Ministry of Health
SAMOA

# 2018

# NATIONAL GUIDELINES ON THE USE OF ANTIRETROVIRAL DRUGS FOR TREATING AND PREVENTING HIV INFECTION

This guideline is an adaptation of the WHO Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infections (Second Edition 2016)

# FOREWORD

*Leausa Toleafoa Dr. Take Naseri*
*Director General/CEO Ministry of Health*

The Ministry of Health is proud to present Samoa's adapted WHO Guidelines for;

1. Use of Anti-retroviral Therapy
2. Preventing Mother to Child Transmission of HIV
3. HIV testing services
4. STI Diagnosis, Treatment and Management

This document is the adaptation of the 2016 WHO guidelines that have been contextualized for Samoa's healthcare system and clinicians. The health sector, stakeholders and partners were consulted in order to tailor these guidelines to better fit Samoa's resources, service delivery systems, multilateral partnerships, and ultimately the needs of patients.

Samoa, as well as the Pacific region as a whole, has long faced high rates of STI's, which are only projected to increase within the coming 5 years. Ensuring quality clinical case management of STI's is an absolutely essential part of the national response to these diseases. Linked to STI management is HIV Testing Services (HTS), which involves clinicians, laboratories, public health, and the communities themselves in detecting infections and connecting people to the services they need. Samoa has historically adopted a treat all approach to those that test positive for HIV, giving all people ART free of cost. It is therefore essential that providers in Samoa are fluent in the latest practices for treatment.

Additionally, Preventing Mother to Child Transmission (PMTCT) encompasses all services, interventions, care, protocols and standards to support patients in maintaining their health and preventing the spread of infection from parent to infant. Samoa has always demonstrated a firm commitment on improving maternal and child health through both the Millennium and the Sustainable Development Goals.

These guidelines serve to provide clinicians a reference for the latest in global best practices, as well as the local context for implementing them. Throughout the document are clinical notes labeled below.

"  "

These notes come from numerous consultations on the guidelines and how to implement the recommendations nationally. We hope that providers will find this useful in their practice.
We are grateful for all of the work from our national and international partners in health that has gone into the development of these guidelines.

Ma lo'u fa'aaloalo lava,

Leausa Toleafoa Dr. Take Naseri

## ACKNOWLEDGMENT

The development of the guideline was supported by UNDP through the Multi-Country Western Pacific Integrated HIV/TB Programme, a regional programme aiming to strengthen control of HIV and TB in 11 Pacific island countries. The programme is supported by the Global Fund to fight AIDS, Tuberculosis and Malaria.

Therefore the Ministry of Health would like to thank the following consultants, individuals and organizations for the development of the updated guidelines. Their valued advice and review was essential for contextualizing these guidelines to Samoa's health system;

World Health Organization

United Nations Development Program - The Global Fund to Fight Malaria, HIV and TB

The National Health Service

Samoa Red Cross Society

Samoa Family Health Association

People living with HIV

Private clinicians

Dr. Dennie Iniakwala (SPC)

Dr. Madeline Salva (WHO)

Dr. Yadav Subhash (WHO)

## ACRONYMS AND ABBREVIATION

| | |
|---|---|
| AIDS | Acquired Immunodeficiency Syndrome |
| ARV | Antiretroviral Drugs |
| ART | Antiretroviral Therapy |
| CoC | Continuum of Care |
| DOT | Directly Observed Treatment |
| EID | Early Infant Diagnosis |
| EWIs | Early Warning Indicators |
| FDC | Fixed Dose Combination |
| HIV | Human Immunodeficiency Virus |
| HBV | Hepatitis B virus |
| HCV | Hepatitis C virus |
| HBsAG | Hepatitis B surface antigen |
| IRIS | Immune Reconstitution Inflammatory Syndrome |
| IVD | In Vitro Diagnostic |
| M and E | Monitoring and Evaluation |
| NAT | Nucleic Acid Test |
| OD | Once daily |
| PEP | Post Exposure Prophylaxis |
| PLHIV | People living with HIV |
| PrEP | Pre-exposure Prophylaxis |
| PMTCT | Prevention of Mother to Child Transmission |
| QA | Quality Assurance |
| RDT | Rapid Diagnostic Test |
| SPC | Pacific Community |
| STI | Sexually Transmitted Infections |
| TB | Tuberculosis |
| UHC | Universal Health Coverage |
| UNAIDS | Joint United Nations Programme on HIV/AIDS |
| UNICEF | United Nations Children's Fund |
| VMMC | Voluntary Medical Male Circumcision |
| WHO | World Health Organization |

## ARV drugs

| | |
|---|---|
| 3TC | lamivudine |
| ABC | abacavir |
| ATV | atazanavir |
| AZT | zidovudine |
| COBI | cobicistat |
| d4T | stavudine |
| ddI | didanosine |
| DRV | darunavir |
| DTG | dolutegravir |
| EFV | efavirenz |
| ETV | etravirine |
| EVG | elvitegravir |
| FTC | emtricitabine |
| FPV | fosamprenavir |
| IDV | indinavir |
| LPV/r | lopinavir/ritonavir |
| NVP | nevirapine |
| RAL | raltegravir |
| RIL | rilpivirine |
| RTV | ritonavir |
| SQV | saquinavir |
| TAF | tenofovir alafenamide fumarate |
| TDF | tenofovir disoproxyl fumarate |
| TPV | tipranavir |

# Contents

National Guideline on the use of Antiretroviral Drugs for treating and preventing HIV Infection has four chapters and annex section.

# [i]DEFINITION OF KEY TERMS

- **General**

HIV refers to the human immunodeficiency virus. There are two types of HIV: HIV-1 and HIV-2. HIV-1 is responsible for the vast majority of HIV infections globally.

Acute infection is the period between a person being infected with HIV and HIV antibodies being detectable by a serological assay.

- **Age groups and populations**

The following definitions for adults, adolescents, children and infants are used in these guidelines for the purpose of implementing recommendations for specific age groups. It is acknowledged that countries may have other definitions under national laws:

- An adult is a person older than 19 years of age.
- An adolescent is a person 10–19 years of age inclusive.
- A child is a person 1 to younger than 10 years of age.
- An infant is a child younger than 1 year of age.

**Key populations** are groups that have a high risk and disproportionate burden of HIV in all epidemic settings. They frequently face legal and social challenges that increase their vulnerability to HIV, including barriers to accessing HIV prevention, treatment and other health and social services. Key populations include (1) men who have sex with men, (2) people who inject drugs, (3) people in prisons and closed settings, (4) sex workers and (5) transgender people.

**Vulnerable populations** are groups of people that are vulnerable to HIV in certain situations or contexts, such as adolescents (especially adolescent girls in sub-Saharan Africa), orphans, people with disabilities and migrant and mobile workers. They may also face social and legal barriers to accessing HIV prevention and treatment. These populations are not affected by HIV uniformly in all countries and epidemics and may include key populations. Each country should define the specific populations that are vulnerable and key to their epidemic and response, based on the epidemiological and social context.

**Substantial risk** of HIV infection is provisionally defined as an incidence of HIV higher than 3 per 100 person-years in the absence of pre-exposure prophylaxis (PrEP). Individual risk varies within groups at substantial risk of HIV infection depending on individual behaviour and the characteristics of sexual partners. People at substantial riskof HIV infection are present in most countries, including some (but not all) people identified with key and vulnerable populations and some people not so identified.

**Serodiscordant couples** are couples in which one partner is living with HIV and the other is HIV non-reactive. A couple refers to two people in an ongoing sexual relationship; each of these people is referred to as a partner in the relationship. How individuals define their relationships will vary according to their cultural and social context.

### ❖ Antiretroviral therapy

**ARV** (antiretroviral) drugs refer to the medicines used to treat HIV.

**ART** (antiretroviral therapy) refers to the use of a combination of three or more ARV drugs for treating HIV infection. ART involves lifelong treatment. Synonyms are combination ART and highly active ART.

**Use of ARV drugs for HIV prevention** refers to the HIV prevention benefits of ARV drugs and includes ARV drugs for preventing the mother-to-child transmission (PMTCT) of HIV, ARV drugs to reduce the transmission of HIV to serodiscordant sexual partners and ARV drugs to prevent the acquisition of HIV when a person is exposed (post-exposure prophylaxis (PEP) and PrEP).

**Viral suppression** refers to a viral load below the detection threshold using viral assays.

**Viral failure** refers to the inability to achieve or maintain viral suppression below a certain threshold. Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/mL (two consecutive viral load measurements within a 3-month interval with adherence support between measurements) after at least 6 months of using ART.

**Universal access to ART** is defined broadly as a high level of treatment coverage (80% or more of the eligible population) that is accessible and affordable. It does not necessarily mean 100% coverage.

**Prevention of mother-to-child transmission of HIV** refers to the use of ARV drugs to prevent the transmission of HIV from the mother during pregnancy and breastfeeding. Previous WHO guidelines have used the terms “options A, B and B+” to refer to different approaches to the prevention of the mother-to-child transmission of HIV.

**Drug interaction** is a condition where two drugs administered at the same time affects the effects of the other drug; either drug effect is decreased (antagonistic effect) leading to therapeutic failure or increased drug effect (synergistic effect) causing toxicity.

**Drug toxicity** is the accumulation of a drug substance in the patient’s blood stream leading to adverse effects in the body.

### ❖ HIV testing and prevention

**Combination prevention** refers to a combination of behavioural, biomedical and structural approaches to HIV prevention to achieve maximum impact on reducing HIV transmission and acquisition.

**Early infant diagnosis** is the testing of infants to determine their HIV status following possible exposure to HIV during pregnancy, delivery and postpartum through breastfeeding.

**Point-of-care testing** is conducted at or near the site at which care is being provided. The test results are usually returned rapidly so that clinical decisions can be made in a timely and cost-effective manner.

**PEP of HIV** is the use of ARV drugs by people who are not infected with HIV but who may have been exposed to HIV to block HIV infection.

**(PrEP): Oral PrEP of HIV** is the use of ARV drugs by people who are not infected with HIV to block the acquisition of HIV.

**Rapid diagnostic test**: in vitro immune-chromatographic or immune-filtration diagnostic test for detecting HIV-1 and -2 antibodies and/or HIV p24 antigen.

- **Health workforce**

**Community health workers** are health workers who have received standardized and nationally endorsed training outside the nursing, midwifery or medical curricula.

**Lay provider** is any person who performs functions related to health-care delivery and has been trained to deliver specific services but has not received a formal professional or paraprofessional certificate or tertiary degree.

**Midwives** are health workers who have successfully completed a midwifery education programme recognized in the country in which the programme is located. This includes registered midwives, community midwives and nurse-midwives.

**Non-physician clinicians** are professional health workers capable of many of the diagnostic and clinical functions of a physician but who are not trained as physicians. These types of health workers are often known as health officers, clinical officers, physician assistants, nurse practitioners or nurse clinicians and are an important cadre for HIV care and treatment in some countries.

**Nurses** are people who have been authorized to practice as a nurse or trained in basic nursing skills. This includes registered nurses, clinical nurse specialists, licensed nurses, auxiliary nurses, dental nurses and primary care nurses.

**Task shifting** and **task sharing** are the rational redistribution of tasks between cadres of health workers with longer training and other cadres with shorter training, such as lay providers.

- **Service delivery**

**Adherence** is the extent to which a person's behaviour – taking medication, following a diet and/or changing lifestyle – corresponds with agreed recommendations from a health worker.

**Continuum of HIV care** refers to a comprehensive package of HIV testing, prevention, treatment and care services provided for people at risk of acquiring HIV and people living with HIV and their families. Examples of these services include combination HIV prevention, including PrEP; HIV testing and linkage to care; managing opportunistic infections and other comorbid conditions; initiating, maintaining and monitoring ART; switching to second-line and third-line ART; and palliative care.

**Dispensing ART** includes dispensing medication to people who are already receiving ART between regular clinic visits and assessing any new signs and symptoms and providing adherence monitoring and support.

**Distribution of ART** is the process of physically transporting ART from one geographical point to another. The following should be distinguished:

- wholesaler distribution: distributing a large quantity of ARV drugs over long distances;
- clinic distribution or refill: selecting, packing and handing over, to specific users or caregivers, ARV drugs that are known to the users and have proven to be the appropriate choice of treatment regimen with the means available; and
- Community distribution: distributing limited quantities of ARV drugs over limited geographical distances destined for specific people who are already receiving ART.

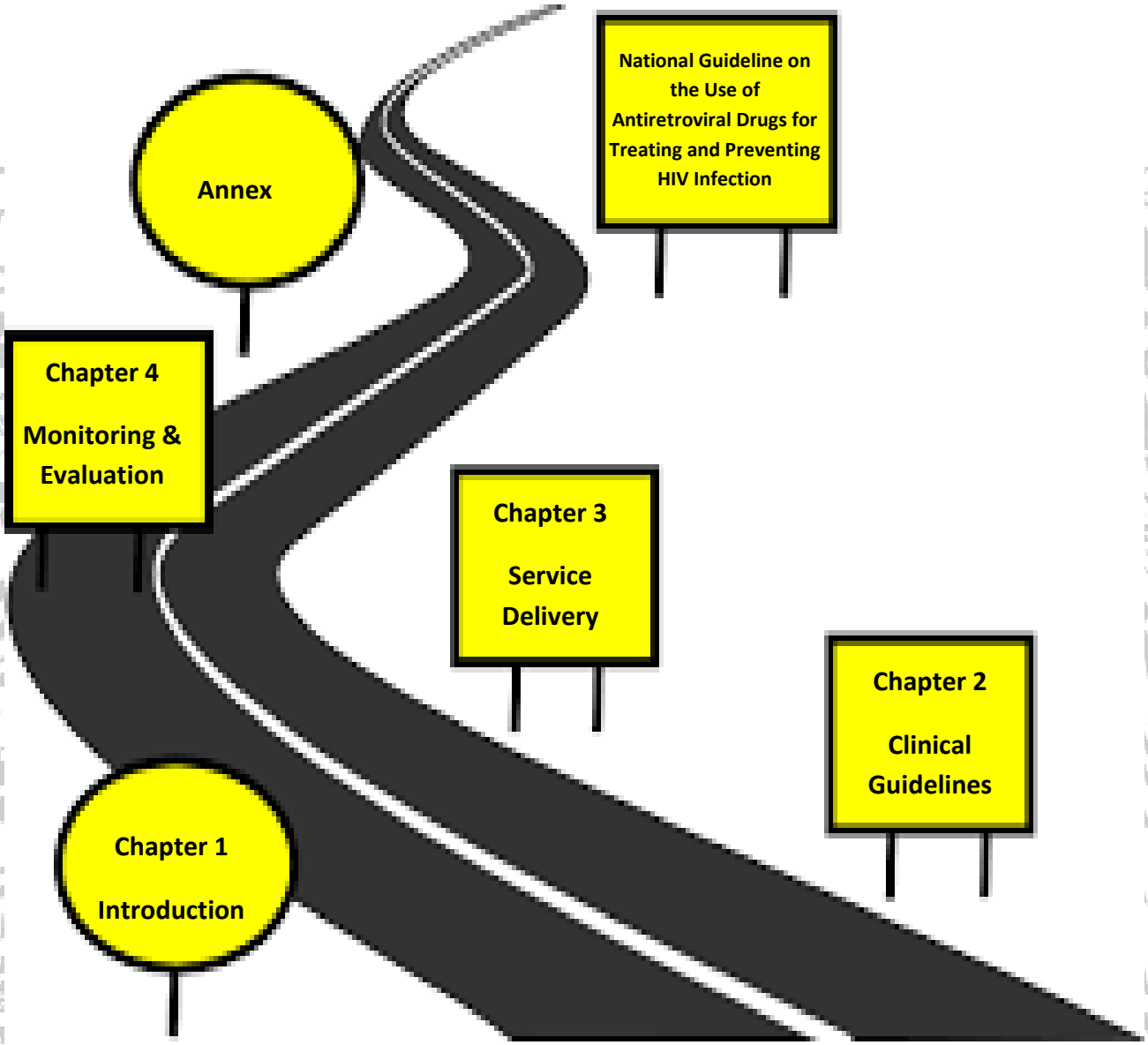
**Integrated health services** are health services that are managed and delivered in a way that ensures that people receive a continuum of health promotion, disease prevention, diagnosis, treatment, disease management, rehabilitation and palliative care services, at the different levels and sites of care within the health system, and according to their needs, throughout their whole life.

**Linkage** is defined as a process of actions and activities that supports people testing for HIV and people diagnosed with HIV in engaging with prevention, treatment and care services as appropriate for their HIV status. For people with HIV, it refers to the period beginning with HIV diagnosis and ending with enrolment in care or treatment.

**Retention** in HIV care means a person living with HIV who is enrolled in HIV care routinely attends these services in accordance with the need. This excludes people who have died or who were lost to follow-up.

**People-centred health services** involve an approach to care that consciously adopts the perspectives of individuals, families and communities and sees them as participants as well as beneficiaries of trusted health systems that respond to their needs and preferences in humane and holistic ways. People-centred care requires that people have the education and support they need to make decisions and participate in their own care. It is organized around the health needs and expectations of people rather than diseases.

**A public health approach** addresses the health needs of a population or the collective health status of the people rather than focusing primarily on managing individual cases. This approach aims to ensure the widest possible access to high-quality services and medicines at the population level, based on simplified and standardized approaches, and to strike a balance between implementing the best-proven standard of care and what is feasible on a large scale in resource-limited settings. For HIV treatment, key elements of a public health approach include: using simplified drug formularies; using fixed-dose combinations on a large scale for first-line treatment for adults, adolescents and children; providing care and drugs free of user charges at the point of service delivery; decentralizing and integrating services, including task shifting; and using simplified approaches to clinical monitoring.


National Guideline on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infection
Annex
Chapter 4
Monitoring & Evaluation
Chapter 3
Service Delivery
Chapter 2
Clinical Guidelines
Chapter 1
Introduction

# CHAPTER 1

# INTRODUCTION

# CHAPTER ONE: INTRODUCTION

## [1]1.1 Background

In Samoa, all living cases of people living with HIV (PLWHIV) are on retroviral therapy (11 individuals). Treatment is managed through the Communicable Disease Clinic located in TTM Hospital, Moto'otua, Apia. Treatment for the 2 cases occurs with private clinicians oversees, where the cases currently reside.

Table 1. ART Profile as of 2017

| ART Demographics | Number | Percent |
|---|---|---|
| **PLWHIV on public ART** | 9 | 81.8 |
| **PLWHIV on private ART treatment** | 2 | 18.8 |
| ***Out of PLWHIV on public treatment…*** | | |
| **Males** | 6 | 62.5 |
| **Females** | 3 | 33.3 |
| **Started ART Same year as diagnosis** | 4 | 44.4 |
| **Had a CD4 test in 2017** | 8 | 88.9 |
| **Healthy CD4 counts (500-1,600)** | 2 | 22.2 |
| **Low CD4 Counts (200-500)** | 4 | 44.4 |
| **Progressed to stage 3 infection (AIDS) <200** | 2 | 22.2 |
| **No CD4 test in 2016** | 1 | 11.1 |
| **Had viral load testing in 2017** | 9 | 100.0 |
| **Have suppressed viral load in 2017** | 6 | 66.7 |

**data from the Global AIDS Monitoring Report for Samoa 2018*

HIV is chronic lifelong infection, with no known cure, and therefore, people living with HIV(PLHIV) have to be followed medically for the rest of their lives. The core component of treatment and care of PLHIV is provision of antiretroviral treatment. Optimal ART increases the length and quality of life of PLHIV, and reduces the onward transmission of the virus. WHO promotes a public health approach to ART, encompassing the rational selection and sequencing of different drug classes into first and second-line regimens; simplified and standardized clinical management; and standardized record

[1]Patient evaluation and antiretroviral treatment for adults and adolescents. Clinical Protocol for the WHO European Region (2012 revision).

keeping in order to preserve therapeutic drug options, minimize adverse drug reactions, maximize patient compliance and thus support the overall goals of providing ART to PLHIV.

The major goals of ART are:

- Clinical: prolongation, preservation and enhanced quality of life;
- Immunological: preservation and improvement (as necessary) of immune function, in order to prevent the onset of opportunistic infections and reduce the risk of AIDS-related cancers;
- Epidemiological: reduction of the risk of onward HIV transmission.

These benefits require achieving the virological goal of a maximum reduction of the viral load for the longest possible time, in order to prevent or delay the development of drug resistance. WHO has produced a series of global guidelines to support ART delivery, which are available on the WHO website. Particular reference is made in this protocol to the guidelines and recommendations for clinical and immunological staging and to the guidelines for ART in adolescents and adults. Medical history, examination findings, exact ART history, laboratory results, findings from other medical procedures and social circumstances need to be documented for the entire treatment period, which may be years or even decades long. Such records are crucial for the individual patient as well as for retrospective analysis. For such purposes, an electronic record-keeping system is advisable, especially at the clinical level. Confidentiality of medical information should be ensured.

Best treatment and care for PLHIV is based on multidisciplinary clinical teams. The core clinical team known in Samoa as the HIV Core Team provides basic medical case-management and consists of a physician (often an infectious disease specialist), a nurse and assistant nurses. Samoa Red Cross Society (SRCS) also provides direct support to PLWHIV, outside of clinical services. Each of the core team members have a distinct role in providing treatment and care as described in the terms of reference (see Annex 1), and their services should be complementary. A network of other specialists and self-help groups should be available to support PLHIV.

[2]WHO first published guidelines on the use of antiretroviral therapy (ART) for HIV infection among adults and adolescents in 2002, and on the use of ARV drugs to prevent mother-to-child HIV transmission in 2004. The 2006 updates of the guidelines introduced the concept of a public health approach, with simplified and harmonized ART regimens. In 2013, for the first time, WHO revised and combined these and other ARV-related guidance documents into consolidated guidelines that address the use of ARV drugs for HIV treatment and prevention across all age groups and

[2] Consolidated Guidelines on the Use of ARV for treating and preventing HIV infections. Second edition. 2016

populations, based on the HIV service continuum. The 2016 edition updates the 2013 consolidated guidelines on the use of antiretroviral drugs following an extensive review of evidence and consultations in mid-2015, shared at the end of 2015, and now published in full in 2016. The **updated consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection recommends that all people living with HIV be provided with antiretroviral therapy (ART).** This will bring one step closer to achieving universal access to HIV treatment and care and ending AIDS as a public health threat. **With the "treat-all" recommendation, all limitations has been removed on eligibility for ART among people living with HIV; all populations and age groups are now eligible for treatment, including pregnant women and children. The same once-per-day combination pill is now recommended for all adults living with HIV, including those with tuberculosis, hepatitis, and other co-infections**. Thus, Ministry of Health of Samoa developed the national ART guideline in 2017 to be consistent with the new WHO recommendations.

## 1.2 Purpose of the guideline and intended audience

This guideline provides guidance on the diagnosis of human immunodeficiency virus (HIV) infection, the use of antiretroviral (ARV) drugs for treating and preventing HIV infection and the care of people living with HIV. It is structured along the continuum of HIV testing, prevention, treatment and care.

The national guideline was developed to provide guidance to the national and provincial programme managers and clinical service providers from the public and private health facilities in Samoa whose normal duties include first-level assessment and treatment of patients and those who work as outreach providers, counsellors or educators at any first-contact health facility. Ensuring standard quality of diagnosis, treatment and care for people living with and affected by HIV. It is also useful to people living with HIV, civil society and community health care workers in order for them to engage meaningfully in the continuum of HIV services. This guideline was adopted from the 2016 WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infections to ensure consistency.

## 1.3 Guiding principles

1. **Anchor on a public health approach**

   Public health approach: addresses the health needs of a population or the collective health status of the people rather than focusing primarily on individual case management. This approach aims to ensure the widest possible access to high-quality services at the population level, based on simplified and standardized approaches, and to strike a balance between implementing the best-proven standard of care and what is feasible on a large scale in resource-limited settings. For HIV, key elements of a public health approach include

simplified drug formularies; large-scale use of fixed-dose combinations; care and drugs provided free of charge at the point of service delivery; decentralization and integration of services, including task shifting; and simplified approaches to clinical monitoring.

2. **Promote the human rights of people living with HIV, key populations at higher risk and other vulnerable female and male populations**

The guideline is based on broad human rights principles reflected in a number of international agreements. This is particularly important in the context of social exclusion of key populations, for whom limited HIV and STI services are available and remain excluded from access to other health related services, or such access is hampered by pervasive stigma, discrimination and criminalization.

Implementation of this guideline will be anchored on setting systems that will allow better access of STI and HIV services by our key populations at higher risk.

3. **Gender equality**

Over the years, the HIV epidemic has helped health systems to recognize that there are differences between sex and age manifestations of diseases and as such delivery of service should recognize these differences. Different populations may require different sets of interventions and different types of services. Comprehensive approaches should include, men, women, girls, boys, as well as, key populations at higher risk such as MSM, transgender people and sex workers.

4. **Operate on continuum of HIV services**

The health system should take into account the need for putting in place continuum or prevention, treatment, care and support services. In addition, it needs to explore most feasible means for integration of STI and HIV prevention, treatment, care and support services and activities into other related health services such as Reproductive Maternal Newborn Child and Adolescent Health (RMNCAH), TB, NCD, Behavioural Health, Mental Health and Hepatitis in order to ensure that total and complete “health for all” is provided.

5. **Achievement of universal health coverage**

Universal health coverage (UHC) means that all people receive the health services they need without suffering financial hardship when paying for them. The full spectrum of essential, quality health services should be covered including health promotion, prevention and treatment, rehabilitation and palliative care.

## 6. A fa'asamoa approach to delivering treatment

The provision of ART to individuals shall take into account the family and community dynamics creating a plan of care for each patient. Emphasis on community based systems of linking people to care and delivering treatment shall be promoted. Protecting the confidentiality and community reputation or standing of the individual within a village setting shall be integral to the plan of care.

# CHAPTER 2

# CLINICAL GUIDELINES

# [ii]CHAPTER TWO: CLINICAL GUIDELINES

## 2.1 HIV Diagnosis

### *2.1.1 The Five C's Principles of HIV Testing Services*

This guideline complements the Samoa National Guidelines on HIV Testing Services (December 2016).

HIV testing is the gateway to HIV prevention, treatment, care and other support services. HIV testing services (HTS) refer to the full range of services that should be provided with HIV testing, including counselling (pre-test information and post-test counselling); linkage to appropriate HIV prevention, treatment and care, and other clinical services; and coordination with laboratory services to support quality assurance (QA) and the delivery of accurate results.

The overarching goals of HTS are as follows:

- to identify people with HIV through the provision of quality testing services for individuals, couples and families;
- to effectively link individuals and their families to HIV treatment, care and support, as well as HIV prevention services, based upon their status; and
- to support the scaling up of high-impact interventions to reduce HIV transmission and HIV-related morbidity and mortality.

The diagnosis of HIV includes testing services in health-care facilities, free-standing sites and a wide range of community-based approaches, as well as HIV self-testing (HIVST). These approaches are described in detail in the 2015 WHO Consolidated guidelines on HIV testing services.

The **WHO Five C's**– consent, confidentiality, counselling, correct test results and connection to care and treatment – are principles that apply to all models of HTS and in all circumstances. The Five C's are as follows:

1) **Consent**: People receiving HTS must give informed consent to be tested and counselled. Verbal consent is sufficient; written consent is not required. They should be informed of the process for HIV testing and counselling and of their right to decline testing.
2) **Confidentiality**: HTS must be confidential, meaning that what the HTS provider and the client discuss will not be disclosed to anyone else without the expressed consent of the person being tested. Confidentiality should be respected, but it should not be allowed to reinforce secrecy, stigma or shame. Shared confidentiality with a partner, family members, trusted other and a health-care provider is often highly beneficial.
3) **Counselling**: Pre-test information can be provided in a group setting, but all people should have the opportunity to ask questions in a private setting if they request it. All HIV testing must be accompanied by appropriate and high-quality post-test counselling, based on the HIV test result

and HIV status reported. QA mechanisms as well as supportive supervision and mentoring systems should be in place to ensure the provision of high-quality counselling.

4) **Correct**: Providers of HIV testing should strive to provide high-quality testing services. Quality management systems (including QA) should be in place for all HTS, regardless of where testing takes place, to ensure that people receive a correct diagnosis. QA should include both internal and external measures, and should receive support from the national reference laboratory. All people who receive a positive HIV diagnosis should be retested to verify their diagnosis before initiation of HIV care or treatment.

5) **Connection**: Linkage to prevention, treatment and care services should include effective and appropriate follow-up, including long-term prevention and treatment support.

**What to do?**

Once **diagnosis is confirmed (whether positive or negative HIV status)** it is important to **ensure linkage** to prevention, treatment and care services.

**REFER** to Fig.1 Continuum of linkage to care and prevention below.

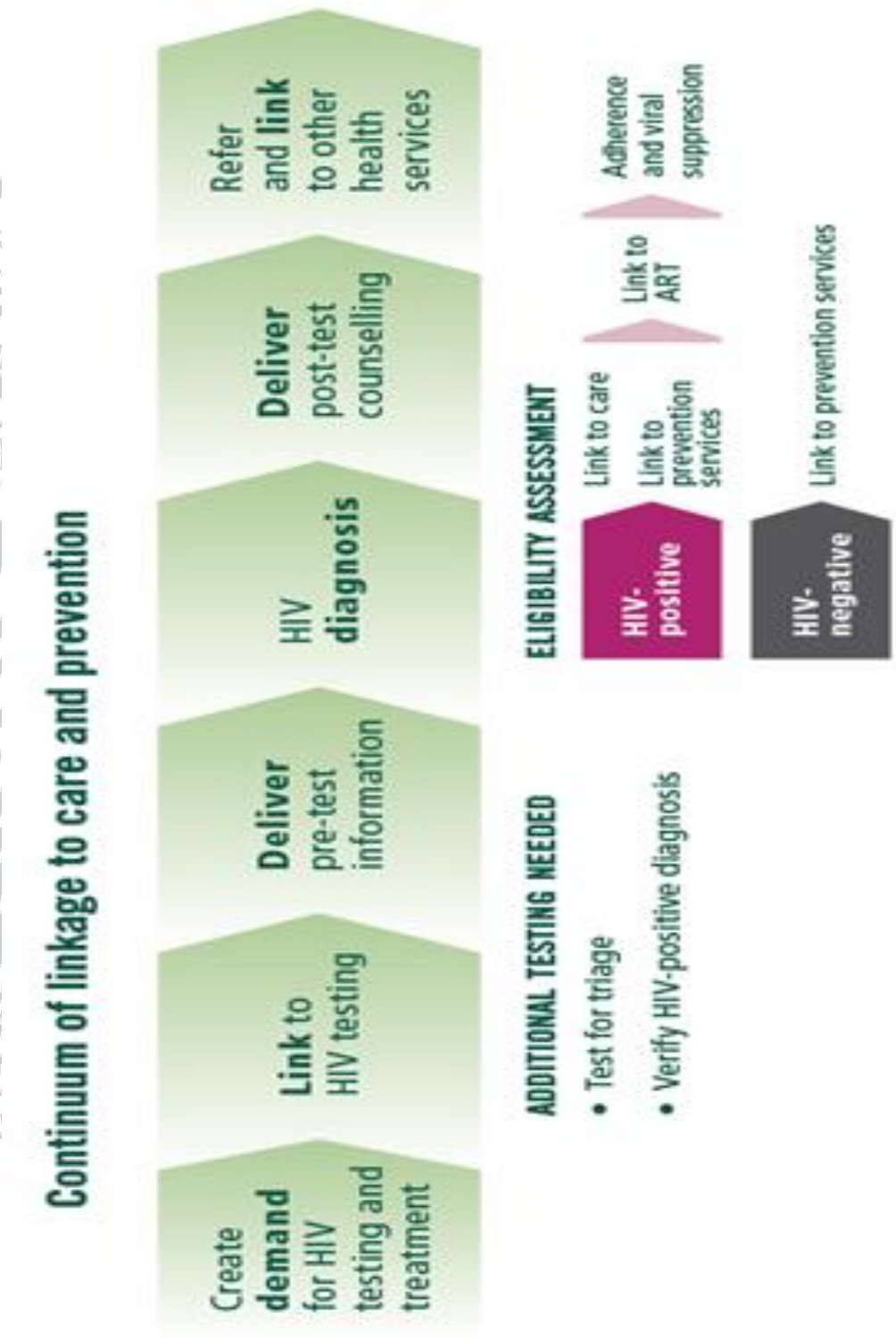
**REMINDER: All HTS should be provided using a validated national testing algorithm**. Based on the HIV prevalence of the population being tested, the WHO-recommended testing strategy for low prevalence will be utilized for Samoa (Refer to **2016 National Guideline on HIV Testing Services, Samoa**).

**For information:** Refer to Annex 2a for the WHO-recommended testing **strategy** for low prevalence countries.

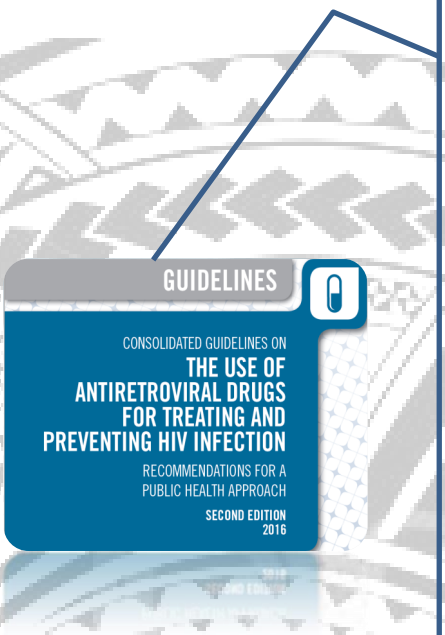
**What to do? USE** the New Validated Testing **Algorithm** for the Pacific Island Countries and Areas (PICs). Refer to **Annex 2b**.

## What to do?

***Fig 1: Continuum of linkage to care and prevention***



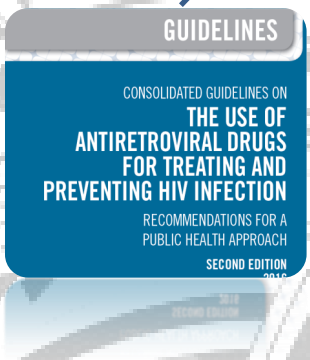
### 2.1.2 HIV diagnosis in infants and children




*Based on the WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd edition; page 28:*

**Mortality in the first year of life is very high among untreated HIV-infected infants**, early HIV testing, prompt return of results and rapid initiations of treatment are essential. In this population**, HIV infection can be definitively confirmed only with virological testing using nucleic acid testing (NAT) technologies**. This is because transplacentally transmitted **maternal HIV antibody may persist in the child up to 18 months of age**, preventing the use of serological testing to diagnose HIV infection. Access to early infant diagnosis (EID) has improved significantly in recent years, but only 50% of all HIV-exposed infants were tested by the second month of age in 2014. For infants who are tested, delays in obtaining results and further losses in the testing-to-treatment cascade still occur, so that only 30% of perinatally infected infants are effectively linked to services and started on ART in a timely manner. Innovative approaches such as **the use of assays at point of care and adding a NAT at or around birth (0–2 days) can improve rapid identification and treatment initiation in infants**.

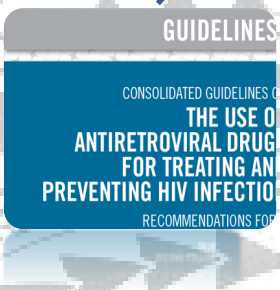
While EID is critical for minimizing early mortality, other opportunities for testing are also essential to capture HIV-infected infants and children who are infected postnatally or who were missed by EID services. In **children older than 18 months of age, serological testing is used in the same manner as in adults following the nationally validated testing algorithm**. As voluntary counselling and testing services are poorly utilized in paediatric populations, **provider-initiated testing is essential to improve identification of children with HIV, especially those who are born to mothers who have not received interventions for PMTCT.**




# What to do?

## RECOMMENDATION

- It is strongly recommended that HIV serological assays used for the purpose of clinical diagnostic testing have a minimum sensitivity of 99% and specificity of 98% under quality-assured laboratory conditions (strong recommendation, moderate-quality evidence).
- It is strongly recommended that **HIV virological assays used for the purpose of clinical diagnostic testing (usually at or after 6 weeks of age) have a sensitivity of at least 95% and ideally more than 98%, and specificity of 98% or more under quality-assured, standardized and validated laboratory conditions** (strong recommendation, moderate-quality evidence).
- It is strongly recommended that **HIV virological testing be used to diagnose HIV infection in infants and children below 18 months of age** (strong recommendation, high-quality evidence).
- In **infants and children undergoing virological testing**, the following assays (and respective specimen types) are strongly recommended for use: **HIV DNA on whole blood specimen or DBS; HIV RNA on plasma or DBS; Us p24Ag on plasma or DBS** (strong recommendation, high-quality evidence).
- It is strongly recommended that **all HIV-exposed infants have HIV virological testing at 4–6 weeks of age or at the earliest opportunity thereafter** (strong recommendation, high-quality evidence).
- In infants with **an initial positive virological test result, it is strongly recommended that ART be started without delay and, at the same time, a second specimen be collected to confirm the initial positive virological test result. Do not delay ART. Immediate initiation of ART saves lives and should not be delayed while waiting for the results of the confirmatory test** (strong recommendation, high-quality evidence).



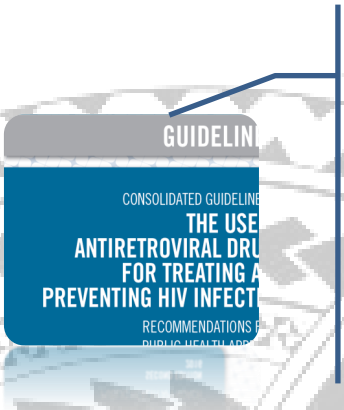

# What to do?

## RECOMMENDATION

- It is strongly recommended that **test results from virological testing in infants be returned to the clinic and child/mother/caregiver as soon as possible, but at the very latest within 4 weeks of specimen collection. Positive test results should be fast-tracked to the mother–baby pair as soon as possible to enable prompt initiation of ART** (strong recommendation, high-quality evidence).
- It is strongly recommended that **all infants with unknown or uncertain HIV exposure being seen in health-care facilities at or around birth or at the first postnatal visit (usually 4–6 weeks) or other child health visit have their HIV exposure status ascertained** (strong recommendation, high-quality evidence).
- It is strongly recommended that **HIV-exposed infants who are well undergo HIV serological testing at around 9 months of age (or at the time of the last immunization visit). Infants who have reactive serological assays at 9 months should have a virological test to identify HIV infection and the need for ART** (strong recommendation, low-quality evidence).
- It is strongly recommended that infants with signs or symptoms suggestive of HIV infection undergo HIV serological testing and, if positive (reactive), virological testing (strong recommendation, low-quality evidence).
- It is strongly recommended that children (18 months or older) with suspected HIV infection or HIV exposure have HIV serological testing performed according to the standard diagnostic HIV serological testing algorithm used in adults (strong recommendation, high-quality evidence)

### 2.1.2.1 *Timing of virologic testing*

The **optimal timing of virological testing** to diagnose HIV infection in infants is **determined by four factors**: (1) when infection occurs (in utero, intrapartum or postpartum during breastfeeding); (2) the sensitivity and specificity, and predictive values of the assay being used; (3) mortality risk by age; and (4) retention in the testing-to-treatment cascade.

