NATIONAL CONSOLIDATED GUIDELINES

FOR THE MANAGEMENT OF HIV IN ADULTS, ADOLESCENTS, CHILDREN AND INFANTS AND PREVENTION OF MOTHER-TO-CHILD TRANSMISSION

South African National Department of Health
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CONTENT

List of Tables

FOREWORD

South Africa is committed to attaining the UNAIDS 90-90-90 targets to control the HIV epidemic through provision of quality health care services using highly effective antiretroviral treatment (ART). The principal goal of ART is to attain and maintain viral suppression, which will prevent new HIV infections, decrease morbidity and mortality as well as improve quality of life for clients.

All HIV positive pregnant and breastfeeding women, infants, children, adolescents and adults have been eligible for ART regardless of CD4 count or WHO staging since 01 September 2016. The “Test and Treat All” approach has made it possible for people living with HIV (PLHIV) to access ART timeously.

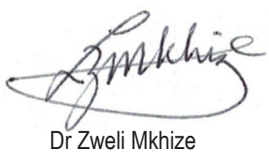
The National Health Council (NHC) has adopted the new World Health Organization (WHO) recommended first- and second-line regimens that include Dolutegravir (DTG) as the preferred antiretroviral drug. The 2019 Consolidated Guidelines have been revised to include a new formulation of the fixed dose combination (FDC) of tenofovir (TDF) 300 mg + lamivudine (3TC) 300 mg + dolutegravir (DTG) 50 mg (TLD) for all eligible adults, adolescents and children 10 years and older and weighing 35 kg or more.

These guidelines have further simplified ART provision and harmonized PMTCT and the management of children, adolescents and adults with HIV/AIDS, TB and other common opportunistic infections. The guidelines provide guidance for clinicians, managers and trainers on the use of available regimens within the context of the continuum of HIV comprehensive care for prevention, treatment and support for all age groups in private and public sector to realize our vision of A LONG AND HEALTHY LIFE FOR ALL.

Implementation of these guidelines will increase access to ART services, advance South Africa’s ability to control the epidemic and help to achieve the 2030 SDG goals.

I would like to thank all the internal and external stakeholders who actively contributed to the development of these guidelines.

It is our sincere wish that all clinicians at PHC clinics, community health centres and hospitals across the board will use these guidelines to offer quality, comprehensive services to the public.



Dr Zweli Mkhize

Minister of Health

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We are grateful to the World Health Organization, the University of Pretoria, and the Technical Working Group for providing expertise, support and guidance towards completion of these guidelines.

Dr T Pillay

Acting Director General: Health

ABBREVIATIONS

3TC	Lamivudine
ABC	Abacavir
ALT	Alanine transaminase
ANC	Antenatal Care
APC	Adult Primary Care
ART	Antiretroviral therapy
ARV	Antiretroviral
ATV/r	Atazanavir/ritonavir
AZT	Zidovudine
BANC plus	Basic Antenatal Care Plus
bd	Twice daily
BMI	Body mass index
CBP	Childbearing potential
CCMDD	Central Chronic Medicines Dispensing and Distribution
CHW	Community Health Worker
CICT	Client initiated counseling and testing
CM	Cryptococcal meningitis
CNS	Central nervous system
CPT	Cotrimoxazole preventive therapy
CrAg	Cryptococcal Antigen
CVS	Cardiovascular
DHIS	District Health Information System
DILI	Drug-induced liver injury
DR	Drug-resistant
DS	Drug-sensitive
DSD	Differentiated service delivery
DST	Drug sensitivity testing
DTG	Dolutegravir
eGFR	Estimated glomerular filtration rate
EFV	Efavirenz
EGK	Electronic gate keeping
EML	Essential Medicines List
EMTCT	Elimination of Mother to Child Transmission of HIV
EPI	Expanded Programme on Immunization
FGR	Foetal Growth Restriction
FDC	Fixed-dose combination
FTC	Emtricitabine
GXP	Gene Expert TB Test
Hb	Haemoglobin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCW	Health Care Worker
HEI	HIV-exposed Infant
HEU	HIV-exposed but uninfected
HIV	Human Immunodeficiency Virus
HIVSS	HIV self-screening
HTAs	High transmission areas
HTS	HIV Testing Services
IEC	Information, education and communication
IM	Intramuscular
IMCI	Integrated management of childhood illnesses
INH	Isoniazid
InSTI	Integrase strand transfer inhibitor
IRIS	Immune reconstitution inflammatory syndrome
IUCD	Intrauterine contraceptive device
IV	Intravenous
KP	Known positive
LAM	Lipoarabinomannan
LGBTI	Lesbian, gay, bisexual, transgender, intersex
LP	Lumbar Puncture
LPA	Line Probe Assay
LPV/r	Lopinavir/ritonavir
LTBI	Latent TB Infection

MCR	Maternity Case Record
MDO	Missed Diagnostic Opportunity
MIP	Mother-infant Pair
MNCH	Maternal, neonatal and child health
MNCWH&N	Maternal Neonatal Child Women's Health and Nutrition
MSM	Men who have sex with men
MTCT	Mother-to-child transmission
MUAC	Mid-upper arm circumference
NA	Not applicable
NCDs	Non-communicable diseases
NHLS	National Health Laboratory System
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NTDs	Neural tube defects
NSA	Non-suppression Algorithm
NVP	Nevirapine
od	Once daily
OI	Opportunistic infection
PCP	Pneumocystis jirovecii Pneumonia
PCR	Polymerase chain reaction test for HIV
PEP	Post Exposure Prophylaxis
PHC	Primary Health Care
PHC EML	Primary Health Care Essential Medicines List
PLHIV	People living with HIV
PI	Protease inhibitor
PICT	Provider Initiated Counselling and Testing
PMTCT	Prevention of Mother to Child Transmission of HIV
PNC	Postnatal Club
PO	Per os (per mouth)
PrEP	Pre-Exposure Prophylaxis
RfA	Results for Action NHLS Reports
RPR	Rapid Plasma Reagin
RTHB	Road to Health Booklet
Rx	Treatment
SA	South Africa
sCR	Serum creatinine
sd	Single dose
SOP	Standard operating procedure
SRH	Sexual and Reproductive Health
STIs	Sexually transmitted infections
TB	Tuberculosis
TDF	Tenofovir disoproxil fumarate
TEE	Tenofovir + emtricitabine + efavirenz
TLD	Tenofovir + lamivudine + dolutegravir
TLE	Tenofovir + lamivudine + efavirenz
TPT	TB preventive therapy
TST	Tuberculin Skin Test
UTI	Urinary Tract Infection
VMMC	Voluntary Medical Male Circumcision
VL	Viral load
VLS	Viral Load Suppression
WASH	Water, Sanitation and Hygiene
WLHIV	Woman Living with HIV
WHO	World Health Organisation
WBOT	Ward-based outreach team
WOCP	Women of childbearing potential

INTRODUCTION

The national HIV programme has made significant strides in the last 20 years since the introduction of antiretroviral treatment (ART) in 2004. These ART Guidelines replace the 2015 National Consolidated Guidelines for the Prevention of Mother to Child Transmission of HIV and the Management of HIV in Children, Adolescents, and Adults.

Background and Rationale

Eligibility criteria for ART according to the 2015 National Antiretroviral Treatment (ART) Guidelines were a CD4 count of less than 500 cells/μL or a WHO stage 3 or 4 defining illness. Special groups including all HIV-positive infants, pregnant women and people with TB and HIV co-infection were also eligible for ART, regardless of CD4 count or percentage. A triple-drug fixed-dose combination (FDC) pill consisting of Tenofovir (TDF), Emtricitabine (FTC)/ Lamivudine (3TC) and Efavirenz (EFV) has been in use as the first-line regimen since 2014 and aimed to reduce morbidity and mortality due to HIV and improve life expectancy. In December 2015, the country introduced birth HIV PCR for all HIV-exposed babies in all facilities.

Evidence has shown that the early use of ART keeps PLHIV alive and healthier and reduces the risk of HIV transmission. For this reason, and in line with the WHO 2016 guidelines on HIV treatment and care, South Africa (SA) introduced “test-and-treat-all” in September 2016, making all populations and age groups eligible for ART regardless of CD4 count. HIV pre-exposure prophylaxis (PrEP) was introduced for all sex workers in June 2016 and was offered in selected sex worker programme sites nationally, gradually expanding to cover more sex worker sites over time. In 2017, PrEP was extended to men who have sex with men (MSM). SA is currently considering PrEP for pregnant and breastfeeding women, adolescent girls and young women (AGYW), and discordant couples who are at substantial risk of HIV acquisition.

In June 2016, the country launched the “She Conquers” campaign focusing on adolescent girls and young women (AGYW) aged 15 - 24 years and the older men who are infecting and impregnating them. The campaign is aimed at reducing new HIV infections among girls and young women, decreasing teenage pregnancies, decreasing sexual and gender-based violence (GBV), keeping girls in school until matric, and increasing economic opportunities for young women to decrease their vulnerability and dependency on older men.

It is estimated that there are 7.9 million people living with HIV in South Africa in 2017, which is 1.6 million higher than the 2012 estimate. The HIV prevalence of all ages was 14.0% (95% CI 13.1-15.0), which is significantly higher than the 12% estimated in 2012. About 4.4 million PLHIV are accessing ART in the public sector, making this the largest ART programme worldwide. Together with the estimated 250,000 PLHIV on ART in the private sector, it is estimated that 4.65 million PLHIV are on ART in South Africa. Around 91% of HIV-positive pregnant women have initiated ART for PMTCT. As a result, MTCT rates at six weeks of age decreased to less than 1.5% by 2015.

SA is committed to achieving the 2020 aspirational targets of having 90% of PLHIV know their HIV status, 90% of those diagnosed with HIV initiated on ART, and 90% of those on treatment virally suppressed. To accelerate progress towards these targets, SA is introducing the new integrase strand transfer inhibitor (InSTI) dolutegravir (DTG). Considered a significant game-changer, DTG has superior efficacy, a high genetic barrier to resistance, and is well tolerated. Tenofovir disoproxil fumarate-lamivudine-dolutegravir (TLD) is, therefore, the preferred first-line ART regimen for those clients initiating ART, experiencing side-effects to EFV, or for those who prefer to use DTG after being given all the necessary information. Transitioning to DTG-based regimens will move SA towards improved retention in care, improved viral suppression, reduced risk of treatment resistance, and improved health outcomes. Furthermore, this document offers guidance on cost-effective differentiated service delivery (DSD) approaches, defined as a client-centred approach that simplifies and adapts HIV services across the cascade to reflect the preferences and expectations of various groups of people living with HIV (PLHIV) while reducing unnecessary burdens on the health system.1 These updated guidelines will provide the necessary direction to improve the management of HIV across different populations and age groups

towards ending the AIDS epidemic as a public health threat by 2030. Figure 1 below provides a summary of the key milestones of the ART Program since its inception in 2004.

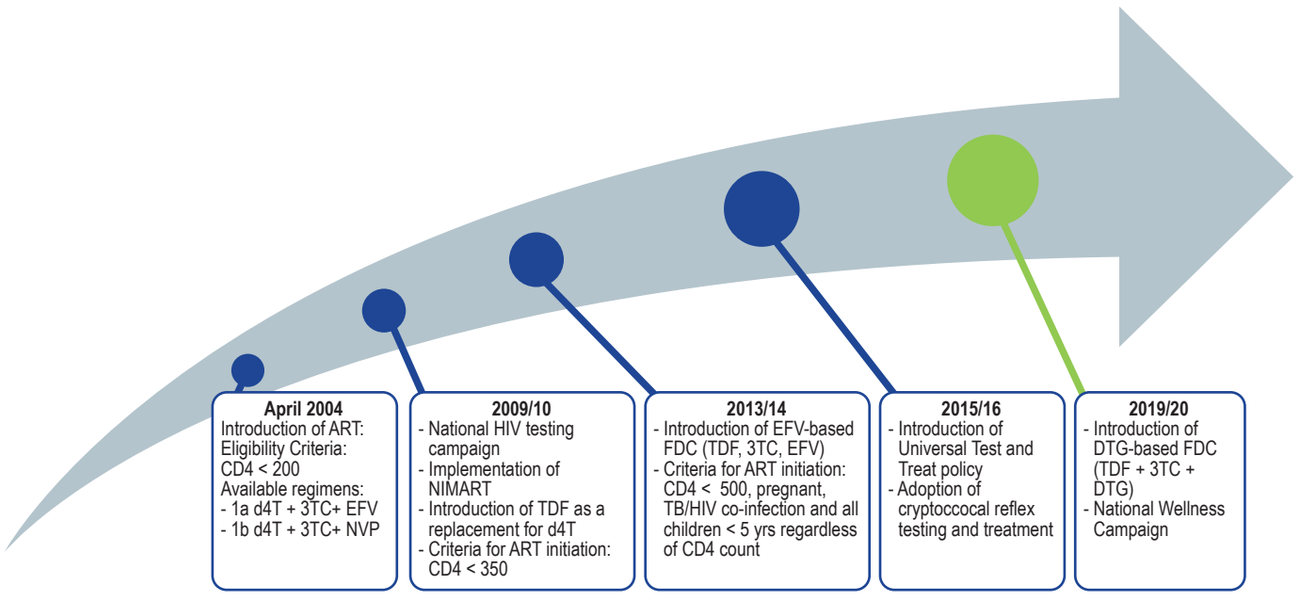


Figure 1: Key Milestones of the National HIV Programme

Target Audience

The target audience of these guidelines are all categories of healthcare providers, programme managers at national, provincial, district and facility level, and community-based organisations working with PLHIV in South Africa. Of particular note are frontline nurses, doctors, and ancillary healthcare workers that provide the continuum of HIV care, treatment, and support services to people living with HIV (PLHIV).

Scope and Content

These guidelines address clinical and programmatic aspects of HIV treatment and prevention amongst adults, adolescents, children, infants, pregnant and breastfeeding women, and key populations along the continuum of care, including:

1. **Part 1:** The minimum package of HIV prevention, care and treatment services to be offered by a facility
2. **Part 2:** HIV prevention, HIV testing services (HTS) and linkage to care
3. **Part 3:** ART initiation, management of the client on ART, and the prevention and management of co-infections and co-morbidities
4. **Part 4:** PMTCT

Certain aspects of care are covered comprehensively in other guidelines such as the National HIV Testing Services (HTS) Policy (2016), the National Adherence Guideline (2016), and the Pre- and post-exposure Prophylaxis Guidelines (PrEP and PEP). While this guideline provides a summary of the most important clinical aspects, it is recommended that healthcare providers refer to these documents for more detail on these aspects of care. Furthermore, these guidelines do not provide detail for complementary programmes such as sexually transmitted infections (STIs), cervical cancer screening, male medical circumcision, contraception, fertility planning and non-communicable diseases (NCDs), as these are covered comprehensively in other guiding documents.

SECTION 1

THE MINIMUM PACKAGE OF HIV PREVENTION, CARE AND TREATMENT SERVICES

The Ideal Facility

What package of services do all facilities need to provide?

SECTION 1: THE MINIMUM PACKAGE OF HIV PREVENTION, CARE AND TREATMENT SERVICES

All South African facilities are expected to provide a minimum package of services for prevention, care, and treatment of HIV for the population they serve. The minimum components of care are outlined in Table 1 below.

TABLE 1 THE MINIMUM PACKAGE OF SERVICE TO BE PROVIDED AT ALL FACILITIES

PREVENTION		REFERENCE
Health Education of HIV Prevention	All facilities should provide education on HIV prevention and risk-reduction both during individual client consultations and as part of daily health talks in the facility.	HTS, 2016
Provision of male and female condoms	Condoms should be routinely promoted and be made available in facility waiting areas, toilets, and in every consultation room. Condoms should be routinely offered during every HTS encounter, as part of dual method family planning, and for clients presenting with STIs. Condoms should be promoted and made available in the community using the WBOT CHWs, through outreach activities and mobile services, and other non-governmental organizations. Condoms should be promoted and made available at hotspots and high transmission areas (HTAs), e.g., truck stops, shebeens, and taverns.	HTS, 2016
Treatment of **STIs**	All facilities should provide screening and syndromic management of STIs and contact tracing according to the National STI guidelines	Sexually Trans-mitted Infections Management Guidelines, 2015.
Voluntary Medical Male Circumcision (VMMC)	All facilities should offer VMMC or refer clients for VMMC. VMMC should be included in health talks and other IEC materials.	South African National Guideline for Medical Male Circumcision (2016)
Post Exposure Prophylaxis (PEP)	All facilities should provide PEP within 72 hours to healthcare workers who are accidentally exposed to HIV through a needle stick injury (occupational exposure), anyone assessed as having a significant risk of sexual exposure (sexual assault, or unprotected sex [in cases of a burst condom] with a known HIV-positive client or high-risk group), or anyone exposed through unintended accidents that lead to contact with blood.	Post Exposure Prophylaxis Guideline, 2019
Pre-exposure Prophylaxis (PrEP)	All facilities should have health care workers trained in PrEP and be able to provide PrEP to those at substantial risk of HIV infection, as outlined in national guidelines	PrEP Guidelines (2019)

HIV TESTING SERVICES (HTS, 2016)		REFERENCE
Facilities should provide **client-initiated counseling and testing (CICT) and provider-initiated counseling and testing (PICT)** for all clients attending the facility, including adults, couples, adolescents, children, pregnant women, and members of the LGBTI community.	HTS services should be provided at, or accessible from, ALL service points, including ANC services, TB services, STI services, mobile services, outpatient clinics, medical, surgical, and paediatric wards, emergency units, maternal, newborn and child health (MNCH) services, mental health services and male circumcision services.	HTS, 2016
Index case testing should be provided to partners of PLHIV and their biological children	Any HIV-positive client is a potential index client, whether newly tested or known to be positive on ART. With the consent of the index client, index testing of their contact list may take place at the facility, in the home (or community) of the index client, or by offering HIV self-screening (HIVSS) kits to the index clients.	HTS, 2016
PICT and distribution of HIVSS kits should be incorporated into **outreach activities and mobile testing services**	General promotion and awareness campaigns for HTS must include children and the hard-to-reach populations. Key Populations (KPs), adolescents and men are three hard-to-reach populations in South Africa, and campaigns should be targeted to reach these populations with carefully tailored messages. Existing technological options such as MomConnect and Be-Wise must be used to encourage individuals to test for HIV.	HTS, 2016
PICT and distribution of HIVSS kits should be provided by **ward-based outreach teams (WBOT)**	WBOT CHWs who have been comprehensively trained should offer the basic HTS package as part of routine household registration or follow-up visits.	HTS, 2016
Community Engagement	All facilities should engage with their governance struc-tures (e.g., hospital boards, clinic committees, ward councilors) and other relevant community-based groups to advocate for the importance of HIV testing and to mobilize clients to attend community and facility-based HTS.	HTS, 2016
Data Analysis	Facilities should analyse their testing data to identify which groups are not accessing HTS, and outreach activities should be targeted accordingly.	

LINKAGE TO CARE (NATIONAL ADHERENCE GUIDELINES, 2016)		REFERENCE
Clients who test negative should be actively **linked to prevention services** (see above)	All HTS service points should provide post-test counseling that is informative as well as reassuring to facilitate linkage to care. All clients should be actively linked to care by providing appointment dates and referral slips. Where feasible: • clients who test HIV positive during community-based testing should be linked to a CHW or community representative • clients who test HIV positive during facility-based testing should be accompanied to the ART initiation services and introduced to the service provider Clear lines of communication and referral pathways should be established between testing sites and relevant service points for follow-up care. Logbooks and appointment systems should be used, and missed appointments should be traced.	National Adherence Guideline
Clients who test positive should be actively **linked to treatment services**		

PROVISION OF ART SERVICES		REFERENCE
ART Initiation	All facilities should provide ART initiation services for adults, adolescents, children, pregnant, and breastfeeding women. Included should be the following: • Baseline clinical assessment and WHO clinical staging • CD4 count/percentage • TB screening, diagnosis, and treatment • TB Preventive Therapy (TPT) • Cotrimoxazole Preventive Therapy (CPT) • Cryptococcal antigen (CrAg) screening and fluconazole prophylaxis • Treatment of Opportunistic Infections (OIs) • Sexual and Reproductive Health Services (SRH) should be integrated into ART services including screening for pregnancy, family planning, STI screening, and screening for cervical cancer • Mental Health Screening • Screening for non-communicable disease • Pregnant women should be initiated in the Antenatal Care Clinic (ANC) • Breastfeeding women should preferably be initiated within routine maternal and child health services in a “one-stop” approach to improve adherence and retention in care. • At Primary Health Care (PHC) level, children should preferably be initiated within Child Health / IMCI services, using the IMCI six steps	See page 20
ART education and adherence counseling	All facilities should provide the following types of education and adherence support: • Fast track initiation counseling: education and support focused on providing skills and identifying potential barriers to adherence • Enhanced adherence counseling: adherence monitoring and targeted intervention for unstable patients • Child and adolescent disclosure for children living with HIV All facilities should monitor linkage and retention and ensure early tracing of all missed appointments	National Adherence Guideline See Key Adherence Messages on page 34

Follow-up for clients on ART	All clients should have the following assessed at ART follow-up visits, until they are assessed as being stable and can enter a differentiated ART delivery model as explained below. Once in a differentiated model, clinical assessments will be done annually, unless the clients become ill. The follow-up of a client should include: • Clinical assessment and WHO clinical staging • Monitoring of weight (adults) and growth and neurodevelopment in children • Screen for medication side effects and potential drug interactions • Monitoring of renal function using creatine and eGFR • VL monitoring and response • TB screening and TPT eligibility • CPT eligibility • Sexual and reproductive health services should be integrated into ART services including screening for pregnancy, family planning, STI screening, and screening for cervical cancer • Mental health screen • Screening for non-communicable diseases • At Primary Health Care level, children should preferably be followed up within child health/IMCI services, using the IMCI seven steps	See Managing a Client on ART on page 35
ART delivery for stable clients A stable client is defined as a client who: • has been on ART for at least 12 months and has attended all scheduled visits on time • has a VL < 50 c/mL • has no current OIs and is clinically well	All facilities should provide a package of differentiated ART delivery for stable clients on ART. One or more of the following strategies may be used, based on context: • Adherence clubs • Spaced, Fast Lane appointment system • Decentralized medication delivery (e.g., CCMDD)	National Adherence Guideline CCMDD SOPs
ART delivery for unstable clients An unstable (or red flag) client is one who: • has missed an appointment or attended late for refills • a VL > 50 c/ml • possible signs or symptoms of treatment failure	Facilities should use TIER.Net early missed appointment lists and have systems in place to trace clients who have missed an appointment. Facilities should ensure effective VL monitoring and response by: • Using the NHLS reports for action (RfA) to identify clients with a VL more than 1000 and recall them to care for further action. • Having a functional results management process in place, so that VL results are captured in the clinical stationery, and into TIER.Net. • Use TIER.net reports to identify those due for a VL, and those who have two VLs more than 1000 c/ml and may require a switch to a second-line regimen. Clinicians should be able to asses a client with a VL > 50 c/ml, implement interventions accordingly, provide enhanced adherence support, and initiate and maintain second-line ART if applicable.	See the Tier.net reports manual v 1.10 See page 92 on how to register for NHLS RfA See page 42 for the management of an elevated VL and how to switch to 2nd line

PROVISION OF INTEGRATED TB/HIV SERVICES		
Facilities should provide **integrated TB and HIV services**	All clients living with HIV should be screened for TB at every visit, and have access to: • further investigations if indicated (GeneXpert MTB/Rif, LPA, culture and DST, CXR, and urinary LAM) • DS- or DR-TB treatment as applicable Clients without TB symptoms may be considered for TPT All TB clients should be screened for HIV Clients who are TB and HIV coinfected should be able to receive treatment for both conditions from the same consulting room.	HTS, 2016

PROVISION OF INTEGRATED SRH/MNCWH&N AND PMTCT SERVICES		
HIV Testing, Care, Treatment, PMTCT and **SRH services should be integrated into Antenatal Care, at Delivery, during Postnatal Care, and into other routine MNCWH&N services**	PMTCT including HTS, ART Initiation, VL monitoring, enhanced infant prophylaxis, and Early Infant Diagnosis (EID) should be part of routine MNCWH&N services. The mother and her infant should receive integrated care as a mother-infant pair until at least the end of the breastfeeding period and ideally up to the child being two years of age. Because infant prophylaxis is dependent on the mother's VL, the clinician treating the child should always enquire about the health of the mother, her adherence to ART, her most recent VL, and if she is still breastfeeding. Every woman attending ART services should be screened for pregnancy and breastfeeding, and be able to receive family planning, STI screening, and other SRH services as a "one-stop" service. All facilities should be able to provide Cervical Cancer screening.	See Section 4 PMTCT on page 65

PROVISION OF INTEGRATED NCD/HIV SERVICES		
Facilities should provide **integrated NCD/HIV services**	All PLHIV should be screened for non-communicable diseases including hypertension, diabetes, and epilepsy, and have their cardiovascular risk assessed as outlined in the PHC EML 2018. All clients on ART should be screened for depression and anxiety at least annually, and at any time if a client presents as unstable/a red flag client (missed appointments, elevated VL, or possible clinical signs of failure). All clients with non-communicable Disease should be screened for HIV.	PHC EML, 2018

PROVISION OF SERVICES FOR KEY POPULATIONS INCLUDING ADOLESCENTS, SEX WORKERS AND PEOPLE FROM LGBTI COMMUNITIES		
Facilities should provide **sensitive and appropriate HIV services for key populations**	All facilities should have HCWs who are trained to provide **adolescent and youth-friendly services** and LGBTI-sensitive and appropriate HIV services in a manner that encourages marginalized populations to access care. Based on their local context, facilities should provide **community-based outreach and mobile services** to deliver HIV prevention interventions such as HTS, condoms, condom-compatible lubricants and targeted communication to people who face barriers to access mainstream services.	National Adolescent and Youth Health Policy (2017) The South African National LGBTI HIV Framework, 2017-2022

PHARMACY		
Facilities are responsible for ensuring a **constant supply of essential medicines and commodities**	Clinicians should have a constant supply of: • 1st and 2nd-line ART • Prophylactic medications, e.g., cotrimoxazole preventive therapy (CPT), TB preventive therapy (TPT), and fluconazole • Medications for the treatment of opportunistic infections (OIs) and sexually transmitted infections (STIs) • Nevirapine and AZT syrup for infant prophylaxis • Anti-TB medications • Contraceptive methods • Male (external) and female (internal) condoms All drug stockouts should be reported to Stop Stockouts: (084) 855-7867 (SMS/please call me/WhatsApp)	National Contraception Clinical Guidelines (2018)

LABORATORY		
Facilities are responsible for ensuring a **constant supply of essential diagnostic kits and commodities for side room investigations**	HIV Rapid Test Kits (screening and confirmatory) HIV SS kits DBS kits for DNA PCR Pregnancy tests Syphilis Rapid tests Haemoglobin Meters and test strips Glucometers and test strips Urine dipsticks Specimen tubes for VL, CD4, FBC, and Biochemistry Sputum jars Urine LAM strips	

INFRASTRUCTURE AND EQUIPMENT		
Essential Infrastructure and Equipment	Running water and electricity Well ventilated rooms for infection control purposes Room that allows for confidential counseling BP machines Stethoscopes Torch and otoscope/auroscope Thermometers Height measuring boards/charts, growth charts for children, MUAC tapes, weighing scales Examination couches Speculum, brushes, slides and fixative, and examination lamp for pap smear Penile and vaginal models for condom demonstration purposes An adequate supply of prescribed clinical stationery	Ideal Clinic policy

MANAGEMENT OF HIV PREVENTION, CARE, AND TREATMENT SERVICES		
Guidelines	Current guidelines as referenced in this document should be available (preferably in each consulting room, if resources allow)	
Data Analysis and Reporting	All data should be checked and verified before submission to DHIS. All facilities should practice good documentation and have functional blood results management processes that will allow accurate data to be captured into TIER.Net. Facilities should use TIER.Net reports to track defaulters and identify clients who are failing ART. Facilities should conduct 3-6 monthly clinical audits to ensure that guidelines are adhered to and that clients are receiving good quality care. Analysis of facility data should enable continuous quality improvement	DHIMS policy TIER.Net reports Manual National Adherence Guideline PHC Supervision Manual, and Ideal Clinic Guidelines
Clinic and Community meetings	Facilities should meet with their supervisor/health area manager to review indicator performance relative to targets and the effectivity of actions outlined in their quality improvement plans (in preparation for sub-district/district quarterly review meetings). Facilities should organize regular clinical case discussion meetings to review difficult cases, adverse events, including positive PCRs and maternal or child deaths or near misses. Facilities should meet quarterly with their governance structures and community leaders to increase the demand for HTS, care, and treatment activities.	PHC Supervision Manual

SECTION 2

HIV TESTING SERVICES (HTS) AND LINKAGE TO CARE

90% of PLHIV should know their status

How do we find those living with HIV and link them to care and treatment?

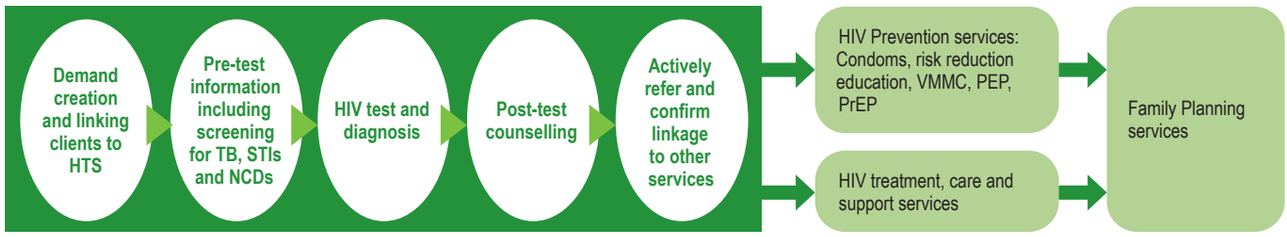
SECTION 2 HIV TESTING SERVICES AND LINKAGE TO CARE

HIV TESTING SERVICES

HIV testing services (HTS), previously HIV counseling and testing (HCT), is the main entry point to the HIV continuum of care.

Key guiding principles for HTS

- Apply a **human-rights-based approach** that prioritizes universal health, gender equality and health-rights;
- Use **integrated** approaches:
- HTS must integrate screening for TB symptoms, STIs and NCDs into the pre-test information session at health facilities and in community settings
- Wherever feasible, HTS should be provided together with family planning services
- HTS services should be integrated into all service delivery areas and offered to all patients attending at health facilities
- Include **high-yield testing strategies** in the mix of facility- and community-based HTS approaches such as facility-based PITC, facility- and community-based **index client testing**, targeted testing of **high-risk populations**, including female sex workers, men who have sex with men (MSM), people who inject drugs (PWID). Low-yield testing strategies (door-to-door community testing, general community campaigns) remain of value in linking those testing HIV-negative to prevention services.
- Implement the 5Cs, namely, **Consent, Confidentiality, Counselling, Correct test results**, and **Connection** along the HTS continuum of care, to ensure clients are not lost to follow-up in the HTS cascade.



Consent for HTS in children

Children may only be tested for HIV if testing is in their best interest, and lawful consent has been given for the test. Any person aged 12 years and older, and/or with sufficient maturity can give consent for HTS in South Africa. Consent for HIV testing for children may be given:

- by a child, if he or she is 12 years or older
- by a child younger than 12 years if he or she has “sufficient maturity”
- by a parent, caregiver or the provincial head of the Department of Social Development if the child is younger than 12 years and is not sufficiently mature

A child will be sufficiently mature to provide independent informed consent if he or she is able to:

- understand information about the benefits, risks and social implications of HIV testing; and
- act accordingly (i.e., agree or refuse to test) based on that understanding.

The Child Act[2] ensures that a wide range of people may assist a child by consenting for HIV testing on the child's behalf. It facilitates HTS for orphans and vulnerable children. According to the Child Act, a caregiver is anyone who cares for a child. Caregivers include:

- grannies, aunts and any other person who cares for a child with the implied or express informed consent of a parent or guardian;
- a foster parent;
- someone offering temporary safe care;
- the head of a shelter or child and youth care centre;
- a child and youth care worker supporting children in the community;
- a child (of 16 years and older) heading a child-headed household.

The Basic Package of HTS services

Where HIV testing is provided by a skilled provider, the package should include:

- Pre- and post-test counseling
- HIV-testing according to the National Testing Algorithm (rapid test, ELISA, or DBS-PCR)
- Active referrals to HIV prevention services (risk reduction education, condoms, VMMC, PEP, PrEP) for those testing negative
- Active referrals to treatment, care, and support services for those who test positive
- Provision of, or referral for, family planning services
- TB, STI, and NCD screening
- Facility and community index testing for partners and biological children of HIV positive clients

For HIV self-screening (HIVSS), the test kit should include:

- Instructions on how to perform the test, and interpret the results
- Information for how and where to link to other services
- A referral card
- National AIDS Helpline contact details for questions and support (0800 012 322)

HIVSS is a pre-screening test and does not provide a definitive diagnosis. A reactive self-test result must always be followed by additional testing following the national testing algorithm by a trained provider or counsellor.

HTS approaches and settings: when, where, who, and what

A combination of facility- and community-based HTS approaches facilitates the early diagnosis of HIV-positive people. Complimentary to **facility based HTS**, working in the **community** increases early diagnosis by reaching first-time testers and people who seldom use clinical services. Men, adolescents, and key populations, for example, visit public health facilities less frequently than women and mothers. Using the principles of differentiated service delivery (DSD), **testing services may be adapted to target both high-risk populations and those that are currently hard to reach.** Table 2 below provides an overview of HIV testing approaches, outlined according to the DSD building blocks of when, where, who, and what.

Members of the LGBTI communities often test late due to fear of stigma and discrimination, thus, increasing risks for poor health outcomes.

TABLE 2 AN OVERVIEW OF HOW HIV TESTING APPROACHES AND SETTINGS CAN BE ADAPTED USING A DSD APPROACH

	WHEN	WHERE	WHO	WHAT
Facility-based PITC for the general population	HTS should be provided within standard operating hours with PITC available overnight and on weekends for inpatients, casualty, and maternity services.	HTS services should be provided at, or accessible from, ALL service points, including ANC services, TB services, STI services, mobile services, outpatient clinics, medical, surgical, and paediatric wards, emergency units, maternal, newborn and child health (MNCH) services, mental health services and male circumcision services.	All healthcare personnel shall be trained in HIV testing services.	
Community-based outreach campaigns and door-to-door testing targeting hard to reach populations including men, young people, and key populations	Community services may provide testing during the early evening, over weekends, or at night (moonlight testing) to increase access for key populations, men and young people (<25 years) who are frequently missed during normal working week hours, or school day visits.	Community-based HTS: •Stand-alone HTS •Home-based HTS through door-to-door campaigns, or targeted testing linked to an index client •Mobile and Outreach HTS •HTS in the workplace, schools or tertiary institutions	The HCW or CHW conducting the outreach service. Clients may perform HIV self-screening (HIVSS). All positive results require confirmation by a trained HCW	
Facility and community index testing for partners and biological children of HIV positive clients	At post-testing counseling of newly diagnosed client, partners and biological children should be identified	Identification of contacts for possible testing should happen at the site of testing whether in the community or at the facility or where known clients on ART receive their follow-up care	HCW carrying out HIV test	Counseling on partner notification, list partners, and biological children with unknown HIV status, screen for intimate partner violence (IPV), offer and action preferred method (see algorithm). Offer HIVST for the partner if this has been selected as the index testing preferred method

Workplace testing targeting men	During work hours	At the workplace clinic, or as an outreach, mobile service	Occupational nurse, or the HCW conducting the outreach service	Workplace rapid testing or workplace HIVSS distribution with the provision of, or access to, confirmatory testing services.
HIV self-screening targeting men, young people, and key populations		Workplaces, community outreach targeting men, young people and key populations, taxi ranks, private pharmacies, and as part of facility services to enable secondary distribution for partners	Client, either assisted or unassisted	Linkage related information, referral card, HIVSS distributor contact information for support, national hotline support All positive results require confirmation by a trained HCW

Frequency of Testing in Different Populations

Table 3 below summarizes the frequency at which HIV testing should be conducted in different populations

TABLE 3 FREQUENCY OF TESTING IN DIFFERENT POPULATIONS

WHO	WHEN
Pregnant women	At confirmation of pregnancy, at every full basic antenatal care (BANC) visit, and at labour (or immediately after delivery)
Breastfeeding women (to detect HIV sero-conver¬sion)	Every three months throughout breastfeeding. Ask about her last testing date at every visit.
HIV-exposed babies	At birth, at ten weeks, at the 6-month integrated well-child visit, at six weeks post-cessation of breastfeeding, at 18 months, and at any time if the child is clinically unwell.
Older children post-breastfeeding to 14 years	At least once post-breastfeeding if mother is known to be living with HIV, is deceased or unavailable, or is unwilling to be tested
Adolescents and young adults (15 – 25 years)	Every six to 12 months if sexually active or more frequently based on exposure
Older adults (> 25 years)	Every 12 months if sexually active or more frequently based on exposure
If exposed to HIV (adults)	Immediately (at the time of assessment for post-exposure prophylaxis [PEP]), at six weeks post-exposure (for window period), and at three months post-exposure
Key populations	Every three months, depending on exposure
Clients on PrEP	At one month, and every three months

Types of tests to use in different age groups

Any HIV diagnosis should always be made using two different HIV tests, a screening test, and a confirmatory test. Table 4 below summarises the types of tests that should be used per age group for screening and confirmation purposes if the screening test is found to be positive.

