilities

3.1 Responsibilities of stakeholders

- MOH – Overseeing the implementation, monitoring compliance, and updating guidelines as needed.
- Healthcare Facilities – Ensuring staff training, resource allocation, and adherence to best practices.
- Healthcare Workers – Providing patient-centered care in line with the guidelines and participating in continuous professional development.
- Community Organizations – Supporting awareness initiatives and patient advocacy efforts

4

Chapter 4: Document history and version control

Chapter 4: Document history and version control

4.1 Document history and version control

Version	Description	Review Date
01	Initial release	
02	Version two	Jan 2003
03	Version three	December 2015
04	Version four	June 2030

4.2 References

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5

Chapter 5: HIV epidemic update

Chapter 5: HIV epidemic update

5.1 Global HIV epidemic update

There were approximately 39.9 [36.1–44.6] million PLHIV at the end of 2023 (Fig. 1) with 1.3 [1.0–1.7] million new HIV infections worldwide (Fig. 2).

Fig. 1: Global number of PLHIV, 1990-2023

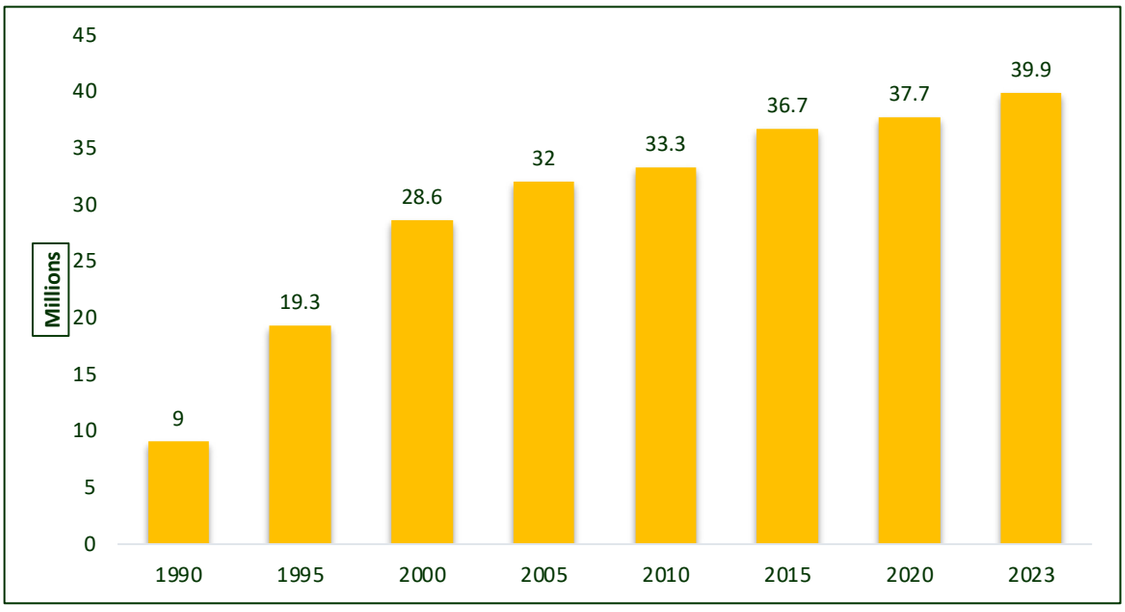
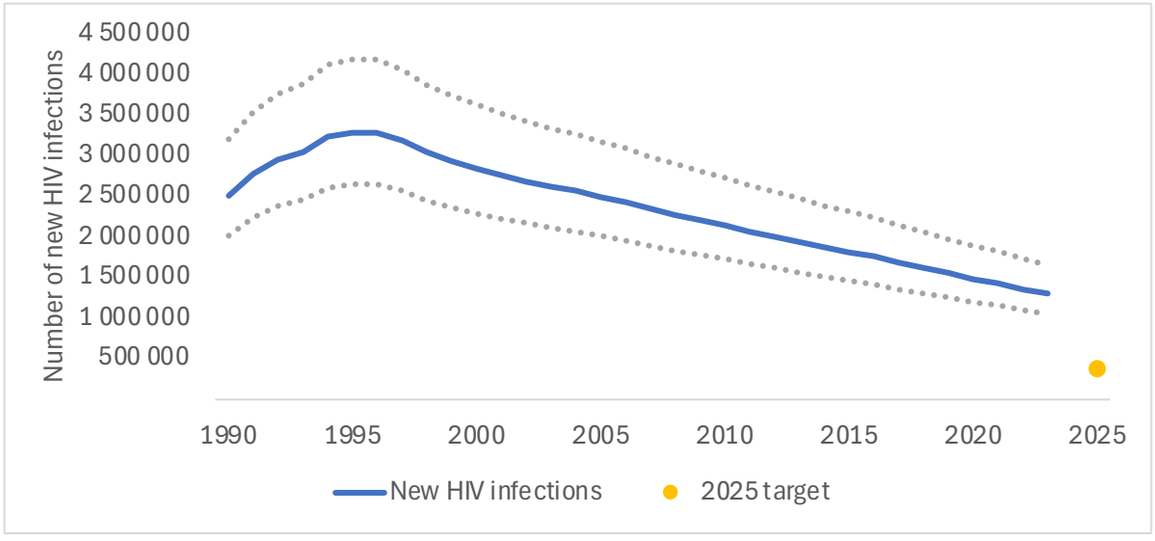
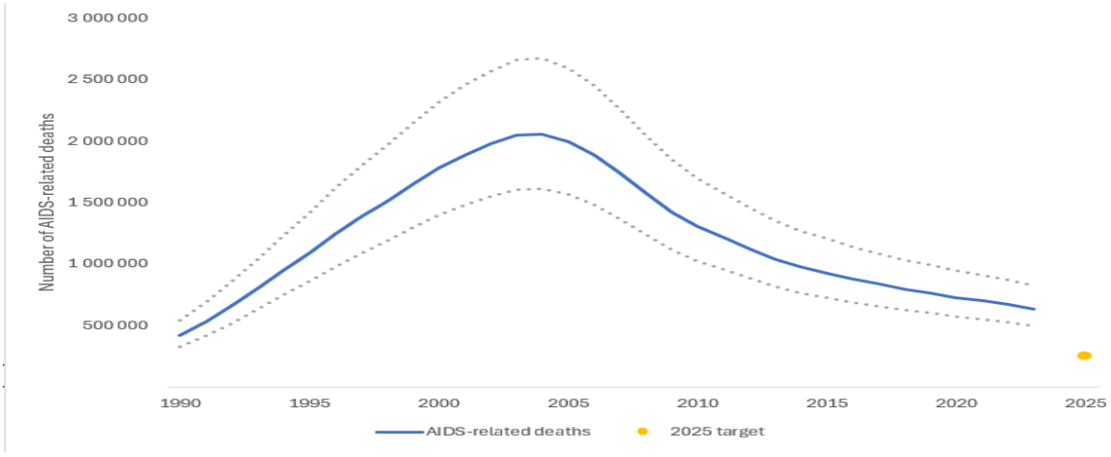


Fig. 2: Global number of new HIV infections, 1990-2023 and 2025 target



In 2023, 30.7 million people [27–31.9 million] were accessing antiretroviral therapy (ART) globally. The improved access to HIV treatment, coupled with a decline in new HIV infections, has led to a 51% reduction in acquired immunodeficiency syndrome (AIDS)-related deaths since 2010 (Fig. 3) (1.3 million in 2010 vs. 630,000 in 2023).

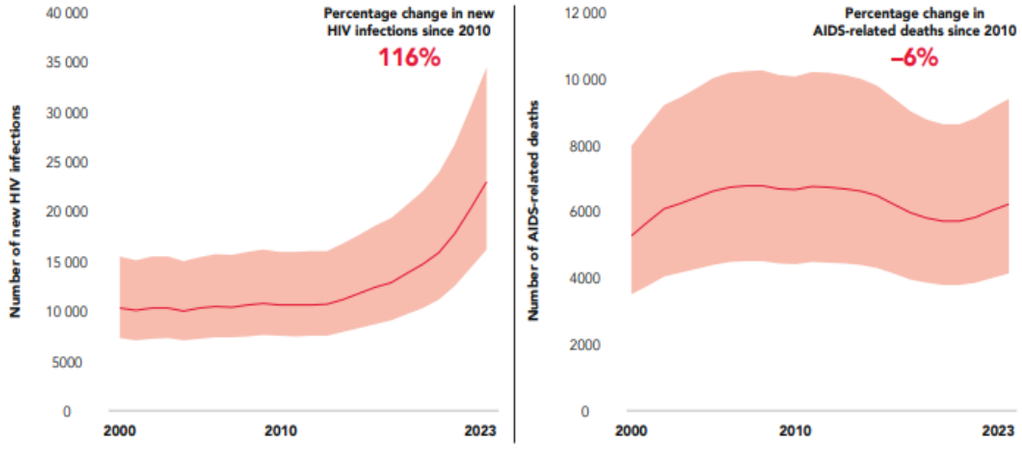
Fig. 3: Global AIDS deaths, 1990-2023 and 2025 target



5.2 Regional HIV epidemic update

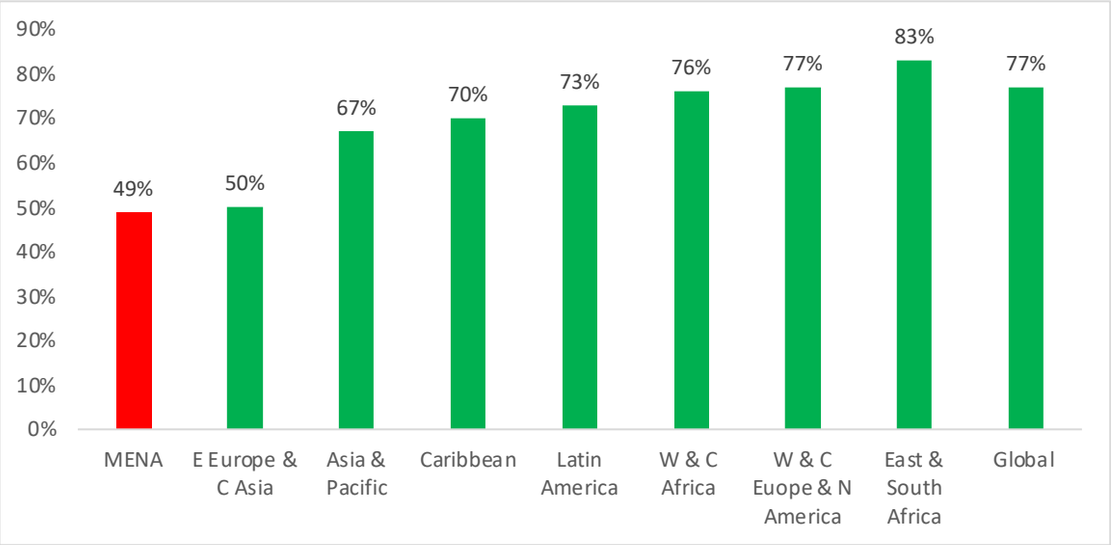
While new infections continue to decline worldwide and the access to ART improves, concerning trends indicate that the HIV epidemic in Middle East & North Africa (MENA) region continues to grow as shown in (Fig. 4).

Fig. 4: Number of new HIV infection and deaths, MENA, 2000-2023



Percentage changes in new HIV infection is increased by 116%, between 2010 and 2023, in contrast to a 39% global decline. AIDS-related deaths in MENA decreased by only 6% during the same period, compared to a 51% global decline.
ART coverage in the MENA region was only 49 percent of the PLHIV, which was the lowest in the world- well below the world average of 77% (Fig.5).

Fig. 5: Percentage coverage of ART in different regions of the world, 2023



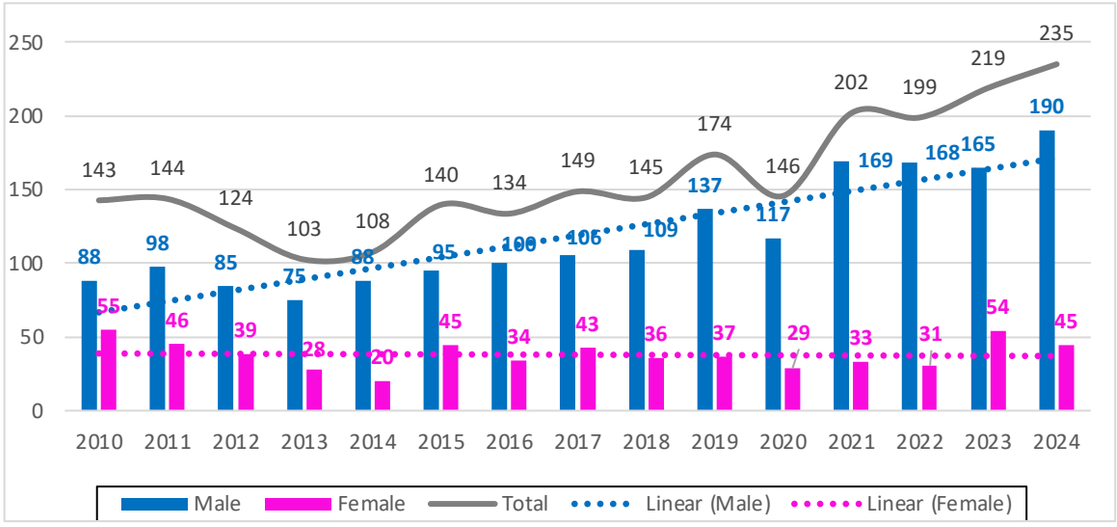
The following are a few challenges that may explain the region-specific HIV epidemic profile:

A. Stigma and discrimination against PLHIV among general population and health care personnel.
B. Inadequate focus on key populations e.g. men who have sex with men (MSM), people who inject drugs (PWID) and sex workers.
C. Health system challenges (e.g. human resources for health, health information systems).
D. War, conflicts, migration and humanitarian crisis affecting population and health services.

5.3 National HIV epidemic update

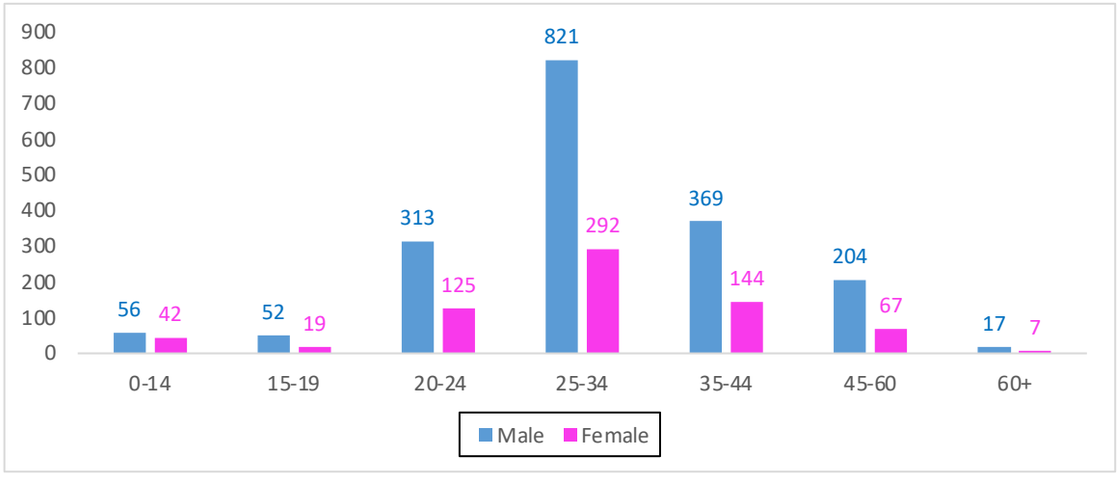
The WHO classifies the HIV epidemic in Oman as a low-prevalence epidemic. The first case of HIV in Oman was detected in 1984, and by the end of 2024, a total 4230 HIV/AIDS cases had been reported among Omanis. Figure 6 shows the trend of HIV case detection from 2010 -2024 by gender. Of the total reported cases, 2528 (60%) were alive at the end of the 2024, with 2243 (89%, 2043/2528) of whom were receiving ART. Heterosexual transmission accounted for the majority of infections (65%), followed by homosexual-bisexual (23%), mother-to-child (4%), injection-drug use (2%) and blood transfusion (1%). In the remaining cases, the mode of HIV acquisition was unknown.

Fig. 6: Newly diagnosed Omani HIV Cases by sex and trend of diagnosis, 2010-2024



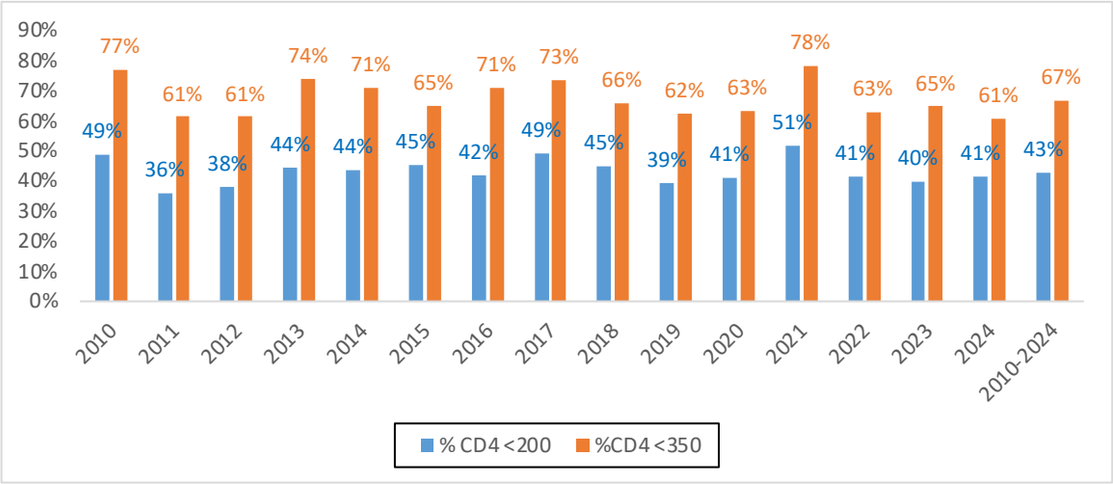
In Oman, the male-to- female ratio of PLHIV in Oman was 72:28 at the end of 2024 (Fig.6). Distribution of PLHIV by age at diagnosis and sex is depicted in Fig 7.

Fig. 7: Distribution of PLHIV in Oman by age and sex at the end of 2024 (n=2528)



Late Diagnosis remains a significant concern. On average, from 2010 to 2024, 43% of PLHIV in Oman were diagnosed with a cluster of differentiation 4 (CD4) cells below 200 cells/mm^3, while 67% were diagnosed with a CD4 below 350 cells/mm^3.

Fig. 8: Proportion of CD4 counts less than 200 and less than 350 among newly diagnosed patients, 2010-2024



HIV treatment is integrated into general health services and is provided through 14 treatment centers spread all over the country, ensuring building capacities and sustainability. Figure 9 shows HIV treatment coverage and viral suppression by the different Governorates and nationwide at the end of 2024.

Fig. 9: ART Coverage and Viral suppression by Governorates 2024

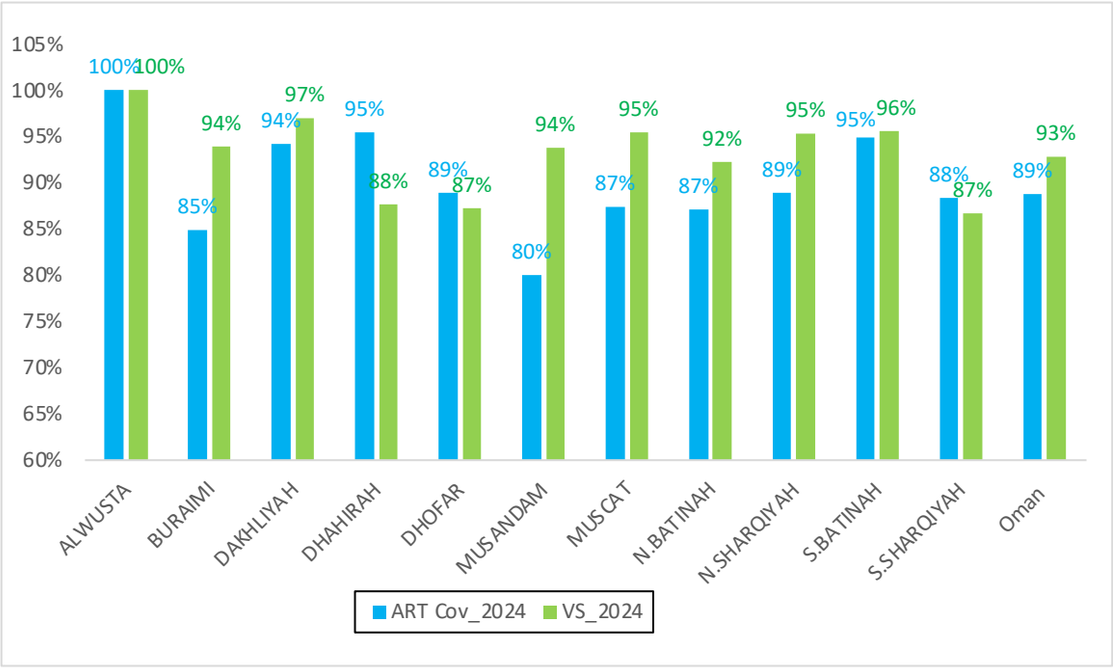
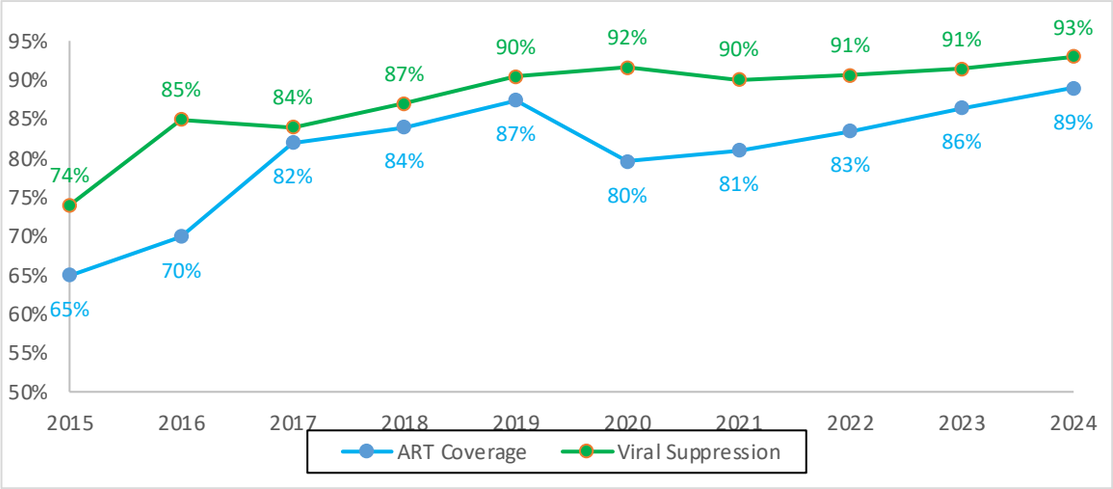
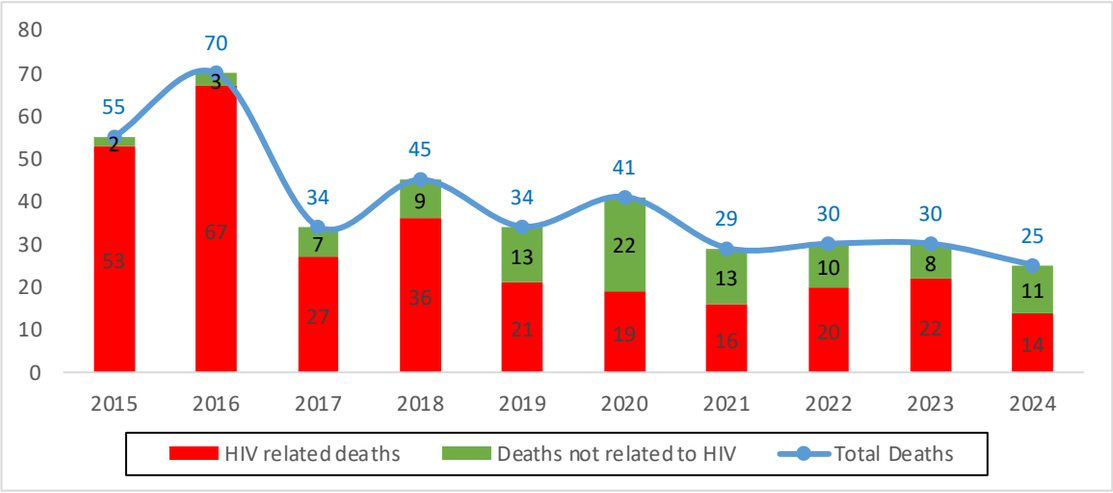


Fig. 10: ART coverage and Viral suppression in Oman, 2015-2024



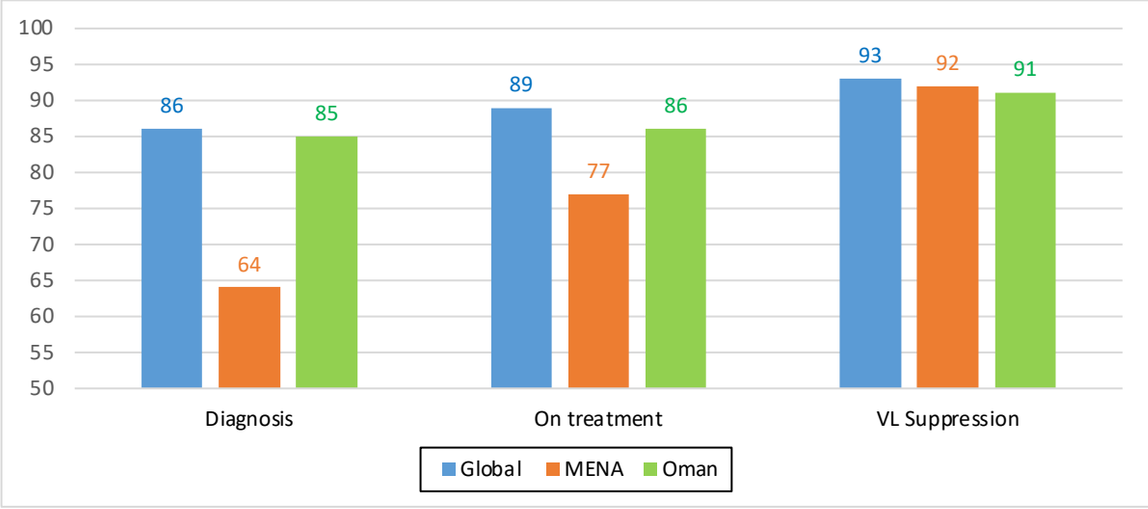
As HIV treatment coverage and viral suppression among PLHIV improved over the years (Fig 10), HIV-related deaths in Oman declined between 2015 and 2024 (Fig 11) by 63%, compared to a 6% decline in the MENA countries and a 51% decline globally during the same period.