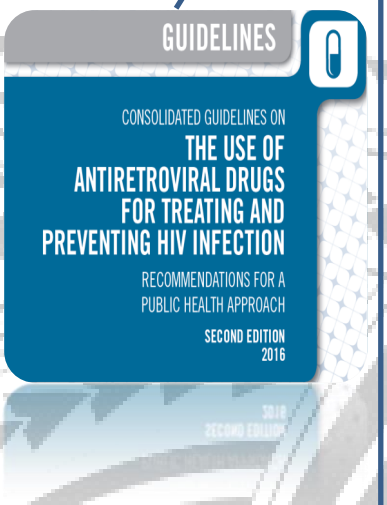



**New recommendation** Based on the WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd edition.

Nucleic acid testing (NAT) at birth to existing early infant diagnosis (EID) testing approaches can be considered to identify HIV infection in HIV-exposed infants (conditional recommendation, low-quality evidence).

- Infants who have HIV detectable by NAT at birth are likely infected in utero, will progress to disease rapidly and, in the absence of treatment, experience high mortality in the first few months of life.
- Infants infected at or around delivery may not have virus detectable by NAT for several days to weeks. The ability of NAT to detect virus in the blood may be affected by ARV drugs taken by the mother or infant for postnatal prophylaxis, resulting in false-negative results. This includes drug that is present in the breast-milk as a result of maternal ART during breastfeeding.
- In addition, as HIV prevalence in the population decreases as a result of effective PMTCT interventions, the proportion of false-positive NAT results increases, underscoring the need to effectively confirm those identified as positive.
- Finally, the ongoing risk of acquiring HIV during breastfeeding can delay final determination of HIV status beyond 18 months.
- For all of these reasons, identifying the optimal timing and frequency of infant testing is very challenging. Existing testing approaches have attempted to enhance programmatic simplicity and maximize uptake of testing by aligning timing of testing with the childhood immunization schedule. However, given the recent cost reduction of assays and the expansion of EID programmes, consideration can now be given to alternative testing approaches that maximize

uptake, retention and timely treatment initiation while responding to changing epidemic and transmission dynamics.




**Implementation consideration**

In light of the risks, benefits, possible acceptability and potential cost–effectiveness, the addition of NAT at or around birth (0–2 days) can be considered where feasible, but only in parallel with efforts to strengthen and expand existing EID testing approaches.

**What to do?**

**Existing recommendations that infants with an initial positive virological test result should start ART without delay remain important.**

**At the same time, a second specimen should be collected to confirm the initial positive virological test result.**

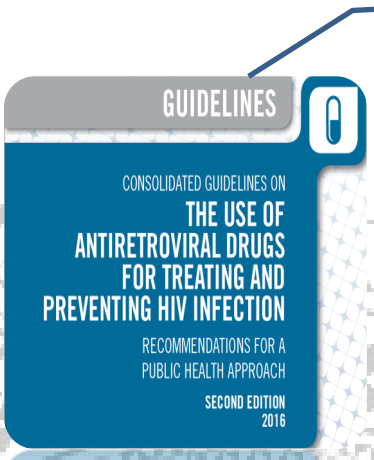
**Immediate initiation of ART saves lives and should not be delayed pending the results of the confirmatory test.**

*In Samoa, confirmatory testing can be processed quickly (within 2-3 days from specimen collection to result notification). Therefore, ART initiation in infants can rely on confirmatory testing. Procurement of ART in the pacific region is difficult, can have long processing windows, and may require confirmatory testing when involving development organizations.*

### *2.1.2.2 Point-of-care technologies for the diagnosis of HIV infection in infants and children*

Based on the WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd edition.

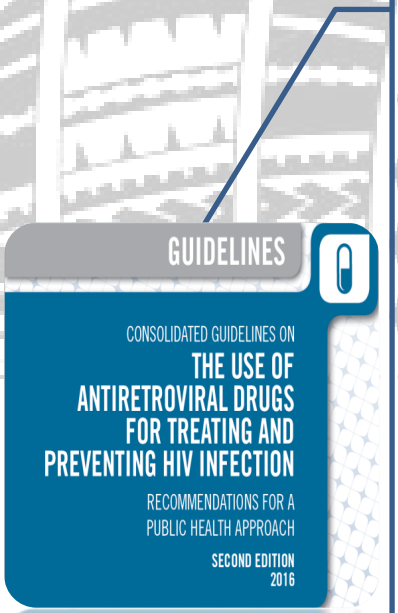
### *2.1.2.3 Point-of-care early infant diagnosis*




**New recommendation**

**Nucleic acid testing (NAT)** technologies that are developed and validated for use at or near to the point of care **can be used for early infant HIV testing** (conditional recommendation, low quality evidence).

### *2.1.2.4 Rapid diagnostic tests for HIV serology*




**New recommendations**

Rapid diagnostic tests (RDTs) for HIV serology can be used to assess HIV exposure only in infants **less than 4 months** of age. HIV-exposure status in infants and children **4–18 months** of age should be ascertained by undertaking HIV serological testing in the mother (conditional recommendation, low-quality evidence).

Rapid diagnostic tests for HIV serology can be used at **9 months** to rule out HIV infection in asymptomatic HIV-exposed infants (conditional recommendation, low-quality evidence).

Rapid diagnostic tests for HIV serology can be used to diagnose HIV infection in children **older than 18 months** following the national testing strategy (strong recommendation, moderate-quality evidence).

## What to do?

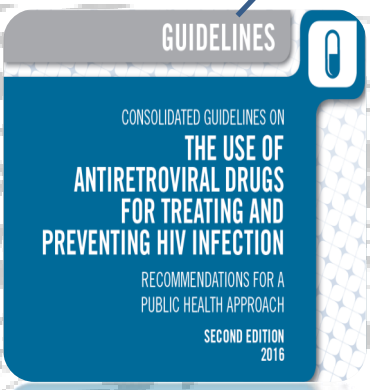
***Table 6 Use of RDT for HIV serology based on age, exposure status and breastfeeding practice***

| Age group | Known HIV exposed | Unknown HIV exposure status and breastfeeding | Unknown HIV exposure status and not breastfeeding[a] |
|---|---|---|---|
| 0–4 months | Not useful, as exposure is known and RDT cannot determine infection status | **Test mother**<br>If mother is not available, RDT in the child can reliably assess exposure. | **Test mother**<br>If mother is not available, RDT in the child reliably determines exposure. |
| 5–8 months | Not useful, as exposure is known and RDT cannot determine infection status at this age | **Test mother**<br>If mother is not available, a positive RDT establishes exposure, but a negative RDT does not fully rule it out. Infants with positive RDT will still need NAT to confirm infection.<br>Infants with negative RDT who are still breastfeeding will need NAT at the end of breastfeeding.<br>If sick and mother is not available, perform NAT directly to assess HIV infection status. | **Test mother**<br>If mother is not available, RDT for the child does not fully rule out exposure.<br>If sick and mother is not available, perform NAT directly to assess HIV infection status. |
| 9–18 months | RDT useful to rule out established HIV infection<br>Infants with *positive* RDT will still need NAT to confirm infection.<br>Infants with *negative* RDT who are still breastfeeding will need NAT at the end of breastfeeding. | **Test mother**<br>If mother is not available, a positive RDT establishes exposure, but a negative RDT does not fully rule it out. Infants with positive RDT will still need NAT to confirm infection.<br>RDT useful to rule out established HIV infection.<br>Infants with positive RDT will still need NAT to confirm infection.<br>Infants with negative RDT who are still breastfeeding will need NAT at the end of breastfeeding.<br>If sick and mother is not available, perform NAT directly to assess HIV infection status.[b] | **Test mother**<br>If mother is not available, RDT in the child does not fully rule out exposure.<br>RDT is useful to rule out established HIV infection.<br>• Infants with positive RDT will still need NAT to confirm infection.<br>• Infants with negative RDT who are not breastfeeding can be considered uninfected.<br>If sick and mother is not available, perform NAT directly to assess HIV infection status. |
| >18 months | Serological testing (including RDT) is recommended to assess HIV infection status unless still breastfed.<br>If still breastfed, serological testing (including RDT) should be provided 3 months after cessation of breastfeeding. | | |

[a] Not breastfed for at least 12 weeks before testing.

[b] Consider initiating ART for presumed HIV infection if there is high degree of suspicion while waiting for NAT results, especially if RDT positive.

### *2.1.2.5 Provider-initiated HIV testing and counselling for infants and children*




**New recommendation** Based on the WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd edition:

- In generalized epidemic settings, infants and children with unknown HIV status who are admitted for inpatient care or attending malnutrition clinics should be routinely tested for HIV (strong recommendation, low-quality evidence).
- In generalized epidemic settings, infants and children with unknown HIV status should be offered HIV testing in outpatient or immunization clinics (conditional recommendation, low-quality evidence.

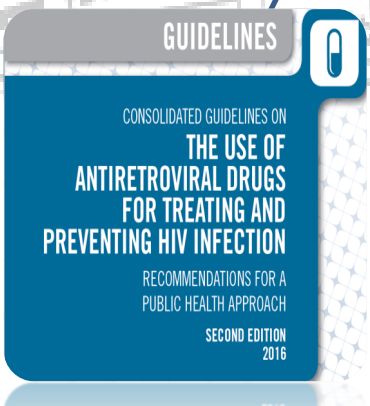
**What to do?**

**In all settings, children with a parent living with HIV should be routinely offered HIV testing and, if found to be either infected or at high risk of infection through breastfeeding, should be linked to services for treatment or prevention**.

**Testing strategy for early infant diagnosis refer to Annex 2c**

## 2.1.3 HIV diagnosis in other priority populations

❖ **Adolescents**




## What to do?

**Recommendations**

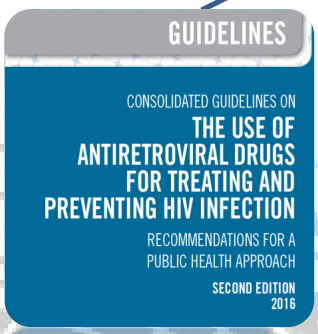
- HIV testing services, with linkages to prevention, treatment and care, should be offered for adolescents from key populations in all settings (strong recommendation, very low-quality evidence).
- Adolescents with HIV should be counselled about the potential benefits and risks of disclosure of their HIV status, and empowered and supported to determine if, when, how and to whom to disclose (conditional recommendation, very low-quality evidence).

 *Due to high social stigma, other methods of family support should be explored, as disclosure could be potentially dangerous for the individual.*

**Concentrated HIV epidemic**

- HIV testing services with linkage to prevention, treatment and care should be accessible to adolescents in low-level and concentrated epidemics (conditional recommendation, very low-quality evidence).

❖ **Pregnant Women**




## What to do?

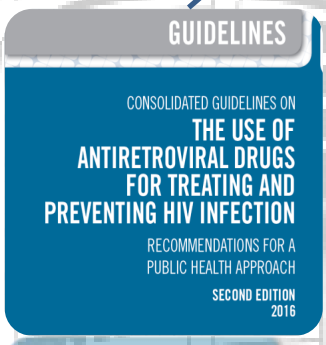
**Recommendation**

**Low-prevalence settings**

PITC can be considered for pregnant women in antenatal care as a key component of the effort:

- ✓ to eliminate mother-to-child transmission of HIV
- ✓ to integrate HIV testing with other key testing (for viral hepatitis, syphilis etc.) as relevant to the setting
- ✓ to retest HIV negative pregnant women who are in a serodiscordant couple, from a key population group or have known ongoing HIV risk.

❖ **Couples and partners**

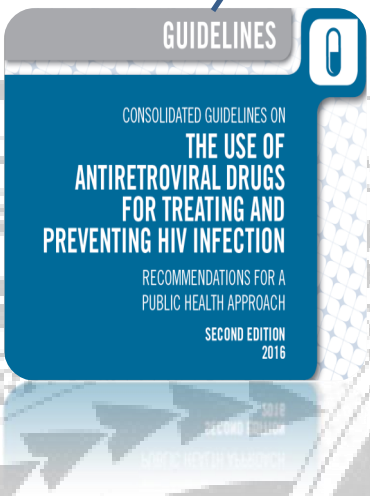



## What to do?

**Recommendation**

- Couples and partners should be offered voluntary HIV testing services with support for mutual disclosure. This applies also to couples and partners from key populations (strong recommendation, low-quality evidence).
- In antenatal care settings, couples and partners should be offered voluntary HIV testing services with support for mutual disclosure (strong recommendation, low-quality evidence).
- HIV testing services for couples and partners, with support for mutual disclosure, should be offered to individuals with known HIV status and their partners (strong recommendation, low-quality evidence for all people with HIV in all epidemic settings; conditional recommendation, low-quality evidence for HIV-negative people depending on the country-specific HIV prevalence).

❖ **Key populations**




## What to do?

**Recommendation**

- HIV testing services should be **routinely offered to all key populations in the community, in closed settings such as prisons and in facility-based settings**.
- Community-based HIV testing services for key populations linked to prevention, treatment and care services are recommended, in addition to routine facility-based
- HIV testing services, in all settings (strong recommendation, low-quality evidence).

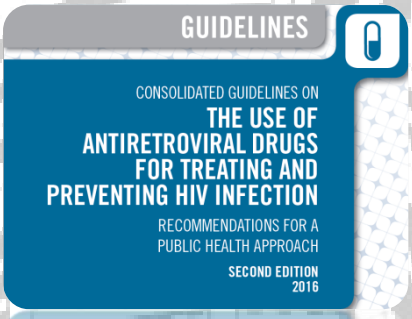
*Key population outreach can be integrated in general population services to protect confidentiality and synergize resources*

In most settings, the incidence of HIV is high in key populations, and they frequently have limited access to HIV services, including testing and ART. They need tailored approaches to and messages for HIV testing. Health-care workers should receive appropriate and recurrent training and sensitization to ensure that they have the skills and understanding to provide services for adults and adolescents from key populations. Health-care workers should respect the rights of all people to health, confidentiality and non-discrimination. Links with key population networks and community-based organizations to support or provide HTS – including services delivered by peers – may increase reach, uptake and acceptability of HTS in these populations.

### 2.1.4 Retesting prior to enrolment in care

WHO reminds national programmes to **retest** all newly diagnosed people with HIV.

*WHO information note – 22 October 2014. Geneva: World Health Organization; 2014 (http://www.who.int/hiv/pub/vct/retest-newly-diagnosed-plhiv-full/en/)*




## What to do?

**RECOMMENDATION**

**Retest all clients diagnosed HIV-positive with a second specimen** and a second operator **using the same testing strategy and algorithm** before enrolling the client in care and/or initiating ART, regardless of whether or not ART initiation depends on CD4 count.

**Retesting people on ART is not recommended**, as there are potential risks of incorrect diagnosis, particularly for in vitro diagnostics (IVDs) that use oral fluid specimens.

It is a priority to retest all people who are diagnosed to be HIV reactive prior to enrolment in HIV care and/or treatment in order to verify their serostatus. Failure to do this may lead, in rare cases, to people being diagnosed incorrectly, with potentially serious adverse long-term consequences.

Retesting a person diagnosed to be HIV reactive to verify the diagnosis should include:

- Retesting of a new specimen for each newly diagnosed individual, preferably conducted by a different provider using the same testing algorithm, prior to initiation of ART; and
- Retesting is preferably conducted at a different site, ideally the site where the decision about ART initiation will be made.

Retesting is aimed to rule out possible technical or clerical errors, including specimen mix-up through mislabeling and transcription errors, as well as random error either by the provider or the test device. While retesting will not exclude misdiagnosis related to poor choice of a testing algorithm, this risk should be minimal with adequate validation of the testing algorithm.

Certain testing services, such as prevention of mother-to-child transmission (PMTCT) services providing ART for all pregnant and postpartum women living with HIV, are programmatically organized to conduct HIV testing, provide a diagnosis and offer immediate initiation of ART. In these programmes, it may not always be feasible to retest at a different site, although it should usually be feasible for a different provider to conduct retesting on a new specimen. If the HIV status is the same upon retesting, the person's HIV-reactive status should be considered verified. If the status is not the same upon retesting, the person or their specimen should be referred for additional testing at a higher-level facility. Specific guidance on retesting in such settings can be found in the annex of the WHO Consolidated guidelines on HIV testing services and technical guidance update on quality assurance for HIV rapid diagnostic tests.[3]

Retesting people on ART is not recommended, as there are potential risks of incorrect diagnosis. The effect of ART in suppressing viral replication may extend to suppression of the immune response and therefore of antibody production. Once a person is started on ART, low antibody titres – particularly if oral fluid-based rapid diagnostic tests are used – make it challenging to discern whether an individual is indeed HIV reactive

People undergoing HIV testing must be made aware of the risk of incorrect diagnosis if they do not disclose that they are on ART. All people receiving HIV testing should be asked if they have been tested previously and told that they are HIV infected and/or if they are now on ART or have ever received ART. The WHO has published a meeting report on misdiagnosis[4]

[3](http://apps.who.int/iris/bitstream/10665/181244/1/WHO_HIV_2015.28_eng.pdf?ua=1&ua=1).
[4](http://www.who.int/hiv/pub/meetingreports/hiv-misdiagnosis-report/en).

### 2.1.5 Pre- and post-test services

Initiatives should be put in place to enforce privacy, protection and institute policy, laws and norms that prevent discrimination and promote the rights of people living with HIV. This can help create environments where disclosure of HIV status is easier.

**What to do?**

**Pre-test information sessions** for people receiving HIV testing should include clear information about:

- The benefits of HIV testing;
- The meaning of an HIV-reactive and an HIV-non-reactive test;
- The services available in the case of an HIV-reactive diagnosis, including where ART is provided;
- A brief description of prevention options and encouragement of partner testing;
- The fact that the test result and any information shared by the client are confidential;
- The fact that the client has the right to refuse to be tested;
- Potential risks to the client, especially for those whose sexual or other behaviour is stigmatized;
- Opportunities for mutual disclosure;
- Opportunity to ask the provider additional questions; and
- Provision of informed consent for testing.

**Post-test information and counselling** for **people who test HIV non-reactive** should include the following:

- An explanation of the test result;
- Information on methods to prevent hiv acquisition and provision of male and/or female condoms, lubricant and guidance on their use;
- Emphasis on the importance of knowing the status of sexual partners and information about the availability of partner and couples testing services;

- Referral And Linkage To Relevant HIV Prevention Services, Such As Post-Exposure Prophylaxis, Pre-Exposure Prophylaxis And, In Priority Countries, Voluntary Medical Male Circumcision (VMMC);
- Advice To People Who Test Negative But Report Recent Risky Behaviour To Return In 4 Weeks For Repeat Testing; If They Again Test HIV Non-Reactive After 4 Weeks, People With Ongoing Risk Should Be Advised To Return For Testing Every 6–12 Months;
- Encouragement Of Partner Testing When Pregnant Women Test HIV Non-Reactive In High-Prevalence Settings, As Incident HIV In Pregnancy And During The Postpartum Period Is Associated With A High Risk Of Mother-To-Child Transmission; And
- No Requirement For Repeat Testing (Window Period) For People Who Report No Recent Risk.

**Post-test information and counselling** for people **who test HIV reactive** should include the following:

- An explanation of the test result and diagnosis, giving the client time to consider the result and helping the client to cope with emotions arising from the diagnosis;
- Discussion of immediate concerns and help for the client to decide who in his or her social network may be available to provide immediate support;
- Assessment of the risk of intimate partner violence and discussion of possible steps to ensure the client's physical safety;
- Assessment of the risk of suicide, depression and other mental health consequences of an HIV-reactive diagnosis and referral to relevant services;
- Clear information on art and its benefits for maintaining health and reducing the risk of HIV transmission, as well as where and how to access art;
- Arranging a specific date and time for active referral and follow-up of clients who are unable to enrol in HIV care on the day of diagnosis;
- Information on how to prevent transmission of HIV, including information on the reduced transmission risks when virally suppressed on art;
- Provision of male or female condoms and lubricants and guidance on their use;
- Discussion of the risks and benefits of disclosure, particularly among couples and to partners, and couples counselling should be offered to support mutual disclosure;
- Encouragement for mutual disclosure and offer of hiv testing for sexual partners, children and other family members, which can be done individually, through couples testing, index case testing, family testing or partner notification;
- Provision of or referral to prevention, counselling, support and other services as appropriate, including screening and treatment for tuberculosis (TB) and sexually transmitted infections

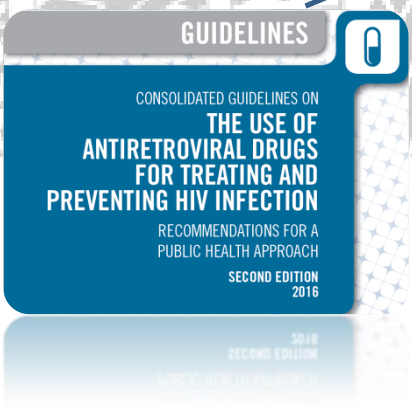
(STIs), prophylaxis for opportunistic infections, contraception, antenatal care, opioid substitution therapy, and access to sterile needles and syringes; and

- Offering time for the client to ask additional questions.

## What to do?

In addition to the information described above, counselling for **pregnant women** whose **test result is HIV reactive** should include the following:

- discussion of childbirth plans and encouragement to deliver in a health facility for personal well-being and to ensure access to services for PMTCT;
- use of ARV drugs both for the client's health and to prevent transmission to the infant;
- the importance of partner testing and information on the availability of couples testing
- services;
- ensuring screening for TB and testing for other infections, such as syphilis and hepatitis B;
- counselling on maternal nutrition, including iron and folic acid, advice on infant-feeding options and support to carry out the mother's infant-feeding choice; and
- HIV testing for the infant and necessary follow up for HIV-exposed infants.




**NOTE:**

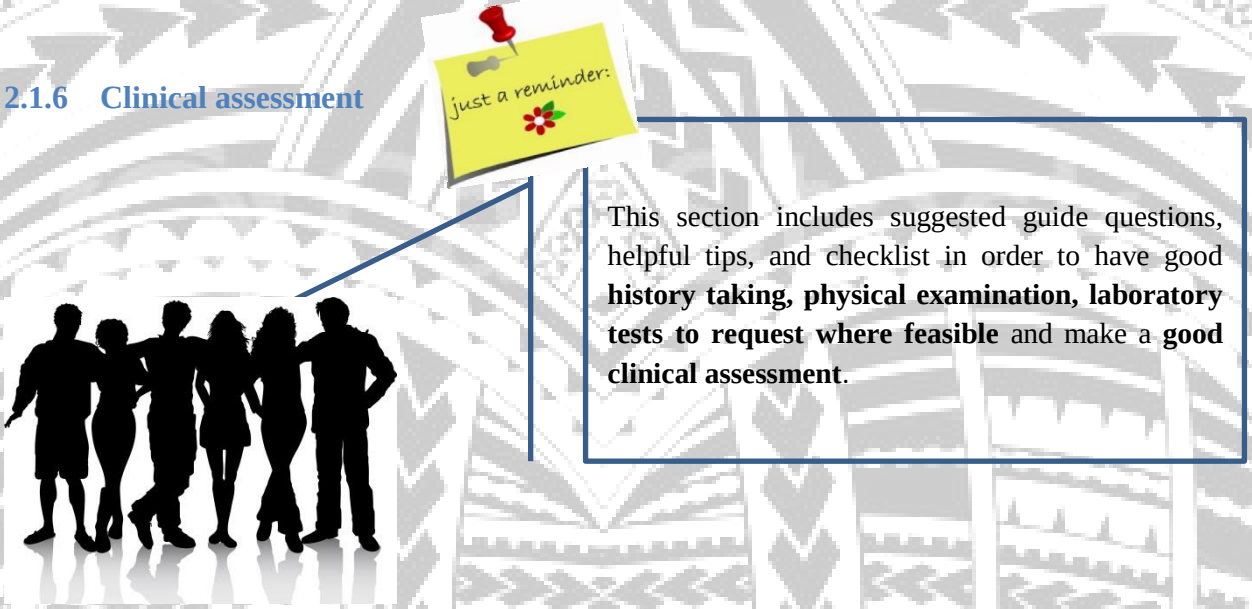
An **inconclusive test result** means that the first reactive test results were not confirmed after additional testing or that the first two test results are reactive but the third assay is non-reactive. All people with an inconclusive status should be encouraged to return in 14 days for additional testing. Inconclusive results may be confusing and stressful for the individual or couple and may be difficult for the provider to explain. Most inconclusive results can be resolved by retesting after 14 days.

Intensified post-test counselling combined with follow-up counselling by certified and registered community health workers may be needed for **key populations who test HIV reactive**. Some people from key populations may lack social networks and/or a supportive family to help them deal with their diagnosis, and additional counselling and peer support may be needed.

In addition to standard messages for all people diagnosed with HIV, post-test counselling for **adolescents whose test result is HIV reactive** should include the following:

- tailored advice with linkage to HIV care and treatment;
- counselling, referral and linkage to specific psychosocial and mental health services tailored to both the situation in which infection happened and the developmental age of the individual;
- information on adolescent rights and responsibilities, especially the right to confidentiality;
- counselling, referral and linkage to specific sexual and reproductive health services, including contraception, and an opportunity to ask questions and discuss issues related to sexuality;
- individualized planning on how, when and to whom to disclose the HIV status; and
- referral for group counselling and peer support groups.

### 2.1.6 Clinical assessment




This section includes suggested guide questions, helpful tips, and checklist in order to have good **history taking, physical examination, laboratory tests to request where feasible** and make a **good clinical assessment**.

### 2.1.6.1 STEP 1 - History taking

## What to do?

A good clinical assessment relies on a **good history taking**.

This needs to take into account the following:

**#1 Setting**

- The layout of the consulting room can assist and facilitate establishing rapport with patients.
- Avoid having obstacles between attending service provider and the patient.
- Greet patient with a welcoming smile. Take care with the opening greeting, as this can set the scene for what follows. It may assist or inhibit rapport.
- Generally, it helps to be warm and welcoming so as to put the patient at ease.
- Good eye contact, shaking hands with the patient and showing an active interest in the patient should help to establish trust and encourage honest and open communication.
- Take care not to let the computer intrude on the consultation. This can be difficult when there is useful information available on a screen. Make use of the time before and after consultations to obtain information from the computer.

**#2 Listening skills**

- Be genuinely interested and attentive to what the patient is saying. Give the patient a chance to tell you their pre-constructed narrative, rather than diving in with a series of questions to delineate detail.

**#3 Type of questions**

- Use open questions to allow patients to express what is on their mind. It is important not to suggest or prompt what is the right or expected answer.
- Questions with multiple answers should be used with care. This technique may lead to danger of getting the answer you wanted rather than what the patient meant.
- Leading questions should be avoided. They tend to lead the patient down an avenue that is framed by your own assumptions.

**#4 Summarizing**

- After taking the history, it's useful to give the patient a run-down of what they've told you as you understand it.
- If there is a nod of approval or expressed agreement with the story then it's fairly certain you're getting what the patient wanted to tell you.
- If not, then you may need to try another approach. This technique can avoid incorrect assumptions by the attending health service provider.

**#5 Sharing understanding**

- It is always a good idea to ask the patient if there is anything they want to ask you at the end of a consultation. This can help you to impart further information if there is something they haven't understood and it can reveal something that has been troubling them that hasn't been touched upon or got to the bottom of. It is an opportunity to confirm that a shared understanding has been reached between attending service provider and patient


*In doing history taking, make sure that you elicit information on the following:*

- ✓ What is the chief or presenting complaint?
- ✓ Get complete history of presenting complaint, including laboratory tests done, treatment and referrals already arranged and provided.
- ✓ Past medical history: significant past diseases/illnesses, surgery, including complications, trauma.
- ✓ Drug history: past, present or currently taking, prescribed and over-the-counter, allergies, adverse reactions
- ✓ Family history: especially parents, siblings and children.
- ✓ Social history: smoking, alcohol, drugs, accommodation and living arrangements, marital status, baseline functioning, occupation, pets and hobbies.
- ✓ Systems review: cardiovascular system, respiratory system, gastrointestinal system, nervous system, musculoskeletal system, genitourinary system.

*In addition,*

- ✓ Try to let patients tell you their story freely.
- ✓ When you use questions, try to keep them as open as possible.
- ✓ Use all your senses to 'listen'.
- ✓ Check that what you think is wrong is what your patient thinks is wrong.
- ✓ Keep an open mind and always ask yourself if you're making assumptions.
- ✓ Be prepared to reconsider the causes of symptoms that you or a colleague has decided upon.

The following **checklist can be used as a guide to elicit key information** from patient who is at risk of HIV infection, or PHLIV initial and succeeding visits.

**Table 1: Sample checklist/guide to elicit key information on risk of HIV infection**

| HIV Testing | HIV Risk |
|---|---|
| Ever tested for HIV in the past?<br>Date and place of first HIV test<br>Reason for the test<br>Documentation of the result<br>Date of any negative HIV test<br>Prior CD4+ cell counts (if available) | Unprotected sexual contact<br>Injection drug use<br>Occupational exposure<br>Perinatal transmission<br>Recipient of blood products<br>Unknown<br>Sex work<br>Partner of the same sex |
| **System Review** | **Past history of HIV-Related Illnesses** |
| Unexplained weight loss<br>Swollen lymph nodes<br>Night sweats and fever<br>Unusual headaches or poor concentration<br>Changes in appetite<br>Skin rashes<br>Sores or white spots in mouth<br>Painful swallowing<br>Chest pain, cough or shortness of breath<br>Stomach pain or Vomiting or Diarrhoea<br>Numbness or tingling in hands or feet<br>Muscle weakness and changes in vision | Oral candidiasis or *Candida* esophagitis<br>Persistent diarrhoea<br>Varicella zoster (shingles)<br>Oral hairy leukoplakia<br>*Pneumocystis jiroveci* pneumonia (PCP)<br>Recurrent bacterial pneumonia<br>Cryptococcal meningitis<br>Toxoplasmosis<br>Kaposi's sarcoma<br>Disseminated *Mycobacterium avium* complex<br>Cytomegalovirus (CMV) infection<br>Tuberculosis<br>Invasive cervical cancer |
| **Tuberculosis History** | **Sexually Transmitted Infections** |
| Last chest X-ray<br>History of past TB<br>Treatment given (drugs and duration)<br>History of exposure to TB<br>BCG and PPD skin test and result | Genital ulcer or other lesion<br>Genital discharge |
| **Gynecologic History** | **General Medical History** |
| Last PAP smear<br>Menstrual irregularities<br>Pelvic pain or discharge | Any other past medical condition such as diabetes, hypertension, cardiovascular diseases, Hepatitis B, Hepatitis C |
| **Pregnancy and Contraception history** | **Vaccination History** |
| Previous preganancies and terminations<br>Living children and HIV status of children<br>Exposure to ARV during pregnancy<br>Drugs and duration of ART<br>Contraception used<br>Last menstrual period | BCG<br>Hepatitis A vaccine<br>Hepatitis B vaccine |
| **Medication** | **Allergies** |
| Past drugs and reasons for taking them<br>Current drugs and reasons for taking them<br>Include traditional remedies | Known allergies to drugs or other substances or materials |

| | |
|---|---|
| Opioid substitution therapy | |
| ART History | Psycho Social History |
| Current and past exposure to ART<br>Which drugs taken and for how long<br>Understanding and readiness to commence<br>ART if never taken | Family history, e.g. other immediate family member with known HIV infection<br>Social history, e.g. marital status, education, occupation, source of income<br>Financial and family support status<br>Disclosure status, readiness to disclose<br>Social relationship within village |
| Substance abuse | Functional status |
| Alcohol, stimulant, opiate and other drug use<br>Smoking history | Able to work, go to school, do housework<br>Ambulatory but not able to work<br>Amount of day to day care needed |

***Source: Myanmar Guidelines for the Clinical Management of HIV Infection in Adults and Adolescents. 2007. Page 12.***

### *2.1.6.2 STEP 2 - Physical Examination*

## What to do?

The **physical examination should document presenting symptoms, signs and reproducible results** so that other attending service providers can assess progress, improvement or worsening of patient's status.

**Table 2: Sample physical examination checklist**

| INITIAL PHYSICAL EXAMINATION |
|---|
| **General appearance:**<br>• height, current and usual weight<br>• body morphology (e.g. lipodystrophy)<br>• overall fitness using standardized scale (e.g. Karnofsky index) |
| **Vital signs:**<br>• blood pressure<br>• temperature<br>• pulse<br>• respiratory rate |
| **Lymph nodes (location of enlargement - if any)** |
| **Skin** (entire body) in particular, assess for:<br>• active or former herpes zoster<br>• liver disease<br>• Kaposi's sarcoma (number of lesions, substance of lesions, lymphatic involvement)<br>• seborrhoeic dermatitis<br>• injection sites in injecting drug users (IDUs) |

| |
|---|
| **Eyes:**<br>• visual impairment<br>• paresis of eye muscle |
| **Oro-pharynx:**<br>• lesion in oral cavity and dental status<br>• signs of:<br>  • oral candidiasis<br>  • oral hairy leukoplakia<br>  • primary syphilis |
| **Thorax and lungs:**<br>• signs and symptoms (respiratory rate, expansion, percussion, auscultation, cough, dyspnoea)<br>• form of thorax<br>• buffalo hump |
| **Breast examination (in female and male PLHIV) to identify tumors** |
| **Cardiac examination** - evidence of ischaemic heart disease (IHD), congestive heart failure or endocarditis (especially in IDUs) |
| **Abdominal examination:**<br>• shape<br>• consistency, size and shape of liver and spleen (enlargement?)<br>• other palpable enlargements<br>• bowel movement<br>• tenderness<br>• rigidity<br>• ascites |
| **Genital and anal region examination for signs of:**<br>• herpes simplex virus infection<br>• syphilis<br>• Human papilloma virus (HPV), (*Condylomata acuminatae,* cervical or anal cancer)<br>• other STIs |
| **Legs** (joint mobility, venous insufficiency, arterial insufficiency, lipoatrophy) |
| **Neurological status** (cognitive function, pareses, also signs of neuropathy) |
| **Mental status** (conscious, answer relevant to questions, disillusional, tardive response) |

### *2.1.6.3 STEP 3 - Laboratory Tests*

## What to do?

**WHO recommends HIV testing and viral load testing as the main pre-requisite to initiate ART.**

*Table 3: Suggested laboratory tests where feasible*

| | LABORATORY TESTING |
|---|---|
| **HIV-related testing** | |
| • HIV serological testing (followed by confirmatory test; a second, separate sample for retesting)<br>• CD4 cell test (absolute count and percentage) - evaluates severity of immunodeficiency (not a prerequisite to initiate ART)<br>• Level of HIV-RNA (copies/mL) in plasma (the viral load [VL]) - reflects level of replication of HIV in the body | |
| **Other infectious disease testing** | |
| **Routine testing:**<br>• test for syphilis<br>• serological tests for hepatitis A, B and C viruses (HAV, HBV and HCV) - i.e. HAV antibodies, hepatitis B virus surface antigen (HBsAg; if positive do HBV-DNA by PCR if available - otherwise HBeAg - and consider delta-antibody screening; if HBsAG negative, do HBs antibodies and if also negative, vaccinate) and HCV antibodies (if positive do HCV-RNA by PCR if available)<br>• toxoplasma immunoglobulin G (IgG) serological test - if negative, provide counselling to avoid infection; if positive and signs of CNS infection, consider toxoplasma encephalitis<br>• CMV immunoglobulin G (IgG) serological test - if negative, provide counselling to avoid infection; if positive and low CD4 cell counts, consider CMV retinitis or gastroenteritis<br>• pap smear for women once annually and consider annual screen for anal cancer in persons engaged in anal sex<br>• if signs of STI: vaginal, urine and anal sampling for gonorrhoea and *Chlamydia trachomatis*<br>• if signs of meningitis/encephalitis and CD4 cell count is < 200/mm: *Cryptococcus* antigen in serum and CSF | |
| **General laboratory testing:** | |
| • complete blood count (leucocyte, lymphocyte and neutrophil and platelet count; erythrocytes, Hb)<br>• liver function - alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatise (elevated levels signify ongoing liver disease, but chronic HCV infection may cause severe liver disease without affecting these enzymes)<br>• bilirubin - sometimes elevated if ongoing liver disease; some ARVs (IDV, STV) also elevate bilirubin (without affecting liver function enzymes) and this does not signify liver damage<br>• renal function - S-creatinine; calculate eGFR (http://www.cphiv.dk/TOOLS/tabid/282/Default.aspx); proteinuria<br>• lactate dehydrogenase (LDH) - general damage/turnover of cells (elevated if lymphomas, several pulmonary infections, myocardial infarcation, muscle damage, etc.)<br>• glucose - if above upper limit of normal do glucose test on a fasting sample<br>• amylase - to detect pancreatitis; maybe normal in chronic pancreatitis<br>• pregnancy test, if relevant<br>* A single quality-assured laboratory is preferable<br><br>* For further information on testing of hepatitis, please refer to Protocols 6 and 7, *Management of hepatitis C and HIV co-infection (2007)* and *Management of hepatitis B and HIV co-infection (2011 revision).* | |

### *2.1.6.4 STEP 4 - Clinical staging*

## What to do?

***Table 4: WHO clinical staging of HIV disease in adults, adolescents and children***

| Adults and adolescents[a] | Children |
|---|---|
| Clinical stage 1 | |
| Asymptomatic<br>Persistent generalized lymphadenopathy | Asymptomatic<br>Persistent generalized lymphadenopathy |
| Clinical stage 2 | |
| Moderate unexplained weight loss (<10% of presumed or measured body weight)<br>Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)<br>Herpes zoster<br>Angular cheilitis<br>Recurrent oral ulceration<br>Papular pruritic eruption<br>Fungal nail infections<br>Seborrhoeic dermatitis | Unexplained persistent hepatosplenomegaly<br>Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)<br>Herpes zoster<br>Lineal gingival erythema<br>Recurrent oral ulceration<br>Papular pruritic eruption<br>Fungal nail infections<br>Extensive wart virus infection<br>Extensive molluscum contagiosum<br>Unexplained persistent parotid enlargement |
| Clinical stage 3 | |
| Unexplained severe weight loss (>10% of presumed or measured body weight)<br>Unexplained chronic diarrhoea for longer than 1 month<br>Unexplained persistent fever (intermittent or constant for longer than 1 month)<br>Persistent oral candidiasis<br>Oral hairy leukoplakia<br>Pulmonary tuberculosis<br>Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)<br>Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis<br>Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 × $10^9$/L) and/or chronic thrombocytopaenia (<50 × $10^9$/L) | Unexplained moderate malnutrition[b] not adequately responding to standard therapy<br>Unexplained persistent diarrhoea (14 days or more)<br>Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one 1 month)<br>Persistent oral candidiasis (after first six weeks of life)<br>Oral hairy leukoplakia<br>Lymph node tuberculosis; pulmonary tuberculosis<br>Severe recurrent bacterial pneumonia<br>Acute necrotizing ulcerative gingivitis or periodontitis<br>Unexplained anaemia (<8 g/dL), neutropaenia (<0.5 × $10^9$/L) or chronic thrombocytopaenia (<50 × $10^9$/L) |
| Clinical stage 3 | |
| | Symptomatic lymphoid interstitial pneumonitis<br>Chronic HIV-associated lung disease, including bronchiectasis |

| Adults and adolescents[a] | Children |
|---|---|
| Clinical stage 4[c] | |
| HIV wasting syndrome<br>*Pneumocystis (jirovecii)* pneumonia<br>Recurrent severe bacterial pneumonia<br>Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month in duration or visceral at any site)<br>Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)<br>Extrapulmonary tuberculosis<br>Kaposi sarcoma<br>Cytomegalovirus infection (retinitis or infection of other organs)<br>Central nervous system toxoplasmosis<br>HIV encephalopathy<br>Extrapulmonary cryptococcosis, including meningitis<br>Disseminated nontuberculous mycobacterial infection<br>Progressive multifocal leukoencephalopathy<br>Chronic cryptosporidiosis<br>Chronic isosporiasis<br>Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis)<br>Lymphoma (cerebral or B-cell non-Hodgkin)<br>Symptomatic HIV-associated nephropathy or cardiomyopathy<br>Recurrent septicaemia (including nontyphoidal *Salmonella*)<br>Invasive cervical carcinoma<br>Atypical disseminated leishmaniasis | Unexplained severe wasting, stunting or severe malnutrition[d] not responding to standard therapy<br>*Pneumocystis (jirovecii)* pneumonia<br>Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)<br>Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month's duration or visceral at any site)<br>Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)<br>Extrapulmonary tuberculosis<br>Kaposi sarcoma<br>Cytomegalovirus infection (retinitis or infection of other organs with onset at age older than one month)<br>Central nervous system toxoplasmosis (after the neonatal period)<br>HIV encephalopathy<br>Extrapulmonary cryptococcosis, including meningitis<br>Disseminated nontuberculous mycobacterial infection<br>Progressive multifocal leukoencephalopathy<br>Chronic cryptosporidiosis (with diarrhoea)<br>Chronic isosporiasis<br>Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis)<br>Cerebral or B-cell non-Hodgkin lymphoma HIV-associated nephropathy or cardiomyopathy |

[a] In the development of this table, adolescents were defined as 15 years or older. For those younger than 15 years, the clinical staging for children should be used.

