

**TUBERCULOSIS SCREENING PRACTICES IN HIV-INFECTED ADULT
PATIENTS ENROLLING AT THE KALINGALINGA ANTI-
RETROVIRAL THERAPY (ART) CLINIC IN LUSAKA, ZAMBIA.**

By

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**A Dissertation submitted to the University of Zambia in partial fulfillment of the
requirement for the degree of Master of Medicine in Internal Medicine.**



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THE UNIVERSITY OF ZAMBIA

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DECLARATION

I declare that this dissertation represents my own work and that it has not previously been submitted for a degree, diploma or other qualification at this or another University.

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ABSTRACT

Title: Tuberculosis (TB) screening practices in human immunodeficiency virus (HIV) infected adult patients enrolling at the Kalingalinga anti- retroviral therapy (ART) clinic in Lusaka, Zambia.

Background: There are currently no studies describing TB screening practices in HIV infected adult patients enrolling at various ART clinics in Lusaka. Such data are critically needed to guide national health policy in areas of TB screening in HIV infected patients as TB is the most common cause of morbidity and mortality in HIV infected patients.

Methods: In this descriptive longitudinal study, TB screening practices in HIV-infected adults at the Kalingalinga ART clinic were assessed by file reviews, parallel TB screening of patients by study staff and by interviews with the ART clinic clinicians. Basic demographic, medical, laboratory and radiological data were obtained to determine factors associated with TB screening.

Results: From May to December 2009, we enrolled 154 consecutive patients eligible for TB screening; in addition 15 patients underwent parallel screening by study staff and 3 ART clinic clinicians were interviewed on their TB screening practices. The median age was 34 years with an inter-quartile range of 29-40, 79 (51%) were female. The CD4 count was below 200cells/ μ l in 72% of the patients while 72% of the patients were either WHO stage III or IV. The median Body Mass Index (BMI) was 19 with an inter-quartile range of 17 to 21. The TB screening form was only used in 39%. Eighty-nine percent had TB symptoms for > 2 weeks. Eighty-four percent presented with a cough plus other symptoms suggestive of TB. Sputum AAFB (acid alcohol fast bacilli) examination was ordered in 42% (65) of patients but only 30% (47) were performed. A CXR was ordered in 38% (58) of patients but only 22% of the 58 (13) were performed, 92% of the total sample did not have a chest x-ray (CXR) done. Out of the 154 patients, 66% (102) were not screened for TB as neither sputum for AAFB nor a CXR was ordered/performed. Fifty-one patients (33%) were diagnosed with TB as follows: sputum positive 15, sputum negative 27, EPTB 5, disseminated TB 1 and PTB without specification of type, 3.

Conclusion: TB screening practices at the Kalingalinga ART clinic are inadequate mainly due to increased workload for the few clinicians, erratic availability of sputum AAFB examination facilities and inability of patients to do chest x-rays due to financial constraints. Policies to improve on workforce in ART clinics, improvement in supply of sputum AAFB examination facilities and reduction in cost of performing x-rays should be considered in this population, given the proven efficacy of anti-tuberculous therapy especially when TB is diagnosed early and this will also lead to reduction in continued spread of TB in the community.

Dedication:

To my late dad, who always believed in me and gave me strength to go on.

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LIST OF ABBREVIATIONS

AAFB – acid alcohol fast bacilli

ART – anti-retroviral therapy

ATT - anti-tuberculous therapy

CXR – chest x-ray

CFR – case fatality rate

DST – drug sensitivity testing

EPTB - extra-pulmonary tuberculosis

HIV – human immunodeficiency virus

NTP – national tuberculosis program

PTB – pulmonary tuberculosis

TB – tuberculosis

TB-IRIS - tuberculosis immune reconstitution inflammatory syndrome

UTH- university teaching hospital

WHO – World health organization

CHAPTER 1

1.0 Background

The burden of tuberculosis (TB) has greatly increased with the high rate of Human immunodeficiency virus (HIV) infection in the developing world. The percentage of TB patients co-infected with HIV is estimated to be 70% in Lusaka, Zambia.¹ This co-infection is of great significance as TB is the most common cause of morbidity and mortality in HIV infected patients.² The increased risk of TB begins within the first year of HIV infection.³ HIV predisposes one to have TB at all CD4 strata.⁴ The risk of developing active TB from latent infection is increased a hundred-fold by HIV infection and primary TB infection is also common accounting for one third of cases.³ Active TB accelerates the rate of HIV progression and is associated with an increase in viral load.⁴ The disease burden is compounded by the ease with which TB is transmitted (airborne).

Delay in TB diagnosis costs lives and earlier diagnosis should decrease case fatality. Lack of TB screening, diagnosis and treatment may also put more people with HIV and unrecognized TB at risk of serious immune reconstitution inflammatory reactions (IRIS) when they are put on anti-retroviral therapy (ART), and could be a factor in high early mortality on ART. Other patients start ART and then die in the first few months of ART as a result of undiagnosed and untreated TB. Clearly, a more aggressive approach to case finding and diagnosis is needed to protect people with HIV from TB. Data suggest that using any one of cough, fever and weight loss could detect up to 80% of the cases.⁴⁰ ART programmes can and must adopt an aggressive approach to TB prevention and treatment.⁴⁰

In Lusaka, Zambia, there are approximately 16,000 new TB cases per year.⁵ Data from the Ministry of Health's (MOH) Smart Care electronic patient record system shows that from June 2007- June 2008, 85 new enrollees at the Kalingalinga anti-retroviral therapy (ART) clinic were on TB treatment at the time of enrolment. However, apart from these 85 patients receiving TB treatment prior to ART clinic enrollment, only 7 patients were commenced on TB treatment during the same period out of 3,110 patients seen. Data from other Lusaka ART clinics also

revealed low incidences of TB case-detection during the same period. The low figure above of those who were diagnosed with TB is likely an underestimate of the true TB burden at Kalingalinga clinic. The exact reasons for low TB case detection in ART clinic enrollees are unknown and merited further investigation. This study documented and summarized the TB screening practices among new enrollees at Kalingalinga ART clinic in Lusaka in order to understand potential reasons for low TB case detection and make recommendations for improving case detection.

1.1 Statement of the Problem

The Ministry of Health's (MOH) Smart Care electronic patient record system shows low rates of TB diagnosis in ART clinics, suggesting that current screening practices in this setting may be inadequate. Delayed diagnosis is an important cause of morbidity and mortality in patients who are smear negative, have extra-pulmonary TB and those with HIV infection²¹⁻²³ hence prompt TB diagnosis in local ART clinics is vital to reduce poor outcomes, decrease the number of patients referred to the tertiary hospital, reduce transmission to other people and reduce the incidence of "unmasking" TB-IRIS. Review of current TB screening practices in Lusaka District HIV clinics is required to determine whether TB diagnostic algorithms are followed consistently and correctly and make recommendations to improve the implementation of TB screening practices.

1.2 Study Justification

In order to improve diagnostic practices at district HIV clinics, it is necessary to first be aware of and understand the current practices.

The purpose of this study was to investigate the reasons behind demonstrated low case detection rates of TB in HIV patients enrolling in the ART clinic at Kalingalinga and make recommendations to the policy makers to implement and improve the current guidelines for TB screening.

1.3 Hypothesis

TB screening algorithms at Kalingalinga ART clinic are followed inconsistently, contributing to low TB case detection rates.

1.4.0 Objectives

1.4.1 Primary Objective

To characterize TB screening practices among new enrollees presenting with symptoms suggestive of TB at the Kalingalinga ART clinic.

1.4.2 Secondary Objectives

1.4.2.1 To determine (a) the percentage of symptomatic patients referred for sputum examination, (b) percentage of referred patients who submitted sputum samples and (c) the percentage of those who returned with sputum results to see a clinician.

1.4.2.2 To determine the percentage of smear-negative suspects who had a chest x-ray: (a) ordered, (b) done and returned with result, and (c) other additional investigations ordered.

1.4.2.3 Among patients who enter the TB diagnostic process, determine the percentage diagnosed with (a) smear-positive PTB, (b) smear-negative PTB, (c) EPTB, (d) no tuberculosis and (e) work-up not completed.

1.4.2.4 To interview clinicians about their screening practices and reasons for doing so.

CHAPTER 2

2.0 Literature Review

Zambia has experienced a rapid increase in TB from 1990s to date. The primary cause of this rise in TB cases has been attributed to co-infection with HIV. In 1990, Zambian adults had a TB incidence of 24,152 (rate of 297/100,000) in all forms of TB with 10,000 being sputum positive (rate of 123/100,000). In 2006, Zambia had a TB incidence of 64,632 (rate 553/100,000) in all forms of TB with 26,697 being sputum positive (rate of 228/100,000). The World Health Organization (WHO) estimates that 37% of these patients were HIV-positive while data from Lusaka district and the MOH estimate that the proportion is currently between 50-70%.^{1, 6}

Many African countries have seen similar increases in TB incidence as experienced in Zambia⁶ and several of them including those with well-organized TB control programmes^{7,8} have had annual TB case notification rates rising more than fivefold since the mid-1980s, reaching more than 400 cases per 100 000 population.⁹ Despite the WHO targets for 2005 calling for smear-positive TB case detection rates of at least 70% and cure rates of 85% under the DOTS strategy, which is part of the WHO's TB control policy,² few of the national TB programs (NTP's) in Sub-Saharan Africa are achieving these targets.¹⁰ If these targets are met, the global burden of TB (per capita prevalence and death rates) will be reduced by 50% by 2015 relative to 1990 levels. If these targets continue to be met, the global incidence of active TB will be less than 1 case per million population per year by 2050.^{6, 11} WHO data for 2006 reveals that Zambia had a TB case detection of 71% for all new cases, but only 53% for smear-positive cases. This is below the expected 70% target for new smear-positive case detection.⁶ As the increase in TB incidence has often exceeded the general health service capacity to deliver TB control interventions, NTPs struggle to provide high-quality provision of TB care.¹⁰

Tuberculosis can affect many organs in the body and is classified as either pulmonary or extra-pulmonary TB (EPTB). Pulmonary TB (PTB) is TB of the lungs while typical forms of EPTB include tuberculomas in the brain, tuberculous meningitis, skeletal TB, pericardial and pleural TB presenting with effusions, genitourinary TB, abdominal TB, tuberculous lymphadenitis

(scrofula), and cutaneous TB.¹² TB can also be disseminated/miliary especially when diagnosis is delayed and this involves haematogenous spread of the tubercle bacilli. EPTB and disseminated TB are common in HIV-infected persons due to immunosuppression.

