PROCESS EVALUATION OF INH PROPHYLAXIS PROGRAM FOR HIV POSITIVE PATIENT IN THE ENARP SITE

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A thesis submitted to the school of graduate studies of Addis Ababa University In partial fulfillment of the requirements for degree of master of public health

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Declaration

I, the undersigned, declare that this thesis is my original work, has not been presented for a degree in this or another university and that all sources of materials used for this thesis have been fully acknowledged.

Name ----------

Signature----------

Place: ----------

Date of submission----------

This thesis work has been submitted for examination with my approval as university advisor

Dr Alemayehu Worku (PHD)

Advisors name ----------

Signature

Acknowledgement

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List of abbreviations

1. **AAU**---------- **Addis Ababa University**
2. **AFB**---------- **Acid Fast Bacilli**
3. **AIDS**---------- **Acquired Immuno- Deficiency Syndrome**
4. **BCG**---------- **Bacillus Calmette-Guerin**
5. **CDC**---------- **Communicable Disease Control**
6. **DOT**---------- **Directly Observed Treatment**
7. **ENARP**---------- **Ethio- Netherlands Aids Research Project**
8. **HIV**---------- **Human Immuno-Deficiency Virus**
9. **ID No**---------- **Identification Number**
10. **INH**---------- **Isoniazid**
11. **IPT**---------- **Isoniazid Prophylaxis Treatment**
12. **PPD**---------- **Purified Protein Derivative**
13. **PT**---------- **Preventive Treatment**
14. **SPSS**---------- **Statistical Package for Social Scientists**
15. **TB**---------- **Tuberculosis**
16. **TST**---------- **Tuberculin Skin Test**
17. **TNF**---------- **Tumor Necrosing Factor**
18. **UNAIDS**---------- **United Nation program on HIV/AIDS**
19. **VCT**---------- **Voluntary Counseling and Testing**
20. **WHO**---------- **World Health Organization**

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Abstract

HIV infection is the greatest known risk factors for the development of active tuberculosis in individuals latently infected with tuberculosis, and there is now strong evidence for the efficacy of prophylaxis treatment in the prevention of TB in HIV infected individuals.

Implementation of Isoniazid PT in developing country presents several problems; therefore this study tried to assess the IPT program implemented in the ENARP sites and its applicability in other VCT centers. The objective of this study was to evaluating operational aspect of INH prophylaxis program for Human immuno-deficiency virus positive patients in the ENARP sites. A crossectional study supplemented with review of available cohort data was conducted. All HIV positive cohort participants, in the two ENARP sites, were included

Of 132 HIV positive participants 61(21.6%) were selected for INH prophylaxis program based on CD4 count who had less than 350 cell/mm3. Among 71(53.8%) participants who were not included in the IPT program, 13(18.3%) died, 37(52.1%) subjects were excluded due to their CD4 count, 13(18.3%) due to recent TB treatment history and 5(7.04%) refused to participate in the IPT program. TST were done to identify the most benefited with IPT, 44.3% were anergic and 26.2% were positive. Of 61 participant 57.4% were completed PT, 24.6% discontinued and 7(11.5%) subjects were on treatment during data collection. The study uptake looks appropriate in that the risk of having TB increases with the CD4 count less than 350 cell/mm3, OR=1.12,95% CI (1.06-1.28) .TST induration size had significant correlation with CD4 count using linear regression model and Pearson correlation analysis. Except 9.8% the rest 84.4% got health care support from the project to enhance adherence, 92.8% were agree on that ENARP staffs has good patient approach. And 86.6% were appreciate the service given to them and recommend to others. Of 61 participants 19(31.1%) missed scheduled appointment. Among 32 who completed 5(15.6%) of them missed ingesting daily pills only for a day. And INH metabolites test were positive in 80.4% of study subjects. IPT doesn't have effect on CD4 count and weight using Wilcoxon sign rank test. Ninety-three point seven of the cost of the program spent before the patient starts PT. The benefit due to PT exceeded the cost of the program by 4.99 factors. Study uptake looks appropriate, screening for active TB was performed as it was recommend by WHO. Even though different methods used to select those most benefited, it needs further evaluation. Adherence to treatment in the project favorably compares with other similar study. Therefore the project has shown the feasibility of IPT in our context.

I- Introduction

The decline in mortality rates from tuberculosis early in the century led some to predict the eradication of the disease in the developed countries. This prediction was based on the idea that infection with tubercle bacilli was harmless and that only re-infection was dangerous. It was reasoned that tuberculosis would disappear when isolating all infectious cases could prevent re-infection. It is now clear, however, that clinical tuberculosis develops largely from reactivation of dormant infections. Therefore, eradication must await the natural disappearance of tubercle bacilli from the population. It is hoped that this process can be accelerated by the judicious use of Isoniazid as prophylactic therapy.

In a setting with high risk of tuberculosis infection, the rate of recurrent tuberculosis infection after curative treatment is higher in HIV infected individuals. HIV increases the risk of recurrent tuberculosis because of an increased risk of re-infection. Recurrent tuberculosis might be due to either relapse or exogenous re-infection. The contribution of re-infection to the epidemiology and pathogenesis of tuberculosis has important implications for tuberculosis control, vaccine design, chemoprophylaxis, and assessment of treatment regimen. HIV positive individuals infected with Mycobacterium tuberculosis might rapidly progress to active tuberculosis, they might also be at high risk of developing infection after active tuberculosis disease and this positive patient might have low immunity to subsequent infection (1).

HIV infection is the single greatest risk factor for the reactivation of latent mycobacterium infection. Although it is still controversial, there is growing evidence that TB may stimulate HIV replication and so speed the progression of HIV disease (2). As

HIV infection can accelerate the natural progression of TB by diminishing cell mediated immune response; host immune reaction to TB can also enhance HIV replication and accelerate HIV disease progression. The mycobacterial antigens activate antigen specific CD4+ T cells releasing interferon gamma, which then activates host macrophages and enhances their ability to contain mycobacterial infection. The activated macrophages release proinflammatory cytokines, such as tumor necrosis factor and interleukin-1. These cytokines enhance HIV replication in monocyte cell lines in vitro. Consequently strategies to control the dissemination of tuberculosis and prevent its occurrence in HIV infected patients may also have great influence on survival. And the rate of recurrent tuberculosis is higher in HIV positive individuals than in HIV negative individuals. And this also has adverse public health outcomes in developing countries suffering from dual HIV and tuberculosis epidemics. Cure rate, in the treatment of recurrent tuberculosis are substantially lower than in the treatment of new tuberculosis. Re-treatment regimens for patients with recurrent tuberculosis are larger and more expensive than first line tuberculosis regimen and further strain the budget of TB control programs in developing countries.

Mantoux testing is widely performed for identification of infected cases in high prevalence countries. Its cutoff value depends on the purpose of testing and the population tested. In relation to the use of IPT in HIV infection, the cutoff value of 5 mm is recommended as IPT initiated according to this interpretation had led to significant protection from active TB, in places with or without a high incidence of TB and with or without routine Bacillus Calmette Guerin vaccination (3).

In high prevalence countries a large proportion of the population is expected to have a positive reaction which limits the specificity of Mantoux test as a screening tool for active tuberculosis. Further more, skin reaction may not correlate with disease severity

Due to epidemiological difference between the industrialized and developing countries, strategies for the diagnosis of TB need to be developed. In low prevalence area heavy reliance was placed on the history of close contact and on positive skin test. In high prevalence countries case contact and skin test was found to be less important.

An early tuberculin survey had shown that there was higher rate of anergy among the HIV positive than HIV negative individuals, including that tuberculin testing in this population would play a limited role in assessing individuals with a latent infection. However tuberculin reaction may be useful in identifying those subjects who would benefit the most from preventive therapy because they are both infected with mycobacterium tuberculosis and not anergic (4)

The annual risk of tuberculosis in the HIV infected adult varies with tuberculin skin test status and ranges from 0-4.5% in tuberculin skin test negative individuals to 5-16% in tuberculin skin test positive individuals (5). In developed countries the chance tuberculin reactor developing clinical tuberculosis from a dormant infection is greater than that of a non-reactor acquiring an infection. Therefore, it is preferable to be tuberculin-negative unless the positive reaction is induced by vaccination. On the other hand, living in the country of high prevalence, a non-reactor would be more likely to become infected than a healthy reactor. Under these circumstances, it would be preferable

to be tuberculin-positive and to have the immunologic protection against acquiring a new infection.

