Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Thuy Thi Thanh Trinh Date

Evaluation of the implementation of tuberculosis (TB) intensified case finding (ICF) among HIV- infected patients in Ho Chi Minh City and Hanoi, Vietnam

By

Thuy Thi Thanh Trinh
Master of Public Health

Department of Global Health

_____

Carlos del Rio, MD
Committee Chair

Evaluation of the implementation of tuberculosis (TB) intensified case finding (ICF) among HIV- infected patients in Ho Chi Minh City and Hanoi, Vietnam

By

Thuy Thi Thanh Trinh
Medical Doctor
Hanoi Medical University
1991

Thesis Committee Chair: Carlos Del Rio, MD

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in the Department of Global Health
2012

Abstract

Evaluation of the implementation of tuberculosis (TB) intensified case finding (ICF) among HIV- infected patients in Ho Chi Minh City (HCMC) and Hanoi, Vietnam

By Thuy Thi Thanh Trinh

Background: In order to reduce the burden of tuberculosis among people living with HIV (PLHIV) the World Health Organization (WHO) recommended intensified case finding as a key component of the 3 I's initiative. In 2007, the Vietnam Ministry of Health issued national guidelines on TB diagnosis on PLHIV.

Objectives: To define the quality and coverage of ICF for PLHIV and identify any barriers to ICF among PLHIV attending HIV care in antiretroviral treatment clinics in Hanoi and HCMC.

Method: Retrospective cohort study designed to collect data from adult HIV-infected patients in 5 out- patient clinics. Data was abstracted from patient's chart regarding TB screening in outpatient clinics OPC and TB diagnosis in TB clinics. A qualitative analysis was conducted to understand ICF practices and associated factors among health care staff in these clinics.

Results: Among 489 eligible patients, 461 (94%) were screened for TB every year. Nine percent of the screened patients in the last visit had one of 3 symptoms (cough, fever, weight loss) and 56% of them were referred to TB clinics to rule out active TB. All of those referred had sputum smears done and 42% had chest x-ray done. There was no association between being screened for 3 symptoms and age group, HIV transmission routes and ART status. Interviews with healthcare workers (HCW) suggested that HIV-infected patients should be screened for cough, fever, weight loss and night sweats and that screening should be done at all visits. HCW indentified barriers for ICF including the fact that TB and HIV services were sometimes not offered at the same location, that patients needed to travel multiple times for TB diagnosis without transportation support, and that patients were at times too sick to travel.

Discussion: Although, health care workers knew that HIV patients should be screened for TB at every visit and that they should be screening for cough, fever, weight loss and/or night sweat, TB-symptom screening was not consistent and 6% of patients had never been screened for TB. Healthcare workers should have more training on the national and WHO guidelines on ICF.

Evaluation of the implementation of tuberculosis (TB) intensified case finding (ICF) among HIV- infected patients in Ho Chi Minh City and Hanoi, Vietnam

By

Thuy Thi Thanh Trinh
Medical Doctor
Hanoi Medical University
1991

Thesis Committee Chair: Carlos del Rio, MD

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in the Department of Global Health
2012

Acknowledgements

I would like to express my thanks to Dr. Carlos del Rio, my thesis advisor, for his critical guidance and instruction throughout my research process. I would like to thank Dr. Bruce Struminger, Dr. Sara Whitehead, Dr. Le Hung Thai and Dr. Nguyen Bui Duc for their technical assistance on the development of my research proposal. To Dr. Vu Thanh Tung, Dr. Vu Thi Khanh, Dr. Han Trung Dien, Dr. Tran Nhu Nguyen and other LIFE-GAP staff, thank you for making my research is possible and useful by sharing with me critical thoughts and advices. To Ms. Maria Sullivan, Ms. Theresa Nash and Ms. Angela Rozo who have guided me in meeting all the program requirements and assuring that I will be successful at Rollins. To the healthcare staff in the out-patient clinics in Hanoi and HCMC who assisted me with data collection and administrative support, thank you. I am grateful to my parents, my husband, my daughter and my son for their love, support and encouragement. Finally, I would like to thank my friends for their invaluable support over the last 2 years.

Table of Contents

1. INTRODUCTION

The HIV epidemic presents a major challenge to the control of tuberculosis (TB) in the world. According to the World Health Organization (WHO) report in 2011, the estimates of the global burden of TB disease were 8.8 million incident cases, 1.1 million deaths among people with TB not infected with HIV and 0.35 million deaths among people with TB infected with HIV. An estimated 13% of HIV-positive people had active TB (WHO, 2011). Tuberculosis is also one of the most common causes of morbidity and one of the leading causes of mortality in people living with HIV (PLHIV)(Cain et al., 2009; Moore et al., 2007). Additionally, the rate of smear-negative pulmonary and extra-pulmonary tuberculosis has been rising in countries with HIV epidemics. The mortality rate among people with both TB disease and HIV infection (TB/HIV) is higher compared to people with TB not infected with HIV. One study in Vietnam found a mortality rate of 26% among HIV-infected TB patients compared to 3% in persons with TB and unknown HIV status (Thuy et al., 2007; WHO, 2009a). The WHO guidelines on improving the diagnosis and treatment of smear negative pulmonary TB and extra-pulmonary TB in 2007 stated that delayed TB diagnosis may be an important cause of excess mortality in PLHIV (WHO, 2007). The guidelines emphasized the timely diagnosis and treatment of all cases of tuberculosis, including smear negative pulmonary and extra-pulmonary tuberculosis through TB intensive case finding. An evaluation in Ethiopia found that the risk of death was 2.4 times higher in patients with symptoms that did not receive TB diagnostic evaluation, compared to patients with HIV without symptoms of TB disease (Feleke et al.). In addition, earlier and accurate TB screening and treatment may also help clinicians identify infectious cases earlier, thereby reducing TB transmission (Getahun et

al., 2011). In 2004, WHO issued an interim policy on collaborative TB/HIV activities, recommending that collaboration between TB and HIV programs should be established and intensified TB case finding be implemented to reduce the TB burden among PLHIV (WHO, 2004).

In August 2007, in response to the WHO TB/HIV policy, the Vietnam Ministry of Health and the National TB program (NTP) issued guidelines for the diagnosis, treatment and management of TB and HIV in Vietnam (Vietnam, 2007). The guidelines recommended annual routine TB screening among PLHIV. The recommended TB screening symptoms included: 1) prolonged cough for more than 2 weeks, 2) hemoptysis, 3) fever and 4) weight loss. If the patient has these symptoms they would receive further evaluations for active TB, including direct acid fast bacilli (AFB) smear, chest x-ray and sputum culture, when available. The guidelines were implemented in Vietnam in early 2008. In addition, the national TB program (NTP) revised its guidelines on diagnosis, treatment and prevention of TB. The guidelines stated that when HIV-infected patients have any one of the four symptoms mentioned above (cough, fever, weight loss or night sweats) for more than 2 weeks, they should receive further TB evaluation to rule out active TB (MOH Vietnam, 2009).

VIETNAM

(http://wwp.greenwichmeantime.com/time-zone/asia/vietnam/map-vietnam/index.htm)

Hanoi and Ho Chi Minh City (HMC) where the study was implemented in 2011

HIV-associated TB in Vietnam

Vietnam has a concentrated HIV epidemic, but tuberculosis infection is generalized and endemic. Vietnam ranks 12th among the 22 highest TB burden countries in the world with an estimated 199 cases per 100,000 population and reporting of 97,000 TB cases in 2009 (WHO, 2009a, 2011). According to the 2010 UNAIDS report, there was an estimated 220,000-350,000 people with HIV aged greater than 15 and HIV prevalence among adults aged 15-49 years was 0.4% in 2009 (UNAIDS). In 2011 there were 197,335 HIV infected patients reported, 48,720 AIDS cases and 52,325 cases that died of AIDS (Vietnam, 2012). The national HIV prevalence among people with TB who were HIV tested was 3.6% in 2009 (Vietnam) and 4 % in 2011(Vietnam, 2011) . For PLHIV in Vietnam, TB is the leading cause of severe illness and death (Klotz et al., 2007). During TB treatment, death rates in people with TB/HIV average 20-30%, with most deaths occurring in the first three months after TB diagnosis (Thuy, et al., 2007).

ART services have expanded rapidly since the initiation of PEPFAR in Vietnam in 2005. So far there have been 404 ART clinics established in the country (Vietnam, 2011). TB/HIV program collaborative activities were also initiated in 2005 in 4 provinces with 29 sites; since then the program has expanded to 26 provinces with 130 service sites. The TB/HIV collaborative initiatives include: improvement of TB and HIV collaboration at the national, provincial and district level; provider initiated testing and counseling (PITC) at TB care settings; intensified TB case finding (ICF) for PLHIV; isoniazid preventive therapy (IPT); and, building of laboratory capacity for diagnosing TB.

HIV-associated TB in Ho Chi Minh City

Ho Chi Minh City is in one of the provinces in Vietnam most affected by both the HIV and TB epidemics. In 2011, 1,943 persons were diagnosed with HIV and 1,470 with AIDS. During this same period, 481 persons died of AIDS. Currently, 46,507 HIV-infected persons are registered in the city's HIV care and ART program out-patient clinics. As of December 2010, PEPFAR supported 22 ART clinics and the Global Fund for AIDS, TB and Malaria (GFATM) supported 7 ART clinics. Since 2003, when ART first became available in HCMC, 26,665 PLHIV have initiated ART. In 2010, 13,916 persons were diagnosed with TB disease, of these, 13% were HIV-infected. The TB/HIV collaborative program started in 2006 and so far 27 clinics have been involved in TB diagnosis for PLHIV. Implementation of TB screening among PLHIV in HIV OPC and TB clinics is believed to be more standardized and systematic after the national TB/HIV standard operating procedures SOP was issued in August 2007 and the revised NTP guidelines in 2009.

HIV-associated TB in Hanoi

Hanoi city has also been greatly affected by both the HIV and TB epidemics. In 2011, 915 persons were diagnosed with HIV, and 352 with AIDS. During this same period, 122 persons died of AIDS. Currently, 8,429 PLHIV are registered in the city's HIV care and ART program through the out-patient clinics. PEPFAR supports 9ART clinics and the GFATM supports 6 ART clinics in the city. Since 2004, when ART first became available in Hanoi, 3,813 PLHIV have initiated ART. In 2010, 4,695 persons were diagnosed with TB disease and, of these, 316 (7%) were HIV-infected (Vietnam, 2009) . The TB/HIV program started in Hanoi in 2005, so far 16 clinics have been involved in TB diagnosis for PLHIV. As is the case with HCMC, implementation of TB screening

among PLHIV in HIV OPC and TB clinics is believed to be more standardized and systematic after the national guidelines on diagnosis, treatment and management of TB and HIV was available in August 2007 and the revised NTP guidelines in 2009. There has been no assessment of the extent to which PLHIV received routine screening for TB following the publication of the national TB screening guidelines by the Ministry of Health. In the most recent PEPFAR program report for 2010, fewer than 10% of PLHIV were referred from the HIV OPC to TB clinics for TB evaluation (PEPFAR Vietnam, unpublished data 2010). We propose to have the US Centers for Disease Control and Prevention (CDC) in Vietnam and its counterparts, the Vietnam Administration of AIDS Control (VAAC) and the national TB program (NTP) of Vietnam work together to evaluate the implementation of TB intensified case finding among PLHIV in select HIV outpatient clinics (OPC) in Hanoi and Ho Chi Minh City. Lesson learned from this evaluation will be used to support scale-up the implementation of TB screening and care linkage in TB clinics and HIV care ART clinics.

