Republic of Zimbabwe

NATIONAL HIV/AIDS AND TUBERCULOSIS CONTROL PROGRAMMES

NATIONAL GUIDELINES FOR TB/HIV CO-MANAGEMENT

Preface

The strong association of HIV/AIDS and tuberculosis (TB) in Zimbabwe calls for new efforts to address the convergence of the dual epidemics in a collaborative fashion. Its primary aim is to promote the use of standard international evidence based best management practices for TB and HIV co-infection care in Zimbabwe.

This document is not intended to serve as a comprehensive clinical guideline: however, general recommendations related to diagnosis, treatment and overall care have been included to promote adherence to standards and best practices. The guidelines are based on the most recently compiled, evidence-based information available at time of writing. In particular, this document draws heavily from the most recent editions (2009) of the World Health Organization (WHO) TB Treatment Guidelines (4th ed.), and the International Standards for TB Care (ISTC) (2nd ed.). These international standards represent an ideal to be attained, while the guidelines herein attempt to describe current best practices for Zimbabwe. It is the intention of the Ministry of Health and Child Welfare (MOHCW) that these guidelines serve to sensitize care providers to best practices for TB and TB/HIV control through in-service training programs. Educators and trainers in health institutions may also find the guidelines useful in developing teaching materials for pre-service education and training.

Although multidrug resistant TB (MDR-TB) is an escalating problem in southern Africa and a serious threat to TB control, relatively little space in this document is devoted to MDR-TB. Specific national guidelines are to be developed based on national progress in establishing drug susceptibility testing (DST) within the context of comprehensive plans for laboratory strengthening.

Ultimately, successful implementation of the approaches described in this document will require strong leadership, political will, social mobilisation, adequate human and financial resources, renewed commitment to the DOTS strategy, and sustainable development of health-care services. The MOHCW is fully committed to the provision and full implementation of comprehensive care packages for all TB/HIV co-infected persons and will strive to provide the necessary resources and support.

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Contents

Background

Tuberculosis is the primary cause of mortality in people living with HIV/AIDS (PLHIV) worldwide, with 79% of the estimated 1.37 million new cases of TB/HIV in 2007 occurring in sub-Saharan Africa (WHO 2009). Tuberculosis (TB) is highly associated with HIV infection in Zimbabwe, and an estimated 80% of TB cases are co-infected with HIV. The increase in TB in Zimbabwe during the last two decades is largely a result of an escalating HIV epidemic in the context of ongoing operational and resource challenges within the country.

Zimbabwe ranks 17th among the world's high TB burden countries, and 4th according to incidence per capita (782/100,000). Case detection in 2006 was estimated at 37% (for all cases), and treatment success at 60% (for new cases). Less than one third of pulmonary TB cases had positive sputum smear microscopy in 2007 and 27% of all patients received TB treatment without smear examination having been performed (NTP).

Zimbabwe has a strong physical health infrastructure, including an elaborate network of laboratories and primary care clinics, and is actively scaling up collaborative TB/HIV activities. The health system has recently been challenged, however, by shortages of adequately trained staff due to high turnover and emigration, insufficient access to and availability of laboratory diagnostic services (including reagents, materials, and staff), and insufficient funding for supervision, monitoring and evaluation, and training at all levels. There are an estimated 180 TB diagnostic centers within the public health system. TB diagnosis and treatment is provided by the public health sector without charge. Fixed-dose combination (FDC) anti-TB drugs were introduced in 2007, and 6 month regimens are used for treatment of new cases. The proportion of multidrug resistant TB (MDR-TB) among new and previously treated cases is estimated at 1.8% and 8.3%, respectively (WHO 2007), though a national prevalence survey has not been carried out since 1995. There is currently no systematic monitoring of TB drug resistance.

Currently, approximately 14% of the adult population aged 15 to 49 years is estimated to be infected with HIV (Zimbabwe HIV Estimates, 2009). Scaling up of HIV testing and counseling of patients with TB began in 2005; it is estimated that 13% of TB patients were screened for HIV in 2007. Rapid HIV testing is now widely available, and 649 health facilities currently provide HIV care and treatment services. In addition, 29.6% of adults and 10% of children who are HIV-infected and meet criteria for antiretroviral (ARV) treatment are currently on ART (ZNASP MTR 2009); about 325,000 (25%) receive cotrimoxazole preventative therapy (CPT).

HIV is the most powerful factor known to increase the risk of TB. HIV increases susceptibility to infection with M. tuberculosis. It also increases the risk of progression of M.tuberculosis infection to TB disease. This risk increases with increasing immunosuppression. HIV increases not only the risk but also the rate of progression of recent or latent M.tuberculosis infection to disease. Compared with an individual who is not infected with HIV, a person infected with HIV has a 10 times increased risk of developing TB.

It is therefore evident that TB and HIV are closely interlinked. TB is the leading cause of HIV-related morbidity and mortality. HIV is the most important factor fuelling the TB epidemic in populations with high HIV prevalence. The need for a coordinated response to the epidemic cannot be over-emphasised. The collaboration between NTP and the OI/ART programme is crucial in supporting general health service providers.

Section One:
Establishing Collaboration between TB and HIV Programmes

TB services are a critical entry point for the promotion of HIV prevention, testing and treatment, as well as for adherence support and ARV drug resistance monitoring. Likewise, HIV services are also a critical entry point for TB care. Both HIV/AIDS and TB care require a chronic disease management approach. Ideally, service delivery should be integrated, providing an accessible continuum of care. For collaboration to be effective, the following steps should be taken:

1.1 Step 1: Reinforce the coordinating body for integration of TB and HIV activities

Important areas of responsibility for the joint coordinating bodies include:

- Joint resource mobilization for TB activities and HIV activities
- Capacity building, including training and supervision
- Ensuring coherence of communications about TB/HIV
- Ensuring the participation of the community in joint TB/HIV activities
- Monitor & evaluate progress toward locally set targets for TB/HIV activities

1.2 Step 2: Conduct surveillance of HIV prevalence among tuberculosis patients

Surveillance is essential to inform programme planning and implementation. Surveillance must contribute to a better understanding of the magnitude of the problem and provide reliable, timely, and cost-efficient information for action. The following are objectives for surveillance of TB and TB/HIV:

- To increase political, professional, and community awareness of the situation
- To provide evidence for the need for collaboration between the programmes (TB and HIV) at the national level, and for formulation and implementation of a TB/HIV strategy
- To provide information on the HIV epidemic and its impact on TB patients and, conversely, the impact of TB on HIV patients
- To quantify the need for providing ART and CPT to TB patients

There should be accurate and timely reporting from both programmes and that reports from each programme are shared with everyone at district, provincial and national level. This kind of communication will enhance the planning and execution of prevention and care programmes.

Data Sources and Indicators

Specific HIV-related indicators useful in integrated case management, such as date of ARV initiation, date of switching of ARV drugs, and cotrimoxazole prophylaxis initiation, have been

recently added to patient tuberculosis treatment cards; patient CD4 count should also be added during the next revision. This data should be summarized from the TB register and routinely reported as NTP programme data. Laboratories, hospitals, health centres, voluntary counseling and testing (VCT) sites and PMTCT clinics should also compile and provide data to the NTP.

