MINISTRY OF HEALTH

NATIONAL GUIDELINES FOR HIV/AIDS TREATMENT AND CARE

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GUIDELINES DEVELOPMENT GROUP

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FOREWORD

Application of antiretroviral (ARVs) treatment of HIV infection has been expanded and there is more scientific evidence regarding the effectiveness of ARV treatment. Good adherence to ARV treatment by people living with HIV helps improving their quality of life as well as reducing transmission to others. In order to enhance the efficiency of antiretroviral treatment (ART), the linkages between counselling, testing and early antiretroviral therapy initiation have been implemented in many countries. In 2016, the World Health Organization (WHO) issued consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. In the new guidelines, clinical recommendations are integrated into the implementation and management of on-going HIV/AIDS treatment and care program. The 2017 WHO Guidelines have supplemented new evidence on the combinations of antiretroviral drugs in treatment of HIV/AIDS, management of new disease models in HIV - positive individuals, including co-infections and non-communicable diseases (NCDs).

Current evidence suggests that the antiretroviral treatment program is being effectively implemented, with growing number of patients on ART and over 90% of HIV - positive individuals receiving ART have achieved viral suppression.

Based on the Recommendations included in the 2016 and 2017 Guidelines of the World Health Organization (WHO), these Guidelines for HIV/AIDS treatment and care, which aim at providing early diagnosis and treatment of HIV infection, and comprehensive care for HIV - positive individuals, have been issued by the Ministry of Health. In this document, update information on new antiretroviral (ARVs) used in HIV/AIDS treatment is integrated in order to improve the effectiveness of the HIV/AIDS treatment program in Vietnam.

The Guidelines Development Group looks forward to receiving feedback from individuals and units during the implementation, so that adjustments and additions can be timely made.

Thank you.

CONTENTS

ABBREVIATIONS

Vietnamese

BC	White blood cell
PLTMC	Prevention of mother-to-child transmission of HIV
NTCH	Opportunistic infections
PHMD	Immune reconstitution
SDD	Malnutrition
TC	Symptoms
TKT	Central nervous system
VG B	Hepatitis B
VG C	Hepatitis C
VK	Bacteria
VMN	Meningitis
XN	Test

English

3TC	Lamivudine
ABC	Abacavir
ADN	acid desoxyribonucleic
AFB	acid fast bacilli
AIDS	acquired immunodeficiency syndrome
ALT	alanin aminotransferase
Anti - HBc	antibody to hepatitis B core antigen
Anti - HCV	antibodies against hepatitis C virus
APRI	AST to Platelet Ratio Index
ARN	acid ribonucleic
ARV	antiretroviral
AST	aspartate aminotransferase
ATV	Atazanavir
BCG	Bacillus Calmette–Guérin
CD4	Lympho T CD4
CMV	Cytomegalovirus
CTX	co-trimoxazole
DCV	Daclatasvir
DRV	Darunavir
DTG	Dolutegravir
EFV	Efavirenz
ELISA	enzyme - linked immunosorbent assay
FTC	Emtricitabine
HBeAg	hepatitis B envelope antigen
HBsAg	hepatitis B surface antigen
HIV	human immunodeficiency virus

INH	Isoniazid
LDV	Ledipasvir
LIP	lymphoid interstitial pneumonia
LPV	Lopinavir
LPV/r	lopinavir/ritonavir
MAC	Mycobacterium avium complex
NNRTI	non - nucleoside reverse transcriptase inhibitor
NRTI	nucleoside reverse transcriptase inhibitor
NtRTI	nucleotide reverse transcriptase inhibitor
NVP	Nevirapine
OPV	oral polio vaccine
PCP	Pneumocystis jiroveci pneumonia
PCR	Polymerase chain reaction
SOF	Sofosbuvir
RAL	Raltegravir
RPV	Rilpivirine
PI	protease inhibitor
TDF	tenofovir disoproxil fumarate
TMP - SMX	trimethoprim – sulfamethoxazol
VEL	Velpatasvir
ZDV	Zidovudine

CHAPTER I
HIV COUNSELLING AND TESTING

1. Principles for HIV counselling and testing

All forms of HIV testing and counselling should be voluntary and adhere to the following 5 principles: **consent, confidentiality, counselling, correct test results and connections to care, treatment and prevention services.**

Consent: People receiving HIV testing must give informed consent to be tested and counselled, and HIV testing should only be done with their consent (except cases where testing is mandatory).

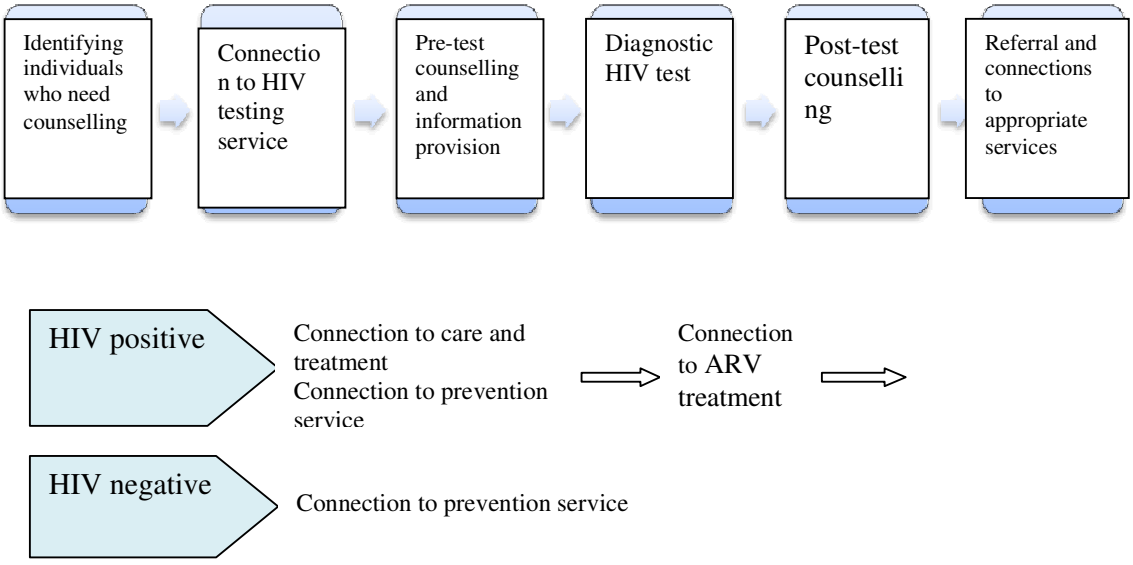
Confidentiality: Personal information of people receiving HIV counselling and testing is kept confidential.

Counselling: People receiving HIV testing must be provided with pre-test information counselling.

Correct test results: Standard Operating Procedures for HIV Testing and national approach to HIV testing should be strictly applied by testing providers, to ensure accuracy of test results.

Connections to care, treatment and prevention services: individuals diagnosed with HIV infection should be referred to care, treatment and prevention services without delay.

Diagram 1. Connections to care, treatment and prevention services



2. Individuals who need HIV counselling and testing

Individuals who need HIV counselling and testing include people who inject drugs, female prostitutes, men who have sex with men (MSM), transgender people; tuberculosis patients; people affected by sexually transmitted infections; pregnant women; spouse/children of HIV

- positive individuals; siblings of HIV positive children, people exposed to HIV, persons who have unprotected sex with drug addicts whose HIV status is inconclusive, and sex workers; HCV infected individuals; patients whose clinical assessment and paraclinical test results fail to determine the cause of illness, but present symptoms suggestive of HIV infection.

Other idividuals who voluntarily wish to get HIV counselling and testing.

3. Forms of HIV counselling and testing

3.1. At a health facility

Voluntary and provider-initiated testing for HIV: testing provided by health workers.

3.2. Community-based HIV counselling and testing

Community-based HIV counselling and testing models include HIV self-testing and testing provided by community health workers.

HIV self-testing is a process whereby a person who wants to know his or her HIV status collects a specimen, performs a test and interprets the test result in private. HIV self-testing can be either assisted or unassisted by community health workers.

Testing provided by community health workers: provided by community or hamlet health workers who have got basic training in HIV testing.

HIV self-testing is only used for initial screening. It does not provide a HIV-positive diagnosis; any reactive (positive) self-test result should be confirmed as per regulations.

4. HIV counselling and testing for adults and children above 18 months in health care settings

Application of HIV testing strategy III.

Procedures:

- Pre-test counselling

-Collecting specimens for HIV testing once informed consent has been obtained.

- Performing diagnostic HIV tests

- Post-test counselling and reruning test results

HIV antibody screening test:

Negative test result: the client should be given counselling and the negative test results. Clients suspected of being in the window period should return for retesting after 3 months. High risk clients should be provided with counselling and advised to return for retesting after 6 months.

Reactive (positive) test result: explanation on the need of retesting should be provided to the client. Blood sample could be taken and sent to the confirmatory laboratory or the client referred to the confirmatory laboratory for retesting. For a pregnant woman, if a rapid HIV test result in labor is reactive, counselling

should be given for antiretroviral (ARV) prophylaxis for the prevention of mother-to-child transmission of HIV without delay.

HIV confirmatory tests: shall be performed at HIV confirmatory labs certified by the Ministry of Health.

Negative test results: counselling provided and test result returned to the client, with confirmation that they are not infected with HIV. Clients suspected of being in the window period should return for retesting after 3 months. Clients of high risk population should be provided with counselling and advised to return for retesting after 6 months.

Indeterminate test results: the presence of HIV antibody is not identified. In this case the client should be given counselling and explanation that his/her HIV status is inconslusive, and advised to return for retesting after 14 days.

Positive confirmatory test result: post-test counselling should be provided and confirmation of HIV infection given. Client should be given the test result and referred to an HIV treatment service and other appropriate services.

5. Early Diagnosis of HIV in Children less than 18 months of age

5.1. Testing

PCR-based assays to detect viral nucleic acid (HIV DNA/RNA) should be performed for HIV- exposed children younger than 18 months within four to six weeks of birth, or at the earliest opportunity thereafter.

5.2. Individuals who need HIV testing

Children born to HIV positive mothers.

Children born to mothers with unknown HIV status, who present symptoms suggestive of HIV infection or are clinically diagnosed with severe HIV / AIDS

5.3. Testing algorithm

See details in Annex 1: Algorithm for early diagnosis of HIV in children less than 18 months of age.

Pre-test counselling/information provision for caregivers.

Type of test used depends on the age of the infant and the mother's HIV status:

Infants born to HIV positive mothers: for infants less than 9 months of age, collect blood samples as the dried blood spots (DBS) for PCR test. For children 9 - 18 months: HIV antibody test should be done first; if test result is positive (reactive), collect dried blood spots for PCR test.

Children born to mothers with unknown HIV status, who present symptoms suggestive of HIV infection or are clinically diagnosed with severe HIV / AIDS: HIV antibody test should be done first; if test result is positive (reactive), collect dried blood spots for PCR test.

Note: The mother should be given counselling on HIV antibody testing if her HIV status is unknown whereas the infant present signs suggestive of infection.

5.4. Explanation and management of PCR test results

5.4.1. Initial PCR test result negative

a. Nonbreastfed children: assume uninfected, HIV antibody test at 9 months of age is required. If negative test result: the child is not HIV infected. If reactive test result: repeating of HIV antibody test is required at 18 months of age to determine HIV status. For children with signs suggestive of HIV: repeating of PCR test is required.

b. Children ever breastfed or currently breastfeeding

Well, exposed infants: HIV antibody tests at 9 months of age and 3 months after breastfeeding cessation.

Negative antibody results: assume uninfected, re-testing is required at 18 months of age if still breastfeeding.
Reactive results: repeating PCR test is required. If the PCR test result is positive, initiate counselling and ART immediately. If the PCR test result is negative, repeating of HIV antibody test is required at 18 months of age to determine HIV status.

Infant or child with signs or symptoms suggestive of HIV:

Infant or child less than 9 months of age: second round PCR test is required. If test result is positive, immediately provide counselling and initiate ART. If test result is negative, monitoring should be applied and repeating of HIV antibody test is required at 18 months of age to determine HIV status.

Infant or child over 9 months of age: HIV antibody test is required. For a child with reactive test result, second PCR test is required. For a child with negative HIV antibody test result, monitoring should be applied and repeating of HIV antibody test is required at 18 months of age to determine HIV status.

5.4.2. Initial PCR test result positive

For infants with an initial positive PCR test result, it is recommended that ART be started without delay and, at the same time, a second specimen be collected to confirm the initial positive test result, to determine the child's HIV status. Parents should be given HIV counselling and testing if their HIV status is inconslusive.

5.4.3. Second PCR test result positive

The child's HIV infection is confirmed and parents/caregiver should be given counselling on the importance of the continuation of ART and treatment adherence.

5.4.4. Initial PCR test result positive and second PCR test result negative

Explanation on reasons why the child's HIV status has not been confirmed will be given, and third PCR test done. If third test result is negative, discontinue ARV treatment.

Note:

1. For children less than 18 months of age with positive antibody results and at the same time, presenting signs of oral candidiasis, severe pneumonia, severe infections or any other illnesses associated with AIDS, it is recommended that

ART be started while waiting for the results of the confirmatory test. If the test result confirms that the child is not HIV infected, discontinue ARV treatment.

2. Early-treated children may have negative HIV antibody results. Therefore HIV antibody test is not recommended for confirmation or exclusion of HIV infection in children on ARV treatment.

6. Connections to care, treatment and prevention services

6.1. Referring clients with high risk behaviors to HIV counselling and testing services

Identification of target groups that need HIV counselling and testing: find information on the groups, their common characteristics via different channels.
Communication on the benefits of awareness of HIV status and benefits of early ARV treatment, on HIV counselling and testing services, community –based HIV prevention, treatment and care services should be conducted, appropriate to each group.
Approach high risk persons via HIV - positive individuals, peer groups, commune or hamlet health workers, social networks, to give them HIV counselling and refer them to appropriate HIV counselling and testing services.

6.2. Referring individual receiving HIV testing to appropriate services

6.2.1. Individuals who test negative

It is recommended that HIV transmission risks and the client's health care needs be assessed and referral to appropriate services made. Clients should be referred to HIV prevention services, including opioid replacement therapy, condom distribution programs, clean needle and syringes programs, etc. for retention of negative HIV status.

Other socio-psychological support services.

6.2.2. Individuals who test positive

Refer HIV - positive individuals to HIV prevention, treatment and care services, including opioid replacement therapy, condom distribution programs, and clean needle and syringes, etc.

Refer HIV - positive individuals to other appropriate services, including counselling, productive health care support, family planning, job support services, legal counselling, etc.

6.3. Post-referral monitoring

The referring provider shall contact the services patients have been referred to by phone, sms, email, feedback forms. Referral results shall be entered in referral registration book. If an HIV - positive individual does not present at the care and treatmetn service, health workers shall coordinate with the HIV/AIDS focal point unit in the area or community outreach group to meet the person to support early ARV treatment.

7. Clinical staging of HIV disease in adults, adolescents and children

Clinical staging of HIV disease is applied as per Annex 2. It is recommended that clinical staging of HIV disease be done at every appointment to health care facility, to evaluate immunodeficiency status, monitor disease progression, and decide when to start or discontinue co-trimoxazole prophylaxis.

8. Diagnostic criteria for advanced HIV, including AIDS

Advanced HIV disease is defined as follows:

For adults and children ≥5 years old, advanced HIV disease is defined as the presence of a CD4 cell count <200cells/ mm^3 or a WHO clinical stage 4.
All children younger than 5 with HIV infection are considered as having advanced HIV disease.

AIDS is the advanced stage of HIV infection AIDS, when HIV-positive individuals are in clinical stage 4 and/or with CD4+ cell count of ≤ 200 cells/mm^3.

CHAPTER II
ANTIRETROVIRAL TREATMENT (ART)

1. Goals of antiretroviral treatment (ART)

Maximizing the long term prevention of HIV replication;

Immune reconstitution.

2. Benefits of early ARV treatment

Reduction of HIV- related morbidity and mortality risks;

Prevention of HIV transmission to others (partners/ peers in the drug use group);

Prevention of mother-to-child transmission of HIV.

3. Principles for ARV treatment

ART should be started as soon as a patient receives a diagnosis of HIV;

Use of the most appropriate combinations of at least three antiretroviral drugs;

Adherence to lifelong, continuous daily treatment is recommended;

4. ARV treatment

4.1. Preparation for ARV treatment

Things to be done prior to initiation of ARV treatment:

Assessment of opportunistic infections, comorbidities, nutrition, and other health conditions (if any) in patients, especially TB and HCV, as well as drug - drug interactions, to inform the choice of ARV regimens or dosing adjustments;

Counselling on the benefits of ARV treatment in improving health, reducing the possibility of mother-to-child transmission of HIV and transmission of HIV to others, particularly sexual transmission of HIV, should be conducted.

Patients should be informed of treatment adherence requirement, possible side effects, follow-up appointments and medication dispensing schedule, testing required prior to therapy commencement and treatment monitoring. For HIV positive children, including adolescents, appropriate timing for disclosure of HIV status should be considered.

It is recommended that testing be reviewed and supplemented as per regulations, including confirmatory tests or positive PCR test results of children less than 18 months of age;

Talking with patients, treatment supporters or children's caregivers about their wishes regarding treatment, treatment adherence issues, and appropriate solutions should be made.

Counselling on other HIV prevention measures, including safe sex, opioid replacement therapy, use of clean needles and referral to HIV prevention services should be conducted;

Advising patients to persuade their spouse/sex partner/peers in the drug use group, children born to HIV positive mothers, and siblings of HIV positive children to get HIV testing.

4.2. Eligibility Criteria for initiating ARV therapy

ART should be started as soon as a patient receives a diagnosis of HIV, regardless of his or her CD4 cell count and clinical stage.

Children less than 18 months of age with initial positive PCR test results, or positive antibody results, together with signs of oral candidiasis, severe pneumonia, severe infections or any other illnesses associated with AIDS. It is recommended that ARV treatment discontinued when test result confirms that a child is not HIV infected.

For an infant born to mother with positive antibody test performed during labor, delivery or while breastfeeding: it is recommended that counselling and ARV treatment provided for the mother without delay, and HIV confirmatory test done. Discontinue ARV treatment if HIV confirmatory test result is negative.

4.3. First line ARV treatment

4.3.1. First line ARV regimens

Table 1: First line ARV regimens

First line ARV regimens	Preferred regimen	Alternative regimens
Adults ≥ 19 years old	TDF + 3TC (or FTC) + EFV	TDF + 3TC (or FTC) + DTG TDF + 3TC (or FTC) + NVP AZT + 3TC + EFV AZT + 3TC + NVP
Pregnant and breastfeeding women	See details in 4.5: Antiretroviral (ARV) prophylaxis for the prevention of mother-to-child transmission of HIV	
Adolescents (10 - 19 years old)	TDF + 3TC (or FTC) + EFV	TDF + 3TC (or FTC) + DTG ABC + 3TC (or FTC) + DTG ABC + 3TC (or FTC)+ EFV TDF + 3TC (or FTC) + NVP AZT + 3TC + EFV AZT + 3TC + NVP
Children 3 - 10 years old	ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + EFV AZT + 3TC + NVP
Children under 3 years old	ABC + 3TC + LPV/r	AZT + 3TC + LPV/r ABC + 3TC + NVP

		AZT + 3TC + NVP

Note: Currently DTG is indicated for the treatment of HIV in children aged over 12 years. In certain cases, due to drug toxicity or interactions, an NNRTI drug can be replaced by ABC or PIs in HIV treatment in adults. See Annexes 4, 5, 6, 7, 8 for dosaging.

4.3.2. ARV treatment of TB and HIV coinfection

Table 2: ARV treatment in children < 10 years old with TB and HIV coinfection

Initiation of ARV therapy in children during TB treatment		
Children < 3 years old		ABC + 3TC + NVP (ensure dose of 200 mg/m^2 body surface area (BSA) or: AZT + 3TC + NVP (ensure dose of 200 mg/m^2 BSA) or Three NRTI drugs (AZT + 3TC + ABC)
Children ≥ 3 - 10 years		ABC + 3TC + EFV or: AZT + 3TC + EFV or: Three NRTI drugs (AZT + 3TC + ABC)
ARV regimens in children diagnosed with tuberculosis while receiving Antiretroviral Therapy		
Children receiving NRTI + EFV or NVP	Children < 3 years old	- Combination of two NRTI drugs + NVP (ensure dose of 200 mg/m^2 BSA) or: - Three NRTI drugs (AZT + 3TC + ABC)
	Children ≥ 3 years old	- Continue with the regimen if the child is receiving EFV - If the child is receiving NVP, replace it with EFV Or: - Three NRTI drugs (AZT + 3TC + ABC)
Children receiving PI -containing regimen (two NRTI drugs + LPV/r)	Children < 3 years old	- Three NRTI drugs (AZT + 3TC + ABC) or: - Continue with LPV/r, increasing RTV dosing to a 1:1 ratio with LPV
	Children ≥ 3 years old	**If the child has not failed NNRTI-based regimen** - Replace LPV/r with EFV, or: - Three NRTI drugs (AZT + 3TC + ABC),

		or: - Continue with LPV/r, increasing RTV dosing to a 1:1 ratio with LPV. **If the child has failed NNRTI-based regimen**: - Three NRTI drugs (AZT + 3TC + ABC) Or - Continue with LPV/r, increasing RTV dosing to a 1:1 ratio with LPV

Body surface area calculation:

$$\text{Body surface area } (m^2) = \sqrt{\frac{\text{Height (cm) x weight (kg)}}{3600}}$$

Table 3: ARV treatment in adults and adolescents with TB and HIV coinfection

Initiation of ARV therapy during TB treatment	
Adults and adolescents	2 NRTI + EFV
Pregnant and breastfeeding women	2 NRTI + LPV/r (or EFV) (Adjust the dose of LPV/r as below)
ARV regimens in patients diagnosed with tuberculosis while receiving Antiretroviral Therapy	
Those receiving 2 NRTI drugs + EFV or NVP	2 NRTI + EFV
Those receiving PI -containing regimen (2 NRTI drugs + LPV/r)	Increasing the dose of RTV to a LPV:RTV 4:4 ratio (LPV400mg/RTV400mg) twice daily or: Doubling the dose to a LPV:RTV ratio 8:2 (LPV800mg/RTV 200mg) twice daily

It is recommended that TB treatment should be commenced first and ART subsequently commenced as soon as possible and within the first eight weeks of

starting TB treatment. For patients with severe immunodefficiency (CD4 < 50 cells/mm³) ARV therapy should start within the first 2 weeks of starting TB treatment.

It is recommended that during treatment of TB and HIV coinfection, assessment of interactions between ARV drugs, TB drugs and other drugs, of treatment adherence and tuberculosis - associated immune reconstitution inflammatory syndrome be conducted.

After discontinuation of rifampicin therapy:

Switch back to previous regimen (2NRTI + 1 NNRTI) instead of regimen containing AZT + 3TC + ABC (3 NRTI drugs)

Switch back to the unadjusted LPV/r dosage.

4.4. Testing before and during ARV treatment

Table 4: Testing before and during ARV treatment

Timing for HIV treatment	Tests
When patients register for treatment	CD4 Blood count, creatinine, AST, ALT HBsAg, anti -HBs, anti - HCV Other tests as per clinical indications
During ARV treatment	Creatinine tests every 6 - 12 months for patients receiving TDF or presenting signs of kidney dysfunction. Blood count test every 6 - 12 months for patients receiving AZT or with signs of anaemia. AST, ALT, blood lipid, blood glucose testing: every 6 – 12 months. HIV viral load: - Routine testing: at 6 months and 12 months after initiation of ARV treatment and every 12 months thereafter. For cases where viral load testing is not available at such time, it should be done at the earliest opportunity thereafter. - Cases presenting signs of clinical or immunological failure, or HIV viral load is 200 - <1000 copies/mL. - Women getting pregnant while on ART: it is recommended that viral load testing be conducted as soon as pregnancy is detected. If testing has been conducted within one month prior to detection,

	retesting is not required. - Breastfeeding women: it is recommended that viral load testing be conducted every 3 – 6 months. CD4: testing should be conducted every 6 months if routine viral load testing is not available or patient is receiving prophylaxis for opportunistic infections (primary or secondary). Anti – HCV testing once a year if the previous test result is negative and there is HCV infection risk. HBsAg test is indicated for patients with treatment failure who are taking a TDF containing regimen. Other tests depending on clinical indications and treatment regimens currently applied to patients.

For children on TDF containing regimens additional tests shoud be conducted:

- Electrolytes - urine test when abnormal blood levels of electrolytes are detected, including that of phosphorus;

- 24-hour urine protein test in cases with abnormal urinalysis results;

- 25-OH vitamin D in cases with abnormal phosphorus level.

4.5. Antiretroviral (ARV) prophylaxis for the prevention of mother-to-child transmission of HIV

4.5.1. Maternal antiretroviral therapy

a. Aims of ARV treatment in HIV-positive pregnant women

It is recommended that ARV treatment be initiated as soon as possible for pregnant women receiving a diagnosis of HIV to ensure maximum prevention of mother-to-child transmission of HIV. ARV treatment in pregnant women aims at achieving viral suppression, and it would be best if viral load is brought below the limits of detection using the most sensitive assay, in the third trimester of pregnancy at the latest, especially before the onset of labor.

Monthly monitoring of HIV-positive pregnant women is advised, and especially close to the estimated delivery date.

b. Events

Events	Management
1. Planning to have baby while on ARV treatment	Continue with current ARV treatment, at the same time providing adherence support. Advise that the best time is when viral load is below the limits of detection using the most sensitive assay.

2. Pregnant women with HIV diagnosis, not receiving ART treatment	Start ARV treatment without delay, as soon as possible: 1. Fetal age < 24 weeks: Initiation of regimen as for adults [*]: Preferred regimen: TDF + 3TC + EFV 2. Fetal age ≥ 24 weeks: cases receiving diagnosis of HIV close to the estimated delivery date or having reactive HIV antibody test result during labor: TDF+ 3TC (FTC) + RAL. If RAL is not available, switch to regimen: TDF +3TC + ATV/r (or LPV/r). If PI drugs are not available: TDF + 3TC + EFV
3. Women getting pregnant while on ARV	HIV viral load test should be performed without delay when pregnant: 1. If HIV viral load is < 1000 copies/ml: Continue with the current regimen. 2. If HIV viral load ≥ 1000 copies/ml and fetal age ≥ 24 weeks: adherence support, consultation and switch to regimens containing RAL or PI drugs (ATV/r or LPV/r). 3. Cases with viral load ≥ 1000 copies/ml and fetal age < 24 weeks: adherence support, HIV viral load testing after one month. Consider alternative regimens, depending on viral load test result. Cases where HIV viral load testing is not available: 1. No clinical and immunological failure: continue with current ARV regimen. 2. With clinical or immunological failure: consultation, switch to a second-line regimen containing PI drugs (ATV/r or LPV/r) or RAL.
4. ARV treatment after delivery	1. Continue with the current ARV regimen. Provide the mother with ART without delay if she has not received ARV treatment. 2. Cases on regimens containing RAL or PI drugs (ATV/r or LPV/r) not due to treatment failure: - No breastfeeding: provide counselling, switch to a first line regimen as for HIV positive adults. - Breastfeeding women: counselling provided and switching to a first line regimen as for HIV positive adults if viral load is below the limits of detection

	using the most sensitive assay in two consecutive tests, or after breastfeeding ends.

*: Initiation of NVP-containing regimens in women with CD4 cell counts ≥250 cells/ml is not recommended.

4.5.2. ARV treatment in children

Table 5: ARVs and duration of prophylaxis in children born to HIV-positive mothers

High risk of mother-to-child transmission of HIV *	Feeding	Prophylaxis and duration
No	Breastfeeding or no breastfeeding	NVP: for 6 weeks after birth
Yes	No breastfeeding	NVP + AZT: for 6 weeks after birth
	Breastfeeding	NVP + AZT: for 12 weeks after birth

**The risk of mother-to-child transmission of HIV is high in the following cases:*

1) The mother has received ARV treatment antenatally for less than 4 weeks or no ARV treatment; 2) HIV viral load > 1000 copies / mL during pregnancy; 3) is diagnosed with HIV during labor or delivery or while breastfeeding.

Note:

1. Start ARV prophylaxis for the infant as soon as possible after birth.

2. If the newborn is over 72 hours old, has not received ART and is not breastfeeding, no ARV treatment is required. If the baby is breastfeeding, it is recommended that the baby start ARV prophylaxis without delay and continue until 12 weeks after birth.

3. In the case where a breastfeeding woman experiences ARV treatment interruptions, regardless of reason, prophylaxis should be provided for the baby and only discontinued after the mother has restarted ART for 6 weeks. If the mother does not receive ART again or the treatment duration is less than 6 weeks, it is recommended that the baby continue taking ARVs until one week after breastfeeding cessation.