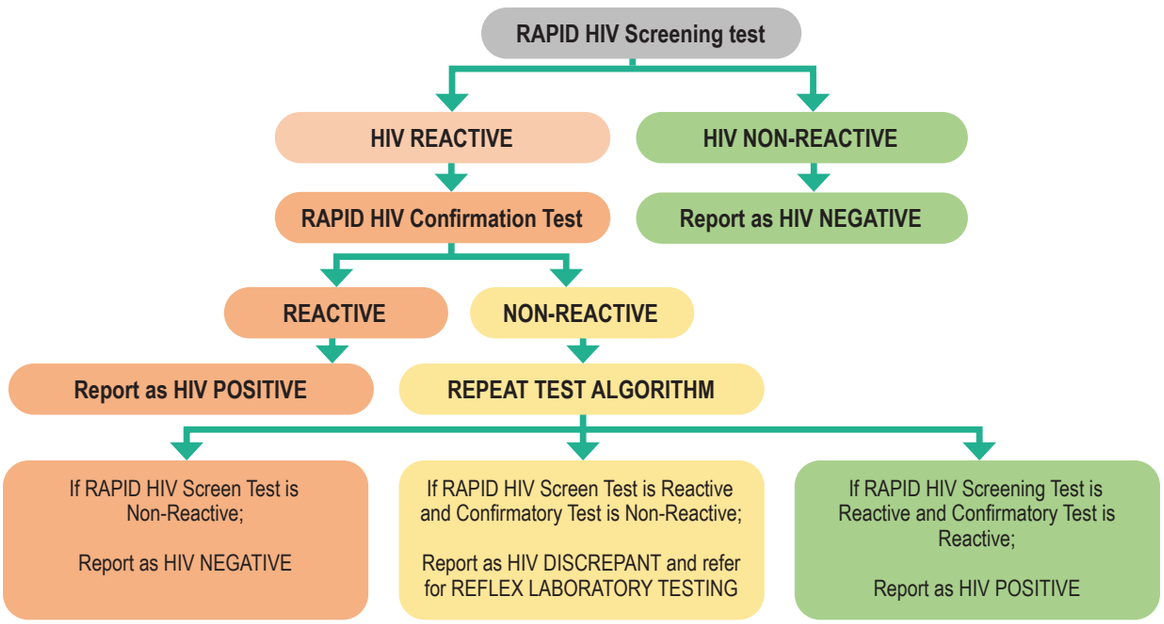
TABLE 4 TYPES OF HIV TESTS TO USE PER AGE GROUP

Age of the client	HIV screening test	Confirmatory HIV Test
Less than 18 months	PCR test	PCR test
18 months to 2 years	HIV Rapid test	PCR test
All adults, adolescents and children older than 2 years	HIV Rapid test	HIV Rapid test

In a small percentage of babies, maternal antibodies are retained beyond 18 months of age, potentially resulting in false-positive HIV diagnoses and inappropriate initiation of ART.[3] For this reason, HIV PCR testing is done as confirmatory testing in all HIV-positive tests in children under two years of age. At the clinician's discretion, the HIV-PCR may be replaced by a viral load test which has the advantage of both confirming the HIV diagnosis and providing a baseline VL for monitoring the child's response to ART. Any child who tests HIV positive should initiate ART according to the Paediatric ART guideline as a matter of urgency. Do not wait for the confirmatory result before initiating ART but ensure that this result is checked.

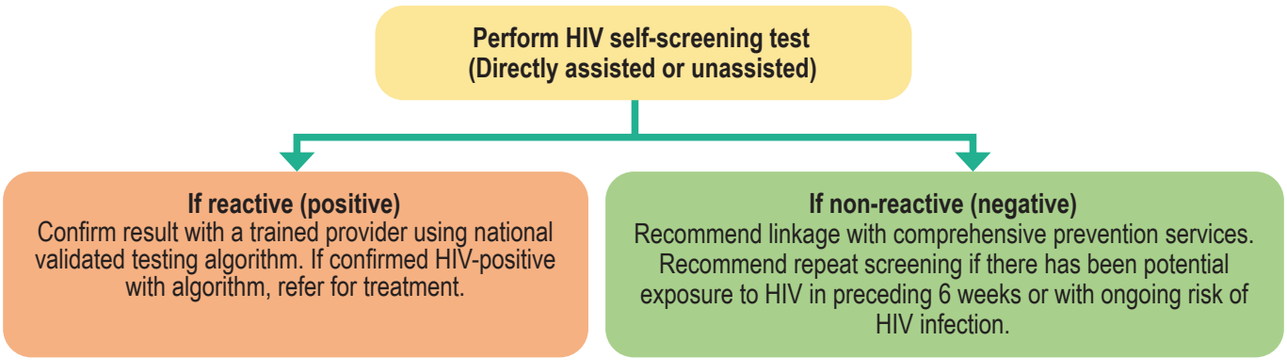
The HIV testing algorithm for all adults, adolescents, and children older than 2 years

When implementing HIV rapid testing, a serial testing algorithm should be followed as indicated in the algorithm below. The first rapid test is run as a screening test, and if reactive, a different rapid test is used to confirm the result of the screening test. If the screening test is non-reactive, a negative result should be reported. However, if the client has had recent exposure to HIV, the client may be in the window period (the time between HIV infection and detection of antibodies on an HIV antibody test). Such clients should be advised to repeat the test after three months.



In cases of discrepant results (first test result is reactive, and the second is non-reactive) the entire testing algorithm must be repeated on a new finger-prick specimen. If the repeat test is also DISCREPANT, a specimen must be submitted for ELISA testing. For more detail on the HIV testing process, refer to the 2016 HTS Policy document.

HIV Self Screening Algorithm

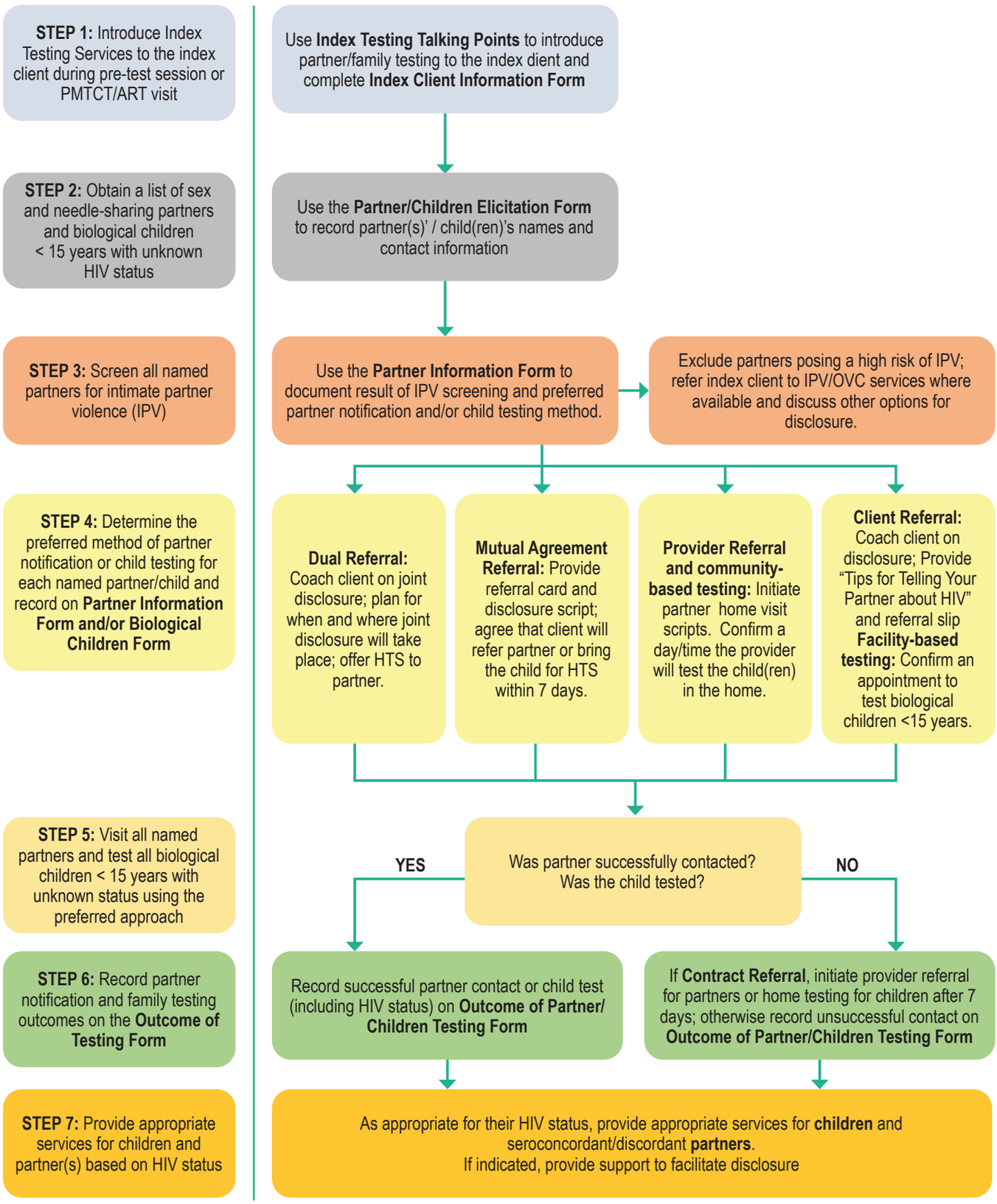


HIV Index Testing Algorithm

To achieve the first 90 of the 90-90-90 targets and identify PLHIV who remain undiagnosed, the country is scaling-up index testing for sexual partners and biological children of PLHIV within all HIV testing and treatment programmes. In this regard:

- Partner testing services should be offered to all HIV-positive adults and adolescents accessing facility or community-based HTS delivery points.
- Family testing of all biological children < 15 years should be offered to all HIV-positive mothers, as well as biological siblings of HIV-positive children.
- Biological children of HIV-positive fathers may also need to be tested if the mother was known to be living with HIV, is deceased or unavailable, or unwilling to be tested.
- HIV index testing is voluntary. Clients have the right to decline or defer index testing. Should a client decline or defer index testing, the offer should be repeated at subsequent visits.

HIV Index Testing Algorithm



LINKAGE TO CARE

Linkage or “connection” to HIV care is defined as a process of actions and activities that support people testing for HIV and people diagnosed with HIV to engage with prevention, treatment and care services as appropriate for their HIV status. It is the responsibility of all HTS providers to ensure that clients are connected to appropriate care.

HTS is of little value if clients that are tested are not linked into prevention and treatment services

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For people living with HIV, it refers to the period beginning with HIV diagnosis and ending with enrolment in care and treatment and other health services, including:

- treatment, care, support and management of the disease
- sexual and reproductive health (i.e., contraception, PMTCT, STI screening, cervical cancer screening, anal cancer, and screening for men)
- testing for partners and families: this includes partner notification and index case testing

For people who test HIV-negative, it refers to the period beginning with HIV testing and ending with enrolment in preventative health services, including:

- HIV risk reduction counseling, PEP, PrEP, dissemination of, and education on, the use of condoms and lubricants, and voluntary medical male circumcision (VMMC)
- sexual and reproductive health (i.e., contraception, STI screening, cervical cancer screening, anal cancer, and screening for men)

Interventions to improve linkage to care

Based on a review of the evidence, the National Adherence Guideline details a minimum package of interventions to be implemented in all health facilities to increase linkage to care.

TABLE 5 INTERVENTIONS TO IMPROVE LINKAGE TO CARE

For all clients diagnosed at a community/workplace site
• Provide **enhanced post-test counseling**, including disclosure support. • Make an **active referral** for a specific time and date. An active referral is one in which the official referring the client makes an appointment for the client and provides a referral letter/form • Inform clients about the tracing and retention in care system. • Ask the client's **consent to be traced** and discuss the best method by which the client would like to be contacted (by phones, SMS, or home visit) • **Obtain accurate contact** details for HIV diagnosed clients and document at the testing site. • Where feasible, the client may be accompanied to the appointment by a community health worker (CHW) or peer (peer navigation to ART initiation service) • **Schedule a follow-up visit** or phone call at a time and date that is convenient to the client • Provide **the list** of name of patients and the date they are expected to come for their appoint¬ment to the referral service at the facility. • Systematically **monitor linkage** to ART initiation services through logbooks • **Identify patients who miss their appointments** by more than five days of set appointment date. • **Trace clients** who have missed appointments, and reintegrate them into care • Provide **additional psychosocial support** for clients who return to the facility after tracing. • All tracing and retention in care processes must be **documented**.
For adolescents, key populations, any client who has previously tested but failed to initiate ART, any client who seems reluctant to initiate ART during post-test counseling, and any client tested/initiated on ART as an inpatient
As above, with the following additional enhancements as appropriate • Peer navigation to ART initiation service • Weekly telephonic support and follow-up until ART has been initiated. • Where the client does not have a telephone or is not responding to telephonic follow-up, a home visit may be conducted.
For all clients diagnosed in a health facility:
Client accompaniment to ART initiation services and introduction to the service provider is preferred, where feasible.

SECTION 3

ART INITIATION AND ACHIEVING VIROLOGICAL SUPPRESSION

90% of PLHIV who know their status should initiate ART

90% of PLHIV on ART should have a suppressed VL

How do we start ART, stay on ART, and thrive on ART?

SECTION 3 ART INITIATION AND ACHIEVING VIROLOGICAL SUPPRESSION

ART ELIGIBILITY

All people living with HIV (PLHIV) are eligible to start ART regardless of age, CD4 cell count, and clinical stage.

An overview of the ART initiation process

TABLE 6 AN OVERVIEW OF THE ART INITIATION PROCESS USING THE DSD APPROACH

WHEN	WHERE	WHO	WHAT
All clients should initiate ART as soon as possible, ideally within one week of diagnosis or linking to care (rapid ART initiation). The timing of ART initiation is determined by the client's **clinical condition** and **psychosocial readiness**.	ART initiation takes place primarily at the facility level but may form part of mobile outreach services	NIMART trained nurse or doctor	• Step 1: Determining the timeframe for ART initiation by performing a **clinical and psychosocial assessment** • Step 2: Determine if the client should be on 1st or 2nd line ART • Step 3: Choose the drugs in the regimen • Step 4: Provide education and skills to adhere to ART

ART INITIATION STEP 1: DETERMINE THE TIMEFRAME FOR ART INITIATION

ART should be delayed only if:

- The concerns about adherence are severe enough to outweigh the risk of HIV disease progression
- Clinical indications exist to defer ART

A clinical assessment (see page 21) and laboratory baseline investigations (see page 23) should be done to initiate ART. From the clinical assessment, the client can be differentiated into one of two categories:

1. **Asymptomatic and clinically well**
   - Most patients that are clinically well should be able to start ART within one week
   - Wherever possible, asymptomatic clients may be able to start on the **same day** as their HIV diagnosis, or on the day they receive their CD4 result, provided that:
     - o They have received counseling on the **key ART adherence messages** (see page 34)
     - o They are motivated to start ART
   - Laboratory results do not need to be available to start clients on ART on the same day, but they should be contactable if any results are abnormal
2. **Advanced disease (symptomatic and/or with low CD4 <200 cells/mm3)**
   - These clients require further investigation and management of their disease condition
   - Table 5 on page 25 outlines the medical indications to defer ART

Baseline Clinical Evaluation for Adults and Adolescents, Pregnant Women, and Children

The baseline clinical evaluation of a client about to start ART requires a thorough **history and clinical examination**. The minimum components of the baseline clinical evaluation are outlined in Table 7 below.

TABLE 7 BASELINE CLINICAL EVALUATION

COMPONENT OF THE BASELINE CLINICAL EVALUATION	PURPOSE	FURTHER ACTION REQUIRED		
		ADOLESCENTS (10-19 YEARS) AND ADULTS	PREGNANT WOMEN	CHILDREN (< 10 YEARS)
Recognise the client with respiratory, neurological, or abdominal **danger signs needing urgent care**	To identify opportunistic infections and conditions needing urgent care or referral	Identify respiratory, neurological, or abdominal danger signs as outlined in Adult Primary Care (APC) guideline	Identify danger signs as outlined in the Maternity Care guidelines	Identify danger signs as classified in the IMCI Chart booklet
Nutritional Assessment	To identify recent weight loss that may indicate an active opportunistic infection (OI) or other pathology. To identify underweight/obese clients requiring nutritional and lifestyle support	Measure weight and height and determine BMI (kg/m^2): < 18.5 = underweight; 18.5 to 25 = normal; > 25 to < 30 = overweight; ≥30 = obese	Measure mid upper arm circumference (MUAC) Women with MUAC < 23 cm require additional nutritional support/referral	Plot weight, height and head circumference (if < 2 years) on growth chart, and measure MUAC to identify moderate and severe malnutrition
Screen for TB	To identify clients with a positive TB screen who require further investigations for TB To identify clients with a negative TB screen who may be eligible for TPT (see page 50)	Identify symptoms of cough, night sweats, fever, recent weight loss as outlined in the TB screening tool	Do a TB symptom screen and **TB GeneXpert** for all HIV-positive women at first visit in antenatal clinic, due to the lower sensitivity of the TB symptom screen in pregnant women	Identify symptoms of cough, fever, recent weight loss or fatigue (always tired) as outlined in the TB screening tool
Screen for symptoms of meningitis	To diagnose and treat clients with cryptococcal and other forms of meningitis and reduce associated morbidity and mortality	**Identify symptoms of headache, confusion** or **visual disturbances.** With cryptococcal meningitis, clients may only present with a recurrent headache. Other symptoms may include fever, neck stiffness or coma. Refer the client for a **lumbar puncture**. Defer ART if meningitis is confirmed as outlined in "Medical Reasons to Defer ART" on page 25		

COMPONENT OF THE BASELINE CLINICAL EVALUATION	PURPOSE	FURTHER ACTION REQUIRED		
		ADOLESCENTS (10-19 YEARS) AND ADULTS	PREGNANT WOMEN	CHILDREN (< 10 YEARS)
Screen for active depression, other **mental health** issues or substance abuse	EFV and, to a lesser extent DTG, are associated with neuropsychiatric side-effects. In general, ART can be initiated, and cautiously monitored. Substance use can affect adherence	Screen for symptoms of depression, psychosis, and substance abuse		Screen for symptoms of depression in older children
Screen for major chronic **non-communicable diseases (NCDs)** (diabetes, hypertension, epilepsy)	To identify and manage clients with major chronic NCDs and/or comorbidities. To identify and prevent potential drug interactions with ART e.g. metformin and anti-epileptic medications	Do blood pressure (BP), and urine dipstix for proteinuria and glucose. Identify other risk factors (smoking, increased waist circumference, age) and determine cardiovascular (CVS) risk. Manage NCDs and CVS risk factors as outlined in the PHC EML	Do blood pressure (BP), and urine dipstix for proteinuria and glucose	Identify the child with epilepsy and be aware of potential drug interactions of anti-epileptic treatment and ART
Screen for **pregnancy** and ask if planning to conceive	To identify pregnancy and facilitate early referral for antenatal care (ANC) and measures to prevent mother-to-child transmission (MTCT). To assess fertility intentions and contraceptive needs if not pregnant. To assess eligibility for DTG-containing regimens	Ask if the client is currently using contraception and if her last menstrual period occurred at the expected time. If she answered "no" to either question, do a urine pregnancy test	N/A	N/A
Symptom screen for **sexually transmitted infections** (STIs)	To identify and treat STIs in sexually active clients	STI screening should include the following three questions: "Do you have any genital discharge?" "Do you have any genital ulcers?" "Has/have your partner(s) been treated for an STI in the last 8 weeks?		N/A
Neurodevelopmental screen	To identify children with neurodevelopmental delay requiring intervention/referral and follow-up	N/A	N/A	Screen for developmental delays as outlined in the child's Road to Health Booklet (RTHB)
WHO clinical stage	**After the baseline clinical evaluation has been completed by means of a thorough history and clinical examination, the client's WHO clinical stage can be determined:** **At ART initiation**, WHO clinical stage helps us to: Understand the severity of the client's clinical condition and the associated risk of mortality Determine the urgency and timing of ART initiation Determine if cotrimoxazole prophylaxis (CPT) is indicated (see "Indications for CPT" on page 49)			

Baseline Laboratory Evaluation for Adults and Adolescents, Pregnant Women, and Children

The following baseline laboratory investigations should be performed routinely before a client initiates ART. Clients are not required to wait for the results of the baseline investigations before starting ART, provided the client is asymptomatic. However, the results should be checked at the next visit.

TABLE 8 BASELINE LABORATORY EVALUATIONS

LABORATORY EVALUATION	PURPOSE	ADOLESCENTS (10-19 YEARS) AND ADULTS	PREGNANT WOMEN	CHILDREN (< 10 YEARS)
Confirm HIV test result	To confirm HIV status for those without documented HIV status	✓	✓	✓
CD4 cell count/ %	To identify eligibility for CPT	See "Indications for starting and stopping cotrimoxazole" in table on page 49		
	To identify eligibility for cryptococcal antigen (CrAg) screening	A reflex CrAg test will be done automatically by the laboratory on all CD4 counts < 100 cells/µL		N/A
Creatinine and eGFR if TDF used	To assess renal insufficiency	See table titled "**Assessing Renal Function**" on page 24		N/A
Haemoglobin (Hb)	To identify and manage anaemia; to determine eligibility for zidovudine (AZT) where necessary	If Hb is low, do a full blood count (FBC). Characterise according to mean corpuscular volume (MCV) as either microcytic, normocytic, or macrocytic and manage accordingly[1]	Treat with ferrous sulphate tds if Hb < 10 g/dL. Refer if < 8 g/dL and symptoms, if anaemia diagnosed at 36 weeks gestation or later, or if no response to treatment	Children < 5 years: Treat with iron supplements and deworm the child[1] Children > 5 years: Do FBC. Characterise according to MCV and manage accordingly[1]
GeneXpert	To diagnose TB	Only for those clients with a **positive TB symptom screen**	**Regardless of TB symptoms**, routinely do a TB GeneXpert for all HIV-positive women at first visit in antenatal clinic, due to the lower sensitivity of the TB symptom screen in pregnant women	Only for those with a **positive TB symptom screen**
Cryptococcal antigen test (CrAg) if CD4 < 100 cells/ µL	To identify asymptomatic clients who need pre-emptive fluconazole treatment	A reflex CrAg test will be done automatically by the laboratory on all CD4 counts < 100 cells/µL If CrAg-negative, no fluconazole is required If CrAg-positive, the client will require treatment of the infection All clients with a positive CrAg should be referred for a lumbar puncture	All pregnant women with a positive CrAg should be referred for a lumbar puncture, regardless of symptoms. The results of the lumbar puncture and further management should be discussed with an expert, or one of the helplines provided on page 42	N/A

Cervical cancer screening	To identify women with cervical lesions and manage appropriately	All HIV-positive women should be screened for cervical cancer at diagnosis and subsequently every 3 years if the screening test is negative. If positive, she should be referred for colposcopy and further interventions	Pregnancy does not preclude screening for cervical cancer and it can be performed up to 20 weeks of gestation. However, pap smear results may be more difficult to interpret in pregnancy, and any abnormal smears should be repeated at 6 to 12 weeks after delivery.	N/A
HBsAg	To identify those co-infected with hepatitis B (HBV)	If positive, exercise caution in stopping TDF-containing regimens, to prevent hepatitis flares		N/A

1 As outlined in the PHC EML 2018

Assessing renal function

TABLE 9 ASSESSING RENAL FUNCTION

ASSESSING RENAL FUNCTION				
	Age/pregnancy Status	**What must be measured?**	**Acceptable level for TDF use**	**Counahan Barratt formula**
	≥ 10 and < 16 years of age	eGFR using Counahan Barratt formula	> 80 mL/min/1.73 m^2	eGFR (mL/min/1.73 m^2) = $\frac{\text{height [cm] x 40}}{\text{creatinine [µmol/L]}}$
	Adults and adolescents ≥ 16 years	eGFR using MDRD equation[1]	> 50 mL/min/1.73m^2	
	Pregnant women	Absolute creatinine level	< 85 µmol/L	

1 Modification of Diet in Renal Disease Study (MDRD) equation. The MDRD formula is automatically calculated by the laboratory for those 18 years and older. For assistance in manually calculating the eGFR for adolescents between 16 and 18 years of age, please contact one of the helplines provided on page 42. Alternatively, use the calculator provided at https://www.mdcalc.com/mdrd-gfr-equation, or one of numerous smartphone applications available for this purpose. Ensure that the website/application uses the correct unit of measurement (i.e. µmol/L) for the creatinine level.

Medical indications to defer ART

Clients with advanced HIV disease should be carefully assessed for opportunistic infections that may necessitate ART deferral. Medical indications to defer ART are outlined in the table below.

TABLE 10 MEDICAL INDICATIONS TO DEFER ART

MEDICAL INDICATIONS TO DEFER ART	
INDICATION	**ACTION**
TB symptoms (cough, night sweats, fever, recent weight loss)	Investigate for TB before initiating ART. If TB is excluded, proceed with ART initiation and TB preventive therapy (after excluding contra-indications to TPT). If TB is diagnosed, initiate TB treatment and defer ART. The timing of ART initiation will be determined by the site of TB infection and the client's CD4 cell count
Diagnosis of drug-sensitive (DS) TB at a non-neurological site (e.g. pulmonary TB, abdominal TB, or TB lymphadenitis)	Defer ART initiation as follows: • If CD4 < 50 cells/µL (any age) – initiate ART within 2 weeks of starting TB treatment, when the client's symptoms are improving, and TB treatment is tolerated • If CD4 ≥ 50 cells/µL (adults and adolescents) – initiate ART 8 weeks after starting TB treatment • If CD4 ≥ 50 cells/µL (infants and children) – initiate ART 2 to 8 weeks after starting TB treatment
Diagnosis of drug-resistant (DR) TB at a non-neurological site (e.g. pulmonary TB, abdominal TB, or TB lymphadenitis)	Initiate ART after 2 weeks of TB treatment, when the client's symptoms are improving, and TB treatment is tolerated
Diagnosis of DS-TB or DR-TB at a neurological site (e.g. TB meningitis or tuberculoma)	Defer ART until 4-8 weeks after start of TB treatment
Signs and symptoms of meningitis	Investigate for meningitis before starting ART
Cryptococcal antigen (CrAg) positive in the absence of symptoms or signs of meningitis	Defer ART until the first 2 weeks of fluconazole prophylaxis has been completed
Confirmed cryptococcal meningitis	Defer ART until 4-6 weeks of antifungal treatment has been completed
Other acute illnesses e.g. *Pneumocystis jirovecii* pneumonia (PJP) or bacterial pneumonia	Defer ART for 1-2 weeks after commencing treatment for the infection
Clinical symptoms or signs of liver disease	Confirm liver injury using ALT and total bilirubin levels. ALT elevations > 120 IU/L with symptoms of hepatitis, and/or total serum bilirubin concentrations > 40 µmol/L are significant. Investigate and manage possible causes including hepatitis B, drug-induced liver injury (DILI), or alcohol abuse
Note: Clients who are already on ART should NOT have their treatment interrupted upon diagnosis of the above conditions	

ART INITIATION STEP 2: DETERMINE IF THE CLIENT SHOULD BE ON FIRST- OR SECOND-LINE ART

Confirm if the client has been on any ART medications for longer than one month in the past.

If not, start a first-line regimen, as outlined in step 3 on page 27.

If the client has been on ART before and is returning to care, follow the steps outlined in the section below:

Re-initiating ART in Clients who have Interrupted Treatment

- Take a thorough history, including:

1) which ART medications the patient was taking, and for how long;

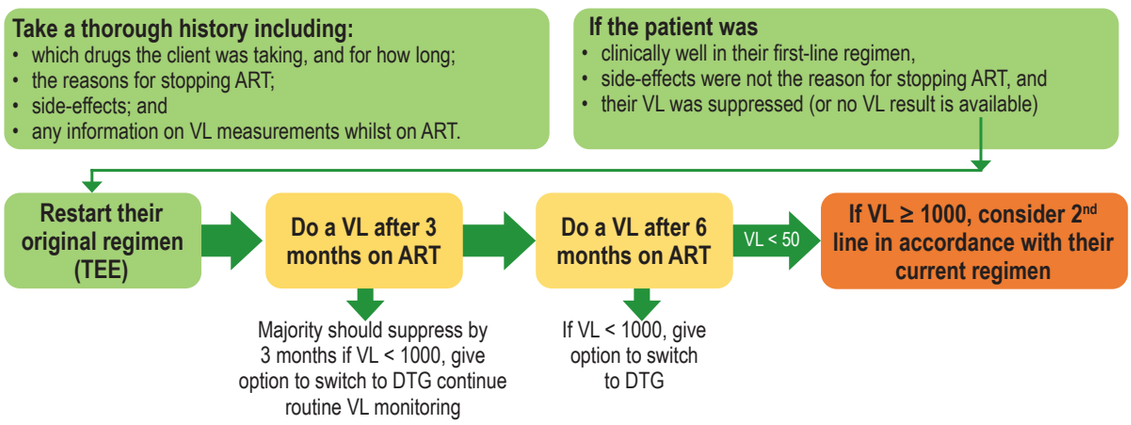
2) the reasons for stopping ART;

3) side-effects; and

4) any information on VL measurements while on ART.

- If the client was well on their first-line regimen, side-effects were not the reason for stopping ART, and their VL was suppressed (or no VL result is available), restart their original regimen they were taking at the time of interruption. Do a VL after three months on ART. The majority of clients should suppress by three months on ART. For those that remain unsuppressed provide enhanced adherence support and repeat the VL at six months on ART (three months later).
- If their VL remains over 1000 c/mL at six months on ART, manage the virological failure in accordance with their specific regimen (see the "Management of VL results" algorithm on page 42).
- If the client restarted an NNRTI-based regimen and they re-suppress to below 1000 c/mL at either the 3-month or 6-month VL test, offer a single drug switch to TLD.
- If the client stopped treatment due to side-effects, manage as outlined on page 93, or contact one of the helplines provided on page 42.
- If the client was failing but is still clinically well, consider restarting their original regimen they were taking at the time of interruption.
- If the client is ill, consider a new regimen, consulting an experienced clinician as necessary.
- For restarting a previously ART-exposed pregnant women on ART see page 68

Re-initiating ART in Treatment interrupters



ART INITIATION STEP 3: CHOOSE THE DRUGS IN THE REGIMEN

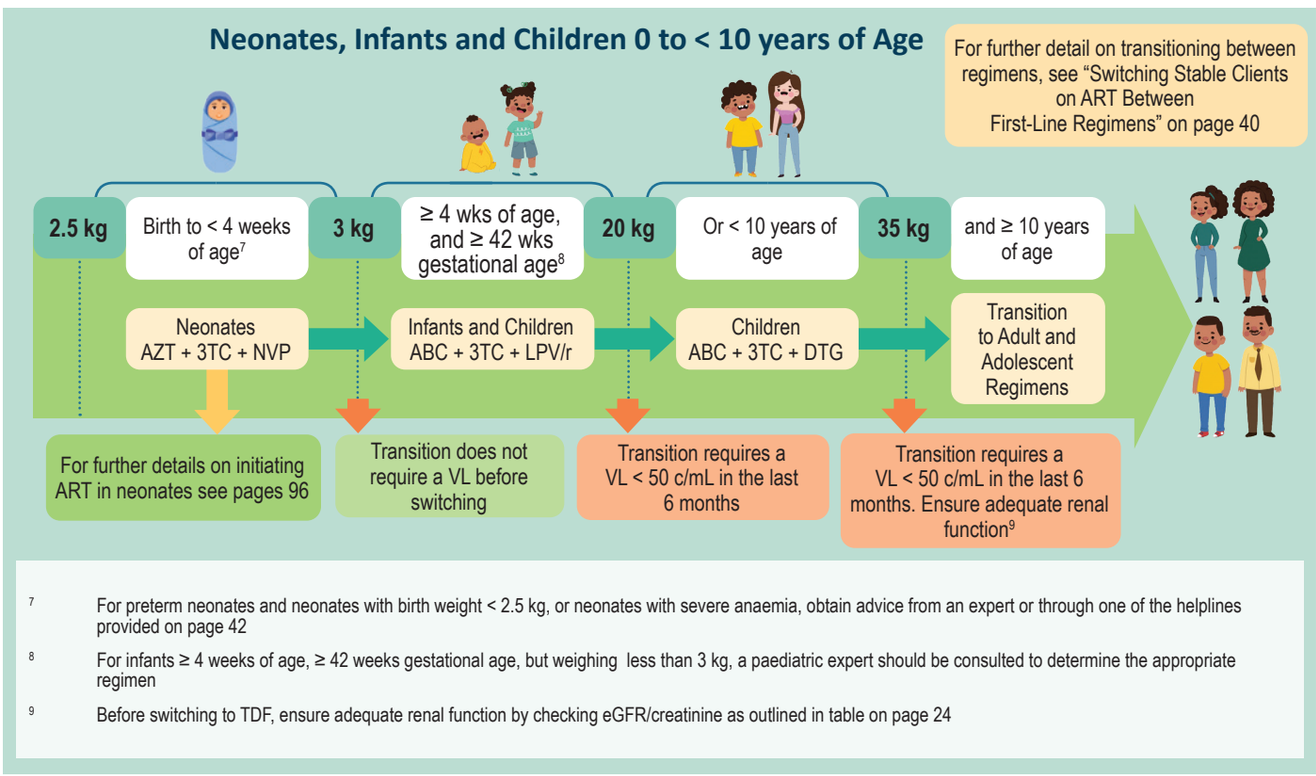
Overview of preferred ART regimens per age group

A significant strategy for achieving and sustaining viral suppression is the new drug **dolutegravir** (DTG). DTG has improved tolerability, has few drug interactions, and the virus does not easily develop drug resistance against it.[4] For this reason, a DTG-containing first-line ART regimen is preferred for

- those clients newly initiating ART and weighing 20 kg or more,
- those clients experiencing side-effects to EFV or
- those clients who prefer to use DTG after being given all the necessary information.

DTG can be used in anyone weighing 20 kg or more. However, TDF can be used from only 35 kg and the age of 10 years or more. Therefore, because of restrictions imposed by TDF, the fixed-dose combination TLD (TDF, 3TC, and DTG) can only be used in clients weighing 35 kg or more and being 10 years of age and older.

The figure below provides an overview of the preferred regimens per age group.



7 For preterm neonates and neonates with birth weight < 2.5 kg, or neonates with severe anaemia, obtain advice from an expert or through one of the helplines provided on page 42

8 For infants ≥ 4 weeks of age, ≥ 42 weeks gestational age, but weighing less than 3 kg, a paediatric expert should be consulted to determine the appropriate regimen

9 Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in table on page 24

Tenofovir disoproxil fumarate (TDF), lamivudine (3TC) and DTG in the fixed-dose formulation known as TLD is the preferred regimen for all adolescent boys (10 years and older) and men weighing more than 35 kg. However, due to concerns around the safety of TLD in the periconception period, tenofovir disoproxil fumarate-emtricitabine-efavirenz (TEE) is recommended for women of childbearing potential who actively want to conceive at the current time, and those who are initiating ART in the first 6 weeks of pregnancy (see page 30 for guidance on how to use DTG in women of childbearing potential).

The preferred first-line regimen in children newly initiating ART and weighing less than 20 kg is abacavir (ABC), 3TC, and lopinavir boosted by ritonavir (LPV/r). Efavirenz is no longer part of the preferred first-line ART regimen in children older than three years due to high levels of pre-treatment resistance. However, children who are already taking an EFV-containing regimen, and who are virally suppressed and clinically well, should remain on that regimen until they reach 20 kg and become eligible to switch to DTG.

DOLUTEGRAVIR

Dolutegravir Overview

Class of ARV: Integrase Inhibitor (InSTI)

Formulations:

- Fixed-dose combination: tenofovir (TDF) 300 mg + lamivudine (3TC) 300 mg + DTG 50 mg (TLD). TLD can be prescribed for clients > 35 kg and > 10 years of age
- DTG 50 mg tablet

Standard Dose: Children > 20 kg; adolescents and adults: DTG 50 mg daily

DTG dose with concomitant TB treatment: DTG dose requires boosting to 50 mg 12-hourly. If on TLD FDC, give a second dose of DTG 50 mg 12 hours after the TLD dose

Side-effects: Usually mild and self-limiting. Side-effects include insomnia, headache, central nervous system (CNS) effects, and gastrointestinal effects. Weight gain has emerged as a side effect of this class of drugs; clients who are overweight should receive lifestyle interventions (see below), and obese clients may be considered for EFV. DTG is known to decrease tubular secretion of creatinine without affecting glomerular filtration. Serum creatinine levels increase early in treatment (by less than 15%), remain stable throughout therapy, and are not an indication to stop DTG. A creatinine level that keeps on rising is, however, a cause for concern and could indicate TDF toxicity or other underlying pathology. DTG can be taken in the evening or the morning as per the clients' preference. However, if the client develops insomnia, TLD should be taken in the morning.

DTG and neural tube defects: DTG may increase the risk of neural tube defects (NTDs). The absolute risk is very low. The risk for NTDs in mothers conceiving on DTG containing ART is 0.3%.5 The risk of NTDs on mothers conceiving on EFV-containing ART is 0,1%. DTG should be used with caution periconception and in the first six weeks of pregnancy. The neural tube closes by the end of the sixth week of pregnancy (fourth week post-conception). DTG appears to be safe if started after the neural tube has closed. Thus, there is no risk of NTDs with TLD use after this period. Women of childbearing potential (WOCP) should be counseled regarding the risk of NTDs and be enabled to make an informed choice. Contraception is recommended for all women who do not currently wish to become pregnant, including those starting DTG. (see page 76 for guidance on how to use DTG in women of childbearing potential).