[b] For children younger than 5 years, moderate malnutrition is defined as weight-for-height < –2 *z*-score or mid-upper arm circumference ≥115 mm to <125 mm.

[c] Some additional specific conditions can be included in regional classifications, such as *penicilliosis* in Asia, HIV-associated rectovaginal fistula in southern Africa and reactivation of trypanosomiasis in Latin America.

[d] For children younger than five years of age, severe wasting is defined as weight-for-height < –3 *z*-score; stunting is defined as length-for-age/height-for-age < –2 *z*-score; and severe acute malnutrition is either weight for height < –3 *z*-score or mid-upper arm circumference <115 mm or the presence of oedema.

*Source*: Adapted from: WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. Geneva, World Health Organization, 2007 (www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf).

### *2.1.6.5 STEP 5 - Management based on clinical stage*

## What to do?

**Table 5: Management and follow up plan based on WHO staging**

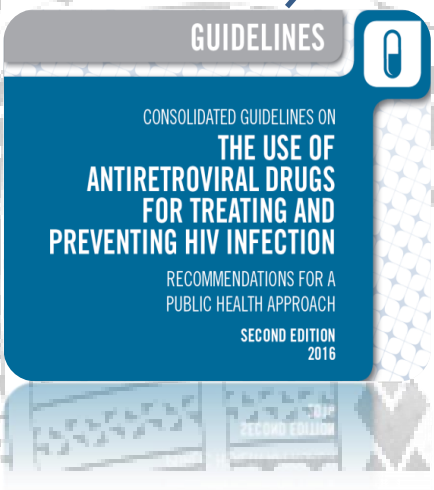
| Management and follow up plan based on WHO staging | |
|---|---|
| WHO Clinical Stage | **Management** |
| Stage 1 | Patients are followed up every 3-6 months<br>Check for clinical signs of progression<br>Informed of the clinical signs of progression that would alert them to go back to their medical doctor.<br>• enlargement of lymph glands<br>• fever lasting more than 2 weeks<br>• weight loss<br>• diarrhoea for more than 2 weeks<br>• cough lasting more than 3 weeks or shortness of breath<br>• persistent headache<br>Total lymphocyte count of CD4 cell count if available<br>Diagnosis and treatment of sexually transmitted infections STIs<br>Counsel on safer sexual practices and contraception |
| Stage 2 | **Patients are followed up every 3-6 months**<br>Check for any symptoms of disease progression (stage III symptoms)<br>• Fever lasting more than 2 weeks<br>• weight loss >10% of body weight<br>• diarrhoea lasting of more than 2 weeks<br>• oral thrush<br>• persistent headache<br>• persistent cough<br>• mucocutaneous manifestations (seborrheic dermatitis, prurigo, recurrent oral ulceration)<br>Symptom directed laboratory evaluation (if available)<br>• Full blood count<br>• ALT<br>• Sputum smear for TB when productive cough<br>• Total lymphocyte count or CD4 cell count<br><br>Follow up STI management counselling as for stage 1 patients<br><br>**Cotrimoxazole prophylaxis**<br>Start prophylaxis in all patients with WHO stage 2, 3 and 4 disease<br>If CD4 testing is available, start prophylaxis in patients with:<br>• Any WHO clinical stage and CD4 <200 cells/mm3 where the aim of cotrimoxazole prophylaxis is the prevention of PCP and toxoplasmosis<br>• Any WHO clinical stage CD4 <350 cells/mm3 where the aim of cotrimoxazole prophylaxis is the reduction of morbidity and mortality associated with malaria, bacterial diarrhoeal disease and bacterial pneumonias in addition to the prevention of PCP and toxoplasmosis<br><br>**Dose**<br>One double strength tablet or two single strength tablets once daily<br>Total daily dose is 960 mg (800 mg SMZ + 160 mg TMP) |

| | |
|---|---|
| Stage III and IV | Frequency of follow up depends on the patient's individual condition.<br>Frequent visits are recommended at initiation of ART (1-2 weekly) then 1-3 monthly once the patient is stable on ART. The main objectives of examination are to detect signs and symptoms of Immune Inflammatory Reconstitution Syndrome (IRIS) and OIs including pulmonary or extra pulmonary tuberculosis.<br>Symptom directed laboratory evaluation (if available)<br>• Full blood count<br>• ALT<br>• Sputum smear for TB when productive cough<br>• Total lymphocyte count of CD4 cell count<br>**Start opportunistic infections (OI) prophylaxis**<br>Start cotrimoxazole (sulfamethoxazole 800 mg and trimethoprim 160 mg) P0 daily if symptom of stage III or stage IV |

*Source: Myanmar Guidelines for the Clinical Management of HIV Infection in Adults and Adolescents. 2007.*

## [iii]2.2 Antiretroviral drugs for HIV prevention

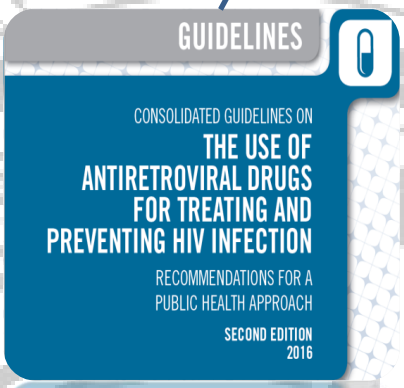
### *2.2.1 Oral pre-exposure prophylaxis*




**Recommendation**

- Oral pre-exposure prophylaxis **(PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches** (strong recommendation, high-quality evidence).

***PreP has been evaluated to be financially unsustainable at this point in time. Samoa will strengthen first and expand implementation of well-established HIV prevention intervention such as condom use in the prevention of sexual transmission of HIV and will assess later feasibility and implications of implementing PrEP.***




**Defining "substantial risk"**
Substantial risk of HIV infection is provisionally defined as **HIV incidence around 3 per 100 person-years or higher in the absence of PrEP**.

HIV incidence higher than 3 per 100 person-years has been identified among some groups of men who have sex with men, transgender women in many settings, and heterosexual men and women who have sexual partners with undiagnosed or untreated HIV infection.

Individual risk varies within groups at substantial risk, depending on individual behaviour and the characteristics of sexual partners.

Most of the PrEP trials reviewed for this recommendation identified and recruited groups at substantial risk of acquiring HIV, as demonstrated by the HIV incidence rate among participants in control arms that ranged between 3 and 9 per 100 person-years in most studies.

Indeed, the HIV incidence in control arms of PrEP trials was often higher than anticipated, suggesting that PrEP attracts people at particularly high risk.

In locations where the overall incidence of HIV infection is low, there may be individuals at substantial risk who would be attracted to and benefit from PrEP services.

HIV incidence higher than 2 per 100 person-years was considered sufficient to warrant offering oral PrEP in the recommendations issued by the International Antiviral Society – USA expert panel in 2014.

Thresholds for offering PrEP may vary depending on a variety of considerations, including epidemiological context or trends, available resources and the relative costs, feasibility and demand for PrEP.

### *2.2.2 Post-exposure prophylaxis*

*Post-exposure Prophylaxis, or PEP, is currently not available in Samoa. The drug is expensive and has not yet been evaluated on financial feasibility for the healthcare system. Through development partners, there is the possibility of procuring PEP in emergency cases, but procedures have not yet been developed. Upon procurement and national distribution of PEP, the following guidelines should be followed.*

## What to do?

### 1) ASSESS eligibility

HIV PEP should be offered and initiated as early as possible in all individuals with an exposure that has the potential for HIV transmission, **preferably within 72 hours**. For individuals who may not be able to access services within this time, providers should consider the range of essential interventions and referrals that should be offered to clients presenting after 72 hours.

Eligibility assessment should be based on the HIV status of the source whenever possible, and may include consideration of background prevalence and local epidemiological patterns.

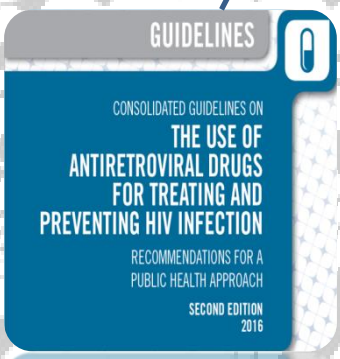
### 2) CHECK if with or without exposures that may warrant HIV PEP.

**2.1 Exposures that may warrant HIV PEP following**:

- ☑ body fluids: blood, bloodstained saliva, breast milk, genital secretions and cerebrospinal, amniotic, peritoneal, synovial, pericardial or pleural fluid
- ☑ fluids carry a high risk of HIV infection, this list is not exhaustive. All cases should be assessed clinically, and health workers should make decisions as to whether the actual exposure constitutes a significant risk.
- ☑ types of exposure: 1) mucous membrane, i.e. sexual exposure; splashes to eye, nose, or oral cavity; and 2) parenteral.

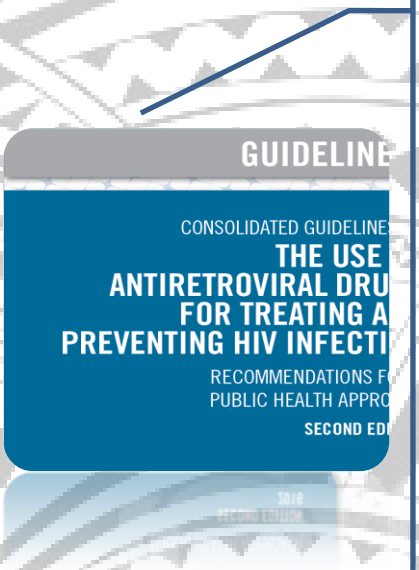
**2.1 Exposures that do NOT require HIV PEP include the following:**

- ☒ when the exposed individual is already HIV positive;
- ☒ when the source is established to be HIV negative; and
- ☒ exposures to bodily fluids that do not pose a significant risk, i.e. tears, non-bloodstained saliva, urine and sweat.




## What to do?

In cases that **do not require PEP**, the exposed person should be counselled about limiting future exposure risk. Although HIV testing is not required, it may be provided if desired by the exposed person.




***Based on the WHO Guidelines on post-exposure prophylaxis for HIV and the use of co-trimoxazole prophylaxis for HIV-related infections among adults, adolescents and children: recommendations for a public health approach – December 2014 supplement to the 2013 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2014 (http://www.who.int/hiv/pub/guidelines/arv2013/arvs2013upplement_dec2014/en).***

# What to do?

## Recommendation

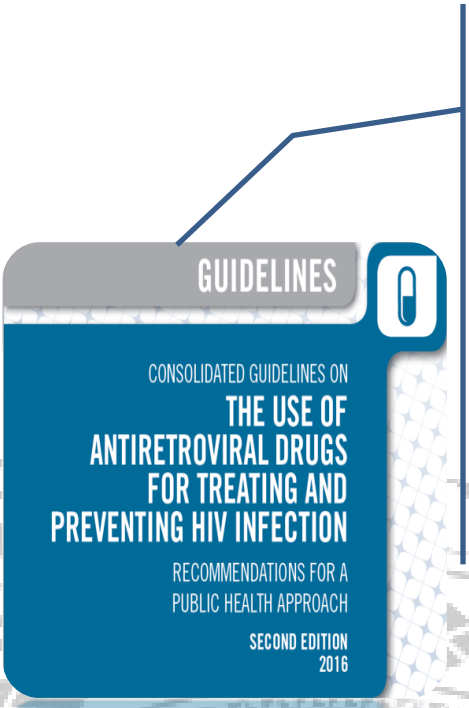
- A regimen for post-exposure prophylaxis for HIV with two drugs is effective, but three drugs are preferred (conditional recommendation, very low-quality evidence).
- Post-exposure prophylaxis ARV regimens for adults and adolescents:
    - TDF + 3TC (or FTC) is recommended as the preferred backbone2 regimen for HIV post-exposure prophylaxis in adults and adolescents (strong recommendation, low-quality evidence).
    - LPV/r or ATV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for adults and adolescents (conditional recommendation, very low-quality evidence). Where available, RAL, DRV/r or EFV can be considered as alternative options.

- Post-exposure prophylaxis ARV regimens for children ≤10 years:
    - AZT + 3TC is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for children aged 10 years and younger.
    - ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens (strong recommendation, low-quality evidence).
    -
- LPV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for children younger than 10 years (conditional recommendation, very low-quality evidence). An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV and NVP.3

**Prescribing practices**

☑ A **full 28-day prescription of antiretroviral drugs should be provided** for HIV post-exposure prophylaxis following initial risk assessment (strong recommendation, low-quality evidence).

☑ Enhanced adherence counselling is suggested for all individuals initiating HIV post-exposure prophylaxis (conditional recommendation, moderate-quality evidence).




- Backbone regimen refers to the two-NRTI component of an ART regimen (normally comprising 3 ARV drugs).
- NVP should not be used in children above the age of two years.
- Enhanced adherence counselling includes baseline individual needs assessment, adherence counselling and education sessions and follow-up telephone calls.

### *2.2.3 Combination HIV prevention*

ARV drugs play a key role in HIV prevention. People taking ART who achieve optimal viral suppression are extremely unlikely to pass HIV to sexual partners. ARV drugs taken by people without HIV as PrEP or PEP are highly effective in preventing HIV acquisition.

Besides use of ARV drugs for prevention, combination prevention can enhance the prevention of HIV transmission.

[5] Combination prevention programmes use a mix of biomedical, behavioural and structural interventions to meet the current HIV prevention needs of particular individuals and communities so as to have the greatest possible impact on reducing new infections. Well-designed combination prevention programmes are carefully tailored to national and local needs and conditions. They focus resources on the mix of programmatic and policy actions required to address both immediate risks and underlying vulnerability. They should be thoughtfully planned and managed to operate synergistically and consistently on multiple levels (e.g. individual, relationship, community and society) and over an adequate period of time. Combination prevention mobilizes communities, the private sector, governments and global resources in a collective undertaking. It requires and benefits from enhanced

[5] Consolidated guidelines on the use of ART in treating and preventing HIV infections. Second edition. 2016

partnership and coordination and should incorporate mechanisms for learning, capacity building and flexibility to permit continual improvement and adaptation to the changing environment.

Other **biomedical interventions** that reduce HIV risk practices and/or the probability of HIV transmission per contact event include the following:

- **Male and female condoms and condom compatible lubricant:** male condoms are estimated to reduce heterosexual transmission by at least 80% and to offer 64% protection in anal sex among men who have sex with men, if used consistently and correctly. Fewer data are available for the efficacy of female condoms, but evidence suggests they can have a similar prevention effect.

- **Needle and syringe programmes** are highly associated with a reduction in HIV transmission through injecting drug use.

- **Opioid substitution therapy** with methadone or buprenorphine is the most effective form of treatment for opioid dependence and has the additional benefit of effectively reducing HIV risk behaviour and transmission through injecting drug use. Opioid substitution therapy also provides adherence support to people on ART.

- **Voluntary medical male circumcision (VMMC):** three randomized clinical trials in Africa demonstrated an approximately 60% reduction in the risk of female-to-male sexual transmission. For high-burden settings, WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS) recommended the inclusion of VMMC as an additional important strategy for presentation of heterosexually acquired HIV infection in men. Male circumcision should be offered as part of a comprehensive HIV prevention package, including safer sex education, providing and promoting condom use, providing HIV testing services (HTS) and linkage to care for those in need, and management of STIs. This intervention has reached over 10 million males in eastern and southern Africa.

**Behavioural interventions** can reduce the frequency of potential transmission events, including the following:

- **Targeted information and education:** these are programmes that use various communication approaches, for example, school-based sex education, peer counselling and community-level and interpersonal counselling, including brief interventions to disseminate behavioural messages. These messages encourage people to reduce risk behaviour and increase behaviour that is protective (such as safer drug use, delaying sexual debut, reducing

the frequency of unprotected sex with multiple partners, using male and female condoms correctly and consistently and knowing your HIV status and that of your partner). There is growing recognition that social media and mobile technology are important tools that can be integrated in HIV prevention programmes, and can be particularly critical in informing about and providing prevention services to populations such as men who have sex with men.

- **Structural and supportive interventions** may increase access to, uptake of and adherence to behavioural and biomedical interventions. Such interventions address the critical social, legal, political and environmental enablers that contribute to HIV transmission, including legal and policy reforms, measures to reduce stigma and discrimination (including in the health sector). In addition, they involve the promotion of women's, fa'afafine and lesbian, gay, bisexual, transgender and intersex (LGBTI) equality and prevention of gender-based and LGBTI violence, economic empowerment, access to schooling and supportive interventions designed to enhance referrals, adherence, retention and community mobilization.

**Combination prevention for key populations**

WHO recommends a comprehensive package of evidence-based HIV-related recommendations for all key populations. The package comprises clinical interventions and a set of critical enablers required for successful implementation of programmes for the key populations.

**Comprehensive package of HIV prevention for key populations**

**a) Essential health sector interventions**

1. Comprehensive condom and lubricant programming
2. Harm-reduction interventions for substance use (in particular, needle and syringe programmes, opioid substitution therapy and naloxone)

*(*  *services not currently available)*

3. Behavioural interventions
4. HIV Testing Services
5. HIV treatment and care
6. Prevention and management of co-infections and other comorbidities, including viral hepatitis, tuberculosis and mental health conditions
7. Sexual and reproductive health interventions

**b) Essential strategies for an enabling environment**

1. Supportive legislation, policy and financial commitment, including decriminalization of certain types of behaviour of key populations
2. Addressing stigma and discrimination, including by making health services available, accessible and acceptable
3. Community empowerment
4. Addressing violence against people from key populations

***Source : Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations. Geneva: World Health Organization; 2014 (http://www.who.int/hiv/pub/guidelines/keypopulations/en)***

## [iv]2.3 Antiretroviral therapy

### *2.3.1 Preparing people living with HIV for ART*


**What to do?**

1. Before people start antiretroviral therapy (ART), health-care providers should initiate a detailed discussion about the willingness and readiness of patients to initiate ART, the antiretroviral (ARV) drug regimen, dosage, scheduling, likely benefits, possible adverse effects and the required follow-up and monitoring visits.

2. In the case of children with HIV, this conversation should directly involve the caregiver and include discussion about disclosing their HIV status.

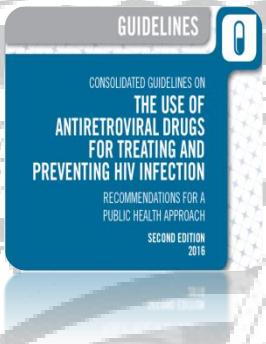
3. Retesting all people living with HIV before initiating ART is recommended to ensure a correct diagnosis of HIV infection.

4. Initiation of ART should always consider nutritional status, any comorbidities and other medications being taken to assess for possible interactions, contraindications and dose adjustment.

5. The choice to accept or decline ART ultimately lies with the person or his or her caregiver, and if they choose to defer initiation, ART can be offered again at subsequent visits.

6. If the person faces mental health or substance use issues or other potential barriers to ART initiation or adherence, appropriate support should be provided and readiness to initiate.

7. ART should be reassessed at regular intervals.




8. Community and peer support can help a person to prepare and make the decision to start therapy.

9. People starting treatment and caregivers should be informed that the first ART regimen offers the best opportunity for effective viral suppression, immune recovery and consequently clinical benefit and that successful ART requires all medications to be taken as prescribed.

10. It is important to acknowledge that there are situations where delays in starting ART can have negative consequences, particularly for people with tuberculosis (TB) or advanced immunosuppression, who are at high risk of death.

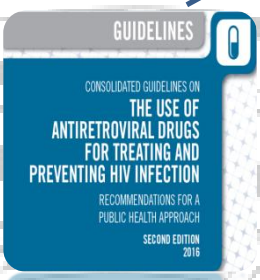
11. People should be advised that many adverse effects are temporary or may be treated, and that substitutions can often be made for the ARV drugs associated with adverse effects.

12. In preparation for treatment initiation, it is important to assess the need for psychosocial support to optimize adherence. People receiving ART and caregivers should also be asked regularly about any other medications that are being taken, including herbal remedies and nutritional supplements.

13. People commencing ART should be given advice on safer sex, including condom use and avoidance of other high-risk activities such as sharing of injecting equipment, to prevent transmitting HIV to other people.

**NOTE:**

WHO recommends TB symptom screening, before initiating PLHIV on ART. All other laboratory tests such as complete blood count, liver function test (SGPT, SGOT) and lipid profile are only desirable and should not delay initiation of ART.




**Good practice statement**

Efforts should be made to reduce the time between HIV diagnosis and ART initiation based on an assessment of a person's readiness.


**It is important to explain to the patient the goals of antiretroviral therapy. As mentioned earlier these include:**

- **Clinical:** prolongation, preservation and enhanced quality of life;
- **Immunological:** preservation and improvement (as necessary) of immune function, in order to prevent the onset of opportunistic infections and reduce the risk of AIDS-related cancers;
- **Epidemiological:** reduction of the risk of onward HIV transmission.

## What to do?

*Table 7: Sample visit schedule and follow up for patients commencing ART*

| Visit<br>(any time if new problems occur) | Test and treat<br>ART medically indicated<br>CD4 count < 350 especially close to 200<br>CD4 <200<br>WHO stage 3 or 4 |
|---|---|
| First visit | Medical History and symptom check list<br>History<br>Examination<br>Document WHO clinical stage<br>Treatment preparedness and understanding of HIV/AIDS, transmission, risk reduction, treatment options<br>Adherence counseling<br>(more than one session may be needed prior to commencing ART) |
| Week 2 | History (new problems)<br>Commence ART if patient is ready |
| Week 4 | History (new problems)<br>Examination<br>If on NVP, any side effects (rash, fever, signs of liver toxicity)<br>Symptom directed liver function testing if available<br>Adherence assessment/support<br>Reassess WHO clinical T stage |
| Week 8 | History (new problems)<br>Symptom checklist<br>Examination<br>Adherence assessment/support<br>Reassess WHO clinical stage |
| **Follow-up** | History (new problems)<br>Symptom checklist<br>Examination<br>Adherence assessment/support<br>Psychosocial support<br>Visit every 1-3 months and more often as needed<br>Viral load count every 6 months if available |

Source: Myanmar Guidelines for the Clinical Management of HIV Infection in Adults and Adolescents. 2007. Page 13.

### 2.3.2 What to expect in the first months of ART

Although ART is a lifelong commitment, the first months of therapy are especially important. Clinical and immunological improvement and viral suppression are expected when individuals adhere to ART, but opportunistic infections (OIs) and/or immune reconstitution inflammatory syndrome (IRIS) may develop, as well as early adverse drug reactions, such as drug hypersensitivity, especially in the first three months of treatment. ART significantly decreases mortality overall, but death rates are also highest in the first three months of ART. These complications are most common when the people starting ART already have advanced HIV disease with severe immunodeficiency and existing co-infections and/or comorbidities, severely low haemoglobin, low body mass index and very low CD4 cell counts or are severely malnourished. Poor adherence in this period is also associated with the risk of early treatment failure and rapid development of drug resistance.

### 2.3.3 When to start ART

| CLINICAL GUIDELINES: ANTIRETROVIRAL THERAPY | |
|---|---|
| **4.1 Preparing people living with HIV for ART** | |
| **4.1.1 Accelerated ART initiation** | Efforts should be made to reduce the time between HIV diagnosis and ART initiation based on an assessment of a person's readiness. |
| **4.2 When to start ART** | |
| **4.3.1 When to start ART in adults (>19 years old)** | ART should be initiated in all adults living with HIV regardless of WHO clinical stage and at any CD4 cell count *(strong recommendation, moderate quality evidence).* |
| | As a priority, ART should be initiated in all adults with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adults with CD4 count ≤350 cells/mm³ *(strong recommendation, moderate quality evidence).* |
| **4.3.2 When to start ART in pregnant and breastfeeding women** | ART should be initiated in all pregnant and breastfeeding women living with HIV regardless of WHO clinical stage and at any CD4 cell count and continued lifelong *(strong recommendation, moderate quality evidence).* |
| **4.3.3 When to start ART in adolescents (10–19 years of age)** | ART should be initiated in all adolescents living with HIV regardless of WHO clinical stage and at any CD4 cell count *(conditional recommendation, low quality evidence).*<br>As a priority, ART should be initiated in all adolescents with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and adolescents with CD4 count ≤350 cells/mm³ *(strong recommendation, moderate quality evidence).* |
| **4.3.4 When to start ART in children younger than 10 years of age** | ART should be initiated in all children living with HIV, regardless of WHO clinical stage or at any CD4 cell count. |
| | Infants diagnosed in the first year of life *(strong recommendation, moderate quality evidence).* |
| | Children living with HIV one year old to less than 10 years old *(conditional recommendation, low quality evidence).* |
| | As a priority, ART should be initiated in; all children ≤2 years old or children younger than 5 years with WHO HIV clinical stage 3 or 4 or CD4 count ≤750 cells/mm³ or CD percentage <25% and children 5 years and older with WHO HIV clinical stage 3 or 4 or with CD4 count ≤350 cells/mm³. |
| **4.3.5 Timing of ART for adults and children with TB** | ART should be started in all TB patients living with HIV regardless of CD4 count *(strong recommendation, high quality evidence).*<br>TB treatment should be initiated first, followed by ART as soon as possible within the first 8 weeks of treatment *(strong recommendation, high quality evidence).*<br>HIV-positive TB patients with profound immunosuppression (e.g. CD4 counts less than 50 cells/mm³) should receive ART within the first two weeks of initiating TB treatment. |
| | ART should be started in any child with active TB disease as soon as possible and within eight weeks following the initiation of anti-tuberculosis treatment regardless of the CD4 count and clinical stage *(strong recommendation, low quality evidence).* |

Helpful Tips

**Assessment of Patients' readiness for therapy**

- Build confidence and assess knowledge
- Explain ART and the objectives of the treatment
  - o to avoid occurrence of OI
  - o to restore immunity
- Ensure the patient has understood
  - o The treatment does not kill the virus
  - o The treatment only suppresses the virus
  - o The treatment has to be taken regularly to avoid resistance
  - o It is a lifelong-treatment
  - o It reduces risk of transmission to partner
- Advise and encourage the patient to disclose his diagnosis to his/ her partner or family and support testing of the partner if status is unknown.

### 2.3.4 *What to start: first-line ART*

| PREFERRED AND ALTERNATIVE FIRST-LINE ART REGIMENS | | |
|---|---|---|
| **First-line ART** | **Preferred first-line regimen** | **Alternative first-line regimens[1,2]** |
| **Adults** | TDF + 3TC (or FTC) + EFV | AZT + 3TC + EFV (or NVP)<br>TDF + 3TC (or FTC) + DTG[3,4]<br>TDF + 3TC (or FTC) + $EFV_{400}$[3,4,5]<br>TDF + 3TC (or FTC) + NVP |
| **Pregnant/breastfeeding women** | TDF + 3TC (or FTC) + EFV | AZT + 3TC + EFV (or NVP)<br>TDF + 3TC (or FTC) + NVP |
| **Adolescents** | TDF + 3TC (or FTC) + EFV | AZT + 3TC + EFV (or NVP)<br>TDF (or ABC) + 3TC (or FTC) + DTG[3,4]<br>TDF (or ABC) + 3TC (or FTC) + $EFV_{400}$[3,4,5]<br>TDF (or ABC) + 3TC (or FTC) + NVP |
| **Children 3 years to less than 10 years** | ABC + 3TC + EFV | ABC + 3TC + NVP<br>AZT + 3TC + EFV (or NVP)<br>TDF + 3TC (or FTC) + EFV (or NVP) |
| **Children less than 3 years** | ABC (or AZT) + 3TC + LPV/r | ABC (or AZT) + 3TC + NVP |

| | |
|---|---|
| **4.4 What to start: first-line ART** | Countries should discontinue d4T use in first-line regimens because of its well-recognized metabolic toxicities *(strong recommendation, moderate quality evidence).* |
| | Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy *(strong recommendation, moderate quality evidence).* |

| | |
|---|---|
| Infant prophylaxis | Infants born to mothers with HIV who are at high risk of acquiring HIV[1] should receive dual prophylaxis with daily AZT and NVP for the first 6 weeks of life, whether they are breastfed or formula-fed *(strong recommendation, moderate quality evidence)*. |
| | Breastfed infants who are at high risk of acquiring HIV,[1] including those first identified as exposed to HIV during the postpartum period, should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks of infant prophylaxis) using either AZT and NVP or NVP alone *(conditional recommendation, low quality evidence)*. |
| | Infants of mothers who are receiving ART and are breastfeeding should receive 6 weeks of infant prophylaxis with daily NVP. If infants are receiving replacement feeding, they should be given 4 to 6 weeks of infant prophylaxis with daily NVP (or twice-daily AZT) *(strong recommendation, moderate quality evidence for breastfeeding infants; strong recommendation, low quality evidence for infants receiving only replacement feeding)*. |
| **Good practice statement** | ART should be initiated urgently in all pregnant and breastfeeding women, even if they are identified late in pregnancy or postpartum, because the most effective way to prevent mother-to-child HIV transmission is to reduce maternal viral load. |

## Sequencing of ARV formulations for newborns starting treatment at around birth

| | 0–2 weeks → | 2 weeks–3 months → | 3–36 months |
|---|---|---|---|
| Preferred | AZT + 3TC + NVP | ABC or AZT + 3TC + LPV/r syrup | ABC or AZT + 3TC + LPV/r pellets |
| Alternative | AZT + 3TC + NVP | | ABC or AZT + 3TC + LPV/r pellets |
| Special circumstances | AZT + 3TC + NVP | ABC or AZT + 3TC + RAL | |

3TC lamivudine, ABC abacavir, AZT zidovudine, LPV lopinavir, NVP nevirapine, r ritonavir, RAL raltegravir.

***Table 8 Summary of recommended ART regimens for children who need TB treatment***

| | | |
|---|---|---|
| **Recommended regimens for children and adolescents initiating ART while on TB treatment[a,b]** | | |
| **Younger than 3 years** | | Triple NRTI (AZT + 3TC + ABC)[c] |
| **3 years and older** | | Two NRTIs + EFV<br>or<br>Triple NRTI (AZT + 3TC + ABC)[c] |
| **Recommended regimen for children and infants initiating TB treatment while receiving ART[a]** | | |
| **Child on standard NNRTI-based regimen**<br>(two NRTIs + EFV or NVP) | Younger than 3 years | Continue NVP, ensuring that the dose is 200 mg/m²<br>or<br>Triple NRTI (AZT + 3TC + ABC)[c] |
| | 3 years and older | If the child is receiving EFV, continue the same regimen<br>If the child is receiving NVP, substitute with EFV<br>or<br>Triple NRTI (AZT + 3TC + ABC)[c] |
| **Recommended regimen for children and infants initiating TB treatment while receiving ART[a]** | | |
| **Child on standard PI-based regimen**<br>(two NRTIs + LPV/r) | Younger than 3 years | Triple NRTI (AZT + 3TC + ABC)[c]<br>or<br>Continue LPV/r, adding RTV to achieve the full therapeutic dose[d] |
| | 3 years and older | If the child has no history of failure of an NNRTI-based regimen:<br>Substitute with EFV[e]<br>or<br>Triple NRTI (AZT + 3TC + ABC)[c]<br>or<br>Continue LPV/r, adding RTV to achieve the full therapeutic dose[d]<br>If the child has a history of failure of an NNRTI-based regimen:<br>Triple NRTI (AZT + 3TC + ABC)[c]<br>or<br>Continue LPV/r, adding RTV to achieve the full therapeutic dose[d]<br>Consider consultation with experts for constructing a second- line regimen |

[a] Ensure optimal dosing of rifampicin based on dosing guidelines (Annex 11c).

[b] Substitute ARV drugs based on an age-appropriate ART regimen in line with nationally recommended first-line ART.

[c] Triple NRTI is only recommended for the duration of TB treatment; an age-appropriate PI- or NNRTI-based regimen should be restarted when rifampicin-based therapy ends. Based on the findings from the ARROW trial *(174)*, this regimen should be considered as the preferred option for children younger than 3 years who are receiving an LPV/r-based regimen when starting TB treatment. The US FDA approval for the use of EFV in children 3 months to 3 years old weighing more than 3.5 kg offers a potential alternative to the triple-NRTI approach *(358)*. An EFV-based regimen in children under 3 years is still not recommended because pharmacokinetic data are needed to ensure that the co-administration of rifampicin does not decrease drug levels below the therapeutic level. Triple NRTI should also be considered as the preferred regimen for children older than 3 years with a history of failure on an NNRTI-based regimen.

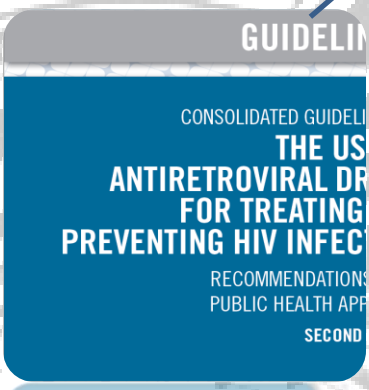
[d] Increase RTV until it reaches the same dose as LPV in mg, in a ratio of 1:1.

[e] Substitution with EFV should be considered as the preferred option *(359)*, and EFV could be maintained after TB treatment ends to enable simplification and harmonization with the ARV drug regimens used for older children.

3TC lamivudine, ABC abacavir, AZT zidovudine, EFV efavirenz, FTC emtricitabine, LPV lopinavir, NNRTI non-nucleoside reverse-transcriptase inhibitor, NRTI nucleoside reverse-transcriptase inhibitor, NVP nevirapine, PI protease inhibitor, r or RTV ritonavir.

**REFER to ANNEX 5** for Doses of recommended ARV drugs.

### *2.3.5 Fixed-dose combinations and once-daily regimens*




**Recommendation**

- Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy (strong recommendation, moderate-quality evidence).
- REFER to ANNEX 5 for Doses of recommended ARV drugs.