1.3 Step 3: Support joint TB/HIV planning

Joint planning and coordinated management is particularly important for:

- **Joint resource mobilization.** Human and financial resources need to be made available if Zimbabwe is to succeed in achieving global Stop TB targets. Preparation and submission of joint TB/HIV proposals would be helpful in soliciting resources for collaborative activities.

- **Capacity building, including training.** Joint capacity building should include recruitment and retention, training, and ongoing supervision and support of health workers in both TB and HIV issues (pre-service and in-service). Human resource capacity is being enhanced by in-service training and increased output from training institutions of health-care workers competent to work in primary health-care services. Task shifting, increased flexibility in health services roles, and a greater reliance on community-based health-care workers are examples of other activities that could contribute to this goal. **Greater resources will be allocated to strengthening the management capacity at all levels to ensure integration of HIV and tuberculosis into primary health-care services as much as possible.**
  Basic systems for managing staff performance, ensuring accountability and for procurement of supplies should be promoted at all levels of care provision.

- **Advocacy and Communications.** Advocacy and communications have at least two goals: (1) to influence policy, programme implementation and resource mobilization; and (2) to communicate directly to the public to create awareness of the interaction between TB and HIV among patients with either disease, in order to increase the likelihood that these persons will actively seek out services. The National TB control program will be increasing these activities in the coming years with progressive expansion to provincial and district levels.

- **Enhancing community involvement in collaborative TB/HIV activities.** Through support groups for people living with HIV/AIDS and community-based organizations, TB prevention and care can be integrated with HIV/AIDS prevention, care, and support. Communities can be mobilized to advocate for resources and help implement collaborative TB/HIV activities.

- **Operational research.** Operational research to determine the most effective and efficient means of delivering collaborative TB/HIV activities is an essential component of

all joint activities. Districts are encouraged to undertake operational research in critical areas identified during routine data analysis.

1.4 Step 4: Monitor and evaluate collaborative TB/HIV activities

Monitoring and evaluation (M&E) provide the critical means to assess quality, effectiveness, coverage, and delivery of collaborative TB/HIV activities and is essential to inform planning of new activities and adjustment of ongoing initiatives. Various methods are available for monitoring and evaluating collaborative TB /HIV activities some of which are external reviews of the programme, situation analysis (using country profile checklist), routine monitoring systems, surveillance and surveys, supportive supervision and health management information systems. More details can to be found in the monitoring and evaluation plan.

A core set of TB/HIV indicators to facilitate the collection of standardized data, avoid duplication of effort in data collection, and help in the interpretation and dissemination of these data for programme improvement are listed below. Data should be collected continuously at the facility level, aggregated periodically (monthly or quarterly) at the district level, and reported annually at the national level. See the ART register and District TB register at annexes A and B respectively.

For more detail on monitoring and evaluation, see the Zimbabwe M&E Plan 2009 - 2013.

Table 1. Zimbabwe TB/HIV Indicators

A. Indicators Measured in HIV Care Settings by National OI/ART Programme

Indicator A1.	Percentage of adults and children enrolled in HIV care who began TB treatment.
Indicator A2.	Percentage of adults and children enrolled in HIV care who underwent TB screening.
Indicator A3.	Percentage of facilities providing HIV care with infection control plans and identifiable infection control practices.
Indicator A4.	Percentage of health care workers notified as having TB in one year.

B. Indicators Measured in TB Care Settings by NTP

Indicator B1.	Percentage of TB patients who had an HIV test result recorded in the TB register.
Indicator B2.	Percentage of HIV+ TB patients who are started on or continue ART during TB treatment.
Indicator B3.	Percentage of HIV+ TB patients who are started on or continue cotrimoxazole preventative therapy (CPT) during TB treatment.
Indicator B4.	Percentage of HIV+ TB patients who are referred for HIV care and support services (per National HIV/AIDS policy) during TB treatment.

Indicator B5.	Percentage of TB patients registered with documented HIV status on TB register who are HIV-positive.
Indicator B6.	Percentage of facilities providing TB care with infection control plans and identifiable infection control policies.
Indicator B7.	Percentage of TB facilities where free condom distribution is practiced.

Section Two:
Decreasing the Burden of TB in Persons Living with HIV

TB is unique among the many other diseases affecting persons living with HIV/AIDS (PLHIV), because it:

- Is a lifelong risk for PLHIV, even in the presence of antiretroviral therapy, and can occur at any stage of HIV-related immunodeficiency.
- Is often the first disease affecting PLHIV during the progression from HIV infection to AIDS.
- Often results in death if not diagnosed early and treated adequately.
- Is a major public health problem, given that it is an airborne disease that can be spread to the general population.

2.1 Intensified TB Case Finding in Persons Living with HIV

Screening for symptoms and signs of TB in settings where HIV-infected people seek care **must be routine practice.** Early identification of signs and symptoms of TB, followed by pursuit of a confirmed diagnosis and prompt treatment, increase the chances of survival, improve quality of life, and reduce transmission of TB in the household and in the community.

The following sites should be prioritized for intensified TB case finding:

- Opportunistic infection (OI) clinics
- VCT and PMTCT centres
- All general outpatient clinics
- Medical and infectious disease wards
- Prisons

The TB screening questions in Table 1 should be asked of *every* patient visiting any of the above sites.

Table 2. TB Screening Questionnaire[1]

Questions	Yes	No
1. Has the patient had a cough for ≥ 2 weeks?		
2. Has the patient had night sweats for ≥ 3 weeks?		
3. Has the patient lost weight (≥ 3 kg if able to quantify) in the past 3-4 months?		
4. Has the patient had fever or "hot body" for ≥ 3 weeks?		
5. Does someone in the patient's household have known active TB?		

Questions should be asked to the patient in a "non-leading" manner. For example, rather than asking "Have you had a cough for 2 weeks or longer?", it is preferable to ask "Do you have a cough? For how long?" (A "yes" answer would be recorded if the patient answers "longer than 2 weeks".)

If "yes" to <u>any</u> of the questions, the patient may have TB disease, and is considered a TB suspect. Collect 2 sputum specimens for AFB smear if patient is able to produce sputum, and continue evaluation for TB (see Figure 1). Refer to higher level of care if necessary. If "no" to all questions, the patient is not a TB suspect. Repeat screening with questionnaire <u>every 3 months</u>.

2.2 Clinical Presentations of TB in the Setting of HIV Infection

Sputum smear-positive pulmonary TB is common among people with HIV infection. However, PLHIV are more likely to present with extrapulmonary or sputum smear-negative TB than patients who are HIV-uninfected, especially as immunosuppression advances (as indicated by clinical status or declining CD4 cell counts). This may result in misdiagnosis or delays in diagnosis, and in turn, higher rates of death. Therefore, implementation of the WHO recommended algorithms to diagnose pulmonary and extrapulmonary TB in HIV prevalent settings is crucial (see Figure 1).

<u>International Standards of TB Care (ISTC) Standard</u>

The diagnosis of sputum smear-negative pulmonary tuberculosis should be based on the following criteria:

- **At least 2 negative sputum smears**
- **Chest radiographic findings suggestive of tuberculosis**
- **Lack of response to a trial of broad-spectrum antimicrobial agents (*<u>NOTE</u>:***

***Because the fluoroquinolone antibiotics [e.g., ciprofloxacin, norfloxacin] are active against* M. tuberculosis *complex, they may cause transient improvement in persons with tuberculosis, and should be avoided.*)**

[1] Adapted from local guidelines and *International Journal of Tuberculosis and Lung Disease*. 2008; 12(3):S39-43.