Because of this relation ship, there has been a dramatic increase in the incidence of TB and TB related deaths in the last 15 years in countries with a high prevalence of TB and HIV. This rise is leading to loss of credibility among health care staff, patients, and the wider community. Reducing death from tuberculosis will require a strengthening of tuberculosis control efforts and research focused on improving the care of HIV positive patients.

There is now strong evidence from several randomized controlled trials for the efficacy of preventive therapy in the prevention of tuberculosis in persons infected with the human immuno-deficiency virus. Prior to the HIV epidemic, the use of IPT in countries with high prevalence of TB was limited to child hood contacts of active cases, since these children have a higher risk of progression to disseminated and sever form of disease. Candidates for TB Preventive Therapy among HIV-infected patients include:

1. All HIV-infected persons with positive TST reactions (equal or greater than 5-mm induration), who have not previously received treatment for M. tuberculosis infection should receive TB preventive therapy regardless of age.

2. HIV-infected persons who have had recent contact with infectious TB patients should receive TB preventive treatment, regardless of age, results of TSTs, or history of previous TB preventive treatment.

3. HIV-infected persons with a history of prior untreated or inadequately treated past TB that healed and no history of adequate treatment for TB should receive TB preventive treatment regardless of their age or results of TSTs.

4. Primary prophylaxis for TST-negative, HIV-infected patients with an ongoing and unavoidable high risk of exposure to M. tuberculosis for the duration of the exposure time (residents of prisons, jails or homeless shelters in which the current prevalence of TB is high) should be considered in some situations.

Preventive therapy against tuberculosis is the use of one or more anti-tuberculosis drugs given to individuals with latent infection of mycobacterium tuberculosis in order to prevent the progression to active disease. Studies of feasibility of IPT demonstrate that the process required targeting appropriate individuals, to exclude active tuberculosis, to deliver preventive treatment and to achieve adherence.

The rational for the use of one or more anti-tuberculosis drugs as preventive therapy is that, INH is cheap and bactericidal against both extra-cellular and intracellular bacilli. In latent TB infection, the bacterial burden is small, allowing the possibility of monotherapy it reduces the small population of dormant bacilli in the body to such levels that the chance of reactivation of this latent infection is significantly reduced.

II- Literature review

2.1Global situation

TB has become the major HIV related disease in sub-Saharan Africa, as high as 70% of HIV positive patients developing TB. As T4 lymphocytes become depleted in HIV infection, the patients are put at risk of reactivation, reinfection and primary

infection with TB. The chance of active TB in HIV increases from 5-10% over a person's lifetime to 8% per year (6)

By the end of 2000 about 1/3 of the 36.1 million people living with HIV/AIDS worldwide were co-infected with tuberculosis, and nearly 95% co-infected persons were living in developing countries. Global estimates indicate that 11%(640000) of the new TB infection that occurred in adults in 2000 were attributable to HIV infection .An HIV infection prevalence of 10% in a community will cause an excess of 40% in TB cases. Some 10% of TB infected HIV positive persons develop TB with in one year (6).

Sub-Saharan Africa, especially the southern region of the continent, is in the grip of a devastating HIV epidemic. Inextricably linked to HIV infection is a twin epidemic of tuberculosis, which threatens to spiral out of control, with serious repercussions for both immuno-compromised and immuno-competent individuals.

2.2-Ethiopian situation

TB is a serious public health threat in Ethiopia, and the advent of HIV epidemic may have a devastating effect on all effort carried out so far to improve the control of the disease, because HIV is the driving force behind the tuberculosis epidemic in sub-Saharan Africa, and stopping the AIDS epidemic is one of the keys to reducing tuberculosis in this region

Forty-two percent of 166TB cases selected from hospital in Tigrai region were HIV positive. A cross-sectional survey of smear positive patient in Addis Ababa showed 45% co-infection with HIV. In 1990, 6.6% of TB patient in the armed forces hospital were HIV positive. In 1994, 44% of 450 TB patient in shashemene (Oremyia region) were HIV -positive (6).

Efforts in the past 20 years to control tuberculosis had been showing some success, however, of late, the number of tuberculosis case in Ethiopia has been rising rapidly as consequence of the spread of HIV. Estimated number of tuberculosis cases which was obtained by taking into account the compounding effect was approximately 50000 in 1984 increased to 82680 in 1989 and in1994 it was 126830.By the year 2014 the number of tuberculosis case is projected, and it will rise to 238820 (7).

In developing countries, preventive therapy has not received much emphasis. Diagnosis, treatment and cure of smear positive cases of TB using the DOTS strategy is considered to be the most important control measure and likely to have the most impact on the incidence of TB. IPT is not an alternative to the DOTS strategy for controlling TB even in areas with a high prevalence of HIV. However it is appropriate to consider PT should have as an addition to DOTS in countries burdened by the dual epidemic of HIV and TB, with the advent of HIV infection TB has emerged as a major opportunistic infection particularly in developing countries. And active TB in HIV infected patient enhance HIV replication and following the initiation of TB treatment, plasma viral lode continued to increase and remained persistently elevated, despite effective treatment of TB, for as long as one year or more (8). Therefore this may contribute to HIV disease progression and large numbers of patients with tuberculosis with out commensurate increase in resources reduce the quality of a patient care (9).

In countries like ours, tuberculosis is a major public-health problem and co-infection is frequent, but many people would rather not know that they are HIV positive, as they believe that there are no medical benefits and that the psychological effect of knowing one is positive is likely to lead to a more rapid demise and progress to AIDS. In

order to increase access to VCT, it is important to publicize the fact that IPT has substantial benefits for persons who are infected both by HIV and TB. The main drawback to a TB PT that are of concern in developing countries are the possibility of the development drug resistance to INH and the drain of financial and human resource away from the treatment of smear positive pulmonary TB patient which remains the most important objective of TB control efforts world wide

Before the HIV era, the efficacy of IPT in person at risk for tuberculosis had been established in numerous controlled trials in different countries and identified that efficacy was influenced by adherence to therapy and ranged from 25-92%, but was over 90% where adherence was guaranteed and it is thought to reduce incidence of TB by more than 80%. Recently, a randomized clinical trial has shown that IPT given to dually infected individuals reduced the incidence of tuberculosis and delayed the onset of HIV related disease and death (10,11). The protective effect appeared to be greatest in subjects who were tuberculin reactive and in those with higher lymphocytes count or hemoglobin level, Person with more advanced immuno-suppression are less likely to benefit from preventive therapy.

Chemo-prophylaxis of tuberculosis may have an important impact on survival of HIV infected patient in population with high prevalence of myco-bacterium tuberculosis infection, especially in developing countries where the incidence of tuberculosis is high and anti-retroviral treatment is not typically available. The potential benefit of providing chemo-prophylaxis for patients with HIV infection in this setting may be at least two fold; the direct effect of prolonged survival in person who receive chemo-prophylaxis and

possibly the effect of preventing transmission of mico-bacterium tuberculosis to others (3).

But implementation of preventive therapy requires the identification of HIV infected individuals, this is difficult, as they are often asymptomatic and don't present for VCT HIV testing. Now a days delivery of PT limited by the number of sites where sufficient number of people know their HIV status, or where there is sufficient demand for and capacity of VCT services. PT should therefore be promoted as an intervention for those living with HIV rather than as a primary strategy to control the public health burden of tuberculosis.