### 2.3.6 Monitoring the response to ART and diagnosing treatment failure

#### *2.3.6.1 Laboratory monitoring before and after initiating ART*

## What to do?

***Recommended tests for HIV screening and monitoring and approaches to screening for coinfections and non-communicable diseases***

| Phase of HIV management | Recommended | Desirable (if feasible) |
|---|---|---|
| **HIV diagnosis** | HIV testing (serology for adults and children 18 months or older; EID for children younger than 18 months)<br>CD4 cell count<br>TB symptom screening | HBV (HBsAg) serology[a]<br>HCV serology<br>Cryptococcus antigen if CD4 cell count ≤100 cells/mm³[b]<br>Screening for STIs<br>Pregnancy test to assess if ART initiation should be prioritized to prevent HIV transmission to the child<br>Assessment for major noncommunicable chronic diseases and comorbidities[c] |
| **Follow-up before ART** | CD4 cell count (every 6–12 months in circumstances where ART initiation is delayed) | |
| **ART initiation** | | Haemoglobin test for starting AZT[d]<br>Pregnancy test<br>Blood pressure measurement<br>Serum creatinine and estimated glomerular filtration rate (eGFR) or starting TDF[e]<br>Alanine aminotransferase for NVP[f]<br>Baseline CD4 cell count |
| **Receiving ART** | HIV viral load (at 6 months and 12 months after initiating ART and every 12 months thereafter)<br>CD4 cell count every 6 months until patients are stable on ART | Serum creatinine and eGFR for TDF[c]<br>Pregnancy test, especially for women of childbearing age not receiving family planning and on treatment with DTG or low-dose EFV |
| **Suspected treatment failure** | Serum creatinine and eGFR for TDF[c]<br>Pregnancy test, especially for women of childbearing age not receiving family planning and on treatment with DTG or low-dose EFV | HBV (HBsAg) serology[a,g] (before switching ART regimen if this testing was not done or if the result was negative at baseline and the patient was not vaccinated thereafter) |

[a] If feasible, HBsAg testing should be performed at baseline to identify people with HIV and HBV coinfection and who should therefore initiate TDF-containing ART.

[b] Can be considered in settings with a high prevalence of cryptococcal antigenaemia (>3%).

[c] Consider assessing for the presence of chronic conditions that can influence ART management, such as hypertension and other cardiovascular diseases, diabetes and TB according to the WHO Package of Essential NCD interventions (PEN), mental health Gap Action Programme (mhGAP) or national standard protocols (*see* section 5.3 "Prevention, screening and management of other comorbidities and chronic care for people living with HIV"). Monitoring may include a range of tests, including serum creatinine and estimated glomerular filtration rate (eGFR), serum phosphate and urine dipsticks for proteinuria and glycosuria. *See* formula for eGFR in the footnote to section 4.6.3.

[d] Among children and adults with a high risk of adverse events associated with AZT (low CD4 or low BMI).

[e] Among people with a high risk of adverse events associated with TDF: underlying renal disease, older age group, low body mass index (BMI), diabetes, hypertension and concomitant use of a boosted PI or potential nephrotoxic drugs.

[f] Among people with a high risk of adverse events associated with NVP, such as being ART-naive, women with HIV with a CD4 count >250 cells/mm³ and hepatitis C virus (HCV) coinfection. However, liver enzymes have low predictive value for monitoring NVP toxicity.

[g] For HIV/HBV coinfected individuals who are already using TDF-containing regimens and develop ART failure, this NRTI should be maintained regardless of the selected second-line regimen.

ART antiretroviral therapy, AZT zidovudine, DTG dolutegravir, EFV efavirenz, eGFR estimated glomerular filtration rate, EID early infant diagnosis, HBV hepatitis B virus, HBsAg hepatitis B surface antigen, HCV hepatitis C virus, STI sexually transmitted infection, TDF tenofovir.

### *2.3.6.2 Monitoring the response to ART and diagnosis of treatment failure*

## What to do?

### Recommendations for routine monitoring

**Routine viral load monitoring can be carried out at 6 months, at 12 months and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting (conditional recommendation, very low-quality evidence).**

**In settings where routine viral load monitoring is available, CD4 cell count monitoring can be stopped in individuals who are stable on ART and virally suppressed (conditional recommendation, low-quality evidence).**

 ***Samoa has implemented this option as development partners have stopped supplying test kits as per this recommendation.***

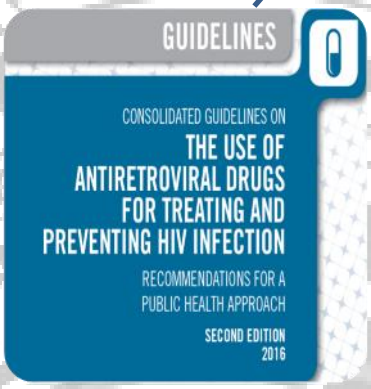
### Recommendations for diagnosis of treatment failure

**Viral load is recommended as the preferred monitoring approach to diagnose and confirm treatment failure. (strong recommendation, low-quality evidence).**

**If viral load is not routinely available, CD4 count and clinical monitoring should be used to diagnose treatment failure (strong recommendation, moderate-quality evidence).**

**Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/mL (that is, two consecutive viral load measurements within a 3-month interval with adherence support between measurements) after at least 6 months of starting a new ART regimen.**

**Dried blood spot specimens using venous or capillary whole blood can be used to determine the HIV viral load. A threshold of 1000 copies/mL can be used to determine viral failure when using dried blood spot samples, as defined for testing in plasma (conditional recommendation, low-quality evidence)**




**Laboratory monitoring before and after initiating ART**

Clinical assessment and laboratory tests play a key role in assessing individuals following a positive HIV diagnosis to assess for coinfections, noncommunicable diseases (NCDs) and other comorbidities that may have an impact on treatment response.

Limited laboratory testing is also recommended for monitoring the response to treatment and possible toxicity of ARV drugs.

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

| Failure | Definition | Comments |
|---|---|---|
| Clinical failure | **Adults and adolescents**<br>New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition)[a] after 6 months of effective treatment<br>**Children**<br>New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with the exception of TB) after 6 months of effective treatment | The condition must be differentiated from immune reconstitution inflammatory syndrome occurring after initiating ART<br>For adults, certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure[a] |
| Immunological failure | **Adults and adolescents**<br>CD4 count at or below 250 cells/mm$^3$ following clinical failure[b]<br>or<br>Persistent CD4 levels below 100 cells/mm$^3$<br>**Children**<br>*Younger than 5 years*<br>Persistent CD4 levels below 200 cells/mm$^3$<br>*Older than 5 years*<br>Persistent CD4 levels below 100 cells/mm$^3$ | Without concomitant or recent infection to cause a transient decline in the CD4 cell count<br>Current WHO clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure. There is currently no proposed alternative definition of treatment failure and no validated alternative definition of immunological failure |
| Virological failure | Viral load above 1000 copies/mL based on two consecutive viral load measurements in 3 months, with adherence support following the first viral load test | An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed |

*Source: WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection, Second Edition, page 135.*

### 2.3.6.2 Monitoring ARV drug resistance

Current approaches to resistance testing remain too costly and complex for routine use as part of a public health approach, and WHO does not currently recommend routine resistance testing to guide ART regimen selection.

Some countries use resistance testing to inform treatment decisions. WHO recognizes the value of resistance testing for individual patients in such situations, provided that adequate treatment options are available and in-country expertise exists to properly interpret results.

**To inform population-level decision-making, WHO recommends routine surveillance for HIV drug resistance (HIV-DR) in populations initiating ART and in populations on ART for 12 months and more than 48 months. The results of these surveys support the choice of recommended first- and second-line ART, and pre- and post-exposure prophylaxis.**

**Emergence of HIV-DR in treated populations is associated with factors related to patient care (and viral suppression at 12 months), patient behaviour (adherence) and clinic-level and programme management (retention on first-line ART, and procurement and supply management of ARV drugs).**

**Many factors are associated with the emergence of HIV-DR. Broadly, these factors may be divided into three categories: (i) viral factors (such as HIV subtype, replication capacity and pre-existing polymorphisms); (ii) drug-related factors (such as drug potency, pharmacokinetics, drug–drug interactions, tolerance and genetic barrier to resistance); and (iii) programme factors (such as adherence to prescribed ART, drug supply continuity and retention of patients on treatment)**.

Although viral and drug-related factors are often beyond the control of public health authorities or programme managers, the monitoring of ART programme factors can alert ART clinics and national programme planners to situations that may favour population-level virological failure and/or the emergence of resistance. Once such situations have been identified, clinic- or programme-level action may be implemented to optimize patient care, thus minimizing the emergence of preventable HIV-DR.

WHO recommends that prevention of HIV-DR be integrated into national HIV programmes, through the annual monitoring of early warning indicators (EWIs) and through the implementation of HIVDR surveillance.

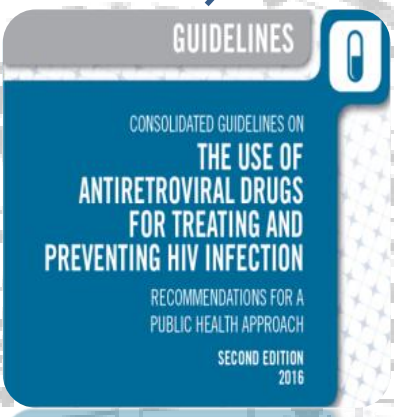
Prescription- or pill-based methods for estimating adherence to ART are objective estimates calculated from routinely captured pharmacy data and have been demonstrated to predict virological and drug-resistance outcomes.

Randomized controlled trials report selection of HIV-DR in at least 70% of patients with virological failure, with some studies documenting no resistance at ART initiation. Numerous studies have documented HIV-DR in substantial proportions of patients with confirmed virological failure.

It should be possible to evaluate the recommended EWIs through routine programme data. Global targets support the indicators. Indicator analysis and action plans based on their results support optimization of HIV treatment and minimize the emergence of HIV-DR.

## 2.3.7 Monitoring of and substitutions for ARV drug toxicities

### *2.3.7.1 Guiding principles*




**GUIDING PRINCIPLES**

- The availability of laboratory monitoring is **not required** for **initiating ART**.
- Symptom-directed laboratory monitoring for safety and toxicity can be used for those receiving ART.

### *2.3.7.2 Major types of ARV toxicities*

## What to do?

**LOOK** for the **different types of toxicities** associated with first-, second- and third-line ARV drugs

| ARV drug | Major types of toxicity | Risk factors | Suggested management |
|---|---|---|---|
| ABC | Hypersensitivity reaction | Presence of HLA-B*5701 allele | Do not use ABC in the presence of HLA-B*5701 allele.<br>Substitute with AZT or TDF. |
| ATV/r | Electrocardiographic abnormalities (PR and QRS interval prolongation) | People with pre-existing conduction system disease<br>Concomitant use of other drugs that may prolong the PR or QRS intervals<br>Congenital long QT syndrome | Use with caution in people with pre-existing conduction disease or who are on concomitant drugs that may prolong the PR or QRS intervals. |
| | Indirect hyperbilirubinaemia (clinical jaundice) | Presence of uridine diphosphate (UDP)-glucuronosyltransferase 1A1*28 (UGT1A1*28) allele | This phenomenon is clinically benign but potentially stigmatizing. Substitute only if adherence is compromised. |
| | Nephrolithiasis | History of nephrolithiasis | Substitute with LPV/r or DRV/r. If boosted PIs are contraindicated and NNRTIs have failed in first-line ART, consider substituting with integrase inhibitors. |
| AZT | Severe anaemia, neutropaenia | CD4 cell count of ≤200 cells/mm³ | Substitute with TDF or ABC.<br>Consider use of low-dose zidovudine *(405)*. |
| | Lactic acidosis or severe hepatomegaly with steatosis<br>Lipoatrophy<br>Lipodystrophy<br>Myopathy | BMI >25 (or body weight >75 kg)<br>Prolonged exposure to NRTIs | Substitute with TDF or ABC. |
| DTG | Hepatotoxicity<br>Hypersensitivity reactions | Hepatitis B or C coinfection<br>Liver disease | If DTG is used in first-line ART, and there are hypersensitivity reactions, substitute with another therapeutic class (EFV or boosted PIs). |
| DRV/r | Hepatotoxicity | Underlying hepatic disease<br>HBV and HCV coinfection<br>Concomitant use of hepatotoxic drugs | Substitute with ATV/r or LPV/r. When it is used in third-line ART, limited options are available.<br>For hypersensitivity reactions, substitute with another therapeutic class. |
| | Severe skin and hypersensitivity reactions | Sulfonamide allergy | |
| EFV | Persistent central nervous system toxicity (such as dizziness, insomnia, abnormal dreams) or mental symptoms (anxiety, depression, mental confusion) | Depression or other mental disorder (previous or at baseline) | For CNS symptoms, dose at night-time. Consider using EFV at a lower dose (400 mg/day) or substitute with NVP or integrase inhibitor (DTG) if EFV 400 mg is not effective in reducing symptoms.<br>For severe hepatotoxicity or hypersensitivity reactions, substitute with another therapeutic class (integrase inhibitors or boosted PIs). |
| | Convulsions | History of seizure | |
| | Hepatotoxicity | Underlying hepatic disease<br>HBV and HCV coinfection<br>Concomitant use of hepatotoxic drugs | |
| | Severe skin and hypersensitivity reactions | Risk factor(s) unknown | |

**Types of toxicities** associated with first-, second- and third-line ARV drugs (continued)

| ARV drug | Major types of toxicity | Risk factors | Suggested management |
|---|---|---|---|
| **EFV** | Gynaecomastia | Risk factor(s) unknown | Substitute with NVP or another therapeutic class (integrase inhibitors or boosted PIs). |
| **ETV** | Severe skin and hypersensitivity reactions | Risk factor(s) unknown | Substitute with another therapeutic class (integrase inhibitors or boosted PIs). |
| **LPV/r** | Electrocardiographic abnormalities (PR and QRS interval prolongation, torsades de pointes) | People with pre-existing conduction system disease<br>Concomitant use of other drugs that may prolong the PR or QRS intervals<br>Congenital long QT syndrome<br>Hypokalaemia | Use with caution in people with pre-existing conduction disease or those on concomitant drugs that may prolong the PR or QRS intervals |
| | Hepatotoxicity | Underlying hepatic disease<br>HBV and HCV coinfection<br>Concomitant use of hepatotoxic drugs | If LPV/r is used in first-line ART for children, substitute with NVP or RAL for children younger than 3 years and EFV for children 3 years and older. ATV can be used for children older than 6 years.<br>If LPV/r is used in second-line ART for adults, and the person has treatment failure with NNRTI in first-line ART, consider integrase inhibitors. |
| | Pancreatitis | Advanced HIV disease, alcohol misuse | |
| | Dyslipidaemia | Cardiovascular risk factors such as obesity and diabetes | Substitute with another therapeutic class (integrase inhibitors). |
| | Diarrhoea | | Substitute with ATV/r, DRV/r or integrase inhibitors. |
| **NVP** | Hepatotoxicity<br>Severe skin rash and hypersensitivity reaction, including Stevens-Johnson syndrome | Underlying hepatic disease<br>HBV and HCV coinfection<br>Concomitant use of hepatotoxic drugs<br>High baseline CD4 cell count (CD4 count >250 cells/mm$^3$ in women or >400 cells/mm$^3$ in men) | If hepatotoxicity is mild, consider substitution with EFV, including in children 3 years and older.<br>For severe hepatotoxicity and hypersensitivity, and in children under the age of 3 years, substitute with another therapeutic class (integrase inhibitors or boosted PIs). |
| **RAL** | Rhabdomyolysis, myopathy, myalgia | Concomitant use of other drugs that increase the risk of myopathy and rhabdomyolysis, including statins | Substitute with another therapeutic class (etravirine, boosted PIs). |
| | Hepatitis and hepatic failure<br>Severe skin rash and hypersensitivity reaction | Risk factors unknown | |

Types of toxicities associated with first-, second- and third-line ARV drugs (continued)

| ARV drug | Major types of toxicity | Risk factors | Suggested management |
|---|---|---|---|
| TDF | Chronic kidney disease<br>Acute kidney injury and Fanconi syndrome | Underlying renal disease<br>Older than 50 years of age<br>BMI <18.5 or low body weight (<50 kg) notably in females<br>Untreated diabetes<br>Untreated hypertension<br>Concomitant use of nephrotoxic drugs or a boosted PI | Substitute with AZT or ABC.<br>Do not initiate TDF at eGFR <50 mL/min, uncontrolled hypertension, untreated diabetes, or presence of renal failure. |
| | Decreases in bone mineral density | History of osteomalacia (in adults) and rickets (in children) and pathological fracture<br>Risk factors for osteoporosis or bone mineral density loss<br>Vitamin D deficiency | |
| | Lactic acidosis or severe hepatomegaly with steatosis | Prolonged exposure to nucleoside analogues<br>Obesity<br>Liver disease | |

ABC abacavir, ATV atazanavir, AZT zidovudine, CNS central nervous system, DRV darunavir, DTG dolutegravir, EFV efavirenz, eGFR estimated glomerular filtration rate, HBV hepatitis B virus, HCV hepatitis C virus, LPV lopinavir, NNRTI non-nucleoside reverse-transcriptase inhibitor, NVP nevirapine, PI protease inhibitor, r ritonavir, RAL raltegravir, TDF tenofovir.

### *2.3.7.3 Special considerations for toxicity monitoring during pregnancy and breastfeeding*

**Safety of efavirenz and tenofovir during pregnancy**

In 2015, updated systematic reviews and meta-analysis showed that data on the safety of EFV and TDF during pregnancy were reassuring, confirming prior reviews conducted for the WHO 2013 Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.

Review of the evidence showed no increased risk in overall congenital anomalies with EFV compared to other ARVs. The risk of neural tube defects associated with EFV remained low (0.05%) and is comparable to the general population in the United States of 0.02–0.2%, confirming studies reviewed for the WHO 2013 Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection.

Review of the evidence showed no increased risk of abnormal pregnancy outcomes such as congenital anomalies, growth, bone health, low or mean birth weight, prematurity, pregnancy loss or miscarriage or other serious maternal adverse reactions with TDF-based ART compared with pregnant women receiving other triple-drug regimens without TDF. The evidence review is consistent with data from the Antiretroviral Pregnancy Registry, which now includes a sufficient number of first-trimester TDF exposures to be able to rule out at least a 1.5-fold increased risk of overall birth defects, with a prevalence of overall birth defects with first-trimester TDF exposure of 2.3%, comparable to the 2.7% prevalence in the general population of the United States. Current human data available suggest that TDF does not increase the risk of major congenital anomalies.

Data on maternal toxicity or infant growth and adverse bone effects associated with TDF exposure remain limited. Only one study directly measured bone mineral density in newborns and found a significant loss of bone mineral density in TDF-exposed newborns compared to those who were not exposed to the drug. However, longitudinal data were not available, and the clinical significance of this finding remains unclear. Although significant differences in anthropometric parameters have not been found in TDF-exposed compared to TDF-unexposed newborns at birth, one study reported slightly lower mean length-for-age-scores in TDF-exposed compared to TDF-unexposed infants at 1 year of age. However, in another study with a follow-up of two years, this difference did not persist.

**Safety of dolutegravir and raltegravir during pregnancy**

There is a lack of data on the safety of INSTIs during pregnancy and breastfeeding. The safety of DTG in pregnancy in particular is not well established, as there are no published safeties or efficacy data on the outcomes of treating women with DTG during pregnancy. Furthermore, calcium or iron supplements frequently used during pregnancy could significantly reduce DTG drug levels (445). Although there are no animal data to suggest that any of the INSTIs have any fetal toxicity, the current update of the Antiretroviral Pregnancy Registry reports only 391 documented INSTI exposures during pregnancy (442). In the absence of well-controlled studies in pregnant women, DTG and RAL should be used only if the perceived benefits outweigh the risk. For practical purposes, in most settings, first-line therapy for pregnant women should continue to be based on drugs for which adequate safety data are available. For these reasons, EFV-based regimens are preferred over DTG-based regimens until more data become available.

**Safety of nevirapine during pregnancy**

Concerns about a higher risk of severe hepatic and skin reactions with NVP compared with EFV were addressed for the 2013 WHO Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. The systematic review conducted at the time suggested that the frequency was increased but no higher than in the general adult population and concluded that NVP needs to be used with caution in pregnant women or women who might become pregnant (294). The higher risk of hepatic and skin reactions with NVP in pregnancy and at higher CD4 counts led to the 2013recommendation favouring EFV as a first-line NNRTI.

**Specific considerations on the safety of ART prior to conception**

Use of ART during pregnancy, particularly when it begins before conception, has been associated in some studies from both high-income and resource-limited countries with increased risk of adverse birth outcomes, such as preterm delivery and low birth weight. In 2015, a systematic review conducted for these guidelines to assess the safety of ART use in terms of pregnancy outcomes compared ART use prior to conception to starting ART during pregnancy Evidence showed an increased risk associated with preconception ART for adverse pregnancy outcomes of preterm delivery (12 studies, low-quality evidence), low birth weight (three studies, moderate-quality evidence), stillbirth (one study, very low-quality evidence), miscarriage (one study, very low-quality evidence), and possible increased risk of pregnancy-induced hypertension and pre-eclampsia (two studies, very low-quality evidence). However, the severity of prematurity and low birth weight were not well delineated in the published literature, with no papers discussing the association of preconception ART with very preterm delivery (<34 weeks gestation) or very low birth weight (<1500 g), which would be expected to have more severe neonatal consequences compared to preterm delivery (34–37 weeks) and low birth weight (1500–2500 g). Although better data on magnitude and impact are needed, the clear benefits of ART use during pregnancy for both child and mother outweigh the risk of adverse reactions. In addition, because pregnancy-induced hypertension and pre-eclampsia have been identified as predictors of pregnancy adverse outcomes, active screening and management of pregnancy-induced hypertension should be prioritized for all high-risk women, including those receiving ART and particularly those receiving ART prior to conception.

#### *2.3.7.4 Drug substitutions for ARV drug toxicity*

Drug regimen or single-agent substitutions may be required to manage drug toxicity and to avoid drug interactions. Delaying substitutions or switches when there are severe adverse drug reactions may cause harm and may affect adherence, leading to drug discontinuation, resistance and treatment failure.

When drug interruptions are required, such as for severe and life-threatening adverse reactions, it is important to consider the various half-lives of ARV drugs. For example, when an NNRTI needs to be discontinued, a staggered approach should be followed, in which the use of the NRTI backbone is prolonged for two to three weeks. Alternatively, the NNRTI could be temporarily substituted with a boosted PI.

### 2.3.8 Key ARV drug interactions

Pharmacological interactions can reduce the efficacy of ART and/or increase ART-related toxicities. Providers should be aware of all drugs that people are taking when ART is initiated, including alternative medicine products such as herbal remedies and dietary supplements as well as new drugs that are added during treatment maintenance.

Management of adverse drug reactions should follow the following principles:

- Prior to starting on ART, the PLHIV should be informed about the adverse drug reactions that may occur and how to react to them. It is essential that the patient can get in contact with a competent health care professional at all times, in particular in the first few weeks after ART is initiated.
- If an adverse drug reaction develops, it should be classified according to severity and the potential for reversibility. Regimens should be switched for patients with treatment-limiting reactions, and those who do not fall into that category should be reassured and carefully monitored.
- Drugs of the same class should preferably be substituted for those provoking the adverse

Adverse drug reactions are common with ARVs and need to be effectively managed.
They can be divided into categories according to:

- Time of onset – early (within the first weeks) or late (after several months or even years of use);
- Frequency – frequent (>10% develop the reaction), common (2–10%) or rare (< 2%);
- Severity – life threatening, severe, moderate, or mild; and

- Spontaneous reversibility – yes (reduced symptoms despite continued use of the ARV), no (once manifested, only discontinuation of the drug will remove the reaction); and required discontinuation – yes (non-reversible reactions irrespective of severity, as well as severe reversible reactions) and no (mild or moderate reversible reactions).

## What to do?

**Key ARV drug interactions and suggested management**

| ARV drug | Key interactions | Suggested management |
|---|---|---|
| AZT | Ribavirin and pegylated-interferon alpha-2a | Substitute AZT with TDF |
| Boosted PI (ATV/r, DRV/r, LPV/r) | Rifampicin | Substitute rifampicin with rifabutin<br>Adjust the dose of LPV/r or substitute with three NRTIs (for children) |
| | Halofantrine and lumefantrine | Use an alternative antimalarial agent |
| | Lovastatin and simvastatin | Use an alternative cholesterol-lowering agent |
| | Hormonal contraceptives | Use alternative or additional contraceptive methods |
| | Methadone and buprenorphine | Adjust methadone and buprenorphine doses as appropriate |
| | Astemizole and terfenadine | Use alternative antihistamine agent |
| | TDF | Monitor renal function |
| | Simeprevir | Use alternative DAA |
| | Ombitasvir + paritaprevir + ritonavir plus dasabuvir | Use alternative DAA |
| DTG | Carbamazepine, phenobarbital and phenytoin | Use alternative anticonvulsant agent |
| | Polyvalent cation products containing Mg, Al, Fe, Ca and Zn | Use DTG at least 2 hours before or at least 6 hours after supplements containing polyvalent cations, including but not limited to the following products: Fe-, Ca-, Mg- or Zn-multivitamin supplements; mineral supplements, cation-containing laxatives and Al-, Ca- or Mg-containing antiacids. Monitor for virological efficacy |
| EFV | Amodiaquine | Use an alternative antimalarial agent |
| | Methadone | Adjust the methadone dose as appropriate |
| | Hormonal contraceptives | Use alternative or additional contraceptive methods to prevent HIV transmission and unintended pregnancies, as EFV may lower efficacy of some long-acting hormonal contraceptives |
| | Astemizole and terfenadine | Use an alternative antihistamine agent |
| | Simeprevir | Use alternative DAA |
| | Ombitasvir + paritaprevir + ritonavir plus dasabuvir | Use alternative DAA |
| NVP | Rifampicin | Substitute NVP with EFV |
| | Methadone | Adjust the methadone dose as appropriate |
| | Astemizole and terfenadine | Use alternative antihistamine agent |
| | Itraconazole and ketoconazole | Use an alternative antifungal agent |
| | Simeprevir | Use alternative DAA |
| | Ombitasvir + paritaprevir + ritonavir plus dasabuvir | Use alternative DAA |

This table was developed using the University of Liverpool's drug interaction charts, which can be found online at www.hiv-druginteractions.org and www.hep-druginteractions.org. A more comprehensive table of ARV drug interactions is available in Annex 13.
AZT zidovudine, ATV atazanavir, DAA direct-acting antiviral (agent), DRV darunavir, DTG dolutegravir, EFV efavirenz, LPV lopinavir, NRTI nucleoside reverse-transcriptase inhibitor, NVP nevirapine, PI protease inhibitor, r ritonavir, TDF tenofovir.

## 2.3.9 What ART regimen to switch to (second- and third-line ART)

### *2.3.9.1 Preferred second-line ART regimens for adults, adolescents, pregnant women and children*

| Population | | Failing first-line regimen | Preferred second-line regimen | Alternative second-line regimens |
|---|---|---|---|---|
| Adults and adolescents | | 2 NRTIs + EFV (or NVP) | 2 NRTIs[b] + ATV/r or LPV/r | 2 NRTIs[b] + DRV/r[c] |
| | | 2 NRTIs + DTG | | |
| Pregnant or breastfeeding women | | 2 NRTIs + EFV (or NVP) | 2 NRTIs[b] + ATV/r or LPV/r | 2 NRTIs[b] + DRV/r |
| Children | Less than 3 years | 2 NRTIs + LPV/r | 2 NRTIs[b] + RAL | Maintain the failing LPV/r-based regimen and switch to 2 NRTIs[b] + EFV at 3 years of age |
| | | 2 NRTIs + NVP | 2 NRTIs[b] + LPV/r | 2 NRTIs[b] + RAL[d] |
| | 3 years to less than 10 years | 2 NRTIs + LPV/r[a] | 2 NRTIs[b] + EFV | 2 NRTIs[b] + RAL[d] |
| | | 2 NRTIs + EFV (or NVP) | 2 NRTIs[b] + LPV/r | 2 NRTIs[b] + ATV/r[d] |

[a] ATV/r can be used as an alternative PI for children older than 3 months of age.

[b] If ABC+ 3TC or TDF + 3TC (or FTC) was used in the first-line failing regimen, AZT + 3TC should be used in second-line and vice versa.

[c] RAL + LPV/r can be used as an alternative second-line regimen in adults and adolescents.

[d] DRV/r can be used as an alternative PI option in special situations.

3TC lamivudine, ABC abacavir, ATV atazanavir, AZT zidovudine, DTG dolutegravir, EFV efavirenz, FTC emtricitabine, LPV lopinavir, NRTI nucleoside reverse-transcriptase inhibitor, NVP nevirapine, PI protease inhibitor, r or RTV ritonavir, RAL raltegravir.

### *2.3.9.2 Preferred second-line ART regimens for adults and adolescents*

| Target population | Preferred second-line regimen[a] | |
|---|---|---|
| Adults and adolescents | If d4T or AZT was used in first-line ART | TDF + 3TC (or FTC) + ATV/r or LPV/r[b,c] |
| | If TDF was used in first-line ART | AZT + 3TC + ATV/r or LPV/r[b,c] |
| Pregnant or breastfeeding women | Same regimens as recommended for adults and adolescents | |
| HIV and TB coinfection | If rifabutin is available | Standard PI-containing regimens as recommended for adults and adolescents |
| | If rifabutin is not available | Same NRTI backbones as recommended for adults and adolescents plus double-dose LPV/r (that is, LPV/r 800 mg/200 mg twice daily)[d] |
| HIV and HBV coinfection | AZT + TDF + 3TC (or FTC) + (ATV/r or LPV/r)[b] | |

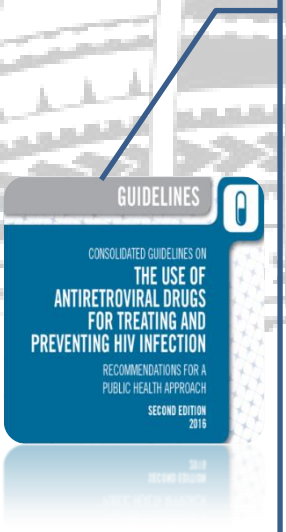
[a] ABC and didanosine (ddI) can be used as NRTI back-up options but add complexity and cost without clinical advantages.

[b] DRV/r can be used as an alternative PI option.

[c] RAL + LPV/r can be used as an alternative second-line regimen (conditional recommendation, low-quality evidence).

[d] Standard LPV/r and RTV-boosted saquinavir (SQV/r) doses with an adjusted dose of RTV (that is, LPV 400 mg/ RTV 400 mg or SQV 400 mg /RTV 400 mg twice daily) can be used as alternative options.

3TC lamivudine, ATV atazanavir, AZT zidovudine, d4T stavudine, FTC emtricitabine, LPV lopinavir, NRTI nucleoside reverse-transcriptase inhibitor, NVP nevirapine, PI protease inhibitor, r or RTV ritonavir, TDF tenofovir.




**RECOMMENDATIONS**

- Second-line ART in adults should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a ritonavir-boosted protease inhibitor (PI).
- The following sequence of second-line NRTI options is recommended:

*– After failure on a TDF + 3TC (or FTC)-based first-line regimen, use AZT + 3TC as the NRTI backbone in second-line regimens.*

*– After failure on an AZT or d4T + 3TC-based first-line regimen, use TDF + 3TC (orC) as the NRTI backbone in second-line regimens.*

- Use of NRTI backbones as a fixed-dose combination is recommended as the preferred approach (strong recommendation, moderate-quality evidence).
- Heat-stable fixed-dose combinations of ATV/r and LPV/r are the preferred boosted PI options for second-line ART (strong recommendation, moderate quality)
- Heat-stable fixed-dose combinations of DRV/r can be used as an alternative boosted PI option for second-line ART (conditional recommendation, low-quality evidence).
- A combination of RAL plus LPV/r can be used as an alternative second-line ART regimen (conditional recommendation, low-quality evidence).

### *2.3.9.3 Preferred second-line ART regimens for children*

Summary of recommended first- and second-line ART regimens for children:

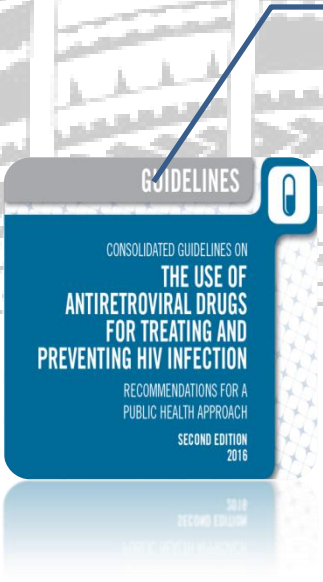
| | Children (including adolescents) | First-line ART regimen | Second-line ART regimen |
|---|---|---|---|
| LPV/r-based first-line regimen | Younger than 3 years | ABC + 3TC + LPV/r | AZT or ABC+ 3TC + RAL[a] |
| | | AZT + 3TC + LPV/r | |
| | 3 years and older | ABC + 3TC + LPV/r | AZT + 3TC + EFV or RAL |
| | | AZT + 3TC + LPV/r | ABC or TDF[b] + 3TC + EFV or RAL |
| NNRTI-based first-line regimen | All ages | ABC + 3TC + EFV (or NVP) | AZT + 3TC + ATV/r or LPV/r[c] |
| | | TDF[b] + 3TC (or FTC) + EFV (or NVP) | |
| | | AZT + 3TC + EFV (or NVP) | ABC or TDF + 3TC[c] (or FTC) + ATV/r or LPV/r[c] |

[a] If RAL is not available, no change is recommended unless in the case of advanced clinical disease progression or lack of adherence specifically due to poor palatability of LPV/r. In this case, switching to a second-line NVP-based regimen should be considered. Based on approval of the use of EFV in children less than 3 years, an EFV-based regimen could be considered as an alternative. However, more data are needed to inform how best to use EFV in this population.

[b] TDF may be given only to children older than 2 years.

[c] ATV/r can be used as an alternative to LPV/r in children older than 3 months. However, the limited availability of suitable formulations for children younger than 6 years, the lack of an FDC and the need for separate administration of the RTV booster should be considered when choosing this regimen.

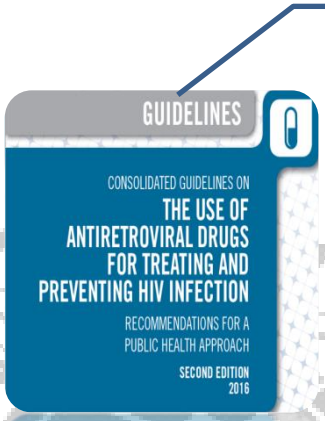
3TC lamivudine, ABC abacavir, ATV atazanavir, AZT zidovudine, EFV efavirenz, FTC emtricitabine, LPV lopinavir, NVP nevirapine, r ritonavir, RAL raltegravir, TDF tenofovir.




**RECOMMENDATIONS**

- After failure of a first-line LPV/r-based regimen, children younger than 3 years should be switched to a RAL-based second-line regimen (conditional recommendation, very low-quality evidence).
- **After failure of a first-line LPV/r-based regimen, children older than 3 years should be switched to a second-line regimen containing two NRTIs plus EFV or RAL (conditional recommendation, very low-quality evidence).**
- After failure of a first-line NNRTI-based regimen, children should be switched to a boosted PI-based regimen. LPV/r or ATV/r are preferred (conditional recommendation, very low-quality evidence).
- After failure of a first-line regimen of ABC or TDF + 3TC (or FTC), the preferred
- NRTI backbone option for second-line ART is AZT + 3TC (strong recommendation, low-quality evidence).
- After failure of a first-line regimen containing AZT or d4T + 3TC (or FTC), the preferred NRTI backbone option for second-line ART is ABC or TDF + 3TC (or FTC) (strong recommendation, low-quality evidence).

### *2.3.9.4 Preferred third-line ART*




**RECOMMENDATIONS**

- National programmes should develop policies for third-line ART (conditional recommendation, low-quality evidence).
- Third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as INSTIs and second-generation NNRTIs and PIs (conditional recommendation, low-quality evidence).
- Patients on a failing second-line regimen with no new ARV drug options should continue with a tolerated regimen (conditional recommendation, very low-quality evidence).

Summary of sequencing options for first-, second- and third-line ART regimens in adults, adolescents, pregnant women and children

| Population | First-line regimens | Second-line regimens | Third-line regimens |
|---|---|---|---|
| Adults and adolescents (>10 years) | 2 NRTIs + EFV | 2 NRTIs + ATV/r or LPV/r[a] | DRV/r [b] + DTG[c] (or RAL) ± 1–2 NRTIs |
| | | 2 NRTI + DRV/r[b] | |
| | 2 NRTIs + DTG | 2 NRTIs + ATV/r or LPV/r | DRV/r[b] + 2 NRTIs ± NNRTI |
| | | 2 NRTI + DRV/r | Optimize regimen using genotype profile |
| Pregnant or breastfeeding women | 2 NRTIs + EFV | 2 NRTIs + ATV/r or LPV/r[a] | DRV/r[b] + DTG[c] (or RAL) ± 1–2 NRTIs |
| | | 2 NRTIs + DRV/r[b] | |
| Children (0–10 years | 2 NRTI + LPV/r | If less than 3 years: 2 NRTIs + RAL[d] | RAL (or DTG)[f] + 2 NRTIs<br>DRV/r[g] + 2 NRTIs<br>DRV/r[g] + RAL (or DTG)[f] ± 1–2 NRTIs |
| | | If older than 3 years: 2 NRTIs + EFV or RAL | |
| | 2 NRTI + EFV | 2 NRTIs + ATV/r[e] or LPV/r | |

[a] RAL + LPV/r can be used as an alternative second-line regimen in adults and adolescents.

[b] In PI-experienced patients, the recommended DRV/r dose should be 600 mg/100 mg twice daily.

[c] Safety and efficacy data on the use of DTG in adolescents younger than 12 years and pregnant women are not yet available.

[d] If RAL is not available, no change is recommended unless in the presence of advanced clinical disease progression or lack of adherence, specifically because of poor palatability of LPV/r. In this case, switching to a second-line NVP-based regimen should be considered. Based on approval of the use of EFV in children less than 3 years of age, an EFV-based regimen could be considered as an alternative. However, more data are needed to inform how best to use EFV in this population (*see* Table 4.18).