For patients with smear-negative pulmonary tuberculosis, sputum cultures should ideally be obtained. In persons who are seriously ill or have known or suspected HIV infection, the diagnostic evaluation should be expedited and if clinical evidence strongly suggests tuberculosis, antituberculosis treatment should be initiated.

Evaluation of suspected HIV-related TB should include a chest radiograph, though reliance on the chest radiograph as the only diagnostic test for tuberculosis will result in both over-diagnosis and missed diagnoses of tuberculosis and other diseases. Several pulmonary diseases can mimic TB on a chest X-ray and in signs and symptoms, and not every HIV-infected patient with an abnormal chest X-ray will have TB; conversely, a normal chest X-ray does not always exclude the possibility of TB. Chest radiograph should also not be used for patients without signs or symptoms of TB (TB screening).

ISTC Standard

All persons with chest radiographic findings suggestive of tuberculosis should have sputum specimens submitted for microbiological examination.

Smear microscopy of the sputum is a reliable diagnostic approach and should be done on all individuals when pulmonary and/or extrapulmonary TB is suspected. The first sputum should be collected (**outdoors, away from patient waiting areas**) and submitted for AFB smear microscopy at the time of initial patient evaluation; the second sputum should be collected the following morning.

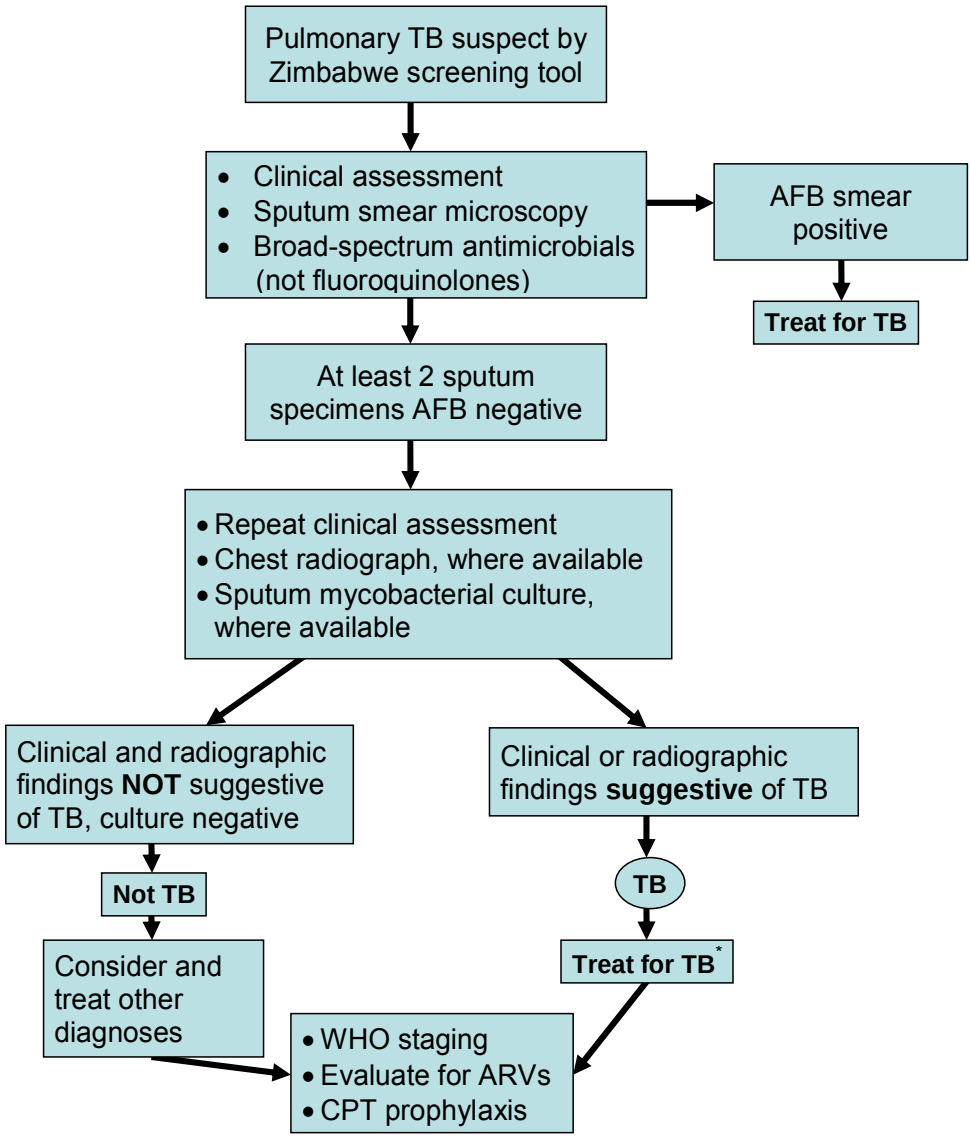
Improper collection of sputum delays diagnosis and may increase laboratory work load. The reasons for and proper technique of sputum collection must be explained to the patient. In particular, (1) patients should understand that spit or saliva is not suitable, and (2) patients should be instructed to cough deeply (demonstrating if possible); clear the back of the throat and produce 5 to 10 ml of sputum in the container, repeating this until a sufficient amount of the best possible sputum is obtained. In general, (1) a specimen collected under supervision of a competent health-care worker is likely to yield better results than a specimen collected without supervision, (2) sputum collection should take place in the open air, taking into consideration the need for the patient's privacy, and (3) an initial specimen should be collected before administration of anti-tuberculosis therapy.

Failure to perform a proper diagnostic evaluation before initiating treatment for tuberculosis potentially exposes the patient to the risks of unnecessary or wrong treatment with no benefit. Moreover, such an approach may delay accurate diagnosis and proper treatment. Age alone is not sufficient justification for failing to attempt to obtain a sputum specimen from a child or adolescent. **TB treatment trials (trials of anti-TB medicines with or without rifampicin) are not acceptable.**

The NTP and collaborating partners will ensure that providers and patients have convenient access to microscopy services. The National Directorate for Laboratories will endeavor to

ensure that all laboratories, public and private, undergo external assessments of quality and have programs for quality improvement.

Figure 1. An Illustrative approach to the diagnosis of pulmonary tuberculosis among patients suspected or known to be HIV-infected[1]



[1] Adapted from *International Standards for Tuberculosis Care*, 2nd edition, 2009

* In patients with severe illness, empiric treatment for TB may be initiated prior to confirmation of diagnosis.

2.3 Prevention of Tuberculosis in HIV-Infected Persons

2.3.1 TB Infection Control

Increased transmission of TB may occur in health care facilities (clinics and hospitals) and congregate settings (e.g., prisons and military barracks) and communities where people with TB and HIV are frequently crowded together.

There are three types of infection control measures: administrative, environmental and personal protective equipment. *National managerial activities* include the NTP's responsibility to assess the problem, develop policy, plan and budget, build human resources, ensure the appropriate development and use of physical infrastructure, and monitor and evaluate progress.

ISTC Standard

Each health care facility caring for patients who have or are suspected of having infectious tuberculosis should develop and implement an appropriate tuberculosis infection control plan.

Administrative controls

Implementation of administrative controls through a clear infection control plan is the most important infection control measure to reduce transmission of TB in health care facilities.

