HIV Care & Antiretroviral Therapy Guideline

THIRD EDITION 2022

MINISTRY OF HEALTH
& MEDICAL SERVICES

World Health Organization

CONTENTS

CONTENTS 2-5
ACKNOWLEDGEMENT 6
ABBREVIATIONS AND ACRONYMS 7-9
SECTION I Introduction .....
Guiding Principle of HIV Care 11
The 5 C's principle of HIV Testing Services 11
Eligibility to conduct HIV Testing Services 11
Overview of Antiretroviral Treatment 12
Goals of Antiretroviral Treatment 12
Antiretroviral (ARV) drug classes and mechanisms of action 12
Antiretroviral treatment recommendation 14
SECTION II HIV Services for Adults and Adolescents .....
Guiding Principles for HIV Services for Adults and Adolescents 15
Pre- and Post-Test Services 16
Pre-test Information 16
Consent 16
Consent by adolescents 17
Post Test Counselling 17
Counselling for those who test HIV-negative 17
Counselling for Inconclusive HIV test result 17
Counselling for Unconfirmed results 18
Counselling for those whose test results is HIV-positive 18
Post test counselling for adolescents 19
Disclosure 20
HIV Diagnosis in adults and adolescents 21
Overview of HIV diagnosis 21
Key considerations in HIV testing 21
Serological testing strategy for HIV diagnosis 23
Outcome summary of HIV testing 25
Retesting prior to enrolment 26
Re-testing during the window period 26
Inconclusive HIV tests 26
Clinical management of HIV positive adults and adolescents 27
Clinical assessment and investigations before initiating ART 27
Clinical Staging 28
Immunological assessment 28
Co-trimoxazole Management of HIV in adults and Adolescents 28
Co-trimoxazole prophylaxis 28
Primary co-trimoxazole prophylaxis 29
Secondary co-trimoxazole prophylaxis 30
Adverse effects to co-trimoxazole 30
Antiretroviral Treatment 30
Treatment Preparedness 30

Antiretroviral initiation 31
Antiretroviral adherence 31
Antiretroviral Drug Classification 32
First Line Antiretroviral Treatment 35
Treatment failure 38
Second line ART recommendations for adult and adolescents 39
Patient Monitoring 39
Routine Monitoring 39
CD4 Cell count Monitoring 39
Viral load monitoring 39
Drug susceptibility Test (DST) 40
Clinical Monitoring 40
Drug to drug Interaction 40
Antiretroviral drug toxicities 42
Management of ARV drug toxicities 45
Immune Reconstitution Inflammatory Response (IRIS) 47
SECTION III HIV in Obstetrics Care & Breastfeeding .....
Guiding Principles for HIV care in obstetrics and the breastfeeding period 49
Pre- and post-test services for antenatal mothers and the early postnatal period 50
Non-consenters to HIV testing 50
Unbooked women in labour 51
Baby born (to unbooked mother) before arrival at any health facility 51
Post test counselling for Pregnant women 52
Negative Pregnant women 53
Retesting in pregnancy 53
HIV diagnosis in Pregnancy 53
Clinical Management of HIV positive pregnant women and breastfeeding mothers. 54
Co- trimoxazole among HIV positive pregnant women and breastfeeding women 54
Antiretroviral treatment 54
Intrapartum Management 56
Post partum management 57
Family Planning 58
SECTION IV Paediatrics Care .....
Guiding principles for HIV services in paediatrics 59
Pre-test and Post-test services in Paediatrics 60
Pre-test Information in Paediatrics 60
Post-test Counselling in Paediatrics 60
Disclosure 61
Disclosure to HIV Positive children 61
Discloser of HIV positive adults to their children 62
Initial Assessment 63
HIV Testing in Infants and Children 64

HIV Testing in Infants and Children 64
HIV Testing Principles for Infants and Children 65
Diagnosing HIV and AIDS in Children 69
Clinical staging 69
Presumptive diagnosis of HIV infection 69
Diagnosis in breastfeeding infants 70
Diagnosis in infants and children of mothers on ART 70
Clinical Management of HIV Positive Infant and Children 71
Therapeutic Management 71
Prophylaxis 72
Antiretroviral therapy for infants and children 73
Treatment Failure 76
Infant ARV Prophylaxis 77
HIV and Infant Feeding 78
Guiding Principles of HIV & Infant Feeding 78
Recommendations for HIV & Infant Feeding 78
New (2016) Infant Feeding Recommendations 79
Revised WHO 2010 Infant Feeding Principles 81
Revised WHO 2010 Infant Feeding Recommendations 84
Infant feeding counselling 87
HIV and opportunistic infection in children 87
Continuum of care for children living with HIV 87
Immunizations 87
Linkage to HIV care 88
SECTION V HIV and General Medicine .....
HIV Co-Infections 89
HIV/TB co-infection 89
Clinical Features 89
Diagnosis 89
Opportunistic Infection 91-102
Metabolic condition and chronic HIV care 103
Metabolic conditions and chronic care of HIV positive patients 103
Management of Metabolic conditions in PLHIV 103
Bone disorders 104
Lipodystrophy 104
Mental disorders 104
Drug use and drug use disorder 105
Nutrition Support 105
Antiretroviral drugs for HIV Prevention 107
Pre-Exposure Prophylaxis (PrEP) 107
Post Exposure Prophylaxis (PrEP) 111
Occupational exposures 111
Recommend post-exposure prophylaxis for HIV 114

Counselling, education, and support to the exposed 115
Post-exposure prophylaxis for non-occupational exposures (NPEP) 116
Surgical care of PLHIV patients 118
Surgical care of HIV positive patients 118
SECTION VI Continuum of Care .....
Guiding principles of the continuum of care 119
The HIV care continuum 119
The HIV Care team 120
The HIV continuum of Care intervention package 121
Linkages to HIV care 122
Palliative care 123
SECTION VII Data Collection and Programme monitoring .....
Guiding principles of Data collection in HIV setting 124
Patient Monitoring System. 124
Current Fiji Patient Monitoring HIV Online System 124
SECTION VIII Annexes 128-155
SECTION IX References 156

ACKNOWLEDGEMENT

In putting together this guideline, the review task force had considered the recommended changes in antiretroviral medicines, laboratory investigations procedures and commodities, information and counselling requirements guided by the WHO Guidelines and other relevant resources available in Fiji.

The Ministry of Health and Medical Services wishes to express its gratitude to the following institutions, technical committees and consultants for their contributions to the revision of the antiretroviral treatment guideline. Acknowledgements are made to the following for their input into this guideline:

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Further appreciation goes to the team that finalized the guideline namely Dr. Torika Tamani, Dr Ravi Naidu [Medical], Dr. Ilisapeci Tuibeqa [Paediatric consultant], Dr. Dashika Balak, Dr. Lavenia Gaunavinaka, Dr. Waisale Turuva, Dr. Asena Tuiketei, Dr. Kelera Sakumeni [Obstetrics and Gynecology consultant], Dr. Stephanie Clarke [CWM Paediatric MO], Dr. Unaisi Sikivou [TB Medical Officer], Mrs. Shazia Ali [CWMH Laboratory] and Mr. Joeli Colati [National HIV program] that has provided the program an extensive personal experience and professional guidance.

A special appreciation is extended to Dr. Dennie Iniakwala, WHO Pacific Representative, and Ms. Renata Ram, UNAIDS Pacific Representative, for their invaluable contribution and support to the process of scaling up HIV and AIDS care in Fiji. The Ministry of Health and Medical Services gratefully acknowledges the financial support from the WHO that facilitated the editing and printing of the guidelines.

ABBREVIATIONS AND ACRONYMS

3TC	Lamivudine
A	Assay
ABC	Abacavir
AFB	Acid-fast bacilli
AIDS	Acquired immunodeficiency syndrome
AHD	Adolescent Health Development
ALT	Serum alanine aminotransferase
AST	Serum aspartate aminotransferase
ANC	Antenatal clinic
ART	Antiretroviral therapy
ARV	Antiretroviral drugs
AZT	Zidovudine
BCG	Bacille Calmette Guerin
BD	Bis diem (Latin for "twice a day")
CCR5	C-C chemokine receptor 5
CD4+	T-lymphocyte bearing CD4 receptor
CDC	Communicable diseases centre
CMV	Cytomegalovirus
CNS	Central nervous system
CoC	Continuum of care
COPD	Chronic obstructive pulmonary disease
CPT	Co-trimoxazole preventative therapy
CSO	Civil Society Organization
CTP	Co-trimoxazole prophylaxis
DAA	Direct-acting antiviral
DBS	Dried blood spots
DNA	Deoxyribonucleic acid
DNA PCR	Deoxyribonucleic acid polymerase chain reaction
DPT	Diphtheria, pertussis, tetanus
DTG	Dolutegravir
DRV	Darunavir
DRV/r	Darunavir/ritonavir
DST	Drug Susceptibility Test
EFV	Efavirenz
eGFR	Estimated glomerular filtration rate
EID	Early Infant Diagnosis

EML	Essential medicines list
EPI	Expanded program on immunization
FBC	Full blood count
FBO	Faith-based organization
FDA	Food and drug administration
FDC	Fixed-dose combinations
FPBS	Fiji Pharmaceutical and Biomedical Services
FTC	Emtricitabine
GP	General Practitioner
GOPD	Surgical outpatient department
HBC	Home-based care
HBV	Hepatitis B virus
HCV	Hepatitis C virus
Hib	Hemophilus influenzae type b
HCW	Health care worker
HIV	Human immunodeficiency virus
HTS	HIV testing services
HUB	Clinic for appropriate care and management of HIV positive cases
IA	Immunoassay
IDU	Injecting Drug User
IEC	Information Education Materials
IgM	Immunoglobulins
INH	Isoniazid
INSTI	Integrase strand transfer inhibitor
IPT	Isoniazid preventive therapy
IRIS	Immune reconstitution inflammatory syndrome
IUD	Intrauterine contraceptive device
LPV/r	Lopinavir/ritonavir
MCH	Maternal and child health
MOHMS	Ministry of Health & Medical Services
MR	Measles-rubella (referring to the vaccine)
MTCT	Mother to child transmission
NAT	Nucleic acid testing
NCD	Non-communicable diseases
NGO	Non-governmental organization
NSAID	Non-steroidal anti-inflammatory agent
NRTI	Nucleoside/nucleotide reverse transcriptase inhibitor
NNRTI	Non-nucleoside reverse transcriptase inhibitor
Nocte	At night (Latin)
NVP	Nevirapine

OD	Once a day
OI	Opportunistic infection
OPV	Oral polio vaccine
PJP	Pneumocystis jiroveci pneumonia (formerly Pneumocystis carinii pneumonia (PCP))
PCR	Polymerase chain reaction
PEP	Post-exposure prophylaxis
PLHIV	Person/people living with HIV
PLWD	People living with disability
PI	Protease inhibitor
PICT	Provider-initiated counselling and testing
PMTCT	Prevention of mother-to-child transmission
PPTCT	Prevention of parent-to-child transmission
PO	Per orem (Latin for "by mouth")
PPD	Purified protein derivative test
PrEP	Pre-Exposure prophylaxis
RAL	Raltegravir
RNA	Ribonucleic acid
RPR	Rapid plasma reagin
SD ANC	Subdivision antenatal clinic
SD HUB	Subdivision Hub for HIV care and management
SD GOPD	Subdivision General out-patient department
SMX	Sulphamethoxazole
SOP	Standard operating procedure
SRH	Sexual and reproductive health
STI	Sexual transmitted infection
T20	Enfuvirtide
TAF	Tenofovir Alafenamide
TMP	Trimethoprim
TST	Tuberculin sensitivity testing; same as Mantoux test or PPD
TB	Tuberculosis
TDF	Tenofovir Disoproxil Fumarate
TDS	Ter die sumendum (Latin for "three times a day")
UNAIDS	Joint United Nations Program for HIV/AIDS
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
VMMC	Voluntary male medical circumcision
WHO	World Health Organization

1

INTRODUCTION

SECTION I Introduction

GUIDING PRINCIPLE OF HIV CARE

The 5 C's principle of HIV Testing Services

HIV testing services (HTS) are available in most health care facilities around Fiji. These facilities provide provider-initiated counselling and testing (PICT). These models of HIV counselling and testing services is voluntary and adheres to the five key consideration listed below:

1. **Consent:** people must give informed consent to be tested and counselled. Verbal consent is sufficient; written consent is not mandatory. They should be informed of the process for HIV testing and counselling, and their right to decline testing.
2. **Confidentiality:** HTS must be confidential. Confidentiality should be respected, but it should not be allowed to reinforce secrecy, stigma and 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.
4. **Correct:** providers of HIV testing should strive to provide high quality testing services. Quality assurance mechanisms must be in place to ensure the provision of correct test results. 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.

Eligibility to conduct HTS

HTS refers to services provided in health facilities including private health care providers. This is often referred to as Provider Initiated Testing and Counselling (PITC). It includes providing pre-test information and obtaining consent, with the option for individuals to decline testing.

Community based HTS includes a number of approaches-door to door/ home-based testing, mobile outreach campaigns, workplaces, prisons, educational and social institutions. This is an important approach to reach first-time testers and people who seldom use health facilities.

All health care workers who have completed the training on HIV clinical management and prevention of parent-to-child transmission (PPTCT) of HIV are expected to provide HIV Testing Services (HTS) in the health care facilities where they are posted.

OVERVIEW OF ANTIRETROVIRAL TREATMENT

Goals of Antiretroviral Treatment

The goals of ART are:

1. Maximal and durable suppression of viral load;
2. Restoration and/or preservation of immunological function;
3. Reduction of HIV-related morbidity, mortality and improvement of quality of life; and
4. Prevention of HIV transmission

The most significant advancement in the medical management of HIV-1 infection has been the treatment of patients with antiretroviral drugs, which can suppress HIV-1infection to undetectable level. Discovering HIV-1 as the causative agent of AIDS and the increasing understanding of the virus replication cycle has been instrumental in the development of more effective and user-friendly therapy.

The World Health Organization (WHO) recommends ART for all people with HIV as soon as possible after diagnosis without any restrictions of CD4 count. The Ministry of Health and Medical Service (MOHMS) Fiji has adopted the Test and Treat strategy for all HIV positive patients accordingly.

Most ARV drugs act by inhibiting the enzymes that are needed for HIV replication, namely: reverse transcriptase, integrase, and protease. ART can rapidly suppress HIV replication leading to a rapid fall in the number of viral particles in the blood (viral load). Thus, the impact of HIV on the immune system is reduced and gradual restoration of immune function (CD4 cells) occurs. ART is not a cure, but it suppresses long-term HIV replication in the body. If ART is ceased, HIV replication returns to pre-treatment levels and promptly begins to damage the immune system once again.

Once ART is commenced, it is generally continued for life.

Antiretroviral (ARV) drug classes and mechanisms of action.

To date, the currently available ARV drugs can be divided into five classes:

1. Entry inhibitors:
   a. Fusion Inhibitors
   b. Chemokine receptor antagonists
2. Nucleoside reverse transcriptase inhibitors (NRTIs);
3. Non-nucleoside reverse transcriptase inhibitors (NNRTIs);
4. Integrase strand transfer inhibitors (INSTIs); and
5. Protease inhibitors (PIs).

To date there are more than 20 approved drugs for the treatment of HIV-1infection, these drugs are classified into more than five distinct classes based on their molecular mechanism and resistance profiles.

Figure 1 ARV mechanisms of action in relation to the HIV replication cycle.

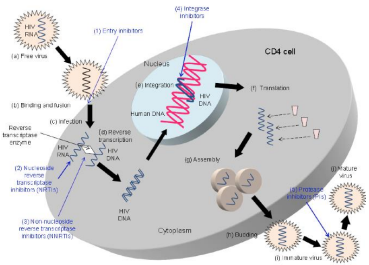


Table 1 Mechanisms of actions of antiretroviral drugs

ARV drug classes	Mechanism of action	Examples
1.Entry inhibitors	Prevent HIV from entering into CD4 cells and infecting them	
a. Fusion inhibitors	Prevent conformational change of gp41 before fusion of HIV to CD4 target cell occurs	Enfuvirtide (T-20)
b. Chemokine receptor antagonists	Blocks the CCR5 co-receptors in CD4 cells which are necessary for HIV entry	Maraviroc (MVC)
2.Nucleoside reverse transcriptase inhibitors (NRTIs)	Terminate the growing HIV DNA chain	Tenofovir (TDF), Zidovudine (AZT), Lamivudine (3TC), Emtricitabine (FTC), Abacavir (ABC)
3.Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Inhibit the conversion of HIV RNA to HIV DNA	Efavirenz (EFV), Nevirapine (NVP)
4.Integrase strand transfer inhibitors (INSTIs)	Prevents the integration of HIV DNA to the human genome	Raltegravir (RAL) Dolutegravir (DTG)
5.Protease inhibitors (PIs)	Prevent maturation of HIV	Lopinavir/ritonavir (LPV/r), Atazanavir/ritonavir (LPV/r), Darunavir/ritonavir (DRV/r)

Antiretroviral treatment recommendation

HIV develops spontaneous genetic mutations at a very high rate. As the virus multiplies, the newly formed virus is often slightly different from the "parent" virus. This is called mutation. The mutant viruses are more successful in multiplying and surviving in the presence of ARVs (viral resistance), rendering treatment less effective.

Effective ART reduces the rate of development of these mutations (and resistance) by continuously suppressing the viral load.

The recommendations for antiretroviral treatment are as follows:

1. A combination of at least three drugs is now the standard treatment for HIV-positive patients.
2. To minimize the development of viral resistance, drugs from two ARV classes should be used.
3. The basic backbone of the ARV regimen is the combination of two NRTIs.
4. The third ARV drug will either be an INSTI or a NNRTI or a PI.
5. The combination of two NRTIs + one INSTI is the preferred combination for first-line ART.
6. The combination of two NRTIs + one NNRTI/PI is reserved as the alternative first-line ART.
7. In special circumstances, a triple NRTI regimen be considered, such as in the treatment of HIV-positive patients co-infected with TB. However, triple NRTI is less effective compared to combinations of three ARV drugs classes.

Single ART is never appropriate due to the rapid development of viral resistance; dual ART can be considered in special circumstances only, such as in the instance of accidental exposure.

Table 2 Recommendations for ARV

At least three ARV drugs should be used **The three drugs should belong to two ARV drug classes** **Two NRTs serve as the backbone of the ART**			
Possible ART:			
ARV Regimen 1	2NRTIs	+	1 INSTI
ARV Regimen 2	2NRTIs	+	1 NNRTI
ARV Regimen 3	2NRTIs	+	1 PI
ARV Regimen 4	3NRTIs	-	Does not fulfil the above pre-requisites; least effective

All HIV positive patients in Fiji will be initiated on the first line regimen, any switch to other regimen requires the endorsement of the HIV care team.

2

SERVICES FOR ADULTS AND ADOLESCENTS

SECTION II HIV Services for Adults and Adolescents

Guiding Principles for HIV Services for Adults and Adolescents

HIV testing services with linkage to prevention, treatment and care are recommended for all people, particularly our key populations which include:

- Pregnant Women (refer to Section III) and their partners.
- Infants and children (refer to Section IV).
- Adolescents.
- Couples and Partners.
- PLHIV & their partners.
- Men.
- Men who have sex with men.
- Transgender people.
- Sex workers and their partners.
- Injecting Drug Users (IDU).
- Other vulnerable populations (such as people living with disabilities (PLWD), inmates, seafarers, frequent travellers, and young people).

Couples and partners should be offered HIV testing services with support for mutual disclosure. Partner testing for HIV negative persons (who may have been exposed to the HIV virus or other sexually transmitted infections) should be offered. For key and vulnerable populations, HIV testing should be routinely offered.

Key principles for starting ART in HIV positive patients include:

- Treatment should be started based on a person's informed decision to initiate ART.
- Interventions to remove barriers to ART initiation once an individual is diagnosed HIV positive should be implemented.
- HIV programmes should promote treatment literacy among all people with HIV, including information on the benefits of early treatment, the lifelong commitment required, the risks of delaying treatment and available adherence support.
- Care providers should be trained to support shared decision-making.
- Although ART initiation is rarely urgent, it may need to be expedited in certain circumstances, such as serious ill health and for pregnant women in labour whose HIV test result is positive.

Pre- and Post-Test Services

Pre-test Information

Lengthy and intensive pre-test counselling and individual risk assessment are not advised, as they may create barriers to service delivery and require significant healthcare worker time and resources, often with minimal benefit to clients (WHO Guideline 2016). Pre-test information which now replaces pre- test counselling can be provided through individual based or group-based information sessions and through IEC materials such as posters, brochures and short video clips shown in the waiting rooms, clinics or during outreach sessions.

When information is being shared with a child or adolescent, information should be shared in an age-appropriate manner to them, or to their guardians as appropriate, to ensure they are being understood.

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

i. the benefits of HIV testing;
ii. the meaning of an HIV-positive and an HIV-negative test;
iii. the services available in the case of an HIV-positive diagnosis, including where ART is provided;
iv. a brief description of prevention options and encouragement of partner testing;
v. the fact that the test result and any information shared by the client are confidential;
vi. the fact that the client has the right to refuse to be tested;
vii. potential risks to the client, (stigma, rejection, violence etc);
viii. an opportunity to ask the provider additional questions; and
ix. provision of informed consent for testing.

Consent

Informed consent remains one of the essential 5Cs of testing services. It should always be obtained individually and in private by a HTS provider. In most settings verbal consent for HIV testing is sufficient. The provider must ensure that the client has learned enough about testing to give informed consent. HTS may provide information about testing and the need for consent in a group setting, such as group health education, but clients should give consent in an individual and private manner. In settings such as ANC or TB clinics, where HIV testing is routine, health workers should carefully explain how a client can decline testing and ensure that each person has a private opportunity to opt out of testing. People who are under the influence of drugs or alcohol or otherwise mentally impaired should not be tested, as they are not able to give informed consent. HTS should ensure that no one coerces clients into being tested.

Consent by adolescents

The MOHMS abides by the Constitution of Fiji Section 38 on the *Right to Health*; and the Convention of the Rights of the Child Article 24 on the *Right to the best healthcare possible* and Article 6 of the CRC on the *Right to Life*. In light of the need to uphold adolescents' rights to make choices about their own health and well-being (with consideration for different levels of maturity and understanding), therefore allows adolescents access to HIV testing and other health services upon their consent.

Post-Test Counselling

Post-test counselling is to be provided to clients according to the HIV test result and status.

Counselling for those who test HIV-negative

Research to date has not demonstrated that a lengthy counselling session is needed or is beneficial. Further, lengthy post-test counselling for people testing negative may divert counselling resources that are needed by those who test HIV-positive, those whose results are inconclusive and those who are found to be in a sero-discordant relationship.

Counselling for those who test HIV-negative should include the following:

- an explanation of the test result and reported HIV status;
- education on methods to prevent HIV acquisition and provision of male or female condoms, lubricant and guidance on their use;
- emphasis on the importance of knowing the status of sexual partner(s) and information about the availability of partner and couples testing services;
- referral and linkage to relevant HIV prevention services, including voluntary male medical circumcision (VMMC) for HIV-negative men, PEP, PrEP (refer to relevant section in this guideline) for people at substantial ongoing HIV risk;
- adolescents who test HIV-negative need information and education about healthy behaviours, such as correct and consistent condom use, reduction of risk-associated behaviours and prevention of HIV and unwanted pregnancy and about the need for retesting if they have new sexual partners.

Counselling for Inconclusive HIV test result

An HIV-inconclusive status means:

- ***in high prevalence settings*** - that the first reactive test result was not confirmed by additional testing using subsequent HIV assays, or that,
- ***in low prevalence settings*** - the first two test results were reactive but the third assay was non-reactive.

Receiving an HIV-inconclusive status may be confusing and stressful for the individual or couple and may be difficult for the provider to explain. As with many other tests for medical conditions, resolving the discrepancy with a third test is not useful, given the high probability that it may equally produce a false-reactive result.

i. All clients with an HIV-inconclusive status should be encouraged to return in 14 days for additional testing to confirm their diagnosis.

ii. Clients with an HIV-inconclusive status should be told that a definitive diagnosis cannot be provided that day and that immediate referral to HIV care or ART initiation is not appropriate.

iii. They should be given a clear plan for follow-up testing.

Most, if not all, HIV inconclusive statuses can be resolved with retesting 14 days later.

Counselling for Unconfirmed results

Unconfirmed results occur when clients who have an initially reactive HIV test result do not receive additional testing in the same visit to confirm their HIV diagnosis. This may occur in community settings where only one assay is performed, an approach known as test for triage.

i. It is the responsibility of HTS providers and counsellors to explain that this initial result is not an HIV diagnosis and needs confirmation and to refer clients with a reactive test result to a site where they can receive an HIV diagnosis.
ii. These providers should encourage clients to go as soon as possible to a facility, such as a clinic or laboratory, for additional HIV testing and a diagnosis.
iii. It is not necessary for these clients to wait 21 days to go to the facility.
iv. After the test result is confirmed and an HIV diagnosis is given, HIV-positive clients should receive post-test counselling.

Every effort is needed to reduce loss to follow-up between a test for triage and additional testing and HIV diagnosis.

To ensure that clients who are misdiagnosed are not needlessly placed on lifelong ART (with potential side-effects, waste of resources and psychosocial and emotional implications), WHO recommends that these clients be retested to verify their HIV diagnosis prior to enrolling in care and/or starting ART. Source: WHO, 2012 (44); WHO, 2014 (57)

Counselling for those whose test results is HIV-positive

An HIV-positive diagnosis is a life-changing event. Before giving HIV-positive test results, the health worker, trained lay provider, or counsellor should keep in mind the 5 Cs of HTS.

All post-test counselling should be "client-centred", which means avoiding formulaic messages that are the same for everyone regardless of their personal needs and circumstances. Instead, counselling should always be responsive to and tailored to the unique situation of each individual or couple.

Health workers, professional counsellors, social workers and trained lay providers can provide counselling.

People with HIV who are trained in counselling may be particularly understanding of the needs and concerns of those who receive an HIV-positive diagnosis.

The information and counselling that health workers, or others, should provide to HIV positive clients is listed below. Absorbing all of this information in one session may be very

challenging, and a follow-up counselling session may be required. Indeed, the shock of learning of an HIV-positive diagnosis may make it difficult or a person to take in further information immediately.

i. Explain the test results and diagnosis.
ii. Give the client time to consider the results and help the client cope with emotions arising from the diagnosis of HIV infection.
iii. Discuss immediate concerns and help the client decide who in her or his social network may be available to provide immediate support.
iv. Provide clear information on ART and its benefits for maintaining health and reducing the risk of HIV transmission, as well as where and how to obtain ART.
v. Make an active referral for a specific time and date. (An active referral is one in which the tester makes an appointment for the client or accompanies the client to an appointment, including an appointment for co-located services, and enrolment into HIV clinical care.) Discuss barriers to linkage to care, same-day enrolment and ART eligibility assessment. Arrange for follow-up of clients who are unable to enrol in HIV care on the day of diagnosis.
vi. Provide information on how to prevent transmission of HIV, including information of the reduced transmission risk when virally suppressed on ART; provide male or female condoms and lubricants and guidance on their use.
vii. Discuss possible disclosure of the result and the risks and benefits of disclosure, particularly among couples and partners. Offer couples counselling to support mutual disclosure.
viii. Encourage and offer HIV testing for sexual partners, children and other family members of the client. This can be done individually, through couples testing, index testing or partner notification.
ix. Assess the risk of intimate partner violence and discuss possible steps to ensure the physical safety of clients, particularly women, who are diagnosed HIV-positive.
x. Assess the risk of suicide, depression and other mental health consequences of a diagnosis of HIV infection.
xi. Provide additional referrals for prevention, counselling, support and other services as appropriate (e.g. TB diagnosis and treatment, prophylaxis for opportunistic infections, STI screening and treatment, contraception, ANC, and brief sexuality counselling).
xii. Encourage and provide time for the client to ask additional questions.

Post-test counselling for adolescents

Along with standard messages for all those diagnosed with an HIV infection, post-test counselling for adolescents with HIV should include:

i. tailored help with linkage to HIV care and treatment;
ii. 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;
iii. information on adolescents' rights and responsibilities, especially their right to confidentiality;
iv. an opportunity to ask questions and discuss issues related to sexuality

and the challenges they may encounter in relationships, marriage and childbearing;

v. individualized planning on how, when and to whom to disclose HIV status and engage families and peers in providing support;

vi. referral for small-group counselling and structured peer support groups, which may particularly benefit adolescents with HIV.

Disclosure

People who test HIV-negative rarely need assistance or support with disclosing their HIV status to others. In contrast, maintaining privacy about testing HIV-positive and deciding about disclosure are serious concerns for many who are diagnosed HIV- positive.

There are three forms of disclosure relevant and appropriate to HIV testing:

- ***Disclosure by the individual to a sexual partner, family member or friend.***
  Such disclosure can have considerable benefits, particularly for couples and sexual partners. However, many clients who learn that they are HIV-positive need time to absorb the diagnosis before they are ready to disclose and may benefit from additional counselling.

- ***Disclosure by a health worker to a sexual partner of the individual.***
  Providers should discuss this with clients before asking for informed consent for testing from partners. Providers need to be sensitive to clients who may be more susceptible to adverse outcomes of disclosure, such as discrimination, violence, abandonment or incarceration; and to, adapt counselling accordingly. Such clients may need additional counselling both before and after testing.

- ***Disclosure by a health worker to other health workers involved in the client's care.***
  Providers need to inform people who test positive that, in order to assure appropriate medical care, the diagnosis will be shared with other medical workers as needed. Such disclosure should respect the client's basic right to privacy and confidentiality of all medical information.

Disclosure by a health worker to the police or other legal authorities is not considered ethical in the context of HTS unless the client has consented to this disclosure. In this case HTS provider should obtain written consent to disclose a client's HIV status to legal authorities.

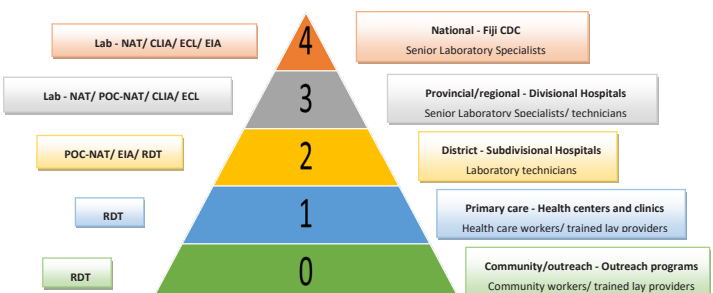
HIV diagnosis in adults and adolescents

Overview of HIV diagnosis

HIV testing may take place at any level of the health-care system, and a diagnosis can be established for a majority of individuals on the same day. Many people will access HIV testing in their community (level 0) or in primary care facilities (level 1). Fig. 5 depicts how HIV testing services are typically organized and shows the different assay formats that could be available at each of the levels (for both facility-based and community-based testing). The degree of infrastructure required for the assay format, such as need for reliable electricity and climate-controlled testing rooms, as well as the staff skills and competencies required, will determine how complex an assay can be used in a given testing setting.

Receipt of a HIV diagnosis empowers individuals to make informed decisions about HIV prevention, treatment and care that will affect both HIV transmission and an individual's health and survival. Linkage to appropriate services following diagnosis should be regarded as a key component of effective and comprehensive HTS.

Figure 2 Available testing services at different service levels



Serological assays are the most commonly used assays for the diagnosis of HIV in adults. The type and format of the assay selected will depend on a variety of factors, most importantly ease of use and the characteristics of the testing site such as storage facilities, infrastructure and level of staff skills.

Key considerations in HIV testing

Serological assays used for HIV diagnosis detect HIV-1/2 antibodies, with fourth generation assays incorporating detection of both HIV-1/2 antibodies and HIV p24 antigen. When initial HIV testing cannot discern a diagnosis, supplemental assays may be used, such as assays that detect HIV p24 antigen only or assays that can detect specific types of HIV-1/2 antibodies.

i. For a period of about 10 days following HIV infection, known as the eclipse period no currently available serological or virological assay can detect any marker of HIV infection.

ii. The end of the eclipse period is marked by the appearance of HIV RNA or DNA detectable by nucleic acid testing (NAT) and then HIV p24 antigen, detectable by immunoassay (IA).

iii. The period prior to detection of HIV-1/2 antibodies is often referred to as "acute infection".

iv. The number of HIV virus particles rises rapidly during acute infection and may be associated with higher infectivity and rate of transmission.

v. As the level of HIV-1/2 antibodies increase, these antibodies form immune complexes with free HIV antigen circulating in the bloodstream. Thus, free HIV antigen is captured (complexed) and, therefore, unable to bind to monoclonal antibody presented on the test device. As a result, the level of detectable HIV antigen decreases.

vi. The detection of HIV-1/2 antibodies by serological assay signals the end of seroconversion and, therefore, the window period for diagnosis.

vii. The duration of the window period depends on three main factors:

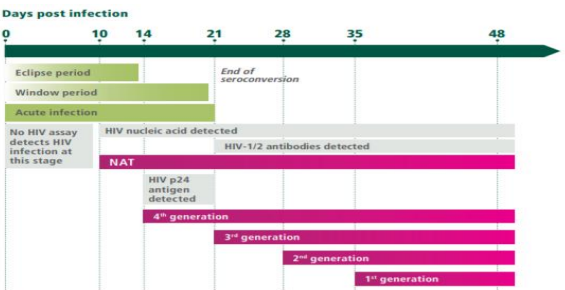
   a. the genetics of the virus,

   b. the genetics and immune competence of the host and,

   c. what exactly the assay detects (antigen, antibodies), the format of the assay determines its ability to detect early HIV antibodies (including IgM, IgA, IgG); this may also depend on the specimen type, such as oral fluid, venous or capillary whole blood and serum/ plasma.