4. If the mother has reactive result of HIV antibody test performed during labor or delivery, counselling on ARV prophylaxis for the baby should be provided. Stop prophylactic treatment if afterwards the mother's confirmatory test result is negative.

Table 6: NVP + AZT prophylaxis dosing for infants born to HIV positive mothers

Age	**Daily dose**	**Recommended daily oral AZT dose**
From birth to 6 weeks		
Birth weight < 2000 g	2 mg/kg once daily	2 mg/kg x 02 times

		daily
Birth weight 2000 - 2499g	10 mg once daily	10 mg x 02 times daily
• Birth weight ≥ 2500 g	15 mg once daily	15 mg x 02 times daily
> 6 weeks - 6 months*	20 mg once daily (2ml syrup once daily or half of 50mg tablet)	Dose of 60mg x 2 times daily (6ml syrup or one 60mg tablet 2 times daily)

4.5.3. Counselling on feeding infants born to HIV positive mothers

Infant and young child feeding counselling should be conducted prior to delivery and depends on the mother's financial conditions and her family; benefits and risks of each feeding choice as well as measures that should be taken should also be considered to ensure maximum prevention of breastmilk transmission of HIV.

Breastfeeding: the mother must be on antiretroviral treatment (ART) and ensure treatment adherence to achieve viral suppression, and it would be best if viral load is below the limits of detection using the most sensitive assay.

Use of breastmilk substitutes: can be chosen on condition that the following requirements are met:

- Sufficient provision of breastmilk substitutes in the first 6 months is ensured, as well as availability of safe drinking water and safe, hygienic preparation of breastmilk substitutes with quantities appropriate to newborn age.
- Family support is available.

5. Monitoring response to ART and diagnosis of treatment failure

5.1. Monitoring response to ARV treatment, follow-up appointments and prescription of medicines

5.1.1. Monitoring clinical response

Monitoring clinical response should be conducted at every follow-up appointment:

- Body weight and clinical stages:

- New or recurrent opportunistic infections: The condition must be differentiated from side effects of ARVs, immune reconstitution inflammatory syndrome occurring after initiating ART, or treatment failure so as appropriate measures can be applied;

Patients responding well to ARV when:

- They gain weight, get appetite back and have good appetite;

- Signs of OIS and HIV-related diseases have disappeared.

5.1.2. Monitoring immune responses

Monitoring immune responses is monitoring the CD4 count changes, especially on two consecutive CD4 measurements; it is one of the parameters to assess response to ARV treatment (See Table 7: Immunological criteria for identifying ART treatment failure).

Monitoring immune responses is conducted when a patient cannot access routine viral load testing, and/or when her/his ARV treatment has not stablilized.

See Table 4 for timing and frequency of CD4 testing.

5.1.3. Virological monitoring

Virological monitoring is conducted through routine viral load monitoring. Routine HIV viral load testing is the best method to monitor response to ARV treatment, and by thus doing, assess treatment adherence and early identify virological treatment failure.

See Table 4 for timing and frequency of viral load testing.

5.1.4. Criteria for defining patients who are stable on ARV treatment

Criteria for stable patients on ARV treatment include:
- Adults who have been receiving ARV for at least one year;
- Results of two consecutive viral load tests are under 200 copies/mL. In cases where viral load testing is not available, rising CD4 counts or CD4 counts above 200 cells/mm3;
- No pregnancy
- No breastfeeding;
- No drug side effects;
- No opportunistic infections or other HIV-related illnesses;
- Good treatment adherence.

5.1.5. Frequency of follow-up appointments, repeat prescriptions and ARV dispensing

For patients who are stable on ARV treatment: follow-up appointments, prescriptions and dispensing of medication, with the maximum 90 days of drug supply prescription could be applied.

For patients with advanced disease: monthly follow-up appointments or at shorter intervals, with the maximum 30 days of drug supply prescription.

5.2. ARV treatment failure

5.2.1. Categories of treatment failures

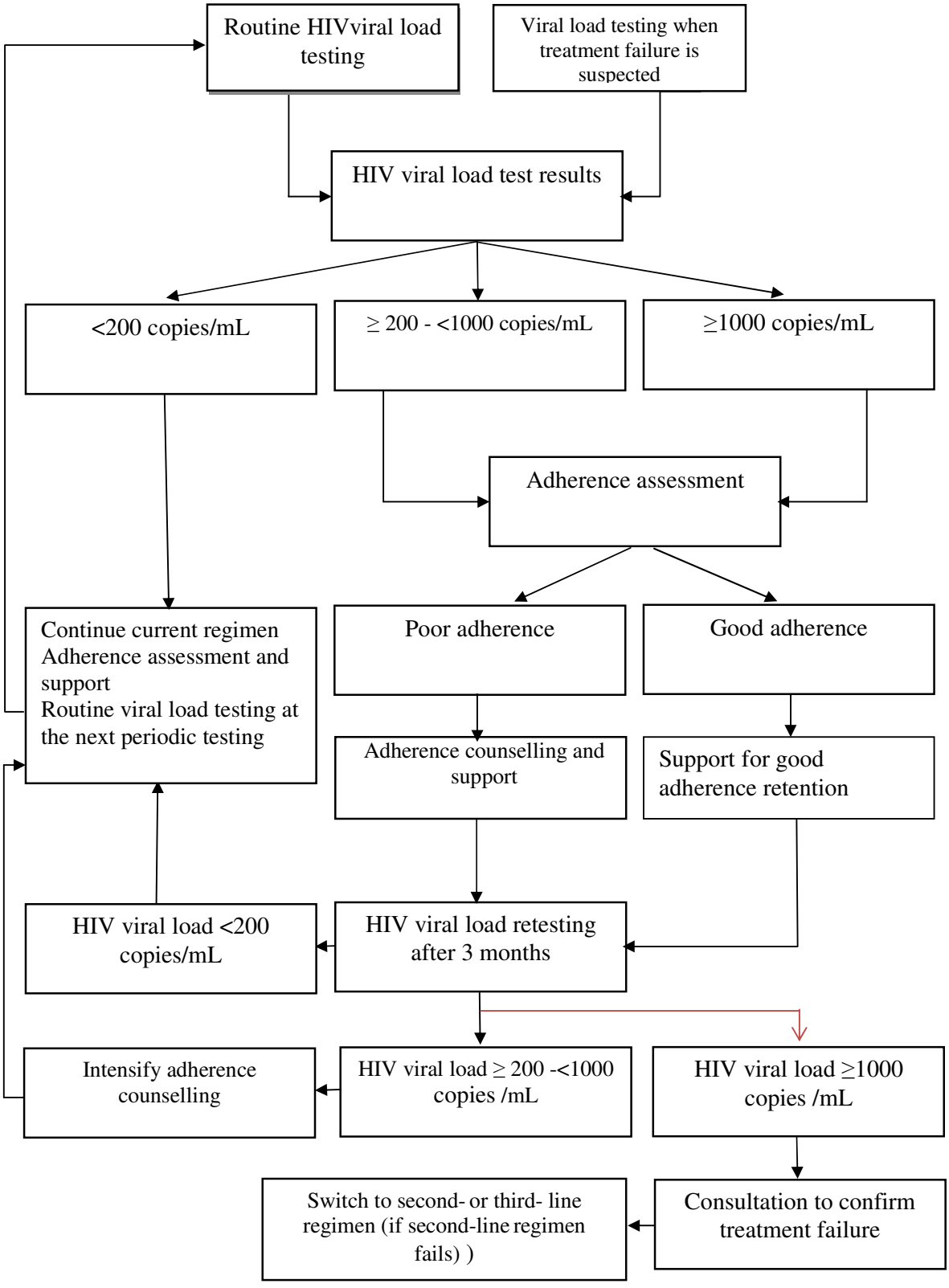
Table 7: Immunological criteria for identifying ART treatment failure

Categories of treatment failures	Criteria
Clinical failure	Adults and adolescents: New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 conditions) after 6 months of effective treatment. Children less than 10 years old: New or recurrent clinical event (WHO clinical stage 3 and 4 clinical conditions) after 6 months of effective treatment
Immunological failure	Adults and children over 10 years old: CD4 count falls to the baseline (or below) or persistent CD4 levels below 100 cells/mm^3 with a CD4 count drop to ≤ pretreatment levels or CD4 count below 100 cells/mm^3 in two consecutive tests (with 6 months interval), and without concomitant or recent infection to cause a transient decline in the CD4 cell count Children 5 - 10 years old: persistent CD4 levels below 100 cells/mm^3 in two consecutive tests (with 6 months interval), and without concomitant or recent infection to cause a transient decline in the CD4 cell count. Children younger than 5: Persistent CD4 levels below 200 cells/mm^3 or <10 % in two consecutive tests (with 6 months interval), and without concomitant or recent infection to cause a transient decline in the CD4 cell count
Virological failure	Plasma viral load above 1000 copies/ml based on two consecutive viral load measurements after 3 months, after 6 months of effective treatment with adherence support

5.2.2. Identifying and management of ARV treatment failure

Treatment failure is identified when patients experience virologic failure. Cases whose initial HIV viral load test result is between 200 copies and 1000 copies/mL, and second viral load test result at 3 months with adherence support >1000 copies/mL are defined as treatment failure, and a switch to second-line or third-line regimen is recommended.

Diagram 2: Identification and management of ARV treatment failure


Routine HIVviral load testing
Viral load testing when treatment failure is suspected
HIV viral load test results
<200 copies/mL
≥ 200 - <1000 copies/mL
≥1000 copies/mL
Adherence assessment
Continue current regimen
Adherence assessment and support
Routine viral load testing at the next periodic testing
Poor adherence
Good adherence
Adherence counselling and support
Support for good adherence retention
HIV viral load <200 copies/mL
HIV viral load retesting after 3 months
Intensify adherence counselling
HIV viral load ≥ 200 -<1000 copies /mL
HIV viral load ≥1000 copies /mL
Switch to second- or third- line regimen (if second-line regimen fails))
Consultation to confirm treatment failure

Note:

1. HIV viral load retesting after 3 months in cases with good treatment adherence. Adherence counselling and support provided as per Section 6.4.

2. Genotypic assays could be performed to detect drug-resistance mutations before switching to a second-line or third-line regimen, if possible.

3. For cases being on a first line ARV regimen and where viral load testing is not available including second HIV viral load test after 3 months: depending on the patients' clinical, immunological status and treatment adherence, consultation is needed to determine treatment failure and switch to a second-line ARV regimen when good treatment adherence is ensured.

5.3. Second-line and third-line ARV regimens

5.3.1. Second-line ARV regimens

Table 8: Second-line ARV regimens in adults and adolescents

HIV -positive individuals	Application of first line regimens	Second-line regimens		
Adults including pregnant and breastfeeding women, and adolescents	First line regimens containing TDF	AZT + 3TC	+	LPV/r or ATV/r
	First line regimens containing AZT	TDF + 3TC or FTC	+	LPV/r or ATV/r
TB and HIV coinfection	Currently receiving TB treatment with rifampicin	ARV regimens in adults and adolescents, using double doses of LPV/r (LPV/r 800 mg/200 mg twice-daily) or increasing the dose of RTV to a LPV:RTV 4:4 ratio (LPV400mg/RTV400mg) twice daily		
	Currently receiving TB treatment with rifabutin	TDF + 3TC (or FTC) + LVP/r (or ATV/r) AZT + 3TC +LVP/r (or ATV/r)		
HIV and HBV coinfection	AZT + TDF + 3TC (or FTC) + LPV/r (or ATV/r)			

Table 9: Second-line ARV regimens in children

	Age group	First-line regimens	Second-line regimens
First line regimens containing LPV/r	< 3 years old	ABC + 3TC + LPV/r	AZT + 3TC + RAL If RAL is not available, continue with current regimen
		AZT + 3TC + LPV/r	ABC + 3TC + RAL If RAL is not available, continue with current regimen
	≥ 3 years old	ABC + 3TC + LPV/r	AZT + 3TC + EFV
		AZT + 3TC + LPV/r	ABC + 3TC + EFV or: TDF + 3TC + EFV
First line regimen containing NNRTI	all ages	ABC + 3TC+ EFV (or NVP)	AZT + 3TC + LPV/r
		TDF + 3TC (or FTC) + EFV (or NVP)	
		AZT + 3TC + EFV (or NVP)	ABC (or TDF) + 3TC (or FTC) + LPV/r (or ATV/r).

Clinical monitoring and testing of patients receiving second-line regimens is similar to that of first-line regimens. Routine HIV viral load testing begins when patients switch to a second-line regimen.

Drug interations monitoring should be paid attention to when using LPV/r, especially when PI is coadministered with rifampicin (see Section 4.3.2. ARV treatment of TB and HIV coinfection).

5.3.2. Failure of second line regimen

Criteria for identification of second-line regimen failure are the same as those for identification of first-line regimen failure.

If third- line regimens are not available, continue with second-line regimens.

5.3.3. Third-line ARV regimens

Table 10: Third-line ARV regimens

<table>
<tr><th colspan="2">Age group</th><th>Second-line regimens</th><th>Third-line regimens</th></tr>
<tr><td colspan="2">Adults and adolescents</td><td>AZT + 3TC + LPV/r
TDF + 3TC (or FTC) + LPV/r
AZT + 3TC + ATV/r
TDF + 3TC (or FTC) + ATV/r</td><td>DRV/r + DTG (or RAL)
± 1–2 NRTI</td></tr>
<tr><td rowspan="3">Children < 10 years old</td><td rowspan="2">Children < 3 years old</td><td>AZT + 3TC + RAL
ABC + 3TC + RAL</td><td>Continue with second-line regimens</td></tr>
<tr><td>AZT (or ABC) + 3TC + LPV/r</td><td>RAL + 2 NRTIs</td></tr>
<tr><td>Children ≥ 3 years old</td><td>AZT (or ABC or TDF) + 3TC + EFV (or LPV/r)
2NRTI + LPV/r or ATV/r</td><td>RAL + 2 NRTIs
Or:
DRV/r + 2 NRTI
Or:
DRV/r + RAL ± 1–2 NRTI</td></tr>
</table>

Currently DTG is indicated for the treatment of HIV in children aged over 12 years; double ARV doses in third-line DTG-containing ART regimens are needed when rifampicin is used with DTG, as rifampicin decreases dolutegravir concentrations.
DRV/r is not recommended for children younger than 3 years, or in combination with rifampicin as the latter decreases DRV concentrations.
Clinical monitoring and testing in administration of third-line regimens is as in first line ARV regimens. Routine viral load testing begins when patients switch to third-line regimen.

6. Treatment adherence assessment and support

6.1. Aims of treatment adherence

Adherence to ARV therapy is defined as a patient's ability to follow a treatment plan, take medications at prescribed times and frequencies, and attending follow-up appointments and getting routine tests as scheduled. Good treatment adherence helps:

- Suppress HIV replications, improving patients' clinical and immunological status;

- Reduce the risks of ARV drug resistance and treatment failure;

- Reduce the risks of HIV transmission to others.

6.2. Assessment of adherence to antiretroviral therapy at HIV clinics

Adherence assessment includes evaluating whether patients take medications at prescribed times and frequencies, attending follow-up appointments and getting routine tests as scheduled.

Assessment of adherence to prescribed medications, times and frequencies: should be done at every appointment, based on pill counts at each patient's clinic visit compared to their expected pill consumption, patient self reporting and medication record chart, and treatment supporter reporting.

Monitoring of patients' attendance at scheduled appointments, theis reception of ARVs and scheduled testing. Patients should be approached by phone or via peer/supporter network, or commune/hamlet health workers, so that they can be reminded to attend scheduled appointments and receive medications.

Treatment adherence assessment by means of routine viral load testing is the best method to assess patients' treatment adherence.

Advice to patients for missed ARV doses:
When you notice that you missed a dose, take your pill right away
For the next dose: If the next planned pill-taking time is 4 hours away or less (twice daily dosing) or 12 hours away or less (once daily dosing), do not take your next dose. Instead wait 4 hours or 12 hours and then take your next dose. Do not take two doses at one time.

The next day follow your regular dosing schedule.

Table 11: Assessment of antiretroviral adherence

Daily dosing	**Adherence level**	**# of missed doses in the month**
Twice-daily dosing	Good	1- 3
	Poor	≥ 4
Once-daily dosing	Good	1
	Poor	≥ 2

Note: If patients have adherence problems, reasons must be found and measures to help them adhere to treatment suggested.

6.3. Treatment adherence support

6.3.1. Assessment of factors affecting treatment adherence

Factors that may affect treatment adherence include:

- Patients' awareness of the necessity of adherence to ARV treatment

- Nature of their work

- Travel distance between patients' home and clinic

- Treatment adherence support provided by family members

- Substance and alcohol abuse, smoking, etc.

- Other coadministered medications include methadone maintenance treatment, tuberculosis treatment and medications for other diseases, etc..

- Inconvenient dosing frequency (multi daily dosing of ARVs).

6.3.2. Treatment adherence support interventions

Treatment adherence support interventions include:

Development and implementation of adherence support plan to provide support for patients at clinics;

Provision of basic information on HIV, currently available ARVs, possible side effects and management;

Counselling, education on treatment adherence, on drug resistance, consequenses of ARV resistance and difficulties in access to second-line and third-line ARVs if they fail first-line ARV regimens;

Talking with patients about adherence, advising them to make use of reminders such as sms, alarm clock, medication administration record chart, etc.

6.3.3 Groups that need special adherence support

Pregnant women before and after delivery: discussing and implementing measures to prevent mother-to-child transmission of HIV.

Adolescents: timing for disclosure of HIV status; explanation on regimens and medication administration; Counselling on adolescent productive health. And ensure convenient transition from paediatric to adult care (see Annex 13: disclosure of HIV status to adolescents living with HIV).

Children: there must be caregivers to ensure provision of care; counselling should be given to the caregivers to help them understand the necessity of treatment adherence; and explanation on types of ARVs and currently applied routes of administration for children.

People with signs of mental health disorders, mental conditions associated with alcohol and drug dependency need special support from their family and friends Those who provide adherence support for this special population should be given counselling on medications, administration, and support patients in attending follow-up appointments to prevent treatment interruptions.

6.4. Adherence counselling and support for patients with HIV viral load ≥ 200 copies/mL

Adherence counselling and support are interventions that aim to support patients on ARV treatment to achive maximum viral suppression, with a focus on patients with viral load ≥ 200 copies/mL.

Adherence support aims at :

- identifying factors that affect adherence and appropriate measures to overcome barriers (relating to knowledge, behaviors, financial conditions and emotions)

- eliminating the possibility of poor adherence before making decisions to switch to a second-line or third-line regimen.

Adherence support must be provided immediately when a patient receives viral load test result > 200 copies/mL, and given again one month later. In the second adherence counselling section adherence reassessment should be made, and a third section given one month later.

7. ARV related toxicity monitoring

7.1. Common toxicities experienced with cetain ARV drugs contained in first line regimens

7.1.1. TDF toxicity

a) Renal toxicity:

TDF can cause renal tubular dysfunction. Serum creatinine test must be done to monitor TDF related renal side effects, especially in patients with high risk factors, such as ageing, history of kidney disease, uncontrolled hypertension, chronic diabetes, use of PI enhancers (e.g. ritonavir) or nephrotoxic drugs. Cockcroft-Gault (CG) formula is used to estimate calculated glomerular filtration rate for renal failure assessment as follows:

- Cockcroft-Gault formula (CG)

$$eGFR = \frac{140 - \text{age(yr)}]*\text{weight(kg)} \text{ multiply by } 0.85 \text{ (for women)}}{72 \; x \text{ serum Cr (mg/dL)}}$$

Formula to convert mg⁄dL values to µmol⁄L Creatinine: 1 mg/dL is equivalent to 88.4 µmol⁄L

TDF should not be used when calculated glomerular filtration rate is <10 ml/min in patients with chronic diabetes, uncontrolled hypertension and renal failure. Adjust TDF dosing for patients who develop renal failure, as per Annex 11. Antiretroviral drug dosing adjustments are based on calculated glomerular filtration rate.

b) Bone toxicity: TDF can cause decline in bone mineral density (BMD) in children, even though the impact of decline in bone mineral density on children's development and fracture risk is not clear. Therefore children's development should be monitored when TDF is used.

7.1.2. Toxicity of other ARV drugs

a) AZT: As zidovudine can cause blood toxicities, hemoglobin testing is required before starting treatment, especially in patients with low body weight, low levels of CD4 count and advanced HIV disease. Avoid the use of zidovudine or switching to another drug in persons having baseline hemoglobin values of less than 8 g⁄dL.

b) NVP: NVP can cause skin rashes and/or hepatotoxicity. Strict monitoring of skin and hepatic reactions in the first 18 months following initiation of treatment, particularly in the first 6 weeks, is recomended. As adults with high levels of pre-ART CD4 counts face increased risk of liver toxicity, regimens containing nevirapine should not be initiated in women with CD4 counts of >250 cells/µL or men with CD4 counts of >400 cells/µL, unless the benefit clearly outweighs the risk.

c) EFV: the major side effect of EFV is central nervous system (CNS) toxicity, which is usually transient, and disappears after a few weeks. However in some cases, it can last several months or never disappear.

7.2. Mangement of ARV related toxicities

(See Annex 10: Toxicity and management of antiretroviral drug toxicity)

Notes:

1. Delayed switching to alternative drugs in cases with serious side effects/toxicity can adversely affect treatment adherence, which, in turn, may consequently lead to drug resistance and treatment failure.

2. For cases where side effects are not serious, temporary disconinuation of ARVs is recommended (e.g. class 3 allergy or ALT levels increase 5 – 10 times higher than upper limit of normal during NVP-based therapy), stop NVP immediately. Continue with the other NRTI drugs for 7 days.

3. For cases with life-threatening reactions, such as Steven Johnson Syndrome or Lyell Syndrome, stop all ARVs without delay.

7.3. ARV - associated drug interactions and management

Table 12: Drug - drug interactions and management

Drug interactions between direct-acting antivirals (DAAs) for hepatitis C and antiretroviral drugs for HIV are presented in Annex 12.

Antiretrovirals	Major interactions	Dosing recommendations
AZT	Ribavirin and peg-interferon alfa-2a	First line regimens: AZT is replaced by TDF
	Methadone	Monitoring toxicity of AZT, such as anaemia, as methadone causes a significant increase in AZT blood levels
(ATV/r, DRV/r, LVP/r) – boosted PI	Rifampicin	Replace rifampicin with rifabutin Adjust PI dose or replace it with three NRTI drugs (in children) Coadminstration with ATV, DRV and LPV is not recommended, or recommended with caution
	Lovastatin and simvastatin	Consider alternative medications for dyslipidemia (e.g. pravastatin)
	Estrogen containing birth control pills	Consider altenative pills or contraceptive methods
	Methadone and buprenorphine	Dosing adjustments in some cases
	Astemizole and terfenadine	Use antihistamines instead
	TDF	Monitor renal function
DTG	Carbamazepine, phenobarbital and phenytoin	Consider alternative anticonvulsants

Antiretrovirals	Major interactions	Dosing recommendations
	Supplements containing Mg, Al, Fe, Ca, Zn	Give DTG at least 2 hours before or at least 6 hours after antacids containing polyvalent cations, including supplements containing Fe, Ca, Mg or Zn; multivitamins with minerals, cation-containing laxativesand Al-, Mg-, and Ca-containing antacids
	Rifampicin	Replace rifampicin with rifabutin. Double doses of DTG is recommended when used concomitantly with rifampicin
RAL	Rifampicin	Replace rifampicin with rifabutin. Doubling raltegravir dose to 800 mg x 2 times daily when coadministered with rifampin as the later reduces RAL concentrations
	Supplements containing Mg, Al, Fe, Ca, Zn	Recommendations as for DTG
EFV	Amodiaquine	Consider alternative malarials
	Methadone	Methadone dose adjustments recommended
	Estrogen containing birth control pills	Consider altenative pills or other contraceptive methods
	Astemizole and terfenadine	Consider altenative antihistamines
	Itraconazol	Consider increasing itraconazole dose
NVP	Rifampicin	Replace NVP with EFV
	Itraconazole and Ketoconazole	Use azole antifungals instead (e.g. fluconazole)
	Methadone	Methadone dose adjustments recommended

7.4. Reporting ARV-related toxicities

Reporting ARV related toxicities must be conducted as per National Guidelines for Pharmacovigilance promulgated under Decision 3551/QD-BYT dated 19 September 2013 of the Minister of Health. Treatment clinics are required to send reports on adverse drug reactions to the National Center for Drug Information and ADR monitoring.

7.4.1. Forms of reporting

Individual adverse event reports*:* all suspected adverse reactions due to ARVs or other drugs used concomitantly in treatment for HIV - positive individuals must be reported. Priority should be given to the following:

Serious adverse events of Grade 3 and grade 4 as per Severity Grading for Treatment-related Adverse Events;

Any adverse drug reaction that results in switching regimen, treatment quitting, discontinuation or requires medical interventions;

Any adverse drug reaction considered by health care professionals as leading to serious clinical consequences;

Adverse reactions to all new drugs or new regimens;

New adverse reactions that have not been known; cases of serious reactions or mild reactions with unusual frequencies.

Periodic reports: monthly reports on ARV-associated adverse reactions. ADRs Reporting form and receivers: as per Decision 3551/QD-BYT dated 19 September 2013 of the Minister of Health.

7.4.2. Reporting implementation

Schedule for individual adverse event reports is as follows:

Unexpected fatal or life-threatening adverse reaction (grade 4): must be filed as soon as possible but no later than 7 working days after first notice of the event.

Serious, unexpected reactions (ADRs) that are not fatal or life-threatening (grade 3) must be filed as soon as possible but no later than 15 working days after first notice of the event.

Reports on other ADRs cases can be collected monthly and filed on the 5th day of the next month.

Preliminary report on an adverse drug reaction must be filed as soon as possible after detection, even when information is insufficient. Further information (if any) shall be included in additional reports.

Monthly ADR reporting: Monthly reporting is conducted at each treatment facility prior to the 5th day of the next month.

8. Immune reconstitution inflammatory syndrome (IRIS)

8.1. Concept

Immune reconstitution inflammatory syndrome is described as a paradoxical deterioration of clinical status on initiation of ART in patients with HIV infection attributable to recovery of the immune system. IRIS is, in nature, the overwhelming inflammatory response of the immune system to a previously acquired opportunistic infection.

IRIS manifestations include:

- Occurence of OIS that have not been diagnosed before ART is started, such as tuberculosis, MAC, cryptococcal meningitis, etc. (unmasking Immune reconstitution inflammatory syndrome).

- Worsening of an existing opportunistic infection or disease process (paradoxical Immune reconstitution inflammatory syndrome).

- Recurrence of co-infections (hepatitis B, HCV) and autoimmune diseases (psoriasis, dermatitis, etc.).

Timing**:** IRIS occurs within 2 - 12 weeks after initiation of antiretroviral therapy, or may be up to months (years).

8.2. Incidence of IRIS and risk factors

IRIS occurs in approximately 10% of patients receiving ARV treatment. Risk factors for IRIS include:

- Low baseline CD4s count (IRIS occurs in around 25% of patients with CD4<50 cells/mm3 when ART is started).

- History of OIS before starting ARV treatment. Starting ART early increases the risk of IRIS in patients with opportunistic infections.

- Use of ARV regimens containing ritonavir-boosted protease inhibitors.

To prevent IRIS, screening for opportunistic infections should be conducted before initiating ART, especially tuberculosis screening and treatment.

8.3. Manifestations of Immune reconstitution inflammatory syndrome

Opportunistic infections and noninfectious conditions associated with IRIS include:

Mycobacterial diseases: tuberculosis (most common), *Mycobacterium avium complex* (MAC) infection.

Fungal infections: infections caused by *C. neoformans, T. marneffei, P. jiroveci*

Viral inifections: *Cytomegalovirus* (*CMV*) *Infection*, *Herpes simplex, Herpes zoster,* Hepatitis B and Hepatitis C, progressive multifocal leukoencephalopathy

Protozoan infections: *Toxoplasmosis*, *Leishmaniasis*

Noninfectious diseases: psoriasis, thyroiditis.

8.4. Diagnosis of Immune reconstitution inflammatory syndrome

IRIS should be suspected when patients start ARV treatment and strictly adhere to therapy, but experience a clinical deterioration, especially those diagnosed with late-stage HIV infection, with low CD4 counts or history of OIS before starting ARV treatment.

Differential diagnoses of IRS to eliminate other reasonable possibilities including:

Side effects of the antiretroviral treatment

New opportunistic infections

OIS treatment failure (such as TB), failure of ART in patients who have received ARV treatment for at least 6 months.