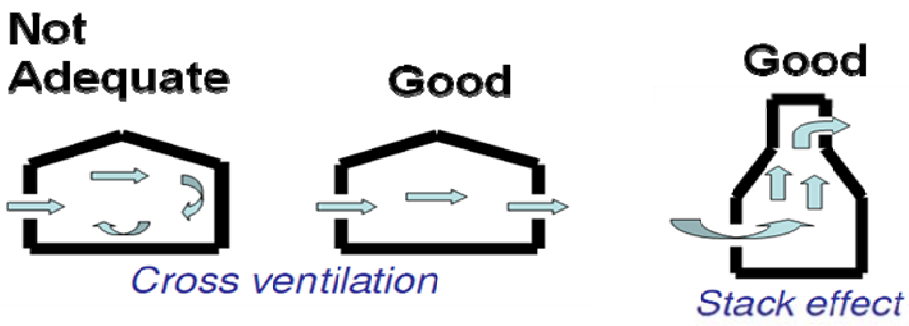
1. Triage. Patients should be screened with the Zimbabwe TB Screening Questionnaire upon arrival. Persons suspected of having TB should be "fast-tracked" for rapid diagnosis and care services or asked to wait near an open window or in an area separate from the general waiting room (outside when possible).
2. Education of patients and community awareness. Respiratory hygiene (covering one's mouth and nose when coughing, careful disposal of soiled tissues) should be emphasised by clinic staff. Every facility should have a poster on TB infection control and cough etiquette in the patient waiting area.
3. Minimize patient waiting time. Patients should be attended to expeditiously in health care facilities.
4. Package of care for health-care workers. Health-care workers (HCWs) should (1) know the symptoms of TB, and (2) be offered HIV testing and TB screening, at least annually. HCWs who are HIV-infected should be offered a change of duties (to minimize exposure to persons with TB), and be offered isoniazid preventive therapy (IPT) when active TB can be safely excluded, and when IPT is available according to national guidelines.
5. Training of staff. Clinic staff and staff working in congregate settings where persons with TB and HIV reside should receive annual refresher training on TB infection control.

Environmental controls

Environmental controls focus on using inexpensive measures to reduce the droplet nuclei in the air. They are the second line of defense after administrative controls.

1. Natural ventilation should be maximized by keeping clinic windows and doors open during working hours, even during winter. Natural ventilation can be maximized through promoting cross ventilation (opening of windows or doors on opposite walls) and "stack effect", which increases airflow using indoor/outdoor temperature difference. (Figure 2.) Open air shelters with a roof to protect patients from sun and rain are recommended. Patients should not wait for services in narrow, poorly ventilated corridors.
2. Sunlight is a natural source of ultraviolet light, which can kill TB bacilli.
3. Reduced crowding in patient waiting areas is very important, and waiting areas in the open air should be favored over enclosed corridors.

Figure 2. Promoting Natural Ventilation [2]



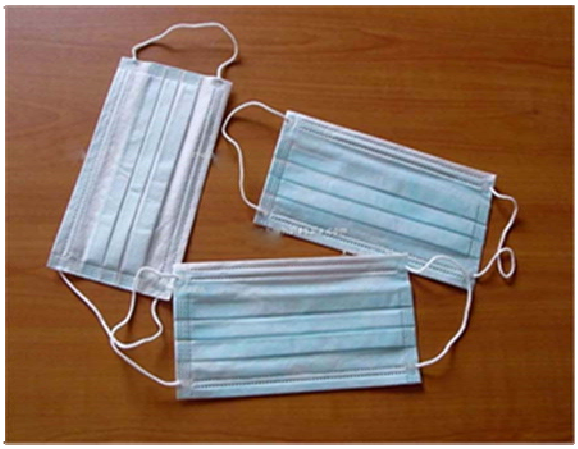
Personal protective equipment

Personal protective equipment should be used together with administrative and environmental controls in situations where there is an increased risk of transmission.

1. Surgical face masks prevent respiratory secretions from becoming airborne, and decrease the risk that **the patient wearing the mask** will infect other people, however they will not avoid the inspiration of bacillus from the air. Health-care workers should therefore not wear surgical face masks, but may wear specialized N95 particulate respirators if available. Whenever possible, a TB suspect or a TB patient who has had less than 1 week of TB treatment should wear a surgical face mask when (1) they cannot be separated from other patients in patient waiting areas, and (2) while moving from one part of a hospital to another.

[2] Credit: Rod Escombe, MRCP DTM&H PhD, Imperial College London, UK

Figure 3. Personal protective equipment



Surgical Face Mask

N95 Particulate Respirator

2.3.2 Isoniazid Preventive Therapy (IPT)

Isoniazid Preventive Therapy (6 to 9 months of isoniazid without other anti-TB medicines) for TB can safely be given to people living with HIV without TB disease, reducing the risk of developing TB by 33 to 67% for up to 48 months. It is currently recommended for all people living with HIV in areas with a prevalence of latent TB infection >30%, and for all people living with HIV with documented latent TB infection or exposure to an infectious TB case, regardless of where they live. More recently, evidence has shown that the combined use of IPT and antiretroviral therapy among people living with HIV significantly reduces the incidence of TB; and the use of IPT in patients who have successfully completed a course of TB therapy has been shown to markedly reduce the risk of subsequent active TB. However, IPT should never be initiated unless active TB can be safely excluded. Due to the high incidence of TB in patients who have begun ART in the past 4 months, it is especially critical to thoroughly exclude active TB before initiating IPT in this group. The following criteria also exclude a patient from consideration for IPT:

- Signs and symptoms of TB, i.e., patients who are currently ill with new or worsening cough or sputum production, hemoptysis, night sweats, fever, or measured weight loss of more than 5%
- Abnormal chest X-ray (even if TB has not been confirmed)
- Poor prognosis (terminal AIDS)
- Presence of jaundice or active hepatitis (acute or chronic)
- Has had TB treatment in the past 2 years
- History of alcoholism (or daily alcohol use)

IPT is used most safely in asymptomatic HIV-infected patients, e.g., those identified early in the course of HIV infection through VCT centres or antenatal clinics.

WHO/UNAIDS Recommendations on IPT in HIV-positive Persons

Before initiating a service to provide routine IPT to PLHIV, the following prerequisites should be in place:

- Strong linkage between HIV care and TB control services
- Adequate capacity for HIV counselling, which should include information, education and counseling about TB
- Health-care staff well-trained in pre-treatment screening to exclude active pulmonary and extrapulmonary TB
- Resources available for close monitoring, supervision and evaluation of IPT outcomes
- TB control programme with high adherence to DOT, high cure rates (≥ 70%) and case detection (≥ 70%) and combined default/failure rates at the end of treatment of less than 10%

Current challenges to the National TB Programme and National OI/ART Programme make programmatic institution of IPT **not** recommended at this time in Zimbabwe as public health policy. Given the clear benefit of IPT to PLHIV, national TB and OI/ART programmatic scale up to meet these requirements in Zimbabwe would be pursued.

Section Three:
Decreasing the Burden of HIV/AIDS in Patients with Tuberculosis

3.1 Provider-Initiated Testing and Counselling in Health Care Facilities

HIV both increases the likelihood of progression from infection with *M. tuberculosis* to active tuberculosis and changes the clinical presentation of TB disease (PLHIV are more likely to present with extrapulmonary or sputum smear-negative TB than HIV-uninfected TB patients, especially as immunosuppression advances). Knowing a TB patient's HIV status, therefore, has very important bearing on his or her TB care. Cotrimoxazole prophylaxis and antiretroviral therapy (ART) reduce morbidity and prolong survival following successful TB treatment, but they cannot be provided if the TB patient's HIV status remains unknown.