The shortest window period is generally observed with fourth generation serological assays, followed by third and then second-generation assays; the first-generation assays have the longest window period.

Figure 3 Detecting HIV-infection with various formats and generations of in vitro diagnostics over the natural history of infection



Source: Rosenberg et al., 2015 *(1)*.

Figure 4 Serological Assays

Generation	Antigen source and attributes of the assays
First generation	Crude viral lysate as antigen
	Relatively sensitive but lacked relative specificity. Detects immunoglobulin G antibodies (IgG) only.
Second generation	Recombinant proteins and synthetic peptides as antigen
	Improved specificity and sensitivity. Detects IgG only.
Third generation	Recombinant proteins as antigen, with same antigen conjugated to enzyme (antigen sandwich)
	Further refines sensitivity and specificity. Detects IgG and immunoglobulin M antibodies (IgM).
Fourth generation	Recombinant proteins as antigen and monoclonal antibodies
	Detects IgM and IgG antibodies and HIV p24 antigen; therefore, increased sensitivity in early infection, that is, during seroconversion.

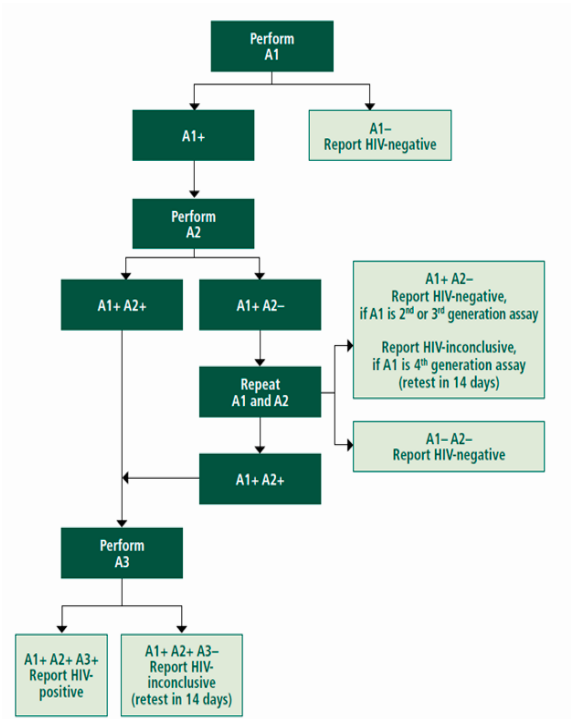
Among Rapid Diagnostic Tests, those using oral fluid specimens exhibit the very longest window period, irrespective of their generation, likely because the concentration of HIV-1/2 antibodies is lower in oral fluid than in other specimen types. However, they have been successfully used in many settings, particularly where high HIV incidence is not expected.

Serological testing strategy for HIV diagnosis

The testing strategy shown in Fig. 4 is recommended for HIV testing in low prevalence settings, that is, with a HIV prevalence of <5% in the population to be tested. This includes settings with low-level HIV epidemics and testing of the general population in areas with concentrated HIV epidemics. Fiji is a low prevalence setting therefore has adopted this testing strategy. This testing strategy is intended for use with serological assays and would require adaptation if NAT technologies were used as A2 or A3.

The figure describes the sequence of assays and number of tests to be performed. Assay 1 (A1), Assay 2 (A2) and Assay 3 (A3) should be three different serological assays that do not share the same false reactivity.

Figure 5 Fiji National HIV Testing Algorithm (adopted from the 2015 WHO HIV Testing Guideline)



These testing strategies apply equally to facility-based testing and non-facility-based testing.

Outcome Summary of HIV testing

All specimens are first tested with one assay (A1), and specimens that are non-reactive (A1−) are considered HIV-negative and reported as such.

A1 should be the most sensitive assay available, taking into account diagnostic sensitivity, seroconversion sensitivity and analytical sensitivity.

Any specimens that are reactive on the first-line assay (A1+) should be retested using a separate and distinct second assay (A2) comprising a different antigen preparation to avoid false cross-reactivity with A1.

Specimens that are reactive on the first-line assay but nonreactive on the second-line assay (A1+; A2−) should be repeated using the same specimen with the same two assays. When the assay uses finger-stick whole blood, a new specimen will have to be taken to be tested with the same two assays.

A specimen that remains reactive following repeat testing with the first assay but is non-reactive on the second assay (A1+; A2−) is considered HIV-negative and reported as an HIV-negative status.

The negative predictive value of the test result of A2− is very high. If the first-line assay (A1) is a fourth-generation assay, however, the test result A1+; A2− should be reported as a HIV-inconclusive status, and the client should be asked to return for retesting in 14 days.

In a low prevalence population, the positive predictive value based on two test results is too low to provide an HIV diagnosis. Therefore, for specimens that are reactive on the first and the second assays (A1+; A2+), a third separate and distinct assay (A3) should be used to confirm the results and issue a HIV-positive diagnosis.

- If the third test result is also reactive (A1+; A2+; A3+), the status is reported as HIV-positive. Retesting to verify the HIV diagnosis should be performed prior to enrolment in care or ART.
- If the result of the third assay is non-reactive (A1+; A2+; A3−), then the test result is discrepant and inconclusive HIV status should be reported. The client should be asked to return in 14 days for additional HIV testing.

In low prevalence populations, for individuals with A1+, then A2− test results, an HIV-negative status should be reported. There is no need for specimens to be reflexed (tested again) on a third assay; the negative predictive value of A2 is high (≥99%), meaning the probably that the negative result observed on A2 is truly negative is ≥99%.

In some settings where HIV testing is offered, it may not be feasible to conduct all three assays on the same day in the same facility. Any individual with an initially reactive result on A1 (A1+) or dual reactive results on A1 and A2 (A1+; A2+) should be referred to a higher-level facility, with a record of their test results, for additional testing.

Table 3 Interpretation of the HIV testing algorithm

HIV Test	Assay 1 (A1)	Assay 2 (A2)	Assay 3 (A3)	HIV Status	Remarks
1	Non-reactive	No test needed	No test needed	Negative	
2	Reactive	Non-reactive	No test needed		Repeat A1 and A2
	Non-reactive	Non-reactive	No test needed	Negative	
	Reactive	Non-reactive	No test needed	Negative	If A1 is 2nd or 3rd generation assay
	Reactive	Non-reactive	No test needed	Inconclusive	If A1 is 4th generation assay; retest in 14 days
3	Reactive	Reactive	Non-reactive	Inconclusive	Retest in 14 days
4	Reactive	Reactive	Reactive	Positive	

Retesting prior to enrolment

Retesting of patients diagnosed as positive with a second specimen using the same testing algorithm before enrolling the patient in care and/or initiating ART will only be done if the patient requests for a retest. The second sample is to be taken on next visit when the patient comes in for results.

If upon retesting, the second result comes back as negative and the clinician is not confident with this result, a third sample is to be sent to the reference lab for verification. If the patient is really sick and requires ART urgently, do not withhold the ART till the third test result is received, but presumptively initiate the patient on ART.

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 the suppression of the immune response and therefore of antibody protection.

Retesting after the window period

Retesting is needed only for HIV negative individuals who report recent or ongoing risk of exposure and pregnant women. Retesting will be done after 21 days of the initial test.

More frequent retesting, that is, every 3–6 months, may be warranted based on individual risks and as part of broader HIV prevention interventions. Those retesting more often would include individuals taking pre-exposure prophylaxis (PrEP), who require quarterly HIV testing, and those from a key population group presenting with an STI.

Inconclusive HIV tests

Inconclusive test result means that the first reactive test result was not confirmed after additional testing or that the first two test results are reactive but the third assay is non-reactive. In this circumstance, the laboratory needs to repeat the testing using the same sample and the same algorithm before reporting the results. If after repeating the test the result is still inconclusive, this will then be reported as inconclusive to the clinicians and a repeat blood test of the patient will be done after 14 days.

Clinical management of HIV positive adults and adolescents

Clinical assessment and investigations before initiating ART

The recommended baseline clinical assessment at the first clinical encounter of a HIV positive patient at any health facility is listed below:

Table 4 Recommended baseline clinical assessment and investigations at initial clinical visit of HIV positive patients

Clinical Assessment
- Vital signs (blood pressure, pulse rate, respiratory rate, temperature, weight (kg), height (cm)) - Physical examination, including eye check (i.e. Visual acuity) and oral health assessment - Screening for other sexually transmitted infections (Syphilis, Hepatitis B and C) - Screening for opportunistic infections (OIs) and other HIV related conditions Other medical conditions e.g. jaundice, hypertension, diabetes mellitus, etc. - Immunizations
Functional Status
- WRK (normal active: able to work, go to school, do housework) - AMB (ambulatory but bed ridden <50% of the day during the last month) - BED (bedridden: >50% of the day during the last month)
Social History
- Prior history of taking ARV drugs or any other drugs - HIV status of partner and/or children and history of ART - Desire for family, size, future pregnancies, family planning, contraception - Sexual activity (including condom use) - Options for infant feeding (if woman desiring pregnancy) HIV diagnostic testing in infants and children - Family history of TB
Tuberculosis (TB) Symptom Screening
- Coughing >2weeks - Persistent fever> 2 weeks - Night sweats >2weeks - Weight loss of >3kg for > 4 weeks
Investigations
- Full Blood Count (FBC) - CD4 cell count (if available) - Urea, Creatinine, and Electrolytes - Liver function tests - Blood glucose - Serum Cholesterol and triglycerides - STI screening: Syphilis, Hepatitis B and Hepatitis C screening - Pregnancy test - Cervical Cancer Screening - Urine dipstick for glycosuria - Chest X-ray - Sputum for acid fast bacilli - G e n e Xpert

Clinical Staging

At the initial visit of the patient with confirmed HIV infection (serological and/or virological evidence of infection), the patient is assessed clinically based on the WHO clinical staging system.

Clinical staging is useful for assessment at baseline (at the time of HIV diagnosis), entry into long-term HIV care, and in the follow up of patients in care and treatment programs. It should be used to guide decisions on when to start co-trimoxazole/ dapsone prophylaxis.

The clinical staging events have been shown to be related to survival, prognosis and progression of clinical disease without ART in adults.

Immunological assessment

The pathogenesis of HIV infection is largely attributable to the decrease in the number of T-cells (a specific type of lymphocyte) that bear the CD4 receptor (CD4+). The immune status of a child or adult living with HIV can be assessed by measuring the absolute number (per mm^3) or percentage of CD4 cells (%CD4). Progressive depletion of CD4+ T-cells associated with progression of HIV disease and an increased likelihood of opportunistic infections (OIs) and other clinical events associated with HIV.

The normal absolute CD4 count in adults and adolescents ranges from 500 to 1,500 cells/mm^3 of blood. Measurement of %CD4 is more valuable in children younger than five years of age. Absolute CD4 counts (and less so the %CD4) fluctuate within an individual and depend on inter-current illness, physiological changes or test variability. At times, measuring the trend over two measurements is therefore more informative than an individual value.

In general, the CD4 cell (absolute count of %CD4) progressively decreases as HIV diseases advances. The CD4 counts usually increase in response to effective combination antiretroviral therapy (ART). The likelihood of disease progression to AIDS or death without ART increases with increasing immunodeficiency (decreasing CD4). Opportunistic infections and other HIV-related conditions are increasingly likely with CD4 counts <200 cells/mm3.

Cotrimoxazole Management of HIV in Adults and Adolescents

Co-trimoxazole Prophylaxis

While preparing the patient for ART initiation, primary prophylaxis with co-trimoxazole or co-trimoxazole preventative therapy (CPT) is given if indicated.

Co-trimoxazole, a fixed-dose combination of sulphamethoxazole (SMX) and trimethoprim (TMP), is a broad-spectrum antimicrobial agent that targets a range of aerobic gram-positive and gram-negative organisms, fungi and protozoa.

Co-trimoxazole prevents Pneumocystis jiroveci pneumonia and toxoplasmosis. It is also active against most salmonella, most methicillin sensitive staphylococcus aureus, streptococcus pneumonia, Haemophilus influenza and most gram-negative bacilli.it is also effective in preventing malaria.

Co-trimoxazole is available in both syrup and tablet formulations at low cost and is on the essential medicines list (EML).

Primary Co-trimoxazole Prophylaxis

Recommendations for primary co-trimoxazole prophylaxis for HIV-positive adults and adolescents

Box 1 Recommendations for primary co-trimoxazole prophylaxis for HIV- positive adults and adolescents

Indications

- CD4 cell count of <350 cells/mm^3 regardless of the WHO clinical stage
- WHO clinical stage 3 or 4 regardless of the CD4 cell count

Co-trimoxazole dose:
Two single-strength tablets PO OD (single-strength tablet = SMX 400mg + TMP 80mg); OR double-strength tablet PO OD (double-strength tablet = SMX 800mg + TMP 160mg)

When to discontinue co-trimoxazole:
Co-trimoxazole can be discontinued if the patient is on ART for 6 months and the CD4 count is persistently ≥350 cells/mm^3 in two measurements within a six-month period.

Table 5 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/mm^3 In settings with high severe bacterial infections [a]: initiate in all regardless of WHO clinical stage or CD4 cell count	May be discontinued in those who are clinically stable, [b] with evidence of immune recovery and/or viral suppression on ART [c] In settings with high prevalence of severe bacterial infections: should be continued
People living with HIV and TB	Initiate in all with active TB regardless of CD4 cell count	Until criteria for discontinuation in adults is met

[a] Settings where severe bacterial infections are highly prevalent includes low-and middle-income countries with high rates of mortality among children less than 5 years.

[b] 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

[c] CD4 count of >350 cells/mm3, with viral load suppression, is considered indicative of immune recovery

Secondary co-trimoxazole prophylaxis

Adults and adolescents with a history of treated PCP should be administered secondary cotrimoxazole prophylaxis with the same regimen recommended for primary prophylaxis.

Adverse effects to co-trimoxazole

Patients should be asked about history of hypersensitivity reaction to sulphur drugs. Severe adverse reactions to co-trimoxazole are uncommon. If non-adverse events occur, every effort should be made to continue prophylaxis with co-trimoxazole. Except in cases of severe adverse reaction, co-trimoxazole should be temporarily interrupted for 2 weeks and then desensitization should be attempted in adults and adolescents, if indicated and feasible. Currently, there is insufficient information in the medical literature on co-trimoxazole desensitization among children in resource-limited settings.

For patients who cannot tolerate co-trimoxazole due to severe adverse reaction, give dapsone 100mg PO OD for HIV-positive adults and adolescents, and dapsone 2mg/kg PO OD for HIV-positive children.

Antiretroviral Treatment

ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count. The following needs to be considered when initiating ART. ART is vital for survival of HIV- positive patients. However, eradication of HIV is not possible with current antiretroviral therapies.

Treatment Preparedness

Before people start antiretroviral therapy (ART), 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 must be discussed.

The choice to accept or decline ART ultimately lies with the person, and if they choose to defer initiation, ART can be offered again at subsequent visits. 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 ART should be reassessed at regular intervals. Community and peer support can help a person to prepare and make the decision to start therapy.

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. 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. 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.

Antiretroviral Initiation

In preparation for treatment initiation, it is important to assess the need for psychosocial support to optimize adherence. Initiation of ART should always consider nutritional status, any comorbidity and other medications being taken to assess for possible interactions, contraindications and dose adjustment.

People receiving ART and caregivers should also be asked regularly about any other medications that are being taken, including herbal remedies and nutritional supplements.

Enrolment into care before the time of ART initiation provides an opportunity for the PLHIV to learn, understand, and prepare for successful lifelong ART.

Antiretroviral Adherence

Treatment readiness of HIV-positive patients is associated with improved adherence once treatment has commenced. In the context of ART, adherence would mean that there is a collaborative process between the patient and the health care provider. The patient plays a more active role in his treatment and makes a commitment to follow the prescribed regiment as best as possible. Adherence to ART greater than 95% is needed to achieve virologic success. In contrast, poor compliance implies the lack of patient participation in the treatment. Table 5 below lists down the important points that need to be discussed with the patient before ART initiation.

Table 6 Checklist for patient education and ARV adherence counselling

Patient assessment	Medical history Knowledge of HIV/AIDS Prior use of ART and other drugs Treatment as prevention Determine social support Disclosure-has the patient disclosed his/her HIV status to anybody? HIV status of partner and members of the family Alcohol/drug use/smoking Mental state Treatment as prevention (discordant couples)
Review health status	Opportunistic infections and WHO clinical staging CD4 count, viral load, and other relevant investigations Nutritional status
Review living conditions and employment	Housing Employment/income

Discuss treatment programme and importance of adherence.	Need for the continued prevention – condom use, ART Cost (if applicable) Side effects of ARVs and what to do Follow-up – clinical and laboratory investigations, e.g. CD4 count, viral load (if required) Importance of adherence and consequences of non- adherence Discuss adherence promotion strategies Discuss role of treatment support person/caregiver Adherence tools – pill diary, alarm clocks, mobile phones, pill boxes, etc. Ongoing adherence counselling
Identify barriers to adherence.	Side effects Poor communication Low literacy Inadequate understanding about HIV/AIDS Lack of social support (family, friends, community) Failure to disclose HIV status Alcohol/drug use/smoking Alternative treatment, e.g. natural/traditional, faith-based Mental state

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

Antiretroviral Drug Classification

Table 7 Antiretroviral classification

ARV drug class	Drug	Dose	Drug administration and process	Adverse effects
Nucleoside reverse transcriptase inhibitors (NRTIs)	Tenofovir (TDF)[a]	300mg PO OD	No food restrictions; must reduce dose if patient has renal dysfunction	Mild side effects; some nausea, vomiting, loss of appetite, renal impairment, lactic acidosis with hepatic steatosis
	TAF (Tenofovir Alafenamide)	25mg PO OD	No food restrictions; must reduce dose if patient has renal dysfunction	Mild side effects; some nausea, vomiting, loss of appetite, renal impairment, lactic acidosis with hepatic steatosis

	Zidovudine (AZT)	300 mg PO BD	No food restrictions	Anaemia, nausea, vomiting, headache, fatigue, muscle aches, bone marrow toxicity, lactic acidosis with hepatic steatosis, body fat changes
	Lamivudine (3TC)	150 mg PO BD or 300 mg PO OD	No food restrictions	Nausea, vomiting, fatigue, headaches, lactic acidosis with hepatic steatosis, body fat changes
	Abacavir (ABC)	300 mg PO BD or 600 mg PO OD	No food restrictions; alcohol boosts abacavir levels	Hypersensitivity reaction in about 5-8% of patients; if hypersensitivity occurs, do not re-challenge at any time
	Emtricitabine (FTC)	200 mg PO OD	No food restrictions	Headache, diarrhea, nausea and rash, lactic acidosis with hepatic steatosis, body fat changes
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	Efavirenz (EFV)	600 mg PO OD or 400mg PO OD	Take on an empty stomach before going to sleep	Headaches, dizziness, insomnia, anxiety, vivid dreams, hallucinations (usually transient and lasts for 3 weeks), rash, nausea, diarrhea
	Nevirapine (NVP)	200 mg PO OD for the first 14 days, then 200 mg PO BD thereafter	No food restrictions	Skin rash, fever, headache, nausea, elevated liver enzymes; be cautious in starting NVP in women with CD4 count >250 cells/mm^3 or in men with CD4 count >400 cells/mm^3 due to high incidence of serious hypersensitivity and hepatoxicity

Protease inhibitors (PIs)	Lopinavir/ ritonavir (LPV/r)	200 mg lopinavir (LPV) + 50 mg ritonavir (RTV), 2 tablets PO BD	No food restrictions; take liquid formulation with food. Keep at room temperature.	Diarrhea, fatigue, headache, nausea, taste perversion, perioral and circumoral paraesthesia
	Atazanavir/ ritonavir (ATV/r)	In ART Naïve: ATV 300mg + RTV 100mg PO OD	Take with food	Indirect hyperbilirubinemia, hyperglycaemia, fat maldistribution, cholelithiasis, nephrolithiasis, renal insufficiency, serum transaminase elevation, hyperlipidaemia, skin rash. Use with caution in patients with underlying conduction defects or in patient with concomitant medications that can cause prolong PR interval
	Darunavir/ ritonavir* (DRV/r)	In ARV Naïve Patient or ARV Experienced Patient with no DRV Mutations: DRV 800mg + RTV 100mg PO OD In ARV Experienced Patient with 1 or more DRV Mutations: DRV 600mg + RTV 100mg PO BD	Take with food	Skin rash (10%)[b] hepatotoxicity, diarrhoea, nausea, headache, hyperlipidaemia, serum transaminase elevation, hyperglycaemia, fat maldistribution
Integrase strand transfer inhibitors (INSTIs)	Dolutegravir[c] (DTG)	ARV Naïve or ARV Experienced INSTI Naïve Patient: 50mg PO OD INSTI Experienced Patient with certain INSTI Mutations or with Clinically Suspected Resistance: 50mg PO BD	Take without regard to meals	Hypersensitive reactions, insomnia, headache, depression and suicidal ideation (rare: usually in patient with pre-existing psychotic conditions)

	Raltegravir (RAL)	400mg PO BD	Take without regard to meal	Rash, including Steven Johnsons syndrome, hypersensitivity reactions, and toxic epidermal necrolysis, nausea, headache, diarrhea, pyrexia, insomnia, CPK elevation, muscle weakness and rhabdomyolysis Depression and suicidal ideation (rare: usually in patient with pre-existing psychotic conditions)

[a] Fixed dose combination (FDC) of antiretroviral drugs are listed in Appendix 9.

[b] The association with NRTIs with body fat changes varies from drug to drug.

[c] Note that exposure to DTG at the time of conception may be associated with neural tube defects among infants. DTG appears to be safe when started later in pregnancy: after the period of risk of neural tube defects and after the first trimester. Adolescent girls and women of childbearing potential who do not currently want to become pregnant can receive DTG together with consistent and reliable contraception.

*DRV has a sulphonamide moiety: Steven Johnsons Syndrome; toxic epidermal necrolysis, acute generalized exanthematous pustulosis.

First Line Antiretroviral Treatment

First line ART recommendations for adults and adolescents (10-19years, ≥ 35kg including pregnant and breastfeeding women.

Figure 5 First line ART recommendation for adults and adolescents

Populations				Preferred first line regimen	Alternative first line regimen(s)	Special situations
Adult men and adolescent boys				TDF + 3TC (or FTC) + DTG	TDF + 3TC (or FTC) + EFV	AZT + 3TC + EFV TDF + 3TC (or FTC) + PI/r[b] ABC + 3TC (or FTC) + DTG TDF + 3TC (or FTC) + RAL
Adult women and adolescent girls	Pregnant or breastfeeding[a]					
	Not of childbearing potential					
	Of childbearing potential	Offered and using effective contraception				
		Offered but not using effective contraception or without access to contraception or want to become pregnant[c]	Choose to use DTG after informed choice			
			Choose to use EFV after informed choice	TDF + 3TC (or FTC) + EFV	TDF + 3TC (or FTC) + PI/r[b]	AZT + 3TC + EFV TDF + 3TC (or FTC) + RAL

[a] *Based on programmatic practicality and uncertainty surrounding possible DTG effects after the neural tube closes at 28 days of gestation as noted by the originator and FDA, previous safe period after 8 weeks is now extended to after the first trimester. In practice, the majority of women will not yet know that they are pregnant during the first 8-12 weeks of pregnancy.*

[b] *If the national prevalence of pre-treatment resistance to EFV or NVP is 10% or higher or if no other alternatives are available.*

[c] *Women of childbearing potential who intend to become pregnant or who are not otherwise using or accessing effective contraception can receive DTG based regimens if they have been informed of the potential increase in the risk of neural tube defects (at conception and up to the end of first trimester). However, many vulnerable and at-risk adolescent girls and women may not be able to negotiate when they want to become pregnant and/or might not be aware they are pregnant.*

The recommended first-line ART for adults and adolescents is a triple therapy consisting of two NRTIs + one INSTI. The use of fixed-dose combinations (FDC) is recommended to be prescribed to the patient whenever possible to enhance patient's drug adherence.

TDF can be substituted with TAF for patients with renal impairment.

Transitioning First Line Antiretroviral Treatment to TDF+3TC+DTG

WHO (2019) recommends that all newly diagnosed HIV positive patients be started on TDF+3TC+DTG regimen but those patients who are already on the previous first-line regimen should follow the following recommendations for adults and adolescents (10-19years, ≥ 35kg including pregnant and breastfeeding women.

Table 8: Transitioning from current regimen to DTG-based regimen

Treatment transition scenario	Preferred approach	Comments
DTG for people living with HIV initiating ART		
Adults and adolescents[a]	Initiate TDF+3TC+DTG	- Potential risk of neural tube defects among infants exposed to DTG during the conception period - Women not using or accessing contraception or who want to be pregnant can use DTG or EFV based on informed choice of the risks and benefits of each regimen
Pregnant and breastfeeding women[b]	Initiate TDF+3TC+DTG	- Possibility of conception during breastfeeding remains
TB co-infection	Initiate TDF+3TC+DTG (DTG dose adjustment needed)	- DTG 50 mg twice daily if rifampicin is being used as the anti-TB regimen
DTG for people living with HIV already using a first-line regimen		
Clinical or immune failure or viral load not suppressed	Switch to AZT+3TC+PI/r[c]	- No evidence to support the efficacy of DTG when used in combination with an inactive NRTI backbone - Provide adherence support
Viral load suppressed	Substitute to TDF+3TC+DTG	- Substitution may confer new side-effects. - Provide adherence support
Clinically and immunologically stable[d]	Give priority to viral load testing or consider	- No evidence to support the efficacy of DTG when used in combination with an inactive NRTI backbone

	clinical indications for substitution to DTG based ART	- Provide adherence support
Stable[d] on suboptimal first-line ART regimens	Substitute to TDF+3TC+DTG	- Substitution may confer new side-effects. - Provide adherence support

[a] Effective contraception should be offered to adult women and adolescent girls of childbearing age or potential. DTG can be prescribed for adult women and adolescent girls of childbearing age or potential who wish to become pregnant or who are not otherwise using or accessing consistent and effective contraception if they have been fully informed of the potential increase in the risk of neural tube defects (at conception and until the end of the first trimester).

[b] If women identify pregnancy after the first trimester, DTG should be initiated or continued for the duration of the pregnancy.

[c] After adherence check and persistent detectable viral load.

[d] Defined as stable based on national guidelines.

HIV Drug Resistance

HIV drug resistance (HIVDR) is caused by a change (mutation) in the genetic structure of HIV that affects the ability of a particular drug or combination of drugs to block the replication of the virus. All current ARV drugs, including newer classes, are at risk of becoming partly or fully inactive because of the emergence of drug-resistant virus. Broadly speaking, there are three main categories of HIVDR.

- **Acquired HIVDR** develops when HIV mutations emerge from viral replication among individuals receiving ARV drugs.
- **Transmitted HIVDR** is detected among ARV drug–naive people with no history of ARV drug exposure. Transmitted HIVDR occurs when previously uninfected individuals are infected with virus that has drug-resistance mutations.
- **Pretreatment HIVDR** is detected among ARV drug–naive people initiating ART or people with prior ARV drug exposure initiating or reinitiating first-line ART. It can result from either transmitted or acquired HIV drug resistance, or both. Pretreatment HIVDR may have been transmitted at the time of infection (transmitted HIVDR) or may be acquired from previous ARV drug exposure (such as among women exposed to ARV drugs for the prevention of mother-to-child transmission (PMTCT) of HIV, among individuals reinitiating first-line ART after a period of treatment interruption without documented treatment failure or among people who have received pre-exposure prophylaxis (PrEP)).

Pretreatment HIVDR

A high prevalence of pretreatment HIV drug resistance to NNRTIs (especially in low- and middle-income countries) negatively affects the success of the HIV program and potentially endangers the attainment of the global target to end AIDS as a global threat. Therefore, the following recommendations have be made by WHO on pretreatment HIVDR:

1. For people initiating first-line ART with pretreatment HIVDR to NNRTIs, a non-NNRTI-containing regimen may be preferable
2. Among people at high risk of pretreatment HIVDR to NNRTIs, a non-NNRTI-containing regimen may be preferable, regardless of the country prevalence of pretreatment HIVDR to NNRTIs and without the need to document the presence of NNRTI resistance by using an HIVDR test.
3. For children, pregnant women and individuals receiving rifampicin for the treatment of TB, the choice of a non-NNRTI-based regimen should be carefully considered in light of the limited options available, existing age-appropriate formulations, safety and potential drug interactions as well as the overall principles for drug optimization in ART programmes.

Treatment Failure

Treatment failure can be classified as:

1. Clinical failure
2. Immunological failure, or
3. Virological failure

An individual must be taking ART for at least six months and the drug adherence is assessed to be 95% before it can be determined that a regimen has failed. Clinical events that occur before the first six months of therapy are excluded from the definition of treatment failure because they represent immune inflammatory reconstitution syndromes related to pre-existing conditions.

Before changing to 2nd line ART, adherence counselling is imperative. Commencement of a second line ART should be reconsidered if there is poor adherence to the first line ART. Second line ART is far more complex and likely to fail with poor adherence. Changing to a second-line ART is not the solution for poor drug adherence.

Table 9 Consideration before diagnosing treatment failure

Prerequisite	**Patients should be on ART for six months and ARV drug adherence assessed to be >95%**	
Definitions	**Clinical failure**	**Adults and Adolescents:** New or recurrent WHO stage 4 condition and certain WHO clinical stage 3 diseases (pulmonary TB and severe bacterial infections). **Children:** New or recurrent WHO clinical stage 3 or 4 with the exception of TB.
	Immunological failure	**Adults and Adolescents:** CD4 count at or below 250 cells/mm^2 following clinical failure OR Persistent CD4 levels below 100cells/mm^3 **Children:** - <5years of age: persistent CD4 levels <200cells/mm^3 or <10%; - >5years of age: persistent CD4 levels <100cells/mm^3
	Virological failure	Plasma viral load >1,000 copies/ml based on 2 consecutive viral load measurements in three months, with adherence support with adherence support following the 1st viral load test.

Second-line ART recommendations for adults and adolescents.

(>= 10years) including pregnant and breastfeeding women.

Table 10 Second-line ART recommendations for adults and adolescents

Population	Failing first-line regimen[a]	Preferred second-line regimen	Alternate second-line regimen
Adults and adolescents	TDF[b] + 3TC (or FTC) + DTG[c]	AZT + 3TC + PI/r	AZT + 3TC + DRV/r
	TDF + 3TC (or FTC) + EFV (or NVP)	AZT + 3TC + DTG[c]	AZT + 3TC + PI/r
	AZT + 3TC (or FTC) + EFV (or NVP)	TDF[b] + 3TC (or FTC) + DTG[c]	TDF[b] + 3TC (or FTC) + PI/r

[a] *Sequencing if PIs are used in the first-line regimen: ATV/r (or LPV/r or DRV/r) + TDF + 3TC (or FTC) and then AZT + 3TC + DTG in second-line ART.*

[b] *TAF can be used as an alternative NRTI in special situations.*

[c] *Effective contraception should be offered to adult women and adolescent girls of childbearing age or potential. DTG can be prescribed to adult women and adolescent girls of childbearing age or potential who wish to become pregnant or who are not otherwise using or accessing consistent and effective contraception if they have been fully informed of the potential increase in risk of neural tube defects (at conception and until the end of first trimester). If women identify pregnancy after first trimester, DTG should be initiated or continued for the duration of the pregnancy.*

Patient Monitoring

Routine Monitoring

CD4 Cell count monitoring

CD4 cell testing at the point of care can be used to prioritize patients for urgent linkage to care and ART initiation. It is the best indicator for gauging the status of the immune system and for determining whether the HIV-positive patient is at risk of certain opportunistic infections. The higher the CD4 count, the risk for OIs will be lower.

It is recommended to monitor CD4 cell counts every 6 months, whether the patient is on ART or not. If the patients are stable on ART, then CD4 counts can be stopped or become yearly. Patients should be informed that CD4 cell counts are variable. Caution patients not to pin emotions and hopes on a single laboratory result. A change of <30% may not be significant. Implausible CD4 cell count results should be re- checked after 2-4 weeks.

Viral Load Monitoring

Routine viral load monitoring can be done at 6 months after initiation, at 12 months and then annually if the patient is stable on ART. WHO defines people stable on ART according to the following criteria: on ART for at least one year, no current illnesses or pregnancy, good understanding of lifelong adherence and evidence of treatment success (two consecutive viral load measurements below 1000 copies/mL). WHO recommends a threshold of 1000 copies/mL based on the fact that the risk of HIV transmission and disease progression is very low when viral load is lower than 1000 copies/mL, this is known as being virally suppressed. Patients should understand that undetectable viral load does not mean that HIV has been eradicated or that the patient is not infectious to others.

Drug Susceptibility Test (DST)

Drug susceptibility test is done to look for mutations in the antiretroviral drugs. Certain mutations are associated with development of resistance. Some ARV needs many mutations before resistance is evident, e.g. protease inhibitors, and some just need one mutation to develop resistance, e.g. non-nucleoside reverse transcriptase inhibitors.