TB deaths comprise 25% of all avoidable adult deaths in developing countries.² In a Zambian study, there were five times more deaths in HIV-positive patients than there were in HIV-negative tuberculosis patients 2 years after the start of treatment.¹³ Studies in Kenya,¹⁴ Tanzania,¹⁵ and Zambia¹³ also showed that risk of death during and after TB treatment is higher among HIV-positive than HIV-negative patients with smear-positive pulmonary TB, and higher still among HIV-positive patients with smear-negative TB, probably reflecting their greater degree of immunosuppression.

The issues surrounding TB and HIV co-infection in settings such as Zambia are complex, and include: (i) an increased TB burden with greater incidence of extra-pulmonary and smear-negative TB due to immunosuppression, (ii) significant diagnostic delays resulting from a limited number of diagnostic facilities and lack of rapid, sensitive TB diagnostics, (iii) increased mortality and (iv) TB-immune reconstitution inflammatory syndrome (TB-IRIS).

Prompt diagnosis of TB is critical to decrease its associated morbidity and mortality in HIV-infected persons. However, diagnosis of TB is challenging and time-intensive, especially in TB/HIV co-infected patients. HIV co-infection compounds patient's clinical presentation with overlap of symptoms from TB, HIV and other opportunistic infections. This can lead to increased time to diagnosis as clinicians may not immediately attribute the symptoms to TB. Even when symptoms are promptly identified, the work-up for smear-negative PTB and EPTB is challenging and time consuming because rapid, simple and accurate diagnostic tools for these types of TB do not exist.¹⁶

Sputum smear microscopy is fast and available in Zambia, but only 31% of new TB cases are sputum smear-positive.⁶ X-ray facilities are available in some urban centers but very few rural clinics. WHO reveals that there are inadequate laboratories at all levels (smear microscopy, TB

culture and drug sensitivity testing (DST) in most countries in Africa.⁶ Zambia has 155 smear microscopy laboratories, 3 culture laboratories and only 1 DST laboratory.⁶

A review of national guidelines for TB diagnosis found that the time to diagnose smear negative TB in Zambia is estimated to take a minimum of 34 days^{17, 18} highlighting the lengthy period required to diagnose smear-negative TB (see appendices A, B & C). Timely diagnosis of TB is important as late diagnosis is associated with dissemination of disease, poorer outcomes, increased mortality and continued spread of the disease to others.¹⁹⁻²² Delayed diagnosis is an important cause of morbidity and mortality in patients who are smear negative, have extra-pulmonary TB and those with HIV infection.²¹⁻²³ In HIV patients, delay in diagnosis has a greater impact on morbidity and mortality because TB presents more commonly with dissemination and the disease progression is more rapid with accelerated increase in viral load.^{19, 20, 24-26}

Another issue associated with delayed or missed diagnoses in an ART clinic setting is “unmasking TB IRIS”.^{27, 28} This occurs when one who had sub-clinical TB develops overt TB due to improvement of the immune system after commencement of ART. TB-IRIS could greatly complicate the delivery of ART in the sub-Saharan region, causing substantial in-programme morbidity and increasing the burden on secondary health-care facilities.³¹ Low CD4 cell count is associated with increased risk of IRIS since advanced HIV-associated immunodeficiency is associated with higher mycobacterial antigen load and greater impairment of immune responses that may rapidly reverse during early ART.³² Evidence suggests that the restoration of *Mycobacterium tuberculosis*-specific immunity is incomplete during at least the first year of HAART³². A prospective study in an HIV-infected cohort (not on TB treatment) in South Africa to determine IRIS incidence during the first 6 months following the initiation of ART, revealed that 44 of 423 (10.4%) of patients developed IRIS with TB accounting for 41% (18/44).³³ Consistent with previous literature,³⁰ the majority of IRIS cases observed in this cohort were due to TB. IRIS usually occurs within the first 90 days of ART, mainly affects patients with lower baseline CD4 cell counts (< 100 cells/μl), and most frequently presents as TB or dermatological manifestations.³³ It is common for Zambian patients to initiate ART when their CD4 counts are

very low, predisposing them to developing TB-IRIS. Diagnosis of TB and treatment initiation prior to ART initiation is a key factor in prevention and management of TB-IRIS.

There are multiple reasons for delay in diagnosis. In a Canadian study on diagnostic delays in hospitalized patients with active tuberculosis, it was found that initially missed or delayed diagnosis and treatment are associated with older age, HIV infection, non-cavitary chest x-ray, absence of cough/sputum and smear-negative disease.³⁶ Delays in diagnosis can be attributed to both patients and providers.³⁷ One of the patient factors for delay in diagnosis is fear of being diagnosed with TB due to the stigma of having HIV as a “partner disease”.³⁸ This was noted in a study on ART scale-up in TB and PMTCT clinics where patients would shun doing sputum tests to avoid being diagnosed with TB and subsequently HIV.³⁸ Provider delays are highlighted in a study of in-patients with TB at a South African hospital which found that only 38% of TB patients had been requested to provide a sputum sample and only 48% requested to undergo chest radiography over an average of 3 visits to primary care centers prior to hospital referral.³⁹ This suggests that few patients with TB symptoms are being screened at primary care centers.

The WHO has recommended “Intensified TB case finding” (ICF) activities intended to detect TB cases as early as possible among people living with HIV, typically through simple questionnaires on the signs and symptoms of TB.⁴⁰ In Zambia, symptom screening for TB is conducted at every ART clinic visit and those reporting any TB-related symptoms (cough, weight loss, chest pains, night sweats, fever, loss of appetite) should be worked up for TB following a TB diagnostic worksheet (see appendix D). Zambia has adopted the WHO algorithm for the diagnosis of TB which gives guidelines for smear positive, smear negative, HIV positive and HIV negative patients (see appendix C). However, there is no data in Zambia on the quality of TB screening in primary care centers.

From the literature above, it can be noted that many studies have been done in relation to delayed diagnosis of TB and its consequences as well as on the impact of HIV /TB morbidity and mortality. However, few studies have focused on actually assessing the screening practices for TB in ART clinics. This study assessed the actual screening practices for TB in an ART clinic so as to identify any inadequacies present.

CHAPTER 3

3.0 Methodology.

3.1 Site:

The Kalingalinga clinic is situated in Lusaka, Zambia and is one of the 22 clinics under the Lusaka District Health Management Team, Ministry of Health. It has in-patient and out-patient facilities including Maternal & Child Health (MCH) and the ART clinic where the study was held. It has a catchment population of 56,491. The ART clinic handles HIV patients referred from the in-patient facilities, MCH as well as referrals from outside the clinic. Consultations in the ART clinic are done daily from Monday to Friday between 08:00 hours and 16:00 hours. On a daily basis, clinicians attend to between 50 and 100 patients in the ART clinic. The ART clinic did not have compiled data on total number of HIV patients notified with TB during this year but the clinic had a total of 4514 adult patients on ART by September, 2009.

3.2 Study population:

Included all consecutive new enrollees at Kalingalinga ART clinic who presented with TB-related symptoms starting from May, 2009 until the sample size was reached in December, 2009.

3.3 Inclusion criteria:

All adult (≥ 16 years) patients enrolling at Kalingalinga ART clinic presenting with tuberculosis related symptom(s) at or within the first month of enrolment.

3.4 Exclusion criteria:

All new enrollees taking treatment for tuberculosis at the time of enrollment into the ART clinic and those who did not present with symptoms suggestive of tuberculosis were excluded.

3.5 Sample size:

In order to estimate the percentage of new enrollees at Kalingalinga ART clinic that present with TB-related symptoms, a chart review was done on one hundred patient files selected randomly.

Starting with the most recently enrolled patient and working backwards, every 10th file was selected. Each selected file was screened for presence of any symptoms suggestive of tuberculosis at enrolment. Those who were already on tuberculosis treatment at enrollment were excluded from the screening. The number of patients found to have symptoms suggestive of tuberculosis at enrolment was used as an estimate of the percentage of patients who exhibit symptoms of tuberculosis at enrolment into the ART clinic. This preliminary chart review showed that 70% of files had symptoms suggestive of tuberculosis at enrolment; thus 70% of new enrollees at Kalingalinga ART clinic will be the population of interest to this study.

A historical review of frequency of patients enrolled at Kalingalinga ART clinic in past months revealed that in four months we could plan to enroll about 366 patients. Based on the chart review described previously, this implied that 256 patients (70% of the 366) would be eligible for TB screening and thus of interest to our study. Using the Epi info statistics calculation method, with the population of 256 (70% of 366), prevalence of 50% as it is unknown as no similar study has been done, an error of 5% and a 95% confidence interval, a sample size of 154 was obtained.

In addition, for the qualitative data, 3 out of the 4 clinicians were interviewed at the Kalingalinga ART clinic. The 4th clinician was on leave and could not be reached.

