Republic of Rwanda

Ministry of Health

National Guidelines for Prevention and Management of HIV, STIs & Other Blood Borne Infections

Edition 2013

RWANDA BIOMEDICAL CENTER

A Healthy People. A Wealthy Nation

PREFACE

Despite many advances in the fight against and control of HIV/AIDS in the last decades, HIV/AIDS still remains a major health problem in developing countries. With about 206,000 people living with HIV/AIDS in Rwanda, the expansion of antiretroviral treatment to reach all patients who meet the eligibility criteria is one of the priorities of the Ministry of Health. There is evidence that starting eligible HIV-infected patients on ART can reduce devastating impact of HIV pandemic.

However, the expansion of antiretroviral treatment is a real challenge that can only be overcome by the participation of all partners, both national and international. Apart from the financial support that is clearly essential, there is the supply of drugs and the monitoring of the mechanisms that have to be set up. Healthcare providers must be trained, infrastructures must be set up or upgraded, education of the community and mobilization of different persons involved in the fight against HIV/AIDS so that they can play their roles, must be carried out.

Human capacity strengthening should occupy an important place during the process of training and mentoring of social workers, nurses, doctors and other people involved in the fight against HIV/AIDS. This capacity strengthening must also motivate healthcare providers so that they are capable of offering quality care services to patients over a long time.

These are integrated National Guidelines 2013 for Prevention and Management of HIV, STIs & Other Blood Borne Infections in accordance with the last guidelines of the World Health Organization (WHO) published in June 2013 and adapted to the Rwandan national context. It thus responds to the need by the Ministry of Health to improve skills of actors in the health sector as well as the quality of care and treatment offered in both public and private health facilities countrywide.

We are fully aware that in spite of the progress made, there is still a lot to be done in prevention and management of HIV, STIs &Other Blood Borne Infections towards a healthy people and wealthy nation.

May this publication contribute to improve the knowledge on HIV/AIDS of all actors in the health sector and in improving the living conditions of our population.

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Dr Agnes BINAGWAHO
Minister of Health

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Dr Sabin NSANZIMANA
Head of HIV/AIDS, STIs and OBBI Division/RBC

Contents

PARTICIPANTS TO THE REVISION OF THE GUIDELINES 2013

No	Names	Institution
1	Dr Agnes Binagwaho	MOH
2	Dr Anita Asiimwe	MOH
3	Dr Jean de Dieu Ngirabega	RBC/IHDPC
4	Dr Sabin Nsanzimana	RBC/IHDPC
5	Dr Muhayimpundu Ribakare	RBC/IHDPC
6	Dr Aimable Mbituyumuremyi	RBC/IHDPC
7	Dr Placidie Mugwaneza	RBC/IHDPC
8	Dr Mwumvaneza Mutagoma	RBC/IHDPC
9	Prof. Baribwira Cyprien	IHV-University of Maryland-Rwanda
10	Dr Jean d'Amour Ndahimana	RBC/IHDPC
11	Dr Chewe Luo	UNICEF /HQ NY
12	Dr Drobac Peter	PIH
13	Dr Karita Etienne	PSF
14	Dr Kayirangwa Eugenie	CDC
15	Dr Mugisha Veronicah	ICAP
16	Dr Musoni Canisious	USAID
17	Dr Nyiramasarabwe Laurence	WHO
18	Dr Sebeza Jackson	IHV-University of Maryland-Rwanda
19	Dr Uwinkindi Francois	RBC/IHDPC
20	Mr. Majyambere Adolphe	RBC/IHDPC
21	Mr. Murindabigwi Augustin	RBC/IHDPC
22	Mr. Niyonsenga Simon Pierre	RBC/IHDPC
23	Mrs. Umutesi Justine	RBC/IHDPC
24	Kenly Sikwese	AEROCAB/IAS
25	Dr Bantura Leonard	AHF RWANDA

26	Lydia Buzaarine	AHF RWANDA
27	Dr Antoine R.Gasasira	CDC
28	Dag Smith	CDC
29	Dr. Felix Ndagije	CDC
30	Dr. Mutwa Philippe	CDC
31	Dr. Patrick Ndimubanzi	CDC
32	Alice Sabino	CHAI
33	Dr. Manzi Olivier	CHUK
34	Dr. Muganga Narcisse	CHUK
35	Nyamuziga Abdoul Karim	CMC/CENTRE
36	Dr Joseph Ryarasa	DOD/US EUSEMY
37	Eugene Zimulinda	DOD-PEPFAR
38	Dr Erick Baganizi	DREW CARES
39	Dr. Fabienne Shumbusho	FHI 360
40	Hakizinka Ida	GLOBAL FUND
41	Helen Von Dadelszen	IAS
42	Dr Anchilla Mary Banegua	JANSSEN
43	Dr Beata Mukarugwiro	JAPIEGO
44	Dr Ida Kankindi	MOH
45	Dr Neil Gupta	PIH
46	Rusanganwa Leon	PSF
47	Rusanganwa Pierre	PSF
48	Dr Vianney Nizeyimana	PSF/APHAR
49	Mugabo Robren	PSF/CMC
50	Dr Fred Rwizibuka	RBC
51	Aimable Mbituyimana	RBC
52	Dr Aimee Muhimpundu	RBC
53	Dr Bizumuremyi Marc	RBC

54	Dr Byiringiro Rusisiro	RBC
55	Dr David Tugizimana	RBC
56	Dr Gilbert Mbaraga	RBC
57	Dr Kayiranga Pascal	RBC
58	Dr Makuza Jean Damascene	RBC
59	Dr Muhire Philbert	RBC
60	Dr Munyampirwa Aloys	RBC
61	Dr Ndagijimana Ntwali	RBC
62	Dr Placidie Mugwaneza	RBC
63	Elyse Tuyishime	RBC
64	Epiphanie Nyirabatsinda	RBC
65	Eric Remera	RBC
66	Hagenimana Marc	RBC
67	Hajabashi Jeanne	RBC
68	Josbert Nyirimigabo	RBC
69	Kamali Fulgence	RBC
70	Leonidas Banamwana	RBC
71	Sr Marie Josée Maliboli	RBC
72	Macara Faustin	RBC
73	Marthe Kubwimana	RBC
74	Mugiraneza Emmanuel	RBC
75	Musabyimana Speciose	RBC
76	Mutunge Elise	RBC
77	Nadege Umuhoza	RBC
78	Niyonsenga Florence	RBC

79	Nsenguwera Jean Helbert	RBC
80	Nyirinkindi Aimé Ernest	RBC
81	Ruhirimbura John	RBC
82	Dr. Rwagasore Edson	RBC
83	Sebuhoro Dieudonne	RBC
84	Singirankabo Joseph Herman	RBC
85	Theobald Habiyaremye	RBC
86	Uwineza Donatille	RBC
87	Uwineza Marie Chantal	RBC
88	Dr Twizeyimana Jean de Dieu	RBC
89	Abimpaye Monique	RBC/HIV
90	Dr Jean Lambert Kabagabo	RBC/HIV
91	Dr Mukamugenzi Violette	RBC/HIV
92	Jean Claude Ntirenganya	RBC/HIV
93	Mariza Clarisse	RBC/HIV
94	Pierre Dongier	RBC/IHDPC
95	Niyibizi Gad	RBC/HIV
96	Dr. Paul De Rire Habineza	RBC
97	Umuhire Marlene	RBC
98	Joyce Icyimpaye	RBC/MPPD
99	Kabasinga Domitille	RBC
100	Dr Joe Dramiga	RBC/NRL
101	Dr John Rusine	RBC/NRL
102	Kayiranga Alphonse	RBC
103	Donata Twizeyemungu	RBC
104	Dr Uwiragiye Furaha Pie	RBC
105	Kagoyire Beatrce	RRP
106	Kamali Innocent	RRP

107	Shengero Solange	SPIU/MOH
108	Dr Pido Nuncil	IHV-University of Maryland-Rwanda
109	Dieudonne Ruturwa	UNAIDS
110	Sibongile Dludlu	UNAIDS
111	Sneke Adriaens	UNAIDS
112	Bernardin Rutazibwa	UNESCO
113	Dr Balachandra	UNHCR
114	Shirisa Bawachanira	UNHCR
115	Dr Fabian Mwayumba	UNICEF
116	Dr Grace Muriisa	UNICEF
117	Noela Slume	UNICEF
118	Dr Jennifer Mbabazi	USAID
119	Dr. Laurence Nyiramasarabwe	WHO
120	Dr Meg Doherty	WHO-Geneva
121	Dr Edozien Anthony	IHV- University of Maryland
122	Dr Kiromera Athanase	IHV- University of Maryland
123	Dr Serge Paul Eholie	ANEPA
124	Dr David Riedel	IHV- University of Maryland
125	Dr Granich Reuben	UNAIDS Switzerland
126	Dr Amitabh Suthar	WHO, Geneva
127	Peter Memiah	IHV- University of Maryland

ACCRONYMS AND ABBREVIATIONS

3TC	Lamivudine
ABC	Abacavir
AES	Accident d'exposition au sang
APRI	Aminotransferase Platelets Ratio Index
ARV	Antiretrovirals
AZT	Azidothymidine
CD4	Cluster of Differentiation 4 (Stands for T4 Lymphocytes
CDC	Center for Diseases Control and Prevention
CMV	Cytomegalovirus
CTM	Cotrimoxazole
ddI	Didanosine
DNA	Deoxyribonucleic Acid
EFV	Efavirenz
FTC	Emtricitabine
HBe Ag	Hepatitis B Envelop Antigens
HBs Ag	Hepatitis B Surface Antigens
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HTC	HIV Testing and Counseling
IDR	Intradermal Reaction
IDV	Indinavir
LDV	Ledipasvir
NFV	Nelfinavir
NNRTI	Non Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NVP	Nevirapine
OI	Opportunistic Infection
PCR	Polymerase Chain Reaction
PEGINF	Pegylated Interferon
PI	Protease inhibitor
PLHIV	Person living with HIV

PMTCT	Prevention of mother to child transmission
RNA	Ribonucleic Acid
RTV	Ritonavir
SMP	Simeprevir
SOF	Sofosbuvir
TDF	Tenofovir
UNAIDS	Joint United Nations Programme on HIV/AIDS
VZV	Varicella zoster virus
WHO	World Health Organization

PART I: HIV PREVENTION

Chapter I: Generalities

1.1. Introduction

This chapter offers background, definitions, summaries of service objectives, and a description of the package of activities associated with each prevention component.

Because prevention of HIV should be part of the minimum package offered by a health center, this chapter describes the standards governing HIV prevention services in Rwanda. These standards cover everything related to the conditions a health center must meet to begin HIV prevention activities. They include, among others, the location of activities and the conditions for opening prevention activities in Health Facility.

1.2. Location of Activities

HIV prevention activities must be integrated into the package of services offered by all public health facilities. However, by agreement of the district hospital, private Health Facilities and some non-health structures may also carry out prevention activities.

1.3. Opening Prevention Activities in Health Facility

Authorization to open a site will be given through the district hospital to any health facility or organization recognized by the Ministry of Health located in its catchment area. The authorization will be offered by the Rwanda Biomedical Center, Ministry of Health.

During the assessment of the health facility, district hospital technicians must ensure that certain criteria are met, including the existence of trained personnel and required infrastructure as well as equipment.

1.4. Training of the Personnel

To provide HIV prevention services, the health facility should have certified staff with relevant trainings. Health care providers are trained using standard training modules validated by Rwanda Biomedical Center. These trainings are integrated and must combine all HIV prevention strategies including HIV testing and counseling (HTC), HIV prevention based on ART (PMTCT, Discordant couples, PEP, and Prevention among KPs), and linkage to Care & treatment services.

The refresher trainings of the personnel should be organized every two years to ensure continuous training of staff.

Every health care provider should be able to provide HIV prevention services. These include Doctors, Nurses, Social workers, Nutritionists, Clinical psychologists, Laboratory technicians and Pharmacists. The services provided will vary according to the professional's area of expertise.

1.5. Required Infrastructures

The infrastructure must enable the provision of high-quality services and be designed in such a way as to respect confidentiality and allow for easy dialogue. The health facility must have at least one reception room, a counseling office, and a laboratory. Health facilities which offer PMTCT services must also have a maternity ward built and equipped according to MOH standards.

1.6. Required Materials and Equipment

To provide clinical HIV prevention services, a health facility must have suitable material and equipment, the list is found in annexes.

Apart from office equipment, the health facility must have national guiding documents to ensure high-quality services. Below are some examples:

- HIV Prevention guiding document including guidelines and training manuals.
- Health provider manuals and training manuals.
- Standards operating procedures (SOP) for all HIV preventions strategies
- IEC materials and demonstration tools.

For details regarding the required infrastructure, materials, and equipment, refer to "Health Facility Evaluation Form".

1.7. Ethical Considerations

1.7.1. Consent for HIV Testing

The decision to be tested must be made by the person concerned. This person has the right to receive all the information related to HIV testing and all the possible outcomes prior to giving consent (verbal consent is sufficient and written consent is not required) to be tested and counseled.

HIV test is accepted for people aged 15 and over. However, the counselor should assess each child's capacity to understand and cope with own seropositivity before undergoing HTC. For children under 15 years, the consent of parents or a legal guardian is required. Due to the young age at which first sexual activity may occur and children's vulnerability to HIV and other STIs, an exception can be made for specific cases (For example sex workers, Men who have sex with men, Drug Users, etc…).

If the person does not have all of his mental faculties to make an informed decision about the test, the procedure will be performed only when it is

certified in his or her medical interest. Under these circumstances, the decision to test should be made by a family member or a legal guardian.

1.7.2. Confidentiality

Confidentiality is believed to be the client's right and an obligation of the provider. Confidentiality must always be guaranteed at all stages of the counseling process.

The files and records of clients must be kept confidential. The system of archiving and storing client files must be designed in a way that guarantees confidentiality. All personnel with access to medical records or test results are bound to confidentiality.

In case of referrals, it is mandatory to observe the rules of shared confidentiality.

1.7.3. Announcement of the Result

HTC providers should strive to provide high-quality testing services, and quality assurance mechanisms should be in place to ensure the provision of correct test results. The results of an HIV rapid test are given within 10-30 minutes. The communication of the results is verbal. For this reason, HIV testing services should not be used for specific reasons (pre-employment, insurance, reasons related to school or travel, etc.). Clients requesting a test under these conditions must be taken to medical facilities authorized to deliver written results.

HIV test results should be given to an individual or to a consenting couple. For adults who do not have command of all of their faculties and did not personally decide to be tested, health care providers will communicate the results to their guardian.

For children and minors, the results will be communicated to the parents or guardian. Minors must themselves be present when the results are communicated, and appropriate counseling for their age must be given.

1.7.4. Pricing

HIV counseling and testing services are offered free of charge at all public health facilities recognized by the Ministry of Health of Rwanda. Accredited private clinics can also offer HIV testing to individual adults or couples at a price determined by the MOH rules and regulations.

Chapter II: HIV Diagnosis and ART for HIV Prevention

2.1. HIV Testing and Counseling (HTC)

The overall HIV testing and counseling goal is to identify as many people living with HIV as early as possible after acquiring HIV infection, and link them appropriately and in a timely manner to prevention, care and treatment services. The people tested who are not infected should receive appropriate counseling to remain HIV negative and be linked to appropriate prevention services.

HTC services include both voluntary HIV counseling and testing (VCT) and provider initiated HIV counseling and testing (PITC). VCT services are provided to the client who decides on his/her own to undertake HTC, while PITC evokes the health care provider's instigation to take HTC for a client who consulted for any other health problem.

2.1.1 HTC Guiding Principles

All forms of HIV testing and counseling should be voluntary and adhere to the **five C's**:

- **C**onsent,
- **C**onfidentiality,
- **C**ounseling,
- **C**orrect test results and
- **C**onnections to care, treatment and prevention services.

Mandatory or coerced testing is never appropriate, whether that coercion comes from a health care provider or from a partner or family member.

Connections to prevention, care and treatment services should include the provision of effective referral to appropriate follow-up services as indicated,

including long-term prevention and treatment support. Each positive case must have an enrollment number (for example TRACnet Number) in the HTC register as an observation.

2.1.2 HIV Testing and Counseling Procedures

For all models, HTC steps include (1) ***Pre-test counseling***, including ***Information, Education and Communication*** (IEC) for behavior change; (2) ***HIV testing*** in the counseling room using rapid testing; (3) ***Post-Test counseling*** and ***delivery*** of the results and its significance. During this session, clients receive appropriate counseling according to their results; (4) ***Linkage to Care and Treatment*** for those tested HIV positive. For each step, it is important to comply with the procedures as outlined below:

2.1.2.1 Pre-test Counseling

Pre-test counseling should be provided to all people seeking or requiring HIV testing. It must be provided individually, to a couple, to a large or small group of people or, if necessary, to a guardian (for children below 15 years, people not in command of all their mental faculties, and people with disabilities).

When Pre-Test counseling is provided in ***small or large groups***, it is an opportunity for Information Education and Communications/Behavior Change Communications (IEC/BCC). Clients receive comprehensive information on HIV/AIDS, including the difference between HIV and AIDS, the importance of being tested, modes of transmission, means of prevention, possible results and their implications, availability of care and treatment services, demonstration of male and female condoms. Then the clients have an opportunity to ask questions and receive answers.

Individual counseling takes place in the counselor's office, where clients are received one by one. It must follow the pre-test approach, which includes (1)

Reception, presentation and screening for eligibility, (2) Assessment of the client's knowledge of HIV and AIDS, (3) HIV risk assessment, (4) Discussion on sexual activities (encouragement of couple testing), (5) HIV risk reduction plan (Abstinence, Being faithful to one partner, Condom use, Don't share needles, Education & Information: ABCDE) and behavior change, (6) Preparation for HIV testing and possible outcomes, (7) Provision of information on availability of Care and Treatment services on case of a positive result, (8) Obtaining free and informed consent for testing.

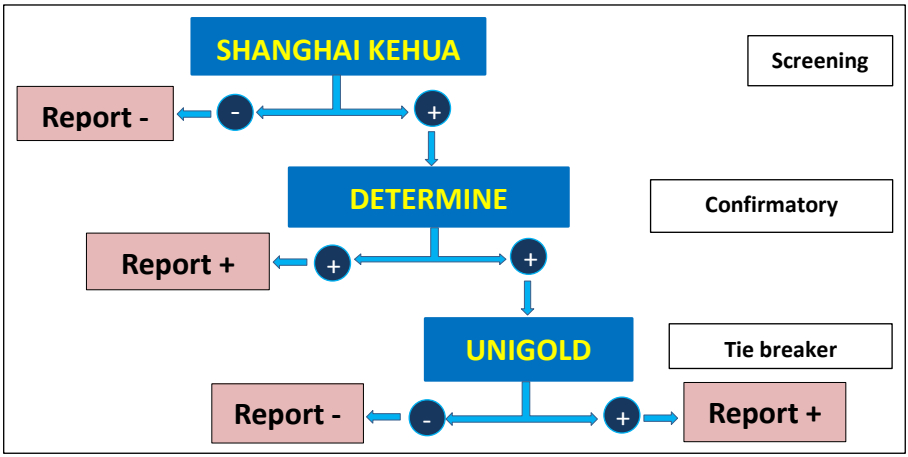
2.1.2.2 HIV Testing

Blood is drawn from capillaries by pricking the finger. This technique called ***"Fingerprick"*** is easy to use, less invasive, and better tolerated by clients. Fingerprick has been recommended by the WHO since 2003 as a method for blood collection for HIV testing. It has several advantages including the use of the whole blood and results are quickly ready. The health worker and non-health worker counselors can be trained and do both counseling and perform HIV testing and laboratory technicians can be used to perform higher level, more complex tasks such as training and supervision. When using blood from the capillaries by pricking the finger, the testing procedure is simple and fast while still maintaining quality. It is less invasive and better tolerated by the clients. Another advantage of HIV rapid test using the fingerpick method is that the time the client spends at the health center is considerably reduced.

The new HIV Testing algorithm **(Algorithm 1)** approved by the Ministry of Health is:

- **First Option**: Shanghai Kehua (Screening) – Determine (Confirmation) – Unigold (Tiebreaker)
- **Backup Option**: First Response (Screening) – Shanghai Kehua (Confirmation)- Determine (Tiebreaker)

Algorithm 1: HIV Testing in Rwanda



Quality control is ensured mainly by using ***Proficiency Testing Programs.*** The National Reference Laboratory (NRL) is the one in charge of supervising this program.

Retesting will be also used for specific cases. Health Facilities are advised to follow the recommendations of the manufacturer and the NRL regarding HIV testing (internal quality control and external quality control).

HIV testing can only be performed by all health care providers and counselors trained on fingerprick and the use of the above mentioned algorithm. This test can be performed in various settings within a health facility (counselor room, maternity, hospitalization wards, consultation room, OPD, etc…) or in the community during outreach activities.

2.1.2.3 Post-Test Counseling

Post-test counseling should be provided by the same person who gave the pre-test counseling. In case of language problems, the counselor may use an

interpreter so that all steps of the counseling process are followed. This must be done with respect to confidentiality.

In case the client is a child below 15 years or not in command of all of his faculties (mental and physical); the counselor will give post-test counseling to the parents or guardian in client's presence.

In case of ***negative results***, post-test counseling will insist on the risk reduction and HIV prevention strategies and the counselor should explain to the client about the seroconversion period and its implications. For high risk clients like Key Populations or negative partners in discordant couples, the counselor will insist on HIV risk reduction behaviors and the importance of retesting. Counselor will also encourage clients to bring their sexual partners for HIV testing. **Negative clients who are not at high risk of HIV infection should be advised to keep protecting themselves against HIV seroconversion and plan to retest only after any other risky contact. Negative clients who are at high risk should be advised to get tested every six months.**

In case of ***positive results***, post-test counseling will insist on risk reduction and secondary prevention of HIV Infection. Clients must be encouraged to live positively, to reduce further exposure and avoid transmitting new infections to others. Clients are advised to disclose their status to their sexual partners and invite them for HIV testing as well as their children if they have them.

HIV Positive clients will be referred to Comprehensive HIV Care and Treatment unit for follow-up and enrolment into the service.

2.1.3 Settings

Diverse models of HTC services delivery are used with the aim to increase population's access to HIV diagnosis. These services are available in health

care facilities, non-health facilities (e.g. Youth Friendly Centers) and in the community. Each setting involves specific HTC approaches.

2.1.3.1 HIV Testing and Counseling in Health Facilities

It is recommended to routinely offer HTC in clinical settings as VCT and PITC. Combined models allow utilization of HIV services by those who wish to know their serostatus, and those may not be aware of availability of services.

PITC was introduced in all clinical settings as an efficient and effective way to identify people with HIV who could benefit from treatment.

PITC in Rwanda is offered in both public and private facilities and it is recommended in cases below:

- Adults, adolescents or children who present in clinical settings with signs and symptoms or medical conditions that could indicate HIV infection, including TB.
- HIV-exposed infants, children born to women living with HIV and children with suspicious symptoms.
- PITC should be considered in sexually transmitted infections, hepatitis and TB services, antenatal care settings and services for key populations (notably sex workers, men who have sex with men and injecting drug users).

PITC activities are guided by the same principles of HTC as mentioned earlier.

The patient follows the process below:

- Before any HIV test, the client must receive a minimum of information to enable him to give his consent.

- For outpatients, HIV counseling and testing is initiated by the provider receiving the patient. If the patient agrees to test, the provider will provide counseling, take a blood sample, and provide the results with post-test counseling.
- For inpatients, it is recommended to have a team of HIV counselors carrying out the tests in all hospital services. These counselors are responsible for pre-test counseling, taking blood samples, communicating results and post-test counseling.

2.1.3.2 Community-Based HIV Testing and Counseling

In addition to providing HTC in clinical settings, HIV testing and counseling can be offered in a variety of settings in the community. The same principles for HTC apply for Community based HTC.

In Rwanda, community-based HTC **(Outreach/Mobile HTC)** is recommended for key populations (specifically sex workers, men who have sex with men, mobile populations, etc.), with linkage to prevention, care and treatment services.

2.1.4 HIV Testing and Counseling in Specific Cases

The following paragraphs describe the procedures for HIV counseling and testing in the case of couples, adolescents, children, key populations, blood transfusions, organ donations, mobile VCT, rape victims, and body fluid exposure accidents.

2.1.4.1 Couples

Couples HIV testing and counseling (CHTC) is recommended in lieu of two different individual HTC for each partner. The CHTC model was proven acceptable, feasible and effective. It allows identifying sero-concordant positive couples who are then linked to care and treatment services. It also

identifies couples with sero-discordant HIV test results who can benefit from HIV prevention interventions.

Services should be offered to married and cohabiting couples, premarital couples, polygamous unions and any other partnerships. It is important to ensure that the process is entirely voluntary and no member of the couple is coerced to take the test. If the counselor suspects any coercion on a member of the couple, he should encourage them to return after they have made the decision jointly and without oppression.

The counseling and testing of couples involves a confidential dialogue between the two people in a couple and a counselor, to enable the couple to overcome stress, assess the risk of HIV transmission within the couple, and make decisions about adopting preventive behaviors.

In all settings, couples and partners should be offered voluntary HTC with support for mutual disclosure.

2.1.4.2 Pregnant Women

HIV testing and counseling for pregnant women as well as linkage to care and treatment are needed to promote the mother's health and prevent new pediatric infections (details see PMTCT).

2.1.4.3 Infants and Children

HIV-exposed infants and children younger than 18 months should be tested within the first 6 weeks of birth so that those already infected with HIV can start ART.

In this population, HIV infection can only be definitively confirmed using virological tests because of the presence of persisting maternal HIV antibody in the child up to 15–18 months of age (details see PMTCT).