There are two types of resistance that can develop:

1. Primary resistance – some HIV strains are naturally resistant to some ARVs.
2. Induced resistance – can occur when there is a high level of virus production and turnover due to non-adherence. The reverse transcriptase of viral DNA into RNA is prone to error.

DST will be done only when treatment failure is suspected, and some random samples will be sent quarterly for surveillance and monitoring purpose.

Clinical Monitoring

Clinical assessment of the patient at each clinic visit (whether ART or not) as well as monitoring the patients adherence to ARV drugs will provide valuable information on patients response to ART. CD4 cell count and viral load testing complement clinical monitoring of patients.

Symptom-directed laboratory monitoring for safety and toxicity is recommended for those on ART. For example, serum creatinine and estimated glomerular filtration rate (eGFR) may need to be monitored in patients on tenofovir (TDF); haemoglobin in patients on zidovudine (AZT); and serum alanine transferase (ALT) in those patients on nevirapine (NVP).

Findings of clinical assessment and laboratory findings should be discussed with patients, treatment and support persons and caregivers. They should be provided with appropriate advice, management, and referral to the relevant health and support services that are required. Provide a schedule for the next laboratory tests as well as for the date of the next clinic follow-up.

Table 11 Recommended schedule for the clinical and laboratory monitoring of HIV- positive patients not initiated with ART (i.e. on HIV care) and for those who are on ART

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) CD4 cell count TB symptom screening	HBV (HBsAg) serology HCV serology Cryptococcus antigen if CD 4 cell count is < 100 cells/mm^2 Screening for STIs Pregnancy test to assess if ART initiation should be prioritized to prevent HIV transmission to the child Assessment for major non communicable chronic diseases and comorbidities
Follow-up before ART	CD 4 cell count (every 6-12 months in circumstances where ART initiation is delayed)	
ART initiation		Haemoglobin test for starting AZT Pregnancy test Blood pressure measurement Serum creatinine and estimated glomerular filtration rate (eGFR) or starting TDF Alanine aminotransferase for NVP Baseline CD4 cell count
Receiving ART	HIV viral load (at 6 months and 12 months after initiating ART and every 12 months thereafter) CD 4 cell count every 6 months until patients are stable on ART	Serum creatinine and eGFR for TDF 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 Pregnancy test, especially for women of childbearing age not receiving family planning and on treatment with DTG or low dose EFV	HBV (HBsAg) serology (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)

Drug- to-Drug Interaction

Drug interactions can decrease the efficacy of ART and/or increase ART-related toxicities. Providers should be aware of all drugs that PLHIV are taking when ART is initiated, these includes:

i. Alternative medicine products such as herbal medicine,
ii. Dietary supplements,
iii. Or new drugs added during treatment maintenance

Table 12 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 Adjust 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 agent
	Methadone and buprenorphine	Adjust methadone and buprenorphine doses as appropriate
	Astemizole and terfenadine	Use alternative antihistamine agent
	TDF	Monitor renal function
	Simeprevir	Use alternative (direct-acting antiviral) 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 antacids. 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
	Rifampicin	Substitute NVP with EFV
	Methadone	Adjust the methadone dose as appropriate
NVP	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

COVID-19

Dexamethasone is used at doses ranging from 6mg upto 20mg daily for short duration for people with COVID-19. At such doses, dexamethasone has a weak to moderate inducing effect that does not warrant any dose adjustment of Efavirenz, Nevirapine, Protease Inhibitors, Dolutegravir or Raltegravir. Conversely, Efavirenz and Nevirapine may decrease dexamethasone concentrations, and doubling of the dexamethasone dose is therefore recommended. No drug-to-drug interactions are expected between ARVs and COVID-19 vaccines.

Antiretroviral Drug Toxicities

Drug related toxicities may occur during any stage of ART, and may vary in severity from mild to severe and can be life-threatening. In general, mild toxicities may be managed symptomatically without interruption of treatment. More severe toxicities may require a change in ART regimen, Life threatening adverse reactions necessitate temporary cessation of the entire ART regimen until the toxicity has resolved.

Table 13 Guiding principles in the management of ARV drug toxicity

Determine the seriousness of the toxicity	
Evaluate the concurrent medication and establish whether the toxicity is attributable to an ARV drug or drugs, or to a non-ARV medication taken at the same time.	
Consider other disease processes (e.g. viral hepatitis in an individual on ARV drugs who developed jaundice) because not all problems that arise during treatment are caused by ARV drugs.	
Manage the adverse event according to severity. In general:	
Mild reactions	These are bothersome but do not require change in therapy.
Moderate reactions:	Consider continuing ART as long as feasible. If the patient does not improve on symptomatic therapy, consider single drug substitutions. For a few moderate toxicities (e.g. peripheral neuropathy or lipodystrophy), single-drug substitution needs to be considered earlier.
Severe reaction	Substitute the offending drug without stopping ART.
Severe life-threatening reactions	Immediately discontinue all ARV drugs, manage the medical event (i.e. symptoms and supportive therapy) and re-introduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilized.
Stress the maintenance adherence despite toxicity for mild and moderate reactions	
If there is a need to discontinue ART because of life threatening toxicity, all ARV drugs should be stopped until the patient is stabilized	

Before concluding that the ARV drugs are the primary cause of toxicity, alternative explanations for the toxicity must be excluded. Adverse reactions that have a non-ARV drug aetiology do not require changing the drug.

Management of ARV Drug Toxicities

Table 14 Toxicities associated with selected 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. Substitute with AZT or TDF/TAF.
ATV/r	Electrocardiographic abnormalities (PR and QRS interval prolongation)	People with pre-existing conduction system disease Concomitant use of other drugs that may prolong the PR or QRS intervals 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 hyperbilirubinemia (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, neutropenia	CD4 cell count of ≤200 cells/mm3	Substitute with TDF or ABC. Consider use of low-dose zidovudine.
	Lactic acidosis or severe hepatomegaly with steatosis, lipoatrophy lipodystrophy, myopathy	BMI >25 (or body weight >75 kg) Prolonged exposure to NRTIs	Substitute with TDF or ABC.
DTG	Hepatotoxicity Hypersensitivity reactions	Hepatitis B or C Coinfection 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 HBV and HCV coinfection Concomitant use of hepatotoxic drugs	Substitute with ATV/r or LPV/r. When it is used in third-line ART, limited options are available.
	Severe skin and hypersensitivity reactions	Sulphonamide allergy	For hypersensitivity reactions, substitute with another therapeutic class.
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. For severe hepatotoxicity or hypersensitivity reactions, substitute with another therapeutic class (integrase inhibitors or boosted PIs).
	Convulsions	History of seizures	
	Hepatotoxicity	Underlying hepatic disease HBV and HCV coinfection Concomitant use of hepatotoxic drugs	
	Severe skin and hypersensitivity reaction	Risk factor(s) unknown	
TDF	Lactic acidosis Severe liver disease	Obesity Increased risk in females Prolonged use of TDF Underlying Hepatitis B infection and any other liver disease Older age (unusual in young children) Pregnancy	Discontinue ART for at least 4 weeks (till lactate levels normalise) Hospital treatment according to severity Substitute TDF or ABC for A Z T .
RAL	More common: Nausea, headache, dizziness, diarrhea, fatigue, itching, and insomnia. Less common: Abdominal pain, vomiting. Patients with chronic active hepatitis B virus infection and/or hepatitis C virus infection are more likely to experience a worsening Grade from baseline for laboratory abnormalities of aspartate, AST, ALT, or total bilirubin than are patients who are not co-infected. Rare: Moderate to severe increase in creatinine phosphokinase.	Use RAL with caution in patients receiving medications associated with myopathy and rhabdomyolysis. Anxiety, depression, and paranoia, especially in those with prior history. Rash, including Stevens-Johnson syndrome, hypersensitivity reaction, and toxic epidermal necrolysis. Thrombocytopenia. Cerebellar ataxia. Hepatic failure (with and without associated hypersensitivity) in patients with underlying liver disease and/ or concomitant medications.	Discuss with HUB medical officer for management of toxicity

Where toxicity is the reason for changing the regimen, and the offending drug is known, this agent alone can be replaced, using another drug that does not have the same toxicity profile. Wherever possible, a single drug substitution because toxicity should be with a drug belonging to the same ARV drug class.

Immune Reconstitution Inflammatory Response (IRIS)

Immune reconstitution inflammatory response is a paradoxical phenomenon that occurs in a newly diagnosed PLHIV who has an underlying stage 3 or 4 opportunistic infection and has been initiated on ART with or before the treatment of that particular opportunistic infection.

IRIS develops within the first 2-3 months of ART commencement but can occur earlier or later. This happens because due to the initiation of ART the number of CD4 cells increase rapidly causing immune recovery in the setting of an untreated or not fully treated opportunistic infection.

There are 2 patterns of IRIS:

1. Paradoxical IRIS – worsening symptoms of an established infectious or inflammatory process
2. Unmasking IRIS – new onset of symptoms or signs of an infectious or inflammatory process that was unsuspected prior to the initiation of ART.

Important elements for an illness to be considered as IRIS:

i. Temporarily related to ART initiation; usually within the first 12 weeks
ii. More frequent in patients with low CD4 at start of ART (<50cells/mm^3)
iii. More likely if antiretroviral naïve
iv. Documented improvement in the immune status, i.e. increase in the CD4 cell count
v. No evidence of new infectious process or drug toxicity
vi. Patient has been previously treated for t his disease "unmasking" of a previously undiagnosed infection
vii. Clinical evidence of inflammatory condition
viii. Common stage 3 and 4 opportunistic infections associated with IRIS are: TB, PJP, toxoplasmosis, CMV, MAC, herpes zoster

The case definition of IRIS is:

i. New onset or worsening symptoms of an infection or inflammatory condition after start of ART
ii. Symptoms not explained by:
    a. Newly acquired infection
    b. Predicted course of previously diagnosed infection
    c. Adverse effects of drug therapy
iii. Decrease in VL>1 log10 copies/mL (if available)

To diagnose IRIS, any one or a combination of case definition can be used.

IRIS is a diagnosis of exclusion! Exclude causes such as:

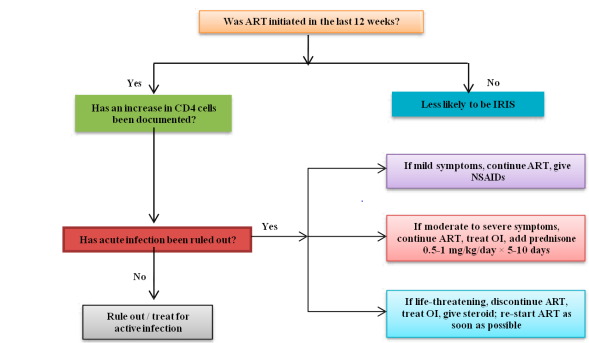
- Drug-resistant infection
- Drug allergy or other adverse drug reactions
- Patient noncompliance
- Reduced drug levels due to drug-drug interactions and mal-absorption

The general management of IRIS includes treatment of the causative pathogen to decrease the antigenic load, continuation of ART, and the use of anti-inflammatory agents.

Table 15 Diagnostic criteria for IRIS, (Adapted from French MA et al. Immune restoration disease after antiretroviral therapy, AIDS, 2004, vol. 18 (pg. 1615-1627)

Major criteria	A. Atypical presentation of OI in patients responding to ART	Localized diseases e.g. lymph nodes, liver and spleen
		Exaggerated inflammatory reaction e.g. severe fever, with exclusion of other causes
		Atypical inflammatory response in affected tissues e.g. granulomas, suppuration, necrosis
		Progression of organ dysfunction or enlargement of pre-existing lesions after definite clinical improvement
	B. Decrease in VL >1 log10 copies/ml (i.e. by 90%)	
Minor	Increased blood CD4 T-cell count after ART	
	Increase in an immune response specific to the relevant pathogen e.g. DTH response to mycobacterial antigens	
	Spontaneous resolution of disease without specific antimicrobial therapy or tumour chemotherapy with continuation of ART	

Figure 6 Algorithm for the management of immune reconstitution inflammatory syndrome



If the above recommended treatment is not responding, **3 doses of Infliximab 5-10 mg/kg infusion 4-6 weeks apart**, can be used as an alternative or adjuvant therapy for severe steroid-resistant IRIS.

3

OBSTETRICS CARE & BREASTFEEDING

Section III HIV in Obstetrics Care & Breastfeeding

Guiding Principles for HIV care in obstetrics and the breastfeeding period

HIV can be transmitted from an HIV positive mother to her child during pregnancy, labour and delivery, and through breastfeeding. To reduce mother-to-child transmission of HIV, there is a need to have a unified approach, throughout pregnancy, labour and delivery, and the breastfeeding period.

Health care providers should be guided by the principles outlined below for the different clinical situations that they may encounter in delivering care to pregnant patients.

The comprehensive strategy for the 'Prevention of Parent to Child Transmission' (PPTCT) of HIV infection has four key principles:

1. Prevention of HIV acquisition among women of childbearing age
2. Prevention of unintended pregnancies among women living with HIV.
3. **Prevention of HIV transmission from women living with HIV to their children.**
4. Provision of care, treatment and support to mothers living with HIV, their partners, their children, and their families.

This section will focus on the third key principle i.e. prevention of mother-to-child PMTCT of HIV (the other three key principles will be covered in the PMTCT policy and procedure manual)

In this strategy ARV drugs are used for HIV positive pregnant and breastfeeding women for their own health and to prevent the exposed child from becoming infected. If used consistently, to the level of viral load reduction, it may also offer benefits for preventing sexual transmission of HIV to sexual partners.

While respecting the confidentiality of the mother and the child, information on a patients HIV status, PPTCT or ART, is shared among health personnel that provide direct care to the patient. This is called confidentiality amongst healthcare workers and is essential for maintaining continuum of care (COC) among women and children.

Pre- and post-test services for antenatal mothers and the early postnatal period

All pregnant women should:

i. Be encouraged to book early into antenatal care, as soon as they believe they are or are confirmed pregnant.
ii. Receive routine antenatal care, including micronutrient supplementation e.g. iron and folic acid.
iii. Be routinely offered HIV pre-test information, counselling and testing, STI screening (including Hepatitis B and syphilis), pap smear and encourage partner counselling and testing (ideally, couple HIV counselling and testing).
iv. Be offered information on the availability of PPTCT interventions during all health care facility visits (and not only during antenatal clinic visits).
v. Be encouraged to involve partners in caring for pregnancy.
vi. Be counselled on safer sex and provided with condoms.
vii. Be counselled on safe infant feeding options, assisted in making an appropriate infant feeding choice, and supported on their choice.

Table 16 List of essential health services to be provided to every pregnant woman

Personal or Individual	Support
- Antenatal screening, Obstetric care, including history-taking and physical examination - Health education information on HIV and STI prevention, screening and management i.e. Syphilis, Hepatitis B - Birth Planning and delivery options - Optimal infant feeding - Family planning counselling (includes desired family size and future pregnancies) - Related health services (e.g. contraception, paps smear) - Tetanus vaccination - Iron and folic acid supplementation - HIV testing, including support for disclosure	- Couple and partner HIV counselling, promotion, testing and provision of condoms - HIV related gender-based violence screening - Maternal and nutrition support - Infant feeding counselling - Psychosocial support - Interventions for PPTCT for HIV- positive pregnant women with referral to appropriate care - ART adherence counselling for women on treatment - HIV counselling and testing, including HIV counselling and testing for women of unknown status at labour and delivery, or postpartum - Care including safer sex practices

Non-consenters to HIV testing

Pregnant women who choose not to be tested for HIV should:

i. Receive another counselling session.
ii. Be offered HIV testing at every subsequent visit in the antenatal clinic in a non-coercive manner.
iii. Also be offered HIV testing at the onset of labour: and if this is not possible, then be offered HIV testing shortly after birth.

Unbooked women in labour

Unbooked women presenting in labour should:

i. Be counselled and have a rapid HIV screening test.
ii. Be offered and receive PPTCT intervention as per guidelines if the HIV screening test is reactive.
iii. Have her HIV screening test confirmed and followed up as early as possible.
iv. Be informed about HIV confirmatory test result
v. Be referred to the HUB centre for appropriate care and management after delivery if the HIV confirmatory test result is positive.
vi. Should be offered HIV counselling and testing after delivery if this was not possible during labour
    a. If A1 positive – administer ARV immediately.
    b. If A2 is negative – stop ART.

Baby born (to unbooked mother) before arrival at any health facility

Women presenting immediately post-partum should:

- Be provided with pre-test information and offered a rapid HIV screening test
- Be offered PPTCT intervention to her baby if the HIV screening test is reactive at labour ward or postnatal ward.
- Have her HIV screening test confirmed and followed up as early as possible.
- Be informed about the HIV confirmatory test result.
- Be referred to the HUB centre for appropriate care and management after delivery if the HIV confirmatory test result is positive.

Post-test counselling for Pregnant women.

Post-test counselling for pregnant women who are diagnosed with an HIV infection should include the following, in addition to the standard messages described for adults and adolescents diagnosed with HIV infection:

i. childbirth plans: providers should encourage HIV-positive pregnant women to deliver in a Divisional health facility or any other health facility providing comprehensive HIV services, to ensure access to PMTCT services;

ii. use of ARVs for the client's health, where indicated and available, as well as the use of ARV to prevent transmission to the infant;

iii. the importance of partner testing and information on the availability of couples testing services;

iv. HIV testing for the infant and needed follow-up for HIV-exposed infants;

v. ensuring screening for TB and testing for other infections such as syphilis and hepatitis;

vi. be offered all other clinical assessment, CD4 count testing, hepatitis C, and other opportunistic infections, and treated appropriately;

vii. counselling on adequate maternal nutrition, including iron and folic acid;

viii. advice on infant feeding options and support to carry out the mother's infant feeding choice;

ix. receive routine antenatal care, including iron and folic acid supplementation;

x. be offered information on the availability of PPTCT interventions at all healthcare facilities;

xi. careful monitoring for the development of pregnancy induced hypertension and pre-eclampsia, especially for women on ART;

xii. offered co-trimoxazole prophylaxis and TB preventative prophylaxis, if indicated.

xiii. started on ART as early as possible, managed appropriately, and monitored regularly; and

xiv. be counselled on safer sex, family planning, cervical screening, postnatal contraception, adherence to treatment, HIV care and regular clinic follow up.

The HUB centre must be notified of all HIV positive pregnant women.

Negative Pregnant Women

Pregnant women who test negative should:

i. Receive post-test counselling, and counselling on the risk reduction interventions including involvement of their partners, mainly focusing on how to maintain their HIV negative status.
ii. Continue to receive routine antenatal care and should be encouraged to use condoms.
iii. Be offered a repeat HIV test 6 weeks after the initial test or at third trimester of pregnancy, (depending on the risks behaviour identified) whichever is earlier, to detect those who may have seroconverted during pregnancy.
iv. Pregnant women who initially tested HIV negative and subsequently test HIV positive during pregnancy, should be referred for appropriate care and management.

Retesting in pregnancy

Although ART prevents vertical transmission of HIV most effectively when given early in pregnancy, it has some efficacy (especially when combined with infant ARV prophylaxis) even when started late in pregnancy, at the time of delivery or during the breastfeeding period.

Pregnant woman who are diagnosed HIV positive should be retested to verify their HIV status prior to enrolling in care and/or treatment, only if the women requests for a retest.

HIV diagnosis in Pregnancy

For screening, testing and diagnosis of HIV in pregnancy, refer to Section 2 on HIV diagnosis in adults and adolescents.

Clinical Management of HIV positive pregnant women and breastfeeding mothers.

Co trimoxazole among HIV positive pregnant women and breastfeeding women.

HIV-positive pregnant and breastfeeding who fulfil the criteria for co-trimoxazole prophylaxis should be given co-trimoxazole. There is no evidence of an increase in co-trimoxazole- related adverse events among pregnant women versus non-pregnant women (refer to relevant section in section II).

Antiretroviral treatment

First line ART recommendations for HIV positive pregnant women and breastfeeding women.

Table 17 First- line ART recommendations for pregnant and breastfeeding women

	Pregnant and Breastfeeding Women[a]
Preferred first-line ART regimen	TDF + 3TC (or FTC) + DTG
Alternative first-line ART regimen	TDF + 3TC (or FTC) + EFV
Special situation	AZT + 3TC (or FTC) + EFV TDF + 3TC (or FTC) + PI/r[b] ABC + 3TC (or FTC) + DTG TDF + 3TC (or FTC) + RAL

[a] *Based on programmatic practicality and uncertainty surrounding possible DTG effects after the neural tube closes at 28 days of gestation as noted by the originator and FDA, previous safe period after 8 weeks is now extended to after the first trimester. In practice, the majority of women will not yet know that they are pregnant during the first 8-12 weeks of pregnancy.*

[b] *If the national prevalence of pre-treatment resistance to EFV or NVP is 10% or higher or if no other alternatives are available.*

Table 18 Treatment guideline recommended for the prevention of PTTCT of HIV (WHO, 2015)

Clinical scenario	Maternal ART	Infant ARV prophylaxis [a]	Duration of infant ARV prophylaxis
Mother diagnosed with HIV during pregnancy	Initiate maternal ART	Zidovudine (AZT) or Nevirapine (NVP)	6 weeks of single ARV, consider extending both ARVs (AZT + NVP) to12 weeks if diagnosed in late pregnancy and falls in the high-risk infant category[b]
Mother diagnosed with HIV during labour or immediately postpartum and plans to breastfeed	Initiate maternal ART	Zidovudine (AZT) and Nevirapine (NVP)	12 weeks of dual ARV (AZT + NVP)
Mother diagnosed with HIV during labour or immediately postpartum and plans replacement feeding	ART initiated by the Obstetrician or Medical Officer.	Zidovudine (AZT) and Nevirapine (NVP)	12 weeks of dual ARV (AZT + NVP) DNA PCR testing at 6 weeks, if negative – cease ARVs
Infants identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is breastfeeding	Initiate maternal ART	Zidovudine (AZT) and Nevirapine (NVP)	Collect DBS for HIV DNA PCR for early infant diagnosis (EID) if infant is > 6 weeks old. If infant is < 6 weeks old, then treat as high-risk infant[b] until diagnosis is established or 12 weeks of dual prophylaxis is completed.
Infants identified as HIV exposed after birth (through infant or maternal HIV antibody testing) and is not breastfeeding	Refer to the Paediatricians for infant and Obstetrician & Hub Centre for maternal care and ART initiation.	No drug	Collect DBS for HIV DNA PCR for EID. Give 6 weeks of dual prophylaxis as high-risk infant[b]. Continue ART if DNA PCR result is positive.
Mother receiving ART but interrupts ART regimen while breastfeeding (infant of any age) (such as toxicity, stockouts or refusal to continue)	Counsel regarding continuing ART without interruption	Zidovudine (AZT) or Nevirapine (NVP)	Continue for 12 weeks after maternal ART is re- started. If mother cannot tolerate or declines ART, the continue NVP throughout the duration of breastfeeding until one week after breastfeeding has ended.

[a] Nevirapine can be used if Zidovudine is not available.

[b] High-risk infant category definition:

- Born to women with established HIV infection who have received less than 4 weeks of ART at the time of delivery; or
- Born to women with established HIV infection with VL>1000 copies/mL in 4 weeks before delivery; or
- Born to women with recent HIV infection during pregnancy or breastfeeding without ART; or
- Identified for the first time during the postpartum period.

Intrapartum Management

Healthcare workers providing antenatal care or any form of clinical care to a pregnant women must always check the pregnant women's HIV status, and if the mother is a PLHIV, then details of her ARV drugs must be obtained and documented.

Standard precautions for infection control should be strictly practiced at all times.

If the pregnant women's status is unknown, and the women is:

- In 1st stage of labour – HIV pre-test information must be shared as soon as possible, and testing, and post-test counselling should be provided at this time.
- 2nd stage of labour just prior to delivery - pre-test information, testing and post-test counselling should be provided as soon as possible after delivery.

Caesarean Section

- Caesarean section should be performed for obstetrics and medical indications and are not generally indicated for the reduction of mother-to-child transmission of HIV.
- Caesarean section is only indicated in pregnant women with HIV who have high viral load or women on ARV for less than 6 weeks.
- For planned elective (as well as emergency) caesarean sections for obstetrics and medical indications, ensure that PLHIV Pregnant women who are already on ART are adherent to their medications.
- All PLHIV Pregnant women who undergo caesarean sections should receive prophylactic antibiotics as per protocol (Antibiotic Guideline).

Post partum management

HIV exposed infants and children are those born to mothers living with HIV or children breastfeeding from mothers living with HIV until exposure stops, i.e. 6 weeks after complete cessation of breastfeeding and HIV infection is excluded.

Care of HIV exposed infants should follow standard neonatal care according to safe motherhood practices:

i. The baby's mouth and nostrils should be wiped as soon as the head is delivered.
ii. Only suction the baby's nose and airway when there is the presence of meconium-stained secretions.
iii. Infants should be handled with gloves until all blood and maternal secretions have been removed (early baby bathing)
iv. The cord should be clamped after birth using delayed clamping procedure, and milking should be avoided.
v. Initiate feeding within the first hour of birth according to the mother's preferred and informed choice.
vi. Paediatricians need to be informed as soon as possible of the delivery of a positive pregnant mother to ensure feeding options are understood. Breastfeeding is highly recommended.
vii. Prophylaxis should have been initiated for baby (refer to Section IV on HIV care in paediatrics).
viii. Infant is booked to relevant paediatric clinic.
ix. Referral needs to be made to the HIV HUB centre for the review and continuum of care for the mother and partner (if not already done so).

Ensure routine postpartum care is provided for both mother and baby.

Family Planning

Emphasis on family planning and the use of contraception must be discussed thoroughly with the mother and her partner. (WHO Family Planning Handbook 2018 Edition). Condoms can be used safely in both people who are infected with STIs and HIV as a dual barrier method (prevention of STIs/ HIV and pregnancy).

Table 19 Family planning options for women living with HIV

Method	Has Sexually Transmitted Infections	Has HIV
Intrauterine device (copper bearing IUD or LNG-IUD)	Do not insert an IUD in a woman who is at high risk for gonorrhoea and chlamydia, or who currently has gonorrhoea, chlamydia, purulent cervicitis, or PID. (A current IUD user becomes infected with gonorrhoea or chlamydia or develops PID can safely continue using IUD during and after treatment).	A woman with HIV Clinical stage that is mild or with no symptoms, including a woman on ARV treatment, can have an IUD inserted. Generally, a woman should not have an IUD inserted if she has HIV clinical disease that is severe or advanced, (WHO stages 3 or 4). A woman, using an IUD who becomes infected with HIV or whose HIV clinical stage becomes severe or advanced (WHO stage 3 or 4) can safely continue using the IUD. A woman using an IUD can keep the IUD in Place when she starts ARV therapy.
Female sterilization	If client has gonorrhoea, chlamydia, purulent cervicitis, or PID, delay sterilization until the condition is treated and cured.	Women with HIV, including women on ARV therapy, can safely undergo female sterilization (tubal ligation). The procedure may be delayed if she currently has an HIV-related illness.
Vasectomy	If client has scrotal skin infections, active STI or swollen, tender tip of penis, sperm ducts, or testicles, delay sterilization until condition is treated and cured.	Men who are living with HIV, including men on ARV treatment, can safely undergo vasectomy. The procedure may need to be delayed if he currently has an HIV related illness.
Spermicides (including when used with diaphragm or cervical cap)	Can safely use spermicides.	Should not use spermicides if at high risk of HIV. Generally, should not use spermicides if she has HIV infection.
Combined oral contraceptives, monthly injectables, combined patch, combined ring	Can safely use combined hormonal methods.	Can safely use combined hormonal methods.
Progestin-only pills, injectables and implants	Can safely use progestin- only methods.	Can safely use progestin only methods.

4

PAEDIATRICS CARE

Guiding principles for HIV services in paediatrics

Mortality is very high in the first year of life among infants infected with HIV who go untreated. In this period early HIV testing, prompt return of results and rapid initiation of treatment are vital. HIV testing for infants should be implemented with the aim of identifying as many HIV-infected infants as possible, and as early as possible.

Infants and children should be tested in the following circumstances:

i. to identify the HIV-exposure status of all infants for the purpose of appropriate follow up, which includes provision of co-trimoxazole prophylaxis, antiretroviral prophylaxis and/or treatment;
ii. at around 4–6 weeks or as soon thereafter as possible for infants known to be exposed to HIV through mother-to-child transmission to enable early diagnosis of HIV with virological testing;
iii. to confirm the HIV infection status of children born to HIV-positive mothers six weeks after exposure to HIV has ceased or at eighteen months, whichever is sooner;
iv. for the purpose of individual diagnosis in a child who is ill (e.g. presenting with an HIV-associated illness, such as tuberculosis or malnutrition, or other recurrent common childhood illnesses such as pneumonia or diarrhea);
v. for the purpose of individual diagnosis where another sibling or parent has been diagnosed with HIV or where there is a history that the parents have died as a result of AIDS or other undiagnosed debilitating illness in the family;
vi. in cases where a child has been exposed or potentially exposed to HIV
   - through sexual abuse or
   - through contaminated needlesticks or receipt of potentially infectious blood or blood products (or through other routes, e.g. wet nursing).

If provision of post-exposure prophylaxis (PEP) is anticipated in response to any of the above situations, HIV testing should be recommended prior to initiation of antiretrovirals. PEP is only relevant to situations of possible exposure.

In all settings, for improved HIV case finding among infants, children and adolescents

- Offer early infant diagnosis for HIV-exposed infants.
- Offer testing to all children and adolescents presenting with indicator conditions or signs and symptoms that suggest HIV, including oral candidiasis, failure to thrive, chronic diarrhoea, chronic cough, chronic skin conditions and severe sepsis.
- Offer HIV testing to all children and adolescents attending TB clinics and malnutrition services.

Pre- and Post-test services in Paediatrics

Pre-test Information in Paediatrics

HIV Pre-test information in children involves the following:

1. Are done for and in the presence of parents or legal guardians.
2. Is carried out at antenatal clinic, postnatal clinic, children's ward or at any other clinic or location convenient to both parties and ensures the privacy and safety of those involved in the information sharing.
3. Parents or legal guardians must give informed consent for HIV testing for the newborn, infant or child (children) who are unable to consent for themselves.
4. 'Verbal consent suffices' (WHO Recommendation).
5. Testing services must be accompanied by appropriate and quality pre-test information sessions.
6. HIV pre-test information and testing services must have connection or linkage to prevention, care and treatment services that include referral to appropriate follow-up services, and long-term prevention and treatment support.
7. HIV Pre-test information and Post-test counselling in Paediatrics must include the following:
    a. Pre-test Information (previously referred to as pre-test counselling), refer to section on infant feeding below.
    b. Infant feeding option counselling, refer to relevant section below.

Post-test Counselling in Paediatrics

Informing children of their HIV diagnosis is complex, and the approach depends on the child's age and understanding; post-test counselling must consider the following:

1. Are done in the presence of parents or legal guardians at the child's discretion.
2. Counselling is done at any other location convenient to both parties, and ensures the privacy and safety of those involved in the information sharing and counselling.
3. Parents or legal guardians must give informed consent for HIV testing for the newborn, infant or child (children) who are unable to consent for themselves.
4. 'Verbal consent suffices' (WHO Recommendation).
5. HIV counselling and testing services are confidential, meaning that any information will not be disclosed to anyone else without the expressed consent of the child and/or the parents /legal guardians of the child being tested.
6. Counselling and testing services must be accompanied by appropriate and quality pre-test information and post-test counselling.
7. Quality assurance mechanisms must be in place to ensure the provision of correct test results.
8. HIV counselling and testing services must have connection or linkage to prevention, care and treatment services that include

referral to appropriate follow-up services, and long-term prevention and treatment support.

9. HIV Pre-test information and Post-test counselling in Paediatrics must include the following:
    a. Pre-test Information (previously referred to as pre-test counselling), refer to Appendix 1.
    b. Post-Test Counselling for HIV- negative test result, refer to Appendix 2.
    c. Post-test counselling for HIV-positive test result, refer to Appendix 3.
    d. Infant feeding option counselling, refer to Appendix 4.

Disclosure

The health care workers' roles and responsibilities in disclosure include the following:

- Respect the disclosure event by scheduling an appointment with family and staff members chosen by the patient (child or caregiver) whom they trust and with whom they feel comfortable.
- Share the diagnosis quickly; do not ''beat around the bush".
- Keep medical facts to a minimum, describing HIV infection as a chronic illness (explain in further detail over the course of time).
- Use language appropriate to the developmental and cognitive level of the child.
- Accept and foster silence, as the youth needs time to process the important information being given.
- Respect and promote the sharing of feelings and support by family members and staff toward the child, and let the child express his or her feelings and needs.
- Explore the child's knowledge about his/her health, HIV and other chronic illnesses.
- Assess the youth's coping skills, family and peer support, school/work progress, skills and interests.
- Establish follow-up plans.

Disclosure to HIV Positive children

There is evidence of health benefit and little evidence of psychological or emotional harm in the disclosure of HIV status to HIV-positive children. Expected and understandable initial emotional reactions dissipate with time and may respond to interventions.

Children of school age should be told of their HIV-positive status; younger children should be informed incrementally to accommodate their cognitive skills and emotional maturity, in preparation for full disclosure.