Within a family-centred approach to HIV testing, once a family member is identified as having HIV, health-care workers should encourage and actively facilitate HIV testing for other family members, where possible and appropriate, through couples or family testing and counselling services. **Especially if found to be living with HIV, household contacts to an infectious case of TB are a high priority for TB screening and treatment.**

ISTC Standard

HIV testing and counseling should be recommended to all patients of all ages with tuberculosis or suspected of having tuberculosis. Because of the close relationship between tuberculosis and HIV infection, integrated approaches to prevention and treatment of both infections are recommended.

ISTC Standard

All providers of care for patients with tuberculosis should ensure that persons who are in close contact with patients who have infectious tuberculosis are evaluated and managed in line with international recommendations. The determination of priorities for contact investigation is based on the likelihood that a contact: 1) has undiagnosed tuberculosis; 2) is at high risk of developing tuberculosis if infected; 3) is at risk of having severe tuberculosis if the disease develops; and 4) is at high risk of having been infected by the index case. The highest priority contacts for evaluation are:

- **Persons with symptoms suggestive of tuberculosis**
- **Children aged <5 years**
- **Contacts with known or suspected immunocompromise, particularly HIV**
- **Contacts of patients with MDR tuberculosis**

Other close contacts are a lower priority group.

TB is often the first clinical indications that a person has underlying HIV infection. As such, TB programmes can be a very important entry point to HIV prevention, care and treatment. Provider-initiated HIV counselling and testing takes place in clinical settings, such as medical wards and TB,

PMTCT and sexually transmitted infection clinics. “Routine” or “opt-out” testing at selected health care settings means that individuals must specifically decline the HIV test after receiving pre-test information if they do not want the test to be performed. Provision of HIV testing in the same facility that provides the TB treatment has been shown to facilitate HIV testing for TB patients.

3.2 Recommendations for Anti-Tuberculosis and Antiretroviral Treatment

Among treated TB patients, HIV-infected patients have a higher risk of death than HIV-uninfected patients. Treatment of HIV-related TB should follow the general principles developed for TB treatment in HIV uninfected individuals. This includes appropriate collection of clinical samples (sputum or lymph node) for staining and microscopy. **This requires that suitable transportation and affordable, quality-controlled diagnostic laboratory facilities are in place**. Suitable transportation means that sputum specimens are to be sent to the district level laboratory within 3 days of collection, and that stocks of TB medicines and supplies are guaranteed in health clinics at all times. Quality-controlled diagnostic laboratory facilities include those that have a functioning external quality control system in place.

ISTC Standard

All patients with tuberculosis and HIV infection should be evaluated to determine if antiretroviral therapy is indicated during the course of treatment for tuberculosis. Appropriate arrangements for access to antiretroviral drugs should be made for patients who meet indications for treatment. However, initiation of treatment for tuberculosis should not be delayed. Patients with tuberculosis and HIV infection should also receive co-trimoxazole as prophylaxis for other infections.

For HIV-infected TB patients, the first priority is to initiate anti-TB treatment (especially in patients with smear-positive pulmonary TB), followed by cotrimoxazole, and then antiretroviral therapy. The optimal time for starting antiretroviral therapy (ART) in patients with HIV-associated TB remains controversial. Beginning ART early (2 to 8 weeks after initiation of TB treatment) improves survival and TB treatment outcome, especially in the setting of advanced HIV disease (CD4 count of < 200). This benefit must be weighed against overlapping toxicity profiles for the drugs used, drug-drug interactions (rifampicin induces the activity of hepatic enzymes, leading to sub-therapeutic concentrations of NNRTIs and certain protease inhibitors [PIs]), potential problems with adherence to multiple medications, and immune reconstitution inflammatory syndrome (IRIS) in some cases. Thus, in patients with early stage HIV infection, it may be safer to defer antiretroviral treatment until at least the completion of the initial phase of tuberculosis treatment.

When available, CD4 cell counts should enter into the decision on ART initiation in TB patients as follows:

- ART is recommended for all people living with HIV and diagnosed with TB whose CD4 counts are 350 cells/mm^3 or below.
- ART should be deferred in pulmonary TB patients whose CD4 cell count exceeds 350 cells/mm^3 as long as there is no other stage 3 or 4 event. Patients whose CD4 count at

TB diagnosis exceeds 350 cells/mm^3 should be re-evaluated 8 weeks after starting TB therapy, and again when TB treatment is completed.

- ART is recommended for all people living with HIV diagnosed with extrapulmonary TB, regardless of the CD4 count.
- Where CD4 is not available, ART is recommended between 2 and 8 weeks.

Table 3. Initiating first-line antiretroviral therapy in relation to starting anti-TB treatment[3].

CD_4 cell count	ART recommendation	Timing of ART in relation to start of anti-TB treatment
CD_4 < 200 cells/mm_3	Start ART[4]	Between 2 and 8 weeks[5]
CD_4 200 - 350 cells/mm_3	Start ART	After 8 weeks
CD_4 > 350 cells/mm_3	Defer ART[6]	Re-evaluate patient at 8 weeks and at the end of anti-TB treatment
CD_4 not available	Recommend ART[7]	Between 2 and 8 weeks

[3] Adapted from *Antiretroviral therapy for HIV infection in adults and adolescents. Recommendations for a public health approach*, 6th revision. Geneva, World Health Organization 2006

[4] A regimen containing efavirenz is the preferred first-line regimen; alternative regimens include nevirapine (NVP) and triple nucleoside reverse transcriptase inhibitors based on regimens using tenofovir disoproxil fumarate or abacavir. For NVP-containing regimens, alanine aminotransferase should be checked at 4, 8 and 12 weeks, and directed by symptoms thereafter.

[5] Start ART as soon as anti-TB treatment is tolerated.

[6] If other non-TB stage 3 or 4 events are present, start ART.

[7] For some TB diagnoses that generally respond well to anti-TB treatment (i.e., TB of the lymph nodes, uncomplicated pleural effusion), consider deferring ART.

TB patients who are HIV-infected should receive the same TB treatment as HIV-uninfected TB patients.

- Category 1: New patients with pulmonary TB should receive a regimen containing 6 months of rifampicin: 2HRZE / 4HR. The recommended treatment approach consists of daily DOT throughout therapy (intensive and continuation phases).
  - Note: The 2HRZE / 6HE treatment regimen is no longer acceptable because of increased treatment relapse and death, and **should no longer be used**.
- Category 2: Patients who have previously defaulted, relapsed, or failed treatment should receive the empiric TB re-treatment regimen 2HRZES / 1HRZE / 5HRE. As scale-up occurs, all previously treated TB patients should ideally have specimens obtained for culture and drug susceptibility testing (DST) before or at the start of treatment. DST should be performed for at least isoniazid and rifampicin.
- In accord with the *Guidelines for Antiretroviral Therapy in Zimbabwe 2007*, a regimen containing efavirenz is preferred for patients while on anti-TB therapy. Following successful completion of TB treatment, a nevirapine-containing regimen can again be prescribed.