Children of school age (7 years) should be told their HIV-positive status and their parents or caregiver's status. The disclosure should be conducted after an attentive assessment of their cognitive and emotional maturity.

2.1.4.4 Adolescents (10-19 years)

Adolescents are often underserved and given insufficient priority in many HIV programs, leading to poor access and uptake of HTC as well as linkage to prevention and care.

Adolescents living with HIV include those surviving perinatal infection and those newly acquiring infection as they become sexually active. Infants infected by their mothers should be diagnosed through PMTCT programs, and initiate antiretroviral treatment immediately.

Adolescents are also vulnerable to HIV infection and would benefit from access to friendly, acceptable and effective HIV services, including HIV testing and counseling.

Consent issues may pose a barrier to access HTC services for adolescents.

- HTC with linkage to prevention, treatment and care, is recommended for adolescents from key populations in all settings.
- Adolescent must receive special post-test counseling from a trained counselor about the potential benefits and risks of disclosure of their HIV status and empowered and supported to determine if, when, how and to whom to disclose.

2.1.4.5 Key Populations

Innovative and tailored models for delivering HIV testing to KPs are needed (e.g., mobile services, home-based testing). Special consideration should be given to different testing models including voluntary, provider-initiated, and

couples and partner testing. Use of rapid test kits with same day results paired with post-test counseling is recommended for KPs. Fingerprick approach is highly recommended for KPs.

HTC should get closer to Key Populations in the community. To reach the majority of key populations, health care providers, in collaboration with peer educators and community health workers, will plan and conduct outreach HTC targeting key populations (mobile VCT) in the catchment areas of the health facilities.

HTC is a gateway to other interventions which will be carried out in compliance with all the steps and procedures as described in this document.

Healthcare providers must address the specific needs of these groups, obtain the informed consent of clients, offer pre-test and post-test counseling, ensure confidentiality and ensure proper client follow up. Everything should be done to get key populations who test HIV positive enrolled into HIV care and treatment services. HIV negative key populations should receive strong risk reduction counseling and be encouraged to get tested for HIV every 6-12 months.

Tab. 1: Summary of HIV Testing & Counseling Recommendations		
Who to Test	**When to Test**	**Where to Test**
People with signs or symptoms of HIV infection	Integrate in health care encounter	Public and private facilities, Outpatient, STI clinics, TB clinics, medical wards, other clinics
Who to Test	**When to Test**	**Where to Test**
Partners of people with HIV	As soon after partner diagnosis as possible For the negative person in serodiscordant couples, offer retesting every 6–12 months	Clinical settings including primary health care settings, ART, TB, sexually transmitted infection clinics, voluntary counselling and testing
Families of index cases	As soon as possible after the family member is diagnosed	ART clinics, maternal and child health and antenatal care settings, homes, community outreach
Key populations: people who inject drugs, men who have sex with men, transgender people and sex workers	Every 6–12 months	Public and private facilities, STI clinics, outreach services for key populations and harm-reduction services
Pregnant women and their partners.	At the first antenatal care visit	In Antenatal care
Infants and children <18 months old	Early infant diagnosis at 6 weeks for all infants whose mothers are living with HIV, HIV Negative mothers with HIV positive partners or if maternal HIV status is unknown; Determine the final infant HIV infection status after 18 months and/or when breastfeeding ends.	Maternal and child health services Pediatric clinics Immunization clinics
Children with signs or symptoms of HIV infection or who have a family member living with HIV	Integrate in health care encounter	In all health settings
Adolescents from key populations	Every 6–12 months	Youth-friendly services, STI clinics, outreach.

2.2. HIV Prevention Based on ART

2.2.1. Prevention of Mother-to-Child Transmission of HIV

The country has embarked on a plan for the Elimination of Mother to Child Transmission of HIV (EMTCT) by 2015. The Prevention of Mother-to-Child Transmission of HIV (PMTCT) program was initiated in the country and was progressively scaled up with the aim of ensuring country's full coverage. The program achieved a lot in terms of services provision, services availability and geographic coverage.

EMTCT strategy emphasizes reorientation and reorganization of existing program activities in order to scale up and expand service coverage, upgrade quality and improve access to and utilization of maternal, neonatal and child health services both at the national and district level. The scale up will be mainly focusing in upgrading PMTCT standalone sites to the level of offering PMTCT full package of services, and increase the coverage of service provision among private health facilities.

In countries where breastfeeding is a common practice like in Rwanda, the probability of transmission of HIV from the mother to her child (MTCT) is very high without any interventions with ART. This probability varies between 20-45% (15-25% during pregnancy and 5-20% during breastfeeding. In developed countries where PMTCT programs are well implemented and where the most efficacious ART is provided to HIV positive pregnant women with limited breastfeeding, the level of MTCT is below 2% at 18 months.

In July 2010, WHO released guidelines with an emphasis on the importance of treating eligible HIV-positive pregnant women (CD4 $\leq$ 350) with lifelong antiretroviral therapy (ART) and recommend two equivalent options of highly effective prophylaxis to HIV-positive pregnant women who do not need ART for their own health. For the first time ARV prophylaxis to either

the mother or child is also recommended during breastfeeding, in settings where breastfeeding is judged to be the safest infant feeding option. Two options were proposed:

- Option A starts treatment of women with Zidovudine (AZT) at 14 weeks of gestation or as soon as possible thereafter until delivery, and the infant receives NVP throughout breastfeeding and until 1-week after exposure to breast milk has ended.
- Option B starts treatment of the mother with triple ARV prophylaxis from 14 weeks or as soon as possible thereafter and continues the maternal triple drug prophylaxis until 1-week after exposure to breast milk has ended. This option encouraged breastfeeding protected by ART.
- A third option (Option B+) proposes further evolution—not only providing the same triple ARV drugs to all HIV-infected pregnant women beginning in the antenatal clinic setting but also **continuing this therapy for all of these women for life**. Important advantages of Option B+ include: further simplification of regimen and service delivery and harmonization with ART programs, protection against mother-to-child transmission in future pregnancies, a continuing prevention benefit against sexual transmission to serodiscordant partners, and avoiding stopping and starting of ARV drugs.

Rwanda is now implementing the Option B+ which insists on starting ART for all HIV positive pregnant women regardless the level of CD4 count, exclusive breastfeeding protected by ART, and mothers continuing ART as a lifelong treatment.

2.2.1.1. Goals

The main goal of PMTCT program in Rwanda is to reduce new pediatric HIV infections by 90% by 2015 and to reduce the overall population based mother to child transmission of HIV to 2% at 18 months by 2015.

Specific objectives include:

- To reduce new HIV infections among women 15-49 years by 50%
- To reduce unmet needs for family planning among women living with HIV to ZERO.
- To reduce transmission of HIV from mother to child to 2% at 18 months.
- To reduce HIV attributable deaths among women and children (<5 years of age) by 90%.

2.2.1.2. PMTCT Package of Services

To prevent mother to child HIV transmission, the program is based on a comprehensive four-pronged approach including (1) Primary prevention of HIV infection among women in childbearing age; (2) Preventing unintended pregnancies among women living with HIV; (3) Preventing HIV transmission from women living with HIV to their infants and (4) Providing appropriate treatment, care and support to mothers living with HIV, their children and families.

HIV counseling and testing (HTC) is recommended for pregnant women as a key component of the package of care in all antenatal services. All pregnant mothers attending ANC will receive HTC preferably with their partners at the time of their first visit to ANC. Strong emphasis will continue being put in male partners' involvement in PMTCT cascade, starting by ANC together with couples HIV counseling and testing.

The new recommendation introduced in this guideline is HIV couple re-testing at the time of labor in addition to the testing done at the time of first ANC visit. The rationale of re-testing is the high risk of acquiring HIV infection during pregnancy and a possibility of seroconversion before delivery.

Tab. 2: Package of Activities in PMTCT

PMTCT Prong I: Primary Prevention	
Services Provided	**Activities**
Prenuptial consultation and related services Couple counseling and Testing	▪ IEC/BCC including HIV, PMTCT, reproductive health and family planning. ▪ HIV Testing and Counseling (HTC) ▪ Family planning ▪ Condom distribution ▪ Referral for HIV positive cases ▪ Referral to others services as needed ▪ STI and TB screening
PMTCT Prong II: Prevention of unintended pregnancies among women living with HIV	
Services Provided	**Activities**
Prenuptial consultation and related services Couple counseling and Testing	▪ IEC/BCC including HIV, PMTCT, reproductive health and family planning. ▪ HIV Testing and Counseling (HTC) ▪ Family planning ▪ Condom distribution ▪ Referral for HIV positive cases ▪ Referral to others services as needed ▪ STI and TB screening
PMTCT Prong III: Preventing HIV transmission from women living with HIV to their infants	
Services Provided	**Activities**
ANC	▪ IEC/BCC including HIV, PMTCT, reproductive health and family planning. ▪ HTC with her partner (if available) ▪ STI Screening and Treatment

PMTCT Prong III: Preventing HIV transmission from women living with HIV to their infants (Continued)	
Services Provided	**Activities**
ANC	**If the woman is tested positive for HIV:** ▪ Open a follow up file for people living with HIV (Green File) ▪ Blood collection for CD4 Count, Full Blood Count (FBC), Liver Function Tests (LFTs) and Renal Function Tests (GFR). ▪ TB Screening ▪ Counseling on nutrition and nutritional support for mothers with moderate or severe malnutrition. ▪ Lifelong ART initiation (Option B+) Cotrimoxazole prophylaxis **If the woman is tested negative and the partner is positive => Serodiscordant Couples:** ▪ Couple counseling on how to remain negative for the woman and positive attitudes for the partner ▪ Provision of prophylaxis to the pregnant woman and her child after delivery according to the protocol. ▪ Referral to Care and treatment for the positive partner and initiate ART regardless CD4 (Treatment as Prevention) HIV Test every 6 months for the woman.
Maternity	**Labor and Delivery** ▪ HIV Test for previously HIV-negative ▪ Lifelong ART initiation as soon as possible for HIV positive mothers identified in delivery room. ▪ Delivery with minimal risk of MTCT ▪ Referral to Care and Treatment after opening the green file if tested positive in the delivery room.

Services Provided	Activities
Maternity	**Immediate post-natal care** ▪ Disinfection of the newborn child ▪ ART Prophylaxis to the newborn ▪ Vaccination ▪ Counseling on the feeding and diet for the mother-child pair. ▪ Counseling on family Planning and offer the appropriate method ▪ Opening a file for exposed infants (Pink file).
PNC/ Mother-Child Follow Up	**Child from HIV+ Mother or Discordant Couple** ▪ Vaccination ▪ HIV testing of the child according to the national protocol ▪ TB screening ▪ Anthropometric measurement ▪ Search for signs of HIV infection ▪ Cotrimoxazole prophylaxis at 6 weeks ▪ Nutritional care of the child ▪ Psychomotor evaluation ▪ Referral of HIV+ children to pediatric care and treatment
Post natal consultation/ Follow up of the mother-child couple.	**HIV + Mother or HIV- Mother in Serodiscordant couple (SDC)** ▪ HIV testing and counseling of mothers whose HIV status is unknown ▪ HIV testing of mothers whose partners are HIV+ every 6 months during the period of breastfeeding and after. ▪ CD4 controls ▪ Regular Biological controls (FBC, LFTs and RFTs) ▪ Verification of CTX prophylaxis ▪ Nutritional counseling and support Family planning (IEC and offer of contraceptive methods)

PMTCT Prong IV: Providing appropriate treatment, care and support to mothers living with HIV, their children and families.	
Services Provided	**Activities**
Facility and Community	▪ HIV testing for all other children ▪ Care and follow up of HIV positive children of HIV infected mothers. ▪ Follow up of the male partner in case of serodiscordant couple where the male partner is negative. ▪ Nutritional counseling and support for infants and young children born to HIV infected mothers.

2.2.1.3. ARV Treatment in Pregnant Women

There are three particularities of provision of ART to pregnant women:

- Adverse side effects are more common and may influence the choice of the ARV drugs (e.g. risk of severe rash with NVP treatment is seven times higher than for men).
- Lactic acidosis and hepatic steatosis are more common when using nucleoside analogues (83% of the first 107 cases that were reported).
- The possibility of an as-yet unknown pregnancy while under treatment.

HIV-infected women should be counseled on family planning.

There are three possibilities relating to pregnancy regarding antiretroviral treatment among women:

- ARV for the woman in the reproductive age group.
- ARV for the pregnant women
- ARV for the woman who is already on triple therapy who becomes pregnant.

2.2.1.4. ARVs for the Woman in the Reproductive Age Group

There is a dual problem:

The problems related to the association of contraception to ARVs:

Several ARVs (PIs and NNRTIs) modify the metabolism of hormonal contraceptives and need special precautions when this mode of contraception is utilized in conjunction with ARV treatment

Tab. 3: Effect of ARV on Plasma Concentration of Contraception

ARV	Effect on Concentration of Ethinyl – Estradiol	Adaptation of dosage
NRTI	No effect	NA
Nelfinavir	Reduction of 47%	↑>30µg ethinyl – estradiol
Lopinavir/r	Reduction of 42%	↑30 µg ethinyl – estradiol
Nevirapine	Reduction of 19%	↑ 30 µg ethinyl – estradiol
Efavirenz	Increase of 37%	↓15 or 20 µg ethinyl – estradiol

- Boosted PIs (Lopinavir or Atazanavir) should not be associated with Estrogen-based hormonal Contraception, Use alternative or additional contraceptive Methods
- Efavirenz should not be combined with Estrogen-based hormonal Contraception, Use alternative or additional contraceptive methods

In case of difficulties in using Ethinyl Estradiol, it is essential to recommend another mode of contraception:

- Either utilization of progesterone only pills: some interactions with ARVs exist in the form of reduction in the plasma concentrations of progesterone.
- Or use an intrauterine device (IUD), but keep in mind the increase risk of infections in the case of severe immune deficiency.

In all cases, the utilization of condoms (male or female) is recommended because they have an important role in preventing re-infection with HIV in case the partner is HIV-infected, and protection against infection if the partner is HIV negative.

The current national PMTCT guideline recommends that EFV-based treatment should no longer be avoided in pregnant women or those who want to conceive.

2.2.1.5. Pregnancy Desire

This phenomenon is very frequent and remains the hardest to manage. It is therefore necessary to regularly discuss this subject with patients during follow up because most patients will not talk about it spontaneously. Ideally, pregnancy in an HIV-infected woman should not be encouraged, even in the presence of PMTCT.

The health care provider together with the client should have more than one counseling discussion, preferably in the presence of the male partner, focusing on the pregnancy desire, associated risk on mother's health and the risk of mother to child HIV transmission. The healthcare provider should accompany the couple in their decision making process.

Therefore, when the couple decides to bear the pregnancy, the healthcare provider will conduct a close follow up of the mother in order to ensure good biological indicators (viral load suppression, good CD4 count and absence of opportunistic infection) and decide the less risky time for conception.

The counseling on infant nutrition, HIV testing and follow up is also a key component.

In a discordant couple where the male partner is HIV positive, the desire for pregnancy should consider seriously the risk of HIV transmission to the

woman. The health care provider should assist the couple to identify the woman's fertile period. It is recommended that conception is attempted during this period, in order to limit repetitive attempts that increase the risk of HIV transmission.

Each PMTCT site should also offer effective family planning services.
Some delicate issues in couples need to be seriously considered. One of them involves the male partner; and here there are 3 possibilities:

- Male partner is ***HIV-infected***: It is obvious that there is a need to counsel this couple on condom use in order to avoid re-infection but it will also be an opening to determine the right moment for conception while at the same time reducing the number of unprotected sexual encounters as much as possible. A focus will be put on early initiation of ART and special adherence follow up.
- Male partner is ***HIV-negative***: In this case there is a risk of eventual transmission through unprotected sexual encounters.
- Male partner's ***HIV status is not known***: in this case, the situation may be further complicated by two scenarios:
    - The woman conceals her HIV status from her partner. In this case, it is very likely that the woman undertakes frequent and unprotected sex. The pregnancy desire with multiple impregnation attempts increases the risk of transmission.
    - The partner refuses to check his HIV status and it is necessary to reduce the risk to both partners by limiting, if possible, the number of unprotected sexual encounters.

In summary, the points to be evaluated when a woman on ARVs wishes to become pregnant are:

- Is the partner's HIV status known?

- Is the disease stable for the HIV positive partner? Check for:
    - Viral load suppression
    - Good evolution in CD4
    - Good clinical evolution
- Is the ARV treatment available and correctly taken?
- Information on the risks to the mother, baby and the partner.
- What is the social support that the patient is receiving?

2.2.1.6. Guidelines on ART Drugs in HIV Positive Pregnant Women and Exposed Infants

It is recommended that any HIV+ pregnant woman receives all care including ART in the same health facility. This will be possible since the process of delegation of powers **(Task Shifting)** from physicians to the nursing staff is being implemented in our health system since 2009. The district hospital must do the maximum to oversee this approach especially for non-ARV sites. A clinical evaluation (Stages WHO) and a biological assessment including CD4 count, hemoglobin, liver function and the renal function must be made before the start of the ART in PMTCT.

In a pregnant woman, it is appropriate to start this treatment as soon as the pregnancy is identified, disregarding the WHO clinical staging or CD4 count. This is a lifelong treatment and thus, should never be discontinued after delivery.

The following situations are possible among HIV-positive pregnant women:

- The first line regimen is composed of **TDF + 3TC + EFV**
- Any woman with impaired renal function or likely to have impaired renal function will receive **ABC + 3TC + EFV**

- In case EFV is contraindicated, Nevirapine can be given only to those with CD4 cell count below 350. For those above 350 CD4 cells, Atazanavir is recommended but can be replaced by Kaletra

NB: Doses are the same as in adults HIV Treatment (see details in care and treatment chapter)

2.2.1.6.1. HIV-Positive Pregnant Women Exposed to SD Nevirapine

All HIV-positive pregnant women who were exposed to SD NVP during their previous pregnancy will receive: **TDF+3TC + ATV/r or LPV/r**
Women with impaired renal function or likely to have impaired renal function who were exposed to NVP during their previous pregnancy will receive:

ABC + 3TC + ATV/r or LPV/r

NB: Monitoring of Renal Function is Important

2.2.1.6.2. HIV-Negative Pregnant Women in a SDC

An HIV-negative woman in a serodiscordant couple (i.e., the partner is HIV-positive and the woman HIV-negative) will need to be tested for HIV every six months, as well as at the onset of labor.

- If she is shown to be HIV-positive: refer to the section on care for HIV-positive pregnant women (see above).
- If she remains HIV-negative, she will receive during labor:
  - A single dose of TDF + 3TC + EFV and continue with TDF + 3TC (one combined tablet per day) for one week after delivery.

Note: For a woman eligible already under ART for life, don't change the regimen except in case of side effects. The woman should continue the same regimen

2.2.1.6.3. Particularities of ARV Treatment in Pregnant Women

There are three particularities of ART provision to pregnant women:

- Adverse side effects are more common and may influence the choice of the ARV drugs (e.g. risk of severe rash with NVP treatment is seven times higher than for men).
- Lactic acidosis and hepatic steatosis are more common when using nucleoside analogues (83% of the first 107 cases that were reported).

There is a dual problem related to the association of contraception to ARVs. Several ARVs (PIs and NNRTIs) modify the metabolism of hormonal contraceptives and need special precautions when this mode of contraception is utilized in conjunction with ARV treatment.

2.2.1.6.4. Biological Monitoring of the Client on ART Drugs

It is recommended that the person living with HIV on ART drugs and followed up in PMTCT undergoes biological monitoring. This recommendation is compelling for mothers living with HIV, and HIV positive partners living in a discordant couple who initiated ART drugs. This includes VL at 6 months after ART initiation and then every 12 months and CD4 every 12 months.

At the time of ANC, for the pregnant mother who tests HIV positive, biological tests will follow the schedule as for adults (See summary table in care and treatment section).

2.2.1.6.5. Prophylaxis in Children Born in a SDC (HIV- Mother)

- The child must take daily NVP syrup since birth until one week after the cessation of breastfeeding unless the mother turns positive during breastfeeding period.
- If the mother is shown to be HIV-positive at the time of breastfeeding, she should be put on ART and the child should continue taking NVP for six weeks after the initiation of the mother's ART.
- The child will start Cotrimoxazole syrup since the age of 6 weeks and will be discontinued after final confirmation of HIV negative status at 18 months.

2.2.1.6.6. ARV Prophylaxis for Infant Born to HIV+ Mothers

All children born to HIV-positive mothers, whether the mothers breastfeed or not, will receive Nevirapine (NVP) syrup since birth for the first six weeks of life. The baby will start Cotrimoxazole syrup since the age of 6 weeks and will be discontinued after final confirmation of HIV negative status at 18 months.

2.2.1.6.7. Postnatal Consultation for the Mother-Child Couple

The follow up of the mother-child couple will include:

(1) Breastfeeding:

Advice on infant diet should be discussed when the results are announced. More details should be availed progressively throughout the pregnancy and during the postpartum period. The recommended feeding method is as follows:

- Exclusive breastfeeding until six months;
- Introduction of healthy, balanced, and appropriate complementary food at six months and continuation of breastfeeding without exceeding the maximum recommended duration of 18 months;
- Weaning should be done gradually over a period of one month and half (advice and nutritional support are necessary during this period);
- Advice on a healthy and balanced diet for the child and the mother must be given continuously to the mother;
- Regular clinical follow up of the mother and child will continue;
- ARV adherence should be continuously ensured;
- Ensure mother's biological regular follow up;
- If a mother wishes not to breastfeed, make sure that safe and adequate replacement food is available. The health care provider should give appropriate advice on substitute milk to use, healthy and balanced complementary foods to offer starting at six months.
- If the mother chooses replacement feeding, the child must be fed exclusively by replacement feeding and never breastfeed.
- From 6 months up to 24 month, complement the milk meals with adequate complementary foods that are locally available.

The success of artificial feeding depends on:

- The quality of the counseling that was given: the issue of infant feeding should be discussed as early as possible following the disclosure of seropositivity.
- It is important to give clear explanations on how to clean the feeding bottles or cups and how to sterilize them using boiling water. Access to clean water is an important factor and must be evaluated before considering artificial feeding.

- The family and/or community support received by the mother.
- The quality of mother infant follow-up done by the health care team.

(2) Infant Growth Monitoring and Evaluation of Nutritional Status

The first two years of life are a period of rapid growth in children. The child's weight at birth is about 3kg. The child doubles his birth weight after six months and triples it after one year. At two years, he weighs about 12kg.
The size of the child is about 50cm at birth. It increases to about 75cm after one year and 85cm after two years. Head circumference is between 33cm and 36cm at birth. It increases to about 45cm after one year and 47cm after two years.

The anthropometric parameters most commonly used for growth monitoring of children are as follows:

- Weight: The naked or lightly dressed (without shoes) child is weighed with a well-calibrated scale by, if possible, the same person each time.
- Height: Children under two years should be measured lying down; older children should be measured upright. Never use a tape measure.
- Head circumference: This should be measured in all children under five years every time they have contact with the health center. A tape measure should be used and should be passed around the frontal and occipital bones.

Regular growth monitoring can allow for early detection of weight, height, and head circumference abnormalities. If any, the exact cause will be sought to undertake appropriate treatment and allow the child to realize his full growth and development potential.

Completing growth charts: At **each** consultation, the weight, height, and head circumference should be recorded on the growth chart in the child's file.

- All children should be completely examined (weight, size, neurological development, suspicious signs of infection) every month until they reach 18 months.
- If the child shows growth or neurological problems, or suspicious signs of infection (fever, impaired general condition, dyspnea, etc.), he will be immediately referred to a doctor.
- Assess nutritional status monthly, and interpret the results to offer appropriate advice and nutritional care given that exposed children are at risk of malnutrition.

(3) Follow up Schedule

The first appointment is after six weeks (child vaccination, PCR, Cotrimoxazole initiation, monitoring of growth and psychomotor development), and monitoring will continue every month following the vaccination schedule. After the vaccinations, monitoring will continue every month until 18 months, and for at-risk cases (non-cessation of breastfeeding at 18 months, malnutrition, HIV infection, etc.), it will be prolonged and overseen by the relevant services.

The appointment at six weeks is crucial. The identification of HIV exposed children in the vaccination service will be facilitated by the immunization card integrating information about the mother's HIV status and interventions in the PMTCT program.

It is important to harmonize follow-up appointments of the child with those of the mother to avoid multiple visits.