Disclosure can be seen as a step in the process of adjusting to an illness and the life challenges it poses.

Discloser of HIV positive adults to their children

Health professionals must support caregivers' decisions whether and when to disclose their HIV diagnosis, and they must respect the individual or family's timing. They do not rush the disclosure process but instead stay alert and sensitive to the families' feelings and needs as they evolve through the phases of disclosure.

- During educational sessions the staff member prepares family members to answer embarrassing or painful questions that children are likely to ask (e.g. about sexual practices or drug use).
- The team of health professionals assists caregivers in revealing other family secrets first, such as adoption.
- Caregivers who have disclosed to their youth with good psychological adjustment serve as peer supporters to other caregivers.
- Staff members must consider the stage of HIV and the child's medical condition because fear, pain and fatigue further compromise the child's and family's emotional energy levels during the disclosure process. They avoid disclosure during a medical crisis or acute illness.
- Emphasizing confidentiality, the staff member engages the patient in a ''partnership'' based on confidence and trust.
- Throughout the sessions the staff member ensures that the child seems curious and ready to learn more about his/her medical condition.
- When the patient is ready to know more about his/her medical condition, the patient can choose which family and staff members he/she wants present at the disclosure session.

There is evidence of health and life planning benefit for the children, with and without HIV, of HIV-positive caregivers if the caregiver discloses to them.
Children of school age should be told of their caregivers' HIV status; younger children should be informed incrementally to accommodate their developing cognitive skills and emotional maturity. Children may need to be reassured as to how the parent/caregiver is feeling and have fears and concerns addressed.

Disclosure of Healthcare workers to Family members and supporters of HIV positive children and dependants involved in their ongoing care.

Initial Assessment

In contemplating conducting an HIV test on a newborn, infant or child, the following initial assessment must be carried out.

Table 20 Summary of the required initial assessment for all suspected or exposed infants and children

Clinical Assessment	
Physical examination	General observation, full physical examination, oral examinations and oral health assessment
Vital signs	Blood Pressure, heart rate, respiratory rate, temperature, weight (kg) and height (cm) with nutritional status (MUAC)
Investigations	FBC, UECR, LFTS. Serology (syphilis, Hep B, HIV, STI), CXR (older children), Sputum AFB, STI/HIV serology
Screening for other 'mother- to-child' transmissible infection	Syphilis, hepatitis, chlamydia infection
Screening for opportunistic infections	TB
Screening for other HIV related conditions	Opportunistic infections
Screen for other medical conditions	DM, liver function, renal function

HIV Testing in Infants and Children

For infants and children under 18 months, HIV infection can be diagnosed only by virological testing; maternal HIV antibodies remain in the infant's bloodstream until 18 months of age, making test results from serological assays ambiguous.

Virological testing using early infant diagnosis (EID) and nucleic acid testing (NAT) technologies can be conducted using dried blood spot (DBS) specimens, which are collected at local sites and sent to centralized laboratories for testing.

For children 18 months of age and older (who were not breastfed or who have stopped breastfeeding at least six weeks earlier), standard HIV serological assays such as RDTs and EIAs can reliably determine HIV status.

> A negative serological test result for an infant does not completely exclude HIV exposure and infection, particularly when certain RDTs are used to test infants between four and 18 months of age, due to imperfect sensitivity during seroconversion for infection acquired postpartum through breastfeeding. During this time virological tests may be used to determine HIV infection.

In line with WHO recommendations:

i. all HIV-exposed infants have HIV virological testing at four to six weeks of age or at the earliest opportunity thereafter.
ii. well HIV-exposed infants undergo HIV serological testing at around nine months of age. Infants who have reactive serological assays at nine months should have a virological test to identify HIV-infected infants who need ART.
iii. children 18 months of age or older with suspected HIV infection or HIV exposure have HIV serological testing performed according to the validated national testing algorithm used in adults.
iv. infants (below 18 months) with signs or symptoms suggestive of HIV infection undergo HIV serological testing and, if reactive, should be referred for virological testing.
v. Children of school age (6–12 years old) should be told their HIV-positive status and their parent's or caregiver's status; younger children should be told their status incrementally to accommodate their cognitive skills and emotional maturity, in preparation for full disclosure.
vi. other health service outlets, in collaboration with the HIV care team of the Division and Subdivision, should test HIV-exposed infants who were not tested for HIV as part of PPTCT services. HIV testing for children and other family members of anyone known to be living with HIV should be prioritized.

HIV Testing Principles for Infants and Children

WHO recommends that HIV Nucleic Acid based Testing (NAT) be used to diagnose HIV infection among infants and children younger than 18 months of age and that ART be started without delay while a second specimen is collected to confirm the initial positive NAT result. Confirmatory testing is critical because of the risk of false positive results, potential contamination with maternal blood (and virus), specimen mislabelling or mix up, laboratory or cross-sample contamination and an observed trend of low detection of HIV among both mothers and infants because of increased exposure to maternal treatment and enhance infant prophylaxis (WHO EID Guideline page 5).

In all settings, infants and children with unknown HIV status who fit the presumptive diagnosis criteria should be routinely tested for HIV. Children with a parent living with HIV should be 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 (WHO Guideline 2nd edition 2016 page 39).

Testing Methodologies in infants and children

Early diagnosis of HIV-exposed infants and children ensures timely treatment and survival. However, making a diagnosis of HIV-exposed infants and children is a challenge. HIV antibody testing is generally used to diagnose HIV infection in adults and children above 18 months of age because of the passive transfer of maternal antibodies (including HIV antibodies) across the placenta to the baby during pregnancy.

HIV antibody testing in infancy cannot be used to confirm HIV infection in the infant but does indicate maternal HIV infection and exposure of the infant. In order to diagnose HIV infection definitively in infants and children below 18 months of age, assays that detect the virus or its components (i.e. virological tests such as HIV DNA PCR through collection of dried blood spots, DBS) are therefore required.

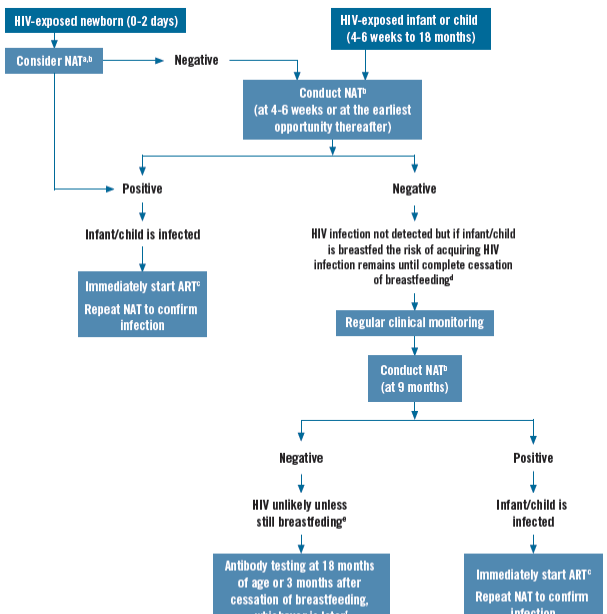
For confirmation of HIV in newborn and infants below 18 months of age, virological testing that detects HIV virus or its components must be used

Specifications for conducting HIV testing in infants and children.

1. All HIV infants should have HIV virological testing at 4-6 weeks of age or at the earliest thereafter.
2. Test results from virological testing in infants are to be returned to the clinic as soon as possible.
3. Mother/caregiver must be notified of the result within 4 weeks of the 1st specimen collection
4. Positive results should be communicated immediately as early as possible.
5. All infants with initial positive virological test results should be started on ART without delay.
6. A second specimen must be collected to confirm the initial test result.
7. Breastfed infants should undergo virological testing at 6 weeks after COMPLETE cessation of breastfeeding.
8. All HIV exposed infants/children who are well are to have a HIV serology test at 18 months of age, preferably during the 18 months MCH immunization visit.
9. Any infants with signs or symptoms suggestive of HIV infection should undergo serological testing and if positive (REACTIVE), virological testing should be done.
10. Children 18 months or older, with suspected HIV infection or exposure, should have serological testing according to the standard diagnostic HIV testing algorithm used in adults – (adapted from WHO recommendations on the use of ART 2nd edition, 2016).
11. MOHMS, Fiji recommends that all siblings of all HIV positive children and children of all HIV positive mothers who have not been previously tested be tested.
12. MOHMS, Fiji recommends that all children (where relevant) admitted into PICU and NICU should be tested for HIV.

Testing strategy for early infant diagnosis using NAT

Figure 7 Early infant diagnosis testing algorithm using NAT

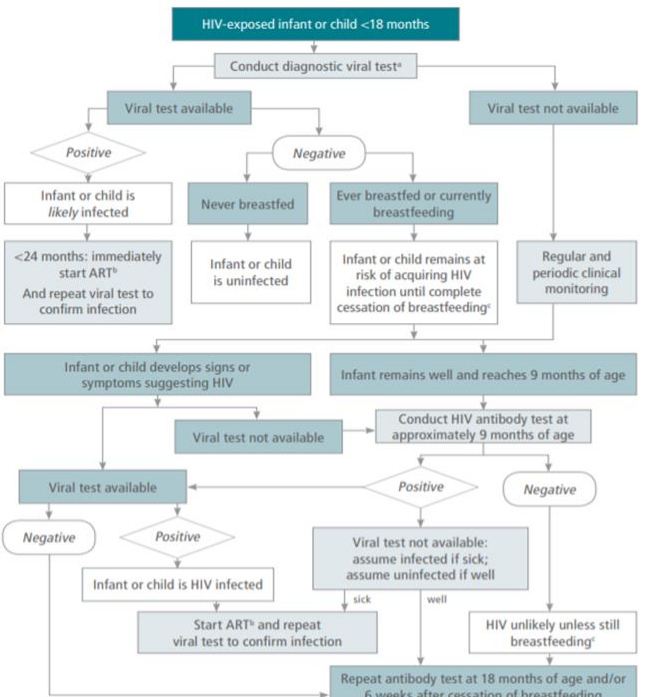


[a] Based on *2016 WHO Consolidated ARV Guidelines*, addition of NAT at birth to the existing testing algorithm can be considered.
[b] POC NAT can be used to diagnose HIV infection as well as to confirm positive results.
[c] Start ART without delay. At the same time, retest to confirm infection. As maternal treatment is scaled up and MTCT transmission rates decrease, false-positive results are expected to increase: retesting after a first positive NAT is hence important to avoid unnecessary treatment, particularly in settings with lower transmission rates. If the second test is negative, a third NAT should be performed before interrupting ART.
[d] For children who were never breastfed, additional testing following a negative NAT at 4–6 weeks is included in this algorithm to account for potential false-negative NAT results.
[e] The risk of HIV transmission remains as long as breastfeeding continues. If the 9-month test is conducted earlier than 3 months after cessation of breastfeeding, infection acquired in the last days of breastfeeding may be missed. Retesting at 18 months or 3 months after cessation of breastfeeding (whichever is later) should be carried out for final assessment of HIV status.
[f] If breastfeeding extends beyond 18 months, the final diagnosis of HIV status can only be assessed at the end of breastfeeding. If breastfeeding ends before 18 months, the final diagnosis of HIV status with antibody testing can only be assessed at 18 months. Antibody testing should be undertaken at least 3 months after cessation of breastfeeding (to allow for development of HIV antibodies). For infants younger than 18 months of age NAT should be performed to confirm infection. If the infant is older than 18 months, negative antibody testing confirms that the infant is uninfected; positive antibody testing confirms infant is infected.

Source: HIV diagnosis and ARV use in HIV-exposed infants: a programmatic update (12).

Early Infant diagnosis – simplified

Figure 8 Establishing the presence of HIV infection in HIV-exposed infants and children less than 18 months of age in resource-limited settings



a For newborns, test first at or around birth or at the first postnatal visit (usually 4–6 weeks).

b Start ART, if indicated, without delay. At the same time, retest to confirm infection.

c The risk of HIV transmission remains as long as breastfeeding continues.

Infants and children diagnosed with HIV infection should be referred to a paediatric specialist care in divisional hospitals as soon as possible where appropriate care and management are provided, in particular ART initiation in HIV-positive infants and children less than 5 years of age.

Diagnosing HIV and AIDS in children

Clinical staging

Clinical staging is useful for assessment at baseline (at the time of HIV diagnosis), entry into long-term HIV care, and in the follow-up of patients in care and treatment programs. It should be used to guide decisions on when to change antiretroviral therapy (ART).

The clinical staging events have been shown to be related to survival, prognosis and progression of clinical disease in adults and children.

The use of CD4 count and viral load is strictly for monitoring of progress and adherence. To calculate the %CD4+, use the following formula:

%CD4+ = (absolute CD4 count [mm3] ×100 / absolute total lymphocyte count (mm3)

Refer to Annex 1 for the WHO clinical staging on HIV disease in adult, adolescent and children.

Presumptive diagnosis of HIV infection

The preferred method of establishing a diagnosis in infants is to conduct a virological testing, however in most instances, virological testing cannot be done readily, therefore a presumptive diagnosis of HIV infection in infants and children less than 18 months of age can be made based on the criteria outlined.

A presumptive clinical diagnosis of severe HIV infection is necessary in order to permit the early initiation of life-saving ART. The diagnosis of HIV infection should be confirmed as soon as possible using DBS for HIV DNA PCR.

Table 21 Criteria for presumptive diagnosis of HIV infection in infants and children less than 18 months of age

The child is confirmed as being HIV antibody positive (which indicates exposure to HIV but not necessarily HIV infection itself)
And
The child is symptomatic with two or more of the following Oral thrush Severe pneumonia Severe sepsis
Or
A diagnosis of any AIDS indicator conditions(s) can be made
Other findings that support the diagnosis of severe HIV disease in an HIV-seropositive child include: Recent HIV-related maternal death or advanced HIV disease; and Child's %CD4<20%

NOTE	Confirm the diagnosis of HIV infection as soon as possible using dried blood spots (DBS) for HIV DNA PCR

Diagnosis in breastfeeding infants

Throughout the breastfeeding period, HIV-exposed infants and children are at risk of acquiring HIV infection. However, breastfeeding should not be stopped while performing collection of DBS for HIV DNA PCR.

Positive HIV DNA PCR results should be considered to reflect HIV infection in a breastfed infant. However, interpreting negative results poses a challenge.

A six-week window period after the complete cessation of breastfeeding is required before negative HIV DNA PCR test results can be assumed to reliably indicate that the child does not have HIV infection.

Diagnosis in infants and children of mothers on ART

HIV DNA PCR assays are reliable for diagnosis of HIV Infection when the mother or infant has been given ARV drugs. HIV DNA detection in the infant is not affected by maternal ART when the mother is breastfeeding.

Table 22 Diagnosis in infants and children of mothers on ART

Clinical Features	Test required	Purpose	Action
Well, HIV-exposed infant	DBS for HIV DNA PCR at 4-6 weeks of age	To diagnose HIV	Start ART if HIV-positive
Infant unknown HIV exposure	Maternal HIV antibody test or infant HIV antibody test	To identify or confirm HIV exposure	Need to do DBS for HIV DNA PCR if HIV-exposed
Well, HIV-exposed infant at 9 months of age	HIV antibody test	To identify infants who have persisting HIV antibody or have seroconverted.	Those who are HIV antibody positive, need to do DBS for HIV DNA PCR and close follow up. Those who are HIV antibody negative, assume that they are not infected with HIV; repeat testing is required if still breastfeeding.

Infant or child with signs and symptoms suggestive of HIV	HIV antibody test	To confirm HIV exposure	Presumptive diagnosis of HIV infection and treat immediately; perform DBS for HIV DNA PCR if <18months of age.
Well or sick child who is antibody positive >9 months and <18 months	DBS for HIV DNA PCR	To diagnose HIV	Reactive – start HIV care and ART.
Infant or child who has completely discontinued breastfeeding	Repeat testing at six weeks or more after complete breastfeeding cessation – usually initial HIV antibody testing followed by DBS for HIV DNA PCR for HIV antibody positive child and <18 months of age.	To exclude HIV infection after exposure to breastfeeding.	Infected infants and children <5years of age need to start HIV care and ART regardless of the WHO clinical stage or CD4%.

Clinical Management of HIV Positive Infant and children

Therapeutic Management

As Fiji has adopted the 'Test and Treat' model of HIV management, all children who have been confirmed HIV positive with a DNA PCR or RDT (>18 months) should be commenced on treatment as soon as possible.

Children who fulfil the presumptive diagnosis criteria should be commenced on treatment while awaiting a DNA PCR confirmation test.

Prophylaxis

Table 23 Recommendations for primary co-trimoxazole and TB preventative prophylaxis for HIV-exposed and HIV-positive infants and children

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
		3-5.9kg	6-9.9kg	10-13.9kg	14-19.9kg	20-24.9kg		25.0-34.9kg
Co-trimoxazole	Suspension 200/40mg per 3ml	2.5ml	5ml	5ml	10ml	10ml	-	-
	Tablets (dispensable) 100/200mg	1	2	2	4	4	-	-
	Tablets 400/80 mg	-	0.5	0.5	1	1	400mg/80mg	2
	Tablets (scored)	-	-	-	0.5	0.5	800mg/160mg	1
Isoniazid (HIV positive with no active TB)	Duration: 6-9 months of daily monotherapy 10 years or older – 5 mg/kg/day < 10 years – 10 mg/kg/day (range, 7-15 mg)							
Rifampicin (HIV positive with no active TB)	Duration: 4 months of daily monotherapy 10 years or older – 10 mg/kg/day < 10 years – 15 mg/kg/day (range, 10-20 mg)							
Rifampicin plus Isoniazid (HIV positive with no active TB)	Duration: 3 months of daily dual therapy Isoniazid: 10 years or older – 5 mg/kg/day < 10 years – 10 mg/kg/day (range, 7-15 mg) Rifampicin: 10 years or older – 10 mg/kg/day < 10 years – 15 mg/kg/day (range, 10-20 mg)							

[a] *Children with history of treated Pneumocystis pneumonia (PJP) should be administered secondary co-trimoxazole prophylaxis with the same regimen recommended for primary prophylaxis.*

[b] *Splitting tablets into quarters is not considered best practice. This should be done only if syrup is unavailable.*

[c] *Children of these ages (6 months – 14 years) may swallow crushed tablets.*

TB preventative prophylaxis in infants must only be given to HIV positives with no active TB.

Antiretroviral therapy for infants and children

First-line ART recommendation for infants and children.

Table 24 Antiretroviral drugs for HIV-positive infants and children (Refer to Annex 4 for weight-based dosing – simplified dosing of single/combination drugs)

ARV drug class	Drug	Formulation	Dose	Side effects	Notes
NRTIs	Zidovudine (AZT)	Liquid:10mg/ml Capsule:100mg, 250 mg Tablets: 60mg, 300mg	**Target dose:** 180–240 mg/m^2 per dose given PO BD (total daily dose of 360-480mg/m^2); maximum daily dose of 300mg PO BD **PMTCT dose** (from birth to 6 weeks): <2,000g: starting dose of 2mg/kg PO OD; 2,000-2,499g: 10mg PO BD; ≥2,500g: 15mg PO BD	Anaemia, neutropenia, head- ache, myopathy, myositis, lactic acidosis (uncommon)	Can be given with food; store at room temperature
	Lamivudine (3TC)	Liquid:10mg/mg Tablet:150mg	<30 days of life: 2mg/kg/dose PO BD >30 days of life: 4mg/kg/dose PO BD <50kg: 150mg PO BD	Headache, fatigue, nausea, skin rash, abdominal disturbances; pancreatitis, peripheral neuropathy, neutropenia, lactic acidosis (uncommon)	Can be given with food; store at room temperature
	Abacavir (ABC)	Liquid:20mg/ml Tablet: 60mg, 30mg Capsule: none	Target dose: 8mg/kg/dose PO BD for age <16 years or weight <37.5kg to a maximum dose 300mg/day PO BD	Nausea, vomiting, fever, headache, diarrhea, anorexia, hypersensitivity rash (5%), pancreatitis, lactic acidosis	Can be given with food; store at room temperature Do not re-challenge after hypersensitivity
	Tenofovir (TDF)	Oral powder: 40mg per 1g of oral powder (1 level scoop = 1g oral powder; supplied with	≥2 to 12 years: 8mg/kg/dose PO OD ≥12 years and weight ≥30kg (same as adult dose):	Diarrhea, abdominal pain, nausea, vomiting, peripheral neuropathy, pancreatitis,	Measured oral powder only with the supplied dosing scoop. Mix oral powder with food that

		dosing scoop)	300mg PO OD	lactic acidosis, ↑ liver enzymes (uncommon)	does not require chewing. Administer immediately after mixing.
NNRTIs	Nevirapine (NVP)	Liquid: 10mg/ml Tablets: 50mg, 200mg	**Maintenance dose:** 160-200mg/m^2 to maximum dose of 200mg PO OD **Induction dose:** half of the maintenance dose OD for the first 14 days then full maintenance dose BD thereafter **Target dose for PMTCT:** birth to 6 weeks of age: <2.5kg: 10mg/day PO >2.5kg: 15mg/day PO 6 weeks to 6 months: 20mg/day PO 6 months to 9 months: 30mg/day PO 9 months to end of breast-feeding: 40 mg/day PO	Rashes, Stevens-Johnson syndrome, ↑liver enzymes, hypersensitivity, hepatitis, fulminant hepatitis (less common)	Can be given with food; store at room temperature Watch for liver toxicity
PIs	Lopinavir/ Ritonavir (LPV/r)	Liquid: LPV (80mg/ml) + RTV (20mg/ml) Paediatric tablet: LPV 100mg + RTV 25mg Adult tablet: LPV 200mg + RTV 50mg	Lopinavir target dose: 230-350mg/m2 PO BD Maximum dose: LPV 400mg + RTV 100mg PO BD	Nausea, vomiting, diarrhea, abdominal pain, headache, anorexia, lipid abnormalities, lipodystrophy syndrome, diabetes, mellitus, haemolytic anaemia, pancreatitis, hepatitis (less common)	Give with food; a high fat meal increases absorption; oral suspension should be refrigerated, but remains stable at room temperature for 2 months
INSTI	For Raltegravir (RAL) and Dolutegravir (DTG) refer to Annex 4 and Figure 9, respectively, on weight based dosing for ARV formulation for infants and children				

Table 25 First-line ART recommendations for infants and children

Population	Preferred first line regimen	Alternative first line regimen	Special situations
Children	ABC + 3TC + DTG[a]	ABC + 3TC + LPV/r ABC + 3TC + RAL[b]	ABC + 3TC + EFV (or NVP) AZT + 3TC + EFV (or NVP) AZT + 3TC + LPV/r (or RAL[b])
Neonates	AZT + 3TC + RAL[b]	AZT + 3TC + NVP	AZT + 3TC + LPV/r[c]

[a] *For age and weight groups approved for DTG dosing. Refer to Figure 9.*

[b] *RAL can be used as an alternative regimen if LPV/r solid formulations are not available.*

[C] *Do not use LPV/r solution in infants <2 weeks of age. LPV/r pellets should not be used in infants <3 months of age.*

Figure 9 Dosing of optimal paediatric ARVs

Formulation	3–5.9 kg		6–9.9 kg		10-13.9 kg		14-19.9 kg		20–24.9 kg		25–29.9 kg		≥30 kg	
	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
ABC/3TC 120/60 mg scored dispersible tablet	1		1.5		2		2.5		3		1 adult tab (600/300 mg)		1 adult tab (600/300 mg)	
LPV/r 40/10 mg pellets (capsules)	2	2	3	3	4	4	5	5	6	6	–		–	
LPV/r 40/10 mg granules (sachets)	2	2	3	3	4	4	5	5	6	6	–		–	
LPV/r 100/25 mg tablets	–	–	–	–	2	1	2	2	2	2	3	3	3	3
4-in-1 ABC/3TC/LPV/r 30/15/40/10 mg (capsules)	2	2	3	3	4	4	5	5	6	6	–	–	–	–
DTG 5 mg dispersible tablets[a]	1		3		4		5		–		–		–	
DTG 10 mg scored dispersible tablet	0.5		1.5		2		2.5		–		–		–	
DTG 50 mg tablet	–		–		–		–		1		1		1	
TDF/3TC (or FTC)/DTG 300/300 (or 200)/50 mg tablet	–		–		–		–		–		–		1	

[a] This dosing was reviewed and confirmed by the Pediatric ARV Working Group on June 19, 2020.

Treatment Failure

Treatment failure can be classified as clinical failure, immunological failure, or virological failure (Table 9).

An individual must be taking ART for at least six months and the drug adherence is assessed to be >95% before it can be determined that a regimen has failed.

Clinical events that occur before the first six months of therapy are excluded from the definition of treatment failure as they represent immune inflammatory reconstitution syndromes related to pre-existing conditions.

(Definitions of clinical, immunological and virological failure, to guide decision to switch to second-line ART, refer to relevant part of Section II).

Before changing to second-line ART, adherence counselling must be conducted.

Commencement of a second-line ART should be re-considered if there is poor adherence to the first-line ART.
Second-line ART is far more complex and likely to fail with poor adherence.

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Changing to a second-line ART is not the solution for poor drug adherence

Table 26 Recommendations for second-line ART for infants and children

Population	Preferred second line regimen	Alternative second line regimen	Special situations
Children and infants	ABC + 3TC + DTG[a]	ABC + 3TC + LPV/r (or ATV/r[b])	ABC + 3TC + DRV/r[c]
	ABC (or AZT) + 3TC + LPV/r	AZT (or ABC) + 3TC + DTG[a]	AZT (or ABC) + 3TC + RAL
	ABC (or AZT) + 3TC + EFV	AZT (or ABC) + 3TC + DTG[a]	AZT (or ABC) + 3TC + LPV/r (or ATV/r[b])
	AZT + 3TC + NVP	ABC + 3TC + DTG[a]	ABC + 3TC + LPV/r (or ATV/r or DRV/r[c])

[a] *For age and weight groups approved for DTG dosing. Refer to Figure 9.*
[b] *ATV/r can be used as an alternate to LPV/r for children older than 3 months, but the limited availability of suitable formulations for children younger than 6 years, the lack of a fixed-dose formulation and the need for separate administration of the ritonavir booster should be considered when choosing the regimen.*
[c] *DRV should not be used for children younger than 3 years and should be combined with appropriate dosing of ritonavir.*

Table 27 Consideration for transition to optimal ART regimens for children who are considered stable on ART

Current regimen	Weight	Optimal regimen for transition	Considerations
AZT + 3TC + NVP AZT + 3TC + EFV ABC + 3TC + NVP	< 20 kg	ABC + 3TC + LPV/r	If stable, children can be transitioned to DTG when they reach 20 kg
	20-30 kg	ABC + 3TC + DTG	If stable, children can be transitioned to TDF + 3TC + DTG when they reach 30 kg
	> 30 kg	TDF + 3TC + DTG	-
ABC + 3TC + EFV	< 20 kg	No change unless they reach 20 kg unless treatment failure occurs	Transition to optimal regimens for these children is of value once they reach 20 kg and DTG can be used maintaining once-daily administration
	20-30 kg	ABC + 3TC + DTG	If stable, children can be transitioned to TDF + 3TC + DTG when they reach 30 kg
	> 30 kg	TDF + 3TC + DTG	-
ABC + 3TC + LPV/r AZT + 3TC + LPV/r	< 20 kg	No change unless they reach 20 kg unless treatment failure occurs	Ensure the use of tablets as soon as possible to reduce pill burden. Transition from AZT + 3TC + LPV/r to ABC + 3TC + LPV/r can also be considered to reduce the pill burden and preserve the antiviral advantage of NRTIs sequencing
	20-30 kg	ABC + 3TC + DTG	If stable, children can be transitioned to TDF + 3TC + DTG when they reach 30 kg
	> 30 kg	TDF + 3TC + DTG	-

HIV exposed or HIV positive infants and children should have access to a comprehensive package of care services in addition to child healthcare services provided to HIV uninfected children.

Routine newborn and infant care, include:
- growth and development monitoring
- co-trimoxazole and TB prophylaxis
- early HIV diagnosis
- testing and diagnosis of HIV related conditions
- diagnosis and management of common childhood illnesses including opportunistic infections, e.g. TB
- immunizations started and completed
- nutritional support
- ART for HIV positive children
- treatment monitoring for children receiving ART
- education and ARV drug adherence counselling for families and caregivers
- continued counselling and support for family members

Infant ARV Prophylaxis

Recommendations for ARV prophylaxis for PPTCT are discussed in the Obstetrics Section.

HIV and Infant Feeding

Breastfeeding is one of the foundations of child health, development and survival, especially where diarrhoea, pneumonia and under-nutrition are common causes of mortality among children younger than five years. For these reasons, exclusive breastfeeding for the first six months of life is the recommended way of feeding infants, followed by continued breastfeeding with appropriate complementary foods for up to two years or beyond.

In 2010, WHO for the first time recommended antiretroviral (ARV) drug interventions to prevent postnatal transmission of HIV through breastfeeding. In the same year, WHO revised its guidelines on HIV and infant feeding to recommend a public health approach that advised national authorities to promote and support one feeding practice to all women living with HIV accessing care in public health facilities.

Guiding Principles of HIV & Infant Feeding

The overall aim is to improve the HIV-free survival of HIV-exposed infants by providing guidance on appropriate infant feeding practices and use of ARV drugs for mothers living with HIV.

This sub-section addresses six aspects of infant feeding in the context of HIV:

a. the duration of breastfeeding by mothers living with HIV;
b. interventions to support infant feeding practices by mothers living with HIV;
c. what to advise when mothers living with HIV do not exclusively breastfeed;
d. what to advise when mothers living with HIV do not plan to breastfeed for 12 months;
e. what guidance on infant feeding should be provided to mothers living with HIV and to health authorities in conflict or emergency settings; and
f. what are the implications of the updated recommendations for monitoring and evaluation?

Recommendation 2 from 2010 has been revised in terms of the duration of breastfeeding, as reflected in recommendation 1 in 2016. A new area of guidance has been introduced (recommendation 2 in 2016).

Recommendations for HIV & Infant Feeding

WHO-recommended breastfeeding is defined as:

i. initiation of breastfeeding within the first hour of life;
ii. exclusive breastfeeding for the first six months of life (that is, the infant only receives breast milk without any additional food or drink, not even water); followed by
iii. continued breastfeeding for up to two years of age or beyond (with the introduction of appropriate complementary foods at six months); and
iv. breastfeeding on demand – that is, as often as the child wants, day and night.

NEW (2016) Infant Feeding RECOMMENDATIONS

Table 28 WHO 2016 Infant feeding recommendations

Guiding Practice Statements	Frequently asked Questions	Recommendation
1. The duration of breastfeeding by mothers living with HIV.	For how long should a mother living with HIV breastfeed if she is receiving ART and there is no evidence of clinical, immune or viral failure?	Mothers living with HIV should breast-feed for at least 12 months and may continue breastfeeding for up to 24 months or longer (similar to the general population) while being fully supported for ART. In settings where health services pro-vide and support lifelong ART, including adherence counselling, and promote and support breastfeeding among women living with HIV, the duration of breastfeeding should not be restricted. "Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter and continue breastfeeding." "Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided." *This recommendation updates the component of the 2010 recommendation on which breastfeeding practices and for how long related to the duration of breastfeeding.* *The components of the 2010 recommendation regarding breastfeeding practices and stopping breastfeeding remain unchanged and valid.*

2. Interventions to support infant feeding practices by mothers living with HIV.	Can facility- and community-based interventions improve the quality of infant feeding practices among mothers living with HIV?	National and local health authorities should actively coordinate and implement services in health facilities and activities in workplaces, communities and homes to protect, promote and support breastfeeding among women living with HIV.
3. When mothers living with HIV do not exclusively breastfeed.	If a mother living with HIV does not exclusively breastfeed, is mixed feeding with ART better than no breastfeeding at all?	Mothers living with HIV and health-care workers can be reassured that ART reduces the risk of postnatal HIV transmission in the context of mixed feeding. Although exclusive breastfeeding is recommended, practising mixed feeding is not a reason to stop breast-feeding in the presence of ARV drugs.
4. When mothers living with HIV do not plan to breastfeed for 12 months.	If a mother living with HIV plans to return to work or school, is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all?	Mothers living with HIV and health-care workers can be reassured that shorter durations of breastfeeding of less than 12 months are better than never initiating breastfeeding at all.

Revised WHO 2010 Infant Feeding Principles.