Possible sites for implementation of tuberculosis preventive therapy service include voluntary counseling and testing centers for HIV, occupational health clinics for military personnel, hospital or company workers. These sits can help as an entry point for access to a range of tuberculosis; HIV care and prevention intervention with the goal of reducing the burden of these diseases in communities most affected. The integration of HIV voluntary counseling and testing centers and AIDS care organization with TB treatment programs may enhance access to TB prevention and treatment but it seems desirable to link education on tuberculosis and prevention to pre and post test counseling for HIV testing (12). Thus a prerequisite for a prevention therapy is an established and operational VCT sits, where clients voluntarily attending, can be educated about tuberculosis. But establishing VCT specifically to deliver IPT will not be a cost effective approach

Knowing this fact, increase utilization of VCT service and they are more likely to seek VCT if they perceive that the personal benefits outweigh the disadvantage (13). And

prevention of tuberculosis should be considered that as one of the feasible medical interventions for HIV infected individual and that should be taken as part of package of care for people living with HIV/AIDS.

Due to perceived poor cost-effectiveness and high-risk re-infection, IPT has never been part of the public health practice in developing countries, although it is widely used in other place. However the increased risk of developing active tuberculosis in HIV infected person might make IPT cost-effective.

When we are trying to implement such a program like IPT, we have to ask our selves about safety, efficacy and effectiveness of the intervention programs. Strong economic case exists for prioritization of preventive intervention and tuberculosis treatment. Where potentially exclusive alternative exist, cost-effectiveness analysis points to an intervention that offers the best value for money. Cost-effectiveness analysis is an essential component of informed debate about priority setting for HIV/AIDS. To ensure that any new resources have the maximum possible effect on the epidemic, cost-effectiveness should be considered in the design of strategies for prevention, care and support.

The question of efficiency to tuberculosis prevention and control can be seen as follows. There are different ways that we can reduce the burden of tuberculosis disease. Developing better mechanism, such as more effective treatment regimens, an effective vaccine, or improved diagnostic tests, expanding the use of existing tools, either option would require increased financial and human resources. And finally giving finite resource and available tools and resources more efficiently reduce burden of TB.

There is little published material on the cost-benefit assessment of preventive therapy. One study modeled on the example of Zambia and assuming a 25% probability that an HIV infected person will develop TB during their lifetime. An isoniazid efficacy of 60%, and assuming that preventing one case of open TB will prevent five additional cases of TB, the benefit/cost ratio was 1.71,i.e, the benefit exceed the cost by a significant margin (14). Economic analysis enables TB control program to identify more efficient uses of their resources. Implementation of preventive therapy is manageable in industrialized countries because it is affordable and the infrastructure is in place to screen, treat and monitor patients on a regular basis, its implementation in developing countries like ours presents several problems.

WHO recommended that HIV infected person who live in settings with high rate of TB is considered candidate for TB prevention therapy (15). Based on this recommendation since 1992, selected HIV positive patient in the ENARP project started to take INH prophylaxis treatment. The main objective of the IPT program stated as follows:

- To reduce the development of active TB in HIV positive population
- To determine which patient benefit optimally from IPT
- Evaluate outcome of IPT during a 5 year follow up after 9 months preventive treatment or until CD4 count reaches >350 cell/mm^3,
- Determine drug resistance rate in subjects whom received IPT and subsequently develop TB.

In Ethiopia only in this project IPT was given for the HIV positive patient as a prophylaxis from tuberculosis infection. Evaluating the success and failure of IPT program initiated by this project using its two cohorts, gives insight how to implement such kind of care for those who are in need of it in similar setup and for continuation and expansion of the program.

Identification of HIV patient, strong counseling system, willingness to participate in the IPT program, capacity to exclude active tuberculosis, drug supply,

monitoring adverse drug reaction, these and other activities indicate how the ENARP sites are strong enough to use for feasibility study of IPT. However to implement IPT program in large scale, feasibility issue such as identification of large numbers of HIV-infected persons, active HIV counseling and testing program, and public interest in obtaining such services, exclusion of active TB, identification of those most likely to benefit, supervision of preventive therapy, monitoring of adverse drug reaction, need to be resolved. Due to that evaluating of this program can provide clear information about the given PT, and idea on how to provide treatment for prevention of active TB in a VCT center where candidates for TB prevention therapy are easily identified, and how to integrate VCT service with IPT program.

III- Objective of the study

Main objective

To assess operational aspect of the isoniazid prophylaxis program for persons infected with HIV in the ENARP project

Specific objectives

1. To assess study uptake, the appropriateness of selection criteria, screening procedure for HIV and active tuberculosis.
2. To assess the appropriateness of drug administered, type of drug used as a prophylaxis, duration of treatment, adverse drug effect, and benefit of prevention therapy
3. To know factors affecting and enhancing adherence to treatment.
4. To assess the cost incurred by implementing the IPT program and its applicability in a VCT setting.

IV- Method and design

Design: A cross-sectional survey supplemented with review of data

4.1 Setting

In the two Ethio-Netherland AIDS Research Project sites.

The Ethio-Netherlands AIDS research project (ENARP) is a bilateral project between the government of Ethiopia and the Netherlands. The main scientific agenda of ENARP has been to set up a large cohort for studying HIV infection progression, and eventually for future testing of anti-retroviral drugs or vaccines and interventions like prophylaxis of opportunistic infection in the Ethiopian context.

The two sites, Akaki and Wonje were selected based on three main criterias, i.e. a sufficient HIV prevalence (around 10% or more), a stable population (median duration of residence longer than 20 years), and high acceptability of long term research project on HIV (more than 95% of participants were willing to participate in the cohort) (16).

Cohort participant living with HIV/AIDS in the ENARP research setting, whose CD4 count dropped below 350 cells/mm^3 were offered preventive treatment for development of active tuberculosis. HIV patients, whose CD4 count above 350 cells/mm^3 at the moment and not consider participant of IPT, when they drop their CD4 below 350 cells/mm^3 gradually will join the IPT program.

Cohort participants were given morning blood sample every six months. HIVSPOT and ELISA were used for screening purpose and all positive and discrepant results were confirmed by a western blot assay. Lymphocyte subsets were determined by flow cytometer using a FACSCAN and assessment of viral load in plasma was done using the nuclisens assay, which has a detection level of 80 copies/ml. All participants

attended an individual HIV pre and post test counseling. And session were available to the study participants at any time five days per week, during which their HIV test results and other related matters like TB could be discussed.

4.2- Study population

All HIV positive participants of the two-cohort project site were involved in the current study. Among 132 HIV positive participants, the project has made selection for INH prophylaxis using the following procedure

Health education was given to all cohort participants concerning IPT.

- HIV positive participant with CD4<=350cells/mm^3 or CD4 <=20% were selected
- Those who are eligible were skin tested with PPD
- Screening for active TB history/physical examination
- Three sputum examination for AFB, store sputum for culture in case of out break
- Chest X-ray
- Liver function test before treatment

Sixty-one participants who fulfilled selection criteria, who were willing to participate in the IPT program, whose CD4 count below 350 cell/mm^3, free from active TB and past tuberculosis history, and free from INH contraindication were selected by the project and given INH 300 Mg, including pyridoxine 50Mg per day. Treatment was self-administered. Supplies were provided monthly. Participant who took more than 80% of INH tablets or who completed 9 months of regular follow up considered as completed. Instructions were given to all participants on signs and symptom, related to adverse reaction to the drug .The participant was asked to return immediately to the site clinic to seek medical help in the event of any adverse reaction developing. To ensure high

compliance rate, for those who missed appointment, the project assignee nurses whom actively traced and made visits to clients working place. If some one missed to collect his drug on the date of appointment, they were traced and interviewed by nurses in order to determine the reason for missing the appointments and encouraged to resume treatment.

4.3-Data collection

In this evaluation study to have more relevant information, in addition to the review of available data in the two cohort sites, all HIV positive participant of the two cohort sites including those who are eligible for IPT were invited and interviewed, on their willingness to participate on the IPT program, past tuberculosis history, knowledge and reason for missed treatment, drug administration and side effect etc. Review was done on CD_4 count, and viral load. For this purpose, pre-tested, structured questionnaire was prepared in English and translated in to Amharic language for better understanding. Four interviewers and two supervisors were recruited from the two-cohort sites and two-days orientation including appropriate guidelines was given in their respective site concerning relevant issue of the research, basic concept of IPT, how to conduct interview and technical problems on the questionnaires. Problems that were raised during pre-testing of questionnaire were properly handled. Based on the finding of the pre-test, questionnaire was revised. In part two, question number two, before correction it was put like this (do you ever attend health education) and it was corrected by adding (if no go to Q-8), and the time needed to fill the questionnaire was adjusted.