Fig. 11: HIV and non-HIV related deaths, 2015-2024



Globally, the 95-95-95 target, initially set for 2030, has been moved to 2025. This means 95% of all PLHIV should be diagnosed, 95% of those diagnosed should be on ART and 95% of on ART should achieve viral suppression. Figure 12 compares 95-95-95 achievements in Oman with MENA and global trends at the end of 2023, emphasizing the need for sustained efforts in Oman and MENA to meet these targets.

Fig. 12: Comparison of Global, MENA and Oman, 95-95-95 achievements at the end of 2023



6

Chapter 6: HIV Testing and Diagnosis

Chapter 6: HIV Testing and Diagnosis

Diagnosis of HIV infection must be confirmed by a laboratory using different validated assays. An individual can approach HIV diagnosis through different models of HIV testing and counseling (HTC) services.

6.1 HIV testing and counseling

With early diagnosis and prompt treatment, PLHIV are expected to have a near-normal life expectancy. Despite this progress, HIV infection remains a major global public health threat. This is largely attributable to late HIV diagnosis, i.e. CD4 count of < 350 cells/mm3 at initial presentation. Late-stage HIV diagnosis is associated with increased morbidity and mortality, onward transmission and high cost of treatment and care [6]. Knowledge of someone's own HIV status results in reduction of the risk of onward transmission of HIV to sexual partners. When people become aware of their HIV infection, they are less likely to engage in high risk-behavior compared to those who remain unaware. Furthermore, patients once they get diagnosed with HIV infection and start HIV treatment, their infectivity is significantly reduced because of the reduction in their HIV viral load (VL).

Evidence shows that HIV patients present to primary and secondary care institutions, with medical conditions closely linked to HIV infection, in the three years preceding their HIV diagnosis. This represents missed opportunities for diagnosing patients at early stage. Late HIV diagnosis has been identified as one of the primary challenges facing the HIV program in Oman. In 2024, 64% (150/235) of newly diagnosed PLHIV in Oman were tested for CD4 count at baseline; 61% of whom were diagnosed late with a CD4 count <350 cells/mm^3.

HTC is intended to allow people to make informed decisions regarding the knowledge of their HIV status and the implications of those decisions. **A range of diverse models and approaches of HTC are available:**

- **Voluntary counseling and testing (VCT):** also known as client-initiated testing and counseling in which the client makes the conscious decision to actively seek HIV testing with no external coercion. VCT services could be stand alone or integrated into other health services, e.g. PHC, NGOs, private health sector etc. Currently VCT is provided at several locations including Al-Khoudh Health Center, Al-Amerat HC, Quriyat PC, Sohar EHC and Buraimi Hospital
- **Provider-initiated testing and counseling:** in which health care providers actively recommending HIV testing to their clients and/or patients for the purpose of diagnosis, further care and treatment, or to offer an ART prevention:

    1. All patients aged 16–65 years admitted to a medical ward, in secondary and local hospitals, regardless of their symptoms.
    2. All patients aged 16–65 years requiring a blood test at select hospitals and polyclinics as per MOH policy.
    3. All patients with confirmed or suspected tuberculosis (TB), hepatitis B and hepatitis C.
    4. Patients with confirmed or suspected sexually transmitted infection (STI).
    5. Patients presenting with symptoms suggestive of primary HIV infection (infectious mononucleosis-like illness) which occurs within 2-4 weeks of HIV infection acquisition. For these patients, repeat the HIV serology test within 2-4 weeks if initial test is negative. Also, enquire about any recent HIV risk. It is important to identify these patients as they are highly infectious due to exceptionally high VL at this stage of the infection.

6. Individuals requesting an HIV test. It is important to explain about the window period (4-12 weeks) as often they might present within few days of an HIV risk exposure. Recommend a repeat test outside the window period and STI screening.
7. All pregnant women as per the national policy; all pregnant women attending ANC should be offered an HIV test at booking. In addition, consider repeat HIV test in the third trimester if the patient discloses high HIV risk, e.g. if the husband is a known HIV case (details in chapter 8).
8. Discordant couples (one of the partners is HIV positive). HIV testing should be offered to the HIV-negative partner at baseline and repeated regularly thereafter to monitor their status. Regular testing is especially important if the couple is sexually active and not consistently using condoms or if the HIV-positive partner is poorly adherent to ART. Testing should generally be conducted every 6 to 12 months, if the HIV-positive partner is virally suppressed.
9. Patients presenting with conditions that are closely linked with undiagnosed HIV or AIDS defining illnesses. (See Table 1 for HIV indictor conditions)
10. Prisoners
11. Individuals who belong to key populations; intravenous drug users, sex workers, transgender people, cisgenders and men who have sex with men.

- ***Community-based approaches*** may include:
  - *Outreach and mobile testing:* especially tailored to access populations at higher risk of HIV, named as hidden populations.
  - *Events and campaigns:* to mobilize HTC services among different sectors of populations e.g. HTC/VCT during Muscat Festival or Kharreef Festival, Salalah and other social and/or health activities.
  - *Self-testing:* Individuals who obtain a reactive (positive) result from an HIV self-test are *strongly advised* to promptly contact the nearest healthcare provider or health facility for confirmatory testing and appropriate follow-up care. Confirmatory testing is essential to establish an accurate diagnosis and to initiate timely treatment and support services as needed.

For a quality and effective HTC service, there are 5 key components, as defined by the WHO, the **"5 Cs"**: consent, confidentiality, counseling, correct test results, and connection to care.

1. ***Consent:*** Provider-initiated counseling and testing does not require a formal consent.
The VCT client should voluntarily agree to have his/her blood tested for HIV. This consent should be based on sufficient, accurate and clear information i.e. "*informed consent*". The minimum package of information needed for an informed consent should cover the following main points:

a. Reasons why HIV testing is being recommended.
b. Details, risks, and implications of HIV testing and meaning of test results.
c. The post-test follow-up prevention and treatment services available, when needed.
d. Assurance of confidentiality and the right to opt-out at any stage of the process without any negative consequences.
e. Disclosure strategy and any further inquiries by the client.

2. ***Confidentiality:*** issues discussed between counselor/health care provider and the client/patient must be always kept confidential and not to be disclosed to a third party without prior consent of the client/patient. VCT clients can be identified by code numbers, however, names may be, sometimes, required to facilitate referral to other services.
3. Counseling: clients voluntarily seeking HIV testing and patients undergoing HIV testing as part of their clinical investigations should receive pre-test information and post-test counseling. Post-test counseling should be done by a well-trained counselor for both positive and negative test result.
4. Correct test result: HTC service delivery should be supported with high quality testing services and quality assurance mechanisms. To minimize false positive and negative test outcomes, HIV testing should be guided by the national reference lab. All the preliminary positive test results should be confirmed by the Central Public Health Laboratory (CPHL).
5. Connection to care: all HTC models should be linked to further prevention and treatment services (e.g. HIV treatment centers) to ensure continuum of HIV care.

Table 1: HIV indicator conditions by specialties

A	**Respiratory/Pulmonology**
1	Tuberculosis
2	Pneumocystis jiroveci pneumonia
3	Pneumonia, recurrent
4	**Mycobacterium avium complex** (MAC) lung disease
5	Histoplasmosis, disseminated/extrapulmonary
6	Herpes simplex bronchitis/pneumonitis
7	Candidiasis bronchial/lungs
8	Community-acquired pneumonia
B	**Neurology and neurosurgery**
1	Cerebral toxoplasmosis
2	Cryptococcosis, extrapulmonary
3	Progressive multifocal leukoencephalopathy
4	Reactivation of American trypanosomiasis (meningoencephalitis or myocarditis)
5	Guillain-Barré syndrome
6	Mononeuritis
7	Subcortical dementia
8	Multiple sclerosis-like disease
9	Peripheral neuropathy
10	Primary space occupying lesion of the brain

C	**Dermatology/dermatovenereology/ genitourinary medicine**
1	Kaposi's sarcoma
2	Herpes Simplex ulcer(s)
3	Atypical disseminated leishmaniasis
4	Penicilliosis, disseminated
5	Seborrheic dermatitis/exanthema
6	Herpes zoster
7	Sexually transmitted infections (STIs)
8	Hepatitis B or C (acute or chronic)
9	Severe or recalcitrant psoriasis
10	Candidemia
11	Candidiasis
D	**Gastroenterology/Hepatology**
1	Cryptosporidiosis diarrhea, > 1 month
2	Microsporidiosis, > 1 month
3	Isosporiasis, > 1 month
4	Candidiasis, esophageal
5	Hepatitis B or C (acute or chronic)
6	Unexplained chronic diarrhea
E	**Oncology**
1	Lymphoma, non-Hodgkin
2	Kaposi's sarcoma
3	Primary lung cancer
4	Anal cancer/dysplasia
5	Cancer requiring aggressive immunosuppressive therapy
F	**Gynecology/ Obstetrics**
1	Cervical cancer
2	STIs
3	Hepatitis B or C (acute or chronic)
4	Pregnancy (implications for the unborn child)
5	Cervical dysplasia
G	**Hematology**
1	Lymphoma, non-Hodgkin
2	Malignant lymphoma
3	Unexplained leukocytopenia/thrombocytopenia lasting > 4 weeks
4	Unexplained lymphadenopathy
5	Thrombotic thrombocytopenic purpura

H	**Infectious Diseases/Internal medicine**
1	Tuberculosis
2	Mycobacterium Tuberculosis, pulmonary or extrapulmonary
3	MAC or Mycobacterium kansasii, disseminated or extrapulmonary
4	Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
5	Pneumonia, recurrent (2 or more episodes in 12 months)
6	Pneumocystis jiroveci pneumonia
7	Cryptococcosis, extrapulmonary
8	Salmonella septicemia
9	Cytomegalovirus, other (except liver, spleen, glands)
10	Herpes Simplex ulcer(s) > 1 month/ bronchitis/pneumonitis
11	Candidiasis bronchial/tracheal/lungs
12	Candidiasis, esophageal
13	Histoplasmosis, disseminated/ extrapulmonary
14	Coccidioidomycosis, disseminated/extrapulmonary
15	Atypical disseminated leishmaniasis
16	Reactivation of American trypanosomiasis (meningoencephalitis or myocarditis)
17	Penicilliosis, disseminated
18	STIs
19	Hepatitis B or C (acute or chronic)
20	Mononucleosis-like illness
21	Invasive pneumococcal disease
22	Herpes zoster
23	Lymphocytic meningitis
24	Visceral leishmaniasis
25	Unexplained weight loss
26	Unexplained fever
27	Unexplained chronic diarrhea
28	Unexplained lymphadenopathy
29	Unexplained leukocytopenia/thrombocytopenia lasting > 4 weeks
I	**Rheumatology**
1	Autoimmune disease treated with aggressive immunosuppressive therapy
J	**Ophthalmology**
1	Cytomegalovirus retinitis
K	**Ear Nose Throat**
1	Candidiasis tracheal/esophageal
2	Mononucleosis-like illness

L	**Nephrology**
1	Unexplained chronic renal impairment
M	**General practice**
1	Symptomatology fitting any of the listed conditions
N	**Emergency medicine**
1	Symptomatology fitting any of the listed conditions
O	**Dentistry**
1	Candidiasis, oral and esophageal
2	Kaposi's sarcoma
3	Oral hairy leukoplakia

	AIDS defining, must test		Strongly recommended for testing		Recommended for testing

6.2 Laboratory diagnosis of HIV infection

HIV diagnosis is a critical step for early and accurate detection of the HIV infection, enabling effective transmission control and the timely initiation of treatment.

HIV screening and confirmation tests are designed to detect HIV antibodies and/or antigens in whole blood, plasma, or serum. The laboratory diagnosis of HIV infection is made by the confirmed detection of HIV antibodies and antigens (HIV serologic assays) using the multi-test algorithm and, in certain circumstances, by direct detection of HIV components (antigen or molecular detection)

Sample collection and transport

All biological specimens from all suspected or confirmed cases of HIV are assumed to be potentially infectious and must be handled with caution. The details of the indication of the test, the type of samples and the collection process are listed in Table 2

Table 2: sampling indication, collection and transport

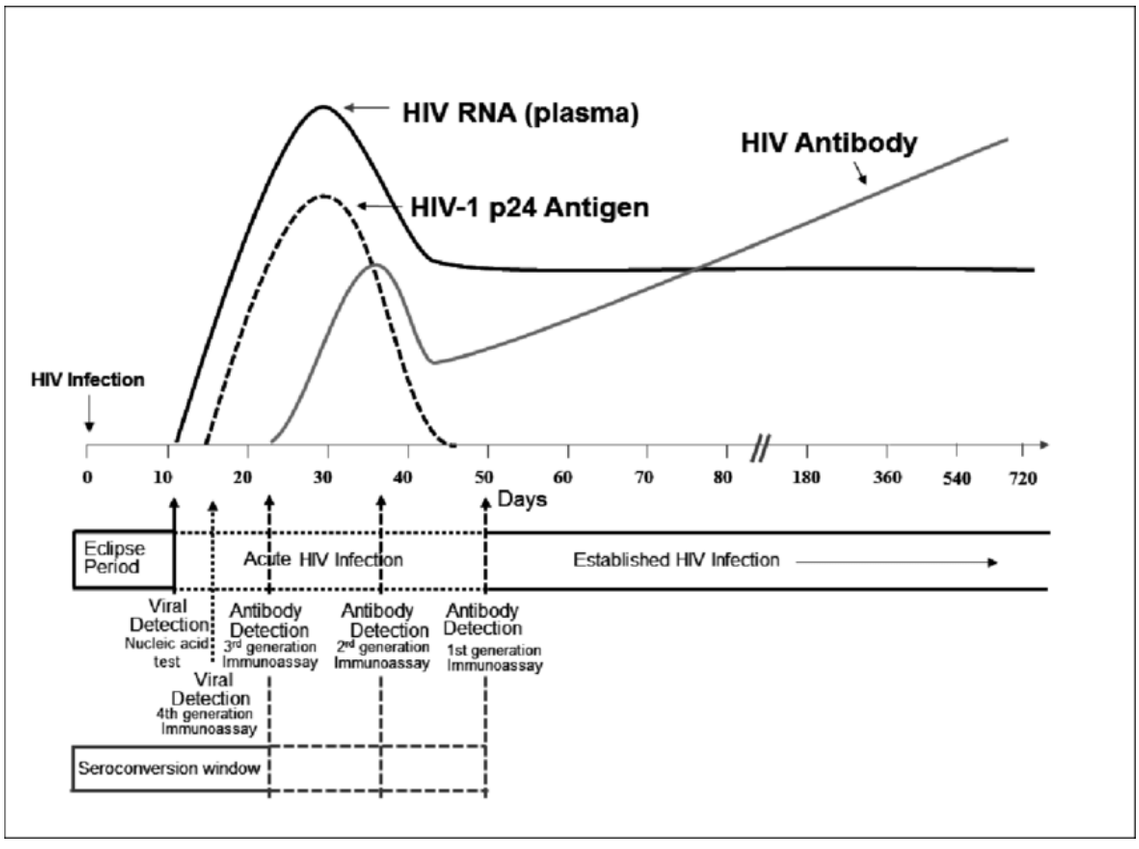
Test	Indication	Location	Sample type and container	Volume	Time to get results from laboratory (days)	Remarks
HIV-1&2 Ab/Ag test	Screening test	CDC Hospitals Polyclinics	Serum sample in serum separation tube	3-5 ml blood	1-3	Separate serum at low speed (1500-3000 rpm) for 5 min at room temperature
Antibody differentiation immunoassay	Confirm HIV diagnosis	CPHL/ Regional Hospitals	Serum sample in serum separation tube	3-5 ml blood	5	Separate serum at low speed (1500-3000 rpm) for 5 min at room temperature

HIV-1 quantitative real time PCR (viral load)	- Baseline RNA level before ART -Monitor ART response -Monitor disease progression -Infants born to HIV positive mothers -Suspected primary HIV -Inconclusive HIV serology results	CPHL, SQUH, MCMSS and other Tertiary hospitals	EDTA whole blood	7-10 ml whole blood to give at least 2 ml of EDTA plasma (only separated plasma should be sent to CPHL)	10	Keep EDTA blood plasma at 2-25 °C before plasma get separated (within 3-6 hours of collection) by centrifugation at 800-1600 X g (1500-2000 rpm) for 20 min at room temperature
CD4 & CD8	- Baseline -Monitor disease progression	Royal Hosp. SQU Hosp. Al Nahdha Hosp. Sohar Hosp. Sur Hosp. Salalah Hosp. Nizwa Hosp.	EDTA whole blood	2-5 ml whole blood	7	No sample processing is required. Keep at ambient temperature. Sample should reach the analyzing laboratory within 24 hours of collection

Serologic assays

HIV antibodies and antigens can be detected in whole blood, serum, or plasma using antibody/antigen combo tests (referred to as fourth-generation HIV screening assays) after the window period. The window period, defined as the time from infection to when a diagnostic test can first detect the marker of infection, varies with the testing method (Fig. 13).

Fig. 13: The sequence of appearance of laboratory markers for HIV-1 infection



Generally, HIV serologic assays are classified as **screening** (or first-line) assays and **supplemental** (or confirmatory) assays.

A. ***Screening assays:*** The current assays are highly sensitive due to the incorporation of the p24 antigen. The following techniques are available for screening:

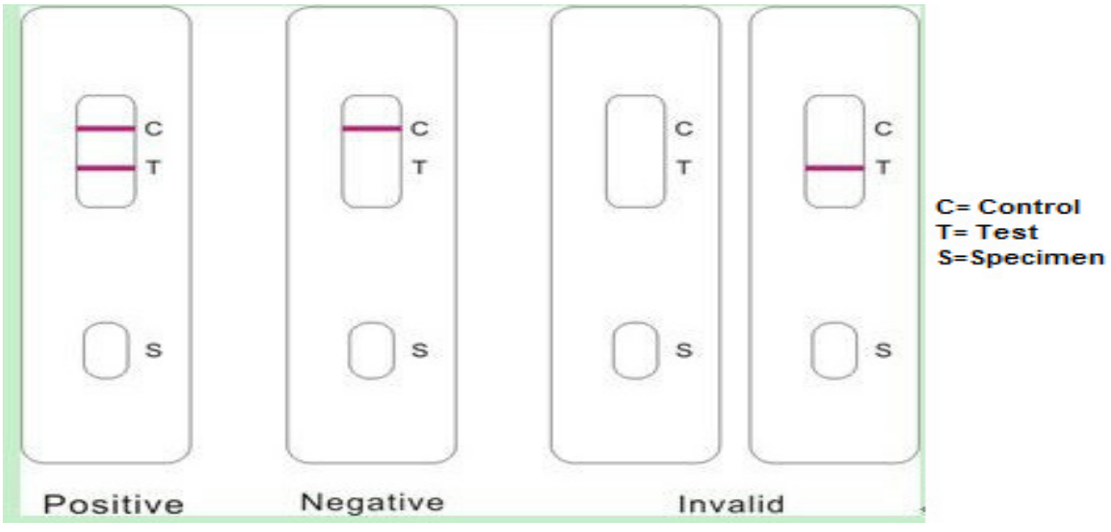
1. Fourth-generation screening ELISA/EIA (enzyme-linked immunosorbent assay/enzyme immunosorbent assay) and chemiluminescent immunoassays (CLIAs):

- Commonly used at health care facilities, e.g. Polyclinic, CDC, blood banks, and secondary tertiary/central laboratories.
- It contains antigens from both Human immunodeficiency virus type 1 (HIV-1) and Human immunodeficiency virus type 2 (HIV-2) and is, therefore, able to detect infections with either of these viruses.
- It requires the use of specialized laboratory equipments and sometimes may take up to 3 hours, to yield results.
- Reported as positive (reactive) or negative (non-reactive) or indeterminate test results.

2. Fourth generation screening Rapid Diagnostic Tests (RDTs):

- It is much easier to use and interpret by non-laboratory personnel, allowing testing, counselling, and referral to be done in one visit.
- Results are available within 20-30 minutes.
- Reported as positive (reactive), negative (non-reactive), or invalid (*Fig2*).

Fig. 14: Possible interpretations of RDTs



- Indications for rapid testing include:
    1. VCT clients.
    2. Awareness campaigns.
    3. Patients admitted to an intensive care unit and suspected of HIV infection (*see section 2.3).*
    4. Occupational exposure to HIV infection.
    5. Pregnant women who have no documented HIV status at the time of delivery.
    6. Needle prick injuries from patients suspected of HIV infection

3. Fifth-generation *ELISA/EIA* assays that detect p24 antigen and differentiate between HIV-1 and HIV-2 antibodies are becoming available. These may be used instead of a fourth-generation assay if they are accessible.

*Please note that Nucleic acid amplification tests (NAATs), typically plasma HIV-1 RNA testing, are not recommended for initial HIV screening because they offer only a marginal advantage over fourth-generation screening assays in detecting recent HIV infection and are more costly and can be associated with false-positive results.

B. *Confirmatory assays*: All specimens with positive (reactive) test results to ELISA/ EIA, CLIA, RDTs and/or self-testing should be confirmed by confirmatory assays, which are more specific than the screening tests. The assay should be done in a laboratory with experience in HIV confirmation.

The following assays should be performed as a confirmatory test :

1. A second fourth generation assay, which is more specific than the initial assay.

2. HIV typing or Antibody differentiation immunoassay (ADI), which is recommended to be used as a supplemental test to confirm and differentiate HIV-1 and HIV-2 antibodies. The ADI incorporates synthetic and recombinant antigenic determinants for HIV-1 and HIV-2. Examples of ADI include Bio-Rad Genius and Bio-Rad Multi-spot tests.

3. Western blot (WB) (line immune assay) detects serum antibodies directed against specific HIV proteins of varying molecular weights. It differentiates between HIV-1 and HIV-2 in most cases. However, WB can produce false negative results in early HIV infection. It is expensive, complex, and requires expertise. It is also time-consuming, resulting in a longer turnaround time for HIV results. Therefore, WB should not be used in national HIV testing strategies and algorithms. However, CPHL will continue to use it for more complicated cases.

Table 3: Conditions causing false positive and false negative HIV test results

False positive test results	False negative test results
• Hematologic malignant disorders • Autoimmune disorders • Multiple myeloma • Primary biliary cirrhosis • Alcoholic hepatitis • Chronic renal failure • Pregnancy	• Window period • Immunosuppressive therapy • Malignant disorders • B-cell dysfunction • Bone marrow transplantation • Late stage of HIV infection (AIDS)

Virological assays

The following assays can directly detect HIV components:

1. ***Antigen (p24) detection assay:***

i. Is used to detect the HIV core protein p24 in blood, serum or plasma.
ii. Is highly specific but has low sensitivity (79% to 89%); it may become positive early during HIV infection before the antibody is detectable. After seroconversion, circulating p24 antigens fall but can be detected in a minority of cases.
iii. Is incorporated with the HIV-1/2 antibody fourth-generation screening assays.

2. ***Polymerase Chain Reaction (PCR) test:***

A. *HIV proviral* deoxyribonucleic acid *(DNA)/ PCR:*

i. It is used to amplify and detect intracellular HIV DNA.
ii. It is indicated in cases with inconclusive serological results and undetectable HIV ribonucleic acid (RNA).

B. *Quantitative PCR (HIV RNA PCR/VL):*

i. VL is mainly used as a tool to monitor the response to ART. It quanti fies HIV RNA in plasma.
ii. It can be used as a confirmatory assay to confirm a reactive HIV screening assay in certain situations, such as inconclusive serological results.
iii. Can be used to screen infants born to HIV-infected mothers.
iv. Can be used as a screening test if acute HIV infection is suspected.

CD4 count

Monitoring CD4 levels is important for assessing immune function and determining the stage of HIV disease; however, treatment should be initiated for all HIV-infected patients regardless of their CD4 level. Whole ethylenediaminetetraacetic acid (EDTA) blood is used for testing. After collection, the tube should be gently inverted to mix. No further processing is required. The sample should be kept at ambient temperature, more than 4°C but always less than 30°C. During transport, if necessary, the specimens can be kept in an insulated cool box with spacers to ensure that the specimens are not kept too cold and do not come in contact with the cool packs. The specimens must not be refrigerated or frozen.

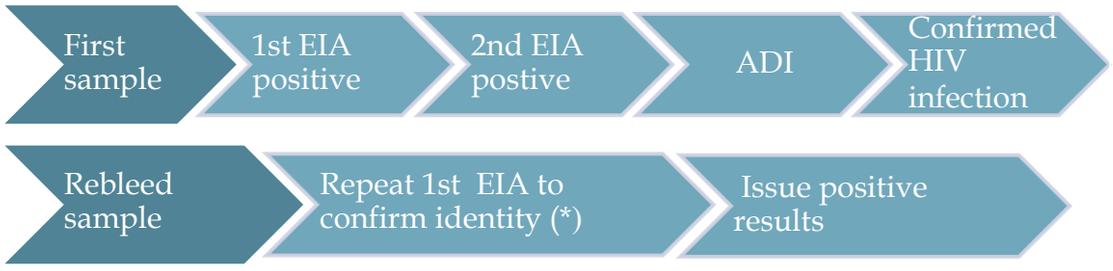
To get accurate results, the blood must be tested within 24 hours of collection time (i.e. the test is done same day or next day of sample collection). There should be good coordination between treatment center and CD4 laboratory. CD4 test is available in several hospitals (Table 2).

6.3 National HIV testing algorithms

Collection and Laboratory screening testing

The serology sample is collected in a serum separation tube (*Table 3*). After collection, the blood should be kept at room temperature for at least 15 minutes before it is separated. Serum should be transferred to a sterile 2 ml O-ring capped polypropylene tube and stored at the fridge before sending to the CPHL within a 4-day period (cold chain must be maintained during transport).

The screening test (EIA1) is done initially at Regional CDCs and other laboratories (polyclinics, hospitals). All reactive serum should be tested by another EIA system (EIA2) which can be done at the level of major Regional hospitals or at the CPHL.



If both EA1 and EIA2 are reactive, then an ADI should be done. This not only confirms the HIV infection but also differentiates HIV-1 from HIV-2 infection. The **Identity check** should be done at the original screening laboratory any time after the initial reactive sample; however, confirmed HIV status should be awaited before disclosing results to the patient. Confirmation of HIV status requires at least 3 different assays to be reactive (EIA1, EIA2, ADI).