Table 29 WHO 2010 infant feeding principles

Principles	Notes	Validity
1. Balancing HIV prevention with protection from other causes of child mortality	Infant feeding practices recommended to mothers known to be living with HIV should support the greatest likelihood of HIV-free survival of their children and not harm the health of mothers. To achieve this, giving priority to preventing HIV transmission needs to be balanced with meeting the nutritional requirements of infants and protecting them from non-HIV morbidity and mortality.	Remains valid
2. Integrating HIV interventions into maternal and child health services	National authorities should aim to integrate HIV testing, care and treatment interventions for all women into maternal and child health services. Such interventions should include access to CD4 count testing and appropriate ART or prophylaxis for the woman's health and to prevent the mother-to-child transmission of HIV.	Remains valid
3. Setting national or subnational recommendations for infant feeding in the context of HIV	National or subnational health authorities should decide whether health services will mainly counsel and support mothers known to be living with HIV to either (1) breastfeed and receive ARV drug interventions or (2) avoid all breastfeeding as the strategy that will most likely give infants the greatest chance of HIV-free survival. This decision should be based on international recommendations and consideration of: □ the socioeconomic and cultural contexts of the populations served by maternal and child health services; □ the availability and quality of health services; □ the local epidemiology, including the prevalence among pregnant women; and □ the main causes of maternal and undernutrition and infant and child mortality.	Remains valid

4. When ARV drugs are not (immediately) available, breastfeeding may still provide infants born to mothers living with HIV a greater chance of HIV-free survival	Every effort should be made to accelerate access to ARV drugs for both maternal health and preventing HIV transmission to infants. While ARV drug interventions are being scaled up, national authorities should not be deterred from recommending that mothers living with HIV breastfeed as the most appropriate infant feeding practice in their setting. Even when ARV drugs are not available, mothers should be counselled to exclusively breastfeed in the first six months of life and continue breastfeeding thereafter unless environmental and social circumstances are safe for and supportive of replacement feeding. In circumstances in which ARV drugs are unlikely to be available, such as acute emergencies, breastfeeding of HIV-exposed infants is also recommended to increase survival.	Remains valid
5. Informing mothers known to be living with HIV about infant feeding alternatives	Pregnant women and mothers known to be living with HIV should be informed of the infant feeding practice recommended by the national or subnational authority to improve the HIV-free survival of HIV-exposed infants and the health of mothers living with HIV and informed that there are alternatives that mothers might want to adopt.	Remain valid
6. Providing services to specifically support mothers to appropriately feed their infants	Skilled counselling and support in appropriate infant feeding practices and ARV drug interventions to promote the HIV-free survival of infants should be available to all pregnant women and mothers.	Updated to a formal recommendation. See recommendation 2 (2016)
7. Avoiding harming infant feeding practices in the general population	Counselling and support to mothers known to be living with HIV and health messaging to the general population should be carefully delivered to avoid undermining optimal breastfeeding practices among the general population.	Remains valid

8. Advising mothers who are HIV uninfected or whose HIV status is unknown	*Mothers who are known to be HIV uninfected or whose HIV status is unknown* should be counselled to exclusively breastfeed their infants for the first six months of life and then to introduce complementary foods while continuing breastfeeding for 24 months or beyond. *Mothers whose status is unknown* should be offered HIV testing. *Mothers who are HIV uninfected* should be counselled about ways to prevent HIV infection and about the services that are available, such as family planning, to help them to remain uninfected.	Remains valid
9. Investing in improving infant feeding practices in the context of HIV	Governments, other stakeholders and donors should greatly increase their commitment to and resources for implementing the Global Strategy for Infant and Young Child Feeding, the United Nations HIV and infant feeding framework for priority action and the global scale-up of the prevention of the mother-to-child transmission of HIV to effectively prevent infants from becoming infected with HIV postnatally, improve HIV-free survival and achieve relevant goals of the United Nations General Assembly Special Session on HIV/AIDS.	Remains valid

Revised WHO 2010 Infant Feeding Recommendations.

Table 30 WHO 2010 infant feeding recommendations

Condition	Recommendation	Validity
1. Ensuring mothers receive the care they need	Mothers known to be living with HIV should be provided with lifelong ART or ARV drug prophylaxis interventions to reduce HIV transmission through breastfeeding.	Remains valid
2. Which breastfeeding practices and for how long?	Mothers known to be living with HIV (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter and continue breastfeeding for the first 12 months of life. Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided.	The 2016 guideline revises the recommended duration of breastfeeding and HIV treatment, see Recommendation 1 (2016): VALID AND UPDATED
3. When mothers decide to stop breast-feeding	Mothers known to be living with HIV who decide to stop breastfeeding at any time should stop gradually within one month. Mothers or infants who have been receiving ARV drug prophylaxis should continue prophylaxis for one week after breastfeeding is fully stopped. Stopping breastfeeding abruptly is not advisable.	Remains valid. *Nevertheless, lifelong ART is recommended now instead of ARV drug prophylaxis*

4. What to feed infants when mothers stop breastfeeding	When mothers known to be living with HIV decide to stop breastfeeding at any time, infants should be provided with safe and adequate replacement feeds to enable normal growth and development. *For infants younger than six months of age:* Alternatives to breastfeeding include: — commercial infant formula milk if the home conditions outlined in recommendation 5 are fulfilled; or — expressed, heat-treated breast milk (see recommendation 6 below). Home-modified animal milk is not recommended as a replacement food in the first six months of life. *For children older than six months of age:* Alternatives to breastfeeding include: — commercial infant formula milk if the home conditions outlined in recommendation 5 are fulfilled; or — animal milk (boiled for infants under 12 months), as part of a diet providing adequate micronutrient intake; meals, including milk-only feeds, other foods and combination of milk feeds and other foods, should be provided four or five times per day. All children need complementary foods from six months of age.	Remains valid

5. Conditions needed to safely formula feed.	*Mothers known to be living with HIV* should only give commercial infant formula milk as a replacement feed to their HIV-uninfected infants or infants who are of unknown HIV status when specific conditions are met: i. safe water and sanitation are assured at the household level and in the community; and ii. the mother or other caregiver can reliably provide sufficient infant formula milk to support the normal growth and development of the infant; and iii. the mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition; and iv. the mother or caregiver can exclusively give infant formula milk in the first six months; and v. the family is supportive of this practice; and vi. the mother or caregiver can access healthcare that offers comprehensive child health services.	Remains valid
6. Heat-treated, expressed breast milk.	Mothers known to be living with HIV may consider expressing and heat-treating breast milk as an interim feeding strategy: in special circumstances, such as when the infant has low birth weight; or, i. is otherwise ill in the neonatal period and unable to breastfeed; or ii. when the mother is unwell and temporarily unable to breastfed, or, iii. has a temporary breast health problem such as mastitis; or iv. to assist mothers in stopping breastfeeding; or if ARV drugs are temporarily not available.	Remains valid
7. When the infant is living with HIV	If infants and young children are known to be living with HIV, mothers are strongly encouraged to exclusively breastfeed for the first six months of life and continue breastfeeding in accordance with the recommendations for the general population: that is, up to two years or beyond.	Remains valid

Infant feeding counselling

It is strongly recommended that HIV-positive mothers are counselled well (as above) about infant feeding choices during pregnancy and must decide on their feeding options before delivery. Breastfeeding HIV-positive mothers should continue taking ART.

It is recommended that HIV positive mothers should have at least 3 infant feeding counselling sessions before delivery/labour.

Without ART, 5-20% of infants breastfed by HIV-infected mothers will acquire HIV through breastfeeding. In Pacific island countries, transmission through breastfeeding is thought to be at the higher end of this range because of poor infant feeding practices, specifically mixed feeding. From six weeks to six months of exclusives breastfeeding, risk of MTCT is 4%. If the breastfed infant is given formula, the risk doubles. If the breastfed infant is given solid foods before six months, the risk is eleven times as high as the exclusively breastfed infant. Choosing the right feeding options for infants and children with HIV is an important step in preventing malnutrition from occurring as a complication of HIV infection.

Mixed feeding (breast milk and formula combined) in the absence of ART is the most hazardous form of infant feeding as the risk for mother-to-child transmission of HIV is at its highest.

HIV and opportunistic infection in children

Refer to section On Opportunistic infections

Continuum of care for children living with HIV

HIV-exposed or HIV positive infants and children should have access to a comprehensive package of care services in addition to child health care services provided to HIV- uninfected children.

- Routine newborn and infant care, including growth and development monitoring
- Diagnosis and management of common childhood illnesses including
- Screening and management of opportunistic infections, e.g. TB
- Immunizations started and completed
- Nutritional Support
- ART for HIV-positive Children
- Education
- Psychosocial support

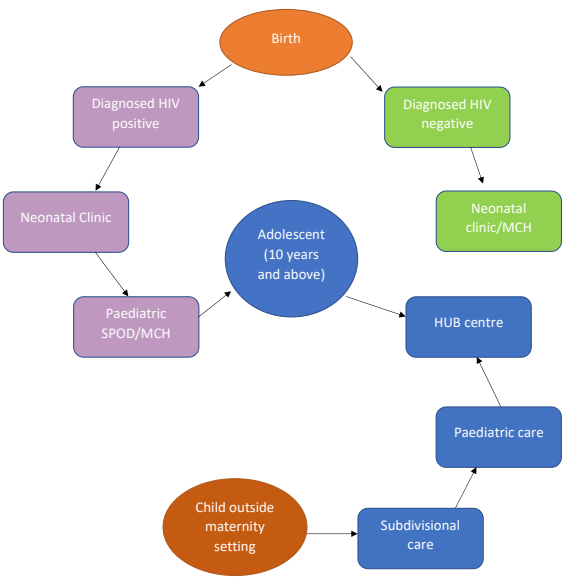
Immunizations

- HIV-exposed infants and children should receive, as much as possible, all vaccines under the Expanded Program for Immunization (EPI). However, modification of EPI schedules may be required for infants and children who have HIV infection.
- HIV-positive infants and children are considered as severely immunocompromised (and vaccine should not be given) if any of the following

conditions are present:

- CD4 <15%;
- Absolute CD4 count that is lower than normal for age; and
- Clinical manifestations of symptomatic HIV infection (refer to WHO clinical staging in annex)

- Once the immune status of the HIV-positive child has improved, resume immunization schedule as deemed appropriate.
- In general, vaccines with live attenuated organisms (e.g. BCG, measles/MMR, oral polio) are not given when the HIV-positive child is severely immune-compromised.
  - BCG vaccine can be given to infants born to mother with an unknown HIV status or those born to HIV-positive mothers but without signs and symptoms suggestive of HIV infection.
  - Measles/MMR vaccine should not be given in HIV-positive children who are severely immunocompromised at the time of the immunization schedule.
  - Haemophilus influenza type B (Hib) conjugate vaccine should be delayed if the HIV-positive child is severely immunocompromised at the time of the immunization schedule.



5

HIV AND GENERAL MEDICINE

HIV Co-Infections

HIV/TB co-infection

Tuberculosis (TB) is a leading cause of death and a common presenting illness among PLHIV. Likewise, HIV is more common among TB patients than among the general population. For this reason, HIV/TB co-infection should be diagnosed as early as possible through HIV testing of TB patients, and TB screening for PLHIV. Therefore, collaboration between HIV and TB programs through cross-referral of patients is essential

Clinical Features

- May present at any stage of HIV infection
- Classically presents with fever, night sweats, productive cough (often with haemoptysis), shortness of breath, and weight loss occurring over weeks to months. However, Tuberculosis (TB) in patients with advanced HIV infection frequently presents with atypical pulmonary or extra-pulmonary manifestations.

Diagnosis

- If pulmonary TB is suspected: sputum for GeneXpert, AFB Smear, Culture and chest Xray
- If nodal TB is suspected: lymph node biopsy for AFB staining, GeneXpert and histopathology
- If CNS TB is suspected: computed tomography (CT) scan and lumbar puncture (LP) for cerebrospinal fluid (CSF) analysis including AFB smear, GeneXpert and Culture
- Alternatively, tissue biopsy of other involved body site for AFB smear, GeneXpert and culture, and histopathology.

Measures to decrease the burden of TB among people living with HIV (the 3Is):

- ***Intensive case finding:***

All HIV-positive patients should be screened for active TB at the time of diagnosis of HIV and at each subsequent visit if symptomatic

- ***Isoniazid preventive therapy (IPT) (now known as TB preventive therapy (TPT),*** for HIV-positive adults and children

- If active TB is ruled out, screen for Latent TB by Mantoux test
- Patient with HIV infection who has been exposed to TB or has a Mantoux test >5mm must be considered to have Latent Tuberculosis Infection or as determined by the health care provider and should be started on either of the following therapy

1. Single - Isoniazid (INH) (Adults:5mg/kg or children:7-15mg/kg) PO OD (max 300mg) daily for six months under DOT strategy + Pyridoxine 10-20mg/day as per indication
2. Combination - Rifampicin (RIF) (Adults:10mg/kg or children:10-20mg/kg) PO OD (max 600mg) daily + Isoniazid (INH) (Adults:5mg/kg or children:7-15mg/kg) PO OD (max 300mg) daily; both for three months under DOT strategy + Pyridoxine 10-20mg/day as per indication

- ***TB Infection Control***

Prevent PLHIV from being infected or re-infected with TB at health care facilities

Recommendations for Treatment of HIV/TB Co-infection

- Treat TB first, if ART naïve.
- Start ART after 2-8 weeks of initiating anti-TB treatment (ATT). For TB meningitis delay ART initiation till 8 weeks.
- Do not stop the ART if the patient is already on ART before the diagnosis of TB.
- Be aware of interactions between ATT and ART, especially between rifampicin and NVP, PIs and INSTI. Rifampicin reduces the levels of these ARVs to sub-therapeutic levels which can lead to HIV treatment failure. Refer to table 31 for the recommendation of ART and ATT in HIV/TB co-infected patients.
- Be aware of adverse effects of ATT and ART:
  - Skin rash
  - Nausea and vomiting
  - Hepatitis
  - Anaemia
  - Arthralgia

Table 31 Recommendation of ART and ATT in HIV/TB co-infection

Population	Drugs	Recommendations
Adults	Rifampicin	Use rifabutin instead of rifampicin
	NVP	Switch to EFV
	LPV/r	Double the dose of LPV/r
	DTG	Double the dose of DTG
Children <20 kg	LPV/r	Double the dose of LPV/r Can use an EFV-based regimen or triple NRTIs for the duration of ATT and return to LPV/r once ATT has been completed
	RAL	Increase the dose to 12 mg/kg BD as an oral chewable formulation
Children >20 kg	DTG	Double the dose of DTG

ART in individuals undergoing TB Treatment is challenging because of overlapping drug toxicities of ARV drugs and anti-TB drugs, as well as increased pill burden, adherence issues, and possible development of immune reconstitution inflammatory syndrome (IRIS). Health care workers should seek expert advice when faced with these clinical situations.

Studies have shown that co-trimoxazole prophylaxis decreases the morbidity and mortality of adults and children with HIV/TB co-infection.

Opportunistic Infections.

According to the Cambridge dictionary definition, opportunistic infection is defined as an infection caused by bacteria or virus that is not harmful to a healthy person, but harms a person whose body's natural defence against infection is damaged or has a weakened defence system.

Table 32 Common opportunistic infections and their management

Opportunistic infections frequently causing skin and mucosal manifestations			
Condition	**Clinical Features**	**Adult Treatment**	**Children Treatment**
Seborrheic dermatitis	Chronic skin infection most likely caused by the dermatophytic fungus Malassezia furfur which characteristically incites an intense inflammatory reaction. The infection manifests as an erythematous, scaling papule or plaque with an oily or dry surface and an indistinct margin. The usual distribution is the mid-facial region with extension to cover the entire face and scalp.	- Aqueous cream as soap. - Selenium sulphide (Selsun) shampoo (or tar shampoo, if available). Application is easier if hair is cut short. - Hydrocortisone cream 1% applied on the skin BD. - If bacterial superinfection occurs, treat with flucloxacillin 500mg PO 6 hourly for 7 days. If patient is allergic to penicillin, give erythromycin 500mg PO 6 hourly for 7 days.	- Aqueous cream as soap. - Hydrocortisone cream 1% applied on the skin BD. - If bacterial superinfection occurs, treat with flucloxacillin 12.5-25mg/kg PO 6 hourly for 7 days. If patient is allergic to penicillin, give erythromycin 7.5-12.5mg/kg PO 6 hourly for 7 days.
Papular pruritic eruptions (PPE)	Aetiology is not defined but may be secondary to an abnormal inflammatory reaction to insect bites. Presents as chronic, severely itchy rash with (hyperkeratotic and hyperpigmented) dark papules and nodules, and scratch marks. • Skin lesions heal as dark spots/marks with pale centres or post- inflammatory hypopigmentation.	Rule out scabies: treat empirically if diagnosis is unclear. - Hydrocortisone ointment 1% cream BD for 10 days to alternate with emollients (Vaseline®) topically BD for 10 days. - For severe itching, give promethazine 10 mg/kg PO nocte to a maximum of 10 mg PO 8 hourly (3 days only). If bacterial superinfection occurs, apply povidone-iodine solution topically BD. If severe, add flucloxacillin 500mg PO 6 hourly for 7days.	Rule out scabies: treat empirically if diagnosis is unclear. - Hydrocortisone ointment 0.5-1% cream BD for 7 days to alternate with emollients (Vaseline®) topically BD for 7 days. - For severe itching, give promethazine 0.1mg/kg PO nocte to a maximum of 0.1mg/kg PO 8-hourly for children >2 years of age for 3 days – further need must be discussed with Paediatrics Consultant.

Fungal nail infections (onychomycosis)	Also called 'tinea uguium The nail thickens and discolours: white, black, yellow or green. As the infection progresses the nail can become brittle, with pieces breaking off. If left untreated, the skin can become inflamed and painful underneath and around the nail.	**Preferred regimen:** Griseofulvin 500mg PO OD for 6-9 months for fingernail infections and 12-18 months for toenail infections. Because of the long duration of treatment, it is recommended to monitor serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) regularly. **Alternative regimen:** Terbinafine 250mg PO OD for 6 weeks for fingernail infections and 12 weeks for toenail infections. Monitor FBC, ALT, and ALT at baseline, then every 4-6 weeks during therapy. **Note:** Griseofulvin is contraindicated in pregnancy; manufacturers also caution against men fathering a child within 6 months after therapy.	**Preferred regimen:** Griseofulvin 10mg/kg PO OD for 6-9 months for fingernail infections and 12-18 months for toenail infections. Because of the long duration of treatment, it is recommended to monitor serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) regularly. **Alternative regimen:** Terbinafine 4-5mg/kg/day PO OD for 6 weeks for fingernail infections and 12 weeks for toenail infections. Monitor FBC, ALT, and ALT at baseline, then every 4-6 weeks during therapy.
Angular cheilitis	It is an inflammatory lesion at the corner of the mouth and often occurs bilaterally. The condition manifests as deep cracks or splits. In severe cases, the splits can bleed when the mouth is opened and shallow ulcers or a crust may form. The sores eventually get infected with Candida species or other pathogens.	Clotrimazole 1% cream applied topically BD for 7-14 days.	Clotrimazole 1% cream applied topically BD for 7-14 days.
Aphthous ulcers	Aphthous ulcers are painful, punched- out ulcers on the mucosal surface. They are usually covered in purulent exudates and tend to bleed when touched. It is difficult to differentiate it with	Advise patient to avoid acidic foods. Oral hygiene with 0.2% chlorhexidine gluconate aqueous mouthwash, 4 times a day for a variable duration (2 weeks to months or even longer until ulcer heals). Lignocaine 2% gel	Advise patient to avoid acidic foods. Oral hygiene with 0.2% chlorhexidine gluconate aqueous mouthwash, 4 times a day for a variable duration (2 weeks to months or even longer until ulcer heals). Lignocaine 2% gel applied to oral ulcers 4 times a

	herpetic ulcers caused by Herpes simplex virus (HSV). Syphilitic ulcer (chancre) is another differential diagnosis but the ulcer is painless.	applied to oral ulcers 4 times a day for 2 weeks or until ulcers heal. **Oral analgesics:** Paracetamol 1gm PO 6 hourly; or Ibuprofen 40 mg PO 8 hourly. **For severe disease (painful persistent ulcers:** Prednisone 30-40 mg PO OD to taper over a month.	day for 2 weeks or until ulcers heal. **Oral analgesics:** Paracetamol 15mg/kg/dose PO 6 hourly. **For severe disease (painful persistent ulcers):** Prednisone 1-2mg/kg PO OD (maximum of 60mg/day) to taper over a month.
Necrotizing stomatitis, necrotizing ulcerative periodontitis, and necrotizing ulcerative gingivitis	Stomatitis is inflammation of the mucosa of the oral cavity. It is often associated with poor oral hygiene and bacterial invasion with anaerobes. Gingivitis is inflammation of the gums with the gums swollen, red and tend to bleed easily. When pus accumulates in the gingival margin around the teeth it is called pyorrhoea. Periodontitis is inflammation of the tissues surrounding the teeth. This is a which there is rapid loss of bone and soft tissue surrounding the teeth. Teeth become loose and fall off and there is bleeding from the gums. Ulceration may occur.	Basic oral health is important to prevent infections of the oral cavity, as these occur with increased frequency in PLHIV. This includes: - Regular brushing and flossing of teeth. - Do not share toothbrush. - Regular visit to the dentist. - Oral hygiene with regular warm saline gargles or chlorhexidine mouthwash. Refer to the dentist for possible local debridement of periodontitis and/ or pyorrhoea. **Preferred regimen:** Metronidazole 200-400 mg PO 8-hourly for 7-10 days. **Alternative regimen:** Amoxicillin/clavulanic acid 125mg, 1 tablet PO 8hourly for 7-10 days.	Basic oral health is important to prevent infections of the oral cavity, as these occur with increased frequency in PLHIV. This includes: - Regular brushing and flossing of teeth. - Do not share toothbrush. - Regular visit to the dentist. - Oral hygiene with regular warm saline gargles or chlorhexidine mouthwash. Refer to the dentist for possible local debridement of periodontitis and/ or pyorrhoea. **Preferred regimen:** Metronidazole 15-50 mg/kg/dose PO 8-hourly for 7-10 days, to a maximum daily dose of 2250 mg/day. **Alternative regimen:** Amoxicillin/clavulanic acid; dose based on amoxicillin: 22.5 mg/kg/dose PO 8 hourly for 7-10 days.
Oral hairy leukoplakia	The condition is caused by Epstein–Barr virus (EBV) and presents as asymptomatic white hyperkeratotic corrugations of the lateral border of the tongue. These lesions are classically adherent and cannot be removed with a spatula. Occurs mostly in adults.	No treatment is necessary, often disappears after ART is initiated.	No treatment is necessary, often disappears after ART is initiated.

Oral, oesophageal, and vaginal candidiasis	**Oral candidiasis:** creamy-white patches on gums, tongue, or lining of the mouth. **Oesophageal candidiasis:** fever, burning retrosternal pain or discomfort, odynophagia, usually in association with oral candidiasis. **Vulvo-vaginal candidiasis:** vaginal irritation, itching, burning, and thick white discharge. Diagnosis A clinical diagnosis of oral or vaginal candidiasis is usually possible based on the above features. Oesophageal candidiasis may be presumptively diagnosed in an HIV positive patient with advanced disease and dysphagia or odynophagia, particularly if oral thrush is evident. Gastroscopy is not routinely performed but may be considered if symptoms fail to respond to antifungal therapy.	**Oral candidiasis:** **Preferred regimen:** Nystatin 500,000 units for 14 days; OR Clotrimazole troches (lozenges) 10 mg dissolved in the mouth TDS for 10-14 days **Alternative regimen:** Fluconazole 150mg PO OD for 7-14 days **Vaginal candidiasis:** Topical therapy usually sufficient. Clotrimazole 100mg pessary inserted per vaginally nocte for 7 nights; or Clotrimazole 500mg pessary inserted per vaginally nocte single dose. **Oesophageal candidiasis:** Fluconazole 100mg PO OD 14-21days. Start ART once patient can swallow tablets comfortably. **Disseminated (systemic) candidiasis:** **Preferred regimen:** Fluconazole 150 mg PO OD (up to 400 mg/day) for 2-3 weeks. **Alternative regimen:** Amphotericin B 0.3-0.6 mg/kg/day IV for 10-14 days. **Prophylaxis:** Not routinely recommended.	**Oral candidiasis:** **Preferred regimen:** Nystatin given 4 times a day for 14 days: - Preterm: 50,000 units per dose - Term: 100,000 – 400,000 units per dose -Children: 400,000 – 600,000 units per dose For all spread inside the oral mucosa, OR Clotrimazole troches (lozenges) 10 mg dissolved slowly in the mouth for 15-30 mins, 5 times a day for 10-14 days (not recommended for children <3 years of age). **Alternative regimen:** Fluconazole 3.3-6.6 mg/kg/day PO OD for 7 days (not recommended for children <3 years of age). **Vaginal candidiasis:** Nystatin 100,000 units (one applicator full) per vagina nocte for 14 days. **Prophylaxis:** Not routinely recommended
Herpes simplex	Typical blisters in the oral, genital, or perianal areas. Diagnosis: Clinical diagnosis based on history and examination. No laboratory tests required.	Acyclovir 400mg 4-6 hourly for 7-14 days. **Prophylaxis:** Primary prophylaxis: Not recommended **Secondary prophylaxis:** In cases of frequency of recurrences of genital herpes, long term suppressive therapy with acyclovir 400mg PO BD.	Acyclovir Neonate: IV 20mg/kg TDS - 21 days for CNS or disseminated - 14 days for skin, eye and mouth. Children: IV 10-15mg/kg TDS for 21 days **Severe mucocutaneous:** IV 5-10mg/kg TDS until all lesions cleared **Encephalitis:** - < 5 years: 20mg/kg IV TDS for 14 to 21 days - 5 to 12 years: 15mg/kg IV

			TDS for 14 to 21 days **Genital or oral labial lesions:** 10 mg/kg PO 8 hours for 7-14 days. Herpes simplex can be chronic and invasive (e.g. oesophagitis, encephalitis, disseminated infection). Patients with suspected systemic infection (such as herpes encephalitis) should receive acyclovir 10 mg/kg IV 8 hourly for a minimum of 2 weeks.
Herpes (varicella) zoster virus	May present as primary varicella infection (chickenpox) or reactivation varicella (shingles). Chickenpox presents with a fever, respiratory prodrome, and a diffuse intensely pruritic vesicular rash. Shingles presents as typical painful blisters along dermatomes (multiple dermatomal involvement can also occur). CNS and respiratory involvement may also occur. It may involve the eyes or the tip of the nose along the trigeminal nerve. Diagnosis: Clinical diagnosis based on history and examination. No laboratory tests required.	**Shingles:** Acyclovir 800 mg/kg PO, 5 times a day for 7 days (maximum of 800 mg PO, 5 times a day). **Chickenpox:** Acyclovir 800mg PO, 5 times a day for 7 days. Treatment should commence within 72 hours of onset of blisters. **Disseminated, ophthalmic nerve involvement, or visceral disease:** Acyclovir 10 mg/kg/day IV 8 hourly for 7-14 days. Adequate hydration is imperative. Acyclovir eye ointment applied to the eye every 4 hours for ophthalmic herpes zoster. Pain relief may be required such as aspirin or paracetamol. If secondary bacterial infection occurs, treat with a suitable antibiotic. **Prophylaxis:** Not required.	**Shingles & Chickenpox:** Acyclovir 20 mg/kg PO, 4 times a day for 7 days (maximum of 800 mg PO, 4 times a day). Treatment should commence within 72 hours of onset of blisters. **Disseminated, ophthalmic nerve involvement, or visceral disease:** Duration is 7 to 10 days or 48 hours after eruption of the last new lesion. - <1 year: Acyclovir 10mg/kg/day IV 8 hourly - >1 year: IV Acyclovir 500 mg/m2 8hrly x 7-14 days Adequate hydration is imperative. Acyclovir eye ointment applied to the eye every 4 hours for ophthalmic herpes zoster. IF SUSPECTED retinopathy, discuss with Paediatrics. Pain relief may be required such as aspirin. If secondary bacterial infection occurs, treat with a suitable antibiotic. **Prophylaxis:** Not required.
Crusted (Norwegian) Scabies	Thick grey keratosis and crusts developed on hands, elbows, knees and ankles, and to the rest of the bodies.	1. Isolate 2. Prolonged topical treatment of permethrin 5% or benzyl benzoate 25% applied every 2nd day for the 1st week	1. Isolate 2. Prolonged topical treatment of permethrin 5% or benzyl benzoate 5% applied every day for the 1st week and then

	Scales and crusts show thousands of mites. Severe form of scabies present in immunocompromised patients.	and then twice a week until healed 3. Prefer to use Ivermectin 200 mcg/kg if available, give 3-15 mg as stat, and repeat in 7days. 4. Keratolytics such as salicylic acid 5-10% needs to be applied to remove the thick crusts; if not available use petroleum jelly or sorbolene cream.	twice a week until healed 3. Prefer to use Ivermectin 200mcg/kg if available, give on day 1, 2,8,9 and 15; in severe infection may require 2 further doses on day 22 and day 29. 4. Keratolytics such as salicylic acid 5-10% needs to be applied to remove the thick crusts; if not available use petroleum jelly or sorbolene cream.
Opportunistic infections frequently causing pulmonary manifestations			
Condition	**Clinical Features**	**Adult Treatment**	**Children Treatment**
Pneumocystis jiroveci pneumonia (PJP)	Usually presents in advanced HIV disease (CD4 count <200 cells/mm^3); uncommon at higher CD4 counts. Generally insidious onset (days to weeks) of progressive shortness of breath, fever, dry cough and fatigue. Examination findings commonly include tachypnoea, hypoxia (more marked with exertion), and bilateral fine crackles (chest may be clear on auscultation). Unusual in patient's adherent to PJP prophylaxis (co-trimoxazole). Diagnosis Chest X-ray: bilateral perihilar interstitial infiltrates; diffuse alveolar shadowing; may be normal. Pneumothorax not uncommon. Pleural effusion rare. Presumptive diagnosis based on the characteristic clinical presentation and radiological findings in a patient with known advanced HIV infection.	Co-trimoxazole (SMX 15-20 mg/kg/day + TMP 75-80 mg/kg/day) given in 3-4 divided doses for 21 days. Usually 4 single-strength or 2 double-strength tablets PO TDS for 21 days. Prednisolone 40mg PO BD for 5 days, then 40mg PO OD for 5 days, then 20mg PO OD for 11 days in adults with severe illness (PaO2 < 70mm Hg or pulse oximetry reading < 93%) If there is a severe drug reaction or a history of severe drug reaction to sulphamethoxazole, give trimethoprim (TMP) 15 mg/kg/ day + dapsone 100 mg/day PO for 21 days. **Prophylaxis:** **Primary prophylaxis:** Refer to section 4. **Secondary prophylaxis:** Patients who have PJP must continue with maintenance therapy of co-trimoxazole 960mg PO OD. Refer to section 2 when to discontinue co-trimoxazole in adults.	Co-trimoxazole (SMX 25mg/kg + TMP 5mg/kg) 4 times a day, minimum duration of 21 days. Prednisolone 0.5mg/kg/dose PO BD for 5 days, then 0.25mg/kg/dose PO BD for 5 days, then 0.25mg/kg/dose PO OD for 11 days in children with severe respiratory distress, with or without IMCI signs; or with pO2 <70 mm Hg in room air; or A-a gradient >35 mm Hg. If there is a severe drug reaction or a history of severe drug reaction to sulphamethoxazole, give trimethoprim (TMP) 5mg/kg/dose PO 4 times a day + dapsone 100mg/day PO for 21 days. **Prophylaxis:** **Primary prophylaxis:** Refer to section 4. **Secondary prophylaxis:** Co- trimoxazole prophylaxis dose is based on standard trimethoprim (TMP) dose of 6-8mg/kg/day PO once a day. Refer to section 4 when to discontinue co-trimoxazole for children <5 years of age. Children >5 years of age, follow adult recommendations as above.