4.4-Operational definition

Evaluation: is the systematic gathering of information in order to make choices among alternative course of action and help us to improve and upgrade the quality by providing feedback on success and failure.

Process evaluation: is a type of evaluation, which responds for the question (how did or does) and compares the manner in which a program is operated against the plan for the program, and it is operations oriented

Refusal: when the subject refused the treatment with out having started taking INH

Completed: when INH had been taken for the required period (9 months)

Defaulter: when the patient did not attend scheduled visit for a period of one or more months after the appointment date, and did not respond to reminders on at least three occasions.

Liver intolerance: increase in SGPT, SGOT, and alkaline phosphate of more than 3 times the base line value were considered to indicate a degree of abnormality of liver function

Adherence: number of persons started on preventive therapy and number completed.

Scheduled attendance: considered if the attainder could collect drug on the date of appointment

Sufficient attainder: considered if the attainder could collect 67% of his total treatment or more than 5 months of treatment

Anergic: Non reactive skin reaction for PPD test.

Normal skin reaction was taken, a reaction of skin with in the range of 1-5mm

Positive skin reaction was considered when the skin reaction ranges above 5mm.

4.5-Variables

Independent variables

Age at enrolment

Sex

Economic status

Educational background

Marital status

Family size

Enrolment weight

Problems which was addressed

Dependent Study variable.

History/physical examination

BCG scar presence

Lab-investigation sputum for AFB

PPD skin test

Liver function test

Chest X-ray

The setup and organization of resources at the two sites

Clear program objective

Staff approaches to the patient

Administrative support incentive for patients for adhering to the program activities

Drug collection and follow up assessment

Drug and supplies

Self-administered treatment

Evaluation of Side effect of the drugs (hepatotoxicity, peripheral neuropathy)

Adherence assessment

Attendance at scheduled follow-up appointments

Dispensing records

Counting of unused pills at the end of every month

Self reported days for which pills were not ingested

Random urine assay for INH metabolites

Defaulters

Tracing mechanism

CD_4 count and viral load

Cost incurred by the project to implement the IPT program

4.6-Data management

To ensure good quality of information there was supervision by the principal investigator. The two cohort's physicians were assigned as supervisors in their respective sites. Both the principal investigator and the supervisors edit the completed questionnaires before entering the data in to computer.

4.7- Statistical analysis

Data was entered, cleaned and analyzed using Epi info (version 6.0) and SPSS (statistical package for social scientists) version 10, computer software. Mainly descriptive statistical method was used for the description of the findings. Comparison of proportions was done by means of X^2 tests with Yates correction or Fishers exact test when the assumptions of chi-square are not fulfilled. Effect of IPT on CD4 count, viral load and weight before and after treatment were analyzed by Willcoxon signed- rank test, Pearson correlation were used to investigate correlation between CD4 count and tuberculosis skin test reaction

4.8-Ethical considerations.

This research was conducted using available data collected in the two cohort sites and interview with the respondents, who are eligible for the study, so ethical clearance was obtained from faculty of medicine AAU, and ENARP ethical and clearance

committee. In addition verbal consent from respondents was obtained during the time of interview. Anonymity and confidentiality were ensured for information obtained from study subjects.

Dissemination and utilization of result

The result of the study will be submitted to AAU department of community health, ENARP, TB center and other stakeholders. Main finding will be published in a reputable journal.

V- Result

During the study period of February 1997 up to 29 December 2003, a total of 1888 employee of two factory workers were admitted to the ENARP cohort, primarily to investigate the natural history of HIV and its disease progression. For these purposes, surveys were carried out in different areas and two sits were selected based on three main criteria, sufficient HIV prevalence, stable population and a high acceptability of long term research on HIV/AIDS.

All participants in the cohort screened for HIV every six-month. HIV positive prevalence at entry was 156 (8.3%). Gradually 23 sero-converters were observed among HIV negative cohort participants, making the incidence rate of 2.3 per 1000 person years (PY).

With in the above-mentioned period of time, among all cohort participants 83 deaths were observed out of which 67 (80.7%) deaths were HIV positive participants. Sixteen deaths were among HIV negative cohort participants. Out of HIV positive deaths, 26 were attributed to tuberculosis and TB related problems (X^2= 504.79; $p < 0.00001$). Therefore the risk of dying due to tuberculosis among HIV positive participants is higher than HIV negative cohort participants.

During the initiation of prophylaxis program, total HIV positive participants were 132.Based on HIV status and CD4 count, 61 individuals were selected for IPT. The rest 71 participants were excluded from the IPT program due to different reasons. Out of those who commenced PT, 7 participants were died, four individuals were died during the treatment period, and 3 of them after completion the PT. Among those who were excluded, 13 deaths were observed.

For the evaluation of INH prophylaxis program, a total of 132 cohort participant's clinical data were reviewed. Out of these, 112 alive HIV positive participants were administered structured questionnaire to assess operational aspect of isoniazide prophylaxis program in the two ENARP cohort sits. For some reason we included 7 individuals who died after commenced PT, to 112 alive participants. The enrolment detail displayed in table-1

Figure -1 -cohort profile.

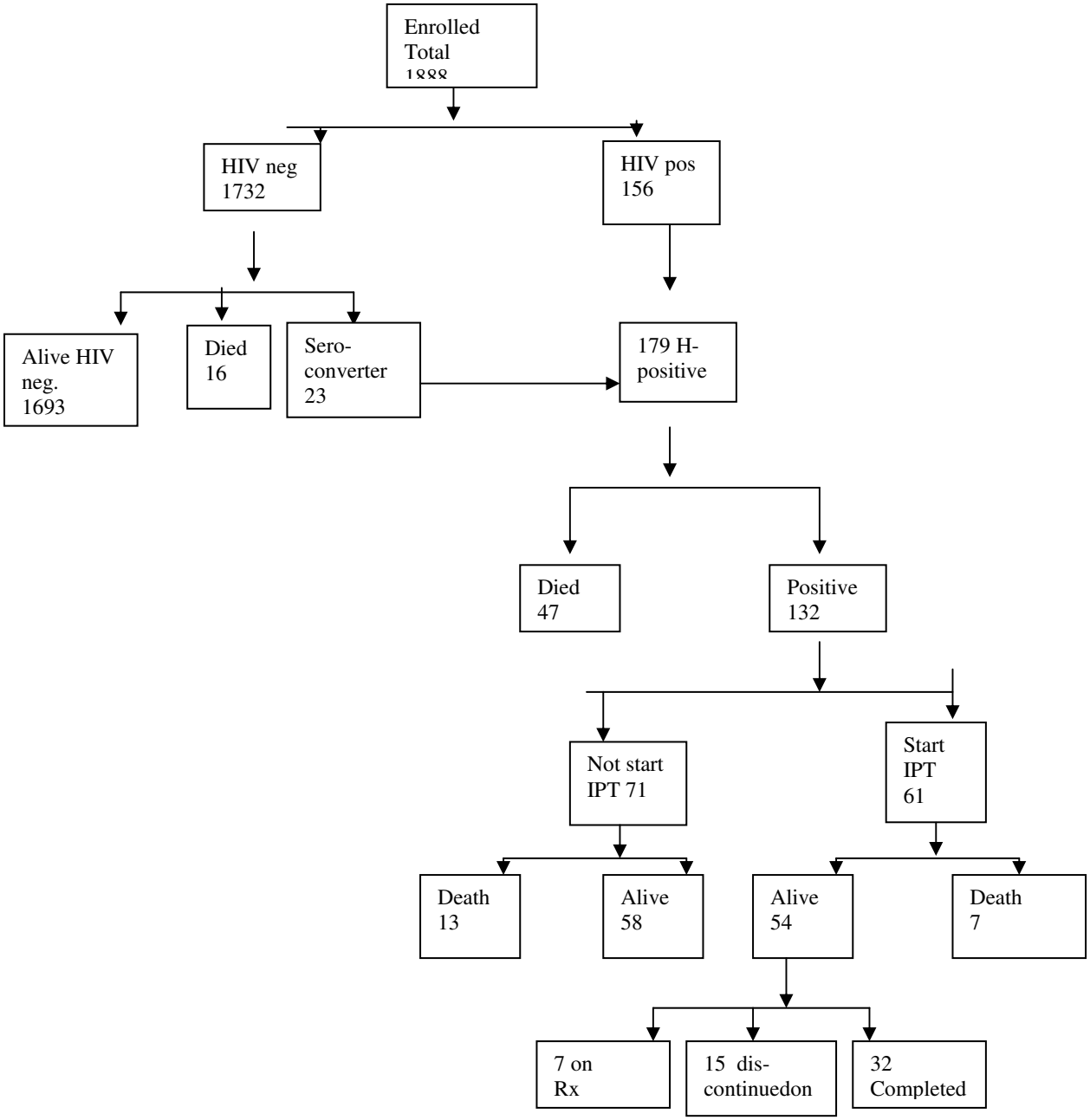

Table-1-Socio demographic characteristics of subjects at enrolment to the study.