3.3 Cotrimoxazole Preventive Therapy (CPT)

In all HIV-infected TB patients, cotrimoxazole preventive therapy should be initiated as soon as possible and given throughout anti-TB treatment. Cotrimoxazole preventive therapy (CPT) substantially reduces mortality in HIV-infected TB patients. CPT is known to prevent *Pneumocystis jirovecii* (formerly *carinii*) pneumonia and malaria, and likely impacts a range of bacterial infections in HIV-infected TB patients. CPT has been shown to be effective even in regions with high levels of bacterial cotrimoxazole resistance, and in patients with CD4 counts greater than 500. **Caution must be exercised when zidovudine (AZT) forms part of the ART regimen, since co-administration of AZT and cotrimoxazole may cause additive hematotoxicity.**

Continuation after TB treatment is completed should be considered in accordance with national guidelines. The current recommendation from the National OI/ART Programme is to provide CPT for all patients with CD4 count less than 350 cells/mm^3 or continue CPT on patients receiving ART until the CD4 count is greater than 200 cells/mm^3 for longer than 6 months.

3.4 Immune Reconstitution Inflammatory Syndrome (IRIS)

In most patients, HIV viral load sharply decreases and the CD4 count rapidly increases within the first few months after starting ART. As a consequence of the improved immune responsiveness, an inflammatory response to infectious or noninfectious antigens may occur, resulting in apparent clinical worsening. This is referred to as immune reconstitution

inflammatory syndrome (IRIS), and is characterized by fever, enlarging lymph nodes, worsening pulmonary infiltrates, or worsened inflammation at other sites temporally related to starting ART; this usually occurs within the first 2 to 3 months, though up to 30% of IRIS cases can present beyond the first 3 months. IRIS may be more common in patients with a low initial CD4 cell count (<50 cells/mm^3), disseminated TB, and a short interval between TB treatment and ART initiation. It is not explained by newly acquired infection or disease, the usual course of a previously acquired disease, or ART toxicity.

IRIS is therefore a diagnosis of exclusion. Patients with advanced AIDS may show clinical deterioration for a number of other reasons. Distinguishing IRIS from treatment failure, antimicrobial resistance, or noncompliance with treatment is important. For mild cases, observation alone with close clinical monitoring may be sufficient. For moderate cases, non-steroidal anti-inflammatory drugs have been used to alleviate symptoms. For severe cases, corticosteroids have been used. However, the optimal dosing and duration of therapy are unknown, and inflammation may take weeks to months to subside. During this time, ART should be continued. IRIS is not a reason to switch patients to second line ART, although adjustments in the ART regimen may be needed to ensure compatibility with the anti-TB treatment.

3.5 Tuberculosis in HIV-Infected Patients Receiving Antiretroviral Therapy

When TB is diagnosed in patients already receiving ART, anti-TB treatment should be started immediately. There are two issues to consider for such patients: (1) Is modification of the ART regimen needed due to drug-drug interactions or to decrease the potential of overlapping toxicities?, and (2) Does this presentation of active TB in a patient on ART constitute ART failure requiring a change in the ART regimen? The diagnosis and management of ART failure is described in *Guidelines for Antiretroviral Therapy in Zimbabwe*.

3.6 Multidrug-Resistant TB and HIV Co-infection

With HIV co-infection, some evidence suggests that drug-resistant TB may be more aggressive, with potential for rapid progression and high mortality. The actual burden of drug-resistant TB disease in Zimbabwe is currently unknown. Because of resource, logistic, and staffing constraints, widespread drug-susceptibility testing (DST) is not currently possible in Zimbabwe. A phased approach for introducing DST will be implemented as follows:

- First for all sputum smear-positive patients whose TB treatment has failed (continued smear positivity **at 3 months** for category 1 **or** category 2 patients);
- Second for all sputum smear-positive patients who have relapsed following completion of prior treatment, or who are returning following treatment default (at least 2 months without treatment after having been on treatment for at least 1 month); and
- Third for all HIV-infected TB patients with advanced disease (WHO stage IV, or CD4 count
  < 200 cells/mm^3 if available), as resources become available. National drug resistance surveys followed by regular surveillance are awaited.

3.7 Treatment Monitoring (Follow-Up)

Patient monitoring is necessary to evaluate the response of the disease to treatment and to identify adverse drug reactions. To judge the treatment response of pulmonary TB, the recommended method is sputum smear microscopy. Sputum cultures in quality-assured laboratories should also be performed for monitoring when resources exist.

ISTC Standard

Response to therapy in patients with pulmonary tuberculosis should be monitored by follow-up sputum microscopy (2 specimens) at the time of completion of the initial phase of treatment (2 months). If the sputum smear is positive at completion of the initial phase, sputum smears should be examined again at 3 months and, if positive, culture and drug susceptibility testing should be performed. In patients with extrapulmonary tuberculosis and in children, the response to treatment is best assessed clinically.

Approximately 80% of patients with sputum smear-positive pulmonary tuberculosis should have negative sputum smears at the time of completion of the initial phase of treatment (2 months of therapy). **Patients who remain sputum smear-positive require particular attention.** A positive sputum smear at the end of the initial phase of treatment should trigger an assessment of the patient's adherence and a careful re-evaluation to determine if co-morbid conditions are present that might interfere with response to treatment**. If the sputum smear is positive at month two, sputum smear examination should be repeated at month three.** However, a **positive smear at the end of month two is not an indication to prolong the intensive phase** of treatment. Having a positive sputum smear after completion of 3 months of treatment raises the possibility of drug resistance and culture and drug susceptibility testing should be performed in a quality assured laboratory, as available, to guide further treatment.

In Zimbabwe, while capacity for culture and drug susceptibility testing is consolidated, patients who are still smear-positive at month three will have additional monitoring only by sputum smear microscopy during the fifth month and during the last month of treatment. If either result is positive, treatment has failed, the patient's TB treatment card should be closed (Outcome = Treatment failure), the patient is re-registered, treatment is changed to the Category 2 regimen and a new card is opened (Type of patient = Treatment after failure). Additionally a sputum specimen should be obtained for culture and drug susceptibility testing and referred to the National Tuberculosis Reference Laboratory.

Radiographic assessments, although commonly used, are often unreliable for evaluating response to treatment. Similarly, clinical assessment can be unreliable and misleading in the monitoring of patients with pulmonary tuberculosis. However, in patients with extrapulmonary tuberculosis and in children, clinical evaluations may be the only available means of assessing the response to treatment.

3.8 Individual Care Plans: Prevention, Treatment, and Support Services

ISTC Standard

All providers should conduct a thorough assessment for co-morbid conditions that could affect tuberculosis treatment response or outcome. At the time the treatment plan is developed, the provider should identify additional services that would support an optimal outcome for each patient and incorporate these services into an individualized plan of care. This plan should include assessment of and referrals for treatment of other illnesses with particular attention to those known to affect treatment outcome, for instance care for diabetes mellitus and malnutrition.