Lifestyle Interventions

All clients should be encouraged to apply the following lifestyle changes as appropriate: Maintain an ideal weight, i.e., BMI < 25 kg/m2. Overweight clients with BMIs > 25 kg/m2 should reduce their weight. Alcohol intake should be reduced to < 2 standard drinks per day for men and < 1 for women on no more than 5 out of 7 days per week. A prudent eating plan should be followed, i.e. low fat, high fiber, and unrefined carbohydrates, with fresh fruit and vegetables. Regular moderate aerobic exercise, e.g., 30 minutes of brisk walking 3-5 times per week (150 minutes/week). The client should be advised to stop smoking.

Drug Interactions with Dolutegravir

Before initiating a client on ART (and at every subsequent visit), it is important to take a thorough medication-related history to identify any potential drug-drug interactions. Ask about TB medications, treatment for NCDs, and any other prescribed medication. Also ask about over the counter (OTC) medications and traditional remedies. Drug interactions can result in suboptimal drug levels, which can cause:

- an elevated viral load
- drug resistance, due to replicating virus in the presence of subtherapeutic drug levels

TABLE 11 DRUG INTERACTIONS WITH DTG

INTERACTING DRUG	EFFECT OF CO-ADMINISTRATION	RECOMMENDATION
Rifampicin	↓ Dolutegravir	Double DTG dose to 50 mg 12-hourly. If on TLD FDC, add DTG 50 mg 12 hours after TLD dose
Polyvalent cations (Mg^{2+}, Fe^{2+}, Ca^{2+}, Al^{3+}, Zn^{2+}) e.g. antacids, sucralfate, multivitamin and nutritional supplements	↓ Dolutegravir	Calcium supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and calcium supplements can be taken at the same time if taken with food. Iron supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and iron supplements can be taken at the same time if taken with food. However, calcium and iron supplements must be taken at least 4 hours apart. Magnesium/aluminium containing antacids decrease DTG concentrations regardless of food intake and should be taken a minimum of 2 hours after or 6 hours before DTG
Anticonvulsants: • Carbamazepine • Phenobarbital • Phenytoin	↓ Dolutegravir	Avoid coadministration if possible. Alternative agents that do not interact with DTG include valproate, lamotrigine, levetiracetam, and topiramate. Remember that valproate is contra-indicated during pregnancy. Double DTG dose to 50 mg 12-hourly for carbamazepine if an alternative anticonvulsant cannot be used
Metformin/DTG	↑ Metformin	DTG increases metformin levels. Maximum metformin dose 500 mg 12-hourly

This table includes some of the most important drug interactions with DTG. Note that efavirenz, lopinavir/r and atazanavir/r also have important drug interactions. For more information, please refer to the following resources:

www.hiv-druginteractions.org/checker,
the **Liverpool HIV iChart application** for smartphones,
the **SA HIV/TB Hotline application** for android smartphones
the **EML-Antiretrovirals Interactions table** available on www.mic.uct.ac.za,
or any of the helplines provided on page 42

Using DTG in women of childbearing potential

Due to concerns around the safety of TLD in the periconception period, tenofovir disoproxil fumarate-emtricitabine-efavirenz (TEE) is recommended for women wanting to conceive and women initiating ART within the first six weeks of pregnancy. For this reason, integration of family planning and ART services are of paramount importance, and issues of family planning and contraception should be discussed at every clinical interaction to understand the client's current fertility desires and healthcare needs.

Care should be provided in ways that respect women's autonomy in decision-making about their health, and services must provide information and options to enable women to make informed choices.

The steps to enable a woman to make an informed choice are as follows:

1. **Understand her current pregnancy status and fertility intentions:**
   - Is she pregnant? If so, what is her gestation?
   - Does she desire a pregnancy at the current time, in the future, or not at all?

2. **Within the context of her fertility intentions, explain the risks and benefits of using either DTG or EFV, as outlined below:**

TABLE 12 THE RISKS AND BENEFITS OF DTG- AND EFV-CONTAINING REGIMENS

BENEFITS OF USING DTG	RISKS OF USING DTG
Provides rapid viral suppression	DTG may increase the risk of neural tube defects (NTDs) if used in the first four weeks after conception
High genetic barrier to resistance	
No interaction with hormonal contraceptives	Drug interactions with Rifampicin
Side-effects are mild and uncommon	

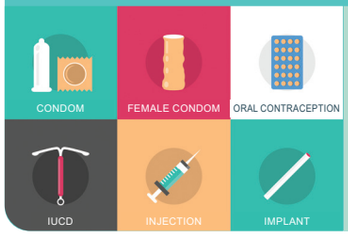
BENEFITS OF USING EFV	RISKS OF USING EFV
Safe in pregnancy	Low genetic barrier to resistance
No significant interaction with TB treatment	Drug interactions with contraceptives
	Neuropsychiatric side-effects

3. **Discuss and provide a choice of contraceptive options as desired**

Women do not currently desire to become pregnant should be provided with a choice of contraceptive options, which includes condoms, oral contraceptives, implants, injectables, and intrauterine contraceptive devices (IUCDs). Dual methods are recommended and consist of:

- a hormonal method or IUCD to prevent pregnancy, and
- a barrier method (male/female condoms) to prevent STIs and HIV transmission.

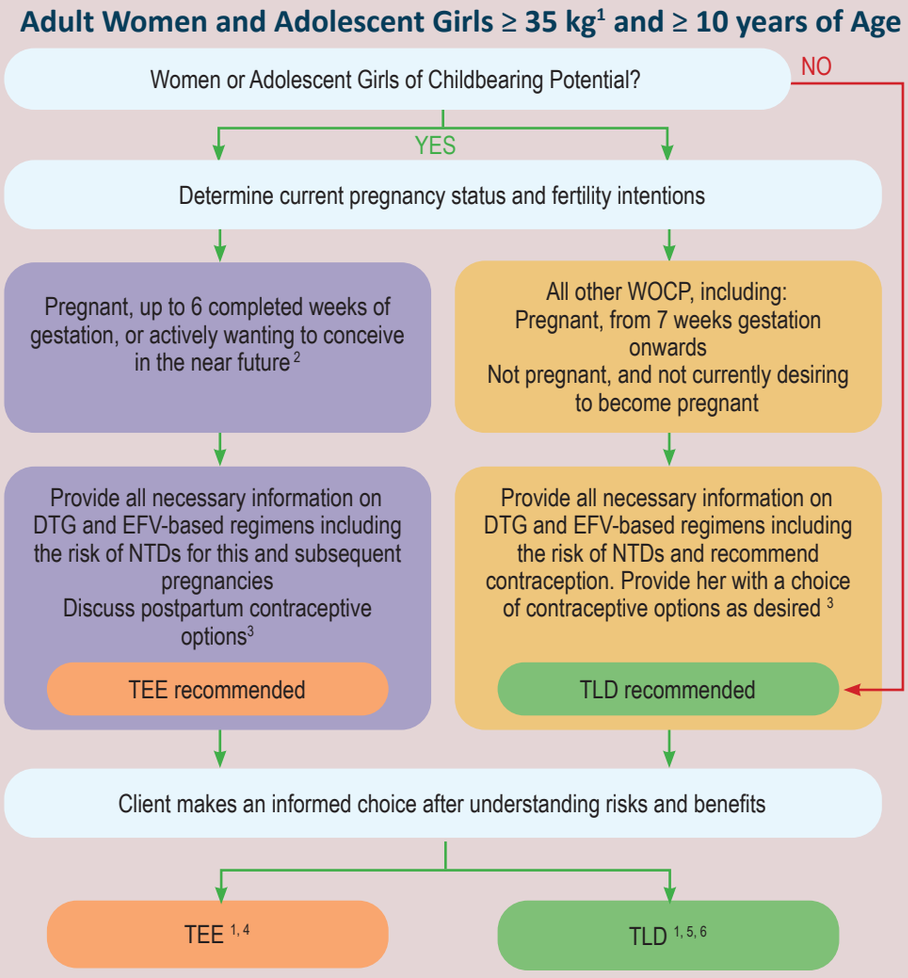
FEMALE CONTRACEPTIVE METHODS



Contraceptive choices need to respect and fulfil human rights and enable clients to make informed choices for themselves. Client contraceptive choices, however, are often influenced directly or indirectly by social, economic, and cultural factors. It is in this context that clients should be given comprehensive, scientifically accurate information to assist them in making an informed, voluntary choice of a contraceptive method.

Algorithm for recommending ART regimens in women and girls

The algorithm below summarises the process for determining the appropriate ART regimen in women and girls



1 For adolescent girls who weigh less than 35 kg, replace tenofovir with abacavir (ABC)

2 Women wanting to conceive should be started on folate and should be counselled to defer attempts to conceive until they are virally suppressed. See also "Contraception and Safe Conception" on page 67.

3 Women should be provided a choice of contraceptive options (which includes condoms, oral contraceptives, implants, injectables, and IUCDs)

4 Women who choose to use TEE around the time of conception can be offered a switch to TLD if their VL is suppressed at 3-months on ART.

5 Documentation that the woman has been counselled and consents to receive DTG must be included in the patient's chart/file.

6 If a woman's fertility intentions change and she is concerned about the risk of NTDs, she can be offered a switch from TLD to TEE, provided that she has a suppressed VL in the last 6 months

ART Initiation in Special Populations

For ART initiation in **neonates**, see page 96
For ART initiation in a **pregnant or breastfeeding women**, see page 75
For ART initiation in women and girls diagnosed during labour, see page 70

Dual Treatment of HIV and Active TB in Neonates, Infants, Children, Adolescents, and Adults

1 **The timing of ART initiation** (see "Indications to defer ART" on page 25)

2 **Drug selection** in clients who are not yet on ART when TB treatment is initiated

3 Drug levels, due to significant **drug interactions** that reduce ART concentrations in the blood

4 **Adherence**, due to increased pill burden

5 **Side-effects** due to overlapping toxicities, e.g. hepatic toxicity

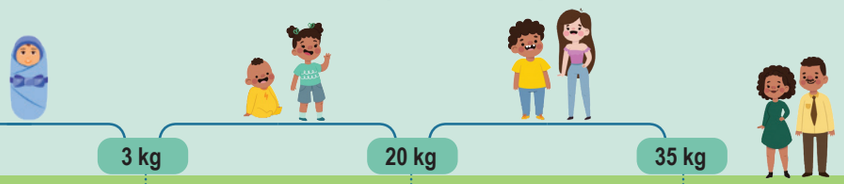
Efavirenz has no significant interaction with rifampicin

Adult clients **who are not yet on ART** when TB treatment is initiated should initiate ART with an EFV-containing regimen.
Adults who are **already on an EFV-containing regimen** when TB treatment is initiated should continue the EFV-containing regimen whilst also taking TB treatment.

In both these situations, the EFV-containing regimen should be continued until two weeks after TB treatment is completed. Thereafter, EFV can be switched to DTG, provided that the process has been followed as outlined in "Switching Stable Clients on ART Between First-Line Regimens" on page 40.

Drug Interactions

Rifampicin-containing TB treatment has significant drug interactions with all paediatric ART regimens, as well as with adult/adolescent regimens containing DTG:



	2.5 kg	3 kg	20 kg	35 kg
ART Regimen	**Neonates** AZT + 3TC + NVP	**Infants and Children** ABC + 3TC + LPV/r	**Children** ABC + 3TC + DTG	**Adolescents and Adults** TDF + 3TC + DTG
Significant drug interaction	! Rifampicin + NVP	! Rifampicin + LPV/r	! Rifampicin + DTG	

Measures to counteract drug interactions with rifampicin

Seek expert advice

LPV/r tablets: Double-dose LPV/r tablets
(See Dosing Chart on page 94). Tablets can be used only if the child is able to swallow whole LPV/r tablets (tablet must not be crushed, broken or chewed).
If the child is unable to tolerate LPV/r at double doses, consult one of the helplines provided on page 42.
LPV/r solution: Super-boosting with additional ritonavir solution or ritonavir powder: maintain standard LPV/r dose but add additional ritonavir twice daily as per Dosing Chart on page 94. If no ritonavir solution or powder is available, consult an expert for a suitable alternative. Ritonavir solution has a shelf-life of only 6 months, whereas ritonavir powder has a shelf-life of 36 months. Note that ritonavir 100 mg tablets must not be crushed, broken or chewed.

Boosting of DTG required
The dosing frequency of DTG should be increased to 50 mg 12-hourly.
If on TLD FDC, then add DTG 50 mg 12 hours after TLD dose

Continue boosting the ART regimen until 2 weeks after stopping rifampicin

ART Dosages, Substitutions, and Side-Effects

For a **summary of dosages, common side effects, and substitutions associated with first- and second-line ART in adults and adolescents**, see page 93
For dosages in children see the **Paediatric ART Dosing Chart** on page 94
For more detail on **ART side effects** see page 46

ART Initiation Step 4: Interventions to support adherence to ART and retention in care

ART education and adherence interventions positively influence adherence outcomes, but lengthy counseling processes that delay ART initiation should be avoided. Conversely, same-day ART initiation is not an adherence support 'short-cut'; ongoing support can occur in the days and weeks immediately after initiation. **Adherence counseling at ART** initiation should focus on:

- providing the client with an understanding of HIV, ART, and the importance of VL suppression
- providing the client with practical skills to adhere to ART
- identifying any potential risk factors for adherence in the future
- An individualized adherence plan should be developed with clear treatment milestones, including an undetectable viral load

Key adherence messages are outlined on the next page.

Child and adolescent disclosure for children living with HIV is a crucial component of ensuring long term adherence in children and adolescents. Child disclosure focuses on the following:

- Disclosure should be addressed pro-actively and should be part of routine support offered by the health worker.
- Caregivers should be educated on the importance and the advantages of progressive disclosure and involved them in the process.
- A step by step approach to disclosure should be applied, providing education on HIV and ART in adapted language that respects the needs of the child.
- Start partial disclosure from the ages of 3 and ensure full disclosure by the age of 10-12.

For a step by step guide to disclosure counseling in children, see Annexure 6 on page 98.

Adherence in young children can be further complicated by unpalatable medications. For practical advice on the administration of ART medications in children, see page 95.

Routine viral load monitoring provides a means of confirming good adherence and viral suppression or timeously detecting clients in need of enhanced adherence support.

Enhanced Adherence Counselling (EAC) is aimed at non-stable clients presenting with adherence issues or poor treatment response and/or signs of treatment failure. Enhance Adherence Counselling focuses on:

- finding patients with less optimal outcomes (e.g., high viral load) and/or adherence problems and referring them for support as soon as possible
- providing education on the outcome of their latest clinical assessment
- assessing the barriers to adherence (including misconceptions and fears linked to taking their medication in case of alcohol or substance consumption or forgetting doses)
- providing information to the patients about their condition and their results
- correcting any misconceptions and allowing flexibility around the most common barriers to adherence (such as alcohol/ drug consumption, forgetting doses due to a rigid schedule, etc.).

- understanding the barriers that affect the client's adherence and developing adherence strategies to overcome these barriers.

Early missed appointment tracing should be in place to ensure that non-attending clients are identified and recalled to the clinic, and that blood results are reviewed and acted on timeously. For further detail on structuring fast track adherence counseling and EAC sessions, and a template for documenting an individualized adherence plan, please refer to the National Adherence Guideline.

Key Adherence Messages (National Adherence Guideline)

STEP 1 EDUCATION ABOUT HIV

- What does HIV do to your body?
- How taking ART can help you?
- The importance of VL suppressions for mother and baby.
- Risks of poor adherence.
- Side-effects of ART.

STEP 2 IDENTIFY LIFE GOALS

- What are the things that make you want to stay healthy and alive?

STEP 3 IDENTIFY SUPPORT SYSTEMS

- Who could support you in taking your treatment?
- Would you agree to have a CHW visit you at home?

STEP 4 COMING TO YOUR APPOINTMENTS

- What will you do if something prevents you from coming to your appointment (such as no money for transport, raining when you usually walk, taxi strike or a sick child, or any other reason)?
- Go to the clinick as soon as possible if you do miss an appointment or run out of ART
- Always take your medication with you to your clinic appointments to enable the HCW to better assist you

STEP 5 ASSESS READINESS TO START ART

- Do you feel ready to start treatment as soon as possible?
  If not, stay supportive. Invite client to express their beliefs or concerns. Correct misconceptions (avoiding judgments).

! Do not turn away an ART client who reports to have run out of treatment and presents without a transfer letter!

STEP 6 MEDICATION SCHEDULE

- According to your schedule, what oould be the best time for you to take your treatment?

STEP 7 REMILLDERS

- What could you use to remind you to take your medication? (e.g. alarm, someone to remind them, when "Generations" is starting on TV, etc.)

STEP 8 MISSED DOSES

- What will you do if you miss a dose? *Advise them to take the treatment as soon as they remember.*

STEP 9 STORING YOUR MEDICATION AND EXTRA DOSES

- Do you worry about people seeing or stealing your treatment?
- Which safe place could you identify to store your treatment? Check that it is outside the reach of children.
- In case you don't have access to your treatment at the time you are supposed to take it, how can you always carry 1 or 2 doses with you?

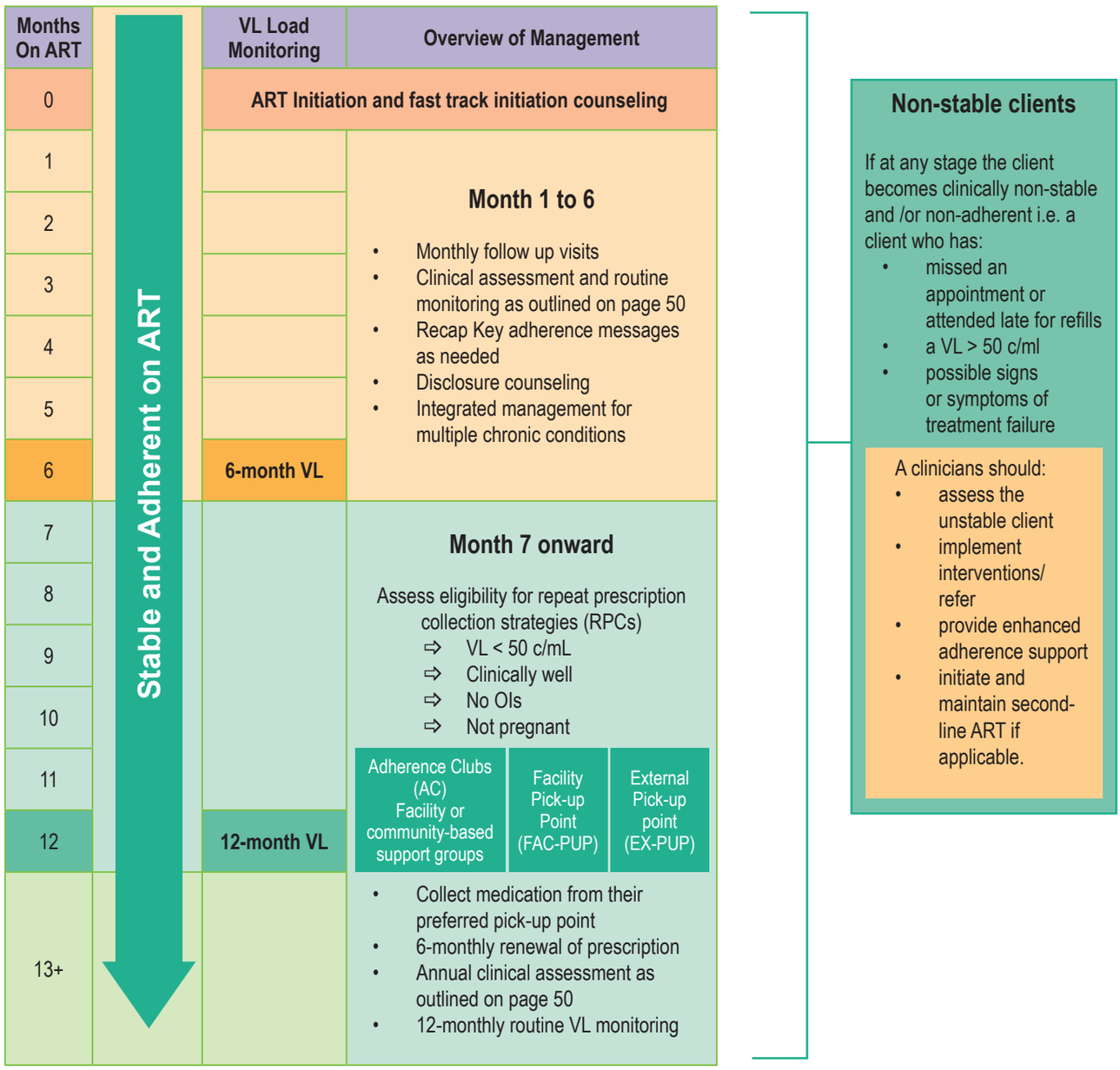
STEP 10 MANAGING SIDE-EFFECTS

- Side·effects such as dizziness, nausea, headache or diarrhea can happen when starting treatment. Most side-effects go away after a few weeks. If you don't vomit up to one hour after taking the medication, take your treatment again. Severe side-effecls are rare. If you don't feel well, it is important you don't stop your treatment and come to the clinic.

MANAGING A CLIENT ON ART

Summary of the Care Continuum for Adult Clients on ART

Clients on ART can be differentiated into those who are 1) clinically well and adherent on ART and 2) those who are non-stable and/or non-adherent. Clients that are well and adherent will continue to see a clinician until they have been on ART for at least 6 months. After that, taking treatment and clinical follow-up should be made as convenient as possible for the client. Therefore, they may continue to receive ART using a differentiated care approach, provided they meet the eligibility criteria of 1) having a suppressed VL, 2) being clinically well with no opportunistic infections (OIs), and 3) not being pregnant. The diagram below provides a summary of the components of care at different visits until the client becomes eligible for alternative repeat prescription strategies. For more detail on repeat prescription strategies, see the National Adherence Guideline and relevant standard operating procedures (SOPs), as well as annexure 10 on page 102: Differentiated models of care (DMoC) Standard Operating Procedures



Summary of the Visit Frequency for Children and Adolescents Clients on ART

Children < 6 months should have a clinic visit at least monthly.
Children 6 to 23 months should have a clinical visit 1-2 monthly, at the clinician's discretion.
Children 2 to 5 years should have a clinical visit at least every three months.
Children > 5 years should have a clinical visit every three months until they are on adult doses. For school-age children and adolescents, appointments should be booked outside school hours whenever possible.
Adolescents who are on adult doses and who are fully disclosed are eligible for alternative prescription collection strategies, provided they meet the eligibility criteria for a stable client.

Monitoring a Client on ART

Providing quality care at the follow-up visit is essential to promote adherence, achieve and sustain viral suppression, minimise side-effects and toxicities, and promote quality of life. A client on ART should be monitored to:

1. Determine clinical response to ART
2. Determine the virological and immunological response to ART
3. Detect and manage any side-effects and toxicities

1 Determine clinical response to ART

The following components should be included in the **clinical assessment:**

Weight (adults)
An assessment of trends in weight in adults

Growth and neurodevelopment (children)
An assessment of trends in weight, height, head circumference, and neurodevelopment

! Remember to adjust ART dosage according to weight!

Screen for TB and other OIs:
to diagnose and provide treatment;
to adjust ART regimen if required;
to determine if TB preventive therapy is required

WHO clinical staging
to determine response to ART, and CPT eligibility

Screen for pregnancy and ask if planning to conceive as outlined in the table for "Baseline Clinical Evaluation" on page 21

2 Determine the virological and immunological response to ART

Viral load should be measured to timeously detect problems with adherence or treatment failure

At month 6 on ART and month 12 on ART
Thereafter, if virally suppressed, repeat every 12 months

! Remember, an elevated VL is a medical emergency! Assess and manage according to the "Management of VL results" algorithm on page 42

The CD4 count
should be measured to monitor susceptibility to opportunistic infections and eligibility for CPT

At month 12 on ART
Thereafter, repeat every 6 months until client meets criteria to discontinue CPT. Stop CD4 monitoring if client's VL remains below 1000 c/mL.
If VL ≥1000 c/mL, monitor CD4 count every 6 months.

3 Detect and manage any side-effects and toxicities

Side-effects and ART toxicities can affect adherence and endanger the client's health:

Drug side-effects
Ask about side-effects at each visit (e.g. sleep or gastrointestinal disturbances)

TDF-induced nephrotoxicity
If on TDF, do creatinine and eGFR* at months 3, 6 and 12
Thereafter, repeat every 12 months

Dyslipidaemia
If on a PI-based regimen (LPV/r, ATV/r, DRV/r), do total cholesterol and triglycerides (TGs) at month 3
If above acceptable range, do fasting cholesterol and TGs and if still above acceptable range, obtain expert advice

Anaemia and neutropaenia
If on AZT, do a full blood count and differential white cell count at months 3 and 6
Thereafter, repeat if clinically indicated

For VL monitoring in pregnant women, see page 77

For the table on Assessing Renal Function, see page 24

In children, collecting blood for VL monitoring can be difficult, and sample rejection rates are high. For this reason, blood for VL monitoring can be collected using a heel or finger prick to collect a minimum of 500 µl (1 full EDTA microtainer) of capillary blood. However, a 1ml sample (2 full EDTA microtainers) is preferred.

Lab results, e.g. creatinine levels, can be abnormal if sample processing is delayed. In general, if results do not correlate with the clinical picture, consider repeating the test. If in doubt, consult one of the helplines provided on page 42.

Principles of Viral Load Monitoring

Achieving and maintaining VL suppression is the first goal of ART and fundamental to good patient outcomes

This guideline uses two VL thresholds:

1. VL < 50 c/mL: This is the threshold for defining VL suppression (previously < 400 c/mL)
2. VL ≥ 1000 c/mL: This is the threshold for defining failure (unchanged from the previous guideline)

Principle 1: Any VL more than 50 c/mL requires action

A VL ≥ 50 c/mL implies that viral replication is taking place in the presence of ART and puts the client at risk of developing treatment resistance. A VL between 50 and 999 may be a viral "blip" that returns to levels below 50 c/mL. Alternatively, the client may be progressing to failure with VLs over 1000 c/ml. A VL of ≥1000 is a medical emergency and may require a full regimen change to second-line ART. **It is therefore important to do a thorough assessment (see** page **39) to identify any modifiable factors leading to the elevated VL as early as possible so that viral suppression can be regained as a matter of urgency.** A small number of clients may maintain a persistent low-level viraemia.

VL > 50 c/mL → Assess (ABCDE) → Intervene → Repeat VL after 3 months to determine if intervention has worked

Principle 2: Never change one drug in a failing regimen (VL > 1000)

If a single drug substitution is made within a failing regimen, the new drug may be the only active drug in the regimen. The client will effectively be on monotherapy, as only one drug may be working. The Dawning study showed that dolutegravir needs to be combined with at least one active NRTI in a treatment regimen for long term virological suppression and to prevent the development of dolutegravir resistance.

An immediate single drug substitution, therefore, requires a VL < 50 c/mL in the last six months. However, someone with a first VL between 50 and 999 may be progressing to failure. They may also return to viral suppression. Therefore, we must exclude that they are not progressing to outright failure by doing a thorough assessment (ABCDE) and repeating the VL in 3 months. If their VL does not progress to over 1000 c/mL at the repeat VL, they can be considered for a single drug switch. If they have two VL's ≥ 1000, they can be switched to DTG, but a full regimen change must be made, including changes in the NRTI backbone (i.e., a switch to second-line ART).

Principle 3: Eligibility for second-line ART will be determined by the client's VL, the current regimen they are failing, and the time they have been on ART

The definition of "confirmed virological failure" remains the same for NNRTI-based regimens, i.e., two VLs ≥ 1000 c/mL on at least two consecutive occasions. However, due to their high genetic barrier to resistance, resistance to DTG and the protease inhibitors (PIs) develops very slowly. An elevated VL on DTG or LPV/r is, therefore, more likely to be related to **suboptimal adherence**. This provides a window of opportunity to address adherence issues, re-suppress the viral load, and prevent the development of resistance. A client should be on DTG or LPV/r for at least two years before considering a switch to second-line ART. Confirmed virological failure for a client on a DTG or PI-based regimen is defined as a VL ≥ 1000 c/mL on at least three occasions over two years, or VL ≥ 1000 c/mL with signs of immunological or clinical failure (i.e., declining CD4 and/or opportunistic infections). Every effort should be made to improve adherence in these clients, while at the same time keeping partners and unborn/breastfeeding children safe by reinforcing condom use, use of prophylaxis in children, and providing feeding advice as appropriate. VL's should not be repeated more frequently than every six months during this period. However, if the client has been on rifampicin at the same time as DTG or a PI and is failing their regimen, consult an expert to determine if resistance testing is indicated before two years on the regimen.

Assessing a Client with an elevated VL

TABLE 13 ASSESSING AN ELEVATED VL

!	**A thorough assessment is essential for any client with a viral load measuring ≥ 50 c/ml**	
A **Adherence**	Is adherence to medication poor? Ask about factors that may influence adherence e.g. • Medication side-effects, • Depression, • Alcohol or substance abuse, • Poor social support or • Non-disclosure. Pregnant women may experience nausea, heartburn, and constipation. Assess the need for symptomatic treatment with an anti-emetic, anti-diarrhea agent, or fiber supplement.	**Tips** Ask open ended questions e.g. "What makes it difficult for you to take your treatment?", and "How many doses have you missed this week?" Be non-judgemental. Statements like "we all miss a dose now and then" can encourage a client to be more open.
B **Bugs (Infections)**	Check for symptoms and signs of infection. Do a TB and STI screen.	Remember that immune compromised and pregnant clients may not exhibit overt symptoms of TB. If in doubt, do a TB GXP.
C **Correct Dose**	Is the client on the correct dose for her weight? This is especially applicable to young or malnourished girls who may have recently gained weight, or clients with previous renal impairment.	
D **Drug Interactions**	Are there any potential drug interactions? Consider: • Other prescribed treatment e.g. rifampicin, anti-epilepsy drugs • Over the counter treatment e.g. antacids • Supplements and herbal/traditional medications e.g. St John's wort	If in any doubt, call the **HIV Hotline** **0800 212 506** or any of the helplines provided on page 42
E **REsistance**	Consider HIV drug resistance if other causes of virological failure have been excluded and the client is adherent to their medication. The need for 2nd-line ART is determined by her current regimen and how long she has been on ART.	Refer to the 2019 Consolidated ART Guideline for further management

TRANSITIONING ADULTS AND ADOLESCENTS WHO ARE ON FIRST-LINE NNRTI-BASED ADULT REGIMENS TO DTG-CONTAINING REGIMENS (SINGLED DRUG SUBSTITUTION)

Switching Adults, and Adolescents who are on First-line Adult Regimens

Routine VL Monitoring:
(First VL at 6 months on ART. If virally suppressed (< 50 c/mL), repeat VL at 12 months on ART, and 12-monthly thereafter if viral load remains suppressed)

Check if client has a VL result in the last 6 months*

VL < 50 c/mL

VL 50 - 999 c/mL⁺

VL ≥ 1000 c/mL

Do a thorough assessment of the cause of an elevated VL as outlined on page 39
Implement interventions and provide enhanced adherence support
Repeat VL in 3 months

Ensure that the elevated VL is correctly managed according to the **VL results management algorithm** on page 42
Do not switch to DTG at this time

VL 50 - 999 c/mL

Provide information on the risks and benefits of DTG, and the use of contraception in WOCP (see page 30). Enable the client to make an informed decision.

Client chooses to remain on their current regimen

Client chooses to switch to DTG

If current regimen is TDF + 3TC/FTC + EFV/NVP

Switch to TDF + 3TC/FTC + DTG[1]

If current regimen is AZT/ABC [2] + 3TC + EFV/NVP

Switch to AZT/ABC + 3TC + DTG[1]

Only switch a **stable pregnant woman** on ART from EFV to DTG if her VL is < 50 copies/mL, and she **is no longer in the** first 6 weeks of pregnancy. A switch to DTG needs to be preceded by WOCP being given all necessary information on DTG and EFV-based regimens including the risk of NTDs. Discuss postpartum contraceptive options and allow her to make an informed choice.

! Warn the client of the new side-effects that may be experienced when switching to DTG (insomnia, headache, GIT disturbances). These are usually mild and self-limiting. If the client experiences insomnia, DTG can be taken in the morning.

! *If a client has not had a VL test in the last 6 months, additional VL testing outside of the routine VL monitoring schedule should NOT be done. The client should await the result of their routine annual VL test to determine their eligibility to switch to DTG.

⁺Clients on CCMDD can be considered for a switch to TLD and remain on CCMDD if they have a VL < 50 c/mL in the last 6 months. For more information see the TLD Transition Guide for Implementers, or the CCMDD SOP: Changing of ARV regimen from TEE to TLD (CCMDD SOP-16).

1 Discuss and provide sexual and reproductive health services for the sexually active adolescent/adult.

2 Assess the reason for the exclusion of TDF from the NRTI backbone. If TDF was excluded due to TDF-induced nephrotoxicity, continue using the same NRTI backbone. If TDF was excluded due to non-TDF related renal failure that has since resolved, the use of TDF can be reconsidered. Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in the table "Assessing Renal Function" on page 24

TRANSITIONING CHILDREN AND ADOLESCENTS ON FIRST-LINE PAEDIATRIC REGIMENS TO DTG-CONTAINING REGIMENS (SINGLED DRUG SUBSTITUTION)

Switching Children and Adolescents who are on First-Line Paediatric Regimens

Children and adolescents currently on the following first-line regimens and weighing ≥ 20 kg:

ABC + 3TC + LPV/r[1] or ABC + 3TC + EFV

Routine VL Monitoring:
(First VL at 6 months on ART. If virally suppressed (< 50 c/mL), repeat VL at 12 months on ART, and 12-monthly thereafter if viral load remains suppressed)

Check if client has a VL result in the last 6 months*

VL < 50 c/mL

VL 50 - 999 c/mL

Do a thorough assessment of the cause of an elevated VL as outlined on page 39
Implement interventions and provide enhanced adherence support
Repeat VL in 3 months

VL 50 - 999 c/mL

VL ≥ 1000 c/mL

Ensure that the elevated VL is correctly managed according to the **VL results management algorithm** on page 42
Do not switch to DTG at this time

Provide information on the risks and benefits of DTG, and the implications for childbearing in later years (see "Dolutegravir" on page 30).
Enable the caregiver/adolescent to make an informed decision

Client chooses to remain on their current regimen

Caregiver/adolescent chooses to switch to DTG

Weight ≥ 20 kg and < 35 kg, or < 10 years of age

Weight ≥ 35 kg and age ≥ 10 years, and renal function normal[3]

ABC + 3TC + DTG[2]

Renal function abnormal

If weight reaches 35 kg or more, and VL < 50 c/mL in the last 6 months, and renal function is normal[3]

TDF[3] + 3TC + DTG[2]

! *If a client has not had a VL test in the last 6 months, additional VL testing outside of the routine VL monitoring schedule should NOT be done. The client should await the result of their routine annual VL test to determine their eligibility to switch to DTG.

1 Switching LPV/r to DTG in this regimen applies strictly to first-line regimens only. If ABC + 3TC + LPV/r is used as a second-line regimen, it is possible that both NRTIs in the regimen are inactive. DTG should not be used without at least 1 active NRTI. If DTG is to be considered within a second-line regimen, expert guidance should be sought to ensure that at least 1 NRTI is active.

2 Discuss and provide sexual and reproductive health services for the sexually active adolescent/adult.

3 Before switching to TDF, ensure adequate renal function by checking eGFR/creatinine as outlined in the table "Assessing Renal Function" on page 24

MANAGEMENT OF VIRAL LOAD RESULTS IN INFANTS, CHILDREN, ADOLESCENTS, AND ADULTS

Routine VL monitoring at 6 months on ART, 12 months on ART, and 12-monthly thereafter

VL < 50 c/mL	VL 50 - 999 c/mL	VL ≥ 1000 c/mL
Continue routine VL monitoring	Do a thorough assessment of the cause of an elevated VL. Consider the possibility of: A. **A**dherence problems B. **B**ugs (Intercurrent infections) C. In-**C**orrect ART dosage D. **D**rug Interactions E. R**E**sistance	

Implement interventions to re-suppress the VL, including **enhanced adherence support** as outlined in the **Adherence Guideline for HIV, TB and NCDs**

Repeat VL after 3 months

VL < 50 c/mL	VL 50 - 999 c/mL	VL ≥ 1000 c/mL
Continue routine VL monitoring	Continue enhanced adherence support Repeat VL in 6 months#	**NNRTI-based regimen (EFV/NVP)** Consider switching to second-line if virological failure confirmed, i.e. VL ≥ 1000 c/mL on **two consecutive occasions** and adherence issues addressed **InSTI (DTG) or PI-based regimen*** Consider switching to second-line if virological failure confirmed, i.e. VL ≥ 1000 c/mL on at least **three occasions over the course of two years,** or VL ≥ 1000 c/mL with signs of **immunological or clinical failure** (i.e. declining CD4 and/or opportunistic infections)

* Due to their high genetic barrier, resistance to DTG and PIs develops very slowly. An elevated VL on DTG or LPV/r is therefore more likely to be related to suboptimal adherence. For this reason, a client should be on DTG or LPV/r for at least 2 years before considering a switch to second-line.

#Clients who have persistent low grade viraemia of between 50 - 999 c/mL should be discussed with one of the helplines listed below on a case-by-case basis. If the client is still on an NNRTI based regimen, a single drug switch to DTG can be considered as outlined in the switching algorithm on page 40

For second and third-line regimens, go to page 44

If in doubt about any aspect of viral load management or switching to second-line, contact one of the following resources:
National HIV & TB Health Care Worker Hotline: **0800 212 506**
Right to Care Adult HIV Helpline: **082 957 6698**
Right to Care Paediatric and Adolescent HIV Helpline: **082 352 6642**
KZN Paediatric Hotline: **0800 006 603**

For the management of an elevated VL in a pregnant woman, see page 79

Clients with a repeat VL of between 50 and 999 c/mL

The results of the viral load repeated after three months may have one of the following results:

- They may revert to VL < 50 c/mL, or
- They may progress to VL ≥ 1000 c/mL, or
- A small minority may be found in the 50 - 1000 category (yellow block in the algorithm).