Base line characteristic	Number	Percent	Mean	Range
age			38.7	25-51
Sex				
Male	71	(59.7)		
Female	48	(40.3)		
Total	119			
weight			57.9	34-87
BCG				
Yes	23	(37.7)		
No	38	(62.3)		
Total	61			
TST				
Anergy	27	(44.3)		
Normal	18	(29.5)		
Positive	16	(26.2)		
Total	61			
Educational background				
Not able read and write	24	(21.4)		
Able read and write	12	(10.7)		
Grade 2-6	23	(20.5)		
Grade 7-12	43	(38.4)		
12 plus	10	(8.9)		
total	112			
CD4 count			308.7	24-974
CD4>350	38	(31.9)		
CD4 between 200 and 350	47	(39.5)		
CD4<200	34	(28.6)		
Total	119			
viral load			80774.83	80-640000
Marital status				
Married	88	(73.9)		
Divorced	7	(5.9)		
Widow	12	(10.1)		
Separated with out divorce	5	(4.2)		
Not married	7	(5.9)		
Total	119			
Income				
Below 200 Birr	15	(13.4)		
From 200-500 Birr	59	(52.7)		
Above 500 Birr	38	(33.9)		
	112			
Family size			4.7	1-10

One hundred twelve alive HIV positive participants, 61 participants started IPT, 119 those who are alive and including 7 participants who died after commencing IPT

Socio-demographic characteristic Total number of participants reported in the table, (for sex, CD4 count, viral load, and marital status) was considered for those who are alive and died after commencing PT. BCG and TST were considered only for those who started PT.

Seventy-one (59.7%) informants were male and the majorities, (73.9%) of them were married. The mean age of the respondents was 38.7 and ranging between 21 and 51 years. Of 112 alive informants (38.4%) had educational background between 7-12 grade and 21.4% of them not able read and write.

The mean number of family size was 4.73 $\pm$ 0.2, and ranging between 1 and 10. Fifty-nine (52.7%) of study subjects gain income of 200 Birr up to 500 Birr per month. The mean income was 502.80 $\pm$ 36Birr and ranging between 0 and 1750 ETB.

Of 61 study subject, who started prophylaxis treatment 23(19.3%) were vaccinated with BCG during their infancy and identified BCG scare. The rest 38 (31.9%) did not have BCG scare. In 25 individuals who completed treatment and in 10 of discontinued individuals BCG scare were not found. Of 20-study subject who had history of tuberculosis in the past two years and earlier, BCG scare was found in 3 only.

Table-2 Characteristics of study participants stratified by CD4 count.

No	characteristics	CD4>350	CD4<350
		n(%)	n(%)
1	**Age**		
	Below 35	12 (31.6)	21 (28.4)
	Above 35	26 (68.4)	53 (71.6)
	total	38	74
2	**Sex**		
	Male	20 (52.6)	51(63.0)
	Female	18 (47.4)	30 (37.0)
	total	38	81
3	**Tuberculosis history**		
	Before 2 years of PT program.	1 (33.0)	6 (35.3)
	With in 2 years of PT program.	2 (66.0)	11 (64.7)
	Total	3	17
4	**TST**		
	Anergy	-	27 (46.6)
	Normal	-	18 (31.0)
	Positive	3 (100)	13 (22.4)
	total	3	58
5	**BCG**		
	Yes	2 (66.7)	21 (36.2)
	No	1 (33.3)	37 (63.8)
	total	3	58

Table-3 Age and sex distribution of alive participants in the two cohorts.

Alive participants, Age and sex in the respective sites.	Akaki	Wonje
	n(%)	n(%)
Alive HIV positive participants	69(61.6)	43(38,4)
Sex		
Male	32 (28.6)	37 (33.0)
female	37 (33.0)	6 (5.4)
Age		
Below 35 years	19 (27.5)	14 (32.6)
Above 35 years	50 (72.5)	29 (67.4)

2. Screening for HIV

Identification of HIV infected person is basic for implementation of preventive therapy. All participants attended an individual HIV pre and post test counseling. And session were available to the study participants at any time five days per week, during which their HIV tests results and other related matters like TB were discussed. Type of health education attended and lessons learnt about tuberculosis prophylaxis were assessed in the study-subjects.

2.1 Health Education attended and heard about tuberculosis prophylaxis

Of the 109 respondents, who attended health education 106 (97.2%) had heard about tuberculosis prophylaxis. Informants said that the staff had explained about the regimen of the drug, the need to take drug regularly, the danger of taking drug with interruption, and possible side effect, including when to seek medical care. The rest 3 (2.8%) participants never heard about IPT (X^2=194.7; P<0.00001). There is significant difference in proportion among those who heard and not heard about prophylaxis treatment.

3. Screening for active tuberculosis

After preliminary acceptance by the study subjects, HIV positive patients were clinically evaluated for the presence of active and past tuberculosis history.

3.1 Contact with TB patient and past TB history

Of the112 study subjects, 29(25.9%) had contact with TB patient either in their Own family or in their working area. Of the 20 (17.9%) individuals who had past TB history, 7 (35.0%) were treated for tuberculosis 2 years before the initiation of TB

prophylaxis program. Thirteen (65.0%) of study subject had history of tuberculosis, and they were treated with in the recent two years of program initiation .The rest 92 (82.1%) doesn't have history of tuberculosis

Of the 83 study subject who denied history of close contact with TB patient 3 (3.6%) developed TB before 2 years and 10 (12.04%) developed TB with in the last 2 years period. There is no statistically significant association between place of contact and the development of tuberculosis (X^2 = 5.67; df=4; P>0.22). Out of 13 who develop tuberculosis with in the recent 2 years period they do have 3-7 family members in their houses. Past tuberculosis history had no association neither with presence of BCG scare (P>0.15) nor with TST status (X^2= 10.41; df=6;P>0.1082).

Among those who had history of tuberculosis 17 of them had CD4 count below 350 cell/mm^3. Three subjects had CD4 count above 350 cell/mm^3. OR=1.12,95% CI=(1.06-1.28) the risk of having tuberculosis increase with the depletion of CD4 count

3.2 Sputum test

Sputum tests performed, but not reveled AFB positive result in subjects eligible for the study.

3.3 Chest-X-Ray

Chest-X-ray was done in 61 study subjects who commenced prophylaxis treatment, except 5 (8.2%) who had abnormal chest x-ray finding which was not compatible with sign of active tuberculosis, the rest 56 (91.8%) individuals x-ray results were normal. Out of these 5 individuals who had abnormal chest x-ray finding in 4 of them tuberculin skin tests was non-reactive. And in one individual PPD test was above

5mm. All 5 individuals had CD4 count below 350 cell/ mm^3, and except one individual 4 of them had completed prophylaxis treatment.