2. LITERATURE REVIEW:

2.1. Introduction of literature review

There are three objectives in this review. The first objective is to describe the association between TB and HIV and describe why HIV-infected patients have a greater risk of developing active TB disease. Second, this review describes tuberculosis intensified case finding (ICF) as it is critical for the diagnosis of TB among HIV infected patients. Finally, the review focused on ICF screening practices in the health services in resource limited settings for HIV-infected patients in accordance with WHO and local guidelines. This review is intended to demonstrate that ICF should be done routinely in HIV infected patients. The review will identify gaps in the current literature on the practice of ICF among HIV infected patients. Studies published in the last 5 years were collected for this review through searches in Pubmed, Google Scholar, WHOLIS, organization specific web-sites, and recommendation, report from subject government, organization especially for low-income setting.

2.2. Epidemiology of Tuberculosis and HIV:

Tuberculosis accounted for 26% of all AIDS related deaths. The risk of developing active TB among HIV-infected patients was 20-37 times higher among persons infected with HIV compared to HIV negative patients. The HIV-infected patient is also 4 times more likely to die from TB as compared to an uninfected one (Getahun, Gunneberg, Granich, & Nunn, 2010). Decentralized HIV services that were integrated with TB services, using HIV services as an entry point to expand access to antiretroviral therapy (ART) and prevent the progression of HIV disease, were all necessary approaches to reduce the morbidity and mortality of HIV patients. In addition, following WHO guidelines, TB

screening for HIV infected persons increased from 600,000 in 2007 to 1.4 million in 2008 (Getahun, et al., 2010).

TB remains the most common serious opportunistic infection in people with HIV infection and the leading cause of death among them. The use of IPT and CPT is addition to starting ART in HIV-infected adults with newly diagnosed TB could significantly reduce mortality. Following the 3I's (as described below) can also help to reduce the TB burden among those with HIV infection (Martinson, Hoffmann, & Chaisson, 2011). Although significant advances have been made in the management of HIV/TB co-infection, additional research is needed in order to reduce the burden of tuberculosis in HIV-infected persons in developing countries. The focus should be on TB diagnosis before and after ART, and TB treatment and prevention for HIV-infected TB patients (Chamie, 2010).

2.3. Intensive case fining (ICF)

Three I's: isoniazid preventive treatment (IPT), intensified case finding (ICF) and TB infection control (IC) are key public health strategies to decrease the impact of TB on people living with HIV (WHO, 2004, 2009b).

ICF is a key component of the WHO 3I's. ICF can increase the number of persons diagnosed with active TB in high TB prevalence countries (TB rate of 100/100,000 or more). An AFB smear done on patients without TB symptoms can yield an additional 4 cases per 100 screening individuals. However, TB screening algorithms tend to be different between countries with variations in both the symptoms screened for and the duration of these symptoms (Kranzer et al., 2010).

ICF has been implemented and shown to be feasible in both clinic and hospital settings, although there appears to be more ICF done in community clinics (48% vs. 18%). Suggested symptoms for the screening of TB included cough, fever and night sweats for more than 2 weeks, weight loss for more than 4 weeks, and chest pain. ICF is considered to be positive if cough is present for more than 2 weeks in addition to one of the other symptoms. At that point it is recommended that sputum be collected on these patients. However, in one study, only about half of screening positive cases returned for sputum testing, of those,16% had a positive sputum smear and 87% of them received TB treatment (Elden et al., 2011).

Data from the Health and Demographic Surveillance Survey (HDSS) was used for sampling to estimate the prevalence of pulmonary TB (PTB) and the fraction attributable to HIV. Symptom screening focused on cough for more than 2 weeks. Case definition was sputum culture positive or sputum smear positive and cough for more than 2 weeks. Fifty one percent of PTB occurred among HIV-infected persons compared to 29% in an official report suggesting that there were more HIV-infected persons in need of ICF. This was critical as 48% of prevalent TB in the study population was attributable to HIV (van't Hoog et al., 2011) .

In 2011 WHO issued updated guidelines on TB intensified case finding and Isoniazid preventive treatment (IPT) for people living with HIV in resource constrained settings. The WHO recommended that the symptoms that should be screened for are 1) current cough, 2) fever, 3) weight loss, and/or 4) night sweats. If one of the four symptoms is positive, the patient should be evaluated for TB and other diseases (WHO, 2010).

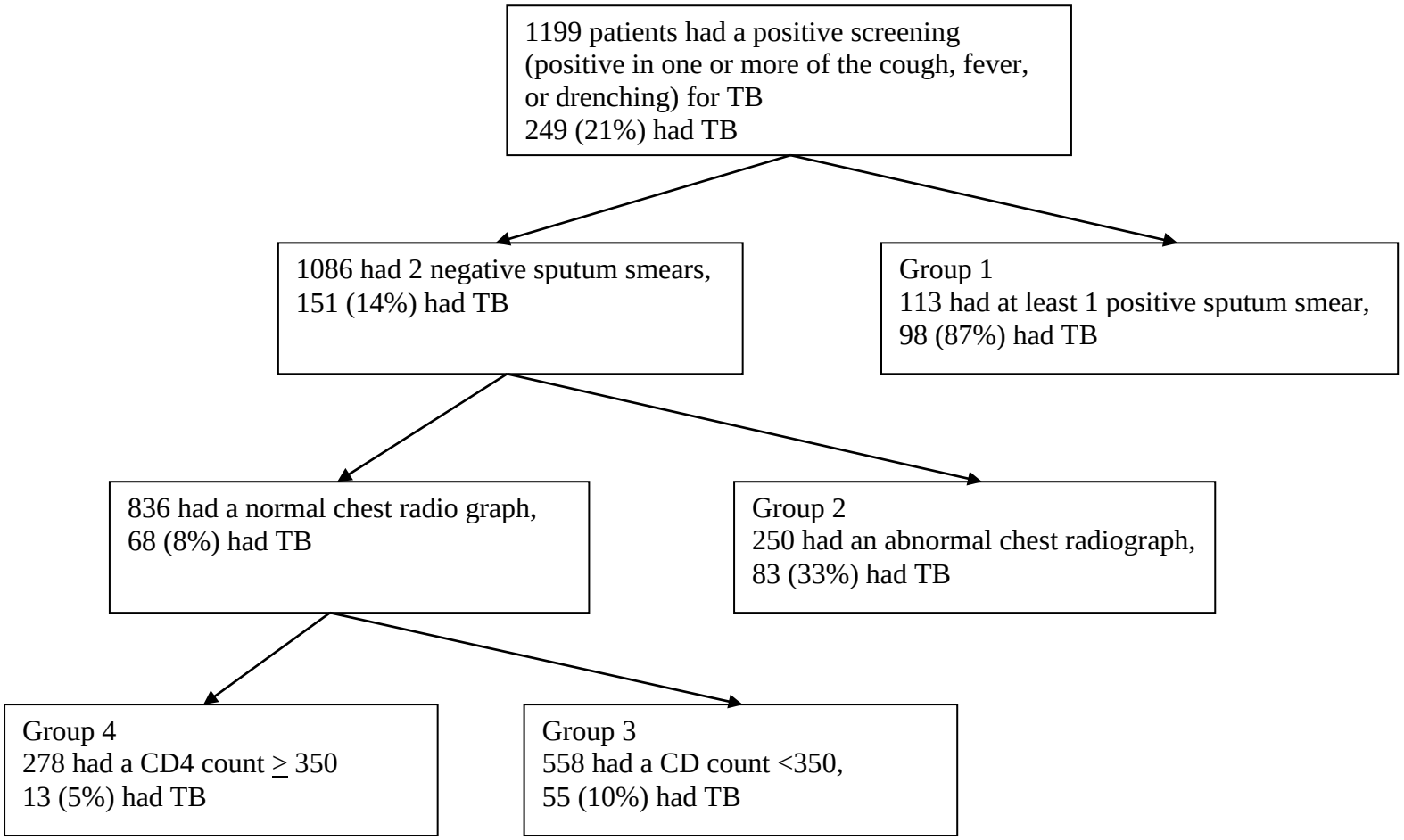
2.4. TB screening of HIV-infected persons

A review of 12 studies with a total of 8,148 HIV-infected patients in resource limited countries where the patients were screened for 5 symptoms that included cough, fever, night sweats, weight loss, and hemoptysis, suggested that cough, fever, night sweats or weight loss had both high sensitivity and specificity when the case definition included at least one smear culture positive . In addition, the study suggested that chest x-ray can increase the sensitivity of symptoms alone for TB screening (Getahun, et al., 2011).

One hundred and fifteen articles and guidelines have also shown that cough alone was a poor screening symptom for TB among HIV-infected persons. Although cough for more than 2 weeks had poor sensitivity, if combined with other symptoms it can increase the sensitivity and specificity of the screening. Sputum smear also has a variable sensitivity that ranges from 31% to 80%. However, it may be lower among HIV-infected persons where the reported sensitivity has been between 24%-61%. In order to reduce the travel burden for HIV-infected patients the number of sputum smears should be reduced with 2 samples collected in 1 day instead of 3 samples in 2 days. It should also be stated that a chest X-ray may not be as useful in HIV infected persons as it may be atypical depending on the immune status of the patient (Reid & Shah, 2009).

In a study in Vietnam, Thailand and Cambodia, Cain et al. (Year) concluded that the presence of cough for 2 to 3 weeks or more during the preceding 4 weeks had very low sensitivity for TB. The presence of cough of any duration, fever of any duration, or night sweats in the last 3 weeks or more in the preceding 4 weeks were 93% sensitivity and 36% specificity for tuberculosis. An HIV-infected patient with any of these symptoms but who has 2 negative sputum smears, a normal chest x-ray and a CD4 count of 350

cells/uL or greater could effective be ruled out for active TB. ART and IPT can be started safely on a patient with 3 negative symptoms (Graphic 1) (Cain, et al., 2010).



Graphic 1. Diagnostic algorithm for Tuberculosis in patients with HIV infection (Cain et al., 2010)

2.5. Conclusion

Evidence from the literature review indicates a strong association between TB and HIV. It shows the need to use HIV services to provide TB intensified case finding among HIV-infected patients as this can help to reduce TB transmission as well as mortality among HIV-infected persons. In addition, WHO guidelines on TB intensified case finding are critical for member countries to implement among HIV-infected persons. Although there are many scientific-based approaches to ICF and TB screening among HIV-infected patients, the screening algorithms are still varied multiple among resourced limited settings. The differences are related to what symptoms should be included in the screening and the duration of the symptoms. There is strong evidence to screen HIV-infected patients with 3 or 4 symptoms that include cough, fever, night sweat and/or weight loss. If none of these 4 symptoms are found then patients can start with IPT or ART. On the other hand, if a patient has one or more of these symptoms then further evaluation for TB is necessary. Moreover, there is an absence of data on the national guidelines for ICF and how healthcare workers adhere to guidelines for tuberculosis ICF on HIV-infected patients. Therefore, additional research is needed to assess health care workers HCW practice regarding the national guidelines on TB ICF screening on HIV infected person in resource limited countries.

3. METHODS:

3.1. Goal and Objectives:

The goal of this study is to define the quality and coverage of ICF for PLHIV and identify any barriers to ICF among PLHIV attending HIV care and antiretroviral treatment (ART) clinics in Hanoi and HCMC.

Objectives:

- To evaluate the extent to which ICF among PLHIV is being implemented according to national guidelines in OPCs in Hanoi and Ho Chi Minh City;
- To evaluate the extent to which PLHIV that screen positive for TB are receiving TB diagnostic and treatment services according to the national guidelines in Hanoi and HCMC; and,
- To provide feedback to the TB and HIV programs on the implementation of the national TB/HIV guidelines in Hanoi and HCMC.