The first screening ELISA or CLIA Test (EIA 1 or CLIA1):

This is offered at the Regional CDC, polyclinics, hospitals, or private sector using routine 4th-generation HIV tests (*see Table 3*). These tests detect HIV-1 p24Ag and antibodies against HIV-1 and HIV-2 but cannot differentiate between them.

Negative EIA1or CLIA1:

Unless an acute infection is suspected, a negative EIA1 result is considered sufficient to exclude infection.

Positive EIA1or CLIA1:

It is good laboratory practice to test the original tube if the aliquot was tested initially and vice versa to exclude errors.

Inconclusive EIA1 or CLIA1

These patients should be followed over time for re-assessment. A re-bleed sample should be collected after 14 days. If acute HIV is suspected, consult with CPHL and arrange for HIV RNA testing.

The supplementary ELISA or CLIA Test (EIA2 /CLIA2and EIA3CLIA1/):

All samples initially reactive by the screening (EIA1/CLIA1) should be tested by an EIA/CLIA system different from the one used for EIA1/CLIA1, with varying antigen and test kit components (EIA2) preparations. EIA2/CLIA2 may be done in a Regional hospital or CPHL. EIA3 is available only at CPHL.

*Negative EIA2/*CLIA2:

Discrepant results between the first and second EIA should be investigated with care. At CPHL, such samples are subjected to a third EIA (EIA3), and a virologist should evaluate the results for proper action and comments. If the EIA2/CLIA1 system is available in the Regional hospitals, the discrepant EIA1+/EIA2- results should be repeated using the same sample with the same two assays. If you have difficulty, please discuss this with a virologist in CPHL. The discrepancies could be due to differences in the test's sensitivity and specificity.

Fig. 15: National HIV testing algorithm for patients older than 18 months

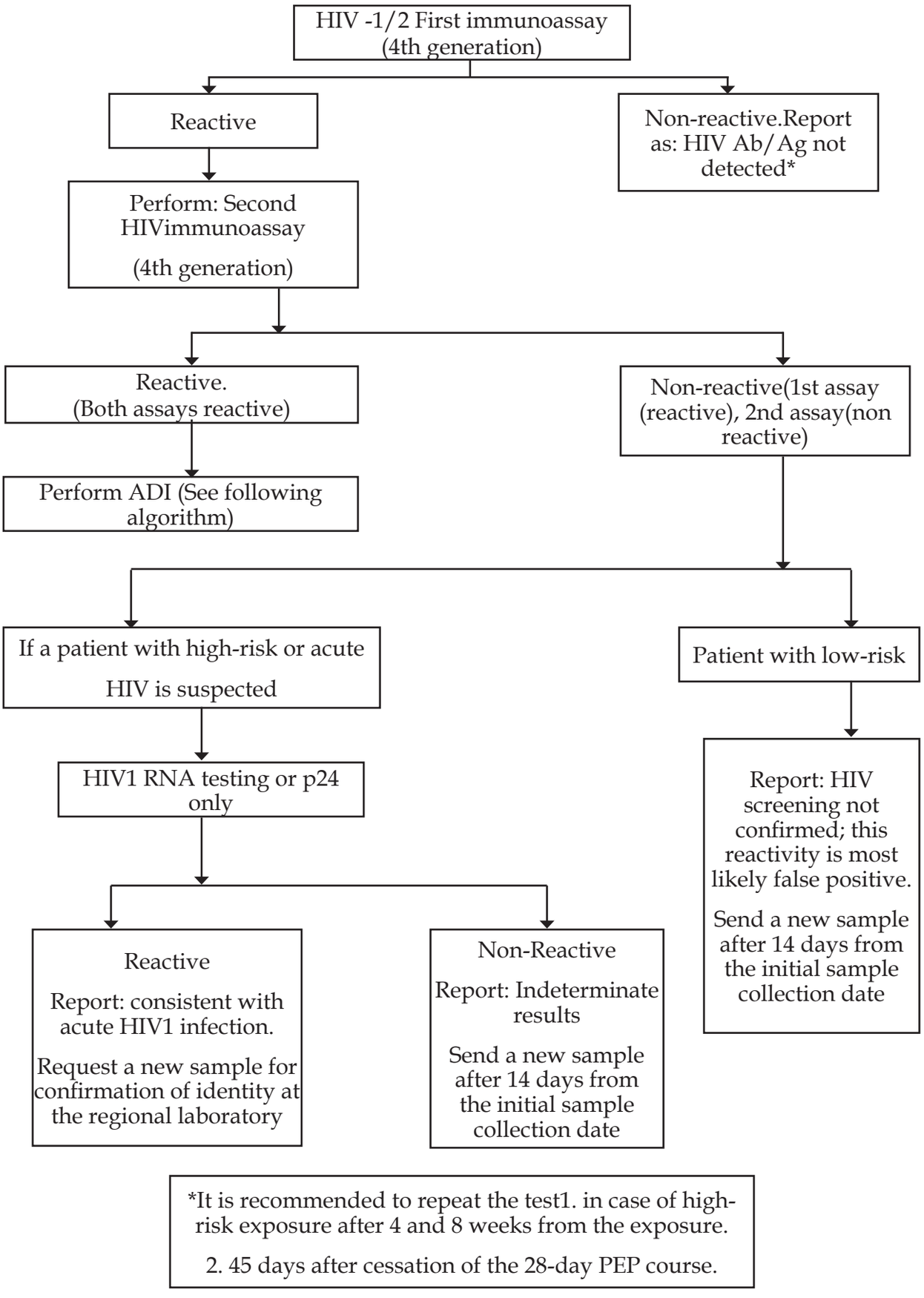
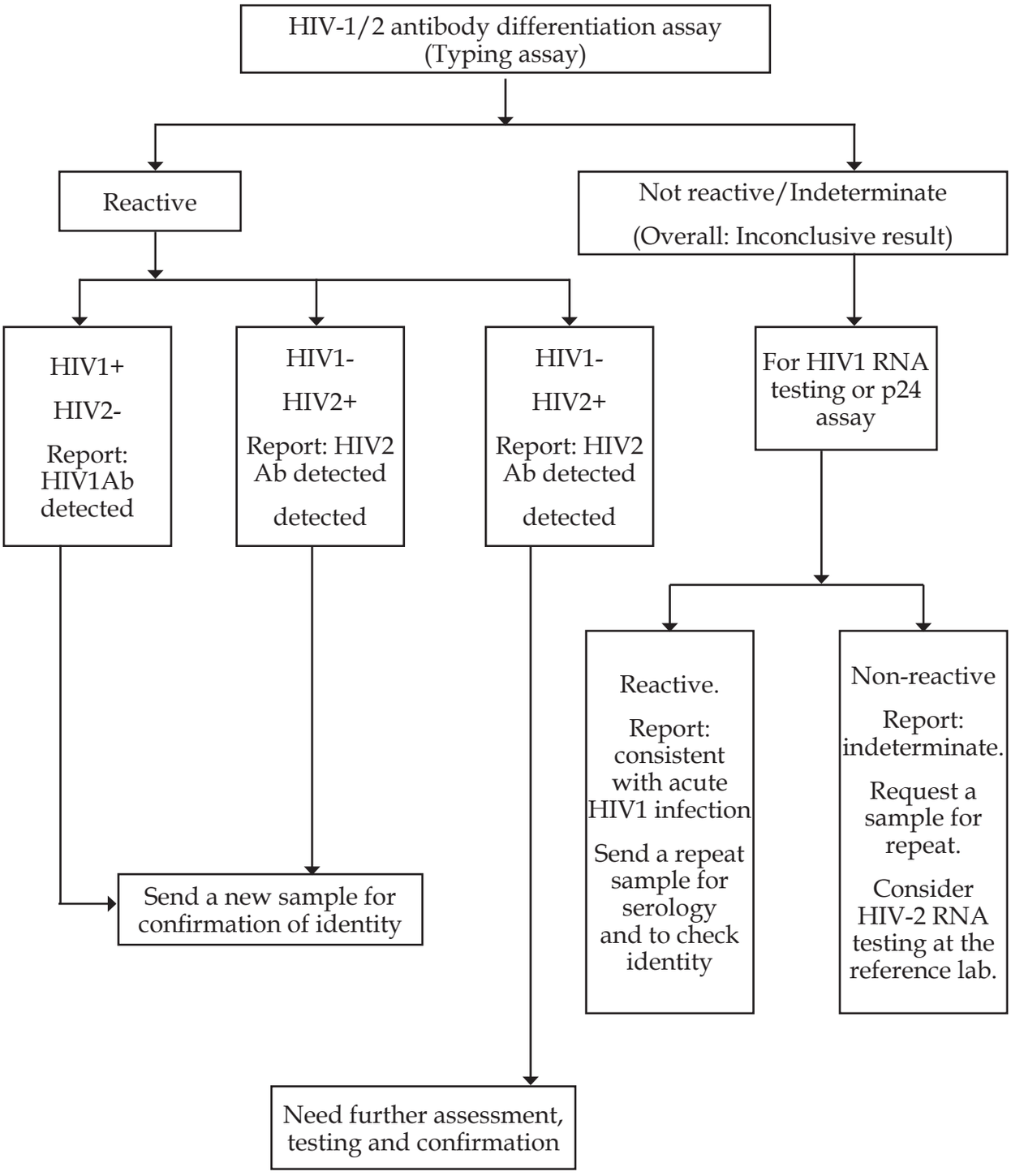


Fig. 16: HIV-1/2 antibody differentiation assay algorithm



- HIV VL testing should not be used as a screening test for HIV in adults. This test is expensive, not licensed for screening and can give false positive results (usually seen as low-level RNA or below detection limit of the assay).
- Only HIV focal point physicians should request HIV RNA/proviral-DNA tests.

7

Chapter 7:

Initial Assessment of newly HIV diagnosed patients

Chapter 7: Initial Assessment of newly HIV diagnosed patients

7.1 Rational for baseline assessment

All patients newly diagnosed with HIV should undergo a process of early assessment involving counseling, medical and laboratory assessment to:

a. Evaluate patient's willingness for ART and likely adherence
b. Assess risk of opportunistic infections (OIs)
c. Assess comorbidities
d. In females, assess plan for conception
e. Identify other prevention, treatment and care needs

7.2 Pre-ART counseling

Counseling prior to initiation of ART should be provided with the objective to:

- Develop a trusting relationship with patients for better care outcome.
- Ensure patient understanding of HIV infection and its transmission.
- Assess risky behaviors (sexual and drug use) and identify strategies to reduce them.
- Describe the benefits of ART for patient's health, explain the importance of adherence to ART and assess patient's readiness for ART.
- Identify social (community, family and occupation networks) and psychological impacts (depression, drug use, cultural factors and disclosure) of HIV infection and help with coping strategies.

7.3 Medical and laboratory evaluation

As summarized in *Table 4*, a complete ***medical and laboratory evaluation*** of PLHIV is to be conducted by a health care provider at baseline to further assess treatment and care needs.

Table 4: Medical and laboratory evaluation prior to ART initiation

Medical evaluation	• Assess weight at baseline and each subsequent visit • Assess 10-year atherosclerotic cardiovascular disease (ASCVD). Use a validated risk assessment tool such as the ASCVD Risk Estimator Plus (by the American College of Cardiology) to estimate 10-year cardiovascular risk in PLHIV aged 40–75 years without a prior history of cardiovascular disease. This assessment should guide decisions on lifestyle modifications and pharmacologic interventions, including statin therapy. • Assess blood pressure at baseline • Assess blood glucose level • Screen for depression and anxiety (See chapter 10) • Assess use of tobacco, recreational drugs and alcohol • Assess the risk of sexually transmitted disease (gonorrhoea, chlamydia, syphilis and herpes simplex virus (HSV) • Explore the contact; partner screening should be planned • Discuss family planning and the importance of pregnancy planning with women of childbearing age • Check immunization status/history

Laboratory evaluation	• Baseline blood investigations: • Complete blood count (CBC) with differential • Fasting blood glucose • Lipid profile • Renal function test • liver function test • Bone profile (Calcium; Phosphate; Alkaline phosphatase) • Glucose-6-phosphate dehydrogenase deficiency(G6PD) • HIV specific testing: • HIV VL (HIV RNA PCR) at baseline • HIV genotypic drug-resistance test: for patients with HIV RNA levels below 1,000 copies/mL, drug resistance testing via viral amplification should still be attempted, although it may not always yield successful results • Human leukocyte antigen (HLA)-B*5701 if Abacavir is being considered • CD4 cell count: CD4 absolute count and %, CD4/CD8 ratio • Tuberculosis Testing using Interferon Gamma Release Assay (IGRA) or Quantiferon-TB Gold • Chest X-ray • Cytomegalovirus (CMV): Immunoglobulin G (IgG); Immunoglobulin M (IgM) if acute infection is suspected. • Toxoplasmosis: IgG; IgM if acute infection is suspected. • Viral hepatitis: Screening for viral hepatitis should be performed prior to initiating ART. If ART needs to be started before screening results are available, a regimen effective against hepatitis B virus (HBV) should be selected. • Hepatitis A virus (HAV): anti-HAV IgG to assess for prior infection or vaccination; anti-HAV IgM if acute infection is suspected.) • HBV: Hepatitis B surface antigen (HBsAg) and Hepatitis B surface antibody (anti-HBs). • Hepatitis Delta Virus (HDV): anti-HDV antibody test (Total or IgG) in all patients with positive HBsAg • Hepatitis C virus (HCV): HCV antibody (HCV RNA if HCV antibody test is positive)

Screening for STIs:

1. Syphilis - At baseline for all patients and annually thereafter for high-risk patients

- **Screening Method:** A combination of serological tests is used:
  - Non-treponemal tests (e.g., rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL)) to screen for active infection and monitor treatment response.
  - Treponemal-specific tests (e.g., Treponema pallidum hemagglutination assay) confirm syphilis if the non-treponemal test is positive.

2. **Gonorrhoea and Chlamydia**

- Screening Method: NAATs are preferred for both gonorrhoea and chlamydia due to their high sensitivity and specificity.
- Sample Types:
- Urine (first catch) for genital infections.
- Swabs for extragenital sites (pharyngeal, rectal) based on exposure history, as HIV patients may have non-genital infections.
- Frequency: Annual screening is recommended for sexually active HIV patients. More frequent screening (e.g., every 3-6 months) is recommended for those with multiple partners or at higher risk of reinfection.

3. **HSV (If clinically indicated)**

- Screening Method: Routine HSV screening is not recommended for asymptomatic. PCR Testing on samples taken from a lesion is the preferred test for symptomatic patients as it directly detects HSV DNA
- Frequency: Screening is not routinely recommended for asymptomatic patients. Test only if symptoms are present

Other investigation at baseline:

Urine analysis:

- Proteins
- Glucose

Cancer screening

- Age-appropriate cancer screening as per national guidelines
- Skin for Kaposi sarcoma, especially in patients with advanced immunosuppression.
- Anal cancer screening with digital anal and rectal exam and anal pap test for key population (MSM who practice anoreceptive sex and/or have history of anogenital warts)

In Women:

- Pregnancy test for women in childbearing age
- Cervical screening including Human Papilloma Virus DNA detection starting at the age of 25 years with regular screening every 3 to 5 years.

As the baseline assessment (counseling and medical and laboratory) is completed and the stage of HIV infection becomes apparent, consideration should be given to ART; initiation and first-line ART regimen (*see section 4.2*).

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Chapter 8: Anti-retroviral therapy (ART) initiation in naïve patients

Chapter 8 Anti-retroviral Therapy (ART) Initiation in Naïve Patients

8.1 Definitions

Treatment- naïve patient is an individual who has never received ART

Treatment-experienced patient is someone who has previously received or is currently receiving ART. These patients could have detectable or undetectable HIV VL. The key characteristics of treatment-experienced patients include treatment history complexity, possible drug resistance and potential virologic failure; this highlights the need to assess prior treatment history and resistance profiles when considering new ART regimens for treatment-experienced individuals. These patients may require second-line or third-line ART with tailored regimens to achieve effective viral suppression and overcome drug resistance challenges.

Elite HIV controllers are a rare group of HIV-positive individuals who can naturally maintain undetectable VL (often <50 copies/mL) without ART. Key Characteristics are:

- Long-term Control: Elite controllers can sustain this control over many years, preventing HIV progression and damage to the immune system.
- Normal CD4 Counts: Many elite controllers maintain stable CD4 cell counts, indicating a healthy immune system.
- Immune Response: They usually have a unique and robust immune response that helps control the virus. Certain genetic factors, such as specific HLA alleles, are often associated with elite HIV controllers.

- Although elite controller patients exhibit low viremia and a strong immune response, current guidelines and expert consensus increasingly recommend initiating ART. Early treatment is advised to address persistent chronic inflammation and reduce the risk of long-term health complications.
- ART is strongly recommended for elite controllers with signs of disease progression, such as declining CD4 counts or HIV-related complications.
- Even in the absence of detectable viremia, ART may offer immunologic and clinical benefits, though the risks of ART toxicity must be weighed.
- If ART is not initiated, elite controllers require close monitoring for CD4 decline, loss of viral control, or HIV-related complications.

8.2 Aim of HIV treatment

The primary objective of HIV treatment is to achieve and maintain an undetectable VL in six months or less, defined as a level of HIV in the blood that is too low to be detected by standard VL assays. Sustaining an undetectable VL is crucial, as it indicates effective suppression of viral replication. Individuals with HIV who consistently maintain an undetectable VL experience significant clinical benefits, including improved immune function, reduced risk of HIV-related complications, and prevention of HIV transmission to sexual partners (consistent with the U=U concept: “Undetectable = Untransmittable”)

8.3 Rapid ART initiation

It is recommended to start **rapid initiation of ART at the first visit** for patients newly diagnosed with HIV, whenever possible. Starting ART promptly, ideally on the same day, can significantly improve health outcomes by reducing the time to viral suppression, preserving immune function, and lowering the risk of HIV transmission.

Before starting, ensure initial assessment and baseline labs are taken and check for any contraindications, but do not delay ART unnecessarily while waiting for results.

ART is recommended for all people with HIV and should be initiated as soon as possible. However, if there is a delay in starting ART, patients should remain engaged in care with periodic monitoring. Table 5 depicts the timing of ART in PLHIV with OIs.

Table 5: Timing of ART initiation in PLHIV with opportunistic infections

opportunistic infection	Timing of ART
Most of OIs	As soon as possible within 2 weeks after starting treatment for the OIs
TB, including TB meningitis	See chapter 7
Cryptococcal meningitis	Defer initiation of ART for at least 4 weeks

8.4 Selection of initial combination regimen for ART-naive patients

General considerations when selecting ART

1. **Pregnancy**: For women who are pregnant or planning to conceive, choose a regimen tailored to their pregnancy stage to ensure both maternal and fetal safety. Pregnant women with positive HIV status should be started on ART as soon as practically possible and preferably on the day of diagnosis.
2. **Opportunistic Infections:** For individuals with opportunistic infections, consult the relevant guidelines on initiating ART in this context (Table 5)**.**
3. **Drug History**: Review for potential drug-drug interactions with other medications the patient is taking.
4. **Swallowing Limitations**: Assess the patient's ability to swallow tablets to ensure adherence to the prescribed medications.
5. Assess alcohol or recreational drug use.
6. Assess risk for metabolic diseases
7. **Pill Burden**: The number of pills required per day.
8. **Pre-Exposure Prophylaxis (PrEP) History**: If the individual acquired HIV while on PrEP, select an appropriate ART regimen to address potential drug resistance.
9. **Resistance Risk**: The propensity for the regimen to select for resistance mutations in cases of suboptimal adherence.
10. **Pre**-treatment VL and CD4 count.
11. **Side Effects**: The likelihood of adverse reactions.

What to start

When initiating ART for ART-naive patients, several regimens are recommended. These regimens generally have comparable efficacy, but the following should be considered:

- It should have demonstrated clinical efficacy.
- It must have a high barrier to resistance.
- It should be well-tolerated.
- It should allow for once-daily therapy.

For HIV treatment to be effective, the regimen should be a combination of:

1. Three effective ART that is usually consisted of:
   A. 2 **Nucleoside/Nucleotide reverse transcriptase inhibitors (**NRTIs) as backbone AND
   B. A third active ART from one of the following:
      - Oral second generation Integrase inhibitors (INSTIs) **OR**
      - PIs **OR**
      - Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
2. Dual ART e.g. Dolutegravir (DTG)/ Lamivudine (3TC) may be used as an initial ART regimen in certain patients when specific criteria are met (only if HIV RNA <500,000 copies/mL, if 3TC resistance not present, and if HBV coinfection not present; not for rapid start).

First-line ART regimens for adults and adolescents

First-line regimen refers to the first regimen of drugs that a person takes. Preferred regimens are shown in *table 6*; alternative regimens are shown in *table 7.*

Table 6: Preferred first-line ART for adults and adolescents

Preferred Regimen	Comments
2 NRTIs + INSTI	
TAF/FTC/BIC	Single tablet regimen
(TAF/FTC) +DTG	
1 NRTI + INSTI	
3TC + DTG	HBsAg negative HIV VL < 500,000 copies/mL No 3TC resistance Not recommended after PrEP failure

Table 7: Alternative first-line ART for adults and adolescents

Alternative Regimen	Comments
2 NRTIs + INSTI	
(TDF/FTC) +DTG	
(TAF/FTC) or (TDF/FTC) + RAL 1200 mg once a day or 400 mg bid	
2 NRTIs + PI/r or cobicistat (c)	
(TAF/FTC) or (TDF/FTC) + DRV/r or c	
(TAF/FTC) or (TDF/FTC) +ATV/r or c	
2 NRTIs + NNRTI	
Doravirine (DOR) plus (TAF/FTC) or (TDF/FTC) or (3TC/TDF)	
TDF/FTC/ Efavirenz (EFV)	Single tablet regimen

Considerations

- INSTI-based regimens have become the ***preferred*** option for initial ART in adults whenever possible due to their virologic efficacy, lack of drug interactions, and favorable toxicity profile.
- Clinical trials have shown that INSTI-containing regimens have superior efficacy compared with PI-containing and NNRTI-containing regimens.
- BIC and DTG has shorter median time to viral suppression and higher genetic barrier to developing drug resistance.
- BIC and DTG has clinical activity against HIV-2 infection.
- DTG has been associated with increased risk of insomnia and other neuropsychiatric adverse reactions.
- 3TC may substitute for FTC or vice versa.

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Chapter 9:
Management of treatment-experienced patients

Chapter 9: Management of treatment-experienced patients

9.1 Virological response definitions

Virological failure is complex and can be due to multiple factors. Unsuppressed VL and persistent HIV replication results in development of resistance-associated mutations, gradual depletion of CD4 cells and clinical progression of HIV infection. The following factors in a patient with virological failure should be assessed and addressed:

- Adherence to ART
- Interaction between ART and other medications or food including over the counter supplements such as Ca, Mg, Fe, Zn
- Adverse effects or intolerance that led to poor adherence or cessation of ART
- Malabsorption
- Reviews of all prior drug resistance testing results, previous treatment experience, and reason for treatment changes or discontinuation

Definitions

- **Virologic Suppression:** Two consecutive HIV-1 RNA measurements <50 copies/mL while prescribed ART.

- **Virologic Failure:** The inability to achieve or maintain suppression of viral replication to HIV RNA level despite a patient's use of recommended ART.

- **Persistent Low-Level Viremia:** Two or more consecutive HIV-1 RNA measurements 50-999 copies/mL at least 30 days apart without progression to higher than 1,000 copies/mL or return to viral suppression.

- **Virologic Rebound:** After virologic suppression, confirmed HIV-RNA level ≥200 copies/mL.

- **Virologic Blip:** After achieving viral suppression, any HIV-1 RNA 50-999 copies/mL that is immediately preceded and followed by an HIV-1 RNA <50 copies/mL without a change in ART.

Table 8 shows the World Health Organization (WHO) definitions of treatment failure.

Table 8: Clinical, immunological, and virological failure to ART

Failure	Definition	Comments
Clinical failure	Adults and adolescents New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition) after 6 months of effective treatment Children New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical conditions with exception of TB) after 6 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 falls to the baseline (or below) ***Or*** Persistent CD4 levels below 100 cells/mm^3 Children • Younger than 5 years ○ Persistent CD4 levels below 200 cells/mm^3 or < 10% • Older than 5 years ○ Persistent CD4 levels below 100 cells/mm^3	Without concomitant or recent infection to cause a transient decline in the CD4 cell count
Virological failure	A confirmed HIV VL ≥200 copies/mL despite a patient's use of recommended ART a VL that rebounds to ≥200 copies/mL after a patient achieves viral suppression.	An individual must be taking ART for at least **6 months** before it can be determined that a regimen has failed

9.2 Causes of virologic failure

Earlier studies on combination ART suggested that poor adherence and drug-related side effects were major contributors to treatment failure and regimen discontinuation. With advancements in ART, modern regimens are generally better tolerated and have a lower pill burden, which may help improve adherence. However, virologic failure can still occur due to various factors, including:

I. **HIV-Related Factors**

- Presence of transmitted (in treatment naïve patients) or acquired drug-resistant virus (in treatment experience patients), whether detected or undetected in past or current resistance tests
- Previous failure with ART

- High pre-treatment HIV-RNA levels (e.g., >100,000 copies/mL), which may reduce the effectiveness of certain regimens

II. **Antiretroviral Regimen-Related Factors**

- Poor drug absorption, metabolism, or distribution in the body (suboptimal pharmacokinetics)
- Insufficient virologic potency
- Low resistance barrier, increasing the risk of treatment failure
- Reduced effectiveness due to prior exposure to weak or outdated regimens (e.g., monotherapy, dual-NRTI therapy, or staggered drug introductions)
- Malabsorption syndrome, bariatric surgery procedures or dietary requirements that impact medication absorption
- Drug interactions with other medications that lower ARV drug levels
- Intolerance and side effects leading to reduced adherence
- Complex regimens with high pill burden or frequent dosing
- Errors in prescribing or dispensing medications

III. **Social and Adherence-Related Factors**

- Substance use, mental health conditions, or cognitive impairment
- Financial barriers or other social challenges
- Missing clinic visits
- Interrupted or inconsistent access to ART

9.3 Management of treatment-experienced patients with virologic failure

Managing ART failure in people with HIV is complex and requires expert consultation. Key steps include:

A. Assessment of Virologic Failure

- Evaluate adherence, drug interactions, tolerability, HIV RNA levels, CD4 trends, ART history, and resistance test results.
- Perform resistance testing while on the failing regimen or within 4 weeks of stopping it.
- For long-acting (LA) CAB/RPV regimens, perform resistance testing regardless of the time since the last dose.