Bacterial pneumonia	Characteristically rapid onset (within days) of fever, cough productive of purulent sputum, and shortness of breath. Diagnosis: Chest X-ray: commonly lobar consolidation. Sputum and blood cultures: routine microbiology tests and culture.	Refer to Fiji MOHMS Antibiotic Guidelines.	Refer to Fiji MOHMS Antibiotic Guidelines.
Tuberculosis (TB)	May present at any stage of HIV infection. Classically presents with fever, night sweats, productive cough (often with haemoptysis), shortness of breath, and weight loss occurring over weeks to months. However, TB in patients with advanced HIV infection frequently presents with atypical pulmonary or extra-pulmonary manifestations. Diagnosis: If pulmonary TB is suspected: sputum for acid-fast bacilli (AFB) smear and culture, and chest X-ray. If nodal TB is suspected: lymph node biopsy for AFB staining and histopathology. If CNS TB is suspected: computed tomography (CT) scan and lumbar puncture (LP) for cerebrospinal fluid (CSF) analysis including AFB smear and culture. Alternatively, tissue biopsy of other involved body site for AFB staining and culture, and histopathology.	Refer to Fiji MOHMS TB treatment guidelines.	Refer to Fiji MOHMS TB treatment guidelines.
Opportunistic infections frequently causing headache and/or neurological manifestations			
Condition	**Clinical Features**	**Adult Treatment**	**Children Treatment**
Toxoplasmosis (Toxoplasma gondii) encephalitis	Usually presents in advanced HIV infection (CD4 count <50 cells/mm3). Most	**Standard therapy:** Co-trimoxazole (sulphamethoxazole [SMX] 75mg/kg/day +	**Standard therapy:** Co-trimoxazole (sulphamethoxazole [SMX] 25mg/kg/day +

	biopsy of other involved body site for AFB staining and culture, and histopathology.		
Opportunistic infections frequently causing headache and/or neurological manifestations			
Condition	**Clinical Features**	**Adult Treatment**	**Children Treatment**
Toxoplasmosis (Toxoplasma gondii) encephalitis	Usually presents in advanced HIV infection (CD4 count <50 cells/mm3). Most commonly presents with fever, headache, altered mental state (confusion, delusional behaviour), with or without focal neurological signs (e.g. hemiparesis, seizures, and coma). It can also affect the eye causing eye pain and reduced vision. Diagnosis: CT scan: usually multiple ring-enhancing lesions (may be single) with associated cerebral oedema. The diagnosis is confirmed by a documented clinical and radiological response to empirical therapy (as below) over 2 weeks.	**Standard therapy:** Co-trimoxazole (sulphamethoxazole [SMX] 75mg/kg/day + trimethoprim [TMP] 15mg/kg/day) given in 3-4 divided doses for 4-6 weeks. Usually provided by 4 single-strength tablets or 2 double-strength tablets PO, three times a day (TDS). **Alternative therapy:** If intolerant to sulfadiazine, clindamycin 600mg IV or PO 6 hourly; OR Dapsone 100mg PO OD may be substituted for 6 weeks.	**Standard therapy:** Co-trimoxazole (sulphamethoxazole [SMX] 25mg/kg/day + trimethoprim [TMP] 5mg/kg/day) given in 3-4 divided doses for 4-6 weeks. **Alternative therapy:** If intolerant to sulfadiazine, clindamycin 450mg/m^2 IV OD or 2 - 5 mg PO 6 hourly; OR Dapsone 100mg PO OD may be substituted for 6 weeks.
Cryptococcal (Cryptococcus neoformans) meningitis	Usually presents in advanced HIV infection (CD4 count <50 cells/mm^3). Characteristically presents with an acute (i.e. days) or subacute (i.e. weeks to months) onset of fever and headache, with or without photophobia, neck stiffness, fatigue, irritability, or altered mental state. Patients may also present with non-specific CNS symptoms including dementia and seizures. Diagnosis: CT scan: Lumbar puncture analysis including opening pressure (usually elevated), fungal stain and culture, and cryptococcal antigen	**Induction Phase** **Preferred regimen:** Amphotericin B (1.0mg/kg/day) and 5-flucytosine (100mg/kg/day, divided into four doses per day) for 1 week, followed by 1 week of fluconazole (1200mg/day) **Alternate regimen:** Two weeks of fluconazole (1200mg daily for adults) + 5-flucytosine (100mg/kg/day, divided into four doses per day), OR Two weeks of amphotericin B (1.0mg/kg/day) + fluconazole (1200mg daily), OR Two weeks of fluconazole (1200mg/day) **Consolidation Phase:**	**Induction Phase** **Preferred regimen:** Amphotericin B (Lyophilized) 3-5mg/kg OD IV and 5-flucytosine (100mg/kg/day, divided into four doses per day) for 1 week, followed by 1 week of fluconazole (12mg/kg/day, up to a maximum dose of 800mg daily) **Alternate regimen:** Two weeks of fluconazole (12mg/kg/day) + 5-flucytosine (100mg/kg/day, divided into four doses per day), OR Two weeks of amphotericin B (1.0mg/kg/day) + fluconazole (12mg/kg/day up to a maximum of 800mg daily), OR Two weeks of fluconazole (12mg/kg/day, up to a maximum dose of 800mg

	with a lymphocyte predominance, and exclusion of a likely alternate diagnosis.	Not required. **Secondary prophylaxis:** Same as maintenance phase. This can be discontinued if the patient is on ART for 6 months and the CD4 count is persistently >250 cells/mm^2 in two measurements within a period of the 6 months, or to be continued indefinitely if no CD4 count is available.	lowering of raised intracranial pressure by serial lumbar puncture, if required. **Prophylaxis** **Primary prophylaxis:** Not required. **Secondary prophylaxis:** Same as maintenance phase. This can be discontinued if the patient is on ART for 6 months and the CD4 count is persistently >250 cells/mm^2 in two measurements within a period of the 6 months, or to be continued indefinitely if no CD4 count is available.
Opportunistic infections frequently causing diarrhoea			
Condition	**Clinical Features**	**Adult Treatment**	**Children Treatment**
Common causes: **Viruses:** **Rotavirus, enterovirus, cytomegalovirus (CMV), HIV** **Bacteria:** **Salmonella, Shigella, Campylobacter, Escherichia coli, Mycobacterium tuberculosis, Mycobacterium avium complex** **Parasites:** **Entamoeba histolytica, Giardia lamblia, Isospora belli, Cryptosporidium, Microsporidium, Strongyloides** **Non-infectious:** **Kaposi sarcoma, non-Hodgkin's lymphoma**	Clinical manifestations with supportive stool and blood cultures. Identification of the causative organism frequently requires multiple stool examinations for routine microscopy and culture (ova, cysts, and parasites) and modified AFB stain. Endoscopy and biopsy should be considered early where diarrhoea persists and the diagnosis remains unclear.	**Symptomatic Rehydration:** Oral or IV fluids with electrolytes. **Anti-motility agents:** Co-phenotrope (diphenoxylate hydrochloride 2.5 mg, atropine sulfate 25 ug PO, 2 tablets as stat dose followed by one tablet PO 8 hourly for each loose stool (exclude bacterial infection first).	**Symptomatic Rehydration:** Oral or IV fluids with electrolytes (use WHO Blue Book). **Anti-motility agents:** are not recommended in children **Organism specific:** Refer to PICU/Antibiotic Guidelines **Isosporiasis:** Co- trimoxazole (SMX 40-50 mg/kg + TMP 8-10 mg/kg) PO, in 2 divided doses for 10 days (this dose is from the RED BOOK 2018-2021 Report of the Committee on Infectious Diseases 31st edition)
Other common opportunistic infections and HIV-related diseases			
Condition	**Clinical Features**	**Adult Treatment**	**Children Treatment**
Cytomegalovirus (CMV)	Usually presents in advanced HIV infection (CD4 count <50 cells/mm^3), most commonly with CMV retinitis but occasionally with disseminated disease, or with other localized end organ	**Induction dose:** Ganciclovir 5mg/kg IV BD, OR Valganciclovir (the drugs that is most likely available) 900mg PO BD for 21 days for CMV retinitis.	**Induction dose:** Ganciclovir 5mg/kg IV BD, OR Valganciclovir (the drugs that is most likely available) 900mg PO BD for 21 days for CMV retinitis.

	involvement. Symptoms are related to the organ system involved. Retinitis: may be asymptomatic, or present with floaters, scotomata's or visual field defects. Central lesions may cause decreased visual acuity and can lead to blindness. Involvement may be unilateral or bilateral. Colitis: fever, abdominal pain, bloody diarrhoea, weight loss. Oesophagitis: pain and difficulty in swallowing, fever. Pneumonitis: fever, dry cough, shortness of breath. Encephalitis: confusion, fever, altered mental state, dementia. Diagnosis Retinitis: Characteristic appearance on ophthalmologic examination. Oesophagitis and colitis: Endoscopy and biopsy for histopathology. Pneumonitis: Pulmonary interstitial infiltrates on chest X-ray. Lung biopsy required for definitive diagnosis. Exclude more common pathogens, especially PCP, pulmonary TB, and bacterial pneumonias. Encephalitis: CT scan and LP for CSF examination to exclude other causes.	Commence ART early. **Maintenance dose:** Ganciclovir 5mg/kg alternate days or 5 days a week skipping the weekend, OR Valganciclovir 15mg/kg/dose PO BD for 21 days **Prophylaxis:** **Primary prophylaxis:** Not required. **Secondary prophylaxis:** Ganciclovir 5mg/kg IV OD, OR Valganciclovir 900mg PO OD for 6 months; can be discontinued in patients who experience immune recovery following the introduction of ART and who have a CD4 count >100 cells/μL for 3 to 6 months. Patients should have a visual acuity test at least once every 6 months and a fundoscopic examination yearly.	Commence ART early. **Maintenance dose:** Ganciclovir 5mg/kg alternate days or 5 days a week skipping the weekend, OR Valganciclovir 15mg/kg/dose (max dose of 900mg/day) PO BD for 21 days **Prophylaxis:** **Primary prophylaxis:** Not required. **Secondary prophylaxis:** Ganciclovir 5mg/kg IV OD, OR Valganciclovir 900mg PO OD for 6 months; can be discontinued in patients who experience immune recovery following the introduction of ART and who have a CD4 count >100 cells/μL for 3 to 6 months. Patients should have a visual acuity test at least once every 6 months and a fundoscopic examination yearly.
Mycobacterium avium complex (MAC)	Disseminated MAC infection presents as a systemic illness characterized by persistent fever, night sweats, fatigue, weight	Clarithromycin 500mg PO OD + ethambutol 15mg/kg/day PO with or without rifabutin 300mg PO OD; OR	Clarithromycin 15mg/kg (max 1g/day) PO BD + ethambutol 15mg/kg/day (max 2.5g/day) PO with or without rifabutin 10-20 mg/kg/dose PO OD (max dose of 300mg)

	loss, cough, anaemia, abdominal pain, and diarrhoea. Diagnosis Confirmed by isolation of the organism (AFB smear and culture) from blood or bone marrow or another normally sterile site, or by histopathology and culture of an appropriate tissue specimen (e.g. lymph node or liver biopsy). Where the above investigations are not available, a presumptive diagnosis may be made based on the characteristic clinical presentation and the presence of typical laboratory (anaemia, elevated alkaline phosphatase [ALP]) and radiological (hepatomegaly, splenomegaly, and mediastinal or intra-abdominal lymphadenopathy) parameters, and exclusion of an alternate likely diagnosis (especially disseminated TB or lymphoma).	Azithromycin 500mg PO OD + ethambutol 15mg/kg/day PO with or without rifabutin 450mg PO OD **Prophylaxis:** **Primary prophylaxis:** Azithromycin 1,200mg PO per week + rifabutin 300mg PO OD; OR Clarithromycin 500mg PO BD + rifabutin 300mg PO OD. **Secondary prophylaxis:** Patient should remain on life-long continuation of therapy on the above doses unless when the HIV viral load has been suppressed and the CD4 cell count is >100 cells/μL for 3 months, after treatment for 12 months.	OR Azithromycin 10mg/kg (max 500mg) PO OD + ethambutol 15mg/kg/day PO with or without rifabutin 300 to 450mg PO OD. If Rifabutin not available, add Ciprofloxacin PO 10-15mg/kg/dose BD (max 1.5g/day). Duration of treatment minimum 12 months. Children receiving ethambutol who are old enough to undergo routine eye testing should have monthly monitoring of visual acuity and colour discrimination. **Prophylaxis:** **Primary prophylaxis:** Azithromycin 20mg/kg (1,200mg maximum weekly dose) PO per week + rifabutin 300mg PO OD; OR Clarithromycin 500mg PO BD + rifabutin 300 mg PO OD. **Primary Prophylaxis Indicated for Children:** - <1 year: CD4 count <750 cells/mm3; - 1 to <2 years: CD4 count <500 cells/mm3; - 2 to <6 years: CD4 count <75 cells/mm3; - ≥6years: CD4 count <50 cells/mm^3 **Criteria for Discontinuing Primary Prophylaxis:** Do not discontinue in children aged <2 years. After≥6months of ART and: - 2 to <6 years: CD4 count >200 cells/ mm^3 for >3 consecutive months - ≥6years: CD4count >100 cells/mm^3 for >3 consecutive months **Criteria for Restarting Primary Prophylaxis:** - 2 to <6 years: CD4 count <200 cells/mm^3 - ≥6years: CD4 count <100 cells/mm^3 **Secondary Prophylaxis Indicated:** - Prior disease **Criteria for Discontinuing Secondary Prophylaxis Fulfillment of All of the Following Criteria:** - Completed ≥6 months of ART - Completed ≥ 12 months MAC therapy - Asymptomatic for signs and

			symptoms of MAC - Aged 2 to <6 years: CD4 count >200 cells/mm^3 for ≥ 6 consecutive months - Aged ≥ 6years: CD4 count >100 cells/mm^3 for ≥ 6 consecutive months **Criteria for Restarting Secondary Prophylaxis:** - Aged 2 to <6 years: CD4 count < 200 cells/mm^3 - Aged ≥ 6 years: CD4 count < 100 cells/mm^3
Cervical cancer	Clinical features: Often asymptomatic. May also present with vaginal discharge, vaginal bleeding, and pelvic pain. Diagnosis: Annual cervical screening is recommended for all HIV positive women as they are at increased risk of cervical dysplasia and cancer. Cervical screening will detect human papilloma virus (HPV), the cause of most cervical cancers, cervical dysplasia, and cancer. Colposcopy and cone biopsy where indicated. Further investigations may be considered (e.g. ultrasonography for hepatic metastases or CT scan for lymph node or bone metastases).	Routine screening: - Conduct cervical cancer screening (pap smear or thin prep) at time of diagnosis; - Repeat at 6 months post diagnosis of HIV; - Then Annual screening thereafter. (if earlier two are within normal) Patients with (abnormal) cervical screening reports refer to Cervical Cancer Screening Policy, for further gynaecological management. Adjuvant therapy may be required.	

Metabolic conditions and chronic HIV care

Metabolic conditions and chronic care of HIV positive patients

People living with HIV are at an increased risk of developing a range of chronic NCDs including cardiovascular disease, hypertension, diabetes, chronic obstructive pulmonary disease (COPD), kidney disease, HIV associated neurocognitive disease (HAND) and cancers. The intersection of HIV and NCD is strongly influenced by increasing survival due to effective ART, lifestyle factors, long term complications of ART and other disease associated with ageing.

ART can lead to multifactorial causes of metabolic conditions such as:

- Lipid abnormalities
- Dysregulation of glucose metabolism
- Body fat redistribution
- Mitochondrial toxicity
- Loss of bone mineral density
- Non-communicable diseases

Due to ART, HIV patients are living longer. Ageing has a lot of impact on HIV; HIV patients have accelerated ageing on top of normal ageing. There can be an accelerated progression of chronic diseases and HIV-related or HIV–unrelated cancers due to inflammation, either from HIV or ageing.

Management of Metabolic conditions in PLHIV

Management of the metabolic condition is not different from non-HIV patients. Integrating interventions as part of HIV care can help reduce the risks of NCD. These interventions can be:

1. Nutrition assessment, dietary counselling and support
2. Smoking and alcohol cessation
3. Exercise promotion
4. Blood pressure and glucose monitoring
5. Cholesterol management
6. Those ARVs (e.g. lopinavir/ritonavir, Tenofovir, zidovudine, etc.) that has contributed to a particular NCD should be substituted with another ARV (refer to relevant section for drug toxicities).
7. PLHIV who have established NCDs should be linked to appropriate clinical care and managed at the same health facility, if possible.

In general, all HIV patients should be screened for NCDs annually, especially those who are on PIs.

Discussions in this section are limited to the conditions listed below. For detailed management – refer to relevant clinical guidelines.

Bone disorders

Due to ageing, PLHIV are at a risk of getting osteoporosis and osteopenia. Men above 50 years of age and post-menopausal women are at an increased risk.

Management

ARVs (e.g. Tenofovir) that causes a decrease in bone mineral density should be substituted (refer to section on drug toxicities).

Lipodystrophy

Lipodystrophy syndrome is the change in body habitus due to fat redistribution. It is associated with long-term use of NRTIs (e.g. zidovudine, abacavir) and PIs (e.g. lopinavir/ritonavir). The overlapping toxicities of NRTIs and PIs result in lipodystrophy syndrome causing metabolic abnormalities i.e. increased blood sugar, serum cholesterol and triglycerides.

There are two mechanisms that occur in lipodystrophy syndrome:

Lipoatrophy – leading to loss of subcutaneous fat and thinning subcutaneous fat in the face, buttocks and extremities.
Lipohypertrophy – deposition of fat tissue subcutaneously in the neck ("bullfrog neck"); dorsocervical spine ("buffalo hump"); breast and upper torso; and abdomen ("pot belly") increasing abdominal girth and waist-to-hip ratio.

Management

1. Monitor blood sugar, cholesterol and triglycerides at least once a year.
2. Lifestyle changes – reduce saturated fat and cholesterol intake; increased physical activity; smoking cessation.
3. Change antiretroviral drugs – currently, the options are quite limited. Among the available NRTIs, the degree of the risk of developing lipodystrophy syndrome is as follows: abacavir (ABC) > zidovudine (AZT) (refer to section 8 for drug toxicities). Even if the ARVs are changed, the changes made to the body due to lipodystrophy syndrome are irreversible.
4. Lipid-lowering drugs – pravastatin (dose: 20–80 mg OD or BD) and atorvastatin (dose: 10–80 mg PO OD) are preferable in HIV-positive patients with dyslipidaemia.
5. Oral hypoglycaemic drugs if patient develops diabetes mellitus – biguanides (metformin).

Mental health disorders

PLHIV are at high risk of mental, neurological and substance abuse disorders. PLHIV who have depression are less likely to achieve optimal treatment adherence. The illness itself is a major source of stress that can lead to mental health disorders. Some opportunistic infections also can contribute to mental disorders as it can affects the nervous system. Assessment, management and appropriate referral of depression should be included in the package of HIV services for all individuals living with HIV.

Management

1. ARV (e.g. efavirenz) drugs that may cause the mental health disorder to worsen, needs to be substituted.
2. Opportunistic infections that can lead to mental health disorders need to be treated appropriately (refer to section II for opportunistic infections).
3. Appropriate referral is needed to a psychiatrist or counsellor, depending on the severity of the mental health disorder

Drug use disorder

Drug use disorders, such as using alcohol, marijuana, cocaine, methamphetamine, opioids, are closely associated with HIV and other STIs. Injecting drug use (IDU) can be a direct route of HIV transmission if people share needles, syringes or other injection materials that are contaminated with HIV. Drinking alcohol and ingesting, smoking or inhaling drugs are also associated with increased risk for HIV. These substances can alter judgment and lead to risky behaviours.
In PLHIV, drug use can fasten the disease progression, affect adherence and worsen the overall consequences of HIV.

Management

1. Appropriate referral to a psychiatrist or counsellor is needed, depending on the severity of the drug use disorder.
2. Appropriate management of any metabolic conditions due to prolonged drug use.
3. Altering ARV drug use leads to mental disorders.

Nutrition Support

ART can improve nutritional status by reducing HIV viral burden and increasing immune function, thereby reducing infections that alter metabolism or decrease intake/absorption. Conversely, optimal nutritional status has the potential to enhance ART efficacy through providing the body with the building blocks for immune system growth and repair. The effects of ART on nutritional status of a PLHIV can be:

- Unplanned weight change
- Diarrhea
- Changes in taste and smell
- Reflux, bloating and other gastrointestinal changes
- Nausea and vomiting
- Hyperlipidaemia
- Insulin resistance
- Osteopenia and osteoporosis

Management

1. HCWs are advised to refer the patient to the dietician for one-to-one counselling.
2. Offer expert advice according to the table below.

Table 33 When and what nutritional advice/interventions to provide for PLHIV

When	What
WHO clinical stage 1	Healthy eating to enhance immune function Food and personal hygiene for prevention of infections
WHO clinical stage 2	Weight gain advice (if unintentional weight loss) Modified textured diet e.g. for oral ulcers
WHO clinical stage 3/4	Diet strategies to manage existing nutrition related problems including: diarrhoea, weight loss, sore mouth
During first 6 weeks of treatment	Identification and provision of dietary strategies to manage symptoms if present e.g. diarrhoea, nausea,
At treatment reviews or when treatment	Nutritional assessment and dietary modification if indicated.

3. During clinical encounters with the patient, health care workers should take the opportunity to remind patients about basic food hygiene.

- Cook food thoroughly
- Food should be steaming hot when served
- Eat cooked food immediately
- Store food carefully
- Re-heat food thoroughly
- Avoid contact between raw and cooked food
- If possible, prepare salads personally to ensure that vegetables are washed thoroughly
- Wash fruits thoroughly. Eat fruits that need to be peeled.
- Keep kitchen surfaces clean protect food from rodents, insects and animals
- Use clean, portable water
- Wash hands thoroughly before and after cooking, before and after eating, before and after using the washroom

Antiretroviral drugs for HIV Prevention

Pre-Exposure Prophylaxis (PrEP)

Oral PrEP is the use of antiretroviral (ARV) drugs before HIV exposure by people who are not infected with HIV in order to block the acquisition of HIV PrEP can be considered for people at substantial risk of acquiring HIV. Oral PrEP containing TDF is to be offered as an additional prevention choice for people with substantial risk of HIV infection as part of combination HIV prevention approaches.

Substantial risk is defined as HIV incidence around 3 per 100 person-years or higher in the absence of PrEP. This has been identified in the following groups:

- Serodiscordant couple
- Injecting drug users
- Men who have sex with men
- Transgender people
- Sex workers

Before starting PrEP, the person seeking PrEP should have the following:

- HIV testing (before and every 3 months after a PrEP)
- Test for other STIs, and Hepatis B
- Adherence counselling & Resistance counselling
- Pregnancy test
- Test and monitor renal function
- Behaviour counselling

Fiji MOHMS is not in the position of providing antiretroviral for PrEP (except to serodiscordant pregnant women), however should an individual require PrEP, they may access PrEP through private providers or from overseas.

Oral PrEP containing **TDF + 3TC** is to be offered as an additional prevention choice for people with substantial risk of HIV infection as part of combination HIV prevention approaches.

PrEP in the setting of PPTCT, should be offered to a HIV negative woman who is in a serodiscordant relationship and wants to become pregnant. PrEP will assist in the prevention of transmission of HIV from the HIV positive partner to the woman and her unborn child.

Eligibility criteria for PrEP in PPTCT

PrEP should be offered in women who are in a serodiscordant relationship, where she is HIV negative and her partner is HIV positive, and wants to conceive, if:

- her partner's recent viral load (done within the last 6 months) is > 1000 copies/mL, or
- her partner is not adherent to ART, or
- her partner is clinically unstable or has OIs/co-infections, or
- her partner has defaulted clinic for at least 6 months

Before starting PrEP, the HCW should discuss the following with the women:

- Potential side effects
    - nausea and headaches which improves within the first few weeks.
    - mild worsening of kidney function which improves upon discontinuation of TDF.
    - decreased bone density greater in people taking TDF, but no increase in fractures.
- Adherence
    - PrEP medication provides 92%-99% reduction in HIV risk for HIV-negative individuals who take the pills every day as directed. If a daily dose is missed, the level of HIV protection may decrease. It only works if you take it.
    - People who use PrEP correctly and consistently have higher levels of protection against HIV. According to data analysis from the iPrEx study that found PrEP to be effective:
        - For people who take 7 PrEP pills per week, their estimated level of protection is 99%.
        - For people who take 4 PrEP pills per week, their estimated level of protection is 96%.
        - For people who take 2 PrEP pills per week, their estimated level of protection is 76%.
- Resistance
    - There is a risk of developing resistance to HIV medications if acute HIV is not identified quickly while on PrEP.
    - The patient should report immediately to clinic if they develop symptoms compatible with acute HIV infection (fever with sore throat, rash, or headache)
- Time to protection
    - Approximately 7 days after starting PrEP in rectal tissue
    - Approximately 20 days in cervicovaginal tissue

Assessment of women before initiating PrEP

- any history of renal or liver disease or osteoporosis: caution or avoid using tenofovir
- recent symptoms of a flu-like illness: test for acute HIV and defer PrEP until test results are back
- willingness and ability to 1) take a medication every day, and 2) return for regular appointments for clinical and laboratory monitoring

Baseline tests before initiating PrEP

- HIV test (preferably done at least 3 weeks prior)
- Test for other STI (e.g. syphilis and hepatitis)
- Kidney function test
- Pregnancy test

Initiating PrEP

- If there are no contraindications to PrEP use and the patient is interested in using PrEP as an HIV prevention tool, PrEP can be initiated.

PrEP medication:

Tenofovir (TDF) 300mg + Lamivudine (3TC) 300mg, per oral once daily

- Timing of initiation: confirm a negative HIV test within the last 3 weeks, normal renal function, and lack of acute HIV symptoms on the day you initiate medications. If it has been more than 3 weeks since baseline labs were obtained, repeat an HIV test.
- Provide adherence counselling, provide anticipatory guidance about common side effects when PrEP is started, and suggest a pill box to help patient with adherence.
- Counsel patients on risk reduction and using condoms – in addition to PrEP – to decrease risk of STIs and provide additional reduction in risk of HIV acquisition.

Remember!

PrEP does not provide any protection from unwanted pregnancies and STIs.

Monitor and provide ongoing support for patients using PrEP

- monthly follow ups at the clinic to monitor side effects, adherence counselling, ongoing risk reduction counselling, assess for signs and symptoms of acute HIV infection, and replenishment of ARV
- 3 monthly blood tests for HIV, STI screening and pregnancy test

When to discontinue PrEP

- If the woman becomes positive for HIV, discontinue PrEP to avoid resistance and start her on ART
- To stop PrEP is the choice of the women. So, after delivery and breastfeeding the woman wants to stop PrEP, you can discontinue it but advise the woman of the risk of transmission of HIV to her from her partner and to her child in future pregnancies.

Post-Exposure Prophylaxis

This section covers consideration and initiation of antiretroviral post-exposure (PEP) prophylaxis in occupational and non-occupational settings. The aim of PEP is to reduce the likelihood of HIV, Hepatitis B and Hepatitis C transmission.

PEP should be offered to a person who may have been exposed to HIV (e.g. health care workers, other occupational exposure, or accidental exposures or those who may have been sexually abused or assaulted etc), after a thorough risk assessment of the possible source, the exposed person, and the circumstances surrounding the exposure to HIV.

Occupational exposures

Prevention is vital. Healthcare workers should practice standard precautions for infection control in delivering care for all patients. The risk of exposure to HIV via the percutaneous (needle stick injuries) route is 0.3%, and 0.09% via the mucous membrane and non-intact skin.

All healthcare workers must ensure that their Hepatitis B vaccination is up-to- date.

Immediate management

- Needle stick injuries and cuts should be washed immediately with soap and running water for at least 2 minutes.
- Aspiration, forced bleeding and wound incision are not recommended.
- Do not use any strong solutions (i.e. iodine) as they may irritate the wound and make the injury worse. If running water is not available, clean the site with an alcohol-based hand rub solution.
- Cover with sterile dressing.
- Splashes to the nose, mouth or non-intact skin should be flushed with water for at least 2 minutes.
- Splashes to the eyes should be irrigated with clean water, saline or sterile water for at least 2 minutes. If wearing contact lenses leave them in place while irrigating, remove after the eye is cleaned, and cleanse the lenses in the usual manner. Do not use soap or disinfectant in the eye.
- Splashes to the mouth or nose should have the fluid immediately spat or blown out, and the site should then be rinsed thoroughly with water or saline and spat or blown out again. Repeat this several times. Do not use soap or disinfectant in the mouth or nose.
- Seek medical attention immediately.

Report the occupational exposure

- Report occupational exposure incident immediately to the supervisor or manager.
- The supervisor should arrange with the infection control officer or the medical officer for assessment of the occupational exposure.
- Health staffs - Complete the prescribed Infection control form.
- The completed form should be sent to the infection control officer who then carries out the risk assessment of the occupational exposure.
- The exposed HCW should be counselled by the infection control officer and/or the immediate supervisor in confidence.

Assess the occupational exposure

- Register the following:
- The name of the person exposed.
- Where the incident occurred.
- Description of the exposure site, body site, and the initial care provided.
- Determine whether the exposure occurred while the HCW was officially working or not.
- Determine the body fluid type, and, exposure type, and volume of exposure.
- Body fluid type and risk of blood borne pathogen transmission.

Table 34 Body fluids and blood-borne pathogen transmission

Body fluids that pose a risk for blood-borne pathogen transmission		
Blood	Semen	Vaginal secretions
Cerebrospinal fluid	Synovial fluid	Pleural fluid
Peritoneal fluid	Pericardial fluid	Amniotic fluid
Body fluids that do not pose a risk of blood-borne pathogen transmission		
Urine	Stool	Tears
Saliva	Vomitus	Sweat
Non purulent sputum	Nasal discharge	

Table 35 Type and volume of exposure to body fluids and risk of blood borne pathogen transmission

Injury	Description	Severity
Percutaneous injuries	Occur when the skin is penetrated by a contaminated sharp object, i.e. needle or instrument	Less severe – superficial injury; penetration with a solid needle, e.g. suture needle. More severe – deep puncture; penetration with a large bore, hollow needles; blood visible on device; needle was used in the patient's artery or vein.
Mucus membrane exposure	Can be inside the eyes, nose or mouth, or exposure to non-intact skin e.g. dermatitis, abrasion, open wound	Small volume exposure – a few drops. Large volume exposure – large splash.

Exposure of intact skin to blood and other body fluids does not constitute an exposure.

Assess the source person

- Assess the source person (where possible)
- Provide counselling and seek consent to access medical information
- Medical history
- Laboratory results
- Interview the source person's doctor
- Record medical information including laboratory results and date

> Do not record the source person's identity on the exposed person's record

If the source person is HIV-positive:

- Assess the clinical status of the HIV disease, e.g. WHO clinical stage
- Obtain results of the most recent CD4 count and viral load
- History of antiretroviral therapy and adherence
- If HBV and HCV status unknown, offer testing of the source person
- If HIV status of the patient is unknown
- Do risk assessment
- Counselling for HIV, HBV, HCV and syphilis
- If the source person refuses testing, decide on the assumption that the source person might be infected with HIV, HBV and HCV

Assess the exposed person or worker

Provide HTS, HBsAg, HCV antibody (on special request), RPR for syphilis, full blood count, liver function tests, serum creatinine, estimated glomerular filtration rate (eGFR), urine dipstick for glycosuria and rule out pregnancy test for females.

Assess hepatitis B immune status of the exposed:

- If the source patient's status is unknown and the exposed is immune (positive anti-HBs) or known responder – the exposed is protected.
- If the exposed is non-immune (anti-HBs negative), administer hepatitis immunoglobulin (0.06 ml/kg intramuscularly) stat; and start hepatitis B immunization (20 µg intramuscularly per dose) as soon possible at 0, 1 and 6 months.
- Consider tetanus immunization.

Recommended post-exposure prophylaxis for HIV

After risk assessment of the occupational exposure, determine the recommended antiretroviral regimen for post-exposure prophylaxis to HIV as below.

Not all occupational/accidental exposures will receive PEP for HIV. The decision for treatment will be based on the risk assessment process that will evaluate the risk of exposure

If the exposed is eligible for PEP, it should be offered immediately without waiting for the results of the HIV test of the source person of the exposure. There is greater benefit if PEP is initiated within 36 hours after exposure and none if given after 72 hours.

Eligibility for PEP:

- Less than 72 hours has elapsed since exposure; *AND*
- The exposed individual is not known to be HIV-positive; *AND*
- The person who is the source of the exposure is HIV-positive or has an unknown HIV status; *AND*
- A defined risk of exposure.

PEP therapy

Table 36 Recommendations for PEP

Population	Recommendations
Adults and adolescents	TDF + 3TC is the recommended backbone regimen
	DTG is recommended as the preferred third drug (refer to section 2 for use in women and adolescent girls of childbearing age)
	When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options
Children	AZT + 3TC is the recommended backbone regimen
	ABC + 3TC or TDF + 3TC can be considered as alternative backbone regimens
	DTG is recommended as the preferred third drug for whom an approved DTG dosing is available
	When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options

Please ensure the following:

- Enhanced adherence counselling is suggested.
- Duration for PEP is 28 days.

Exposures that do not require PEP are:

- when the exposed individual is already HIV positive or,
- when the source is established to be HIV negative or
- when exposed to bodily fluids that do not pose a significant risk.

Counselling, education, and support to the exposed

Counselling should be provided regarding PEP and this should be continued until follow-up is completed (i.e. for 3 months). The following issues should be discussed during counselling:

- Confidentiality and disclosure
- HIV, HBV and HCV infection and their respective consequences
- Procedure of HIV testing and the meaning of results
- Assessment of risk related to past and current sexual and other risk behaviours, as well as any previous exposures
- Assessment of risk related to the current exposure
- Explanation of risk of transmission associated with exposure
- Assessment of anxiety level and coping mechanisms
- Obtaining informed consent for testing (including stat pregnancy test)
- Planning for precautions while awaiting test results (and while taking PEP, if indicated) including:
- Safe sexual practices, e.g. provide condoms
- Cessation of breast feeding is an option, after full counselling with the breastfeeding mother (refer to breastfeeding/nutritional counselling), if lactating
- Any required modification of occupational duties, if indicated
- Not to donate blood
- Wound management.
- Providing information about the need to take PEP; when to start and what are the drugs to take; duration of PEP; PEP side effects and management

Repeat blood tests:

- HIV antibody: 4-6 weeks and 3 months.
- Anti-HBs: Individuals with evidence of previous immunity to hepatitis B (HBsAb positive) will require no further follow-up Non-immune individuals require immunisation and follow-up to 6 months).
- Anti-HCV: 6 months (with serum alanine transferase, ALT)
- Regular follow-up
- Arranging support while awaiting results and while taking PEP, if PEP is indicated
- Provision of exposure risk reduction education in a sensitive and non-judgmental way
- Referral for appropriate care and management if repeat blood test is confirmed HIV-positive.

Post-exposure p rophylaxis for non-occupational exposures (NPEP)

Post-exposure prophylaxis for HIV infection (PEP-HIV) will be provided to the person who has been raped and/or sexually abused by a known HIV-positive person and also to individual cases where a high risk of transmission has been identified.