The latter group who have a repeat VL result between 50 and 999 may fall into two categories:

A. Those with persistent low-grade vireamia (defined as at least 2 VLs in the range of 50-999 c/ml)

These clients had a first VL of between 50 and 999 c/mL, and their repeat VL after three months remained in the range of 50 -999 c/mL.

- If they are on DTG/PI based regimen, they should continue to have enhanced adherence support and have their VL repeated in 6 months. They may be discussed with an expert, but they are unlikely to have any regimen changes if they have not been on a PI/DTG based regimen for at least two years.
- If they are still on an NNRTI-based regimen and their second VL remains in the 50-999 category (i.e., persistent low-grade viraemia), they may do a single drug switch to TLD. This is consistent with the switching algorithm on page 40, as we have excluded that they are progressing to a VL of ≥ 1000 c/ml and outright failure.

B. Those that are still on an NNRTI-based regimen and who's second VL goes back into the 50-999 c/mL range

These clients had a first VL of ≥ 1000 c/mL, but after interventions, it re-suppressed to below 1000 c/mL again:

- These clients may also do a single drug switch to TLD as we have been able to re-suppress them. If a client's VL can be re-suppressed to below 1000 with improved adherence, the risk of having both a K65R mutation to TDF and an M184V mutation to 3TC is very low.

The overarching message is that a single drug substitution from EFV to DTG can be made provided we have excluded outright failure by proving that their VL's are not persistently over 1000.

Remember that a switch from an EFV-containing regimen to a DTG-containing regimen should always be accompanied by the following:

- Counseling on the risks and benefits of DTG vs. EFV, and the low risk for NTDs in subsequent pregnancies in WOCP
- Counseling on contraception for WOCP
- A check for potential drug interactions
- A warning to the client about new side effects that may be experienced when switching to a new drug
- The client making an informed a choice regarding their preferred regimen

SECOND- AND THIRD-LINE ART REGIMENS FOR CLIENTS WITH CONFIRMED VIROLOGICAL FAILURE

TABLE 14 SECOND-LINE ART REGIMENS FOR ADULTS

	First-Line Regimens				Second-Line Regimens	
	NNRTI-based Regimen		InSTI-based Regimen for > 2 years		PI-based or InSTI-based Regimen for > 2 years	
Regimen	TDF + 3TC/FTC + EFV/NVP		TDF + 3TC/FTC + DTG		AZT/TDF + 3TC/FTC + LPV/r or ATV/r or DTG	
Resistance Testing	Resistance test not required		Resistance testing not required[4]		Resistance test required	
Resistance Test results	Not applicable		Not applicable		No PI or InSTI resistance	PI or InSTI resistance
HBV Co-infection Status [1]	HBV-negative	HBV-positive	HBV-negative	HBV-positive	HBV-positive or -negative	
New Regimen	AZT + 3TC/FTC + DTG[2]	TDF[1] + AZT + 3TC/FTC + DTG[2]	AZT + 3TC/FTC + LPV/r	TDF + 3TC/FTC + LPV/r [3]	Continue current regimen and address adherence. If intolerance to LPV/r is affecting adherence, discuss possible substitutions with an expert	Refer to Third-Line Committee. Regimen will be determined by results of resistance test
	If DTG not suitable[2], AZT + 3TC/FTC + LPV/r	If DTG not suitable[2], TDF + 3TC + LPV/r[3]				

TABLE 15 SECOND AND THIRD-LINE ART REGIMENS FOR CHILDREN AND ADOLESCENTS

All children and adolescents with confirmed virological failure should be discussed with an expert.

	NNRTI-based Regimen		PI-based Regimen for > 2 years			InSTI-based Regimen for > 2 years	
Regimen	ABC/AZT/TDF + 3TC/FTC + EFV/NVP		ABC/AZT/TDF + 3TC/FTC + LPV/r or ATV/r			ABC/AZT/TDF + 3TC/FTC + DTG	
Resistance Testing	Resistance test not required		Resistance test required			Resistance test required	
Resistance Test Results	Not applicable		No PI resistance		PI resistance (or genotype unsuccessful)	No InSTI resistance	InSTI resistance
Weight	< 20 kg	≥ 20 kg	< 20 kg	≥ 20 kg	All	All children/adolescents on DTG will be ≥ 20 kg	
New Regimen or Other Action Required	ABC/AZT + 3TC + LPV/r [3]	2 NRTIs + DTG[2] In consultation with an expert, ensure that at least 1 NRTI is active[5, 6]	Continue current regimen and address adherence	2 NRTIs + DTG[2] In consultation with an expert, ensure that at least 1 NRTI is active[5]	Refer to Third- line committee	2 NRTIs + DTG[2] In consultation with an expert, ensure that at least 1 NRTI is active[5]	Refer to Third-line committee
		If NRTI activity cannot be confirmed, expert will recommend **2 NRTIs + PI/r**		If NRTI activity cannot be confirmed, expert will recommend **2 NRTIs + PI/r**. Adherence must be addressed		If NRTI activity cannot be confirmed, refer to Third-line committee	

1 Always check hepatitis B status before stopping TDF. If a client has chronic hepatitis B, stopping TDF may lead to a severe hepatitis flare. If hepatitis B-positive, TDF should be continued in the second-line regimen.

2 Before DTG initiation, all women and adolescent girls of childbearing potential must be appropriately counseled on the potential risk of NTDs with DTG use around conception and within the first 6 weeks of pregnancy. They should be provided with contraceptives as desired (see "Using Dolutegravir in WOCP" on page 30).

3 In the EARNEST study, LPV/r was shown to be effective even if combined with two NRTIs that are known to have genotypic resistance.[7] For this reason, AZT is omitted from LPV/r-containing regimens when TDF is continued due to HBV co-infection. Resistant NRTIs may be recycled with an active PI if no other feasible options are available.

4 Current resources do not allow for resistance testing for adults and adolescents failing a first-line DTG-based regimen, and it is as yet unclear whether INSTI resistance testing is of any value in first-line DTG failure.

5 From the DAWNING study, DTG was shown to achieve viral suppression when used in combination with two NRTIs, at least one of which was fully active.[6] It is as yet unknown if DTG will work if combined with two NRTIs, neither of which are fully active.

6 For adolescents failing an ABC, 3TC and EFV containing regimen, TDF, 3TC and DTG (TLD) may be considered for their second-line regimen. Being a once daily, well tolerated regimen, TLD has significant adherence advantages, while the risk of cross-resistance between ABC and TDF is relatively low.

RESISTANCE TESTING

Indications for resistance testing in adults and adolescents

- Any client failing a PI-based regimen and who meets the definition of confirmed virological failure, i.e., a VL ≥ 1000 c/ml on at least three occasions over two years.
- Resistance testing for adults and adolescents failing a DTG-based regimen and who meet the definition of confirmed virological failure may be authorized by an expert on a case-by-case basis.
- Any adult with an elevated VL on a PI or DTG-based regimen (irrespective of time on the regimen) who received concurrent rifampicin-containing TB treatment and unboosted ART.
- Any newly diagnosed client who has received PrEP in the last six months

Indications for resistance testing in infants and children

- Any child failing a PI or DTG-based regimen and who meets the definition of confirmed virological failure, i.e., a VL ≥ 1000 c/ml on at least three occasions over two years.
- Any child with an elevated VL on a PI or DTG-based regimen (irrespective of time on the regimen) who received concurrent rifampicin-containing TB treatment and ART.
- Any newly diagnosed child < 2 years of age whose mother was receiving PI-based ART during pregnancy and/or during breastfeeding.

Third-line review committee

- The third-line review committee coordinates the management of patients failing a second-line DTG- or PI-based regimen
- Adults and children are considered to have confirmed virological failure if they have a VL ≥ 1000 c/mL on at least three occasions over two years, or VL ≥ 1000 c/mL with signs of immunological or clinical failure (i.e., declining CD4 and/or opportunistic infections).
- A full treatment history using the standard motivation form (see annexure 8 on page 101) must be submitted together with the resistance test result to the third line review committee for consideration. Once consensus is reached, a decision is conveyed to the provincial pharmacy and local facility with a recommended management plan. If third-line ART is indicated, the medication is ordered by the facility on a named patient basis.

Important considerations before doing a resistance test

- All indications for resistance testing should be discussed and confirmed with an expert. An expert is defined as an infectious disease (ID) specialist at the relevant referral hospital, one of the hotlines provided on page 42, or a member of the third-line committee.
- For best results, a client needs to be adherent to their regimen for at least 1 month prior to the resistance test.
- Resistance tests cannot be interpreted in isolation. If resistance to earlier antiretroviral medications has been detected on earlier resistance tests, assume those mutations are still present.
- A resistance test requires two EDTA tubes to be sent to the laboratory.

ART SIDE EFFECTS

- ARVs can cause a wide range of toxicities, from low-grade intolerance that may be self-limiting, to life-threatening side-effects.
- It may be difficult to differentiate between complications of HIV disease, ART toxicity, or adverse reactions to other medications.
- ARV toxicity can occur immediately, or early within the few days or weeks of treatment, or late, after months of treatment. It is important to know how long a client has been on a regimen to understand which toxicities might occur.
- Adverse reactions can vary in severity from mild to severe to life-threatening and may be specific to the drug or generic to the class of drugs in use.
- Side-effects are far less common in children than in adults.
- Generally, it is recommended that patients continue with the medication if the side-effects are mild.

Neural tube defects: DTG may increase the risk of neural tube defects (NTDs). The absolute risk is very low and translates into a risk difference of two additional NTDs per 1000 periconception exposures to DTG (0.3% risk), compared to EFV ART at conception (0.1% risk).5 DTG should be avoided periconception and in the first six weeks of pregnancy. The neural tube closes by the end of the sixth week of pregnancy (fourth week post-conception). DTG appears to be safe if started after the neural tube has closed. Women of childbearing potential (WOCP) should be counseled regarding the risk of NTDs and be allowed to make an informed choice. Contraception is recommended for all women who do not currently wish to become pregnant.

Weight gain: Weight gain has emerged as a side effect of the INSTI class of drugs; clients who are overweight should receive lifestyle interventions as outlined in the EML, and obese clients may be considered for EFV.

Increased creatinine due to DTG. DTG may cause a small increase in serum creatinine (usually ≤ 15%) because of interference with tubular secretion. This does not represent renal damage and is not an indication to discontinue DTG. A creatinine level that keeps on rising is, however, a cause for concern and could indicate TDF toxicity or other underlying pathology.

Renal tubular dysfunction due to TDF Regular monitoring of the estimated glomerular filtration rate (eGFR) is necessary, particularly if TDF is used with a PI such as lopinavir/ritonavir. Urine dipstix should be performed as per monitoring guidelines. eGFR should be measured at baseline (before ART initiation), three months, six months, 12 months, and 12-monthly after that. It is important that eGFR tests are followed up to ensure results are received as quickly as possible (preferably 1–4 weeks), and TDF replaced as needed. Renal function should be interpreted as per the table below.

***ASSESSING RENAL FUNCTION**

Age/pregnancy status	What must be measured?	Acceptable level for TDF use
> 10 and < 16 years of age	eGFR using Counahan Barratt formula	> 80 mL/min/1.73 m^2
Adults and adolescents ≥ 16 years	eGFR using MDRD equation[1]	> 50 mL/min/1.73m^2
Pregnant women	Absolute creatinine level	< 85 µmol/L

Counahan Barratt formula

$$\text{eGFR (mL/min/1.73 m}^2\text{)} = \frac{\text{height [cm]} \times 40}{\text{creatinine [µmol/L]}}$$

[1] Modification of Diet in Renal Disease Study (MDRD) equation. The MDRD formula is automatically calculated by the laboratory for those 18 years and older. For assistance in manually calculating the eGFR for adolescents between 16 and 18 years of age, please contact one of the helplines provided on page 42. Alternatively, use the calculator provided at https://www.mdcalc.com/mdrd-gfr-equation, or one of the numerous smartphone applications available for this purpose. Ensure that the website/application uses the correct unit of measurement (i.e. µmol/L) for the creatinine level.

Bone density reduction due to TDF. HIV itself is a risk factor for bone density reduction, but studies show an initial increase in bone loss, which seems to plateau after about 24 weeks. Any signs of possible osteoporosis (e.g., vertebrae, rib, hip, wrists or other fractures not adequately explained by the degree of trauma fractures) warrant investigation.

Anaemia. Patients should have a full clinical history, an examination, a full blood count (FBC), a peripheral blood smear, and reticulocyte count to characterize the anaemia and determine further investigations that may be needed. AZT should be avoided or used with caution and close monitoring in anaemic patients.

Anaemia is very common in patients with low CD4 counts. Those who are relatively asymptomatic or who have a serious opportunistic infection (OI) such as TB, that explains the anaemia, should have their ART started right away and monitored carefully. In other patients, an Hb < 8 g/dL with no clear cause should generally trigger additional investigations; usually, there is an underlying serious OI, often TB, and this requires urgent diagnosis and treatment. A low Hb is an independent poor prognostic factor in HIV, so these patients should not delay ART if at all possible.

Where anaemia occurs immediately after ART initiation, confirm that the Hb has dropped, by comparing previous results. Again, a full history, examination, and interpretation of an FBC/smear/reticulocyte count are helpful. Common causes of anaemia in the first few weeks and months of treatment include IRIS, disseminated TB, and AZT-containing regimens, although many other conditions can cause this.

Anaemia in patients established on ART is unusual and often suggests a serious OI or a condition unrelated to HIV. However, drugs should still be considered as AZT, pure red cell aplasia from 3TC or FTC, or cotrimoxazole may also cause FBC abnormalities.

Lipoatrophy is caused by NRTIs, i.e., AZT. Signs include loss of subcutaneous fat and facial wasting. It is important for clinicians to recognise signs of lipoatrophy, as they may contribute to body image problems, are stigmatizing, and can result in poor adherence.

Abacavir related hypersensitivity reaction (ABC HSR). ABC HSR is uncommon in Black African patients but may occur in up to 5% of Caucasian patients. It usually occurs within the first six weeks of initiation and is suspected with the presence of at least two symptoms from the following: fever, rash, constitutional symptoms, gastrointestinal symptoms, and respiratory symptoms. There is a strong association with HLA B5701 typing, rarely investigated locally.

The ABC HSR typically gets worse with each dose of ABC. If in doubt as to the cause of the symptoms, the client can be admitted to hospital and be given the next dose of ABC under direct observation. If ABC HSR develops, supportive therapy, usually including hospital admission, is required. ABC can be switched if the client is stable. However, all ART must be discontinued if the client is unstable. When the client has stabilized, ART can be restarted, but ABC must never be included in the regimen as re-exposure is potentially life-threatening.

Hyperlipidaemia. Protease inhibitors and stavudine are associated with increased risk of abnormal lipid profile. Lopinavir causes hypertriglyceridaemia.

Breast enlargement and lipomastia. Breast enlargement may be due to benign glandular breast tissue proliferation or abnormal fat deposition (lipomastia), or both. It occurs in both males (known as gynaecomastia) and females and can occur at any age. It has most consistently been associated with the use of EFV, although d4T and ddI have also been implicated. The onset occurs several months after initiation of ART, and it may be bilateral or unilateral. The mechanism appears to be related to oestrogen receptor activation in breast tissues by EFV.

In males, it is important to exclude other common causes of gynaecomastia, such as other medications (including spironolactone, calcium channel blockers, metoclopramide). A serum testosterone level is useful in excluding hypogonadism as a cause. If the serum testosterone is low, other appropriate investigations should be performed to identify the cause and manage accordingly. If the serum testosterone level is normal, then EFV should be substituted, bearing in mind the general principles of single-drug substitutions (patients who are virologically suppressed should be switched to DTG).

The resolution of gynaecomastia is generally slow, taking months and may be incomplete or may remain. It is, therefore, important to manage the expectations of the patient in this regard.

Hepatotoxicity is common with ARV drugs. NNRTIs and PIs are often associated with hepatotoxicity. InSTIs such as DTG have, on rare occasions, been associated with hepatotoxicity. TDF and AZT may cause lactic acidosis or severe hepatomegaly with steatosis. ATZ/r causes indirect hyperbilirubinaemia (clinical jaundice), which can be stigmatizing. RAL can cause hepatitis and hepatic failure. For these reasons, screening for symptoms of underlying liver disease is an integral part of PLHIV evaluation at presentation and prior to ART initiation. Routine monitoring of baseline ALT is not recommended unless indicated by the client's history or clinical examination.

Skin and hypersensitivity reactions are seen with the use of ARV drugs, particularly with NNRTIs (NVP, EFV). In addition, cotrimoxazole, ABC, DTG, DRV/r, and RAL are associated with varying degrees of skin and hypersensitivity reactions (mild to severe).

Immune Reconstitution Inflammatory Syndrome (IRIS). IRIS occurs when improving immune function unmasks a previously occult opportunistic infection, which subsequently presents with an unusually aggressive inflammatory presentation or causes paradoxical deterioration of an existing opportunistic disease.

- Patients with advanced HIV disease, particularly those with a CD4 count < 100 cells/μL, may become ill with IRIS, usually during the first three months of ART.
- Most cases can be managed on an outpatient basis with disease-specific therapies and anti-inflammatories. Very ill or complex patients may need to be referred for advice regarding investigation and management.
- TB is the most common IRIS reaction in South Africa. Some patients starting ART when on treatment for TB will experience recurrence or worsening of their TB symptoms/signs or new manifestations.
- The most common of these presentations is with enlarging lymph nodes, often with extensive caseous necrosis. In addition, respiratory symptoms, lung infiltrates, or effusions may worsen. It is important to exclude multi-drug resistant (MDR) TB in all these cases, as well as non-adherence to TB medication.
- MDR or extensively drug-resistant (XDR) TB needs to be excluded before IRIS is diagnosed. TB culture of sputum, blood, lymph nodes, and other affected tissue is essential.
- Opportunistic infections may also present in atypical ways during this phase of immune reconstitution.
- Rashes (including zoster, herpes, molluscum, and others) and cryptococcal meningitis that occur in the first weeks and months of ART initiation are other manifestations of IRIS.

IRIS is not indicative of drug failure or drug side effects. It is **not a reason to stop ART** or to change the ARV regimen. However, careful counseling is needed to ensure that the patient understands this.

PREVENTION, SCREENING, AND MANAGEMENT OF COMMON CO-INFECTIONS AND CO-MORBIDITIES

Various co-infections, co-morbidities, and other concomitant health conditions are common among PLHIV and have implications for their treatment and care, including the timing and choice of ARV drugs. Below is a brief overview of the most common and important conditions, with a focus on screening, prophylaxis, and timing of ART for these conditions.

Co-trimoxazole Prophylaxis (CPT)

Co-trimoxazole (CTX) is a fixed-dose combination of two antimicrobial agents, namely sulfamethoxazole (SMX) and trimethoprim (TMP). CPT is used to treat a variety of bacterial, fungal and protozoal infections, in particular, *pneumocystis jirovecii* (previously P. carinii) pneumonia (PJP) and toxoplasmosis.

The baseline clinical evaluation allows the determination of the client's WHO clinical stage. The WHO clinical stage, together with the CD4 count (or CD4 percentage in children under five years of age), will determine the clients' eligibility for cotrimoxazole preventive therapy (CPT). The table below presents the indications for CPT in infants, children, adolescents, and adults **living with HIV.**

TABLE 16 INDICATIONS FOR STARTING AND STOPPING CPT

AGE AND HIV STATUS	WHEN TO START	WHEN TO STOP
HIV-positive infant under 1 year of age	All children under 1 year should be on cotrimoxazole irrespective of CD4% or clinical stage	
HIV-positive child 1-5 years of age	CD4% ≤ 25 %, WHO Stage 2, 3, and 4	Discontinue if CD4 count > 25 %, regardless of clinical stage
HIV-positive child under 5 years of age with PJP infection	Start CPT after PJP treatment is completed	Continue CPT until 5 years of age and stop thereafter only if CD4 criteria in the older-than-five category are met
HIV-positive adults and children older than 5 years	CD4 count ≤ 200 cells/μL, WHO Stage 2, 3 and 4	Discontinue if CD4 count > 200 cells/μL, regardless of clinical stage

Certain clients may qualify for CPT based on their clinical stage, even though their CD4 count at CPT initiation was above 200. Such clients may stop CPT after receiving 6-12 months of ART, regardless of clinical stage.

HIV-exposed infants should initiate CPT at six weeks of age. CPT should be stopped when the PCR is negative ≥ six weeks after full cessation of breastfeeding, and the infant is clinically HIV negative. For further information on prophylaxis in the HIV-exposed infant, please see page 81.

TABLE 17 CPT DOSING CHART

WEIGHT BAND	ORAL DOSE, GIVEN ONCE DAILY	SUSPENSION 200 MG SMX/ 40 MG TMP PER 5 ML OR	SINGLE-STRENGTH TABLET 400 MG SMX/80 MG TMP OR	DOUBLE-STRENGTH TABLET 800 MG SMX/160 MG TMP
<5 kg	100 mg SMX/20 mg TMP	2.5 mL	¼ tablet	–
≥5 to <14 kg	200 mg SMX/40 mg TMP	5 mL	½ tablet	–
≥14 to <30 kg	400 mg SMX/80 mg TMP	10 mL	1 tablet	½ tablet
≥30 kg	800 mg SMX/160 mg TMP	–	2 tablets	1 tablet

Source: Paediatric Hospital EML Standard Treatment Guideline 2017 edition

TB Preventive Therapy

All clients starting ART, or already on ART, and who have not yet received TB Preventive Therapy (TPT), should be considered for TPT. Before initiating TPT, active TB should be ruled out by screening for TB.

A Tuberculin skin test (TST) is not required before starting TPT.

The TB APPRISE study, a randomized control trial, reported adverse pregnancy outcomes for women who received INH during pregnancy. Therefore, only pregnant women with CD4 counts below 350 c/μL, who are most at risk for TB and poor health outcomes, should be offered TPT. Those with a CD4 count greater than 350 c/μL should have TPT deferred until six weeks post-delivery

TABLE 18 TPT PER CATEGORY OF CLIENTS

Category of Client	Specific Eligibility Criteria	Treatment and Duration
Adult or adolescent > 15 years (non-pregnant)	Any CD4 count. Exclude active liver disease, alcohol abuse, or known hypersensitivity to isoniazid	Isoniazid, oral, 300 mg daily for 12 months and pyridoxine 25 mg daily
Children who are contacts of index TB cases	Children < 5 years (regardless of HIV status), and children 5-14 years who are HIV-positive	Isoniazid, oral, 10 mg/kg/day for 6 months (maximum dose 300 mg daily) and pyridoxine daily
Pregnant women	Eligible if CD4 count ≤ 350 cells/μL. If CD4 > 350 cells/uL, defer TPT till 6 weeks after delivery*	Isoniazid, oral, 300 mg daily for 12 months and pyridoxine 25 mg daily

TPT in Children

Give TPT to all children living with HIV, and all uninfected children < 5 years, who have been exposed to a close contact with infectious pulmonary TB (sputum microscopy smear-positive, culture-positive or M. tuberculosis PCR test positive), or who are newly found to be TST positive, but in whom no evidence of TB disease is present.

Repeat the course if an HIV-infected child is re-exposed to a TB contact at any point after completing TB treatment or prophylaxis. If the child has been exposed to a known MDR or XDR-TB source case or the source case has failed standard TB treatment, refer for an expert opinion.

Tuberculosis (TB)

People living with HIV have an increased risk of developing TB disease compared to people who are HIV-negative. Tuberculosis can occur at any point in the course of HIV infection. Pulmonary tuberculosis is the most common manifestation of tuberculosis in adults infected with HIV. The clinical pattern of tuberculosis correlates with the patient's immune status:

- in the early stages of HIV infection, when immunity is only partially compromised, the features are more typical of post-primary TB (i.e. similar to TB in non-HIV infected persons).
- As immune deficiency worsens, HIV-infected patients present with an atypical pulmonary disease resembling primary TB, or with extra-pulmonary TB or disseminated disease.

While the principles of TB diagnosis and treatment are similar for those clients living with HIV and those who are HIV-negative (see the National Tuberculosis Management Guidelines), clinicians should be aware of the following aspects that may delay TB diagnosis or complicate the management of a TB/HIV co-infected client:

- Clients living with HIV have reduced numbers of alveolar macrophages, are less likely to form cavities, and are more likely to have smear-or GeneXpert negative TB.
- The clinical presentation of TB is more likely to be atypical or at extra-pulmonary sites.
- TB/HIV co-infected clients have increased mortality due to faster TB disease progression and delayed diagnosis and treatment.
- Drug interactions and side-effects are more prevalent in TB/HIV coinfected patients
- Active TB increases HIV viral replication and accelerates HIV disease progression
- The risk for other opportunistic infections is higher in HIV/TB-co-infected persons than in HIV-positive persons without TB

Early identification of TB among PLHIV through careful assessment of symptoms and signs, diagnosis using Xpert MTB/RIF, and prompt initiation of anti-TB treatment is important to improve survival and quality of life as well as reduce transmission of TB.

TB Screening

Clients living with HIV should be screened for TB at every clinical encounter. The main symptoms of TB in adults and adolescents are:

- Persistent cough of 2 weeks or more or any duration if HIV positive
- Fever for more than two weeks
- Drenching night sweats
- Unexplained weight loss (more than 1.5 kg in a month)

The most common symptoms in children are:

- Cough of two weeks or more
- Persistent fever of more than two weeks
- Documented weight loss/ failure to thrive
- Fatigue (less playful/ always tired)

A productive cough, often accompanied by systemic symptoms such as fever, night sweats, or loss of weight, is the commonest presentation of pulmonary tuberculosis. Not all those with TB will have a cough; therefore, a high index of suspicion is required, particularly in PLHIV who may only have one of the above symptoms. Every patient with a positive symptom screen must be investigated appropriately, as outlined in the National Tuberculosis Management Guidelines.

TB is an important cause of maternal and infant mortality in pregnant and breastfeeding women. The possibility of TB and its prevention should be considered at every encounter during ANC, delivery, and in the postnatal period. However, new evidence has shown that screening for TB using a TB symptom screening may have lower sensitivity in pregnant women. For this reason, a TB GXP should be done for the following women, regardless of TB symptoms:

- Any pregnant women with a new HIV diagnosis
- Any known positive women (whether on ART or not on ART) with a new pregnancy diagnosis

For more information on **screening, diagnosing, and managing TB in pregnant women**, see page 87.
For the **dual treatment of HIV and active TB in neonates, children, adolescents and adults**, see page 32.

Cryptococcal Disease

Cryptococcal meningitis is a common opportunistic infection, and a leading cause of death in PLHIV before and after ART is initiated. The main reasons for this high death rate include late presentation and delayed diagnosis.

Prevention and Screening of Cryptococcal Disease

- HIV-positive adults and adolescents with a CD4 count <100 cells/µl should be screened for cryptococcal disease before initiating ART.
- A cryptococcal antigen (CrAg) assay is used to detect cryptococcal antigenaemia. A reflex CrAg test will be done automatically by the laboratory on all CD4 counts < 100 cells/µL.
- All clients, including pregnant women, with a positive cryptococcal antigen (CrAg) blood test have disseminated cryptococcal disease and should be referred for lumbar puncture (LP) to exclude cryptococcal meningitis.[13]
- If cryptococcal meningitis is confirmed on LP, patients should be managed in hospital (for at least two weeks), and ART deferred for four weeks.
- For CrAg-positive patients without suspected meningitis, oral fluconazole (1200 mg for two weeks, followed by standard consolidation and maintenance treatment) is recommended, as well as for patients with an LP that is cryptococcal test-negative.
- For patients without signs or evidence of meningitis, ART is recommended to be started two weeks after anti-fungal therapy is initiated.
- Fluconazole should be avoided in the 1st trimester, but pregnant women should be counselled that the benefits of fluconazole may outweigh the risks in the management of cryptococcosis.
- All pregnant women <20 weeks gestation exposed to fluconazole should have an ultrasound scan to detect congenital abnormalities.
- For management of breastfeeding mothers, consult a specialist, as fluconazole is present at concentrations similar to maternal plasma concentrations in breast milk that will be transmitted to the breastfed infant.
- Liver disease: evidence of clinical liver disease warrants careful monitoring because fluconazole may cause liver injury.
- Patients with a prior diagnosis of cryptococcal meningitis do not need to be screened.
- Screening and primary prophylaxis are not recommended for children under 10 years of age, given the low incidence of cryptococcal meningitis in this age group.

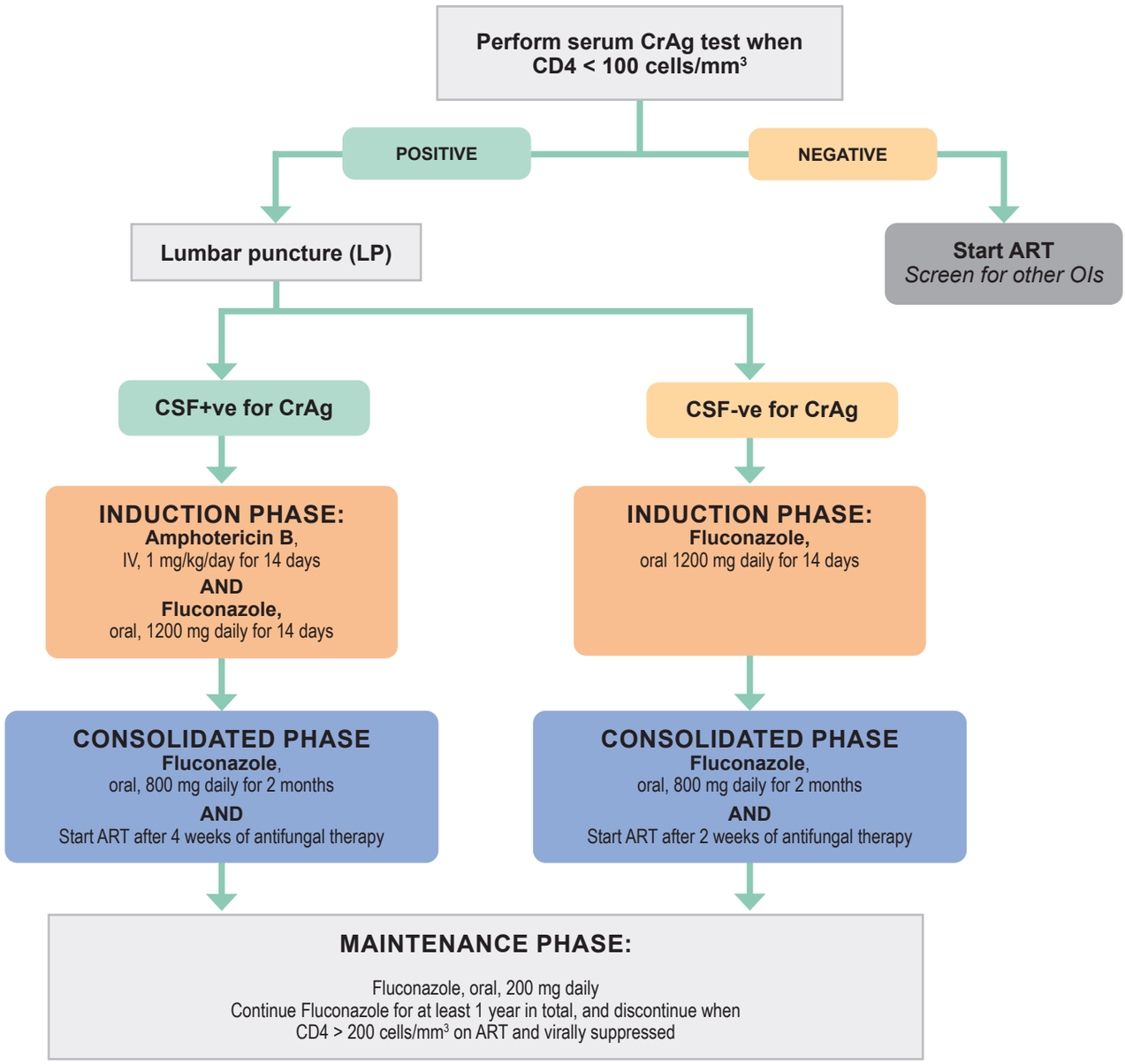
13. Republic of South Africa. Essential Drugs Programme. Hospital level (Adults) Standard Treatment Guidelines and Essential Medicines List. 5th ed. South Africa: National Department of Health; 2019.

Diagnosis of Cryptococcal Disease

For adults, adolescents and children living with HIV suspected of having a first episode of cryptococcal meningitis, prompt lumbar puncture with measurement of CSF opening pressure and rapid CSF cryptococcal antigen (CrAg) assay or rapid serum CrAg (either LA or LFA) is the preferred diagnostic approach

Treatment of Cryptococcal Disease

Treatment of symptomatic and asymptomatic clients with cryptococcal infection is outlined in the algorithm below:



Note: If there is a delay in performing LP, obtaining LP results or in starting amphotericin B therapy, start fluconazole 1200 mg immediately.

Adapted from: Govender NP, Meintjes G (Chairpersons), Bicanic T, Dawood H, Harrison TS, Jarvis JN, Karstaedt AS, Maartens G, McCarthy KM, Rabie H, Variava E, Venter WDF (Expert panel members), Boulware DR, Chiller T, Meya DB, Scriven J (Reviewers). Guideline for the prevention, diagnosis and management of cryptococcal meningitis among HIV-infected persons: 2013 update. S Afr J HIV Med 2013;14(2):76-86. http://www.sajhivmed.org.za/index.php/hivmed/article/view/82/128

Using Adjunctive Systemic Corticosteroids in Treating Cryptococcal Meningitis

Adjunctive corticosteroids have been shown to be detrimental. Therefore, routine use of adjunctive corticosteroid therapy during the induction phase is not recommended in treating HIV-associated cryptococcal meningitis among adults, adolescents, and children.

Timing of ART

For those clients with confirmed cryptococcal meningitis on lumbar puncture, ART initiation should be deferred by four weeks from the initiation of antifungal treatment. For asymptomatic clients and clients with a negative lumbar puncture, ART initiation should be deferred by two weeks from the initiation of antifungal treatment.

Management of Hepatitis B and C Coinfection

Increasingly, viral hepatitis is a cause of morbidity and mortality among PLHIV, including among people on ART.

Management of HIV and Hepatitis B Coinfection

HIV coinfection has a profound impact on the course of Hepatitis B virus (HBV) infection, including more rapid progression to cirrhosis and hepatocellular carcinoma, higher liver-related mortality, and decreased treatment response compared with HIV-negative people. Hepatitis B infection is unusual in children because children are immunized against Hepatitis B. However, any child with raised liver enzymes should be screened for Hepatitis B.

The use of NRTIs or entecavir is recommended in people with chronic hepatitis B infection. The recommended NRTI drugs for ART, namely, TDF with 3TC (or FTC), are active against HBV. However, only TDF is recommended for HBV mono-infection.

- Treatment of HIV-HBV coinfection without the use of TDF in the regimen may lead to flares of hepatitis B due to ART-associated immune reconstitution.
- Likewise, treatment discontinuation, especially of 3TC, has been associated with HBV reactivation, ALT flares, and in rare cases, hepatic decompensation.
- If ARV drugs need to be changed because of HIV drug resistance or toxicity, then TDF with 3TC (or FTC) should be continued together with the new ARV regimen.
- For children < 10 years or <35kg with Hepatitis B and HIV co-infection, an expert should be consulted.

The risk of HBV infection may be higher in HIV-infected adults and as such,

- All people newly diagnosed with HIV should be screened for hepatitis B surface antigen (HBsAg) and vaccinated if non-immune.
- People coinfected with HIV and HBV, with evidence of severe chronic liver disease, should be considered a priority for ART. High alanine aminotransferase (ALT) levels, hepatitis B e antigen (HBeAg) positivity, or high HBV DNA levels are not a contraindication or reason for delaying ART initiation.

Management of HIV and Hepatitis C coinfection

Hepatitis C virus (HCV)-related liver disease progresses more rapidly in people coinfected with HIV. Treatment of HCV is, therefore, a priority for people with HIV-HCV coinfection. The decision to initiate treatment for HCV in the latter population is more complex than in those with HCV mono-infection because response rates are lower, the risk of potential toxicities is higher, and treatment is complicated by a high pill burden, overlapping toxicities, and interactions between drugs used for treating HCV and HIV.

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

- Careful consideration of drug-drug interactions is important to avoid toxicity and to ensure the efficacy of regimens used to treat both HIV and HCV.
- HCV treatment using older regimens (pegylated interferon and ribavirin) has generally yielded low rates of success among HCV/HIV co-infected patients, but outcomes for HCV therapy with DAAs in people with HIV coinfection are comparable to those with HCV mono-infection.
- The newer all-oral DAAs also have fewer drug-drug interactions than earlier interferon-based regimens

The decision to start ART among people coinfected with HCV should follow the same principles as in HIV mono-infection.

- The potential harmful effects of ARV drugs include their hepatotoxic effects.
- The highest rates of hepatotoxicity have been observed with ARV drugs that are no longer commonly used or recommended, including stavudine, didanosine, and nevirapine.
- For most HIV-HCV coinfected people, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury (DILI).