8.5. IRIS management

In some cases IRIS is mild and no treatment is required as IRIS resolves over time; Continue ART if patients respond well to drugs; Continue therapy against the primary opportunistic pathogen or start therapy against newly emerged OIs; adjust ART regimens and doses if there appear drug interactions between ARVs and non- ARV drugs (e.g: replacing NVP with EFV if TB treatment regimen containing rifampicin is coadministered). In case of life-threatening forms of IRIS, stopping ARV temporarily should be considered.

Use nonsteroidal anti-inflammatory drugs (diclophenac, ibuprofen) if these are not contraindicated.

Treatment with corticosteroids: prednisolone or methylprednisolone oral or for injection, dose of 0.5mg/kg/day for 5 – 10 days, in patients with moderate to severe IRIS.

ART interruption is only recommended in severe IRIS cases where patients do not respond to medications. Standard protocols should be applied: discontinuation of ARV regimens containing NNRTI drugs (stop NVP or EFV first; continue with other NRTI drugs for 7 days before stopping regimen). Restart ART regimens when IRIS is treated and patients can respond to medications.

Other interventions could be applied if needed, such as pus drainage from a lymph node abscess, surgery to remove obstructions in case of small intestinal obstruction or airway obstruction.

9. Antiretroviral (ARV) prophylaxis for the prevention of HIV infection

9.1. HIV post-exposure prophylaxis following occupational exposure to HIV

Occupational exposure to HIV is defined when direct contact with the blood or body fluids of patients with HIV infection or suspected HIV infection, leading to risk for acquisition of HIV infection.

9.1.1. Types of exposure

Needlestick injury that occur when performing medical procedures: injections, blood sample collection for testing, punctures, etc.

Sharps injury caused by scalpel or other sharp equipment contaminated with blood or other body fluids of patients.

Accidental puncture from broken glass when a tube containing a patient's blood or body fluid breaks.

Blood or body fluids splash onto damaged skin surface (due to previous eczema, burn, ulcers) or mucous membrane (eyes, nose, throat).

Exposure to HIV infected blood when a person is intentionally stabbed with a contaminated needle or accidental exposure while pursuing a criminal, etc.

9.1.2. Procedure for post-exposure prophylaxis

Steps involved

Step 1: Treat exposure site.

Step 2: Report the incident to the in-charge/supervisor immediately and document (all details of the accident should be provided in the Exposure Record).

Step 3: Risk assessment for potential exposure to infection, based on injury severity and contact area.

Step 4: Determine the HIV status of the source person.

Step 5: Determine the HIV status of the HIV- exposed person.

Step 6: Counselling provided for the HIV- exposed person.

Step 7: ARV prophylaxis.

Treat exposure site

- Bleeding cut or wound: Wash the exposed body area immediately under running water with soap. Encourage bleeding for a while; Do not squeeze or rub the injured side.

- Exposure through eye mucous membrane: irrigate eyes with distilled water, saline solution Nacl 0.9 continuously for 5 minutes. Use laboratory eyewash station (provided at confirmatory laboratories) if available.

- Exposure through nose or mouth mucous membrane: irrigate the nose with distilled water, saline solution Nacl 0.9; gargle several times with saline solution Nacl 0.9.

Report the incident to the in-charge/supervisor immediately and filling report form

Give the date and time of incident, circumstance, injury assessment and potential exposure to infection. Get the signatures of the witness and supervisor.

Exposure risk assessment

- Presence of exposure risk: Injuries caused by blood containing needlestick causing bleeding; deep injury with a large bore- hollow needle contaning much blood poses higher risk than a superficial injury caused by a small bore, hollow needle that contains little blood. Or deep skin cuts caused by scalpel or broken glass when a tube containing a patient's blood or body fluid breaks. Splash of a patient's blood and body fluids onto previously damaged or abrasive skin surface, mucous membranes (even when it is not known if there are ulcers or not). Extensive ulcers pose higher risks.

- No presence of risk: splash of blood and body fluids of patients onto undamaged skin surface.

Determine the HIV status of the source person

- The source person is diagnosed with HIV infection: collect information on his/her history of HIV treatment and response to ARVs.

- HIV status of the source person is unknown: Counselling provided and blood sample collected for HIV testing.

- Cases where the HIV status of the source person is inconclusive are considered as posing potential risk and must be made clear in the report.

Determining the HIV status of people exposed to HIV

- Provide pre-and post-test counselling as per regulations.

- If the result of an HIV test performed immediately after exposure is positive: the HIV-exposed person was already infected with HIV before exposure. Stop post-exposure prophylaxis. Provide the HIV-exposed person with counselling, and refer him/her to HIV treatment service.

The HIV exposed person should be given counselling on:

- HIV infection risk and HBV, HCV

- The HIV-exposed person should be provided with information and appropriate counselling on ARV treatment for the prevention of HIV infection, the benefits and risks of prophylaxis.

- Explanation on the side effects of ARVs and symptoms of primary HIV infection: fever, rashes, nausea or vomitting, anaamia with swollen lymph nodes, etc. should be given.

- Counselling on prevention of transmission of HIV to others: a HIV-exposed person can transmit the virus to others even though s/he tests negative (window period), therefore preventive measures must be applied.

- Adherence counselling and psychological support.

9.2. Prevention of non- occupational exposure to HIV

Non - occupational exposure to HIV occurs in a non - occupational environment where a person is exposed to blood and/or body fluids that may transmit HIV virus.

9.2.1. Events of non- occupational exposure to HIV

- Exposure through sexual acts: unprotected intercourse, i.e. sexual intercourse without a condom, the condom is broken or torn, or sexual assaults.

- Injection drug users sharing syringes and needles.

- Injuries caused by a needle or sharp object scattered in a public place, visibly blood stained.

- Someone bitten by a person with suspected HIV infection, which causes bleeding.

9.2.2. Factors that need assessing and management in cases of non-occupational exposure to HIV

- HIV status of the HIV- exposed person.

- Scope, frequency and time of exposure risks. Efforts should be made to find out the HIV status of the source person.

- Pre-test counselling.

- Hepatitis B and C testing; testing to assess pregnancy status.

9.2.3. Assess the HIV status of the source person

Provide HIV testing for the source person if his/her HIV status is unknown. If the test result is positive, s/he should be given counselling and post-exposure prophylaxis provided for the HIV-exposed person.

It is recommended that post-exposure prophylaxis be initiated in the following cases:

- The source person is at high risk of HIV infection, such as an injection drug user, an MSM, or sex worker;

- The HIV status of the source person is inconslusive;

Stop post-exposure prophylaxis when the source person is not diagnosed with HIV infection.

In sexual assault cases, post-exposure prophylaxis should be started after risk assessment and counselling for the HIV-exposed person have been conducted.

9.3. Post prophylaxis used for HIV-exposed persons

9.3.1. Indication

Exposure through mucous membrane or blood (through sexual acts, splash of body fluids to eye, nose or mouth): contact with body fluids that pose a risk of transmitting HIV, including blood, bloody saliva, breastmilk, genital secretions, cerebrospinal fluid, amniotic fluid, rectal fluid, peritoneal fluid, synovial fluid, pericardial fluid or pleural fluid.

Post-exposure prophylaxis should be started as soon as possible for all individuals at risk of HIV infection; optimal time for initiation is within the first 6 hours following exposure and no later than 72 hours after exposure.

Post-exposure prophylaxis is not recommended in the following cases:

-The HIV-exposed person is already infected with HIV;

- The source person tests negative;

- Exposure to body fluids that do not pose potential risk of infection, including tears, saliva not contaminated with blood, urine and sweat.

- On-going HIV exposure, such as routinely having sex with HIV -positive individuals or prostitutes and rarely using condoms; injection drug users sharing needles and syringes.

Table 13: Post – exposure prophylaxis

Subjects	ARV regimens	Treatment duration
Adults	TDF + 3TC (or FTC) + LPV/r (or EFV) or AZT + 3TC + LPV/r (or EFV)	28 days
Children ≤ 10 years old	AZT + 3TC + LPV/r	

9.3.2. Mornitoring plan

Mornitoring of ARV side effects: discontinuation of ART is not recommended when side effects are mild and transient. Cases with severe side effects must be sent to health care facilities immediately.

Psychological support is recommended when necessary.

Retesting at 3 months after exposure.

Advising patients not to donate blood, apply safe injection drug use and sex practices, and not to breastfeed until HIV infection is excluded.

Counselling on vaccination against hepatitis B.

10. Pre-exposure prophylaxis

Pre-exposure prophylaxis is the use of ARVs for the prevention of HIV infection in individuals with high risk behaviors.

Pre-exposure prophylaxis has maximum preventive effects in those practicing anal sex if received in 7 consecutive days.

Pre-exposure prophylaxis has maximum preventive effects in those practicing varginal sex and in the prevention of HIV transmision through blood after application in 21 consecutive days.

10.1. Individuals who need pre-exposure prophylaxis

People with high risk behaviors of such groups as men who have sex with men, transgender women, sex workers.

Individuals whose spouse/sex partner is HIV positive: start ARV treatment for their spouse/sex partner and apply periodic testing to monitor HIV viral load. If the HIV- positive spouse/partner's HIV viral load is <200 copies/ml, no pre-exposure prophylaxis is required for the HIV-uninfected spouse/sex partner. Pre-exposure prophylaxis is recommended in special cases where HIV - positive individuals do not receive ARV treatment or they are receiving ARVs but their viral load is over 200 copies/ml.

10.2. Procedure for examination and pre-exposure prophylaxis

Step 1: Screening to assess high risk behaviors in the last 6 months that may result in HIV infection.

Step 2: HIV counselling and testing.

Step 3: Counselling on pre-exposure prophylaxis provided for those at high risk of infection who test negative, including:

- Benefits and effectiveness of pre-exposure prophylaxis;

- Medications and possible side effects;

- Importance of adherence to prophylactic treatment;

- Additional preventive measures.

Step 4: Physical examination and asking about history of kidney disease, STDs, mental disease, epilepsy, etc. Determine if a client has experienced signs and symptoms of influenza-like illness (signs of primary HIV infection) during the last month.

Step 5: Perform creatinine test and HbsAg test

Step 6: Eligibility for Pre-exposure prophylaxis:

- HIV test results are negative;

- No signs of primary HIV infection;

- No renal failure; no history of mental disease of epilepsy

- Voluntarily acceptance of pre-exposure prophylaxis;

- Awareness of the importance of treatment adherence and commiment to adherence

Step 7: Indication of ARV regimen containing TDF + FTC or once-daily single-tablet regimen of tenofovir disoproxil fumarate (TDF).

Step 8: Monitoring and follow-up visits.

First follow-up visit: after 1 month, HIV antibody testing, assessment of side effects, treatment adherence, identifying problems in treatment adherence.

Next follow-up visits: every three months for patients with good adherence: testing to assess HIV status, drug supply prescription for the next 3 months (90 days), assessment of side effects and adherence, and answers to patients' questions. For cases with poor adherence, apply monthly appointments and 30 days of drug supply prescription.

Creatinine testing every 6 – 12 months for patients with signs of renal dysfunction.

Examination and screeing tests to detect sexually transmitted infections, and assessement of the need to continue treatment.

10.3. Management of certain events in Pre-exposure prophylaxis

Table 14. Management of certain events in Pre-exposure prophylaxis

Events	**Management**
Side effects	
Head ache, dizziness, nightmares, nausea…	Counselling and psychological support provided; such side effects will disappear in 1 – 2 weeks.
If side effects are persistent, seriously affecting health	Discontinuation of prophylaxis if needed
Missing HIV medications	
1 – 3 days of missed HIV medications	Continuation of routine medication schedule
4 – 7 days of missed HIV medications	Conduction of risk behaviors assessment for the days of missed HIV doses; if There are no risk behaviors: continue prophylaxis schedule. Presence of risk behaviors: continue with treatment and conducting HIV test at 3 months after risk behaviors.
> 7 days of missed HIV medications	Restart treatment as for new cases registered for prophylaxis.
Test HIV	
Negative test results	Continue with prophylaxis.
Positive HIV confirmatory test results	Counselling, switch to ARV treatment
Becoming pregnant while on prophylaxis	Counselling, encouraging to continue prophylaxis if there remain HIV infection risk
Renal failure	
Calculated glomerular filtration rate (eCrCL < 60 ml/min)	No prophylaxis. Referral to a specialist clinic

10.4. Discontinuation of Pre-exposure prophylaxis

If a client wishes to discontinue pre-exposure prophylaxis, s/he should be advised to take ARV medicines every day for 28 days following the last exposure.

Discontinuation of Pre-exposure prophylaxis can be applied in the following cases:

- Behaviors have changed, there is no HIV infection risk;

- Diagnosis of HIV during prophylaxis: clients should be referred to HIV care and treatment services;

- Persistant side effects (renal failure) despite treatment, affecting health.

Things to do before discontinuing pre-exposure prophylaxis:

- HIV antibody testing

- Finding reasons for discontinuation

- Assessing client's risk behavior

- Recording all above information in client's outpatient medical record.

CHAPTER III
PREVENTION AND MANAGEMENT OF COMMON CORMOBIDITIES

1. Prophylaxis

1.1. Prophylaxis of some opportunistic infections

Co-trimoxazole preventive therapy (CTX or trimethoprim-sulfamethoxazole, TMP-SMX) is effective to prevent some opportunistic infections like *Pneumocystis jiroveci* pneumonia, *Toxoplasmosis* and other infections. CTX prophylaxis is recommended for adults, pregnant and breastfeeding women, HIV-exposed or HIV-infected children.

Figure 15: Criteria for initiating and discontinuing co-trimoxazol preventive therapy

Age	Criteria for initiation	Criteria for discontinuation	Dose of co-trimoxazole
HIV-exposed children	In all, starting at 4 - 6 weeks after birth	Until the risk of HIV transmission ends or HIV infection is excluded	See appendix 10
HIV-infected children ≤ 5 years	In all	No discontinuation until 5 years of age.	See appendix 9
HIV-infected children ≥ 5 years	CD4 ≤ 350 cells/mm^3 or clinical stages 3 or 4	Stable (at least 12 months of ART and no manifestations of clinical stages 2, 3, 4) and CD4 > 350 cells/mm^3 or suppressed viral load	See appendix 9. For children with weight > 30 kg, use 960 mg daily
Adults, pregnant and breastfeeding women living with HIV	CD4 ≤ 350 cells/mm^3 or clinical stages 3 or 4	Stable and CD4 > 350 cells/mm^3 or suppressed viral load	See appendix 9

Note:

1. In case of ART initiation and patient with clinical stages 1 or 2 without CD4 count, co-trimoxazole preventive therapy is still recommended.

2. Discontinue co-trimoxazole if patient has Stevens-Johnson syndrome, drug allergy grade 3 - 4, severe liver disease, severe anemia, severe pancytopenia.

3. Suppression level: < 1000 copies/mL

1.2. Tuberculosis prophylaxis

HIV care settings should synchromously implement 3 strategies including intensified-tuberculosis finding, isoniazid preventive therapy and infection control at healthcare facilities.

Early treatment of ART for HIV infected people who meet the criteria will reduce the prevalence and mortality rate of tuberculosis (TB).

1.2.1. Screening and active diagnosis for TB eradication

People with HIV need TB screening according to the following figure 3 and 4 in any visit to heath facility.

TB suspected symptoms and signs in people living with HIV:

Adults and aldolescents with HIV are likely to have TB if they have any one of symptoms sush as cough, fever, weight loss and night sweats.

Children with HIV have any one of the following symptoms:

- Body weight: no weight gain; underweight to age; weigth loss (>5%) since the last visit or growth curve flattening;

- Fever;

- Current cough/wheeze;

- Contact history with a TB case.

- Children with contact history with multiple drug resistance TB case need stricly monitoring of symptoms for at least 2 years, who can not require TB prophylaxis.

Figure 3: TB Screening in adults and adolescents with HIV

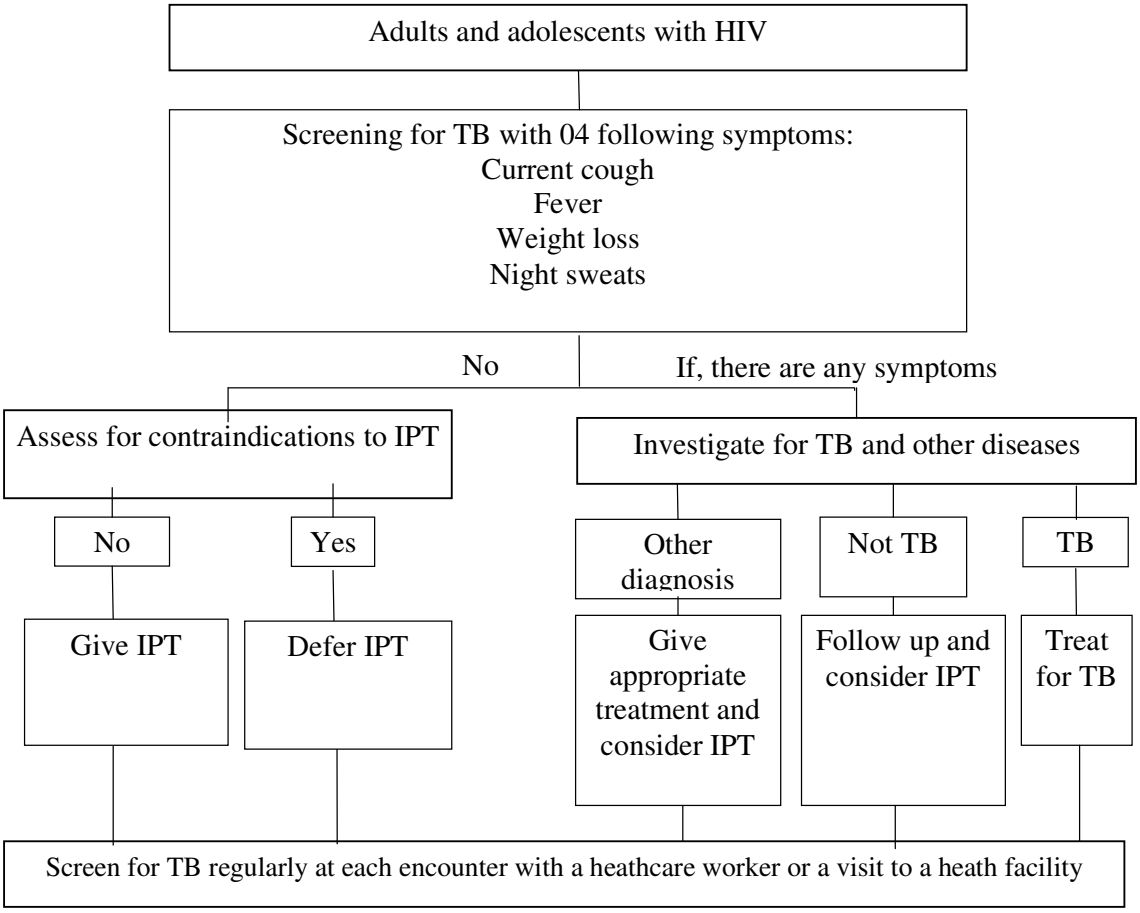
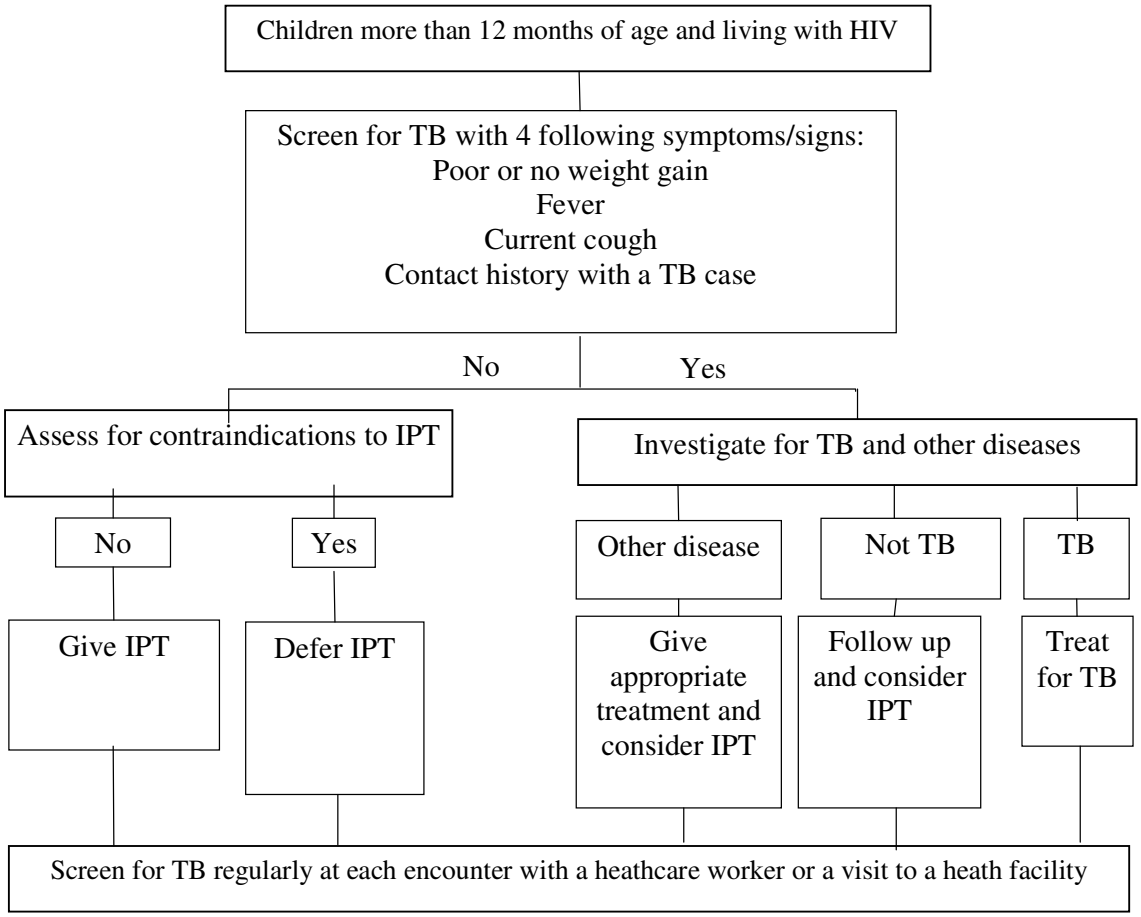

Adults and adolescents with HIV
Screening for TB with 04 following symptoms:
Current cough
Fever
Weight loss
Night sweats
No
If, there are any symptoms
Assess for contraindications to IPT
Investigate for TB and other diseases
No
Yes
Other diagnosis
Not TB
TB
Give IPT
Defer IPT
Give appropriate treatment and consider IPT
Follow up and consider IPT
Treat for TB
Screen for TB regularly at each encounter with a heathcare worker or a visit to a heath facility

Figure 4: TB Screening in children more than 12 months of age and living with HIV



Any case with suspected TB need differential diagnosis with other opportunistic infections and receive investigations for TB diagnosis including chest X-ray, AFB smear in sputum and other tests (gene Xpert, AFB smear in lymph node or TB culture if possible)

For children with HIV:

- Sputum specimens could be collected from gastric aspiration or sputum induction if possible. In case of no sputum, TB diagnosis could be made by 3 factors: contact history of a TB case, clinical symptoms and suggestion of TB lesions on chest X-ray.
- Follow up, differential diagnose with BCG disease**:** Disseminated BCG disease often occurs in HIV infected children under 1 year with BCG vaccincation: abscess at injected site, ipsilateral or bilateral lymphadenopathy after BCG infection. Lymph node aspiration for histopathology, culture if possible.

Diagnosis and treatment of TB in people living with HIV is permitted in accordance with regulations in Decision No. 4263/QĐ-MoH 13/10/2015 on recommendations of diagnosis, treatment and prevention of TB.

HIV infected people with diagnosis of TB need registration and early treatment for TB.

1.2.2. Isoniazid preventive therapy (IPT)

a. Indication

Adults and adolescents living with HIV who are unlikely to have active TB irrespective of the degree of immunosuppression, to those on ART, pregnant woman and to those who have previosly been treated for TB.

Children living with HIV:

- Children > 12 months of age: Give IPT to children who are unlikely to have active TB on symptom-based screening and have no contact with a TB case (Figure 4). Only children who have contact with a TB case, give IPT if the examination and investigations show no active TB.

- Children ≤ 12 months of age: Give IPT to any child who has contact with a TB case and rule out active TB.

All patient with TB who have successfully complete treatment for TB should receive IPT immediately after that.

b. Contraindication

Absolute contraindications: patient with allergic history to INH (who peviously have fever, rash or hepatitis related to INH).

Defer IPT in any following cases:

- Active hepatitis, cirrhosis, severe alcoholism: patient with clinical manifestations of hepatitis (fatigue, anorexia, dark urine, abdominal pain, nausea, vomiting, jaundice) and/or elevated liver enzymes (ALT > 5 times upper reference limit). Defer IPT until liver enzymes normalize or fall down < 5 times upper reference limit.

- Peripheral nervous disorders: numbness, tingling, weakness or burning in extremities. Defer IPT until patient are stable.

c. Dose

INH dose:

- Adult: 300mg/day

- Children: 10mg/kg/day, maximum 300 mg/day (see appendix 9)

Take INH once daily at certain time and on an empty stomach, after meals.

Duration: 9 months for adults and 6 months for children.

d. Managing patients who forget to take medications

< 50% total doses: continue treatment until taking 270 doses;

> 50% total doses or discontinue for more than 2 consecutive months : restart treatment.

e. Monitoring during TB preventive therapy

Follow up side effects:

Healthcare workers should explain the reason for TB prevention and emphasize the importance of completing treatment, regularly monitor clinical symptoms of HIV infected patients in scheduled visits. Patients must contact immediately with healthcare workers if they have any symptoms sush as vomiting, nausea, abdominal pain, persistent lethargy, dark urine, light-colored stool or jaundice.

Baseline investigations should include AST, ALT, bilirubin level in HIV infected person with risk factors as liver disease, alcoholism, chronic liver disease, age over 35 years and pregnant women or newly giving birth (within 3 months). If there are any abnormal results, retest regularly to follow up.

Follow up adherence to treatment and completion of preventive therapy:

- Counsel, encourage HIV infected person and caregiver (children) to obey and complete the TB preventive therapy.

- Record and report information of TB preventive therapy.

1.2.3. Managing TB transmission at HIV/AIDS care facility

5 steps in managing TB transmission at HIV/AIDS care facility:

Screening: Early recognize people with suspected TB. Patients, who have cough for more than 2 weeks or diagnosis or treatment for TB, need priority to receive immediately examination or services without lining up with others.

Education: Educate patient about cough etiquette: cover mouth and nose when coughing and sneezing, and provide face masks or tissues if possible.

Isolation: Patients with suspectd TB or confirmed TB should be seperated from others and stayed in isolation room, receive face masks or tissues while waiting.

Delivery of HIV services: Patients with suspected TB have priority to meet their requirements (sush as HIV counselling, taking medications...) in order to reduce the contact time with other patients. In facility with integrated services, HIV services should be prior to TB examination if possible.

Diagnosis: TB diagnosis should be performed in facility with adequate equipments. If HIV care facility can not perform TB tests or treat for TB, refer people with suspected or confirmed TB to TB settings for diagnosis and treatment.

1.3. *Cryptococcal infection prophylaxis*

Screening of *Cryptococcus neoformans* Antigen (CrAg) and early prophylaxis with fluconazole prevent from the development of meningitis in asymtopmatic individuals with cryptococcal antigenemia.

1.3.1. Screening of *Cryptococcal antigen*

Screening of *Cryptococcal antigen* (CrAg) should be performed in all ART-naive adults with CD4 count < 100 cells/mm^3.

1.3.2. Prophylaxis of *Cryptococcal infections*

a. Indication

Prophylaxis with fluconazole is indicated for HIV infected patients with CrAg-positive after ruling out *Cryptococcal* meningitis with clinical manifestations or laboratory.

b. Regimen

Induction phase: fluconazole 800 – 900 mg/day (or 12 mg/kg/day and up to 900 mg/day if below 18 years) x 2 weeks

Consolidation phase: fluconazole 400 - 450 mg/day (or 6 mg/kg/day and up to 450 mg/day if below 18 years) x 8 weeks.

Maintenance phase: fluconazole 150-200 mg/day (or 6 mg/kg/day up to 200 mg/day if below 18 years).

Discontinuation of maintencance treatment is recommended when patients are stable and adhere to ART treatment for at least 1 year, and have CD4 > 200 cells/mm³ for over 6 months or CD4 > 100 cells/mm³ for over 6 months and have undetectable viral loads. Discontinutaion of maintenance treatment is not recommended in children under 2 years.