B. Treatment Goals & Regimen Selection

- The primary goal is to achieve virologic suppression (HIV RNA undetectable).
- A new regimen should ideally include two fully active drugs, with at least one having a high resistance barrier (e.g., second-generation INSTI or boosted PI) (Table 9).
- If no high-resistance barrier drug is available, aim to include three fully active drugs.
- Fully active drugs may include:
    - Drugs in classes for which the person has not previously selected for drug-resistant virus.
    - Newer drugs in existing drug classes that are predicted to be fully active against HIV isolates despite the presence of resistance mutations for some drugs in the same drug class. For example, etravirine (ETR) and possibly doravirine (DOR) in NNRTIs class, the DRV/r in PIs class and DTG and BIC in INSIs. However, clinical data supporting the use of DOR or BIC in the setting of virologic failure are limited for now.
    - Drugs with novel mechanisms of action that the person with HIV has not received before, such as the post-attachment inhibitor ibalizumab (IBA), the gp120 attachment inhibitor fostemsavir (FTR), the capsid inhibitor lenacapavir (LEN), the fusion inhibitor enfuvirtide (T-20), or the CCR5 antagonist maraviroc (MVC) in people with no detectable CXCR4-using virus.

C. Important Considerations

- Adding a single ARV to a failing regimen is not recommended due to the risk of further resistance.
- In cases of extensive drug resistance, ART should still be continued to maintain CD4 levels and delay disease progression.
- Provide adherence support before and after regimen changes.
- For individuals with HBV/HIV coinfection, continue an HBV-active drug (TAF, TDF, or entecavir) to prevent HBV rebound.
- ART should not be discontinued or interrupted, as this can lead to rapid viral rebound and immune decline.
- In cases with suspected drug resistance and limited or incomplete ART and resistance history, please refer to an HIV expert
- In cases with multiple or extensive drug resistance with few/limited treatment options, please refer the patient to an HIV expert for consideration of novel ARV such as IBA, FTR, LEN, T-20), or MVC.

Table 9: Antiretroviral Options for Patients with Virologic Failure

Clinical Scenario	Type of Failing Regimen	New Regimen Options
First Regimen Failure	NNRTI plus two NRTIs	• DTG (or BIC) plus two NRTIs (preferably at least one fully active) • Boosted PI plus two NRTIs (preferably at least one fully active) • Boosted PI plus INSTI (boosted DRV plus DTG)
	Boosted PI plus two NRTIs	• DTG, or BIC, plus two NRTIs (preferably at least one fully active) • Continue same regimen with adherence support • Boosted PI plus INSTI (boosted DRV plus DTG) • Another boosted PI plus two NRTIs (at least one fully active)
	INSTI plus two NRTIs	If failure with no INSTI resistance • Boosted PI plus two NRTIs (preferably at least one fully active) • DTG, or BIC, plus two NRTIs (preferably at least one fully active) • DRV/r plus DTG If failure with INSTI resistance • Boosted PI plus two NRTIs (preferably at least one fully active) • DTG twice daily or possibly BIC (if HIV is sensitive) plus two fully active NRTIs • DTG twice daily or possibly BIC (if HIV is sensitive) plus a boosted PI (preferably DRV/r)
	INSTI plus NNRTI (DTG/RPV or LA CAB/ RPV)	• Use ART history and past and current resistance testing to design a new regimen. • Consult an HIV specialist

Second Regimen Failure and Beyond (Drug resistance with fully active treatment options	i) Second line with resistance to DTG/BIC but not to Boosted PI second-	i) Boosted PI with two NRTIs (preferably at least one fully active)
	ii) Second line with resistance to boosted PI but not to DTG/BIC	ii) DTG or BIC with two NRTIs (preferably at least one fully active)
	iii) Second line with Both PI and INSTI fully active	(iii) The two options above or boosted PI with INSTI

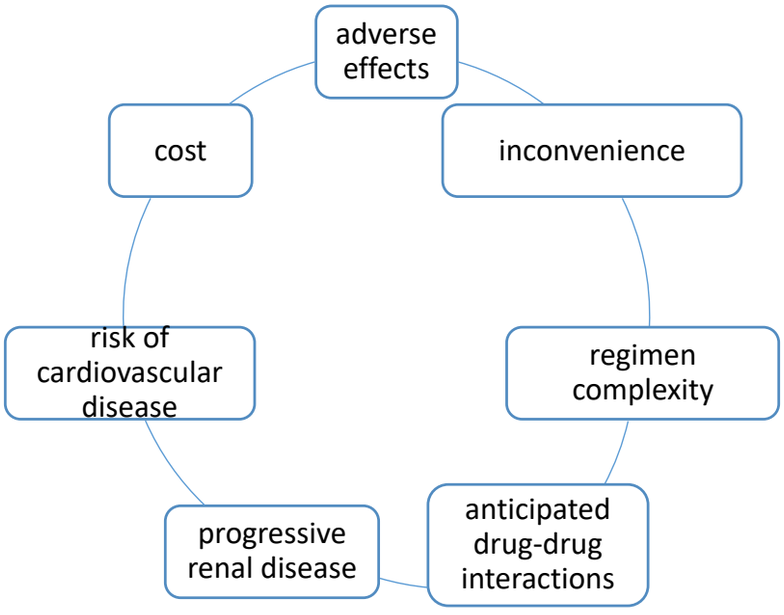
9.4 Management of treatment-experienced patients with undetectable plasma VL

In the absence of virologic failure, switching ART is possible if viral suppression is maintained and future treatment options are preserved.

Reasons for ART switch in the setting of virologic suppression include (Fig. 17):

- Adverse events
- Drug interactions
- Pill burden
- Pregnancy
- Cost
- Stigma
- Inconvenience
- Desire for regimen simplification

Fig. 17: Reasons for ART switch in the setting of virologic suppression



Pre-switch evaluation and review should include:

- Full ART history
- Virologic responses
- Past toxicities
- Intolerances
- Resistance test results

Table 11 shows ART options when switching ART in patients with viral suppression. Close monitoring of tolerability, viral suppression, adherence and safety for the first 3 months is warranted.

Table 10: Guidance for ART switch in the Setting of Virologic Suppression

Scenario	ART Options
No History of Resistance or Virologic Failure	Can switch to any highly effective regimen for ARV-naïve individuals or NRTI-sparing options like DTG + RPV or LA CAB/RPV.
Existing NRTI Resistance	Include two NRTIs (TAF or TDF + FTC or 3TC) plus a fully active high-resistance barrier drug (DTG, BIC, or boosted darunavir). NRTI-sparing options (DTG/RPV or LA CAB/RPV) may be used if no INSTI or RPV resistance.
History of Resistance to Two or More Drug Classes	Consult an HIV specialist.
HIV/HBV Coinfection	Use HBV-active drugs with a high barrier to resistance (TAF, TDF, or entecavir). Avoid discontinuation to prevent HBV reactivation and liver damage – see chapter xxxx
Monotherapy	Not recommended due to high risk of virologic failure and resistance development.

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Chapter 10: Management of ART

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Once a person begins ART, adherence is crucial for its effectiveness. Regular monitoring by a doctor and a counselor is essential to ensure the treatment is achieving its intended goals.

After the initial ART prescription, the assigned healthcare provider should establish a schedule for regular follow-up visits to:

- Monitor **adherence** to treatment and discuss strategies to support optimal adherence.
- Identify and report potential **toxicities** of ART
- Assess the need for modifying or **substituting** ART
- Screen for and manage potential **OIs.**
- **Detect** early signs of **treatment failure**.

10.1 Laboratory monitoring

Table 11 provides an outline of laboratory tests recommended for all PLHIV at baseline assessment (previously discussed in *section 4.1*) as well as during follow-up.

Table 11: Laboratory monitoring and follow-up of HIV-infected individuals

	Entry into care	ART initiation or modification	2-8 weeks post-ART initiation or modification	Every 3-6 months	Every 6 months	Every 12 months	Treatment failure	Clinically indicated
HIV serology	√ If diagnosis has not been confirmed							
CD4 count	√	√		√ Every 3 months < 300 cell/mm3	√ During the first 2 years if CD4>300 cell/ mm3	√ After 2 years of ART if CD4 300-500cell/ mm3 If CD4 >500 monitoring is optional	√	√
HIV VL	√	√	√	√	√*		√	√
Resistance testing	√	√					√	√

HLA-B*5701 testing		√ If considering ABC						
Hepatitis B Serology (HBsAg, anti-HBc, anti-HBs)	√	√ if patient is not vaccinated/immune and considering a regimen that doesn't contain tenofovir						√
Hepatitis C serology	√					√ Repeat for high-risk patients		√
Cryptococcus serum antigen	√ If CD4 count <100 cells/mm^3							√
(STIs (syphilis	√	√						√
Renal Functions Test	√	√	√	√				√
Liver function Tests	√	√	√	√				√
CBC with differential	√	√		√				√

Fasting lipid profile	√	√	√ Consider 4–8 weeks after starting new ART regimen that affects lipids		√ If normal at last Measure-ment			√
Fasting glucose or haemoglobin A1C	√	√			√ If normal at last measure-ment		√	√
Urinalysis	√	√			√ If on TDF	√		√
Pregnancy test	√	√ If starting EFV						√

*For patients on ART, VL typically is measured every 3–6 months. More frequent monitoring may be considered in individuals having difficulties with ART adherence or at risk for nonadherence. However, for adherent patients with consistently suppressed VL and stable immunologic status for more than 1 year, monitoring can be extended to 6-month intervals.

10.2 Adherence to ART

Adherence refers to a patient's commitment to taking medications correctly, as agreed upon with their healthcare provider. Adherence involves taking the **right drugs** in **the right doses** and **the right frequency** at **the right time**.

For a successful HIV treatment outcome, PLHIV must maintain at least 95% adherence to their prescribed ART, which means taking their ART exactly as they are prescribed, 95% of the time. In other words, 95% adherence (or optimum adherence) means:

- Not missing more than 1 dose a month in a once daily regimen.
- Not missing more than 3 doses a month in a twice daily regimen.

Adherence below 95% has been linked to increased VL and the development of drug resistance. Therefore, it is essential for patients to understand the critical role of adherence in achieving virological suppression, maintaining CD4 cell count, and reducing mortality. Optimal adherence is crucial to prevent treatment failure.

Barriers to adherence

Studies have revealed many factors that may interfere with optimum adherence to ART. These factors include:

- Nondisclosure of HIV serostatus
- Denial
- Stigma
- Low health literacy
- Busy or unstructured daily routines
- Depression and other mental illnesses
- Neurocognitive impairment
- High pill burden and complexity of treatment
- ART side effects and toxicities
- Severe illness and distance to facility
- Lack of social support
- Active substance abuse
- Poverty

Monitoring adherence

Virologic success in antiretroviral therapy (ART) is highly dependent on adherence. Adherence is typically measured by calculating the percentage of prescribed doses that a patient has taken. While there is no universally accepted 'gold standard' for monitoring adherence, several tools can be used to assess it, including:

1. ***Pill count method***: this method is conducted by the dispensing healthcare worker. The adherence level is calculated by determining the number of pills a patient was supposed to take over a given period (A) and subtracting the number of pills missed (B). The adherence percentage is then determined using the following formula: [(A-B)/A]*100.
2. ***Two-day recall method***: for twice-daily regimens or cases involving a large number of pills, this method uses 'sun and moon' charts to assess the consistency of medication intake over the past two days. For once-daily regimens, the recall period can be extended to seven days.
3. ***Visual analogue method:*** ART users will indicate their adherence rate by marking a 10 cm visual analogue scale. The distance from zero to the marked point will be multiplied by 10 to estimate the percentage adherence rate.

Measuring adherence remains a challenge, as no single method can accurately assess it. However, a combination of approaches can provide a more comprehensive evaluation. In addition to the previously mentioned methods, other approaches include patient self-reporting, electronic monitoring devices, pharmacy refill tracking, provider assessments, and measuring medication levels in the bloodstream

Strategies to support adherence

Adherence is a dynamic behavior that changes over time. Adherence can be influenced by several factors, including a person's social situation, clinical condition, the prescribed regimen, and the patient–provider relationship. Optimum adherence requires an integrated multidisciplinary approach that involves physicians, nurses, counselors and pharmacists. It requires a combination of adherence promoting strategies. The following are some strategies to support adherence through the course of ART:

Adherence support prior to initiating ART: adherence counseling done by a professional counselor or a peer counselor to all PLHIV before initiating ART is a first step to ensure success of treatment and effective outcome. Adherence counseling prior to initiating ART should include:

1. *Education* of patients about HIV and treatment (e.g.: basic information on HIV, its transmission, benefits and side effects of ART).
2. *Assessment* of patient understanding of the therapy (e.g. how the medications should be taken and the importance of not missing any dose).
3. Patient *readiness* for treatment (e.g. social and family support and patient's lifestyle).

Adherence consideration at initiation of ART:

- The number of pills.
- Frequency of dosing.
- Food restrictions.
- Adjusting ART to the patient's lifestyle.
- Involving relatives, friends and/or community members.

Adherence support during therapy: it is essential to continue with adherence counseling. This should involve:

- Assessment during every visit.
- Emphasis on importance of adherence.
- Addressing adherence barriers such as substance abuse, mental health, and lack of social support.
- Continuous involvement of relatives, friends, peers and/or community support personnel.

10.3 Management of ART toxicities

Table 12 shows the common ART-induced toxicities, their risk factors and management.

Table 12: ART toxicities (major types, risk factors and management)

ARV drug	Major types of toxicity	Risk factors	Suggested management
ABC	Hypersensitivity reaction Increase risk of MI in some cohort studies	-Presence of HLA-B*5701 gene	Substitute with TAF or TDF
ATV/r	Electrocardiographic abnormalities (PR interval prolongation)	-Preexisting conduction disease -Concomitant use of other drugs that may prolong the PR interval	Change to Integrase inhibitor, boosted DRV or NNRTI)
	Indirect hyperbilirubinemia (clinical jaundice)	-Underlying hepatic disease -HBV and HCV co-infection -Concomitant use of hepatotoxic drugs	
	Nephrolithiasis and risk of prematurity	-Risk factors unknown Median onset 42 months after starting medications	
AZT	Anemia, neutropenia, myopathy, lipoatrophy or lipodystrophy	-Baseline anemia or neutropenia -CD4 count ≤ 200 cells/mm3	Substitute with TAF or TDF
	Lactic acidosis or severe hepatomegaly with steatosis	-BMI > 25 (or body weight > 75 kg) -Prolonged exposure to nucleoside analogues	
DRV/r	Hepatotoxicity GI upset Increase TG	-Underlying hepatic disease -HBV and HCV co-infection -Concomitant use of hepatotoxic drugs	Change to Integrase inhibitor or ATV/r
	Severe skin and hypersensitivity reactions (not there in guidelines)	Sulfonamide allergy	

EFV	Persistent central nervous system (CNS) toxicity (such as abnormal dreams, depression or mental confusion)	-Depression or other mental disorder	Change to Integrase inhibitor or boosted DRV
	Hepatotoxicity	-Underlying hepatic disease -HBV and HCV co-infection -Concomitant use of hepatotoxic drug	
	Convulsions	History of seizure	
	-Hypersensitivity reaction -Stevens-Johnson syndrome -Potential risk of neural tube birth defects (very low risk in humans) -Male gynecomastia	Unknown	
ETV	Severe skin and hypersensitivity reactions	Unknown	Change to Integrase inhibitor or boosted DRV

LPV/r	Electrocardiographic abnormalities (PR and QT interval prolongation, torsades de pointes)	-People with preexisting conduction system disease -Concomitant use of other drugs that may prolong the PR interval	-If LPV/r is used in first-line ART for children, use an integrase inhibit or an age-appropriate NNRTI (NVP for children younger than 3 years and EFV for children 3 years and older) -ATV can be used for children older than 6 years -In adults, Change to Integrase inhibitor or boosted DRV or ATV/r or NNRTI
	QT interval prolongation	-Congenital long QT syndrome -Hypokalemia -Concomitant use of drugs that may prolong the QT interval	
	Hepatotoxicity	-Underlying hepatic disease HBV and HCV co-infection -Concomitant use of hepatotoxic drugs	
	Pancreatitis	Advanced HIV disease	
	Risk of prematurity, lipoatrophy or metabolic syndrome, dyslipidemia or severe diarrhea	Risk factors unknown	
NVP	Hepatotoxicity	-Underlying hepatic disease -HBV and HCV co-infection -Concomitant use of hepatotoxic drugs -CD4 > 250 cells/mm3 in women -CD4 > 400 cells/mm3 in men -First month of therapy (if lead-in dose is not used)	Change to Integrase inhibitor or boosted DRV
	Severe skin rash and hypersensitivity reaction (Stevens-Johnson syndrome)	Risk factors unknown	

RAL	Rhabdomyolysis, myopathy, myalgia Insomnia, headache	Concomitant use of other drugs that increase the risk of myopathy and rhabdomyolysis	Change to DTG or BIC, or boosted DRV or ATV/r
DTG	Increase CK level and myositis CNS (insomnia, headache), less frequently(-depression) Hepatotoxicity Weight gain	Depression more likely in those with pre-existing condition	Change to boosted DRV
BIC	Increase CK level and myositis GI upset with diarrhoea and vomiting Rarely CNS side effects(headache) Weight gain	Weight gain is more in combination with TAF	Change to boosted DRV
TDF	-Renal tubular dysfunction, -Fanconi syndrome	-Underlying renal disease Older age -BMI < 18.5 (or body weight < 50 kg) -Untreated diabetes mellitus -Untreated hypertension -Concomitant use of nephrotoxic drugs or a boosted PI	Change to TAF or discuss with a specialist if considering nuke-sparing regimen
	Decreases in bone mineral density	-History of osteomalacia and pathological fracture -Risk factors for osteoporosis or bone loss	
	Lactic acidosis or severe hepatomegaly with steatosis	-Prolonged exposure to nucleoside analogues -Obesity	
	Exacerbation of hepatitis B (hepatic flares)	Discontinuation of TDF due to toxicity	Use alternative drug for hepatitis B treatment (such as entecavir)

10.4 Management of drug-drug interactions

Table 13 illustrates the key ART drug-drug interactions and their management.

Table 13: Key ART drug-drug interactions and their management

ARV drug	Key interactions	Effect	Suggested management
BIC	Antacid	**Al/Mg hydroxide antacid:** decrease BIC level by 47%-79% if administered simultaneously **Ca containing antacid:** decrease BIC level by 33% if administered under fasting condition	For antacid containing Al/Mg: Give antacid 6 hrs before or 2 hrs after BIC For antacid containing Ca: Give antacid with food
	Rifampicin	decrease BIC level by 75% of BIC concentration	Change to DTG bid
	Metformin	increase Metformin level by 39%	Monitor for side effects of metformin
DTG	Antacid	decrease DTG level by 74% if administered simultaneously with antacid	Give DTG 2 hrs before or 6 hrs after antacid containing polyvalent cations
	Rifampicin	decrease DTG level by 54%	Increase the dose to bid Or Change Rifampicin to Rifabutin (without changing DTG dose)
	Metformin	increase Metformin by 79%	Start Metformin at lower dose and monitor for side effects
AZT	Ribavirin and peg-interferon alfa-2a	Increased risk of anemia and hepatic decompensation	- Substitute AZT with TDF, ABC or d4T -Discuss with a specialist

Boosted PI (ATV/r, LPV/r)	Rifampicin	Hepatotoxicity and gastrointestinal intolerance Decrease PI concentration by 75%	-Substitute rifampicin with rifabutin (150mg od) - Use integrase inhibitor -Discuss with a specialist
	Lovastatin and simvastatin	Increased risk of myopathy	Use an alternative dyslipidemia agent (e.g. Atorvastatin)
	Estrogen-based hormonal contraception	Increase/decrease bioavailability of steroid hormones	Use alternative or additional contraceptive methods
	Methadone and Buprenorphine	Decreased Methadone concentrations which may lead to withdrawal symptoms and relapse to opioid use	Adjust methadone and buprenorphine doses as appropriate
	Astemizole and terfenadine	Cardiac arrhythmia	Use alternative antihistamine agent
	Protein Pump Inhibitors	Decrease bioavailability of ART	PPI should be given at least 12 hours before ATV
	Clarithromycin	Increase concentration of clarithromycin	Use Azithromycin or change ART to integrase inhibitor
	Warfarin Rivaroxiban	Increase concentration of warfarin Increase concentration of Rivaroxiban	Closely monitor INR Avoid using rivaroxiban or change to integrase inhibitor
	Clopidogrel	Decrease concentration of clopidogrel	Do not co-administer or change to Integrase inhibitor
	Steroids	Increase concentration of steroids	Do not co-administer, or change to Integrase inhibitor
EFV	Methadone	Decreased Methadone concentrations which may lead to withdrawal symptoms and relapse to opioid use	- Close monitoring - Adjust the methadone dose as appropriate
	Estrogen-based hormonal contraception	Increase/decrease bioavailability of steroid hormones	Change ART regimen or use alternative or additional contraceptive Methods
	Itraconazole Posaconazole Voriconazole	Decrease itraconazole AUC by 86% Decrease posaconazle AUC by 50% Decrease voriconazole AUC by 77% and increase EFV AUC by 44%	Do not co-administer Do not co-administer Adjust the dose to voriconazole 400mg bid + EFV 300mg od

NVP	Rifampicin	Hepatotoxicity and gastrointestinal intolerance	Substitute NVP with EFV
	Itraconazole and ketoconazole	Decreased concentration of itraconazole and ketoconazole to sub-therapeutic levels	Use an alternative antifungal agent (for example fluconazole)

11

Chapter 11: HIV and co-Infections

Chapter 11: HIV and Co-infections

11.1: Vaccinations for adult PLHIV

Vaccination plays a crucial role in preventing infections among PLHIV and PWID. Table 14 summarizes the recommended vaccinations in PLHIV and PWID, including those that may not be readily available.

Table 14: Recommended vaccinations for people living with HIV and people who inject drugs

Group	Vaccine name	Doses	Schedule	Comments
PLHIV	**Seasonal Influenza vaccine** "Inactivated"	Annually	At any visit every fall or winter, yearly	All PLHIV
	PCV 13 vaccine "Conjugated" **followed by** **PPSV 23** "Polysaccharide" **OR** **PCV 20 vaccine**	Single dose Single dose Single dose	1st vaccination visit. At least 8 weeks after PCV 13 1st vaccination visit	All PLHIV. PPSV 23 should preferably be deferred until after an individual's CD4 count increases to >200 cells/mm^3 while on ART All PLHIV
	Meningococcal vaccine "Conjugated"	2 doses	After 1st visit, 2 doses at 8 weeks interval.	All PLHIV
	Hepatitis A virus vaccine "Inactivated"	If CD4 count >350 cells/mm^3 to be given 2 doses at 0- & 6-months' interval If CD4 < 350 cells/mm^3 to be given 3 doses at 0, 1 & 6 months	Can be given at the same time of HBV vaccine or separately	To be given for those at-risk group if HAV IgG is negative: Travel, close contact with children, MSM, IVDU, active HBV or HCV infection, chronic liver disease)

	Hepatitis B virus (HBV) vaccine "Subunit"	3 doses	If non-immune anti-Hbs <10 IU/L to be given 3 doses at 0,1 and 6 months Measure anti-HBs 4 weeks after the last dose of the vaccine: -If repeated anti-Hbs <100 IU/L give a booster dose -If anti-Hbs <10 IU/L repeat 3 doses	All non-immune PLHIV
	Human Papilloma virus vaccine "Subunit"	3 doses	At 0, 1 and 6 months	All PLHIV, as early as age 9 years and for PLHIV who are aged 13 to 26 years and who were not vaccinated previously, regardless of gender. Patients aged 27 to 45 years old can be considered. Contraindicated in pregnancy
	Varicella vaccine (Chickenpox) "Live attenuated"	2 doses 4–8 weeks apart		Contraindicated if CD4 <200 **cells/mm^3.** All non-immune **if CD4 >200 cells/mm^3** Contraindicated in pregnancy
	Herpes zoster (Shingles) "Live attenuated"	Shingrix 2 doses 2–6 months apart		All HIV-positive adults aged 19 years and older to be given if CD4 >200 cells/mm^3

	Mpox vaccine "Live nonreplicating"	2 doses At any CD4 count	28 days apart	For PLHV who have potential for mpox exposure or anticipate potential exposure to mpox, including high-risk MSM. For unvaccinated PLHIV who experience a known or presumed mpox exposure
PWID "People who inject drugs"	**Hepatitis B virus (HBV) vaccine** "Subunit"	3 doses	0, 1 and 6 months	

11.2 Prevention of OIs

Table 15 summarizes the recommended prophylactic therapy and prevention of common opportunistic infections

Table 15: Primary and secondary prophylaxis for opportunistic infections

Primary prophylaxis	Preferred regimen	Indications to d/c primary prophylaxis	Indications for restarting primary prophylaxis	Secondary prophylaxis
Pneumocystis jirovecii pneumonia (PJP); formely known as pneumocystis carinii pneumonia (PCP)				
• CD4 count <200 cells/ mm^3, or • CD4 percentage <14% of total lymphocyte count, or • CD4 count >200 cells/ mm^3, but <250 cells/ mm^3 if ART initiation must be delayed and if CD4 count monitoring (e.g., every 3 months) is not possible Note: Patients who are receiving pyrimethamine/ sulfadiazine for treatment or suppression of toxoplasmosis do not require additional prophylaxis for PCP.	Preferred Therapy: • **TMP-SMX,** (960 mg PO daily, or 480 mg PO daily) Alternative Therapy: • **TMP-SMX** 960 mg PO three times weekly, or • **Dapsone** 50 mg PO daily with (**pyrimethamine** 50 mg plus **leucovorin** 25 mg) PO weekly, or • (**Dapsone** 200 mg plus **pyrimethamine** 75 mg plus **leucovorin** 25 mg) PO weekly, or • **Atovaquone** 1500 mg PO daily with food, The following should only be used in people who are seronegative for Toxoplasma gondii: • **Dapsone** 100 mg PO daily or 50 mg twice daily, or • **Aerosolized pentamidine** 300 mg via Respigard IITM nebulizer every month, or • **Intravenous pentamidine** 300 mg every 28 days		• CD4 count <100 cells/ mm3 regardless of HIV RNA • CD4 count 100–200 cells/ mm^3 and HIV RNA above detection limit	Indication for initiation: Prior PJP infection Indication for d/c secondary prophylaxis: Same as indication of stopping primary prophylaxis For patients in whom PJP occurs at a CD4 count >200 cells/mm^3 while not on ART, discontinuation of prophylaxis can be considered once HIV RNA levels are suppressed to below limits of detection for ≥3 to 6 months, although there are no data to support ecommendations in this setting Note: If an episode of PCP occurs at a CD4 count >200 cells/mm3 while a patient is on ART, it would be prudent to continue PCP prophylaxis for life, regardless of how high the CD4 cell count rises because of ART

Toxoplasmosis				
• CD4 count <200 cells/mm^3, or • CD4 percentage <14% of total lymphocyte count	Preferred regimen: • **TMP-SMX** (960 mg PO daily, or 480 mg PO daily, or 960 mg PO three times weekly) Alternative regimens: • **Atovaquone** suspension 1500 mg PO daily, or • **Dapsone** 200 mg plus **pyrimethamine** 75 mg plus **leucovorin** 25 mg) PO weekly, or • **Atovaquone** 1500 mg plus **pyrimethamine** 25 mg plus **leucovorin** 10 mg) PO daily with food	CD4 count >200 cells/mm^3 for >3 months in response to ART, or • Can consider if CD4 count is 100-200 cells/mm^3 and HIV RNA levels remain below limits of detection for at least 3-6 months	CD4 count <100 to 200 cells/mm^3	After completion of the acute therapy, all patients should be continued on chronic maintenance therapy if they remain asymptomatic, and CD4 count >200 cells/mm^3 for >6 months in response to ART Criteria for Restarting Secondary Prophylaxis/ Chronic Maintenance • CD4 count <200 cells/mm^3
Cryptococcosis				
Primary prophylaxis is not recommended Pre-emptive therapy to be used in case of: -Positive Cryptococcus Serum Antigen **and** -Asymptomatic individuals with CD4 < 100 cells/mm^3	Preferred regimen: **Fluconazole** 800 mg PO daily for 2 weeks followed by 400 mg PO daily for 8 weeks then maintenance of 200 mg PO daily			-Secondary prophylaxis duration for at least 12 months - Stop secondary prophylaxis if CD4 > 100 cells/mm^3 and HIV VL undetectable over 3 months **or** - CD4 > 200 cells/ mm^3

Non-tuberculous *Mycobacterium* (NTM)				
Not recommended if ART is started immediately May be considered for persons with CD4 count < 50 cells/ mm^3 who remain viremic on ART (drug resistant HIV with no option to achieve virologic control). Exclude disseminated MAC before starting.	Preferred regimen: **Azithromycin** 1250 mg/week PO (or 500 mg twice weekly), or **Clarithromycin** 500 mg bid PO, or Alternative therapy: **Rifabutin** 300 mg PO daily *Note: Consider DDI and dose adjustment when used with ART) Active TB should be ruled out before starting Rifabutin	Initiation of effective ART	CD4 count < 50 cells/ mm3 (only if not on fully suppressive ART)	Stop if CD4 count > 100 cells/ mm^3 and HIV VL undetectable over 6 months and MAC treatment received for at least 12 months

11.3 HIV and TB

It is recommended that, in case of TB/HIV co-infections, both infections are addressed together. However, co-treatment of HIV and TB is complex because of the following challenges:

-Adherence of multi drug therapy.
-Drug-drug interactions between the rifampicin (for TB treatment) and many ART.
-Overlapping side effects of anti-tuberculosis and ART drugs.