The TB programme should provide the following to all TB suspects and TB patients:

- Routine HIV counselling and testing
- Condom provision
- For all patients who are found to be HIV-infected:
    - Cotrimoxazole preventative therapy (CPT)
    - Antiretroviral therapy according to national guidelines
    - Referral to HIV program for comprehensive AIDS care

A comprehensive AIDS care strategy includes clinical management (early diagnosis, treatment and follow-up care for opportunistic infections, TB preventive treatment (IPT) [when available according to national policy]), nursing care (promoting hygiene and nutritional support), palliative care, counselling and social support. This package of care includes a core set of effective interventions listed below:

- Screening for TB.
- Psychosocial counselling and support.
- Disclosure of HIV status, partner notification and testing and counselling.
- Cotrimoxazole prophylaxis.
- Fungal infection prevention.
- Prevention of sexually transmitted and other reproductive tract infections.
- Malaria prevention.
- Selected vaccines (hepatitis-B, pneumococcal, and influenza, where available).
- Nutrition.
- Family planning.
- Prevention of mother-to-child transmission of HIV.
- Water, sanitation, and hygiene.

Section Four:
Tuberculosis in the HIV-Infected Child

HIV-infected children are more vulnerable to the development of TB because of increased exposure within the household, young age and immune compromise related to HIV infection and malnutrition.

4.1 Prevention

Improving uptake of antenatal HIV testing, improving maternal access to ART, and strengthening prevention of mother-to-child transmission of HIV programmes will decrease the number of children born with HIV. Further, **early diagnosis of HIV in infants is one of the keys for managing TB**, because placing HIV-uninfected children on ART leads to a substantial reduction in TB incidence.

It is important to remember that **both TB and HIV are communicable family diseases.** Therefore, all HIV-infected children, and all household contacts (whether HIV-infected or not) of a pulmonary TB patient should be screened for TB disease. HIV-infected children should be screened for TB during every clinic visit. Consideration for isoniazid prophylaxis after the exclusion of active tuberculosis should also be made in accordance with National TB Control Programme Guidelines, especially for infants born to a mother with sputum positive TB. Similarly, all children of an HIV-infected patient, and any child with TB, should be screened for HIV.

4.2 TB Diagnosis in Children Living with HIV

Diagnostic difficulties due to low yield of positive smears and cultures pose a great challenge to childhood tuberculosis management. Increased tuberculosis incidence and mortality rates are seen in HIV-infected children compared with children without HIV. In addition to being at risk of tuberculosis, HIV-infected children are also at risk for other lung diseases, including pneumocystis pneumonia (PCP), lymphoid interstitial pneumonitis (LIP), and viral and bacterial pneumonias. As in adults, children with HIV may have multiple and concurrent opportunistic infections, so the presence of one diagnosis does not exclude other causes of illness. Due to radiographic similarities and chronic symptoms resembling TB, LIP is often difficult to distinguish from TB.

The approach to diagnosing TB in HIV-infected children is essentially the same as for HIV-uninfected children. In addition to HIV-infection, age less than 5 years, severe malnutrition, and household contact with a newly diagnosed smear-positive case are key risk factors for TB. The presence of three or more of the following should strongly suggest the diagnosis of TB:

- Chronic symptoms suggestive of TB (e.g., cough, fevers, night sweats)
- Physical signs highly suggestive of TB (e.g., weight loss)
- A positive tuberculin skin test (TST) (diameter of induration equal or greater than 5 mm)

- Chest X-ray suggestive of TB

ISTC Standard

In all children suspected of having intrathoracic (i.e., pulmonary, pleural, and mediastinal or hilar lymph node) tuberculosis, bacteriological confirmation should be sought through examination of sputum (by expectoration, gastric washings, or induced sputum, where available) for smear microscopy and culture.

In the event of negative bacteriological results, a diagnosis of tuberculosis should be based on the presence of abnormalities consistent with tuberculosis on chest radiography, a history of exposure to an infectious case, evidence of tuberculosis infection (e.g., positive tuberculin skin test, where available) and clinical findings suggestive of tuberculosis.

For children suspected of having extrapulmonary tuberculosis, appropriate specimens from the suspected sites of involvement should be obtained for microscopy and for culture and histopathological examination.

Children able to produce sputum should have 2 specimens submitted for smear microscopy. With proper instruction and supervision many children 5 years of age and older can generate a specimen. Adolescents, although often classified as children at least until the age of 15 years, can generally produce sputum. Hypertonic saline-induced sputum collection and gastric aspiration are viable alternatives when children are unable to produce sputum spontaneously, though consideration should be given to involvement of TB experts in order to perform these procedures safely.

4.3 Treatment Recommendations for Children with TB/HIV Co-infection

4.3.1 Anti-TB Treatment

Because of the high risk of dissemination of TB in children aged less than 5 years, TB treatment should begin as soon as the diagnosis of TB is suspected. HIV-infected children benefit from treatment with ART, though the initiation of anti-TB treatment is the first priority. The principles for treatment of TB are the same in the HIV-infected child and in the HIV-uninfected child. **As in adults and children not infected with HIV, a trial of anti-TB treatment should not be practiced. A decision to treat any child for TB should be carefully considered; once this decision is made, the child should receive a full course of treatment.**

- HIV-infected children are more likely to have severe disease, thus requiring a fourth drug during the intensive phase. The initial phase of TB treatment should consist of a four-drug regimen: rifampicin, isoniazid, pyrazinamide, and either ethambutol or streptomycin. Streptomycin should replace ethambutol in the treatment of TB meningitis. Most children with TB, including those with HIV, have a good response to a 6-month regimen that includes rifampicin.
- In the continuation phase, isoniazid and rifampicin should then be continued daily to complete 6 months of therapy (4 months following the initial phase).
- Children should be regularly followed and drug dosages (both anti-TB and ARV) adjusted for weight gain.

For the recommended doses of First-Line Anti-TB Drugs for Children see the DOTS charts for paediatric formulations on annex C.

The risk of peripheral neuropathy with isoniazid is greater in children with HIV. Therefore, the administration of supplemental pyridoxine (5 to 10 mg/day) is necessary. Supplemental pyridoxine is also recommended for: (1) malnourished children, (2) breastfeeding infants and (3) pregnant adolescents.

4.3.2 Multi-Drug Resistant TB (MDR-TB)

Children with known adult MDR-TB source-cases should be treated as MDR-TB (in consultation with a TB expert) until proven otherwise. Drug resistant TB should also be considered if the child is not responding to or has not been adherent to first-line therapy.

4.3.3 Treatment Monitoring (Follow-Up)

During treatment, every child should be assessed at least at the following intervals: 2 weeks after treatment initiation, at the end of the intensive phase, and every 2 months until treatment completion. Assessment of symptoms, treatment adherence, adverse events and weight should be included at each visit. Medication dosages should be adjusted to account for any weight gain. Adherence should be assessed by reviewing the child's treatment card. A follow-up sputum sample for smear microscopy at 2 months after treatment initiation should be obtained for any child who was smear-positive at diagnosis.

4.3.4 Recording and Reporting of Cases of TB among Children

Children with TB and HIV should always be notified, registered for treatment (including ART) and have their treatment outcomes recorded so that they are included in routine NTP recording and reporting systems. Recording and reporting of two age groups for children (0 to 4 years and 5 to 14 years) in the TB registers is recommended for planning the procurement of anti-TB drugs in child-friendly formulations, and for monitoring and evaluation purposes.

4.4 Malnutrition

Malnutrition is commonly associated with both TB and HIV. Supplemental nutritional support should be made available if necessary. Regular monitoring for weight gain is mandatory to assess response to treatment in the presence of adequate nutrition.

4.5 Antiretroviral Therapy for Children

4.5.1 When to Begin Treatment

ART should be deferred for 2 to 8 weeks in children starting anti-TB treatment who have not yet started ARVs (e.g., ARV "naive" patients). DOT should be strictly enforced in order to ensure adherence and to better monitor and reduce potential toxicities.