3.2. Data collection

A retrospective cohort study were designed to collect data from HIV-infected patients who were 18 years old or older in Dong Anh and Dong Da outpatient clinics in Hanoi and District 1, District 2 and District 4 outpatient clinics in Ho Chi Minh City (HCMC). The patients needed to be enrolled in the OPC between January 2008 and July 2011. A list of patients during this time period was provided to randomly select patients using the formula of randbetween (a,b) in order to select 100 patients from each clinic (Appendix E). The study team included 2 PhD, 4 medical doctors, and one public health officer. At study initiation, a meeting was held with leaders and staff of each HIV out-patient clinic (OPC) to present the goals and objectives of the study. The study team then reviewed patient charts that were selected randomly and data was abstracted to a structured data

collection form (appendix A). We collected both categorical and continuous data. The data includes variables of site evaluation ID number, 01DD for Dong Da clinic, 01DA for Dong Anh Clinic, 0201 for District 1 clinic, 0202 for District 2 clinic and 0204 for District 4. Then HIV patient unique numbers, assigned by the OPC, were recorded. Other variables were: patient age, gender (male=1, female=0), the date first seen at OPC (day/month/year), HIV transmission route (IDU=1, SEX=2, blood transfusion=3, unknown=9), most recent CD4 cell count variable recoded dichotomized into two levels (<200 and $\geq$ 200), and eligibility for ART (yes=1, no=0). If the answer was "no" to this last question, the data collectors skipped the next question that asked for the ART initiation date (day/month/year), data on the question "currently on ART" (yes=1, no=0) was collected. Data on patients screening for TB at the OPC, if "ever", "at the first 2 weeks of admission", "at every visit" and "most recent visit", number of TB screening, patients screening (yes=1, no=0), if yes then TB symptom (Cough=1, no cough=0, fever=1, no fever=0, drenching=1, no drenching=1, wasting=1 no wasting=0, and others), sputum smear (sample 1, positive=1, negative=0, sample 2, positive=1, negative=0; sample 3, positive=1, negative=0), and chest x-ray (yes=1, no=0) was abstracted. If the answer was "no" then the person doing the abstraction skipped the next question, "chest x-ray result" (Abnormal TB=1, Abnormal not TB=2, normal=0). The name of the TB center that the patient was referred to, co-trimoxazol prophylaxis (CPT) with day/month/year, and CPT stop date (day/month/year) were recorded. Follow-up status at OPC (alive, death day/month/year, transfer out day/month/year, lost follow-up day/month/year) were also included. It could be possible that health care workers could not record in the patient chart if a patient had been referred to a TB clinic for further TB

evaluation. In those cases, we had to find indirect evidence - such as information if the patient was on TB treatment or if chest X-ray, sputum smear or sputum culture test requisition forms were attached with the patient chart to track for the results on the TB evaluation at the TB clinics. Appendix A includes the recorded information on TB evaluation and diagnosis that was then used to later locate patients in TB clinics.

The questions in appendix B were used to collect data from the HIV-infected patients who went to TB clinics. That included the same unique site evaluation ID number, name of TB clinic, and if the patient was seen at the TB clinic (yes=1, no=0, unknown=9). We recorded name of the clinic referred patients (Dong Da clinic=01DD, Dong Anh clinic=01DA, District 1=0201, District 2=0202, district 4=0204), date that patient self referred to clinic (day/month/year), date patient diagnosed with TB (yes=2, day/month/year, no=0), number of sputum samples and sputum result (#1: positive=1, negative=2 , # 2: positive=1, negative=2, # 3: positive=1, negative=2), sputum conversion after 2 months of treatment (positive=1, negative=0, not done=2), chest x-ray result (abnormal TB=1, abnormal not TB=2, normal=0), if the chest x-ray was abnormal TB, if there was a cavity on x-ray (yes=1, no=0, unknown=9), TB status (smear+=1, smear-=, EPTB=3, not TB=4, unknown status=5), patient stared on TB treatment (yes=1, day/month/year, no=0), date treatment end, day/month/year. Treatment outcomes (cure=1, completed=2, failure=3, died=4; default=5, transferred out=6, change of diagnosis=7), mortality status after 2 months of treatment (alive=1, dead=2, unknown=9), mortality status between 2-8 months of treatment (alive=1, dead=2, unknown=9), and mortality status after 8 months of treatment (alive=1, dead=2, unknown=9) were also collected.

The 2 PhDs and 2 MDs in our team took turns to interview staff of the 5 OPC clinics in order to assess challenges, barriers, and suggestions for improvement in the conduct of TB screening services for PLWHIV. A questionnaire was developed (Appendix C) to interview staff at the clinics. The questions focused on knowledge on TB/HIV, their practice of TB screening on HIV-infected patients in their clinics. The questions included: 1) What is the estimated percentage of HIV-infected persons routinely screened for TB at each visit; 2) When are the patients screened for TB (only at the first visit=1, during every visit=2, prior to staring INH, ARV, other=4); 3) How are persons with HIV screened for TB (asked about cough >2 weeks, chest x-ray, sputum smear, sputum culture, others); 4) other symptom screening (no=0, weight loss=1, night sweat=2, fever=3, lymphadenophathy=4, others=5); 5) Are HIV-infected persons referred to a TB clinic (no referred=0, TB clinic); 6) How are they referred (verbal=1, MOH form=2, other=3); 7). How does the clinic follow-up after the referral (Communication with TB clinics=1, patient provided information=2, other =3); 8) Where is TB treatment started for active TB (TB clinic=1, OPC=2, Other=3); and 9) Where does the TB treatment for continuous phase occur (TB clinic=1, OPC=2, other=3).

Another questionnaire was developed (Appendix D) to interview senior staff, such as the head of the OPCs, about their knowledge of the national guidelines on TB screening for HIV-infected patients. In addition, we wanted to know the barriers that existed about TB screening of HIV-infected patients. The question included: 1) proportion of HIV-infected patients who have TB; 2) Current policy, guidelines on TB screening on HIV-infected persons, what do they do; 3) What TB services are provided at the clinic; 4) According to them who is the best suited for TB screening; 5) How patients are referred to TB clinics;

6) What patient characteristics can effect negatively in the screening; and, 7) What factors from the health care systems are barriers to screening.

3.3. Ethical Considerations

This project involves minimal risk to patients and staff. For staff interviews, staff names were not recorded. This minimized the risk that sensitive or critical comments by individual staff members would become known by higher level officials.

For retrospective chart reviews, as noted above, no personal identifiers were recorded except temporarily in a single paper logbook to allow linkage of HIV and TB clinic data. The confidentiality measures noted above minimized the risk of breach of confidentiality of patient data through this study.

Determination of "exempt status" was obtained from the Emory IRB. In addition, the Centers for Disease Control and Prevention (CDC) determined the study as "non-human subject research" because the purpose of the project is to perform a programmatic evaluation of an existing screening program for TB among patients attending OPC clinics in Hanoi and HCMC. Data will be used to provide feedback to the ministry of health to improve coordination of the TB/HIV program in these sites. The findings are expected to be of use to local and national health officials, and will not lead to generalizable knowledge.

Data collection, consent and privacy protection

Verbal consent for staff interviews was obtained. Identifying information was not collected from staff. The evaluation teams briefly interviewed the assigned clinic staff regarding TB screening policies and practice at the clinic (Appendix C and D). Only

aggregated results of staff interviews will be shared with the Ministry of Health representatives.

Records from a sample of patients attending OPC were randomly selected and reviewed. For patients found to be TB suspects, identifying data was collected temporarily for linkage to the TB clinics, and later destroyed after successful linkage could be established. Data on TB screening and on initiation of TB treatment was will be abstracted to document TB diagnostic and treatment services (Appendix A and B).

For review and abstraction of patient records, no names or personal identifiers were collected except temporarily for service linkage as specified below. Patient informed consent was not sought, as this evaluation consisted only of retrospective chart review with no personal identifiers included in the study data file. In order to protect patient confidentiality, each patient was assigned a unique identifier. No names or personal identifiers were recorded for any patients except those referred from OPC to TB clinics. Names of these patients were recorded to allow linkage to records at the TB laboratory and treatment referral centers. We maintained a logbook linking the unique identifier to the identifier assigned at the clinic until this linkage is made, and the logbooks have destroyed after data cleaning completed. No personal identifiers will be entered in the electronic database.

All data collected was kept in the same secure location with other patient records at the OPC. Only authorized health staff could access the files. The electronic data was stored in a password-protected computer database with restricted access. The number of people who had access to the information was limited to the evaluation personnel. All study

forms were collected at the clinics and transported to the central data processing center located in the CDC office in Hanoi, Vietnam.

3.4. Data analysis:

Quantitative analysis:

The evaluation data was entered into eCRF designer database web and imported to Microsoft Access version 2010 for data storage. SAS 9.3 for Windows was used for all statistical analyses (SAS Institute, Cary, NC). The dataset was checked for any missing and implausible values.

Univariate analysis was performed to describe demographic information of patients such as name of OPC, age, and gender by sites (Dong Anh, Dong Da, District 1, District 2, District 5). Included in the analysis was: proportion of PLHA who have been seen at the OPCs by year from 2008-2011; the follow-up outcome of the patients at the time of data abstraction on July 2011; patient age by clinic with 4 age groups (20-29, 30-39, 40-49 and $\geq$ 50); mean, median and range of age of the population, number of visits, number of TB screenings, CD4 count results, follow-up time for survivors, and non-survivors. Then HIV transmission routes such as IDU, sexual transmission and blood transmission and combined IDU/sexual transmission were analyzed by gender In addition, those patients eligible for ART, eligible and initiated, and currently on ART were also counted. The number of TB symptoms screened for at every visit, the proportion screened for TB within the first 2 weeks of admission to OPC, and the proportion screened for TB at every visit were analyzed. Screening for TB symptoms at the most recent visit were analyzed using Chi-square test to compare the proportion between TB symptom

screening by site with CD4 counts and currently on ART. We went into more detail for the most recent visit by July 2011, looking at the proportion of patients who had TB screening (both symptom screening and laboratory screening), then the proportion of who had only TB symptom screening, followed by the proportion who had TB symptom including cough, fever, drenching, wasting, headache, abdominal pain, diarrhea, and lymphadenopathy. The proportion of patients screened for cough, fever, drenching and wasting, and the proportion with 1, 2, 3 or all 4 symptoms present were also counted. Then the proportion of patients screened for cough only, cough and fever, cough, fever, and drenching, and cough, fever, drenching and wasting were counted. Those found positive at screening for any of these were counted and also included were those with sputum smear, and CXR results by OPC site. Cotrimoxazol prophylaxis treatment (CPT) status by CD4 level (<200, ≥ 200) was analyzed. The proportion of presumptive active TB was counted with a combination of CXR result (abnormal TB), having one of the 4 symptoms, and a positive sputum smear or culture. Kaplan Meier and Cox Model were used to analyze mortality and survival. The model was also used to estimate for survival overall and its association with gender (male vs. female), CD4 count levels, location (Hanoi vs. HCMC), and number of TB screenings.

As shown in appendix B, we determined TB status (smear positive, smear negative, extra pulmonary TB, not TB, other lung disease). Of those diagnosed and treated, outcomes were categorized as cured, completed, died, transferred out, and treatment not completed. Proportions of sputum smear result, chest x-ray result, survival status of TB cases was counted. Patients diagnosed with TB using the methods above were counted. Among the patients referred to the TB clinic, TB status, ART treatment and survival status, and TB

treatment outcome were analyzed by univariate analysis. Patients who went to the TB clinic and time to TB diagnosis and treatment before and after OPC admission date were studied for mean, median and range of months. The length of TB treatment, median and range were analyzed.