(4) Infant Biological Follow up

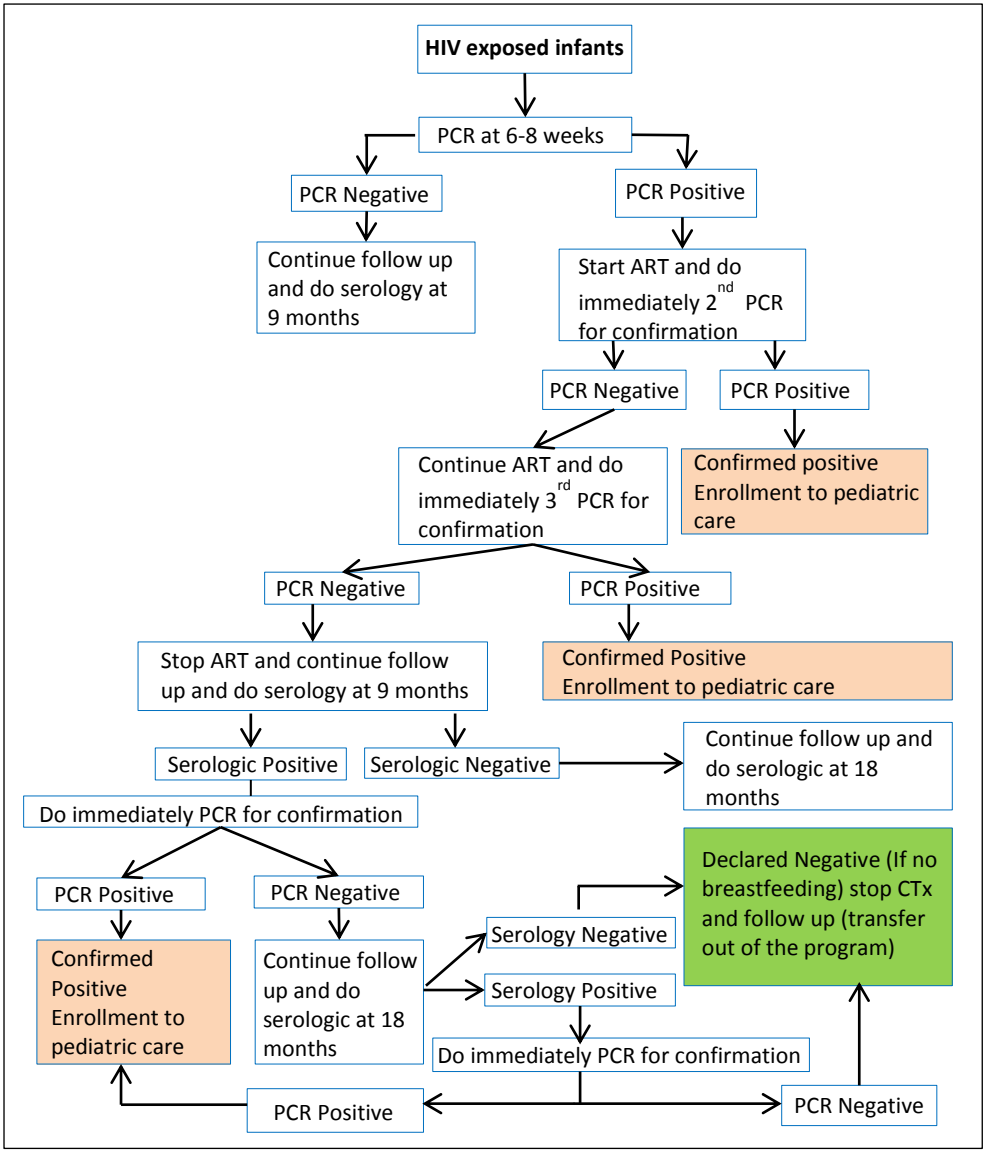
HIV exposed children will be closely monitored, clinically and biologically, in order to diagnose and provide early treatment to those needing ARVs before 18 months. The biological follow-up includes PCR at six weeks and serological tests at 9 and 18 months. **(Refer to Algorithm 2)**

It is worth noting two important instructions:

☞ When an HIV exposed infant tests indeterminate on serological tests used at the health facility, the health care provider should collect immediately a DBS/PCR for confirmation.

☞ At completion of the follow up period in PMTCT (18 months), the health care provider should be certain of the infant's serostatus. When the infant tests negative on rapid tests used at the health facility, but the result accuracy is suspected for any reason (e.g. suspected that mother did not stop breastfeeding 1.5 months earlier) the health care provider should collect a DBS/PCR for final confirmation and declare the infant' status upon reception of the result.

Algorithm2: HIV Testing Among HIV Exposed Infants



2.2.2. HIV Prevention Among Discordant Couples

Evidence-based interventions package for HIV Discordant Couples can be provided through facility based and/or community interventions. Although these interventions are delivered in a package, providers must ensure that they contextualize the specific, particular needs of the couple since different couples may have different needs.

Overall, the intervention package for discordant couples consists of the following: (1) Risk Reduction Counseling and Condom Provision, (2) Family Planning Counseling and Service Provision, (3) Repeat HIV Testing for the uninfected partner every 6 months, (4) Care and Treatment for the HIV positive partner, (5) STI screening and treatment.

The objectives of these interventions are (1) to protect the negative partners from HIV infection, (2) to provide Care and Treatment to HIV positive partners, (3) to protect future children from HIV infections and (4) to get their sex partners and children tested for HIV.

All HIV positive partners in discordant couples will be started on lifelong ART regardless any eligibility criteria. The choice of ART regimen is based on the recommendations for the first line in Rwanda like for any other HIV positive person.

People with HIV in discordant couples who start ART for their own health should be advised that ART is also recommended to reduce HIV transmission to the uninfected partner.

2.2.3. ART Post Exposure Prophylaxis

Every person who has been a victim of accidental exposure to blood/body fluids or rape victim must have access to an early evaluation of the risk of HIV infection and antiretroviral prophylaxis if indicated. This is why it is

necessary to have functional services that work 24 hours a day. It has been shown that initiating prophylaxis early diminishes the risk of HIV infection by about 80%.

Post-exposure prophylaxis is short-term ART to reduce the likelihood of acquiring HIV infection after potential exposure either occupationally or through sexual intercourse.

2.2.3.1. Accidental Exposure to Blood (AEB) or to Other Biological Fluids

Within the health sector, post-exposure prophylaxis should be provided as part of a comprehensive package of universal precautions that reduces the exposure of personnel to infectious hazards at work. An HIV serology test should be performed for the exposed caregiver as soon as possible (ideally ***within four hours***). If it turns out negative, serologic monitoring will be done, in particular in the third month and before the end of the sixth month.

The actual risk for a given patient must be evaluated by one of the health care providers from the health facility. This evaluation includes (1) the severity of the exposure, which is directly linked to the depth of the wound and the type of needle that was responsible for the injury (Venipuncture needle, needle for injection, non-sharp instrument); (2) external contact of secretions with the skin or mucosa (splash), the risk is higher with blood than with any other body secretions (amniotic fluid, serous fluid).

The source person of the exposure should be assessed on his or her HIV status, clinical and immunological status and history of ART. If the HIV status is not known, it is important to establish it with his/her free consent. In any case, if the HIV status of the source person cannot be obtained within 4 hours, prophylaxis should be started immediately. If eventually the source

person of the exposure is proven to be HIV negative, then ARV prophylactic treatment should be stopped.

In case of AEB, always clean the exposed area immediately. In case of exposure through ***needle stick or skin injury***, clean the wound immediately with clean water and soap. In case of ***Splash on the mucous membranes (particularly the conjunctiva)***, rinse at least for 5 minutes with copious amounts of water or preferably physiological saline and do not apply disinfectant on the mucous membranes. The post exposure prophylaxis (PEP) depends on degree of exposure, and HIV status of the source of exposure as per the following table:

Table 4: Recommendations on Post Exposure Prophylaxis

Source	Exposure		
	Massive	Moderate	Minimum
HIV + with low CD4 or Opportunistic Infections	Recommended	Recommended	Recommended
HIV + Asymptomatic	Recommended	Recommended	Discuss
HIV status unknown, but risk factor for HIV (≥ 1 risk factor)	Recommended	Recommended	Discuss
HIV status unknown or unknown source without risk factors	Recommended	Discuss	Discuss

2.2.3.2. Sexual Assault or Rape

In case of rape, the provider must first follow the HIV counseling and testing steps described in the above paragraphs before giving prophylactic treatment. Consider HIV post-exposure prophylaxis for women presenting within 48 - 72 hours of a sexual assault.

Table 5: Management of Sexual Assault or Rape

Source Person HIV Status	Exposed Person HIV Status	Recommendation
Positive or negative	Known positive	No prophylaxis is indicated
Known positive*	Known negative	Immediate prophylaxis indicated
Known positive	Not known	Immediate HIV Rapid test done on the victim. - If HIV negative, give prophylaxis - If HIV positive, stop prophylaxis and refer victim to HIV treatment clinic. - Provide emergency contraception if the victim accepts.
Not known but accepts HIV test	Known negative	Immediate HIV Rapid test done on the rapist - Give prophylaxis as you wait for the results. - If the rapist is HIV negative, stop prophylaxis - If rapist is HIV positive, continue with prophylaxis - Provide emergency contraception if the victim accepts.

Source Person HIV Status	Exposed Person HIV Status	Recommendation
Not known but accepts HIV test	Not known	Immediate HIV Rapid test done on the rapist and the victim - Give prophylaxis as you await the results, if the rapist is negative, stop the prophylaxis - If the victim is positive, stop prophylaxis and refer her to the HIV care and treatment clinic. - Provide emergency contraception if the victim accepts.
Not known and either refuses the test or is not available	Known negative	Counsel the victim and inform her of the risks and benefits of prophylaxis and explain the options; then give prophylaxis if the victim accepts. Provide emergency contraception if the victim accepts.
Not known and either refuses the test or is not available	Not known	Immediate HIV Rapid test done on the rape victim - If the victim is HIV negative, then give prophylaxis; - Counsel the victim and inform her about the risks and benefits of prophylaxis and give options. - Provide emergency contraception if the victim accepts.

2.2.3.3. ART Prophylaxis

The current recommended duration of post-exposure prophylaxis for HIV infection is 28 days. Treatment should start as early as possible, within the first 4 hours following the exposure, without waiting for results of HIV serology of the source person. A limit of 48 hours is reasonable in seeking maximum efficacy. The recommended post-exposure prophylaxis drugs are based on the current second and first line regimen:

1. TDF + 3TC / FTC + ATV/r
2. AZT + 3TC/ FTC + ATV/r (If no TDF or a contraindication)
3. TDF + 3TC/ FTC + EFV

NB: The recommended ART Prophylaxis is the same in rape/sexual assault and exposure to biological fluids

Table 6: Follow up of Person on Post Exposure Prophylaxis

Date	Not on Prophylaxis	On Prophylaxis
Initial	HIV Test (Serology)	- HIV Test (Serology)
		- Creatinin (Renal Clearance)
		- Pregnancy Test
Week 2	NA	- Creatinin (Renal Clearance)
M1	HIV Test (Serology)	- HIV Test (Serology)
		- Creatinin (Renal Clearance)
M3	NA	- HIV Test (Serology)
M6	HIV Test (Serology)	- HIV Test (Serology)

2.2.4. HIV Prevention Among Key Populations (KP)

Key populations are persons with behaviors that put them at risk of contracting and/or transmitting STIs/HIV, particularly because of multiple partners and the low rate of condoms use. They are often affected, stigmatized and marginalized, and disproportionately affected by HIV.

Classic KPs include Men who have sex with Men and transgender persons, People who inject Drugs, and male and female sex workers (M/FSWs); while vulnerable populations include prisoners, uniformed personnel, mobile populations (migrant workers, truck drivers), people living with Disabilities and Refugees. In Rwanda, KPs are defined as Female sex workers, MSM, and vulnerable groups include prisoners, Mobile populations and uniformed personnel.

1. ***HIV Testing and Counseling:*** Described in HTC chapter, in special cases
2. ***Peer education and outreach services***: Peer outreach service relies on community members to reach key and vulnerable populations with HIV prevention information and linkage to clinical services. These services emphasize on risk reduction counseling and provisioning of supplies (e.g. condoms, lubricants, FP commodities).
3. ***Sexual and drug use assessment, and risk reduction counseling***: Taking a sexual and individual drug using history ensures that service providers know and do not assume the needs of their clients. Risk reduction counseling is an effective intervention for KPs, whether delivered through peer outreach or in health facility settings and can address both drug and sexual risk behaviors, as appropriate.
4. ***Condom and water based lubricant promotion and distribution***: Programs need to ensure a consistent supply and availability of quality

male and female condoms as well as water based lubricants compatible with condoms especially for MSM.

5. ***Sexually Transmitted Infections (STI) screening and treatment***: Existence of an STI may facilitate sexual transmission and acquisition of HIV Routine STI assessment and treatment should be an integral component of KP package of services. Key populations (especially Sex workers and MSM) should get screened for STIs every 3 months.

   STI services are also useful in attracting KPs into services/programs, providing an opportunity to reach KPs with other HIV prevention services.

6. ***Referrals to HIV care and treatment, including PMTCT:*** Initiation of ART at the earliest possible point is a critical intervention for KPs. FSW and MSM should be rapidly linked to friendly ART services upon diagnosis with HIV, and ***should get started on ART as soon as possible regardless any other eligibility criteria***. KP programs should include support for adherence and retention designed around the needs of these populations. Good treatment adherence has been demonstrated among KPs when approaches are implemented to facilitate access and acceptability. Innovative approaches to increasing successful linkage into PMTCT, care and treatment services should be implemented. All KP programs need to ensure adequate monitoring of linkages to services. Prevention programs for KP need to link up and help facilitate training for clinical PMTCT and ART service providers to make existing services key population friendly and accessible.

7. ***Referrals to substance abuse treatment***: although substances abuse seems to be very low in the Rwandan population, substance abuse treatment reduces the frequency of drug use, which in turn reduces HIV risk behaviors. It also improves adherence to disease treatment regimens.

Treatment modalities include non-pharmacological and pharmacological approaches; often, a combination of the two is used.

8. ***Linkages to other health, social, and legal services***: KPs and other vulnerable populations should be provided with or referred to other health services including family planning, primary health care as well as psychosocial and legal support.

Service delivery models (e.g., mobile versus fixed sites, hours of operations, type of health service provider, etc.) for these core prevention interventions may need to be adapted to reach, engage and retain KPs.

Chapter III: Combination Prevention

3.1. Biomedical Prevention

3.1.1. Male and Female Condoms

Condom use is a critical element in a comprehensive, effective, and sustainable approach to HIV prevention across the continuum of response. Condom distribution and promotion should be key components of all packages of interventions for all populations, where appropriate. Male condoms reduce heterosexual transmission by at least 80% and offer 64% protection in anal sex among men who have sex with men, if used consistently and correctly. Fewer data are available for the efficacy of female condoms, but evidence suggests they can have a similar prevention effect.

Condom programming should engage the public, social marketing and private sectors in condom distribution and promotion and should include a plan for increasing sustainability of condom programming. Social marketing programs should provide subsidized and marketed commodities to poor and vulnerable populations where the private sector does not supply these commodities. Free public sector condoms should primarily be distributed to population segments lacking disposable income and/or those most at risk of HIV transmission or acquisition.

Specifically for Key populations (Female sex workers and Men who have sex with men), condom programming and distribution should go hand in hand with the distribution of water-based lubricants.

3.1.2. Voluntary Medical Male Circumcision (VMMC)

Three randomized controlled trials (RCT) demonstrated that VMMC reduces men's risk of HIV acquisition by approximately 60 percent, making it one of the most effective HIV prevention interventions known. WHO/UNAIDS issued normative guidance in March 2007, recognizing that VMMC is an additional important intervention to reduce the risk of male heterosexually acquired HIV infection and that VMMC should always be implemented as part of a comprehensive HIV prevention package.

The minimum VMMC package includes (1) the provision of HTC services; (2) clinical evaluation of the client, and (3) an informed consent. Also the package may include the treatment for STIs; the promotion of safer sex practices, such as abstinence from penetrative sex, reduction in the number of sex partners, and delay in the onset of sexual relations; and the provision of male and female condoms, and promotion of their correct and consistent use.

After the VMMC procedure, the client should receive all the information regarding possible complications (Bleeding, Important pain, difficulty urinating, swelling or local infection). The client is advised to avoid any sexual intercourse or masturbation for at least 4-6 weeks after VMMC. When the VMMC is device based, the counseling is based on the manufacturer recommendations.

In case of complications beyond the health facility competencies or by the client's request, transfer should be done according to referral system applicable in Rwanda.

3.1.2.1. VMMC Setting

VMMC package is offered in public and private health facilities fulfilling the conditions required by the Ministry of Health.

Conditions for health facilities to start VMMC programs include (1) to have an operation room for at least minor surgery, (2) to have at least one health care providers trained on VMMC procedures, (3) to have necessary equipment for sterilization of materials, (4) to have necessary materials for the performance of MC (depending to the VMMC method), (5) to respect scrubbing and infection prevention principles

VMMC can be provided by using classic surgical methods or a device based method. In Rwanda, the Prepex device has been tested and found to be safe and effective as a means of performing bloodless adult male circumcision that can be carried out by non-physician staff without need for anesthesia, suturing, or sterile settings.

3.1.2.2. Newborn Circumcision

Rwanda is a traditionally a non-circumcising society and the prevalence of male circumcision among men age 15-59 is only 13%. These data are mainly applicable to adult population, and data on children are not yet available.

Efforts to increase the male circumcision prevalence in the country took into account all age groups of the population. For young children, these efforts sometimes face obstacles such as pain related to the procedure and parents' fear of potential side effects to their children. The introduction of infants' specific program in the country aims at breaking such barriers and reverses the trend towards a circumcising society.

The Early Infant Male Circumcision (EIMC) in the country is using Mogen clamp procedure. It is clamp-based procedure validated by the WHO and performed on infants between 7 and 60 days of life. It has got several advantages as it takes less time to be performed, the wound heals quickly, the procedure is cost effective and it causes less pain to the infant.

3.1.3. Prevention with People Living with HIV (PWP)

HIV prevention with people living with HIV (PLHIV) integrated into routine care is a core component of a comprehensive and integrated HIV prevention, care, and treatment strategy. Prevention services for HIV-positive persons include both behavioral and biomedical activities aimed at reducing the morbidity and mortality experienced by HIV-positive individuals and reducing the risk of transmission to HIV-negative partner(s) and infants.

By focusing on partner and couples HIV testing and counseling (HTC), PwP service provision can contribute to the identification of HIV-positive individuals and serodiscordant couples and partnerships. Partners who are newly identified as HIV-positive can then be linked into HIV prevention, care and treatment services.

The Prevention with people living with HIV is summarized in 5 steps:

STEP 1: Give prevention recommendations to the HIV-positive patient during each visit

STEP 2: Evaluate the patient's adherence to ARV treatment and/or other treatments at each visit.

STEP 3: Evaluate the patient for possible signs and symptoms of STIs at each visit.

STEP 4: Evaluate the state of pregnancy and the intention of the patient or her partner to have a child.

STEP 5: Give condoms to the patient at each visit

The provider must refer patients needing specialized care to the appropriate health care services.

3.2. Behavioral Interventions

The goal of behavioral interventions is to reduce HIV risk behaviors and the frequency of HIV transmission events. To reach this goal, interventions attempt:

(1) to decrease the number of sexual partners,
(2) to increase the number of sexual acts that are protected,
(3) to encourage adherence to clinical strategies for preventing HIV transmission

Programs use various communication approaches – ***for example, school-based sex education, peer Education/counseling and community-level and interpersonal counseling*** – to disseminate behavioral messages designed to encourage people to reduce behavior that increases the risk of HIV and increase the behavior that is protective (***such as safer drug use, delaying sexual debut, reducing the frequency of unprotected sex with multiple partners, using male and female condoms correctly and consistently and knowing own and partner's HIV status***).

3.3. Structural and Supportive Interventions

Structural approaches aim to mitigate the impact of HIV by altering structural factors, which include physical, social, cultural, organizational, community, economic, legal or policy aspects of the environment that determine HIV risk and vulnerability. Structural interventions involve more than the service providers and beneficiaries; it includes working with various stakeholders

including governmental and non-governmental agencies and addressing the factors that impede or facilitate efforts to prevent HIV infection.

These interventions affect access to, uptake of and adherence to behavioral and biomedical interventions. Such interventions address the critical social, legal, political and environmental enablers that contribute to HIV transmission. This includes legal and policy reform, measures to reduce stigma and discrimination, the promotion of gender equality and prevention of gender-based violence, economic empowerment, access to schooling and supportive interventions designed to enhance referrals, adherence, retention and community mobilization.

Chapter IV: Linking HIV Testing Services to Care and Treatment

Knowledge of HIV status allows people to make informed decisions about HIV prevention and treatment. Strong linkages to effective HIV prevention, treatment, care and support services are essential if people are to carry out these decisions.

For individuals identified as HIV-negative or seroconcordant negative couples, HTC provides access to HIV prevention services, including condoms, male circumcision and risk reduction counseling. In the absence of linkages to these services, HTC will have only a moderate impact on HIV prevention.

The post-test counseling is the key to ensure all clients who test HIV-positive are referred to the general care and treatment of HIV. In this case, HTC provides a gateway to treatment services. It enables women and couples with HIV to access services both for themselves and to aid safer conception and prevent transmission to their infants.

For couples that are serodiscordant, HTC provides access to services to prevent HIV transmission to the uninfected partner and to HIV care, support and treatment services for the partner with HIV. It can support the uptake and effective use of PMTCT interventions and safer conception options.

The general care and treatment is composed of medical, psychosocial, and nutritional services which consider all aspects of the client's problems to ensure the patient leads a normal family, social and professional life.

It is critical for people living with HIV to enroll in care as early as possible. This enables both early assessment of their eligibility for ART and timely initiation of ART as well as access to interventions to prevent the further

transmission of HIV, prevent other infections and comorbidities and thereby to minimize loss to follow-up.

Several good practices are proposed to improve linkage to care. These include:

(1) Integrating HIV testing and counseling and care services;
(2) Providing on-site or immediate CD4 testing with same-day results;
(3) Assisting with transport if the ART site is far from the HIV testing and counseling site;
(4) Involving community health workers to identify the people lost to follow-up;
(5) Ensuring support from peer patients;
(6) Using new technologies, such as mobile phone text messaging for follow up.

Connecting individuals and couples that have been tested for HIV to prevention, care and treatment services is one of the guiding principles of HTC conduct. This is the responsibility of HTC providers; to support the strengthening of linkages. HTC providers must be informed that the obligation of linking their clients to the appropriate services lies with them. HTC providers must collaborate with other service providers to ensure that individuals or couples undergoing HTC are effectively linked to appropriate services. Programs and facilities should explore appropriate interventions to maximize effective linkages.

PART II: HIV CARE AND TREATMENT

1.1. Goals of Antiretroviral Therapy

- Suppress the viral load to undetectable levels
- Increase the number of CD4 cells so as to improve the immune reconstitution;
- Reduce the transmission of HIV
- Minimize the risk of cross resistance
- Minimize long term toxicity
- Improve the clinical status of the patient
- Improve the quality of life of the patient
- Maximize growth and development
- Minimize the cost of care

1.2. Initial Evaluation of HIV Infected Clients

1.2.1. Clinical Evaluation

- History, review of systems, and past medical history
  - General health status
  - Drug history
  - Sexual History (if applicable)
  - Past medical history: STI; past or present HIV-related illness; Risks for opportunistic infections
  - Screening for opportunistic infections and HIV staging
- Comprehensive physical examination

1.2.2. Laboratory Evaluation

- Baseline:
  - CD4 Cell Count (Repeated every year),
  - Hepatitis B surface antigen,
  - Hepatitis C antibody,
  - Cryptococcus antigen (if CD4 count < 200cells/mm3)
- Additional studies as clinically indicated

1.3. Criteria for Eligibility to ART in Adults

Any adult with confirmed HIV sero-positive status is eligible for ART if the individual has one of the following criteria:

- WHO Stage 3 or 4
- WHO Stage 1 or 2 with CD4 < 500/mm^3
- HIV-TB co-infection
- HIV-Hepatitis B co-infection
- HIV-Hepatitis C co-infection
- All HIV-positive sexual partners in stable discordant couples
- All men who have sex with men (MSM)
- All female sex workers (FSW)

1.4. Initial Biological Assessment Before Initiation of ART

Area	Biological Test
OIs	Cryptococcus antigen if CD4 < 200 cells/mm3
Liver Function	ALAT*, ASAT*
Renal Function	Creatinine and calculation of creatinine clearance
Viral Hepatitis	Ag HBs; HCV Ab
Immunology	CD4 Cell count
Hematology	FBC*

*Not to be done on a routine basis but rather on a case to case basis

1.5. First-line ART Regimen for Adults

- **ART Options in Adults**

There are four options recommended in first line regimen (Adult):

	NRTI	NNRTI
1	Tenofovir(TDF)+Lamivudine(3TC)*	Efavirenz(EFV)
2	Tenofovir(TDF)+Lamivudine(3TC)*	Nevirapine(NVP)
3	Abacavir(ABC)+ Lamivudine(3TC)*	Efavirenz(EFV)
4	Abacavir(ABC)+ Lamivudine(3TC)*	Nevirapine(NVP)
***Lamivudine can be substituted by FTC**		

- If contre indication to Efavirenz then give, Niverapine
- If contre indication to TDF then give Abacavir

- **Dosing and Administration of First-Line Drugs**

Molecule	Dosage
Tenofovir(TDF)	300 mg once a day
Abacavir(ABC)	300 mg twice a day or 600 mg once a day
Lamivudine(3TC)	150 mg twice a day or 300 mg once a day
Emtricitabine(FTC)	200 mg once a day
Efavirenz(EFV)	600 mg once evening
Nevirapine(NVP)	200 mg once a day for 14 days and then 200 mg twice a day

- **Prescription of ART First Line**

1) TDF + 3TC + EFV (FDC): TDF 300mg + 3TC 300mg + EFV 600mg
2) ABC + 3TC + EFV: ABC 600mg+ 3TC300mg+ EFV 600mg (Evening*)
3) ABC** + 3TC + NVP:

- Initial Phase (15 Days): ABC 600mg + 3TC 300mg + NVP (200 mg OD)
- Maintenance phase: ABC600mg+ 3TC300mg + NVP (200 mg BID)

(*) Encourage taking drugs in the evening before 8:00pm due to daytime side effects of EFV

(**) Give the formulation of ABC 600mg to facilitate once daily dosage

4) TDF + 3TC + NVP: TDF 300mg + 3TC 300mg (OD) + NVP 200mg (Twice a day).

Note: The association of 3 NRTIs (ABC+3TC+AZT) is possible but because of the reduced potency should not be considered except in cases of extreme necessity or after expert opinion.