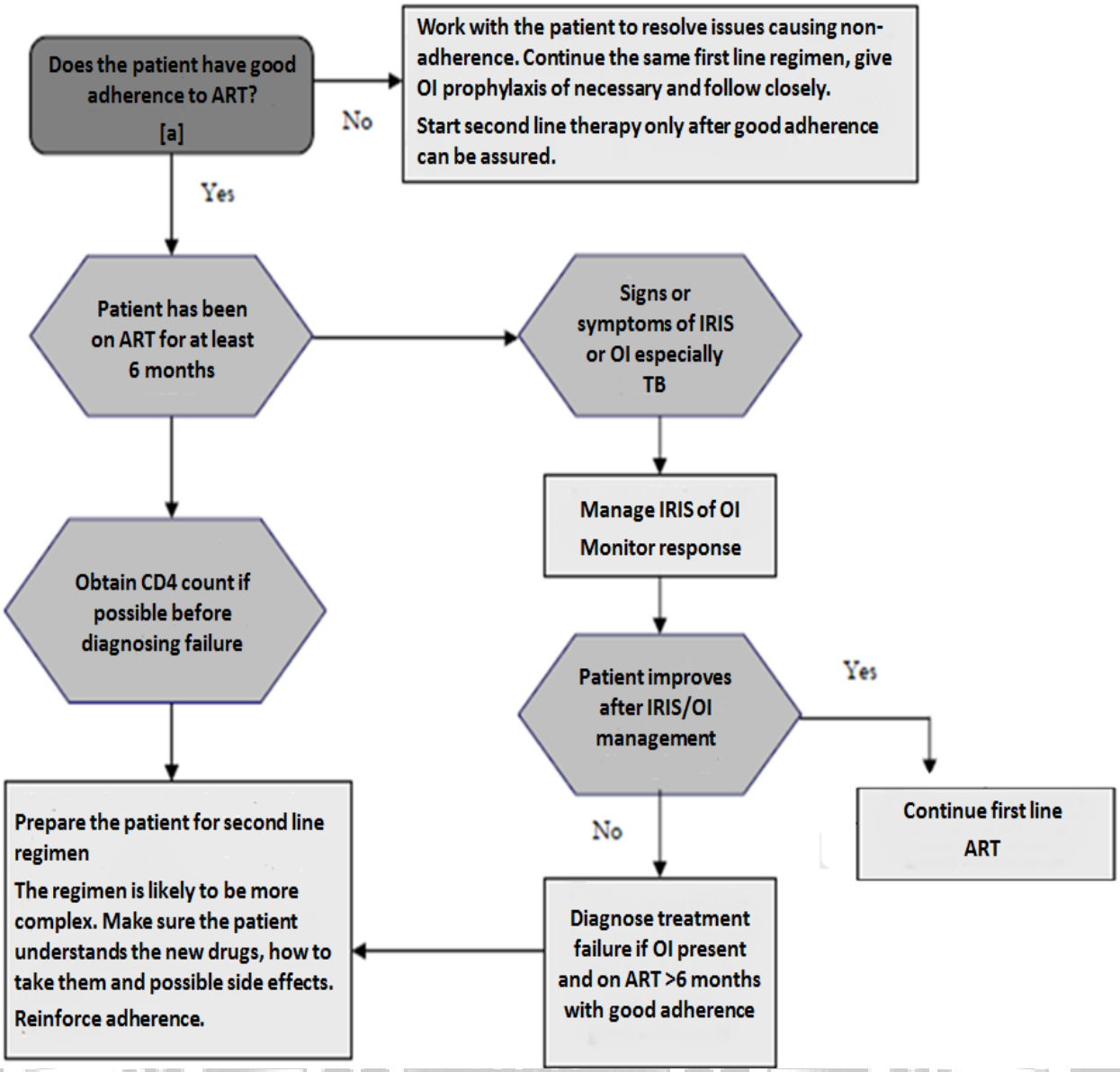
[e] ATV/r can be used as an alternative to LPV/r in children older than 3 months of age. However, the limited availability of suitable formulations for children younger than 6 years of age, the lack of an FDC and the need for separate administration of RTV booster should be considered when choosing this regimen.

[f] RAL can be used in children failing PI-based second-line treatment when DTG is not available and when RAL has not been not used in a previous regimen. DTG is currently approved only for children 12 years and older; however, studies are ongoing to determine dosing in younger children, and approval for lower age groups is expected in the near future

[g] DRV/r should not be used in children younger than 3 years of age.

ATV atazanavir, DRV darunavir, DTG dolutegravir, EFV efavirenz, LPV lopinavir, NNRTI non-nucleoside reverse-transcriptase inhibitor, NRTI nucleoside reverse-transcriptase inhibitor, NVP nevirapine, PI protease inhibitor, r ritonavir, RAL raltegravir.

*Fig 3: ART failure and when to switch therapy*




### 2.3.10 Monitoring ARV drug resistance

Current approaches to resistance testing remain too costly and complex for routine use as part of a public health approach, and WHO does not currently recommend routine resistance testing to guide ART regimen selection.

Some countries use resistance testing to inform treatment decisions. WHO recognizes the value of resistance testing for individual patients in such situations, provided that adequate treatment options are available and in-country expertise exists to properly interpret results.

To inform population-level decision-making, WHO recommends routine surveillance for HIV drug resistance (HIV-DR) in populations initiating ART and in populations on ART for 12 months and more than 48 months. The results of these surveys support the choice of recommended first- and second-line ART, and pre- and post-exposure prophylaxis.

Emergence of HIV-DR in treated populations is associated with factors related to patient care (and viral suppression at 12 months), patient behaviour (adherence) and clinic-level and programme management (retention on first-line ART, and procurement and supply management of ARV drugs).

Many factors are associated with the emergence of HIV-DR. Broadly, these factors may be divided into three categories: (i) viral factors (such as HIV subtype, replication capacity and pre-existing polymorphisms); (ii) drug-related factors (such as drug potency, pharmacokinetics, drug–drug interactions, tolerance and genetic barrier to resistance); and (iii) programme factors (such as adherence to prescribed ART, drug supply continuity and retention of patients on treatment). Although viral and drug-related factors are often beyond the control of public health authorities or programme managers, the monitoring of ART programme factors can alert ART clinics and national programme planners to situations that may favour population-level virological failure and/or the emergence of resistance. Once such situations have been identified, clinic- or programme-level action may be implemented to optimize patient care, thus minimizing the emergence of preventable HIV-DR.

WHO recommends that prevention of HIV-DR be integrated into national HIV programmes, through the annual monitoring of early warning indicators (EWIs) and through the implementation of HIVDR surveillance.

Prescription- or pill-based methods for estimating adherence to ART are objective estimates calculated from routinely captured pharmacy data and have been demonstrated to predict virological and drug-resistance outcomes.

Randomized controlled trials report selection of HIV-DR in at least 70% of patients with virological failure, with some studies documenting no resistance at ART initiation. Numerous studies have documented HIV-DR in substantial proportions of patients with confirmed virological failure.

It should be possible to evaluate the recommended EWIs through routine programme data. Global targets support the indicators. Indicator analysis and action plans based on their results support optimization of HIV treatment and minimize the emergence of HIV-DR.

### 2.3.11. Diagnosis and management of Immune Reconstitution Inflammatory Syndrome (IRIS)

Immune reconstitution inflammatory syndrome (IRIS), also known as immune restoration disease, refers to a disease or pathogen-specific inflammatory response in HIV-infected patients that can be triggered after:

- Institution or re-initiation of ARV therapy;
- Change to more active ARV therapy.

Frequency: Ten percent (10%) in all patients initiating ART and up to 25% among patient initiating ART with CD4 cell count less than 50 cells / $mm^3$

Timing: Typically within 2-12 weeks of initiation of ART but may present later.

Signs and symptoms:

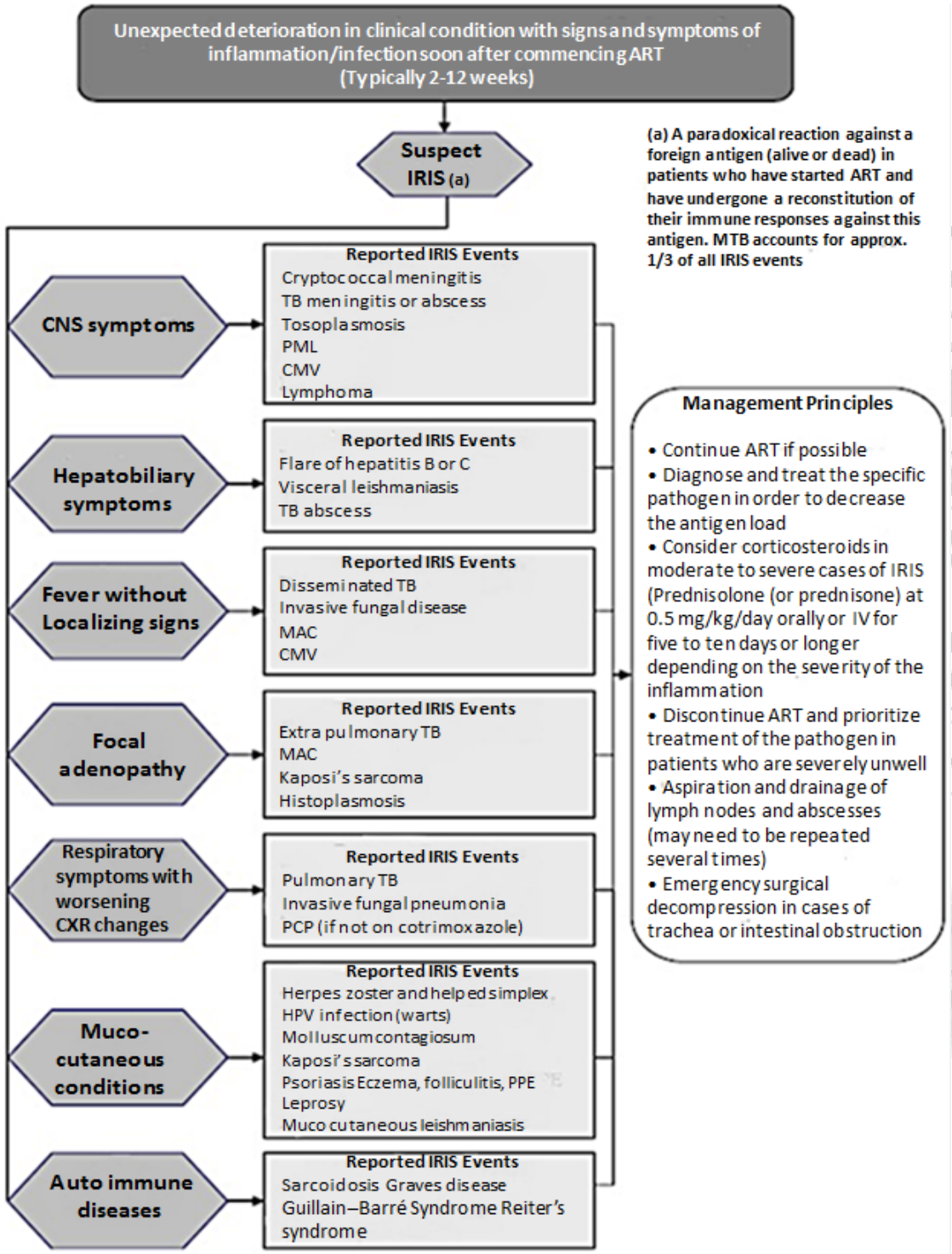
- Unexpected deterioration of clinical status after commencing ART.
- Unmasking of subclinical infection such as TB, this may be presented as new active disease.
- Worsening of co-existing infection such as a flare of hepatitis B or C.

Most common IRIS events: Sixty percent (60%) are of TB, MAC or Cryptococcal disease

Management:

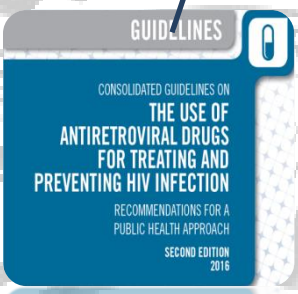
- IRIS may be mild and resolve without treatment.
- Continue ART if possible. Treat unmasked OI, such as TB.
- This may mean temporary interruption of ART until the patient is stable on TB drugs, then reintroduction of ART.
- Corticosteroid treatment to suppress exaggerated inflammatory response may be indicated.
- For example, an acute hepatic flare where viral hepatitis co-infection is known or suspected.
- If the patient is taking nevirapine, clinical hepatitis and/or rising hepatic enzymes in associated with rash and fever is more likely to be due to nevirapine than IRIS and switching to efavirenz is recommended.
- Prednisone 0.5mg/kg/day for 5-10 days is suggested in moderate to severe cases of IRIS.

**Fig 4: Suspected IRIS management**




*Source: Myanmar Guidelines for the Clinical Management of HIV Infection in Adults and Adolescents. 2007, page 13.*

### 2.3.12 Infant feeding in the context of HIV




**RECOMMENDATION**

National or subnational health authorities should decide whether health services will principally counsel and support mothers known to be HIV infected to either breastfeed and receive ARV interventions or avoid all breastfeeding.

In settings where national authorities have decided that maternal and child health services will principally promote and support breastfeeding and antiretroviral interventions as the strategy that will most likely give infants born to mothers known to be HIV infected the greatest chance of HIV-free survival, mothers known to be infected with HIV should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for the first 12 months of life.

Breastfeeding should then stop only once a nutritionally adequate and safe diet without breast milk can be provided (strong recommendation, high-quality evidence for the first 6 months; low-quality evidence for the recommendation of 12 months).

*Due to adherence issues, clinicians in Samoa have recommended to discourage HIV positive mothers from breastfeeding and to focus instead on supporting their access to synthetic milk products.*

## [v]2.4 Managing co-infections and co-morbidities

Various coinfections, comorbidities and other concomitant health conditions are common among people living with HIV and have implications for their treatment and care, including the timing and choice of ARV drugs. This section provides a brief overview of the most common and important conditions. It summarizes selected key recommendations from existing WHO guidelines and related materials, focusing on the screening, prophylaxis and timing of ART for these conditions; it does not cover their management in detail. Sources are provided for relevant, previously published recommendations. These recommendations were not reviewed during the 2015 guideline development process.

Evidence reviews were undertaken in 2015 with regard to presumptive treatment for tuberculosis (TB), depression and cardiovascular disease in people living with HIV. Although no formal recommendation on presumptive TB treatment is made, guidance is provided. New recommendations are presented for the screening and management of cardiovascular disease and depression in people living with HIV.

### *2.4.1 Prevention, screening and management of common coinfections*

| **What to do?** |
| --- |
| **1. Co-trimoxazole prophylaxis** |
| Co-trimoxazole prophylaxis is recommended for adults (including pregnant women) with severe or advanced HIV clinical disease (WHO stage 3 or 4) and/or with a CD4 count ≤350 cells/mm3 (strong recommendation, moderate-quality evidence).<br>• In settings where malaria and/or severe bacterial infections (SBIs) are highly prevalent, co-trimoxazole prophylaxis should be initiated regardless of CD4 cell count or WHO stage (conditional recommendation, moderate-quality evidence).<br>• Co-trimoxazole prophylaxis may be discontinued in adults (including pregnant women) with HIV who are clinically stable on ART, with evidence of immune recovery and viral suppression (conditional recommendation, low-quality evidence).<br>• In settings where malaria and/or severe bacterial infections are highly prevalent, co-trimoxazole prophylaxis should be continued regardless of CD4 cell count or WHO clinical stage (conditional recommendation, moderate-quality evidence). |

- Routine co-trimoxazole prophylaxis should be given to all HIV-infected patients with active TB disease regardless of CD4 cell count (strong recommendation, high-quality evidence).
- Co-trimoxazole prophylaxis is recommended for infants, children, and adolescents with HIV, irrespective of clinical and immune conditions. Priority should be given to all children less than 5 years old regardless of CD4 cell count or clinical stage, and children with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) and/or those with CD4 ≤350 cells/mm3 (strong recommendation, high-quality evidence).

- In settings where malaria and/or severe bacterial infections are highly prevalent, co-trimoxazole prophylaxis should be continued until adulthood, irrespective of whether ART is provided (conditional recommendation, moderate-quality evidence).
- In settings with low prevalence for both malaria and bacterial infections, co-trimoxazole prophylaxis may be discontinued for children 5 years of age and older who are clinically stable and/or virally suppressed on ART for at least 6 months and with a CD4 count >350 cells/mm3 (strong recommendation, very low-quality evidence).
- Co-trimoxazole prophylaxis is recommended for HIV-exposed infants from 4 to 6 weeks of age and should be continued until HIV infection has been excluded by an age-appropriate HIV test to establish final diagnosis after complete cessation of breastfeeding (strong recommendation, very low-quality evidence).

Source: *Guidelines on post-exposure prophylaxis and the use of co-trimoxazole prophylaxis for HIV-related infections among adults, adolescents and children: recommendations for a public health approach – December 2014 supplement to the 2013 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2013 (http://www.who.int/hiv/ pub/guidelines/arv2013/arvs2013upplement_dec2014/en).*

## Criteria for initiation and discontinuation of co-trimoxazole prophylaxis

| Population | Recommendation | |
|---|---|---|
| | **Criteria for initiation of co-trimoxazole prophylaxis** | **Criteria for discontinuation of co-trimoxazole prophylaxis** |
| **Adults (including pregnant women) with HIV** | • Initiate in all with severe /advanced HIV disease (WHO clinical stage 3 or 4) or CD4 count ≤350 cells/mm³[a]<br>• **In settings with a high prevalence of malaria and/or severe bacterial infections**[b]: initiate in all regardless of WHO clinical stage or CD4 cell count | • May be discontinued in those who are clinically stable,[c] with evidence of immune recovery and/or viral suppression on ART[d,e]<br>• In settings with a high prevalence of malaria and/or severe bacterial infections: should be continued |
| **Children and adolescents with HIV** | • Initiate in all regardless of WHO clinical stage or CD4 cell count<br>• **As a priority:** (1) initiate in all less than 5 years of age, regardless of WHO clinical stage or CD4 cell count; (2) initiate in all older than 5 years of age and with severe /advanced HIV disease (WHO clinical stage 3 or 4) or CD4 count ≤350 cells/mm³ | • **In settings with a high prevalence of malaria and/or severe bacterial infections:** should be continued until adulthood<br>• **In settings with a low prevalence of both malaria and severe bacterial infections:** may be discontinued for those older than 5 years of age who are clinically stable, with evidence of immune recovery[f] and/or viral suppression on ART |
| **HIV-exposed uninfected infants** | • Initiate in all starting at 4–6 weeks after birth | • Until the risk of HIV transmission ends or HIV infection is excluded[g] |
| **People living with HIV and TB**[h] | • Initiate in all with active TB regardless of CD4 cell count | • Until criteria for discontinuation in adults or children are met |

[a] This group is also prioritized for ART initiation (as recommended for ART in the 2013 WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection).

[b] Settings where malaria and/or SBIs are highly prevalent includes low- and middle-income countries with high rates of mortality among children less than 5 years old (http://www.who.int/gho/child_health/mortality/mortality_under_five/en).

[c] Clinically stable adults are defined as those individuals on ART for at least one year without any new WHO clinical stage 2, 3 or 4 events.

[d] CD4 count >350 cells/mm³, with viral load suppression, is considered indicative of immune recovery (some countries may adopt a threshold of CD4 count >500 cells/mm³).

[e] WHO recognizes that in settings with a low prevalence of malaria and SBIs where CTX is used primarily as prophylaxis for some AIDS-associated opportunistic infections (PCP and toxoplasmosis), guidelines exist for discontinuing CTX in adults with HIV infection when there is evidence of viral suppression and immune recovery at CD4 cell counts >200 cells/mm³ and being on ART for at least 1 year.

[f] Parameter for immune recovery in children when >5 years old: CD4 cell count >350 cells/mm³, with viral load suppression.

[g] In settings with a high malaria transmission, consideration may be given to extend CTX prophylaxis in HIV-exposed uninfected infants up to 2 years of age.

[h] Recommendation maintained from: WHO policy on collaborative TB/HIV policy activities: guidelines for national programmes and other stakeholders. Geneva: WHO; 2012.

## What to do?

### 2. Tuberculosis

- Xpert MTB/RIF should be used rather than conventional microscopy, culture and drug susceptibility testing (DST) as the initial diagnostic test in adults and children suspected of having HIV-associated TB or multidrug resistant TB (strong recommendation, adults: high-quality evidence; children: very low-quality evidence).
- Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test for cerebrospinal fluid specimens from patients suspected of having TB meningitis (strong recommendation, very low-quality evidence).
- Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture or histopathology) for testing specific non-respiratory specimens (lymph nodes and other tissues) from patients suspected of having extrapulmonary TB (conditional recommendation, very low-quality evidence).

Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB in adults and children:

*WHO policy update. Geneva: World Health Organization; 2013 (http://www.who.int/tb/laboratory/xpert_policyupdate/en).*

- Except as specifically described below for people with HIV infection with low CD4 counts or who are seriously ill,1 urine lateral flow (LF)-LAM should not be used for the diagnosis of TB (strong recommendation, low-quality evidence).
- LF-LAM may be used to assist in the diagnosis of active TB in adult inpatients living with HIV, with signs and symptoms of TB (pulmonary and/or extrapulmonary), who have a CD4 cell count less than or equal to 100 cells/mm3 or people living with HIV who are seriously ill regardless of CD4 count or with unknown CD4 count (conditional recommendation, low quality evidence).
- LF-LAM should not be used as a screening test for active TB (strong recommendation, low quality evidence).

Source: *The use of lateral flow urine lipoarabinomannan assay (LF-LAM) for the diagnosis and screening of active tuberculosis.in people living with HIV: Policy guidance. Geneva: World Health Organization; 2015 (http://apps.who.int/iris/bitstream/10665/193633/1/9789241509633_eng.pdf).*

- TB patients with known positive HIV status and TB patients living in HIV-prevalent settings should receive at least 6 months of a rifampicin-containing treatment regimen.
- The optimal dosing frequency is daily during the intensive and continuation phases (strong
- recommendation, high-quality evidence).

Source: *WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders. Geneva: World Health Organization; 2012 http://www.who.int/tb/publications/2012/tb_hiv_policy_9789241503006/en).*

## What to do?

### 3. Isoniazid preventive therapy (IPT)

- Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT (strong recommendation, moderate-quality evidence).
- Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive at least 6 months of IPT as part of a comprehensive package of HIV care. IPT should be given to such individuals regardless of the degree of immunosuppression and also to those on ART, those who have previously been treated for TB and pregnant women (strong recommendation, high-quality evidence).
- Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test status and among whom active TB disease has been safely ruled out should receive at least 36 months of IPT. IPT should be given to such individuals regardless of whether or not they are receiving ART. IPT should also be given irrespective of the degree of immunosuppression, history of previous TB treatment, and pregnancy (conditional recommendation, moderate-quality evidence).
- Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB. Children living with HIV who have poor weight gain, fever or current cough or contact history with a TB case may have TB and should be evaluated for TB and other conditions. If the evaluation shows no TB, they should be offered IPT preventive therapy regardless of their age (strong recommendation, low-quality evidence).
- Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening and have no contact with a TB case should receive 6 months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care (strong recommendation, moderate-quality evidence).

Note:

- Seriously ill is defined as four danger signs: respiratory rate >30/min, temperature >39°C, heart rate >120/min and unable to walk unaided.
- 2 This recommendation also applies to adults living with HIV who are outpatients with signs and symptoms of TB (pulmonary and/or extrapulmonary) who have a CD4 cell count less

than or equal to 100 cells/mm3, or who are seriously ill regardless of CD4 count or with unknown CD4 count, based on the generalization of data from inpatients. This recommendation also applies to children living with HIV, with signs and symptoms of TB (pulmonary and/or extrapulmonary) based on the generalization of data from adults, while acknowledging that data are very limited and that there are concerns regarding low specificity of the LF-LAM assay in children.

- In children living with HIV who are less than 12 months of age, only those who have contact with a TB case and who are evaluated for TB (using investigations) should receive 6 months of IPT if the evaluation shows no TB disease (strong recommendation, low-quality evidence).
- All children living with HIV, after successful completion of treatment for TB, should receive IPT for an additional 6 months (conditional recommendation, low-quality evidence).

*Source: Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living withHIV in resource-constrained settings. Geneva: World Health Organization; 2011 (http://apps.who.int/iris/bitstream/10665/44472/1/9789241500708_eng.pdf).*

# What to do?

### 4. Multi drug resistant TB and HIV

- Antiretroviral therapy is recommended for all patients with HIV and drug-resistant TB requiring second-line anti-tuberculosis drugs irrespective of CD4 cell count, as early as possible (within the first 8 weeks) following initiation of anti-tuberculosis treatment (strong recommendation, very low-quality evidence).

Source: *Guidelines for the programmatic management of drug-resistant tuberculosis: 2011 update. Geneva: World Health Organization; 2011 (http://apps.who.int/iris/bitstream/10665/44597/1/9789241501583_eng.pdf).*

## What to do?

### 5. Cryptococcal disease

#### 5.1 Diagnosis of cryptococcal disease

- Prompt lumbar puncture with measurement of CSF opening pressure and rapid CSF cryptococcal antigen (CrAg) assay or rapid serum CrAg (either LA or LFA) is the preferred diagnostic approach. (Strong recommendation, moderate-quality evidence).

#### 5.2 Prevention of cryptococcal disease

- The routine use of antifungal primary prophylaxis for cryptococcal disease in HIV-infected adults, adolescents and children with a CD4 count less than 100 cells/mm3, and who are CrAg negativeor where CrAg status is unknown, is not recommended prior to ART initiation, un less a prolonged delay in ART initiation is likely (strong recommendation, high-quality evidence).
- The use of routine serum or plasma CrAg screening in ART-naive adults, followed by preemptive antifungal therapy if CrAg-positive to reduce the development of cryptococcal disease, may be considered prior to ART initiation in:a) patients with a CD4 count less than 100 cells/mm3; andb) where this population also has a high prevalence (>3%)1 of cryptococcal anti-genaemia (conditional recommendation, low-quality evidence).
- The use of routine CrAg screening in ART-naive adolescents and children with pre-emptive antifungal therapy if CrAG positive, prior to ART initiation is not recommended (conditional recommendation, low-quality evidence).

## What to do?

*Induction, consolidation, and maintenance antifungal treatment regimens*

- For the induction phase of treatment in HIV-infected adults, adolescents and children with cryptococcal disease (meningeal and disseminated non-meningeal), the following two-week antifungal regimens are recommended in order of preference:
    - Amphotericin B + flucytosine (strong recommendation, high-quality evidence).
    - Amphotericin B + fluconazole (strong recommendation, moderate-quality evidence).
    - Amphotericin B short course (5–7 days) + high dose fluconazole (to complete 2 weeks of induction) when a minimum package of pre-emptive hydration and electrolyte replacement and toxicity monitoring and management cannot be provided for the full 2-week induction period (conditional recommendation, low-quality evidence).
    - Fluconazole high dose + flucytosine, when amphotericin B is not available (conditional recommendation, low-quality evidence).
    - Fluconazole high dose alone, when amphotericin B is not available (conditional recommendation, low-quality evidence).

- For the consolidation phase treatment of HIV infected adults, adolescents and children with cryptococcal meningitis or disseminated non-meningeal disease, the following 8-week antifungal regimen is recommended:
    - Fluconazole 400–800mg/day after a two-week induction with amphotericin B regimen (6–12 mg/kg/day up to 400–800 mg/day if below 19 years).
    - Fluconazole 800 mg/day after induction treatment with short-course amphotericin B or fluconazole-based induction regimen (fluconazole 12 mg/kg/day up to 800 mg/day if below 19 years) (strong recommendation, low-quality evidence).

- For maintenance treatment of cryptococcal disease in HIV-infected adults, adolescents and children, oral fluconazole 200 mg daily (6 mg/kg/day up to 200 mg/day if below 19 years) is

recommended (strong recommendation, high-quality evidence).

- For localized non-meningeal disease, or in patients with isolated serum CrAg positivity (where active cryptococcal meningitis has been excluded). Fluconazole 800 mg/day (or 12 mg/kg/ day if below 19 years) for two weeks, then 400 mg/day (or 6 mg/kg/day up to 400–800 mg/day if below 19 years) for 8 weeks, and continued maintenance with fluconazole 200 mg/day is recommended. The optimal antifungal regimen in this population remains to be determined (conditional recommendation, low-quality evidence).

## What to do?

***Prevention, monitoring and management of amphotericin B toxicity***

- In HIV-infected adults receiving amphotericin B–containing regimens for treatment of cryptococcal disease, a minimum package of toxicity prevention, monitoring and management is recommended to minimize the serious amphotericin B–related toxicities of hypokalaemia and nephrotoxicity (strong recommendation, moderate-quality evidence).

***Timing of ART initiation***

- Immediate ART initiation is not recommended in HIV-infected patients with cryptococcal meningitis due to the high risk of IRIS, which may be life-threatening (conditional recommendation, low-quality evidence).
- In HIV-infected adults, adolescents and children with a recent diagnosis of cryptococcal meningitis, ART initiation should be deferred until there is evidence of a sustained clinical response to antifungal therapy, and after 4 weeks of induction and consolidation treatment with amphotericin B–containing regimens combined with flucytosine or fluconazole, or after 4–6 weeks of treatment with a high-dose oral fluconazole induction and consolidation regimen (conditional recommendation, low-quality evidence).

***Discontinuation of azole maintenance treatment (secondary prophylaxis)***

- In HIV-infected adults and adolescents with successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal maintenance treatment is recommended based on the following criteria:

  a. If HIV viral load monitoring is available: when patients are stable and adherent to ART and antifungal maintenance therapy for at least 1 year and have a CD4 cell count of greater than

or equal to 200 cells/mm3 (two measurements 6 months apart) (strong recommendation, low-quality evidence). b. If HIV viral load monitoring is available: when patients are stable and adherent to ART and antifungal maintenance treatment for at least one year and with CD4 cell count of greater than or equal to 100 cells/mm3 (two measurements 6 months apart) and a suppressed viral load (conditional recommendation, low-quality evidence).

- In children aged less than two years with successfully treated cryptococcal disease, antifungal maintenance treatment should NOT be discontinued (strong recommendation, low-quality evidence).

- In HIV-infected children aged between 2 and 5 years with successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal treatment maintenance is recommended if the child is stable and adherent to ART and antifungal maintenance treatment for at least one year and with a CD4 cell count percentage greater than 25% or absolute count greater than 750 cells/mm3 (two measurements 6 months apart) (strong recommendation, low-quality evidence).

- Maintenance therapy for cryptococcal disease should not be discontinued in children less than two years (strong recommendation, low-quality evidence).

- Maintenance treatment for cryptococcal disease should be restarted if CD4 count drops to 100 cells/mm3, or below in HIV-infected adults and adolescents (or CD4 cell count less than or equal to 25% or 750 cells/mm3 in children aged between 2 and 5 years), or if a WHO stage 4 clinical event occurs, irrespective of patient age (strong recommendation, low-quality evidence).

Source: *Rapid advice: diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children. Geneva: World Health Organization; 2011 www.who.int/hiv/pub/cryptococcal disease2011/en).*

## What to do?

### 6. Hepatitis B and C

**Chronic hepatitis B virus (HBV) infection** affects 5–20% of the 36 million people living with HIV worldwide, and hepatitis C virus (HCV) affects 5-15%, rising to 90% among people who inject drugs. The burden of coinfection is highest in low- and middle-income countries, particularly in South-East Asia and sub-Saharan Africa for hepatitis B.

Viral hepatitis is an increasing cause of morbidity and mortality among people living with HIV in some regions, including among people on ART. A comprehensive approach includes prevention, HBV and HCV testing, hepatitis B vaccination and treatment and care for people with HIV who are co-infected with hepatitis B and/or hepatitis C.

WHO recommends that adults, adolescents and children with chronic hepatitis B and clinical evidence of cirrhosis (or cirrhosis based on the non-invasive APRI test score >2 in adults) should be treated regardless of alanine aminotransferase (ALT) levels, hepatitis B e antigen (HBeAg) status or HBV DNA levels. WHO guidelines for the prevention, care and treatment of people with chronic hepatitis B infection *(63)* provide recommendations on who should receive HBV treatment and recommend the use of NRTIs or entecavir for this treatment.

The recommended NRTI drugs for ART – TDF with 3TC or FTC – are active against HBV. However, of these, only TDF is recommended in the WHO HBV guidelines for patients with HBV mono-infection. Furthermore, treatment of HIV-HBV co-infection without the use of TDF in the regimen may lead to flares of hepatitis B due to ART-associated immune reconstitution. Similarly, treatment discontinuation, especially of 3TC, has been associated with HBV reactivation, ALT flares and, in rare cases, hepatic de-compensation. If ARV drugs need to be changed because of HIV drug resistance or toxicity, then TDF with 3TC or FTC should be continued together with the new ARV drugs.

The risk of HBV infection may be higher in HIV-infected adults. All people newly diagnosed with HIV should therefore be screened for hepatitis B surface antigen (HBsAg) and vaccinated if non-immune.

**Hepatitis C virus (HCV)-related liver disease** progresses more rapidly in people co-infected with HIV. Treatment of HCV is therefore a priority for people with HIV/HCV co-infection.

The decision to initiate treatment for HCV is more complex than in those with HCV mono-infection, because response rates are lower, the risk of potential toxicities is higher and treatment is complicated by a high pill burden, overlapping toxicities and interactions between drugs used for treating HCV

and HIV. In general, clinical stabilization of HIV disease with ART is advisable prior to starting treatment for HCV, especially in people with advanced immunosuppression (CD4 count below 200 cells/mm3). The newer, all-oral direct-acting antiviral HCV regimens (DAAs) produce similar rates of sustained virological response regardless of HIV status.

Careful consideration of drug–drug interactions is important to avoid toxicity and to ensure the efficacy of regimens used to treat both HIV and HCV. Further information regarding choice of anti-HCV regimen, including potential drug–drug interactions with ARV drugs, is provided in the 2014 WHO Global guidelines for the screening, care and treatment of persons living with hepatitis C infection, HCV treatment using older regimens (pegylated interferon and ribavirin) generally yielded low rates of success among HCV/HIV co-infected patients, but outcomes for HCV therapy with DAAs in people with HIV coinfection are comparable to those with HCV mono-infection. Updated WHO guidelines for the treatment of people with HCV infection, including management of HCVin HIV-co-infected patients, will be released in 2016. The newer all-oral DAAs also have fewer drug–drug interactions than earlier interferon-based regimens.

The decision to start ART among people co-infected with HCV should follow the same principles as in HIV mono-infection. Potential harmful effects of ARV drugs include their hepatotoxic effects. However, the highest rates of hepatotoxicity have been observed with ARV drugs that are no longer commonly used or recommended, including stavudine, didanosine, nevirapine or full-dose ritonavir (600 mg twice a day). For most HIV/HCV co-infected people, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury.

## What to do?

### 7. Malaria

- Key interventions to control malaria include early diagnosis, prompt and effective treatment with artemisinin-based combination therapies and use of insecticide-treated nets and indoor residual insecticide spraying to control the vector mosquitoes. In areas of stable malaria transmission, people with HIV (as for the general population) should routinely use insecticide-treated bed-nets or have access to indoor residual spraying to reduce their exposure to malaria. Intermittent preventive treatment during pregnancy and seasonal malaria chemoprophylaxis are also recommended in areas of high transmission.
- Treatment or intermittent preventive treatment with sulfadoxine pyrimethamine should not be given to patients with HIV or HIV-exposed infants who are taking CTX prophylaxis.
- People with HIV who develop malaria should receive prompt, effective antimalarialtreatment.
- Parasitological confirmation should be undertaken for all suspected malariacases using either

microscopy or a rapid diagnostic test. However, absence or delay of parasitological diagnosis should not delay the immediate start of antimalarial treatment.

- Some drugs used to treat malaria and ARV drugs may share toxicities (particularlysulfa-based drugs) and may have important pharmacokinetic interactions (especially artemesinins, lumefantrine, NNRTIs and PIs). For this reason, people receiving treatment for both HIV and malaria should be monitored closely for adverse drug reactions, and people with HIV receiving AZT or EFV should, if possible, avoid amodiaquine-containing artemisinin-based combination regimens because of the increased risk of neutropenia in combination with AZT and hepatotoxicity in combination with EFV.
- In settings where malaria and/or severe bacterial infections are highly prevalent, co-trimoxazole prophylaxis should be initiated regardless of CD4 cell count or WHO stage (conditional recommendation, moderate-quality evidence).

**Good practice statement**

In people who have HIV and uncomplicated P. falciparum malaria, avoid artesunate + sulfadoxine-pyrimethamine if they are being treated with cotrimoxazole and avoid artesunate + amodiaquine if they are being treated with efavirenz or zidovudine.

Intermittent preventive treatment for malaria in pregnancy should not be provided in addition to CTX prophylaxis.

*Source: Guidelines for the treatment of malaria, third edition. Geneva: World Health Organization; 2015 (http://www.who.int/malaria/publications/atoz/9789241549127/en).*

## What to do?

### 8. STI and cervical cancer

**REFER to the National STI Guidelines, 2016**

**REFER to the following guidelines:**

- Comprehensive cervical cancer control: a guide to essential practice, second edition. Geneva: World Health Organization; 2014 (http://www.who.int/reproductivehealth/publications/cancers/cervical-cancer-guide/en).
- Treatment of cervical intraepithelial neoplasia 2–3 and adenocarcinoma in situ: cryotherapy, large

loop excision of the transformation zone, and cold knife conization: WHO guidelines. Geneva: World Health Organization; 2014 (http://www.who.int/ reproductive health/publications/cancers/treatment_CIN_2-3/en).

- Human papillomavirus vaccines: WHO position paper. *Wkly Epidemiol Rec. 2009;84:118–31 (www.who.int/wer/2009/wer8415.pdf).*

## What to do?

### 9. Vaccines for PLHIV

Immunizations are an important component of the HIV care package in many international guidelines, and people living with HIV should be assessed for eligibility for vaccination at all stages of care.

In general, HIV-exposed infants, children and adolescents with HIV should receive all vaccines under routine vaccination according to recommended national immunization schedules *(84,85)*. In adults living with HIV, immunization against some diseases such as influenza, hepatitis B, pneumococcal disease and tetanus are frequently indicated. Other immunizations may be recommended based on age, risk factors or travel plans.

Source: For currently recommended vaccination schedules and detailed guidance on immunization for all age groups, see WHO recommendations for routine immunization – summary tables at www.who.int/immunization/policy/immunization_tables/en/index.html.

## What to do?

### 10. HIV-related skin and oral conditions

HIV infection increases the prevalence and severity of skin and oral diseases, especially when the person's CD4 count declines below 200 cells/mm3. As a result, skin and oral conditions affect up to 90% of adults and children with HIV in resource-limited settings. Adverse drug reactions of the skin are also 100 times more common in people living with HIV compared to the general population, and their prevalence increases as immunodeficiency worsens. Skin and oral manifestations of HIV infection can aggravate stigma in some societies, as physical signs in the form of skin diseases, such as papular pruritic eruptions, which suggest the possibility of HIV infection, could make the affected person more vulnerable to discrimination.