Sexually Transmitted Infections (STIs)

The epidemiological synergy between HIV and STIs is well established, and they frequently coexist. Most of these infections are asymptomatic, especially among women. However, even asymptomatic STIs can cause complications, be transmitted to sexual partners, and enhance HIV transmission. There is empirical evidence that:

- Neisseria gonorrhoeae substantially increases the shedding of HIV-1 from the male genital tract in seminal fluid.
- Herpes simplex virus (HSV) is associated with increased acquisition and transmission of HIV. HIV infection may also alter the natural history of STIs.
- HIV infection changes the natural history of HSV infection, resulting in more frequent recurrences in coinfected individuals, many of which are subclinical.
- Serious clinical manifestations of HSV, human papillomavirus (HPV), syphilis, and other STIs are seen among people with advanced HIV disease.

From a WHO commissioned systematic review, the prevalence of STI among PLHIV on ART and not on ART was found to be equally high. This suggests that STI coinfection could undermine efforts to use ART for prevention unless STIs are appropriately treated.

- It is necessary to appropriately screen, diagnose, and treat STIs, especially among the most vulnerable populations and PLHIV.
- STI services should be an important part of comprehensive HIV care among adults and adolescents.

For further information on the syndromic management of STIs, see the Sexually Transmitted Infections Management Guidelines.

Cervical Cancer

Cervical cancer is a preventable disease and is curable if diagnosed and treated early. The most effective strategy available to primarily prevent this infection is by vaccination against the most common oncogenic HPV types, namely types 16 and 18. HPV vaccines are indicated for pre-pubertal girls and offer most hope to effectively stop the epidemic of cervical cancer in South Africa. Furthermore, studies have shown sufficient immune response in HIV positive children; hence they too can receive the HPV vaccine.

Women living with HIV (WLHIV) have a higher risk of pre-cancer and invasive cervical cancer. The risk and persistence of HPV infection increases with low CD4 count and high HIV viral load. Cervical cancer screening leads to early detection of precancerous and cancerous cervical lesions that will prevent serious morbidity and mortality.

- WLHIV should be screened every three years for evidence of precancerous changes in the cervix, regardless of whether they are taking ART or their CD4 count or viral load.
- All WLHIV should be screened for cervical cancer regardless of age.
- Immediate management for precancerous and cancerous lesions should be provided.

For more detail, refer to the National Cervical Cancer Prevention and Control Policy.

Management of Non-Communicable Disease and Other Conditions

Cardiovascular Disease (CVD)

PLHIV have an increased risk of CVD compared to HIV-negative people in the same age ranges.

The mechanisms underlying the association between HIV and CVD are multifactorial and include HIV-related chronic immune activation and inflammation, immunodeficiency, and higher burdens of traditional CVD risk factors in PLHIV.

Exposure to some classes of ARV drugs (e.g., PIs) can cause lipid abnormalities and may increase the risk of premature CVD. Although some ARV medications may increase the risk of CVD, the overall beneficial role of ART on HIV morbidity and mortality has been demonstrated to outweigh potential CVD risks in PLHIV.

All PLHIV should be screened for non-communicable diseases, including hypertension, diabetes, and epilepsy. Do blood pressure (BP), and urine dipstix for proteinuria and glucose. Identify other risk factors (smoking, increased waist circumference, age) and determine the client's cardiovascular (CVS) risk. Manage NCDs and CVS risk factors, as outlined in the PHC EML.

All clients should be encouraged to maintain an ideal weight, i.e., BMI < 25 kg/m2. Overweight clients with BMIs > 25 kg/m2 should apply the following lifestyle changes to reduce their weight:

- alcohol intake should be reduced to < 2 standard drinks per day for men, and < 1 for women on no more than 5 out of 7 days per week;
- a prudent eating plan should be followed, i.e. low fat, high fibre, and unrefined carbohydrates, with fresh fruit and vegetables;
- regular moderate aerobic exercise, e.g., 30 minutes of brisk walking 3-5 times per week (150 minutes/week);
- the client should be advised to stop smoking.

Depression

- PLHIV are at high risk of mental, neurological, and substance use disorders.
- Depression is often overlooked and unrecognized by health-care providers during routine HIV care.
- Treatment, or lack of it, for mental health disorders can affect general health, adherence to ART, and retention in care, and may lead to potential side-effects and drug interactions being overlooked.
- All clients on ART should be screened for depression and anxiety at least annually, and at any time if a client presents as unstable/a red flag client (missed appointments, elevated VL, or possible clinical signs of failure).
- Manage as outlined in the PHC EML.
- Be aware of potential drug-drug interactions between ART and psychiatric medications.

NATIONAL PHARMACOVIGILANCE PROGRAMME

The NDoH Pharmacovigilance Centre for Public Health Products (NPC) coordinates the programmatic implementation of pharmacovigilance (PV). Currently, the mainstay of NPC PV activities in SA involves creating awareness of the need for detecting and reporting suspected ADRs through targeted spontaneous reporting. ADR report forms and guides for detecting and reporting ADRs have been designed and are in distribution to HCP nationwide. The decentralized approach to PV emphasizes improved patient care at the facility level where ADRs are identified, thereby increasing awareness of ADRs and simultaneously improving the associated patient outcomes. The NPC organizes provincial and regional training workshops for HCWs in government institutions nationwide.

What is Pharmacovigilance?

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding, and prevention of adverse reactions to medicines (i.e., adverse drug reactions). The ultimate goal of this activity is to improve the safe and rational use of medicines, thereby improving patient care and public health.

What is an Adverse Drug Reaction (ADR)?

ADRs are commonly defined as a response to a medicine that is noxious and unintended, including lack of efficacy, which occurs at any dosage and can also result from an overdose, misuse, or abuse of a medicine.

Who should report Adverse Drug Reactions?

All healthcare workers, including doctors, dentists, pharmacists, nurses, and other health professionals are encouraged to report all suspected adverse reactions to medicines (including vaccines, X-ray contrast media, traditional and herbal remedies), especially when the reaction is not in the package insert, potentially serious or clinically significant.

What happens to a report?

All ADR reports are entered into a national ADR database. Each report is evaluated to assess the causal relationship between the event and the medicine. The purpose of ADR reporting is to reduce the risks associated with the use of medicines and improve patient care.

A well-completed adverse drug reaction/product quality form submitted could result in any of the following:

- Additional investigations into the use of the medicine in South Africa
- Educational initiatives to improve the safe use of the medicine
- Appropriate package insert changes
- Changes in the scheduling or manufacture of the medicine
- Changes to treatment guidelines
- Removal of the medicine from the market

Will reporting have any negative consequences on the health worker or the patient?

An adverse drug reaction report does not constitute an admission of liability or that the health professional contributed to the event in any way. The details of a report are stored in a confidential database. The names of the reporter or any other health professionals named on a report and the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others

What types of reactions should be reported?

The following adverse drug reactions should be reported (even if you are not certain the medicine caused the event):

- All suspected ADRs, expected or unexpected, to a medicine, including over-the-counter and traditional/herbal medicines.
- All suspected drug-drug interactions, drug-food interactions, and drug-herbal/traditional medicines.
- Lack of efficacy
- Treatment failures
- All suspected ADRs associated with medicine errors or overdose
- All serious reactions and interactions
- All adverse reactions or poisonings to traditional or herbal remedies

What product quality problems should be reported?

The following product quality problems should be reported:

- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labeling
- Therapeutic failures

How can ADRs be prevented from occurring?

Some ADRs are unavoidable and cannot be prevented. However, most ADRs can be prevented by following the basic principles of rational use of medicines.

How are adverse drug reactions reported?

An adverse drug reaction/product quality report form is provided on page 61 and should be completed in as much detail as possible before returning it by email, fax, or post to any of the addresses provided on the next page.

Additional forms can be obtained by contacting the National Pharmacovigilance Centre at the address below:

The National Pharmacovigilance Coordinator

National Pharmacovigilance Centre,

Private Bag X828,

Pretoria, 0001

Tel: (012) 395 9506/8099/9641

Fax2email: 086 241 2473

email: npc@health.gov.za

SAHPRA / National Adverse Drug Event Monitoring Centre at (021) 447 1618

SUSPECTED ADVERSE DRUG REACTION REPORT HIV/AIDS AND TB TREATMENT PROGRAMME

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

NDoH Pharmacovigilance Centre for Public Health Programmes (NPC)
Adverse Drug Reaction (ADR) / Product Quality Problem Report Form
This report will be shared with SAHPRA

Reporting Health Care Facility/Practice			
Tel: 012 395 9506 (NPC)	Facility/Practice		
Fax: 086 241 2473	District		Tel
Email: npc@health.gov.za	Province		Fax

Patient Details									
Patient Initials		File/Reference Number			Date of Birth/Age				
Sex	□M □F □Unk	Race		Weight (kg)		Height (cm)		Pregnant?	□N □Y
Allergies				Estimated Gestational Age at time of reaction					

Suspect Medicine(s) **[Medicines suspected to have caused the ADR]**

Trade Name [Generic Name if Trade Name is unknown]	Name of Manufacturer	Route	Dose (mg) and Interval	Date Started	Date Stopped	Reason for use	Batch Number / Expiry Date

All other Medicines Patient was taking at time of reaction [Including over-the-counter and herbal products]

Trade Name [Generic Name if Trade Name is unknown]	Name of Manufacturer	Route	Dose (mg) and Interval	Date Started	Date Stopped	Reason for use	Batch Number / Expiry Date

Adverse Drug Reaction/Product Quality Problem

Date and time of onset of reaction		Date reaction resolved/duration	

Please describe Adverse Reaction/Product Quality Problem: (kindly add as much clinical information as possible)

Intervention **[tick all that apply]**	**Patient Outcomes** **[tick all that apply]**
□ No intervention	□ Patient recovered □ Patient recovering
□ Intervention unknown	□ Patient not recovering
□ Patient counselled/non-medical treatment	□ Patient died: Date of death:_____
□ Discontinued Suspect Drug; **Replaced with**:_____	□ Impairment/Disability □ Congenital Anomaly
□ Decreased Suspect Drug Dosage; **New Dose**:_____	□ Patient hospitalised or hospitalisation prolonged
□ Treated ADR with:_____	□ Life threatening □ Other:_____
□ Referred to hospital; **Hospital Name**_____	□ ADR reappeared after restarting suspect drug/similar drug (rechallenge)?: □N □Y □ Not done □ Unknown
□ Other Intervention (e.g. dialysis): _____	

Laboratory Results			**Additional Laboratory Results**		
Lab Test	**Test Result**	**Test Date**	**Lab Test**	**Test Result**	**Test Date**

Co-morbidities/Other Medical Condition(s) **[tick all that apply]**

□ Hypertension □ Diabetes □ Asthma □ Tuberculosis □ HIV/AIDS □ Other:

Reported by			
Name		E-mail	
Designation	□ Nurse □ Pharmacist □ Doctor □ Other:	Date Reported	
Telephone	Signature	**VERSION 33.0 June 2016**	

THIS ADR REPORT IS NOT A CONFIRMATION THAT THE REPORTER OR THE SUSPECT MEDICINE(S) CAUSED THE ADR

SECTION 4

PREVENTION OF MOTHER-TO-CHILD TRANSMISSION OF HIV

Zero HIV transmissions from mother to child

How do we achieve VL suppression in pregnant and breastfeeding mothers, promote and protect breastfeeding, and realize an HIV-free generation?

SECTION 4 PMTCT

Overview of the Structure of Section 4 for PMTCT

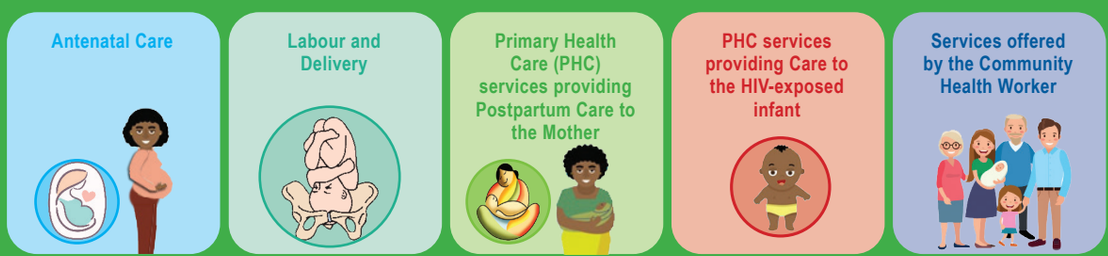
The PMTCT section of this guideline is divided into four parts:

1. **Part One: Introduction** provides an introduction and background to this guideline

2. **Part Two: Prevention** gives guidance around the universal measures to prevent transmission of infections during pregnancy and breastfeeding, prevent HIV, prevent unintended pregnancies, as well as safe conception.

3. **Part Three: Charts per Service Delivery Area** is structured by service delivery point across the continuum of care. It deals with the care and treatment of the woman living with HIV, her partner and children, and preventing mother-to-child-transmission (MTCT) to her exposed infant.

START BY SELECTING THE SERVICE POINT AT WHICH SERVICES ARE PROVIDED



For each service delivery point **in the facility** the following components of care are outlined:
1. HIV testing,
2. Antiretroviral therapy (ART) as treatment or prophylaxis,
3. Viral load (VL) monitoring and management,
4. Tuberculosis (TB) screening, TB Preventative Therapy (TPT), and opportunistic infection (OI) prophylaxis,
5. Prevention of mother to child transmission of syphilis, hepatitis B virus (HBV) and other infections, and
6. Other care required, e.g. basic antenatal care (BANC) services, immunization services (EPI), growth monitoring and nutrition.

For care provided by the **community** health worker (CHW) at home the following components of care are outlined:
7. Care of the non-pregnant woman of child bearing potential (CBP) at home,
8. Home-based care during the antenatal period, and
9. Home-based care after delivery for the mother and infant

Where additional information is needed you will be redirected to the relevant sections in Part Four.

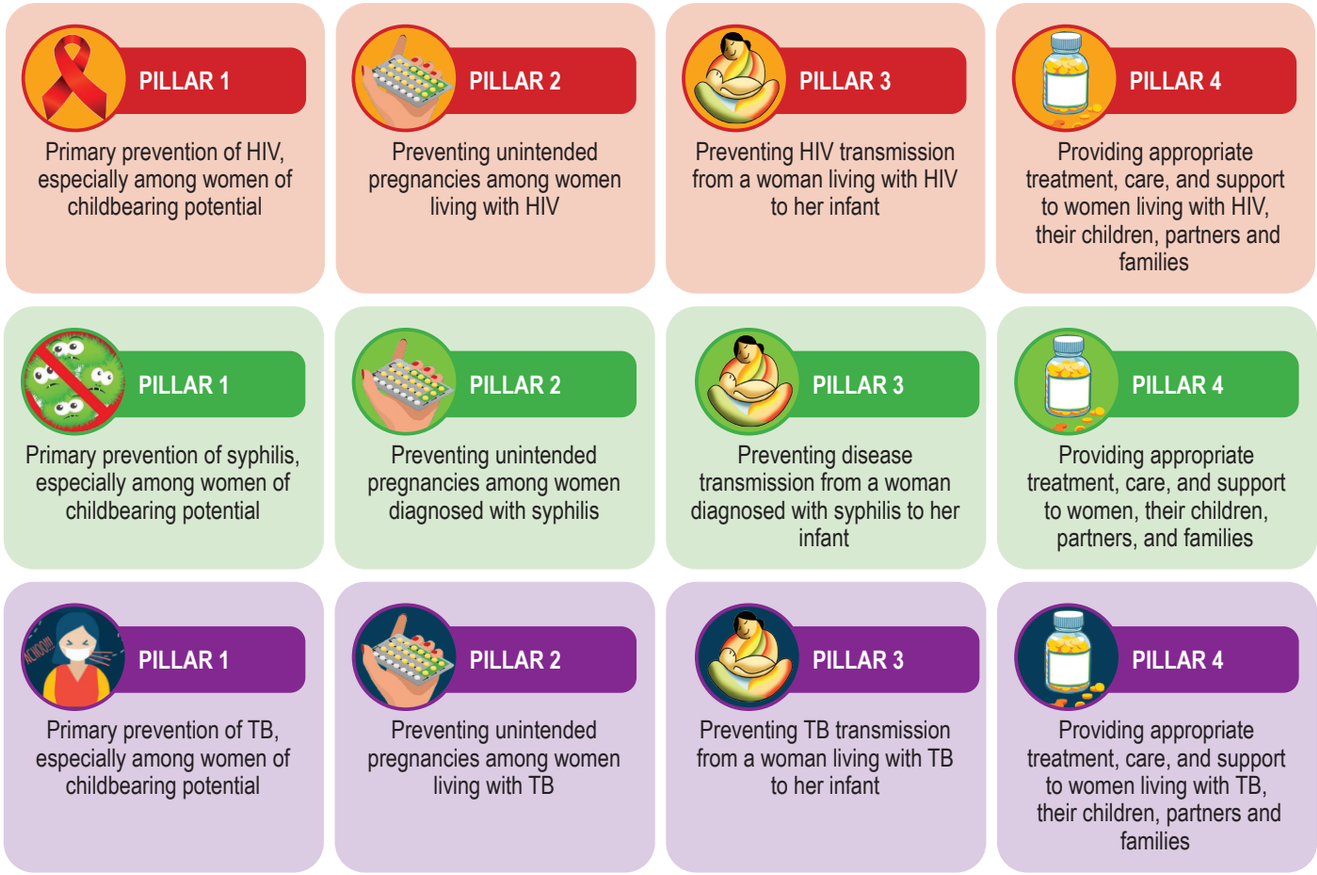
4. **Part Four: Algorithms and Decision Tools** provides algorithms and decision tools that may apply to any service point, e.g. how to manage an elevated VL, how to screen for TB and initiate TPT, important adherence messages, etc.

The PMTCT guideline aims to outline the minimum standards for routine care for women of childbearing age and their families relating to:

- the prevention of new HIV cases, TB cases, and syphilis cases
- the prevention of unintended pregnancies
- the prevention of mother-to-child transmission of HIV, syphilis, and
- the care and treatment of the women living with, and their children exposed to HIV, TB, and syphilis

South Africa (SA) is committed to achieving the elimination targets outlined in the Last Mile Plan. While significant progress has been made in preventing HIV infections in children, HIV remains the third leading cause of maternal mortality and a significant contributor to under-five deaths in SA. Therefore, managing the health of women living with HIV and preventing mother-to-child transmission of HIV remains a critical intervention for ensuring that women and children survive and thrive in South Africa. PMTCT Option B Plus entailed initiating ART for life in all pregnant and breastfeeding women regardless of CD4 count or clinical stage and was launched in SA in January 2015. Now, three years down the line, it is necessary to reflect on new evidence, both scientific and operational, to ensure that SA's HIV PMTCT program remains relevant, practical, and evidence-based.

The PMTCT program outlines four pillars by which to achieve the targets of zero HIV, syphilis, and TB transmissions from mothers to their infants. They are outlined in the three figures below.



Prevention of HIV

All persons of reproductive age need access to comprehensive information, as well as non-judgmental, confidential, and (as necessary), youth friendly SRH services.

WHO should be offered HIV prevention services?

- All HIV negative women, including adolecent girls, young women, and sex workers
- HIV negative partners and other men
- HIV positive persons

WHAT
HIV prevention options should be offered?

BASIC PREVENTION PACKAGE

HTS services
Couples Counselling and partner testing
Screen and treat STI's
Safe sex education*
Post Exposure Prophylaxis (PEP)
Pre-Exposure Prophylaxis (PrEP) as applicable & available #

BASIC PREVENTION PACKAGE +

Voluntary Medical Male Circumcision (VMMC) and communication for men

TREATMENT AS PREVENTION

HTS, couples counselling and partner testing, Linkage to Care, ART and VL suppression

Remember, condoms are recommended for all couples regardless of HIV status

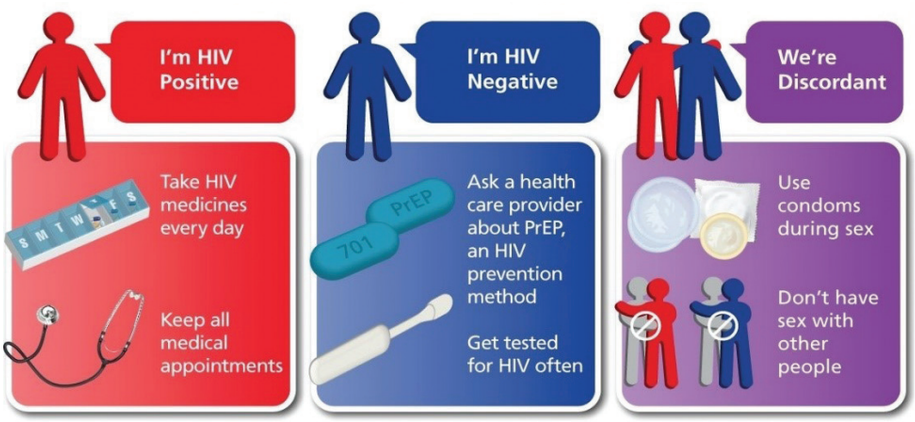
WHERE
should HIV prevention services be offered?

At all contact points with the health system, including PHC, SRH services, MNCWH&N services, Chronic and Acute Care services (including hospitals)

Community based services, including mobile/outreach services for sex workers and other working persons

School based prevention (in the context of comprehensive sexuality education)

Ways to prevent HIV transmission within a discordant couple



***Safe Sex Education:**
Counsel the women to avoid the following sexual practices that could put her at risk for contracting HIV and other STI's:

- The woman or her regular partner having new or multiple sexual partners
- Unreliable use of condoms
- Alcohol abuse

 # PrEP *is routinely available for adolescent girls and young women, as well as for sex workers. For PrEP in other populations consult the current PrEP guideline.*

Prevention of Unintended Pregnancies and Safe Conception in Women

Regularly discuss issues of childbearing and contraception to understand current fertility desires and health care needs. Ideally, engage the women living with HIV and her current partner in a couples-based approach, as the health and co-operation of both partners is important for safe contraception or conception.[8]

Classify client

A. Currently wanting to conceive

Recommend, discuss, and agree on steps before conception

Optimise HIV treatment in the partner living with HIV (serodiscordant couple), or in both partners living with HIV (sero-concordant couple).

- Continue to use condoms
- Document HIV status of both partners
- Identify and manage co-morbidities, including syphilis and other STIs
- Initiate ART and support good adherence
- Maintain an undetectable VL, ideally for 4-6 months before conception
- Start folate supplementation and do an Hb if clinically pale
- Consider PrEP for the uninfected partner

! Initiating **Dolutegravir (DTG)** in women wanting to conceive now or in the future may carry risks. Counsel the mother on use of DTG in pregnancy and allow her to make an informed choice. See **Dolutegravir in Pregnancy** on page 30

Once viral load suppression is achieved in the HIV positive partner(s), the following additional options are available to make conception safer

- timed, limited, peri-ovulatory, sex without a condom
- intravaginal insemination
- male circumcision
- intra-uterine insemination
- sperm washing
- surrogate sperm donation

Not readily available in the public sector

If pregnancy confirmed, counsel the mother to book at ANC before 14 weeks and to continue using condoms consistently during pregnancy and the breastfeeding period

B. Not currently desiring a child, but may do so in the future

Counsel about options for contraception including long-acting reversible contraceptives (IUCD and implants), and barrier methods

C. No desire for a child now or in the future

Counsel about options for contraception including permanent methods (male and female voluntary sterilisation), long-acting reversible contraceptives (IUCD and implants) and barrier methods. If permanent methods are not appropriate, proceed to an alternative dual method as outlined below

Dual method is always recommended:

A hormonal method (including implants) or intra-uterine contraceptive device to prevent pregnancy

A barrier method (male/female condoms) to augment the hormonal method, and prevent STIs and HIV

Discuss the different contraceptive options available for use in the women living with HIV (See PC101, and the National Contraceptive Clinical Guideline, 2018)
Available options include:

- Injectable progestins
- Combined oral contraceptive pills.
- Intra-uterine contraceptive device
- Emergency contraception

All hormonal methods including implants (e.g. Implanon NXT®) and the long acting injectables (e.g. Depo Provera®) are effective when used with Dolutegravir. Women should be counseled about the possibility of reduced efficacy when using **progestin subdermal implants (e.g. Implanon NXT®)** with enzyme inducing drugs such as **Efavirenz, Rifampicin,** and certain epilepsy drugs. Women who are already using an implant should consider an alternative non-hormonal method for contraception e.g. the IUCD, and should continue to use condoms correctly and consistently.

ANTENATAL CLINIC

When caring for a pregnant woman, always be sure to:

- Recognise the pregnant client that requires urgent attention as outlined in BANC Plus and manage/refer as appropriate
- Identify the pregnant client who needs secondary level antenatal care as outlined in BANC Plus and manage/refer as appropriate
- Provide routine antenatal care to the woman not requiring urgent referral.

TESTING for HIV

HIV Testing: Provider Initiated Counselling and Testing (PICT) should be provided to all women with unknown or HIV-negative status:

- Offer an HIV test at ANC first/booking visit.
- Retest the HIV-negative mother at every routine BANC Plus visit.
- Offer couple/partner testing to promote prevention, access to HIV care and treatment, and/or manage discordant results (when one partner is HIV-positive and the other partner HIV-negative).
- If the woman and/or her partner test HIV-negative, provide **HIV prevention** information (Go to **HIV Prevention** on page 66).
- Women who choose not to be tested should be offered 'post-refusal' counselling and offered a re-test at every subsequent visit.
- If a woman tests HIV-positive at any stage, encourage testing of her other children, and linkage to HIV care and treatment as necessary.
- For the **HIV testing algorithm**, including the management of discrepant HIV test results, refer to the HTS Guideline.

TREATMENT for HIV

- Pregnant women already on ART should continue their current ART regimen pending their 1st VL result (see below). If she will now collect her ART at ANC, ensure that she is documented as a transfer-out from her former clinic, and not classified as lost-to-follow-up.
- All newly diagnosed HIV-positive pregnant women are eligible for lifelong ART regardless of gestation, CD4 count, or clinical stage.
- Creatinine and CD4 count should still be done to determine renal function and the need for prophylaxis (TB, PCP and CM).
- TDF, 3TC, and DTG (as a fixed dose combination) is the preferred regimen for women who are newly initiating ART. However, each mother should understand the risks and benefits of DTG and EFV-based regimens, and be enabled to make an informed choice. ART should be initiated on the same day as HIV diagnosis[10], and after contra-indications to ART have been excluded (Go to **ART Initiation Algorithm** on page 75).
- Pregnant women already on ART should continue their current ART regimen pending the result of their 1st VL (to be done at entry into antenatal care as outlined below). Only if her VL is <50 c/ml, and she is no longer in the 1st six weeks of pregnancy, offer her the option of switching to DTG (If her VL is ≥ 50 c/ml, manage her as per the VL Non-suppression algorithm on page 79). A switch to DTG needs to be preceded by appropriate counseling on the risk for NTDs for subsequent pregnancies, postpartum contraception, and the new side-effects that may be experienced when switching to a new drug (see **DTG in pregnancy** on page 30. If she will now collect her ART at ANC, ensure that she is documented as a transfer-out from her former clinic, and not classified as lost-to-follow-up.
- Known HIV positive women, who are not currently on ART, but are ART-exposed (e.g. previous PMTCT, or previous LTFU on ART) should initiate a DTG-containing regimen. If she has a documented VL that was suppressed while she was previously on ART, start TLD. If no VL result is available, or her VL was not suppressed, start AZT, 3TC, and DTG.
- Appropriate ART literacy education should be given to the woman before she leaves the facility. (Go to **Key Adherence Messages** on page 34)
- All women living with HIV should be referred to a CHW to support adherence, breastfeeding and retention in care pre- and post-delivery.

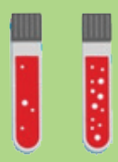
PRIMARY OBJECTIVES

1. Identify HIV infection and achieve viral suppression
2. Identify and treat syphilis and other infections

! Initiating Dolutegravir in pregnant women in the 1st 6 weeks may carry risks. Counsel the mother on use of DTG in pregnancy and allow her to make an informed choice.

Remember to put the PMTCT code: **C#PMTCT** in the EGK code field of the lab form for each VL done to ensure the electronic gatekeeping rules (EGK) do not lead to sample rejection

VL MONITORING and Management (Go to **VL Monitoring Schedule** on page 77)



Newly diagnosed and initiated ART for the first time:
- Do 1st VL at 3 months on ART.
- If VL < 50 c/ml, repeat VL at delivery.

Known HIV-positive women already on ART:
- VL at first/booking visit in ANC,
- If VL < 50 c/ml, repeat VL at delivery.

Known HIV-positive women, who are not currently on ART, but are ART exposed (e.g. previous PMTCT, or ART LTFU) and who are initiating a DTG-containing regimen:
- Do 1st VL at 3 months on ART.
- If VL < 50 c/ml, repeat VL at delivery.

If the VL is ≥50 c/ml in any of the above scenarios, go to **the VL Non-suppression Algorithm on** page 79.

✓ Early referral to community-based services improves adherence to ART, exclusive breastfeeding and retention in care

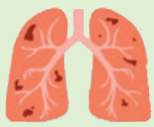
! Pregnant adolescents are at a higher risk for poor adherence and poor viral suppression and require more intense support. Go to **"The Pregnant Adolescent"** on page 80

! Remember to insert the laboratory barcode sticker and record all VL, TB, and syphilis results in the Maternity Case Record/ANC Card, and the ART Clinical Stationery (if available in that facility)

SCREENING for TB and other OI's

Screen for TB at every visit regardless of HIV status and consider TPT if eligible. Ensure any woman diagnosed with TB is adherent to TB treatment and that she is aware that her newborn may require TB prophylaxis (Go to **TB screening and TPT** on page 87). Initiate Cotrimoxazole Prophylaxis (CPT) if CD4 count ≤ 200 cells/μL, or WHO clinical stage 2, 3, or 4.

If CD4 ≤100 cells/uL the lab will automatically perform a Cryptococcal Antigen test (CrAg). CrAg-positive clients who are pregnant should be offered an LP (regardless of symptoms) and discussed with an expert before a decision is made regarding management.



PREVENTION of transmission of Syphilis, HBV and other infections

Syphilis: Test all women for syphilis and screen for other STI's, e.g. gonorrhoea, at their first ANC visit. (Go to **Syphilis** on page 90)
- If the first test is performed before 20 weeks gestation and is negative, a second test should be done at 32 to 34 weeks.
- Treat all women with a positive syphilis screening test, irrespective of titer (MCG, PC101).

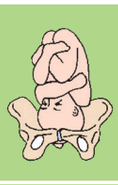
HBV: All woman living with HIV will automatically be treated for HBV when they start routine 1st line ART containing TDF and 3TC/FTC. If she should need to switch to 2nd line ART, HBsAg should be checked. If HBsAg is positive, TDF should be retained as a fourth drug in her new regimen. If a HIV negative pregnant woman is known to have HBV infection, she should be referred for further tests to determine eligibility for treatment. All babies should receive hepatitis B vaccinations in accordance with the EPI schedule.

Malaria: Although MTCT is rare, malaria in pregnancy poses serious risks for both the mother and the baby. Malaria presents as a febrile illness and is often unrecognised or misdiagnosed with severe consequences. The most important aspect of making a diagnosis of malaria is having a high index of suspicion. If a woman presents with fever in pregnancy, always ask about her travel history. Refer any woman with signs of severe illness or danger signs as outlined in PC101. Comprehensive information on Malaria in Pregnancy is available in the Guideline for Maternity Care in South Africa, and the National Guideline for the Treatment of Malaria SA.

Other Care

- Routine antenatal care according to the BANC Plus guideline. Encourage male partner involvement throughout antenatal care.
- Nutritional screening for mother. Refer any woman with a BMI of less than 23 to a dietician
- Counselling on infant feeding. See the **Infant and Young Child Feeding Policy**.
- Mental health screen for mother
- Assist the mother to register on Mom-Connect
- Identify any potential psychosocial risk factors that may require additional support (see page 100 Psychosocial risk factors)

! TB and other non-pregnancy related infections remain an important cause of maternal and neonatal mortality



LABOUR AND DELIVERY

PRIMARY OBJECTIVES

1. Safe delivery for mother and infant
2. Prevent MTCT during labour

TESTING for HIV

PICT should be provided to all women presenting in labour ward who are not known to be HIV-positive (including born-before-arrivals [BBAs]):

- Offer couples counselling and partner testing. For the management of the discordant couple, go to the **HIV Prevention** section on page 66.
- Women who choose not to be tested should be offered 'post-refusal' counselling and offered a re-test at every subsequent visit.
- If a woman tests positive at any stage, encourage testing of her other children, and linkage to HIV care and treatment as necessary.
- If a woman has indeterminate or discrepant HIV test results, treat the baby as a high-risk HIV-exposed infant until mother's HIV status can be confirmed. Communicate clearly to the mother and document the results and plan of action in the maternal record and RTHB.

Antiretrovirals

Pregnant women already on ART should continue their current ART regimen at usual dosing times during labour.

Newly diagnosed, or known HIV positive women not on ART:

- Give a stat single fixed dose combination tablet of TDF, 3TC and DTG (TLD) and a stat single dose of NVP.
- Lifelong ART should be initiated the following day after contra-indications to ART have been excluded (Go to **ART Initiation Algorithm** on page 75). TLD is the preferred regimen, provided the mother has been provided with all necessary information on DTG and EFV-based regimens including the risk of NTDs. A contraceptive method is recommended. Provide her with a choice of contraceptive options as desired.
- Appropriate ART literacy education should be given to the women before she leaves the facility. (Go to **Key Adherence Messages** on page 34).
- Mothers must understand and anticipate the adherence challenges that may be experienced in the postpartum period.

! An elevated viral load at delivery increases the risk for poor maternal outcomes and MTCT during labour and through breastfeeding.

VL MONITORING and Management

Check if the mother has had a VL result in the last 12 weeks and categorize the risk for the infant:

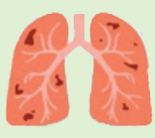
- VL < 1000c/ml = Low risk
- VL ≥ 1000 c/ml = High risk
- No VL result in the last 12 weeks = High risk

All women must have a VL test done at the time of delivery.
Although this VL result will mostly still be unknown when infant prophylaxis is initiated, remember to insert the laboratory barcode sticker into the postnatal discharge form and the RTHB.
The results of the delivery VL must be checked at the 3-6-day postnatal visit, and the management of the mother-infant pair adjusted accordingly.

Remember to put the correct PMTCT code in the EGK code field of the lab form for each VL done to ensure the electronic gatekeeping rules (EGK) do not lead to sample rejection.
Use the code **C#Delivery** for all VLs done at the time of delivery.

SCREENING for TB and other OI's

- Screen all women for TB at entry to the labour ward, and initiate TPT for women living with HIV before discharge, if eligible (Go to **TB Screening and TPT** on page 87).
- Initiate Cotrimoxazole Prophylaxis before discharge if CD4 count ≤ 200 cells/uL, or WHO clinical stage 2, 3, or 4.



Other Care for the Mother living with HIV at delivery

Provide routine labour and delivery management according to the Maternity Guidelines of SA, including safe delivery techniques for the HIV positive mother:

- Avoid episiotomy & assisted delivery unless essential. Avoid prolonged rupture of membranes. Avoid unnecessary suctioning of the infant.
- If C/section required: Provide prophylactic antibiotics for all HIV-positive women according to the Maternity Care Guidelines 2016.

Within 1 hour of delivery

- Encourage skin-to-skin contact with baby and initiate exclusive breastfeeding. Hospitals and labour wards can support mothers to breastfeed by following the WHO **10 Steps to Successful Breastfeeding** on page 85 of the PMTCT guideline. In addition, counsel mother on **Breastfeeding** on page 84.

At discharge

- Ensure contraception has been administered after appropriate counselling (go to **Contraception and Safe Conception** page 86).
- Provide the mother with two-months' supply of ART and six-weeks supply of infant prophylaxis.
- Communicate follow-up appointment dates for the six-day post-natal visit at a named facility. Provide necessary referral letters. Provide an ART transfer-out letter, if she will receive her ART at a different facility. However, it is recommended that the mother-baby pair continue to receive integrated care within the maternal and child health stream until the baby is two years old or no longer breastfeeding.
- Identify any potential psychosocial risk factors that may require additional support (see page 100 **Psychosocial risk factors**)

Care of the HIV-exposed Infant at Delivery

All HIV-exposed Infants should receive a birth HIV-PCR to identify HIV transmission that occurred in-utero.
All HIV-exposed Infants should receive a minimum of six weeks post exposure prophylaxis with NVP.

Identify the high-risk infants for whom additional prophylaxis must be provided:

- Mother with a VL of ≥ 1000 c/ml at delivery (or most recent VL taken during the last 12 weeks of antenatal care), or
- Mother with no VL result in the last 12 weeks.
- These infants should be provided with high-risk prophylaxis until the result of the delivery-VL can be checked at the 3-6-day postnatal visit. When the delivery-VL result is known, the infant can be re-classified as high/ low-risk and prophylaxis adjusted accordingly.

All high-risk infants who are breastfed should receive additional AZT for the first six weeks of life and should receive NVP for a minimum of 12 weeks. NVP should only be stopped when the breastfeeding mother has a VL of less than 1000 c/ml, or until four weeks after she has stopped breastfeeding. All high risk infants who are exclusively formula fed should receive AZT for 6 weeks and NVP for 6 weeks. (Go to **HEI Prophylaxis Infographic and the NVP and AZT dosing chart** on page 81 and 99)

Provide oral polio vaccine, BCG and other routine neonatal care as per the Maternity Care and Neonatal Care Guidelines. Do not give BCG if baby is TB-exposed, and will be receiving TB prophylaxis (Go to **Management of the TB-Exposed Infant** on page 88).