Available fixed dose combination (FDC) in Rwanda:

(1) TDF + 3TC + EFV (FDC)

(2) **TDF + 3TC**

(3) AZT+3TC+NVP

(4) AZT+3TC

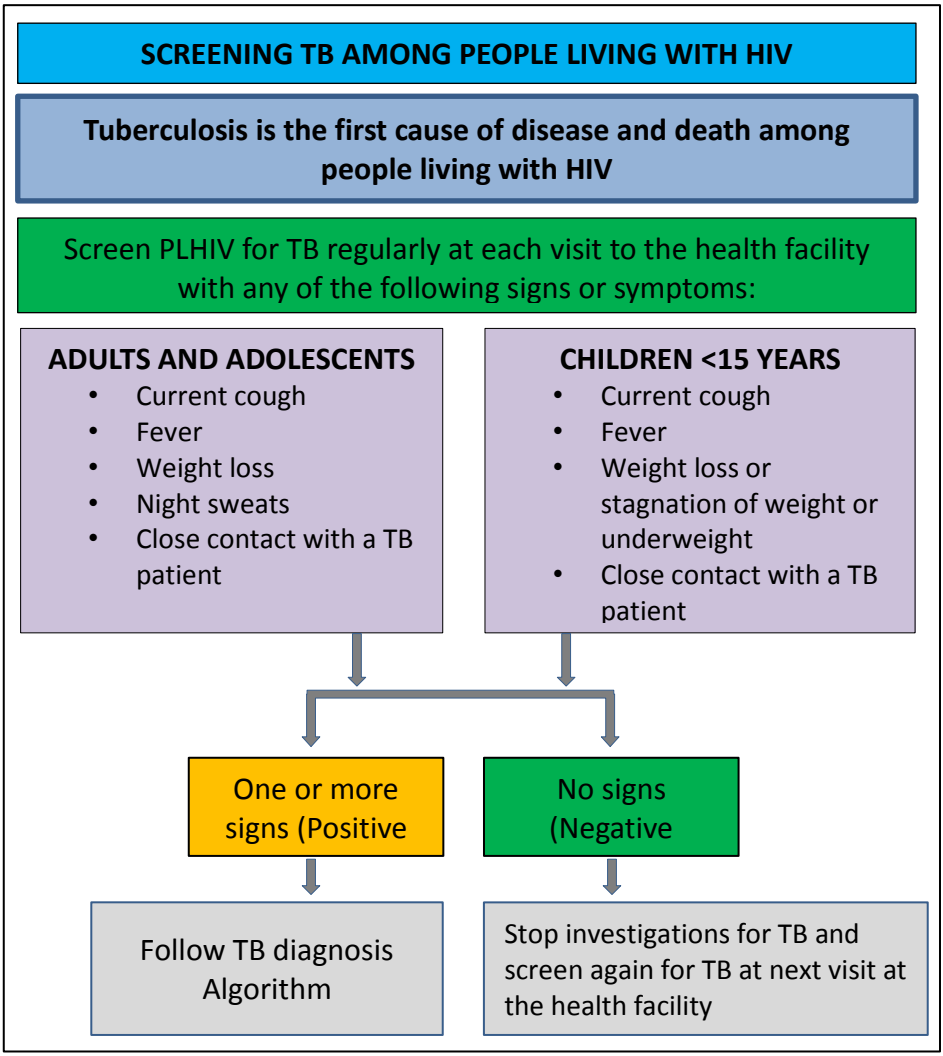
(5) ABC+3TC

1.6. Recommendations for HIV-TB co-infection in Adults

1.6.1. Screening of TB-HIV co-infection in Adults

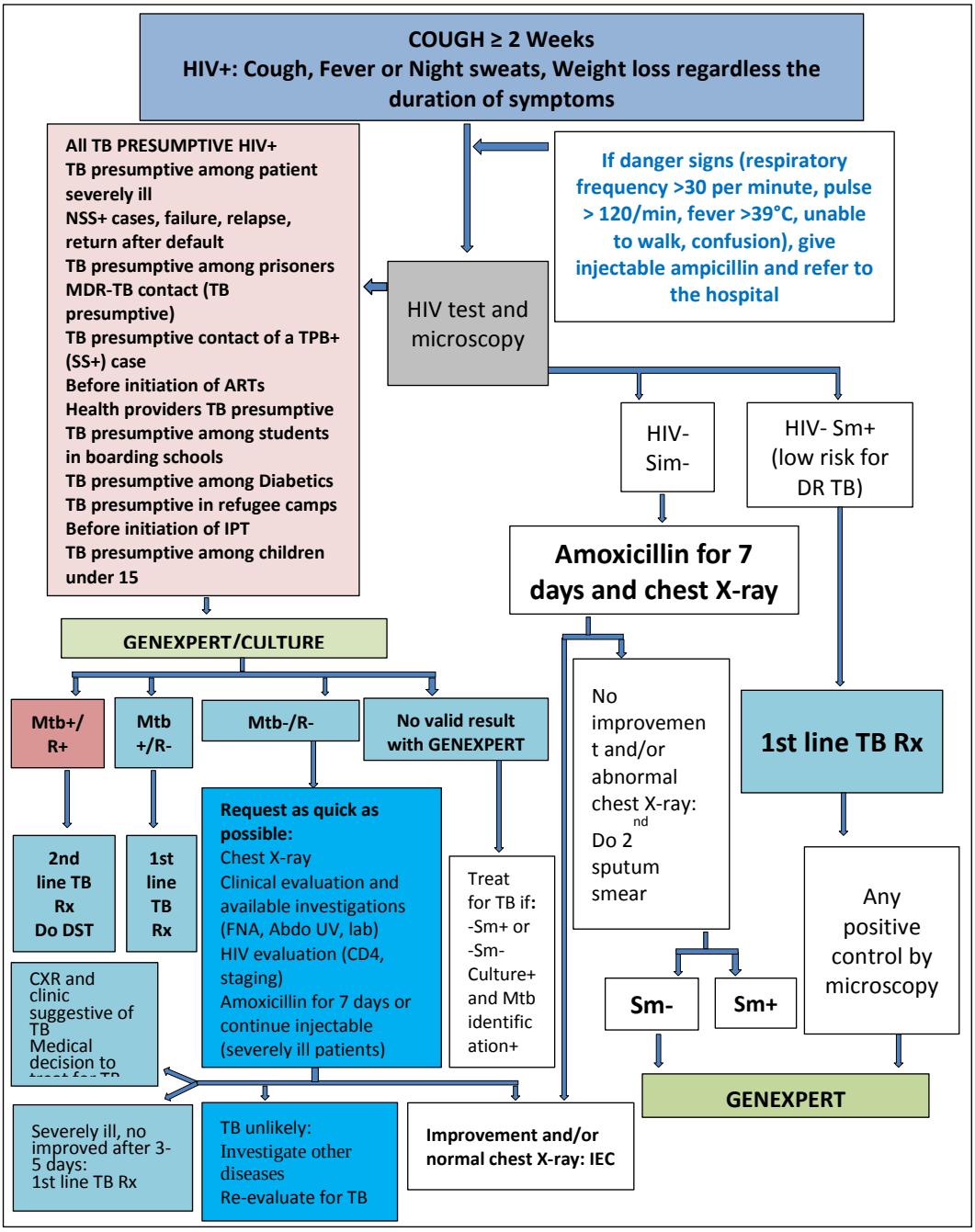
All HIV-positive adults and adolescents should be screened for active TB infection at enrollment and regularly at each clinical encounter with a clinical algorithm using the following symptoms or signs:

1) Cough
2) Fever or night sweats
3) Weight-loss
4) Contact with someone known to have TB



1.6.2. Diagnosis of TB-HIV Co-infection

Algorithm 4: Diagnosis of TB in HIV-Positive People


COUGH ≥ 2 Weeks
HIV+: Cough, Fever or Night sweats, Weight loss regardless the duration of symptoms
All TB PRESUMPTIVE HIV+
TB presumptive among patient severely ill
NSS+ cases, failure, relapse, return after default
TB presumptive among prisoners
MDR-TB contact (TB presumptive)
TB presumptive contact of a TPB+ (SS+) case
Before initiation of ARTs
Health providers TB presumptive
TB presumptive among students in boarding schools
TB presumptive among Diabetics
TB presumptive in refugee camps
Before initiation of IPT
TB presumptive among children under 15
If danger signs (respiratory frequency >30 per minute, pulse > 120/min, fever >39°C, unable to walk, confusion), give injectable ampicillin and refer to the hospital
HIV test and microscopy
HIV- Sim-
HIV- Sm+ (low risk for DR TB)
Amoxicillin for 7 days and chest X-ray
GENEXPERT/CULTURE
Mtb+/ R+
Mtb +/R-
Mtb-/R-
No valid result with GENEXPERT
No improvement and/or abnormal chest X-ray: Do 2nd sputum smear
1st line TB Rx
2nd line TB Rx Do DST
1st line TB Rx
Request as quick as possible:
Chest X-ray
Clinical evaluation and available investigations (FNA, Abdo UV, lab)
HIV evaluation (CD4, staging)
Amoxicillin for 7 days or continue injectable (severely ill patients)
Treat for TB if:
-Sm+ or
-Sm- Culture+ and Mtb identification+
Any positive control by microscopy
Sm-
Sm+
CXR and clinic suggestive of TB
Medical decision to
GENEXPERT
Severely ill, no improved after 3-5 days:
1st line TB Rx
TB unlikely:
Investigate other diseases
Re-evaluate for TB
Improvement and/or normal chest X-ray: IEC

Note:

- Do not give Fluoquinolones (Ciprofloxacin) in case of TB suspicion
- Patients suspected of having extrapulmonary TB should be managed by a physician or at a referral center

1.6.3. Treatment of TB-HIV Co-infection

The following are national recommendations on TB-HIV Management:

1) All HIV-positive patients with confirmed TB co-infection are eligible for ARVs regardless of CD4 count and clinical stage.
2) The standard first-line anti-tuberculosis regimen in Rwanda is $2RHZE_7/4RH_7$ (see Rwanda National TB Guidelines for detailed instructions regarding management of TB).
3) Co-infected patients (TB-HIV) should receive anti TB treatment based on Rifabutin to replace Rifampicin
4) Patients with MDR TB should be referred to appropriate treatment centers
5) Co-infected patients (TB-HIV) should receive Pyridoxine 25mg daily (100mg daily for MDR-TB/HIV).
6) If a patient has contra-indication to EFV, it can be substituted by LPV/r (with doubled dose of LPV/r) or Atazanavir
7) If a patient has contra-indications to both EFV and LPV/r, triple NRTI regimen of AZT/3TC/ABC is acceptable during the TB treatment period.
8) In co-infected patients, the priority is to first treat TB basing on patient's clinical status and CD4 count. Time for ART initiation varies between 2 and 8 weeks as follows:

Tab 7: Recommendations on TB-HIV Management

Situation	When to Start	ART Regimen	ART Adjustment
Patient already on ARV	Continue ARV	TDF/ABC/AZT + 3TC + EFV	No adjustment (EFV remains 600mg daily)
		TDF/ABC/AZT + 3TC + NVP	Substitute NVP with EFV
		TDF/ABC/AZT + 3TC + LPV/r	Double dosing of LPV/r during antituberculosis therapy or substitute Rifampin with Rifabutin
		TDF/ABC/AZT + 3TC + ATV/r	Substitute ATV/r with double-dosing of LPV/r or substitute Rifampin with Rifabutin
Pre-ART Patient and CD4<50	Start ARV with 2 weeks	Start EFV-based first-line regimen	No adjustment
Pre-ART Patient and CD4>50	Start ARV with 8 weeks	Start EFV-based first-line regimen	No adjustment

1.7. Screening and Management of Opportunistic Infections

1.7.1. Cryptococcal Infection

- **Introduction**

Cryptococcal infections are common in patients with AIDS and lowest CD4 (+) cell counts.

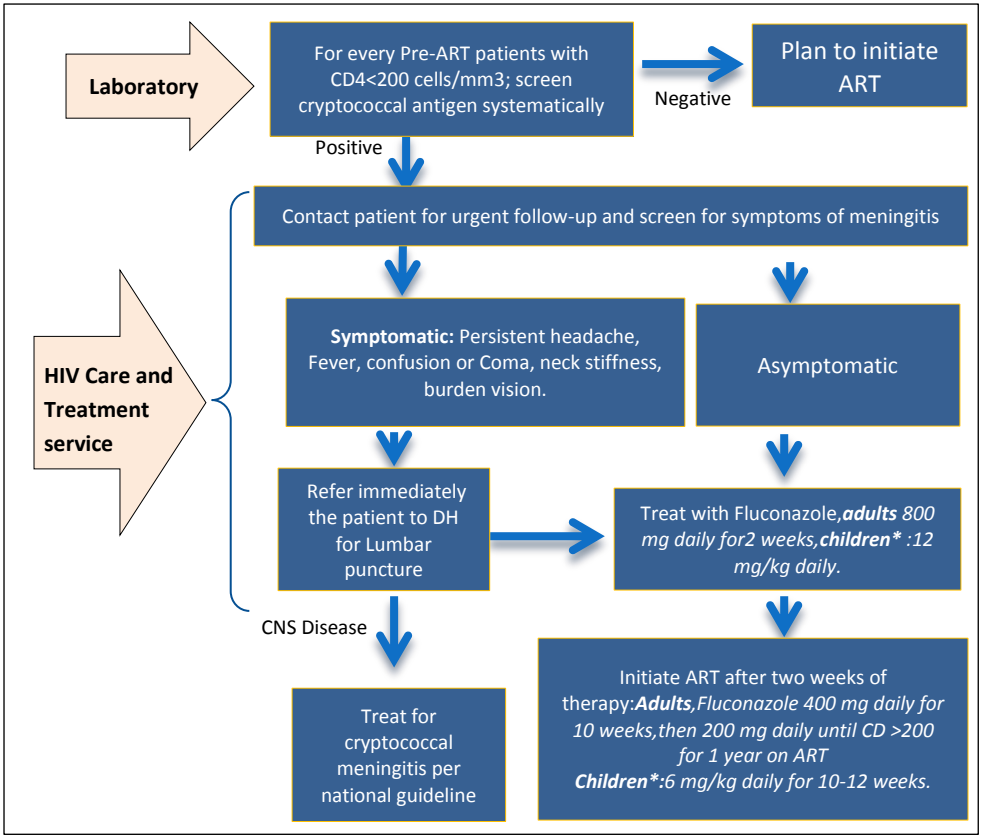
In this case, prolonged anti-fungal therapy and secondary prophylaxis is necessary. For meningitis both anti-fungal therapy and aggressive cerebrospinal fluid pressure management are required.

Antifungal agents (Amphotericin B or Fluconazole) are given into the following phases:

- Induction (2 weeks)
- Consolidation (10 Weeks)
- Maintenance (1 Year)

- **Cryptococcal Infection Screening**

Algorithm 5: Screening of Cryptococcal Infection



- *:For children the dosage will be based on medical Judgment of the patient's response to therapy, and not exceed 600mg/day in some older children.
- Avoid combination of Fluco with NVP: use EFV
- Do not use Fluconazole in the first trimester of pregnancy
- Rifampicine decreases Fluco concentration: increase Fluco from 800 to maxim dose (1200 mg) and double dosing if maintenance.

1.8. Diagnosis and Management of Other OIs

CD: 200-500/mm^3		
Pneumococcal and other bacterial pneumonia		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
Symptoms: - Fever and Productive cough of acute onset, - Pleuritic chest pain, - Malaise, - Chills and dyspnea **Clinical findings:** - Fever, - Signs of consolidation on the diseased side or simply crackles, - Low blood pressure, - Tachypnea, sometimes leading to confusion or decreased level of consciousness in advances cases.	- CXR - Sputum M, C &S - Blood Culture The assessment of severity is important to decide about the right treatment. If the patient presents with 3 of severity signs, transfer to a facility with ventilation should be considered	O2 and rehydration Analgesics and antipyretics Antibiotics - First choice: Amoxycillin 500 mg tds po X 7days - Second choice: Amoxy-clavulinic acid po or IV or cefuroxime IV X 7 days. - If staphylococcus suspected : Cloxacillin 500mg quid po or IV X 7 days - If general condition is not good, consider IV drugs in first 2-3 days and then change to oral therapy.
Oral Hairy Leukoplakia		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
Signs: - White asymptomatic lesion with corrugated surface, - Very often on lateral surface of the tongue. **Diagnosis** : Biopsy	Clinical but sometimes biopsy	Indicated if pain: Acyclovir 800mg po 5x/day for 2 to 3 weeks ARV

Pulmonary TB		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
Symptoms - Cough for more than 2 weeks - Fever - Night sweating - Loss of weight - Poor appetite - Other Risk factors (HIV+, Smoker, Health worker, Diabetic, Malnourished) - Bacterial pneumonia not responding to ATB **Signs:** - Fever - LOW - Adenopathies - Signs of pneumonia, bronchopneumonia	**Imaging:** CXR **Lab:** - Sputum ZN stain - Hemogram (Anemia) - Low Na, High ESR)	2RHZE(7)4RH(7)
Kaposi's Sarcoma		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
Signs: - Hyper pigmented nodules, - Purpurish or erythematous plaques sometimes progressing to ulcerative lesions on the face, trunk, limbs, or oral cavity. - They are usually asymptomatic-neither painful nor pruritic. - Lymphadenopathy, - Respiratory,GIT,pericardial or ocular symptoms	Clinical diagnosis,may need histology by biopsies	- ARV - Bleomycine alone or associated with Vincristine

Herpes Zoster (Zona)		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
- Lesions are vesicles, painful and involve several dermatomes, - Lesions can take a long time to heal when they become necrotic. - They can show secondary infection and deep scarring. - Zoster Ophthalmic is when the ophthalmic branch of the trigeminal nerve is often involved and cause corneal scarring with loss of vision in that eye.	**Diagnosis:** - Based on clinical symptoms and signs. - A Tzanck test show multinucleated giant cells with inclusion bodies which are pathognomonic.	- Acyclovir 10mg /kg IV every 8 hours; for7-14 days (For encephalitis: 21d) Or - Acyclovir 800mg PO 5 times daily for 7 days +Systemic antibiotics + Analgesics for pain and fever +NSAID or Carbamazepine 200-600mg daily or Amitriptyline 25-75 mg (effective in controlling post – zoster neuralgias)
CD4: <200/mm^3		
Miliary TB		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
Fever, night sweats, weakness, weight loss, cough sometimes and dyspnea, hepatomegaly, splenomegaly, lymphadenopathy, choroidal tubercules on eye examination.	CXR: Miliary pattern. Lab: Sputum ZN staining is negative in 80% Anemia, leucopenia, DIC.	2 RHZE7 4RH7.

CD4: <200/mm^3		
Pneumocystis Jirovecii Pneumonia		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
Symptoms: - Sub-acute onset of shortness of breath. - Dry cough - Fever, fatigue, chest pain - HIV + not on Cotrimoxazole prophylaxis yet with low CD 4 Count **Clinical Findings:** - Fever, - Tachypnea, - Tachycardia, - Normal chest exam in 50%, rales/ rhonchi, - Cyanosis.	- Hypoxia (Low saturation on walking - Elevated LDH: Sensitive but not specific. - CXR: Usually a diffuse, bilateral interstitial pattern, pneumothorax - CXR normal in early disease in up to 10 to 20%. - Sputum induction and staining	- Oxygenation - Rehydration - IV Trimethoprim 15-20 mg/kg/day + sulfamethoxazole 75-100 mg/kg/day for 21 days in 3-4 divided doses. Alternative for non-complicated cases is 2 DS (960 mg) 3 x /day for 21 days. - Any patient with hypoxia (pa O2 <70mm Hg or a A-a gradient >35 mmHg) should receive prednisone p o as per following regimen:D1-5 40mg BD p o; D6-10 40 mg OD p o;D11-21 20 mg OD p o . - In case of allergy to cotrimoxazole, the other options are either - Trimethoprim 15mg /kg /day P.O + Dapsone 100 mg/day for 21 days or - Clindamycin 600-900mg qid X 21 days P.O + Primaquine 15-30mg OD P.O. - Then secondary prophylaxis

Progressive Multifocal Leukoencephalopathy (PML)		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
- Cognitive disorder ranges from mild impairment of concentration to dementia. Insidious onset. - Focal neurological deficit seizures, loss of sensation. - Fever and headache are rare.	CT scan but MRI is the best imaging modality to exclude other pathologies - CSF: elevated protein	No prophylaxis or curative Rx available ARV Therapy remains the only hope for patients.
Lymphomas(NHL)		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
NHL B Cell Types Stage 4 disease with B symptoms Weight loss,Fever,hepatic dysfunction,marrow failure,lung disease and effusion,CNS signs.	Biopsy	Chemotherapy: CHOP Cyclophosphamide, Doxorubicin, Vincristine, Prednisone.
CD4: <100/mm^3		
Cryptococcosis		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
Symptoms: - Insidious onset of fever, - Malaise - Headache with / without vomiting **Clinical Findings:** - Features of AIDS - Neck stiffness - Behavioral changes - Confusion and sometime seizures	CT Scan Brain Lumber puncture and India Ink staining, Cryptococcal Ag testing	- Amphotericin B 0.7-1 mg/ kg/day, slow IV infusion x 2 weeks followed by - Fluconazole (Consolidation and Maintenance Phases). - Repetitive lumbar punctures to decrease ICP. - Antiepileptic if seizures. - Management of Coma if comatose.

Toxoplasmosis		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
- Focal neurological signs (hemiparesis/hemiplegia) - Cognitive dysfunction - Seizures - Headache and Fever - Symptoms of diffuse encephalopathy - Meningeal irritation is less frequent - Sometimes signs of raised ICP (papilledema/ vomiting).	**LP:** - CSF may be normal or nonspecific (Mild mononuclear pleocytosis and mild to moderately elevated protein). - Toxoplasma antibody absence has a high negative predictive value of 94-97%. - CT Scan Brain	- Pyrimethamine 200mg loading dose, then 50mg OD po+ Sulfadiazine 1-1.5g qid PO.+ Folinic acid 10mg OD.X 6-8 weeks - Cotrimoxazole 2 tabs(480mg) PO 3x/day or 5 tabs 2x/day PO for 6 weeks - Clindamycin 600mg qid PO +Pyrimethamine 200 mg loading then 50mg OD PO +Folinic acid 10mg OD (in case of allergy to sulfa). - Prednisone 40mg qid or Dexamethasone IV 4 mg qid in case of raised intracranial pressure. - Antiepileptic in case of seizure: Phenytoin 300 mg OD - Secondary prophylaxis with cotrimoxazole.
Candida Esophagitis		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
Diffuse retrosternal pain, dysphagia, odynophagia, thrush.	**Clinical:** Oral thrush and retrosternal chest pain.	Fluconazole 200 mg OD PO for 2-3 weeks

CD4: <50/mm^3		
Disseminated CMV		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
- Retinitis/esophagitis, - Colitis/encephalitis, - Polyradiculo myelopathy, - Dementia/pneumonitis.	Fundoscopy/biopsy/CSF/ BAL fluid	Ganciclovir 5mg/kg IV BD for 3-4 weeks
Disseminated *M. Avium* Complex		
Symptoms & Signs	**Diagnostic Test(s)**	**Treatment**
- Fever, - Night sweats, - Weight loss, - Diarrhea, - Abdominal pain	- Culture from non-pulmonary sterile site, - AFB blood culture - Biopsy from liver, bone marrow or lymph node	- Clarithromycin 500mg bid po + Ethambutol 15 mg/kg/day - ARV simultaneously or in 1-2 weeks

Chapter II: Monitoring of Patient (Pre and On-ART)

2.1. Introduction

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

Note that once started, ART is a treatment for life but should be changed in the following cases:

- Drug toxicity or severe side effect
- Drug interaction
- Co-infection
- Treatment failure confirmed by viral load

2.2. Recommendations on Monitoring of Adult Patients

Monitoring of Patient on PreART and on ART			
Date	Laboratory	Clinical	Psychosocial
PreART			
Baseline	CD4, HBsAg, HCV Ab, CRAG if CD4<200/ml	TB and STI Screening	+
M3	None	TB and STI Screening	+
M6	CD4	TB and STI Screening	+
ART Initiation	CD4, ALT, Creatinine (Clearance)	TB and STI Screening	+
On ART			
M1	Creatinine (Clearance) if TDF	+	+
M2	None	+	+
M3	Creatinine (Clearance) if TDF	+	+
M4	None	+	+
M5	None	+	+
M6	VL, Creatinine (Clearance) if TDF	+	+
M12	CD4	+	+

Note:

(1) VL shall be done at M6 after ART initiation thereafter every 12 months

In case of treatment failure, VL will be done 3 months after adherence intervention

(2) CD4 will be controlled every 6 M in pre ART and every 12 M after ART initiation

(3) After the first year adherence shall be assessed every 3 months in patients demonstrating excellent adherence for the first year

(3) After the first year, pharmacy refill shall be done every 3 months (not monthly) coinciding with clinical and adherence assessment

1) FBC, ALAT and amylase will be done if clinically indicated

Genotyping is recommended for patients failing second line or some special cases failing first line before ART switching.