3.6 Data collection:

Most of the data collection was based on file reviews; however, 10% of patients were screened in a parallel manner for comparison by the study investigator. There was no interaction between study staff and patients other than those selected for parallel testing. No names of patients were used in data entry at any point; only file numbers were recorded. Files of all new ART clinic enrollees were reviewed three times a week. Files from patients that met the inclusion criteria were followed up from time of first presentation of symptoms until the patient reached a study endpoint. Pertinent patient data was entered into the study database at enrolment and each consecutive visit. Data recorded included dates of visits, TB-related symptoms, investigations ordered, results of investigations, antibiotics prescribed and diagnoses made.

Only those who presented with symptoms suggestive of TB at enrolment or within the first month of enrolment were included in the study. The investigations ordered were recorded. Investigators also reviewed laboratory and radiography department registers to record whether the ordered tests were actually obtained by the patient and ART clinic files were followed up to see whether results were recorded. If a sample was received by the laboratory or an x-ray was performed but results are not in patient's file, a follow-up was made to the laboratory or x-ray department to ensure results were not lost. Lost results or unprocessed samples were taken note of as well.

Following clinician's review of the results, the decisions or diagnosis made were noted as well as any further tests ordered. Treatment given was also recorded. Each time an additional investigation was ordered, the same procedure of follow-up to the laboratory or x-ray department was carried out for verification. Follow-up of a patient's file was discontinued once a study end-point was reached.

Patient history, physical examination results and symptoms of patients presenting with TB symptoms but not worked-up were also noted.

An interview with the attending clinicians at Kalingalinga ART clinic (after obtaining their consent) was conducted on their screening practices in patients presenting with symptoms suggestive of TB with focus on the following questions:

- i. What symptoms did the clinician consider necessary to screen a patient for TB?
- ii. When did the clinician think it was not necessary to screen for TB?
- iii. What were their criteria for ordering chest x-rays?
- iv. Did they do lymph node aspirates for TB screening?
- v. When did they consider referring patients?
- vi. What challenges they faced in screening for TB?
- vii. What concerns they had in relation to TB screening?
- viii. How their workload affected their practice?

The questions included in the questionnaire above had been piloted by interviewing clinicians who work at ART clinics other than Kalingalinga. The interview was conducted verbally by the study investigator and the responses were written down as they were being given.

The investigator conducted parallel testing screening on 10% of the sample size that is, 15 patients; these patients had to be first screened by the ART clinic clinicians during their scheduled visit then they would undergo parallel screening by the study investigator. Informed consent was obtained from these patients prior to screening them. The standard MOH diagnostic TB worksheet was used by study staff and this ensured uniformity in the screening. These patients were given a transport allowance of K15, 000=00 for participating in the study.

3.7 Study end points:

Patients in whom a TB work-up was initiated were followed up until they reached one of the following endpoints:

- Diagnosis of TB (smear positive, smear negative or extra-pulmonary)
- TB ruled out (other diagnosis made or symptoms resolved)
- Patient death
- Transfer to another health center
- Work-up not completed
- Patient lost to follow up (defined as not attending clinic visits for >60 days)

3.8 Statistical analysis:

Patient information was transcribed from the data forms to an access dataset. The data was then analyzed using statistical analysis program, SAS, version 9.1.3. Frequencies were obtained for demographic characteristics of the patients. Frequencies were obtained for numbers of patients referred for sputum examination, those who submitted sputum samples and those who returned to see clinician with sputum results. The number of those who had a chest x-ray ordered and performed or other additional investigations of those who were found to be smear-negative were

tabulated. The outcome of patients who entered the TB diagnostic process: percentage smear-positive, smear-negative, extra-pulmonary tuberculosis and no tuberculosis were also tabulated.

The qualitative data from the interviews with the ART clinicians was used to provide possible explanation for trends seen in the quantitative data.

In addition, the difference in TB screening between clinicians at Kalingalinga ART clinic and the study investigator were compared by proportions and confidence intervals.

3.9 Ethics:

Ethics approval was obtained from the University of Zambia Research Ethics Committee and the University of Alabama Internal Regulatory Board (IRB). Permission was granted by the Lusaka District Director of Health and the Clinical Superintendent at Kalingalinga clinic. The MOH approval was also granted. There was no patient contact except for the patients that were screened for parallel testing by the study investigator; this study was based on file reviews. There was no use or disclosure of any patients' names as only file numbers were used in the data entry. The actual file numbers were used as patients' files were reviewed more than once in the process of data collection. Informed consent was obtained from patients who were screened for parallel testing. A patient information sheet in English or Nyanja was given to the patient. The study posed no risk to any patient. The principal investigator has and will keep all data confidential.

The data will be kept for a period of two years and thereafter destroyed. Strict confidentiality was maintained at all times during the study and subjects' rights were respected at all times.

CHAPTER 4

4.0 Results.

4.1 General description of results.

Of the 154 patients whose files were reviewed on whether/how they were screened for TB, 79 (51%) were female. The age range was 18 years to 72 years and the median age was 34 years with an inter-quartile range of 29-40. Some laboratory results were not available for some subjects with regards to CD4 counts. The CD4 count was below 200cells/ μ l in 72% of the patients while 72% of the patients were either WHO stage III or IV. The median Body Mass Index (BMI) was 19 with an inter-quartile range of 17 to 21. Sixty-two percent of the patients had a BMI below the normal range (<20) (Table1).

The TB screening form was only used in 39%. For duration of TB symptoms, 89% had them for more than 2 weeks. Ninety percent presented with at least a cough as one of the symptoms and 84% presented with a cough plus other symptoms suggestive of TB (Table1).

Seventeen (11%) patients were noted to have lymphadenopathy of which only one was diagnosed with TB adenitis. Ninety-nine percent (153) had a full blood count ordered and 50% (77) had liver and renal function tests ordered as well as part of the pre-antiretroviral therapy assessment.

Diagnosis made at first visit revealed that 30% were suspected to have TB (Table2).

4.2 Sputum AAFB examination.

Patients that had a sputum AAFB examination ordered accounted for 42% (65) and of these, only 47 (72% of the 65) were performed, which is 30% of the total sample that presented with symptoms suggestive of TB. Sixty-nine percent of the patients did not submit sputum samples for AAFB examination. Ninety-two percent of those who had a sputum AAFB examination ordered submitted 3 samples each. Smear positive results were noted in 15 patients (10%) and smear negative in 32 patients (21%) (Table 3).

4.3 CXR details.

Those who had a CXR ordered were 38% (58). Of those 38%, only 13 (22% of the 58) were performed as evidenced by results in the file and this equated to 92% of the total sample not having had a CXR done. The findings on the CXRs included infiltrates, hilar adenopathy, cavities, effusions and miliary picture. Two were just interpreted as being abnormal and suggestive of TB and 1 was interpreted as a normal CXR. Twenty-one of the 27 patients who were diagnosed with sputum-negative TB had no CXR performed and of the 6 who did do CXR's, 2 were said to be normal (Table 3).

4.4.0 Diagnosis.

Fifty-one patients were diagnosed with TB as follows: sputum positive 15, sputum negative 27, EPTB 5, disseminated TB 1 and PTB without specification of type, 3. Five patients were diagnosed with EPTB and these included 2 with pleural effusions, 1 with pericardial effusion (basis of the pericardial effusion was not indicated) and 2 with TB-adenitis. Only one patient was diagnosed with disseminated TB based on a miliary picture on CXR (Table 4).

Of the 46 (30%) patients who were suspected to have TB at the initial visit, 31(20%) were eventually diagnosed with TB.

4.4.1 Mean days to diagnosis.

Patients who were diagnosed with sputum positive TB had 7.7 mean days to diagnosis whereas those diagnosed with sputum negative TB had 19.9 days. EPTB patients had 11.8 mean days to diagnosis, disseminated TB had 3 days, PTB (basis not indicated) 29 days and the combined mean for all those diagnosed with TB was 15.6 days (Table 5).

4.5 Parallel TB screening results.

Three out of 15 [20% 95 CI (-0.0024 to 0.4024)] had TB forms used by clinician at ART clinic and 2 out of 15 [13% 95% CI (-0.0387 to 0.3054)] had sputum and CXR tests ordered by clinician at ART clinic (Table 6).

4.6 Correlation of Sputum positive/negative TB with CD4 count, BMI, Sex and WHO staging.

Fifty percent of patients diagnosed with sputum positive TB had a CD4 count > 200 cells/ul and 50% had a value < 200 cells/ul. Of those diagnosed with sputum negative TB, 85% had a CD4 count < 200 cells/ul. Eighty-one percent of sputum positive patients had a BMI < 20 whereas 88% of sputum negative patients had a BMI < 20 . With reference to sex, 87% of sputum positive patients were male and 52% of sputum negative patients were female. Ninety-three percent of sputum positive patients and 81% of sputum negative TB had a WHO staging of III or IV.