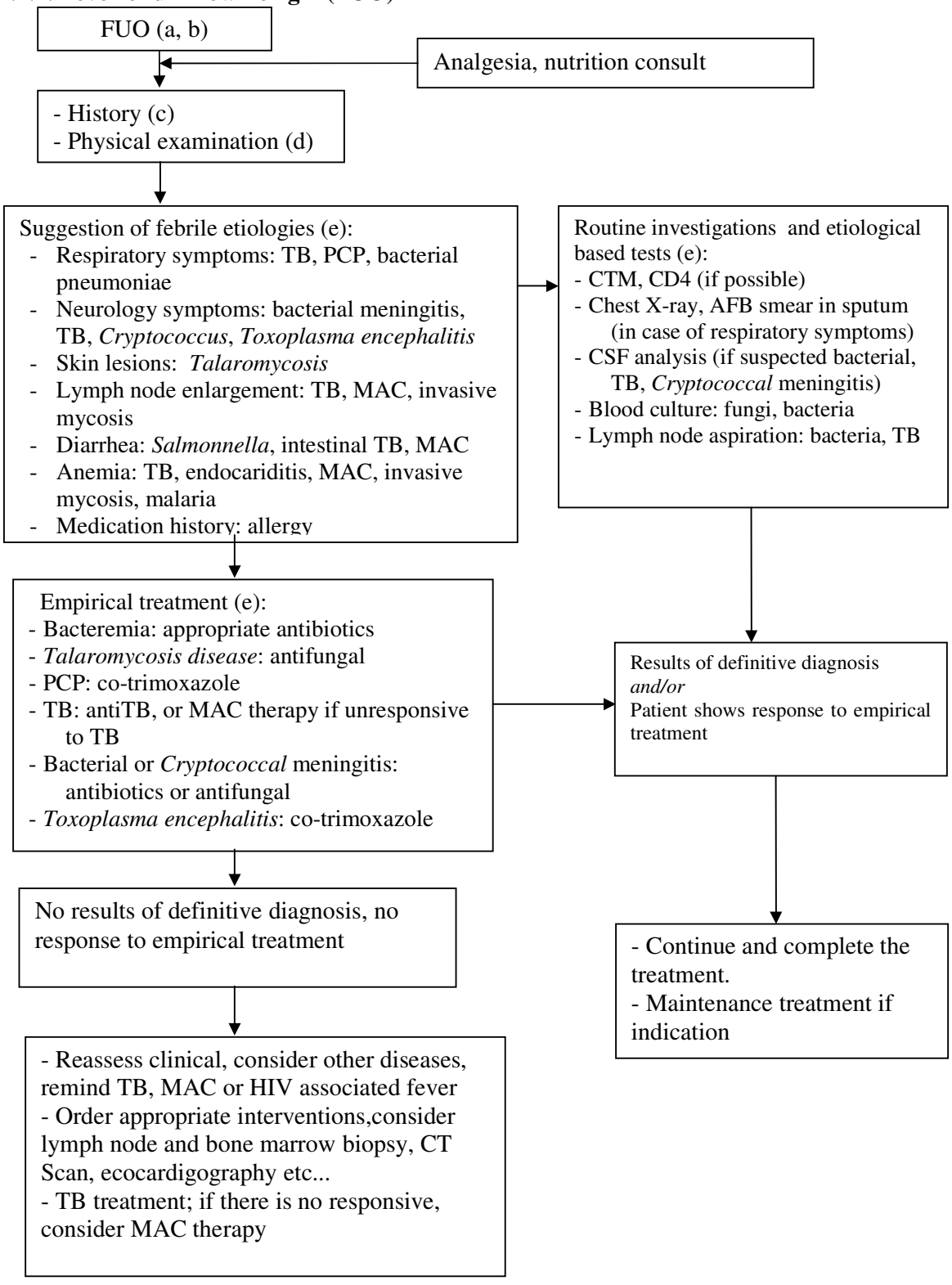
1.3.3. Timing of ART in asymptomatic patients with *Cryptococcal antigen* (CrAg)

In asymptomatic patients with *Cryptococcal antigen* (CrAg), ART initiation should be deferred after 4 weeks of prophylaxis with fluconazole in order to reduce the presence of immune reconstitution inflammatory syndrome (IRIS).

2. Approach to common clinical syndromes in people living with HIV

2.1. In adults

2.1.1. Fever of unknown origin (FUO)



Guidance:

(a) Definition: Fever of unknown origin is defined when temperature is greater than $38^{o}5$ and prolongs for more than 14 days without confirmation of etiology.

(b) Common etiology of FUO

Opportunistic infections (OIs): tuberculosis, T*alaromyces marneffei* infection, meningitis and fungemia due to *Cryptococcu*s, bacteremia due to *Salmonella* and other pathogens, MAC, etc...

HIV associated malignant disease: lymphoma

Drug eruptions: allergy to co-trimoxazole, NVP, ABC, v.v...

HIV associated fever, malaria.

(c) Present and past medical history*:*

Symptoms: headache (bacterial or fungal meningitis *Toxoplasmosis*), diarrhea (bacteremia due to *Salmonella,* MAC, etc..), cough (pulmonary tuberculosis), rash (*T. Marneffei* infection, drug eruptions), etc...

Medications: co-trimoxazole, ARV, other drugs

History of OIs and HIV associated diseases (recurrence of OIs if there were no secondary prophylaxis or no ART)

History of medication allergy and other diseases

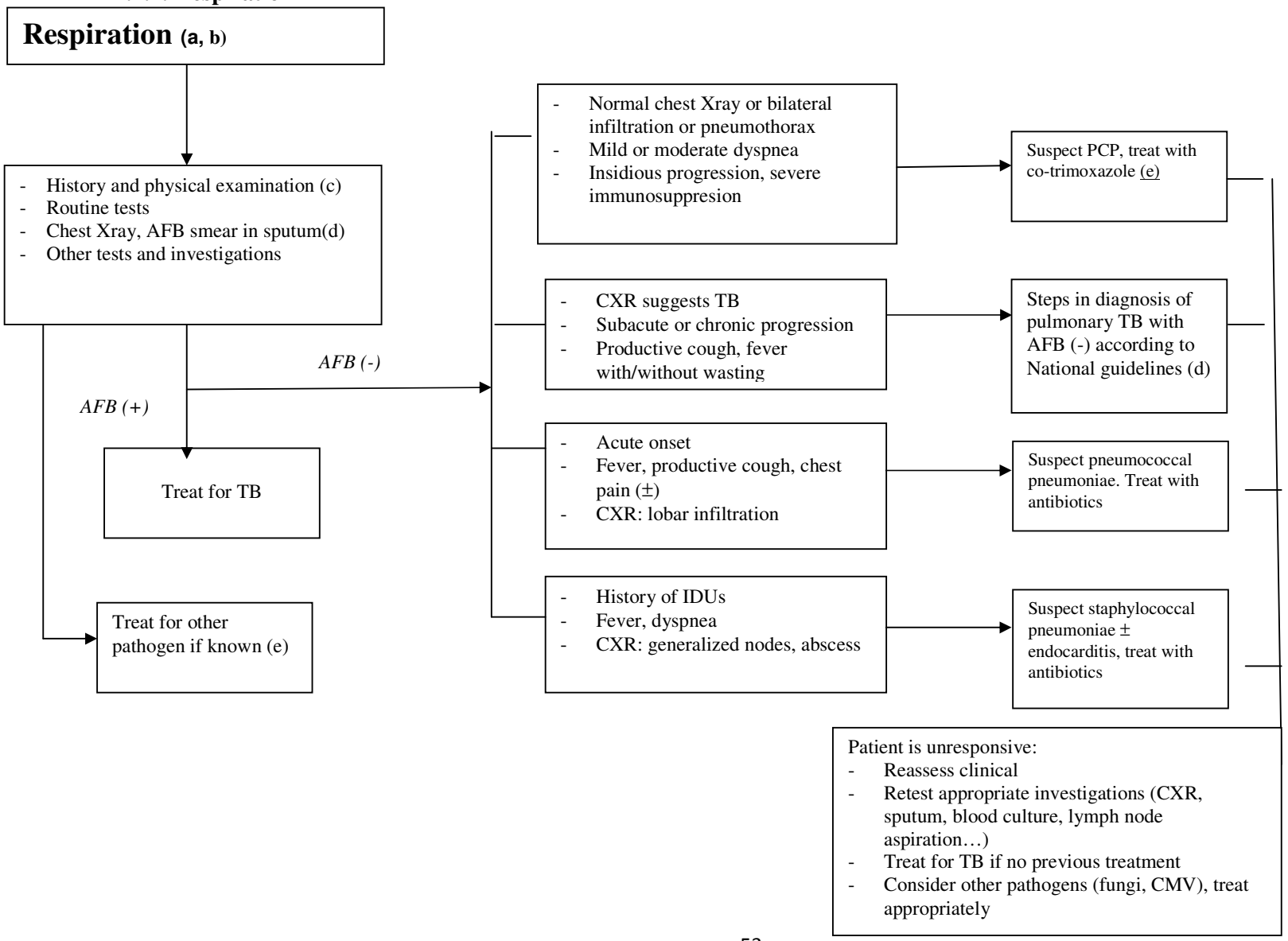
History of injecting drug user (bacteremia due to S.aureus), unprotected intercourse (gonorrhea, syphilis and other sexually transmitted diseases)

Family history: tuberculosis, cough and other infectious diseases.

(d) Physical examination: Exam all organs and systems, focus on symptomatic organs.

(e) See part 3, Chapter III: Diagnosis and management of common cormobidities.

2.1.2. Respiration



Guidance:

(a) Respiratory manifestations: cough, dyspnea; usually associated with fever

(b) Etiology:

Common etiologies: Pulmonary and pleural tuberculosis, PCP, MAC, bacterial pneumonia.

Other etiologies: *T. marneffei infection, Cryptococcosis, Histoplasmosis* (lung manifestations in invasive infection); *Cytomegalovirus infection;* noninfectious etiologies: lymphoma, kaposi sarcoma.

c) Key points in taking medical history and physcal examination:

Medical history:	***Examination:***
- Acute, subacute onset - Dyspnea on exertion - Sputum characteristics - Associated symptoms: fever, chest pain… - History of IDUs - History of tuberculosis in family and themselve	- Respiratory distress: dyspnea, cyanosis - Generalized manifestations: fever, weight loss, rash, lymphadenopathy etc… - Respiratory examination: rales, crepitations… - Other signs of immunosuppression : oral thrush, wasting…

(d) Diagnostic investigations*:* Based on clinical symptoms and history

Routine tests, CD4 count

Chest Xray, AFB smear in sputum; smear for other bacteria

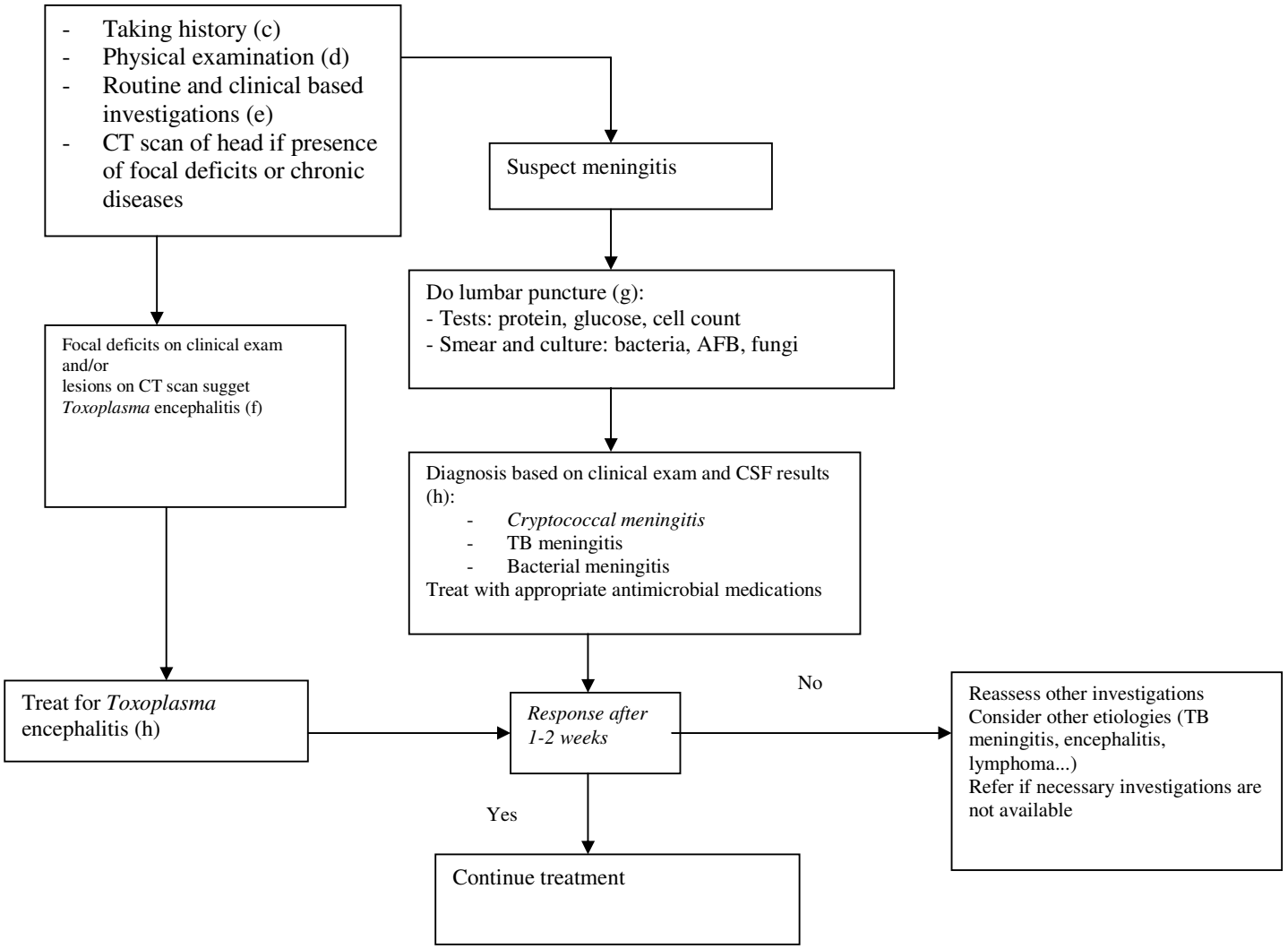
Blood culture if patient presented with fever

Thoracentesis, lymph node aspiration if presence of pleural effusion or lymph node enlargement; send samples for tests

If available: CT Scan .

(e) See part 3, Chapter III: Diagnosis and management of common cormobidities.

2.1.3. Neurology (a, b)



Guidance:

(a) Neurology manifestations: headache, altered level of consiousness, focal deficits.

(b) Etiology:

Central nervous system OIs: *Toxoplasma* encephalitis, *Cryptococcal* meningitis, TB meningitis, bacterial meningitis

Other etiologies: lymphoma, HIV associated neuropathy, progressive multifocal leukoencephalopathy (PML)

Medications: EFV…

(c) Medical history:

Duration of symptoms, associated symptoms: fever, rash, weight loss...

History of tuberculosis in family and patient.

(d) Physical examination:

Find neurological signs: mental disorders, meningismus (headache, neck stiffness, photophobia), focal deficits (hemiplegia, cranial nerve palsy)

Find generalized signs: fever, lymph node enlargement, rash, immunodeficiency signs.

(e) Investigations: based on history and physical examination

Blood culture in case of fever

Chest Xray and other tests for TB if suspected TB meningitis.

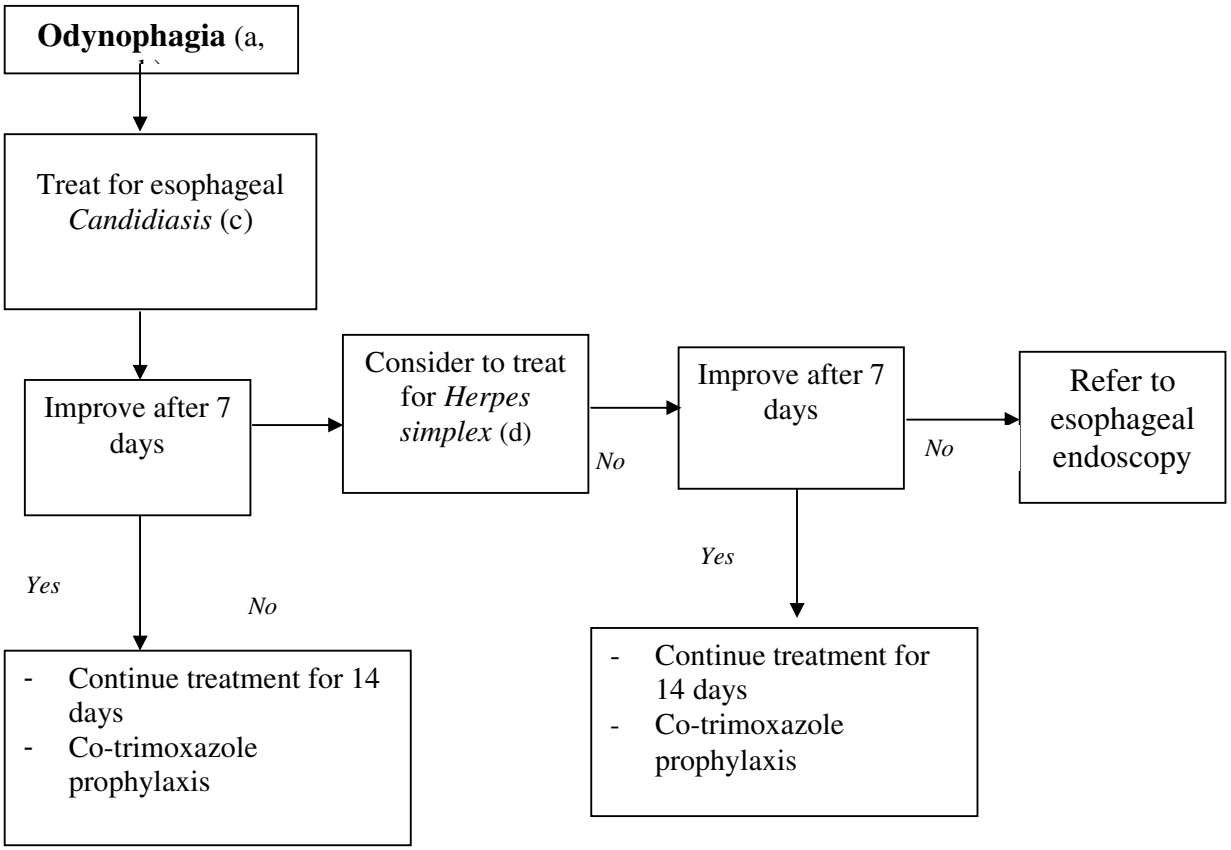
(f) Typical imaging of *Toxoplasma* encephalitis: ring enhancing lesions.

(g) Differential diagnosis based on CSF analysis (DNT):

Etiology	Pressure	Protein	Cell count	Smear	Culture
Cryptococcal meningitis	Significantly Elevate	Mild increase or normal	Mild increase or normal	+ India ink stain	+
TB meningitis	Elevate or normal	Increase from mild to significant	Increase (lymphocyte)	+/- - -	+/-
Bacterial meningitis	Elevate	Significantly increase	Leucocytosis	+/-	+
Toxoplasma encephalitis	Normal	Normal or mild increase	Normal	-	-
Lymphoma	Normal	Normal	Normal	-	-

h) Treatment for *Toxoplasma* encephalitis (see part 3, Chapter III: Diagnosis and management of common cormobidities)

2.1.4. Odynophagia



Guidance:

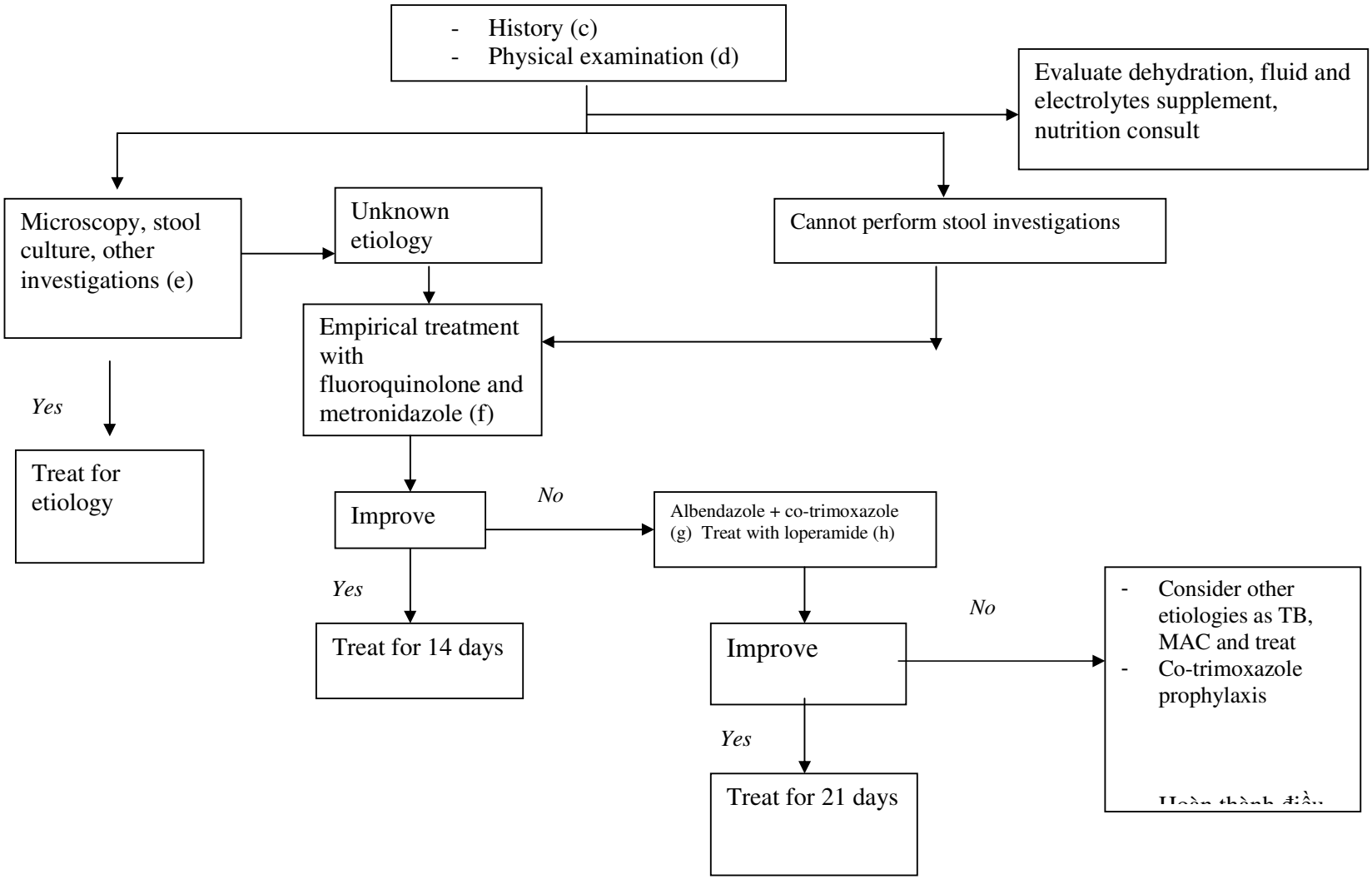
(a) Definition*:* Odynophagia refers feeling of pain in throat or retrosternum when patient swallows, may comes with difficulty in swallowing, which usually is a symptom of esophagitis.

(b) Etiology causing odynophagia in patients living with HIV*:*

- *Candidiasis*
- *Herpes simplex*
- *Cytomegalovirus*
- Aphthous ulcer
- Kaposi sarcoma, lymphoma

(c) Treatment for esophagitis due to *Candidiasis, Herpes simplex* (see part 3, Chapter III: Diagnosis and management of common cormobidities).

2.1.5. Chronic diarrhea (a, b)



Guidance:

(a) Definition: Chronic diarrhea is defined when patient passed loose or watery stool more than 3 times per day, lasting longer than 14 days.

(b) Etiology:

- Bacterial infections: *Salmonella, Shigella, Campylobacter*

- Protozoa and helmiths: *Giardia, Amoeba, Cryptosporidium, Isospora, Microspora, Strongyloides*

- *Mycobacterium* infection: TB, MAC

- Virus: CMV

- HIV associated malignant disease: Kaposi sarcoma, lymphoma

- HIV

(c) Medical history:

- Frequency of diarrhea, stool characteristics

- Associated symptoms: fever, abdominal pain, location and patterns of pain

- History of ART and other medications; antibiotics used to treat diarrhea

- History of TB and other infectious diseases in family.

(d) Physical examination:

- General assessment, dehydration status, nutrition

- Generalized symptoms: fever, lymphadenopathy; respiratory and cardiovascular examination

- Abdominal examination: pain, ascites, hepatomegaly, intraabdominal lymph nodes.

(e) Investigations:

- Fecal blood and leucocyte tests (invasive diarrhea); ova and parasites tests (amoeba, giardia), strongyloides larva, hook worm, helmith ova. Look for *Cryptosporidium, Microsporidium* and *Isospora*; AFB smear (TB and MAC), if available

- Blood culture in case of fever, suspected diarrhea with bacterial septicemia

- Chest X-ray, sputum tests in case of suspected TB or pulmonary TB

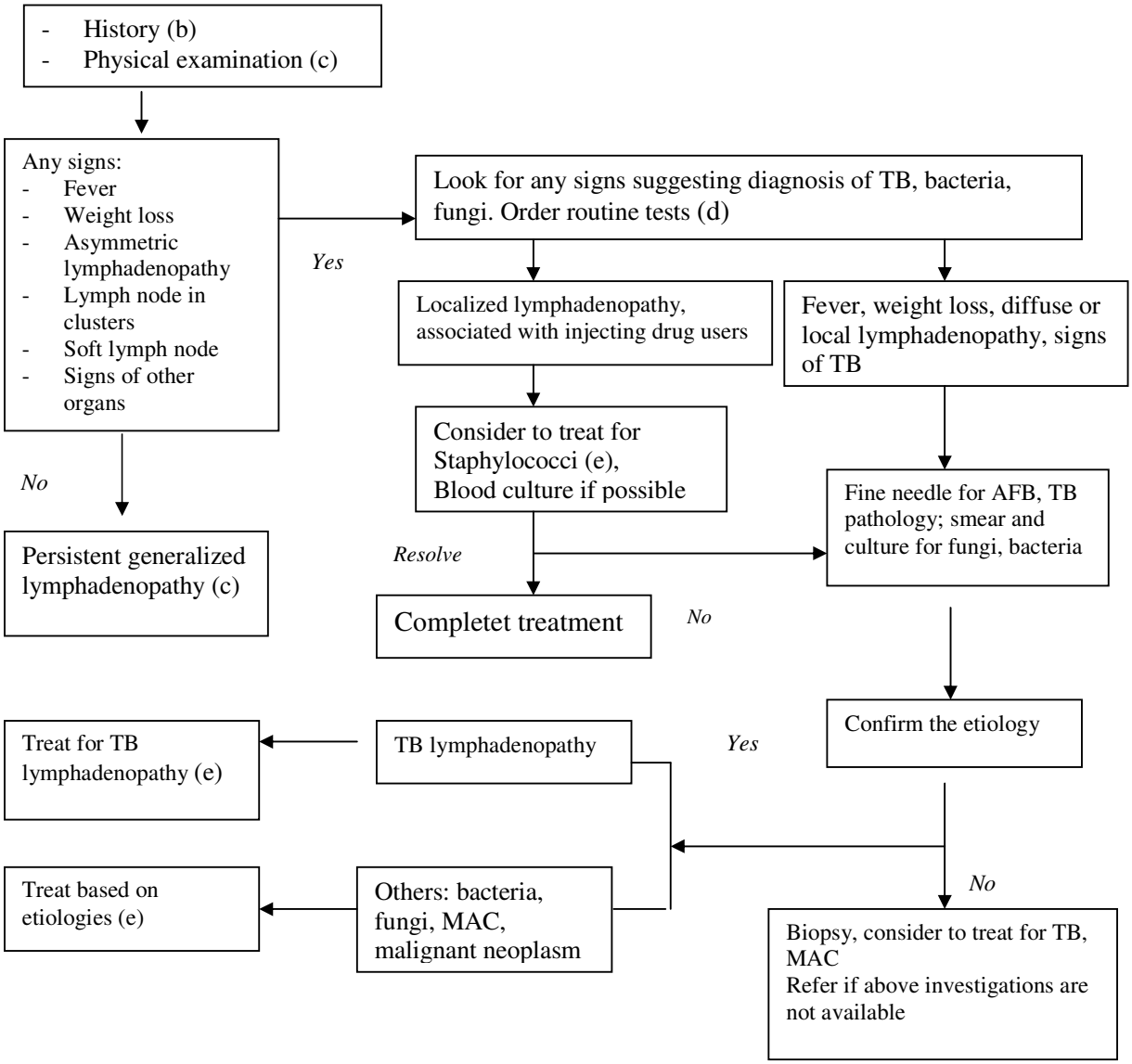
- Abdominal ultrasound if possible, indicating hepatosplenomegaly, lymph node enlargement, ascites.