3.4 Liver function test

Blood test for liver function were performed in order to detect possible contraindication to INH and to provide baseline values

4. Targeting, the most likely to benefit with IPT.

4.1 Tuberculin skin test result

Skin test was performed in all participants who commenced prophylaxis treatment Out of the 61 subjects in 27(44.34%) the skin test was non-reactive. In 18 (29.5%) of them the skin reaction were between1 and 5mm. In 16 (26.2%) individuals identified positive skin reaction (X^2= 5.07; df=2; P>0.079). Among 23 participants who had BCG scare in 9 of them PPD were non-reactive, Out of 38 individuals who doesn't have BCG scare 20 (52.6%) subjects were tuberculin skin reaction were non-reactive. And in 8 (21.1%) subjects reactions were more than 5mm (X^2=121.55; df=6; P<0.00001). Among 27 subjects who had TST result non-reactive 2 (7.4%) individuals had history of tuberculosis. Out of those who had normal TST reaction 4 (22.2%) subjects had past tuberculosis history.

All respondents who had TST reaction above normal hadn't had history of TB in the past. Past tuberculosis history doesn't have association with TST status (X^2=10.41; df 6;P>0.1082)

4.2 Tuberculin skin test Vs CD4 counts There is statistically significant correlation between TST status and CD4 lymphocyte count in these study groups using Pearson correlation. Among the 119 study subjects 81(68.1%) had CD4 count below 350

cells/ mm^3. Out of the 61 individuals who had CD4 count less than 350-cells/ mm^3, in 27 of them tuberculin skin test was significantly depressed. Out of 16 participants who had TST result above normal 13 of them had CD4 cell count below 350 cell/ mm^3 the rest 3 subjects had CD4 count above 350 cell/ mm^3 (X^2=43.93; df=3;P<0.00001).

4.3 Table-4-CD4 and viral load before and after treatment

	Before treatment				After treatment					
	mean	**min**	**max**	**S.D**	**mean**	**min**	**max**	**S.D**	**Wilcoxon signed-rank test**	
									Z	**P-value.**
CD4	308.7	24	974	15.5	312.2	24	999	18.7	-0.4888	0.626
V. load	80774	80	640000	16746.6	96391.2	80	790000	18453.3	-1.772	0.076
Weight	57.69	34	87	0.91	57.05	37	87	1.05	-0.399	0.690

There is no statistical significant difference before and after prophylaxis treatment use, on CD4 count, viral load and weight using Wilcoxon Signed- rank test

Table-5- Willingness and reason to take IPT

N0	Willingness to take IPT	n(%)
12	agree	100(89.3)
	disagree	12(10.7)
	Total	112
	Reason to agree	
	I know TB is serious	30(26.8)
	Friend died of TB	1(0.9)
	Had close contact with TB patient	6(5.4)
	Advised by doctors	63(56.3)
	Total	100

	Reason not to agree	n(%)
1	**I am not convinced on the benefit of the drug**	5(4.5)
2	**Taking drug will make me suspicious to partners**	4(3.6)
3	**Not convenient to collect drug**	2(1.8)
4	**I am not advised by doctors**	1(0.9)
	Total	12

Of the 112 study subjects, 100 (89.3%) were found to be in favor of taking IPT. And 10.7% disagree (X^2=138.3; P<0.00001). Out of the100 study participants, who agreed to take IPT, 30 (26.8%) of them said, they agree because they know tuberculosis is serious health problem. Sixty-three (56.3%) said, they will agree if they were told about the benefit by the doctors. six (5.4%) of respondents were agree because they had close contact with TB patient so they believe it is important to them.

5.1 Reasons for not participating in IPT

Among 12-study subjects who were not willing to participate in IPT, 5 of them (41.7%) said they were not convinced on the benefit of the drug. Four (33.3%) of them said they were afraid of taking drug daily that will make them suspicious to their partner and others. Two (16.7%) of them said that it was not convenient to them.

6. Reason for exclusion

Of the 71 study subjects, who did not start TB treatment, the reason for exclusion among the 58 subjects were assessed, out of these 37 (63.8%) were had CD4 count above 350 cell/mm^3, 13 (22.4%) of them were excluded from the study because they developed tuberculosis and had recent TB treatment history, five (8.6%) participants refused to

enrolled in the study because of their personal reason. Thirteen (18.3%) participants died. The causes of death for 4 (30.8%) of them stated in their clinical chart were related to tuberculosis. Even though active TB and pregnancy were put under exclusion criteria no body was found with these problems.

7. Provision of IPT

Isoniazid is the recommended drug, self-administered 5mg/kg (max.300mg) and supplemented with vitamin B6 50mg daily, for 9 months.

The clinical record of One hundred thirty two-study subjects was surveyed. IPT were commenced for 61(46.2%)-study subject. There were 7 (11.5%) deaths among patients who started chemoprophylaxis. Out of these, 4(6.6%) subjects died while they were on treatment. Three subjects (4.9%) died after completion of treatment. Questionnaire was administered to all these 54 participants who were alive and eligible for the program. Among 61 study subject 35 were successfully completed 9 months prophylaxis treatments, making completion rate 57.4% of those who started IPT. Fifteen participants (24.6%) discontinued due to different reason and. Seven (11.5%) subjects are still on treatment. If these 7 subjects would have completed the required period of treatment, the completion rate would have risen to 68.9%. There is significant statistical difference in sex among those who commenced IPT (X^2= 9.57; df= 3; p< 0.02).

8. Out come of those who started IPT

Out of 35 subjects who were completed preventive treatment, 3(8.6%) of them died of other reason which is not related to TB problem. Out of the 15 subjects who discontinued treatment, 3 of them (20.0%) subsequently developed tuberculosis. And their CD4 count before the initiation of IPT were below 200 cells/ mm^3 and their TST

status showed that 2 of them had reaction less than 5mm, one subject had non reactive test result. Among 11 (18.1%) study subjects who were on treatment 4 of them (6.6%) died while they were on treatment, due to other problem related to their immune status.

Twenty participants had history of tuberculosis prior to initiation of IPT, thirteen of them excluded from the study due to recent TB. Among 7 participants who had history of TB before 3 or 4 years of the initiation of prophylaxis program 4 of them enrolled in the study and out of these individuals one subject discontinued treatment, subsequently he developed tuberculosis. Making the incidence rate of tuberculosis during the study period 2.6/100 PY.

9. Adherence enhancement

Table-6-Organizational support and staff approach.

Org.support&staff approach	Agree n (%)	Disagree n (%)	X^2-test	p-value
Project support	101(90.2%)	11(9.8%)	144.6	<0.00001
Listen actively	102(91.1%)	10(8.9%)	151.1	**
supportive	99(88.4%)	13(11.6%)	132.1	**
Talks culturally	103(92.0%)	9(8.0%)	151.9	**
Fell comfort	110(98.2%)	2(1.8%)	208.3	**

The majority of informants agree on that ENARP staffs are supportive, good listeners, and they fell comfort to discus health issue with them. There is significant difference in proportion among those informants who agree and not agree.

10. Factors affecting adherence

10.1 Waiting time

The mean waiting time spent by the client to get first appointment and to get HIV test results were 16.9 $\pm$ 13.2,ranging between 5 and 60 minuets. The mean waiting time spent by the client to see a medical doctor was 16.8 $\pm$ 13.1, and ranging between 5 and 60 minuets.

10.2 Habit of drug administration

Of the 112 clients, ninety-eight (87.5%) of study subjects had habit of regular drug administration according to scheduled time. Twelve (10.7%) of respondent said that, they some times missed to take drug prescribed by the doctors .Two (1.8%) informants said that, they take drug prescribed when somebody remind them. There is statistical significant difference in the habit of drug administration among the informants (X^2=223.8; df=2; P<0.00001).

Among those study subjects who discontinued treatment, 12 (80.0%) participants, even though they discontinued taking drug they do have habit of taking drug regularly at scheduled time while they were on treatment. The rest 3 (20.0%) subjects only sometimes missed to take drug prescribed to them. Neither sex (P>0.48) nor educational background was associated with habit of drug administration (X^2=11.18; df=8; P>0.191)

10.3 Acceptance of length of treatment

Of 54 study subjects who are still on follow up, 3(5.6%) of them get taking tablet for 9 months was difficult, 6(11.1%) of them said the 9 months prophylaxis treatment was sometimes difficult. For the rest of 45 (83.3%) respondents the scheduled 9 months prophylaxis treatment was ok (X^2=91.5;df=2;P<0.00001).