Bivariate analysis was used to look for an association between "ever screening" and the variables - follow-up outcome, gender, age groups, number of visits to OPCs, HIV transmission route, CD4 count level and currently on ART. The same analysis was also done for "TB screening at every visit". Chi-square test was use to count the p-value of the associations.

Associations between screening of 3 symptoms (cough, fever, weigh loss) and age groups, HIV transmission route, CD4 count, and current ART also were analyzed. Likewise, associations between begin screening of 4 symptoms (cough, fever, drenching and weight loss) and age group, HIV transmission route, CD4 count, current ART also was analyzed. Moreover, the association between being referred to TB clinics and gender, age group, CD4 count levels, HIV transmission route and ARV status were analyzed by using Chi-square test.

Qualitative analysis

Data from appendix C and D were entered into Excel 2007 and was then used for qualitative analysis to describe findings on the HCW's knowledge, practices and barriers on ICF, TB screening in HIV infected patients.

4. RESULTS

The demographic characteristics of patients from the 5 clinics are summarized in Table 1. There were 489 patient charts reviewed, of these 93 (19%) were from Dong Da clinic, 98 (20%) from Dong Anh clinic, 116 (24%) from District 1, 91 (18%) from District 2 and 91 (18%) from District 4 clinic. Two hundred and four patients (41.7%) were admitted to the OPCs in 2008, 156 (40%) in 2009, 88 (18%) in 2010, and 41 (8.4%) in the first 6 months of 2011. Three hundred and forty eight (71%) patients were male. Their mean age was 33 (20-64) years-old and the median was 31 (29- 36). The mean CD4+ T-cell count was 313 cells/uL (5-1589) and the median was 297 cells/uL (130-448). The mean number of visit to OPC was 22 (1-70) and the median was 19 (7-34). There was a significant difference in the number of visits between site ($p<0.0001$) as the median for District 4 was 31 compared to other OPC where it was 14 (District 2), 15 (district 1) and 16 (Dong Anh). The mean number of times TB screening occurred was 12 (0-48) and the median was 10 (3-17). There was also a significant difference in the number of times TB screening occurred between clinics ($p<0.0001$) as this was 13 in District 4, 7 in District 1 and 8 in Dong Da.

Table.1 Demographic information of patients in the 5 clinics in Hanoi and HCMC

	Dong Da (n=93)	Dong Anh (n=98)	District 1 (n=116)	District 2 (n=91)	District 4 (n=91)	Overall (n=489)	p-value
Year seen in OPC clinic							
2008 (n,%)	28 (30)	42 (43)	50 (43)	46 (51)	38 (42)	204 (42)	
2009 (n,%)	41 (44)	27 (28)	36 (31)	30 (33)	22 (24)	156 (32)	
2010 (n,%)	17 (18)	21 (21)	22 (19)	10 (11)	18 (20)	88 (18)	
2011 (n,%)	7 (8)	8 (8)	8 (7)	5 (6)	13 (14)	41 (8)	
Gender							

Male (n,%)	59 (63)	71 (72)	87 (75)	68 (75)	63 (69)	348 (71)	
Age (median, range)	34 (21,57)	34 (23,57)	33 (22,54)	31 (20,50)	33 (21,64)	33 (20,64)	
Number of visits to OPC (median, range)	23 (30, 37)	16 (2, 32)	15 (6, 33)	14 (5, 31)	31 (29, 37)	19 (7, 34)	<0.0001
Number of TB screening (median, range)	8 (4,13)	9 (2,17)	12 (3, 27)	7 (1, 16)	13 (7, 21)	10 (3, 17)	<0.0001
CD4 count (median, range)	271 (159, 406)	301 (143, 483)	315 (109, 503)	270 (114, 416)	280 (134, 436)	297 (130-448)	

The patients were categorized into 4 age groups, 20-29, 30-39, 40-49 and ≥ 50 years old (Vietnam, 2011). Of the 489 patients, 160 (32.7%) were between 20 and 29 years-old, 262 (53.6%) 30-39 years-old, 50 (10%) 40-49 years-old, and 17 (3.5%) older than 50 years. The differences of age groups and among sites was significant (p=0.02). There were 138 patients (34.3%) that had a CD4 count less than 200 cells/uL, there was no significant differences in the CD4 counts among the 5 clinics (p=0.97) (Table 2).

Table.2 Age groups, CD4 count level of HIV infected patients in the 5 clinics in Vietnam

	Dong Da (n=93)	Dong Anh (n=98)	District 1 (n=116)	District 2 (n=91)	District 4 (n=91)	Overall (n=489)	p-value
Age groups							
20-29 (n,%)	22 (24)	25 (26)	42 (36)	41 (45)	30 (33)	160 (33)	0.02
30-39 (n,%)	55 (59)	57 (58)	54 (47)	45 (50)	51 (56)	262 (54)	
40-49 (n,%)	9 (10)	11 (11)	17 (15)	4 (4)	9 (10)	50 (10)	
≥50 (n,%)	7 (8)	5 (5)	3 (3)	1 (1)	1 (1)	17 (4)	
CD4 count levels							0.97
<200	34 (37)	32 (35)	38 (34)	30 (34)	34 (37)	168 (35)	

(n,%)							
≥200 (n,%)	58 (63)	59 (65)	75 (66)	58 (66)	58 (63)	307 (65)	

The most common HIV risk factor was injection drug use (IDU) which was present in 236 (48%) patients. Of these, 218 (92%) were male. Sexual transmission was the next most frequent risk behavior present in 153 (31%) of the patients and, of these, 92 (60%) were female. In 103 (21%) patients the transmission route was unknown as it was not recorded in the patient chart.

Three hundred and thirty four (68%) patients were eligible for antiretroviral therapy (ART) according to the national guidelines and 331 (99%) had been initiated on ART and 299 (90%) were currently on ART by July 2011. Three hundred and ninety five (86%) patients had TB screening in the first 2 weeks of entry into the OPC. Four hundred and sixty one (94%) patients had TB screening at least one time per year, however, there were only 75 (16%) patients who had TB screening at every visit. There were 384 (83%) patients who received TB screening at the most recent visit by July 2011 (Table 3).

Table 3. TB screening on HIV-infected patients in the 5 clinics in Hanoi and HCMC, Vietnam

	Dong Da (n=93)	Dong Anh (n=98)	District 1 (n=116)	District 2 (n=91)	District 4 (n=91)	Overall (n=489)	p-value
TB symptom screening "Ever" (n,%)	93 (100)	96 (98)	109 (94)	73 (80)	90 (99)	461 (94)	
TB screening in the first 2 weeks (n,%)	84 (90)	86 (90)	96 (88)	49 (67)	80 (89)	395 (86)	
TB	8 (9)	21 (22)	27 (25)	11 (15)	8 (9)	75 (16)	

screening at every visit (n,%)						
TB screening in the most recent visit (n,%)	63 (68)	75 (78)	106 (97)	62 (85)	77 (86)	383 (83)

Of the 384 patients who received TB screening that includes symptom screening and laboratory tests at the most recent visit, 262 (94%) had TB symptom screening only. Three hundred and thirty three (89%) were screened for cough, and, of these, 59 (18%) had cough, 326 (87%) were screened for cough and fever and, of these, 50 (16%) had cough and fever. One hundred and seventy four were screened for cough, fever and drenching sweats (47%) and, of these, 26 (15%) were positive for all three symptoms (cough, fever and drenching sweats).

Thirty four patients (9%) were screened for cough, fever and weight loss, of these, 9 (27%) had these 3 symptoms positive. There were differences in the screening algorithm for cough, fever and weight loss among the 5 clinics, as none of the patients screened for these 3 symptoms in Dong Da clinic, 21 % screened at Dong Anh clinic and there was equal range (7-9%) of these screening in the 3 clinics in HCMC (p-value=0.001).

Twenty five patients (7%) were screened for cough, fever, drenching and wasting, of these 4 (16%) had all these symptoms (Table 4). Less than 1% of the screened patients had either headache, abdominal pain, diarrhea or lymphadenopathy.

Table 4. Symptoms screened in the most recent visit at the 5 OPC in Hanoi and HCMC, Vietnam.

	Dong Da (n=62)	Dong Anh (n=68)	District 1 (n=101)	District 2 (n=61)	District 4 (n=82)	Overall (n=374)	p-value
Cough screened (n,%)	53 (86)	46 (68)	96 (95)	56 (92)	82 (100)	333 (89)	
Cough and fever screened (n,%)	51 (82)	43 (63)	94 (93)	56 (92)	82 (100)	326 (87)	
Cough, fever and night sweats screened (n,%)	6 (10)	19 (28)	30 (30)	50 (82)	72 (88)	177 (47)	
Cough, fever and weight loss screened (n,%)	0 (0)	14 (21)	9 (9)	5 (8)	6 (7)	34 (9)	0.001
Cough, fever and night sweats and weight loss screened (n,%)	0 (0)	14 (21)	6 (6)	3 (5)	3 (4)	26 (7)	0.002

None of the 5 clinics performed chest x-rays (CXR) or sputum smear for TB diagnosis. CXR and smears were done at TB clinics, the results were then returned to the OPCs and were incorporated into the patient chart. There was 1 patient whose record suggested that they had 1 sputum smear positive for TB and 4 patients (1%) had 3 sputum smears positive on their chart. One hundred and forty nine (31%) had CXR records in the patient chart, of these, 21 (14%) had an abnormal CXR suggestive of TB and 23 (15%) had an abnormal CXR but considered as not consistent with TB.

There were 92 patients who had information of having at least one TB evaluation at one of the 25 TB clinics in Hanoi, Ninh Binh, Ha Giang, Bac Ninh, Hung Yen, Quang Ninh, Thai Nguyen, Ninh Binh, Tuyen Quang, Hai Duong, Hai Phong, Ba Vi, Soc Son, Gia Lam, Vung Tau, Dong Nai with 97 records (3 patients had 2 visits, 1 patient had 3 visits to TB clinics). Of these, Dong Da clinic referred 2 (2%), Dong Anh 12 (13%), District 1 13 (14%), District 2 16 (17%), and District 4 23 (25%). There were 25 (27%) patients that referred themselves to a TB clinic before HIV-diagnosis.

Of these 92 patients, 70 (76%) had sputum smears done, 26 (37%) had 3 sputum smears positive, 2 (3%) had 2 sputum smears positive, and 2 (3%) had 1 sputum smear positive (3%). Thirty five (38%) had a CXR done and in 19 of those (54%) the CXR was reported as “abnormal TB”. Of the 92 patients, 62 (67%) were diagnosed with active TB. Of these 62, 31 (50%) had smear positive TB, 2 (6%) had smear negative TB, and 27 (44%) had extra-pulmonary TB (EPTB). Of the 62 TB cases, 46 (74%) finished TB treatment and 20 (43%) of them were considered to be cured, 19 (41%) completed treatment, 4 (9%) transferred out, and 3 (7%) died during TB treatment. Sixteen (26%) has not completed TB treatment. (Table5).

Table 5. TB evaluation, TB diagnosis and TB treatment outcomes among 92 HIV infected patients who were seen at the TB clinics.