(f) Fluoroquinolone P.O (ciprofloxacine 500mg, twice daily or ofloxacine 200mg, twice daily) + metronidazole P.O 500 mg twice daily. Useful against *Shigella, Salmonella, Campylobacter*, amoeba and *Giardia*. Note: rule out TB before giving fluoroquinolone.

(g) Albendazole 200 mg 2- 4 times per day + co-trimoxazole 960 mg 1-2 times per day. Useful against *Isospora, Microsporidia*, stronglyloides.

(h) Loperamide begin with 4 mg, followed by 2 mg after 4 hour if stool is still loosen, maximum 16 mg/day. Loperamide should not be used in patient with bloody stool.

2.1.6. Lymph node enlargement (a)



Guidance:

(a) Etiology*:* Lymph node enlargement in symptomatic patients are usually caused by infection or malignant diseases.

- Infection: TB, *T. marneffei, Cryptococcosis*, Staphylococci, maybe *MAC, Nocardia*, Syphilis, *Histoplasmosis, Leishmaniasis*

- Malignancy: Lymphoma, Kaposi sarcoma

- HIV (persistent generalized lymphadenopathy in asymptomatic patient with HIV).

(b) Medical history:

- Duration, associated symptoms: fever, pain, rash, cough…

- History of presence and treatment of OIs (*T. marneffei* infection, TB, etc..) and other diseases.

(c) Physical examination: general evaluation, finding of any signs: fever, wasting, oral thrush, rash, anemia…

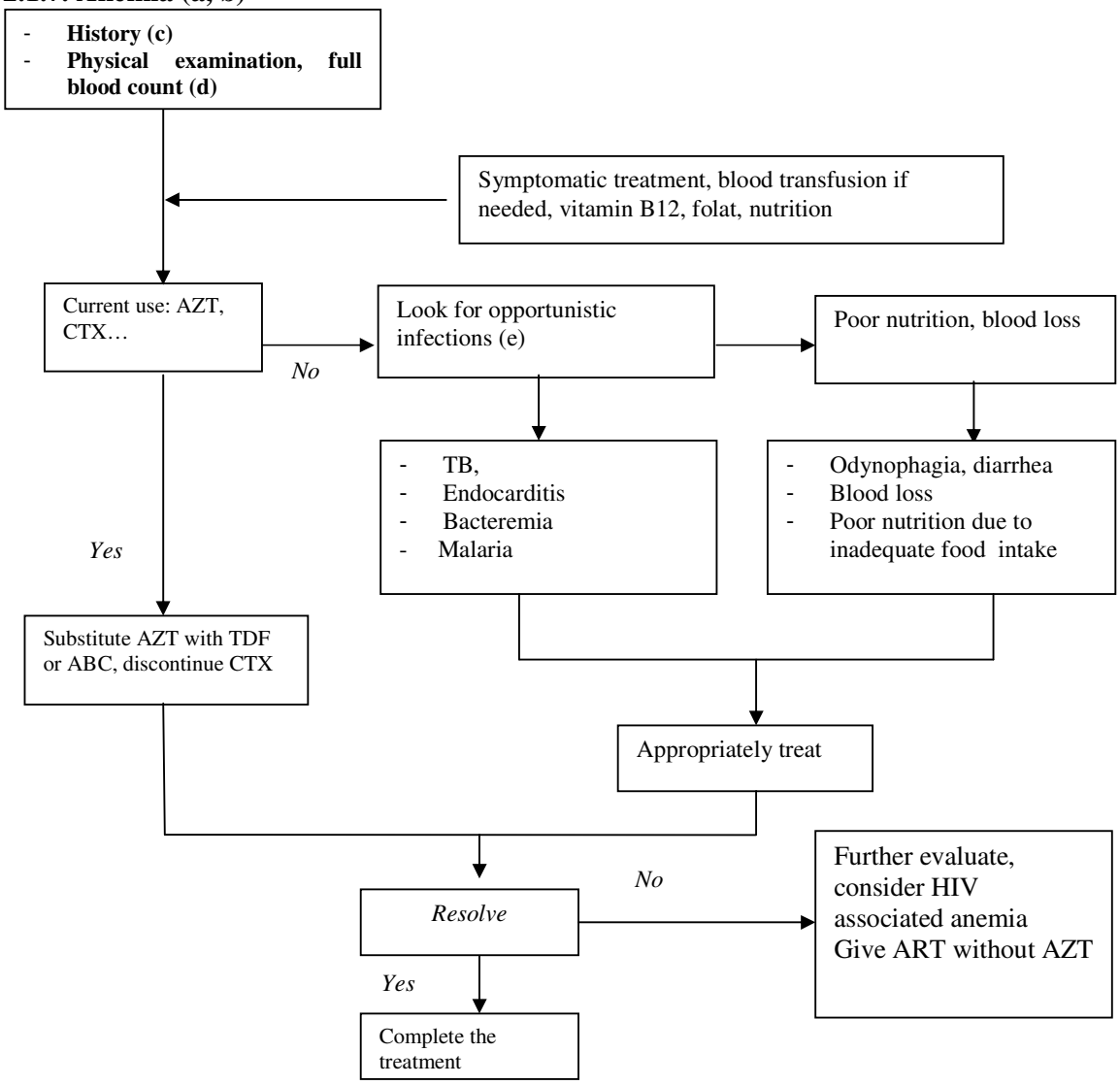
- Exam the lymph node, access the size and characteristics

- Look for signs of other organs, intraabdominal lymph node, hepatosplenomegaly.

(d) Routine investigations: full blood count, CD4 count, chest X-ray

(e) See part 3, Chapter III: Diagnosis and management of common cormobidities.

2.1.7. Anemia (a, b)



Guidance:

***(a) Definition**:*

Anemia is defined as Hb < 120g/L in men and < 100 g/L in women

***(b) Etiology**:*

Infection: TB, invasive mycosis, endocarditis, MAC, malaria…

Lack of nutrition, dysphagia, chronic diarrhea

Medications: AZT, CTX…

Blood loss, bone marrow failure due to internal diseases …

Malignant diseases, HIV.

(c) Medical history:

Duration of associated symptoms (fatigue, tinnitus, dizzeness)

Any signs such as fever, diarrhea, odynophagia, cough, rash…

History of opportunistic infections (OIs)

Medication history of co-trimoxazole, AZT and others

History of IDU, travelling to malaria endemic area

History of blood loss, nutrition diet.

(d) Physical examination

Assess the severity of anemia, nutrition, look for signs of OIs.

(e) Investigations:

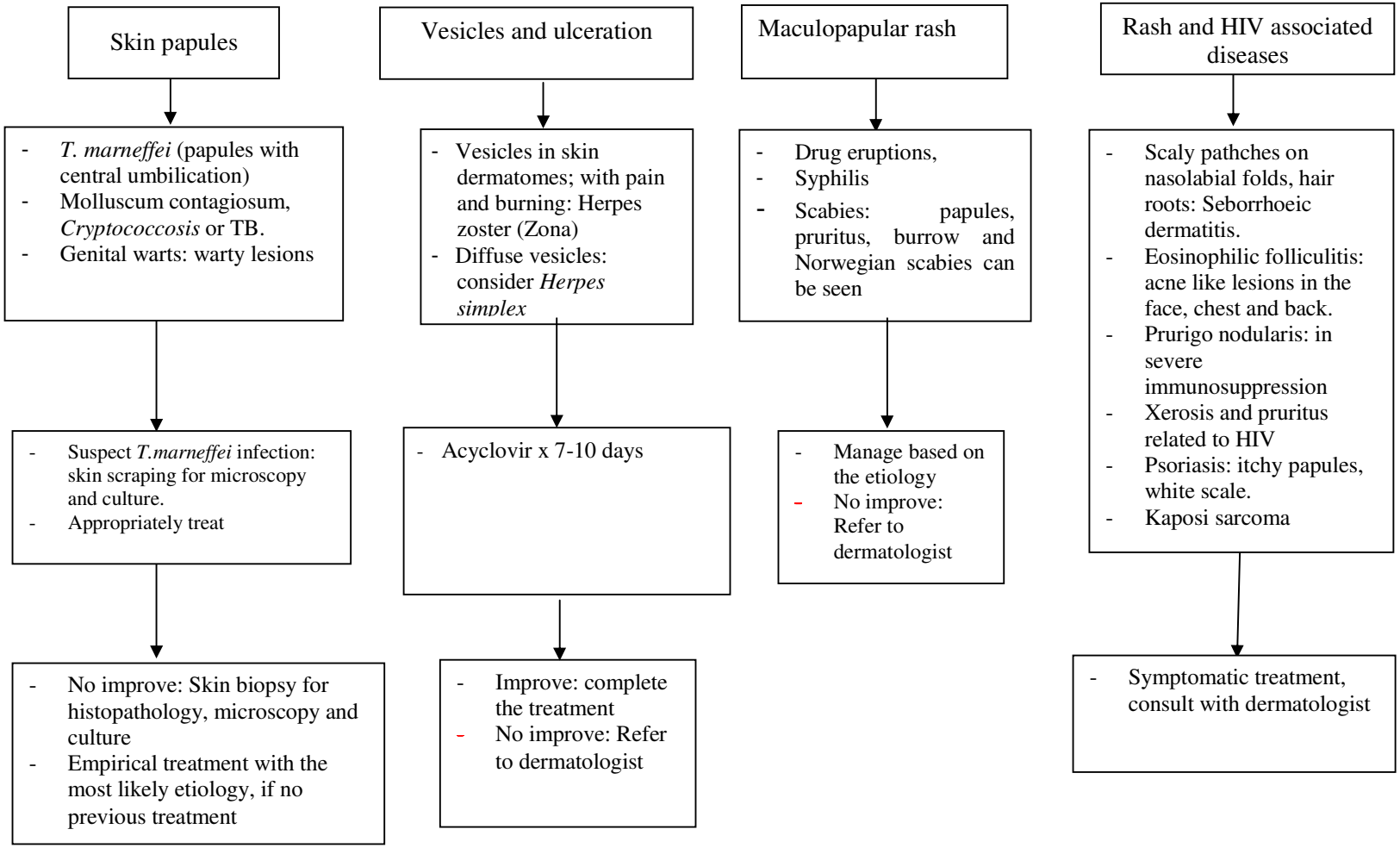
Full blood count: Hb, blood cells with differentiation; mean corpuscular volume (MCV) (macrocytic anemia: vitamin B12 deficiency, co-trimoxazole, AZT; microcytic anemia: OIs, blood loss)

Tests for malaria

Diagnostic tests for OIs: AFB smear in sputum, smear and culture for fungi

Bone marrow aspiration, lymph node and marrow biopsy, other tests if needed.

2.1.8. Mucocutaneous manifestations



Guidance:

(a) Etiology with mucocutaneous manifestations:

- Bacteria: folliculitis, impetigo due to cocci, cellulitis, lupus vulgaris

- Virus: *Herpes simplex*, *Herpes zoster*, molluscum contagiosum (*Poxvirus*), human papilloma virus (HPV), hairy leukoplakia (*Epstein-Barr virus*)

- Fungi: *Candida, T. marneffei*, cutaneous fungal infections (dermatophytosis, onychomycosis), *Cryptococcal infections*

- Parasites: scabies

- Neoplasm: Kaposi sarcoma, lymphoma

- Other dermatitis: eosinophilic folliculitis, pruritic papule eruption (PPE), psoriasis, xenosis

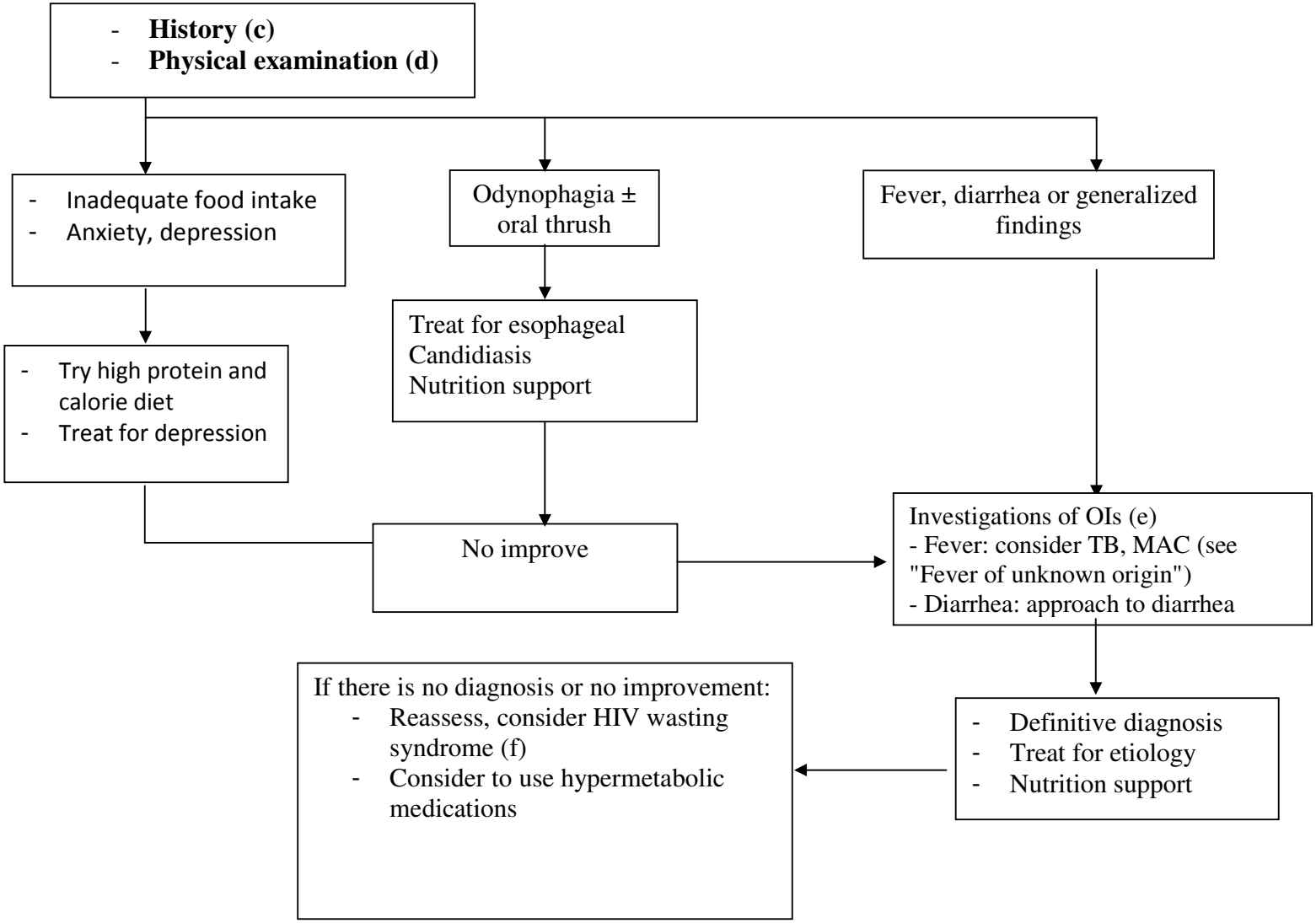
- Drug reactions: co-trimoxazol, ARV drugs can cause rash, generalized exanthema, bullous or skin detachment.

(b) Key points in taking history and examing a patient with skin lesions:

Medical hítory:	**Physical exam:**
- Duration ? - When did the lesion begin? - Was it itchy or not? - History of allergic diseases: asthma, weather allergy? - Current medications? How long did the patient use? - Associated symptoms : fever …	- Types of lesions: papules with central umbilication, vesicles, ulcers, macules… - Distribution - Assessment of the lesion progression - Signs of immunosuppression: oral thrush, wasting - Associated findings: fever, hepatosplenomagaly, neurological signs…

(c) Diagnosis and treatment based on etiology (see part 3, Chapter III: Diagnosis and management of common cormobidities)

2.1.9. Wasting (a, b)



Guidance:

(a) The severity of weight loss is defined when patient reported or healthcare worker compared between current weigth and weight by height.

(b) Etiology*:*

Infections: OIs such as TB, chronic diarrhea due to protozoa, invasive mycosis and MAC

Poor nutrition due to inadequate food intake

Poor intake due to odynophagia (Esophageal Candidiasis)

Metal disorders: anxiety, depression.

(c) History:

Timing and severity of weight loss

Findings: fever, diarrhea, odynophagia, cough...

History of OIs

Nutrition diet

Signs of anxiety, depression.

(d) Physical examination:

Evaluate the severity of weight loss, presence of edema, anemia

Look for any signs of OIs (oral thrush, lymph node enlargement, etc...)

(e) Investigations*:*

Chest X-ray, AFB smear in sputum if suspected TB

Blood culture in case of bacteremia and fungemia

Stool microscopic examination for parasites and protozoa.

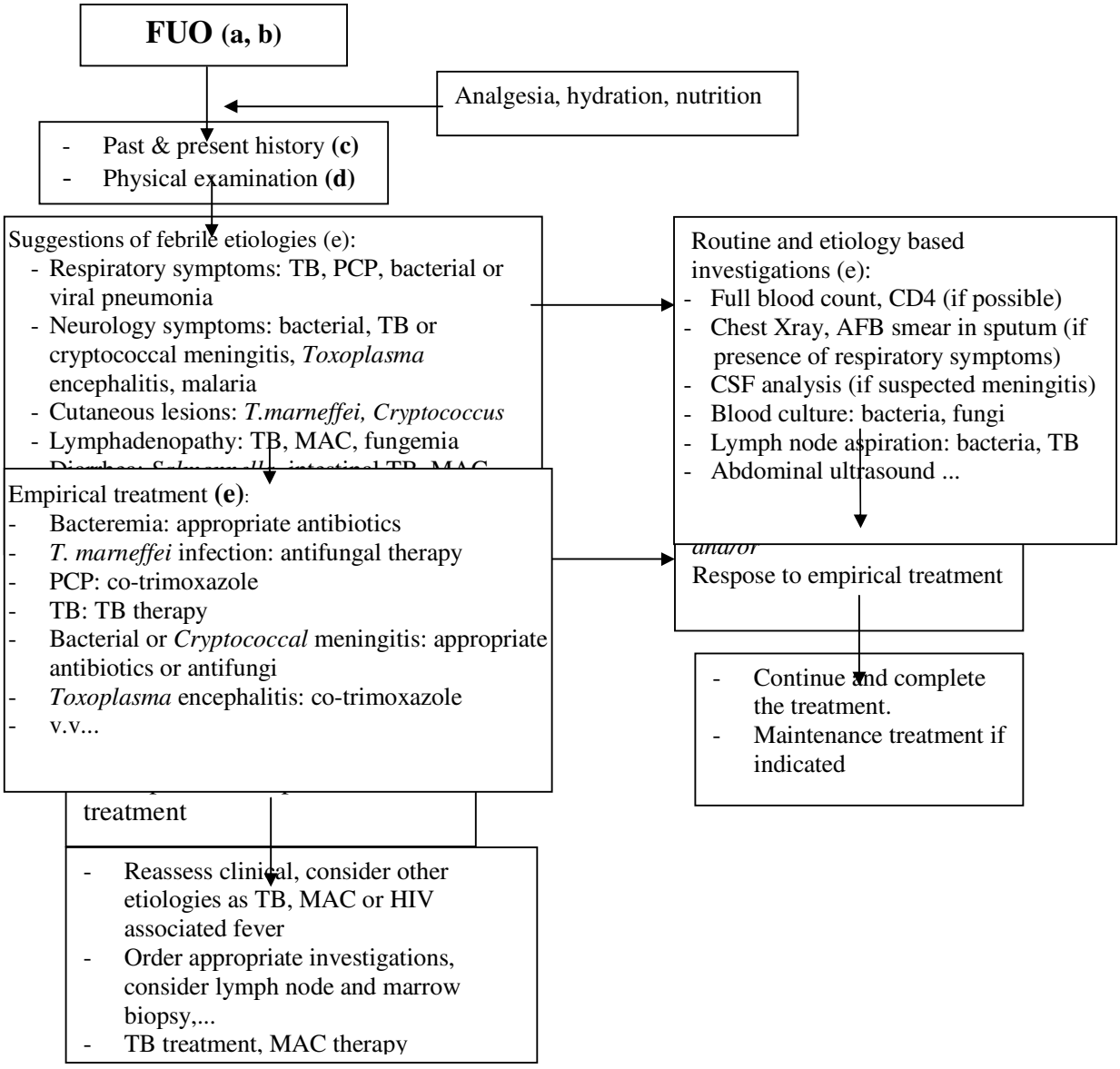
(f) HIV wasting syndrome:

Weight loss > 10% body weight

Presence of persistent diarrhea (loose stool > 2 times per day) or documented fever for at least 30 days.

2.2. In children

2.2.1. Fever of unknown origin (FUO)



Guidance:

(a) Definition: Fever of unknown origin is defined as temperature over $37^0$5, lasting longer than 14 days.

(b) Common etiologies causing fever of unknown origin:

Common etiologies in HIV and immunosuppression:

TB, MAC, *T. marneffei* infection, *Cryptococcosis*, bacteremia due to *Salmonella* and others, Cytomegavirus disease ...

HIV associated malignant diseases: lymphoma

HIV associated fever, malaria

Drug reactions: CTX or ARV (like NVP, ABC….)

(c) Past and present history*:*

Duration, pattern of onset (acute or subacute)

Organ symptoms: headache, diarrhea, cough, rash…

Medications: CTX, ARV, others

History of OIs and HIV associated diseases (recurrence of OIs if there were no secondary prophylaxis or no ART)

History of medication allergy and other diseases

Family history: TB and other infectious diseases

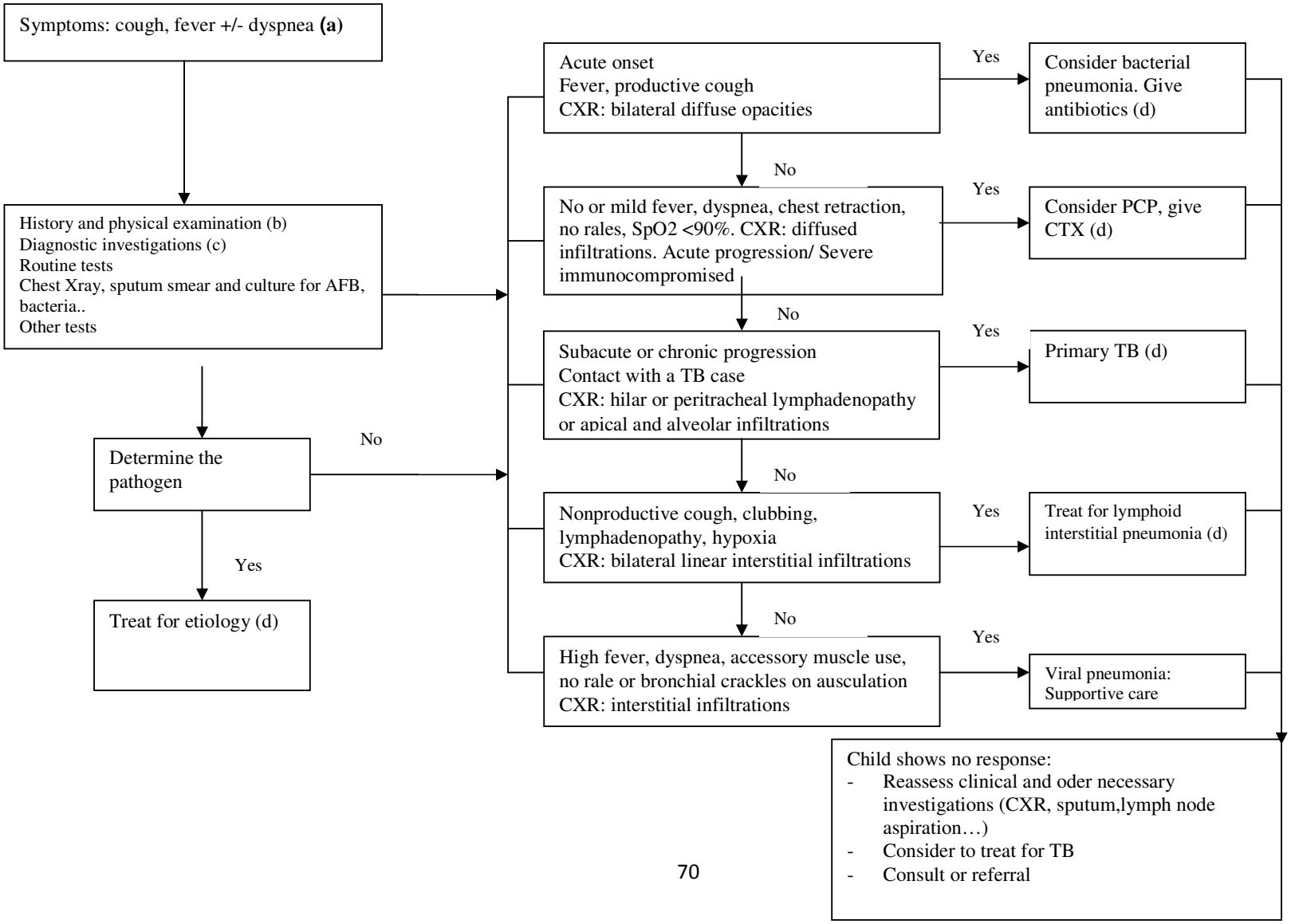
(d) Physical examination:

Full body examination, focus on symptomatic organs.

If children have low percentage of CD4, notice opthalmologic examination (funduscopy) to find CMV, *Toxoplasma* and blood culture for fungi, bacteria.

(e) Look for pathogens resulting to opportunistic infections *(*see part 3, Chapter III: Diagnosis and management of common cormobidities)

2.2.2. Respiration



Guidance:

(a) Etiology:

Common etiologies: bacterial pneumonia, PCP, primary TB, lymphoid interstitial pneumonia, viral pneumonia

Others: mycosis, noninfectious diseases.

(b) Key points in history taking and physical examination:

History:	**Examination:**
- Acute, subacute onset - Non-productive or productive cough - Associated symptoms: fever, weight loss, night sweats … - History of TB in family and the child	- Respiratory distress: dyspnea, cyanosis - Generalized signs: fever, weight loss, rash, lymphadenopathy, clubbing... - Respiratory exam: rales, crepitations… - Other signs: mental and growth development, immunosuppression (oral thrush, wasting…).

(c) Diagnostic investigations: Based on clinical symptoms and history

Routine tests, CD4 count,

Chest X-ray, sputum and gastric lavage for AFB smear; smear and sputum culture for other bacteria.