2.3. Management of Most Common Side Effects

Molecule	Major Type of Toxicity	Suggested Management
TDF	- Tubular renal dysfunction - Fanconi syndrome - Decreases in bone mineral Density - Lactic acidosis or severe hepatomegaly with steatosis	- If TDF is being used in first-line ART, substitute with AZT or ABC - If TDF is being used in second-line ART (after d4T + AZT use in first line - ART), substitute with ABC or DDI - Use alternative drug for hepatitis B treatment (such as entecavir) to avoid Hepatic flares if TDF is replaced due to toxicity
ABC	-Hypersensitivity reaction -Gastrointestinal intolerance	- If ABC is being used in first-line ART, substitute with TDF or AZT - If ABC is being used in second line ART, substitute with TDF
AZT	- Anemia, neutropenia, Myopathy, - Lipoatrophy or lipodystrophy - Lactic acidosis - Severe hepatomegaly with steatosis	- If AZT is being used in first-line ART, substitute with TDF or ABC - If AZT is being used in second-line ART, discuss another alternative
NVP	- Hepatotoxicity - Severe skin rash and hypersensitivity reaction (Stevens-Johnson syndrome)	Substitute with EFV. If the person cannot tolerate either NNRTI, use boosted PIs

Molecule	Major Type of Toxicity	Suggested Management
EFV	- Persistent central nervous system toxicity (such as abnormal dreams, depression or mental confusion, Convulsions) - Hepatotoxicity - Hypersensitivity reaction, Stevens-Johnson syndrome - Potential risk of neural tube birth defects (very low risk in humans) - Male gynecomastia	Substitute with NVP (Be careful if high CD4). If the person cannot tolerate either NNRTI, use boosted PIs
ETV	- Severe skin and hypersensitivity reactions	Limited options are available Seek consult with expert advice
RAL	Rhabdomyolysis, myopathy, myalgia	Limited options are available Seek consult with expert advice
ATV/r	- Indirect hyperbilirubinemia (clinical jaundice, although not pathologic just cosmetic) - Nephrolithiasis and risk of prematurity	LPV/r or DRV/r. If boosted PIs are contraindicated and NNRTIs have failed in first-line ART, consider integrase inhibitors
DRV/r	- Hepatotoxicity - Severe skin and hypersensitivity reactions	- If DRV/r is being used in second line ART, substituting with ATV/r or LPV/r can be considered. When it is used in third-line ART, limited options are available - Seek consult with expert advice

Molecule	Major Type of Toxicity	Suggested Management
LPV/r	- Electrocardiographic abnormalities (PR and QT interval prolongation, torsades de pointes) - Hepatotoxicity - Pancreatitis, lipoatrophy or metabolic syndrome, dyslipidemia or severe diarrhea - Risk of prematurity	- If LPV/r is used in first-line ART for children, use an age-appropriate NNRTI (NVP for children younger than 3 years and EFV for children 3 years and older). - ATV can be used for children older than 6 years - If LPV/r is used in second-line ART for adults, use ATV/r or DRV/r. - If boosted PIs are contraindicated and the person has failed on treatment with NNRTI in first-line ART, consider integrase inhibitors Seek consult with expert advice
Cotrimoxazole	- Anemia - GI Intolerance (Nausea, vomiting, etc.) - Hepatotoxicity - Skin Rash	Dapsone

2.4. Evaluation of Dermatological Toxicity

Grade 1	Grade 2	Grade 3*	Grade 4
Erythema, pruritis	Widespread maculopapular eruptions of dry desquamation	Appearance of blisters or humid desquamation or ulceration or association with fever or pain	Appearance of the following signs: affecting the mucosa, Stevens Johnson syndrome, Erythema multiforme, necrosis, or exfoliative dermatitis.

2.5. Evaluation of Hepatotoxicity

	Normal	Grade 1	Grade 2	Grade 3*	Grade 4
ALAT(SGPT) (UI/l)	< 40	50-100	100-200	200-400	>400

*Note that the suspected molecule will be stopped only if the toxicity is ≥ Grade 3

2.6. Creatinine Clearance Calculation

If Creatinine machine reports in mg/dL:

$$\frac{(140\text{-age}) \times \text{weight (kg) (weight at present)}}{72 \times \text{creatinine (mg/dL)}} \times 0.85 \text{ for a woman}$$

or

If Creatinine machine reports in µmol/L:

$$\frac{(140\text{-age}) \times \text{weight (kg)}}{0.81 \times \text{creatinine (µmol/L)}} \times 0.85 \text{ for a woman}$$

Interpretation of Renal Creatinine Clearance

≥ 90 ml/min. = Normal

60-89 mL/min = Mild Renal insuffisancy

30-59 ml/min = Moderate Renal insuffisancy

≤ 29 mL/min = Severe Renal insuffisancy

Note:

- If clearance > 50 mL/min, OK for TDF; if clearance < 50 mL/min, give ABC
- If decrease in creatinine clearance ≥ 15%, consider possible TDF toxicity and switch to ABC.

Important Notice

- In Case Drug Toxicity, change only the suspected molecule not all drugs
- NNRTIs remain in blood for a very long period after stopping the drug. It is advised that after stopping EFV or NVP the patient should continue with their 2–NRTI based regimen (e.g. TDF + 3TC) for 7 days after stopping the NNRTIs to avoid likelihood of resistance.

Chapter III: Management of Treatment Failure

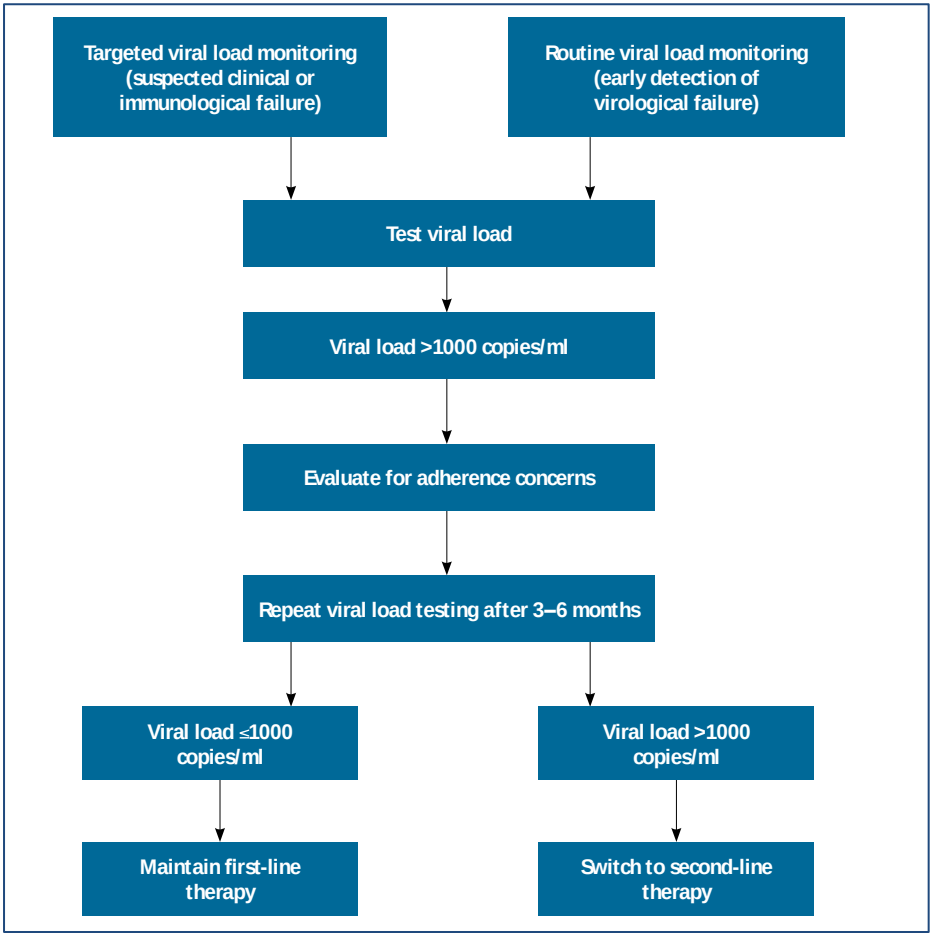
3.1. Identification of Treatment Failure

Monitoring individuals receiving ART is important to ensure successful treatment, identify adherence problems and determine whether and which ART regimens should be switched in case of treatment failure.

The treatment failure is defined by the virological failure (plasma viral load above 1000 copies/ ml) based on two consecutive viral load measurements after 3 months with adherence support.

A poor immune reconstitution despite a good virological control is frequent during the first year of HAART. This condition seems mainly driven by the age and the low baseline CD4 count of the patients.

Algorithm 6: Treatment Failure and Viral Load Testing Strategies



(WHO ART Guidelines 2013)

NB: VL is the gold standard for defining the treatment failure but when not available, the CD4 and Clinical status may be used to decide.

3.2. Recommended Regimens for Second-line ART

First-line Regimens	Second-line Regimens
TDF+3TC + EFV/NVP	AZT+3TC+ATV/r or LPV/r *
ABC+ 3TC+EFV/NVP	AZT+3TC+ATV/r or LPV/r *
AZT+ 3TC+EFV/NVP	TDF+ 3TC+ATV/r or LPV/r *

* In case of Hepatitis B co-infection, maintain TDF: AZT + TDF + 3TC + ATV/r or LPV/r

Dosing of Second Line Drugs

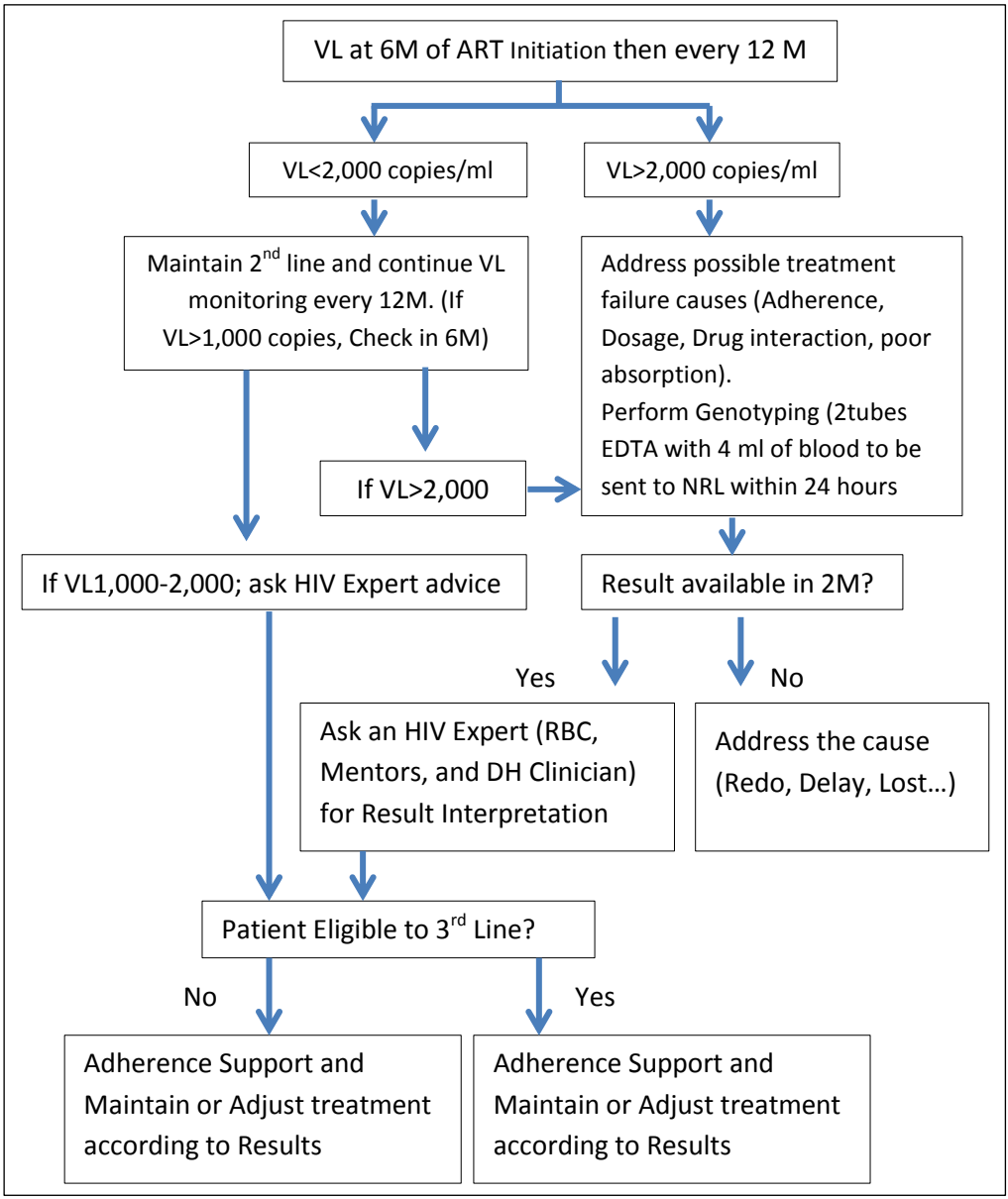
Molecule	Dosage
ATV/r 300 mg /100 mg (FDC)	300/100 mg orally once a day
LPV/r 200mg/50 mg (FDC)	400/100 mg twice a day

For TDF, ABC, AZT refers to the dosing table for the first line regimen
NB: The pill burden for Lop/rit regimen is 2 pills twice a day compared to ATV which is one pill once per day (Both in combination with NRTIs.

3.3. Recommended Regimens for Third-line ART

Any patient on the second-line with VL > 2,000 copies/ml based on two consecutive viral load measurements after 3 months with adherence support is eligible for third-line ART. Identification of treatment failure to the second-line follows the following algorithm.

Algorithm 7: Genotyping and Third Line Initiation



NB:
- Third line doses: Refer to Section below (Dose tables)
- Patients on 3rd line should receive nutrition supplement (at least 400 kcal e.g. 500 ml of porridge per dose)
- Consider 2,000 Copies/ml as Genotyping Threshold and 1,000 Copies as Treatment Failure Threshold

In Rwanda, the 3rd line regimen combination is: RAL/ETV/DRV/r*

- The 3rd line regimen must only be given upon expert consultation and usually with the assistance of genotyping test.
- Before prescribing third-line therapy, the patient MUST undergo extensive additional adherence counseling and should have a treatment partner involved with assisting in adherence.
- Third-line regimens will only be prescribed at specialized centers with trained providers.
- Third line combination can be adjusted based on Genotyping results and upon HIV Expert view
- NRTI backbone may be necessary based on genotyping test or in case of Hepatitis B co-infection

Dosing of Third Line Drugs

Molecule	Dosage
Raltegravir	400 mg twice a day
Ritonavir	100 mg twice a day
Darunavir	600 mg twice a day
Etravirine	200 mg twice a day

Chapter IV. Antiretroviral Treatment in Children

4.1. Initial Evaluation of HIV-infected Children

4.1.1. Clinical Evaluation

- Comprehensive physical examination
- WHO HIV staging in children
- Growth assessment and malnutrition screening
- Neurodevelopment and intellectual assessment
- Drug history for the child and mother

4.1.2. Laboratory Evaluation

- Baseline:
  - CD4% preferred if < 5years old
  - Hepatitis B surface antigen,
  - Hepatitis C antibody,
  - Cryptococcus antigen (if CD4 count < 200cells/mm3) < 5years old consider CD4<20%.
- Additional studies as clinically indicated

Creatinine clearance in children in developing countries (except infants) is calculated using the following formula :

eGFR = 0.42 9 * (Ht in cm /scr in mg/dl)

ht = height in cm,
scr = serum creatinine in mg/dl
or if using umlo/l **:**

e GFR= 40 X ht(cm)/serum creatinine(umol/l)

4.2. Eligibility Criteria for ART Initiation

Any child with confirmed HIV-positive status is eligible for ART if the child has one of the following criteria:

- Any child aged less than 5 years regardless CD4 and WHO Stage
- Any child aged more than 5 years with one of the following criteria:
    - WHO Stage 3 and 4
    - WHO Stage 1, 2 and CD4 < 500/mm^3
    - HIV-TB co-infection
    - HIV-Hepatitis B co-infection
    - HIV-Hepatitis C co-infection

4.3. Initial Biological Assessment before Initiation of ART

Area	**Biological Test**
OIs	Cryptococcus antigen if CD4 < 200 cells/mm3
Liver Function	ALAT*, ASAT*
Renal Function	Creatinine and calculation of creatinine clearance
Viral Hepatitis	HBs Ag; HCV Ab
Immunology	CD4 Cells count

4.4. First-line ART Regimens in Children and Adolescents

In children the ARV regimen depends on the age of the child:

	Children < 3 years	**Children 3 to 10 years and adolescents <35 kg**	**Adolescents (10-19 years) > 35 kg**
Preferred	ABC+ 3TC+ LPV/r	ABC+3TC+ EFV	TDF + 3TC + EFV
Alternatives	a) ABC + 3TC + NVP b) AZT + 3TC + LPV/r c) AZT + 3TC + NVP	ABC + 3TC + NVP AZT + 3TC + EFV or NVP HBV co-infection: TDF + 3TC + EFV or NVP***	1) TDF + 3TC + NVP 2) ABC + 3TC + EFV or NVP

Note:

- In Hepatitis B co-infection, TDF may be considered in children older than 2 years
- By 3 years of age, a child should be switched from LPV/r to EFV based regimen if the VL is suppressed
- These recommendations apply to children and adolescents who are initiating first-line ART
- Adolescents >35kg who are already taking ABC-containing regimens can safely substitute TDF for ABC.
- Adolescents >35kg should be given once-daily dosing when possible to maximize adherence (e.g. ABC 600mg + 3TC 300mg)

4.5. HIV-TB Co-infection Management in Children

4.5.1. Screening of TB-HIV Co-infection in Children

All HIV positive children should be screened for active TB infection at enrollment and regularly at each encounter with a health worker or visit to a health facility. Children having the following symptoms should be evaluated for TB (refer to TB Screening Algorithm above).

4.5.2. Isoniazid Preventive Therapy (IPT) in Children

Children living with HIV who are unlikely to have active TB on symptom-based screening and have known contact with a TB case should receive six months of IPT (10 mg/kg/day).

4.5.3. Diagnosis of TB-HIV Co-infection in Children

The following examinations are used to diagnose active TB infection:

- Sputum if child is able to produce sputum sample, induced sputum if available, or gastric aspirate if child unable to provide sputum sample (typically younger than 5-10 years old)
- AFB Microscopy with Ziehl Nelson stain and culture, if available
- GeneXpert (based on availability).
- Tuberculin skin test: A negative TST does not exclude TB disease. It may be negative despite the child having TB, especially in severe disseminated TB, malnutrition and HIV disease
- Chest X-ray

Note: Children suspected of having extra-pulmonary TB should be managed at a referral center. Fine needle aspiration (FNA) or a lymph node biopsy may be performed if a lymph node is suspicious for tuberculosis.

4.5.4. Co-Treatment TB and HIV Co-infections in Children

- All HIV-positive children with confirmed TB co-infection are eligible for ART regardless of CD4 count and clinical stage
- ART should be started in any child with active TB disease as soon as possible and within eight weeks following the initiation of anti-TB treatment irrespective of the CD4 count and clinical stage
- For TB treatment in children refer to the Rwanda Childhood Tuberculosis National Guidelines

Table 7: HIV and TB Co-Treatment in Children

Current ART	**ART Adjustment with Anti-TB Therapy**	
	Children < 3 Years Old	**Children > 3 Years Old**
ABC/AZT+ 3TC + EFV	EFV currently not recommended under 3 years*	No change
ABC/AZT+ 3TC + NVP	Increase NVP by 30%* Or switch to EFV if > 3.5kg	Substitute NVP with EFV
ABC/AZT+ 3TC+LPV/r	Replace Rifampicin by Rifabutin Or switch to EFV if > 3.5kg and VL suppression	Substitute LPV/r with EFV (if no history of failure on NNRTI-based regimen)
	Alternative: Substitute LPV/r with NVP for < 3.5 kg	Increase Ritonavir dose for 1:1 ration Lop/Rit Alternative: ABC + 3TC + AZT (not a strong combination)

Note:

1) EFV may be used in children > 3.5 Kg
2) If NVP dosing increased, ALAT shall be done at 2 weeks, 1 month, 3 and 6 months
3) EFV shall be increased by 30% in children with EFV dosing less than 600 mg /day

(Refer to the pediatric dosing table)

4.6. Management of Opportunistic Infections in Children

Oral Thrush: Candida albicans	
First Line Treatment	**Comments/ Side Effects**
Nystatin 100,000-200,000 iu gargled or delivered to the cheeks in children 4-5 x day for 14 days	- Nausea, - Vomiting, - Diarrhea, - Abdominal pain - Hepatotoxicity, - Agranulocytosis, - Seizures, - Nausea, - Vomiting
1% aqueous solution of gentian violet, local application 2 x daily x 7 days	
Fluconazole - oral 6mg/kg stat day 1 then 3mg/kg/day for 14 days	With Fluconazole, hepatotoxicity, nausea, vomiting, abdominal pain, pancytopaenia can occur
Esophagitis: Candida albicans	
Fluconazole - oral 6mg/kg stat day 1 then 3mg/kg/day for 14-21 days	With fluconazole, hepatotoxicity, nausea, vomiting abdominal pain, pancytopaenia may occur
Ketoconazole 3.3-6.6mg/kg/day x 14-21 days	Avoid use of Ketoconazole with NVP

Oral Herpes: Herpes simplex virus 1 and 2	
If severe: I.V Acyclovir 5mg/kg/dose TID or orally 40-80mg/kg/day TID for 5-10 days. Topical antiseptics to avoid secondary bacterial infections. Analgesics.	Nausea, vomiting, diarrhea, headache, malaise, rash, seizures, renal dysfunction
Pneumocystis Pneumonia (PCP): Pneumocystis jirovecii (carinii)	
Acute: Trimethoprim (TMP) 20mg/kg/day PO or iv x 21 days (3-4 divided doses) Or Dapsone 2mg/kg daily max. 100mg/ day x 21 days Or Pentamidine 4mg/kg/day iv x 21 days; Or Clindamycin 10-30mg/kg/day i.v. tid x 14-21 days **For severe disease:** PO2 <90mmHg: add Prednisolone 2mg/kg/day x 7-14 days Prophylaxis: CTX 6-8mg/kg/day PO daily	Complications of drug treatment: - Severe reactions, - Stevens-Johnson syndrome, - Toxic epidermal necrolysis, - Anemia, - Hepatitis, - Hemolysis in G6PD deficient patients
Lymphoid interstitial pneumonitis (LIP): Epstein Barr Virus	
If severe : - Steroids (prednisolone 2mg/kg/day x 6 weeks, taper off) - Oxygen - Bronchodilators (salbutamol) - Chest physiotherapy - Referral to specialist (pediatric specialist)	Complications of therapy with prednisolone include: - Hypertension, - Gastritis, - Adrenal insufficiency, - Seizures, - Pseudo tumor cerebri, - Hypokalemia, - Fluid retention, - Glucose intolerance and possible acute infections

CNS Herpes	
First Line Treatment	**Comments/ Side Effects**
IV Acyclovir 20mg/kg TID x 21days	
Herpes zoster (Shingles, Zona): Varicella zoster	
IV Acyclovir 30mg/kg/day tds x 7 days Analgesics – NSAIDS, carbamazepine, amitriptyline Local application of calamine lotion; Topical application of Acyclovir cream	Refer intractable cases for specialist care.
Toxoplasmosis: Toxoplasma gondii	
- Pyrimethamine 2mg/kg/dose/day max 50mg x 2 days - Maintenance 1mg/kg/day max 25mg + Sulphadiazine 50mg/kg/every 12 hours - Then treat 4 weeks after symptoms Pyrimethamine + Folinic acid 5-20 mg 3x/wk + Clindamycin 10-30mg/kg/day tds x 6 wks Corticosteroids to reduce edema/mass effect. **Prophylaxis:** CTZ	Complications of drug treatment - Megaloblastic anemia, pancytopenia, rash, Stevens Johnson Syndrome, nausea, vomiting, abdominal pain, photosensitivity Folinic acid 5-20 mg should be given to prevent deficiency
Cryptococcal Meningitis: Cryptococcus neoformans	
Induction : Amphotericin B 1mg/kg/day x 2 wks Plus Flucytosine orally 100mg/kg/day for 14 days followed by fluconazole (10–12 mg/kg per day orally) for 8 weeks. **Maintenance :** Fluconazole 6mg/kg/day oral Discontinuation of maintenance therapy in children receiving HAART is poorly studied and must be individualized	Refer to infectious disease specialist

4.7. Management of Treatment Failure in Children

4.7.1. Introduction

The monitoring of ART response and identification of treatment failure are the same as for adults except the following specifics to children:

NB:
Clinical follow up and pharmacy refill shall be done every month in children less than 10 years and every 3 months in stable and adherent children more than 10 years old or in boarding school.

Identification of treatment failure to the second-line follows the same algorithm as for failure to the second-line in adults (See algorithm above)
The treatment failure is defined by the virological failure (plasma viral load above 1000 copies/ ml) based on two consecutive viral load measurements after 3 months with adherence support.