Table 1. Baseline characteristic of the 154 HIV infected patients enrolling at Kalingalinga		
a. Characteristic	N	value
Age , median (IQR)	153	34(29-40)
BMI , median (IQR)	149	19(17-21)
Age in years		
<20	1	1(0.65%)
20-30	47	47(30.7%)
31-40	68	68(44.4%)
41-50	26	26(17%)
51-60	10	10(6.53%)
>=61	1	1(0.65%)
BMI: Body mass Index		
<16	13(9%)	Severely malnourished
16<18.5	48(33%)	Malnourished
18.5<20	29(20%)	Underweight
20-25	45(31%)	Normal
>25<30	7(5%)	Overweight
>30	1(1%)	Obese
Sex, n (%)		
male	75	75(49%)
female	79	79(51%)
WHO staging, n (%)		
I	8	8(5%)
II	36	36(23%)
III	100	100(65%)
IV	10	10(6%)
CD4 count, cells/ul, n (%)		
< 50	45	45(31%)
50-100	29	29(20%)
>100-200	31	31(21%)
>200	40	40(28%)
TB Symptoms		
Cough only	9	9(6%)
Cough + other TB symptoms	130	130(84%)
No cough but with other TB symptoms	15	15(10%)
Duration of symptoms		
< 2 weeks	10	10 (10%)
> 2 weeks	87	87 (89%)
TB screening form used		
Yes	60	60(39%)
No	94	94(61%)

Table 2: Diagnosis made at Initial visit:		
Diagnosis	No.	%
TB	46	30
RTI	31	20
Pneumonia	3	2
Other	7	5
No diagnosis made	67	43

Table 3. Investigation details of the 154 HIV infected patients enrolling at Kalingalinga ART		
Sputum test ordered, n (%)	N	Value
Yes	65	65(42%)
No	89	89(58%)
Sputum test performed, n (%)		
Yes	47	47(72%) (30% of 154)
No (of those ordered)	18	18(28%) (12% of 154)
No (of total sample)	106	106 (69%)
Sputum Samples submitted		
3 samples	43	43(92%)
2 samples	3	3(6%)
1 sample	1	1(2%)
Sputum results		
Smear negative	32	32 (21% of 154)
3 samples	27	27 (17.5% of 154)
2 samples	4	4 (3% of 154)
1 sample	1	1(2% of 154)
Smear positive	15	15 (10% of 154)
3 samples	12	12 (8% of 154)
2 samples	0	0 (0%)
1 sample	3	3 (2% of 154)
CXR ordered		
Yes	58	58(38%)
No	96	96(62%)
CXR performed		
Yes	13	13(22%) (8% of 154)
No (of those ordered)	45	45(78%) (29% of 154)
No (of total sample)	141	141 (92%)

Table 4: Diagnosis made after investigations			
Diagnoses made:		No.	% of 154 patients
Smear positive		15	10%
Smear negative		27	17.5%
Disseminated TB (Miliary CXR)		1	0.6%
PTB (basis not indicated)		3	2%
EPTB	2 Pleural effusions	5	3%
	2 TB adenitis		
	1 Pericardial effusion		
Total no. diagnosed with TB		51	33%

Table 5: Mean days to diagnosis.	
Diagnosis	Average no. of days to diagnosis
Sputum positive	7.7
Sputum negative	19.9
EPTB	11.8
Disseminated TB	3
PTB (not specified)	29
Combined for all	15.6

Table 6: Parallel TB screening by study investigator.			
Study investigator		ART Clinician	
Tests ordered	TB form used	Tests ordered	TB form used
Sputum for AAFB, CXR	Yes	Sputum for AAFB, CXR	Yes
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	Sputum for AAFB, CXR	Yes
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	Yes
Sputum for AAFB, CXR	Yes	None	No
Sputum for AAFB, CXR	Yes	None	No

Table 7: Correlation of Sputum positive/negative TB with CD4 count, BMI, Sex & WHO staging			
	Sputum positive	Sputum negative	P-value
CD4 count, n (%)			
< 50	4(29)	9(35)	
50-100	2(14)	6(23)	0.14
>100-200	1(7)	7(27)	
>200	7(50)	4(15)	
BMI, n (%)			
<16	1(7)	5(19)	
16 to <18.5	7(47)	13(50)	
18.5to <20	4(27)	5(19)	0.61
20 to 25	3(20)	3(12)	
>25 to 30	0(0)	0(0)	
>30	0(0)	0(0)	
Sex n (%)			
female	2(13)	14(52)	0.01
male	13(87)	13(48)	
WHO staging n (%)			
I	1(7)	1(4)	
II	0(0)	4(15)	0.12
III	14(93)	18(67)	
IV	0(0)	4(15)	

4.7 Mortalities

There were 9 mortalities of the 154 patients included in the study. Six were female and 3 males. Six of them had an initial CD4 count below 50cells/ul and for 3 patients it was between 50 and 100. The average time to death from initial visit was 6 weeks in 7 patients whereas the other 2 patients died 4 days and 1 day after initial presentation respectively. In 6 patients, no tests for TB screening were ordered and hence not performed; in 3 patients sputum AAFB and CXR were ordered. One patient was diagnosed with sputum-negative TB based on sputum and CXR findings; had been on anti-tuberculous therapy (ATT) for 8 weeks at time of his death. The other patient had a negative sputum AAFB result but was diagnosed with EPTB (pericardial effusion) and put on ATT despite no results of a CXR in the file, basis of this diagnosis was not clear. This patient died 3 weeks after her initial visit. Two of the patients had renal impairment evidenced by deranged creatinine results.

4.8 Referrals, loss to follow-up and work-up not completed

There was only one patient referred to UTH 27 days after the initial visit due to renal failure. No TB screening tests were performed by this patient despite the tests having been ordered by the clinician.

One patient was lost to follow-up. This patient had sputum AAFB ordered but was not done and CXR was not ordered.

Out of the 154 patients, 102 (66%) were not screened for TB as neither sputum for AAFB nor CXRs were ordered/performed.

4.9 Qualitative data: Interview with the clinicians at the ART clinic.

There are currently 4 clinicians in the ART clinic but only 3 were interviewed as the 4th is on leave. The qualitative interview that was carried out with the clinicians at the Kalingalinga ART clinic using a structured open-ended questionnaire revealed the following:

Question (i): What symptoms does a clinician consider necessary to screen a patient for TB?

- ♣ Cough (productive) lasting 2 or more weeks with or without chest pains, fever, night sweats, loss of appetite and weight loss.
- ♣ Cough (productive) lasting less than 2 weeks but with chest pains, fever, night sweats, loss of appetite or weight loss.
- ♣ Recurrent cough or cough not responding to antibiotics.

Question (ii): When does the clinician think it is not necessary to screen a patient for TB?

- ♣ Dry cough with flu-like symptoms

- ♣ Cough that improves after a course of antibiotics
- ♣ Patient with no symptoms suggestive of TB
- ♣ Cough lasting less than a week with no constitutional symptoms of TB
- ♣ Despite the above reasons, they still ensure having a high index of suspicion for TB as a possibility

Question (iii): What are their criteria for ordering chest x-rays?

- ♣ When the laboratory is not able to do sputum AAFB examinations for various reasons listed below
- ♣ When patient has symptoms suggestive of TB
- ♣ When patient is found to have either bronchial breath sounds, crepitations or reduced air entry on auscultation

Question (iv): Do they do lymph node aspirates for TB?

- ♣ No, but would like to have some training to be able to do the procedure

Question (v): When do they consider referring patients?

- ♣ Clinic is not doing sputum AAFB examinations
- ♣ Wards are full and patient needs admission
- ♣ Suspect that patient could have multi-drug resistant TB (MDR)

♣ Patient is critically ill or has co-morbidities like severe anaemia

♣ Patient needs lymph node aspirate or biopsy to rule out TB adenitis

Question (vi): What challenges are faced when screening for TB?

♣ Sputum AAFB examinations not being done on a regular basis due lack of reagents, slides, sputum containers and sometimes even water

♣ Patients often can not afford to pay K25, 000=00 for an x-ray to be done

♣ Sometimes the x-ray machine does not function properly

♣ Patients neglecting the sputum examination or CXR to avoid being diagnosed with TB

♣ Patients presenting with classical symptoms of TB, sputum AAFB examination negative and CXR not revealing signs suggestive of TB

Question (vii): What concerns do they have in relation to TB screening?

♣ Delay of patients in seeking medical care

♣ Clinicians not always having a high index of suspicion for TB

♣ Overcrowding at the ART clinic

♣ Poor ventilation in screening rooms

♣ Convincing the other patients that those patients who are ill (TB suspects) be prioritised when being seen by the clinician during hospital visits

- ♣ The erratic sputum examinations by the laboratory
- ♣ Inability of patients to pay for x-rays
- ♣ Some patients deny having any presenting complaints (cough, fever and so on) in order to be attended to quickly

Question (viii): How does their workload affect their practice?

- ♣ Tedious to fill in an extra form for TB screening when clinician has too many patients waiting to be screened
- ♣ When clinician has too many patients waiting to be screened he/she will just ask if patient has suffered from TB before rather than using the TB form
- ♣ When too busy, clinician does not ask for the TB form from the nurse (the TB form is only put in patients file at the initial visit)
- ♣ When too busy, clinician does not always ask patients whether they have symptoms suggestive of TB and little attention is paid to the patients complaints in an attempt to see as many patients as possible
- ♣ Seeing an average of 50-100 patients per shift on a busy day is a lot of work giving the clinicians little time to carry out thorough patient assessment

CHAPTER 5

5.0 Discussion

Patients who present with symptoms suggestive of TB at the Kalingalinga ART clinic are not being screened consistently for TB. This is evidenced by the results showing that patients that underwent TB screening by sputum AAFB examination were only 30% (42% having had a sputum AAFB examination ordered) and those screened by CXR were only 8% despite 38% having had a CXR ordered. Only 33% of the 154 symptomatic patients were diagnosed with TB. Majority of the patients (84%) presented with a cough and other symptoms suggestive of TB with 89% having had symptoms of > 2 weeks duration which should have warranted TB screening. Despite all the patients having presented with symptoms suggestive of TB, only 39% had a TB form used. It was also noted that not all patients that had a TB form used had sputum AAFB or CXR ordered. Out of the 154 patients, 102 (66%) were not screened for TB as neither sputum for AAFB nor CXRs were ordered/performed.