	Hanoi		HCMC			Overall
	Dong Da (n=2)	Dong Anh (n=19)	District1 (n=20)	District 2 (n=22)	District 4 (n=29)	N=92
Sputum smear done	0	12	20	12	26	70
1 (+)(n, %)	0	0	0	1 (8)	1 (3)	2 (3)
2 (+)(n, %)	0	1 (8)	0	1 (8)	0	2 (3)
3 (+)(n, %)	0	6 (50)	5 (25)	5 (42)	10 (39)	26 (37)
TB status						
Not TB	0	3 (17)	9 (45)	2 (9)	15 (52)	29 (33)

(n, %)						
TB (n,%)	2 (100)	15 (79)	11 (55)	20 (91)	14 (48)	62 (67)
Smear + (n, %)	0	7 (47)	7 (64)	6 (30)	11 (39)	31 (50)
Smear -(n, %)	0	1 (7)	1 (1)	2 (10)	0	4 (6)
EPTB (n, %)	2 (100)	7 (47)	3 (28)	12 (60)	3 (21)	27 (44)
Finished treatment (n,%)	1	11	6	17	11	46 (74)
Cured	0	5 (45)	2 (33)	5 (29)	8 (72)	20 (43)
Completed (n, %)	1 (50)	5 (45)	1 (17)	9 (53)	3 (27)	19 (41)
Died (n, %)	0	0	0	3 (15)	0	3 (7)
Transferred out (n, %)	0	1 (7)	3 (50)	0	0	4 (9)

Of the 92 patients, 25 self-referred to a TB clinic before OPC admission and could have been diagnosed as HIV-infected as a result of the HIV counseling and testing program (PITC) that is available at TB clinics in Vietnam.

Of these 62 TB patients, 57 (92%) were alive after TB treatment and 3 (5%) died during treatment. Data on ART initiation were available in all 62 TB patients, of these, 53 (85%) were on ART during TB treatment. The TB treatment outcome was much better in the ART group compared to the non-ART group as there was only 1 (11%) patient that completed TB treatment among the non- ART group compared to 18 (34%) among the ART group. In addition, there were 3 (33%) deaths during TB treatment among the non-ART treatment group compared to no death among those in the ART group (p=0.001) (Table 6).

Table 6. Associations between TB treatment outcome and ART status among TB patients in Hanoi and HCMC, Vietnam.

	ART initiated/NO (n=9)	ART initiated/YES (n=53)	Overall	P-value
TB treatment outcomes				0.001
Treatment completed (n, %)	1 (11)	18 (34)	19 (31)	
Died (n, %)	3 (33)	0 (0)	3 (5)	

There were 26 cases that had either one of the 4 symptoms positive. Of these, 19 (73%) patients were successfully referred to TB clinics. Eight (43%) of them had a CXR and 19 (100%) sputum smears. All of those who underwent smear were diagnosed with TB (Table 7).

Table 7. Patients referred to TB clinics due to one of 4 symptoms positive

	Referred to TB clinics (n=26)	CXR at TB clinics (n=19)	Sputum smear at TB clinics (n=19)	TB diagnosis (n=19)	p-value
Referred to TB clinic due to 1 of 4 symptoms positive (n,%)	19 (73)	8 (43)	19 (100)	19 (100)	

There were 34 cases that had either one of the 3 symptoms (cough, fever and weight loss), and of these 19 (56%) were successfully referred to a TB clinic. Eight (43%) of them had a CXR, 19 (100 %) a sputum smear and all of them were diagnosed with TB (Table 8).

Table 8. Patients referred to TB clinics due to one of 3 symptoms positive

	Referred to TB clinics (n=34)	CXR at TB clinics (n=19)	Sputum smear at TB clinics (n=19)	TB diagnosis (n=19)	p-value
Referred to TB clinic due to 1 of 3 symptoms positive (n,%)	19 (56)	8 (43)	19 (100)	19 (100)	

Of the 489 patients, 340 (70%) were alive at the time of the study, 40 (8%) had died, 80 (16%) were lost to follow-up, and 29 (6%) had transferred out. TB treatment outcomes were different among the 5 clinics (p=0.01).

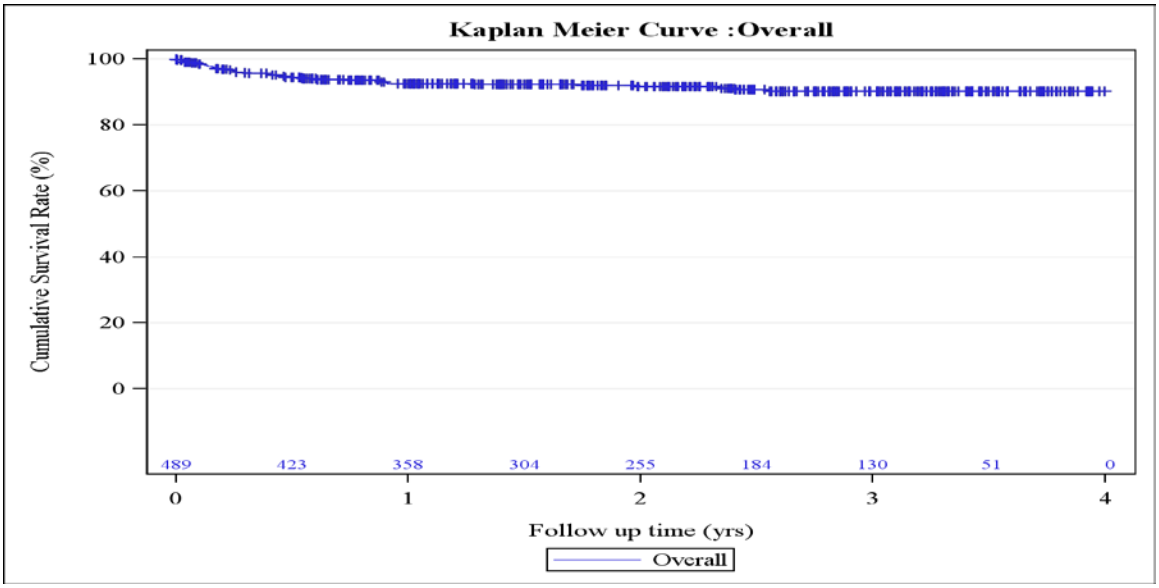
For example, District 2 had 50% alive while Dong Da had 86% alive. Lost to follow-up were also different among clinics with 25% lost to follow up in District 2 compared to only 5.5% in District 4 (Table 9).

Table 9. Follow-up of 489 HIV infected patients by clinics in Hanoi and HCMC, Vietnam.

	Dong Da (n=93)	Dong Anh (n=98)	District 1 (n=116)	District 2 (n=91)	District 4 (n=91)	Overall (n=489)	p-value
Patient outcomes							0.01
Alive (n, %)	80 (86)	70 (71)	74 (64)	46 (51)	70 (77)	340 (70)	
Dead (n, %)	3 (3)	8 (8)	7 (6)	13 (14)	9 (10)	40 (8.2)	
Lost of follow-up (n, %)	9 (10)	15 (15)	28 (24)	23 (25)	5 (6)	80 (16)	
Transferred (n, %)	1 (1)	5 (5)	7 (6)	9 (10)	7 (8)	29 (6)	

Survival analysis performed using Kaplan-Meier methods suggested that the highest survival was in the first 6 months, survival was reduced between the third and fourth year of follow up (99.8% vs. 90%). The risk of death was lower for women compared to men (OR=0.42, p=0.05, 95%CI 0.18-1.00), however the association is at the marginal significant level. In addition, the risk of death was lower for those with a CD4 count ≥ 200 cells/uL compared to those with a CD4 count < 200 cells/uL (OR=0.09, 95%CI=0.04-0.21, p<0.01) the association was statistically significant (Graphic. 2).

Graphic 2. Kaplan Meier Curve for CD4 categories (log rank test p-value < 0.0001)



The risk of death was also higher for patients in HCMC (0R=1.84, 95%CI=0.92-3.69, p=0.08), however the association is not significant. Risk of death decreased by 55% when the number of times TB screening occurred was 5 or greater (OR=O.85, 95%CI=0.8-0.91, p<0.01); this association is statistically significant. In addition, the risk of death is increased by 1% for each 10 year increase in age (OR=1, 95%CI=0.96-1.05, P=O.97), however the association was not significant (Table 10).

Table 10. Factors associated with survival of 489 HIV infected patients in 5 clinics in Vietnam.

Characteristics	Covariate	Hazard ratio (95%CI)	p-value
Gender	Female	0.42 (0.18-100)	0.05
CD4 count	CD4≥	0.09 (0.05-0.21)	<0.01
Location City	HCMC	1.84	0.08
Number of TB screening	Continuous	0.85	<0.01

When comparing patients "ever screened for TB" to those "never screened for TB" the percent alive was significantly different with 336 (73%) of those "ever screened for TB" alive, compared to 4 (14%) in the "never screened for TB" category. Lost to follow-up was also 3 times higher in "never screened for TB" patients (50% vs. 14%). These differences were statistically significant ($p<0.0001$) (Table 11).

Table 11. "Ever screened for TB" and follow-up outcome of 489 patients from 5 clinics in Hanoi and HCMC, Vietnam

	Ever screened TB symptoms "yes" n=461	Ever screened TB symptoms "no" n=28	Overall (n=489)	p-value
Patient outcome				<0.0001
Alive	336 (73%)	4 (14%)	340 (70%)	
Dead	34 (7%)	6 (21%)	40 (8%)	
Lost to follow-up	66 (14%)	14 (50%)	80 (16%)	
Transferred	25 (5%)	4 (14%)	29 (6%)	

Of the 28 (6%) patients who were never screened for TB, 18 (20%) were from District 2, 7 (6%) was from District 1, and 2 (2%) from Dong Anh clinic. There was only 1 (1%) District 4 patient not screened for TB, and all of the patients of Dong Da clinic were ever screened for TB. There was no difference in the "ever screened for TB" and "never screened for TB" by age group. The median number of visits to the clinic of "ever screened for TB" group was 4 times higher than was in the group of "never screened for TB". This difference is statistically significant ($p<0.0001$). There was no association between "ever screened TB" and HIV route of transmission ($p=0.07$) in Kruskal_Wallis test. There was also a significant association between "ever screened TB" and currently on ART, 90% "ever screened for TB" patients were on ART vs. 71% in "never screened for TB" group ($p=0.03$) (Table 12).

Table 12. Association between number of visits to clinic, ART treatment and "ever screened for TB" in 489 HIV-infected patients in Hanoi and HCMC, Vietnam.

	Ever screening TB symptoms YES (n=461)	Ever screened TB symptom NO (n=28)	Overall (n=489)	p-value
Number of visit to OPC (median, range)	21 (8,36)	4 (2,9)	19 (7,34)	<0.0001
Currently on ART				0.03
No (n,%)	21 (7)	2 (29)	23 (7)	
Yes (n,%)	294 (91)	5 (71)	299 (90)	

There were only 75 (16%) patients screened for TB at every visit. The median number of visits to the clinics for patients "TB screening at every visit" was 2 (1-9), compared to the median number of clinic visits for all patients which was 19 (7-34). Of the 75 patients

that were screened for TB at every visit, 21 (22%) were from Dong Anh clinic, 27 (25%) from District 1, 11 (15%) from District 2, 8 (9%) from District 4 and 8 (9%) from Dong Da clinic.

There was no association between "screened for TB at every visit" and gender or age groups. There was also no association between "screened for TB at every visit" and follow-up outcome (p-value =0.9), HIV transmission route (p-value=0.4) or currently on ART (p-value=0.7) (Table 13).

Table 13. Association between "screened for TB at every visit" and follow-up outcomes, HIV transmission routes and ART status.

	Screened TB symptoms at every visit/YES (n=75)	Screened TB symptoms at every visit/NO (n=386)	Overall (n=416)	p-value
Gender				
Female (n,%)	22 (29)	115 (30)	137 (30)	0.9
Male (n,%)	53 (71)	271 (70)	324 (70)	
Patient outcome at the end of the evaluation				
Alive (n,%)	40 (53)	296 (77)	336 (73)	0.3
Dead (n,%)	6 (8)	28 (7)	34 (7)	
Lost follow-up (n,%)	26 (35)	40 (12)	66 (14)	
Transferred (n,%)	3 (4)	22 (6)	25 (5)	
HIV transmission route				
Sexual transmission (n,%)	27 (36)	116 (30)	143 (31)	0.4
Injecting transmission (n,%)	38 (51)	175 (45)	213 (46)	

Currently on ART				
No (n,%)	2 (8)	19 (6)	21 (7)	0.7
Yes (n,%)	22 (88)	272 (91)	294 (91)	

There was no difference among age group with the screening algorithm of cough, fever and weight loss among 34 patients who were screened for these 3 symptoms (p-value=0.9) (Table 14).