PREVENTION of transmission of Syphilis, HBV and other infections

Syphilis: Examine and treat the newborn of the RPR positive mother (go to Syphilis on page 90):
Well (asymptomatic) baby: Treat baby with benzathine penicillin 50 000u/kg IM stat only if:

- Mother was not treated, or
- If the mother has received < 3 doses of benzathine benzylpenicillin, or
- If the mother delivers within 4 weeks of commencing treatment.

Symptomatic baby (hepatosplenomegaly, pseudoparesis, snuffles, oedema, jaundice, anaemia, purpura, desquamative rash -especially involving palms and soles): Refer all symptomatic babies for treatment of congenital syphilis: procaine penicillin 50 000 u/kg IM daily for 10 days, or benzyl penicillin (penicillin G) 50 000 u/kg/dose 12-hourly IV for 10 days.

HBV: All babies should receive hepatitis B vaccinations in accordance with the EPI schedule.

CARE OF THE MOTHER AFTER BIRTH

	6 DAYS	6 WEEKS	10 WEEKS	6 MONTHS	18 MONTHS
TESTING for HIV 	Retest the HIV-negative mother if she was not retested in labour		Retest every HIV-negative mother at the **10-week visit** (~ three months postpartum), the **six-month visit**, and every **three months** whilst breastfeeding Remember to offer partner testing. If no longer breastfeeding, ensure that the mother receives an HIV test at least every year		
Antiretrovirals 	**Mother to continue ART** during the postpartum period and **for life**. If she is **newly diagnosed during the breastfeeding period**, initiate ART after contra-indications to ART have been excluded (Go to **ART Initiation Algorithm** on page 75). Provide appropriate counselling on available ART options. TDF, 3TC, and DTG (TLD) is the preferred regimen, provided the mother has been given all necessary information on DTG and EFV-based regimens including the risk of NTDs. This is a high-risk period for poor **adherence**. Ensure that the mother understands the importance of continued viral suppression for her own health and that of her baby. She must also understand and anticipate the adherence challenges that may be experienced in the postpartum period. Link the mother to mom-connect, a CHW, a mentor mother, or a support group/club if available. Whether continued ART care is provided at MNCWH services (preferred) or at PHC/Wellness services, ensure that mother is **retained in care, adherent to ART, and maintains a suppressed viral load.**				
VL MONITORING and Management 	Check ART adherence Follow-up on result of **delivery-VL**. (If not yet available, follow-up again in 1 week. If VL not done at delivery, do VL at this visit) **If VL ≥ 50 c/ml:** manage mother as per **VL Non-suppression Algorithm** on page 79. **If VL ≥ 1000 c/ml:** manage infant as a high-risk infant i.e. add AZT for six weeks, and extend NVP until mother's VL is <1000 c/ml.	Check ART adherence Repeat VL if delivery-VL was ≥ 1000 c/ml. Check mother's ART supply and confirm where she will be receiving her ongoing ART care	Check ART adherence Check, record and act on any earlier VL tests Check mother's ART supply and confirm where she will be receiving her ongoing ART care ! Viral Load suppression is critical for the health of the mother, her baby, her subsequent pregnancies, and her partner!	Check ART adherence at every visit. Check, record and act on results of any earlier VL tests Do a VL for all HIV-positive mothers on ART at six months. Continue VL monitoring every six months (at 12,18, and 24 months) whilst breastfeeding. Ensure that the results of any VL test are checked within 1 week. If VL ≥ 50c/ml: • Recall the mother-infant pair to the facility • Manage mother as per **VL Non-suppression Algorithm** on page 79. If VL ≥ 1000 c/ml: • Restart/extend infant prophylaxis if mother is still breastfeeding. Go to **Management of a High Maternal VL after Delivery** on page 83.	
SCREENING for TB and other OI's	• Routine postpartum care as per the Maternity Care Guideline • TB screening, TPT, and CTMX according to guidelines • Mental Health: Screen for postpartum depression • Contraception and STI screening • Infant feeding counselling and support according to the Infant and Young Child Feeding Policy • Counselling on safe use of water, sanitation and hygiene (WASH) • A papsmear can be done from six weeks onwards		• TB screening, TPT, and CTMX according to guidelines • Mental Health: Screen for postpartum depression • Contraception and STI screening • Infant feeding counselling and support according to the Infant and Young Child Feeding Policy • Counselling on safe use of water, sanitation and hygiene (WASH) • Papsmear (if indicated)		

PRIMARY OBJECTIVES

1. Prevent MTCT through Breastfeeding
2. Retain Mother in Care
3. Achieve and Maintain Viral Suppression

CARE OF THE HIV-EXPOSED INFANT AFTER BIRTH

HIV Testing and Early Infant Diagnosis

3-6 DAYS	6 WEEKS	10 WEEKS	6 MONTHS	18 MONTHS	OTHER TESTS (at any time)
Follow-up results of birth PCR and manage accordingly. Any HIV positive neonate should be discussed/referred to a clinician experienced in managing an HIV-positive neonate. ART should be initiated even if the infants weighs less than 2,5 kg.	Ensure that birth PCR and mother's VL results were checked, recorded and acted upon correctly.	HIV-PCR for all HIV-exposed infants who previously tested HIV-PCR negative.	**Known HIV-exposed infants:** • Do HIV-PCR test at 6 months in all HIV-exposed infants, except in those who previously tested positive and are on ART. **Infants not known to be HIV-exposed:** • At six months of age, establish the HIV status of all infants not already known to be HIV-exposed • Offer an HIV test to the mother. If she tests HIV negative, no infant test is required • If the mother is not available, or refuses an HIV test, get consent and do an HIV rapid test on the infant • All positive infant rapid tests need to be confirmed with an HIV-PCR.	Universal HIV testing at 18 months (HIV rapid test for ALL infants regardless of HIV exposure, except in those who previously tested HIV positive and are on ART)	Do an age-appropriate HIV test 6 weeks post cessation of breastfeeding, even if breastfeeding continues beyond 18 months of age. Test a symptomatic child at any age according to IMCI guideline.

! The HIV-exposed but uninfected (HEU) child is at higher risk for poor outcomes and requires careful follow-up. Go to **"Care of the HEU Infant"** on page 89

! Use the **NHLS Results for Action (RfA) Reports** to follow up on lab results (See page 92). Any child with a positive, indeterminate, or not-resulted PCR should be traced to come back to the clinic urgently. A clinical audit can provide insight into reasons for the failed PMTCT

Confirmatory test for HIV

Any child under two years with a positive HIV-PCR or a positive HIV rapid test should have their HIV status confirmed with a **HIV-PCR test on a new sample**. At the clinician's discretion, the HIV-PCR may be replaced by a viral load test which has the advantage of both confirming the HIV diagnosis and providing a baseline VL for monitoring the child's response to ART. **Any child who tests HIV positive should initiate ART** according to the Paediatric ART guideline as a matter of urgency. Do not wait for the confirmatory result before initiating ART **but ensure that this result is checked**. For the **Management of Indeterminate HIV PCR results**, go to page 86.

AGE OF CHILD	HIV SCREENING TEST	HIV CONFIRMATORY TEST
Less than 18 months	PCR	PCR
18 months to 2 years	Rapid	PCR
More than 2 years	Rapid	Rapid

Infant Prophylaxis

Check **adherence**/ tolerance to NVP (and AZT, if applicable). Ask the mother to explain how she administers the infant's medication. Check result of mother's delivery-VL.

If necessary re-classify infant as high/ low-risk and adjust prophylaxis accordingly.

See the **Infant Prophylaxis Infographic** and the **NVP and AZT dosing chart** on page 99.

All HEI's: Start cotrimoxazole prophylaxis therapy (CPT), even if birth PCR was negative. Go to **Cotrimoxazole Dosing Chart** on page 99.

Low-risk infant: Stop NVP if mother's VL at delivery was <1000 c/ml.

High-risk infants:
- **stop AZT**,
- **continue NVP** for a minimum of 12 weeks, or until four weeks after all breastfeeding has stopped.

High-risk infants: Continue NVP prophylaxis. Ask mother to return at 12 weeks to evaluate VL result and stop/ extend NVP as necessary

At every visit, check results of mother's most recent VL. An elevated VL may require high-risk infant prophylaxis (6 weeks AZT twice daily and 12 weeks NVP daily) to be restarted or existing NVP prophylaxis to be extended. Go to **Management of a High Maternal VL after Delivery** on page 83.

! Remember to adjust NVP dosages according to weight

Stop NVP after 12 weeks only if mother's VL is < 1000 c/ml. If the maternal VL is not suppressed by 12 weeks, continued NVP **until mother's VL is <1000 c/ml**, or until four weeks after all breastfeeding has stopped.

Continue **cotrimoxazole prophylaxis** until infant is confirmed HIV negative six weeks post cessation of breastfeeding. For formula fed infants, CPT may be stopped if the infant is confirmed to be HIV negative at the 10-weeks PCR test, provided that no breastfeeding has occurred in the six weeks prior to the 10-week PCR test.

If a child tests **HIV positive** at any stage, **stop NVP** prophylaxis, **initiate ART**, do a confirmatory HIV PCR, and continue cotrimoxazole prophylaxis according to guidelines.

If mother diagnosed with HIV after delivery or during the breastfeeding period go to **Management of a High Maternal VL (due to HIV Diagnosis) after Delivery** on page 83

! For any child that tests HIV-positive ensure that:
- Confirmatory testing has been done and the child is tracked and linked to care,
- The mother and other significant caregivers are counselled appropriately,
- CHWs are involved,
- The child is registered on Tier.net & retained in care.

Other Routine Care

Routine growth monitoring, immunisations, nutritional support. Provide advice to support breastfeeding. Go to **Breastfeeding Plus** on page 84

Routine growth monitoring, immunisations, vit A, deworming and nutritional support. Provide advice to support **breastfeeding**. Go to **Breastfeeding Plus** on page 84

Early referral to community-based services improves adherence to ART, exclusive breastfeeding and retention in care. Where resources allow, all women should be linked with a CHW during antenatal care. In areas with insufficient numbers of CHWs to meet the demand, women should be prioritised as outlined on page 100

Care offered in the Community Setting

Care of the non-pregnant woman of child bearing potential (CBP) at home

- Ask if she is using reliable family planning, and if not, refer to the clinic. Discuss the advantages of planned parenthood.
- Screen all woman of child bearing potential (CBP) for pregnancy. If she is not on reliable contraception or her period is late, provide/refer her for a pregnancy test.
- Encourage all girls, boys, women, and men to test for HIV if they are sexually active. Offer an HIV test to the woman and her partner if they have not tested in the last year.
- Discuss healthy nutrition with the family.

Encourage pregnant women to attend at the antenatal clinic

- Identify pregnant woman early.
- Encourage booking at the antenatal clinic before 14 weeks.
- Encourage attendance of all 8 antenatal appointments.
- Track and trace any woman who missed their clinic appointments.

Identify the pregnant woman living with HIV

- Check that she has been offered an HIV test during this pregnancy.
- Encourage partner testing.
- Encourage testing of any other children living in the household if she tests positive for HIV.

Counsel all pregnant women on good nutrition and following a healthy lifestyle

- Discuss infant feeding.
- Follow a healthy diet.
- Avoid tobacco, alcohol, drugs and traditional remedies.
- Wash your hands after using the toilet, before and after preparing food, or after changing a baby's diaper/nappy.
- Practice safe sex and continue to use condoms.

Prevent mother to child transmission of HIV, syphilis and TB

- Provide education on STI's, HIV, ART and the importance of viral load suppression.
- Encourage adherence to ART and all other treatment provided by the clinic.
- Counsel on the importance of exclusive breastfeeding
- Screen all woman for TB and STI's

Promote safety during pregnancy and delivery

- Educate her and her family on danger signs in pregnancy.
- Educate her on the signs of labour.
- Encourage the mother to deliver in a clinic or hospital.
- Encourage her to plan her mode of transport to the delivery site.

Postnatal care for mother and baby

- Check mother for bleeding, infections, mastitis, and depression. Screen the mother for TB.
- Refer mother or baby at any stage if ill, including the jaundiced (yellow-skinned) baby.
- Educate mother on universal infection control practices if either mom or baby are ill (Go to **Universal Measures to Prevent Infections during Pregnancy** on page 7 of the PMTCT guideline).
- Provide support for exclusive breastfeeding and advise on latching and positioning of baby whilst feeding.
- Educate on hygienic cord care and keeping the baby warm (thermal care).
- Continue to support good adherence to ART, cotrimoxazole (if indicated), and other treatment.
- Make sure that the mother is giving infant NVP (and AZT) correctly (NVP once daily and AZT twice daily).
- Make sure mother and baby attend all postnatal check-ups and immunisation appointments.
- Check that baby is growing well.
- Educate mother on contents of RTHB, including infant nutrition and danger signs in infants and children.

ART Initiation in a Pregnant Women

Any pregnant or breastfeeding women with a new HIV diagnosis, or any known positive woman (not currently on ART) with a new pregnancy diagnosis

* Known HIV positive women, who are not currently on ART, but are ART-exposed (e.g. previous PMTCT, or previous LTFU on ART) should initiate a DTG-containing regimen. If she has a documented VL that was suppressed while she was previously on ART, start TLD. If no VL result is available, or her VL was not suppressed, start AZT, 3TC, and DTG

! Timing of ART initiation in pregnancy is critical. Every week a mother is on ART further decreases her risk of MTCT[9]

Take a history and do a clinical examination:
Exclude contra-indications to starting ART on the same day. Ask about TB symptoms, a history of renal disease, or current psychiatric symptoms. Determine the client's WHO Clinical Stage. Start cotrimoxazole (CPT) if eligible.
Do the following tests on ALL HIV positive pregnant women, regardless of symptoms or history: **CD4 count, s-Creatinine, sputum for TB Gene Expert (GXP), and urine dipstix**

TB Symptoms with danger signs:
If the woman appears very ill with any of the following signs, **discuss with a doctor or refer for further assessment. Do not start ART until TB is excluded/diagnosed as these women may be at a higher risk of developing IRIS:** weight loss > 5%, difficulty breathing, respiratory rate >30/min, temperature > 38°C, pulse > 100min, BP < 90/60, coughing up blood, confusion, agitation, or unable to walk unaided.

TB Symptoms without danger signs

History of renal disease

If no abnormal history

Initiate ART same day: TDF, 3TC/FTC, and DTG preferred*
(See algorithm on **Recommendations Regarding the Use of DTG in WOCP** on page 30)
If TDF contraindicated due to history of/suspected renal disease replace TDF with ABC.
Review results in 3-7 days

Ensure a thorough evaluation for TB

TB GXP negative, but still TB symptoms

TB GXP positive

Investigate with CXR, 2nd sputum for culture/line probe assay (LPA) +/- antibiotics as per National TB Guidelines. If CD4 <100, do a urine LAM.

TB Diagnosis confirmed → **Initiate TB Rx**

Review in 2 weeks. If stable and tolerating TB Rx, initiate ART (if not already initiated). DTG requires boosting with TB treatment to 50 mg twice daily. If TB symptoms worsen after ART initiation, consider TB IRIS and refer/discuss with the HIV hotline. If TB meningitis, defer ART for 4 to 6 weeks.

TB GXP negative (or unable to produce sputum), AND no TB symptoms

Continue ART: TDF, 3TC/FTC, DTG*

If CD4 < 350 and the client is tolerating ART, **initiate TPT for 12 months**.
Ensure that active TB has been excluded, and check for other contra-indications to TPT. No TST necessary.
(Go to **TB Screening and TPT algorithm** on page 26)

CD 4 ≤ 100

Do CrAG

CrAG neg

CrAG pos

Refer Urgently for LP

Creatinine > 85 umol/L

Continue/adjust ART to **ABC**, 3TC and DTG.
Adjust dose of 3TC (and any other drugs) as needed.
Discuss with an expert/HIV-hotline re further investigations and management.

No abnormal results and CD4 more than 100

Continue ART
If CD4 ≥ 350, defer TPT until 6 weeks after delivery

[$]Only switch an existing, stable client from EFV to DTG if her VL is <50c/ml and she is no longer in the first 6 weeks of pregnancy. A switch to DTG needs to be preceded by appropriate counseling on the risk for NTDs for subsequent pregnancies, postpartum contraception, and the new side-effects that may be experienced when switching to a new drug. See DTG in pregnancy on page 30.

For a **Summary of 1st line ART Regimens** go to page 76

Remember that same-day ART initiation is not an adherence support 'short-cut.' Provide her with the "Key Adherence Messages" as outlined on page 34. Ongoing support can occur in the days and weeks immediately after initiation.

DTG-USE IN PREGNANT AND BREASTFEEDING WOMEN

There are some concerns regarding the risk of neural tube defects (NTD) if a woman should fall pregnant on DTG. Therefore, TLD is the preferred regimen in all women of childbearing potential who are not actively trying to conceive and who are not in the first six weeks of pregnancy (see algorithm on the use of DTG in WOCP on page 76). Due to the low risk of NTDs in women using DTG, the following precautions are required:

- Women should be counseled about the potential risk of NTDs when DTG is taken around the time of conception and be allowed to make an informed choice.
- Any non-pregnant woman taking or starting DTG should be advised to use contraception and folic acid supplements.
- Once a non-pregnant woman is taking DTG, fertility intentions should be discussed at every visit. Should she desire a pregnancy, and she is concerned about the risk of NTDs, she can be offered a switch from TLD to TEE, provided that she has a suppressed VL in the last six months.
- Women who fall pregnant on DTG should be entered into the antiretroviral pregnancy register (http://www.APRegistry.com/). She should continue her DTG containing regimen.
- Pregnant women already on an EFV containing ART regimen may switch to DTG containing regimen provided that:
    - Her most recent VL in the last six months is < 50 c/ml.
    - She has been counseled on the risk for NTDs for subsequent pregnancies, and the need for postpartum contraception.
    - She is aware of the side-effects that may be experienced when switching to DTG (insomnia, headache, GIT disturbances). These are usually mild and self-limiting. If she does not feel well, encourage her not to stop her ART, but rather to report to the clinic.
    - She is aware that while her previous TEE regimen was taken at night, TLD may be taken in the morning or at night. However, should she experience insomnia, it is recommended that TLD be taken in the morning. For additional information on using DTG in WOCP see page 30

Summary of First-line ART Regimens for Women of Childbearing Potential

TABLE 19 SUMMARY OF FIRST-LINE ART REGIMENS IN WOCP

SUMMARY OF 1ST LINE ART REGIMENS FOR ADOLESCENTS GIRLS (10 – 19 YEARS) AND ADULT WOMAN		
Any WOCP with normal renal function, with or without TB, and who chooses to use DTG after understanding the risk and benefits	Weight ≥ 35 kg	TDF 300 mg, 3TC 300 mg, DTG 50 mg (TLD) as a single fixed dose combination tablet taken once daily
	Weight < 35 kg	Replace TDF with Abacavir 300mg bd (or 600mg once daily)
	DTG requires boosting with TB treatment to 50 mg twice daily. This will require one standard fixed dose combination tablet of TLD to be taken at the normal time, and an additional single tablet of DTG 50 mg to be taken 12 hours later.	
Clients who currently wish to conceive and are concerned about the risk for NTDs on DTG	Weight ≥ 40 kg	TDF 300 mg, FTC 200 mg, EFV 600 mg (TEE) as a single fixed dose combination tablet taken once daily in the evening
	Weight < 40 kg	TDF 300 mg daily, 3TC 300 mg daily, Efavirenz 400 mg daily
Abnormal renal function	Tenofovir (TDF) is contraindicated	Replace TDF with Abacavir 300mg bd (or 600mg once daily), or dose-adjusted AZT
Active psychiatric illness	Efavirenz (EFV) is contraindicated	Replace EFV with DTG. If DTG not suitable, give LPV/r or ATZ/r.
Known HIV positive women, who are not currently on ART, but are ART-exposed (e.g. previous PMTCT, or previous LTFU on ART)	VL < 50 c/ml while previously on ART	TDF 300 mg, 3TC 300 mg, DTG 50 mg (TLD) as a single fixed dose combination tablet taken once daily
	Unsuppressed VL, or no documented VL while previously on ART	AZT 300 mg twice daily, 3TC 150 mg twice daily (or 300 mg once daily), and DTG 50 mg daily

CD4 Count and Toxicity Monitoring in the Pregnant or Breastfeeding Women

Monitoring of the response to ART by CD4 count and monitoring for ART toxicity are the same in pregnant and non-pregnant populations. Monitoring is outlined on page 36 and summarised in the table below:

TABLE 20 CD4 AND TOXICITY MONITORING IN THE PREGNANT OR BREASTFEEDING WOMAN

MONITORING BLOODS ON ART

These monitoring bloods are in addition to the **VL monitoring schedule** on page 77

Time on ART	Creatinine (only if on TDF)	CD4	FBC (only if on AZT)	ALT (only if on NVP)
At ART Initiation	✓	✓	✓	Only if client develops rash or symptoms of hepatitis
Month 3	✓		✓	
Month 6	✓		✓	
At 1 year	✓	✓		
Annually	✓	If clinically indicated	✓	

Do HB and HBsAg if switching from 1st to 2nd line ART

VL Monitoring in Pregnant and Breastfeeding Women

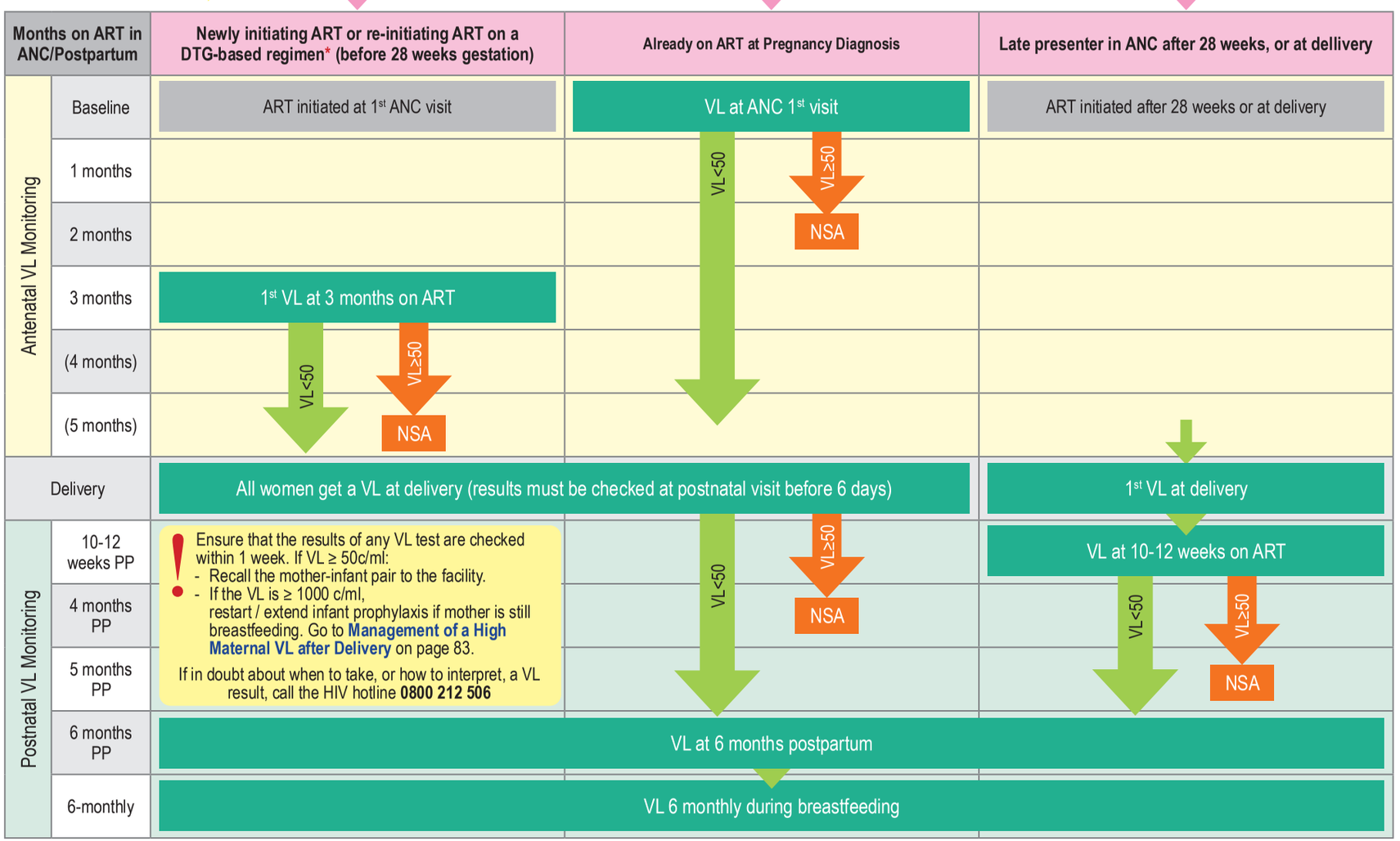
While the principles of viral load monitoring outlined on page 36 are the same for pregnant and non-pregnant clients, the timing of VL monitoring is different in pregnant and breastfeeding women. Viral load monitoring per category of women is outlined in Table 21 on the next page:

NSA refers to the **VL Non-Suppression Algorithm** on page 79

Remember to put the correct PMTCT code in the EGK code field of the lab form for each VL done to ensure the electronic gatekeeping rules (EGK) do not lead to sample rejection. Use the code **C#PMTCT** for all VLs done during ANC or the breastfeeding period.
Use the code **C#Delivery** for all VLs done at the time of delivery.

START HERE

Select a category for the woman starting ART from the pink blocks below:

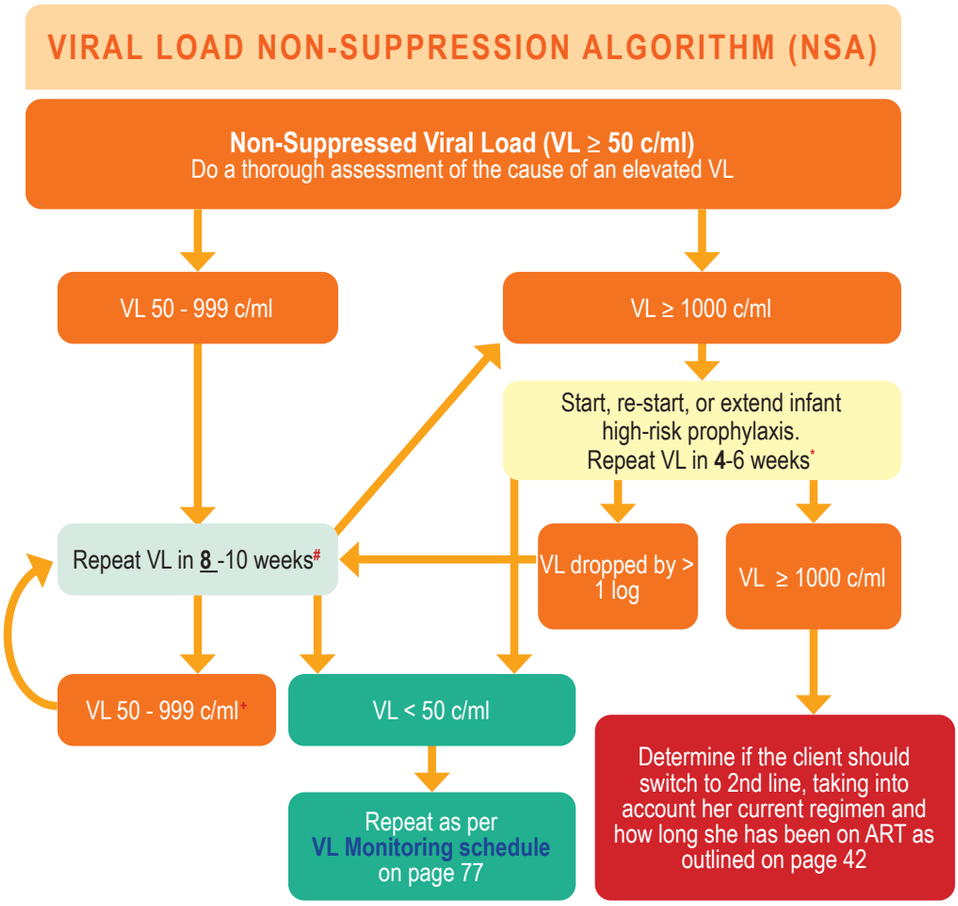


* If a women who is previously ART exposed chooses to re-initiate EFV rather than DTG, do a VL before re-starting ART. Repeat the VL in one month. If more than one log drop in VL is achieved, continue current regimen and repeat VL in two months. If VL < 50 c/ml, repeat VL at delivery. If the repeat VL is ≥ 50 c/ml, manage according to the **VL non-suppression algorithm** on page 79

MANAGEMENT OF THE WOMEN WITH AN ELEVATED VL

Remember, an elevated VL in a pregnant or breastfeeding mother is a MEDICAL EMERGENCY! Every week she continues with an elevated VL increases her risk for MTCT!

A thorough assessment is essential for any woman with a VL measuring more than 50 c/ml. Follow the "ABCDE" acronym for assessing the reasons for an elevated VL as outlined on page 39.

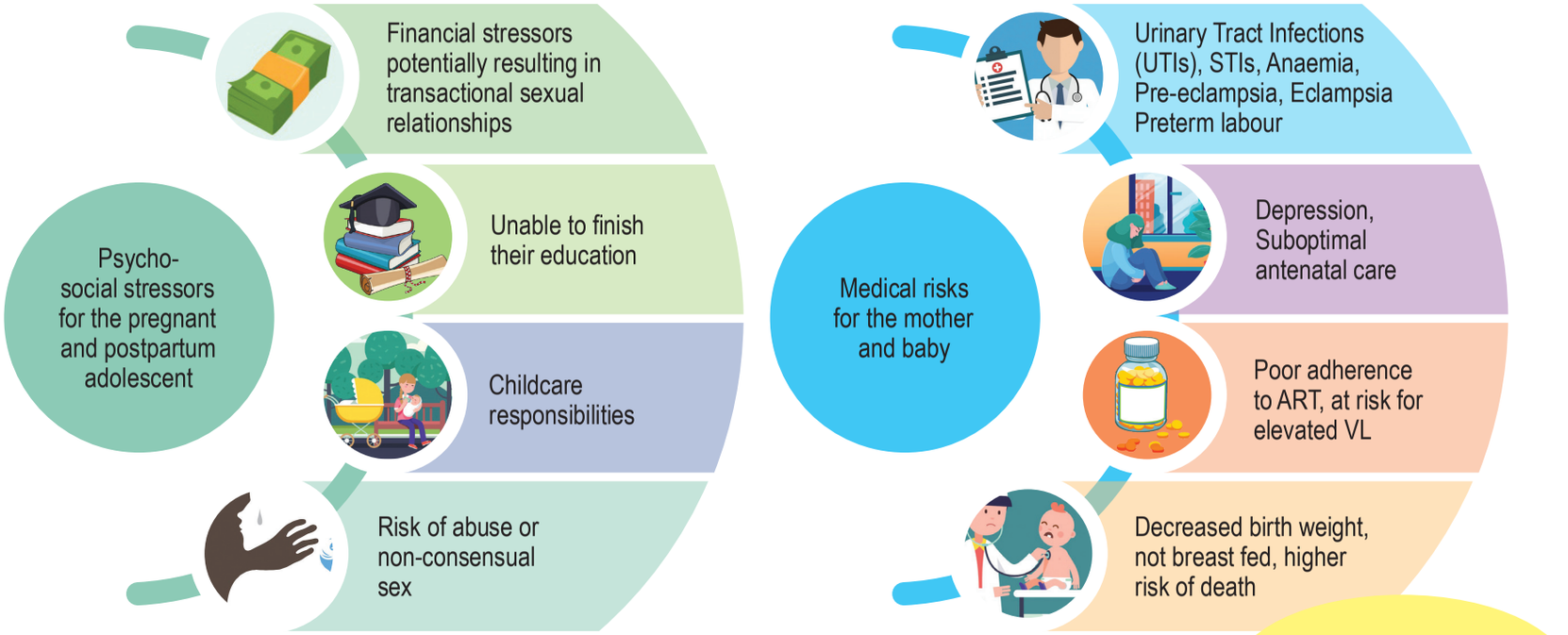


* The shorter 4-week interval between the first VL above 1000 and the repeat VL is preferred wherever possible. However, if the first elevated VL is the **delivery-VL**, the next visit may only occur at the 6-weeks post-natal visit. A HBVsAg and HB can also be done at the same time to inform the switch to 2nd line if this becomes necessary.

The shorter 8-week interval between the first VL of 50 - 999 c/ml and the repeat VL is preferred wherever possible. However, if the first elevated VL is the **delivery-VL**, and the mother opts to remain in the maternal and child stream for follow-up ART care, the closest coinciding visit will occur at the 10-week EPI visit.

+ Women on an EFV-containing regimen who have a second VL result of between 50 and 999 c/ml may be considered for a switch to a DTG-containing regimen, provided she has been thoroughly assessed for her elevated VL, and has been appropriately counseled as outlined on page 40.

Pregnant adolescents are a vulnerable group that have psycho-social stressors and medical risks that may result poor health outcomes[10]



For a **Summary of 1st line ART Regimens** applicable to adolescents go to page 76

The pregnant adolescent requires non-judgmental, confidential, and quality youth friendly SRH services that are sensitive to the challenges and stressors experienced by adolescents. This care should include:

A determination of whether or not the pregnancy was intended/unintended? wanted/unwanted? Provide counselling about options in terms of proceeding/not proceeding with the pregnancy.

High quality basic antenatal care, considering the additional medical risks in an adolescent.

Intensive ART adherence support during ANC, breastfeeding and there-after. If available, she should attend a peer-led support group.

Education and intensive support for **breastfeeding and PMTCT**. Adolescent are more likely not to breastfeed.

Counselling on **contraceptives, STIs** as well as **re-entering the education system**. Long-acting reversible contraceptive methods are preferred.

An exploration of the **possibility of abuse or non-consensual sex** to ensure that she is in a safe environment. If not, the involvement of the police and social services should be facilitated.

PROPHYLAXIS FOR THE HIV-EXPOSED INFANT AT BIRTH

The PMTCT guideline uses two VL thresholds. If any client on ART, including mothers, surpasses the first VL threshold of 50 c/ml, action is required to timeously assess for possible causes that may lead to confirmed virological failure. Once the maternal VL exceeds 1000 c/ml, the risk for MTCT warrants the use of high-risk prophylaxis.