4.7.2. Second-line ART in Children and Adolescents

First-line Regimen	Preferred Second-line Regimen	Alternative Second-line Regimen
Children < 3 years		
ABC + 3TC + LPV/r	AZT+ 3TC + LPV/r	AZT + 3TC + NVP
ABC + 3TC + NVP	AZT+ 3TC + LPV/r	
AZT + 3TC + LPV/r	ABC + 3TC + LPV/r	ABC + 3TC + NVP
AZT + 3TC + NVP	ABC + 3TC + LPV/r	
Children 3 YO to 10 YO and Adolescents <35 kg		
ABC + 3TC + EFV/NVP	AZT + 3TC + ATV/r if > 6 YO	AZT+ 3TC + LPV/r if children less than 6 years
AZT + 3TC + EFV/NVP	ABC + 3TC + ATV/r if > 6 YO	ABC+3TC+ LPV/r if children less than 6 years
Children >10 YO and Adolescents >35 kg		
TDF/ABC+ 3TC + EFV/NVP	AZT + 3TC + ATV/r	AZT + 3TC + LPV/r
AZT + 3TC + EFV/NVP	TDF + 3TC + ATV/r	ABC + 3TC + ATV/r or LPV/r

NB:

1) Keep TDF in second line if HBV infection
2) ATV cannot be co-administered with rifampicin, use Rifabutin
3) ATV boosted with RTV (ATV/r) is preferred for children aged at least 6 years and adolescents (see dosing below)

Dosing of Second-line Drugs in Children

- ABC/TDF/3TC and LPV/r refer to the first line regimen dosing (Pediatric dosing)
- ATV capsules: 100 mg, 150 mg, 200 mg, and 300 mg

Weight (kg)	Once-Daily Dose
15–<20 kg	ATV 150 mg + RTV 100 mg, both once daily with food
20–<32 kg	ATV 200 mg + RTV 100 mg, both once daily with food
32–<40 kg	ATV 250 mg* + RTV 100 mg, both once daily with food
≥40 kg	ATV 300 mg + RTV 100 mg, both once daily with food

Note:
*FDC is preferred
*Dose requires two different capsule strengths of ATV

4.7.3. Regimens for Third-line ART in Children and Adolescents

	NNRTIs	PIs	IIs
1	**Etravirine (ETV)**	**Darunavir (DRV/r)**	**Raltegravir (RAL)**
In some cases, TDF and 3TC should be associated			

Note:
1) Third line is given by Expert only
2) Genotyping & VL are required before switching to third line.
3) In some case, switching to second line may require genotyping (clinical decisions in case of poor adherence suspicion)

PART III: STIs PREVENTION AND TREATMENT

Chapter I: Generalities on Sexually Transmitted Infections

1.1. Introduction

Sexually transmitted Infections (STIs) are a major public health concern and constitute a high risk of HIV transmission.
Therefore, they should be timely and efficiently prevented, diagnosed and treated.

1.2. Principles Guiding STIs Prevention and Treatment

The policy in the area of the care of STIs is based on the following principles:

- The integration of STI control activities in the minimum activity package of health services ;
- Advocacy and mobilization of resources ;
- Implementation of multi-sector participation;
- Mobilization of the community and specific groups;
- To avoid stigmatization.

1.3. Strategies

The prevention and the control of STIs are based especially on five major strategies:

- Education and counselling of high risk persons on changing their sexual behaviour;
- The identification of infected persons with clinical signs (symptomatic) or without clinical signs (asymptomatic) that should consult services in charge of diagnosing and the treatment of STI;

- Efficient and early diagnosis and treatment of persons infected by STIs;
- Evaluation, treatment, and counselling of partners of persons infected by STIs;
- Vaccination of persons with high risk to STI.

1.4. Major Components of STIs Complete Care

Complete care of STIs includes:

1) IEC/BCC (focus on risk factors, STIs and HIV relationship)
2) Systematic screening of syphilis in pregnant women
3) Systematic screening of STIs for newborn, adolescents and adults
4) Screening and systematic treatment of FSW and MSM
5) Carry out the correct diagnosis;
6) Provide correct antimicrobial treatment corresponding to the syndrome of STI, corresponding to the clinical diagnostic of STI or corresponding to the micro-organism of the STI;
7) Explain the adherence of the treatment;
8) Demonstrate the correct condom use and to make them available and accessible;
9) Provide counselling on the treatment of partners and to give the patient an orientation form for the sexual partner so that he/she can send it to his/her partner (s);
10) Systematic HTC.

Chapter II: Prevention of Sexually Transmitted Infections

2.1. Primary Prevention: Reduction of the Risk of Infection

- Reduction of the number of partners
- Low risk sexual practices
- Consistent and correct use of condoms
- Counseling for MC

2.2. Secondary Prevention of STIs

This is the prevention of STIs complications and constitutes primary prevention of HIV infection

- Promotion of the attitude to seek treatment
- Provision of quality care services
- Offer of support and counseling services

Chapter III: Management of Sexually Transmitted Infections

In Rwanda, the management of STIs uses two approaches implemented at different levels:

- Syndromic approach (recommended at all Health Centers and District Hospitals)
- Etiologic approach (recommended at Referral and provincial hospitals and some district hospitals which have lab capability)

3.1. Syndromic Management of STIs

3.1.1. Definition

The syndrome approach is based on the identification and treatment of a set of symptoms and signs called "syndrome", which is easy to recognize basing on the information and symptoms observed during the history and physical examination.

3.1.2. Different STI Syndromes

These syndromes, which may be caused by one or several STI germs, are the following:

1. Urethral discharge in men;
2. Vaginal discharge;
3. Genital ulceration;
4. Inguinal bubo;
5. Painful swelling of the scrotum;
6. Pelvic pain in women;
7. Venereal vegetation or growth (Condyloma);
8. Purulent conjunctivitis of the new born baby.

The syndrome approach enables one to carry out rapid presumptive diagnosis and to administer immediate treatment beginning with the first consultation. It enables the client to receive treatment without delay and increases the chances of healing.

Below is the summary of syndromic management of STIs and we recommend you refer to STIs Provider manual and specific algorithms (see on annexes different STI algorithms) for more detailed information on STIs management approach.

3.2. Etiologic Diagnosis and Management of STIs

3.2.1. Definition

The etiological approach uses laboratory tests with the support of information obtained from the interview and physical examination. It constitutes an ideal strategy in the care of STI but it requires adequate laboratory and highly qualified personnel.

Table 8: STIs Syndromes and Signs and Management

Syndrome	Symptom	Signs	Frequent Causes	Treatment
Urethral discharge in men	▪ Urethral discharge ▪ Dysuria ▪ Frequent urination	▪ Urethral discharge (if necessary, ask the patient to empty his/her glans)	▪ Gonococcus ▪ Chlamydia	**1st Choice:** ▪ Ciprofloxacine, tab, 500mg SD ▪ Doxycycline, tab 100mg *2/d/7d **2nd Choice:** ▪ Ceftriaxone, 250 mg in IM single dose. ▪ Erythromycin, 1g x2/ d /7 days
Genital ulcerations	▪ Genital wound	▪ Genital ulceration ▪ Inguinal lymphadenopathy	▪ Syphilis ▪ Wet Chancre ▪ Genital herpes	**1st Choice:** ▪ Benzedrine penicillin 2.4 Million IU IM single dose unique. ▪ Ciprofloxacin 500 mg x2/day /3 days ▪ Acyclovir 400 mg x2/ day/5 days **2nd Choice:** ▪ Erythromycin 1 g x 2/ day/14 days in case of allergy to penicillin. ▪ Ceftriaxone, 250 mg in IM single dose. ▪ Acyclovir 400 mg x2/ day/5 days

Syndrome	Symptom	Signs	Frequent Causes	Treatment
Vaginal discharge	▪ Vaginal discharge ▪ Itching vulva ▪ Dysuria ▪ Dyspareunia	▪ Vaginal discharge (leukorrhea)	**Vaginitis :** Trichomonas ▪ Candida ▪ Bacterial vaginosis **Cervicitis:** ▪ Gonococcus ▪ Chlamydia	▪ Metronidazole or Tinidazole, 2 g in a SD **1st Choice:** ▪ Ciprofloxaine,tab,500mg SD ▪ Doxycycline ,tab 100mg *2/d/7d **2nd Choice:** ▪ Ceftriaxone, 250 mg in IM single dose. ▪ Erythromycin, 1g x2/ d /7 days

Syndrome	Symptom	Signs	Frequent Causes	Treatment
Pelvic pain in women	▪ Abdominal pain during sexual relations ▪ Dyspareunia	▪ Vaginal discharge ▪ Sensitivity of the lower abdomen to palpation Temperature > 38° (inconstant)	▪ Gonococcus ▪ Chlamydia ▪ Mixed Anaerobes	**1st Choice:** ▪ Ciprofloxacin,tab,1gr SD ▪ Doxycycline ,tab 100mg *2/d/21d ▪ Metronidazole, tab 1g*2/d/14days **2nd Choice:** ▪ Ceftriaxone, 250 mg in IM single dose. ▪ Erythromycin, 1g x2/ d /21 days ▪ Tinidazole, 1g x2/d/14days
Painful swelling of the scrotum	▪ Pain and swelling of the scrotum	▪ Swelling of the scrotum	▪ Gonococcus ▪ Chlamydia	**1st Choice:** ▪ Ciprofloxacin,tab,500mg SD ▪ Doxycycline ,tab 100mg *2/d/7d **2nd Choice:** ▪ Ceftriaxone, 250 mg in IM single dose. ▪ Erythromycin, 1g x2/ d /7 days

Syndrome	Symptom	Signs	Frequent Causes	Treatment
Inguinal bubo	▪ Inguinal Adenopathy	▪ Ganglion Tumefaction ▪ Fluctuation ▪ Abscess or fistulas	▪ Wet chancre ▪ Venereal Lympho-granulomatosis	**1st Choice:** ▪ Ciprofloxacin,tab,500mg SD ▪ Doxycycline ,tab 100mg *2/d/7d **2nd Choice:** ▪ Ceftriaxone, 250 mg in IM SD ▪ Erythromycin, 1g x2/ d /7 days
Purulent conjunctivitis of the newborn	▪ Swollen eyelids ▪ Baby cannot open its eyes ▪ Ocular discharge	▪ Eyelids oedema ▪ Purulent discharge	▪ Gonococcus ▪ Chlamydia	▪ Ceftriaxone, 50 mg per kg in IM single dose. ▪ Erythromycin, 50mg per kgx2/ d /7 days
Venereal vegetations (Condyloma)	▪ Genital/anal external growths	▪ Genito-anal external growths	▪ Papilloma virus	▪ Destruction of the condylomatous tissue by physical and clinical method (Use of podophylline cream, liquid nitrogen, silver nitrate crayon, curettage followed by the application of iodine dye).

Table 9: STIs Etiologies and Management

Symptoms and Signs	Etiologies	Laboratory Tests	Disease	Treatment
Bacterial Infections				
- Urethral discharge; - Cervicitis and lower abdominal pain in women; - Conjunctivitis of the new born may be asymptomatic	Neisseria Gonorrhea	Specimen types are: Urethral, Urine, Cervical, Vaginal, Rectal, Oropharyngeal, Conjunctiva, Sterile body fluids. - Direct microscopic examination after gram staining , - Culture and PCR are the diagnostic tools for gonococcus infection - The collection of the discharge must be done at the level of the urethra in men and at the level of the cervix in women.	Gonorrhea	**1st Choice:** ▪ Ciprofloxacin, 1gr SD **2nd Choice:** ▪ Ceftriaxone, 250 mg in IM single dose.

Symptoms and Signs	Etiologies	Laboratory Tests	Disease	Treatment
- Urethral discharge; - Cervicitis and lower abdominal pain in women; - Conjunctivitis of the new born may be asymptomatic	Chlamydia trachomatis	Direct cytological examination to look for intracytoplasmic inclusions, culture, antigen detection and PCR	Infection due to Chlamydia	**1st Choice:** ▪ Doxycycline, 100 mg x 2 day 7 days during meals **2nd Choice:** ▪ Erythromycin, 1g x2 day /7 days
- Ano-genital ulcers (chancre); - Inguinal tumefaction; - Generalized itching.	Treponema pallidum	Microscopic examination on a dark background is used in primary and secondary syphilis. At later stages, nontreponemal VDRL and RPR are the commonly used tests, but they require confirmation with more specific treponemal tests such as FTA-ABS and TPHA	Syphilis	**1st Choice:** ▪ Benzedrine penicillin 2.4 Million IU IM single dose unique. **2nd Choice:** ▪ Erythromycin 1 g x 2/ day/14 days in case of allergy to penicillin.

Symptoms and Signs	Etiologies	Laboratory Tests	Disease	Treatment
Genital ulcers with inguinal tumefaction(bubo) in most of the cases	Haemophilis ducreyi	Haemophilus ducreyi can be isolated by direct examination after gam stain or Toluidine or culture	Wet Chancre	**1st Choice:** ▪ Ciprofloxacin 500 mg x2/day /3 days **2nd Choice:** ▪ Ceftriaxone,250 mg in IM single dose ▪ Erythromycin, 1g x2/day /14 days in case of pregnancy
Viral Infections				
Vesicular lesions and ano-genital ulcerations	Herpes virus of the simplex type 2 (HSV-2)	The most common diagnostic tests are: Direct Fluorescence, Tzanck test to search for Herpes cytopathogenic effect, culture in cellular media and Western blot	Genital Herpes	▪ Acyclovir 400 mg x3/ day/5 days

Symptoms and Signs	Etiologies	Laboratory Tests	Disease	Treatment
Swollen ano-genital Condylomas; Cervical condylomas; cervix cancer in women.	Human papilloma Virus (HPV)	Clinical examination	Genital Condylomas	Consists in the destruction of the condylomatous tissue by physical and clinical method (Use of podophylline cream, liquid nitrogen, silver nitrate crayon, curettage followed by the application of iodine dye).
Others				
Asymptomatic; abundant mucous vaginal discharge	Trichomonas vaginalis	Trichomonas is diagnosed through direct specimen examination	Trichomonas	Metronidazole or Tinidazole, 2 g in a single dose If persistence of signs despite good observance, give: Metronidazole 500 mg x 2/ day /7 days or Tinidazole 500 mg x 2 day /5 days
Thick vaginal discharge; itching and vulvar burning	Candida albicans	Direct examination and culture are the most common methods for the diagnosis of Candida infection	Candida	Fluconazole gynae tab 150 mg in single dose

3.3. Special Cases

3.3.1. Female Sexual Workers (FSW)

Sex workers are vulnerable groups and core groups for the transmission of STI and HIV. Their care and treatment is a process that is both classic and specific. It is specific, given the profession of sex workers and the prevalence of STI/HIV in women. Consequently, active diagnosis of STI is highly recommended.

In practice, presumptive treatment of the commonest and the most morbid STI (risk of the Pelvic Inflammatory Syndrome, infertility) is recommended during the first visit in the absence of obvious clinical signs of STI. (See specific algorithm).

3.3.2. Men Who Have Sex with Men (MSM)

MSM, including those with HIV infection, should routinely undergo nonjudgmental STI/HIV risk assessment and client-centered prevention counseling to reduce the likelihood of acquiring or transmitting HIV or other STIs.

Healthcare providers should be informed about the local community resources available to assist MSM (Condom, lubricants, drugs, etc.).
Clinicians also should routinely ask MSM about symptoms consistent with common STIs, including urethral discharge, dysuria, genital and perianal ulcers, regional lymphadenopathy, skin rash, and anorectal symptoms consistent with proctitis, including discharge and pain on defecation or during anal intercourse.

Care providers should perform appropriate diagnostic testing on all symptomatic patients.

Routine laboratory screening for common STIs (HIV serology, syphilis serology, a test for urethral infection with *N. gonorrhoeae* and *C. trachomatis* in men who have had insertive anal intercourse, a test for rectal infections with *N. gonorrhoeae* and *C. trachomatis* in men who have had receptive anal intercourse, a test for pharyngeal infection with *N. gonorrhoeae* in men who have had receptive oral intercourse is indicated for all sexually active MSM.

3.3.3. Persons in Correctional Facilities

Screening for symptomatic and asymptomatic STIs in detention facilities and jails facilitates the identification and treatment of persons with infections. This will eliminate complications for the individual and will reduce the prevalence of STIs among detainees who are released back into the local community.

3.3.4. Management of Sexual Abuse and Aggression of Children

a. Definition

Sexual abuse occurs when a child is engaged in sexual activities that it may not understand for which its psychomotor development is not prepared and therefore the child cannot give its consent and/or these activities violate the law or the taboos of the society.

These sexual activities include any forms of sexual contacts: Sexual intercourse (oral, genital, ano-genital, genito-genital).

b. Initial Examination

- To collect data and information on the circumstances in which the sexual abuse occurred;
- To determine if possible, the time separating the aggression and the date of consultation ;
- To carry out meticulous physical examination in search of the signs of STI (genital discharges, ulcerations and genital vesicles, condylomas) ;
- To collect anal samples in the two sexes, vaginal swab in case of a young girl, and urethral samples in case of a boy in the view to search for gonococcus, Trichomonas vaginalis;
- To carry out serological tests for HIV, hepatitis B and syphilis;
- To carry out the pregnancy test in case of a young girl who has already started having menstruations.
- To search for clinical signs of STI and carry out serological tests for HIV, hepatitis B and syphilis of the aggressor or the suspected perpetrator of the aggression if he/she has been identified.

c. Suggestive Clinical Signs of Sexual Abuse

Major genital signs are: genital discharges, tear or the absence of the hymen, fissure or anal gaping, trauma of the perineum, recto vaginal fistula or vesico-vaginal fistula, and pelvic pain. There are also signs linked to physical trauma and behavioral disorders.

Signs	Girls	Boys
Genitals	✦ Absence or tear of the hymen ; ✦ Fissure or anal openness; ✦ Trauma of the perineum; ✦ Vesico-vaginal fistula; ✦ Recto vaginal fistula; ✦ Pelvic pain ; ✦ Presence of STI.	✦ Anal gaping ✦ Anal fissure ✦ Recto anal fistula Presence of STI.
Other Signs : ✦ Cutaneous trauma; ✦ Marked docility on examination; ✦ Exaggerated fear by the patient of a parent or close relative.		

d. Management of Sexual Abuse in a Child

- **Treatment**

- If the pregnancy test is negative, prescribe within 72 hours (following the aggression or sexual abuse) urgent contraception;
- If HIV serology is positive in the aggressor, treat the child and start the ARV treatment (PEP). The results are the best when treatment is started within 6 hours that follow the aggression quite before 24 hours and do not exceed 72 hours;
- If a germ is isolated, it is necessary to treat the child by taking into account its sensitivity to antibiotics (or treatment according to the STI syndrome identified);
- If no germ is isolated and if there exists other risk factors that have been identified in the aggressor or if the aggressor presents STI or has recent precedents of STI, in this case there is need to provide presumptive treatment. This treatment must take into account the syndrome of the suspected STI in the aggressor.

- To propose care, treatment and psychological monitoring.

  - **Follow up at 3 Months**

It is recommended to repeat the serological tests for HIV, hepatitis B and syphilis in the child (especially if the initial tests were negative).

In case the HIV serology is positive, monitoring and treatment of the child must respect the recommendations for the medical care of people living with HIV in the rest of this document.

PART IV: MANAGEMENT OF HEPATITIS B & HEPATITIS C

1.1. Definitions

1.1.1. Hepatitis

Hepatitis is a general term meaning inflammation of the liver and can be caused by several mechanisms, including viral agents. The most common causes of viral hepatitis are Hepatitis A, B, C, D, and E.

1.1.2. Blood-borne Infection

A blood borne infection is one that can be spread through contamination by blood.

Blood borne pathogens are viruses or infectious agents carried by human blood and body fluids.

They can enter our bodies, live in human blood and can cause disease or immune deficiencies which can sometimes lead to death.

The most common blood borne pathogens are Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV) and Viral Hemorragic Fevers Viruses (HFV).

The following sections will focus on blood borne hepatitis caused by Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV).

1.2. Transmission of HBV and HCV

Both viruses share the same mode of transmission with HIV:

1. Blood and biological fluids contact (including needlestick injury)
2. Sexual contact
3. Mother to child

Both infections may be acute or chronic based on the duration of the condition.

1.3. Prevention of HBV and HCV Infections

Prevention activities aim at reducing or eliminating potential risk for HBV/HCV transmission through:

1.3.1. General Measures

- ✓ Safe injections
- ✓ Safe sex
- ✓ Routine screening of blood and blood products for HBV/HCV infections
- ✓ Screening and management of HBV/HCV infected people

1.3.2. Specific Measures

- **Passive Immunisation for HBV**

- ✓ Consists of administration of hepatitis B immune globulin (HBIg) following exposure directed against HBV
- ✓ Administration of HBIg in conjunction with HBV vaccination to infants born to HBsAg-positive mothers

- **Active Immunisation or HBV Vaccination**

HBV vaccination is recommended to all HBV non-immune people (unvaccinated or non-exposed)

The following high risk groups need to be prioritized for hepatitis B vaccination:

- ✓ All infants from 6 weeks of age
- ✓ All infants borne to HBsAg + mothers within 24 hours after birth

- ✓ Persons with HIV infection
- ✓ Persons with HCV infection
- ✓ Susceptible sex partners of HBsAg positive persons
- ✓ Health care and public safety workers at risk (exposure to body fluids)
- ✓ Susceptible household contacts of HBsAg-positive persons
- ✓ All other persons seeking protection from HBV infection

Vaccination Schedule and Recommended HBV Vaccines				
N°	**Group**	**Dose 1**	**Dose 2**	**Dose 3**
1	Newborn	Week 6*	Week 10	Week 14
2	Adult	1st Contact	Month 1	Month 6*

NB*:

1) In Rwanda, we recommend to vaccine all babies at 6 weeks*

2) Infants born to HBsAg positive mothers will require both hepatitis B immunoglobulin and first dose of vaccine within the first 24 hours of life.

3) Whenever possible, we recommend to test anti-HBsAg 2 months after the last dose of vaccination to check if the client is protected (> 10 UI/l)

4) We advise people to get screened for HBs Ag and Anti-HBs Ag (Optional) prior vaccination.

1.4. HBV and HCV C Post Exposure Prophylaxis

1.4.1. Introduction

HBV and HCV may be transmitted by significant exposure to blood or other body fluids through:

- Percutaneous injury
- Contact of mucous membrane

- Non intact skin
- Semen and vaginal secretions

1.4.2. Recommendations on HBV& HCV Post Exposure Prophylaxis

- **Immediate Care of the Exposed Person**

After exposure to blood or other body substances the following is recommended as soon as possible:

- ✓ Wash the exposure site with soap and water;
- ✓ If eyes are contaminated then rinse them, while they are open, gently but thoroughly with water or normal saline;
- ✓ If blood or other body substances get in the mouth, spit them out and then rinse the mouth with water several times;
- ✓ If clothing is contaminated remove clothing and shower if necessary;
- ✓ Inform an appropriate person to ensure that necessary further action is undertaken.
- ✓ Where water is not available use of a non-water cleanser or antiseptic should replace the use of soap and water for washing cuts or punctures of the skin or intact skin.

- **Specific Measures for Hepatitis B**

Hepatitis B exposure management depends on the following:

- ✓ Is the HBV immunity status of the exposed person known?
- ✓ Is the exposed person fully or partially immunized and/or immune?
- ✓ Note that both HBIG and first dose of HBV vaccination series should ideally be administered within 24 hours of exposure; HBIG should not be given later than 14 days post exposure **(Algorithm 8).**

NB: percutaneous, mucous membrane or cutaneous exposure to (non-blood stained) urine or saliva does not require further assessment, clinical follow up or immunization.

- **Specific Measures for Hepatitis C**

At present there is no prophylaxis proven to be effective following exposure to HCV.

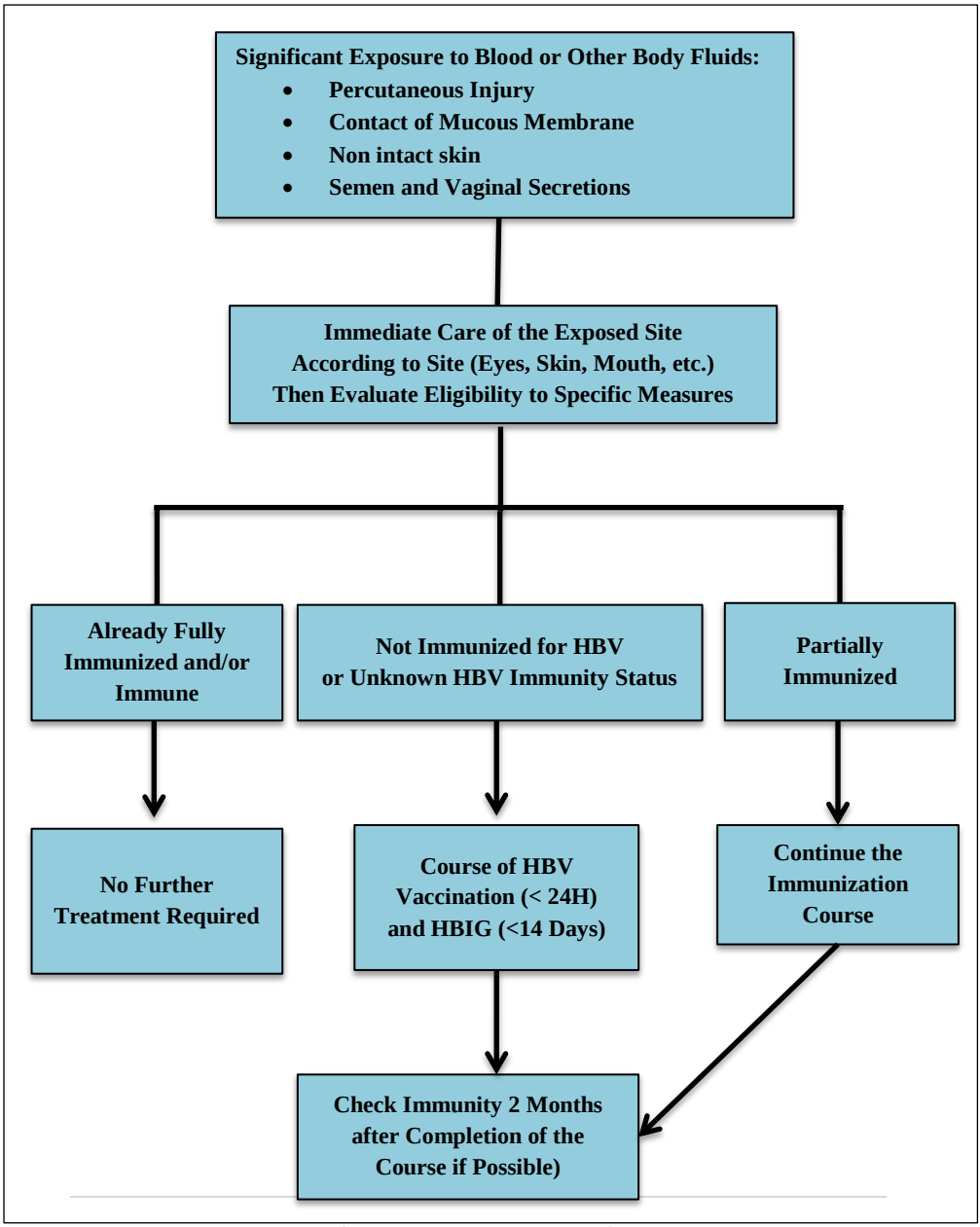
The aim of follow up is to detect acute hepatitis C so that appropriate management can be instituted.