Table 14. TB screening for 3 symptoms and age groups among HIV-infected patients in Hanoi and HCMC, Vietnam

	20-29 years old (n=160)	30-39 years old (n=262)	40-49 years old (n=50)	50 years old and older (n=17)	Overall (n=489)	p-value
Cough, fever and wasting screened						
No (n, %)	112 (90)	181 (91)	35 (92)	12 (92)	340	0.9
Yes (n, %)	12 (9)	18 (9)	3 (8)	1 (8)	34	

Among 34 patients screened for the 3 symptoms, 20 had a CD4 count less than 200 cells/uL compared to 14 who had a CD4 count equal or greater than 200 cells/uL (RR=3, p-value=0.002) (Table 15).

Table 15. Screening algorithm of 3 symptoms and CD4 counts for HIV-infected patients in Hanoi and HCMC, Vietnam.

	CD4 count less than 200 (n=169)	CD4 count $\geq$ 200	Overall (n=492)	p-value

Cough, fever and weight loss screened				
No (n, %)	108 (84)	230 (94)	340 (91)	0.002
Yes (n, %)	20 (16)	14 (6)	34 (9%)	

Screening for the 3 symptoms was not associated with being on ART (p-value=0.7) (Table 16) or HIV transmission risk (Tables 17 and 18).

Table 16. Screening algorithm of 3 symptoms and ART status on HIV-infected patients In Hanoi and HCMC, Vietnam

	Currently on ART/YES (n=299)	Currently on ART/NO (n=23)	Overall (n=322)	p-value
No (n, %)	210 (89)	13 (87)	223 (89)	0.78
Yes (n, %)	26 (11)	2 (13)	28 (11)	

Table 17. Screening algorithm of 3 symptoms and HIV transmission through sexual route on HIV-infected patients in Hanoi and HCMC, Vietnam

	Sex/YES (n=120)	Sex/NO (N=254)	Overall (n=374)	P-value
Cough, fever, wasting screened				
No (n, %)	109 (91)	231 (91)	340 (91)	0.9
Yes (n, %)	11 (9)	23 (9)	34 (9)	

Table 18. Screening algorithm of 3 symptoms and HIV transmission through injecting drug route on HIV-infected patients in Hanoi and HCMC, Vietnam

	IUC/YES (n=183)	IDU/NO (N=191)	Overall (n=374)	p-value
Cough, fever, wasting				

screened				
No (n, %)	162 (89)	178 (93)	340 (91)	0.1
Yes (n, %)	21 (12)	13 (7)	34 (9)	

When all four symptoms (cough, fever, weight loss and drenching sweats) were used for TB screening, there was no difference by age group between those that were screened and those that were not(p-value=0.9) (Table 19).

Table 19. TB screening algorithm of 4 symptoms and age groups among HIV-infected patients in Hanoi and HCMC, Vietnam

	20-29 years old (n=160)	30-39 years old (n=262)	40-49 years old (n=50)	50 years old and older (n=17)	Overall (n=489)	p-value
Cough, fever, drenching and wasting screened						
No (n, %)	115 (93)	184 (93)	36 (95)	13 (100)	340 (93)	0.9
Yes (n, %)	9 (7)	15 (8)	2 (5)	0 (0)	26 (7)	

However, more patients with a CD4 count with < 200 cells/uL were screened for the 4 symptoms compared to patients with a CD4count greater or equal to 200 cells/uL (RR=2.8 p=0.01) (Table 20).

Table 20. Screening algorithm of the 4 symptoms and CD4 counts on HIV-infected patients in Hanoi and HCMC, Vietnam

	CD4 count less than 200 (n=128)	CD4 count $\geq$ 200 (n=239)	Overall (n=367)	P-value
Cough, fever				

and weight loss screened				
No (n, %)	113 (88)	228 (95)	341 (93)	0.01
Yes (n, %)	15 (12)	11 (5)	26 (7)	

Of patients on ART, 9 % were screened for 4 symptoms compared to none on non-ART group. However, this did not reach statistical significance (p-value=0.22) (Table 21).

Table 21. Screening algorithm of 4 symptoms and ART status on HIV-infected patients In Hanoi and HCMC, Vietnam.

	Currently on ART/YES (n=299)	Currently on ART/NO (n=23)	Overall (n=322)	P-value
Cough, fever, drenching and wasting				
No (n, %)	214 (91)	15 (100)	229 (91)	0.22
Yes (n, %)	22 (9)	0 (0)	22 (9)	

Finally, those who had acquired HIV through IDU were more likely to have been screened for 4 symptoms compared to those who had not (RR=2.5, p=0.03), but there was no difference among those who had acquired HIV sexually (p-value= 0.3) (Table 22 and 23).

Table 22. Screening algorithm of 4 symptoms and HIV transmission through sexual route on HIV-infected patients in Hanoi and HCMC, Vietnam

	Sex/YES (n=120)	Sex/NO (N=254)	Overall (n=374)	P-value

Cough, fever, drenching and wasting screened				
No (n, %)	114 (95)	234 (92)	348 (93)	0.3
Yes (n, %)	6 (5)	20 (8)	26 (7)	

Table 23. Screening algorithm of 4 symptoms and HIV transmission through injecting drug route on HIV-infected patients in Hanoi and HCMC, Vietnam

	IUC/YES (n=183)	IDU/NO (N=191)	Overall (n=374)	P-value
Cough, fever, drenching and wasting screened				
No (n, %)	165 (90)	183 (96)	348 (91)	0.03
Yes (n, %)	18 (10)	8 (4)	26 (7)	

Among 34 patients screened for cough, fever and weight loss, 19 patients were successfully referred to TB clinics. Of these 16 (84%) were male and 13 (68%) had a CD4 count $\geq$ 200 cells/uL. Seventy nine percent of patients who initiated ART and were referred to the TB clinics went.

There were 12 health care workers who participated in the individual interviews for the questions in Appendix C. Of these, 11 (92%) estimated that patients were screened for TB, all of them estimated that patients were screened for at least 1 time, only one thought that only 80% had ever been screened for TB. Ten (83%) of the 12 interviewees thought that 100% of the patients were screened for TB at every visit to their clinic. Regarding when HIV-infected patients should be screened for TB, 4 thought that it should be at the first visit, 11 though it should be prior to starting IPT or ART, and 1 said that TB

screening should be done when patients had lymphadenopathy. In addition, 1 out of 12 interviewees thought that TB screening should be at the first visit and before starting IPT or ART. Four staff answered that the screening should be at the first visit and before starting IPT and ART and 7 thought that TB screening should be done at every visit and before starting IPT and ART. All12 interviewees asked patients if they had cough for more than 2 weeks, 11 used CXR, 11 ordered AFB smears and 9 used smears and culture for TB screening. Regarding other symptoms screened, 1 staff asked patients about weight loss, 10 for night sweats, 9 for fever and 10 for lymphadenopathy. When asked where to refer patients with suspected TB most referred to TB clinics with a few also mentioning the provincial TB clinic, the National TB hospital and Pham Ngoc Thach hospital. When asked how to refer patients to TB clinic, 11 answered using the ministry of health form. Regarding how the clinic followed up after patients had been referred to TB clinic, 3 said they exchanged information during meetings with TB partner, 5 waited for patients to provide information and 1 checked with the TB clinics. Regarding where HIV-infected patients should receive the intensive phase (first 2 months) of TB treatment, the TB clinics was the most frequent answer followed by community health centers and rehabilitation centers if the patients admitted there. However, when asked about where patients should receive the continuation phase of TB treatment, more suggested community health centers rather than TB clinics.

We carried out another set of interviews with 12 health care staff of these 5 clinics. When asked about how to conduct TB screening 9 out of 28 answers (31%) mentioned TB screening questions (3 symptoms), and 5 mentioned the 4 symptoms. CXR was mentioned by 2 persons. Other items mentioned were sputum smear, skin test, ultrasound

, and lymph node aspiration. When asked what TB services were provided at the clinic, 8 (22%) out of 36 answers listed symptom screening, 6 (17%) answered AFB smear, 4 (8%) CXR, 3 (6%) follow-up TB treatment, 6 (12%) referrals to TB clinics, and 1 (2%) mentioned TB treatment. When asked who should provide TB screening for HIV-infected patients, 7 out of 12 answered that it should be the doctor and 5 said that it should be both doctors and nurses. Answering what method should be used to refer patients to TB clinics, 3 said patients should be escorted to the TB clinic (especially if the TB and OPC clinic were located at the same place), 10 indicated the use of MOH referral form, and 3 by contacting the TB clinics. When asked about barriers faced during TB screening 3 (16%) out of 19 answered that there was no difficulty, 1 (5%) mentioned the lack of available chest x-ray, 1 (5%) said that TB symptoms in HIV patients were not clear, 2 (10%) said there were many AFB smears that need to be done before TB was diagnosed, 6 (30%) reported that patients had to travel a long way to get to a TB clinic, 3 (15%) answered that there was not transportation support for patients and, 3 (15%) reported that patients were too sick to travel to TB clinics. Additional barriers identified by the staff included the fact that cultures were not available, lymph node aspiration was not available, AFB smear was not available, and the fact that not all staff had received training. Others barriers mentioned were that “patients did not care” about TB, a lack of feedback from the TB clinics, and the time it took to get back results from smear and culture. Finally, about a third stated that the fact that patients were poor was also a barrier for TB screening, especially for patients who were from other provinces.

5. DISCUSSION:

Among 489 HIV-infected patients enrolled in 5 HIV OPC in Vietnam 461(94%) were screened for TB at least once a year following the National guidelines for diagnosis, treatment and management of TB and HIV in Vietnam. According to the guidelines, the screening symptoms include cough for more than 2 weeks, hemoptysis, fever and weight loss. However, during the qualitative research interviews conducted with a group of healthcare workers none mentioned hemoptysis as a symptom that should be included in screening for TB and thus we took it out from the list of symptoms that we included in our study. In addition, healthcare workers usually asked if the patient had symptoms or not without recording the duration of the symptom, so duration was also not included in the TB symptom screening of this study.

At the most recent clinic visit by July 2011, 383 (83%) patients had received TB screening. There were 34 (9%) cases that had at least one of the 3 symptoms (cough, fever and weight loss), of these, 19 (56%) were referred successfully to TB clinics. Eight (42%) had a CXR, 19 (100%) a sputum smear and all 19 were diagnosed with TB. There were 26 (7%) patients that had at least one of the 4 symptoms positive (cough, fever, weight loss and drenching), of these, 19 (73%) were referred to TB clinics. 8 (43%) had a CXR, 19 (100%) had sputum smear and all 19 were diagnosed with TB. Screening for 4 symptoms is now recommended in the new NTP guidelines on diagnosis, treatment and management of TB. Evaluating the guidelines was not the main objective of our study but we recorded when the 4 symptoms were noted in the patient's chart as the guidelines should be utilized at the OPC for screening HIV-infected patients for TB. Our study found no association between TB screening algorithm using 3 or 4 symptoms and age groups, HIV transmission risk and being currently on ART. However, patients

that had a CD4 count greater than 200 cells/uL were less likely to be screened for either 3 or 4 symptoms.