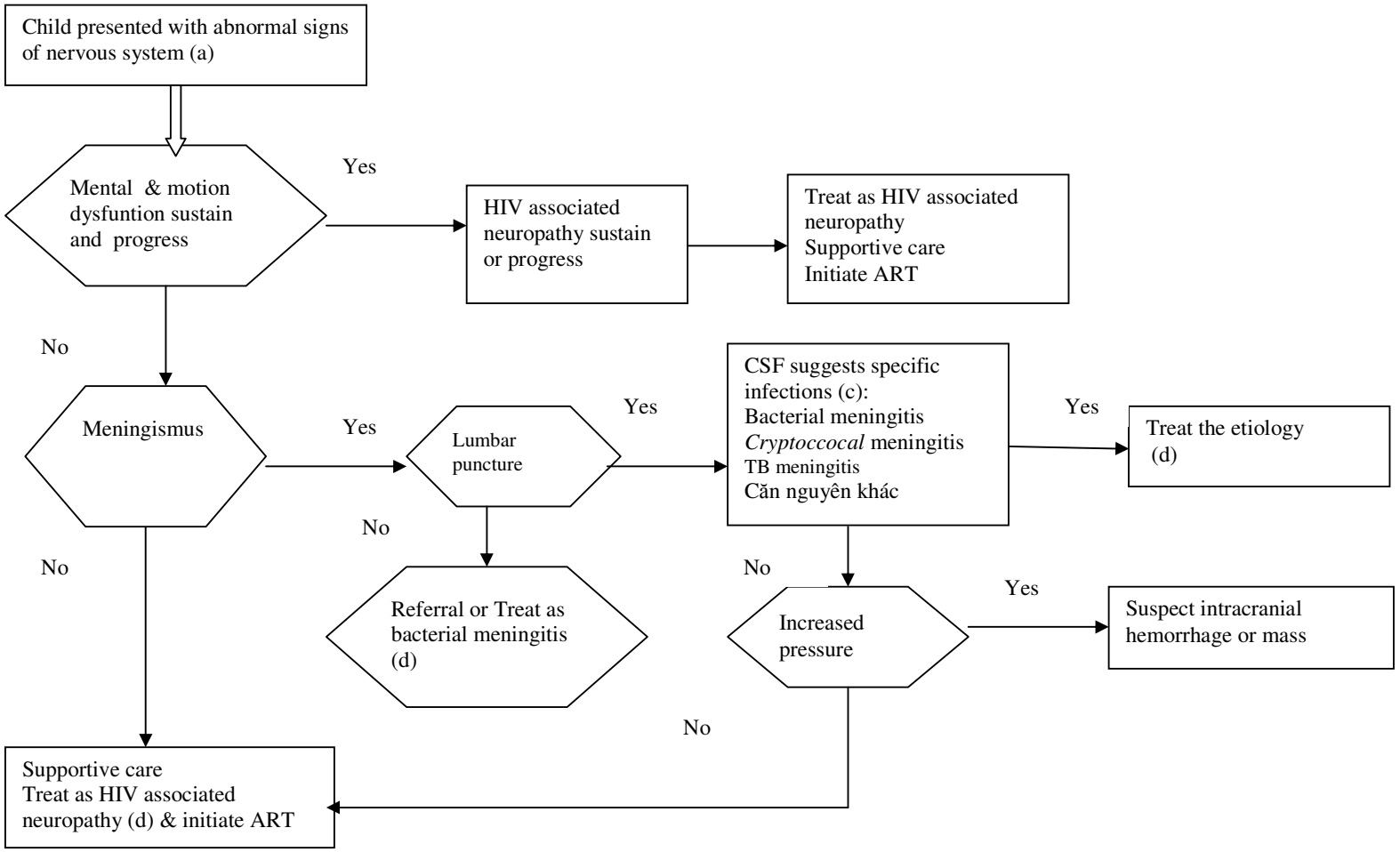
Blood culture if presence of fever

Thoracentesis, lymph node aspiration if presence of pleural effusion or lymph node enlargement; take samples for investigations

If available: CT Scan of lung

(d) Treatment: see part 3, Chapter III: Diagnosis and management of common cormobidities

2.2.2. Neurology



Guidance:

(a) Definition: Neuropathy diseases in children include:

Progressive encephalopathy: slow decrease in motion, cogitive and language function. Child has delayed growth or did not reach the developmental milestones; usually has early onset in first few years; however, child can present at any time.

Sustained encephalopathy: motion dysfunction and growth impairment with varied severity, but no progression in any visit.

HIV sustained encephalopathy: it is defined when there are no other etiologies causing delayed growth, neurological dysfunction (sush as preterm birth, distress at bith, brain injury or drug and alcohol influence during pregnancy).

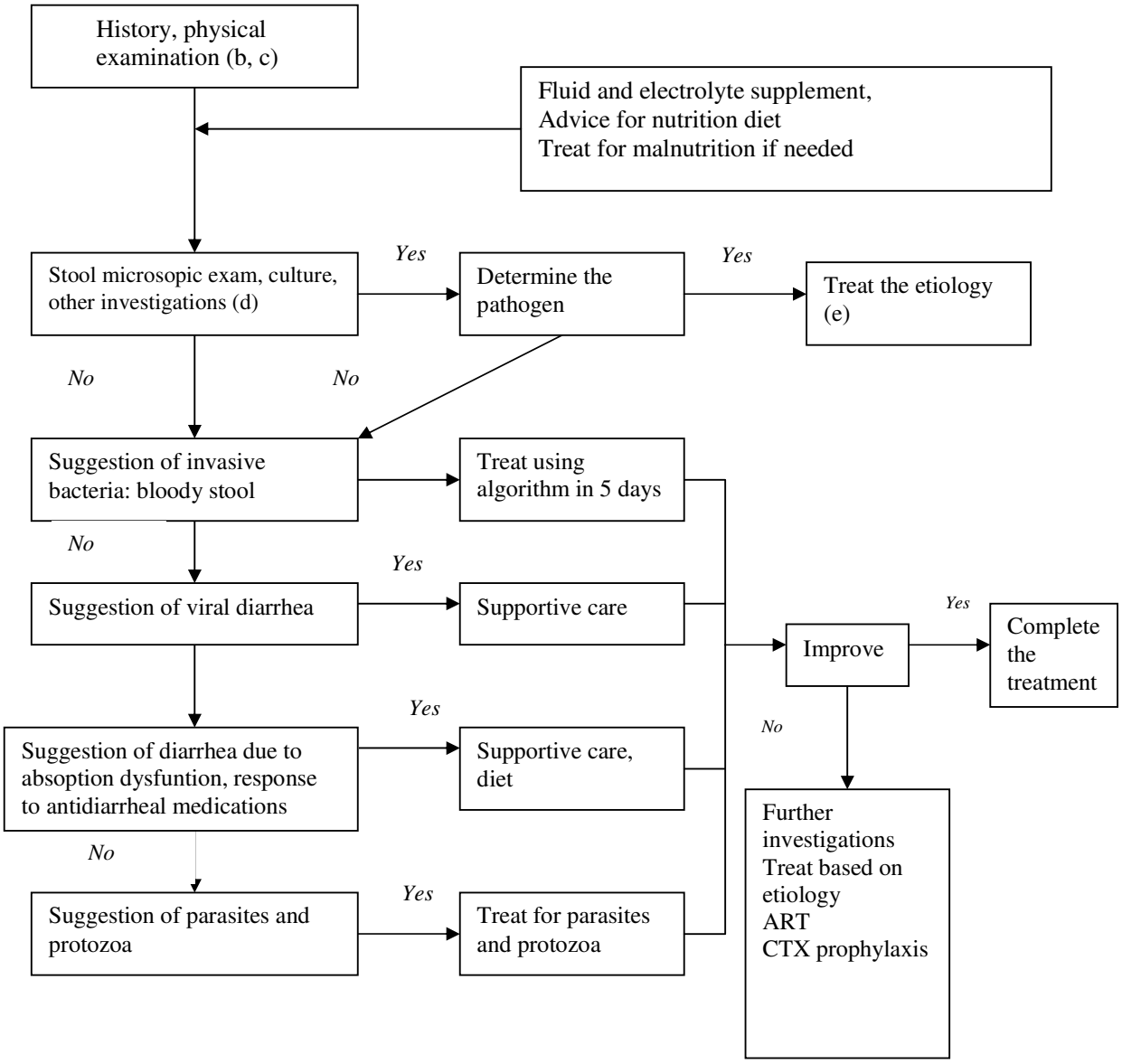
Acute infections: acute onset with seizures, localized paralysis and meningismus, usually caused by bacterial meningitis, cryptococcal meningitis, TB meningitis.

(b) Acute manifestations can occur in asymptomatic children with HIV or those with HIV associated neuropathy.

(c) Base on CSF results: biochemistry, cell count, smear and culture for bacteria and fungi.

(d) Etiology and treatment: see part 3, Chapter III: Diagnosis and management of common cormobidities.

2.2.4. Persistent diarrhea (a)



Guidance:

(a) Definition: Persistent (chronic) diarrhea is defined when the child passed loose stool more than 3 times per day, lasting longer than 14 days

(b) Medical history:

Frequency, stool characteristics

Associated symptoms: fever, abdominal pain, location and pattern of pain

Nutrition history

History of TB and other infectious diseases in family.

(c) Physical examination:

General assessment, dehydration status, nutrition

Assessment of physical growth

Generalized symptoms: fever, lymphadenopathy; weight loss

Respiratory and cardiovascular examination

Abdominal examination: pain, ascites, hepatomegaly, intraabdominal lymph nodes.

(d) Investigations:

Stool examination:

- Fecal blood and leucocyte tests (diarrhea due to shigellosis and bacteria); protozoa and parasites (amoeba, giardia, strongyloides larva, hook worm, helmith ova); look for AFB (TB and MAC)

- Look for *Cryptosporidium, Microsporidium* and *Isospora*; if available

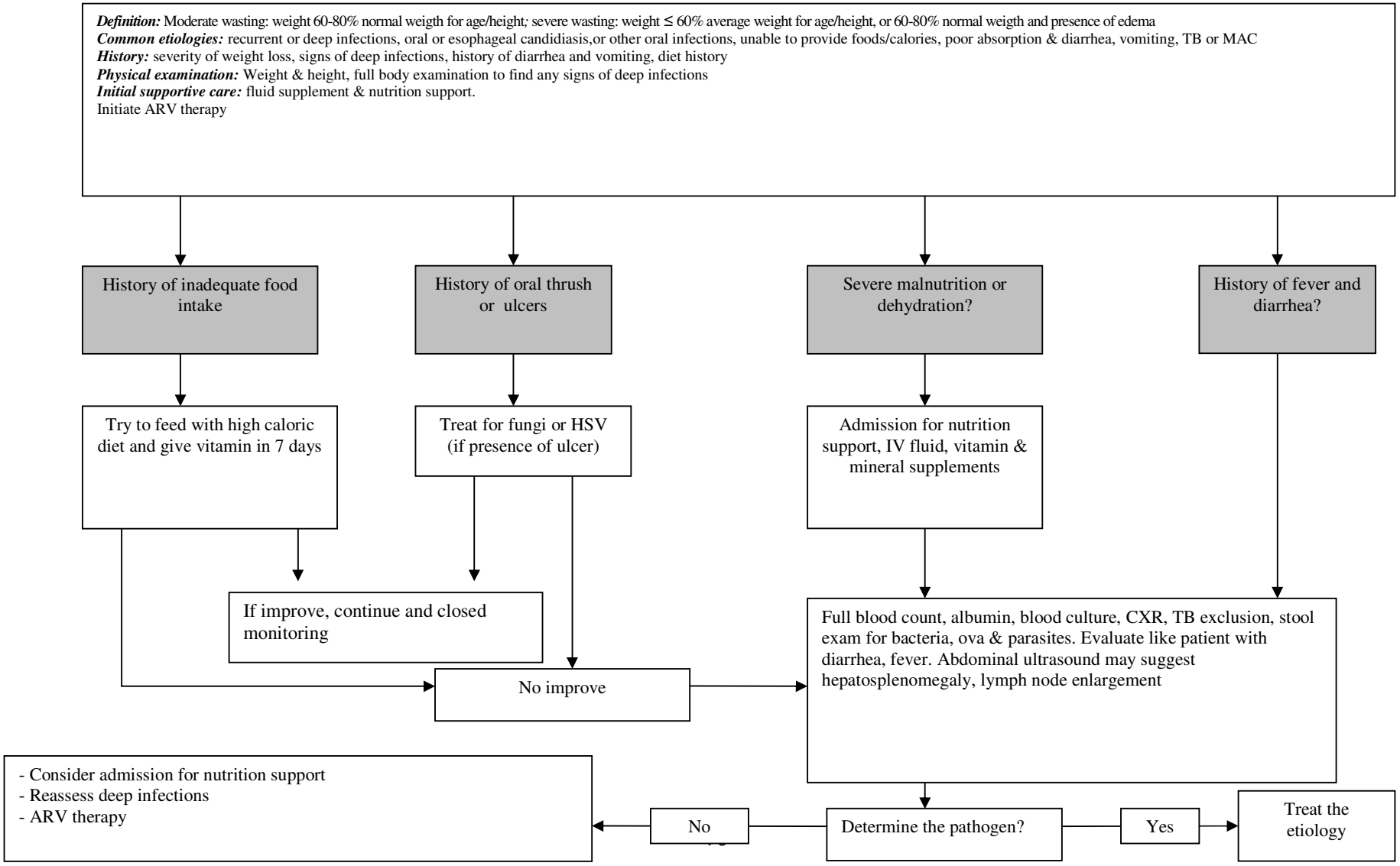
Blood culture in case of fever, suspected diarrhea with bacterial septicemia

Chest X-ray, sputum tests in case of suspected TB or pulmonary TB

Abdominal ultrasound indicates hepatosplenomegaly, lymph node enlargement, ascites.

(e) Etiology and treatment: see part 3, Chapter III: Diagnosis and management of common cormobidities.

2.2.5. Stunting and Wasting



3. Diagnosis and treatment of common cormobidites

3.1. *Pneumocystis jiroveci* pneumonia(PCP)

3.1.1. Diagnosis

PCP is subacute onset within 1- 2 weeks. The common manifestations are cough, progressive dyspnea, fever and night sweats. In children, PCP usually occurs in those below 1 year with severe progression and high mortality. Above 90% patients present with normal chest X-ray; typical radiograph are bilateral, diffuse interstitial infiltrations.

Diagnosis is made by clinical presentations and response to co-trimoxazole treatment.

If available: take bronchoalveolar lavage fluid for Giemsa, silver or immunofluorescent stains to diagnose *P. jiroveci*.

3.1.2 Treatment

a) Preferred therapy

Co-trimoxazole (CTX) (other names : trimethoprim-sulfamethoxazole, TMP-SMX), based on TMP dose for both adults and children, is 15-20 mg TMP/kg/day in divided 3 doses x 21 days.

b) Alternative therapy (in case of sulfamide allergy)

Adult: primaquine 30 mg base P.O once daily x 21 days plus clindamycin 600 mg I.V q8h in 10 days, followed by 300 mg P.O q6h x 11 days after.

Children: primaquin 0,3 mg base/kg P.O once daily plus clindamycin 10 mg/kg q8h x 21 days.

c) In case of respiratory distress: If PaO_2 <70 mm Hg or SpO2 < 90% at room air, give adjunctive prednisolon within 72 hours after starting PCP therapy

Adult:

- Prednisolon 40 mg P.O twice daily x 5 days, followed by 40 mg once daily x 5 days then 20 mg once daily from day 11 to 21.

- IV methyprednisolon can be used as 75% of prednisolon dose

Children: prednisone 1 mg/kg twice daily x 5 days, followed by 0,5 mg/kg twice daily x 5 days, then 0,5 mg/kg once daily from day 11 to 21, discontinue based on the disease condition.

d) Maintenance therapy

CTX dose 960 mg P.O once daily in adults and 5 mg TMP/kg/day in children until patients who receive ART at least 12 months, are stable and have CD4 count > 350 cells/mm^3 or undetactable viral load. Maintenance therapy should not be discontinued for children below 5 years.

3.2. *Cryptococcosis*

3.2.1. Diagnosis

a. Fungemia: fever, skin lesions with necrosis papule, lung infiltrates. Investigations: skin biopsy or lymph node aspiration for fungi smear; blood culture.

b. Meningitis: headache, photophobia, meningismus, altered mental status, focal neurological deficits, fever. Investigations: CSF analysis usually shows mild change; india ink staining, *Cryptococcal* antigen (CrAg) and culture should be performed in CSF.

Cryptococcosis rarely presents in children, often when they are greater than 6 years old.

3.2.2. Treatment

Induction phase: use one of any following regimens in 2 weeks:

Amphotericin B 0,7 -1 mg/kg/day + flucytosine 100 mg/kg/day

OR: Amphotericin B 0,7 -1 mg/kg/day + fluconazole 800- 900 mg/day (12 mg/kg/day and up to 900 mg/day if below 18 years);

OR: Fluconazole dose 800 - 1200 mg/day if amphotericin B is unavailable

Consolidation phase: fluconazole 800-900 mg/day (or 12 mg/kg/day and up to 900 mg/day if below 18 years) in 8 weeks

Maintenance phase: fluconazole 150 - 200 mg/day (or 6 mg/kg/day and up to 200 mg/day if below 18 years). Discontinuation of maintenance treatment is recommended when patients are stable and adhere to ART treatment for at least 1 year, and have CD4 > 200 cells/mm³ for over 6 months or CD4 > 100 cells/mm³ for sustained 6 months and have undetectable viral loads. Discontinutaion of maintenance treatment is not recommended in children under 2 years.

For *Cryptococcal* meningitis, repeat lumbar puncture daily to reduce increased intracranial pressure, drain at least 15 - 20 ml each time or until patients have headache relieved (mannitol and corticoid are ineffective).

3.2.3. When to start ART

ART should not be initiated in patients with cryptococcal meningitis due to high risk of IRIS and life-threatening neuropathy.

In HIV patients with recent diagnosis of cryptococcal meningitis, delay ART until there is proof of stable clinical response to induction and consolidation antifungal therapy at least after 4 weeks in case of amphotericin B or 4-6 weeks in case of fluconazole, respectively.

3.3. *Candidiasis*

3.3.1. Diagnosis

Oral candidiasis: creamy white, plaque like lesions or patches on the tongue, gingiva, buccal surface, soft palate, anterior tonsils and posterior pharynx.

Esophageal candidiasis: odynophagia; maybe associated with oropharyngeal thrush. Diagnosis is usually made by clinical presentations; only in atypical clinical manifestations or unresponse to treatment are fungal smear and culture indicated. Endoscopy should be performed in patients who showed no improvement to antifungal treatment.

Genital candidiasis: women presents with mucosal itching and burning; white adherent vaginal discharge like cottage cheese; redness, swelling and pain in vulva or vagina; episodes

recur more frequently. Vulvovaginal candidiasis is usually diagnosed based on clinical manifestations; fungal microscopic and culture confirmation is required if there is no clinical response or ineffective treatment.

3.3.2. Treatment

Oral candidiasis:

- Adult: fluconazole 100 - 200 mg/day x 7 - 14 days

- Children: fluconazole 3-6 mg/kg once daily x 7-14 days

Esophageal candidiasis:

- Adult: fluconazole 200 - 300 mg/day x 14 - 21 days, or itraconazole 200 mg/day x 14 – 21 days.

- Children: fluconazole 3-6 mg/kg once daily x 14 - 21 days

Genital candidiasis: fluconazole 150 - 200 mg P.O a single dose; in patient with severe immunocompromised, give higher doses and longer duration; or itraconazole 100 mg P.O twice daily x 3 consecutive days; or topical clotrimazole 100 mg/miconazole 100 mg once daily x 3-7 days; or clotrimazole 500 mg daily.

3.4. *Talaromyces marneffei* infection *(former name: Penicillium marneffei)*

3.4.1. Diagnosis

Clinical manifestations

Isolated cutaneous presentation: painless, non-pruritic skin papules with central necrosis umbilication; lesions usually appear on the face or have generalized distribution.

Fungemia: fever, skin lesions, anemia, heptosplenomegaly, lymph node enlargement, wasting.

Lung involment: nonproductive cough, fever, mild to moderate dyspnea.

Investigations

Fungal microscopic examination and culture in specimens of skin, bone marrow or lymph node.

Blood culture and other specimen culture on media Sabbouraud at 25 - 37°C.

3.4.2. Treatment

Induction therapy

Preferred therapy: amphotericin B (0,7 - 1,5 mg/kg/day) in 2 weeks, followed by itraconazole 200 mg twice daily (in childern: 5 - 6 mg/kg twice daily) x 8 - 10 weeks.

Alternative therapy (in mild case or without amphotericin B): itraconazole 200 mg twice daily x 8 weeks.

Maintenance therapy: itraconazole 200 mg/day in adults and 3 mg/kg/day in children; discontinue in patients with ART who have CD4 counts > 200 cells/mm^3 for at least 6 months.

3.5. *Toxoplasma gondii* encephalitis

3.5.1. Diagnosis

Headache, dizziness, seizures, fever

Focal neurological deficits

A single or multiple lesions with mass effect on CT Scan or MRI of the brain

Response to specific therapy can support the diagnosis

Children: *Toxoplasma* infection can occur before giving birth (congenital) or postnatally. Early manifestations of *Toxoplasma* infection: fever, sore throat, myalgia, lymphadenopathy, rash and hepatosplenomegaly. Late manifestations: encephalitis, fever, confusion, seizures and retinal damage.

5.5.2. Treatment

Adult

Therapy: co-trimoxazole, 10 mg TMP/kg/day in divided 2 doses in 6 weeks.

Maintenance treatment: co-trimoxazole P.O 960 mg/day; discontinue in patients with ART have CD4 counts > 350 cells/mm^3 for at least 6 months.

Children

Congenital toxoplasmosis: Duration should be 12 months or decided by experienced physicians. Use one of two following regimens:

- Co-trimoxazole (CTX): 10 mg TMP/kg/day in divided 2 doses

- Pyrimethamine 2 mg/kg/day P.O daily x 2 days; followed by 1 mg/kg/day P.O daily in 2 - 6 months; then 1 mg/kg/day P.O (3 times/week) + sulfadiazine 50 mg/kg P.O in divided 2 doses + acid folinic 10 mg P.O or I.M in each dose of pyrimethamin.

Postnatal Toxoplasmosis: use one of two following regimens in 6-8 weeks:

- Co-trimoxazole (CTX) 10 - 15 mg TMP /kg/day in divided 2 doses

- Pyrimethamine 2 mg/kg P.O once daily in 3 days, followed by 1 mg/kg daily + acid folinic 10 - 25 mg P.O daily + sulfadiazin 25mg/kg P.O 4 times per day.

- **Maintenance treatment**: co-trimoxazole (CTX) dose 5 mg TMP/kg/day. Treatment should be stopped similarly to adult therapy in children over 5 years; no discontinuation in children below 5 years.

3.6. Disease due to *Mycobacterium avium complex* (MAC)

3.6.1. Diagnosis

Presistent or recurrent fever, weight loss, fatigue, anemia, hepatosplenomegaly, lymph node enlargement. Differential diagnosis should include tuberculosis.

Diagnosis: Isolation of MAC from blood or other sites is usually difficult; consider diagnosis of MAC in patients who show no response to TB therapy after 2 - 4 weeks.

3.6.2. Treatment

Adult

Preferred therapy: clarithromycin 500 mg P.O twice daily + ethambutol 15 mg/kg/day P.O.

Alternative therapy: azithromycin 500 mg P.O + ethambutol 15mg/kg/day P.O.

Consider adjunctive medications in patients with severe immunosuppression (CD4 count < 50 cells/mm^3):

- Rifabutin 300 mg P.O daily or Fluoroquinolone such as levofloxacin 500 mg P.O daily or moxifloxacin 400 mg P.O daily.

Discontinue MAC therapy when patients have completed treatment for ≥ 12 months, have no MAC signs and symptoms, and have ART with increase in CD4 count > 100 cells/mm^3 over 6 months.

Children

Clarithromycin: 7,5 - 15 mg/kg twice daily (maximum 500 mg) or azithromycin 10-12 mg/kg (maximum 500 mg/day) P.O daily plus ethambutol 15 - 25 mg/kg P.O daily (maximum 1000 mg)

No discontinuation in children < 2 years. For children over 2 years, criteria for discontinuation is same as that in adults.

3.7. Herpes simplex

3.7.1. Diagnosis

Clinical presentations:

- Mucocutaneous manifestations: vesicles in clusters, leading to skin detachment and ulcer after rupture; lesions usually appear in genital, anal, perianal and orolabial area; sometimes they can spread to esophagus causing dysphagia, odynophagia and bronchotracheal involvement. Disease is more recurrent and severe than that in patient without HIV.

- Herpes encephalitis: Atypical presentations with focal lesions on the frontotemporal lobe

3.7.3. Treatment

Mild case (Mucocutaneous herpes):

Adults: acyclovir 200mg P.O x 5 times/day (or 400mg x 3 times/day) x 5 - 10 day.

Children: acyclovir 20 mg/kg P.O x 3 times/day x 5 -10 days

In severe cases including encephalitis: Acyclovir 5 - 10mg/kg I.V q8h x 14 -21 days.

Topical treatment with antiseptics sush as methylene blue or gentian.

3.8. Herpes zoster

3.8.1. Diagnosis

Clinical presentations: blisters in clusters, pain, distribution in dermatomes, maybe with eye involvement.

3.8.2. Treatment

Adults: acyclovir 800 mg P.O x 5 times/day x 5-7 days in mild case and acyclovir 15 mg/kg I.V q8h x 7-10 days in severe case.

Children: acyclovir 20 mg/kg P.O x 4 times/day x 7 - 10 days in uncomplicated case and acyclovir 10 mg/kg I.V q8h x 10 -14 days in severe and complicated case.

Topical agents with gentian or chlorhexidine

Herpes zoster opthalmicust: topical and oral acyclovir

3.9. *Cytomegalovirus* infection

3.9.1. Diagnosis

Retinitis: blurred vision, floaters, scotoma, photophobia, retinal detachment and blindness if untreated. It may occur in one side or presents as bilateral disease. Retinal damages are usually irreversible.

Colitis: weight loss, abdominal pain, diarrhea, fever, maybe perforation, gastrointestinal bleeding.

Esophagitis: odynophagia

Central nervous system involvement: dementia, encephalitis, polyradiculopathy, CSF analysis shows pleocytosis, elevated or normal protein; it is high mortality.

3.9.2. Diagnosis

Retinitis: Funduscopy indicates necrotizing (white) lesions in retina, with or without intraretinal hemorrhage, with single or diffuse damage.

Colitis, esophagitis, encephatitis: If available, take specimens from brain biopsy, CSF and blood to cultre or perform PCR.

3.9.3. Treatment

a) Adult

CMV retinitis

Induction therapy (acute phase):

Preferred therapy: intravitreal injection of ganciclovir 2 mg in 0,05 - 0,1 ml twice weekly x 2 weeks plus valganciclovir 900 mg P.O twice daily x 14 – 21 days

Alternative therapy: combine intravitreal injection of ganciclovir 2 mg in 0,05 - 0,1 ml twice weekly x 2 weeks and one of any following regimens:

- Ganciclovir 5 mg/kg I.V twice daily x 14-21 days
- Foscarnet 60 mg/kg I.V x 3 times/day or 90 mg/kg twice daily in 14–21 days

Maintenance therapy: use one of any following regimens:

- Valganciclovir 900 mg P.O daily
- Gancyclovir 5 mg/kg I.V daily
- Foscarnet 90–120 mg/kg I.V daily

Discontinuation: patients receive CMV treatment for at least 3 – 6 months, have inactive CMV lesions and have sustained CD4 count > 100 cells/mm^3 for 3-6 months in response to ART.

Other manifestations (CMV colitis and esophagitis): Use oral and intravenous medications as above.

b) Children

CMV dissemiation and retinitis

Induction therapy:

Preferred therapy: ganciclovir 5 mg/kg I.V twice daily x 14-21 days.

Alternative therapy: foscarnet 60 mg/kg I.V t.i.d x 14 - 21 days or valganciclovir 900 mg P.O (older children) b.i.d x 14-21 days

Maintenance therapy: use one of any following regimens:

- Ganciclovir 5 mg/kg I.V daily

- Valganciclovir 900 mg P.O daily (older children and take with meals)

- Foscarnet 90-120 mg/kg I.V daily

Maintencance therapy for retinitis: intravitreal injection of ganciclovir every 6 - 9 months + ganciclovir 90 mg/kg/day P.O in divided 3 doses.

Discontinuation: in case of at least 6 months of ARV treatment and CD4 count > 100 cells/mm^3 for children ≥ 6 years and CD4 percentage > 15% for children below 6 months in sustained 6 months.

3.10. Lymphoid interstitial pneumonina (LIP)

3.10.1. Symptoms and signs

LIP can present in children with HIV from 8 months to 4 years old. LIP is associated with immune response to HIV and/or *Epstein Barr* virus (EBV), seldomly resulting to death; however, it usually has prolonged duration, episodic recurrence and no fever unless bacterial coinfection. LIP can cause chronic respiratory distress.

Manifestations:

- Nonproductice cough, dyspnea, clubbing, parotitis, lymphadenopathy

- Hypoxia in children with pre-existing respiratory disease

- Chest X-ray: diffuse linear – nodule infiltrations, bronchiectasis.

3.10.2. Diagnosis

Clinical manifestations, chest X-ray

Rule out pulmonary tuberculosis and other lung diseases

3.10.3. Treatment

Patients show partial improvement with prednisolon 1-2mg/kg/day (if PaO2 < 85-90 mm Hg); titrating dose after clinical response.

Symptoms usually reoccur after discontinuation of prednisolon. Avoid prednisolon in case of contraindications due to other comorbidites.

It is stable when patients have ART

Symptomatic treatment: oxygen therapy in respiratory distress

Antibiotics if bacterial coinfection.