The majority of patients are in their productive age group (20-40 years), 62% were noted to have a BMI below 20 meaning these patients are underweight and malnourished and 72% had a CD4 count < 200 cells/ul indicating their susceptibility to getting TB and other opportunistic infections.

Twenty-seven patients were diagnosed with sputum negative TB and 21 of these patients had no CXR performed. Of the 6 patients with sputum negative TB who did have a CXR performed, 2 of the CXR results were noted to have been normal. This indicates that sputum negative TB in some patients is being diagnosed on clinical basis alone.

Of the 32 samples that were sputum negative, 27 were diagnosed to be sputum negative TB, 3 of them were part of those diagnosed as EPTB (Pleural effusion, TB adenitis, pericardial effusion) and 2 of them were diagnosed as not having TB but CXRs were not done to support this. This shows that there are areas that need improvement in TB screening at the ART clinic.

Of the 13 patients that had a CXR performed, 2 patients were not diagnosed with TB despite having had TB symptoms for > 2 weeks and CXR findings suggestive of TB (pleural effusion and infiltrates). This shows that certain patients could have had TB but it was not diagnosed even when an investigation had been done. The low percentage of those diagnosed with EPTB could be due to only a few patients having performed a CXR, inadequate examination (due to high patient load) leading to effusions, ascites and lymphadenopathy not being noted even when present.

Three patients were diagnosed with PTB without a basis. Two of these had no CXR performed, none of them had a sputum AAFB examination done and only one had a CXR result which was stated as being abnormal without other details. This is an inappropriate way of diagnosing TB and proper information should always be recorded in a patients file on how TB has been diagnosed whether it is by clinical, laboratory or radiological examination. Of the 17 patients that were noted to have lymphadenopathy on examination, only one was diagnosed with TB adenitis but a lymph node aspirate was not performed. The other patient that was diagnosed with TB adenitis had no presence of lymph nodes on examination at initial visit. This could have been due to the clinician not entering all the relevant physical findings of the patient in the file.

Data collected also revealed that of the diagnoses made at the initial visit only 46 (30%) patients were suspected to have TB despite 154 presenting with symptoms suggestive of TB. After investigations were performed, 31 of the 46 (20%) were diagnosed with TB. This figure could have been higher but it was noted that despite some patients being suspected to have had TB at the initial visit, they were not screened for TB. It is very important for clinicians to have a high index of suspicion for TB as well as investigate the suspects. Of the 33% that were diagnosed with TB, 12% were not suspected to have had TB from their initial visit despite having presented with symptoms suggestive of TB.

The mean days to diagnosis revealed that diagnosis of PTB which had no basis indicated had the longest of 29 days followed by those who had sputum negative TB (19.9 days). The overall mean days to diagnosis were 15.6. Making a conclusion from these figures may not be appropriate as

the number of patients used to calculate these days were few as only 33% were diagnosed with TB.

The parallel screening results revealed that only 20% had TB forms used and 13% had sputum AAFB and CXR tests ordered by the clinician at the ART clinic in comparison to the study investigator. These results confirm the inconsistencies in TB screening noted from the file reviews that were performed in this study. However, in 2 patients it was noted that the patient did not give the same presenting complaint to the ART clinician and the study investigator.

Correlation of sputum positive/negative TB diagnosis with CD4 count, BMI, Sex and WHO staging revealed that the results were not significant with reference to the p-value except for sex which gave a p-value of 0.01. This could be due to the low figure of those diagnosed with sputum positive/negative TB.

The qualitative data obtained from an interview with the clinicians who work at the ART clinic revealed that the clinicians are well versed with the symptoms suggestive of TB, when to screen and when not to screen for TB, when to order a CXR and when to refer patients. They are not able to perform lymph node aspirates but would like to be trained in that area. The main challenges they face in TB screening included irregular facilities for sputum AAFB examination, CXR machine malfunctioning sometimes, patients' lack of affordability to do CXRs, patients neglect in performing tests and grey cases. Their concerns included delay of patients in seeking medical care, clinicians not always having a high index of suspicion for TB, overcrowding at the ART clinic and poor ventilation in screening rooms. The clinicians admitted that their workload does affect their TB screening practices.

Some of the ways in which TB screening can be improved at the Kalingalinga ART clinic include increasing the number of clinicians screening patients per shift, improvement in availability of facilities for sputum and CXR to be performed regularly, improving ventilation in screening rooms, reducing the cost of performing a CXR, sensitizing patients through health talks on the importance of diagnosing and treating TB and conducting refresher courses on TB screening including training on how to perform a lymph node aspirate for the ART clinicians.

The ART clinic has a “TB corner” next to it and it was noted that patients that go through the TB corner were more likely to be screened for TB than those who were just seen in the ART clinic. This can be used to improve TB screening by sensitizing patients who have any symptoms suggestive of TB to go through the TB corner for screening. Patients should also be frequently educated /reminded that TB is curable and ARVs do not cure TB.

CHAPTER 6

6.0 Study limitation:

The main data was collected by file reviews and this was limiting as certain files had missing information and certain data could not be verified. Another limitation was the lack of information from patients which could have revealed their reasons for low rates of TB screening. Capturing data on all deaths that may have occurred was also a limitation as not every patient dies at a health center. Some patients go to other health facilities and if they die there or at home, such data will not be obtained unless a relative reports such a death to the clinic.

Due to time and budget constraints, the study was conducted at only one ART clinic in Lusaka. As a result, study findings will not be directly generalizable to all other Lusaka district clinics. However, due to the similarities in clinician training, clinic organization, resources available, use of a standard TB diagnostic worksheet, and support from CIDRZ as a technical partner across Lusaka District ART clinics, it is hoped that the study results will provide insight to issues with TB screening practices in the other Lusaka District ART clinics as well.

6.1 Conclusion and Recommendations:

TB screening practices at the Kalingalinga ART clinic are inadequate mainly due to increased workload for the few clinicians, erratic availability of sputum AAFB examination facilities and inability of patients to do chest x-rays due to financial constraints. There is a serious human resource crisis in the Zambian health sector which is derailing existing health programs including the millennium development goals.⁴¹ Diagnosis of TB is challenging as there are no rapid diagnostics tests available as there are for HIV and malaria.

Given the observations in this study, the integration of HIV/TB has to be implemented more aggressively. Policies to improve on workforce in ART clinics are vital. This can be aided by use of community health workers being involved in intensified case finding of TB suspects in the communities. In addition, HIV patients have to be sensitized of the presence of the TB corner

which they can access at any time when they develop symptoms suggestive of TB (which they should be aware of through health talks given at the health center). This will improve TB screening in that patients will not have to wait for their review dates at the congested ART clinic if they develop symptoms of TB but can simply seek medical attention at the TB corner. Improvement in supply of sputum AAFB examination facilities and reduction in cost of performing x-rays should be considered in this population, given the proven efficacy of anti-tuberculous therapy especially when TB is diagnosed early and this will also lead to reduction in continued spread of TB in the community.

Results of this study can be used as a pilot for a bigger study that can be done involving several ART clinics to study TB screening practices so as to get data that will reflect what is happening in Lusaka district. Increase in the number of clinicians working in the ART clinics is vital in order to reduce workload and improve patient care. There is also need to improve ventilation in screening rooms used for patients.

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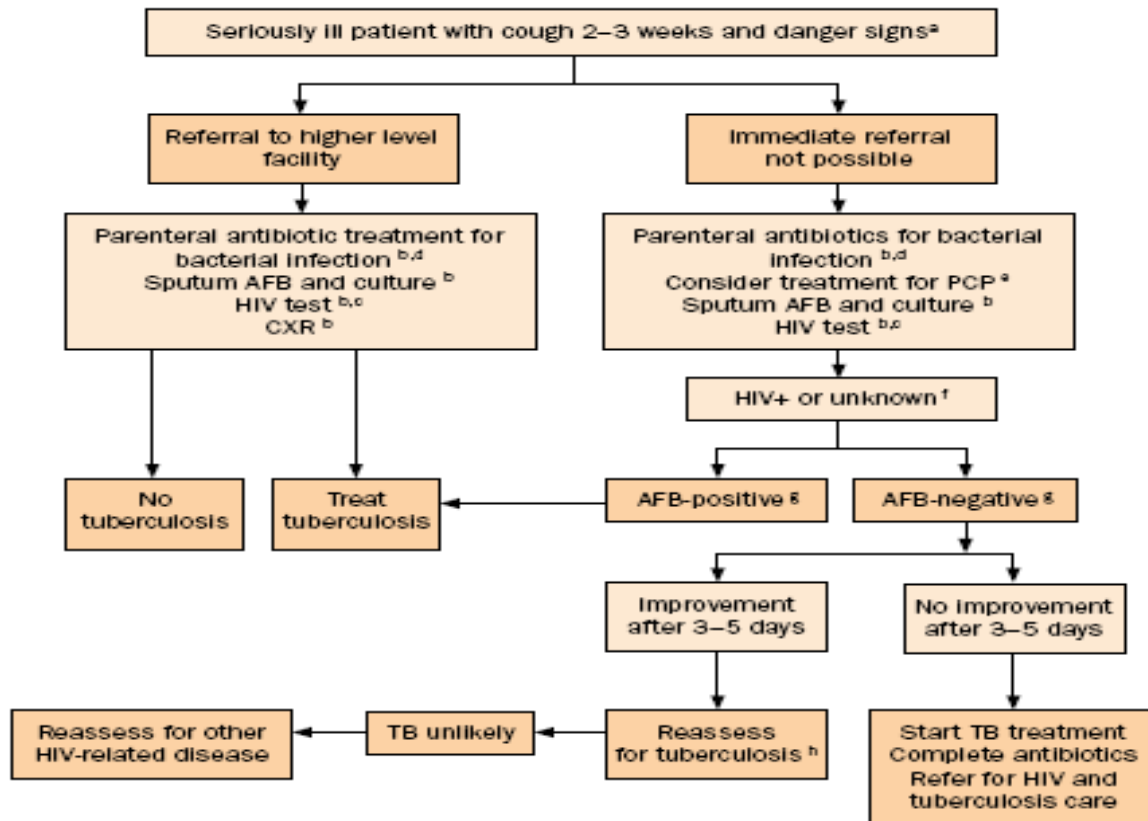
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Appendices:

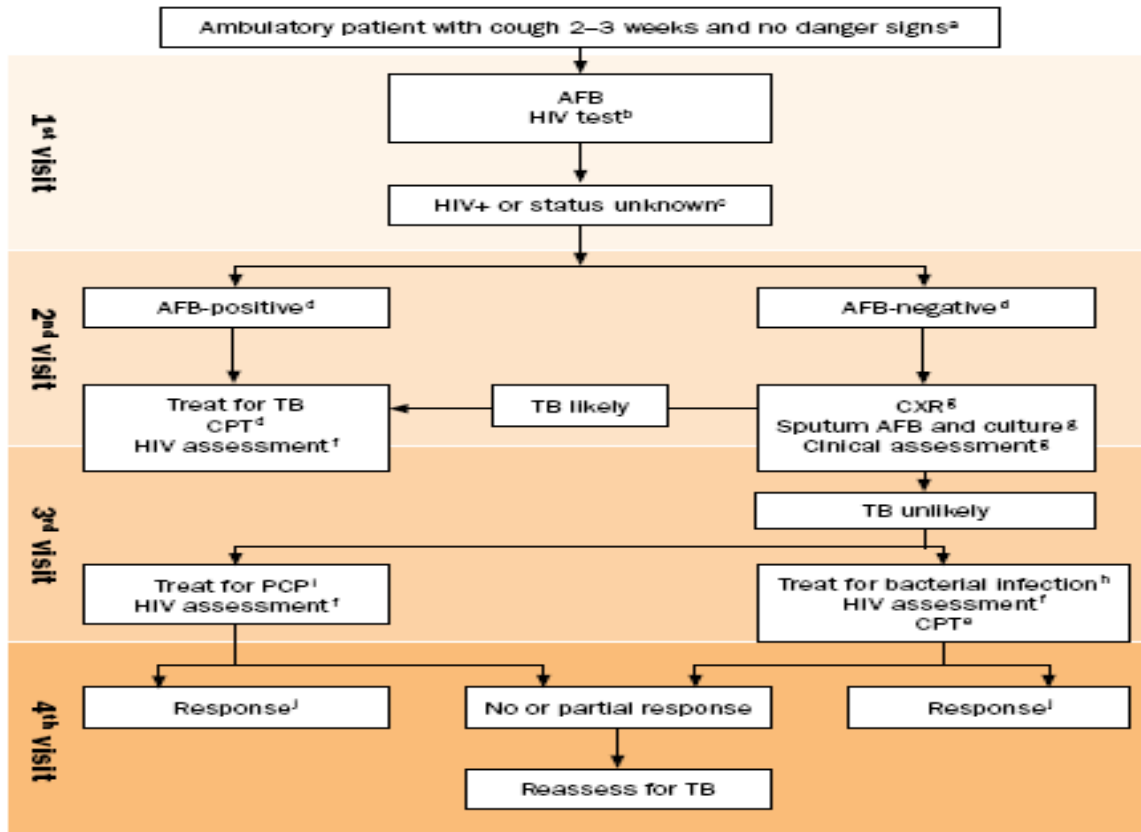
Appendix A

Algorithm for the diagnosis of tuberculosis in seriously ill HIV-positive patient

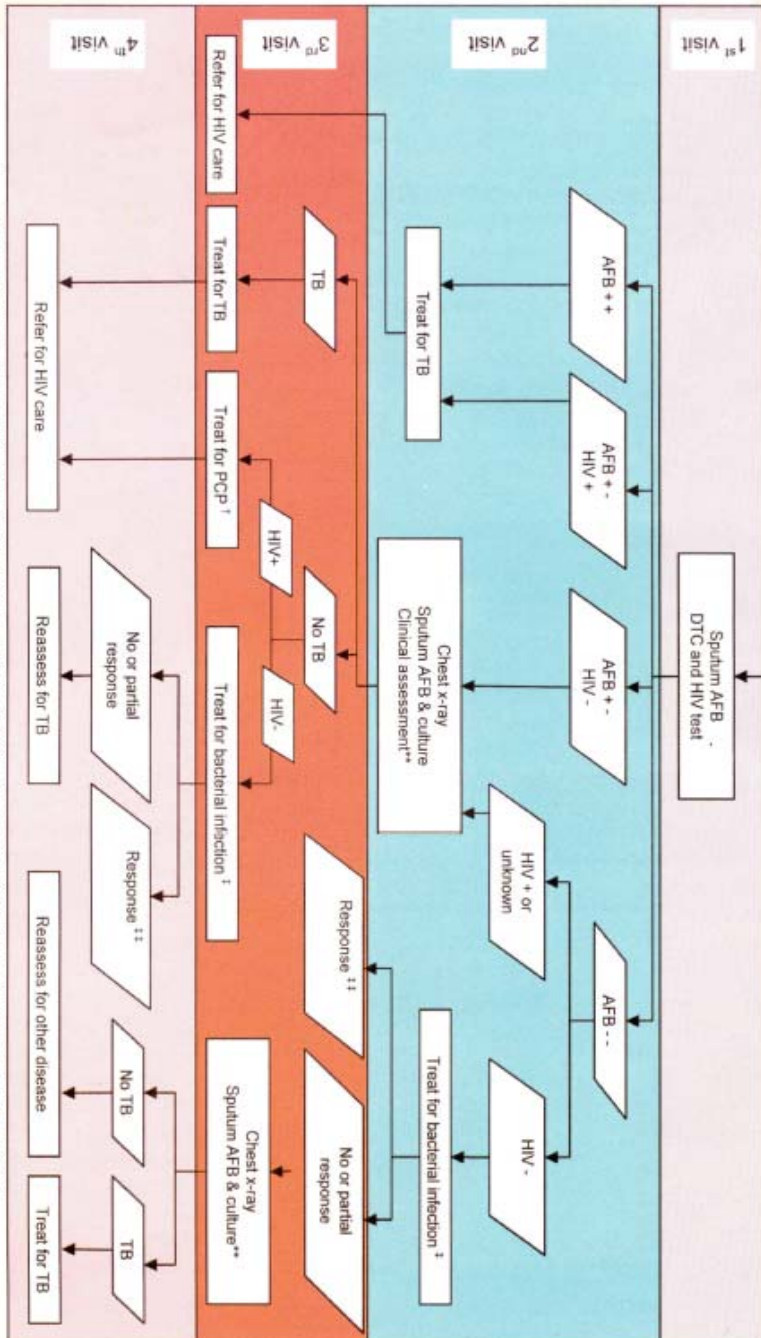


Appendix B

Algorithm for the diagnosis of tuberculosis in ambulatory HIV-positive patient



Ambulatory patient with suspected TB and no danger signs*



Danger signs respiratory rate $>30/\text{minute}$, fever $>39^\circ\text{C}$, pulse rate $>120/\text{min}$ and unable to walk unaided
Investigations within the same box should be done at the same time, wherever it is possible, to decrease the number of visits for the client and speed up diagnosis
Antibiotics (except Fluoroquinolones) to cover both typical and atypical bacteria should be considered
PCP: *Pneumocystis carinii* pneumonia also known as *Pneumocystis jirovecii* pneumonia
Advise to return if symptoms recur

⁴ Adapted from WHO

Appendix D



TUBERCULOSIS DIAGNOSTIC WORKSHEET

Patient ID - -		Facility ID (if different)	
Patient Last Name		Patient First Name	
Clinic code			

TB SCREENING VISIT day month year		Current TB episode diagnosed elsewhere ☐ Yes ☐ No	
Past TB history: ☐ None ☐ Unknown ☐ Yes If yes, # of treatments lasting > 1 mo.	Last episode: ☐ Pulmonary ☐ Extrapulmonary ☐ Unknown Treatment started (mo/yr) Treatment ended (mo/yr)	Reasons for suspecting TB today: Symptoms: ☐ Cough > 2 weeks ☐ Weight loss ☐ Fever ☐ Night sweats ☐ Loss of appetite ☐ Haemoptysis ☐ TB meningitis / focal neuro abnormality	
		Locating signs: ☐ Lung ☐ Spinal lesion ☐ Ascites ☐ Pericardial effusion ☐ Skin lesion ☐ Lymph nodes	Other: ☐ TB contact ☐ Abnormal CXR ☐ HIV infection ☐ Other, specify:
Comments: 		INVESTIGATIONS ☐ Sputum for AFB ☐ Chest X-ray ☐ Other	Prescribed antibiotic ☐ Yes ☐ No Date of next visit: / / Day Month Year

TB FOLLOW UP VISIT day month year		CXR results. Date: / /	
Sputa results: Date / / ☐ Positive ☐ Negative ☐ Not done Date / / ☐ Positive ☐ Negative ☐ Not done Date / / ☐ Positive ☐ Negative ☐ Not done	Other results: Date / / ☐ Positive ☐ Negative	☐ Normal ☐ Infiltrate ☐ Pleural effusion ☐ Cavity ☐ Pericardial effusion ☐ Other	
TB status: ☐ TB diagnosed by: (tick all that apply) ☐ smear ☐ biopsy ☐ culture ☐ history ☐ exam ☐ xray ☐ Diagnosis unclear* Observe, refer, further tests ☐ Patient does not have TB		Plan: ☐ Treat for TB. Go to TB Assessment and Plan. ☐ Treat with antibiotics ☐ Order other tests* ☐ sputum AFB ☐ sputum culture ☐ CXR ☐ Other ☐ Continue usual HIV care	
Comments: 		*For additional follow up visits, use another TB Diagnostic Worksheet Date of next visit: / / Day Month Year	

TB ASSESSMENT AND PLAN day month year	
Type of patient: ☐ New ☐ Relapsed ☐ Failure ☐ Resumed (treatment after default)	
Type of TB: ☐ PTB smear positive ☐ PTB smear neg., culture not ordered ☐ PTB smear neg., culture pending ☐ EPTB	
TB treatment category and medications: ☐ New case: RHZE x2 mos intensive phase; EH x6 mos continuation phase ☐ Failure/relapsed/resumed: S(RHZE) x2 mos/(RHZE) x1 mo intensive phase; RHE x5 mos continuation phase ☐ Paediatric: RHZ x2 mos intensive phase; RH x4 mos continuation phase ☐ Paediatric TB meningitis/disseminated TB: SRHZ x2 mos intensive phase; RH x10 mos continuation phase	
Comments: 	Date of next visit (should be in 2 weeks) / / Day Month Year

Appendix E

INFORMATION SHEET FOR PARTICIPANTS.