Among the 32 study subject who completed the prophylaxis program, for 30(93.7%) of them taking the treatment for 9 months was ok and 2(6.25%) subjects said that this might be sometimes difficult. Even though 15 participants discontinued treatment, 9(60.0%) of them thought that taking treatment for 9 months was not difficult and 3 of them said difficult, the rest 3(20.0%) subjects replied that sometimes hard to take treatment for 9 months regularly (X^2=134.8; df =9;P<0.00001).

10.4 Adverse drug effect

Of 54 subjects those who started prophylaxis treatment and still on follow up, except 7 of them which is 12.9 %, the rest are not experienced any sickness while and after they took IPT (X^2=59.3; df=1;P< 0.00001)

Among those who discontinued prophylaxis treatment 5 (33.3%) of them they did so because of adverse drug effect, the rest 10 (66.7%) never experienced sickness while they are on treatment. Among those who completed 30 of them and out of those who are on treatment at the time of data collection never experienced adverse effect of INH (X^2 128.26; df=6; P< 0.00001). Of those individuals, who discontinued preventive treatment and subsequently developed tuberculosis, in none of them seen drug resistance to INH, while they were on treatment.

10.5 Health problem due to drug

Among those who experienced adverse drug effect non-of them develop either liver or neurological problem. Only 5 (4.5%) mentioned other problem like dyspepsia.

10.6 Knowledge about IPT Of 112 informants, seventy-five (65%) of them said they would develop tuberculosis. And the rest 37(33%) informants replies they don't know what will happen to them if they don't take IPT (X^2=23.15;df=1;P<0.00001).

Among 100 study subject who agreed to take IPT, 74 (74%) subjects knew they will develop tuberculosis if they don't take IPT. There is significant statistical difference of knowledge in those respondent who are willing to take IPT and those who refused (X^2=18.02; P<0.00001). Among 75 individuals who attend either counseling or all type of session, 72 (96%) of them know what will happen to them if they don't take IPT (X^2= 9.77; df=2; P<00756).

10.7 Living with a partner, and knowledge of sero-status among partners.

Among the 112 respondents, 84 (75%) of them live with partner. The rest 28 (25%) live with out partner (X^2=56.0; P<0.00001). Forty-five (40.2%) of the respondent said that their partners know their sero-status. The rest 67 (59.8%) either doesn't know or doesn't want to tell their partner at all (X^2=8.64; df=1; P<0.003). Of 84-study subject, who live with partner, 34 (40.5%) of them did not want to tell about their sero-status for their partners. And out of those who were not live with partner 11 of them refused to tell about their HIV status to their partner. But knowledge of sero-status among partners doesn't differ whether living with partner or not (X^2= 4.23; df=2;P>0.1206). Out of 81 married 80 (98.7%) of them live with partner, among 12 widowed 2 and out of 7 not married 2 of them live with causal partner.

10.8 Difficulty to take tablet in front of partner

Two (1.8%) of study subject replies that, they face difficulties to take tablet in front of their partner, 86 (76.8%) never face difficulties to take tablet in front of their partner. The rest 24 (21.4%) will not do that in front of their partner due to inconvenience (X^2=152.5;df=2;P<0.00001).

Among 45 informants who doesn't want to tell for their partner about their sero-status, 25 (55.6%) of them they never face difficulty to take tablet in front of their partner. The rest 20 (44.4%) respondents they never do it in front of their partner (X^2= 1.11; df =1; P>0.29).

Out of 15 who discontinued 1of they face difficulties to take tablet, and 6(40.0%) of them will not take tablet in front of their partners due to inconvenience.

11. Assessment of adherence

Among 54 study subjects who are still on follow up 19(35.2%) said that they missed collecting drug on the date of appointment, 32 (59.3%) of respondent said they never missed collecting drug on their date of appointment. The rest 3 (5.6 %) individuals said that sometimes missed their date of appointment (X^2=35.2;df=2;P< 0.00001). Out of 45 study subjects who were in favor of 9 months treatment, 12(37.8) of them missed collecting drug on the date of appointment, and 3(6.6) individuals missed sometimes their date of appointment, the rest 30 (66.7) never missed (X^2=37.8; df =2;P<0.00001).

11.1 Time for missed treatment

Out of those who started treatment and said missed collecting drugs on their date of appointment, 9 (47.3%) of them missed treatment between the first two months. Six (31.6%) missed in between third and forth months. The rest 4 (21.1%) missed collecting drug on their date of appointment after they had taken 5 months of treatment (X^2=3.0; P>0.223).

Among 32 who successfully completed treatment 4 (12.5%) of them missed taking the drug only for a day. Out of 7 who are still on treatment one subject missed to

ingest his drug for a week. The rest 15 who discontinued treatment they missed taking drug for more than months (X^2=193.31; df =9; P<0.00001).

11.2 Self report about missed pills.

Among 5 informants who missed ingesting daily treatment for days they all took treatment the next day, doses of that day only. Out of those who missed ingesting drug for a week one subject said I would take double the next day if I missed ingesting. Out of 15 subjects who missed taking drug for more than months, 3 of them said they would take double the next day if they missed daily dose. The rest 12 (80.0%) subjects said that they would take in the next day, doses of that day only if they missed to take daily dos

11.3 Tracing by the staff

Out of 19 study subjects who started treatment and missed collecting drug on their date of appointment 16 (84.2%) of them remind by active tracing of ENARP staff. The rest 3 said they remember them selves to collect treatment again (X^2=150.89; df=9; P< 0.00001).

11.4 Sufficient Scheduled attendance

Sixty-one subject were followed during the study period, out of which 46 (75.4%) were had sufficient attendance. The rest 15(24.6%) subjects attend less than 5 months of follow up (X^2=31.51;df=1;P<0.00001). Among 15 individuals who discontinued treatment 11(73.3%) of them were had less than 5 months of follow up, the rest 4 (26.7%) individuals even though they discontinued taking IPT they had sufficient scheduled attendance (X^2=6.53; df=1;P<0.01). Among 45 study subjects who were in favor of 9 months treatment, 38 (84.4%) of them had sufficient attendance (X^2= 42.7; df=1; P<0.00001)

11.5 INH metabolite test

The test was performed in 46 (75.4%) individuals out of 61 who commenced treatment, Out of 46-study subject who had tested for INH metabolite in 37 (80.4%) of them had positive test result. The rest 9 (19.6%) participants test results were negative. Out of 46 individuals who had sufficient scheduled attendance the tests were performed in 40 of study subjects. Out of 40 individuals who had test results in 35 (87.5%) of them was positive and in five (12.5%) subjects the tests were negative

All 112 interviewees were asked, about their experience, regarding the probable reason for missing to take IPT displayed in the next table.

Table-7-Reason why some one missed treatment

No	reason	lack	agree	disagree	X^2-test	p-value
1	If he or she feel well	**information**	22(19.6%)	90(80.4%)	82.57	<0.00001
2	If he or she thought that not have TB		23(20.5%)	89(79.5%)	77.79	<0.00001
3	Presumed side effect		32(28.6%)	80(71.4%)	41.14	<0.00001
4	If busy	**motivation**	20(17.9%)	92(82.1%)	92.57	<0.00001
5	No interest		12(10.7%)	100(89.3%)	138.21	<0.00001
6	Discourage due to inconvenience		18(16.1%)	94(83.9%)	103.14	<0.00001
7	Denial, had no accepted HIV disease		11(9.8%)	101(90.2%)	144.64	<0.00001
8	Moved far away	**support**	35(31.3%)	77(68.8%)	31.5	<0.00001
9	Family problem		26(23.2%)	86(76.8%)	64.29	<0.00001
10	Too sick		41(36.6%)	71(63.4%)	16.07	<0.00006
11	Discourage by relatives		16(14.3%)	96(85.7%)	114.29	<0.00001

The majority of respondents agree on that lack of information, motivation, and support plays important role in missed drug collection.