4. Management of patient with HBV, HCV and HIV coinfections

4.1. Diagnosis and treatment of HBV/HIV coinfection

4.1.1. Screening of HBV in patient living with HIV

HBsAg is indicated in all people living with HIV. Test should be repeated anually if the previous result was negative and patient is at risk of HBV infection

4.1.2. Diagnosis of chronic hepatitis B in patient living with HIV

Diagnosis of chronic HBV infection: HBsAg positive for > 6 months

Diagnosis of active chronic hepatitis B:

- HBsAg positive for > 6 months and AST, ALT > 2 times upper reference limit intermittently or persistently over 6 months OR
- Evidence of advanced histopathology injury, cirrhosis (confirmed by liver biopsy or fibroscan, fibrotest or APRI) without other etiologies

Diagnosis of hepatitis B flares in ARV treatment: the flares after few months of ART may be caused by IRIS, or discontinuation of ARV drugs that are effective against hepatitis B virus (3TC, TDF)

4.1.3. Treatment of chronic hepatitis B in patient living with HIV

Preferred first-line ART are both effective against HIV and HBV:

TDF + 3TC (or FTC) + EFV

Management of hepatitis B flares in patients receiving ART: manage similarly to hepatotoxicity from ART and continue ART including TDF and 3TC

Patients with HBV/HIV coinfection should not stop ARV medication by themselves to prevent hepatitis B flares.

In case of switching to second-line ART in patients with HBV/HIV coinfection, keep medications against HBV as TDF, 3TC.

4.2. Diagnosis and treatment of HCV/HIV coinfection

4.2.1. Screening of HCV in patient living with HIV

All patients with HIV should be screened for anti- HCV. Anti-HCV test can be repeated annually if the previous result was negative and patient is at risk of HCV infection.

4.2.2. Diagnosis of chronic hepatitis C in patient living with HIV

Anti-HCV positive for > 6 months and HCV RNA or HCV core antigen is positive

4.2.3. Treatment of chronic hepatitis C in patient living with HIV

Treatment is indicated for all patients with chronic hepatitis C. Patients with HIV/HCV coinfection need the priority of hepatitis C treament to reduce the prevalence and mortality rate of end stage liver diseases and hepatocellular carcinoma.

Regimens and medications for hepatitis C treatment: See Guidelines on diagnosis and treatment of hepatitis C- Decision 5012 QĐ/MoH 2016.

Preferred regimens of hepatitis C treatment include direct acting antivirals (DAAs). Choosing the ART and DAAs should be aware of drug interactions. See appendix 12. Drug - drug interactions between DAAs and ARV and table 15. Choose regimens of ART and DAAs in patients with HIV/HCV coinfection

Patient with naive ART:

CD4>500 cells/mm³: first, treat for hepatitis C. Duration: 12 – 24 weeks, depending on the liver fibrosis. Initiate ART after completing the hepatitis C treatment.

CD4 from 200- 500 cells/mm³: Consider in specific cases, prefer ART. After ART tolerance, begin treatment for hepatitis C.

CD4<200 cells/mm³: Prefer ART until CD4 count >200 cells/mm^3 or undetectable viral load, then begin treatment for chronic hepatitis C.

Patient with ongoing ART

CD4>200 cells/mm^3 or undetectable viral load: begin treatment for chronic hepatitis C.

Table 15. Choose regimens of ART and DAAs in patients with HIV/HCV coinfection

ARV regimens	**Treatment for hepatitis C**	
	Regimens	**Genotype**
TDF + 3TC (FTC) + EFV (NVP)	**DCV + SOF**: Increase dose of DCV 90 mg	1,2,3,4,5,6
	LDV + SOF: Monitor nephrotoxicity of LDV. Do not use LDV plus TDF if GFR <60ml/min	1,4,5,6
TDF + 3TC(FTC) + DTG (RAL)	**DCV + SOF**	1,2,3,4,5,6
	VEL + SOF: Monitor nephrotoxicity of VEL	
	LDV + SOF: Monitor nephrotoxicity of LDV. Do not use LDV plus TDF if GFR <60ml/min	1,4,5,6
	GZR/EBR	1,4
AZT* + 3TC	**LDV + SOF**	1,4,5,6

+ EFV (NVP)	**DCV + SOF**: Increase dose of DCV 90 mg	1,2,3,4,5,6
TDF + 3TC + LPV/r	**DCV + SOF**	1,2,3,4,5,6
	VEL + SOF: Monitor nephrotoxicity of VEL	
AZT * + 3TC + LPV/r	**DCV + SOF**	1,2,3,4,5,6
	VEL + SOF	
	LDV + SOF	1,4,5,6
TDF + 3TC (FTC) + ATV	**DCV + SOF**: Decrease dose of DCV 30 mg	1,2,3,4,5,6
	VEL + SOF: Monitor nephrotoxicity of VEL	
	LDV + SOF: Monitor nephrotoxicity of LDV. Do not use LDV plus TDF if GFR <60ml/min	1,4,5,6

** Note: Ribavirin should not be combined with AZT in patients with HCV/HIV coinfection*

4.3. Follow up

- Assess and support the treatment adherence

- Follow up and manage the flares of hepatitis B in patient with HIV

- Follow up and manage drug interactions between ART and medications for HCV

- Follow up and manage side effects of ART, DAAs, especially nephrotoxicity of TDF.

- Follow up complications of hepatitis B, screen for hepatocellular carcinoma

- Follow up treatment response to hepatitis B

- Follow up treatment response to hepatitis C with HCV-RNA viral load: Sustained virologic response is defined as undetectable viral load 24 weeks after completion of treatment (reach SVR12).

4.4. Recommendation, education and prevention of HBV, HCV transmission in patient living with HIV

- Evaluate the severity of alcoholism, give advice and aids to cease alcohol consumption, treat for alcoholism.

- No taking medications, even herbs by themselves.
- Implement a healthy and balance diet; avoid obesity, do regular excersices, relax and rest, stop or reduce smoking.
- Vaccinate against hepatitis B
- Apply the preventive methods of HBV and HCV transmission in patient with HIV
- In patients with HBV, HCV/HIV coinfection: apply preventive methods to protect community from HBV, HCV and prevent reinfection, especially HCV reinfection after treatment.

CHAPTER IV
PREVENTION AND MANAGEMENT OF NON-COMMUNICABLE DISEASES IN PATIENT LIVING WITH HIV

1. Counselling and supporting patient with alcoholism or opioid dependence
1.1. Alcoholism

Counselling for the influence of alcoholism or alcohol abuse on ART adherence and liver funtions; the increase in toxicity of ARV drugs.

Counselling for alcohol cessation and enhancement of treatment adherence**.**

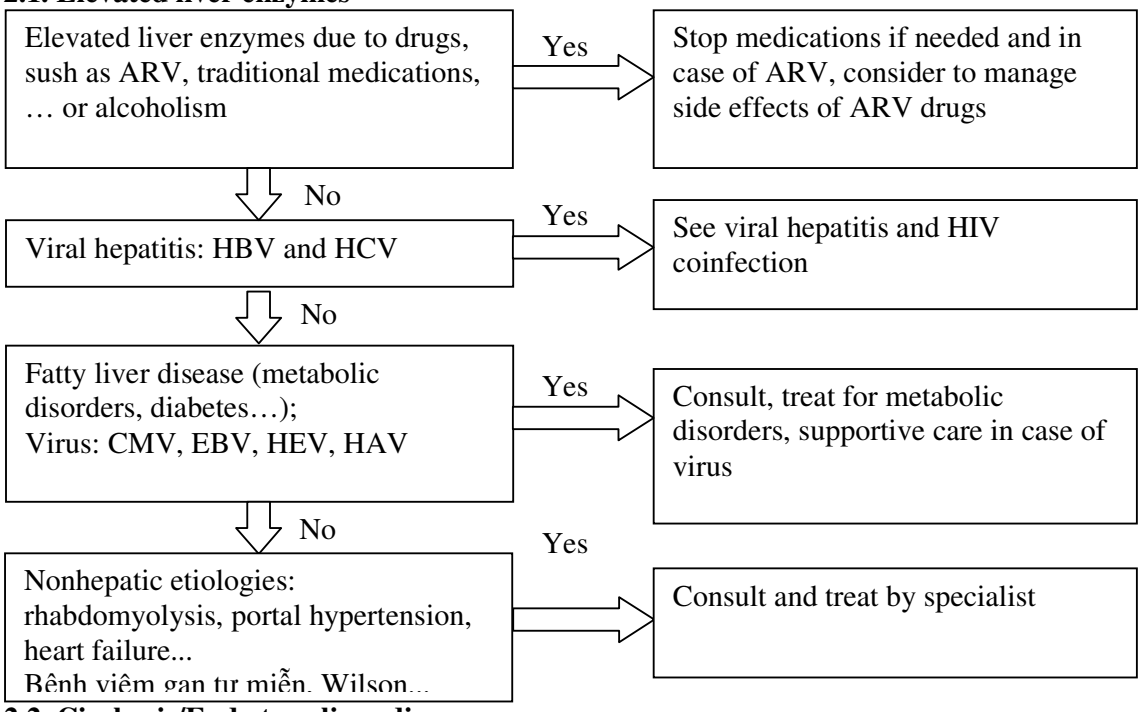
1.2. Opioid dependence

Counselling for affects of opiod dependence, HIV transmission, hepatitis B, hepatitis C and treatment adherence.

Counselling for preventive methods to reduce HIV transmission sush as using single needle and syringe, using condoms, treating with opioid substitution therapy (methadone)...and referring to methadone treatment services.

Note:
- Interactions between methadone and ARV drugs (AZT and NNRTI)
- Early initiation of ART, enhancement of treatment adherence.

2. Management of liver disease
2.1. Elevated liver enzymes



2.2. Cirrhosis/End-stage liver disease

2.2.1. Cirrhosis classification by Child- Pugh score

Table 17. Cirrhosis classfication by Child-Pugh

Parameters	Points

	1	2	3
Toral bilirubin mg/dL (µmol/L)	< 2 (< 34)	2-3 (34-50)	> 3 (> 50)
Serum albumin g/L (µmol/L)	> 35 (> 507)	28-35 (406-507)	< 28 (< 406)
INR (or prothrombin time, second)	< 1,7 (<4)	1,7-2,2 (4-6)	> 2,2 (>6)
Ascites	No	Mild/moderate (diuretic responsive)	severe (diuretic refractory)
Encephalopathy	No	Grade I-II (or controlled by medications)	Grade III-IV (or irreversible)

Classification: class A: 5-6 points, class B: 7-9 points; class C 10-15 points

2.2.2. Prevention and management of cirrhosis/end-stage liver disease

Table 18: Prevention and management of cirrhosis/end-stage liver disease

	Cirrhosis/End-stage liver disease
Risk factors	- HBV, HCV coinfection - Alcoholism - Other chronic liver diseases (Metabolic disorders, autoimmune diseases, etc..)
Screening and diagnosis	- Clinical presentations: collateral circulation; hepatorenal syndrome, or hepatic encephalopathy - Calculating APRI index and classification by Child- Pugh score - Cirrhosis imaging on liver ultrasound, including fibroscan and liver biopsy; - Esophageal endoscopy to evaluate esophageal varices; - Consulting with hepatobiliary specialist and develop plan, follow up and treat. - Monitoring liver function every 6 months and until presentations - Screening for hepatocellular carcinoma
Prevention and management	- Treat underlying diseases related to cirrhosis (sush as hepatitis B, hepatitis C and other liver diseases) - Counsel for no alcohol consumption. - Counsel for appropriate nutrition: enough energy, supplement of essential vitamins, low salt intake.

	- Treat for esophageal varices and give prophylaxis with diuretics, propranolol. - Treat for decompensated cirrhosis, hepatic encephalopathy, hepatorenal syndrome, bleeding complications, infections. - Take cautions with hepatotoxic medications like paracetamol; avoid non-steroid anti-inflammatory drugs due to risk of bleeding and renal failure

2.2.3. Dosing adjustment of ARV in liver failure

Table 19. Dosing adjustment of ARV based on Child-Pugh Score

	Child -Pugh		
	A	**B**	**C**
ABC	200 mg twice daily	Contraindication	
FTC hoặc 3TC	No adjustment required		
TDF hoặc TDF/3TC	No adjustment required		
ZDV	No adjustment required	No adjustment required	Taper ½ dose or extend the timing
EFV	No adjustment required	Caution in liver failure	
NVP		Contraindication	
ATV		300 mg daily	No recommended
RTV		No boosted RTV	
LPV		Caution in liver failure	

3. Screening for cancer

HIV infected people have a higher risk of cancer, especially cervical carcinoma, than normal populations. Therefore, they need regular screening to recognize and treat promptly. Counselling for prevention of cervical carcinoma with HPV vaccination should be recommended to women if indicated.

Steps in screening process for carcinoma in patient living with HIV should be based on guidelines of Ministry of health..

4. Cardiovascular diseases, dyslipidemia and diabetes

HIV infected people are at higher risk of suffering from cardiovascular diseases, dyslipidemia and diabetes. In addition to risk factors of cardiovascular diseases, dyslipidemia and diabetes like patients without HIV, there are many risks related to ARV treatment. The increase in occurrence of these diseases is related to the duration of ART, particularly NNRTTs and PI.

People with HIV need regularly screening for these diseases to treat promptly. Educating nutrion and appropriate diet, stop smoking, encouraging exercises, mornitoring blood pressure and choleterol level, glucose level facilitate a decrease in risk of non-communicable diseases in patient living with HIV.

When patient with HIV have cardiovascular diseases, dyslipidemia or diabetes, physicians consider to adjust the ART, substitute to other drugs with same efficacy.

5. Nephropathy

Chronic kidney diseases usually occurring in patient with HIV include HIV associated nephropathy, proximal tubular disease, distal tubular disease and interstitial nephritis.

In addition to risk factors of nephropathy sush as hypertension, diabetes, dyslipidemia..., HIV infected patients also deal with ARV related nephrotoxicity (TDF, boosted PI) in advanced stage of HIV.

HIV infected patients with ongoing ART should be tested creatinine to estimate glomerular filtration rate (GFR). Alteration in ART should be considered with substitution of drugs, dosing adjustment, which is based on GFR. Appendex 11. Dosing adjusment of ARV based on glomerular filtration rate. Consultation with nephrologist if needed.

6. Bone diseases

Bone diseases occuring in patient with HIV are bone mineral loss, osteopenia, osteoporosis...Therefore, patients with HIV are at higher risk of fracture. Risks due to ART should be taken account in addition with risk factors like patient without HIV. The occurence of bone diseases is associated with duration of ART, especially in the presence of TDF and PI.

Assess diseases, risk factors related to bone disease. Consult with osteologist and nutrionist, implement prevention of osteoporosis and treat if patients have any bone diseases.

If HIV infected patients are suffered from bone diseases, consider to adjust ART (TDF, PI drugs). Substitute ARV if needed.

7. Depression

The proportion of depression in patient living with HIV is greater than that of normal population (20-40% versus 7%). Depression increases the risk of treatment failure and mortality rate of infected individual. Infected patients with history of addictive drugs, EFV and antipsychotic medicines should be considered to be at risk of depression.

HIV infected person needs examination and early screening for symptoms and signs related to depression. Consultation with psychiatric specialty is recommended to recognize and early treat. Discontinue EFV and substitute to appropriate ARV

8. HIV associated neurocognitive disease

HIV Associated Neuro-cognitive Disease (HAND) is a disorder of many important neurological functions including cognition, behavior and motion in patient with HIV. It is associated with the invasion of HIV in central nervous system and neurological injury due to HIV.

Many functions should be evaluated in patient with HIV, consisting of language, concentration, short-term memory, speed of thinking, learning and movement. Opportunistic infections and brain tumor must be excluded. In case of suspected HAND, consult with psychiatric specialty.

Patient with naive ART: initiate ART.

Patient with ongoing ART: order HIV viral load, reassess treatment failure, change therapy if indicated.

Consider to give ARV drugs that permeate through blood-meningeal barrier in following descending order (AZT, ABC, EFV, NVP, LPV/r, DRV/r).

CHAPTER V
PREVENTIVE INTERVENTIONS FOR PEOPLE LIVING WITH HIV

In addition to ART, people living with HIV should receive preventive interventions including: behaviour change communication, clean needle and syringe, condoms and methadone substitution therapy.

1. Behaviour change communication

A diversity of methods in health communication should be implemented in community, priority to target populations. Direct communication styles like personal counselling by peer partners or healthcare workers combine with community counselling through papers, media or seminars to distribute messages about risk of HIV transmisson, preventive methods and benefits of behaviour change, regular HIV investigation and early ARV treament. Educating knowledge, building skills and trust in high risk populations allow patients to maintain safety and preventive behaviours (sush as using clean needles without sharing, using condoms in sexual active, reducing the frequency of unprotected intercourse) and require regular HIV testing.

Men who have sex with man and transgender people: Enhance awareness of safe sexual behavior and knowledge of HIV testing and counselling from Internet and direct communication with social marketing strategies and community based approaches. Implement interventions in individual and community level.

Men who inject drugs: Deliver information and education about safe injection and prevention of drug overdose. Encourage the injecting users to take part in building and sharing information. Access to condoms in addition to clean needles and syringes.

Sex workes: Thanks to interventions of peer groups and community, communicate and build skill of condom usage and demand for HIV testing, screening of sexually transmitted diseases and connecting with HIV care and treatment.

2. Condoms

All high risk populations must use condoms regularly and in the right way with lubricants to prevent HIV transmission and sexually transmitted diseases. Regular and proper use of condoms can reduce the risk of sexually transmitting HIV by 94% as well as other sexually transmitted diseases.

Men who have sex with men and transgender people are at high risk of HIV infection through anal sex. Therefore, they must use condoms and lubricants in every intercourse.

Sex workers or their partners need to use condoms and lubricants regulary and properly. For female sex workers, using female condoms should be initiated before sex.

Implementation of condoms and lubricants should pay attention to following points:

Ensure condom delivery with high quality, variety of size and meeting the demand for both men and women. Place condoms in places where can be reached by high risk populations. Implement campaigns to increase the awareness and community acceptance of condoms.

Use lubricants to reduce the risk of tearing and slipping off as well as the discomfort during sex. In case of anal sex, use more lubricants. Avoid using oil based lubricants with latex condoms.

3. Clean needles and syringes

Using clean needles and syringes is a safe method in order to decrease the risk of transmitting HIV in people who inject drugs. In addition to clean needles, people who inject drugs should receive the information about risk of HIV transmission due to sharing needles. Used needles and syringes should be collected with medical sharps containers and disposed safely.

4. Opioid substitution therapy

Opioid substitution therapy with methadone or buprenorphine is the most effective way for people with opioid dependence and supports the adherence to ART. HIV infected people with methadone therapy should be referred to HIV care settings for prompt treatment of ART.

5. Prevention of HIV transmission in healthcare settings

Healthcare settings must implement safe blood transfusions, safe infusions and standard precautions including hand hygiene, using personal protective equipments for exposure prophylaxis, safe disposal of sharps and waste materials, antiseptics and safety of environment and equipment. Clinical settings develop and apply the protocol of post-exposure prophylaxis to healthcare workers.

6. Immunization for HIV exposed children and HIV infected children

Immunizations for HIV-exposed and HIV-infected children are similar to normal children; however, there are some cautions with live attenuated vaccines:

6.1. BCG vaccine

HIV exposed children:

Vaccinate BCG if there is no evidence of HIV infection

Closely monitor HIV exposed children after BCG vaccination to recognize disease associated with BCG injection: ulcers at injected site, lymphadenopathy, disseminated BCG disease (wasting, hepatosplenomegaly, lymph node enlargement).

Delay BCG vaccination for children with weight < 2000g or HIV suspected symptoms until HIV infection is confirmed.

HIV infected children: No BCG vaccination

6.2. Other live attenuated vaccines: polio, measles, rubella, ...

HIV exposed children: No vaccincation for children with HIV suspected symptoms.

HIV infected children: Delay live vaccinations if child presents with severe HIV infection, CD4 count < 15% or clinical stage 4. When children are stable and have sustained ART, continue to vaccinate children following national immunization schedule as children without HIV.

CHAPTER VI
HOME AND COMMUNITY BASED CARE

1. Objectives

Community based care for patient living with HIV are implemented by healthcare staff in primary care settings, local and district level, peer group and HIV working group.

Activities include: support high risk populations to access HIV testing services and connect patient with HIV to HIV/AIDS treatment and care services; support prevention of HIV transmission; support adherence to treatment; support HIV infected people who missed any visit and/or dose delivery, were lost to follow-up or treatment to retain the care; manage common symptoms at home, community and support socio-psychological problems.

2. Contents of care

2.1. Support for access to HIV testing and treatment services

Activites include the assistance of HIV infected people in registration, treatment at HIV care settings. Introduce people with high risk behaviors to HIV testing and counselling services. Counsel and introduce wife, husband or sex partners of people living with HIV and their offsprings to HIV testing, counselling and treatment services. Provide information about the importance and benefits of HIV treatment so people with HIV could go to the facilities to receive the care and services immediately after knowing their HIV status.

2.2. Counselling for prevention of HIV transmission

People living with HIV should be educated about protected sex, safe injected drugs and prevention of mother-to-child transmission.

2.3. Support for adherence to treatment

People living with HIV need support for ART adherence, taking medications as prescribed, using reminder tools, remembering the visit and tests on time. Guide patient who missed the visit and refused treatment to come back to care settings; guide the storage and preservation of medicines at home

2.4. Support for physical care

Support HIV infected people in monitoring, care and managment of mild side

effects of medications. Guide them and their caregivers how to face with common symptoms like pain, fever, diarrhea, constipation, vomiting and nausea, cough....

Provide information about sanitation and nutrition at home and community

2.5. Socio-psychological support

Provide support and encouragement for people living with HIV and their family.

People with HIV and children affected by HIV/AIDS have access to social

services and community integration.

Patient with HIV usually have strong feelings at the time of diagnosis and at the end of life. They have mental breakdown; fear of disease and death, feeling of guilt, self-punishment, fear of isolation, anxiety about their future and family; loss of income and social position; they also worry that their children will loss opportunities. Therefore, they need mental and psychological support.

Encourage patients to buy medical insurance so their treatment could be paid. Find support resources in community from friends, family, peer partners, clubs or social organizations....

Resolve the issues sush as finance, accommodation, food, transport, cemetary fees…

Planning support in the future: making a will, future plan for children…

CHAPTER VII
QUALITY IMPROVEMENT IN HIV/AIDS CARE AND TREATMENT

1. Objectives of quality improvement in care and treatment

To ensure good implementations of standards and national guidelines on diagnosis, treatment and care for HIV/AIDS.

Enhance the access to high-quality services in HIV counselling, testing and care in order to increase the adherence, reduce the mortality rate and drug resistance, decrease the risk of transmitting HIV to community.

2. Principles in quality improvement

Base on measurable data

Implement continuously over time

Base on a system of quality improvement

Focus on implementation of current protocols and guidelines on HIV/AIDS published by Ministry of health.

3. Steps in process of quality improvement

- Measure and evaluate quality improvement parameters. Quality improvement parameters should be collected through random sampling with medical charts and records of HIV patient. Parameters for measurement and assessment usually are established by authorities or settings to improve the quality of services. Measuring parameters should be carried out every 6 months or annually.

- Planning for quality improvement. Review the results and select priority parameters to improve

- Analyse to find etiology: Use paragraphs to make a list of causes. Draw fishbone diagram and problem tree analysis to arrange causes in a logical sequence.

- Identify the possibility of interventions for each etiology (full, partial or no intervention). Ask questions “why; how” to find the root. Choose priority cause to intervene.

- Identify the objective of improvement: Objectives should be clarified what issue, for whom, where, when and how much. Consider related informations to estimate the possibility of changing with interventions. Ensure objectives fullfill 5 criteria: specific, measurable, attainable, relevant and timely (SMART).

- Introduce and choose appropriate interventions: feasible, acceptable, efficient, high effective and sustainable. Use table for solution choosen by scoring the effectiveness and efficiency. Determine the product by multiplying the effectiveness and the efficiency. Choose methods with higher score.

- Build the plan: Categorize necessary activities to implement each intervention. Determine the timing for carrying out activities. Identify the workers, people who are responsible for, coordinators and supervisors. Identify the place, necessary resources and expected results.

- Implement quality improvement based on the plan

- Evaluate the progress of implementing qualtity improvement.

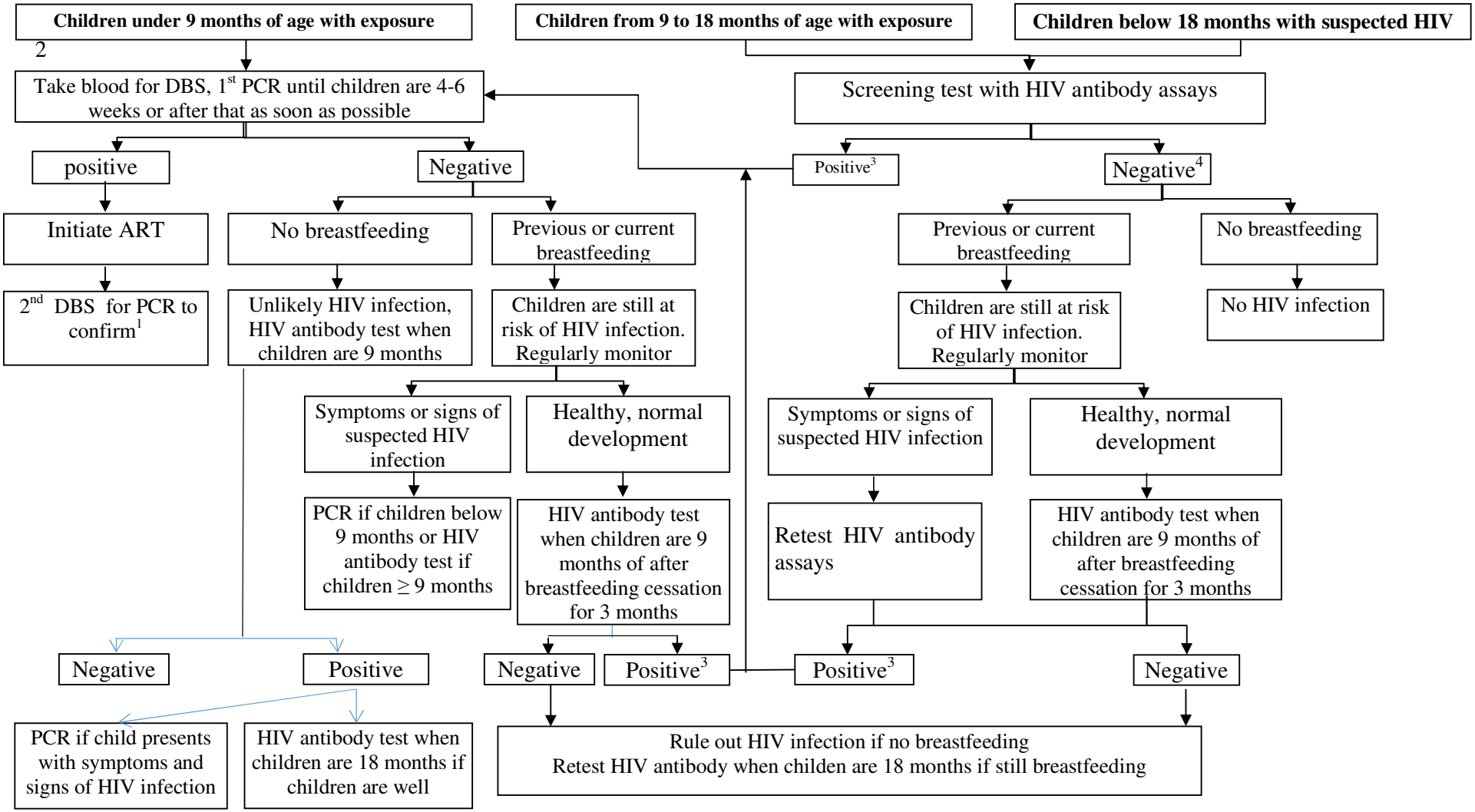
- Monitor, support and assess to ensure the implementation of quality improvement as planned. Preliminary assessment of result after completing a half of timing in a quality improvement cycle. Adjust the plan if needed.

Based on the results of quality improvement, healthcare settings organize a disscussion about implemented plan and adjust if neccessary to be suitable for the next period.

After completing a cycle, HIV/AIDS care settings should continue to select parameters that need improvement to start the next cycle of quality improvement.

APPENDIX

Appendix 1: Algorithm of early diagnostic investigations of HIV for children below 18 months of age



[1] Repeat PCR if 1st PCR was positive and 2nd was negative

[2] PCR positive, initiate ART and repeat PCR immediately to confirm

[3] Order PCR.