Certain systemic diseases, such as Kaposi sarcoma, may initially be noted on the skin and may require urgent ART to reduce mortality. Others, while not always a major cause of mortality, can be a source of severe morbidity through, for example, itching that provokes scratching, secondary infections, disfigurement, sleep disturbance and psychological stress. In the case of candidiasis, it can cause pain on swallowing, limiting a person's ability to take ARV drugs.

In 2014, WHO released guidelines for the treatment of common HIV-associated skin and oral conditions in low- and middle-income countries. These guidelines are applicable for all adults, pregnant women, adolescents and children living with HIV and recommend HIV testing for all those with unknown HIV status presenting with the discussed skin conditions. If the HIV status is known, they should be evaluated for initiation of ART.

**ART is the initial treatment of choice for a number of these conditions (e.g. Kaposi sarcoma, papular pruritic eruption, eosinophilic folliculitis, molluscum contagiosum).**

**Additional resources**

Guidelines on the treatment of skin and oral HIV-associated conditions in children and adults. Geneva: World Health Organization; 2014 *(http://apps.who.int/iris/ bitstream/10665/136863/1/9789241548915_eng.pdf?ua=1&ua=1).*

## 2.4.2 Prevention, screening and management of other co-morbidities and chronic care for people living with HIV

### *2.4.2.1 Assessment and management of noncommunicable diseases*

**What to do?**

#### 2.4.2.1.1 General

REFER to the WHO essential NCD interventions (WHO PEN)

WHO has defined a package of essential NCD interventions (WHO PEN) and published recommendations on assessment and management of the major NCDs from the primary care level to the district hospital level. The interventions are mainly focused on assessment and management of CVD risk, including high blood pressure, type 2 diabetes, chronic respiratory diseases (asthma and COPD) and early identification of breast and cervical cancer. More information and additional guidance on WHO PEN and management of NCDs are available in the following resources:

- Package of essential non-communicable (PEN) disease interventions for primary health care in low-resource settings. Geneva: World Health Organization; 2010
- *(www.who.int/ cardiovascular_diseases/publications/pen2010/en).*

- Prevention and control of non-communicable diseases: guidelines for primary health care in low-resource settings. Geneva: World Health Organization; 2012 (http://apps.who.int/iris/bitstream/10665/76173/1/9789241548397_eng.pdf).

#### 2.4.2.1.2 Assessment and management of cardiovascular diseases

Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population (conditional recommendation, very low-quality evidence). The WHO PEN protocol targets the following populations for CVD screening: age >40 years, smokers, people with known hypertension or diabetes mellitus, waist circumference >90 cm in women and >110 cm in men and family history of diabetes mellitus or premature CVD. See more about PEN at www.who.int/cardiovascular_diseases/ publications/ pen2010/en.

**Good practice statement**

Strategies for the prevention and risk reduction of cardiovascular diseases by addressing modifiable factors such as high blood pressure, smoking, obesity, unhealthy diet and lack of physical activity should be applied to all people living with HIV.

## What to do?

### 2.4.2.2 Assessment and management of depression in people living with HIV

Assessment and management of depression should be included in the package of HIV care services for all individuals living with HIV (conditional recommendation, very low-quality evidence).

## What to do?

### 2.4.2.3 Drug use and drug use disorders

People living with HIV who use drugs may experience a range of disorders related to drug use, including drug dependence, intoxication, withdrawal and overdose. Injecting drug use is associated with a range of diseases and infections, including viral hepatitis, TB, septicaemia and bacterial endocarditis, in addition to HIV.

WHO, the United Nations Office on Drugs and Crime (UNODC) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) recommend a comprehensive package of nine interventions for HIV prevention, treatment and care for people who inject drugs; these are needle and syringe programmes, OST, HIV testing and counselling, ART, preventing and treating STIs, condom programmes, targeted behaviour change communication, preventing and treating viral hepatitis and preventing, diagnosing and treating TB.

## What to do?

### 2.4.2.4 Nutritional care and support

*Nutrition for adults and adolescents living with HIV*

- Low energy intake combined with increased energy demands due to HIV infection and related infections may lead to HIV-related weight loss and wasting. In addition, altered metabolism, reduced appetite and higher incidence of diarrhoea may lower nutrient intake and absorption and lead to nutrient losses.
- These effects may all be compounded in low-income and food-insecure contexts. Low body mass in adults (body mass index less than 18.5 kg/m2) and weight loss and wasting in children are all independent risk factors for HIV disease progression and mortality.
- Nutritional assessment (anthropometry, clinical and dietary assessment), counselling and support should be an integral component of HIV care and conducted at enrolment in care and monitored across the care continuum.
- Malnourished HIV-infected patients, especially in food-insecure contexts, may require food supplements in addition to ART to support nutritional recovery. Weight loss or failure to regain or maintain a healthy weight at any stage of HIV infection and/or while on ART should trigger further assessment and appropriate interventions.

NOTE: WHO is revising recommendations for nutritional care and support of adolescents and adults living with HIV, including pregnant and lactating women.

*Nutrition for children living with HIV*

- Nutritional assessment is essential to identify malnutrition and growth faltering early. Infants and children should undergo initial nutritional assessment (evaluation of nutritional status, diet and symptoms) and then be weighed and have height measured at each visit, and monitored with reference to WHO or national growth curves.
- Growth monitoring should also be integrated into the assessment of ART response *(179)*. If poor growth is identified, then further assessment should be performed to determine the cause, and plan an appropriate response. The 2009 guidelines for an integrated approach to the nutritional care of children living with HIV provide details of nutritional interventions.

Additional guidance

- Nutrition assessment, education, counselling and support for adolescents and adults living with

HIV: A programming guide. Food and nutrition in the context of HIV and TB. Geneva: World Food Programme, PEPFAR, USAID, UNAIDS 2014. (http://reliefweb.int/sites/reliefweb.int/files/resources/wfp271543.pdf).

- Guidelines on HIV and infant feeding 2010: principles and recommendations for infant feeding in the context of HIV and a summary of evidence. Geneva: World Health Organization; 2010 http://whqlibdoc.who.int/publications/2010/9789241599535_eng.pdf).

*Guidelines for an integrated approach to the nutritional care of HIV-infected children(6 months–14 years): handbook. Preliminary version for country introduction. Geneva:World Health Organization; 2009 (http://whqlibdoc.who.int/publications/2009/9789241597524_eng_Handbook.pdf).WHO, FAO. Nutritional care and support for people living with HIV/AIDS: a training course. Geneva: World Health Organization; 2009 (www.who.int/nutrition/publications/hivaids/9789241591898/en/index.html).*

## What to do?

### 2.4.2.5 General care

Countries should establish a package of general HIV care interventions, in addition to ART, for people living with HIV to reduce HIV transmission, prevent illness and improve their quality of life. General care includes basic HIV prevention, promoting the health of people living with HIV, and screening, prophylaxis and management of HIV-related co-infections and comorbidities. WHO has produced summary guidance on general care and prevention interventions, and recommends a package of 13 prevention interventions for adults and adolescents living with HIV in resource-limited settings. These are (1) psychosocial counselling and support; (2) disclosure and partner notification; (3) CTX prophylaxis; (4) TB counselling, screening and preventive therapy; (5) preventing common fungal infections; (6) treatment of STIs and supporting reproductive health needs, including prevention of and screening for cervical cancer; (7) preventing malaria (CTX, bed-nets and particularly preventing malaria among pregnant women); (8) the use of vaccines for the prevention of pneumococcal disease, influenza, hepatitis B and yellow fever; (9) provision of adequate nutrition; (10) family planning services; (11) prevention of mother-to-child HIV transmission; (12) needle and

syringe programmes for people who inject drugs; and (13) water, sanitation and hygiene.

A general care package will vary according to the epidemic type, populations affected and prevalence of co-infections, other comorbidities and health conditions. Table 5.2 provides an overview of the elements of a general care package for people living with HIV. In the era of universal treatment for all people with HIV, the time between HIV diagnosis, enrolment into care and initiation of ART may be addressed in one visit or in an expedient manner to reduce loss to follow-up and provide life-saving ART as soon as possible.

Overview of key elements of general care over the continuum of HIV care for people living with HIV.

| Service | At HIV diagnosis | At enrolment into care | At initiation of ART | Stable while receiving ART | At treatment failure and switching of ART regimen |
|---|---|---|---|---|---|
| **General care** | | | | | |
| **WHO clinical staging**<br>Past and current HIV- related conditions | ✔ | ✔ | ✔ | | |
| **Preparing people for ART** | ✔ | ✔ | ✔ | | |
| **Preparing, assessing and supporting adherence** | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Current medications** | | ✔ | ✔ | ✔ | ✔ |
| **Pregnancy status**<br>Family planning and contraception | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Support for disclosure and partner notification** | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Risk reduction counselling and combination HIV prevention approaches** | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Assessing, preventing and managing noncommunicable diseases** | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Screening for and managing mental health problems and substance use**<br>**Psychosocial counselling and support** | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Managing pain and symptoms** | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Nutritional assessment and counselling** | ✔ | ✔ | ✔ | ✔ | ✔ |
| **Nutritional, growth and development assessment in children and adolescents**<br>Infant and child feeding | ✔ | ✔ | ✔ | ✔ | ✔ |

Overview of key elements of general care over the continuum of HIV care for people living with HIV (continued).

| Service | At HIV diagnosis | At enrolment into care | At initiation of ART | Stable while receiving ART | At treatment failure and switching of ART regimen |
|---|---|---|---|---|---|
| **Preventing and treating coinfections** | | | | | |
| Co-trimoxazole preventive therapy | ✔ | ✔ | ✔ | ✔ | ✔ |
| Intensified TB case-finding | ✔ | ✔ | ✔ | | ✔ |
| Isoniazid preventive therapy | | ✔ | ✔ | | |
| Screening for cryptococcal infection and fungal prophylaxis | | ✔ | ✔ | | |
| Screening for hepatitis B and C | | ✔ | ✔ | | ✔ |
| Malaria prevention (insecticide-treated bed-nets and prophylaxis) | ✔ | ✔ | ✔ | ✔ | ✔ |
| Screening for sexually transmitted infections | ✔ | ✔ | ✔ | ✔ | ✔ |
| Prevention of and screening for cervical cancer | | ✔ | ✔ | ✔ | ✔ |
| Assessing for vaccine-preventable diseases | ✔ | ✔ | ✔ | ✔ | ✔ |

# CHAPTER 3

# SERVICE DELIVERY

## CHAPTER THREE: SERVICE DELIVERY

This chapter provides guidance in three service delivery areas:

**1. Differentiated care:**

- ✓ addressing the diversity of needs of people in care
- ✓ community ARV drug delivery approaches.

**2. Recommendations to strengthen the continuum of treatment and care:**

- ✓ linkage from HIV testing to enrolment in care
- ✓ retention
- ✓ adherence
- ✓ frequency of clinic visits and medication pickup
- ✓ task shifting
- ✓ decentralization
- ✓ integration
- ✓ adolescent-friendly health services.

**3. Considerations for continuity and high quality of service delivery:**

- ✓ quality service delivery
- ✓ ensuring a stable supply chain of ARV drugs
- ✓ laboratory and diagnostic services.

## 3.1 Approaches for service delivery

In order to help increase number of PLHIV accessing early diagnosis and treatment, quality and efficiency of HIV testing should be improved through integration of HIV testing services where relevant (TB clinics, Antenatal Clinic (ANC), Family Planning (FP) and Adolescent Reproductive Health (ARH) clinics).3.1.1 Differentiated care

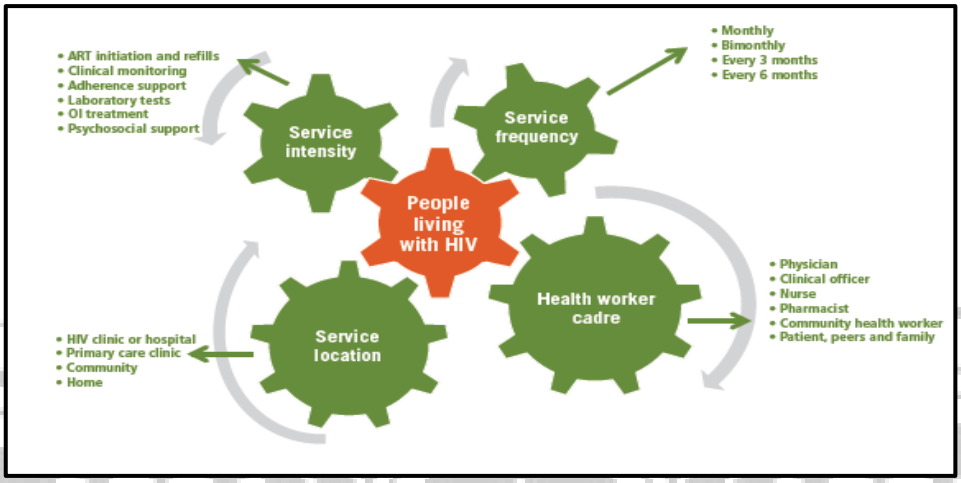
### *3.1.1 Differentiated care*

The care package elements for people living with HIV are a minimum and may be expanded according to the epidemic, clinical setting and health-care system. These packages are further supported by the differentiated care framework, which proposes the delivery of care in facilities for those who need clinic-based services, with less frequent clinical contact for those who are stable. Differentiating between the service needs of those who are unwell – either because they present late for care or due to treatment failure – and those who are stable on ART, and determining where and how those services are to be delivered, are key to maximizing treatment outcomes and efficiencies. A number of national HIV programmes have already adopted differentiated approaches to care as they scale up ART.

**Diversity of care needs for people living with HIV.**

| People living with HIV | Care package elements |
|---|---|
| People presenting when well | Adherence and retention support |
| People with advanced disease | Clinical package to reduce mortality and morbidity |
| Stable individuals | Reduced frequency of clinic visits and community ART delivery models |
| Unstable individuals | Adherence support, viral load testing, switch to second- or third-line ART if indicated, monitoring for HIV drug resistance (HIV-DR) |

The **differentiated care framework is characterized by four delivery components**: (i) the types of services delivered; (ii) the location of service delivery; (iii) the provider of services; and (iv) the frequency of services. How these components are combined into a service delivery framework will vary across countries and populations, but the common intention should be to improve acceptability and care outcomes.




**Two key groups of people** require specific approaches that will involve different resource requirements – people who present late to care and people who are stable on ART. To support differentiated care approaches for these two groups, the following WHO consensus definitions and related package of care were reached in a Delphi survey of experts.

**People with advanced disease** are defined as those presenting to care with a CD4 count below 200 cells/mm3 or WHO disease stages 3 and 4. The package of care for these people should include the following: rapid initiation of ART (once the risk of immune reconstitution inflammatory syndrome [IRIS]2 is ruled out); systematic screening for Cryptococcus antigen; screening and treatment for tuberculosis (TB) or isoniazid preventive treatment (IPT) as indicated;3 screening for toxoplasmosis and co-trimoxazole (CTX) prophylaxis; and intensive follow-up.

**Stable individuals** are defined as those who have received ART for at least one year and have no adverse drug reactions that require regular monitoring, no current illnesses or pregnancy, are not currently breastfeeding and have good understanding of lifelong adherence and evidence of treatment success (i.e. two consecutive viral load measurements below 1000 copies/mL). In the absence of viral load monitoring, risingCD4 cell counts or CD4 counts above 200 cells/mm3, an objective adherence measure,

can be used to indicate treatment success. The package of care for stable individuals can include the following:

- less frequent (3–6-monthly) clinic visits;
- less frequent (3–6-monthly) medication pickup;

• community-based care; and

• cessation of CD4 count monitoring if viral load testing is available.

While less frequent clinic visits are recommended for stable individuals, rapidly growing children (0–5 years old) and adolescents will need to be monitored more frequently for treatment dosing/weight changes and adherence support.

### 3.1.2 Models of community delivery

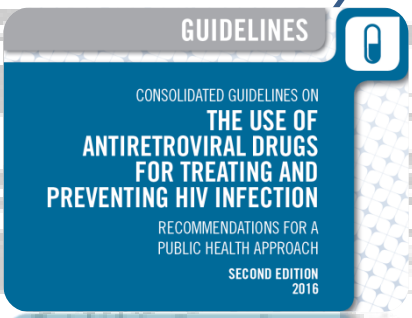
**Summary of strategies for alternative community delivery of long-term ART**

Health service driven → Patient driven

| Key objective | Appointment spacing and fast-track ARV refill | At enrolment into care | | Community ART distribution points | Community ART groups |
|---|---|---|---|---|---|
| | | Facility-based clubs | Community-based clubs | | |
| **Patient perspective** | | | | | |
| Reduce costs (time and transport) | Yes | Yes | Yes | Yes | Yes |
| Increase peer support | No | Yes | Yes | Yes | Yes |
| Enhance community participation | No | Potentially | Potentially | Potentially | Yes |
| **Health-care perspective** | | | | | |
| Reduce workload | | | | | |
| Nurse | Yes | Yes | Yes | Yes | Yes |
| Pharmacist | Yes | Yes | No | Yes | Yes |
| Counsellor/health-care worker/peer supporter | N/A | No | No | No | No |
| Maintain and improve health care | | | | | |
| Retention | Yes | Yes | Yes | Yes | Yes |
| Improve self-management of patients | Yes | Yes | Yes | Yes | Yes |

Moving towards community-based testing, community ART delivery will be explored once facility-based testing and treatment and support services has been fully established in key areas in Samoa.

### 3.1.3 Linkage from HIV testing to enrolment in care




**RECOMMENDATIONS**

Following an HIV diagnosis, a package of support interventions should be offered to ensure timely linkage to care for all people living with HIV (strong recommendation, moderate-quality evidence).

**The following interventions have demonstrated benefit in improving linkage to care** following an HIV diagnosis:

- ✓ streamlined interventions to reduce time between diagnosis and engagement in care, including (i) enhanced linkage with case management, (ii) support for HIV disclosure, (iii) patient tracing, (iv) training staff to provide multiple services and (v) streamlined services (moderate-quality evidence);
- ✓ peer support and navigation approaches for linkage (moderate-quality evidence); and
- ✓ quality improvement approaches using data to improve linkage (low-quality evidence).

### 3.1.4 Retention in care

Programmes should provide community support for people living with HIV to improve retention in HIV care (strong recommendation, low-quality evidence).

The following community-level interventions have demonstrated benefit in improving retention in care:

- package of community based interventions (children low-quality and adults very low-quality evidence)
- adherence clubs (moderate-quality evidence)
- extra care for high-risk people (very low-quality evidence).

### 3.1.5 Adherence

Adherence support interventions should be provided to people on ART (strong recommendation, moderate-quality evidence).

The following interventions have demonstrated benefit in improving adherence and viral suppression:

- peer counsellors (moderate-quality evidence)

- mobile phone text messages (moderate-quality evidence)
- reminder devices (moderate-quality evidence)
- cognitive-behavioural therapy (moderate-quality evidence)
- behavioural skills training/medication adherence training (moderate-quality evidence)
- fixed-dose combinations and once-daily regimens (moderate-quality evidence)

**Key Elements of treatment adherence counselling**

• Establishing trusting relationship with health workers

• Providing necessary information and advice

• Encouraging peer participation and help identify treatment support persons/organizations

• Developing individual treatment plan fitting ART into patient's lifestyle/daily events and identifying treatment reminders

• Assessing readiness and commitment of patients for ART. Readiness to commence ART may be assessed by:

- past ability to attend regular clinic visits and not miss appointments
- past ability to take OI prophylaxis, such as cotrimoxazole
- past ability to complete full course of TB therapy
- adequate understanding

• Treatment adherence should be strict and adherence to recommended regimens should be greater than 95% to avoid resistance. This means that missing more than **3 doses per month** is associated with increased risk of drug resistance and failure

• If regular dose are missed or late, reinforce adherence counselling. Enlist community outreach teams and PLHIV peer support groups as appropriate

• Treatment has to be continued for life

• Timing of drug intake is critical (e.g. drugs taken twice daily must be taken every 12 hours +/- one hour).

• Missed doses can be taken up to 6 hours in a BID regimen. If > 6 hours late, skip dose and take next normal dose.

• Some drugs are taken with food, some drugs are taken on an empty stomach, and some require an increased intake of water.

• Drug side effects have to be understood and explained to the patient in advance of commencing ART

• People on ART need to continue to use condoms regularly and practice safe injecting use

• Other medications, including herbal products, may interact with ART. Patients need careful counselling about which medications are allowed and which are not permitted with their ART

• Regular clinic attendance for monitoring of efficacy and adherence is essential

• If patient cannot make clinic appointment, they need to call or make home visit

[6]A durable favorable response to ART requires strict adherence to the indicated dosing schedule from day one of ART initiation. By strict adherence is implied that the total daily intake of the prescribed doses of medicine is maintained at all times. Low or insufficient adherence has consequences for the patients, public health and national economies, as follows.

- Their future treatment options may be reduced, as insufficient adherence leads to the selection of virus-carrying, drug-related resistance mutations.
- Once a virus has acquired a sufficient number of such mutations to make it non-susceptible to a given drug, it is unlikely that the person will ever again be able to use the drug.
- When viral resistance mutations appear they often mean that the virus is not just resistant to the drug(s) in the regimen but also to other drugs in the same class(cross resistance), which may further reduce future drug options.
- The selection for resistant viruses leads to increased probability of such viruses being transmitted to other people . Transmitted drug resistant virus reduces the choice of active first-line drugs and, if resistance testing prior to ART initiation is not performed, impairs the response to first-line ART.
- The presence of resistant strains will result in increased use of second-line, third-line and salvage regimens, which are in general more expensive than first-line regimens.
- Low adherence also means a higher risk of disease progression , resulting in higher costs for treating opportunistic infections.
- It is the patient's responsibility to ensure reliable intake of the prescribed medication, and it is the responsibility of the provider prescribing the medication to ensure that the patient understands why optimal adherence is critically important, and to provide the necessary support to optimize the chances of full adherence.

Health care workers should identify possible factors that might lead to poor treatment adherence and try to address them accordingly.

It is the patient who determines when to take the medicine. It has proven impossible to reliably predict who will have suboptimal adherence based on demographic or social characteristics, and individual adherence rates also vary over time. Most PLHIV under treatment will exhibit low adherence at some time.

[6]Patient evaluation and antiretroviral treatment for adults and adolescents. Clinical Protocol for the WHO European Region (2012 revision).

**Barriers to adherence include:**

• Illicit drug and alcohol use (may impair regular intake of all medication)

• Poor diet

• religious beliefs

• fear of disclosing hiv status through routine medications

• fear of adverse drug reactions and doubts about the necessity of medication

• psychiatric conditions, including depression

• lack of access to art (including difficulty accessing health care service)

• pill fatigue

• incarceration

**Methods to support adherence include:**

• ongoing education on ART and adherence

• prompt response to patients' misconceptions

• regular evaluation of patients' commitment to ART

• peer interventions

• regular assessment of mental health problems

• assessing behavioural skills needed for adherence

• contacting specialized social care services and other institutions.

**Role of health care workers:**

Health care providers should clearly understand adherence and its role in the development of resistance

when providing adherence support. Professionals working in the area of HIV/AIDS require continuous

education in adherence issues. There are several strategies that health care workers should apply to increase adherence.

- Every HIV treatment centre should have a written and regularly reviewed adherence strategy.
- Health professionals need to be engaged in multidisciplinary adherence support programmes
- Exploring patient preferences for involvement may act as a catalyst to adherence.
- Adherence services should be offered to all PLHIV, taking into account the varying degrees of adherence that they all show over the course of treatment.
- Adherence support should be continued for second-line and salvage regimens. Viral failure usually reflects poor adherence, and hence is a key point for reinforcing the requirements for adherence and support interventions.

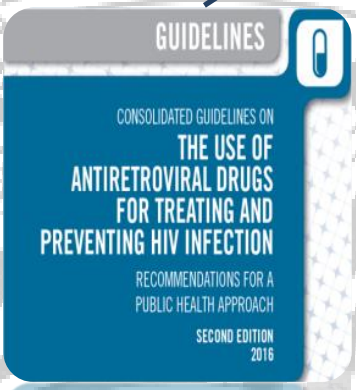
- As maintaining optimal adherence is a continuous process and not a single event, support must be offered when starting ART, changing ART and as a part of routine follow-up.
- Providers must ensure that PLHIV have sufficient understanding of HIV, the relationship between adherence and resistance and potential adverse drug reactions. Verbal information should be supported by written information.
- Pill diaries, pill charts, medication containers, electronic reminders and enlistment of family and friends as reminders can all be recommended.
- Adherence to ART is improved where PLHIV view their relationship with their doctor and other health care providers positively.
- Early follow-up (e.g. via telephone) should occur two days after initiating or changing a regimen, to evaluate whether the patient needs more information or has unregistered problems.
- When interviewing PLHIV about adherence, encourage dialogue and use open-ended question (e.g. “Please tell me how you have taken the medication during the past week?”)
- Partnership between clinics and community-based organizations can improve the uptake of information, especially among hard-to-reach populations and some ethnic groups.
- Continuous access to ART should be provided to the patient at all times once initiated.

Some important tips to support adherence:

- adjusting the regiment to lifestyle patterns such as eating, sleeping and working;
- assessing individual preferences for pill size, formulation, burden, dietary restrictions, etc.;
- showing PLHIV the pills prior to regimen selection;
- educating about adverse reactions prior to prescribing a drug (type of reaction, when it may emerge,
- the potential for reversibility with continued intake, how to reduce symptoms, how to react if drug
- reactions occur (i.e. contacting the treatment centre for advice, never ceasing the regimen without
- prior consultation with the treatment centre, etc.).
- dispensing medication in small amounts at frequent intervals once ART is first initiated, which can
- facilitate opportunities to address adherence problems before they lead to resistance; limiting treatment disruptions and misuse; utilizing QD options and FDCs, which can lower the pill burden and be beneficial early in treatment;

- using directly observed treatment (DOT), particularly in hospitals and among drug users; addressing lifestyle barriers to adherence (social and psychological support, psychiatric disorders, OST, disulfiram) and contacting patients regularly.

### *3.1.6 Frequency of clinic visits*

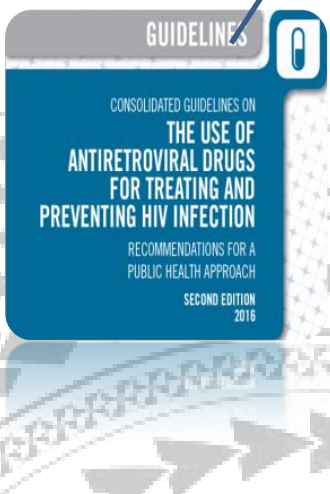



**RECOMMENDATIONS:**

- Less frequent clinical visits (3–6 months) are recommended for people stable on ART (strong recommendation, moderate-quality evidence).
- Less frequent medication pickup (3–6 months) is recommended for people stable on ART (strong recommendation, low-quality evidence).

When routine clinical consultations are due, they should be coordinated with planned medication pickup to reduce visit frequency. b ARV supply management should be strengthened to ensure availability of ARV medicines and prevent stock-outs in the context of less frequent medication pickup.

### *3.1.7 Decentralization*




**RECOMMENDATIONS**

Decentralization of HIV treatment and care should be considered as a way to increase access to and improve retention in care:

- initiation of ART in hospitals with maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence);
- initiation and maintenance of ART in peripheral health facilities (strong recommendation, low-quality evidence); and
- initiation of ART at peripheral health facilities with maintenance at the community level (strong recommendation, moderate-quality evidence).

### *3.1.8 Integrating and linking services*

Chronic care requires integrating and linking related services to ensure comprehensive and consistent patient management over time, including provision of related services in the same settings, systems to share information and effective referrals across settings and providers. Integrating and linking services are likely to reduce missed opportunities for initiating ART, enhance adherence support and optimize retention in care.

Linkages with maternal and child health-care settings, TB clinics, STI clinics are being strengthened.

## 3.2Service delivery sites

Clinical management of HIV infection are provided in the following health facilities in Samoa:

- Communicable Disease Clinic, TTM Hospital, Moto'otua, Apia
- National Laboratory, TTM Hospital, Moto'otua, Apia

There is a structure known as the HIV Core Team that is composed of the following core members:

- Physician
- Nurse Specialist, Senior Nurse
- 2-5 Nurses
- Community Nurse Focal Points for Rural Districts
- Laboratory technicians

- Principal Officer HIV/STI/TB Coordination (National Programme)
- Epidemiologist (National Programme)

Main roles include:

- Develop and coordinates comprehensive management plan for PLHIV from the time of diagnosis, during treatment and follow up.
- Coordinate care of PLHIV
- Serve as Antiretroviral Treatment Committee
- Develop training plan, mentorship and support for health care workers involved in HIV care.
- Report to the designated person or committee for matters that need decision.
- Coordinate clinical and public health response to HIV, STI's and TB

Full terms of reference in Annex 1

# CHAPTER 4

# MONITORING & EVALUATION

## CHAPTER FOUR:[7]MONITORING AND EVALUATION

A monitoring and evaluation framework and system needs to be strengthened to collect and analyse information to track the implementation and impact of the recommendations. Monitoring and evaluation will help programme managers to assess the effectiveness of interventions and linkages between services along the cascade of treatment and care for HIV and associated conditions. Such information is essential to detect and respond to bottlenecks or gaps in programme performance and to adequately characterize and respond to patient attrition. As the National HIV programme matures, monitoring individual- and population-level outcomes, including toxicity and adverse events, drug resistance, viral suppression, mortality, survival and incidence, is also essential to assess the impact of programmes.

### 4.1Monitoring and evaluating the HIV treatment cascade

***Table 13: Overview of data areas for monitoring and evaluating the HIV treatment cascade***

| *Step in the cascade* | Indicator areas | Relevance |
|---|---|---|
| *People living with HIV* | Estimated number of people living with HIV in various categories | - Estimates the distribution of people living with HIV among the population<br>- Estimates the size of relevant populations and need for HIV interventions, to help focus planning |
| *HIV diagnosis* | Percentage of the general population with known HIV test status and within specific populations as well | - The level of testing coverage of relevant populations indicates efforts to scale-up HIV testing and counselling, including provider-initiated testing and counselling<br>- Measuring the proportion of population groups aware of their HIV status<br>- Identifies where more effort may be needed |
| | Number of people newly diagnosed with HIV infection | - Number of people living with HIV newly diagnosed with HIV infection in a given period indicates the pool of people who should be linked to care |
| *Linkage and enrolment in HIV care* | Percentage of people newly diagnosed with HIV infection enrolled in HIV care<br><br>Percentage of people currently receiving HIV care | - Measures strength of link between diagnosis and enrolment in care Indicates access to and uptake of HIV care following a positive HIV test |

[7]Samoa National ART Guidelines

| | | |
|---|---|---|
| | (Number of people enrolled in HIV care, as proxies by receipt of at least one of the following: clinical assessment (WHO staging); CD4 count; viral load; or currently receiving antiretroviral therapy.) | |
| | Profile of people living with HIV initiating HIV care | - Identifies who is enrolled in care and whether key populations and priority groups are linked to care |
| | Retention in care of people living with HIV not yet initiating ART, including HIV-exposed infants | - Acts as a proxy measure for maintained linkage to the care of adults and children who may start ART in the future |
| *Antiretroviral drugs: coverage* | Number of people receiving ART (and coverage)<br><br>Percentage of adults and children receiving antiretroviral therapy among all adults and children living with HIV | - Coverage of ART among eligible people living with HIV, by population groups of interest and regimen<br>- Indicates trends in the number of people receiving ART, to be used to review programme expansion and plan drug supply<br>- Helps estimate unmet need for ART and equity in access to ART |
| | Number of people receiving ARV drugs for PMTCT (and coverage) | - Coverage of ARV drugs for PMTCT among pregnant women with HIV<br>- Estimates unmet need for ARV drugs for PMTCT<br>- Input to model the impact of services for PMTCT |
| *Antiretroviral drugs: drug supply* | Percentage of ART facilities with ARV drug stock-outs in a given period | - Indicates stock-outs, which could directly affect treatment adherence and clinical outcomes, and may contribute to HIV drug resistance |
| *Antiretroviral drugs: adherence and* | Adherence | - Indicates the quality of care and the likelihood of viral suppression<br>- Adherence acts as an early warning indicator |

| | | |
|---|---|---|
| *retention* | Percentage of adults and children with HIV known to be on treatment 12 months after starting antiretroviral therapy<br><br>Percentage of adults and children with HIV known to be on treatment 24 months after starting antiretroviral therapy<br><br>Percentage of adults and children with HIV known to be on treatment 60 months after starting antiretroviral therapy | of drug resistance |
| | Percentage retained on ART and PMTCT | - Indicates retention over time and the success of ART programmes<br>- Helps to monitor losses and identify where to strengthen engagement in care<br>- Low retention acts as an early warning indicator for HIV drug resistance |
| *Viral suppression* | Percentage of viral suppression<br><br>Percentage of adults and children receiving antiretroviral therapy who were virally suppressed in the reporting period (last 12 months) | - Effectiveness of ART programmes in achieving viral suppression |
| *Impact* | Mortality | - Decline in HIV-related deaths and even overall mortality in countries with a high |

| | | |
|---|---|---|
| | | - burden of HIV indicates successful HIV programmes |
| | Incidence and the number of adults and children acquiring HIV infection | - Decline in incidence indicates how successful HIV prevention and treatment programmes are in limiting the number of people acquiring HIV infection<br>- Identifying who is acquiring HIV infection and where the infection was acquired helps to focus planning<br>- Elimination of new HIV infections among<br>- children is a measure of the success of<br>- PMTCT programmes |
| | Mother-to-child transmission rate | - The mother-to-child transmission rate indicates how much vertical transmission occurs |
| | Survival<br><br>Total number who have died of AIDS-related illness | - Increased survival and extended life-years of people living with HIV receiving ART is a measure of the impact of ART<br>- Survival, including HIV-exposed children and children living with HIV, indicates the levels of access to and the quality of health care |

The following are additional indicators to monitor treatment outcome, adherence and adverse reactions.

- Total number of people living with HIV, having active TB expressed as a percentage of those who are newly enrolled in HIV care (pre-antiretroviral therapy or antiretroviral therapy) during the reporting period.
- Number of patients started on treatment for latent TB infection, expressed as a percentage of the total number newly enrolled in HIV care during the reporting period.
- Proportion of people in HIV care who were tested for hepatitis B
- Proportion of HIV-HBV co-infected persons currently on combined treatment
- Proportion of people in HIV care who were tested for hepatitis C virus (HCV)
- Proportion of people diagnosed with HIV/HCV co-infection started on treatment for HCV during a specified time frame (e.g. 12 months)
- Proportion of patients reporting side-effects

## 4.2Other monitoring considerations

Programmes are increasingly moving beyond coverage indicators to focus on critical outcomes, such as viral load suppression and immune reconstitution, and on the broader impact of HIV treatment, including HIV-related mortality and HIV incidence. However, programmes also need to measure potential unintended outcomes, such as HIV drug resistance and ARV-related toxicities. Periodic evaluations and implementation research are also central to reviewing programmes.

- **HIV drug resistance**

WHO recommends the use of early warning indicators to help identify deficits in programme performance that favour the emergence of HIV drug resistance. WHO also recommends that countries undertake surveillance of HIV drug resistance and provides specific guidance on how to do the surveys required.

- **Sentinel surveillance for ARV toxicity monitoring**

Surveillance of the toxicity of ARV drugs is essential to identify and address preventable adverse events. Various approaches have been developed to monitor the toxicity of ARV drugs, including targeted and systematic surveillance reporting on specific types of toxicity and serious adverse events caused by a specific drug in targeted populations, and the pregnancy exposure registry following a cohort of pregnant women exposed to ART, including birth defect surveillance. WHO technical guidance on implementing toxicity monitoring at sentinel sites was released in 2013

- **Evaluation, including impact and programme performance and implementation research**

Routine monitoring should be complemented by systematic evaluations and programme reviews to assess the performance and effects of HIV programmes, either comprehensively or with respect to specific priority areas. Social science and implementation research are important to assess perceptions and values of service recipients and communities along with barriers, facilitators and experiences in delivering and receiving services.

Impact indicators, such as incidence, morbidity and mortality, are often difficult to measure. Guidance on the use of assays for recent infection to estimate HIV incidence at the population level has been developed, and guidance on monitoring mortality, including the cause of death, was also released in 2013. A short guide summarizing five methods to measure the impact of programmes for PMTCT is already available, and detailed guidance that can be adapted to implement each method was also released in 2013.

Mathematical modelling is often undertaken to project various scenarios for programme planning and evaluating impact. Ensuring the availability of robust data is especially important when estimating the prevention impact of ARV drugs at the population level, as multiple sources of information and uncertainty come into play. Specific data collection efforts and models for particular contexts may provide more accurate estimates.

### *4.3Suggested way of reviewing and strengthening M&E system*

The recommendations in these guidelines may require certain adaptations to the monitoring and evaluation system. Guidance is available on the 12 components of a monitoring and evaluation system and tools to review and strengthen national HIV monitoring and evaluation

systems. Table 14 below highlights some specific areas to review to ensure that monitoring and evaluation systems are aligned to the new ARV guidelines.