- Risk of IRIS particularly with disseminated TB and TB meningitis.

Screening for latent/ active TB

- All persons with HIV should be tested for LTBI at the time of HIV diagnosis.
- The IGRA is the recommended test for adults.
- The Tuberculin Skin Test (TST) is an alternative test; a result is considered positive if there is ≥ 5 mm of skin induration at 48–72 hours.
- All persons with a positive TST or IGRA should be evaluated for the possibility of active TB disease.
- Once TB disease is excluded and in the absence of other medical contraindications, persons with HIV and a positive TB screening test should receive LTBI treatment, unless there is documentation of prior treatment for active TB or LTBI.

Latent TB management

Table 16 shows treatment regimens for latent TB.

Table 16: Latent TB treatment regimens

Regimen	Dose timing	Duration	Comments
Isoniazid 300 mg PO daily + pyridoxine 40-50mg PO daily	Daily	6-9 months	Preferred regimen
Rifampicin 600 mg PO daily	Daily	4 months	Check DDI with ART and other medications
3HR: Rifampicin 600 mg PO daily + Isoniazid 300 mg PO daily + pyridoxine 40-50 mg PO daily	Daily	3 months	Check DDI with ART and other medications
3HP: Rifapentine 900 mg PO x 1/ week + Isoniazid 900 mg PO x 1/ week + pyridoxine 40 -50 mg PO x 1/ week	Once weekly	3 months	3HP is recommended only for virally suppressed persons receiving EFV, RAL, or once daily DTG-based ART regimen
Rifapentine 450 mg (<45 kg) or 600 mg (>45 kg) PO daily + Isoniazid 300 mg PO daily + pyridoxine 40 -50mg PO daily	Daily		

Active TB management

- After collecting the required specimens for culture and molecular diagnostic tests, empiric treatment should be initiated in PLWH with clinical and radiographic presentation suggestive of HIV-related TB.
- Treatment regimens for active TB are shown in table 17.
- Doses should be calculated based on body weight (Table 18).
- Timing of ART in PLHIV with active TB is depicted in table 19

Table 17: Recommended regimens for active tuberculosis

Drug susceptible TB		
Intensive phase	Type of TB	Duration of treatment
2 months of Isoniazid plus (**rifampin** or **rifabutin**) plus **pyrazinamide** plus **ethambutol** **Followed by** continuation phase of Isoniazid plus (rifampin or rifabutin) daily	Pulmonary & extrapulmonary (except CNS or bone involvement)	**6 months**
	Extensive pulmonary	**12 months**
	Osteo-articular TB	**12 months**
	TB meningitis / TB CNS involvement	**9-12 months** Corticosteroids are recommended as adjuvant treatment in TB meningitis / TB CNS involvement
Drug resistant TB		
Isoniazid and ethambutol	Rifampicin (rifabutin), pyrazinamide and a fluoroquinolone (levofloxacin or moxifloxacin)	**6-9 months**
Isoniazid and pyrazinamide	Rifampicin (rifabutin), pyrazinamide and a fluoroquinolone (levofloxacin or moxifloxacin)	**9-12 months**
Isoniazid, ethambutol and pyrazinamide	Rifampicin (rifabutin), a fluoroquinolone (levofloxacin or moxifloxacin) and one or two additional oral agents to which the isolate is susceptible (possible additional agents include, linezolid, or clofazimine; use of bedaquiline with rifampicin is contraindicated)	**9-12 months**

Empiric Therapy for Resistance to Rifamycin plus/minus Resistance to Other Drugs:	Discuss with HIV/Infectious diseases Specialist Note: Definitive therapy should be individualized based on drug susceptibility test results, clinical and microbiological responses, to include 5 active drugs, and with close consultation with experienced specialists	Duration: **12 to 24 months** Refer to WHO guidelines on management of MDR/XDR-TB and National guidelines on management of TB

Adjunctive corticosteroid improves survival for patients with HIV-related TB involving the CNS.

- Dexamethasone has been used for CNS disease with the following dosing schedule: 0.3–0.4 mg/kg/day for 2–4 weeks, then taper 0.1 mg/kg per week until 0.1 mg/kg, then 4 mg per day and taper by 1 mg/week; total duration of 12 weeks.
- Despite the potential of drug-drug interactions, a rifamycin remains the most potent TB drug and should remain as part of the TB regimen unless a rifamycin-resistant isolate is detected, or the patient has a severe adverse effect that is likely due to the rifamycin.
- Intermittent use of rifamycin can result in development of resistance in patients with HIV and is not recommended.
- Paradoxical reaction in patients with tuberculosis, is characterized by either worsening of pre-existing tuberculous lesions or the appearance of new tuberculous lesions in patients who show initial improvement following anti-tuberculosis treatment. Paradoxical reaction that is not severe may be treated symptomatically.
- TB-IRIS is a paradoxical worsening or recurring of preexisting tuberculous lesions, or a development of new lesions in patients on effective antituberculosis treatment. It may occur during or even after completion of anti-TB therapy. TB-IRIS might be misdiagnosed as superimposed infections, treatment failure following inadequate anti-TB treatment, drug-resistant TB, or TB relapse. Therefore, the following strict criteria must be applied to diagnose TB-IRIS :
- (1) initial improvement of TB-related symptoms and/or radiographic findings after adequate anti-TB treatment for a certain time.
- (2) paradoxical deterioration of TB-related symptoms and/or radiologic findings at the primary or at new locations during or after anti-TB treatment.
- (3) absence of conditions that reduce the efficacy of anti-TB drugs (e.g., poor compliance, drug malabsorption, drugs side effects).
- (4) exclusion of other possible causes of clinical deterioration.

- There are two forms of IRIS: paradoxical or unmasking. Paradoxical IRIS is defined as recurrent, new, or worsening symptoms of a treated case. Unmasking IRIS is an antiretroviral (ART)-associated inflammatory manifestation of a subclinical infection with a hastened presentation. In this latter form signs and symptoms not clinically apparent before, appear during ART.
- For moderately severe paradoxical reaction, use of corticosteroid may be considered. Taper over 4 weeks (or longer) based on clinical symptoms.

Table 18: Dosing recommendations for anti-TB drugs for treatment of active drug sensitive TB

TB Drug	ARV Drugs	Daily Dose
Isoniazid	All ARTs	5 mg/kg (usual dose 300 mg)
Rifampin Note: DTG, RAL, and MVC doses need to be adjusted when used with rifampin	With HIV PIs, DOR, ETR, RPV, BIC, or EVG/c	**Not recommended**
	With TAF	Use with caution at dose indicated below
	With other ARV drugs	10 mg/kg (usual dose 600 mg)
Rifabutin Note: DOR and RPV doses need to be adjusted when used with rifabutin	With PI with COBI, TAF, BIC, or EVG/c containing regimens	**Not recommended**
	With DTG, RAL, EFV, DOR, RPV	5 mg/kg (usual dose 300 mg)
	With HIV PIs with RTV	150 mgd
	With EFV	450–600 mg
Pyrazinamide	All ARTs	Weight-Based Dosing • Weighing 40–55 kg: 1,000 mg (18.2–25.0 mg/kg) • Weighing 56–75 kg: 1,500 mg (20.0–26.8 mg/kg) • Weighing 76–90 kg: 2,000 mg (22.2–26.3 mg/kg) • Weighing >90 kg: 2,000 mg
Ethambutol	All ARTs	Weight-Based Dosing • Weighing 40–55 kg: 800 mg (14.5–20.0 mg/kg) • Weighing 56–75 kg: 1,200 mg (16.0–21.4 mg/kg) • Weighing 76-90 kg: 1,600 mg (17.8–21.1 mg/kg) • Weighing >90 kg: 1,600 mg

Table 19: When to start ATT and ART for TB/HIV co-infection

<table>
<tr><td rowspan="5">Patients diagnosed with TB while already receiving ART</td><td colspan="2">• Start ATT immediately
• Assess and, if needed, modify ART regimen to avoid potential pharmacokinetic interactions with rifampicin*
• If suboptimal HIV suppression or suboptimal response to ATT, assess:
○ Anti-TB drug adherence or resistance
○ ART drug adherence or resistance</td></tr>
<tr><td rowspan="4">Patients diagnosed with TB while not yet receiving ART</td><td colspan="2">Initiate ATT immediately with particular attention to potential pharmacokinetic interactions with ART drugs*</td></tr>
<tr><td>CD4 < 50 cells/ mm^3</td><td>Initiate ART as soon as possible, but within 2 weeks of starting ATT</td></tr>
<tr><td>CD4 counts ≥50 cells/mm^3</td><td>Initiate ART within 2 to 8 weeks of starting ATT</td></tr>
<tr><td>Patients with TB meningitis</td><td>Initiate ART after TB meningitis is under control and after at least 2 weeks of ATT to reduce the risk of IRIS</td></tr>
<tr><td>During pregnancy</td><td>Initiate ART as early as possible</td></tr>
</table>

Multidrug Resistant TB (MDR-TB) / Extensively Drug Resistant-TB (XDR-TB)
MDR-TB: Resistance to Rifampicin AND Isoniazid
XDR-TB: Resistance to Rifampicin AND Isoniazid AND Fluoroquinolone AND at least 1 additional Group A drug

MDR/XDR-TB should be suspected in case of:
-Previous or incomplete TB treatment
-Contact with MDR/XDR-TB index case
-Birth, travel or work in an area endemic for MDR-TB
-History of poor adherence
-No clinical improvement on standard therapy and/or sputum smear positive after 2 months of TB therapy or culture positive at 3 months
-Homeless/ hostel living and, in some countries, recent/current incarceration
-From an area with very high MDR-XDR-TB prevalence

Gene Xpert or similar technology has the advantage of rapid detection of rifampicin resistance. Drug susceptibility testing is important for optimizing treatment.

HIV and Viral Hepatitis

Table 20 shows screening and confirmatory tests for hepatitis B and C in PLHIV.

Table 20: Screening and confirmatory tests for hepatitis B and C in PLHIV

• **Initial screening tests** All patients should have the following screening tests during initial visit and no **later than 3 months of HIV diagnosis**/ initiation of ART:
• **HBV screening** -If clinically indicated, persons who are hepatitis B core antibody (anti-HBc) positive, anti-Hbs negative and HBsAg negative might be screened for HBV-DNA in addition to HBsAg to rule out occult HBV infection with detectable viremia. - HDV antibodies should be screened for in all HBsAg positive persons -HBV (Hbs Ag, anti-Hbs, Hbe Ag, anti-Hbe, anti-Hbc and anti-HDV if HBV positive) -Genotype of HBV is not required to determine initial treatment.
• **HCV screening** -HCV should be screened for at time of diagnosis and annually thereafter. -Screening should use an anti-HCV antibody test. -A positive result should be followed by HCV-RNA and genotype determination. Persons engaging in activities associated with increased risk of HCV transmission should be tested for HCV infection every 3 to 6 months. -Persons suspected of recently acquired primary HCV infection with a negative anti-HCV antibody test should be tested for HCV-RNA. -HCV-RNA is also recommended in persons with ongoing risk behavior for HCV re-infection after successful treatment or spontaneous clearance at 3 to 6-monthly intervals.
• Persons with viral hepatitis co-infection **should be assessed for concurrent causes of liver disease** such as alcohol consumption, cardiac disease, renal impairment, autoimmunity, genetic or metabolic liver diseases (e.g. genetic haemochromatosis, diabetes mellitus or obesity) and drug-induced hepato-toxicity

11.4: HIV and Hepatitis B

Table 21 illustrates treatment and follow up of hepatitis B in PLHIV.

Table 21: Treatment and follow up of hepatitis B in PLHIV

• **Treatment indication** - HBV/HIV coinfection is defined as the diagnosis of HIV in the presence of positive HBsAg for longer than 6 months. - Coinfection has a significant impact on progression of chronic HBV infection and associated liver disease mortality. But, the natural history of HBV-HIV coinfection has improved after initiation of ART which they need to take for life. -All persons with HBV/HIV co-infection should receive ART that includes TDF or TAF unless history of tenofovir intolerance - Stopping anti-HBV active ART should be avoided in persons with HIV/ HBV co-infection because of the high risk of severe hepatitis flares and decompensation following HBV reactivation hepatitis
• **Treatment selection** -ART fully suppressive combination therapy should **include tenofovir based regimen** (**tenofovir-DF or tenofovir-AF**). -**Combination therapy tenofovir-DF/emtricitabine** or **tenofovir-AF/ emtricitabine** should be used **unless there is evidence of lamivudine/ emtricitabine-resistant HBV or HIV**, lamivudine/emtricitabine may be omitted from the ART regimen and tenofovir-DF or tenofovir-AF be given as the sole anti-HBV active agent. -Tenofovir-DF should be used in patients without renal disease or osteoporosis. -Tenofovir-AF should be given to those patients with established renal disease with a creatinine clearance >30ml/min or osteoporosis or significant predisposing factors for their development. -**Neither lamivudine nor emtricitabine should be used as the sole active drug** against HBV.
• **Treatment goal** The optimal treatment duration for nucleos(t)ide analogues with anti-HBV activity has not yet been determined and experts recommend life-long therapy.
• **Follow up laboratory monitoring of liver disease and effect of ART:** -All patients should have the following blood tests performed at follow up: -HBV PCR should be monitored every 3-6 months during the first year, then: -HBV PCR every 6 months if HBV is not fully suppressed **(if HBV VL >2000 IU/ml)** -HBV PCR every 2 years **if suppressed**. -HBsAg should be checked every 12 months at least until loss of HBsAg -LFT should be performed every 3 months during the first year and every 6-12 months thereafter -RFT "if no renal risk factors" and bone profile monitoring: every 12 months.

•	**Referral to hepatology:** **-All decompensated liver disease patients** should be referred to a hepatologist or a gastroenterologist with interest in hepatology.
•	**Assessment of extension of liver disease:** -Elastography should be performed to screen **all patients for cirrhosis**. -OGD should be performed to screen for gastro-oesophageal varices in **all patients with decompensated liver cirrhosis.** -FRAX score should be measured for **all HBV-HIV co-infected patients**. -Dexa scan in **cirrhotic patients**. -Liver biopsy should be offered when: 1: Transient elastography score between **6 and 10 kPa** and **normal LFT** or 2: Transient elastography score is **less than 6 kPa and patients are younger than 30 years and have HBV DNA greater than 2000 IU/ml and abnormal ALT** (greater than or equal to 30 IU/L for males and greater than or equal to 19 IU/L for females) on 2 consecutive tests conducted 3 months apart.
•	**HCC screening is indicated in:** -All cirrhotic patients (irrespective of viral suppression for HBV) -Non-cirrhotic HBV (irrespective of HBV suppression) in persons with one of the following: family history of HCC; Asian/African ethnicity, HDV-co-infection, age >45 years, Caucasian patients with PAGE-B score ≥10 -US liver and AFP **every 6 months**
1.	**HDV:** -In persons with positive HDV antibodies, HDV-RNA should be measured in order to assess activity of the disease -In persons with chronic HDV co-infection and significant liver fibrosis (≥ F2), long-term (at least 12 months) treatment with PEG-IFN might be considered in association with TDF-based ART. -Non-invasive fibrosis markers (transient elastography and serum markers) should be used with caution in HIV/HBV co-infected persons with chronic HDV infection as there are no well-established thresholds. -Because of its anti-HBV activity, TDF/TAF should be added, as part of ART, to PEG-IFN in order to reduce HBV-DNA load. -Bulevirtide (2mg/d; s.c.) in combination with TDF/TAF is recommended in HDV-RNA positive persons with compensated liver disease and should be used where available. The optimal duration of treatment remains unclear. Treatment should be performed in centers with sufficient experience. -Treatment efficacy should be monitored with HBV-DNA and HDV-RNA measurements, when available, and with follow-up of biochemical and liver fibrosis estimates. -Persistent off-treatment HDV-RNA negativity and anti-HBs seroconversion are the ideal goals of antiviral treatment for HDV even if they can only be obtained in a minority of persons. Histological remission of liver disease is a less ambitious but more likely achievable goal. -In persons with HDV and ESLD or HCC, liver transplantation from HBsAg negative donors should be strongly considered.

11.5 HIV and Hepatitis C

Table 22 illustrates treatment and follow up of hepatitis C in PLHIV.

Table 22: Treatment and follow up of hepatitis C in PLHIV

• **Treatment indication-** Every person with HCV/HIV co-infection should receive Direct-Acting Antiviral drug (DAA) therapy to eradicate HCV, regardless of liver fibrosis stage. -Cure of HCV infection substantially reduces the risk for hepatic and extrahepatic complications and eliminates onward HCV transmission. - DAAs achieve similar cure rates and tolerability in HCV/HIV co-infected compared to HCV mono-infected persons. Therefore, treatment indication and regimens are the same as in HCV mono-infected persons.
• **Treatment selection** -DAA combinations are now standard of care for chronic HCV infection. -IFN-based therapies and first-generation PIs (boceprevir and telaprevir) are not recommended because of insufficient efficacy and increased toxicities. -Selection of DAA combinations is based upon stage of liver fibrosis, HCV genotype, pre-treatment history and resistance-associated substitutions (RAS) if tested. -Due to drug-drug interactions with HIV and HCV PIs, careful checking for interactions is urgently recommended prior to starting HCV therapy.
• **Treatment goal** -The primary aim of HCV treatment is SVR_{12} defined as undetectable HCV-RNA 12 weeks after the end of therapy (evaluated using sensitive molecular tests). SVR_{12} corresponds to a definitive cure of HCV infection in most cases
• **Referral to hepatology** -All patients with HCV infection should be referred to hepatologist for management once diagnosed.
• **Treatment monitoring:** -In persons with advanced fibrosis (≥ F3), measurement of the following after 2-4 weeks of therapy is recommended: CBC, creatinine, liver enzymes, bilirubin, albumin and INR. -In HBsAg negative persons with positive anti-HBc, monitoring of ALT and HBV-DNA in case of ALT elevation is recommended. -In persons with impaired renal function undergoing Sofosbuvir based treatment creatinine should also be monitored. - HCV-RNA measurement during therapy should only be performed in order to assess compliance and/or break-through in persons experienced to oral DAA **-HCV-RNA should be measured at end-of-treatment at week 12 and week 24 after treatment cessation (to assess SVR) and not during therapy.**

- **Post treatment monitoring**
  -Surveillance for HCC and for oesophageal varices should be continued if the respective indications were present pre-treatment, despite achieving SVR.
  - All persons with concurrent causes of liver disease should undergo periodical clinical assessments.
  - Increase in body weight and changes in lipid and glucose metabolism have been described after SVR. Thus, surveillance, counseling and treatment for obesity and metabolic alterations should be enforced after SVR.

- **Treatment of recently acquired HCV infection- refer to Hepatologist**
  - IFN-containing HCV regimens are no longer recommended.
  - HCV treatment immediately after diagnosis is recommended in all persons particularly in those with ongoing risk behavior to reduce onward transmission.
  -IFN-free treatment with DAAs is recommended as in treatment naïve persons without cirrhosis (except for those with pre-existing cirrhosis).
  - If pangenotypic regimens are foreseen, HCV GT determination is not mandatory before starting treatment. HCV GT determination should be considered in persons at risk of reinfection in order to differentiate between relapse and re-infection in case of reemergence of HCV RNA after therapy.

- **HCC screening**

  It is indicated in:
  -All cirrhotic patients (irrespective of viral clearance for HCV).
  -Consider HCC screening for non-cirrhotic F3 patients, regardless of etiology, based on individual risk assessment (e.g. family history of HCC).

- US liver and AFP **every 6 months**

12

Chapter 12: Management of HIV infection in pregnancy

Chapter 12: Management of HIV infection in pregnancy

One of the most significant successes in the management of HIV-positive patients has been the prevention of mother-to-child transmission (MTCT) of HIV.

In Oman, the current recommendations for universal prenatal HIV counseling and testing, treatment with ART, avoidance of breastfeeding, appropriate antenatal care and management of delivery have reduced the MTCT of HIV rates to almost nil.

12.1 Preconception care and counseling

- Couples, where one or both partners are HIV seropositive and are planning a pregnancy, should be referred to a joint Obstetrics Infectious Diseases clinic, if available locally, for counselling about interventions to prevent perinatal HIV transmission, including ART.
- Both partners should be informed that individuals with HIV should achieve maximum viral suppression before attempting conception to prevent sexual HIV transmission to partners and to minimize the risk of MTCT of HIV, including in-utero HIV transmission in infants.
- Couples considering or planning a pregnancy should be informed that if ART is initiated before conception and maintained throughout pregnancy, with an undetectable VL at delivery, the risk of HIV transmission to the infant is virtually zero. The implications of initiating therapy before conception, the selection of ART for the woman trying to conceive, and the need for adherence to achieve durable viral suppression should be discussed with both partners.
- Refer to Chapter 4 to select the recommended ART during pregnancy to minimize the possible adverse outcomes for the pregnant women and her fetus.
- Screening for genital tract infections and HBV for both partners should be done, and any infection should be treated as genital tract inflammation is associated with increase in genital tract shedding of HIV.
- Information on contraceptive methods should be made available and accessible for couples to reduce the likelihood of unintended pregnancy. Couples are advised to delay conception until VL is suppressed.
- For partners with discordant HIV status in which the partner with HIV is on ART and has achieved sustained viral suppression for at least 2 years, sexual intercourse without a condom is a safe method of conception that will not result in sexual transmission to the partner without HIV. It is not known how frequently VL testing should be conducted when a patient is relying on ART and viral suppression as a prevention strategy. Consider monitoring the VL every 4-6 months in these individuals, taking into consideration the adherence level and durability of viral suppression of the HIV positive partner.
- Pregnant women who test HIV seronegative and have partners with HIV should continue to be counseled regularly regarding consistent condom use and the option for PrEP to decrease their risk of sexual acquisition of HIV if the partner with HIV has not achieved sustained virologic suppression. They also should be counseled on the importance of their partners' adherence to ART and the need for their partners to achieve sustained virologic suppression to reduce the risk of sexual transmission of HIV.

- When both partners have HIV, both should be on ART with sustained viral suppression before attempting conception to optimize the health of the parents and reduce perinatal transmission. The risk of HIV superinfection or infection with a resistant virus is negligible when both partners are on ART and have fully suppressed plasma VL.
- Condom use should be encouraged during pregnancy when there is a risk of STI.

12.2 Antenatal HIV screening

Timely diagnosis of HIV and rapid initiation of ART are crucial to reducing the risk of perinatal vertical HIV transmission and maintaining the health of pregnant women and their infants.

- All pregnant women should be offered screening for HIV infection at their booking antenatal visit, with appropriate pre and post-test counselling; repeat HIV testing is recommended for pregnant women with a STI or with signs and symptoms of acute HIV infection or ongoing exposure to HIV.
- Healthcare practitioners should take informed consent before HIV testing. Women must be explained the importance and benefit of the testing.
- If a woman declines the initial HIV test, this should be documented clearly in the antenatal card, and screening should be offered again around 28 weeks.
- Repeat HIV testing in the third trimester is recommended for pregnant women with initial negative test results who remain at increased risk of acquiring the HIV infection: who are incarcerated; or who have signs and symptoms consistent with acute HIV infection (eg, fever, lymphadenopathy, skin rash, myalgias, arthralgias, headache, oral ulcers, leukopenia, thrombocytopenia, or transaminase elevation), those who have been diagnosed with another STI in the past year, those who are injection drug users or whose sex partners are injection drug users, those who exchange sex for money or drugs, those women with a new sex partner, more than one sex partner during this pregnancy, or partners at high risk of HIV. Healthcare providers should make every effort to identify these women who at high risk of HIV infection and offer them a repeat HIV testing in the third trimester. A sensitive and non-judgmental approach is essential in these situations.
- Those women who present late in pregnancy or in labor with undocumented HIV status should have a rapid HIV screening test. Results are to be available within 30-45 minutes. Confirmatory tests should be done if a rapid test is positive. Meanwhile, the post-test counselling and medications can be started immediately.

Confidentiality

- A negative test is documented on the antenatal green card.
- A positive test is documented on the green card without highlighting, fonts or underlying.
- Information about the woman's VL, receiving ART, mode of delivery, etc, can be written in the follow up notes in the antenatal card.
- The husband's HIV status should not be mentioned in the antenatal card.