Regarding the successful at being referred to TB clinics after screening for 3 and/or 4 symptoms, men and patients with CD4 counts greater than 200 cells/uL were more likely to be successfully referred to TB clinic. Moreover, more patients who initiated ART were successfully referred to TB clinics than those who were not on ART.

Eighty six percent of patients had TB screening in the first 2 weeks of admission into the OPC and 94% of the patients had TB screenings at least once per year. According to the national guidelines, 100% of the HIV patients should be screened for TB (Vietnam, 2007). There were only 16% of the patients who had TB screenings performed at every visit. According to WHO guidelines the patients should be screened for TB at each time that they visit the clinic (WHO, 2010).

There were 28 (6%) patients who had never been screened for TB. Of these, 18 (64%) were from District 2 clinic, 7 (25%) from District 1 clinic, 2 (7%) from Dong Anh clinic, 1 (4%) from District 1 and none from Dong Da clinics. Compared to patients "ever screened for TB", patients who had never been screened for TB had much worse outcomes. For example, the death rate was 3 times higher, lost to follow-up was nearly 4 times higher and transfer out was 3 times higher ($p<0.0001$). There was no association between no screening for TB and gender, age, CD4 level and HIV transmission routes. Patients who were not on ART were at increased risk of not having been screened for TB ($p=0.03$).

There were 75 (16%) patients that received TB screening at all the visit to the clinics. Of these, 27 (36%) were from District 1, 21 (28%) from Dong Anh clinic, 11 (15%) from

District 2, 8 (11%) from District 4, and 8 (11%) from Dong Da clinic. There was no association between being screened for TB at every visit and gender, age, CD4 count, HIV transmission risk and ART status.

Of the successfully referred patients, one fourth was from District 4. Interestingly, the TB clinic is located at the same place as the District 4 clinic, thus co-location is likely the reason why more patients referred from this clinic successfully went to the TB clinic for TB evaluation. At Dong Da clinic most of the suspected TB cases were diagnosed and treated there as the clinic is located in the hospital where doctors have experience diagnosing and treating TB patients. However, patients had to pay for TB diagnosis and treatment that are otherwise free under the national TB program in the TB clinics. Thirty-eight percent of patients who screened positive for TB had a CXR done and 54% were found to have an abnormal CXR compatible with TB. Of all patients that were successfully referred to a TB clinic, 67% were diagnosed with active TB. Of these patients 50% had a positive sputum smear, compared to 83% smear positive among HIV-infected patients in another study in Vietnam (Thuy, et al., 2007). Of the 62 patients with active TB the cure and completed rate was 84 %. which is higher to the rate found in another study whose rate was 71% (Thuy, et al., 2007; WHO, 2011). Eighty five percent of HIV/TB patients were on ART treatment concomitantly with TB treatment which may have helped to improve TB treatment outcomes, as there were no deaths among patients on ART compared to 3 deaths in the non-ART group. This is similar to the finding from a study in South India (Vijay, Kumar, Chauhan, Rao, & Vaidyanathan, 2011).

HIV-infected patients with a CD4 count equal or greater than 200 cells/uL had a lower risk of death compared to patients who had a CD4 count less than 200 cells/uL. This is

not surprising and was confirmed by other studies in the literature (Sieleunou, Souleymanou, Schonenberger, Menten, & Boelaert, 2009). Risk of death was also lower for women, which is similar to a conclusion of a study conducted in China on gender and survival (Dou et al., 2011). Finally, the risk of death was decreased when the number of times a patient was screened for TB was 5 or higher. This finding was not collaborated in the literature review of similar studies.

Although this study was conducted in a convenience sample of patients enrolled in 5 OPCs in Vietnam, the age distribution, gender and HIV transmission risk of the study population were similar with those of the HIV-infected patients in Vietnam (Vietnam, 2011). Ninety nine percent of ART eligible patients in the study were initiated on ART. Regarding ART treatment, there was as high as 90% of the patients currently on ART suggesting that ART is widely available and that the program does a good job to initiate patients on ART in the country.

Findings from the qualitative study helped us to understand the current practice of TB screening and barriers to TB screening among HIV infected patients in OPCs in Vietnam. Most of the healthcare staff thought that patients should be screened for TB at the first visit and at every visit, however there were only 16% of patients screened at every visit suggesting a disconnect between knowledge and practice. Healthcare staff knew about TB screening for 3 symptoms (cough, fever and weight loss), as well as the need for AFB smear and CXR and most of them agreed to refer patients to a TB clinic if they were "suspected of having TB". It was however, not clear to them if patients with one of the 3 or one of the 4 symptoms should be referred even though the guidelines say so. Most of them think that physicians should work with nurses in TB screening. In addition, the

MOH referred form was widely used to refer HIV-infected patients to TB clinics. Barriers to screening identified in the qualitative study included the fact that, except for Dong Anh and District 4 clinics, TB clinics are far away from HIV clinics. Dong Anh and District 4 had nearly 100% of patients screened for TB at the clinics, compared to 94% in District 1 and 80% in District 2 where TB clinics are far from the OPC. In addition, they provided TB screening for 90% of patients within the first 2 weeks after admission. Also Dong Anh clinic had 22% of patients screened for TB at every visit. These findings suggest that co-location or at least proximity of HIV and TB clinics may improve screening for TB among HIV-infected patients.

There were some limitations to this study. First, the screening algorithm could only be evaluated for the most recent visit and this may not reflect TB screening at others visits. Second, the duration of the suspected TB symptoms were not recorded in the patient chart and thus it could not be collected for this study. Finally, there was no consistent method to document TB screening in the patient chart and the information on suspected TB and referral to TB clinics was also not systematically recorded in the patient chart which could lead to underestimation of both screening and referral.

6. RECOMMENDATIONS:

Both TB and HIV programs should work together to address factors that limit TB intensified case finding among HIV-infected patients. Although the national guidelines recommend that TB patients should be screened for cough, fever, weight loss and/or night sweats, there were only 9% of HIV patients screened for 3 TB suspected symptoms and 7% screened for 4 TB suspected symptoms in the study. It is thus necessary to conduct further trainings of healthcare workers on the updated guidelines so that they are

familiar with the symptoms for which screening is now recommended. In addition, healthcare workers should be reminded that all HIV-infected patients should be screened for TB independent of CD4. The successful referral of patients that screened positive for TB to a TB clinic needs to be improved. This study found that women, patients, younger (20-39 years old) as well as older (greater than 50 years old), with a CD4 count less than 200, and patients who were not on ART were less likely to be successfully referred to TB clinics. Finally, in order to implement routinely ICF, programs should address the concerns noted by the HCW in the qualitative part of this study. Findings suggest that TB and HIV services should be provided as a "one stop" setting for HIV-infected patients as a way to improve ICF in HIV infected patients. Future evaluations of the implementation of ICF should also be conducted but it is important that patient's charts be standardized in order to document in a manner to easy abstract information on TB screening at OPCs as well as information on patient's referrals to TB clinics and their outcome.

APPENDIX

Appendix A: Data to be collected on individual patients at OPC clinic

Data element	Content
1.Unique site evaluation ID number *(study ID number: 100 number at the each clinic* *01=Hanoi city* *+01DD000-01DD100= Dong Da clinic* *+01DA000-01DA100= Dong Anh clinic* *02=Ho Chi Minh city:* *+0201000-0201100= District1 clinic* *+0202000-0202100= District2 clinic* *+0204000-0204100= District4 clinic)*	
2.Patient unique # *(HIV ID number that issued by the clinic not by the study team)*	
3.Name of OPC:	+ 01DD=Dong Da clinic +01DA= Dong Anh clinic +0201=District1 clinic +0202=District2 clinic +0204=District4 clinic
4.Age (in years)	Age
5.Sex	1=Male, 0=Female
6.Date first seen at OPC	Day/Month/Year
7.Number of visits to center *(from January 2008-July 2011)*	##
8.Date when patient was diagnosed with HIV	Day/month/year
9.Transmission route	1=IDU; 2=SEX; 3=Blood transfusion; 9=unknown
10.Most recent CD4 cell count *(the last CD4 cell count by July 2011)*	####
11.Eligible for ART	1=Yes; 0=No if no skip question 12
12.ART initiation date	Day/Month/Year OR [Not yet started]
13.Currently on ART	1=Yes; 0=No
14.Patients symptom-screened for TB at OPC . Ever . At visits within the first 2 weeks of admission *(linked to No.6 above)* . At every visit *(linked to question 7)* . At the most recent visit *(by July 2011)*	 1=Yes; 0=No 1=Yes; 0=No 1=Yes; 0=No 1=Yes; 0=No

15.Number of TB screening *(From Jan.2008 to July 2011)*	##
16.Patients screened for TB *(at the most recent visit by July 2011)* 1. TB symptom 2. Sputum smear 3. CXR	 1=Yes; 0=No If yes, please describe the 1=Yes; 0=No if yes, please describe Cough: 1=yes 0=no Fever: 1=yes 0=no Drenching: 1=yes 0=no Wasting: 1=yes 0=no Others: specify[1] Sample1: 1=positive 0=negative Sample2: 1=positive 0=negative Sample3:1=positive 0=negative 1=Yes 0=No=0 if no skip the question 17 If yes, date: Day/Month/Year
17.Chest x-ray	0=Normal 1=Abnormal consistent TB 2=Abnormal not TB
18. If screening positive referred to TB clinic due to: (Linked to Question 16) Any symptom Smear CXR Prior to ART Prior to IPT	 1=Yes Day/month/year 0=No 1=Yes Day/month/year 0=No 1=Yes Day/month/year 0=No 1=Yes Day/month/year 0=No 1=Yes Day/month/year 0=No
19.If screened positive, was patient refereed to TB clinic for TB diagnosis?	1=Yes; 0=No; 9=Unknown
20.Name of TB center	1=HNTBH 2=NLRH 3=DTUDD 4=DTUDA 5=PNTTB 6=DTUD1 7=DTUD2 8=DTUD4

	Other (please specify)[2]
21.CPT treatment date *(opportunistic prophylaxis treatment)*	Day/month/year
22.CPT stop	Day/month/year
23. Follow-up status at OPC *(by July 2011)*	Alive (by July 2011) Dead Day/month/year Transferred Day/month/year Lost follow-up Day/month/year *(when patient did not show-up after 3 months with non-ART patients and after 6 months with ART patients by July 2011)* ***Linked to Q.13 for ARV*** Unknown *(when patient did not show-up for less than 3 months with non-ART patients and less than 6 months with ART patients by July 2011)* ***Linked to Q.13 for ARV***

[1.] Q.16: Other TB symptom:
Headache
Abdominal pain
Diarrhea

[2.] Q.20: Other TB center
DTUNHBE
TRUONG4
DTUQ9
VTAU
DNAI
BVNHD
DTULBIEN
NINHBINH
MELINH
HAGIANG
BVLSNDHN
BACNINH
HUNGYEN
QNINH
THNGUYEN
NBINH
TQUANG
HDUONG
HPHONG
BAVI
SSON
GILAM

Appendix B: Data to be collected on individual patients at the TB clinic (on referred patients only)*

1. Unique site evaluation ID number *(this is the same number with question1 in the Appendix A)*	
2.Name of TB clinic *(link to question 20 in the Appendix A)*	1=HNTBH 2=NLRH 3=DTUDD 4=DTUDA 5=PNTTB 6=DTUD1 7=DTUD2 8=DTUD4 Other (please specify): see others in page 3
3.Was patient ever been seen in TB clinic	1=Yes; 0=no; 9=unknown
4.When was patient first seen at this clinic	Day/month/year
5.Name of the clinic referred patient *(link to question 3 in the Appendix A)*	+ 01DD=Dong Da clinic +01DA= Dong Anh clinic +0201=District1 clinic +0202=District2 clinic +0204=District4 clinic +Other (please specify): +Unknown *(when this information was not recorded in the patient chart)*
6. If patient self referred to this clinic, please listed	1=Yes Day/month/year 1=Yes Day/month/year 1=Yes Day/month/year 1=Yes Day/month/year 0=No
7.Has the patient diagnosed TB at this clinic?	1=Yes Day/month/year 1=Yes Day/month/year 1=Yes Day/month/year 1=Yes Day/month/year 0=No
8.Number of sputum samples collected for microscopy at the most recent time *(by July 2011)*	#