Principles for Infant Prophylaxis:

Principle 1: The delivery-VL will determine the risk profile of the infant. If the result of delivery VL is not yet available, use the result of the most recent VL in the last 12 weeks of antenatal care

Principle 2: At birth, treat the infant as high risk unless there is evidence to prove they are low risk. When the delivery-VL result becomes known at the 3-6-day postnatal visit, the infant can be re-classified as high-/ low-risk and prophylaxis adjusted accordingly

Principle 3: Continue high-risk prophylaxis until mom's VL is suppressed. NVP should be stopped after 12 weeks only if the mother's VL is confirmed to be less than 1000c/ml

Definition of a low-risk infant at birth: Infant born to a mother with a VL < 1000 c/mL (delivery VL, or VL in last 12 weeks of ANC if delivery VL not yet available)

Definition of a high-risk infant at birth: Infant born to a mother with a VL > 1000 c/mL (delivery VL, or VL in last 12 weeks of ANC if delivery VL not yet available, or no VL available in last 12 weeks)

TABLE 22 PROPHYLAXIS FOR THE HIV-EXPOSED INFANT

For Prophylactic Dosages for the HIV-Exposed Infant see Annexure 6 on page 100

Risk Profile	Antenatal	Labour and Delivery	Postnatal Period (6 weeks PP / 12 weeks PP)
Low-Risk Mom	Mom booked early in ANC, and is adherent to treatment	**Delivery VL < 1000 c/ml**	Mom's VL: Continue the VL monitoring and management schedule on page 78
Low-Risk Infant	Keeping the mom's VL suppressed is the best way to protect her infant	Infant gets Birth PCR	**NVP** Once daily: Baby gets NVP for 6 weeks only → STOP NVP → Start cotrimoxazole from 6 weeks onwards ★★
High Risk Mom	Mother with a VL of ≥ 1000 c/ml (most recent VL taken during the last 12 weeks of antenatal care), or a mother with no VL result in the last 12 weeks.	**Delivery VL ≥ 1000 c/ml**	Mom's VL: Get the mom's VL suppressed as a matter of urgency! Even though NVP prophylaxis to the infant can be stopped if her VL is < 1000 c/ml, any detectable VL ≥ 50 c/ml means the virus is replicating and puts her at risk for developing resistance mutations. Follow the **VL Non-suppression algorithm** on page 79 → Mom's VL < 1000c/ml
High Risk Infant	Any situation that causes mom to have an elevated VL puts her infant at risk for HIV infection	**Infant gets Birth PCR.** If at discharge no VL result is available (delivery-VL or a VL in the last 12 weeks), initiate the baby on high risk prophylaxis until result can be checked at 3-6-day postnatal visit	**NVP** Once daily: The breastfed baby gets NVP for a minimum of 12 weeks, and if needed, ongoing until mothers VL is < 1000 c/ml, or until 4 weeks after cessation of all breastfeeding. The exclusive formula-fed baby will receive NVP for 6 weeks. → STOP NVP **AZT** Twice daily: Baby gets AZT for 6 weeks only, whether breastfed or formula fed → STOP AZT → Start cotrimoxazole from 6 weeks onwards ★★

STOP ★★ *Stop cotrimoxazole when PCR is negative ≥ 6 weeks after full cessation of breastfeeding AND infant is clinically HIV negative*

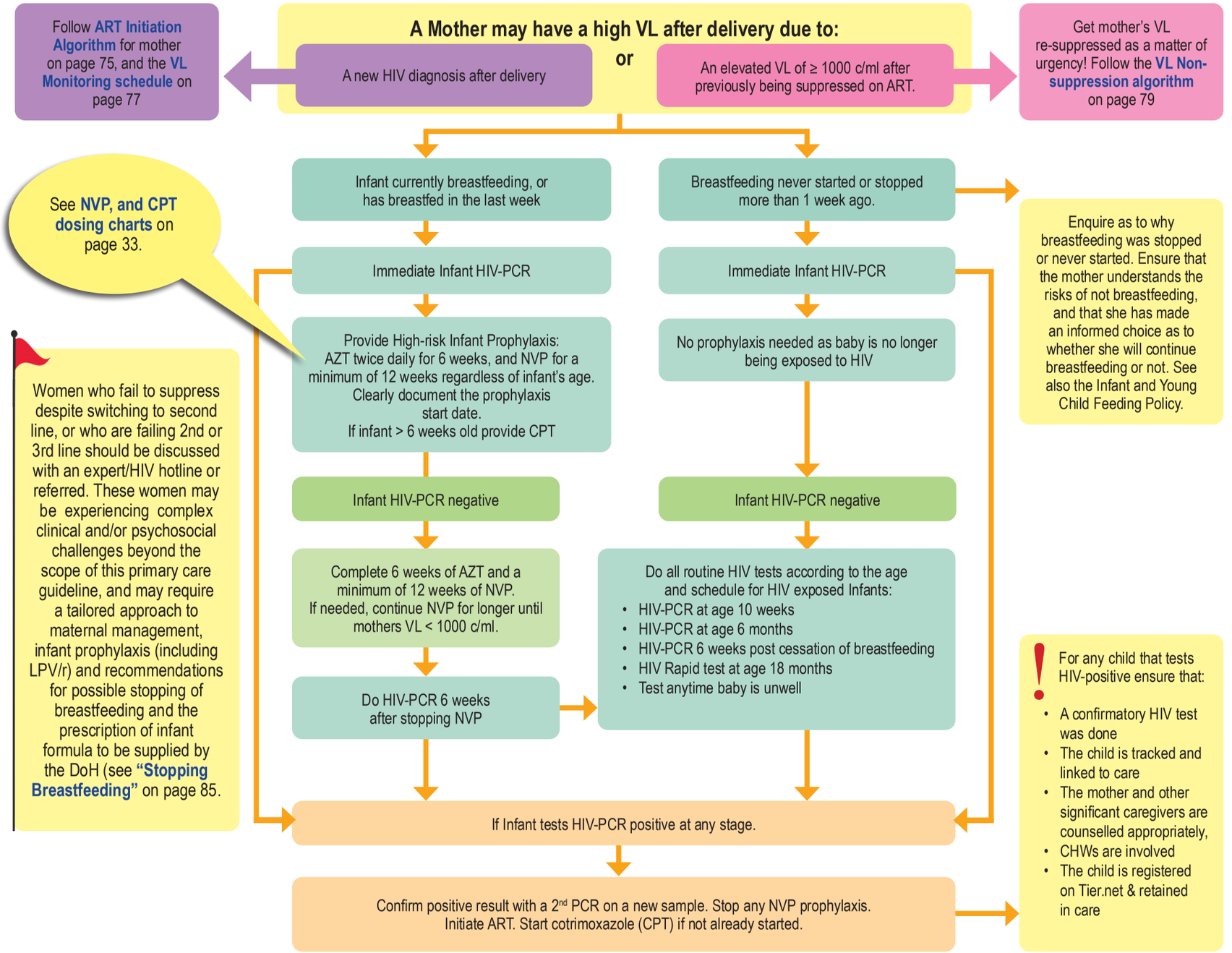
Prophylaxis for the HIV-exposed Infant during Breastfeeding

A mother may have an elevated VL during breastfeeding due to 1) a new HIV diagnosis during breastfeeding, or 2) an unsuppressed VL on ART. Regardless of the cause, an elevated viral load in a breastfeeding mother should be considered a “medical emergency.” Every effort should be made to re-suppress the mother’s VL according to the VL non-suppression algorithm on page 79. Her infant should receive high-risk prophylaxis which “buys time” to regain maternal viral suppression while allowing breastfeeding to be protected. High-risk prophylaxis consists of AZT twice daily for six weeks, and NVP daily for a minimum of 12 weeks. NVP to the infant should only be stopped if the mother’s VL has confirmed to be suppressed, or she has stopped breastfeeding.

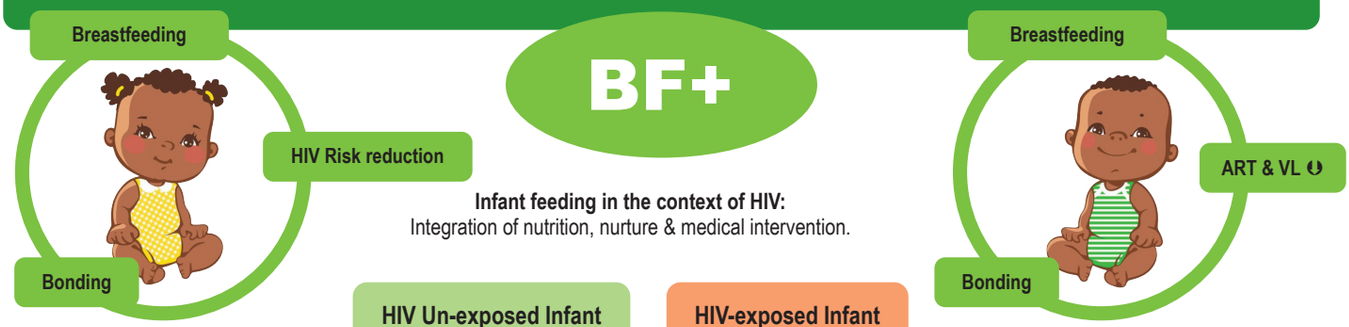
SUMMARY OF THE INDICATIONS FOR HIGH- AND LOW-RISK INFANT PROPHYLAXIS

TABLE 23 SUMMARY OF THE INDICATIONS FOR HIGH-AND LOW-RISK INFANT PROPHYLAXIS

Risk Profile	Indications	Prophylaxis
Low-risk prophylaxis at birth, whether breastfed or exclusively formula-fed	At birth: • VL at delivery is < 1000 cop-ies/mL	NVP at birth and then daily for six weeks.
High-risk prophylaxis at birth in the breastfeeding infant	At birth: • Mother on ART with VL ≥ 1000 c/mL at delivery or no HIV viral load available at deliv-ery (or within the last 12 weeks prior to birth) • Mother not on ART at delivery.	AZT twice daily for six weeks. NVP for a minimum of 12 weeks. Stop infant NVP only af-ter confirmation of VL being less than 1000 c/mL, or until four weeks after cessation of all breastfeeding.
High-risk prophylaxis at birth in the exclusively formula-fed infant from birth	At birth: • Mother on ART with VL ≥ 1000 c/mL at delivery or no HIV viral load available at delivery (or within the last 12 weeks prior to birth) • Mother not on ART at delivery.	AZT twice daily for six weeks NVP at birth and then daily for six weeks.
High-risk prophylaxis during breastfeeding	During breastfeeding: • Breastfeeding mother diagnosed HIV positive > 72 hours after delivery • Mother on ART with latest VL ≥ 1000 copies/mL during breastfeeding.	AZT twice daily for six weeks. NVP for a minimum of 12 weeks. Stop infant NVP only after confirmation of VL being less than 1000 c/mL, or until four weeks after cessation of all breastfeeding.


Follow ART Initiation Algorithm for mother on page 75, and the VL Monitoring schedule on page 77
A Mother may have a high VL after delivery due to:
A new HIV diagnosis after delivery
or
An elevated VL of ≥ 1000 c/ml after previously being suppressed on ART.
Get mother's VL re-suppressed as a matter of urgency! Follow the VL Non-suppression algorithm on page 79
See NVP, and CPT dosing charts on page 33.
Infant currently breastfeeding, or has breastfed in the last week
Breastfeeding never started or stopped more than 1 week ago.
Enquire as to why breastfeeding was stopped or never started. Ensure that the mother understands the risks of not breastfeeding, and that she has made an informed choice as to whether she will continue breastfeeding or not. See also the Infant and Young Child Feeding Policy.
Immediate Infant HIV-PCR
Immediate Infant HIV-PCR
Provide High-risk Infant Prophylaxis: AZT twice daily for 6 weeks, and NVP for a minimum of 12 weeks regardless of infant's age. Clearly document the prophylaxis start date. If infant > 6 weeks old provide CPT
No prophylaxis needed as baby is no longer being exposed to HIV
Women who fail to suppress despite switching to second line, or who are failing 2nd or 3rd line should be discussed with an expert/HIV hotline or referred. These women may be experiencing complex clinical and/or psychosocial challenges beyond the scope of this primary care guideline, and may require a tailored approach to maternal management, infant prophylaxis (including LPV/r) and recommendations for possible stopping of breastfeeding and the prescription of infant formula to be supplied by the DoH (see "Stopping Breastfeeding" on page 85.
Infant HIV-PCR negative
Infant HIV-PCR negative
Complete 6 weeks of AZT and a minimum of 12 weeks of NVP. If needed, continue NVP for longer until mothers VL < 1000 c/ml.
Do all routine HIV tests according to the age and schedule for HIV exposed Infants:
• HIV-PCR at age 10 weeks
• HIV-PCR at age 6 months
• HIV-PCR 6 weeks post cessation of breastfeeding
• HIV Rapid test at age 18 months
• Test anytime baby is unwell
Do HIV-PCR 6 weeks after stopping NVP
For any child that tests HIV-positive ensure that:
• A confirmatory HIV test was done
• The child is tracked and linked to care
• The mother and other significant caregivers are counselled appropriately,
• CHWs are involved
• The child is registered on Tier.net & retained in care
If Infant tests HIV-PCR positive at any stage.
Confirm positive result with a 2nd PCR on a new sample. Stop any NVP prophylaxis. Initiate ART. Start cotrimoxazole (CPT) if not already started.

Breastfeeding Plus



Infant feeding in the context of HIV:
Integration of nutrition, nurture & medical intervention.

HIV Un-exposed Infant

HIV NEGATIVE WOMEN

1. HIV Risk Reduction
   - Number of sexual partners
   - Condom use
   - Partner testing
   - Partner ART and viral suppression
   - PrEP (as available and applicable)
2. Regular HIV Testing
3. Infant Feeding advice and support

HIV-exposed Infant

WOMEN LIVING WITH HIV

1. ART and VL suppression
2. Infant prophylaxis
3. Infant testing
4. HIV Risk reduction (re-infection and risk to partner)
   - Number of sexual partners
   - Condom use
   - Partner testing
   - Partner ART and viral suppression
5. Infant Feeding advice and support

Whether a woman is living with HIV or HIV-uninfected, recommendations for Infant feeding remain the same

HIV VL suppression in mother is essential to prevent MTCT through breastfeeding!

Infant Feeding Advice

For all women, exclusive breastfeeding (EBF) is recommended for the 1st six months of life. Thereafter, breastfeeding should continue for two years or longer, with the introduction of nutritionally adequate, appropriate and safe complementary feeding. Women living with HIV should be fully supported for ART adherence during the breastfeeding period and thereafter

Antenatal	6 months	12 months	18 months	2 years
Counselling on the benefits of breastfeeding should start during the antenatal period	Early initiation of BF within 1 hour after birth. EBF for 1st 6 months of life	**Continue breastfeeding until 2 years of age or longer**		
		Start introducing age appropriate solid foods from 6 months onwards as outlined in the RTHB		

Introducing solids before 6 months is strongly discouraged! The younger the infant, the higher the risk to the infant's health.

WHO Practice Statements for Women Living with HIV

- Any mother that is mixed feeding in the first 6 months should be encouraged to return to exclusive breastfeeding.
- However, 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, practicing mixed feeding with formula milk is not a reason to stop breastfeeding in the presence of ARV drugs.
- 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.

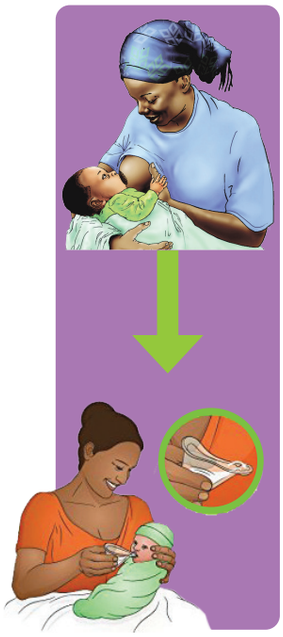
WHO PRACTICE STATEMENTS FOR WOMEN LIVING WITH HIV

- Any mother that is mixed feeding in the first six months should be encouraged to return to exclusive breastfeeding.
- However, 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, practicing mixed feeding with formula milk is not a reason to stop breastfeeding in the presence of ARV drugs and maternal viral suppression.
- 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.

Breastfeeding in a Women with an Elevated VL

It is recommended that women with a VL ≥ 1000 c/ml on first-line ART continue to breastfeed. Infant prophylaxis should be extended/restarted while a concerted effort is made to re-suppress the mother's VL (see Management of a High Maternal Viral Load after Delivery on page 83). Breastfeeding in women who are failing 2nd and 3rd line ART is not recommended. These women should be referred or discussed with a team of experts. See also Stopping Breastfeeding and Indications for Formula Feeding below.

Stopping Breastfeeding



Stopping Breastfeeding

Mothers living with HIV who decide to stop breastfeeding should do so gradually over a period of a month. Abrupt cessation of breastfeeding is not recommended and may increase the VL in breastmilk. If subsequent intermittent breastfeeding should occur, the infant is at increased risk of becoming HIV infected.

Infants who have been receiving ART prophylaxis should continue prophylaxis for four weeks after all breastfeeding has stopped.

Children must receive an adequate diet following cessation of breastfeeding as outlined in the Infant and Young Child Feeding Policy.

Indications for Formula Feeding to be provided by the Dept of Health Supplementation Scheme

1. Infants of mothers who are failing second or third-line ARV treatment (VL ≥1000 copies/ml) should be advised not to breastfeed.
2. The mother has died, or the infant has been abandoned.
3. Other individual circumstances deemed necessary by a multidisciplinary team including certain metabolic conditions in the infant, medical conditions in the mother, or certain maternal medications as outlined in the PHC EML.

MANAGEMENT OF INDETERMINATE PCR RESULTS IN INFANTS

Indeterminate HIV-PCR result
(This result is not positive, but not negative either)

Check for prior HIV-PCR and VL results

- Prior HIV-PCR is positive or indeterminate And/or Prior HIV VL is detectable → Treat infant as HIV infected Initiate ART
- Prior HIV-PCR or VL is negative or undetectable, or No prior HIV-PCR or VL done → Repeat HIV-PCR and HIV VL urgently
  - HIV-PCR is positive or indeterminate and/or HIV VL is detectable → Treat infant as HIV infected Initiate ART
  - HIV-PCR is negative and HIV VL is undetectable # → Further HIV testing as per PMTCT guidelines

Final HIV status cannot be determined until the infant has stopped all antiretroviral prophylaxis and is at least 6 weeks post-cessation of breastfeeding. In cases where clients have been initiated on ART and diagnosis remains uncertain, clients should be referred for further management by a specialist clinical and laboratory team. ART should never be stopped without specialist supervision.

! If in doubt, discuss with a virologist, or contact the NICD at HIV@nicd.ac.za Document all test barcodes in the RTHB and referral letters

PCR, polymerase chain reaction; VL, viral load; ART, antiretroviral therapy

THE ABANDONED INFANT

Abandoned infant with unknown HIV exposure
Treat infant as a high-risk, HIV-exposed infant

Perform an HIV-PCR and HIV rapid test[$].
Provide high-risk infant prophylaxis.

Start NVP once daily for 6 weeks and AZT twice daily for 6 weeks

- HIV-PCR is negative → Do HIV-PCR at 10 weeks of age or 4 weeks after stopping NVP
  - HIV- PCR is negative → Go to **Management of HEU infant** on page 89
  - HIV-PCR is positive → Initiate ART as per guidelines and confirm with a second HIV-PCR or VL.
- HIV-PCR is positive → Stop NVP (and AZT) → Initiate ART as per guidelines and confirm with a second HIV-PCR or VL.

[$] A positive HIV rapid test will confirm HIV exposure and assist clinical management. However, a negative HIV rapid test may be falsely negative. Due to the unavailability of the mother, the HIV-exposure status of an infant with a negative rapid test can therefore not be definitively established. For this reason, all abandoned infants should have an HIV-PCR test performed and be managed as a high-risk HIV-exposed infant. An HIV rapid test therefore adds value if it is positive but does not change the management of the infant if it should be negative.

ALL women should be screened for TB at every visit

At 1st / Booking visit in ANC

All pregnant women with a new HIV diagnosis, or
All known HIV positive woman with new pregnancy diagnosis
(whether on ART or not on ART)

Assess TB symptoms and clinical condition:
If TB symptoms without danger signs, or no TB symptoms present, **initiate ART**.
If the woman appears very ill with any of the following signs, **discuss with a doctor or refer for further assessment. Do not start ART until TB is excluded/diagnosed as these women may be at a higher risk of developing IRIS:**
weight loss > 5%, difficulty breathing, respiratory rate >30/min, temperature > 38°C, pulse > 100min, BP < 90/60, coughing up blood, confusion or agitation, or unable to walk unaided.

Do a TB GXP for all women at 1st visit in ANC, due to the lower sensitivity of the symptom screen in pregnant women.

- GXP neg, but TB symptoms still present → Additional investigations as per National TB Guidelines If CD4 ≤ 100, do a urine LAM → TB diagnosis confirmed → Initiate TB Rx
- GXP positive → Initiate TB Rx
- TB GXP negative (or unable to produce sputum) AND no TB symptoms → Initiate/continue ART
  - CD4 more than 350 → Defer TPT until 6 weeks after delivery
  - CD4 350 or less → Initiate TPT after contra-indications have been excluded*

Review in 2 weeks: If stable and tolerating TB Rx, continue TB Rx and initiate/continue ART:
TDF, 3TC/FTC, EFV/DTG$
If TB meningitis, defer ART for 4 to 6 weeks

At Follow-up visits

HIV positive woman currently on TPT

Check:
1. Adherence to TPT, ART and CPT
2. Side-effects of TPT
3. TB symptoms

- 1 or more TB symptoms present → Investigate as per National TB Guideline → If TB diagnosed, stop TPT, initiate full TB Rx and send a sputum sample for LPA, or culture and drug sensitivity test (DST)
- No TB symptoms present → Continue TPT for a total of 12 months

All HIV positive women from 6 weeks after birth who had TPT deferred in pregnancy (CD4 count above 350 during antenatal care)

TB symptom screen

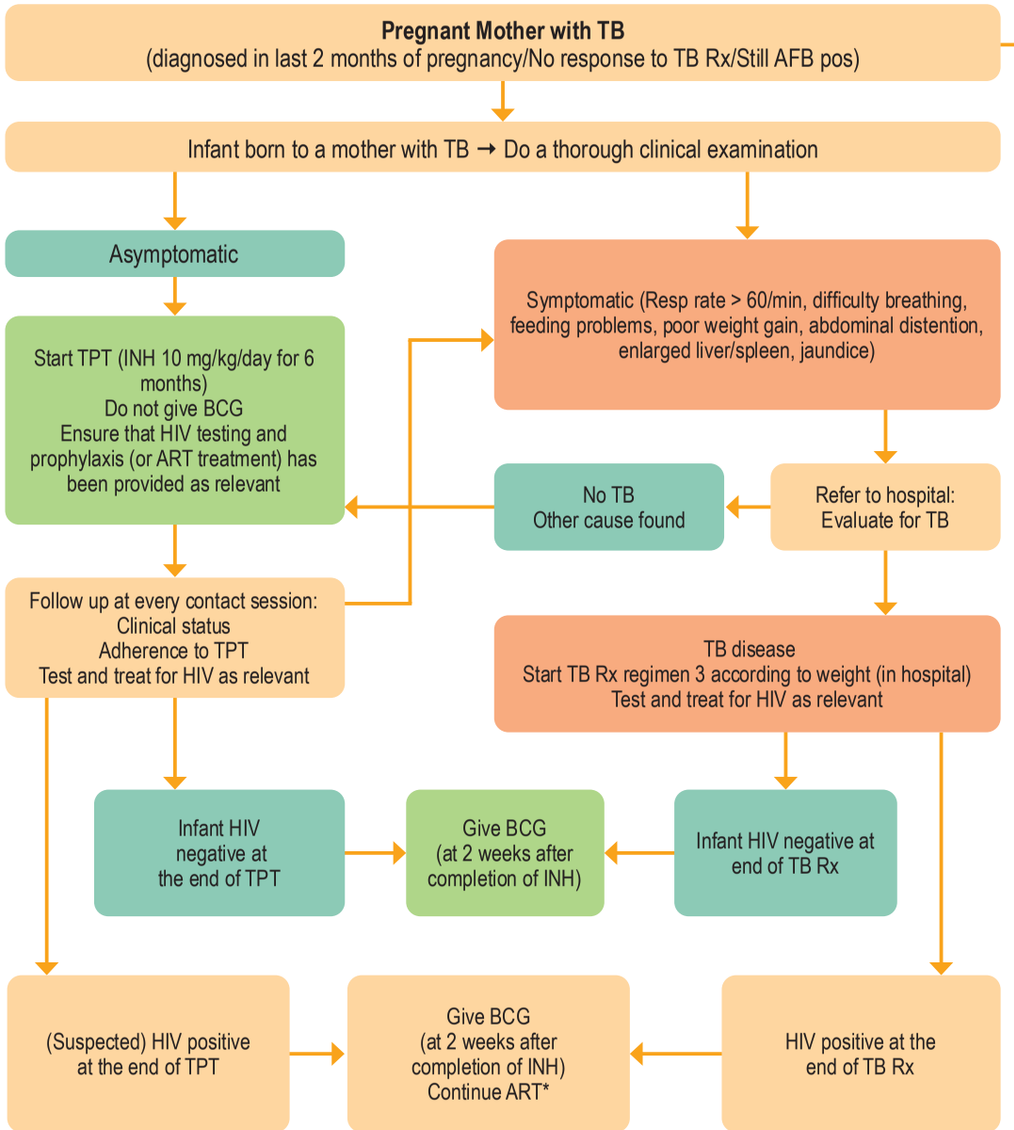
- No TB symptoms present → Initiate TPT for 12 months (after excluding other contra-indications to TPT *) Record start date of TPT
- 1 or more TB symptoms present → Investigate as per **National TB Guideline**

***Contra-indications to TPT**
- Positive TB symptom screen
- Alcohol abuse
- Liver disease
- Known hypersensitivity to INH

TPT dosage: Isoniazid (INH) 300 mg daily PO, and Pyridoxine 25 mg OD PO x 12 months

The **APPRISE** randomised control trial found a higher incidence of adverse pregnancy outcomes in mothers who used TPT in pregnancy[11, 12, 13]

DTG requires boosting with rifampicin-containing TB treatment.
See page 32 on **drug interactions with DTG**



Refer/discuss any mother diagnosed with **drug resistant TB** with an expert or call the HIV Hotline 0800 212 506

INH Dosing Chart	
Isoniazid (INH), oral, 10 mg/kg daily for 6 months. Maximum dose 300 mg daily	
Weight (kg)	**Daily INH (100mg tablet)**
>2-3,4 kg	¼ tablet
>3,5-6,9 kg	½ tablet
>7-9,9 kg	1 tablet
>10-14,9 kg	1 ½ tablets
>15-19,9 kg	2 tablets
>20-24,9 kg	2 ½ tablets
>25 kg	3 tablets

*If ART is delayed due to other clinical complications, discuss with an expert or the HIV Hotline to determine the best course of action regarding BCG vaccination

CARE OF THE HIV-EXPOSED BUT UNINFECTED INFANT

More than 25% of the total infant population in SA are HIV-exposed and more than 98% of these infants are HIV negative. Yet, having escaped HIV infection, they may still suffer the consequences of being born to a woman living with HIV. HIV-exposed but Uninfected (HEU) children still require:

Routine Child Health Management

- Manage and treat acute problems according to the IMCI guidelines
- Provide feeding counselling and support
- Monitor growth and development
- Provide routine immunizations, Vit A, and deworming
- Screen for TB symptoms and TB index cases and manage accordingly
- Ask about mother's health, ART adherence, and family planning needs
- Provide social support and counselling for age-appropriate parental disclosure

Routine Management for the HIV-Exposed Infant

- Ongoing interventions to prevent vertical transmission through breastfeeding
- All routine HIV tests as indicated in this guideline for HIV-exposed infants

Additional Management for the HEU Infant

HEU infants may experience poorer outcomes despite being HIV uninfected, and may require more regular follow-up.
Identify high-risk HEU infants who may require closer monitoring, including those with:

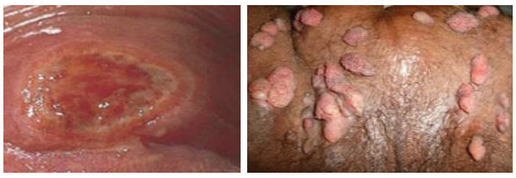
- Poor birth outcomes
- Symptoms of anaemia
- Impaired growth and/or neurodevelopment
- History of hospitalisation
- Maternal illness or death

Ongoing Care for the Mother and her Family

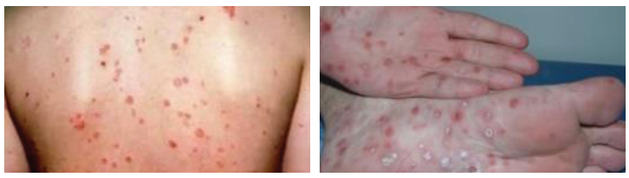
- Remember to provide appropriate ongoing care to the women living with HIV and her family.
- If a breastfeeding mother is sick or hospitalised, consider appropriate ways she can continue breastfeeding. If not, ensure that baby receives appropriate care whilst mother is hospitalised.
- Screen partner and other children for HIV and other infectious disease as indicated (e.g. TB)

SYPHILIS

Syphilis is a sexually transmitted infection that can have multiple different presentations but also be asymptomatic. The signs of secondary syphilis occur six to eight weeks after the primary ulcer (chancre) and include a generalized rash (including palms and soles), flu-like symptoms, flat wart-like genital lesions (condylomata lata), mouth ulcers and patchy hair loss. Tertiary syphilis occurs many years later and affects skin, bone, heart and nervous system.

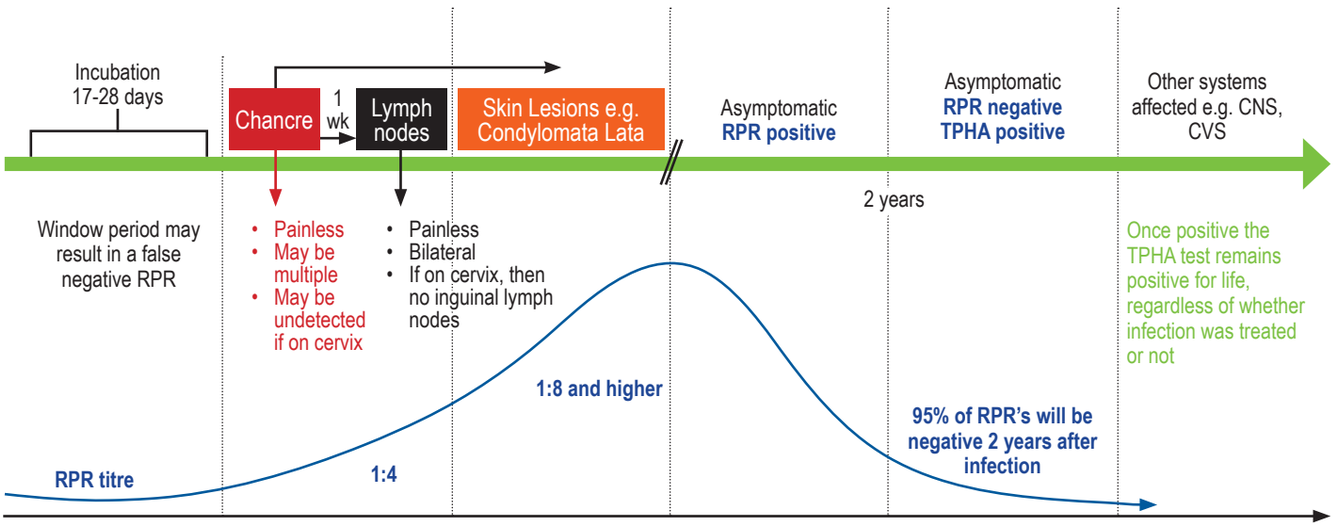


Painless ulcer/chancre and condylomata lata on genitals



Rash involving palms and soles

The stages of disease progression of syphilis are illustrated in the figure below, together with the typical clinical presentation in each stage, and the level of the RPR titer (blue graph). Note that a genital ulcer caused by syphilis will resolve spontaneously within four to six weeks without treatment; however, the syphilis infection persists, and the ulcer resolving does not represent cure.



Testing for Syphilis	First test	Confirmatory test
Use of RPR	RPR (rapid or laboratory)	TPHA (laboratory)
If rapid syphilis testing used (dual and standalone)	TPHA (HIV-syphilis combination or standalone syphilis test)	RPR (rapid or laboratory)

Testing for Syphilis

It is important to know what type of test is being used to test for syphilis. Older syphilis tests are of the RPR type (non-treponemal test). False positive RPR's can occur. It is therefore good practice to confirm any positive RPR with a TPHA/FTA test (treponemal test). TPHA remains positive for life, but an RPR changes in titer in response to treatment or disease progression. Consider re-infection if the RPR titer increases by four times or more. Conversely, if a TPHA is used as the first test (as what is used in the HIV-syphilis combination or standalone syphilis rapid test), the positive result should be confirmed using an RPR. The RPR will determine if the positive TPHA result indicates a current active infection or an earlier infection.

Congenital Syphilis

Vertical transmission occurs in 40% of mothers with untreated syphilis, and can result in miscarriage, still birth, non-immune hydrops fetalis and congenital syphilis of the newborn. Signs of congenital syphilis are desquamative rash (red/blue spots or bruising especially on soles and palms), jaundice, pallor, distended abdomen due to enlarged liver or spleen, low birthweight, respiratory distress, large, pale placenta, and hypoglycaemia.

Treating the Newborn Infant

Examine and treat the newborn of the mother with syphilis:
Well (asymptomatic) baby: Treat baby with Benzathine penicillin 50 000 u/kg intramuscularly (IM) stat only if:

- Mother was not treated, or
- If the mother has received less than three doses of benzathine benzylpenicillin, or
- If the mother delivers within four weeks of commencing treatment.

Symptomatic baby:

- Refer all symptomatic babies for treatment of congenital syphilis:
- Procaine penicillin 50 000 u/kg IM daily for 10 days, or benzyl penicillin (penicillin G) 50 000 u/kg/dose 12-hourly intravenously (IV) for 10 days
- Erythromycin does not reliably cure syphilis in either the mother or the baby

SYPHILIS IN PREGNANCY

All pregnant women at first visit and repeat testing at 32-34 weeks for women testing negative in the first trimester

Take history and examine, explain needs for syphilis screening, do pre-test counselling for HIV

Do a syphilis test, an HIV test, and any other tests according to the BANC Plus protocol

Any STI syndrome or illness?

Y

Use appropriate flowchart, manage appropriately

Syphilis positive?

Y

Treat pregnant woman with:

- **Benzathine penicillin** 2.4MU imi once weekly for 3 weeks. Reconstitute with 6mL of lidocaine 1% without epinephrine (adrenaline)

OR In case of penicilin allergy:

- Refer for penicillin desensitisation

HIV test positive?

Y

Post test counselling, same day TB screen, HIV education, CD4 count, creatinine, clinical staging, support, and same day ART start

N

Repeat HIV testing **monthly** at every full BANC Plus visit throughout pregnancy, at labour/delivery, at 10-week EPI visit, and every 3 months throughout breastfeeding

Symptomatic newborns of mothers with positive syphilis test during pregnancy:

- Refer all symptomatic babies

Notify: Notification of medical conditions, form GW17/5

Treat asymptomatic newborns of mothers with positive syphilis test if mother was not treated, ***OR*** if mother received < 3 doses of Benzathine penicillin, ***OR*** if mother delivers within 4 weeks of commencing treatment, with:

- **Benzathine penicillin** (depot formulation), IM, 50,000 units/kg as a single dose into lateral thigh*

** Benzathine penicillin (depot formulation) must never be given IV*

Follow up at 3 months after the last injection to confirm a fourfold (i.e. 2 dilution) reduction in RPR litres, provided the initial litre was > 1:8. If the initial litre was ≤ 1:8, further reduction may not occur.

All pregnant women:

- Educate, ensure compliance and counsel; promote couple-counselling if applicable
- Explain the risk of vertical transmission
- Promote consistent condom use particularly during pregnancy, demonstrate condom use, provide condoms
- Stress the importance of partner treatment, issue one notification slip for each sexual partner
- Promote HIV counselling and testing of partner

Source: Sexually Transmitted Infections Management Guidelines 2015, Adapted from: Standard Treatment Guidelines and Essential Drugs List PHC

DOCUMENTATION IN THE CLIENT RECORD

Document all clinical findings, results and decisions clearly, and insert the barcode stickers of any blood tests taken in the following client records as applicable:

1. The Maternity Case Record
2. The Adult Clinical Record (ART Stationery) for HIV positive women, if available in that facility
3. The Road to Health Booklet for the HIV-exposed infant

USING NHLS REPORTS FOR QUALITY IMPROVEMENT AND CLIENT TRACKING

These reports are compiled from NHLS HIV laboratory data and are e-mailed in different formats depending on the user's requirements. The purpose of these reports is to assist with monitoring of the HIV PMTCT program, identify HIV-infected pregnant women with high viral loads and link HIV-infected infants to care.

REPORT NAME	REPORT NO.	DESCRIPTION	USEFUL FOR
HIV PCR Facility Report	RPT01001	• Provincial level data disaggregated per facility • Number of PCR tests and results at each facility per age range • Reported per month with comparison to previous year • Can be used to check accuracy of DHIS stats • Total MDOs per facility reported	▲●
HIV National Report (Birth Testing)	RPT01008	• National monthly report • Number of PCR tests done within 7 days of birth with results and MDOs • Reports intra-uterine infection case rates	▲●
HIV PCR RfA Report	RPT01002 W/D	• All verified PCR results (with client identifiers) since the previous weekly (W)/daily (D) report • To assist with tracing HIV-exposed infants and linkage to care • All previous HIV PCR results per client are also reported (within limitations of demographic linking)	●■
HIV VL RfA Report (all ages)	RPT00001 W/D	• All VL ≥ 1000 c/ml (with client identifiers) since previous weekly (W)/daily (D) report • Previous consecutive VL ≥ 1000 c/ml per client are also reported (within limitations of demographic inking)	●■
HIV PCR MDO Report	RPT01004/5/6/7 (monthly)	• Facilities with the highest number of MDOs are listed at either National, Provincial, District or Facility level • The 10 facilities with the most MDOs in a region receive a detailed report of their MDOs (e.g. rejection type, rejection reason and test result text) • A laboratory report is also available for laboratorians • To improve the quality of specimen collection and processing	▲●■★

RfA, Results for Action; MDOs, Missed Diagnostic Opportunities = registered HIV PCR tests that are neither positive or negative (includes rejections, invalid and indeterminate results); DHIS, District Health Information System

DESCRIPTION	DESCRIPTION
▲	National/ Provincial/ District Manager
●	Facility Manager
■	Clinical Healthcare Worker
★	Laboratorian

Registering on the self-service portal and requesting reports
STEP 1: Go to **www.nicd.ac.za**
→ Click on the "M&E Dashboards" and "HIV"
→ Select "Guest User"
→ Click on "Self Service Registration"
→ Self-Service Portal Landing Page
STEP 2: Select "New User Registration" → Complete the registration form, and follow further instructions

Please direct any queries to **HIV@nicd.ac.za**

ANNEXURE 1 SUMMARY OF DOSAGES, COMMON SIDE EFFECTS, AND SUBSTITUTIONS ASSOCIATED WITH FIRST- AND SECOND-LINE ART IN ADULTS AND ADOLESCENTS

Generic name	Drug Class *	Recommended dosage	Common or severe side effects (Life-threatening reactions are indicated in bold)	Replacement Drug
Tenofovir (TDF) (for those > 35 kg and > 10 years of age)	NtRTI	300 mg daily	Renal failure, tubular wasting syndrome (rare), reduced bone mineral density, nausea. TDF should not be used in patients with uncontrolled hypertension or diabetes with renal failure. Assess renal function as per the table on page 24	ABC
Lamivudine (3TC)	NRTI	150 mg 12-hourly or 300 mg daily	Anaemia (pure red cell aplasia) (rare), hyperlactataemia (rare)	
Emtricitabine (FTC)	NRTI	200 mg daily	Palmar hyperpigmentation, hyperlactataemia (rare)	
Abacavir (ABC)	NRTI	300 mg 12-hourly or 600 mg daily	Hypersensitivity reaction (rare), hyperlactataemia (rare)	AZT or TDF
Zidovudine (AZT)	NRTI	300 mg 12-hourly	Anaemia, neutropenia, GI upset, headache, myopathy, hyperlactataemia or steatohepatitis (medium potential), lipoatrophy	Discuss with an ex-pert*
Dolutegravir (DTG) (for those > 20 kg)	InSTI	50 mg daily Add a single tablet of DTG 50 mg 12 hours after TLD if on TB treatment (rifampicin)	Insomnia, dizziness, headache and other CNS side effects, GI upset, weight gain, hepatitis, rash (rare),	EFV
Efavirenz (EFV)	NNRTI	600 mg at night (400 mg at night if < 40 kg)	Central nervous system symptoms (vivid dreams, problems with concentration, dizziness, confusion, mood disturbance, psychosis), rash, hepatitis, gynaeco-mastia. EFV is contraindicated if active psychiatric illness present	DTG or LPV/r if DTG is contra-indicated
Atazanavir (ATV)	PI*	300 mg with ritonavir 100 mg daily	Unconjugated hyperbilirubinaemia (visible jaundice in minority of patients), dyslipidaemia (low potential), renal stones, hepatitis (uncommon)	
Lopinavir/ ritonavir (LPV/r)	Boosted PI	400/100 mg 12-hourly or 800/200 mg daily (only if PI-naive)	GI upset, dyslipidaemia, hepatitis	ATV/r or DTG (discuss with an ex-pert)
Nevirapine (NVP)	NNRTI	200mg daily for 14 days, then 200mg twice daily. In unbooked women in labour, sdNVP is used as a 200mg tablet together with a stat dose of TLD	Hepatotoxicity, hypersensitivity reaction, Stevens-Johnson syndrome. Avoid NVP if CD4 count ≥250cells/µl for women, and ≥400cells/µl for men. NVP is no longer advocated for general use and should be used only on the recommendations of an expert.	NVP should only be considered if DTG, EFV, and a PI are contraindicated

* AZT will usually be used as part of a second-line regimen. If the second line regimen contains a PI, AZT can be replaced by either TDF or ABC. However, if the second line regimen contains DTG, TDF/ABC will no longer be suitable as at least one active NRTI is required in a second-line regimen containing DTG. Stavudine may be an option in the short term until the underlying issue has resolved.