1. The individual should receive medical care and other support services:
2. Initial crisis intervention (such as emotional support) and first aid;
3. Explain to the survivor the care and interventions that will be provided;
4. Obtain medical history;
5. Conduct a general examination, including overall status and recording injuries;
6. Assess the risk of HIV transmission (see below);

The individual risk of HIV transmission depends on the type of exposure. Co- factors such as sexually transmitted infections (STIs), viral load, and trauma may affect the risk estimate. The estimated per-act probability of acquiring HIV from an infected source, by exposure act is as follows: receptive anal intercourse, 0.5%; receptive penile-vaginal intercourse, 0.1%; insertive anal intercourse, 0.065%; insertive penile-vaginal intercourse, 0.05%. Accurate risk estimates for receptive oral or insertive oral intercourse are not available.

Box 2 Eligibility criteria for post-exposure prophylaxis (NPEP) among people who have been sexually assaulted

- Less than 72 hours has elapsed since exposure; AND
- The exposed individual is not known to be HIV-positive; AND
- The person who is the source of the exposure is HIV-positive or has an unknown HIV status: AND
- A defined risk of exposure, such as:
  - Receptive vaginal or anal intercourse without a condom or with a condom that broke or slipped; OR
  - Contact between the perpetrator's blood or ejaculate and mucous membrane or non-intact skin during the assault: OR
  - Receptive oral sex with ejaculation; OR
  - The person who was sexually assaulted was drugged or otherwise unconscious at the time of the alleged assault and is uncertain about the nature of the potential exposure: OR
  - The person was gang-raped

The use of PEP following potential sexual exposure to HIV is only recommended where the victim presents within 72 hours of exposure. Within that time frame, it is recommended that HIV-PEP (if given) should be administered as early as possible.

HIV-PEP is not appropriate in the context of chronic exposures to HIV such as regular and ongoing unprotected sex with an intimate partner.

It is recommended that a three-drug ARV regimen should be used as indicated in the table below.

PEP therapy

Table 37 Recommendations for PEP

Population	Recommendations
Adults and adolescents	TDF + 3TC is the recommended backbone regimen
	DTG is recommended as the preferred third drug (refer to section 2 for use in women and adolescent girls of childbearing age)
	When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options
Children	AZT + 3TC is the recommended backbone regimen
	ABC + 3TC or TDF + 3TC can be considered as alternative backbone regimens
	DTG is recommended as the preferred third drug for whom an approved DTG dosing is available
	When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options

Please ensure the following:

- Enhanced adherence counselling is suggested.
- Duration for PEP is 28 days.

Screening services;

- Baseline full blood count, liver function tests, serum creatinine, estimated glomerular filtration rate (eGFR) and urine dipstick for glycosuria;
- STI screening and treatment, including hepatitis B, hepatitis C, and syphilis;
- Pregnancy test, emergency contraceptive, and other sexual and reproductive health services; and

Counselling for the exposed

The exposed person should be counselled on:

1. The need to take PEP; when to start, what drugs to take and for how long; adherence to PEP; the side effects of PEP and how to manage them
2. How to prevent HIV transmission
3. Repeat laboratory tests:
   - Repeat pregnancy test 4-6 weeks after exposure
   - HIV antibody: 4-6 weeks and 3 months
   - Anti-HBs: Individuals with evidence of previous immunity to hepatitis B (HBsAb positive) will require no further follow-up Non-immune individuals require immunisation and follow-up (to 6 months).
   - Anti-HCV: 6months (with serum alanine transferase, ALT)
4. Referral for appropriate care and management if repeat blood test is confirmed HIV-positive.
5. Referral for psychosocial support.

Surgical care of PLHIV patients

Surgical care of HIV positive patients

This section provides guidance for surgeons in the care of HIV positive patients undergoing surgery. It does not cover details on surgical procedures on particular opportunistic infections and other HIV related conditions.

It is reasonable to consider all patients for surgery to be potentially HIV infected and infectious. However, HIV testing is not mandatory. Universal precautions must be practiced at all times.

Surgeons have professional responsibility to provide the best possible quality of care to their patients regardless of HIV status.

1. Pre-operative evaluation and preparation of HIV-positive patients are similar to that of the general population which includes asking patients whether they are suffering from any chronic medical condition or on long term medications.
2. CD4 cell count or HIV viral load should not be used as sole determinants in assessing patient's surgical risk.
3. All patients on ART should continue with their treatment protocol during the peri-operative period. When ART interruption is necessary, the surgeon or anaesthetist should consult the patient's attending physician.
4. For patients who are able to receive liquids but not solids for more than one week, consideration should be given to converting the ART regimen that is available in liquid preparation temporarily and resume to tablet formulations once the patient is allowed to take solids.
5. Surgeons should adhere to universal standard precaution of infection control using the most effective known sterile barriers for all surgical procedures.

To reduce the risk of intra-operative exposure to blood and bodily fluids, the following are being suggested:

- Avoidance of hand-to-hand passage of sharp instruments;
- Use of staple devices instead of suturing, if available;
- Placing sharp instruments on a sterile instrument stand between the scrub nurse and the surgeon, especially in short, low-risk surgical procedures;
- Use of blunted needles for facial closure.

Knowledge of the HIV status of the patients should not affect in any way the behaviour of health professionals in the operating theatre.

6

CONTINUUM OF CARE

Section VI Continuum of Care

Guiding principles of the continuum of care

Positive prevention interventions should focus on prevention of initial illness or episodes of opportunistic infections and other HIV-related conditions or prevention of recurrence. HIV care involves medical care, psychological, social, and legal support; enhancing economically productive activities; and creation of enabling environments.

HIV is now considered a chronic disease because of increasing accessibility of PLHIV to effective ART. As with other chronic diseases, the continuum of care (CoC) for HIV is the system that provides humane, effective, quality, comprehensive and continuous care for PLHIV as well as their families. CoC is a valuable approach to comprehensive care for PLHIV and their involvement in their care:

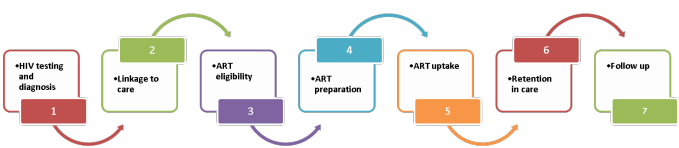
1. It enhances the quality of life of PLHIV;
2. It promotes better ARV adherence and retention in HIV care;
3. It reduces stigma and discrimination; and
4. It reduces service delivery costs.

The HIV care continuum

Successful patient outcome of HIV care depends on a high degree of success at each and every point of the HIV care continuum steps or processes:

Figure 1 1 The HIV continuum of care. Adapted from Ahonkai et al (2012)

Processes



Negative Outcomes

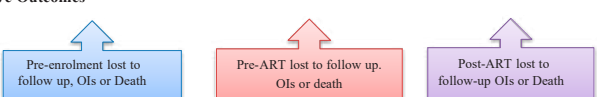
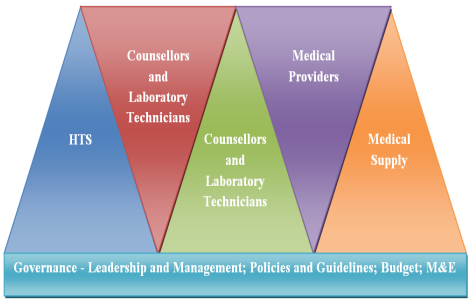


Figure 12 HIV Service Structure



The HIV Care team

Prescription of ART is complex and requires complete understanding of the rationale, pharmacology and adverse effects of drugs. In addition, the health practitioner needs to be knowledgeable or should have completed relevant training about the treatment of co-existing conditions and the management of HIV in special groups such as pregnant women and children.

The HIV care team may consist of three or more of the following personnel:

Medical officer HIV HUB, Physician, Paediatrician, Surgeon and Obstetrician from the hospital where treatment is being provided, TB specialist, Counsellor, Midwife, Nurse, Pharmacist, laboratory officer, dietician and dental personnel. The HIV HUB will be the secretariat to the team. Other healthcare professionals and support personnel will be co-opted when the need arises.

The HIV care team coordinates the continuum of clinical care activities for an individual. The team will facilitate the linkages of the PLHIV to other services.

The roles and functions of the HIV care team includes:

1. Develop and co-ordinate management plan for people infected with and affected by HIV from the time of diagnosis, treatment and long-term chronic care.
2. Conduct HIV surveillance in the country.
3. Act as advocates for ART treatment adherence and follow up; and also strengthen initiative for contact notification and testing.

The HIV continuum of Care intervention package

Throughout the course of HIV infection, PLHIV face a lot of challenges, this includes:

- Deteriorating physical health – e.g. Opportunistic infections; ARV drug reactions
- Mental health issues - Fear of rejection and isolation
- Economic issues – inability to work; health care costs, poverty; and
- Social and legal issues – stigma, discrimination, human rights violation

To mitigate these challenges, PLHIV should have access to:

- Physical and mental health awareness
- Reduce vulnerability and risk behaviours
- Reduce the risk of HIV transmission to others
- Get involved in community activities
- Be supported to address diseases the most impact the quality and duration of their lives.

The minimum package of service and interventions essential for a successful and quality HIV management and care is in the box below.

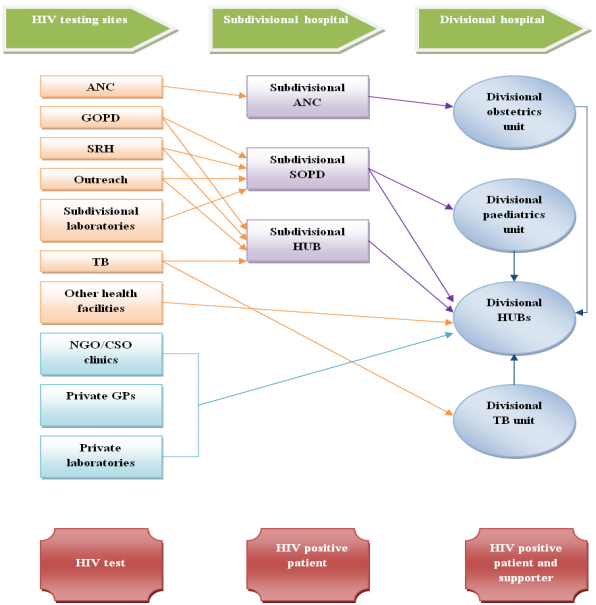
Box 3 Package of Continuum of care interventions for people living with HIV

1. Refer and retain PLHIV to treatment, care and support services; disclosure; partner management
2. Co-trimoxazole prophylaxis
3. Prevention, early detection and treatment of TB
4. Diagnosis and treatment of other sexually transmitted infections
5. Prevention and treatment of opportunistic infections and other HIV-related conditions
6. Antiretroviral therapy and adherence counselling and support
7. Immunizations
8. Antenatal (ANC), maternal and child health (MCH), sexual and reproductive health (SRH) services
9. Prevention of mother-to-child transmission (PPTCT) for HIV-positive pregnant women linked to ANC, MCH and SRH (e.g. family planning, contraception)
10. Infant feeding and ongoing support
11. Care and diagnostic testing for HIV-exposed infants
12. Adolescent health and development (AHD) and peer support services
13. Nutritional therapy
14. Palliative care
15. PLHIV support groups
16. Psychosocial support
17. Care and support of orphans
18. Financial and legal support
19. Prevention services for gender-based and domestic violence
20. Spiritual support
21. Respite for caregivers

Linkages to HIV care

After the patient is diagnosed HIV positive and has received post-test counselling, the patient is referred to the HUB as early as possible (for further assessment and initiation of ART).

Figure 12 Referral pathway to the HUB from the HTS sites and laboratories



Continuum of care is a network that links, coordinates and consolidates care, treatment, and support services for PLHIV. These services are provided in their homes, in the communities where they live, and in the health facilities that serve them.

Palliative care

The aim of palliative care is to provide the best quality of life for PLHIV. It begins when:

- Medical treatment is no longer effective and side effects outweigh the benefits;
- The patient does not want to continue aggressive therapy; or
- The patient's vital organs fail

Management

As with any chronic, terminal illness, palliative care for PLHIV follows these basic principles:

- Keep the patient nourished and hydrated
- Maintain basic physical care
- Provide medications for confusion and dementia
- Clean and treat skin ulcers and abscesses
- Address emotional distress appropriately
- Provide effective pain relief (follow WHO analgesia ladder below)

Table 38 WHO Analgesia ladder

Stage	Medication	Adults	Children
Step 1	Paracetamol	Paracetamol 1g PO	Paracetamol 15mg/kg PO 6 hourly (max 500mg)
Step 2	Codeine, with or without NSAIDs	Codeine 30mg orally 8 hourly when needed; ibuprofen 400mg 8 hourly when needed	Codeine 0.5 – 1mg/kg PO 4-6 hourly when needed Ibuprofen 10mg/kg PO 8 hourly (max 400mg) when needed
Step 3	Morphine	Morphine 5mg orally 8hourly, and increased by 5-10mg increments Add ibuprofen 400mg orally every 8 hours, if needed.	Morphine 0.2 - 0.5mg/kg PO 4-6 hourly when needed, Morphine 0.1mg/kg IV 2-6 hourly when needed Morphine infusion 1mg/kg in 50mls Normal saline at a rate of 1 – 4mls/hour (20-80mcg/kg/hour).

For counselling PLHIV on palliative care, the following issues are to be the core points of discussion:

- Fear of death (patient and close family members).
- Loneliness and depression.
- Feelings of guilt and regret.
- Spiritual support.
- Making a will (where applicable) and use of financial gains like superannuation, insurance, etc.
- Preparation for death & Bereavement counselling for partner and family.
- Provide care for caregivers.

7

DATA COLLECTION AND PROGRAMME MONITORING

Section VII Data collection and Programme monitoring

Guiding principles of data collection in HIV setting

With the advent of antiretroviral therapy, HIV is now considered a chronic disease similar to non-communicable diseases (NCDs). As such, it is critical for the health system to provide and sustain effective long-term HIV care with ART and prevention. This requires an effective patient monitoring system (PMS) integrated care, prevention, and treatment at all health facility levels that provide HIV related services.

Patient monitoring captures data on patients over time and across health facilities that provide HIV care/ART services. Aggregated patient data from HIV care/ART sites (i.e. HUBs) will provide routine tracking information about the program and its intended outcomes.

Patient Reporting and Monitoring System

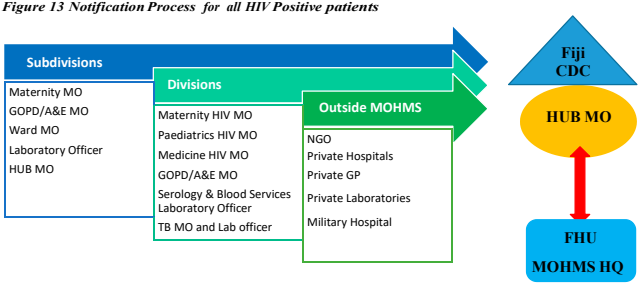
Current Fiji HIV Patient Reporting and Monitoring System

Once a patient is diagnosed HIV positive or has an inconclusive result (or unable to confirm due to stock outs) at any testing laboratories, the laboratories need to generate 3 copies of the result. The copies generated are sent to the following authorities:

1. Copy 1 – sent to the MO ordering the test;
2. Copy 2 – sent to the respective SRH clinic (HUB) MO; and
3. Copy 3 – sent to Fiji CDC.

All the patients need to be notified and referred to the HUBs for further monitoring and continuum of care. The paediatric patients also need to be referred to the respective divisional paediatric units and the pregnant women also need to be referred to the divisional maternity units. The paediatric units and the maternity units need to notify and report all their cases to the HUBs on a quarterly basis so none of the patients are missed out.

Figure 13 Notification Process for all HIV Positive patients



The indicators on which the respective HIV care team counterparts need to report against are derived from the HIV Estimates Spectrum software and Global AIDS Monitoring (GAM). These indicators will need to be updated in the respective international reporting portals annually. The number of indicators being reported on depends on the countries programme, therefore, some indicators may not be reported on.

For national reporting, the HUB consolidates all the reports from the different units on a quarterly basis and reports it to the Family Health Unit (FHU). The FHU consolidates all the reports from the 3 HUBs for internal reporting.

The following are the indicators as per Spectrum and GAM reporting tools:

➢ Spectrum:

1. Number/Percentage of pregnant women who started ART before the current pregnancy.
2. Number/Percentage of pregnant women who started ART during current pregnancy >4 weeks before delivery.
3. Number/Percentage of pregnant women who started ART during current pregnancy <4 weeks before delivery.
4. Number of pregnant women who had their first ANC visit.
5. Number of pregnant women who received at least one HIV test.
6. Number of pregnant women who tested positive at their first HIV test.
7. Number of pregnant women who were re-tested.
8. Number of pregnant women who tested positive at re-testing.
9. Number of pregnant women who were known to be HIV positive at first ANC visit (including on ART).
10. Number/Percentage of children receiving co-trimoxazole prophylaxis.
11. Number of children newly infected with HIV.
12. Number/Percentage of children receiving ART.
13. Number/Percentage of children receiving ART, desegrated in age groups 0-4 years, 5-9 years and 10-14 years.
14. Percentage to of children lost to follow-up each year.
15. Number/Percentage of adults receiving ART, desegregated into gender.
16. Percentage lost to follow up each year.
17. Number initiating ART desegregated into gender.
18. Number re-initiating ART.
19. Number PLHIV who know their HIV status, desegregated into adults (with gender) and children.
20. Number of PLHIV on ART, desegregated into 5-year age groups.
21. Number of PLHIV tested for viral suppression among those on ART.
22. Number of PLHIV tested who are virally suppressed.

➢ GAM:

1. Percentage of people living with HIV who know their HIV status at the end of the reporting period.
2. Percentage and number of adults and children on antiretroviral therapy among all adults and children living with HIV at the end of the reporting period.
3. Percentage of adults and children living with HIV known to be on antiretroviral therapy 12 months after starting.
4. Percentage and number of adults and children living with HIV who have suppressed viral loads at the end of the reporting period.

5. Percentage and number of adults and children newly diagnosed with HIV with an the initial CD4 cell count <200 cells/mm^3 and <350 cells/ mm^3 during the reporting period.
6. Percentage of treatment sites that had a stock-out of one or more required antiretroviral medicines during a defined period.
7. Total number of people who have died from AIDS-related causes per 100 000 population.
8. The number of HIV tests conducted (testing volume) and the percentage of HIV -positive results returned to people (positivity) in the calendar year.
9. Percentage of infants born to women living with HIV receiving a virological test for HIV within two months of birth.
10. Estimated percentage of children newly infected with HIV from mother-to-child transmission among women living with HIV delivering in the past 12 months.
11. Percentage of pregnant women living with HIV who received antiretroviral medicine to reduce the risk of mother-to-child transmission of HIV.
12. Percentage of women accessing antenatal care services who were tested for syphilis, tested positive and treated.
13. Percentage of reported congenital syphilis cases (live births and stillbirths).
14. Percentage of pregnant women with known HIV status.
15. Number of people newly infected with HIV in the reporting period per 1000 uninfected population.
16. Percentage of specific key populations (sex workers, men who have sex with men, people who inject drugs, transgender people, prisoners) living with HIV.
17. Percentage of people of a key population who tested for HIV in the past 12 months, or who know their current HIV status.
18. Percentage of the people living with HIV in a key population receiving antiretroviral therapy in the past 12 months.
19. Percentage of sex workers reporting using a condom with their most recent client.
20. Percentage of sex workers reporting using a condom with their most recent client.
21. Percentage of sex workers reporting using a condom with their most recent client.
22. Percentage of transgender people reporting using a condom during their most recent sexual intercourse or anal sex.
23. Coverage of HIV prevention programmes: percentage of people in a key population reporting having received a combined set of HIV prevention interventions.
24. Percentage of people who inject drugs reporting using sterile injecting equipment the last time they injected.
25. Number of needles and syringes distributed per person who injects drugs per year by needle and syringe programmes.
26. Percentage of people who inject drugs receiving opioid substitution therapy.
27. Percentage of sex workers with active syphilis.
28. Percentage of men who have sex with men with active syphilis.
29. HIV prevention and treatment programmes offered to prisoners while detained.
30. Prevalence of hepatitis and coinfection with HIV among key populations.
31. Number of people who received oral pre-exposure prophylaxis (PrEP) at least once during the reporting period.
32. Percentage of men 15–49 that are circumcised.
33. Number of male circumcisions performed according to national standards during the past 12 months.

34. The percent of respondents who say they used a condom the last time they had sex with a non-marital, non-cohabiting partner, of those who have had sex with such a partner in the last 12 months.
35. Percentage of women and men 15–49 years old who report discriminatory attitudes towards people living with HIV.
36. Avoidance of health care among key populations because of stigma and discrimination.
37. Proportion of ever-married or partnered women 15–49 years old who experienced physical or sexual violence from a male intimate partner in the past 12 months.
38. Percentage of people living with HIV who report experiences of HIV-related discrimination in healthcare settings.
39. Percentage of women and men 15–24 years old who correctly identify both ways of preventing the sexual transmission of HIV and reject major misconceptions about HIV transmission.
40. Percentage of women of reproductive age (15–49 years old) who have their demand for family planning satisfied with modern methods.
41. Domestic and international HIV expenditure by programme categories and financing sources.
42. Percentage of estimated HIV-positive incident tuberculosis (TB) cases that received treatment for both TB and HIV.
43. Total number of people living with HIV with 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.
44. Number of people who started treatment for latent TB infection, expressed as a percentage of the total number of people newly enrolled in HIV care during the reporting period.
45. Number of men reporting urethral discharge in the past 12 months.
46. Rate of laboratory-diagnosed gonorrhoea among men in countries with laboratory capacity for diagnosis.
47. Proportion of people starting antiretroviral therapy who were tested for hepatitis B.
48. Proportion of people coinfected with HIV and HBV receiving combined treatment.
49. Proportion of people starting antiretroviral therapy who were tested for hepatitis C virus (HCV).
50. Proportion of people coinfected with HIV and HCV starting HCV treatment.
51. Proportion of women living with HIV (aged 30–49) old who report being screened for cervical cancer using any of the following methods: visual inspection with acetic acid (VIA), Pap smear or human papillomavirus (HPV) test.

8

Annex

Annex 1

WHO Clinical Staging of HIV disease in adults, adolescents and children

Adults and adolescents[a]	Children
Clinical stage 1	
Asymptomatic Persistent generalized lymphadenopathy	Asymptomatic Persistent generalized lymphadenopathy
Clinical stage 2	
Moderate unexplained weight loss (<10% of presumed or measured body weight) Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis) Herpes zoster Angular cheilitis Recurrent oral ulceration Papular pruritic eruption Fungal nail infections Seborrhoeic dermatitis	Unexplained persistent hepatosplenomegaly Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) Herpes zoster Lineal gingival erythema Recurrent oral ulceration Papular pruritic eruption Fungal nail infections Extensive wart virus infection Extensive molluscum contagiosum Unexplained persistent parotid enlargement
Clinical stage 3	
Unexplained severe weight loss (>10% of presumed or measured body weight) Unexplained chronic diarrhoea for longer than 1 month Unexplained persistent fever (intermittent or constant for longer than 1 month) Persistent oral candidiasis Oral hairy leukoplakia Pulmonary tuberculosis Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia) Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis Unexplained anaemia (<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 Unexplained persistent diarrhoea (14 days or more) Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one 1 month) Persistent oral candidiasis (after first six weeks of life) Oral hairy leukoplakia Lymph node tuberculosis; pulmonary tuberculosis Severe recurrent bacterial pneumonia Acute necrotizing ulcerative gingivitis or periodontitis 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 Chronic HIV-associated lung disease, including bronchiectasis

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

(Reference – Annex 10, page 386, WHO Consolidated guideline on the use of ART for prevention and treating HIV)

Annex 2

Doses of recommended antiretroviral drugs

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 In the presence of rifabutin, no dose adjustment required. In the presence of rifampicin, adjusted dose of LPV/r: (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 (1 ml of syrup once daily)	10 mg twice daily (1 ml of syrup twice daily)
Birth weight ≥2500 g	15 mg once daily (1.5 ml of syrup once daily)	15 mg twice daily (1.5 ml of syrup twice daily)
>6 weeks to 12 weeks		
	20 mg once daily (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 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.

(For weight-based dosing for ARV formulations for infants and children refer to WHO UPDATED RECOMMENDATIONS FOR FIRST LINE AND SECOND LINE ARV REGIMENS AND ARV PROPHYLAXIS AND RECOMEDATIONS FOR EARLY INFANT DIAGNOSIS
2018, pages 62 -75)

Annex 3
ARV dosage for adults and adolescents

Dosages of ARV drugs for adults and adolescents

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
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 (Please note that NVP based regimens are no longer recommended and should only be used in special circumstances).
Proteases inhibitors (PIs)	
Atazanavir + ritonavir (ATV/r)	300 mg + 100 mg once daily
Darunavir + ritonavir (DRV/r)	800 mg + 100 mg once daily or 600 mg + 100 mg twice daily
Lopinavir + ritonavir (LPV/r)	400 mg + 100 mg twice daily
	Considerations for individuals receiving TB therapy In the presence of rifampicin, adjusted dose of LPV/r (LPV 800 mg + ritonavir 200 mg twice daily or LPV 400 mg + ritonavir 400 mg twice daily), with close monitoring. In the presence of rifabutin, no dose adjustment required.
Integrase strand transfer inhibitors INSTI	
Dolutegravir (DTG)	50 mg once daily*
Raltegravir (RAL)	400 mg twice daily
	Considerations for individuals receiving TB therapy In the presence of rifampicin, adjusted dose of DTG (50 mg twice daily) and RAL (800 mg twice daily), with close monitoring. In the presence of rifabutin, no dose adjustment required.

* TLD (Tenofovir 300 mg, Lamivudine 300 mg, Dolutegravir 50 mg fixed dose combination) can be used once daily in adolescents living with HIV weighting at least 30 kg.

Annex 4
Weight based dosing for ARV formulation 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 paediatric indications, formulations or sufficient information and evidence to provide guidance on prescribing and dosing in infants, children and adolescents less than 18 years of age. The work to develop and update simplified guidance on ARV drugs for use in children has been undertaken by WHO 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 expected body surface area of children from low- and middle-income countries in each 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 expert paediatric pharmacology consultations. 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 in no case would a child receive more than 25% above the maximum target dose or more than 5% below the minimum target dose. PK efficacy and safety studies have also confirmed the overall safety of this dosing approach. For simplification, ARV drugs no longer considered preferred or alternative options for children have been removed from the dosing guidance.

In the context of increasing implementation of virological testing at birth, and the shift towards treating infants earlier in an effort to reduce early mortality, these guidelines include weight-based dosing for term infants aged <4 weeks, including those weighing less than 3 kg. However, there is limited experience with initiating treatment in HIV-infected newborns aged <2 weeks, and a paucity of PK data to fully inform accurate dosing for most drugs in neonates, who are undergoing rapid growth and maturation in renal and liver function. PK data in preterm infants are available only for AZT; there is considerable uncertainty of appropriate dosing for NVP, RAL and 3TC in preterm and low birth weight infants. In addition, LPV/r solution should not be given to preterm infants until they have reached 42 weeks gestational age, because of the risk of adverse effects that may occur in this population. The management of HIV treatment in preterm neonates extremely is challenging because of the lack of appropriate pharmacokinetic, safety, and dosing information as well as suitable formulations. Dosing for postnatal prophylaxis for HIV-exposed infants is not provided here but can be found at http://www.who.int/hiv/pub/arv/annexes-5Sep2016.pdf?ua=1.

In this 2018 ARV guidelines revision, integrase inhibitors have been included more prominently among the preferred regimens recommended by WHO. At the time of this guidelines update, DTG was only approved for children above 6 years and 15 kg in Europe and above 30 kg in the United States. The registration trial is anticipated to generate data for dosing DTG in children down to age 4 weeks in early 2019, with potential regulatory approval in late 2019. This dosing annex includes approved DTG dosing as well as simplified dosing based on pk and safety data from an ongoing multicounty study, which is also investigating the pharmacokinetics of DTG in TB co-treated children. In some weight bands (14-24.9 kg) the simplified dosing is based on preliminary findings, which are expected to be confirmed in early 2019. As the introduction of paediatric DTG will take time, programmes are encouraged to begin planning for the use of DTG in paediatric populations while the simplified dosing is being confirmed.

RAL granules were also added with the goal of providing a suitable formulation to deliver RAL to neonates. Due to concerns about the complexity of administration of the granule formulation, the 25 mg chewable tablets as dispersible tablets have been endorsed by the PAWG for infants and children older than 4 weeks of age and weighting at least 3 kg. This decision was largely based on in vitro data on solubility and bioequivalence between RAL tablets and granules as well as considering the limited availability of adequate alternative formulations for this age group. This dosing annex and the simplified dosing schedule will be regularly reviewed and updated as additional data and new formulations become available.

Antiretroviral drugs and formulations are available from several manufacturers, and available dosage strengths of tablets, capsules and liquid formulations may vary from the information provided here. Several optimal paediatric dosage forms are currently in development but have not yet received regulatory approval at the time of writing these updated guidelines. National programme managers should ensure that products planned for use have received stringent regulatory approval and of appropriate quality and stability. For guidance on the quality assurance of medicines, see the WHO medicines web site (http://www.who.int/medicines/areas/quality_safety/quality_assurance/about/en/index.html) and the Access to HIV/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 https://www.fda.gov/InternationalPrograms/ PEPFAR/ucm119231.htm. For the policy of the Global Fund to Fight AIDS, Tuberculosis and Malaria on procurement and quality assurance, see https://www.theglobalfund.org/en/sourcing-management/quality-assurance/medicines/.

General principles

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

- Use of an age-appropriate fixed dose combination is preferred for any regimen if such a formulation is available.
- Oral liquid or syrup formulations should be avoided where possible. Dispersible tablets (or granules for oral solution) are the preferred solid oral dosage forms, since each tablet can be made into liquid at the point of use.
- If suitable dispersible FDC's 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
- While dosing neonates generally necessitates use of oral liquid formulations for administrating precise dosing, switching to solid oral dosage form as soon as possible is recommended
- Where children have to use adult formulations, care must be taken to avoid under-dosing and overdosing. Use of scored tablets are preferred to ensure accurate dosing is provided, particularly if adult dosage forms are used. Splitting of unscored tablets should be avoided as uniform distribution of active drug product cannot be assured in tablet fragments.
- 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 bioavailability is seriously reduced when not swallowed whole.
- At each clinic visit, children should be weighed and doses should be adjusted based on observed growth and change in body weight.
- Country programs should consider the national regulatory status and local availability status of specific dosage forms when developing national paediatric treatment recommendations.
- Research is ongoing for several antiretroviral medications to establish dosing guidance in neonates, 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 1

Simplified dosing of child-friendly fixed-dose solid formulations for twice-daily dosing in infants and children 4 weeks of age and older

Drug	Strength of paediatric tablets	Number of tablets by weight band morning and evening										Strength of adult tablet	Number of tablets by weight band	
		3–5.9kg		6–9.9kg		10–13.9kg		14–19.9kg		20–24.9kg			25–34.9kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
AZT/3TC	Tablet (dispersible) 60mg/30mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300mg/150mg	1	1
AZT/3TC/NVP[b]	Tablet (dispersible) 60mg/30mg/50mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300mg/150mg/200mg	1	1
ABC/3TC	Tablet (dispersible) 60mg/30mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600mg/300mg	0.5	0.5
ABC/3TC	Tablet (dispersible) 120/60mg	0.5	0.5	0.5	1	1	1	1	1.5	1.5	1.5	600mg/300mg	0.5	0.5

[a] For infants younger than 4 weeks of age refer to table 4 for more accurate dosing which is reduced due to the decreased ability to excrete and metabolize medications. For infants who are at least 4 weeks of age but less than 3 kg, immaturity of renal and hepatic pathways of elimination are less of a concern but uncertainty still exists on the appropriate dosing of ARVs in preterm and low birth weight infants.

[b] Please note that this regimen and formulation is no longer recommended and should only be used in special circumstances where other age appropriate formulations are not available.

Table 2 Simplified dosing of child-friendly solid formulations for once-daily dosing in infants and children 4 weeks of age and older[a]

Drug	Strength of paediatric tablet	Number of tablets or capsules by weight band once daily					Strength of adult tablet	Number of tablets or capsules by weight band once daily
		3–5.9 kg	6–9.9 kg	10–13.9 kg	14–19.9 kg	20–24.9 kg		25–34.9 kg
EFV[b]	Tablet (scored) 200 mg	–	–	1	1.5	1.5	–	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	–	–	2	2	2	300 mg	1[d]
	Capsules 200 mg	–	–	1	1	1		
DRV[e]	Tablet 600 mg	–	–	–	1	1	600 mg	1
	Tablet 150 mg	–	–	–	4	4		
RTV[f]	Tablet 25 mg	–	–	–	4	4	100 mg	1
	Tablet 50 mg	–	–	–	2	2		
DTG[g]	Tablet 50 mg	–	–	–	–	TBC[g]	50 mg	1

[a] See table 4 for dosing recommendations for infants younger than 4 weeks old. Doses for this age group are reduced to account for the decreased ability to excrete and metabolize medications. For infants who are at least 4 weeks of age but less than 3 kg, immaturity of renal and hepatic pathways of elimination are less of a concern but uncertainty still exists on the appropriate dosing of ARVs in preterm and low birth weight infants.

[b] EFV is not recommended for children younger than 3 years and weighing less than 10 kg.