The person should be informed and advised on the risk of transmission to secondary contacts, especially during the first 6 months following the incident.

The exposed person should have baseline testing for HCV antibody, if negative be retested at 6 months for HCV as well as for other blood borne viruses.

If HCV antibody is positive, the person should be referred for HCV PCR testing and follow up if necessary.

Algorithm 8: HBV Post Exposure Prophylaxis



Chapter II: Diagnosis of HBV and HCV

2.1. Diagnosis of HBV

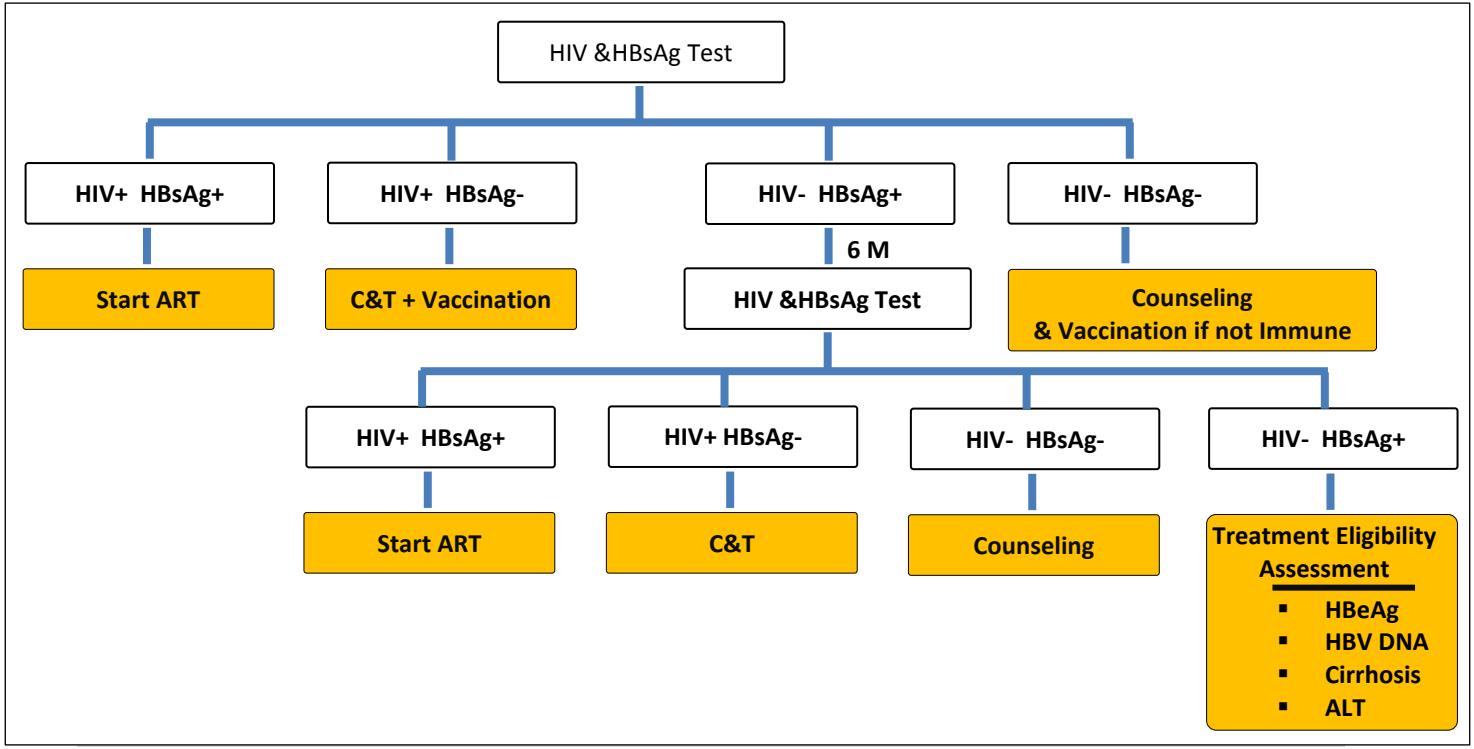
Hepatitis B infection can present in two forms:

- **Acute Infection:** Acute viral hepatitis refers to the short-term infection with HBV which the body's immune system clears within 6 months (first 6 months after someone is exposed to the virus)
- **Chronic Infection:** It is generally defined as the presence of HBsAg for > 6 months. Over time, the chronic infection can cause liver fibrosis, cirrhosis and hepatocellular carcinoma (HCC).

Anybody seeking HBV screening should be offered the service. However, the following are key target groups for HBV screening:

1) Pregnant women
2) Individuals infected with HIV or HCV
3) Health care workers exposed to biological fluids
4) Blood donors
5) Inmates of correctional facilities
6) Individual with chronically elevated ALAT or ASAT
7) Household and sexual contacts of HBsAg-positive person
8) Female sex workers
9) Male having sex with men (MSM)
10) Patients undergoing renal dialysis
11) Persons needing immunosuppressive therapy
12) Persons who have ever injected drugs

Algorithm 9: Diagnosis of HBV in HIV Negative People



2.2. HBV Screening in HIV-Positive People

HIV-Positive people who stand to most benefit from HBV screening are:

1) Those not eligible for ART based on the current guidelines (CD4/mm^3, WHO stage, TB/HIV, SDC, > 5 years, etc.)
2) Those eligible to ART but with contraindication to TDF (new patients)
3) Those on non-TDF based regimen
4) Those on TDF-based regimen but in need of switching to other regimen
5) All children with unknown HBV status and not on TDF

Note: It is known that almost all HIV positive people who have acute HBV infection will not clear the infection and will develop chronic HBV. The presence of HBs Ag in HIV-Positive will confirm the chronicity of the infection and therefore, there is no need to confirm after six months.

2.3. Diagnosis of HCV and Treatment Eligibility

HCV diagnosis depends on the presence of anti-HCV antibodies. Anti-HCV is generally not detectable in patients with initial signs or symptoms of hepatitis C. Anti-HCV develop in acute infection generally between 2 and 8 weeks after evidence of liver injury. Some persons may not test positive for 6-9 months after onset of illness.

Hepatitis C viremia may be detected by RT-PCR within days after infection.

In general, the screening for hepatitis C should be done with anti-HCV by ELISA technique, and positive samples should be tested by PCR for HCV-RNA.

In Rwanda, the screening of HCV will be done based on:

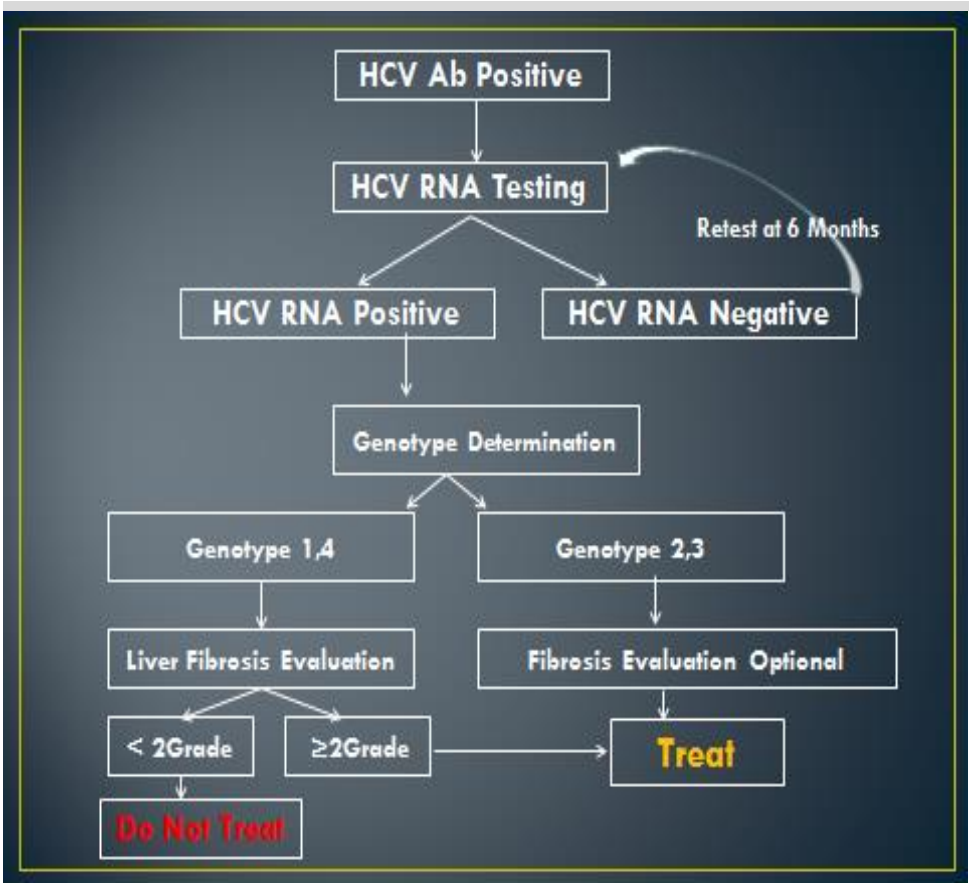
- Presence of HCV Ab (ELISA/RIBA or Rapid Test) then confirm with PCR.
- For people with Immunosuppression (Always use PCR in case of severe immunosuppression below 200 CD4/ml) as HCV Ab may be negative.

Persons who are positive for anti-HCV but negative for HCV-RNA should be retested by PCR after 3-6 months.

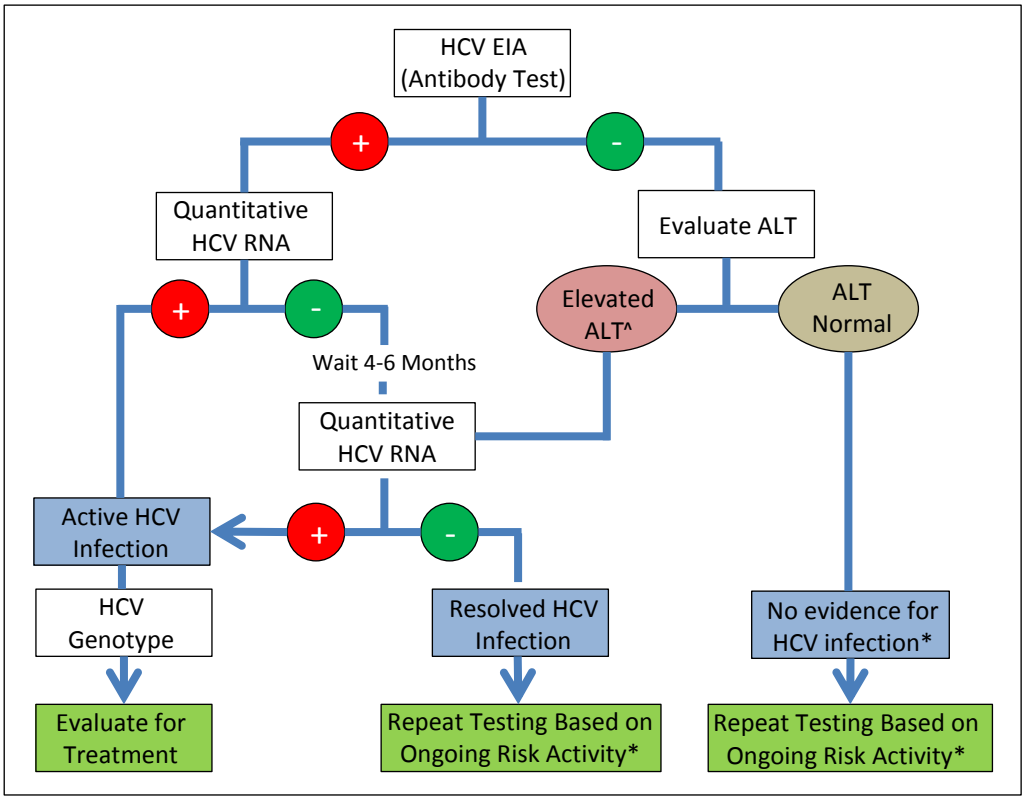
The following key populations are recommended to be tested for hepatitis C virus:

1. Patients infected with HBV
2. HIV-Positive people
3. Current and former drug users
4. Patients who received blood products or organ transplants prior to the introduction of anti-HCV screening (HCV screening started in Rwanda in 1999)
5. Patients undergoing renal dialysis
6. Children born of hepatitis C infected mothers
7. Health-care workers exposed to needle stick injuries
8. Patients with persistently elevated ALT (>50 IU/L for males and >35 IU/L for females)
9. Persons with evidence of chronic liver disease
10. Populations in correctional institutions, drug treatment programs, programs for high risk youth

Algorithm 10: Diagnosis of HCV Infection in General Population



Algorithm 11: Diagnosis of HCV Infection in HIV-Positive People



NB: Liver biopsy is the gold standard for evaluation for the stage of liver disease progression.

Other noninvasive methods are less accurate in assessing liver fibrosis but are can be used (Fibroscan, APRI)

Chapter III: Management of HBV

3.1. Management of HBV Mono-infection

3.1.1. Evaluation of Patients with Chronic HBV Infection

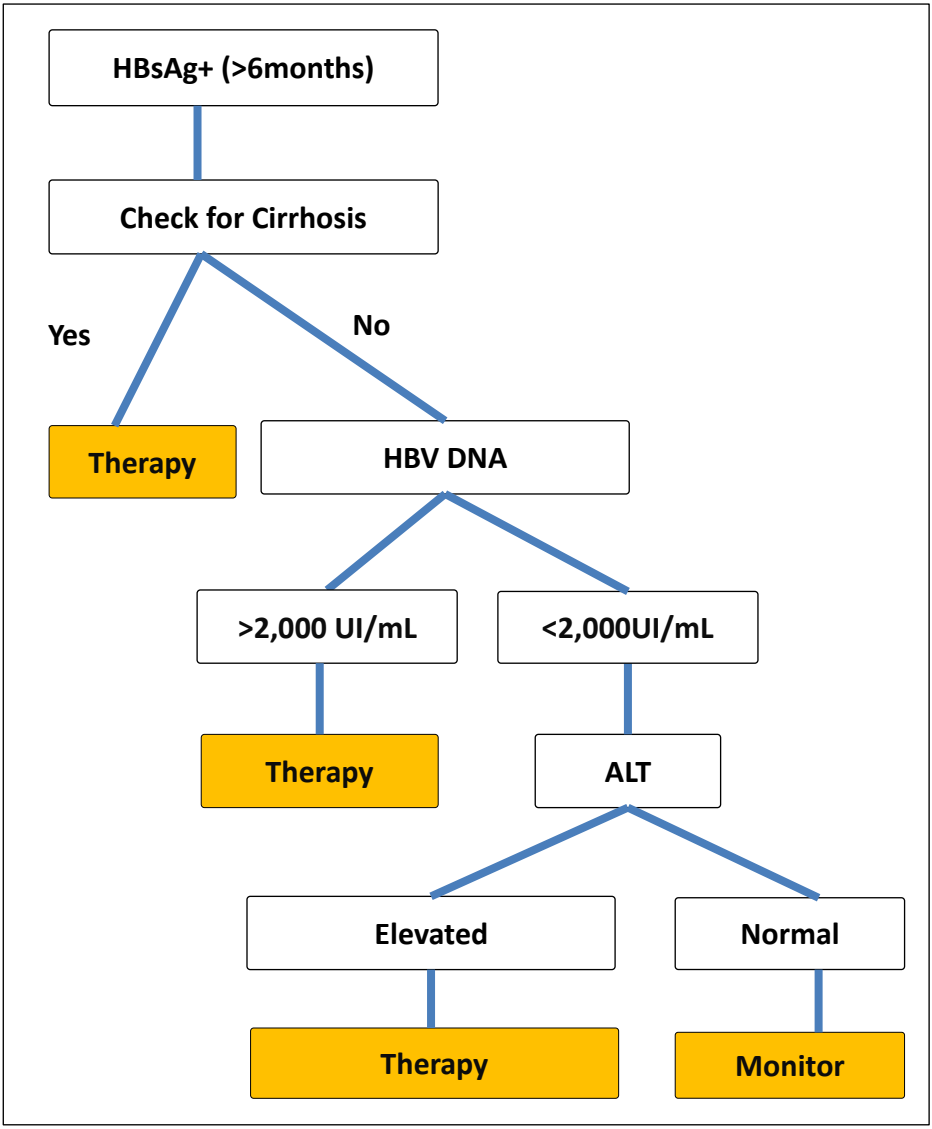
The initial evaluation includes:

1) History (including **alcohol** usage) and physical examination
2) Family History of liver disease, Hepatocellular carcinoma (HCC)
3) Laboratory tests to assess liver disease:
   - Complete blood counts (CBC) with platelets,
   - Hepatic panel, and prothrombin time
4) Tests for HBV replication:
   - HBeAg
   - Anti-HBe,
   - HBV DNA
5) Tests to rule out viral co-infections:
   - Anti-HCV,
   - Anti-HIV
6) Tests to screen for HCC:
   - Alpha fetoprotein (AFP) at baseline and, in high risk patients,
   - Ultrasound
7) Liver biopsy

This aims at grading and staging liver disease - for patients who meet criteria for chronic hepatitis

3.1.2. HBV Treatment Eligibility Criteria

Algorithm 12: Criteria for HBV Treatment in HIV-Negative People



3.1.3. HBV Treatment Options in Rwanda

Drug	Dose	Duration
Tenofovir **(1)**	300mg 1x/day	See endpoint
Entecavir **(2)**	1mg 1x/day	See endpoint
Adefovir **(3)**	10mg 1x/day	See endpoint
Lamivudine **(4)**	300mg 1x/day	See endpoint
Peginterferon alfa-2a **(5)**	180 µg SQ weekly	See endpoint

3.2. HBV Treatment in Special Patient Groups

3.2.1. HBV Infection and Immunosuppressive Therapy or Cancer Chemotherapy

Approximately 20-50% of HBV carriers undergoing immunosuppressive therapy or cancer chemotherapy develop reactivation of HBV replication, presenting with hepatitis flare and rarely hepatic decompensation. This may occur even in those with occult HBV infection. Administration of lamivudine prior to these treatments is associated with reduced frequency and severity of hepatitis B flare and improved survival in these patients.

3.2.2. HBV Infection and Pregnancy

Data in HIV-positive pregnant women suggest that the use of lamivudine, emtricitabine and tenofovir is safe.

Lamivudine or tenofovir are recommended in the last trimester in HBsAg-positive women with high viral loads (serum HBV DNA >1 x 10^{6-7} IU/ml), to prevent intra-uterine and perinatal HBV transmission. Nucleos (tide) s analogues therapy can be discontinued 3 months post-delivery if only

required for prevention of perinatal transmission. In this situation HBV-infected women should be monitored closely after delivery as flares may occur.

Lamivudine treatment should be combined with hepatitis B immunoglobulin and HBV vaccination of the newborns.

3.2.3. Hepatitis B in Children

Children usually display an immune tolerant course of their HBV infection. Treatment decision should be guided by liver biopsy results.

- Only standard interferon alpha, lamivudine and adefovir have been evaluated in children.
- Tenofovir can be given to children aged ≥2 years upon specialist advice

3.2.4. Hepatitis B in Healthcare Workers

Healthcare workers who are HBsAg positive and have HBV DNA levels ≥2,000 IU/ml should be treated with either TDF or entecavir. The HBV DNA level should preferably be undetectable or at least <2,000 IU/ml before such an individual may return to exposure-prone procedures.

3.2.5. Chronic HBV Infection with Persistently Normal Transaminases

Chronic HBV infection may present with high level of serum HBV DNA, but persistently normal transaminases. These patients usually have milder hepatic inflammation and tend to have a poor serological response to antiviral therapy. It is recommended that a liver biopsy be considered in these patients and for those who have histological evidence of active and/or advanced HBV disease, HBV treatment should be considered.

3.2.6. Treatment of Patients with Compensated Cirrhosis

Treatment should be considered in patients with compensated cirrhosis and detectable HBV DNA levels.

Life-long combined TDF and Lamivudine therapy is required and regular monitoring of HBV DNA levels is essential. Combined treatment can stabilize and even prevent or delay the need for liver transplantation when it is associated with sustained virologic suppression.

3.2.7. Treatment of Decompensated Cirrhosis

All patients with decompensated cirrhosis should be considered for urgent treatment. Lifelong treatment with nucleos (tide) s is indicated even if the HBV DNA level is low or undetectable, in order to prevent flares/reactivation. TDF may be replaced by entecavir dosed at 1mg/day.

3.3. Biological Follow up of Patient on HBV Treatment

Date	Test
1 Month	ALAT/ASAT; creatinine (Renal Clearance)
3 Months	ALAT/ASAT; creatinine (Renal Clearance)
6 Months	HBV DNA; HBe Anti-bodies
12 Months	HBsAg if HBe sero-conversion or undetectable HBV DNA in HBeAg negative

3.4. Endpoints in HBV Treatment: Summary Recommendation on Treatment Duration

Therapy	HBe Ag-Positive Disease	HBe Ag-Negative Disease
Nucleotide Or Nucleoside Analogue	- Sustained HBs Ag loss[1] due to therapy +/- anti-HBs - Durable[2] HBe Ag loss and seroconversion to anti-HBe - Durable[2] suppression of HBV DNA to low or undetectable levels - Normalization of ALAT	- Sustained HBs Ag loss[1] off therapy +/- anti-HBs - Durable[2] suppression of HBV DNA to low or undetectable levels (below 10-15UI/ml) - Normalization of ALAT
Peginterferon	48 Weeks	48 Weeks
Standard IFN	16 Weeks	48 Weeks

Note :

[1] HBs Ag loss is ideal but not always required to stop the treatment (Most patients receiving nucleos/tide analogue therapy will require at least four to five years of treatment, and some may require indefinite treatment).

[2]Patients in whom HBeAg seroconversion has occurred and serum HBV DNA has become undetectable should be treated for at least 12 more months after HBeAg seroconversion has been confirmed (by testing on two occasions at least two months apart) to reduce the rate of relapse.

3.5. Side Effect Monitoring

Drug	Side Effect	Monitoring Test	Frequency
Tenofovir	- Renal Toxicity - Fanconi's Syndrome	Creatinine and Creatinine Clearance	Every 3 months
Adenofovir	Renal Toxicity	Creatinine and Creatinine Clearance	Every 3 months
Entecavir	- Lactic Acidosis - Severe Hepatomegaly - Steatosis	- Hepatomegaly - Steatosis or - Elevated ALT/AST	Every 3 months
Interferon	- Psychiatric - Endocrinologic - Hematologic	- Clinical - CBC, TSH - Liver panel	Every 3 months

3.6. Treatment of Drug-Resistant Hepatitis B

HBV DNA monitoring is critical to detect treatment failure.

- Undetectable HBV DNA levels by real-time PCR (level of detection <10 - 15 IU/ml) need to be achieved to prevent the development of resistance.
- Partial responses (HBV DNA level detectable but <2,000 IU/ ml) are assessed at 24 weeks for lamivudine and at 48 weeks for tenofovir and entecavir.
- If HBV DNA levels are still positive, but declining at 48 weeks on tenofovir or entecavir, monotherapy can be continued

There is no documented resistance to TDF. In case of resistance to other nucleosides it is recommended to add Tenofovir to the failing regimen except in case of Adefovir where a switch to TDF and 3TC is advised (Renal toxicity of Adefovir).

3.7. Management of HIV-HBV Co-infection

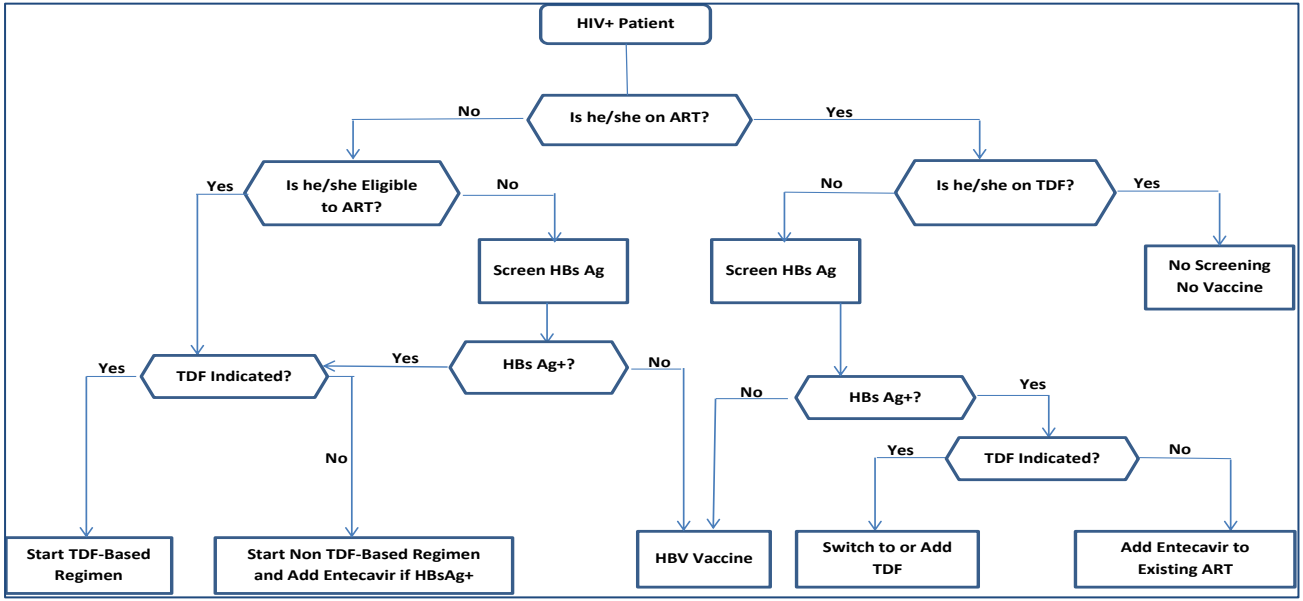
3.7.1.General Recommendations

1- HIV-HBV Infected Patient is eligible to begin treatment for both infections regardless the number of CD4 Cells, regardless the WHO clinical staging.
2- Chronic Hepatitis B infection is diagnosed based on HBs Ag (no need to confirm at 6 months).
3- The HIV treatment should include TDF and 3TC/FTC and the treatment is for life.