Table adapted from: Meintjes, G., Moorhouse, M., Carmona, S., Davies, N., Dlamini, S., Van Vuuren, C., Manzini, T., Mathe, M., Moosa, Y., Nash, J., Nel, J., Pakade, Y., Woods, J., Van Zyl, G., Conradie, F., Venter, F. Adult antiretroviral therapy guidelines 2017. Southern African Journal of HIV Medicine, 18 Jul 20

Abbreviations: NtRTI, nucleotide reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; GI, gastrointestinal; NNRTI, non- nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; InSTI, integrase inhibitor (integrase strand transfer inhibitor); TDF, tenofovir

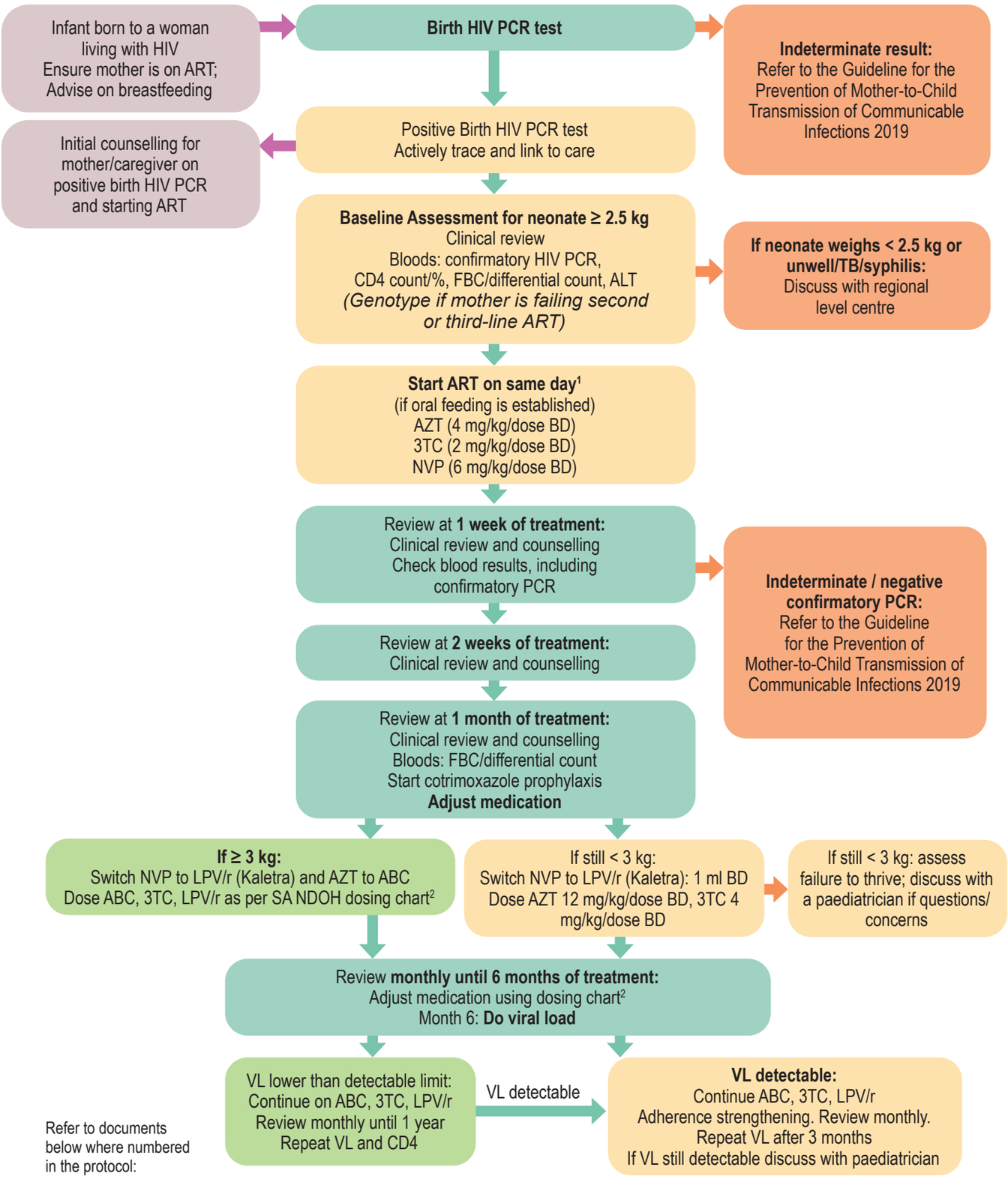
	Abacavir (ABC)		Lamivudine (3TC)		Zidovudine (AZT)	Lopinavir / ritonavir (LPV/r)	Lopinavir/ritonavir when on rifampicin (and for 2 weeks after stopping rifampicin) Choose one of the 3 options below as appropriate			[#]Atazanavir (ATV) + ritonavir (RTV)	Dolutegravir (DTG)	Dolutegravir when on rifampicin	Efavirenz (EFV)	
Target dose	8 mg/kg/dose **TWICE daily** OR **If ≥ 10 kg:** 16 mg/kg/dose **ONCE daily**		4 mg/kg/dose **TWICE daily** OR **If ≥ 10 kg:** 8 mg/kg/dose **ONCE daily**		180-240 mg/m²/dose **TWICE daily**	300/75 mg/m²/dose LPV/r **TWICE daily**	**LPV/r std dose + super-boosting with ritonavir (RTV)** solution **TWICE daily** (≥ 0,75 x LPV dose bd)	**LPV/r std dose + super-boosting with ritonavir (RTV)** powder **TWICE daily** (≥ 0,75 x LPV dose bd)	**Double-dose LPV/r tabs ONLY if able to swallow whole LPV/r tabs TWICE daily**	By weight band **ONCE daily**	By weight band **ONCE daily**	By weight band **TWICE daily**	By weight band **ONCE daily**	**Target dose**
Available formulations	Sol. 20 mg/ml Tabs 60 mg (scored, dispersible), 300 mg (not scored), FDC: ABC/3TC 600/300 mg		Sol. 10 mg/ml Tabs 150 mg (scored), FDC: ABC/3TC 600/300 mg		Sol. 10 mg/ml Tabs 100 mg, 300 mg (not scored), FDC: AZT/3TC 300/150 mg	Sol. 80/20 mg/ml Adult tabs 200/50 mg, Paeds tabs 100/25 mg **TABLETS MUST BE SWALLOWED WHOLE**	Solution 80 mg/ml	Oral powder 100 mg/packet	Adult tabs 200/50 mg, Paed tabs 100/25 mg	ATV caps 150, 200 mg: RTV tabs 100 mg	Tabs 50 mg, FDC: TLD 300/300/50 mg	Tabs 50 mg	Caps/tabs 50, 200, 600 mg (not scored); FDC: TEE 300/200/600 mg	**Available formulations**
Wt. (kg)	Currently available tablet formulations of abacavir (except 60 mg), zidovudine, lopinavir/ritonavir, ritonavir, dolutegravir & efavirenz must be swallowed whole and NOT chewed, divided or crushed													**Wt. (kg)**
< 3	Consult with a clinician experienced in paediatric ARV prescribing for neonates (< 28 days of age) and infants weighing < 3kg													**< 3**
3 - 3.9	2 ml bd		2 ml bd		6 ml bd	*1 ml bd	1 ml bd	100 mg (1 packet) bd	Do not use double-dose LPV/r tabs	Avoid ATV capsules when < 15 kg or < 6 years	Not currently recommended: dosing and formulations not available	Not currently recommended: dosing and formulations not available	Avoid using when < 10 kg or < 3 years	**3 - 3.9**
4 - 4.9														**4 - 4.9**
5 - 5.9	3 ml bd		3 ml bd		9 ml bd	*1.5 ml bd	1.5 ml bd							**5 - 5.9**
6 - 6.9														**6 - 6.9**
7 - 7.9	4 ml bd		4 ml bd		12 ml bd OR 1 x 100 mg tab bd									**7 - 7.9**
8 - 8.9														**8 - 8.9**
9 - 9.9														**9 - 9.9**
10 - 10.9	**Choose only one option**		**Choose only one option**			2 ml bd OR 2 x 100/25 mg **paed tabs** am + 1 x 100/25 mg **paed tab** pm	1.5 ml bd		3 x 100/25 mg tabs bd				1 x 200 mg caps/tabs nocte	**10 - 10.9**
11 - 13.9	6 ml bd OR 2 x 60 mg abs bd	12 ml od OR 4 x 60 mg tabs od	6 ml bd	12 ml od										**11 - 13.9**
14 - 14.9	8 ml bd OR 2.5 x 60 mg tabs bd	5 x 60 mg tabs od OR 1 x 300 mg tab od OR 15 ml od	½ x 150 mg tab bd OR 8 ml bd	1 x 150 mg tab od OR 15 ml od	2 x 100 mg tabs am + 1 x 100 mg tab pm OR 15 ml bd	Choose only one option: 2.5 ml bd OR 2 x 100/25 mg **paed tabs** bd OR 1 x 200/50 mg **adult tab** bd	2 ml bd	200 mg (2 packets) bd	4 x 100/25 mg tabs bd OR 2 x 200/50 mg tabs bd	ATV 1 x 200 mg cap od + RTV 1 x 100 mg tab od	1 x 50 mg tab od	1 x 50 mg tab bd	1 x 200 mg cap/tab + 2 x 50 mg caps/tabs nocte	**14 - 14.9**
15 - 16.9														**15 - 16.9**
17 - 19.9														**17 - 19.9**
20 - 22.9	10 ml bd OR 3 x 60 mg tabs bd	1 x 300 mg tab + 1 x 60 mg tab od	1 x 150 mg tab bd OR 15 ml bd	2 x 150 mg tab od OR 30 ml od	2 x 100 mg tabs bd OR 20 ml bd	Choose only one option: 3 ml bd OR 2 x 100/25 mg **paed tabs** bd OR 1 x 200/50 mg **adult tab** bd	2.5 ml bd							**20 - 22.9**
23 - 24.9		1 x 300 mg tab + 2 x 60 mg tab od												**23 - 24.9**
25 - 29.9	1 x 300 mg tab bd	2 x 300 mg tabs od OR 1 x ABC/3TC 600/300 mg tab od	1 x 150 mg tab bd	2 x 150 mg tab od OR 1 x ABC/3TC 600/300 mg tab od	1 x 300 mg tab bd OR 1 x AZT/3TC 300/150 mg tab bd	Choose only one option: 3.5 ml bd OR 3 x 100/25 mg **paed tabs** bd OR +1 x 200/50 mg a**dult tab** bd + 1 x 100/25 mg **paed tab** bd	3 ml bd	300 mg (3 packets) bd	6 x 100/25 mg tabs bd OR 3 x 200/50 mg tabs bd				2 x 200 mg caps/tabs nocte	**25 - 29.9**
30 - 34.9						Choose only one option: 5 ml bd OR 4 x 100/25 mg **paed tabs** bd OR -2 x 200/50 mg **adult tabs** bd	4 ml bd	400 mg (4 packets) bd	4 x 200/50 mg tabs bd OR 8 x 100/25 mg tabs bd	ATV 2 x 150 mg cap od + RTV 1 x 100 mg tab od	1 x 50 mg tab od OR FDC: TLD if eligible od	1 x 50 mg tab bd OR FDC: TLD if eligible od + 50 mg 12 hours after TLD dose		**30 - 34.9**
35 - 39.9														**35 - 39.9**
≥ 40													1 x 600 mg tab nocte OR FDC: TEE if eligible od nocte	**≥ 40**

ARV Drug	Formulations (as used in dosing chart)	Can tablets be split/crushed if unable to swallow?	Comment
Abacavir (ABC)	Oral solution: 20 mg/ml Tablets: 60 mg, 300 mg FDC tablet: ABC/3TC 600/300 mg	Tablets: **YES** Limited data on FDC, preferably swallow whole or use individual drugs.	Hypersensitivity reaction (fever, rash, GIT & respiratory symptoms) may occur during first 6 weeks of therapy, very uncommon in black African patients. Symptoms typically worsen in the hours immediately after the dose and after each subsequent dose. Caregivers or patients should discuss symptoms early with the clinician rather than stopping therapy. Stop ABC permanently if hypersensitivity reaction has occurred.
Lamivudine (3TC)	Oral solution: 10 mg/ml Tablets: 150 mg; FDC tablets: ABC/3TC 600/300 mg, TLD 300/300/50 mg		Well tolerated, adverse-effects uncommon. Pure red cell aplasia causing anaemia can occur but is very rare.
Zidovudine (AZT)	Oral solution: 10 mg/ml Tablets: 100 mg, 300 mg Capsules: 100 mg FDC tablet: AZT/3TC 300/150 mg	Tablets and FDC: **YES** Capsules: **YES**. Open and add to a small amount of soft food/liquid and ingest immediately.	Avoid or use with caution in neonates or children with anaemia (Hb < 8 g/dl) due to potential to cause bone marrow suppression.
Tenofovir (TDF)	Tablets: 300 mg FDC tablets: TDF/FTC 300/200 mg, TEE 300/200/600 mg, TDF/3TC/EFV 300/300/600 mg, TLD 300/300/50 mg	Data is lacking: preferably swallow whole or use individual drugs.	TDF may be prescribed for adolescents ≥ 10 years of age AND ≥ 35 kg body weight after ensuring adequate renal function by checking eGFR/creatinine using the appropriate formula (refer to 2019 ART Clinical Guidelines). TDF is usually prescribed as part of an FDC tablet: TDF/FTC, TDF/FTC/EFV, TDF/3TC/EFV or TDF/3TC/DTG. To assess for TDF-induced nephrotoxicity, do creatinine and eGFR at months 3, 6 and 12 and thereafter repeat every 12 months.
Lopinavir/ritonavir (LPV/r)	Oral solution: 80/20 mg/ml Tablets: 200/50 mg, 100/25 mg	Tablets: **NO** Must be swallowed whole and not divided, crushed or chewed.	Oral solution should be refrigerated/stored at room temperature (if < 25°C) for up to 6 weeks. Preferably administer oral solution with food as increases absorption. Strategies to improve tolerance and palatability of oral solution: coat mouth with peanut butter, dull taste buds with ice, follow dose with sweet foods. LPV/r has many drug-drug interactions. #
Ritonavir (RTV)	Oral solution: 80 mg/ml Oral powder: 100 mg/packet Tablets: 100 mg		Ritonavir oral solution should be stored at room temperature. It's shelf-life is approximately 6 months. Strategies to improve tolerance and palatability of oral solution: coat mouth with peanut butter, dull taste buds with ice, follow dose with sweet foods. Each 100 mg packet of RTV powder should be mixed with a small amount of water or soft food and immediately ingested. RTV has many drug-drug interactions. #
Atazanavir (ATV)	Capsules: 150 mg, 200 mg	Capsules: **NO** **Must be swallowed whole and not divided, crushed or chewed.**	ATV is used in combination with RTV which must be dosed separately as a co-formulation is not available. May cause unconjugated hyperbilirubinaemia resulting in jaundice, but this does not indicate hepatic toxicity and is not a reason to discontinue the drug unless it is worrying the patient. Consider drug-drug interactions. #
Dolutegravir (DTG)	Tablets: 50 mg FDC tablet: TLD 300/300/50 mg	Tablet: **YES** Data on crushing FDC tablet is lacking: swallow whole or use individual drugs.	Iron supplements decrease DTG concentrations if taken together on an empty stomach. To prevent this, DTG and iron supplements can be taken at the same time if taken **with food**. It may be helpful to administer as a morning dose rather than an evening dose if insomnia occurs with evening dosing. DTG may raise creatinine levels by up to 15% without affecting renal function. Consider drug-drug interactions.#
Efavirenz (EFV)	Capsules: 50 mg, 200 mg Tablets: 50 mg, 200 mg, 600 mg FDC tablet: TEE 300/200/600 mg	Tablets: **NO** **Must be swallowed whole and not divided, crushed or chewed.** Capsules: **YES**. Open and add to small amount of soft food and ingest immediately.	Best given at bedtime to reduce CNS side-effects, especially during first 2 weeks. Consider drug-drug interactions. #

FDC = fixed dose combination; eGFR = estimated glomerular filtration rate; GIT = gastrointestinal tract; TEE = Tenofovir/Emtricitabine/Efavirenz; TLD = Tenofovir/Lamivudine/Dolutegravir;# EML-Antiretroviral interactions table (http://www.mic.uct.ac.za) OR www.hiv-druginteractions.org/checker OR the Liverpool HIV iChart application for smart phones, or any of the helplines listed on page 42

ANNEXURE 4: INITIATING ART IN HIV-INFECTED NEONATES WEIGHING ≥ 2.5 KG AT BIRTH

Protocol for initiation of ART in HIV-infected neonates ≥ 2.5 kg at birth



Refer to documents below where numbered in the protocol:

1. Dosage chart if < 28 days of age (see page 97)
2. SA NDOH dosing chart (see page 94)

Please note, this protocol is meant as a guide, and there is allowance for flexibility after discussion with an expert.

ANNEXURE 5: ARV DRUG DOSING CHART FOR CHILDREN FROM BIRTH - 28 DAYS OF AGE WITH BIRTH WEIGHT ≥ 2.5 KG (≥ 35 WEEKS GESTATIONAL AGE AT BIRTH)

	Lamivudine (3TC)		Zidovudine (AZT)		Nevirapine (NVP)	
Target dose	2 mg/kg/dose TWICE daily (BD)		4 mg/kg/dose TWICE daily (BD)		6 mg/kg/dose TWICE daily (BD)	
Available formulation	**10 mg/mL**		**10 mg/mL**		**10 mg/mL**	
Weight (kg)	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**	**Dose in mL**	**Dose in mg**
≥ 2.5 - < 3	0.5 mL BD	5 mg BD	1 mL BD	10 mg BD	1.5 mL BD	15 mg BD
≥ 3 - < 4	0.8 mL BD	8 mg BD	1.5 mL BD	15 mg BD	2 mL BD	20 mg BD
≥ 4 - < 5	1 mL BD	10 mg BD	2 mL BD	20 mg BD	3 mL BD	30 mg BD

Dosing is based on the birth weight of the child, and it is not necessary to change the dose before 28 days of age (for example if the weight decreases in the first week or two of life)

- Caregivers who will be administering ARV medication to the child must be supplied with a syringe (2 mL or 5 mL) for each of the 3 ARVs and shown how to prepare and administer the correct dose. If required, bottles and syringes should be colour coded with stickers and a sticker of the relevant colour used to mark the correct dose on the syringe.

Adapted from: Updated recommendations on first- and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: interim guidelines. Supplement to the 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2018

STEP BY STEP GUIDE TO DISCLOSURE TO CHILDREN REGARDING THEIR HIV STATUS

- Remains a difficult process for all concerned
- Effective conversations are dependent on the age and understanding (developmental level) of the child
- Aim to build up a body of knowledge in the child that leads to the point of disclosure of HIV diagnosis
- The first step is to find out what the child already knows (often more than adults think)

Failure of full disclosure by early teenage years can lead to:

- Poor adherence
- Emotional difficulties
- Poor school performance
- HIV transmission if sexually active

VERY YOUNG

0 – 4 Years
NO DISCLOSURE YET

DEVELOPMENTAL LEVEL

- Depends on adult for all needs and information
- Child needs comfort, support and most of all security

WHAT DO YOU EXPLAIN:

- Carry on consultation with child present
- Child too young for direct information about HIV but explanations to caregiver about how HIV can affect the child remain important
- Provide ideas to help caregiver support child taking medicine
- Congratulate child on taking medicines well
- Address caregiver anxieties
- Build relationship with the child through play/singing
- Provide a safe and welcoming clinic

AIM

BUILD UP CONFIDENCE of CHILD in HEALTH WORKERS and MEDICINE TAKING

YOUNG CHILD

(PRE-SCHOOL)
5 – 7 Years
EARLY DISCLOSURE

DEVELOPMENTAL LEVEL

- Can understand concrete based ideas e.g. real events in the present and past
- Thinking is based in the present
- Take the lead from confidence of caregiver interactions with health workers
- Beginning to link medicines and health

WHAT DO YOU EXPLAIN:

Child needs to learn about illness but not HIV by name yet

- Introduce ideas of good and bad health by eating healthy food, keeping clean, exercising, looking after teeth etc.
- Medicines help to keep a body healthy and strong
- Introduce infections as 'germs' that can hurt or damage the body/make you sick or hurt
- Introduce (white) blood cells as the part of the body that look for and kill infections or germs
- Some germs hide and you need to take medicines to help fight the germs

AIM

UNDERSTANDING that MEDICINES SUPPORT the BODY to KEEP YOU WELL

SCHOOL GOING CHILD

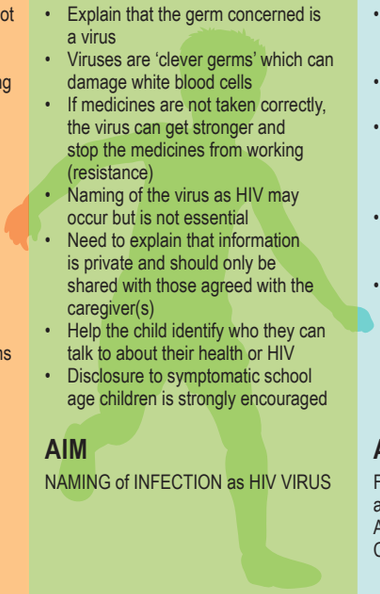
8 – 11 YRS
PARTIAL DISCLOSURE

DEVELOPMENTAL LEVEL:

- Able to hold onto ideas and apply them to new situations
- Can understand past, present and future
- Has social and moral awareness about right & wrong behaviour
- Beginning to be more curious and take some control over their lives

WHAT DO YOU EXPLAIN:

- Explain that the germ concerned is a virus
- Viruses are 'clever germs' which can damage white blood cells
- If medicines are not taken correctly, the virus can get stronger and stop the medicines from working (resistance)
- Naming of the virus as HIV may occur but is not essential
- Need to explain that information is private and should only be shared with those agreed with the caregiver(s)
- Help the child identify who they can talk to about their health or HIV
- Disclosure to symptomatic school age children is strongly encouraged



AIM

NAMING of INFECTION as HIV VIRUS

TEENAGER

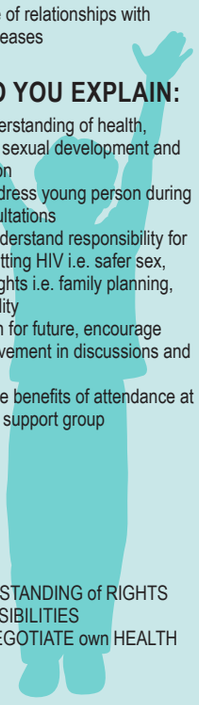
11 – 14 Years
FULL DISCLOSURE

DEVELOPMENTAL LEVEL:

- More abstract thinking (understands future consequences of actions)
- Increasingly making decisions on their own regarding identity, independence, school, career
- Puberty/sexual development
- Dependence on caregivers decreases
- Importance of relationships with friends increases

WHAT DO YOU EXPLAIN:

- Check understanding of health, medicines, sexual development and HIV infection
- Directly address young person during clinic consultations
- Need to understand responsibility for not transmitting HIV i.e. safer sex, and their rights i.e. family planning, confidentiality
- Preparation for future, encourage direct involvement in discussions and decisions
- Promote the benefits of attendance at adolescent support group



AIM

FULL UNDERSTANDING of RIGHTS and RESPONSIBILITIES
ABILITY to NEGOTIATE own HEALTH CARE

ANNEXURE 7: PROPHYLACTIC DOSAGES FOR THE HIV-EXPOSED INFANT

Summary of Infant Prophylaxis Regimens		
Risk Profile	**NVP**	**AZT**
Low risk, whether breastfed or formula fed	6 weeks	no AZT
High Risk, and breastfed	minimum of 12 weeks	6 weeks
High risk, and exclusively formula fed	6 weeks	6 weeks

Nevirapine (NVP)		
Age	**Current weight**	**Once daily dose**
Birth to 6 weeks	2,0 - 2,49 kg★	1 ml (10 mg) daily
	> 2,5 kg	1,5 ml (15 mg) daily
> 6 weeks to 6 months		2 ml (20 mg) daily
> 6 to 9 months		3 ml (30 mg) daily
9 months until 4 weeks after all breastfeeding has stopped		4 ml (40 mg) daily

Zidovudine (AZT)		
Age	**Current weight**	**Twice daily dose**
Birth to 6 weeks	< 2 kg, > 35 weeks gestation★	4 mg/kg/dose twice daily
	2,0 to 2,49 kg	1 ml (10 mg) twice daily
	> 2,5 kg	1,5 ml (15 mg) twice daily
> 6 weeks (doses according to ART Drug Dosing Chart for Children)	< 3 kg	4 mg/kg/dose 12 hourly (0.4 ml/kg/dose 12 hourly)
	3,0 to 5,9 kg	6 ml (60 mg) twice daily
	6 to 7,9 kg	9 ml twice daily
	8 kg to 13,9 kg	12 ml twice daily

Cotrimoxazole syrup (200/40 mg per 5 ml)	
Weight	**Once daily dosage**
2,5 to < 5 kg	2,5 ml
5 to < 14 kg	5 ml
STOP ★★ Stop cotrimoxazole when PCR is negative ≥ 6 weeks after full cessation of breastfeeding AND infant is clinically HIV negative	

Premature infants < 35 weeks gestational age should be dosed using expert guidance.

- For infants weighing < 2000 g, the suggested NVP dose is 2 mg/kg/dose (0.2 ml/kg/dose) once daily from birth – 2 weeks of age followed by 4 mg/kg/dose (0.4 ml/kg/dose) once daily from 2 – 6 weeks of age.
- If the infant still weighs < 2 kg at 6 weeks of age, continue with dosage of 4 mg/kg/dose (0.4 ml/kg/dose) once daily until reaches 2 kg.

Certain babies are at higher risk e.g. premature and malnourished infants. Closer monitoring is recommended. If in doubt, discuss with an expert and refer as needed.

ANNEXURE 8: PSYCHOSOCIAL SUPPORT FOR PREGNANT AND BREASTFEEDING WOMEN

A number medical, mental health and social risk factors may put a mother-infant-pair at risk of poorer outcomes. These factors are identified within currently used clinical records e.g. the maternity case record, the RTHB, and the WBOT household risk assessment form, and are summarised below. These mother-infant-pairs may require closer follow-up and additional support from both clinicians and CHWs.

ANTENATAL RISK FACTORS
Teenage pregnancy
Primigravida
Lives in an informal settlement
Single
Unemployed
Any medical problem (including HIV)
Any obstetric problem
Any psychiatric problem
Use of tobacco, drugs, or alcohol
Any other relevant reason e.g. violence/abuse at home, lack of social support, food insecurity, being a refugee, recent bereavement, etc.

PERINATAL RISK FACTORS
Low birth weight baby (<2500 grams)
Delivery before 37 weeks (premature baby)
Neonatal death or stillbirth
Any neonatal problem: e.g. Low Apgar (<7); breast-feeding problems; suspected hypoxic ischaemic encephalopathy (HIE); congenital problems
Any maternal problem that arose during delivery or post-delivery: e.g. bleeding, tears, infection, re-tained placenta
Any other relevant reason e.g. violence/abuse at home, lack of social support, food insecurity, being a refugee, recent bereavement, etc.

Screening Pregnant Women for Referral to a CHW

Early referral to community-based services improves adherence to ART, retention in care, exclusive breastfeeding and care of the child up to two years of age. Where resources allow, all women should be linked with a CHW during antenatal care. However, in areas with insufficient numbers of CHWs to meet the demand, the factors listed above can be used to screen and prioritise women to be referred. Any woman who has one or more of the listed criteria should be prioritised. Screening should be done antenatally and after the birth of the baby before discharge from labour ward. The screening assessment can be done by a midwife, a BANC nurse, or a lay counsellor in the facility. Each facility should decide which of the above categories of staff are best placed in their facility to conduct the screening and referral.

Screening and referring women for antenatal and postnatal depression and anxiety

The prevalence of depression and anxiety is high in antenatal and postnatal women. It is therefore important to screen women for these conditions and refer as appropriate. The validated screening tool below is able to identify women with potential depression and/or anxiety. Those who answer “yes” to two or more questions, should be referred for a definitive diagnosis and further counselling.

	ANTENATAL RISK FACTORS	YES	NO
1.	In the last 2 weeks, have you on some or on most days felt unable to stop worrying, or thinking too much?		
2.	In the last 2 weeks, have you on some or on most days felt down, depressed or hopeless?		
3.	In the last 2 weeks, have you on some or most days had thoughts and plans to harm yourself or com-mit suicide?*		

*the self-harm question will require urgent referral if there are both thoughts AND plans. If there is a history of previous attempt, referral is required even if there are thoughts alone.

ANNEXURE 9: THIRD-LINE APPLICATION FORM

APPLICATION - THIRD LINE ANTIRETROVIRAL THERAPY					
please ensure all fields are completed before submitting					
Patient First Name					
Patient Surname					
Date of Birth day/month/year		*Patient Number*			
Identity number		Age		*Gender*	
Weight		BMI (kg/m^2)		*Height (Child)*	
FACILITY DETAILS					
Facility Name					
Province					
Doctor in Charge Of Patient/Authorised Prescriber					
Doctor's Contact Number					
Doctor and Pharmacist Email Addresses					
		DATE *day/month/year*			

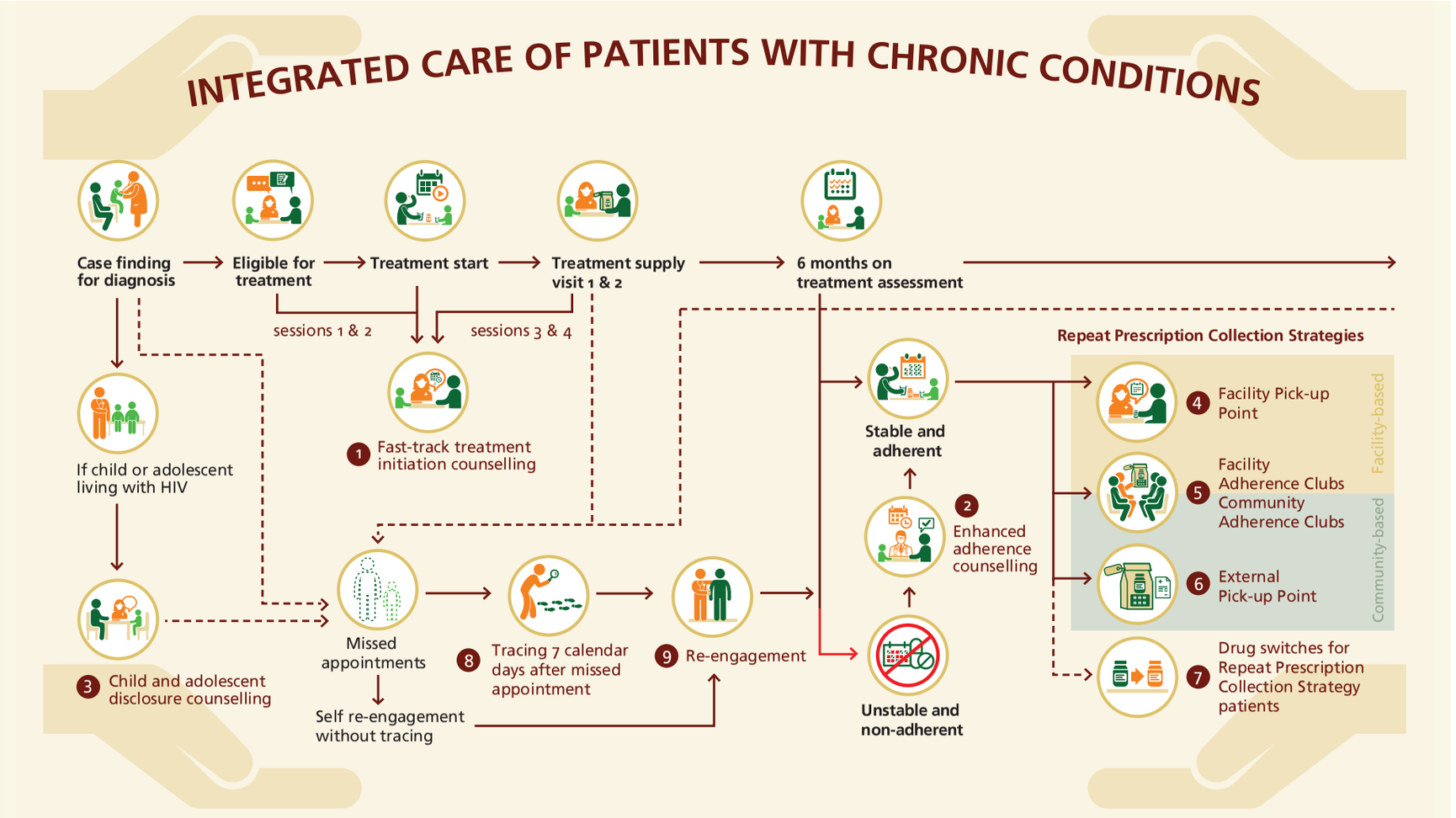
PAST MEDICATION HISTORY				
Timelines *day/month/year*		Past Regimens Only	Reason for discontinuation	Concurrent TB Treatment
Date started				
Date stopped				
Date started				
Date stopped				
Date started				
Date stopped				
Date started				
Date stopped				
Reason for discontinuation codes? SE = Side effect, F = Failure, FC = Formulary change, NC = Non adherent				

CURRENT REGIMEN ONLY			
Date Started *day/month/year*		**Regimen**	

CHILDREN PMTC HISTORY	
Was the mother on therapy during pregnancy or breastfeeding?	
What treatment did the mother take and for how long?	
Was child breastfed?	
Did child receive any ARV at birth/ after birth/ during breastfeeding? State ARV and dura-tion	

Differentiated Models of Care (DMoC) Standard Operating Procedures: Minimum package of interventions to support linkage to care, adherence and retention in care.

Differentiated care aims to strengthen linkage, adherence and retention using a patient-centred approach throughout the treatment cascade. DMoC take into consideration the patient's population group, clinical characteristics and context. It enhances maximum adherence and retention and recognizes the importance of integrated chronic care service provision. The standard operating procedures (SOPs) for the minimum package of interventions are contained in the SOP booklet entitled "Minimum package of interventions to support linkage to care, adherence and retention in care" (February 2020). The interventions are numbered in the continuum of care flow diagram below. Numbers in the diagram correspond to the numbered list of SOPs on the following page.



Standard Operating Procedures (SOPs) for minimum package of interventions according to the continuum of care flow diagram

STANDARD OPERATING PROCEDURES	BRIEF EXPLANATION
Treatment education and counselling	
SOP 1: Fast track initiation counselling including a focus on adaptation for same-day initiation and post-initiation counselling aligned with treatment supply return dates (FTIC)	Standardized education sessions and counselling approach for: i) Treatment initiation ii) Patients struggling with adherence (while in care or when re-engaging in care)
SOP 2: Enhanced adherence counselling for patients struggling with adherence (EAC)	
SOP 3: Child and adolescent disclosure counselling	An incremental and standardized approach to HIV disclosure counselling in children and adolescents.
Repeat prescription collection strategies for stable patients with chronic conditions	
SOP 4: Facility pick-up point (FAC-PUP)	Repeat Prescription Collection strategies (RPCs) after 6 months on treatment: FAC-PUP = health facility-based individual RPCs AC = health facility or community-based support group RPCs EX-PUP = out-of-facility individual RPCs
SOP 5: Adherence Club (AC)	
SOP 6: External pick-up point (EX-PUP)	
SOP 7: Switching first-line regimens for stable patients utilizing a Repeat Prescription Strategy	Managing stable patients first-line regimen drug switches when receiving treatment through RPCs: FAC-PUP/AC/EX-PUP
Patient tracing and re-engagement	
SOP 8: Tracing and Retention in Care (TRIC)	Tracing early missed appointment in order of priority based on abnormal results, treatment interruptions and missed clinical appointments
SOP 9: Re-engagement in care	Re-engagement in care involves assessing treatment interruption, adherence challenges, including reviewing documented suppressed viral loads. The patient can be referred for EAC or preferred RPCs modality

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