In HIV-infected children who are not yet on ART, the clinical and immunological condition of the child should guide the decision of when to start ART:

- WHO clinical stage 4 (extra-pulmonary TB other than lymph node TB) and 3 (pulmonary and lymph node TB): **Start ART treatment soon (2 to 8 weeks) after the start of anti-TB treatment**
- If mild or no immunodeficiency and the child is stable: **May delay start of ART until anti-TB treatment is completed.**

For a child who is already receiving ART, a careful review of any possible drug interactions between ART and anti-TB medications should be performed; medication regimen modifications should be determined with the guidance of an HIV treatment expert.

4.5.2 Recommended ART Regimens for Children who Develop TB *before* commencement of ART

- Child aged 3 years or above: 2 NRTIs + efavirenz.

- Child younger than 3 years: 2 NRTIs and (1) increased dose nevirapine (the patient must be closely monitored for drug reactions) **or** (2) switch to boosted LPV/r (if available).

Note: the safety of efavirenz has not been established for children younger than 3 years.

4.5.3 Recommendations for Children who Develop TB while on ART

- If on nevirapine and 3 years or older, weighing over 10 kg: switch to efavirenz.
- If on nevirapine and under 3 years old, or weighs less than 10kg: switch to boosted Lopinavir/Ritonavir (if available).

Following completion of anti-TB therapy, it is preferable to remain on the ART regimen to which the patient was previously switched.

Because recommendations on combinations of anti-TB drugs and antiretroviral drugs are frequently revised, it is advisable to obtain the most recent information from the WHO website (http://www.who.int/hiv/mediacentre), or the website of the United States Centers for Disease Control and Prevention (http://www.cdc.gov/nchstp/tb/).

4.5.4 TB Immune Reconstitution Inflammatory Syndrome (IRIS)

Transient clinical deterioration (worsening disease, fever, and increased size of lymph nodes or tuberculomas) in children on TB treatment who start ART occasionally occurs due to restoration of the immune system. In addition to ART, improved nutrition or TB treatment have also been known to trigger similar events. Reactions also have been described in children who had received the bacillus Calmette-Guérin (BCG) vaccine and later initiated ART.

4.6 Cotrimoxazole Prophylaxis

Daily cotrimoxazole (20 mg trimethoprim (TMP) + 100 mg sulfamethoxazole (SMX) if under 6 months of age; 40 mg TMP + 200 mg SMX if aged under 5 years; 80 mg TMP + 400mg SMX if

5 years or older) prolongs survival in HIV-infected children and reduces the incidence of respiratory infections and hospitalization. As in adults, cotrimoxazole preventative therapy (CPT) should be given throughout TB treatment course and continued thereafter according to national guidelines.

4.7 BCG Vaccination

Bacillus Calmette-Guérin (BCG) is a vaccine derived from a weakened strain of the live bovine tuberculosis bacillus. Although data suggest that it has mixed success at preventing pulmonary TB, it does appear to protect against more serious forms of disease, such as miliary TB and TB meningitis, in HIV-uninfected children. In children living with HIV, these benefits are less clear, and BCG has been associated with development of disseminated BCG infections with high rates of death. Four scenarios have been outlined by WHO that address the balance of risks and benefits of BCG vaccination in settings such as Zimbabwe with high burdens of tuberculosis and HIV infection.

1. Infants born to women of unknown HIV status

Recommendation: The benefits of BCG vaccination outweigh the risks, and infants should be vaccinated.

2. Infants whose HIV infection status is unknown and who demonstrate no sign or symptom of HIV infection, but who are born to women known to be HIV-infected

Recommendation: The benefits of BCG vaccination usually outweigh the risks, and infants should receive the vaccine after consideration of local factors.

3. Infants who are known to be HIV-infected, with or without signs or symptoms of HIV infection

Recommendation: The risks of BCG vaccination outweigh the benefits and infants should not receive the vaccine, but they should receive other routine vaccines.

4. Infants with unknown HIV infection status but who have signs or symptoms of HIV infection and were born to HIV-infected mothers

Recommendation: The risks of BCG vaccination usually outweigh the benefits, and children should not be vaccinated during the first few weeks of life, since clinical symptoms of HIV infection typically occur after 3 months of age. However, the vaccine can be given if HIV infection is ruled out by early virological testing.

In practice, selective vaccination strategies (delaying vaccination of HIV-exposed infants from birth until 10 to 14 weeks of age following a negative HIV PCR testing result), is not currently feasible in Zimbabwe. Universal BCG immunisation of infants should continue in Zimbabwe until early infant diagnosis is widely available for implementing selective deferral of HIV-exposed infants.

Annexes

Annex A: ART Register

Annex B: District TB Register

Annex C: Anti-Tuberculosis FDCs Drugs Daily Dosage Tables

Key to Drug Abbreviations

R = Rifampicin, H = Isoniazid, Z = Pyrazinamide, E = Ethambutol, S = Streptomycin

CATEGORY I ANTI- TB TREATMENT FOR CHILDREN

Pre-Treatment Weight	*INTENSIVE PHASE OF TREATMENT 2 MONTHS DAILY RHE/RHZE TABLETS*		*CONTINUATION PHASE OF TREATMENT 4 MONTHS DAILY RH TABLETS*
	Children		**Children**
	$R_{60}H_{30}Z_{150}$ (Paediatric formulation)		$R_{60}H_{30}$ (Paediatric formulation)
	Rifampicin 60mg + Isoniazid 30mg + Pyrazinamide 150mg)		(Rifampicin 60mg + Isoniazid 30mg)
Under 7kg	1		1
8- 9 kg	1.5		1.5
10- 14 kg	2		2
15- 19 kg	3		3
20- 24kg	4		4
25- 29kg	5		5

NB:

* EH is recommended in the continuation phase for <u>all</u> Cat I TB patients for

- sputum negative TB
- extra pulmonary TB
- patient on Nevirapine based ART

However please also note that in line with current recommendations from WHO this combination will eventually and gradually be phased out.

- Streptomycin dose for children is calculated as 15mg/kg body weight.

	INTENSIVE PHASE 3 months			**CONTINUATION PHASE 5 months**	
	Daily streptomycin injection*	***Daily Supervised RHZ***	***Daily Supervised RHZE***	***Daily Supervised RH***	***Daily Supervised RHE***
Pre-Treatment Weight		**Rifampicin 60mg + Isoniazid 30mg + Pyrazinamide 150mg**	**Rifampicin 150mg + Isoniazid 75mg + Pyrazinamide 400mg + Ethambutol 275mg**	**Rifampicin 60mg + Isoniazid 30mg**	**Rifampicin 150mg + Isoniazid 75mg + Ethambutol 275mg**
	Month 1 and 2 only	**Months 1, 2 and 3**	**Months 1, 2 and 3**	**Months 4, 5, 6, 7, 8**	**Months 4, 5, 6, 7, 8**
Under 7kg	**100mg**	**1**		**1**	
8- 9 kg	**150mg**	**1.5**		**1.5**	
10- 14 kg	**200mg**	**2**		**2**	
15- 19 kg	**300mg**	**3**		**3**	
20- 24kg	**500mg**	**4**		**4**	
25- 29kg	**500mg**	**5**		**5**	

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