12.3 Approach to the ANC of women who are HIV positive

Management should be provided by a multidisciplinary team, including an HIV/ID physician (whenever available), obstetrician, neonatologist and Pediatric ID (if available).

Women who are HIV positive should be assured that their confidentiality will be maintained. Care should be taken to avoid inadvertent disclosure to a woman's partner or family members based on a woman's wish, as they may be unaware of her HIV diagnosis. However, the disclosure of the woman's HIV status to her partner should be done as per the MOH protocol.

Women living with HIV should be made aware that with consistent use of combination ART and abstinence from breastfeeding, the risk of perinatal transmission is <1 %.

Women living with HIV with existing children of unknown HIV status should have them tested for HIV; all children <13 years old (especially <10 years) should be tested for HIV.

12.4 Antepartum care

Use of ART drugs during pregnancy

First-line ART for pregnant women

Start ART ASAP upon diagnosis, regardless of CD4 count or VL, and continue through pregnancy, delivery, and postpartum to lower VL and transmission risks.

Preferred Regimens:

- **Dolutegravir-based ART** is now preferred for its high efficacy and safety profile.
- **Bictegravir-based ART** is an alternative option

Continuation of Effective ART:

- Pregnant women already on ART should continue their regimen unless there are safety concerns for the fetus. Dose adjustments in certain ART (e.g. DRV/r) may be necessary for pregnancy-related changes.

Breastfeeding Guidance:

For mothers on ART with a sustained undetectable HIV VL during and after pregnancy, the risk of transmission through breastfeeding is less than 1%, but not zero. In settings, like Oman, with access to clean water and formula, breastfeeding is not recommended to avoid postnatal transmission.

One preferred and 4 alternative regimens *(*Table 23*)* are recommended for first-line ART regimen in ART-naïve pregnant women in Oman.

Table 23: First-line ART for pregnant women

Recommendation	Regimen
Preferred	(TAF/FTC) or (TDF/FTC) + DTG
Alternatives	BIC/FTC/TAF
	*TDF/FTC/EFV
	(TAF/FTC) or (TDF/FTC) +ATV/r
	(TAF/FTC) or (TDF/FTC) + DRV/r 600 mg bid/100 mg bid
*NOT BEFORE 14 WEEKS	

Considerations for ART in pregnancy

- (TAF/FTC) or (TDF/FTC) + DTG is the *Preferred* first-line ART for treatment-naïve pregnant women.
- DTG has High rates of viral suppression
- Dose adjustments of the preferred first line ART during pregnancy are not required.
- DTG is the preferred regimen for initial treatment without a history of long acting injectable cabotegravir (CAB-LA) exposure for pre- exposure prophylaxis (PrEP).
- TDF has potential renal toxicity and should be used with caution in patients with renal insufficiency.
- TAF/FTC is associated with fewer adverse birth outcomes and less risk of insufficient weight gain in pregnancy.
- EFV is the preferred alternative ART during pregnancy. However,
  - In ART-naïve pregnant women, initiation of EFV should be done after the first 14 weeks of pregnancy due to the risk of neural tube defects to the fetus.
  - EFV-containing regimen can be continued in previously diagnosed HIV-positive pregnant women presenting for ANC in first trimester and who have achieved virologic suppression (if virologic suppression is not achieved, refer the patient to an HIV specialist in Muscat).
- ATV/r is preferred for initial alternative PI that can be administrated once daily.
- DRV/r is a preferred for initial alternative ART only in certain circumstances (e.g., exposure to CAB-LA)
- No routine dose alterations are recommended for most ART during pregnancy; DRV/r requires twice-daily dosing during pregnancy, and it requires administration with food.
- In case of significant nausea during pregnancy, ART should not be started until her nausea is adequately controlled – discuss the alternative options with HIV/ID specialist. Most antiemetics used in pregnancy can be given with ART.

Laboratory Monitoring of HIV positive pregnant women

Newly diagnosed HIV-positive pregnant women do not require any additional baseline investigations compared with non-pregnant HIV- positive women (Table 5, chapter 3). Table 24 highlights some of the important tests that are monitored during pregnancy.

Table 24: Timing and frequency of some of the key tests during pregnancy

Type of test	Timing and frequency
Screening for syphilis, hepatitis B and rubella	At the booking visit
Screen for genital infections	At booking
Screening for hepatitis C virus	If not done already
HIV genotype test	At initial HIV clinic visit
HIV viral load	✓ 2—4 weeks after commencing or changing ART ✓ Monthly until complete viral suppression ✓ Once every trimester and at 36 weeks
CD4 counts	At initial visit and • For patients who have been on ART for ≥2 years, have had consistent viral suppression and CD4 counts that are consistently >300 cells/mm3, and are tolerating ART during pregnancy, CD4 count should be monitored only at the initial antenatal visit • Patients who have been on ART for <٢ years and have CD٤ counts of <٣٠٠ cells/mm٣, those with inconsistent adherence, or those with detectable VL should have CD4 counts monitored every 3 months during pregnancy. • Patients who have been on ART <2 years and have CD4 counts of ≥300 cells/mm3 should have CD4 counts monitored every 6 months.
Liver function tests	At initiation of ART, then at each antenatal visit. Hepatotoxicity may occur because of the drugs or the development of obstetric complications.

12.5 Obstetric management

At booking

- Review of prior and current HIV-related illnesses, CD4 counts and plasma HIV RNA levels.
- History of prior and current ART use.
- HIV status of the partner and children, if any.
- Previous Obstetric history.

Immunization

- Hepatitis B and pneumococcal vaccination is recommended for all individuals who are HIV positive and can be safely administered during pregnancy.
- Influenza, Tdap and SARS CoV- 2 vaccination can also be safely administered in pregnancy.
- Live vaccines including Varicella Zoster, Measles, Mumps and Rubella vaccines are contraindicated in pregnancy.

Antenatal Care

- As per National Guidelines for dating and anomaly scans.
- Additional ultrasounds for fetal growth and amniotic fluid volume are recommended at least each trimester or as obstetric indications guide.
- Women taking ART at the time of booking should be screened for gestational diabetes, as those on protease inhibitor-based ART are at higher risk for gestational diabetes. wo
- Invasive prenatal diagnostic testing should not be performed until after the HIV status of the mother is known and should ideally be deferred until the HIV VL has been adequately suppressed.
- External cephalic version (ECV) can be performed in women with HIV.
- There is no contraindication to membrane sweep or the use of prostaglandins.

12.6 Intrapartum care and mode of delivery

Pregnant women who present in labor with unknown HIV status and women with an increased risk of HIV infection who were not retested in the third trimester should undergo expedited antigen/antibody HIV testing.

- If the results are positive, an HIV-1/HIV-2 antibody differentiation test and an HIV-1 RNA assay should be performed as soon as possible. Pending the differentiation test's result, intravenous (IV) zidovudine (AZT) should be initiated.
- If acute or recent HIV infection is suspected or if a woman has had recent HIV exposure, an HIV RNA assay should also be done at the time of expedited antigen/antibody testing.

A plan for the mode of delivery (MOD) should be made jointly with the ID physician (if available). The approach to delivery mode depends on the VL obtained within four weeks of delivery at 34-36 weeks gestation, obstetric factors and the patient's choice. The options should be discussed with the patient, and the plan should be documented in the antenatal card and the progress notes.

- For women with a plasma VL of < 50 HIV RNA copies/ml at 36 weeks, and in the absence of obstetric contraindications, a planned vaginal delivery is recommended.
- Where the VL is 50-399 HIV RNA copies/ml at 36 weeks, elective Cesarean section should be considered, taking into account the actual VL, the trajectory of VL, length of time on ART, adherence issues, obstetric factors and the patient's wishes.
- Where the VL is ≥ 400 HIV RNA copies/ml at 36 weeks, elective Cesarean section is recommended.

Elective Cesarean Section:

- Planned cesarean section (PLCS) to reduce the risk of perinatal transmission should be undertaken at 38 weeks gestation to prevent labor and/or ruptured membranes.
- The timing of PLCS is a balance between the risks of transient tachypnoea of the newborn and the risk of labor before the scheduled Caesarean Section.
- The surgical field should be kept as hemostatic as possible and avoid rupturing the membranes until the head is delivered through the incision.
- Administer prophylactic antibiotics according to guidelines for the general population.
- Women taking ART should have their medications prescribed and administered before and after delivery.

Planned Vaginal Delivery

- Planned vaginal delivery should only be offered to women taking ART who have a VL of less than 50 copies/ml.
- ART should be administered throughout labor and postpartum.
- Epidural Anesthesia can be used safely regardless of a patient's ART regimen.
- There are concerns about possible discordance between plasma and genital tract VL. Hence, routine use of fetal scalp electrodes should be avoided unless clear obstetric indications exist.
- If labor progress is expected, avoid early amniotomy.
- Amniotomy and oxytocin may be considered for augmentation of labor.
- Electronic fetal monitoring should be performed according to national guidelines. HIV infection per se is not an indication for continuous fetal monitoring.
- Operative vaginal delivery with forceps or a vacuum extractor should follow standard obstetric indications but should be avoided if possible in those with HIV RNA ≥50 copies/mL.
- Fetal scalp electrodes for fetal monitoring should be avoided, when maternal HIV RNA is not suppressed (≥50 copies/mL) or is unknown because of the potential risk of HIV transmission.
- Delayed cord clamping for 30 to 60 seconds after birth in vigorous term and preterm infants is recommended to improve the infant's iron stores and hemoglobin levels. This practice does not appear to affect the risk of HIV transmission.
- Because of potential drug interactions with some ART, consider the drug regimen when treating postpartum bleeding.

- Methergine should be used cautiously in women on Cytochrome P450 CYP3A4 enzyme-inhibiting drugs. Concomitant use of ergotamines with Protease inhibitors has been associated with exaggerated vasoconstrictive responses. If methergine is used, it should be administered at the lowest effective dose for the shortest possible duration.
- In contrast, additional uterotonic agents may be needed when using ART drugs that are CYP3A4 inducers (e.g., Nevirapine, efavirenz, etravirine) because of the potential for decreased methergine levels and inadequate treatment effect.

Vaginal birth after Cesarean section:

A trial of scar can be considered for women on ART whose plasma VL is less than 50 copies/ml. Where the VL is 50-399 HIV RNA copies/ml at 36 weeks, a trial of scar can be considered, taking into account the actual VL, the trajectory of VL, length of time on ART, adherence issues, obstetric factors and the patient's wishes.

HIV diagnosed in labour

- Women who test positive on the initial HIV test during labor should be presumed to have HIV until follow-up testing clarifies their HIV status.
- The pediatrician should be informed, and urgent advice should be sought from the Pediatric ID regarding optimum medications.
- Delivery should be by Cesarean section. Where possible, this should be timed to address antiretroviral administration.

Zidovudine (AZT) infusion

Intrapartum administration of IV AZT provides antiretroviral pre-exposure prophylaxis at a time when infants are at increased risk of exposure to maternal blood and body fluids.

If indicated, IV AZT (2 mg/kg loading dose followed by a continuous infusion of 1 mg/kg/hour until delivery) should be given regardless of the presence of drug resistance to Zidovudine.

Women should continue taking their ART regimen as much as possible during labor and delivery or scheduled Cesarean delivery. Additional administration of intrapartum intravenous AZT depends on the maternal HIV VL within four weeks of anticipated delivery.

- For women on ART with HIV RNA ≤50 copies/mL consistently in late pregnancy and near the time of delivery (i.e., four weeks before delivery) and no concerns regarding adherence or resistance to the regimen, IV AZT is not recommended as it does not appear further to reduce the risk of vertical transmission in this setting.
- For women on ART with HIV RNA between 50 and 399 (ie, four weeks before delivery) or those who have had challenges consistently taking ART, IV ZDV should be started at the time the woman presents in labor or prior to scheduled cesarean delivery; however, data are insufficient to determine whether administration of IV ZDV to people with HIV RNA levels between 50 copies/mL and 399 copies/mL provides any additional protection against perinatal HIV transmission.

- For women with HIV RNA ≥400 copies/mL within four weeks before delivery, possible poor adherence, unknown HIV RNA levels or known or suspected lack of adherence since the last HIV RNA result, or a positive expedited antigen/antibody HIV test result during labour, IV AZT should be started. Additionally, IV AZT should be given for women with acute or primary HIV during pregnancy.

    - For women scheduled for Cesarean delivery, IV AZT should be given at least three hours before cesarean delivery.
      Pharmacokinetics – the ratio of cord blood to maternal blood concentration shows that an interval of at least 3 hours provides adequate time to reach equilibrium across the placenta.
    - Women with HIV who present in labour should be given IV AZT immediately to decrease the risk of vertical transmission.

Management of Pre- labor Rupture of Membranes at Term

- In all cases of term pre-labor spontaneous rupture of the membranes after 37 weeks, vaginal delivery or Cesarean section should be expedited according to the plan of delivery.
- Artificial rupture of membranes and operative vaginal delivery with forceps or a vacuum extractor should follow standard obstetric indications but should be avoided, if possible, in those with HIV RNA ≥50 copies/mL.
- Chorioamnionitis has been associated with perinatal transmission.
- If maternal HIV VL is suppressed, immediate induction of labor is recommended, with low threshold for treatment of intra partum pyrexia.
- If maternal HIV VL is 400 RNA copies/mL and above, immediate Caesarean should be considered.
- Management of prolonged premature rupture of membranes (PPROM) at >= 34 weeks is the same as term rupture of membranes.
- When membrane rupture occurs before 34 weeks gestation, decisions about timing of delivery should be based on best obstetric practices, considering risks to the infant of prematurity and of HIV transmission. Antibiotics to prolong the time from membrane rupture to onset of labor (the latency period), magnesium sulfate for fetal neuroprotection, and antenatal corticosteroids should be given in accordance with usual obstetric guidelines because no data exist to suggest that these recommendations need to be altered for pregnant people with HIV.

Management of PPROM at less than 34 weeks

When PPROM occurs at < 34 weeks of gestation –

- In pregnant women on ART with HIV RNA ≤400 copies/mL, duration of ruptured membranes is not associated with an increased risk of perinatal transmission and is not an indication for Cesarean delivery to prevent HIV transmission.
- Decisions on optimum management require assessment of factors - exact gestation, maternal VL, infection and obstetric factors.
- Administration of corticosteroids to improve fetal lung maturation should be given if appropriate.
- Oral erythromycin and intravenous Amoxicillin should be started in accordance with guidelines for the general population.
- Evidence of chorioamnionitis and fetal distress are indications for prompt delivery otherwise, there should be multidisciplinary discussion along with the neonatologist about the timing of delivery.

12.7 Postpartum care

- It is well established that HIV can be transmitted from mother to child by breastfeeding. Women should be given advice about formula feeding. However, if an HIV positive woman insists on breastfeeding, refer her to an HIV expert in Muscat for further counselling and support.
- An immediate dose of carbegoline should be given to suppress lactation.
- Continue ART to reduce risk of disease progression and prevent sexual transmission.
- Guidance about contraception should be given in the postpartum period.
- A cervical smear should be done at 6 weeks postpartum if not done in the past 1 year.

13

Chapter 13: Pediatric HIV Care

Chapter 13: Pediatric HIV Care

13.1 Diagnosis of HIV in infants and children under 18 months

An HIV-positive pregnant woman will always give birth to an HIV sero-positive baby because of transplacental transfer of maternal HIV antibodies during pregnancy. These passive antibodies can be detected in the blood of babies born to HIV-positive mothers for up to 18 months of age. As a result, HIV serological assays do not confirm the presence of HIV infection in infants and children under 18 months; instead, virologic testing should be used for accurate diagnosis (*Fig. 14*).

Unique Aspects of Paediatric HIV infection and care

- The transmission of maternal anti-HIV antibodies to the infant complicates the diagnosis of HIV in newborns.
- Since newborns and young children with HIV are at risk for rapid disease progression and death, ART should be started immediately after diagnosis.
- In infants and children, ART have age-specific and weight -specific approvals with different dosing requirements.
- Adherence to ART is particularly challenging in children.

Time of diagnosis:

I. **HIV virologic test (RNA or DNA) by PCR**

Should be performed for early diagnosis of infants and children under 18 months at the following ages:

- At birth
- At 2 weeks for high risk - If the newborn is considered at high risk (see below for criteria of high risk) for perinatal HIV transmission, an additional early HIV RNA testing at 2 weeks of age should be considered by the pediatric HIV specialist.
- At 4-6 weeks of age
- At 4-6 months of age

II. **HIV serology**

- At 18 months of age

Late seroconversion: Up until the age of 24 months, non-breastfed children who had perinatal HIV exposure, but no other risk factors for HIV transmission, and no virologic or clinical or laboratory evidence of HIV infection may still carry maternal HIV antibodies. One study showed that 14% of children with HIV exposure who did not have HIV infection seroconverted after age 18 months.

- Due to the possibility of residual maternal HIV antibodies, virologic testing is necessary to definitively exclude or confirm HIV infection in children with perinatal HIV exposure who have a positive HIV antibody (or antigen/antibody) test at age 18 months to 24 months; if the virologic test is negative, repeat antibody testing at a later date should be done to confirm seroconversion.

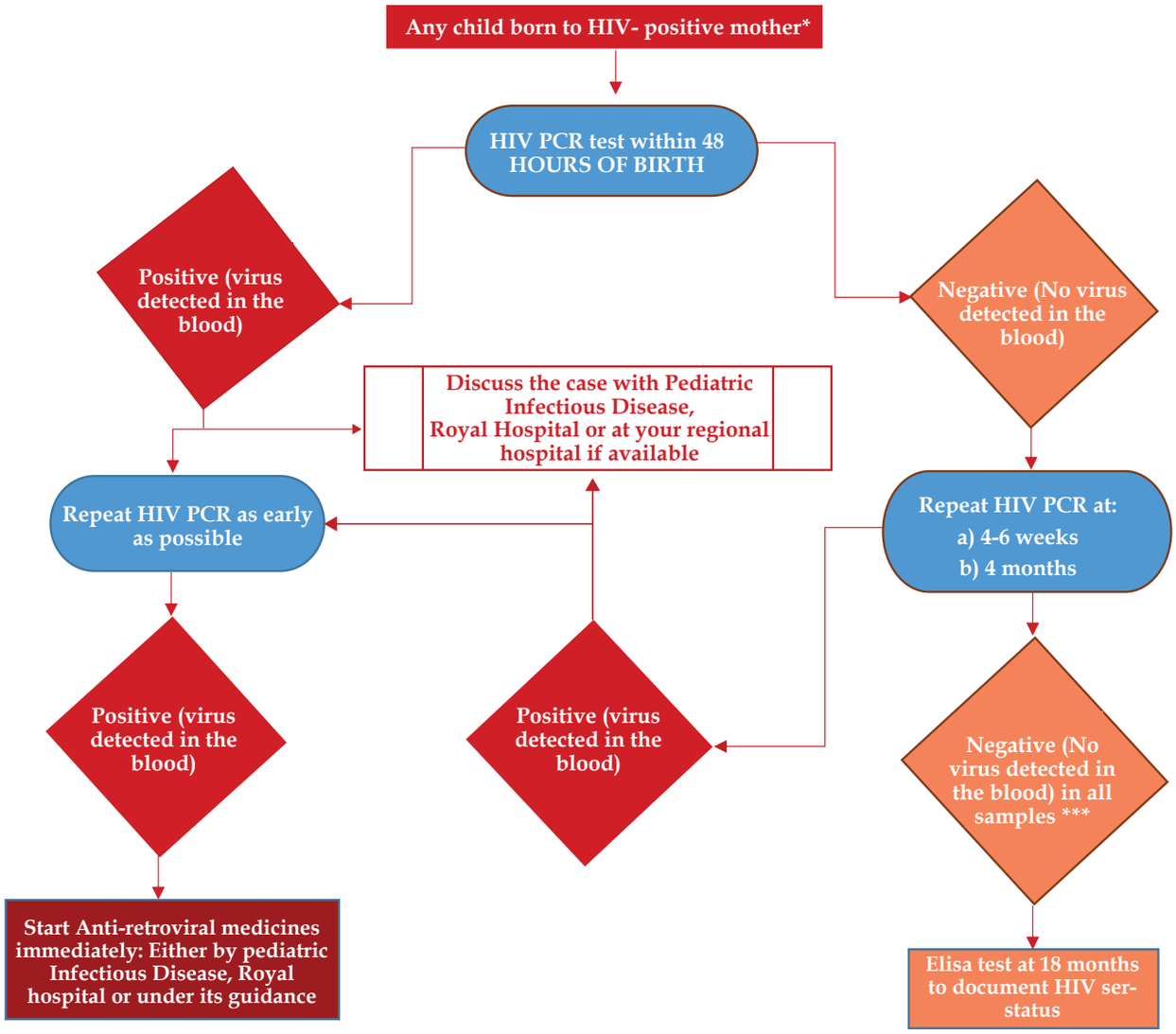
Interpretation of test results

- Positive HIV virologic test by PCRresults at any age should be confirmed by repeat testing as soon as possible on a new sample. Two independent HIV PCR positive test results definitively diagnose pediatric HIV infection in HIV-exposed infants and subsequent testing is not necessary.

  Two negative HIV virologic test by PCR results, one obtained ≥ 4 weeks of age and one obtained ≥ 4 months of age, definitively exclude pediatric HIV infection in HIV-exposed infants (in the absence of breastfeeding). However, it is important to perform antibody test at 18 months of age to document negative HIV serostatus.

A child who is in age group of 4 to 17 months and is not tested previously should be tested for HIV PCR for diagnosis. If HIV PCR is negative, then repeat ELISA test at 18 months for a definitive diagnosis. If HIV PCR is positive, then repeat urgently the HIV PCR test and refer the child to a **Pediatric Infectious Disease specialist.**

Fig. 18: National HIV testing algorithm for children under 18 months



*1) No breast feeding, 2) Avoid live vaccines like BCG, OPV, 3) Start on AZT prophylaxis, 4) Notify HIV focal point**1) Discontinue AZT at 6 weeks, 2) Start Co-trimoxazole at 6 weeks***1) Discontinue CT if all tree PCR negative, 2) Give BCG now, 3) Give MMR vaccine as per schedule, 4) Give IPV and do not give OPV

Counseling HIV positive mother after delivery

Before counseling make sure of the following information:

- Detailed history on the pregnancy.
- VL during and before delivery.
- Maternal viral resistance genotyping if available.
- Medication received during pregnancy and compliance.
- Medication during delivery.
- Father/partner status and his VL if it is available.
- Presence or exclusion of other sexually transmitted diseases (STD) in both parents.

General principles of management

1. **Ensure confidentiality of maternal and infant HIV status.**
2. Standard precautions for blood and fluid should be observed in the management of mother and infant. No additional precautions are required.
3. Newborn infants should be cleaned well in order to remove maternal blood or amniotic fluid prior to intramuscular injections or blood sampling.
4. Breastfeeding should be avoided irrespective of maternal clinical, immunologic and virological status or ART. In case of discordant couple where father is positive and mother is negative, it is preferable to avoid breastfeeding as chances of transmission to mother and subsequently to the child during the breastfeeding cannot be ruled out.
5. Consultation with the HIV focal point in pediatric is mandatory for all mother infant pairs when the mother is known or suspected to be HIV-positive.
6. All newborns of HIV-infected mothers who need referral as referred in algorithm for diagnosis of HIV in children under 18 months of age or other children with HIV should be referred to the Pediatric Infectious Diseases Clinic at Royal Hospital for management and follow-up. **Please call 24599000 and ask for 3091 pager during working hours or else page 3004 asking for contact number of Pediatric ID specialist on call. Alternatively, you can contact Pediatric ID specialist at your regional hospital (if Pediatric HIV service is available).**

13.2 ART prophylaxis for infants born to HIV-infected mothers

- All newborns who were exposed perinatally to HIV should receive postpartum ART to reduce the risk of perinatal transmission of HIV.
- A newborn's ART regimen should be determined based on maternal and infant factors that influence the risk of perinatal transmission of HIV.

A. <u>For newborns at low risk of perinatal HIV acquisition</u>

A **<u>4-week zidovudine (ZDV) regimen</u>** is recommended for ARV prophylaxis if the newborn is ≥37 weeks gestation and is born to a mother with HIV who:

- is currently receiving and has received at least 10 consecutive weeks of ART during pregnancy; and
- has achieved and/or maintained viral suppression (defined as at least two consecutive tests with HIV RNA <50 copies/mL obtained at least 4 weeks apart) for the remainder of the pregnancy; and
- has a VL <50 copies/mL at or after 36 weeks; and

- did not have acute HIV infection during pregnancy; and
- has reported good ART adherence, and adherence concerns have not been identified

B. <u>For newborns at (High- risk) of perinatal HIV acquisition</u>

- **A pre-emptive 3-drug regimen ART administered for 6 weeks is indicated**

The following scenarios are considered high risk for perinatal acquisition of HIV:

Infants born to mothers who:

- have not received antepartum ART, or
- have received only intrapartum ART, or
- have received antepartum ART but who did not achieve viral suppression (defined as at least two consecutive tests with HIV RNA level <50 copies/mL obtained at least 4 weeks apart) within 4 weeks of delivery, or
- have primary or acute HIV infection during pregnancy

- **Regimens for High- risk newborns:**

Table 25 shows the recommended preferred and alternative regimens for high-risk newborns.

Table 25: ART regimens for high-risk newborns

	ART	Comments	
Preferred First line Second line	Three-drug regimen: Zidovudine (AZT) plus Lamivudine (3TC) plus Nevirapine (NVP) or Zidovudine (AZT) plus Lamivudine (3TC) plus Raltegravir (RAL)	To be continued from birth to 6 weeks, but if duration of the 3-drug regimen is shorter than 6 weeks, ZDV should be at least continued for total of 6 weeks	See *Table* 26 for dosing recommendations
Alternative regimen	Two-drug regimen of 6-week of AZT + 3 doses of NVP in the first week of life	This regimen may be considered on case-by-case basis as alternative if maternal HIV viral load is less than 200 copies/mL within 4 weeks prior to delivery, likelihood of HIV transmission is not very high **<u>and 3-drug regimen is not available</u>**	See *Table* 26 for dosing recommendations

C. Infants born to mothers with unknown HIV infection status

Conduct rapid HIV testing on the mother. Results should be available within 30 minutes:

- Assess maternal risk factors of HIV infection.
- Consider the risk of window period in case of high-risk mother (detection of HIV antibodies can take up to 45 days, while HIV antigen may be detected as soon as 18 days).
- In High-risk maternal history, start the newborn on preemptive therapy as above.

- Hold on breast feeding till risk assessment and maternal and newborn investigations are available.
- If supplemental test results on the mother are negative and no concern of the potential that the mother is in the window period, discontinue ART prophylaxis in the infant.