9.Sputum result: can be up to 6 times Number 1 Number 2 Number 3	 1=Positive; 2=negative 1=Positive; 2=negative 1=Positive; 2=negative
10.Sputum conversation result after initial phase (≥2 months)	0=Negative; 1=positive; 2=not done;
11.The most recent chest x-ray *(by July 2011)*	0=Normal; 1=Abnormal TB; 2=Not performed or 9=unknown *(if it is not in the patient's chart)* If abnormal TB please continue question 12
12.If chest x-ray "abnormal TB", cavity on x-ray	1=Yes=1; 0=no; 9=unknown
13. TB status *(linked to question 9, question11)*	1=smear+; 2=smear -; 3=EPTB; 4=not TB; 5=unknown status (when diagnosis has not been made)
14.Patient started on TB treatment	1=Yes;2= no; if yes, day/month/year
15.Date treatment ended	Day/month/year
16. Treatment outcome	1=Cured; 2=completed; 3=failure; 4=died; 5=default;6= transferred out; 7=change of diagnosis
17.Mortality status after less than 2 months of treatment	1=Alive; 2=dead;9= unknown
18.Mortality status between 2 months and 8 months of treatment	1=Alive; 2=dead;9= unknown
19.Mortality status at the end of 8 month of treatment	1=Alive; 2=dead;9= unknown

*This form should be filled for each successful referral

** Positive result: 1+, 2+, 3+, 1-9 AFB/100 HPF (specific count recorded), negative result: 0 AFB/100 HPF

Appendix C: Data to be collected at HIV OPC clinic

Question	Response
1.What is the estimated percentage of HIV-infected persons routinely screened for TB at each visit What percent ever screened? What percent screened at each visit?	
2. When are HIV-infected patients screened for TB?	1=only at the first visit 2=during every visit 3=prior to starting INH, ARV 4=other ***(check all that apply)***
3. How are persons with HIV screened for TB?	Patient asked about cough > 2 weeks yes=1; no=0 Chest x-ray yes=1; no=0 Sputum smear yes=1; no=0 Sputum culture yes=1; no=0 Others (specify)
4. Are patients screened for other symptoms	Not screen for other symptom=0 Weight loss=1 Night sweat=2 Fever=3 Lymphadenophathy=4 Others=5
5. Where are HIV-infected persons referred for TB diagnosis?	No referral=0 TB clinic=1 Other specify _____
6. How are HIV-infected patients referred to TB clinic	Verbally =1 MOH form=2 Other=3
7. How does this clinic follow-up on TB suspects referred to TB clinic?	Regular communication between TB and HIV by phone or quarterly meeting=1 Information provided by patients=2 Other=3
9. Where are HIV(+) TB patients receiving intensive TB treatment?	TB clinic=1 OPC=2 Other=3
10. Where are HIV(+) TB patients receiving continuation TB treatment?	TB clinic=1 OPC=2 Other=3

Appendix D: OPC clinical staff interview guide: screening for TB among HIV patients

1. What proportion of PLHIVV patients have TB?

2. What is the current policy, guidelines on TB screening of your HIV patients? Do you follow the national TB/HIV SOP? (if yes, please describe the SOP)

Follow the national TB/HIV SOP 8/2007:

Follow the SOP of the ICF/IPT study:

3. What TB services are provided for HIV patients at this clinic?

4. Who is best suited to do TB screening?

5. How are your HIV-infected patients referred to TB diagnostic and treatment services?

6. What are the issues around TB screening for HIV-infected (too sick, TB clinic is far, no transportation fee, TB diagnosis has not been made after several visits?)

7. What barriers do you face in caring for your patients in what you consider to be an adequate TB/HIV care (lab capacity to carry out AFB smear, culture, lymph node or other site aspiration, coordinate with NTP about result, technical consultation of TB and HIV staff, knowledge and skills for clinical management of HIV-associated TB?

Appendix E: Random number generator using Microsoft Excel

1. Create a new blank column (right click→insert new) or use an existing empty column to generate your numbers

2. In the top cell of this column type "=randbetween(a,b)" where a=the lower limit of the range of your random numbers, and where b=the top of the range of numbers. For example, =randbetween(1,100) will generate a randomly selected number between 1 and 100 for the cell.

3. To create multiple random numbers across several cells within your selected number range, grab the cell by the lower right corner and drag downwards.

   NOTE: Any time these generated numbered are copied and pasted they will generate NEW numbers. This also happens when you try to list them in order (and why we were having trouble with this in lab today.)
   - To get around this problem, highlight your randomly generated numbers, copy them, and select "paste special"
   - Select the option to paste Values. This will let you move around and manipulate the numbers without having them change on you.

REFERENCES

Cain, K. P., Anekthananon, T., Burapat, C., Akksilp, S., Mankhatitham, W., Srinak, C., . . . Varma, J. K. (2009). Causes of death in HIV-infected persons who have tuberculosis, Thailand. *Emerg Infect Dis, 15*(2), 258-264.

Cain, K. P., McCarthy, K. D., Heilig, C. M., Monkongdee, P., Tasaneeyapan, T., Kanara, N., . . . Varma, J. K. (2010). An algorithm for tuberculosis screening and diagnosis in people with HIV. *N Engl J Med, 362*(8), 707-716. doi: 10.1056/NEJMoa0907488

Chamie, G. (2010). Tuberculosis as Part of the Natural History of HIV Infection in Developing Countries. *Clinical Infectious Diseases, Clin Infect Dis. (2010) 50 (Supplement 3): S245-S254.* . doi: 10.1086/651498

Dou, Z., Xu, J., Jiao, J. H., Ma, Y., Durako, S., Yu, L., . . . Zhang, F. (2011). Gender difference in 2-year mortality and immunological response to ART in an HIV-infected Chinese population, 2006-2008. *PLoS One, 6*(8), e22707. doi: 10.1371/journal.pone.0022707

Elden, S., Lawes, T., Kudsk-Iversen, S., Vandelanotte, J., Nkawanyana, S., Welfare, W., . . . Wright, J. (2011). Integrating intensified case finding of tuberculosis into HIV care: an evaluation from rural Swaziland. *BMC Health Serv Res, 11*, 118. doi: 10.1186/1472-6963-11-118

Feleke, B., Desai, M., Fantu1, R., Ahmed, J., Demissie, G. W. M., E Vitek, . . . Cain, K. Evaluation of Integrated Management of Adolescent and Adult Illness guidelines for TB/HIV co-management — Ethiopia.

Getahun, H., Gunneberg, C., Granich, R., & Nunn, P. (2010). HIV infection-associated tuberculosis: the epidemiology and the response. *Clin Infect Dis, 50 Suppl 3*, S201-207. doi: 10.1086/651492

Getahun, H., Kittikraisak, W., Heilig, C. M., Corbett, E. L., Ayles, H., Cain, K. P., . . . Varma, J. K. (2011). Development of a standardized screening rule for tuberculosis in people living with HIV in resource-constrained settings: individual participant data meta-analysis of observational studies. *PLoS Med, 8*(1), e1000391. doi: 10.1371/journal.pmed.1000391

Klotz, S. A., Nguyen, H. C., Van Pham, T., Nguyen, L. T., Ngo, D. T., & Vu, S. N. (2007). Clinical features of HIV/AIDS patients presenting to an inner city clinic in Ho Chi Minh City, Vietnam. *Int J STD AIDS, 18*(7), 482-485. doi: 10.1258/095646207781147265

Kranzer, K., Houben, R. M., Glynn, J. R., Bekker, L. G., Wood, R., & Lawn, S. D. (2010). Yield of HIV-associated tuberculosis during intensified case finding in resource-limited settings: a systematic review and meta-analysis. *Lancet Infect Dis, 10*(2), 93-102. doi: 10.1016/s1473-3099(09)70326-3

Martinson, N. A., Hoffmann, C. J., & Chaisson, R. E. (2011). Epidemiology of tuberculosis and HIV: recent advances in understanding and responses. *Proc Am Thorac Soc, 8*(3), 288-293. doi: 10.1513/pats.201010-064WR

MOH Vietnam. (2009). Guidelines: Diagnosis, treatment and prevention of Tuberculosis.

Moore, D., Liechty, C., Ekwaru, P., Were, W., Mwima, G., Solberg, P., . . . Mermin, J. (2007). Prevalence, incidence and mortality associated with tuberculosis in HIV-

infected patients initiating antiretroviral therapy in rural Uganda. *AIDS, 21*(6), 713-719. doi: 10.1097/QAD.0b013e328013f632
Reid, M. J., & Shah, N. S. (2009). Approaches to tuberculosis screening and diagnosis in people with HIV in resource-limited settings. *Lancet Infect Dis, 9*(3), 173-184. doi: 10.1016/s1473-3099(09)70043-x
Sieleunou, I., Souleymanou, M., Schonenberger, A. M., Menten, J., & Boelaert, M. (2009). Determinants of survival in AIDS patients on antiretroviral therapy in a rural centre in the Far-North Province, Cameroon. *Trop Med Int Health, 14*(1), 36-43. doi: 10.1111/j.1365-3156.2008.02183.x
Thuy, T. T., Shah, N. S., Anh, M. H., Nghia do, T., Thom, D., Linh, T., . . . Varma, J. K. (2007). HIV-associated TB in An Giang Province, Vietnam, 2001-2004: epidemiology and TB treatment outcomes. *PLoS One, 2*(6), e507. doi: 10.1371/journal.pone.0000507
UNAIDS. Global Report: UNAIDS Report on the Glolabal AIDS Epidemic 2010.
van't Hoog, A. H., Laserson, K. F., Githui, W. A., Meme, H. K., Agaya, J. A., Odeny, L. O., . . . Borgdorff, M. W. (2011). High prevalence of pulmonary tuberculosis and inadequate case finding in rural western Kenya. *Am J Respir Crit Care Med, 183*(9), 1245-1253. doi: 10.1164/rccm.201008-1269OC
Vietnam. Year-End Report: Performance of TB Control Program in 2010, Direction and Plans for 2011.
Vietnam. (2007). Standard of procedure (SOP) for diagnosis, treatment and management of TB and HIV in Vietnam.
Vietnam. (2009). Yearly report of Vietnam Administration of HIV/AIDS Control (VAAC).
Vietnam. (2011). Vietnam Administration AIDS Control report.
Vietnam. (2012). Vietnam Administration of AIDS Control (VAAC) report, 2012.
Vijay, S., Kumar, P., Chauhan, L. S., Rao, S. V., & Vaidyanathan, P. (2011). Treatment outcome and mortality at one and half year follow-up of HIV infected TB patients under TB control programme in a district of South India. *PLoS One, 6*(7), e21008. doi: 10.1371/journal.pone.0021008
WHO. (2004). Interim policy on collaborative TB/HIV activities. *WHO/HTM/TB 2004.330*.
WHO. (2007). Improving the diagnosis and treatment of smear negative pulmonary TB and extrapulmonary TB among adults and adolescens.
WHO. (2009a). Global Tuberculosis control: epidemiology, stratery, finaning, WHO report 2009.
WHO. (2009b). WHO Three I's Meeting.
WHO. (2010). Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resourceconstrained settings.
WHO. (2011). 2011 GLOBAL TUBERCULOSIS CONTROL.