Title of Study: Tuberculosis screening practices in HIV infected adult patients enrolling at the Kalingalinga anti- retroviral therapy (ART) clinic in Lusaka, Zambia.

Introduction:

Dear participant,

My name is I am hereby requesting you to participate in a research study that will assess the screening practices used in diagnosing tuberculosis in HIV infected adult patients enrolling at the Kalingalinga anti- retroviral therapy (ART) clinic. This study is being conducted by Dr. Sally Trollip who is a postgraduate student at the University of Zambia in the School of Medicine, department of Internal Medicine. The study is being carried out as a partial fulfillment for the degree of Masters of Medicine in Internal medicine.

Purpose of the Study: The purpose of this study is to determine the current practices used in screening tuberculosis at Kalingalinga ART clinic. The information obtained will be used to help improve the screening practices for tuberculosis.

This information sheet gives you information about the study. If you understand and agree to take part in the study, you will be required to sign a consent form. For persons who are illiterate, a witness will observe the consenting procedures.

Voluntary Participation: Your participation in the study is voluntary. You will not be paid to participate in the study. The information you give is confidential .The screening form will not have your name but will have numbers. You are free to withdraw from the interview at any given time should you wish to discontinue.

Problems/questions: If you have any questions regarding the study, please contact Dr. Sally Trollip on cell 0977 788069. Any queries regarding ethics should be addressed to the Chair of

the research Ethics committee of the University of Zambia, Ridgeway Campus, P O. Box 50110 Lusaka, Zambia. Phone +260 211 252641. Email: unzarec@zamtel.zm.

If you agree to take part in the study you can sign the consent form.

Explanation of Procedures: You will not be exposed to any experimental therapy in this study. The screening that will be carried out during the study will use standard procedures for tuberculosis screening. You would still need to undergo them even if you decided not to take part in the study. Tests that you would have already been requested to do by the ART clinic staff will not be unnecessarily repeated.

Physical Examination: A routine general physical examination will be performed by a qualified medical doctor.

Handling of specimens: The sputum specimens you will submit will be sent to the laboratory for examination. You will then receive appropriate standard care depending on results of your specimen.

Alternative screening methods: Other investigations such as chest x-rays will be ordered and results will be communicated to you. Some blood tests maybe required as deemed necessary by the medical officer.

Risks and Discomforts: You will not encounter any additional risks or discomforts by virtue of your participation in the study. The above procedures are standard and are generally harmless. You will not be subjected to any experimental therapies.

Benefits: Your participation in this study will be of benefit to you as you will be thoroughly screened for tuberculosis. In the event that an important investigation is not requested by the staff at the ART clinic, the study screening will ensure you undergo the test. This will benefit you as the time for your screening and ultimately treatment will be faster and prevent you from worsening. The study will also provide valuable information to policy makers on current tuberculosis screening practices.

Confidentiality: All information collected during the study will be kept in strict confidence. However core study staff and representatives of the research ethics committee of the University of Zambia will have access to your medical records. Collected information including laboratory findings may be published for scientific purposes, but your personal identity will not be made public at any time.

Withdrawal without prejudice: You are free to withdraw from this study without prejudice of further care that you may enjoy at this institution.

Cost of participation: There will be no cost to you for participating in the study.

Payment for participation in study: You will be given K15, 000 as transport allowance for participating in this study.

Appendix F

Informed consent

Title of Study: Tuberculosis screening practices in HIV infected adult patients enrolling at the Kalingalinga anti- retroviral therapy (ART) clinic in Lusaka, Zambia.

I have understood the purpose and procedures that will be involved in this study. I have willingly agreed to participate in the study and indicate this agreement by my signature below:

_____	_____	_____
Participant's name	Participant's signature/ Thumb print	Date
_____	_____	_____
Witness's name	Signature of Witness	Date
_____	_____	_____
Name of person obtaining consent	Signature of person obtaining consent	Date

Appendix G

Chihepala cha Chibvomekezo

Dzina la Maphunziro: Njila zopimilamo matenda a chifuwa cha TB (tuberculosis) mu anthu amene ali ndi HIV amene alikulembesa pa chipatala cha mankhwala a HIV (ART) clinic) ku Kalingalinga mu Lusaka, Zambia bungwe la (Fogarty International Clinical Research Scholars Support Center ku Vanderbilt-AAMC)

Nambala ya Maphunziro (UAB IRB Protocol Number): X090429001

Akhulu a Ofufuza: Dr. Sally Trollip

Opeleka Ndalama: Fogarty International Center at the National Institutes of Health, USA

Chiyambi:

Kuli Otengako Mbali, Dzina langa ndine Ndili pano kukupepani inu kutengako mbali mu maphunziro akufufuza amene adzaziwa njila zopimilamo zimene zitsewenzesedwa pakupeza matenda a chifuwa cha TB (tuberculosis) mu anthu amene ali ndi HIV amene alikulembesa pa chipatala cha mankhwala a HIV (ART) clinic) ku Kalingalinga. Maphunziro aya ali kuchitidwa ndi a Dr. Sally Trollip amene alipamaphunziro awo pa sukulu lapamwamba la za umoyo mu Zambia (University of Zambia in the School of Medicine, department of Internal Medicine). Maphunziro ali kuchitidwa monga mbali yakukwanisa maphunziro amadigili (*degree of Masters of Medicine in Internal medicine*).

Kufotokoza kwa Ndongomeko:

Cholinga cha maphunziro aya ndi kudziwa njila zatsopano zimene zitsewenzesedwa mukupima matenda a chifuwa cha TB (*tuberculosis*) ku chipatala cha mankhwala a HIV ku Kalingalinga (*ART clinic*). Nkhani idzapezedwa idzasewenzesedwa mukuthandiza kuongola njila zopimilamo matenda a chifuwa cha TB (*tuberculosis*). Chihepala cha chibvomekezo ichi chikupatsilani nkhani paza maphunziro. Ngati mwamvetsetsa ndipo mumvomela kutengako mbali mu maphunziro, mudzayenela kusaina chihepala ichi. Ku anthu amene sakwanitsa kuwelenga ndi

kulemba (*illiterate*), mboni idzakhalapo pa nthawi ya ndondomeko ya chibvomekezo. Simuzakhala ndi kuchilitsa kwakuyetsa kuli konse (*experimental therapies*) mu maphunziro aya. Kupima kumene kudzachitidwa panthawi yamaphunziro kudzatsewenzetsa ndondomeko zoyenela za kupima matenda a chifuwa cha TB (*tuberculosis screening*). Mudzafunikila kuchita zipimo idzi angakhale kuti munasakha kusatengako mbali mu maphunziro. Zipimo zimene munachita kale ku chipatala cha mankhwala a HIV (*ART Clinic*) sizizabwezedwapo kuchitidwa.

Chipimo Cha Pathupi:

Chipimo cha pathupi cha nthawi zonse chizachitidwa ndi a dotolo azaumoyo ophunzila bwino (*qualified medical doctor*).

Kusunga kwa Zopima: Zikolala zopima zimene mudzapatsila zizatumidwa ku malo opimilako ku chipatala (*laboratory*) kukapimidwa. Ndipo mudzalandila chisamalilo choyenela kulingana ndi zotulukamo za zopima zanu.

Njila Zina Zopimilamo:

Kufufuza kwina monga chipimo chapa chifuwa (*chest x-rays*) chidzachitidwa ndipo zotulukamo zizapatsidwa kwainu. Zipimo zina za magazi zingafunike monga kwaonedwa ndi anchito azaumoyo (*medical officer*) kuti ndikofunikila.

Ziopyezo ndi Zotsamvetsa Bwino:

Simuzakhala ndi ziopyezo zoonjezelapo zili zonse kapena zotsamvetsa bwino pakutengako mbali kwanu mu maphunziro. Ndongomeko zili pamwamba apa ndi zoyenela ndipo zilibe chiopyezo. Simuzakhala ndi kuchilitsa kwakuyetsa kuli konse (*experimental therapies*).