Table 26 shows the dosing of ART for infant prophylaxis.

Table 26: Dosing of ART for infant prophylaxis

Infant age	Dosing	
AZT		
Birth to 6 weeks 1) ≥ 35 weeks of gestation 2) ≥ 30 to 35 weeks of gestation 3) 30 weeks of gestation	Start within 6-12 hours of birth to 6 weeks 1) 4 mg/kg/dose PO twice daily 2) 2 mg/kg/dose PO twice daily and change to 3 mg/kg/dose PO twice daily at age 15 days 3) 2 mg/kg/dose PO twice daily and change to 3 mg/kg/dose PO twice daily at age 29 days Note: newborns who are not able to tolerate orally, the IV dose is 75% of the oral dose while maintaining the same dosing interval.	
NVP for 2-drug regimen		
Birth weight 1500-2000 g Birth weight ≥ 2000 g	8 mg/dose 12 mg/dose	3 doses in the first week of life: -1st dose: birth-48 hrs. -2nd dose: 48 hrs. after 1st -3rd dose: 96 hrs. from 2nd
NVP for 3-drug regimen		
≥37 weeks' gestation at birth ≥34 to <37 weeks' gestation at birth: ≥32 to <34 weeks' gestation at birth	6 mg/kg per dose orally twice daily. Birth to age 1 week: 4 mg/kg per dose orally twice daily and change to 6 mg/kg per dose orally twice daily at age 8 days. Birth to age 2 weeks: 2 mg/kg per dose orally twice daily and change to 4 mg/kg per dose orally twice daily at age 15 days, then change to 6 mg/kg per dose orally twice daily at age 29 days.	
Lamivudine (3TC): in >= 32 weeks		
Birth to age 4 Weeks: Age >4 Weeks:	2 mg/kg per dose orally twice daily. 4 mg/kg per dose orally twice daily.	
Raltegravir (RAL)		

□37 weeks' gestation at birth and weighing □2 kg: No dosing information is available for preterm infants or infants weighing <2 kg at birth.	Birth to age 6 weeks: ~1.5 mg/kg per dose once daily from birth to 1 week, then ~3 mg/kg per dose twice daily from 1-4 weeks of life, then ~6 mg/kg per dose twice daily for 4-6 weeks of life. **Note:** If the mother has taken RAL 2 to 24 hours prior to delivery, the neonate's first dose of RAL should be delayed until 24 to 48 hours after birth; additional ARV drugs should be started as soon as possible.

13.3 Initial (at birth) and postnatal management of HIV-exposed infants

1. A CBC and differential should be performed on HIV-exposed newborns before initiation of infant ART prophylaxis. Anemia is the primary complication seen in neonates given the standard 6-week postnatal zidovudine regimen.
2. At birth, glucose-6-phosphate dehydrogenase deficiency should also be performed to know the status prior to starting PJP prophylaxis at 6 weeks of age.
3. Virologic tests (HIV PCR) are required to diagnose HIV infection in infants < 18 months of age and should be performed as shown in algorithm for diagnosis of HIV in children less than 18 months of age (Fig. 18).
4. The HIV focal point in pediatrics will see the mother and baby prior to discharge to ensure appropriate investigation and management plan is started, parents are counseled, and proper arrangements are made for follow-up of the child both in the Royal and regional hospitals.
5. BCG vaccine should not be given to infants born to HIV-positive mothers and a note should be placed in the child's health card, "**No live vaccines**". Please cross over OPV (oral polio vaccine) in vaccine card and replace with IPV (inactivated polio vaccine) instead.
6. All HIV-exposed infants will be followed up in the Pediatric Infectious Diseases Clinic between 4 to 6 weeks of age, at which point ART prophylaxis or preemptive therapy will be discontinued, and cotrimoxazole will be initiated for PJP prophylaxis. High-risk infants will be reviewed at 2 weeks of age for additional HIV PCR testing.

   To prevent PJP, all infants born to women with HIV infection should begin PJP prophylaxis at age 6 weeks, after completing their ART prophylaxis/ preemptive regimen, unless there is adequate test information to presumptively exclude HIV infection.

13.4 Vaccinations for infants and children living with HIV

- All routinely recommended inactivated vaccines can be administered safely to infants and children living with HIV.

- The exposed infant will remain on PJP prophylaxis (Cotrimoxazole) until HIV excluded. If the child is confirmed to be positive for HIV, continue Cotrimoxazole until 5 years of age.
- After ruling out HIV infection in newborn, the BCG vaccine should be given, and infant can have other live attenuated vaccines.

- All live attenuated vaccines (e.g. BCG vaccine) are contraindicated for severely immunosuppressed children (i.e. CD4 < 15%).
    - Varicella vaccines can be considered only for children with CD4 > 15% and those older than 5 years with CD4 > 200 cell/ mm3.
    - Two doses of measles, mumps and rubella (MMR) vaccine are recommended for children older than 12 months with no evidence of severe immunosuppression.
    - Rota virus vaccine can be administered to infants with HIV exposure or infection irrespective of CD4 count and percentage.
    - IPV should be given instead of OPV
- Specific vaccines:
    - Pneumococcal 20 Valent Conjugate Vaccine.
    - Trivalent influenza vaccine is recommended annually.
- Re-immunization with MMR should be considered after improved immune response following ART regimen.

13.5 Clinical and laboratory monitoring of pediatric HIV infection

- Absolute CD4 count, and plasma HIV RNA VL should be measured at the time of HIV diagnosis, and, if a child is not started on ART after diagnosis, this monitoring should be repeated at least every 3 to 4 months thereafter.
- Absolute CD4 count is recommended for monitoring immune status in children with HIV of all ages, with CD4 percentage as an alternative for children aged <5 years.
- Additional CD4 count and plasma VL monitoring should be performed to evaluate children with suspected clinical, immunologic, or virologic deterioration or to confirm an abnormal value.
- Antiretroviral drug-resistance testing is recommended at the time of HIV diagnosis, before initiation of therapy in all ART-naive patients, and before switching regimens in patients with treatment failure. Genotypic resistance testing is preferred for this purpose, and it should be done while patient is still on the failing regimen.
- Laboratory testing should also be performed to assess for HIV- associated conditions, including the following:
    - Anemia, leukopenia, thrombocytopenia
    - Hypoalbuminemia
    - Nephropathy (urinalysis)
    - Renal insufficiency (creatinine)
    - Hyperglycemia
    - Hepatic transaminitis
- Baseline screening tests for coinfections and OIs, including tests for the following, should be performed:
- Tuberculosis, with tuberculin skin test, or an interferon gamma release assay
- HBV, with HBV surface antibody, HBV surface antigen, and HBV core antibody tests.
- HCV, with HCV nucleic acid (HCV RNA) testing if aged <18 months or HCV antibody if aged >18 months.
- CMV, with CMV antibody tests if aged >12 months.

Table 27 shows a suggested schedule for clinical and laboratory monitoring of children before and after initiation of ART.

Table 27: Clinical and laboratory monitoring of children living with HIV

Laboratory Testing	Entry Into Care	ART Initiation	Weeks 1–2 on Therapy	Weeks 2–4 on Therapy	Every 3–4 Months	Every 6–12 Months	Virologic Failure (Prior to Switching ART Regimens)
Medical history and physical examination	√	√	√	√	√	√	√
Adherence Evaluation		√	√	√	√		√
CD4 Count	√	√			√	√	√
Plasma Viral Load	√	√		√	√		√
Resistance Testing	√						√
CBC with Differential	√	√		√	√	√	√
Chemistries	√	√		√	√	√	√
Lipid profile	√	√				√	
Random Plasma Glucose		√				√	
Urinalysis	√	√				√	
HBV screening	√						√
HCV screening	√						
TB screening	√					√	
CMV serology	√						
HLA-B*5701 (if ABC is considered)	√					√	

13.6 Initiation of ART in children and adolescents with HIV infection

- ART should be initiated in all infants and children with HIV infection.
- Rapid ART initiation (defined as initiating ART immediately or within days of HIV diagnosis), accompanied by a discussion of the importance of adherence and provision of subsequent adherence support, is recommended for all children with HIV.

First-line ART for children

The selection of an initial ART for the treatment of HIV infection in infants, children and adolescents (Tables 28, 29, 30 and 31) should be individualized based on factors that include patient characteristics (e.g., age, weight), regimen characteristics (e.g., efficacy, safety, tolerability), clinical and practical considerations, patient and family preferences, the results of HIV resistance testing and availability of the recommended agents.

Table 28: Recommended initial ART regimens for infants and children aged <30 Days

Term infants (≥37 weeks gestation) or preterm infants with a postmenstrual age ≥37 weeks at the time of treatment initiation	
Preferred regimen	RAL (for infants >= 2 kg) + AZT +3TC OR NVP + AZT +3TC
Alternative regimen: >= 42 weeks & postnatal age >= 14 days >= 37 weeks	LPV/r + AZT +3TC ABC + 3TC + (RAL or NVP) – (if HLA*B5701 negative)
Preterm infants with postmenstrual age >=32 weeks to < 37 weeks at the time of treatment initiation	
Preferred regimen	NVP + AZT +3TC
Preterm infants with postmenstrual age < 32 weeks at the time of treatment initiation: Consult Paediatric ID specialist.	

Considerations for infants and children aged <30 Days

- INSTI-based regimens have become the Preferred option for initial ART regimens in infants and children whenever possible due to their virologic efficacy, lack of drug interactions, and favorable toxicity profile.
- Increasing number of efficacy studies have evaluated the PK, safety, tolerability, and efficacy of these drugs in infants, children, and adolescents.
- RAL is a first-generation INSTI and is the only INSTI option Food and Drug Administration (FDA) approved for use in infants aged <30 days. INSTI-based regimens using second-generation INSTIs that have greater efficacy and a higher barrier to resistance than RAL (i.e., Dolutegravir, DTG or Bictegravir, BIC depending on age and weight), are recommended for initial therapy in children.
- RAL: Granule formulation requires multistep preparation before administration. Caregiver must be carefully taught how to prepare it.
- LPV/r oral liquid should be avoided in premature babies or in full-term babies younger than 14 days because of potential side effects. In addition, it has poor palatability and bitter taste, which may cause incomplete dosing if infant spits it out. Therefore, it is not a preferred ARV outside the neonatal period if other options are available.
- Compared to NVP, LPV/r, if used, is associated with less risk of discontinuing treatment and virological failure among children less than 3 years.
- LPV/r is known to have a better resistance profile that protects against the selection of NRTI resistance without compromising the use of other PIs in second-line regimens.

Table 29: Recommended initial ART regimens for infants and children aged ≥30 Days to <2 years

Aged >= 30 days to < 2 years and weighing >= 3 kg	
Preferred regimen (INSTI-based)	DTG +ABC + 3TC if HLA-B*5701 negative OR DTG + AZT +3TC
Alternative regimen	AZT + 3TC + LPV/r OR NVP
Aged >= 3 months to < 2 years and weighing >=6 kg to < 25 kg	
Preferred regimen	DTG/ABC/3TC as a FDC tablet if HLA-B*5701 negative
Alternative regimen	AZT +3TC +LPV/r OR NVP

Considerations for infants and children Aged ≥30 Days to <2 Years

- For infants > =30 days old but weighing < 3 kg; regimen should be same as for those < 30 days old.
- DTG is a second-generation INSTI that has a higher barrier to resistance than RAL and is FDA approved for use in this age group. Young infants may initially have very high HIV VL and continue to have low level viremia during the first year of life. For those >= 30 days & weighing >= 3 kg: it is available as dispersible tablets. For those >= 6 kg: it is available as FDC tablet. Tablet should be dissolved in water only (no other liquids, including milk).
- INSTIs have better efficacy and safety profiles than NNRTIs or PIs, and DTG has been studied extensively in children.
- Importantly, the FDC of DTG/ABC/3TC has proven efficacy and a good safety profile.

Table 30: Recommended initial ART regimens for infants and children aged ≥ 2 years to < 12 years

Children aged >= 2 years to < 12 years who are <u>NOT ABLE</u> to swallow pills		
Preferred regimen		
HLA-B*5701 status	Weight	Regimen
negative	6 to < 25 kg	DTG/ABC/3TC: as FDC- PD) once daily
	>= 25 kg	DTG film-coated tablets + ABC +3TC in liquid formulations
positive or unknown or ABC not available	>= 14 kg	DTG + (FTC/TAF) OR DTG in dispersible tablets plus AZT+3TC in liquid formulations.
	< 14 kg	DTG (dispersible tablet) once daily +(AZT + 3TC both twice daily).
Children aged >= 2 years to < 12 years who are <u>ABLE</u> to swallow pills		
positive or unknown or ABC not available	< 14 kg	DTG (dispersible tablet) once daily + (AZT + 3TC both twice daily).
	>= 14 kg	BIC/FTC/ TAF OR DTG + (FTC/TAF)
Negative	>= 25 kg	DTG plus ABC plus 3TC (FDC)
Alternative anchor drugs in an ART regimen with a preferred 2 NRTI backbone		
Weight / years	Regimen	

>=15 to <=25kg	ATV powder plus RTV powder (boosted PI)
>= 15 kg	ATV capsules plus RTV tablets (boosted PI)
>= 35 kg	ATV plus RTV (boosted PI)
>= 20 kg	DRV plus RTV (boosted PI)
>= 40 kg	DRV plus RTV (, boosted PI): >= 40 kg
	NVP
>= 6 years	NVP XR: >= 6 years
>= 3 years & >= 10 kg	EFV (capsules can be opened & used as a sprinkle formulation for children unable to swallow pills)
>= 35 kg	DOR (available as single tablet regimen (DOR/3TC/TDF)

Consideration for infants and children aged ≥ 2 years to < 12 years

- In this age group, older patients may be able to swallow pills. Therefore, it is important to counsel family to teach children how to swallow pills (as young as 4 years old). This will increase ARV options and improves compliance.
- BIC/ FTC/TAF as a FDC tablet: use lower strength tablet for children weighing ≥14 kg. For children who are unable to swallow a whole tablet, it may not be crushed or dissolved, but it can be split and each part taken separately, as long as all parts are ingested within approximately 10 minutes. BIC plus FTC plus TAF is a good option for transition to tablet once young patients are able to swallow pills.
- DTG/ABC/ 3TC as a FDC pill is much larger than the BIC/ FTCTAF as a FDC tablet pill and might be more challenging to swallow, particularly for younger children. It is non-dispersible. On the other hand, DTG/ ABC/ 3TC as a FDC tablet PD is dispersible & should be dissolved in water.
- TAF is a prodrug of tenofovir, available as a single-strength tablet and in combination with FTC and DTG or other INSTIs. Studies have suggested improved renal and bone safety markers compared with TDF

Table 31: Recommended regimens for children and adolescents aged ≥12 Years

Recommended Regimens for Children and Adolescents Aged ≥12 Years, weight >= 25 kg	
Preferred regimen	
Weight/ years/others	Regimen
If no previous exposure to CAB-LA for pre-exposure prophylaxis:	
>= 25 kg >= 35 kg	BIC/FTC/ TAF as a FDC tablet, OR DTG/ABC/ 3TC as a FDC tablet DTG + (FTC +TAF)
If there is previous exposure to CAB-LA for pre-exposure prophylaxis	
DRV-based regimens are recommended for initial therapy	

Note: If adolescent is not able to swallow pills or weight is less than 25 kg, please refer to the *Preferred* regimens in the 2- to 12-year age group.	
Alternative regimen	
>= 40 kg	(FTC +TAF) or (FTC+TDF) +DRV/r once daily. Note: Avoid TAF in obesity or lipid issues and avoid TDF in bone and renal disease.

Second-line ART and beyond for children

- All children with HIV infection who are treatment-experienced, especially those with treatment failure, should be promptly referred to a pediatric ID specialist at **Royal Hospital** for expert evaluation and management.
- Resistance testing should be performed while a patient is still receiving the failing regimen.
- Follow-up should include a measurement of plasma VL at 4 weeks (and not >8 weeks) after the switch to ensure that the new regimen is effective.

13.7 Adherence to ART in children and adolescents with HIV

- Strategies to maximize adherence should be discussed before and/or at initiation of ART and before changing regimens.
- Adherence to ART must be assessed and promoted at each visit, and strategies to maintain and/or improve adherence must be continually explored.
- In addition to VL monitoring, at least one other method of measuring adherence to ART should be used.

13.8 OIs in children infected with HIV

The most common Opportunistic infection include:

- Serious bacterial infections (most commonly pneumonia, often presumptively diagnosed, and bacteremia)
- Herpes zoster
- Disseminated Mycobacterium avium complex (MAC)
- PJP
- Candidiasis (esophageal and tracheobronchial disease)
- Less commonly observed OIs (event rate <1 per 100 child-years) included CMV disease, cryptosporidiosis, TB, systemic fungal infections, and toxoplasmosis.

PJP prophylaxis

***Indication*:**

- Children ≥6 years who have CD4 T lymphocyte (CD4) cell counts <200 cells/ mm3 or CD4 percentage <15%
- Children aged 1 to <6 years with CD4 counts <500 cells/mm3 or CD4 percentage <15%.
- All HIV-infected infants aged <12 months regardless of CD4 count or percentage.
- Choice: TMP–SMX (cotrimoxazole) is the drug of choice for prophylaxis because of its high efficacy, relative safety, low cost, and broad antimicrobial spectrum. TMP alone has little, if any, anti-Pneumocystis activity, but it enhances the activity of the sulfonamide.

Dose: (based on trimethoprim)

- TMP-SMX 150 mg/m2 body surface area per day (~ 5-10 mg/kg/day), administered orally once daily, OR
- TMP-SMX 2.5-5 mg/kg/dose twice daily on 3 consecutive days per week or every other day (e.g., Monday, Wednesday, Friday).
- The total daily dose should not exceed 320 mg TMP and 1600 mg SMX.
- In patients with impaired renal function, a reduced dose may be necessary.
- TMP-SMX, preferably given daily, also is effective in preventing toxoplasmosis and some bacterial infections (e.g., Salmonella, Haemophilus, and Staphylococcus).
- For patients who are not able to take TMP-SMX, consult pediatric infectious diseases specialist for other options (e.g. atovaquone, dapsone).

14

Chapter 14:
Psychosocial Support and Mental Health

Chapter 14: Psychosocial Support and Mental Health

14.1 Background

The interplay between HIV and mental disorders is bi-directional, therefore, addressing mental health of PLHIV is essential. Mental disorders increase an individual's risk for HIV infection through increased social vulnerability, altered behavior, substance misuse and high-risk sexual behaviors. PLHIV with mental disorders are at risk of non-compliance, lack of retention of care and thus affects risk of transmission to others.

Mental disorders may also arise because of HIV neuro-invasion or psychosocial stressors associated with the diagnosis, or due to ART side effects. Integrating mental health in HIV care pathways addresses both the physical and psychological aspects, which promotes a more holistic approach to PLHIV treatment and support. Therefore, regular screening of mental health issues is important in PLHIV for early intervention.

Stigma, the fear of HIV disclosure, discrimination, and uncertainty about the future often exacerbate psychological vulnerabilities in PLHIV. Therefore, integrating interventions for stigma reduction at all levels is essential at individual and community level.

In Oman, the prevalence rate of depressive symptoms in PLHIV is 41.6%. Globally, the prevalence of depression is reported as 20-40% in PLHIV versus 7% in general population. Anxiety disorders include the following: panic disorder (10% in PLHIV), generalized anxiety disorder (5.6% in PLHIV), social anxiety disorder (9% in PLHIV), and post-traumatic stress disorder (PTSD). Anxiety and depression are associated with significant disability and poorer HIV treatment outcomes.

This strong relation between HIV and mental health mandates integrating psychosocial health in HIV regular care to ensure that individuals receive comprehensive care that supports both their medical and psychological needs. Mental disorders are underdiagnosed or inadequately managed in PLHIV. It's important for clinicians to screen, diagnose and manage mental disorders in the population.

14.2 Screening and diagnosis of anxiety and depression

It is essential to screen PLHIV for any underlying mental health disorders for early identification and to ensure timely referral to mental health expert assessment and intervention. Table 32 shows the screening and diagnosis of anxiety.

Table 32: Screening and diagnosis of anxiety

Who?	How to screen?	How to diagnose?
Screening all PLHIV at each clinic visit (every 6 months) is recommended Populations at particularly high risk: - Positive history of anxiety disorders in family - Anxious personality - Alcohol excess - As part of investigation of cognitive impairment. - Multiple stressful life events	Generalized anxiety disoders-2 (GAD-2) screening tool: Over the last 2 weeks, how often have you been bothered by the following problems? - Feeling nervous, anxious or on edge - Not being able to stop or control worrying Score each question and calculate sum: **0-** Not at all **1-** Several days **2-** More than half the days **3-** Nearly everyday	If GAD-2 cut-of score of >= 3, ask the following questions to diagnose generalized anxiety disorder: - Excessive anxiety for more days than not over 6 months - Difficulty controlling worry - Associated with at least three of these symptoms (restlessness, fatigue, difficulty concentrating, irritability, muscle tension, sleep disturbances) - Significant life impairment - Not attributable to another substance or medical condition - Not being better explained by another medical disorder Seek expert advice to diagnose panic attacks, PTSD and social phobia Rule out hyperthyroidism, hypoglycemia and hyperadrenocorticism. Exclude caffeine excess and other stimulants, such as cocaine, crystal meth, amphetamines)
Source: EACS guideline version 11.1 Oct 2022 (10)		

Screening, diagnosis and management of depression are shown on table 33.

Table 33: Screening, diagnosis and management of depression

Who?	How to screen?	How to diagnose?
Screening of all PLHIV for depression Populations at particularly high risk: ▪ Positive family history of depression ▪ Positive personal history of depression ▪ Older age ▪ Adolescence ▪ Persons with a history of drug addiction, psychiatric, neurologic or severe somatic co-morbidity ▪ Use of EFV ▪ Use of neurotropic and recreational drugs ▪ Neurocognitive impairment. ▪ Socially isolated	Screen every year Ask Two questions: 1- Have you often felt depressed, sad or without hope in the last few months? 2. Have you lost interest in activities that you usually enjoy? • Rule out other medical conditions (such as hypothyroidism, hypogonadism, Cushing's syndrome, vitamin B12 deficiency) • Rule out depressive symptoms secondary to ART (such as EFV) and non-ART medication • Assessment of the risk of suicide should be done with the following questions: - Are these just ideas? - Are they intrusive and how many? - How much control do you have over these ideas? - Have you planned? - Are you about to act?	Evaluate symptoms regularly At least 2 weeks of Depressed mood (A) (or) Loss of interest (B) (or) Diminished sense of pleasure (C) PLUS 4 out of 7 of the following: 1. Weight change of ≥ 5% in one month or a persistent change of appetite 2. Insomnia or hypersomnia on most days 3. Changes in speed of thought and movement 4. Fatigue 5. Feelings of guilt and worthlessness 6. Diminished concentration and decisiveness 7. Suicidal ideation or a suicide attempt
Management of depression		
Degree of depression	Number of symptoms (A, B, (or C +4/7	Management
No	4>	No

Mild	4	- Problem-focused consultation - Consider referral to expert - Physical activity
Intermediate	5-6	Refer to expert to start anti-depressant treatment
Severe	>6	Refer to expert (essential)
Source: EACS guideline version 11.1 Oct 2022 (10)		

14.3 Integration of mental health with HIV Care

Psychosocial and mental health integration into HIV care is essential. This holistic approach improves adherence to antiretroviral therapy (ART), reduces HIV transmission, lowers the risk of mental health exacerbations and improves quality of life. The inclusion of psychosocial support in HIV can be achieved through the below system pathways:

A. Collaboration between HIV and Mental Health Professionals: Integrating mental health care requires regular screening in clinical encounters and appropriate collaboration between HIV care providers and mental health professionals.

B. Social Support system: Social support services, such as housing support, employment assistance, and case management are integral to managing the mental health needs of individuals with HIV. These formal and informal services help individuals explore and navigate the socio-economic challenges that may underlie mental health problems. These challenges include unemployment, transportation issues, financial constraints, or stresses. These services can also assist patients in overcoming barriers to accessing medical and mental health care, ensuring that patients receive the comprehensive support they need.

14.4 Stigma and discrimination

HIV-related stigma remains a significant barrier to both prevention and treatment of HIV, negatively affecting testing, disclosure of diagnosis, and engagement in care. HIV-related stigma originates from misconceptions about transmission, fear of moral judgments and discrimination. Stigma can lead to social isolation, anxiety, depression, and reduce access to healthcare services. It is critical to address stigma within the community, and through legal and policy reforms to improve HIV care and prevent further transmission. Below are some strategies that have been identified to combat HIV-related stigma (Table 34):

- **Public Education and Awareness Campaigns**: Public education campaigns should provide accurate information about HIV transmission, prevention, and treatment; HIV is now a treatable chronic disease with average life expectancy, with 0% sexual transmission when the HIV VL is undetectable [Undetectable = Untransmissible]. These campaigns aim to challenge misconceptions, correct myths, and reduce fear associated with HIV. Media plays an essential role in normalizing HIV and show casting positive view of PLHIV.

- Internalized Stigma Reduction: Psychological interventions such as counselling and cognitive behavioral therapy help PLHIV confront and reduce internalized stigma. Internalizing negative societal views about HIV results in a feeling of shame and isolation. Addressing internalized stigma improves access to healthcare, well-being and enhances treatment outcomes.
- Healthcare Provider Training: HIV care providers should undergo training on the role of non-judgmental attitudes, cultural sensitivity, and maintaining confidentiality in reducing stigma. Empathy and understanding of PLHIV create a safe environment for disclosing diagnosis, accessing treatment, and receiving holistic care. Such training can help reduce the likelihood of discrimination and increase the trust and engagement of PLHIV.
- Empowerment and Community-Based Approaches: Peer educators and community health workers provide information, emotional support, and guidance on coping strategies to PLHIV. This approach strengthens social networks, reduces stigma and empowers health management and diagnosis disclosure.

Table 34: World health organization intervention approaches for stigma reduction

Level of stigma	Intervention focuses and strategies
Intra-personal ((self-stigma	Self-help, counselling, treatment of stigmatized condition
Interpersonal	Enhance care and social support
Community	Reduce stigmatizing attitudes and behaviors in the community through education, awareness-raising, social marketing, contact, advocacy, and working with media to reduce perpetuation of stigmatizing attitudes
Organizational, institutional	Institute training programmes and institutional policies
Governmental, structural level	Establish and enhance legal, policy and rights-based structure

14.5 Legal and policy considerations

Legal and policy considerations contribute significantly to HIV care landscape. Implementing non-discrimination laws, ensuring access to healthcare, protecting confidentiality, and promoting human rights are essential to reduce stigma and to encourage engagement with HIV care. Effective laws and policies not only safeguard the rights of individuals but also play a key role in creating an environment that encourages HIV testing, treatment, and care. The following legal and policy considerations are crucial for HIV care guidelines:

- Access to Healthcare and Treatment: Laws and policies must ensure universal access to healthcare for all individuals, regardless of their HIV status. This includes ensuring access to antiretroviral therapy (ART), testing, and prevention services. Policies that facilitate access to healthcare such as free service for HIV care are essential for reducing barriers to treatment and care.
- Protection of Confidentiality and Privacy: Legal protections around confidentiality and privacy are critical in encouraging individuals to seek HIV testing and care. Laws must protect patients' rights to keep their HIV status private and prevent unauthorized disclosure of HIV-related information.
- Advocacy for Human Rights: Legal frameworks should actively promote the human rights of PLHIV. Human rights focus on treating PLHIV with dignity and respect, ensuring that they have the same rights as any other person to live free from discrimination and violence.