***Table 14: Critical aspects of monitoring and evaluation systems and implications of guidelines***

| Selected elements of M&E systems | Key considerations to review with new guidelines |
|---|---|
| Patient monitoring system | - Improving the monitoring of enrolment and retention in HIV care<br>- Accurate accounting for transfers and losses<br>- Updating data elements required for patient monitoring in line with new guidelines, such as changes in regimen and including viral load (where available)<br>- Revisit disaggregation categories and links and synergy for systems for<br>- monitoring ARV drugs for PMTCT, TB and ART Move to electronic systems where feasible |
| Data flow and integration | - One standardized monitoring and evaluation system, agreed on by all partners and stakeholders, including necessary updates based on evolving<br>- ARV drug policies and practices<br>- Common country standards and data flow, based on any changes in service delivery<br>- Clarify integration of programmes for PMTCT, TB programmes and ART programmes and transfer to ART programmes<br>- Consider a unique patient identifier<br>- Use of mobile phones where proven opportunities exist<br>- Functional links between HIV and health management information systems |
| Data generation and quality assurance approach | - Clear protocols for data generation, standard operating procedures for aggregation, where they do not exist, for any new indicators and for new service delivery scenarios<br>- Review available laboratory data as a source of key information<br>- Regular assessment of the data quality in facilities and at the subnational level<br>- Supportive supervision, including new elements of ARV drug policy and implementation plans<br>- Update national reporting forms to capture any new national-level data, including identifying the frequency of data collection necessary for various indicators |
| Data use at various levels and programme reviews | - Regular review of standardized data at the facility, regional and national levels to identify issues and improve programmes, including a review of early warning indicators for HIV drug resistance<br>- Review and update the strategy for using data based on new ARV drug policies and a corresponding monitoring and evaluation framework and plan |

| Selected elements of M&E systems | Key considerations to review with new guidelines |
|---|---|
| Periodic reporting and data accessibility | - Maintaining national and subnational databases, to include new data elements<br>- Regular data dissemination and public accessibility of data related to the evolving HIV programme<br>- Periodic (sub-) national and international reports to reflect and document the roll-out of new ARV drug policies and their impact |
| Monitoring and evaluation system capacity | - Human and institutional capacity for data generation and analysis at the facility, subnational and national levels, for monitoring and evaluation that is relevant to updated ARV drug guidance and policies<br>- Appropriate investment in monitoring and evaluation and reflection in grants (including those from the Global Fund to Fight AIDS, Tuberculosis and Malaria) of the monitoring and evaluation adjustments required to strengthen existing capacity and capture new guidance on ARV drugs |
| Monitoring and evaluation plan | - A costed national plan with a list of core indicators and planned evaluations, with focus on results and accountability, revisited in light of new guidelines on ARV drugs<br>- Regular assessment of the implementation of the monitoring and evaluation plan, based on the updated plan |
| Evaluation and operational and implementation research | - Plan and strategy for evaluating impact, considering the rollout of the new guidelines on ARV drugs<br>- Agenda and plan for implementation research, considering the rollout of the new guidelines on ARV drugs<br>- Review of research results for improving programmes |
| Monitoring and evaluation partnerships and coordination | - Coordinating programme monitoring and reporting activities among key stakeholders and partners<br>- Alignment with national health strategy, link with other programme strategies (maternal and child health services, TB and key populations) and international initiatives (Commission for Information and Accountability for Women's and<br>- Children's Health, ending mother-to-child transmission of HIV (eMTCT) and Global AIDS Response Progress Reporting |

### *4.4 Suggested minimum data to be collected at the clinical level*

The suggested minimum data to be collected are important in the development of key indicators on access to treatment and its success, which assist managers in decision-making on ways to strengthen and expand these services to all who need them.

Statistics should be collected at each clinical facility on a regular basis (e.g. quarterly or semi-annually):

- seen for care at least once in the previous 12 months;

- seen for care who are eligible for ART;
- receiving ART;
- receiving first-line ART by end of reporting period;
- switching from first-line ART to second-line ART within last reporting period;
- switching from second-line ART to salvage ART within last reporting period;
- interrupting ART treatment in the last reporting period, with the reason (e.g. death, toxicity/side effects, loss to follow-up, ARVs not available, etc);
- with a viral load; and
- CD4 cell count (  *discontinued except for annual basis*)

### *4.5 Essential information on personal history of HIV treatment and care*

Below is a suggested outline of the minimal information that each clinic should record routinely as part of routine care for individual patients. The information can be recorded electronically.

| Visit date | CD4 cells/ mm3 | % | VL copies/ ml | Current ART | Date interrupting ART | Suboptimal adherence (Y/N)? | Reason for switching ART | Other medication | Significant laboratory or clinical events since last visit |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | |

# ANNEXES

## Annex 1: Terms of Reference: HIV Core Team

### 1.0 Introduction

The impact of HIV infection is experienced across the full spectrum of the lives of people who are living with the virus, including the biological, psychological, and social dimensions.

Similarly, successful treatment for HIV infection requires a bio-psycho-social perspective because factors across all these dimensions will bear on the person's ability to adhere accurately to treatment and to stay engaged with the care team.

As well as providing support and encouragement to their patients and clients, health care workers should have an advocacy role in ensuring that appropriate services are made available for people living with HIV in their communities.

The establishment of HIV management core team is essential to ensure effective communication, coordination, improved referral systems, optimization of available resources and protection in maintaining confidentiality of any privileged communication between the health care workers and people living with HIV.

### 2.0 Roles and Functions

- Develop and coordinates comprehensive management plan for PLHIV from the time of diagnosis, during treatment and follow up.
- Coordinate care of PLHIV to the [site name] Continuum of Care (CoC) coordinating committee
- Serve as Antiretroviral Treatment Committee
- Develop training plan, mentorship and support for health care workers involved in HIV care
- Report to the [add the appropriate person or committee to report to- it needs to be someone with sufficient power to authorise decisions of the core team]

### 3.0 Members

The following are core members who will serve the full term of the committee [add and remove as appropriate]:

- Team leader – Must be a Doctor
- Additional doctor to relieve
- A&E Medical Officer
- Obstetrician
- Midwife
- Paediatrician
- Infection control officer
- Pharmacist
- Laboratory technician
- A Person Living with HIV
- Nurse Specialist, Senior Nurse

- 2-5 Nurses
- Community Nurse Focal Points for Rural Districts
- Principal Officer HIV/STI/TB Coordination (National Programme)
- Epidemiologist (National Programme)

There are also ad hoc members who will be invited when needed such as the dentist, surgeon, psychiatrist, physiotherapist and dietician.

4.0 The tenure

5.0 Security

All members are expected to protect and maintain any confidential information divulged during the deliberations of the committee.

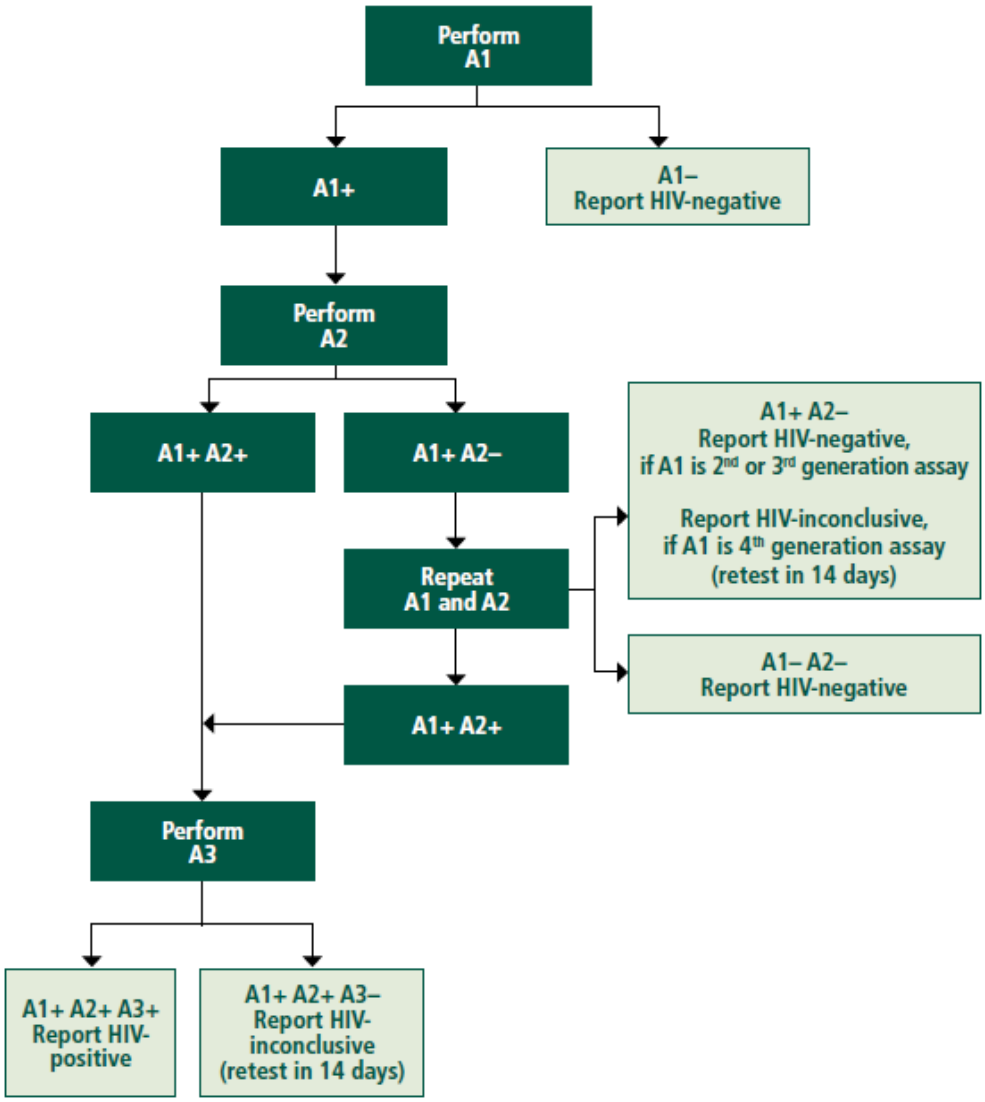
**6.0 Conduct of Business**

- The agenda and any specific issues for discussions are determined by the team leader.
- The team leader will send the invitation to attend the meeting.
- Members will receive the agenda, briefing materials and other documentations in advance of meetings.
- Schedule of meetings
- Quorum
- Manner of discussions
- Minutes of the meetings

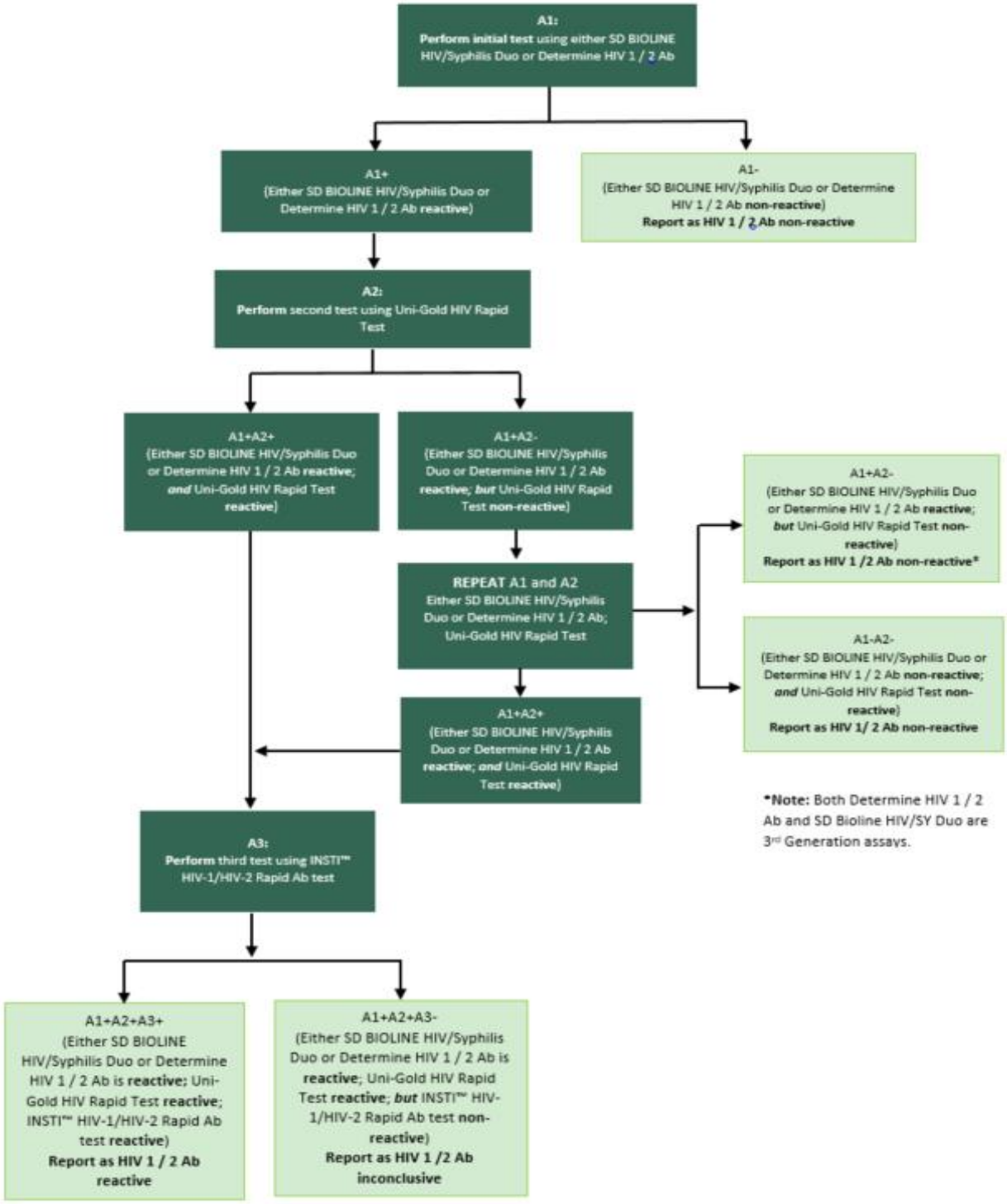
**7.0 Proposed Agenda**

- Members present in the last meeting
- Welcome
- Apologies
- Review of minutes
- Adoption of minutes of last meeting
- Business arising from action sheet
- Matters arising from minutes of last meeting
- Report from members
- New business
- Date, time and venue of next meeting

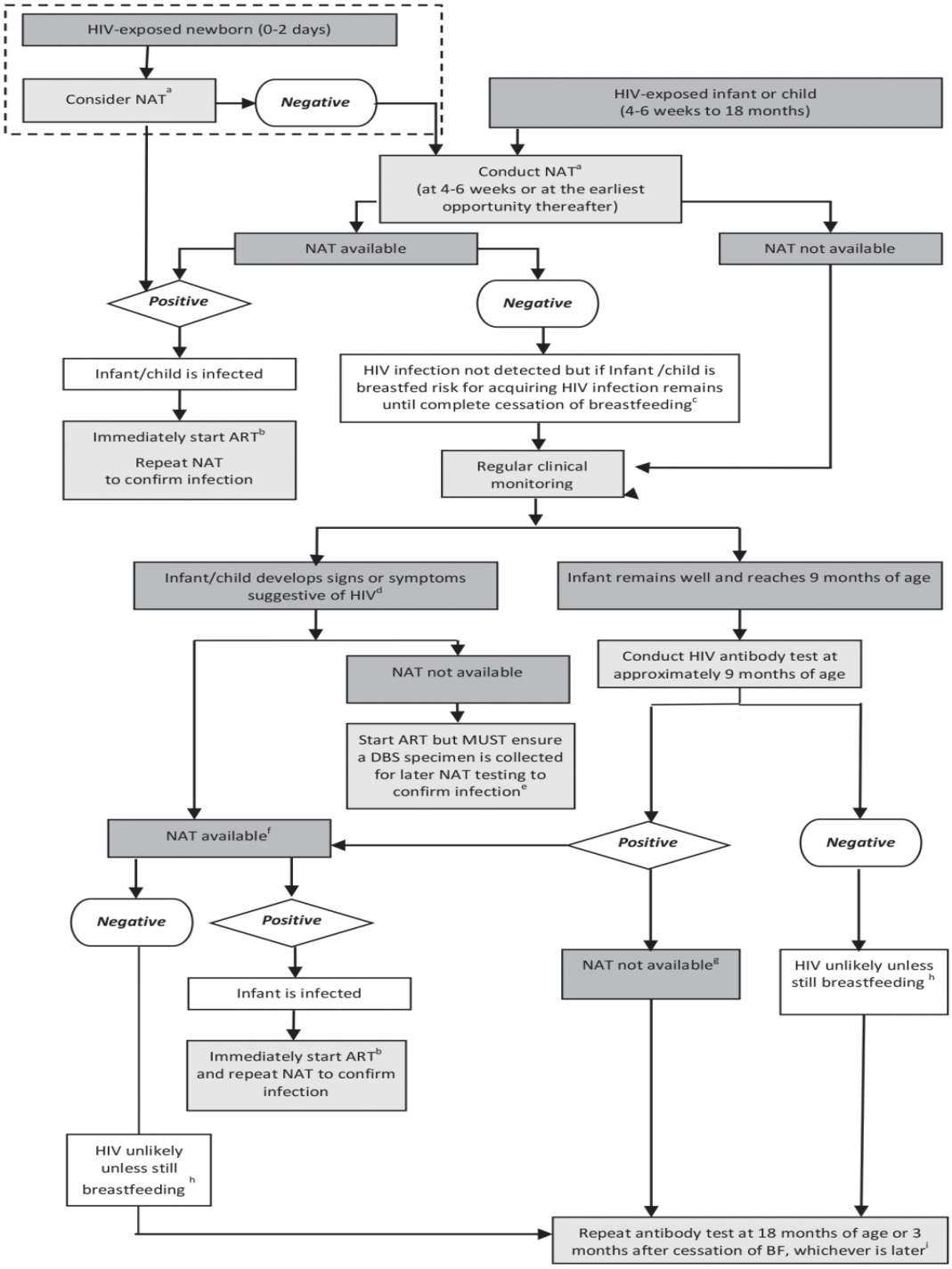
## Annex 2a:HIV testing strategy for HIV diagnosis in low prevalence setting



## Annex 2b: Recommended HIV Testing Algorithm for HIV diagnosis in Pacific Island Countries (PICs) using either Determine HIV 1 / 2 Ab or SD BIOLINE HIV/Syphilis Duo as first assay



## Annex 2c Testing strategy for early infant diagnosis



## Annex 3: HIV Testing Sites in Samoa

List of active HIV Testing Services Sites in Samoa–(year)

| Basic Information | | | | Location | | | Operational | | |
|---|---|---|---|---|---|---|---|---|---|
| **Facility ID** | **Name of Facility** | **Alternate Name (Village Name)** | **Designation** | **Province** | **Island** | **Health Zone** | **Ownership** | **Setting** | **Current Status (month/year)** |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |
| | | | | | | | | | |

## Annex 4 Karnofsky Performance Scale

| Condition | Value | Level of functionality |
|---|---|---|
| Able to carry on normal activity and to work no special care needed. | 100 | Normal no complaints, no evidence of disease |
| | 90 | Able to carry on normal activity, minor signs or symptoms of disease. |
| | 80 | Normal activity with effort; some signs or symptoms of disease. |
| Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed. | 70 | Cares for self; unable to carry on normal activity or to do active work. |
| | 60 | Requires occasional assistance, but is able to care for most of his personal needs. |
| | 50 | Requires considerable assistance and frequent medical care. |
| Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly. | 40 | Disabled; requires special care and assistance. |
| | 30 | Severely disabled; hospital admission is indicated although death not imminent. |
| | 20 | Very sick; hospital admission necessary; active supportive treatment necessary. |
| | 10 | Moribund/declining; fatal processes progressing rapidly. |
| | 0 | Dead |

## Annex 5Doses of recommended ARV drugs

Based on the WHO Consolidated Guidelines on the Use of Antiretroviral Drugs for Treating and Preventing HIV Infections (Second Edition 2016); pages 388-395.

### A. Dosages of antiretroviral drugs for adults and adolescents

| Generic name | Dose |
|---|---|
| Nucleoside reverse-transcriptase inhibitors (NRTIs) | |
| Abacavir (ABC) | 300 mg twice daily or 600 mg once daily |
| Emtricitabine (FTC) | 200 mg once daily |
| Lamivudine (3TC) | 150 mg twice daily or 300 mg once daily |
| Zidovudine (AZT) | 250–300 mg twice daily |
| Nucleotide reverse-transcriptase inhibitors (NtRTIs) | |
| Tenofovir (TDF) | 300 mg once daily |
| Non-nucleoside reverse-transcriptase inhibitors (NNRTIs) | |
| Efavirenz (EFV) | 400–600 mg once daily |
| Etravirine (ETV) | 200 mg twice daily |
| Nevirapine (NVP) | 200 mg once daily for 14 days, followed by 200 mg twice daily |
| Proteases inhibitors (PIs) | |
| Atazanavir + ritonavir (ATV/r) | 300 mg + 100 mg once daily |
| Darunavir + ritonavir (DRV/r) | 800 mg + 100 mg once daily[a] or 600 mg + 100 mg twice daily[b] |
| Lopinavir/ritonavir (LPV/r) | 400 mg/100 mg twice daily |
| | **Considerations for individuals receiving TB therapy**<br>In the presence of rifabutin, no dose adjustment required. In the presence of rifampicin, adjusted dose of LPV/r:<br>(LPV 800 mg + RTV 200 mg twice daily or LPV 400 mg + RTV 400 mg twice daily).or, SQV/r (SQV 400 mg + RTV 400 mg twice daily), with close monitoring. |
| Integrase strand transfer inhibitors (INSTIs) | |
| Dolutegravir (DTG) | 50 mg once daily |
| Raltegravir (RAL) | 400 mg twice daily |

[a] For individuals with no previous use of protease inhibitors.
[b] For individuals with previous use of protease inhibitors.

### B. Simplified infant prophylaxis dosing

| Infant age | Dosing of NVP | Dosing of AZT |
|---|---|---|
| Birth to 6 weeks | | |
| Birth weight 2000–2499 g[a] | 10 mg once daily<br>(1 ml of syrup once daily) | 10 mg twice daily<br>(1 ml of syrup twice daily) |
| Birth weight ≥2500 g | 15 mg once daily<br>(1.5 ml of syrup once daily) | 15 mg twice daily<br>(1.5 ml of syrup twice daily) |
| >6 weeks to 12 weeks | | |
| | 20 mg once daily<br>(2 ml of syrup once daily or half a 50 mg tablet once daily) | No dose established for prophylaxis; use treatment dose 60 mg twice daily<br>6 ml of syrup twice daily or a 60 mg tablet twice daily) |

[a] For infants weighing <2000 g and older than 35 weeks of gestational age, the suggested doses are: NVP 2 mg/kg per dose once daily and AZT 4 mg/kg per dose twice daily. Premature infants younger than 35 weeks of gestational age should be dosed using expert guidance.

## C. Weight-based dosing for ARV formulations for infants and children

### Prescribing information and weight-based dosing of available ARV formulations for infants and children

This annex contains information on ARV drugs for which there are indications or formulations for children or sufficient information and evidence to provide guidance on prescribing and dosing among infants, children and adolescents younger than 18 years of age. WHO has undertaken the work to develop and update simplified guidance on ARV drugs for use among children through the Paediatric Antiretroviral Working Group.1

For simplification and ease of implementation, doses are expressed per weight band rather than per kilogram or per square metre of body surface area. When this simplified weight-band dosing was developed, careful consideration was given to the usual body surface area of children from low- and middle-income countries in that weight band. The primary source of information for the guidance provided is the manufacturer's package insert. This was supplemented with data from other clinical studies as well as consultations of experts in pharmacology for children. For fixed-dose combinations, a dose-modelling tool (http://www.who.int/hiv/paediatric/generictool/en/index.html) was used to predict the dose delivered for each component drug against the recommended dosing schedule. In some cases, the dose for a component in a particular weight band may be somewhat above or below the target dose recommended by the manufacturer. This is inevitable given the limitations imposed by a fixed-dose combination, but care was taken to ensure that no child would receive more than 25% above the maximum target dose or more than 5% below the minimum target dose. Pharmacokinetic studies have also confirmed the overall safety of this dosing approach. For simplification, ARV drugs that are no longer considered preferred or alternative options for children have been removed from the dosing guidance.

In the context of future introduction of virological testing at birth, and the shift towards treating infants earlier in an effort to reduce early mortality, these guidelines provide drug weight-based dosing for term infants aged <4 weeks, including those weighing less than 3 kg. However, experience is limited with initiating treatment among newborns living with HIV aged <2 weeks, and few pharmacokinetic data can fully inform accurate dosing for drugs other than AZT among newborns, who are undergoing rapid changes in renal and liver function. The dosing provided for newborns is aligned with that used in ongoing trials; updates will be provided as soon as trial results are available. In addition, reliable pharmacokinetic data in preterm infants are available only for AZT; there is considerable

uncertainty about the appropriate dosing for NVP and 3TC, and LPV/r solution should not be given to preterm infants until they have reached 42 weeks of gestational age, making managing HIV treatment in preterm newborns extremely challenging. Dosing for postnatal prophylaxis for HIV-exposed infants is not provided here.

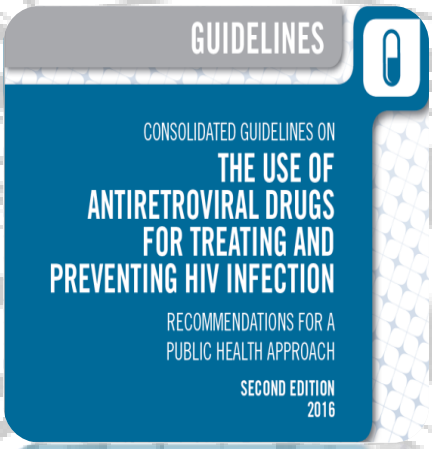
In 2013, the United States Food and Drug Administration approved the use of EFV among children 3 months to 3 years old and weighing at least 3.5 kg. Although the Clinical Guideline Development Group recognized the opportunity to provide an additional drug option to young children and allow further harmonization across age groups, the Group highlighted the need for further data before recommending EFV as a treatment option among children younger than 3 years. These data are still lacking, and the recommended dosing schedule for EFV was not amended in this version of the dosing guidance.

National programmes are advised to consider the most recent product labelling for up-to-date information. Additional information can also be found in specific drug information sheets provided at http://emtct-iatt.org/resources-main.ARV drugs and formulations are available from several manufacturers, and the available dosage strengths of tablets, capsules and liquid formulations may vary from the information given here. Several optimal dosage forms for children are currently being developed but have not yet received regulatory approval during the writing of these guidelines. National programme managers should ensure that products planned for useare currently available and of appropriate quality and stability. For guidance on the quality assurance of medicines, see the WHO medicines:

**Website**

*(http://www.who.int/medicines/areas/quality_safety/quality_assurance/about/en/index.html) and Access toHIV/AIDS drugs and diagnostics of acceptable quality, which is available and updated at http://www.who.int/hiv/amds/selection/en/index.html . The current list of WHO prequalified drugs is available at http://apps.who.int/prequal. For the current list of ARV drugs approved and tentatively approved by the United States Food and Drug Administration, see http://www.fda.gov/ForPatients/Illness/HIVAIDS/Treatment/ucm118915.htm.*

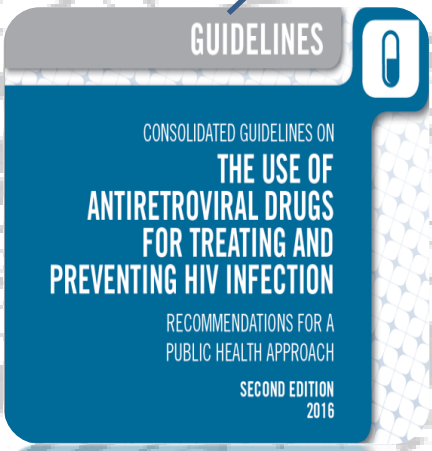
For the policy of the Global Fund to Fight AIDS, Tuberculosis and Malaria on procurement and quality assurance, see http://www.theglobalfund.org/en/healthproducts/qualityassurance/pharmaceutical.




## General principles

The principles followed in developing the WHO simplified tables include the following.

- Using an age-appropriate fixed-dose combination is preferable for any regimen if such a formulation is available.
- Oral liquid or syrup formulations should be avoided where possible. Dispersible tablets (or tablets for oral solution) are the preferred solid oral dosage forms, since each dispersible tablet can be made into liquid at the point of use.
- If suitable dispersible fixed-dose combinations are not available and oral liquids must be used, it is recommended that children be switched to a solid oral dosage form as soon as possible.
- Where children have to use adult formulations, care must be taken to avoid under-dosing and overdosing. Using functionally scored tablets is preferable to ensure accurate dosing, especially if adult dosage forms are used. Splitting un-scored tablets should be avoided, since uniform distribution of the active drug product cannot be assured in tablet fragments.




**General principles (continued)**

- Some tablets such as LPV/r or ATV heat-stable tablets are made in a special embedded matrix formulation (a proprietary melt extrusion technology that stabilizes drug molecules that are normally heat labile) and should not be cut, split, dissolved, chewed or crushed, since these products have variable bioavailability when not swallowed whole.
- Different dosing between morning and evening doses should be avoided if possible.
- Children have to be weighed at each clinic visit, and dose changes are required as children grow and/or change weight.
- Country programmes should consider the national regulatory status and local availability status and availability of specific dosage forms when developing national treatment recommendations for children.
- Research is ongoing for several ARV medications to establish dosing guidance for newborns, infants and young children. The age indications for each drug mentioned in the drug pages are based on current evidence and will be updated as new recommendations become available.

**Table 10 Simplified dosing of child-friendly fixed dose solid formulations for twice –daily dosing for infants and children 4 weeks of age and older.**

| Drug | Strength of tablets (mg) | Number of tablets by weight band morning and evening | | | | | | | | | | Strength of adult tablet (mg) | Number of tablets by weight band | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 3.0–5.9 kg | | 6.0–9.9 kg | | 10.0–13.9 kg | | 14.0–19.9 kg | | 20.0–24.9 kg | | | 25.0–34.9 kg | |
| | | AM | PM | AM | PM | AM | PM | AM | PM | AM | PM | | AM | PM |
| AZT/3TC[a] | Tablet (dispersible) 60 mg/30 mg | 1 | 1 | 1.5 | 1.5 | 2 | 2 | 2.5 | 2.5 | 3 | 3 | 300 mg/ 150 mg | 1 | 1 |
| AZT/3TC/ NVP[a] | Tablet (dispersible) 60 mg/30 mg/50 mg | 1 | 1 | 1.5 | 1.5 | 2 | 2 | 2.5 | 2.5 | 3 | 3 | 300 mg/ 150 mg/200 mg | 1 | 1 |
| ABC/3TC | Tablet (dispersible) 60 mg/30 mg | 1 | 1 | 1.5 | 1.5 | 2 | 2 | 2.5 | 2.5 | 3 | 3 | 600 mg/ 300 mg | 0.5 | 0.5 |
| ABC/3TC | Tablet (dispersible) 120/60 mg | 0.5 | 0.5 | 0.5 | 1 | 1 | 1 | 1 | 1.5 | 1.5 | 1.5 | 600 mg/ 300 mg | 0.5 | 0.5 |

[a] For infants younger than 4 weeks of age, see Table 4 for more accurate dosing, which is reduced because of the decreased ability to excrete and metabolize medication. For infants who are at least 4 weeks of age but less than 3 kg, the immaturity of renal and hepatic pathways of elimination is less of a concern, but uncertainty still exists on the appropriate dosing of ARV drugs for preterm and low-birth-weight infants.

**Table 11 Simplified dosing of child-friendly solid and oral liquid formulations for once-daily dosing for infants and children 4 weeks of age and older[a]**

| Drug | Strength of tablet (mg) | Number of tablets or capsules by weight band once daily | | | | | Strength of adult tablet (mg) | Number of tablets or capsules by weight band once daily |
|---|---|---|---|---|---|---|---|---|
| | | 3.0–5.9 kg | 6.0–9.9 kg | 10.0–13.9 kg | 14.0–19.9 kg | 20.0–24.9 kg | | 25.0–34.9 kg |
| EFV[b] | Tablet (scored) 200 mg | – | – | 1 | 1.5 | 1.5 | 200 mg | 2 |
| ABC/3TC | Tablet (dispersible) 60/30 mg | 2 | 3 | 4 | 5 | 6 | 600 mg/ 300 mg | 1 |
| ABC/3TC | Tablet (dispersible) 120/60 mg | 1 | 1.5 | 2 | 2.5 | 3 | 600 mg/ 300 mg | 1 |
| ATV[c] | Capsules 100 mg | – | – | 1 | 2 | 2 | 300 mg | 2 (100 mg)[d] or 1 (300 mg) |
| TDF[e] | Oral powder scoops 40 mg/scoop | – | – | 3 | – | – | 300 mg | 1 (200 mg)[d] or 1 (300 mg) |
| | Tablets 150 mg or 200 mg | – | – | – | 1 (150 mg) | 1 (200 mg) | | |

[a] For infants younger than 4 weeks of age, see Table 4 for more accurate dosing, which is reduced because of the decreased ability to excrete and metabolize medication. For infants who are at least 4 weeks of age but less than 3 kg, the immaturity of renal and hepatic pathways of elimination is less of a concern, but uncertainty still exists on the appropriate dosing of ARV drugs for preterm and low-birth-weight infants.

[b] EFV is not recommended for children younger than 3 years and weighing less than 10 kg. The United States Food and Drug Administration approved EFV for use for children younger than 3 years weighing more than 3.5 kg during the finalization of these guidelines (3.5–5.0 kg: two 50-mg capsules; 5.0–7.5 kg: three 50-mg capsules; 7.5–15.0 kg: one 200-mg capsule), but more data are urgently needed to inform recommendations for using EFV in this age group.

[c] ATV is only approved for use for children 3 months and older. ATV single-strength capsules should be administered with RTV 100 mg for all weight bands. The ATV powder formulation enables administration of ATV to infants and children as young as 3 months. Infants and children weighing 5–10 kg should be administered 200 mg of ATV powder (4 packets, 50 mg per packet) with 80 mg of RTV oral solution (5 ml). http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206352s003,021567s038lbl.pdf

[d] 200 mg should be used for weight 25.0–29.9 kg and 300-mg tablets for 30.0–34.9 kg.

[e] TDF is only approved for use for children 2 years and older. Target dose: 8 mg/kg or 200 mg/m$^2$ (maximum 300 mg). The Paediatric Antiretroviral Working Group developed this guidance to harmonize TDF dosing with WHO weight bands and to reduce the numbers of strengths to be made available. The WHO generic tool was used based on the target dose provided by the manufacturer's package insert. In accordance with the standard Paediatric Antiretroviral Working Group approach, dosing was developed ensuring that a child would not receive more than 25% above the maximum target dose or more than 5% below the minimum target dose.

**Table 12 Simplified dosing of child-friendly solid and oral liquid formulations for twicedaily dosing for infants and children 4 weeks of age and older**

| Drug | Strength of tablets (mg) or oral liquid (mg/ml) | Number of tablets or ml by weight-band morning (AM) and evening (PM) | | | | | | | | | | Strength of adult tablet (mg) | Number of tablets by weight band | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 3.0–5.9 kg | | 6.0–9.9 kg | | 10.0–13.9 kg | | 14.0–19.9 kg | | 20.0–24.9 kg | | | 25.0–34.9 kg | |
| | | AM | PM | AM | PM | AM | PM | AM | PM | AM | PM | | AM | PM |
| **Solid formulations** | | | | | | | | | | | | | | |
| AZT | Tablet (dispersible) 60 mg | 1 | 1 | 1.5 | 1.5 | 2 | 2 | 2.5 | 2.5 | 3 | 3 | 300 mg | 1 | 1 |
| ABC | Tablet (dispersible) 60 mg | 1 | 1 | 1.5 | 1.5 | 2 | 2 | 2.5 | 2.5 | 3 | 3 | 300 mg | 1 | 1 |
| NVP[b] | Tablet (dispersible) 50 mg | 1 | 1 | 1.5 | 1.5 | 2 | 2 | 2.5 | 2.5 | 3 | 3 | 200 mg | 1 | 1 |
| LPV/r[c] | Tablet[d] 100 mg/ 25 mg | – | – | – | – | 2 | 1 | 2 | 2 | 2 | 2 | 100 mg/ 25 mg | 3 | 3 |
| | Pellets[e] 40 mg/ 10 mg | 2 | 2 | 3 | 3 | 4 | 4 | 5 | 5 | 6 | 6 | 100 mg/ 25 mg | 3 | 3 |
| DRV[f] | Tablet 75 mg | – | – | – | – | 3 | 3 | 5 | 5 | 5 | 5 | | | |
| RAL | Chewable tablets 25 mg | – | – | – | – | 3 | 3 | 4 | 4 | 6 | 6 | 400 mg | 1 | 1 |
| | Chewable tablets 100 mg | – | – | – | – | – | – | 1 | 1 | 1.5 | 1.5 | 400 mg | 1 | 1 |
| | Granules[g] (100 mg/sachet) | 0.25 | 0.25 | 0.5 | 0.5 | – | – | – | – | – | – | | – | – |
| **Liquid formulations** | | | | | | | | | | | | | | |
| AZT | 10 mg/ml | 6 ml | 6 ml | 9 ml | 9 ml | 12 ml | 12 ml | – | – | – | – | – | – | – |
| ABC | 20 mg/ml | 3 ml | 3 ml | 4 ml | 4 ml | 6 ml | 6 ml | – | – | – | – | – | – | – |
| 3TC | 10 mg/ml | 3 ml | 3 ml | 4 ml | 4 ml | 6 ml | 6 ml | – | – | – | – | – | – | – |
| NVP[b] | 10 mg/ml | 5 ml | 5 ml | 8 ml | 8 ml | 10 ml | 10 ml | – | – | – | – | – | – | – |
| LPV/r[c] | 80/20 mg/ml | 1 ml | 1 ml | 1.5 ml | 1.5 ml | 2 ml | 2 ml | 2.5 ml | 2.5 ml | 3 ml | 3 ml | – | – | – |
| DRV[f] | 100 mg/ml | – | – | – | – | 2.5 ml | 2.5 ml | 3.5 ml | 3.5 ml | – | – | | | |

[a] For infants younger than 4 weeks of age, see Table 4 for more accurate dosing, which is reduced because of the decreased ability to excrete and metabolize medication. For infants who are at least 4 weeks of age but less than 3 kg, the immaturity of renal and hepatic pathways of elimination is less of a concern, but uncertainty still exists on the dosing of ARV drugs for preterm and low-birth-weight infants.

[b] NVP dose escalation with half dose for 2 weeks when initiating ART is still recommended to avoid toxicity from high initial NVP levels. However, secondary analysis from the (CHAPAS)-1 trial recently suggested that younger children have a lower risk of toxicity, and consideration can be given to starting with a full dose (Fillekes Q et al. Is nevirapine dose escalation appropriate in young African HIV+ children? 20th Annual Conference on Retroviruses and Opportunistic Infections, Atlanta, GA, USA, 3–6 March 2013 (http://retroconference.org/2013b/Abstracts/46904.htm, accessed 15 May 2015). More definitive evidence is expected from an ongoing trial.

[c] LPV/r liquid requires a cold chain during transport and storage. The LPV/r heat-stable tablet formulation must be swallowed whole and should not be split, chewed, dissolved or crushed.

[d] The adult 200/50 ml tablet could be used for children 14.0–24.9 kg (1 tablet in the morning and 1 tablet in the evening) and for children 25.0–34.9 kg (2 tablets in the morning and 1 tablet in the evening)

[e] The LPV/r pellets formulation should not be used for infants younger than 3 months. More details on the administration of LPV/r pellets is available at http://www.emtct-iatt.org/wp-content/uploads/2015/09/IATT-LPVr-Factsheet-Final-30-September-2015.pdf.