Maphindu:

Kutengako mbali kwanu mu maphunziro aya kudzakhalala ndi maphindu kwainu pakuti mudzapimidwa bwino bwino pa matenda a chifuwa (*tuberculosis*). Pa nthawi yakuti kufufuza

uku kofunika sikunafunikile kulingana ndi anchito apa chipatala cha mankhwala a HIV (*ART clinic*), chipimo cha maphunziro chidzasimikiza kuti mwapimidwa. Ichi chidzapidula kwainu pakuti kupimidwa ndi kuchilitsidwa kudzachitika mwam'sanga ndi kukulengani inu kusadwala kwambili (*worsening*). Maphunziro adzapatsila nkhani zofunikila ku anthu opanga malamulo (*policy makers*) pa njila zatsopano zopimilamo matenda a chifuwa (*tuberculosis*).

Njila Zina Zakutengako Mbali:

Njila ina ndi kusatengako mbali mu maphunziro aya, ndipo ndi kulandila kuchilitsidwa kwa nthawi zonse.

Chisinsi:

Nkhani zonse zizatengedwa pa nthawi yamaphunziro zizasungidwa mwachisinsi. Tidzalemba chabe nambala yanu yokudziwilaniko pa mapepala athu amaphunziro ndi mosungila nkhani (*mu database*); dzina lanu silidzalembedwa kuli konse. Mapepala onse amaphunziro adzasungidwa mukabati mokomedwa (*locked filing cabinet*) ndipo nkhani imene idzaikidwa mu computer idzatetezedwa ndi nambala kuti anchito amaphunziro ndi amene angaonepo chabe. Komabe, nkhani yofufuza imene ilenga imwe kuziwika ingayanganidwe ndi bungwe la sukulu lapamwamba yamu Zambia (*University of Zambia Research Ethics Committee*) ndi sukulu lapamwamba laku Alabama ku Birmingham (*University of Alabama at Birmingham Institutional Review Board (IRB)*), kupatikizapo anthu oyimililako bungwe la National institute of health (*NIH*) kapena bungwe la Fogarty International; ndi ofesi ya Human Research Protections (*OHRP*). Nkhani zotengedwa kupatikizapo zotulukapo zaku malo opimilako ku chipatala (*laboratory*) zingaulusidwe pazolinga za kufufuza (*scientific purposes*), koma kuziwika kwanu sikuzabvumbululidwa pa nthawi ili yonse.

Kuleka Maphunziro Kopanda Kupatsidwa M'landu:

Kutengako mbali kwanu mu maphunziro ndikozipeleka. Nkhani imene mupatsa ndi ya chisinsi. Chi pepala chakusakha (*screening*) sichizakhala ndi dzina lanu koma chidzakhala ndi ma nambala chabe. Muli omasuka kuleka mafunso (*interview*) pa nthawi ili yonse ngati mufuna kuleka kopanda kukuza kuchisamalilo chaumoyo pa chipatala chino.

M'tengo pa Kutengako Mbali:

Kulibe m'tengo kwainu pakutengako mbali mu maphunziro.

Kulipila pa Kutengako Mbali mu Maphunziro:

Mudzapatsidwa K15, 000 monga ndalama yokwelela pa kutengako mbali mu maphunziro aya.

Kulipila pa Kudzichita Kokuzana ndi Kufufuza:

Sukulu lapamwamba laku Alabama ku Birmingham ndi opeleka ndalama za maphunziro sanapange njila yolipililamo ngati inu mwazichita kuchokela mukutengako mbali mu maphunziro aya. Ngati kuzichita kwam'tundu uyu kwachitika, kuchilitsidwa kuzapatsidwa. Komabe, kuchilitsa uku sikuzapatsidwa kwaulele. Bungwe la Centre for Infectious Disease Research in Zambia (CIDRZ) lidzakonza makonzedwe olipililamo kukuchilitsa kwa kuzichita kuchokela kukufufuza. Ngati mwazichita pachifukwa chakutengamo mbali mu maphunziro aya, mudzachelitsidwa mwam'sanga kulingana ndi kuchilitsa kumene kuliko muzipatala za boma mu Zambia.

Munthu Owona pa Mabvuto kapena Mafunso:

Ngati muli ndi mabvuto ali yonse kapena mafunso paza maphunziro, kuli anthu amene mungaone. A kansela (*counselors*) ndi anchito awo angakuthandizeni kuona anthu oyenekela kuti ayakhe mafunso ali yonse amene mungakhale nawo. Paza mafunso, zondondometsa (*concerns*), kapena zondandaulitsa paza kufufuza kapena kudzichita kokuzana ndi kufufuza kupatikizapo kuchilitsa kumene kulipo, mungaone a: Dr Sally Trollip, pa nambala ya lamy 0977 788069. Pa mafunso paza ufulu wanu monga otengako mbali mukufufuza, kapena zondondometsa (*concerns*) kapena zondandaulitsa paza kufufuza, mungaone a:

Kum'pando

Research Ethics Committee

Ridgeway Campus

P.O. BOX 50110

Lusaka, Zambia

Tel: 260-211-256-067

Email: unzarec@zamtel.zm.

Ufulu Walamulo: Simutaya ufulu wanu uli onse pa kusaina chi pepala cha chibvomekezo ichi.

Kusaina

Ndamvetsetsa cholinga ndi ndondomeko zizachitidwa mu maphunziro aya. Ndamvomela mozipeleka kutengemo mbali mu maphunziro ndi kuonetsa ichi pakusaina chi pepala cha chibvomekezo ichi pansi apa:

_____	_____	_____
Dzina la otengako mbali	Otengeko mbali kusaina	Tsiku
	Kapena kusindikiza ndi chala	
_____	_____	_____
Dzina la mboni	Kusaina kwa mboni	Tsiku
_____	_____	_____
Dzina la munthu wamene	Kusaina kwa munthu wamene	Tsiku
alikutenga chibvomekezo	alikutenga chibvomekezo	

Appendix H

P.O. Box 50827
Lusaka
Tel: +260-211-235554
Fax: +260-211-236429



Republic of Zambia

MINISTRY OF HEALTH LUSAKA DISTRICT HEALTH MANAGEMENT TEAM

In reply please quote

No.



19TH May, 2009

Sally Trollip
University Teaching Hospital
Private bag RW 1x
Ridgeway
LUSAKA.

Dear Madam,

RE: REQUEST FOR PERMISSION TO DO A RESEARCH AT KALINGALINGA ART CLINIC.

Refer to the above subject.

Lusaka District Health Management Team (DHMT) has no objection to your request to do a research at Kalingalinga ART clinic which will be conducted in collaboration with the CIRDZ TB/HIV department. The study is entitled "Tuberculosis screening practices in adult HIV patients."

However, we ask you to avail DHMT with your study results after the research.

By copy of this letter the Kalingalinga Health Centre In-charge is hereby informed.

Yours faithfully,


for/ **DR. MATIMBA CHIKO**
MANAGER PLANNING & DEVELOPMENT
For/DISTRICT DIRECTOR OF HEALTH.

CC: The Health centre In-charge Kalingalinga.

Appendix I



THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
Fax: + 260-1-250753
E-mail: unzarec@zamtel.zm

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia

Assurance No. FWA00000338
IRB00001131 of IORG0000774

27 April, 2009
Ref.: 007-04-09

Dr Sally Trollip
Principal Investigator
UTH Department of Internal Medicine
P/Bag RWIX
LUSAKA

Dear Dr Trollip,

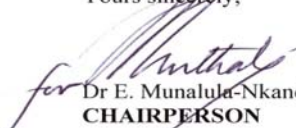
RE: SUBMITTED RESEARCH PROPOSAL: "TUBERCULOSIS SCREENING PRACTICES IN HIV INFECTED ADULT PATIENTS ENROLLING AT THE KALINGALINGA ANTI-RETROVIRAL THERAPY (ART) CLINIC IN LUSAKA, ZAMBIA"

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee extra-ordinary meeting held 15 April, 2009, where changes were recommended. We would like to acknowledge receipt of the corrected version with clarifications. The proposal is approved.

CONDITIONS:

- This approval is based strictly on your submitted proposal. Should there be need for you to modify or change the study design or methodology, you will need to seek clearance from the Research Ethics Committee.
- If you have need for further clarification please consult this office. Please note that it is mandatory that you submit a detailed progress report of your study to this Committee every six months and a final copy of your report at the end of the study.
- Any serious adverse events must be reported at once to this Committee.
- Please note that when your approval expires you may need to request for renewal. The request should be accompanied by a Progress Report (Progress Report Forms can be obtained from the Secretariat).

Yours sincerely,


Dr E. Munalula-Nkandu, BSc (Hons), MSc, PgD R/Ethics, PhD
CHAIRPERSON

Date of approval: 27 April, 2009

Date of expiry: 26 April, 2010

Appendix J



THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

Telephone: 260-1-256067
Telegrams: UNZA, LUSAKA
Telex: UNZALU ZA 44370
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Assurance No. FWA00000338
IRB00001131 of IORG0000774

Ridgeway Campus
P.O. Box 50110
Lusaka, Zambia

15 December, 2009
Ref.: 007-04-09

Dr Sally J. Trollip
Principal Investigator
Department of Internal Medicine
University Teaching Hospital
P/Bag RWIX
LUSAKA

Dear Dr Trollip,

RE: **APPROVAL REQUEST FOR TRANSLATIONS OF INFORMED CONSENT FORMS
FOR THE PREVIOUSLY APPROVED PROTOCOL: "TUBERCULOSIS SCREENING
PRACTICES IN HIV-INFECTED ADULT PATIENT ENROLLING AT THE
KALINGALINGA ART CLINIC IN LUSAKA"**

We acknowledge receipt of your letter dated 9 June, 2009.

The translated consent forms have been reviewed and approved, and these are:-

- a. Approved English Informed Consent Form (ICF), version 1.0
- b. Nyanja translation and back translation of ICF, version 1.0

Yours sincerely,

Mrs Mercy Mbewe
A/VICE CHAIRPERSON