[c] ATV is only approved for use in children 3 months and older. ATV single strength capsules should be administered with RTV 100 mg for all weight bands. ATV powder formulation has limited availability in LMIC, but enables administration of ATV to infants and children as young as 3 months. Infants and children 5-15 kg should be administered 200 mg of ATV powder (4 packets, 50 mg/packet) with 80 mg of RTV oral solution (1 ml). https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021567s042,206352s007lbl.pdf

[d] A 300 mg dose for 25-29.9 kg is recommended on the basis of findings from the PRINCE-2 study[26].

[e] DRV in combination with RTV should be used in children older than 3 years, once daily when this is used without previous exposure to PI. While approved dosing for 30-35 kg is 675 mg, preliminary data from adult studies suggest that even lower DRV doses may be effective, therefore use of 600 mg dose was extended to the entire 25-35 kg weight band.

[f] RTV should only be use as a boosting agent in combination with ATV or DRV.

[g] At the time of this update, DTG film coated tables were approved for children above 6 years by the FDA (35mg for weight 30 to < 40 kg, 50 mg for weight ≥ 40 kg)[36] and by the EMA (20 mg 15 to < 20, 25 mg for 20 to < 30, and 35 for 30 to < 40, 50 mg for weight ≥ 40 kg)[37] based on data from the IMPAACT 1093 trial[38]. Simplified weight band dosing is being investigated in the Odyssey trial which supports the use of 50 mg dose for all children ≥ 25 kg, as proposed here. An anticipated dose of 50 mg in children 20-25kg is based on predicted exposure derived from PK results on DTG 2mg (FCT) in this weight band, more data to confirm this and further inform optimal dosing in the 14 to 25 kg weight bands is expected at the beginning of 2019 and will be included in an updated version of this annex. For adolescents living with HIV weighting more than 30 Kg a fixed dose formulation of TDF 300mg /3TC 300mg /DTG 50mg (TLD) can be used and is preferred.

Table 3

Simplified dosing of child-friendly solid and oral liquid formulations for twice-daily dosing in infants and children 4 weeks of age and older[a]

Drug	Strength of paediatric tablets or oral liquid	Number of tablets or MLS by weight-band morning (AM) and evening (PM)										Strength of adult tablet	Number of tablets by weight band	
		3–5.9 kg		6–9.9 kg		10–13.9 kg		14–19.9 kg		20–24.9 kg			25–34.9 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 100 mg/25 mg	–	–	–	–	2	1	2	2	2	2	–	3	3
	Pellets 40 mg/10 mg	2	2	3	3	4	4	5	5	6	6	–	–	–
DRV[d]	Tablet 75 mg	–	–	–	–	–	–	5	5	5	5	400 mg	1	1
RTV[e]	Tablet 25 mg	–	–	–	–	–	–	2	2	2	2	100 mg	1	1
	Tablet 50 mg	–	–	–	–	–	–	1	1	1	1			
RAL[f]	Chewable tablets 25 mg	1	1	2	2	3	3	4	4	6	6	400 mg	1	1
	Chewable tablets 100 mg	–	–	–	–	–	–	1	1	1.5	1.5	400 mg	1	1

Drug	Strength of paediatric tablets or oral liquid	Number of tablets or MLS by weight-band morning (AM) and evening(PM)										Strength of adult tablet	Number of tablets by weight band	
		3–5.9 kg		6–9.9 kg		10–13.9 kg		14–19.9 kg		20–24.9 kg			25–34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
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[d]	100 mg/ml	–	–	–	–	2.5 ml	2.5 ml	3.5 ml	3.5 ml	–	–	–	–	–
RTV	80 mg/ml	–	–	–	–	0.5 ml	0.5 ml	0.6 ml	0.6 ml	–	–	–	–	–
RAL[f]	10 mg/mL (Oral granules for suspension: 100 mg/sachet)	3 mL	3 mL	5 mL	5 mL	8 mL	8 mL	10 mL	10 mL	–	–	–	–	–

[a] See table 4 for dosing recommendations for infants younger than 4 weeks old. Doses for this age group are reduced to account for the decreased ability to excrete and metabolize medications. For infants who are at least 4 weeks of age but less than 3 kg, immaturity of renal and hepatic pathways of elimination are less of a concern but uncertainty still exists on the dosing of ARVs in 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[a]. More definitive evidence is expected from an ongoing trial. Please note that this regimen and formulation is no longer recommended and should only be used in special circumstances where other age appropriate formulations are not available.

[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. Adult 200/50 tablet could be used for patients 14-24.9kg (1 tab qam and 1 tab qpm) and for patients 25-34.9 kg (2 tab qam and 1 tab qpm). LPV/r pellets formulation should not be used in infants younger than 3 months. More details on the administration of LPV/r pellets can be found at http://apps.who.int/iris/bitstream/handle/10665/193543/FactsheetIATT_WHO_UNICEF_lopinavir_eng.pdf?sequence=1. This dosing schedule applies to equivalent solid dosage forms that may become available in the near future (ie granules).

[d] DRV, to be used in children older than 3 years, must be administered with 0.5 ml of RTV 80 mg/ml oral suspension if less than 15 kg and with RTV 25 or 50 mg solid formulation in children 15 to 30 kg.

[e] RTV should only be use as a boosting agent in combination with ATV or DRV.

[f] RAL granules are approved from birth. Feasibility and acceptability of such formulations has not been widely investigated and concerns have been raised regarding administration in resource limited settings. Due to the administration challenges presented by the granule formulation the use of the 25 mg chewable tablets as dispersible has been endorsed by the PAWG for infants and children older than 4 weeks and weighting at least 3 kg. This was largely based on in vitro data on solubility and bioequivalence between tablets and granules[a] as well as considering the limited availability of adequate alternatives for this age group. However, findings from a feasibility and acceptability assessment conducted in South Africa demonstrate that administration of RAL granules in rural settings is feasible as long as supported with adequate training and counselling.

Table 4

Drug dosing of liquid formulations in infants less than 4 weeks of age[a]

Drug	Strength of oral liquid		2-3 kg		3-4 kg		4-5 kg	
			AM	PM	AM	PM	AM	PM
AZT	10 mg/mL		1 mL	1 mL	1.5 mL	1.5 mL	2 mL	2 mL
NVP	10 mg/mL		1.5 mL	1.5 mL	2 mL	2 mL	3 mL	3 mL
3TC	10 mg/mL		0.5 mL	0.5 mL	0.8 mL	0.8 mL	1 mL	1 mL
LPV/r[b]	80/20 mg/mL		0.6 mL	0.6 mL	0.8 mL	0.8 mL	1 mL	1 mL
RAL	10 mg/mL	<1 week	0.4 mL (once daily)[c]		0.5 mL (once daily)[c]		0.7 mL (once daily)[c]	
	(Oral granules for suspension: 100 mg/sachet)[c]	>1 week	0.8 mL	0.8 mL	1 mL	1 mL	1.5 mL	1.5 mL

[a] PK data in preterm infants are available only for AZT; there is considerable uncertainty of appropriate dosing for NVP, RAL and 3TC in preterm and low birth weight infants. In addition, LPV/r solution should not be given to preterm infants until they have reached 42 weeks gestational age, because of the risk of adverse effects that may occur in this population. This guidance will be updated when more evidence is available from ongoing trials.

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

[c] RAL granules for oral suspension should use in neonates of at least 2 kg and be administered in once a day during the first week of life (http://www.merck.com/product/usa/pi_circulars/i/isentress/isentress_pi.pdf)

Table 5 Dosing for RTV super-boosting of LPV/r for children receiving rifampicin-containing TB treatment[a]

Drug	Strength of paediatric tablets or oral liquid	Number of tablets or mLs by weight-band morning (AM) and evening (PM)										Strength of adult tablet	Number of tablets by weight band	
		3–5.9 kg		6–9.9 kg		10–13.9 kg		14–19.9 kg		20–24.9 kg			25–34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
For children able to swallow tablets														
LPV/r[b]	Tablet 100/25 mg	–	–	–	–	2	1	2	2	2	2	–	3	3
RTV	Tablet 100 mg	–	–	–	–	1	1	1	2	1	2	100 mg	2	2
	Tablet 50 mg	–	–	–	–	2	2	3	3	3	3			
	Tablet 25 mg	–	–	–	–	4	4	6	6	6	6			
For children unable to swallow tablets														
LPV/r	Oral solution[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	-	-	-
	Pellets[d] 40 mg/10 mg	2	2	3	3	4	4	5	5	6	6	-	-	-
RTV[e]	Oral solution 80 mg/ml	0.8 ml	0.8 ml	1.2 ml	1.2 ml	1.5 ml	1.5 ml	2 ml	2 ml	2.3 ml	2.3 ml	-	-	-
RTV	Powder 100 mg/packet	-	-	1	1	1	1	1	2	1	2	-	-	-

[a] Suggested RTV dose for super-boosting to achieve the same dose as LPV in mg, in a ratio equal or approaching to 1:1. This dosing approach is supported by a study which explored this approach in young children receiving LPV/r12.

[b] The LPV/r heat-stable tablet formulation must be swallowed whole and should not be split, chewed, dissolved or crushed. Adult 200/50 tablet could be used for patients 14-24.9kg (1 tab am and 1 tab pm) and for patients 25-34.9kg (2 tab am and 1 tab pm).

[c] RTV liquid requires a cold chain during transport and storage.

[d] LPVr pellets formulation should not be used in infants younger than 3 months. More details on the administration of LPVr pellets can be found at http://www.emtct-iatt.org/wp-content/uploads/2015/09/IATT-LPVr-Factsheet-Final-30-September-2015.pdf. The dosing schedule provided applies to equivalent solid dosage forms that may become available such as LPVr granules.

[e] RTV oral solution dosing is based on the dosing tested in the trial that supports the use of superboosting.

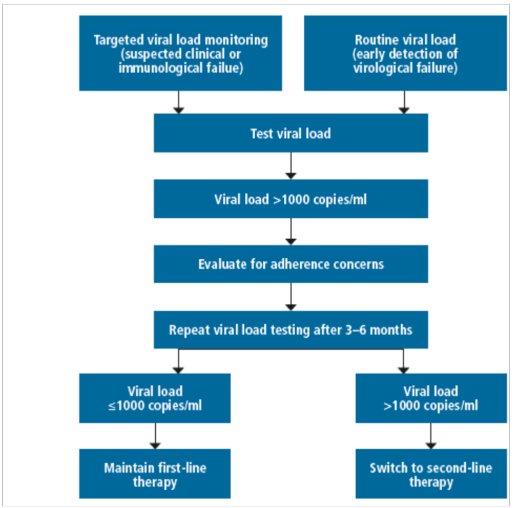
Table 6

Simplified dosing of isoniazid (INH) and co-trimoxazole (CTX) prophylaxis for infants and children who are at least 4 weeks of age

Drug	Strength of paediatric tablet or oral liquid	Number of tablets or ml by weight band once daily					Strength of adult tablet	Number of tablets by weight band
		3–5.9 kg	6–9.9 kg	10–13.9 kg	14–19.9 kg	20–24.9 kg		25–34.9 kg
INH	100 mg	0.5	1	1.5	2	2.5	300 mg	1
CTX	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
INH/CTX/B6[a]	Tablets (scored) 300 mg/960 mg/25 mg	–	–	–	0.5	0.5	960 mg/300 mg/25 mg	1

[a] A scored tablet (480 mg/150 mg/12.5 mg) is under development.

Annex 5
Viral load testing strategy



Annex 6

Key drug-to-drug interactions for antiretroviral drugs

	ABC	TDF	AZT	3TC	ddI	FTC	d4T	ATV	LPV	DRV	RTV	EFV	ETR	NVP	RPV	DTG	RAL	EVG + COB
Antibiotics (including drugs for TB)																		
Rifampicin								1	2	3			4	5	6			
Rifabutin															7			
Rifapentine													8		9			
Isoniazid																		
Pyrazinamide																		
Ethambutol																		
Ethionamide																		
Ofloxacin																		
Kanamycin																		
Cycloserine																		
Bedaquiline																		
Co-trimoxazole																		
Opioid substitution therapy																		
Methadone																		
Buprenorphine																		
Antiviral drugs (including drugs for hepatitis B, hepatitis C and herpesviruses)																		
Ribavirin			10		11													
Adefovir		12																
Peginterferon alpha-2a			13															
Telaprevir																		
Boceprevir																		
Entecavir																		
Ganciclovir																		
Aciclovir																		
Sofosbuvir																		
Ledipasvir + sofosbuvir																		
Daclatasvir																		
Simeprevir								14	15	16	17	18	19	20				21
Tenofovir			NA															
Tabihxudin																		


ABC
TDF
AZT
3TC
ddI
FTC
d4T
ATV
LPV
DRV
RTV
EFV
ETR
NVP
RPV
DTG
RAL
EVG + COB
Antiparasitic drugs
Metronidazole
Spectinomycin
Antimalarial drugs
Amodiaquine
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Artemisinin
Halofantrine
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27
Pyrimethamine
Sulfadoxine
Lumefantrine
Mefloquine
Antifungal drugs
Itraconazole
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Ketoconazole
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Voriconazole
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Fluconazole
Amphotericin B
Flucytosine
Antihistamines
Astemizole
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Terfenadine
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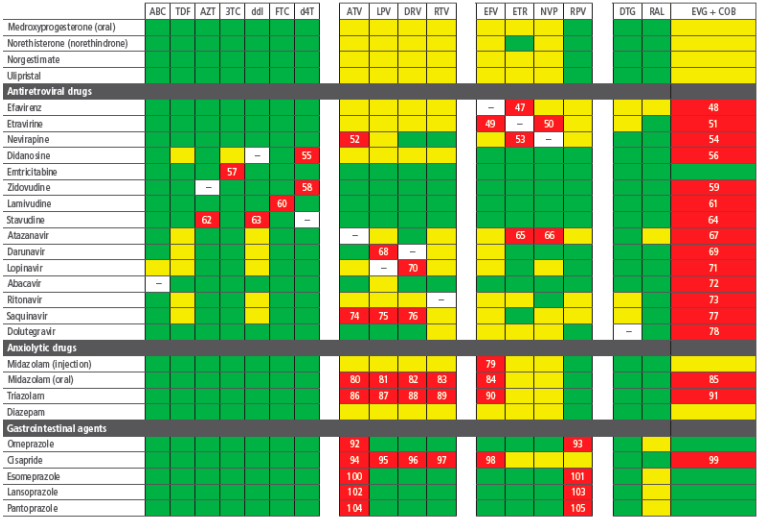
Fluticasone
Hormonal contraceptives
Desogestrel
Drospirenone
Dydrogesterone
Estradiol
Ethinylestradiol
Etonogestrel
Levonorgestrel
Medroxyprogesterone (intramuscular)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FTC
d4T
ATV
LPV
DRV
RTV
EFV
ETR
NVP
RPV
DTG
RAL
EVG + COB
Medroxyprogesterone (oral)
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
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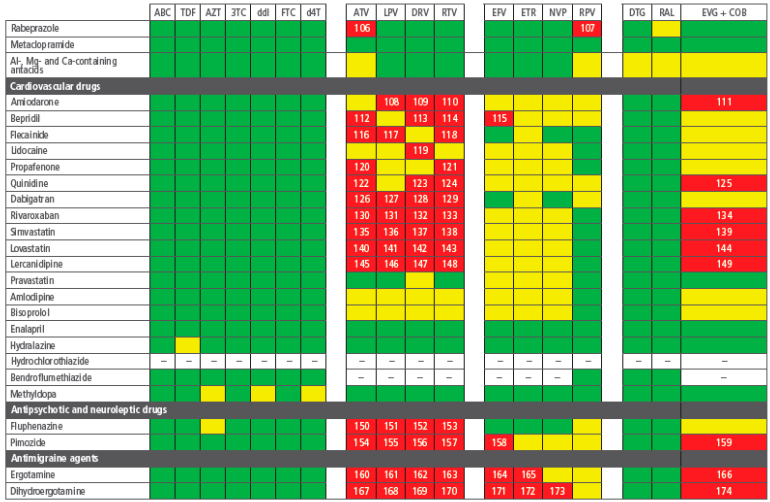
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ATV
LPV
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EFV
ETR
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RPV
DTG
RAL
EVG + COB
Rabeprazole
106
107
Metoclopramide
Al-, Mg- and Ca-containing antacids
Cardiovascular drugs
Amiodarone
108
109
110
111
Bepridil
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114
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Flecainide
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Lidocaine
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Propafenone
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Quinidine
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Dabigatran
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Simvastatin
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Lercanidipine
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Pravastatin
Amlodipine
Bisoprolol
Enalapril
Hydralazine
Hydrochlorothiazide
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Bendroflumethiazide
Methyldopa
Antipsychotic and neuroleptic drugs
Fluphenazine
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Pimozide
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Antimigraine agents
Ergotamine
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Dihydroergotamine
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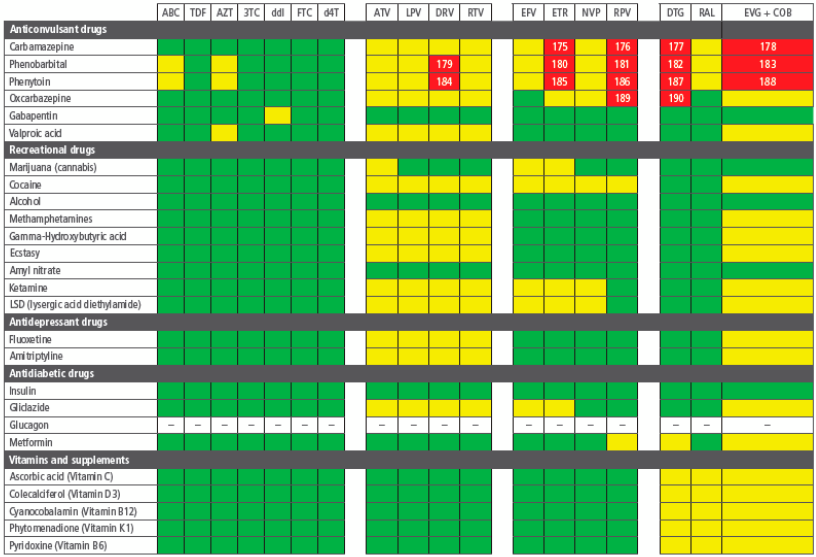
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3TC
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ATV
LPV
DRV
RTV
EFV
ETR
NVP
RPV
DTG
RAL
EVG + COB
Anticonvulsant drugs
Carbamazepine
175
176
177
178
Phenobarbital
179
180
181
182
183
Phenytoin
184
185
186
187
188
Oxcarbazepine
189
190
Gabapentin
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 B2)
Thiamine (Vitamin B1)
Vitamin E
Magnesium
Iron
Zinc
Calcium
Other drugs
Hydroxyurea
191
192
Sildenafil – pulmonary arterial hypertension
193
194
195
196
Sildenafil – erectile dysfunction
Allopurinol
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Alfuzosin
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Dexamethasone
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Piroxicam
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St John's wort
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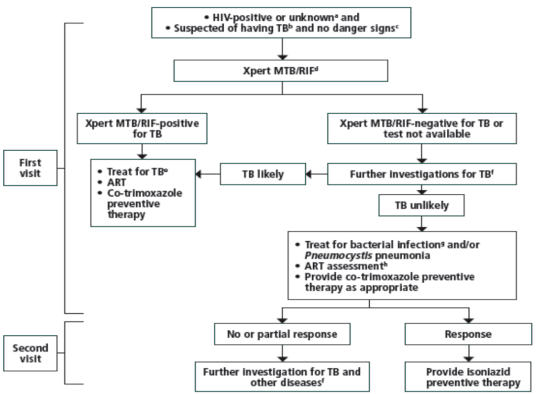
Orlistat
Figure Legend
No clinically significant interaction or interaction unlikely based on knowledge of drug metabolism.
Potential interaction that may require close monitoring, alteration of drug dosage or timing of administration.
Interaction likely: do not use or use with caution (# indicates cross-reference to interaction explanation).
– No clear data, actual or theoretical, indicate whether an interaction will occur.

Annex 7

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.

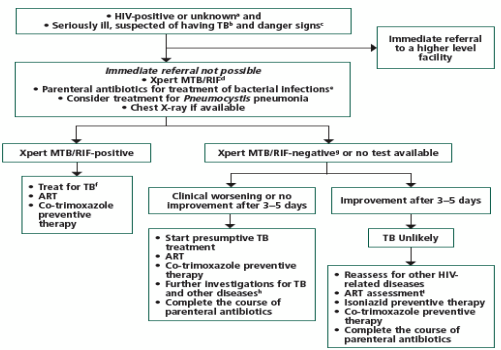
[g] Antibiotics with broad-spectrum antibacterial activity (except fluoroquinolones) should be used.

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

Annex 8

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

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.

Annex 9

Drug Toxicity and drug-to-drug interactions of ARV drugs

Table 1 Types of toxicity 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* gene	Do not use ABC in presence of the *HLA-B*5701* gene. Substitute with AZT or TDF.
ATV/r	Electrocardiographic abnormalities (PR and QRS interval prolongation)	People with pre-existing conduction system disease Concomitant use of other drugs that may prolong the PR or QRS intervals Congenital long QT syndrome	Use with caution in people with pre-existing conduction disease or who are taking concomitant drugs that may prolong the PR or QRS intervals.
	Indirect hyperbilirubinaemia (clinical jaundice)	Presence of UDP-glucuronosyltransferase 1-1 enzyme (*UGT1A1*28* gene)	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	Anaemia, neutropaenia	Baseline anaemia or neutropaenia CD4 cell count of ≤200 cells/mm^3	Substitute with TDF or ABC. Consider using low-dose zidovudine.
	Lactic acidosis or severe hepatomegaly with steatosis lipoatrophy, lipodystrophy myopathy	BMI >25 (or body weight >75 kg) Prolonged exposure to NRTIs	Substitute with TDF or ABC.
DTG[a]	Hepatotoxicity Hypersensitivity reactions	Coinfection with hepatitis B or C Liver disease	Substitute with another therapeutic class: EFV or boosted PIs.
	Insomnia	Older than 60 years Female	Consider morning dose or substitute with EFV, boosted PI or RAL.
DRV/r	Hepatotoxicity	Underlying hepatic disease Coinfection with hepatitis B or C Concomitant use of hepatotoxic drugs	Substitute with ATV/r or LPV/r. When it is used in third-line ART, limited options are available. For hypersensitivity reactions, substitute with another therapeutic class.
	Severe skin and hypersensitivity reactions	Sulfonamide allergy	

ARV drug	Major types of toxicity	Risk factors	Suggested management
EFV	Persistent central nervous system toxicity (such as dizziness, insomnia and abnormal dreams) or mental symptoms (anxiety, depression and mental confusion)	Depression or other mental disorder (previous or at baseline) Daytime dosing	For central nervous system symptoms, dosing at bedtime. Consider using EFV at a lower dose (400 mg/day or an integrase inhibitor (DTG) if EFV 400 mg is not effective in reducing symptoms.
	Convulsions	History of seizure	
	Hepatotoxicity	Underlying hepatic disease Coinfection with hepatitis B or C Concomitant use of hepatotoxic drugs	For severe hepatotoxicity or hypersensitivity reactions, substitute with another therapeutic class (integrase inhibitors or boosted PIs).
	Severe skin and hypersensitivity reactions	Risk factors unknown	
	Gynaecomastia	Risk factors unknown	Substitute with another therapeutic class (integrase inhibitors or boosted PIs).
ETV	Severe skin and hypersensitivity reactions	Risk factors 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 Concomitant use of other drugs that may prolong the PR or QRS intervals Congenital long QT syndrome Hypokalaemia	Use with caution for people with pre-existing conduction disease or taking concomitant drugs that may prolong the PR or QRS intervals.
	Hepatotoxicity	Underlying hepatic disease Coinfection with hepatitis B or C Concomitant use of hepatotoxic drugs	If LPV/r is used in first-line ART for children, substitute with RAL or DTG if younger or older than 6 years repectively. If integrase inhibitors are not available EFV, NVP or boosted ATV can be used. If LPV/r is used in second-line ART for adults and the person has treatment failure with NNRTIs in first-line ART, consider integrase inhibitors.
	Pancreatitis	Advanced HIV disease, alcohol	Substitute with another therapeutic class (integrase inhibitors).
	Dyslipidaemia	Cardiovascular risk factors such as obesity and diabetes	Substitute with another therapeutic class (integrase inhibitors).
	Diarrhoea	Risk factors unknown	Substitute with atazanavir/r, darunavir/r or integrase inhibitors.

ARV drug	Major types of toxicity	Risk factors	Suggested management
NVP	Hepatotoxicity Severe skin rash and hypersensitivity reaction, including Stevens-Johnson syndrome	Underlying hepatic disease Coinfection with hepatitis B or C Concomitant use of hepatotoxic drugs High baseline CD4 cell count (CD4 count >250 cells/mm^3 for women or >400 cells/mm^3 for men)	If hepatotoxicity is mild, consider substituting with EFV, including for children three years and older. For severe hepatotoxicity and hypersensitivity, and for children younger than three years, substitute with another therapeutic class (integrase inhibitors or boosted PIs).
RAL	Rhabdomyolysis, myopathy and myalgia	Concomitant use of other drugs that increase the risk of myopathy and rhabdomyolysis, including statins	Stop ART. When symptoms are resolved, substitute with another therapeutic class (etravirine, boosted PIs).
	Hepatitis and hepatic failure Severe skin rash and hypersensitivity reaction	Risk factor(s) unknown	
TDF	Chronic kidney disease Acute kidney injury and Fanconi syndrome	Underlying renal disease Older than 50 years old BMI <18.5 or low body weight (<50 kg), notably in females Untreated diabetes Untreated hypertension Concomitant use of nephrotoxic drugs or a boosted PI	Substitute with AZT or ABC Do not initiate TDF at an estimated glomerular filtration rate of <50 mL/min, uncontrolled hypertension, untreated diabetes or kidney failure
	Decreases in bone mineral density	History of osteomalacia (adults) and rickets (children) and pathological fracture Risk factors for osteoporosis or bone mineral density loss Vitamin D deficiency	
	Lactic acidosis or severe hepatomegaly with steatosis	Prolonged exposure to nucleoside analogues Obesity Liver disease	

• Potential signal of neural tube defect in neonates exposed to DTG during the first trimester of pregnancy.
See Box 1 for clinical considerations for women and adolescent girls of childbearing potential.

Table 2 Key ARV drug interactions with DTG, EFV and boosted PIs and suggested management

ARV drug	Key interactions	Suggested management
Boosted PIs (ATV/r, DRV/r and LPV/r)	Rifampicin	Substitute rifampicin with rifabutin Adjust the dose of LPV/r or substitute with three NRTIs (for children)
	Halofantrine	Use an alternative antimalarial agent
	Lovastatin and simvastatin	Use an alternative statin (such as pravastatin)
	Hormonal contraceptives	Use alternative or additional contraceptive methods
	Metformin	Adjust methadone and buprenorphine doses as appropriate
	Astemizole and terfenadine	Use an alternative antihistamine agent
	TDF	Monitor renal function
	Simeprevir	Use an alternative direct-acting antiviral agent
	Ombitasvir + paritaprevir/ritonavir + dasabuvir	Use an alternative direct-acting antiviral agent
DTG	Dofetilide	Use an alternative antiarrhythmic agent
	Rifampicin	Adjust the dose of DTG or substitute rifampicin with rifabutin
	Carbamazepine, phenobarbital and phenytoin	Use an alternative anticonvulsant agent (esuch as valproic acid or gabapentin)
	Polyvalent cation products containing Mg, Al, Fe, Ca and Zn	Use DTG at least two hours before or at least six hours after supplements containing polyvalent cations, including but not limited to the following products: multivitamin supplements containing Fe, Ca, Mg or Zn; mineral supplements, cation-containing laxatives and antacids containing Al, Ca or Mg. Monitor for efficacy in suppressing viral load.
EFV	Amodiaquine	Use an alternative antimalarial agent
	Cisapride	Use an alternative gastrointestinal agent
	Methadone	Adjust the methadone dose as appropriate
	Hormonal contraceptives	Use alternative or additional contraceptive methods
	Astemizole and terfenadine	Use an alternative antihistamine agent
	Ergotamine and dihydroergotamine	Use an alternative antimigraine agent
	Simeprevir	Use an alternative direct-acting antiviral agent
	Midazolam and triazolam	Use an alternative anxiolytic agent

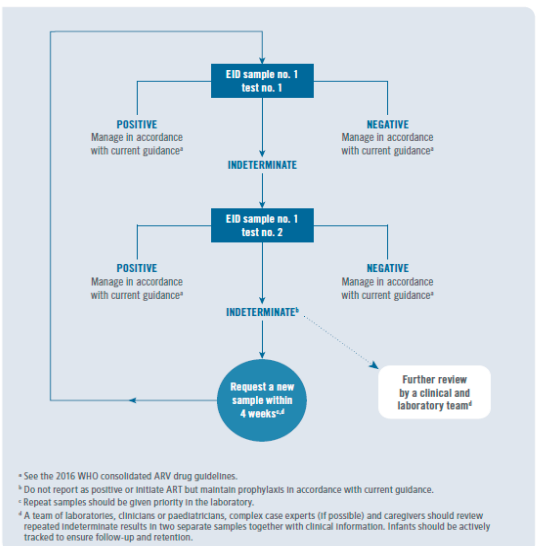
* This table was developed using the University of Liverpool's drug–drug interaction charts: www.hiv-druginteractions.org and www.hep-druginteractions.org. Web Annex 1 provides a more comprehensive table of ARV drug interactions.

(Reference – Annex 2, WHO UPDATED RECOMMENDATIONS FOR FIRST LINE AND SECOND LINE ARV REGIMENS AND ARV PROPHYLAXIS AND RECOMEDATIONS FOR EARLY INFANT DIAGNOSIS 2018)

Annex 10
Standard operating procedure for early infant diagnosis testing

All indeterminate tests should be repeat tested on the same specimen, if and when available. If the same specimen cannot be repeat tested, then a new specimen should be requested and tested as quickly as possible.

For specimens with two indeterminate test results, a new specimen should be requested. For infants repeatedly testing indeterminate, it is suggested that a team of experts review clinical and test information to determine the best follow-up care.

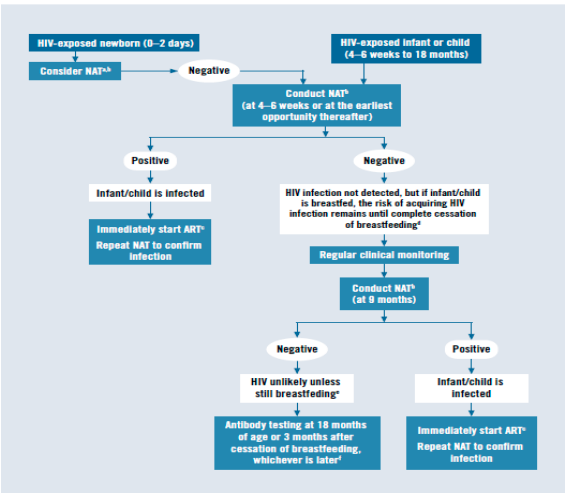


[a] See the 2016 WHO consolidated ARV drug guidelines.
[b] Do not report as positive or initiate ART but maintain prophylaxis in accordance with current guidance.
[c] Repeat samples should be given priority in the laboratory.
[d] A team of laboratories, clinicians or paediatricians, complex case experts (if possible) and caregivers should review repeated indeterminate results in two separate samples together with clinical information. Infants should be actively tracked to ensure follow-up and retention.

Annex 11
Revised simplified early infant diagnosis algorithm

The key principles for establishing whether HIV-exposed infants and children younger than 18 months are infected with HIV in low- and middle-income countries are based on existing WHO recommendations.

- Assess HIV exposure status by antibody testing the mother.
- Perform NAT test for any HIV exposed child that presents outside of national infant testing algorithm with clinical symptoms irrespective of previous NAT results.
- At 9 months, perform NAT for HIV-exposed infants, symptomatic and asymptomatic, regardless of previous NAT results after delivery.
- Ensure that confirmatory testing is undertaken following any positive result.
- Ensure that indeterminate test results are repeat tested immediately and given priority for rapid resolution.
- Ensure regular follow-up for all HIV-exposed infants until final diagnosis, including providing co-trimoxazole prophylaxis and clinical and nutritional assessment.



Annex 12

Overview of key elements of general care over the continuum of HIV care for infants and children living with HIV

SERVICES	At HIV diagnosis	At enrolment in care	At initiation of ART	Stable while receiving ART	At treatment failure and switching ART regimen
General care					
WHO clinical staging	+	+	+		
Past and current HIV-related conditions	+	+	+		
Preparing people for ART	+	+	+		
Preparing, assessing and support adherence	+	+	+	+	+
Current medications		+	+	+	+
Support for disclosure	+	+	+	+	+
Risk reduction counselling and combination HIV prevention approaches	+	+	+	+	+
Assessing, preventing and managing NCDs	+	+	+	+	+
Screening for and managing mental health problems and substance use	+	+	+	+	+
Psychological counselling and support					
Managing pain and symptoms	+	+	+	+	+
Nutritional assessment and counselling	+	+	+	+	+
Nutrition, growth and development assessment in children and adolescents	+	+	+	+	+
Infant and child feeding	+	+	+	+	+
Prevention and treating co-infections					
Co-trimoxazole preventative therapy	+	+	+	+	+
Intensified TB case finding	+	+	+	+	+
TB preventative therapy		+	+		
Screening for hepatitis B and C		+	+		+
Screening for STIs	+	+	+	+	+
Assessing for vaccine preventable disease	+	+	+	+	+

9

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