14.6 Grievances redressal mechanisms

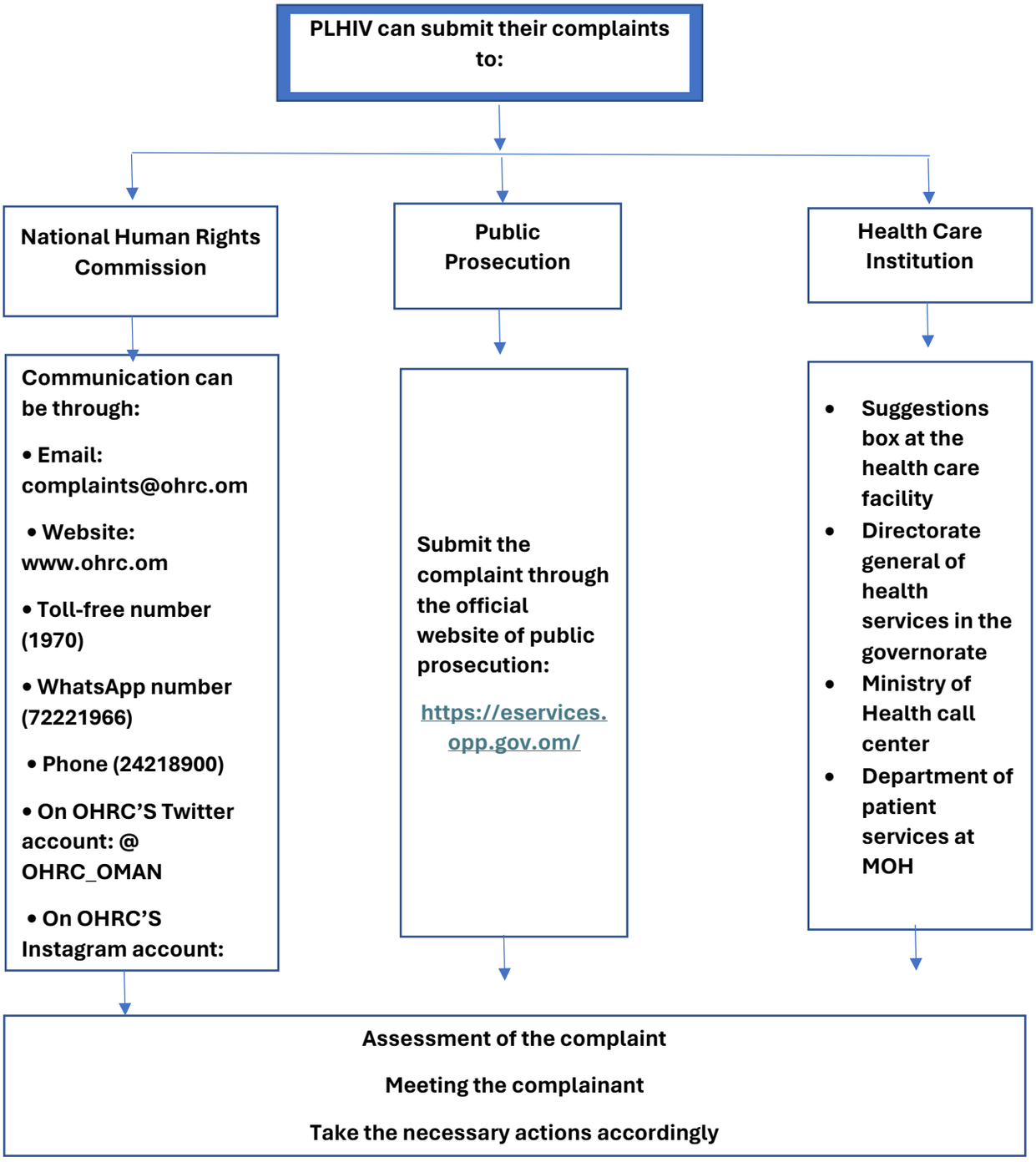
Grievance redressal mechanisms should be a formalized process to allow PLHIV to seek resolution for any discrimination. Discrimination against PLHIV can significantly hinder access to necessary services and negatively impact mental and physical health outcomes. A well-established grievance redressal system is essential for protecting the rights of PLHIV and ensuring they are treated with dignity and equality in all aspects of life. Below we expand on these domains of discrimination:

1- Employment discrimination: Grievance redressal mechanisms for employment-related discrimination are essential for protecting the rights of PLHIV in the workplace. Denial of job opportunities, unfair treatment, wrongful termination, or inadequate workplace accommodations based on HIV diagnosis bias can significantly impact the mental health and quality of life of PLHIV.

2- Social benefits discrimination: PLHIV has the right to have equal access to financial, healthcare, housing, and other social support services without facing discrimination or bias due to their HIV status. Discriminatory denial or delayed access to social benefits can increase vulnerability, and perpetuate stigma, thereby undermining the overall well-being of PLHIV.

3- Healthcare discrimination: Discrimination in healthcare settings, whether it involves denial of care, sub-standard treatment, or the breach of confidentiality, can significantly impact both physical and mental health outcomes for PLHIV.

Fig. 19: Procedure for PLHIV complaints' submission



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Chapter 15: Pre-exposure prophylaxis (PrEP)

Chapter 15: Pre-Exposure Prophylaxis (PrEP)

PrEP) involves the use of ART in HIV-negative individuals to prevent the acquisition of HIV. When taken daily as prescribed, PrEP reduces the risk of sexual transmission of HIV by approximately 99% among MSM and by about 90% among heterosexual individuals. Among PWID, PrEP reduces the risk of HIV acquisition by at least 74% when taken consistently

15.1 Indications

Strong Recommendation

- **MSM** who report sexual behaviors associated with HIV infection (e.g., condomless anal sex).
- **Heterosexually active persons** who have sex with partners who are at high risk of HIV infection (e.g., partners from high HIV prevalence areas, partners who inject drugs).
- **PWID.**

Consideration

- HIV-negative heterosexual individuals in a **serodiscordant relationship** when the HIV-positive partner is **not virally suppressed** or their **suppression status is unknown or unreliable**.

- **Heterosexual women** who have, in the last six months, engaged in condomless sex with male partners who are at high risk of HIV infection.
- **Heterosexual men** who have, in the last six months, been diagnosed with a bacterial STI or have engaged in condomless sex with partners from areas of low general HIV prevalence but who are at high risk of HIV infection (e.g., sex workers, persons who inject drugs).

15.2 Risk assessment

To determine if a patient is at risk for HIV acquisition through sexual transmission, clinicians should assess sexual risk behaviors over the last 6 months. This includes:

- **Partner's HIV status and risk behaviors:** If known, assess the HIV status and risk behaviors of the patient's sexual partners.
- **Monogamous relationships:** If the patient is in a monogamous relationship with someone living with HIV, assess the partner's viral suppression status.
- **Condomless sex:** Determine if the patient has had condomless penile-anal or penile-vaginal sex with partners other than their main partner.
- **Number of sexual partners.**
- **History of STIs:** Assess the history of any bacterial STIs.

  To assess a patient's risk for HIV acquisition through drug use, clinicians should ask about their drug use history over the last 6 months, including:

- **Injecting drugs:** Injecting heroin, fentanyl, cocaine, and/or methamphetamine.
- **Needle sharing:** Sharing needles or equipment for injecting drugs.
- **Drug use during sex:** Using non-parenteral drugs (particularly methamphetamine) during sex.

15.3 PrEP Regimens

- **TDF-FTC (tenofovir disoproxil fumarate + emtricitabine); can be given daily or event driven.**
  - **Daily:** 1 tablet once daily. **It is recommended for MSM and heterosexuals**.
  - **Event-driven** indicated for persons who engage in anal sex less than 2 events per month and when events are planned)**:** 2 tablets (2-24 hours before the event) then once daily until 48 hours post-event. **It is recommended only for MSM.**
  - **Benefits:** Well-tolerated, most studied regimen, can be used in most populations, can be administered as event-driven therapy for some individuals.
  - **Risks:** Can reduce renal function, can result in bone loss, risk of liver flare in patients with chronic HBV if discontinued.
  - **Considerations:** Not recommended for patients with an eGFR < 60 mL/min/1.73m2. Requires monitoring of renal function.
- **TAF-FTC (tenofovir alafenamide + emtricitabine):**
  - **Daily:** 1 tablet once daily.
  - **Event-driven:** Not recommended due to insufficient data.
  - **Benefits:** Well-tolerated, less bone and renal toxicity than TDF-FTC.
  - **Risks:** Higher rates of mild triglyceride elevations and weight gain compared to TDF-FTC. Not recommended for those whose main risk is vaginal sex or who inject drugs. Less experience in certain populations. Risk of liver flare in patients with chronic HBV if discontinued.
  - **Considerations:** Not well studied for vaginal sex, pregnancy, or in people who inject drugs.
- **CAB-LA, if available:**
  - **Administration:** Injected intramuscularly every other month.
  - **Benefits:** Well-tolerated, long-acting, clinical trials suggest higher efficacy than TDF-FTC (possibly due to improved adherence). Can be considered for patients with conditions that increase the risk of adverse events with oral PrEP.
  - **Risks:** Long half-life (drug may be detectable in blood for over a year), potential limitations on future HIV treatment options if infection occurs, need for access to injection sites, injection site reactions.
  - **Considerations:** Limited data in pregnant or pregnancy-desiring individuals, not studied in people who inject drugs.

15.4 Baseline investigations prior to starting PrEP

- **HIV-1 RNA:** An HIV-1 RNA test is recommended as part of the initial evaluation for all individuals initiating CAB-LA. For individuals starting oral HIV PrEP with TDF-FTC or TAF-FTC, a baseline qualitative or quantitative HIV-1 RNA polymerase chain reaction (PCR) assay is not routinely recommended, but it is indicated in the following circumstances:
  - Has taken oral HIV PrEP or HIV PEP within the past 3 months, or
  - Received CAB-LA for HIV PrEP within the past 12 months, or
  - Had high-risk HIV exposure in prior 4 weeks (e.g., condom broke during sex with partner known to have HIV), or
  - Symptoms in prior 4 weeks consistent with acute HIV infection.

Note, if the HIV-1 RNA test is indicated, it should be drawn within 7 days of starting HIV PrEP. For persons who take an oral cabotegravir lead-in prior to starting CAB-LA, the HIV-1 RNA should be done within 7 days of starting the oral lead-in and then repeated within 7 days of receiving the first injection of CAB-LA.

- HIV Antigen-Antibody Immunoassay: The HIV-1/2 antigen-antibody test must be performed in the 7-day period prior to starting PrEP. For example, if a person had a negative HIV test 4 weeks ago, the HIV testing must be within the 7-day period prior to starting PrEP. Ideally, a laboratory-based blood HIV-1/2 antigen-antibody immunoassay is performed; a blood rapid HIV-1/2 antigen-antibody test is an acceptable but less preferable option. Oral fluid samples should not be used for HIV testing in this setting.
- Estimated Creatinine Clearance (eCrCl): A serum creatinine is recommended to assess renal function. This test is important to order at baseline due to restrictions on the use of TDF-FTC and TAF-FTC for individuals with renal insufficiency.
- Syphilis Serology: Testing for syphilis requires a serum sample that can be used for either the reverse screening method (treponemal-specific antibody screening testing followed by a nontreponemal assay) or the traditional method (screening with a nontreponemal assay). For the nontreponemal tests, two options can be used: RPR or VDRL. Persons with a known prior history of syphilis should have a nontreponemal assay (RPR or VDRL) as their screening test, since they will likely have a positive treponemal-specific antibody test for life.
- Gonorrhea and Chlamydia: The preferred tests are NAATs. Testing should consist of obtaining samples from all sites involved with sexual activity, such as throat, urethra, vagina, and rectum. Swabs can be self-collected by patients or by a clinician. Urine samples can be used instead of swabs for testing urethral and cervical/vaginal infection.
- Hepatitis B Serology: The recommended screening for HBV consists of a 3-test panel: HBsAg, anti-HBs and anti-HBc. The oral PrEP options, TDF-FTC and TAF-FTC are active against HBV, so baseline testing for individuals starting these PrEP regimens is important, since starting and then stopping these medications can lead to an HBV flare in persons with underlying chronic HBV infection. Individuals who are HBV-seronegative should receive HBV vaccination.
- Hepatitis C Serology: The recommended serologic testing for HCV infection is an anti-HCV antibody test, with HCV PCR testing for all positive antibody results. Repeat annual testing should also be performed for persons who have ongoing risk of acquiring HCV, including PWID and MSM. If a person is seronegative and at risk, counseling can be performed to reduce the risk of acquiring HCV. Persons who test positive for both HCV antibody and HCV PCR (indicating active infection) should be evaluated or referred for HCV treatment.
- Lipid Panel: The recommended lipid panel to order should include total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides. Several studies have shown that taking TAF-FTC may lead to minor unfavorable changes in serum lipid parameters, but these changes are not seen with TDF-FTC or injectable CAB-LA. Accordingly, a baseline serum lipid panel is recommended only for individuals who initiate TAF-FTC for PrEP.

- Pregnancy Testing: For women with childbearing potential, a baseline pregnancy test is recommended prior to starting PrEP, primarily for counseling purposes. CAB-LA has not been adequately studied for use in pregnancy and is not recommended for pregnant women. The oral PrEP regimens, TDF-FTC and TAF-FTC, have both been shown to be safe and effective for the treatment of HIV during pregnancy, but there are limited data for their use as PrEP during pregnancy.
- Bone mineral density (DEXA scan) in patients with history of osteoporosis.

15.5 Follow up visits and investigations after starting PrEP

Each Follow-up:

- Review Sexual history
- Adherence assessment and support (Table 35).
- Monitor for side effects.
- Perform laboratory tests.

- Laboratory tests: Oral PrEP

    - At least every 3 months: HIV Ag/Ab, HIV RNA, screen for STIs (see Baseline list), pregnancy test when applicable
    - Every 6 months: eGFR for persons age ≥ 50 or eCrCl < 90
    - Every 12 months: cholesterol and triglyceride levels. HCV Ab for MSM, transgender women, people who inject drugs.

- Laboratory tests: Injectable PrEP

    - 1 month: HIV RNA
    - Every 2 months: HIV Ag/Ab and HIV RNA. Pregnancy test when applicable
    - Every 4 months: HIV RNA, STI testing (see Baseline list)

Follow up visits: Oral PrEP

- 1 week: Call to assess adherence and side effects
- 1 month (optional)
- At least every 3 months

Follow up visits: Injectable PrEP

- 1 month (at time of 2nd injection)
- Every 2 months (timed with subsequent injections)

Table 35: Key components of oral medication adherence counselling

Establish Trust and Bidirectional Communication
Provide simple explanations and education
• Medication dosage and schedule
• Management of common side effects
• Relationship of adherence to the efficacy of PrEP
• Signs and symptoms of acute HIV infection and recommended action
Support adherence
• Tailor daily dose to patient's daily routine
• Identify reminders and devices to minimize forgetting doses
• Identify and address barriers to adherence
• Reinforce benefit relative to uncommon harms
Monitor medication adherence in a non-judgmental manner
• Normalize occasional missed doses, while ensuring patient understands importance of daily dosing for optimal protection
• Reinforce success
• Identify factors interfering with adherence and plan with patient to address them
• Assess side effects and plan how to manage them

16

Chapter 16: Post-Exposure Prophylaxis (PEP)

Chapter 16: Post-Exposure Prophylaxis (PEP)

16.1 Background

PEP refers to the short-term use of ART initiated after potential exposure to HIV, with the goal of preventing infection. PEP is indicated in both occupational settings—such as needlestick injuries among HCWs—and non-occupational exposures, including unprotected sexual contact or sharing of injection equipment.

The rationale behind PEP is based on the window of opportunity following exposure, during which HIV has not yet established systemic infection. When initiated promptly—within 72 hours after exposure—PEP can significantly reduce the risk of HIV acquisition. The regimen typically consists of a 28-day course of combination ART, and effectiveness is highest when adherence is maintained throughout the full course.

PEP should be considered after any exposure where there is a non-negligible risk of HIV transmission, guided by the type of exposure, the HIV status of the source (if known), and clinical judgment. Timely evaluation, risk assessment, and counselling are essential components of PEP provision.

HCWs are at risk of acquiring bloodborne pathogens, including HIV, HCV and HBV, following an occupational exposure. Although of minimal risk (Table 36), the transmission of HIV in health care settings is often a cause of anxiety.

Table 36: Risk of transmission of HIV, HCV and HBV infections per exposure

Bloodborne pathogens	Route/condition	Estimated risk
HIV	Percutaneous	(CI, 0.2%-0.5% 95%) 0.3%
	Mucous membrane	(CI, 0.006%-0.5% 95%) 0.09%
	Non-intact skin	(CI, 0.006%-0.5% 95%) 0.09% >
HCV	Percutaneous	(0%-7%) 1.8%
HBV	HBsAg +ve and HBeAg +ve	22%-31%
	HBsAg +ve and HBeAg –ve	1-6%

An occupational exposure is defined as "a percutaneous (a needlestick or cut with a sharp object), mucous membrane (eye, nose and mouth) or non-intact skin (exposed skin that is chapped, abraded, or afflicted with dermatitis) exposure to blood or body fluids (Table 28) that occurs during the course of an individual's employment. It mainly applies to HCWs in health care settings; however, other workers, such as emergency rescue staff, waste disposal workers, law enforcement personnel and fire fighters, may also be exposed".

First aid

First aid refers to the set of actions that should be taken immediately after potential exposure occurs. The aim of first aid is to reduce contact time with the source person's blood, body fluids or tissues and to clean and decontaminate the site of exposure. The specific first aid treatment used will depend on the type of exposure as summarized in Table 37.

Following first aid, the exposed person should immediately report the incident to the designated person (HIV focal point and infection prevention and control focal point). The designated person should report the incidence using form MR-4.

Table 37: First aid following occupational exposure to HIV infection

Injury with a used needle or sharp instrument	Splash to the eyes	Splash to the mouth
- Do not squeeze or rub the injury site - Wash the site immediately with soap or a mild disinfectant (chlorhexidine gluconate solution) - If running water is not available clean the site with a gel or other hand-cleaning solution - Do not use strong disinfectant	- Irrigate the exposed eye immediately with water or normal saline - Sit in a chair, tilt the head back and have a colleague gently pour water or normal saline over the eye, pulling the eyelids up and down to make sure the eye is cleaned thoroughly - Leave contact lenses in place while irrigating the eye -Do not use soap or disinfectant on the eye	- Spit the fluid out immediately - Rinse the mouth thoroughly, using water or saline, and spit again. Repeat this process several times - Do not use soap or disinfectant in the mouth

16.2 Establishing eligibility for PEP

Establishing eligibility for PEP after occupational exposure

Obtain the following history from the exposed person:

- Baseline health information and any known chronic diseases or medications
- Exposed person's risk for acquiring HIV through other exposures
- Details of the exposure incident, e.g.:
  - Type and size of the needle or sharp instrument.
  - The amount of blood or body fluids or tissues to which the individual was exposed.
  - Whether injury was with a sharp object and whether the wound bled.
  - Whether the injury was through gloves or clothing.
  - When the exposure occurred.

Individuals are eligible for HIV PEP if any the following 4 criteria are met:

1. Exposure occurred within the past 72 hours*
   - PEP is more effective when given within the first 72 hours following exposure.
   - A first dose of PEP drugs should be made readily available to potentially exposed individuals (starter dose).

   *In patients with high-risk exposure (e.g. blood percutaneous injury with a needle that was in the source patient's artery or vein where the source patient is known to be HIV positive) PEP can be considered in up to 1 week on a case-by-case basis with HIV expert consultation as the benefit of this is unknown
2. The potentially exposed individual is not infected or not known to be infected with HIV.
   - HIV infection of the exposed person should first be ruled out by using rapid testing. However, an HIV test should NOT be a condition for initiating PEP, nor should PEP be delayed until the results of an HIV test become available (unless rapid testing is used).

3. The source is HIV-infected, or the HIV status is unknown.
   Note: PEP is typically not recommended following a sharps injury if the source patient has been on ART for at least six months, maintains an undetectable HIV VL (confirmed at their most recent measurement within the past 3 to 6 months), and has demonstrated good adherence. However, due to the absence of definitive evidence, decisions should be individualized based on the specifics of the injury.
4. An exposure that may place a health care worker at risk for HIV infection.
   Exposure to high risk or potentially infectious bodily fluid (Table 38) via:

- A percutaneous injury (e.g., a needlestick or cut with a sharp instrument used on a patient)
- Contact of mucous membrane or nonintact skin (e.g., exposed skin that is chapped, abraded, or afflicted with dermatitis)

High risk body fluids	• Blood, any visibly blood-stained fluid or substance • Semen* • Vaginal secretions*
Potentially Infectious	• Amniotic fluid • Cerebrospinal fluid • Pericardial fluid • Pleural fluid • Synovial fluid
No-risk body fluids¥	Saliva, urine, faeces, vomit, sweat, tears, sputum, nasal secretions
*** Fluids that have not been implicated in occupational transmission**	

Table 38: Examples of high risk, potentially infectious and no-risk body fluids

Establishing eligibility for PEP after non-occupational exposure

PEP should be considered for individuals who have had a potential sexual exposure to HIV within the past 72 hours. Eligibility is based on the risk level of the exposure and the HIV status or risk profile of the source partner. Key scenarios that warrant consideration for PEP include:

- Unprotected receptive or insertive anal or vaginal intercourse with a partner known to be HIV-positive or of unknown status.
- Condom failure (e.g., breakage or slippage) during intercourse with a partner at risk for or known to be living with HIV.
- Sexual assault, especially if the assailant's HIV status is unknown or positive.
- Exposure involving a high-risk partner, such as someone from a high-prevalence population (e.g., MSM, PWID) or with known risk factors.

16.3 Prescribing PEP

1. Counselling

Persons receiving PEP should be advised to use precautions (e.g., use of barrier contraception and avoidance of blood or tissue donations, pregnancy, and, if possible, breast-feeding) to prevent secondary transmission, especially during the first 6–12 weeks after exposure.

2. For exposures for which PEP is prescribed, people should be informed regarding the following:

- Possible drug toxicities (e.g., rash and hypersensitivity reactions that could imitate acute HIV seroconversion and the need for monitoring)
- Possible drug interactions
- The need for adherence to PEP regimens

3. Obtain baseline testing for the following:

1. Renal function test
2. Alanine transaminase
3. 4th generation test HIV-1&2 Ag/Ab
4. Hepatitis B serology (HBs Ag, anti HBs Ab, anti HBc Ab)
5. Hepatitis C serology (HCV antibody)
6. Pregnancy test for any female patient of childbearing age

However, in personss not previously known to have kidney disease or liver disease or risk factors for kidney or liver disease, do not delay initiation of treatment until baseline testing results are available as earlier initiation of PEP leads to improved outcomes.

Repeat lab tests may need to be obtained if there are abnormalities at baseline.

Starting PEP

Time: PEP should be initiated as quickly as possible, preferably within 1-2 hours of exposure and up to 72 hours post-exposure. Preferred and recommended PEP regimens are shown in table 39.

Duration: 28 days

Table 39: Recommended PEP regimens

(A three-drug regimen is preferred (28-day course Note: dosing is for patient with normal renal function Dose or regimen may need to change based on kidney function and creatinine clearance ((CrCl) (Please, contact the pharmacist if CrCl is <30 mL/min	
Preferred	Tenofovir AF 25 mg OD + Emtricitabine 200 mg OD + Dolutegravir 50 mg OD
Alternative	Tenofovir AF 25 mg OD + Emtricitabine 200 mg OD + Raltegravir 400 mg BID
Alternative Tenofovir AF 25 mg OD + Emtricitabine 200 mg OD + Darunavir 800 mg OD + Ritonavir 100 mg OD	

16.4 Follow-up

A follow-up visit should be scheduled at 2 weeks to monitor adherence and to identify and manage side effects.

HIV serology should be performed at the time of exposure and repeated at 6 weeks, 3 months and 6 months. It should also be repeated at 12 months in HCWs who acquired HCV with the exposure, since this may delay HIV seroconversion.

If there is no recent positive or negative serology available, serology for HIV should be done along with serology for HBV and HCV.

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Chapter 17: Monitoring and evaluation (M & E)

Chapter 17: Monitoring and evaluation

Monitoring and evaluation (M&E) is an integral part of the effective implementation of these guidelines. It helps to measure performance and identify gaps of the service provision. M&E identifies responsibilities of all stakeholders involved in the operationalizing of HIV management.

17.1 HIV treatment and care cascade

It is important to recognize that HIV is a chronic communicable disease, which necessitate monitoring each of the above-mentioned steps of cascade using Key Performance Indicators (KPI). However, the overall objectives of these indicators are captured in the target of 95-95-95 by 2030, which aim to ensure that by 2025, 95% of PLWH are diagnosed, 95% of diagnosed persons are on ART and 95% of those on ART achieve sustained viral suppression.

Early diagnosis of PLHIV, starting ART among them and achieving sustained viral suppression among the majority of PLWH reduces transmission and helps in decreasing the incidence of new HIV infection in the community, and bring the epidemic to a level where HIV is no longer a public health problem.

17.2 Clinical audit of HIV treatment centers

The MOH is conducting regular clinical audits for HIV treatment centers, enabling the evaluation of key processes such as initiating ART, ensuring adherence to ART among PLWH and achieving viral suppression. These audits identify areas for improvement, that subsequently can be addressed through training programs or by providing mentorship to HIV clinic teams. Monitoring efforts also include periodic site visits and stakeholder feedback to assess compliance with guidelines and identify the challenges faced by healthcare providers.

17.3 Global AIDS Monitoring

Since 2010, the MOH has been reporting online on the joint platform of WHO, UNICEF, and UNAIDS for global AIDS monitoring, covering all aspects of HIV/AIDS. Additionally, the MOH participates in the HIV estimation exercise using Spectrum software. These collaborations enable the evaluation of national HIV services against global benchmarks, ensuring alignment with international standards and best practices.