[f] DRV must be administered with 0.5 ml of RTV 80 mg/mL oral suspension if the child weighs less than 15 kg and with RTV 50 mg solid formulation for children weighing 15–30 kg.

[g] RAL granules are approved for use for children as young as 4 weeks, but the feasibility and acceptability of such formulations has not been widely investigated, and concerns have been raised regarding administration in resource-limited settings. The bioequivalence of RAL chewable tablets dispersed in liquid is currently being explored, and more guidance will be provided as soon as additional evidence becomes available.

**Table 13 Drug dosing of liquid formulations for twice-daily dosing for infants younger than 4 weeks of age[a]**

| Drug | Strength of oral liquid (mg/ml) | 2–3 kg | 3–4 kg | 4–5 kg |
|---|---|---|---|---|
| AZT | 10 mg/mL | 1 mL | 1.5 mL | 2 mL |
| NVP | 10 mg/mL | 1.5 mL | 2 mL | 3 mL |
| 3TC | 10 mg/mL | 0.5 mL | 0.8 mL | 1 mL |
| LPV/r[b] | 80/20 mg/mL | 0.6 mL | 0.8 mL | 1 mL |

[a] There is limited experience with initiating treatment among newborns living with HIV <2 weeks of age, with few pharmacokinetic data to fully inform accurate dosing for drugs other than AZT during a time that renal and liver functioning is rapidly maturing , and LPV/r solution should not be given to infants aged <2 weeks, making management of HIV treatment in newborns challenging. In addition, reliable pharmacokinetic data for preterm infants are available only for AZT, with uncertainty of dosing for NVP and 3TC; LPV/r solution should not be given in preterm infants until they have reached 42 weeks of gestational age. This guidance will be updated when more evidence is available from ongoing trials.

[b] Do not use LPV/r solution for infants <2 weeks of age. LPV/r pellets should not be used for infants younger than 3 months. More details on the administration of LPVr pellets is available at http://www.emtct-iatt.org/wp-content/uploads/2015/09/IATT-LPVr-Factsheet-Final-30-September-2015.pdf.

**Table 14 Simplified dosing of isoniazid and co-trimoxazole prophylaxis for infants and children who are at least 4 weeks of age**

| Drug | Strength of tablet or oral liquid (mg or mg/5ml) | Number of tablets or millilitres by weight band once daily | | | | | Strength of adult tablet (mg) | Number of tablets by weight band |
|---|---|---|---|---|---|---|---|---|
| | | 3.0–5.9 kg | 6.0–9.9 kg | 10.0–13.9 kg | 14.0–19.9 kg | 20.0–24.9 kg | | 25.0–34.9 kg |
| Isoniazid | 100 mg | 0.5 | 1 | 1.5 | 2 | 2.5 | 300 mg | 1 |
| Co-trimoxazole | Suspension 200/40 per 5 ml | 2.5 ml | 5 ml | 5 ml | 10 ml | 10 ml | – | – |
| | Tablets (dispersible) 100/20 mg | 1 | 2 | 2 | 4 | 4 | – | – |
| | Tablets (scored) 400/80 mg | – | 0.5 | 0.5 | 1 | 1 | 400 mg/ 80 mg | 2 |
| | Tablets (scored) 800/160 mg | – | – | – | 0.5 | 0.5 | 800 mg/ 160 mg | 1 |
| Isoniazid + co-trimoxazole + B6[a] | Tablets (scored) 300 mg/960 mg/25 mg | – | – | – | 0.5 | 0.5 | 960 mg/ 300 mg/ 25 mg | 1 |

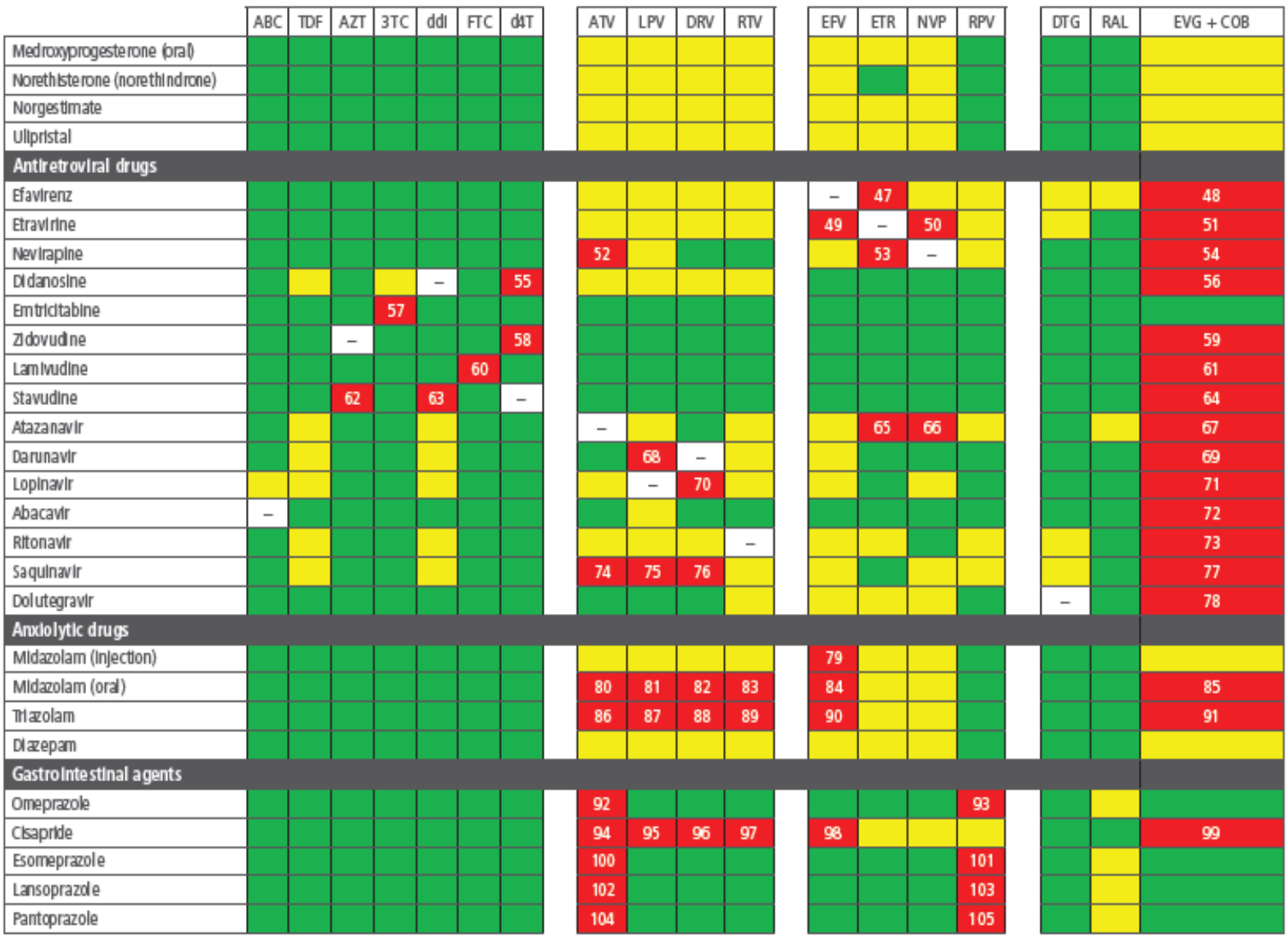
[a] This formulation is currently awaiting regulatory approval, and a scored tablet (480 mg/150 mg/12.5 mg) is also being developed.

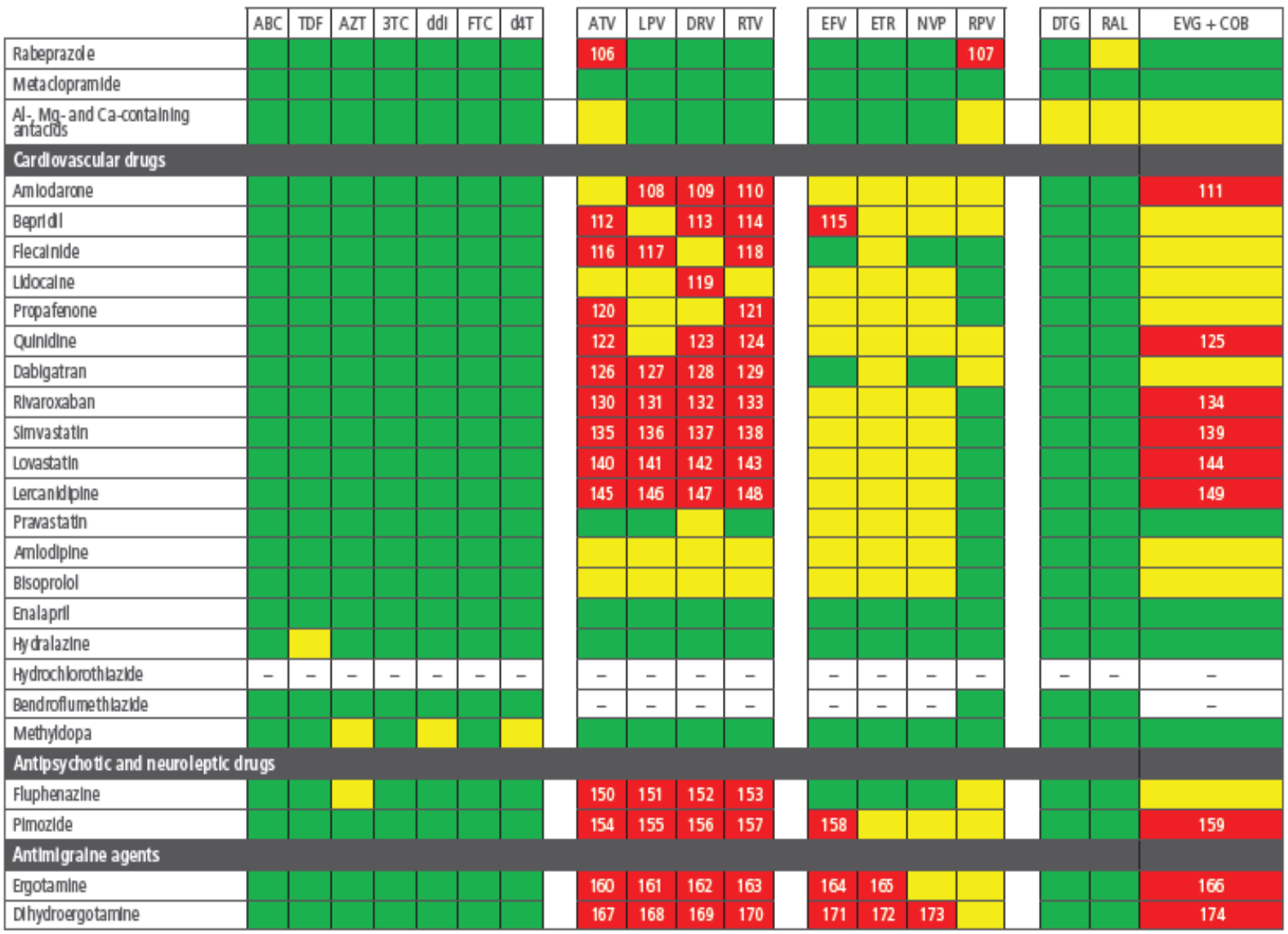
**Table 15 Simplified dosing for urgently needed ARV drugs for children recommended by the Paediatric Antiretroviral Drug Optimization groups**

| Drug | Strength of dosage form (mg) | Number of tablets or sprinkle capsules or sachets by weight band | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 3.0–5.9 kg | | 6.0–9.9 kg | | 10.0–13.9 kg | | 14.0–19.9 kg | | 20.0–24.9 kg | | 25.0–34.9 kg | |
| | | AM | PM | AM | PM | AM | PM | AM | PM | AM | PM | AM | PM |
| ABC + 3TC + LPV/r | 30 mg/15 mg/40 mg/10 mg | 2 | 2 | 3 | 3 | 4 | 4 | 5 | 5 | 6 | 6 | – | |
| AZT + 3TC + LPV/r | 30 mg/15 mg/40 mg/10 mg | 2 | 2 | 3 | 3 | 4 | 4 | 5 | 5 | 6 | 6 | – | |
| DRV/r | 120 mg/20 mg | – | – | – | – | 2 | 2 | 3 | 3 | 3 | 3 | 4 | 4 |
| ATV/r[a] | 100 mg/33 mg | – | | – | | 1 | | 2 | | 2 | | – | |
| ABC + 3TC + EFV | 150 mg/75 mg/150 mg | | | | | 1.5 | | 2 | | 2.5 | | 3 | |

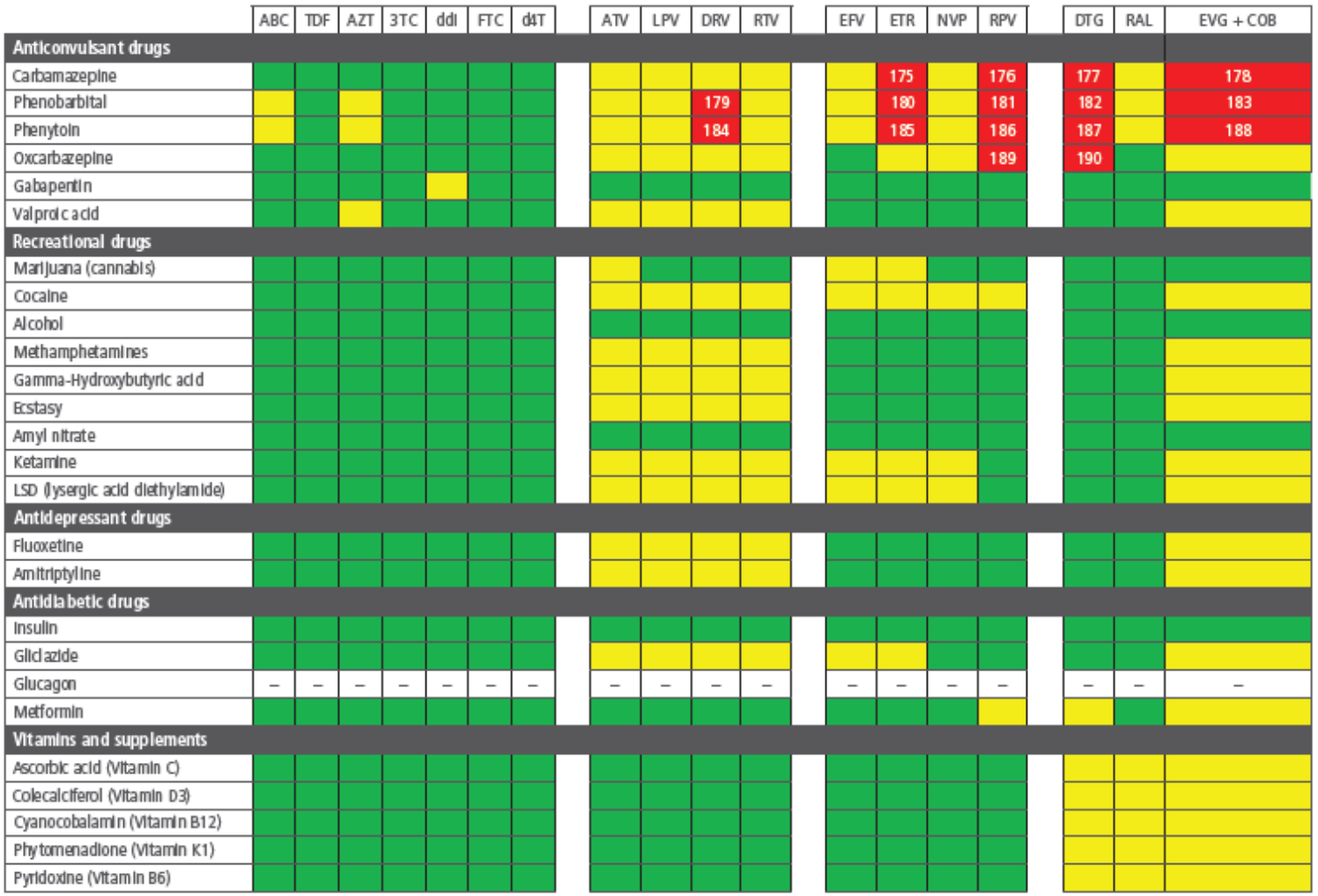
[a] Dosing for ATV/r at 14.0–19.9 kg has been adjusted since previous versions of this annex to address concerns of potential underdosing of ATV.


## Annex 6Key drug interactions


ABC
TDF
AZT
3TC
ddI
FTC
d4T
ATV
LPV
DRV
RTV
EFV
ETR
NVP
RPV
DTG
RAL
EVG + COB
Medroxyprogesterone (oral)
Norethisterone (norethindrone)
Norgestimate
Ulipristal
Antiretroviral drugs
Efavirenz
Etravirine
Nevirapine
Didanosine
Emtricitabine
Zidovudine
Lamivudine
Stavudine
Atazanavir
Darunavir
Lopinavir
Abacavir
Ritonavir
Saquinavir
Dolutegravir
Anxiolytic drugs
Midazolam (injection)
Midazolam (oral)
Triazolam
Diazepam
Gastrointestinal agents
Omeprazole
Cisapride
Esomeprazole
Lansoprazole
Pantoprazole
48
51
54
56
59
61
64
67
69
71
72
73
77
78
85
91
99



| | ABC | TDF | AZT | 3TC | ddI | FTC | d4T | ATV | LPV | DRV | RTV | EFV | ETR | NVP | RPV | DTG | RAL | EVG + COB |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Rabeprazole | | | | | | | | 106 | | | | | | | 107 | | | |
| Metoclopramide | | | | | | | | | | | | | | | | | | |
| Al-, Mg- and Ca-containing antacids | | | | | | | | | | | | | | | | | | |
| **Cardiovascular drugs** | | | | | | | | | | | | | | | | | | |
| Amiodarone | | | | | | | | | 108 | 109 | 110 | | | | | | | 111 |
| Bepridil | | | | | | | | 112 | | 113 | 114 | 115 | | | | | | |
| Flecainide | | | | | | | | 116 | 117 | | 118 | | | | | | | |
| Lidocaine | | | | | | | | | | 119 | | | | | | | | |
| Propafenone | | | | | | | | 120 | | | 121 | | | | | | | |
| Quinidine | | | | | | | | 122 | | 123 | 124 | | | | | | | 125 |
| Dabigatran | | | | | | | | 126 | 127 | 128 | 129 | | | | | | | |
| Rivaroxaban | | | | | | | | 130 | 131 | 132 | 133 | | | | | | | 134 |
| Simvastatin | | | | | | | | 135 | 136 | 137 | 138 | | | | | | | 139 |
| Lovastatin | | | | | | | | 140 | 141 | 142 | 143 | | | | | | | 144 |
| Lercanidipine | | | | | | | | 145 | 146 | 147 | 148 | | | | | | | 149 |
| Pravastatin | | | | | | | | | | | | | | | | | | |
| Amlodipine | | | | | | | | | | | | | | | | | | |
| Bisoprolol | | | | | | | | | | | | | | | | | | |
| Enalapril | | | | | | | | | | | | | | | | | | |
| Hydralazine | | | | | | | | | | | | | | | | | | |
| Hydrochlorothiazide | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Bendroflumethiazide | | | | | | | | – | – | – | – | – | – | – | | | | – |
| Methyldopa | | | | | | | | | | | | | | | | | | |
| **Antipsychotic and neuroleptic drugs** | | | | | | | | | | | | | | | | | | |
| Fluphenazine | | | | | | | | 150 | 151 | 152 | 153 | | | | | | | |
| Pimozide | | | | | | | | 154 | 155 | 156 | 157 | 158 | | | | | | 159 |
| **Antimigraine agents** | | | | | | | | | | | | | | | | | | |
| Ergotamine | | | | | | | | 160 | 161 | 162 | 163 | 164 | 165 | | | | | 166 |
| Dihydroergotamine | | | | | | | | 167 | 168 | 169 | 170 | 171 | 172 | 173 | | | | 174 |



| | ABC | TDF | AZT | 3TC | ddI | FTC | d4T | ATV | LPV | DRV | RTV | EFV | ETR | NVP | RPV | DTG | RAL | EVG + COB |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Anticonvulsant drugs** | | | | | | | | | | | | | | | | | | |
| Carbamazepine | | | | | | | | | | | | | 175 | | 176 | 177 | | 178 |
| Phenobarbital | | | | | | | | | | 179 | | | 180 | | 181 | 182 | | 183 |
| Phenytoin | | | | | | | | | | 184 | | | 185 | | 186 | 187 | | 188 |
| Oxcarbazepine | | | | | | | | | | | | | | | 189 | 190 | | |
| Gabapentin | | | | | | | | | | | | | | | | | | |
| Valproic acid | | | | | | | | | | | | | | | | | | |
| **Recreational drugs** | | | | | | | | | | | | | | | | | | |
| Marijuana (cannabis) | | | | | | | | | | | | | | | | | | |
| Cocaine | | | | | | | | | | | | | | | | | | |
| Alcohol | | | | | | | | | | | | | | | | | | |
| Methamphetamines | | | | | | | | | | | | | | | | | | |
| Gamma-Hydroxybutyric acid | | | | | | | | | | | | | | | | | | |
| Ecstasy | | | | | | | | | | | | | | | | | | |
| Amyl nitrate | | | | | | | | | | | | | | | | | | |
| Ketamine | | | | | | | | | | | | | | | | | | |
| LSD (lysergic acid diethylamide) | | | | | | | | | | | | | | | | | | |
| **Antidepressant drugs** | | | | | | | | | | | | | | | | | | |
| Fluoxetine | | | | | | | | | | | | | | | | | | |
| Amitriptyline | | | | | | | | | | | | | | | | | | |
| **Antidiabetic drugs** | | | | | | | | | | | | | | | | | | |
| Insulin | | | | | | | | | | | | | | | | | | |
| Gliclazide | | | | | | | | | | | | | | | | | | |
| Glucagon | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – | – |
| Metformin | | | | | | | | | | | | | | | | | | |
| **Vitamins and supplements** | | | | | | | | | | | | | | | | | | |
| Ascorbic acid (Vitamin C) | | | | | | | | | | | | | | | | | | |
| Colecalciferol (Vitamin D3) | | | | | | | | | | | | | | | | | | |
| Cyanocobalamin (Vitamin B12) | | | | | | | | | | | | | | | | | | |
| Phytomenadione (Vitamin K1) | | | | | | | | | | | | | | | | | | |
| Pyridoxine (Vitamin B6) | | | | | | | | | | | | | | | | | | |

| | ABC | TDF | AZT | 3TC | ddI | FTC | d4T | ATV | LPV | DRV | RTV | EFV | ETR | NVP | RPV | DTG | RAL | EVG + COB |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Folic acid | | | | | | | | | | | | | | | | | | |
| Retinol (Vitamin A) | | | | | | | | | | | | | | | | | | |
| Riboflavin (Vitamin $B_2$) | | | | | | | | | | | | | | | | | | |
| Thiamine (Vitamin $B_1$) | | | | | | | | | | | | | | | | | | |
| Vitamin E | | | | | | | | | | | | | | | | | | |
| Magnesium | | | | | | | | | | | | | | | | | | |
| Iron | | | | | | | | | | | | | | | | | | |
| Zinc | | | | | | | | | | | | | | | | | | |
| Calcium | | | | | | | | | | | | | | | | | | |
| **Other drugs** | | | | | | | | | | | | | | | | | | |
| Hydroxyurea | | | | | 191 | | 192 | | | | | | | | | | | |
| Sildenafil – pulmonary arterial hypertension | | | | | | | | 193 | 194 | 195 | 196 | | | | | | | |
| Sildenafil – erectile dysfunction | | | | | | | | | | | | | | | | | | |
| Allopurinol | | | | | 197 | | | | | | | | | | | | | |
| Alfuzosin | | | | | | | | 198 | 199 | 200 | 201 | | | | | | | 202 |
| Dexamethasone | | | | | | | | | | | | | | | 203 | | | |
| Piroxicam | | | | | | | | | | | 204 | | | | | | | |
| St John's wort | | | | | | | | 205 | 206 | 207 | 208 | 209 | 210 | 211 | 212 | 213 | | 214 |
| Orlistat | | | | | | | | | | | | | | | | | | |

Figure Legend

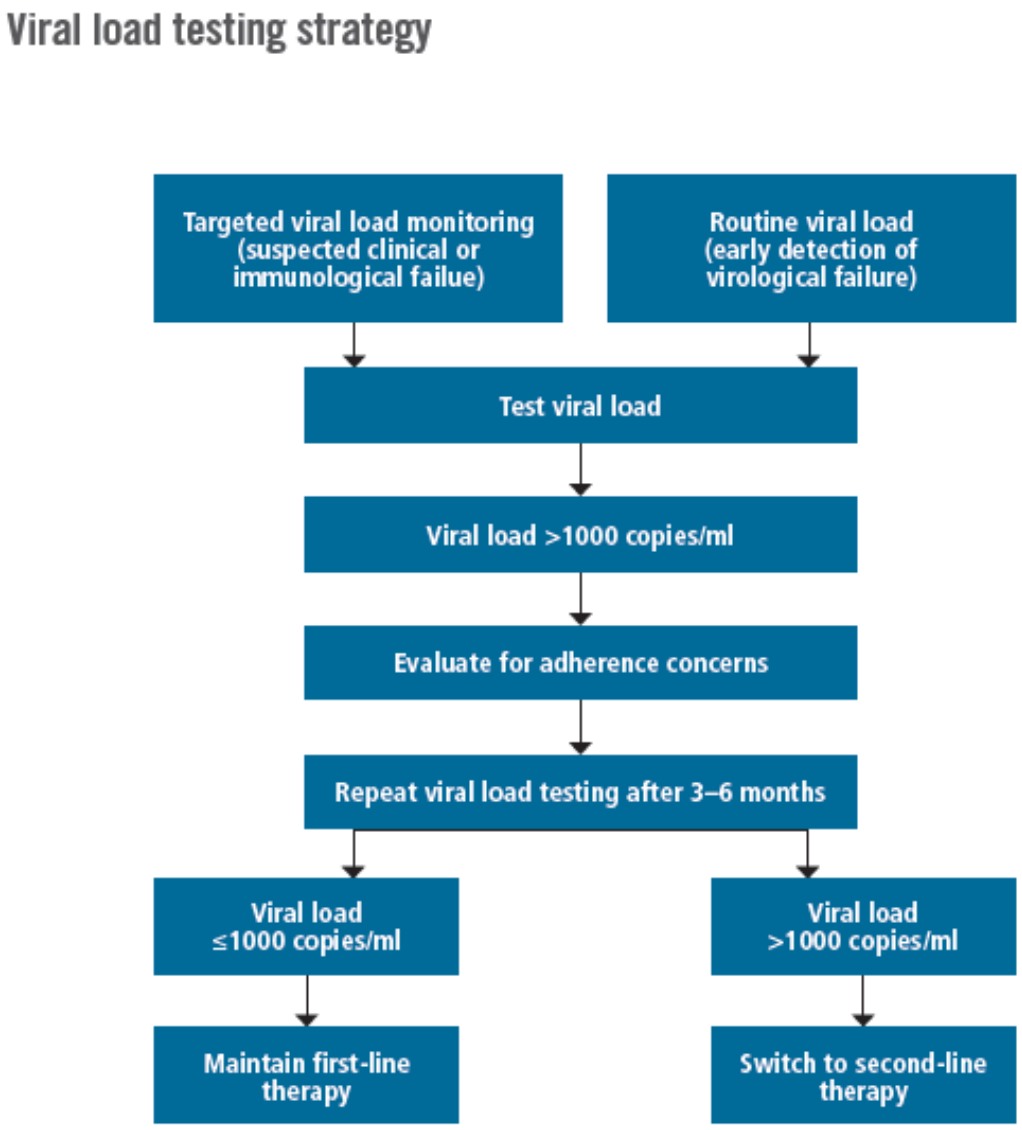
No clinically significant interaction or interaction unlikely based on knowledge of drug metabolism.

Potential interaction that may require close monitoring, alteration of drug dosage or timing of administration.

Interaction likely: do not use or use with caution (# indicates cross-reference to interaction explanation).

– No clear data, actual or theoretical, indicate whether an interaction will occur.

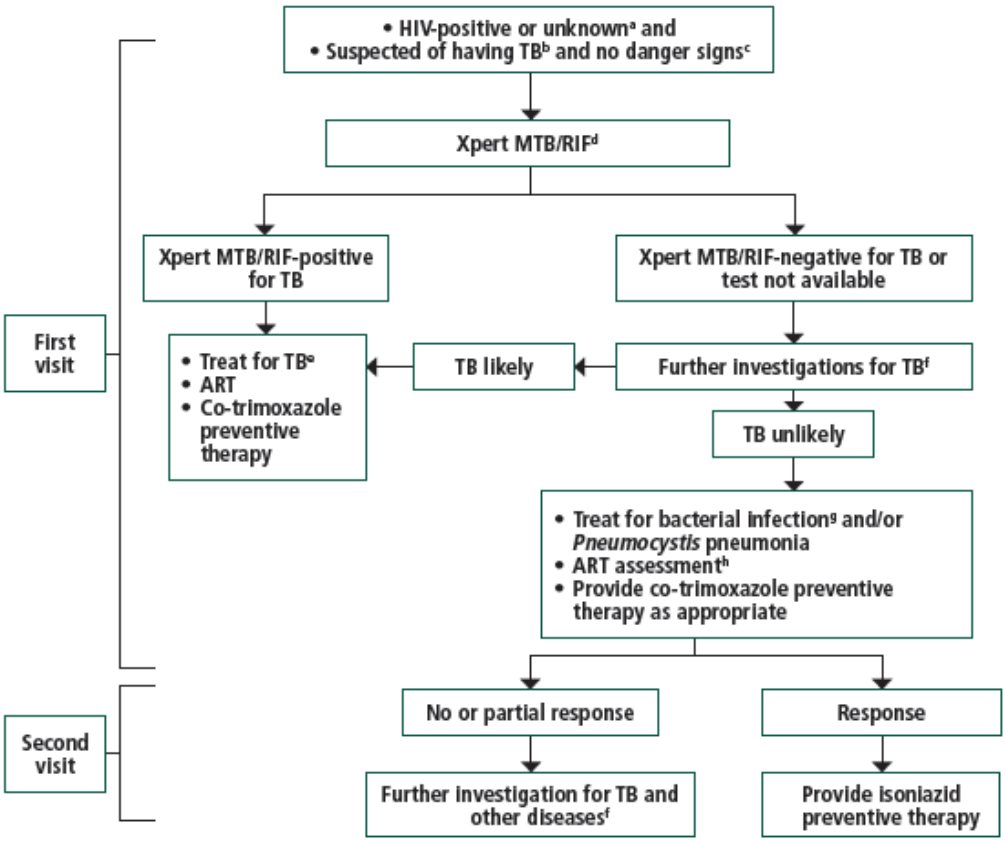
## Annex7 Viral Load Testing Strategy



## Annex 8 Algorithm of managing people living with HIV who are suspected of having TB (ambulatory)

## Annex 9 Algorithm for managing PLHIV and suspected of having TB (seriously ill)

### Algorithm for managing people living with HIV who are suspected of having TB (ambulatory)




[a] For all people with unknown HIV status, HIV testing should be performed according to national guidelines.

[b] Suspicion of TB is defined by the presence of any one of the following symptoms.
– For adults and adolescents living with HIV: current cough, fever, weight loss or night sweats.
– For children living with HIV: poor weight gain, fever, current cough or history of contact with a TB case.

[c] Danger signs include any one of the following: respiratory rate >30 per minute, temperature >39°C, heart rate >120 beats per minute and unable to walk unaided.

[d] For people suspected of having extrapulmonary TB, extrapulmonary specimens should be obtained for Xpert MTB/RIF (cerebrospinal fluid, lymph nodes and other tissues: Xpert MTB/RIF has low sensitivity for pleural fluid and data are limited for stool, urine or blood).

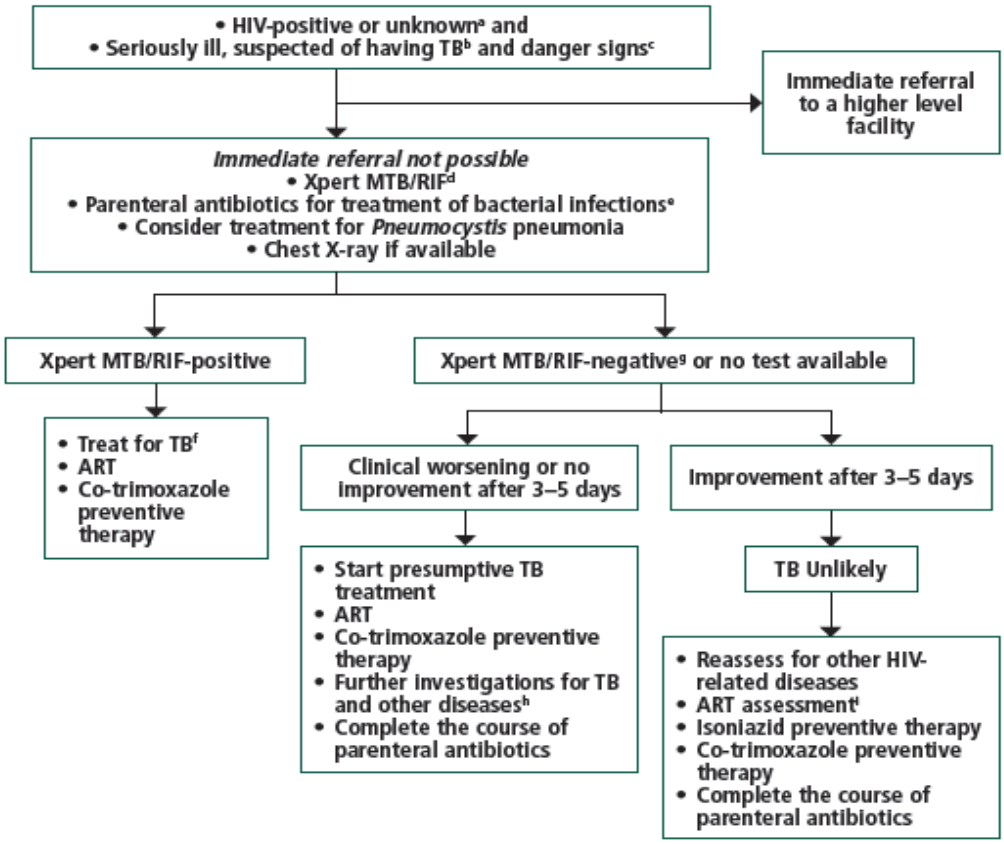
[e] If Xpert MTB/RIF shows rifampicin resistance, treatment for multidrug-reistant TB should be initiated. If the person is considered at low risk for rifampicin resistance, a second Xpert MTB/RIF test should be performed on a fresh specimen. Collect and refer a sample for culture and additional drug sensitivity testing.

[f] Further investigations for TB include chest X-ray, clinical assessment and a repeat Xpert MTB/RIF using a fresh specimen. Refer a sample for TB culture where feasible. If Xpert MTB/RIF is not available, conduct acid-fast bacillus (AFB) microscopy. AFB-positive is defined as at least one positive smear, and AFB-negative as two or more negative smears. If extrapulmonary TB is suspected, extrapulmonary specimens should be obtained and sent for culture and abdominal ultrasound may be performed. These investigations may require additional visits. A urine lateral flow lipoarabinomannan (LF-LAM) assay should not be performed for people with no danger sign.

[g] Antibiotics with broad-spectrum antibacterial activity (except fluoroquinolones) should be used.

[h] ART should be recommended for all adults, regardless of CD4 cell count or clinical stage.

## Algorithm for managing people living with HIV and suspected of having TB (seriously ill)




[a] For all people with unknown HIV status, HIV testing should be performed according to national guidelines.

[b] Suspicion of TB is defined by the presence of any one of the following symptoms.
– For adults and adolescents living with HIV: current cough, fever, weight loss or night sweats.
– For children living with HIV: poor weight gain, fever, current cough or history of contact with a TB case.

[c] Danger signs include any one of the following: respiratory rate >30 per minute, temperature >39°C, heart rate >120 beats per minute and unable to walk unaided.

[d] For people suspected of having extrapulmonary TB, extrapulmonary specimens should be obtained for Xpert MTB/RIF (cerebrospinal fluid, lymph nodes and other tissues: Xpert MTB/RIF has low sensitivity for pleural fluid and data are limited for stool, urine or blood).
The urine lateral flow lipoarabinomannan (LF-LAM) assay may be used to assist in diagnosing active TB among seriously ill adults and children living with HIV, regardless of CD4 count.
If Xpert MTB/RIF is not available, conduct AFB microscopy. AFB-positive is defined as at least one positive smear and AFB-negative as two or more negative smears. Refer the specimen for TB culture where feasible.

[e] Antibiotics with broad-spectrum antibacterial activity (except fluoroquinolones) should be used.

[f] If Xpert MTB/RIF shows rifampicin resistance, treatment for multidrug-reistant TB should be initiated. If the person is considered at low risk for rifampicin resistance, a second Xpert MTB/RIF test should be performed on a fresh specimen. Collect and refer a sample for culture and additional drug sensitivity testing.

[g] If Xpert MTB/RIF shows negative results, the test can be repeated using a fresh specimen.

[h] Further investigations for TB include chest X-ray, clinical assessment, a repeat Xpert MTB/RIF using a fresh specimen an culture. If extrapulmonary TB is suspected, extrapulmonary specimens should be obtained and sent for culture and abdominal ultrasound may be performed.

[i] ART should be recommended for all adults, regardless of CD4 cell count or clinical stage.

[i] WHO Consolidated Guidelines on the use of ART for treating and preventing HIV infection. Second Edition.2016.
[ii] WHO Consolidated Guidelines on the use of ART for treating and preventing HIV infection. Second Edition.2016.
[iii] WHO Consolidated Guidelines on the use of ART for treating and preventing HIV infection. Second Edition.2016.
[iv] WHO Consolidated Guidelines on the use of ART for treating and preventing HIV infection. Second Edition.2016.
[v] WHO Consolidated Guidelines on the use of ART for treating and preventing HIV infection. Second Edition.2016.