[4] Order HIV antibody test for mother;in case of negative result, HIV infection in child was excluded

Appendix 2: Clinical staging of HIV disease in adults, adolescents and children

Adults and adolescents[a]	**Children**
Clinical stage 1	
Asymptomatic Persistent generalized lymphadenopathy	Asymptomatic Persistent generalized lymphadenopathy
Clinical stage 2	
Moderate unexplained weight loss (<10% body weight) Recurrent respiratory tract infections (sinusitis, tonsilitis, otitis media, pharyngitis) Herpes zoster Angular cheilitis Recurrent oral ulceration Papular pruritic eruption Fungal nail infections Seborrhoeic dermatitis	Unexplained persistent hepatoslenomegaly Recurrent or chronic upper respiratory tract infections (otitis media, otorrhea, sinusitis, tonsillitis) Herpes zoster Lineal gingival erythema Recurrent oral ulceration Papular pruritic eruption Fungal nail infections Extensive wart virus infections Extensive molluscum contagiosum Generalized exfoliative dermatitis Unexplained persistent parotid enlargement
Clinical stage 3	
Severe unexplained weight loss (>10% body weight) Unexplained chronic diarrhea for longer than 1 month Unexplained persistent fever (intermittent or constant for longer than 1 month) Persistent oral candidiaisis Oral hairy leukoplakia Pulmonary tuberculosis Severe bacterial infections (sush as empyema, pyomyositis, bone or joint infection, meningitis, bacterimia) Periodonitis, acute necrotizing ulcerative stomatitis and gingivitis Unexplained anemia (<8 g /dl), neutropeniagiảm bạch cầu trung tính (<0.5 x 109 /l) or chronic thrombocytopenia (<50 x 109 /l)	Unexplained moderate malnutrition[b] not adequately responding to standard therapy Unexplained persistent diarrhea (14 days or more) Unexplained persistent fever (above 37.5°C, intermittent or constant for longer than 1 month) Persistent oral candidiasis (after first 6 weeks of life) Oral hairy leukoplakia Lymph node tuberculosis Pulmonary tuberculosis Severe recurrent bacterial pneumonia acute necrotizing ulcerative periodontitis and gingivitis Unexplained anemia (<8 g /dl), neutropenia (<0.5 x 109 /l) or chronic thrombocytopenia (<50 x 109 /l) Symptomatic lymphoid interstitial pneumonia. Chronic HIV associated lung disease,

Adults and adolescents[a]	Children
	including bronchiectasis.
Clinical stage 4	
HIV wasting syndrome Pneumocystis jirovecii pneumonia (PCP) Severe recurrent bacterial pneumonia Chronic herpes simplex infection (orolabial, genital or anorectal for longer than 1 month, or visceral herpes at any site) Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs) Extrapulmonary tuberculosis Kaposi sarcoma Cytomegalovirus infection (retinitis or infection of other organs) Central nervous system toxoplasmamosis (after neonatal period) HIV encephalopathy Extrapulmonary cryptococcosis, including meningitis Disseminated nontuberculosis mycobacterial infection Progressive multifocal leukoencephalopathy Chronic cryptosporidiosis Chronic isosporiosis Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, talaromycosis) Lymphoma (cerebral or B cell non Hodgkin) HIV associated nephropathy or cardiopathy Recurrent bacteremia (including nontyphoidal Salmonella) Invasive cervical carcinoma Atypical disseminated leishmaniasis	Unexplained severe wasting, stunting or severe malnutrition[c] not responding to standard therapy Pneumocystis jirovecii pneumonia (PCP) Recurrent severe bacterial infections, sush as empyema, pyomyositis, bone and joint infection, or meningitis but excluding pneumonia Chronic herpes simplex infection (chronic orobabial or cutaneous herpes simplex infection more than 1 month or visceral infection at any site) Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs) Extrapulmonary tuberculosis Kaposi sarcoma Cytomegalovirus infection (retinitis or infection of other organs with onset at age more than 1 month) Central nervous system toxoplasmamosis (after neonatal period) HIV encephalopathy Extrapulmonary cryptococcosis, including meningitis Disseminated nontuberculosis mycobacterial infection Progressive multifocal leukoencephalopathy Chronic cryptosporidiosis (with diarrhea) Chronic isosporiasis Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, talaromycosis) Lymphoma (cerebral or B-cell non Hodgkin) HIV associated nephropathy or cardiopathy

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

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

[c] For children younger than 5 years, wasting is defined as weight for height ≤ 3 z – score; stunting is definded as length for age/height for age <–2 z-score; severer acute malnutrition is defined as weight for height ≤ 3 z-score or mid-upper arm circumference <115 mm or the presence of edema.

Appendex 3: Dosages of ARV drugs for aduls and children > 35 kg

Generic name	Dose
Nucleoside reverse transcriptase inhibitors (NRTIs)/ Nucleotide reverse transcriptase inhibitors (NtRTIs)	
Abacavir (ABC)	300 mg twice daily or 600 mg once daily
Emtricitabine (FTC)	200 mg once daily
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily
Zidovudine (AZT)	250–300 mg twice daily
Tenofovir (TDF)	300 mg once daily
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	
Efavirenz (EFV)	400 or 600 mg once daily
Nevirapine (NVP)	200 mg once daily for 14 days, followed by 200 mg twice daily. In the presence of rifammycin treatment, use dose of NVP 200 mg twice daily
Protease inhibitors (PIs)	
Atazanavir + ritonavir (ATV/r)	300 mg + 100 mg once daily
Darunavir + ritonavir (DRV/r)	800 mg + 100 mg once daily or 600mg + 100 mg twice daily
Lopinavir/ritonavir (LPV/r)	400 mg/100 mg twice daily Considerations for people with TB therapy In the presence of rifabutin, no dose adjustment required. In the presence of rifampicin, adjust dose of LPV/r (LPV 800 mg + RTV200 mg twice daily or LPV 400 mg + RTV 400 mg twice daily) or SQV/r (SQV 400 mg + RTV 400 mg twice daily), with close monitoring
Integrase stand transfer inhibitors (INSTIs)	
Raltegravir (RAL)	400 mg twice daily
Dolutegravir (DTG)	50 mg once daily

Appendix 4: Dosing of fixed-dose solid formulations for twice daily dosing among children

Drug	Strength of tablets (mg)	Number of tablets by weight band morning and evening										Strenght of adult tablets (mg)	Number of tablets by weight band	
		3 - 5.9 kg		6 - 9.9 kg		10 - 13,9 kg		14 - 19.9 kg		20 - 24.9 kg			25 - 34.9 kg	
		am	pm	am	pm	am	pm	am	pm	am	pm		am	pm
AZT/3TC	tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150	1	1
AZT/3TC / NVP	tablet (dispersible) 60 mg/30 mg/50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150/200	1	1
ABC/ AZT/3TC	tablet (dispersible) 60 mg/60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/300/150	1	1
ABC/3TC	tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600/300	0.5	0.5

Appendix 5: Simplified dosing of solid formulations for once daily dosing in children

Drug	Strength of tablets (mg)	Number of tablets or capsules by weigth band, once daily					Strenght of tablet (mg)	Number of tablets or capsules by weight band, once daily
		3 - 5.9 kg	6 - 9.9 kg	10 - 13.9 kg	14 - 19.9 kg	20 - 24.9 kg		25 - 34.9 kg
EFV*	Tablet (scored) 200 mg	–	–	1	1.5	1.5	200	2
	Tablet (double scored) 600 mg	–	–	1/3	1/2	2/3	600	2/3
ABC/3TC	Tablet dispersible 60/30 mg	2	3	4	5	6	600 + 300	1

* EFV is not recommended for children under 3 years and weight less than 10 kg

The double scored tablet has two score lines in one side and one score line on the other side, enabling the tablet to be divided into thirds and halves as needed.

Appendix 6: Simplified dosing of solid, oral liquid formulations for twice daily dosing in children

Drug	Strenght of tablets (mg)	Number of tablets by weight band morning and evening										Strenght of adult tablets (mg)	Number of tablets by weight band	
		3 - 5.9 kg		6 - 9.9 kg		10 - 13,9 kg		14 - 19.9 kg		20 - 24.9 kg			25 - 34.9 kg	
		am	pm	am	pm	am	pm	am	pm	am	pm		am	pm
		Solid formulations												
3TC	tablet (dispersible) 30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	150	1	1
AZT	tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300	1	1
ABC	tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300	1	1
NVP[a]	tablet (dispersible) 50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	200	1	1
LPV/r[b]	tablet (heat stable) 100 mg/25 mg	–	–	–	–	2	1	2	2	2	2	100/25	3	3
		Liquid formulations												
AZT	10 mg/ml	6 ml	6 ml	9 ml	9 ml	12 ml	12 ml	–	–	–	–	–	–	–
ABC	20 mg/ml	3 ml	3 ml	4 ml	4 ml	6 ml	6 ml	–	–	–	–	–	–	–
3TC	10 mg/ml	3 ml	3 ml	4 ml	4 ml	6 ml	6 ml	–	–	–	–	–		
NVP[a]	10 mg/ml	5 ml	5 ml	8 ml	8 ml	10 ml	10 ml	–	–	–	–	–	–	–
LPV/r[b]	80/20 mg/ml	1 ml	1 ml	1.5 ml	1.5 ml	2 ml	2 ml	2.5 ml	2.5 ml	3 ml	3 ml	–	–	–

[a] When initating ARV, NVP dose decreased with half dose to avoid toxicity. For children with presence TB therapy with rifamycin, initiate with ARV, dose of NVP: 200mg/m^2 /1 time twice daily.

[b] LPV/r liquid requires cold chain during transport and storage. The LPV/r heat stable tablet must be swallowed whole and should not be split or crushed.

Appendix 7: Simplified dosing for currently available TDF formulations for children

Drug	Size of powder scoop (mg) or stenght of tablet (mg)	Number of scoops or tablets by weight band once daily					Strength of adult tablet (mg)	Number of tablets by weight band, once daily
		3 - 5.9 kg	6 - 9.9 kg	10 - 13.9 kg	14 - 19.9 kg	20 - 24.9 kg		25 - 34.9 kg
TDF [a]	Oral power scoops 40 mg/scoops	–	–	3	–	–	300 mg	1 (200 mg)[b] or 1 (300 mg)
	tablets 150 mg or 200 mg	–	–	–	1 (150 mg)	1 (200 mg)		

[a] Target dose: 8 mg/kg or 200 mg/m2 (maximum 300 mg).

[b] Tablet 200 mg should be used for children with weight of 25 - 29.9 kg and tablet 300 mg should be used for weight of 30 - 34.9 kg.

Appendix 8: Simplified dosing of isoniazid (INH) and cotrimoxazole (CTX) prophyaxis

Drug	Strenght of tablets or oral liquids (mg or mg/5 ml)	Number of scoops or tablets by weight band once daily					Strenght of adult tablet (mg)	Number of tablets by weight band once daily
		3 - 5.9 kg	6 - 9.9 kg	10 - 13.9 kg	14 - 19.9 kg	20 - 24.9 kg		25 - 34.9 kg
INH	100 mg	0.5	1	1.5	2	2.5	300 mg	1
CTX	Suspension 200/40 per 5 ml	2.5 ml	5 ml	5 ml	10 ml	10 ml	–	–
	Tablet (once scored) 100/20 mg	1	2	2	4	4	–	–
	Tablet (double scored) 400/80 mg	–	Once half	Once half	1	1	480/80 mg	2
	Tablet (double scored) 800/160 mg	–	–	–	Once half	Once half	800/160 mg	1
INH/CTX /B6	Tablet (double scored) 960 mg/300 mg/25 mg	–	–	–	Once half	Once half	960 mg/300 mg/25 mg	1

Appendix 9: Dosing of CTX prophyaxis for children with exposure or HIV

Weight (kg) Dose: 5 mg (TMP)/kg/day	Syrup TMP 40 mg/SMX 200 mg /5ml once daily	Tablet TMP 20mg/SMX 100mg once daily	Suspension TMP 40mg/ SMX 200 mg once daily	Tablet TMP 80 mg/SMX 400 mg once daily	Tablet TMP 160 mg/SMX 800 mg once daily
3,0 - 5,9	2.5ml	1 tablet	½ suspension	¼ tablet	
6,0 - 9,9	5ml	2 tablets	1 suspension	½ tablet	
10 - 13,9	5ml	2 tablets	1 suspension	½ tablet	
14 - 19,9	10ml	4 tablets	2 suspensions	1 tablet	
20 - 24,9	10ml	4 tablets	2 suspensions	1 tablet	
25 - 34,9				2 tablets	1 tablet
>= 35				2 tablets	1 tablet

Appendix 10. Toxicity of ARV drugs and management

ARV drug	Major types of toxicity	Risk factors	Management
ABC	Hypersensitivity reaction	Presence of HLA-B*5701 gence	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
ATV/r	ECG abnormalities (PR interval prolongation)	Pre-existing conduction disease Concomitent use of other drugs that may prolong PR interval	LPV/r or DRV/r. If boosted PIs are contraindications and NNRTIs have failed in first line ART, consider integrase inhibitors
	Indirect hyperbilirubinemia (clinical jaundice)	Underlying hepatic disease sush as HBV and HCV coinfection Concomitent use of hepatotoxic drugs	
	Nephrolithiasis and risk of prematurity	Risk factors unknown	
AZT	Anemia, neutropenia, myopathy, lipoatrophy or lipodystrophy	Baseline anemia or neutropenia CD4 count ≤ 200 cells/mm^3	If AZT is being used in first line ART, substitute with TDF or ABC
	Lactic acidosis or hepatomegaly with severe steatosis	BMI > 25 (or body weight > 75 kg) Prolonged exposure to nucleoside analogues	
DRV/r	Hepatotoxicity	Underlying hepatic disease sush as HBV and HCV coinfection Concomitent use of hepatotoxic drugs	If DRV/r is being used in second line ART, substitute with ATV/r or LPV/r.
	Hypersensitivity and severe skin reactions	Sulfonamide allergy	
DTG	Hepatoxicity and hypersensitivity reactions	HBV, HCV coinfection Hepatic disease	If DTG is being used in first line ART, substitute with ARV drugs in other class (EFV or boosted PIs)
EFV	Persistent central nervous system (sush as abnormal dreams, depression	Trầm cảm hoặc các rối loạn tâm thần khác (có từ trước hoặc khi bắt đầu điều trị) Daytime using	Consider to substitute with NVP in case of neurotoxicity. If there is allergy grad 3, 4 or severe hepatotoxicity, use

ARV drug	Major types of toxicity	Risk factors	Management
	or mental confusion)		boosted PI. If there are no choice, use 3 drugs of NRTI.
	Hepatotoxicity	Underlying hepatic disease sush as HBV and HCV coinfection Concomitent use of hepatotoxic drugs	
	Convulsions	History of seizure	
	Hypersensitivity reaction, Stevens-Johnson syndrome	Risk factor unknown	
	Potential risk of neural tube birth defects (very low risk in humans)	Risk factor unknown	
	Male gynaecomastia		
LVP/r	ECG abnormalities (PR and QT interval prolongation, torsades de pointes)	People with pre-existing conduction disease Concomitent use of other drugs that may prolong the PR interval	If LPV/r is being used in first line ART for children, use age appropriate NNRTI (NVP for children younger than 3 years and EFV for children 3 years and olders). ATV can be used for children older than 6 years. If LPV/r is being used in second line ART for adults, use ATV/r or DRV/r. If boosted PIs are contraindicated and patient has failed on first line treatment with NNRTI, consider intergrase inhibitors.
	QT interval prolongation	Congenital long QT syndrome Hypokalemia Concomitent use of other drugs that may prolong the QT interval	
	Hepatotoxicity	Underlying hepatic disease sush as HBV and HCV coinfection Concomitent use of hepatotoxic drugs	
	Pancreatitis	Advanced HIV disease	
	Risk of prematurity, lipodystrophy or metabolic syndrome, dyslipidemia or severe diarrhea	Risk factors unknown	
NVP	Hepatotoxicity	Underlying hepatic disease sush	Subsititute with EFV if

ARV drug	Major types of toxicity	Risk factors	Management
		as HBV and HCV coinfection Concomitent use of hepatotoxic drugs CD4 > 250 cells/mm^3 in women CD4 >400 cells/mm^3 in men First month of therapy (if lead-in dose is not used)	patient cannot tolerate NNRTI (severe hepatoxicity), use boosted PIs or 3 drugs of NRTI if there is no other choices
	Hypersensiticity and severe skin reactions (Stevens-Johnson syndrome)	CD4 > 250 cells/mm^3 in women CD4 >400 cells/mm^3 in men	Discontinue if moderate and severe allergy. When the person is stable, retreat with PIs, or 3 drugs of NRTI if there is no other choices
RAL	Rhabdomyolysis, myopathy, myalgia	Concomitent use of other drugs that increase the risk of myopathy and rabdomyolysis	Substitute with other class of ARV (boosted PI)
	Hepatitis and liver failure, severe rash, hypersensitivity reaction	Risk factors unknown	
TDF	Chronic kidney disease. Acute kidney injiry and Fanconi syndrome	Underlying renal disease Age > 50 years BMI < 18.5 or low body weight (<50kg) Untreated comorbidities sush as diabetes, hypertension Concomitent use of nephrotoxic drugs or boosted PI	Substitute with AZT or ABC No initiate with TDF if GFR < 50 ml/min; uncontrolled hypertension, untreated diabetes or presence of renal failure
	Decreases in bone mineral density	History of osteomalacia, rickets, pathological fracture. Risk factors for osteoporosis and bone loss Vitamin D deficiency	
	Lactic acidosis, hepatomegaly with steatotis	History of prolonged treatment with nucleoside analogues Obesity Hepatic disease	

Appendex 11. Dosing adjustment of ARV by glomerular filtration rate (GFR)

ARV drug	**GFR (mL/min)**				Hemodialysis if GFR < 10
	≥ 50	30-49	10-29	< 10	
ABC	No adjustment required				
FTC 200 mg once daily	200 mg once every 2 days		200 mg once daily	200 mg once every 4 days	200 mg once every 4 days
3TC 300 mg once daily	150 mg once daily		100 mg once daily	50-25 mg once daily	50-25 mg
TDF 300 mg once daily	300 mg q48h		Alternative drugs If no others available: 300 mg twice per week (every 72-96 hour)	No recommendation	300 mg once per week
AZT 300 mg q12h	No adjustment required			100 mg q8h	100 mg q8h
NNRTIs (EFV, NVP)	No adjustment required				
PIs	No adjustment required				

Appendix 12.Drug - drug interactions between HCV DAAs and ARV

DAAs drugs	ARV drugs										
	Efavirenz (EFV)	Nevirapine (NVP)	Abacavir (ABC)	Lamivudine/ emtricitabine 3TC/FTC	Tenofovir (TDF)	Zidovudine (AZT)	Lopinavir/r (LPV/r)	Atanazavir (ATV/r)	Darunavir (DRV/r)	Dolutegravir (DTG)	Raltegravir (RAL)
Sofosbuvir											
Daclatasvir	↑ dose of daclatasvir 90mg	↑ dose of daclatasvir 90mg						↓ dose of daclatasvir 30mg			
Sofosbuvir/ Ledipasvir		NA			Monitor renal toxicity		Monitor renal toxicity if coadminister with TDF	Monitor renal toxicity if coadminister with TDF	Monitor renal toxicity if coadminister with TDF		
Grazoprevir/ Elbasvir	No coadminister	No coadminister					No coadminister	No coadminister	No coadminister		
Sofosbuvir/ Velpatasvir	No coadminister	No coadminister			Monitor renal toxicity						
Sofosbuvir/ Velpatasvir/ Voxilaprevir	No coadminister	NA	NA		Monitor renal toxicity	NA	No coadminister	No coadminister	No coadminister		
Simeprevir	No coadminister	No coadminister					No coadminister	No coadminister	No coadminister		
Paritaprevir/ Ombitasvir/r +/- Dasabuvir	No coadminister	No coadminister					No coadminister	No coadminister	No coadminister		
Ribavirin						No coadminister					

No significant interaction

Close monitoring/dose adjustment

Interactions, no coadminister Both

No data or not available

Appendix 13: Disclosure of HIV status to adolescents

Objectives	Help adolescents understand about HIV status and deliver education about self-care, treatment adherence and prevention of HIV transmission
Process of disclosure to adolescents	
Step 1. Identify the children with full criteria of disclosure	- Children over 7 years; the most appropriate age for full disclosure of HIV status is 10-12 years - Children live with caregivers and receive continuous support - Children and caregivers have no severe diseases - Children have no severe impairment of mental growth and suicide ideation.
	Cases with urgent disclosure: - Children know HIV status by chance - Children suspect HIV infection - Children do not adhere to treatment - Children reach puberty - Caregivers want to inform
Step 2. Evaluate whether caregivers and children are ready	*a.* ***Evaluate the ready of caregivers*** - Desire to announce, have good attitude and less anxiety - Understand disease thoroughly, benefits and disadvantages of disclosure - Be able to actively communiate with children (prepare appropriate response to adverse conditions in process of disclosure to children…) ***b. Evaluate the ready of children*** - Be able to comprehend and communicate - Be able to feel about yourself and relationships in family, be responsible to yourself - Have experience in dealing with stress and solving problem - Security. **c.** ***Evaluate the ready of counselling and treatment team*** - Understand the development of children and family situation… - Have counselling skills - Have communication skills with children
Step 3. Inform about HIV status	- Tell the truth, no tell lies (disclosure of HIV status, explain the reason of infection) - Provide the knowledge: transmission route and prevention, differentiation between HIV and AIDS, self-care, adherence to ART, prognosis…

	- Evaluate the feelings of children and respond appropriately - Discuss about strategies to deal with, including security issue
Step 4. Follow up and evaluate children and caregivers after disclosure	Follow up and assess children and caregivers immediately after disclosure, 1-2 weeks later, 2 months and 6 months later or whener if necessary: - Evaluate the feelings of children, from the opinion of caregivers - Review and supplement knowledge about HIV, AIDS, treatment adherence and self-care - Guide children about information security of HIV status

REFERRENCES

Tài liệu tiếng Việt:

1. Bộ Y tế: "Hướng dẫn tư vấn phòng, chống HIV/AIDS tại cơ sở y tế" ban hành kèm theo Thông tư số 01/2015/TT-BYT ngày 27 tháng 02 năm 2015.

2. Bộ Y tế: "Hướng dẫn quản lý, theo dõi điều trị người nhiễm HIV và người phơi nhiễm với HIV" ban hành kèm theo Thông tư số 32/2013/TT-BYT ngày 17 tháng 10 năm 2013 của Bộ Y tế.

3. Bộ Y tế: "Hướng dẫn điều kiện và phạm vi chuyên môn của cơ sở y tế điều trị bằng thuốc kháng HIV" ban hành kèm theo Thông tư số 09/2011/TT-BYT ngày 26 tháng 01 năm 2011 của Bộ Y tế.

4. Bộ Y tế: "Hướng dẫn chẩn đoán và điều trị HIV/AIDS" ban hành kèm theo Quyết định số 3003/QĐ-BYT ngày 19 tháng 8 năm 2009 của Bộ Y tế.

5. Bộ Y tế: "Quy định chế độ báo cáo công tác phòng, chống HIV/AIDS" ban hành kèm theo Thông tư số 03/2015/TT-BYT ngày 16 tháng 3 năm 2015.

6. Bộ Y tế: "Quy định chức năng, nhiệm vụ, quyền hạn và cơ cấu tổ chức của Trung tâm Phòng, chống HIV/AIDS tỉnh, thành phố trực thuộc Trung ương" ban hành kèm theo Thông tư số 02/2015/TT-BYT ngày 04 tháng 3 năm 2015 của Bộ Y tế.

7. Bộ Y tế: Quyết định số 4139/QĐ-BYT ngày 02 tháng 11 năm 2011 của Bộ trưởng Bộ Y tế về việc sửa đổi, bổ sung một số nội dung trong "Hướng dẫn chẩn đoán và điều trị HIV/AIDS" ban hành kèm theo Quyết định số 3003/QĐ-BYT ngày 19 tháng 8 năm 2009 của Bộ trưởng Bộ Y tế.

8. Bộ Y tế: Về việc ban hành "Hướng dẫn thực hiện chăm sóc người nhiễm HIV tại nhà và cộng đồng" ban hành kèm theo Quyết định số 1781/QĐ-BYT ngày 27 tháng 05 năm 2010 của Bộ trưởng Bộ Y tế.

9. Bộ Y tế: "Về việc ban hành hướng dẫn phát hiện tích cực bệnh lao và điều trị dự phòng mắc lao bằng Isoniazid (INH) ở người nhiễm HIV" ban hành kèm theo Quyết định số 2495/QĐ-BYT ngày 18 tháng 7 năm 2012 của Bộ trưởng Bộ Y tế.

10. Bộ Y tế: "Về việc ban hành Quy chế phối hợp giữa chương trình mục tiêu quốc gia phòng, chống HIV/AIDS và dự án phòng, chống bệnh lao thuộc chương trình mục tiêu quốc gia y tế" ban hành kèm theo Quyết định số 2496/QĐ-BYT ngày 18 tháng 7 năm 2012 của Bộ trưởng Bộ Y tế.

11. Bộ Y tế: "Về việc ban hành quy trình chăm sóc và điều trị dự phòng lây truyền HIV từ mẹ sang con" ban hành kèm theo Quyết định số 4361/QĐ-BYT ngày 07 tháng 11 năm 2007 của Bộ trưởng Bộ Y tế.

12. Bộ Y tế: "Về việc ban hành Hướng dẫn thực hiện cải tiến chất lượng chăm sóc và điều trị HIV/AIDS đối với hoạt động khám ngoại trú" ban hành kèm theo Quyết định 471/QĐ-BYT ngày 11 tháng 02 năm 2014 của Bộ trưởng Bộ Y tế.

13. Cục Phòng, chống HIV/AIDS: "Ban hành Hướng dẫn quản lý cung ứng thuốc kháng HIV (ARV) trong Chương trình phòng, chống HIV/AIDS" ban hành kèm theo Quyết định số 165/QĐ-AIDS ngày 25 tháng 8 năm 2014 của Cục trưởng Cục Phòng, chống HIV/AIDS.

14. Bộ Y tế (2014). Hướng dẫn chẩn đoán, điều trị bệnh viêm gan vi rút B. Quyết định số 5448/QĐ-BYT ngày 30 tháng 12 năm 2014

15. Bộ Y tế (2016). Hướng dẫn chẩn đoán, điều trị bệnh viêm gan vi rút C. Quyết định số 5012/QĐ-BYT ngày 20 tháng 9 năm 2016

16. Bộ Y tế (2015). Hướng dẫn, chẩn đoán điều trị và dự phòng bệnh lao. Quyết định số 4263/QĐ-BYT ngày 13/10/2015

Tài liệu tiếng Anh:

1. AIDS info, Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents, Aug 2017
2. European AIDS Clinical Society (EASL), Guidelines, 1/2017
3. India: Antiretrovial therapy guidelines for HIV-Infected adults and adolescents, May 2013.
4. Malaysia: Guidelines for the management of adult HIV infection with antiretroviral therapy, December 2011.
5. South Africa: The south african antiretroviral treatment guidelines , March 2013.
6. United States Centers for Disease Control and Prevention, the National Institutes of Health and the Infectious Diseases Society of America, Treating Opportunistic Infections Among HIV-Exposed and Infected Children, MMWR December 3, 2004 / 53(RR14);1-63
7. WHO (2008), Operations manual for delivery of HIV prevention, care and treatment at primary health care centres in high-prevalence, resource-constrained settings.
8. WHO (2011), Rapid advice: Diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children.
9. WHO (2011), Intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings.
10. WHO (2012), Guidance on prevention of viral hepatitis B and C among people who inject drugs
11. WHO (2013), Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach.
12. WHO (2013), Guidance on prevention of viral hepatitis B and C among people who inject drugs.
13. WHO (2013), HIV and adolescents: Guidance for HIV testing and counselling and care for adolescents living with HIV: Guidance document.
14. WHO (2014), Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations.
15. WHO (2014), Guidelines on post-exposure prophylaxis for HIV and the use of co-trimoxazole prophylaxis for HIV-related infections among adults, adolescents and children: Recommendations for a public health approach - December 2014 supplement to the 2013 consolidated ARV guidelines.
16. WHO (2014) , Guidelines for the screening, care and treatment of persons with hepatitis C infection.

17. WHO (2014), March 2014 supplement to the 2013 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: Recommendations for a public health approach.
18. WHO (2014), July 2014 Global update on the health sector response to HIV, 2014.
19. WHO (2015), Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection.
20. WHO (2016) Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach.
21. WHO (2017) Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy
22. WHO (2016). Guidelines for the screening, care and treatment of persons with hepatitis C infection.
23. WHO (2017). Guideline on hepatitis B and C testing.
24. WHO- UNITAID (2017). Technology and market landscape. Hepatitis C medicines