Note:

1. When there is a need to switch from TDF (Side effect or HIV treatment failure), always check if the HBV infection is cured first; otherwise keep TDF or replace with another effective anti-HBV molecule.
2. 3TC may be replaced by FTC
3. Patients on second or third line ART should receive additional TDF+3TC if their HIV treatment does not include those two molecules
4. In case TDF is contraindicated, add Entecavir or Adefovir

Algorithm 13: Management of HBV in HIV- Positive People



4.1. Initial Evaluation

Persons tested for HCV infection and determined to be anti-HCV positive should be evaluated for the presence of active infection, presence or development of chronic liver disease (CLD), and possible treatment. Quantitative HCV RNA will be necessary to confirm active infection and to predict response to treatment and to monitor therapy. Genotype analysis is used to predict response to therapy and to adjust the dosage of Ribavirin. Hepatic transaminases reflect liver inflammation but their values fluctuate and may be normal with advanced liver disease. CT scan or ultrasound is the preferred method for the detection of hepatocellular carcinoma.

To evaluate the liver fibrosis, liver biopsy is considered as the gold standard method. There are other noninvasive methods to stage the liver disease, but they are variable in sensitivity and specificity. In Rwanda, as a resource-limited settings country, we recommend that the aminotransferase/platelet ratio index (APRI) or FIB4 tests be used for the assessment of hepatic fibrosis and where possible, other noninvasive tests that require more resources such as elastography (Fibroscan) or Fibrotest can be used.

The initial laboratory evaluation should include:

- Total and direct bilirubin
- ALAT, ASAT
- Alkaline phosphatase,
- Prothrombin time, Coagulation tests
- Total protein, albumin,
- Globulin,
- Complete blood count (CBC)

4.2. Treatment of HCV Mono-infection

The goal of the treatment is to eradicate the virus, prevent liver cirrhosis and its complications including hepatocellular carcinoma. When histology is available, treatment may be indicated in patients with moderate to bridging fibrosis or compensated cirrhosis.

4.2.1. Indication for Hepatitis C Infection Treatment

- **Eligibility for Chronic HCV Treatment**

All patients with chronic hepatitis C infection should be considered potential candidates for drug therapy.

Treatment is recommended for patients who are at risk of developing cirrhosis, generally defined by a measurable hepatitis C RNA level and liver biopsy showing portal or bridging fibrosis along with moderate inflammation and necrosis.

In fact, patients with less advanced fibrosis respond better to treatment, while those with more advanced disease are at higher risk of developing cirrhosis and hepatocellular carcinoma.

In view of this, patients with advanced fibrosis and cirrhosis (METAVIR stages F3 and F4) should be prioritized for treatment as they are at higher risk of developing cirrhosis and hepatocellular carcinoma. If resources permit, then persons with less advanced fibrosis (METAVIR stages F1 and F2) could also be considered for treatment.

METAVIR LIVER BIOPSY SCORING SYSTEM					
METAVIR Stage	F0	F1	F2	F3	F4
Definition	No Fibrosis	Portal Fibrosis without Septa	Portal Fibrosis with Septa	Numerous Septa without Cirrhosis	Cirrhosis

Treatment is also recommended for patients with elevated serum ALAT levels who meet the following criteria:

- Age >18 years
- Positive HCV antibody and serum HCV RNA test results
- HIV-HCV Co-Infection
- Compensated liver cirrhosis (e.g., no hepatic encephalopathy or ascites)
- Acceptable hematologic and biochemical indices (hemoglobin at least 13 g/dL for men and 12 g/dL for women; neutrophil count >1500/mm3, serum creatinine < 1.5 mg/dL)
- Patients with symptomatic extrahepatic manifestations even in the absence of liver damage
- Willingness to be treated and to adhere to treatment requirements
- No contraindications for treatment

4.2.2. Pre-therapeutic Evaluation

Liver function is assessed by clinical examination, and the following laboratory analysis:

- **ALAT/ASAT**
- Hematology (hemoglobin, platelets and leucocytes including differential count)
- Bilirubin
- Alkaline phosphatase
- Prothrombin time/INR
- Albumin
- Alpha-fetoprotein (AFP)

Patients for whom treatment is not indicated should have their liver tests and hematology performed at intervals of 6-12 months. Until now, progression of fibrosis has required a new liver biopsy with 3-5 years interval.

Current trend is to evaluate liver fibrosis/cirrhosis with noninvasive methods. In Rwanda, we recommend that the aminotransferase/platelet ratio index (APRI) or FIB4 tests be used for the assessment of hepatic fibrosis and where possible, other noninvasive tests that require more resources such as elastography or Fibrotest can be used.

Note that FIB4 was evaluated only for the diagnosis of significant fibrosis (METAVIR stage ≥F2), while APRI* was validated for the diagnosis of both significant fibrosis.

APRI SCORE AND LIVER FIBROSIS

APRI= [{AST (IU/L)/AST_ULN (IU/L)} x100]/Platelet Count (10^9/L)

FIB4= Age (Years) x AST (IU/L)/ Platelets Count (10^9/L) x [ALT (IU/L) $^{1/2}$]

$$\text{APRI} = \frac{\dfrac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet Count } (10^9/\text{L})} \times 100$$

NB: Three Zeros in Platelets count are chopped off, e.g. if you have 137,000 you only consider 137

Low and High Cut-off Values for the Detection of Significant Cirrhosis and Fibrosis					
	APRI (LCO)	**APRI (HCO)**	**FIB4 (LCO)**	**FIB4(HCO)**	**Transient Elastography (Fibroscan)**
Significant Fibrosis (METAVIRF2)	**0.5**	**1.5**	**1.45**	**3.25**	**7-8.5kPa**
Cirrhosis (METAVIR F4)	**1**	**2**	**-**	**-**	**11-14kPa**

APRI: Aminotransferase Platelet Ratio Indice
LCO: Low Cut-Off
HCO: High Cut-Off
kPa: Kilo Pascal

Interpretation of Aminotransferase Platelet Ratio Index (APRI)

APRI Value	Interpretation	Recommendation
>1.5	High Probability (94%) of F4 Cirrhosis	Start Treatment
0.5-1.5	Intermediary Risk of Advanced Fibrosis	Discuss Treatment or Retest Every Year
<0.5	Very Low Probability (18%) of Advanced Fibrosis (F2 fibrosis or Higher)	Defer Treatment and Reassure

A strategy that uses a combination of the high and low cut-off values was assessed. Using this strategy, patients with values above the APRI high cut-off value would be prioritized for treatment as they have a high probability (94%) of having F4 cirrhosis. For patients with an APRI score below the low cut-off value, treatment could be deferred as they have a very low probability (18%) of having advanced fibrosis (F2 fibrosis or higher) and could thus be reassured and reassessed periodically. Those patients with APRI values between low and high cut-off values could either be retested every one or two years or, if resources are available, could be treated.

A pretreatment liver biopsy is not mandatory but may be helpful in patients with normal transaminase levels, particularly those with a history of alcohol dependence, in whom little correlation may exist between liver enzyme levels and histologic findings.

4.2.3. HCV Drugs Available (Recommended in Rwanda)

Genotype	Drug	Dose
Protease Inhibitors		
1	Simeprevir	150 mg PO Once Daily with Food
Polymerase Nucleotide Inhibitor		
1,2,3,4	Sofosbuvir	400 mg PO Once Daily +/-Food
NS5A Inhibitor		
1	Ledipasvir*	90 mg PO Once Daily +/-Food
Interferon		
1,2,3,4,5,6	Pegylated IFN alpha-2b	1.5mg/kg/Week
	Pegylated IFN alpha-2a	Fixed dose of 180 µg/Week
Ribavirin		
1,4,5,6	Ribavirin PO (Weight-based dose)	600mg AM and 400mg PM (< 75kg) 600mg AM and 600mg PM (> 75kg) (or 15mg/kg/day ranging 1000- 1400mg)
2,3	Ribavirin PO (Fixed dose)	400mg AM and 400mg PM
*Ledipasvir is to be approved very soon		

HCV Treatment Options and Duration			
Genotype	**Drug**	**Dose**	**Duration**
Genotype 1	Sofosbuvir	400mg OD	12 weeks
	Ribavirine Weight Based	600mg AM + 400mg PM <75 kg OD	
		600mg AM + 600mg PM >75 Kg OD	
	Pegylated IFN Alpha -2	Fixed dose of 180 µg/Week	
Genotype 1 Not Eligible to IFN	Sofosbuvir	400mg OD	12 weeks
	Simeprevir	150 mg OD	
	Ribavirine Weight- Base Optional		
Genotype 2	Sofosbuvir	400mg OD	12 weeks
	Ribavirine Weight -Based	600mg+400mg PM if <75 Kg	
		600mg +600mg PM if >75 Kg	
Genotype 3	Sofosbuvir	400mg OD	24 weeks
	Ribavirine Weight -Based	600mg +400mg PM if <75 kg	
		600mg + 600mg Pm if >75 Kg	
Genotype 4	Sofosbuvir	400mg OD	12 weeks
	Ribavirine Weight -Based	600mg AM + 400mg PM <75 kg OD	
		600mg AM + 600mg PM >75 Kg OD	
	Pegylated IFN alpha -2	Fixed dose of 180 µg/Week	
Genotype 4 Not Eligible to IFN	Sofosbuvir	400mg OD	24 weeks
	Ribavirine Weight -Based	600mg AM +400mg PM if <75 Kg	
		600mg AM +600mg PM if >75 kg	
Genotype 5 and 6	Sofosbuvir	400mg OD	12weeks
	Ribavirine Weight -Based	600mg AM +400mg PM if <75 kg	
		600mg AM+600mg PM if >75 Kg	

4.3. HIV-HCV Co-infection

4.3.1. Introduction

According to WHO guidelines 2014, coinfection with HIV adversely affects the course of HCV infection, and coinfected persons have a significantly accelerated progression of liver disease to cirrhosis, decompensated liver cirrhosis and HCC than HCV-monoinfected persons, particularly those with advanced immunodeficiency (CD4 count <200 cells/mm3).

Furthermore, co-infected patients have a lower likelihood of achieving sustained virological response to treatment compared with mono-infected ones. Two large European cohorts have shown that after ART initiation, CD4 recovery was impaired in HIV/HCV-coinfected persons when compared to those infected with HIV alone. HIV/HCV-coinfected persons also demonstrated more rapid HIV disease progression compared to those who were HIV-infected alone, and had an impaired recovery of CD4 cells.

4.3.2. National Recommendations for HIV-HCV Co-infection

- Whenever possible, HIV-infected patients should be screened for hepatitis C virus (HCV) infection, preferably before starting antiretroviral therapy (ART).
- The HCV genotype must be assessed prior to antiviral treatment initiation and will determine the dose of ribavirin and treatment decision.
- Treat all regardless CD4 Cell count
- Initial ART combination regimens for most HIV/HCV co-infected patients are the same as those for individuals without HCV infection.
- However, when treatment for both HIV and HCV is indicated, consideration of potential drug-drug interactions and overlapping toxicities should guide ART regimen selection or modification

- Although ART should be initiated for most HIV/HCV co-infected patients regardless of CD4 cell count, in ART naive patients with CD4 counts >500 cells/mm^3, it is recommended to defer ART until completion of HCV treatment.
- In patients with lower CD4 counts (e.g., <200 cells/mm3), it is recommended to initiate ART and delay HCV therapy until CD4 counts increase as a result of ART.

4.3.3. ART and Anti HCV Combinations

Due to drug-drugs interactions and overlapping toxicities between anti HIV and anti HCV drugs, combined antiretroviral therapy and anti HCV treatment options are limited.

HCV infection among persons with HIV co-infection can be treated with PEG-IFN/RBV.

These persons can also be treated with PEG-IFN/RBV and boceprevir, telaprevir or simeprevir (for genotype 1 infection) and may also be treated with Sofosbuvir/RBV or PEG-IFN/RBV/Sofosbuvir. Persons coinfected with HCV/HIV treated with PEG-IFN/RBV with or without an additional agent (PI or Sofosbuvir) who require treatment for HIV should receive compatible ART.

Persons with HIV require special consideration regarding the selection of an antiretroviral regimen. The safety profile in HCV/HIV-1 co-infected subjects treated with sofosbuvir is similar to that observed in HCV-monoinfected subjects. Elevated total bilirubin (grade 3 or 4) occurs extremely commonly in persons treated with sofosbuvir and atazanavir as part of the antiretroviral regimen. Tipranivir/sofosbuvir is not recommended but darunavir/ritonavir, efavirenz, emtricitabine, raltegravir, rilpivirine and

tenofovir have been tested and no dose adjustment is currently recommended.

It is extremely important to consider known and potential pharmacokinetic (PK) interactions when selecting an ARV regimen for patients for whom initiation of Simeprevir and Sofosbuvir is being considered.

✓ **Simeprevir**

- The concentration of Simeprevir decreases in presence of efavirenz;
- The concentration of Simeprevir increases in presence of darunavir/ritonavir, ritonavir (100mg bid) and cobicistat-containing products and it is not recommended to co-administer simeprevir with any HIV protease inhibitor (with or without ritonavir).
- No clinically significant interactions of Simeprevir with raltegravir, rilpivirine, tenofovir

✓ **Sofosbuvir**

- The concentrations of Sofosbuvir decreases in presence of tipranavir/ritonavir and co-administration is not recommended.
- No clinically significant interactions of Sofosbuvir with darunavir/ritonavir, efavirenz, emtricitabine, raltegravir, rilpivirine, or tenofovir

✓ **Pegylated IFN and Ribavirin**

Do not combine pegylated interferon-alpha and ribavirin treatment with:

- **Didanosine** (increased to toxic levels and may lead to mitochondrial toxicity and lactate acidosis).
- **Stavudine** (may possibly also lead to mitochondrial injury)
- **Zidovudine** (may worsen the anemia caused by ribavirin)

Treatment Options for HIV-HCV Confection

ART Combination	HCV Treatment
2NRTI +EFV	G 1, 4,5,6 Sofosbuvir + Ribavirin+ Peg IFN
	G1 : Not Eligible to IFN : Sofosbuvir+Ribavirine
	G2,3 : Sofosbuvir+ Ribavirine
2NRTI +NVP	G2, 3 : Sofosbuvir + Ribavirine
	G1, 4, 5,6 : Sofosbuvir+ Ribavirine+Peg IFN
2NRTI + ATV/r	G1,4,5,6 : Sofosbuvir + Ribavirine+ Peg IFN
	G2,3 : Sofosbuvir + Ribavirine
2NRTI + Lop/r	G1,4,5,6 : Sofosbuvir+Ribavirine+ Peg IFN
	G2,3 : Sofosbuvir + Ribavirine
2 NRTI+ Raltegravir	G1,4,5,6 : Sofosbuvir + Ribavirine + Peg IFN
	G1 : Sofosbuvir+ Simeprevir
	G2,3 : Sofosbuvir + Ribavirine
Darunavir+Etravirin+Raltegravir	G1,4,5,6 : Sofosbuvir +Ribavirine+ Peg IFN
	G2,3 : Sofosbuvir+Ribavirine
Avoid Ribavirin –AZT Combination whenever possible because of increased frequency in anemia	

4.4. Management of Special Cases of HCV Infection

4.4.1. Patients with Hepatitis C and Cirrhosis

Between 15% and 30% of persons infected with HCV will go on to develop cirrhosis of the liver within 20 years and a proportion of these will progress to HCC.

Persons with compensated cirrhosis have the least time available for treatment, the most to lose and much to gain from achieving SVR. Treatment of HCV infection with IFN-containing regimens must be commenced before the onset of decompensated disease as it may precipitate liver failure and death if administered at this stage.

In addition to clinical care offered to all HCV patients with blood tests for ALAT, cirrhotic patients should be screened for HCC with AFP every 6 months and ultrasonography of the liver every year. Screening for esophageal varices should be performed every second year.

Patients with decompensated cirrhosis should be evaluated for liver transplantation by a gastroenterologist/hepatologist.

4.4.2. Treatment of Patients with Renal Failure

In patients with decreased renal function the dose of pegylated interferon should be reduced. Approximately 30% of pegylated-interferon-alpha2b is excreted by the kidneys. The dose should be reduced by 25% if creatinine clearance is reduced to 30-50 mL/min, and by 50% in the interval 15-29 mL/min. With a creatinine clearance below 15mL/min pegylated-interferon- alpha2b should not be used.

Pegylated-interferon-alpha2a is less influenced by renal function. The dose should be reduced to 135 µg/week if the creatinine clearance <10mL/min.

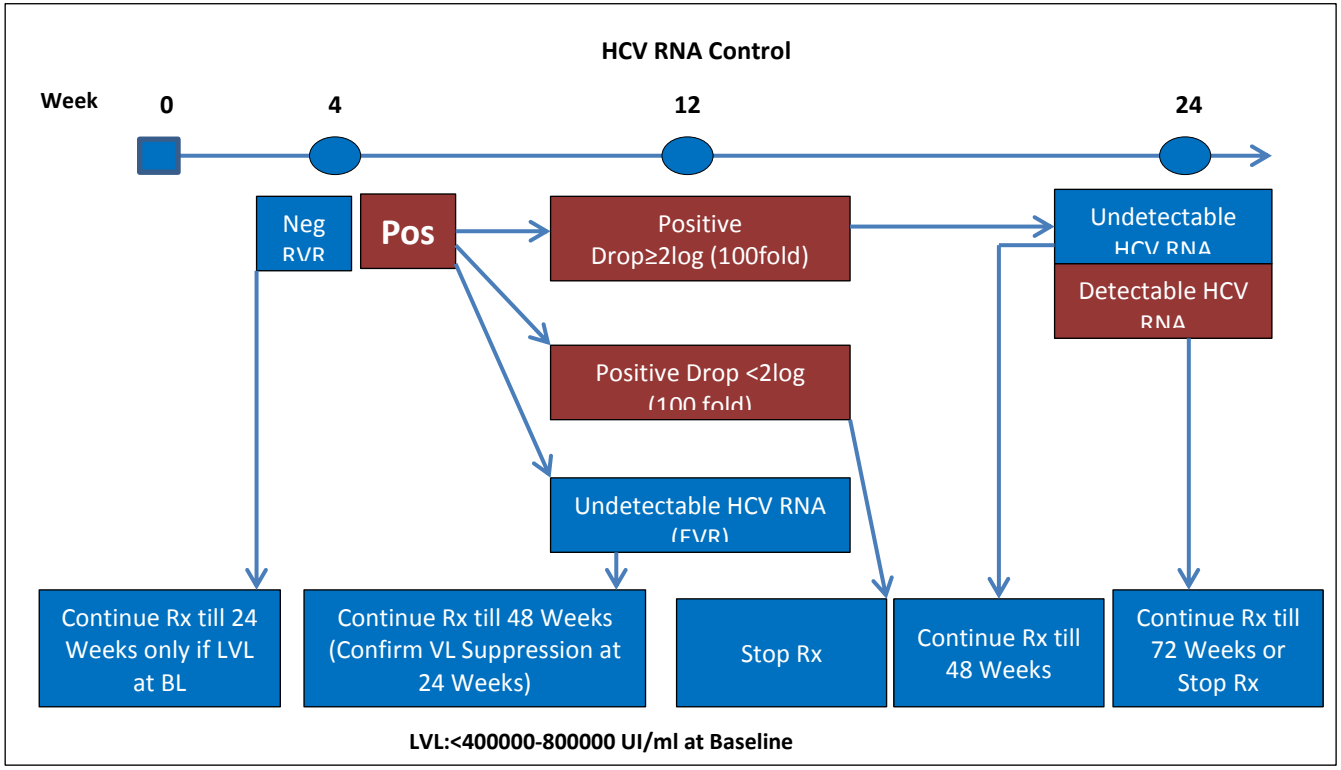
Ribavirin is predominantly excreted by the kidneys and the drug should

normally not be used in patients with a creatinine clearance <50mL/min. On an individual basis ribavirin may be administered cautiously to patients with renal failure. This requires careful monitoring of hemoglobin and plasma ribavirin levels and this treatment should be centralized at referral centers.

4.5. HCV Infected Patient Monitoring

Patients treated with pegylated IFN-a and ribavirin should be seen at a minimum of weeks 4 and 12 after initiation of treatment then at a minimum of every 12 weeks until the end of treatment for both efficacy and side effects, and 24 weeks after the end of therapy to assess the SVR.

4.5.1. HCV-RNA Response Guided Therapy



4.5.2. Virologic Monitoring of on-Therapy Response to PegIFN+ RBV

Sustained Virological response (SVR)	**Undetectable HCV RNA level (<50 IU/ml), 24 weeks after treatment**
Rapid Virological Response (RVR)	Undetectable HCV in a sensitive essay (lower limit of detection ≤50 IU/ml) at week 4 of therapy, maintained up to end of treatment
Early Virological Response (EVR)	HVC detectable at week 4 but undetectable at week 12, maintained up to end of treatment
Delayed Virological Response (DVR)	More than $2\log_{10}$ drop but detectable HCV RNA at week 12, HCV RNA undetectable at week 24, maintained up to end of treatment
Null Response (NR)	Less than 2 $\log_{10}$ IU/ml decrease in HCV RNA level from baseline at 12 weeks of therapy
Partial Nonresponse (PR)	More than 2 $\log_{10}$ IU/ml decrease in HCV RNA level from baseline at 12 weeks of therapy but detectable HCV RNA at week 12 and 24
Breakthrough (BT)	Reappearance of HCV RNA at any time during treatment after virological response

4.5.3. Most Common HCV Treatment Side Effects

Side effects are observed in almost 80% of patients receiving peginterferon (PEG-IFN) and ribavirin (RBV) combination therapy for chronic hepatitis C virus (HCV) infection.

Both interferon-alpha and ribavirin have a number of side effects.

Molecule	Side Effects
Interferon	- Fever, Fatigue, - Muscle/joint pain, - Nausea, Diarrhea, Dry mucosa - Psychic instability, Depression, Aggravation of preexisting epilepsy. - Bone marrow depression, - Visual disturbance, - Hyper- and hypothyroidism dermatitis, Alopecia
Ribavirin	Anemia and may cause dyspepsia and rash. Birth defects have been produced in animal experiments and contraception should be used during treatment and until 4 month after (female)/7 month after (males) end of treatment
Sofosbuvir	Fatigue and Headache
Simeprevir	Rash (including a potentially serious photosensitivity reaction), Pruritus, and Nausea

4.5.4. Monitoring Plan of Patient on HCV Therapy

Monitoring Plan During Treatment for HCV Infection									
	Weeks of Treatment								
Test	Baseline	2	4	8	12	16	20	24	24-48
CBC	X	X	X	X	X	X	X	X	X
LFTs	X		X	X	X	X	X	X	q4Wk
Metabolic Panel	X		X	X	X	X	X	X	q4Wk
HCV RNA	X		X		X			X	q12Wk
TSH	X				X			X	q12Wk
Depression	X	X	X	X	X	X	X	X	Ongoing
Ophthalmologic Exam	X				X			X	q12 Wk
Prothrombin Time	X					X			q12 Wk
Pregnancy Test	Perform at regular intervals if appropriate								

4.5.5. Contraindication to HCV Treatment (IFN-RBV Based)

The following are the absolute contraindications to treatment:

1. Severe uncontrolled psychiatric disease,
2. Decompensated cirrhosis,
3. Advanced cardiac or pulmonary disease,
4. Autoimmune liver disease,
5. Insufficiently controlled epilepsy,
6. Untreated severe anemia
7. Poorly controlled diabetes.
8. Pregnancy, or insufficient use of contraceptives, is a contraindication to treatment (Ribavirin). Contraception must be used until 4 months after treatment for women and 7 months for men.
9. Precautions must be taken when treating cirrhotic patients with prior decompensation, or those with neutrophils $<0.75x10^9/L$ or platelets <50 $x10^9/L$, and when treating patients with poorly controlled diabetes.
10. Patients with alcohol overconsumption and/or ongoing drug abuse will often have considerable problems with compliance. Alcohol may decrease the chances of SVR and injecting drug users have a risk of repeated infection.
11. Ribavirin is contraindicated in patients with renal insufficiency (creatinine clearance <50ml/min). However treatment with low dose ribavirin and frequent monitoring of hemoglobin and plasma ribavirin concentration may be considered in some cases

Patients with unstable cardiopulmonary disease, pre-existing anemia not responding to Erythropoietin or in case of hemoglobinopathy, may be treated with pegylated interferon monotherapy though the optimal therapy remains the combination of pegylated interferon with Ribavirin.