12. Appreciation of IPT and recommending to others

Among all respondents 98 (87.5%) said they advised that IPT is important to some one who are prone to tuberculosis disease. Nine (8.0%) of the respondents they don't want to advice IPT to anybody. The rest 5 (4.5%) don't know whether to advised to some one like them to go for IPT (X^2=222.13;df=2;P<0.00001). Among those who started prophylaxis except 9 who discontinued treatment they all adviced someone to go for IPT. Out of 100 subjects who are willing to take IPT 91 (91%) of them would like to give advice about IPT to everybody who are prone to tuberculosis. Even among 12 subjects who were against to take IPT 7 of them advice IPT to some one very essential

13. Effects of IPT, on CD4 count and body weight.

Using Wilcoxon signed- rank test we tried to see the difference between CD4 counts before and after treatment with IPT based on positive rank, but the test doesn't reveal significant difference. (P> 0.626) There is no statistically significant difference in weight before and after IPT using Wilcoxon sign rank test analysis.

14. Analysis of cost incurred by implementing IPT program.

The analysis had taken account the additional cost incurred by implementing this prophylaxis program in the existing ENARP sites. And tried to look two main benefits saving to the project services on TB treatment cost averted, and loss of monthly income of tuberculosis patients who are unable to work to capacity for two months.

The averted treatment cost includes those of the index patients who didn't develop TB as a result of preventive therapy, and those of additional causes averted.

14.1 Others benefit which were not coasted.

1. Early detection of cases of TB.
2. Benefit to the individual as well as to the community and their household patient cost of seeking diagnosis, time costs of other household
3. Income of the patients estimated by taking the mean of salary gained by the participants

Table-8. Estimated costs for TB preventive therapy program in the tow cohorts

1	**HIV testing and counseling** unit cost 10 Birr	
2	**Screening for active TB**	
	PPD test	5.25 birr
	AFB test	15.00 birr
	LFT	30.00 birr
	C-X-ray	40.00 birr
	Clinical examination	1.00 birr

The cost for AFB, LFT, and chest X-Ray was taken from the average cost requested by privet clinic in Addis. The cost for PPD was taken from MOH drug dispensing unit.

1	Begin TB preventive therapy	61(46.2%)
2	Complete regimen	35(57.4%)
3	Efficacious preventive therapy (60%)	60% of 35=21
4	Likelihood of developing active TB	25% of 21=5
5	Additional cases caused by index case	2 new cases/index n=10

The costs for short course treatment and INH with B6 for 9 months were taken from ministry of health drug dispensing unit. The cost for active TB screening was taken from average cost requested in privet clinic.

Table 9. Summary value of Cost of screening for HIV, active tuberculosis and short course TB treatment.

	cost	Birr (ETH)
1	TB therapy short course(8 months)	71.62 birr
2	Counseling and HIV testing	10.00 birr
3	Screening for active TB	90.27 birr
4	INH and vitamin B6 for 9 months	6.48 birr
5	Salary(mean income for 2 months)	502.75*2=1107.50 birr

A	cost	Unit cost	N=	Total
1	HIV testing and counseling	10	132	1320 Birr
2	Screening for active TB	90.27	61	5506.47 Birr
3	Provision of IPT			
a	No starting IPT		61	
b	INH/B6 (For 9 months)	6.48 Birr	61	395.28 Birr
c	Service cost	1 Birr	61	61.00 Birr
d	No completing IPT	--	35	--
e	Efficacy of preventive therapy (60%)	--	21	--
f	Probability of developing TB (25%)	--	5	--
g	Two additional case/index case	--	10	--
h	Total cost of program	--	--	7287.75 Birr

Table 10-The benefit gained due to prophylaxis treatment Vs the cost of the program

B	Saving benefit		
1	Treatment cost saved index plus added cases	15.75*71.62	1128.02 birr
	Benefit cost ratio 1	1128.02/7287.75	0.154
2	Treatment costs saved plus lost income		36323.32
	Benefit cost ratio 2:treatment saving plus incomes	36323.32/7278.8	4.99

The benefit exceeded by 4.99 factors the cost of the IPT program.

VI- Discussion

This study was designed to assess the operational aspect of INH prophylaxis program for HIV positive patients in the two cohort sites.

Although appropriate use of IPT has proved to be effective in preventing active illness in subjects at high risk for tuberculosis, its effectiveness has often been limited due to several reasons. Therefore, the aim of this particular study mainly focus on the operational aspect of INH prophylaxis program and tried to evaluate the prerequisites which should be in place before a PT service is considered.

Identification of HIV infected person and confirms the association observed between TB and HIV is the first requirement for the implementation of IPT. And this needs active HIV counseling and testing program, public interest in obtaining such service, adequate capacity for HIV testing and counseling, sufficient trained health care staff. However VCT services are not widely used and therefore candidate for IPT are not easily identified.

Our finding indicate that, 89.3 % of informants were willing to participate in the IPT program, And this finding is inline with the study conducted in Botswana (17), where more than 90% of study population showed willingness to seek VCT, in exchange for a medical benefit, care such as TB PT are offered, if they are found infected.

Based on WHO recommendation (15) the project evaluate participants for active tuberculosis. Clinically cohort's physicians assessed them for presence of prolonged cough, blood spiting, fever, night sweating, and weight loss. Laboratory investigations like sputum test for AFB, and also liver function test to determine base line value done.

As WHO recommended, these procedures must be performed prior to preventive therapy initiation. During screening time it is important to have an accurate medical examination and it is essential for both public and individual health reasons to quickly identify and treat active tuberculosis cases. However it is known that it adds further time, expense, and an additional step where patients are lost to follow up. In the study conducted in Uganda at a VCT center there was significant attrition of members at all level of screening (18) in contrary to that, due to these procedures the ENARP project had not lost participant.

To identify those who are most benefited with preventive therapy, tuberculin skin test and CD4 count were performed. In the study conducted by ES.Lugada (19) in addition to ours they used WHO HIV clinical staging 1, 2 and 3. In Zambia study conducted by Godfrey et al (20) instead of CD4 count they used serial absolute lymphocyte counts. Determination of CD4 count needs CD4 counter, which require capital investment. Its cost, availability and access to get at VCT center make the procedure untouchable, especially in developing countries. But this should not be obstacle to the wide spread introduction of INH prophylaxis.

Although serial absolute lymphocyte counts aren't very stable, they do correlate with CD4 lymphocyte counts in HIV sero-positive individuals and may therefore be used as a crude measure of the progression of HIV disease. And this can be seen in the study by Yared et al, unpublished document in the ENARP project and Zambian (21), where he showed that simple biological markers to replace CD4 count and viral load in resource poor setting. Screening potential recipient of tuberculosis preventive therapy by total lymphocytes count may be an important strategy that will be more practical to implement

in many settings. This has the added advantage that facilities for differential white blood cell counts are more widely available than those for tuberculin skin test.

The cut of point used for the selection of eligible participant for the prophylaxis program was taken CD4 count of less than 350 cell/ mm^3. Our study indicates that, among 20 study subjects who had history of tuberculosis, except 3 participants all developed tuberculosis while their CD4 dropped below 350 cells/ mm^3. Therefore the risk of having tuberculosis increases with CD4 count below 350 cells. In contrast to our finding, studies conducted in Uganda and Zaire showed that significant proportion of HIV infected patient develop TB while their CD4 count above 500 cells and immune system is still effective (18) the argument is that, our finding might be considered in view of that, the low absolute CD4 count of Ethiopians in general could contribute to this outcome (22)

Tuberculin skin test studies to date indicate that those who are TST positive individuals are most likely to benefit from preventive therapy. And tuberculin skin test is useful in identifying those subjects who would benefit the most from preventive therapy. Because they are both infected with mico-bacterium tuberculosis, and not anergic. According to our finding, of 61 studies subject who commenced prophylaxis treatment only 16 (26.2%) subjects could have been started preventive treatment. Twenty-seven (44.2%) individuals had skin test reaction significantly depressed and it showed anergy. An early limited tuberculin survey conducted in Zambia has also shown that there was a higher rate of anergy among HIV positive than HIV negative individuals. Similar finding also observed in Uganda where they reported in the cohort 25% anergy to PPD (cohort study in Entebbe by AM Elliott) (23).

But the project has given IPT irrespective of TST status, and this measure is inline with the study conducted in Pakistan Karachi (24). The reason is that in high TB prevalence areas large proportion of population is expected to have positive reaction, which limits the specificity of mountoux test as a screening tool. In this population TST would play a limited role in assessing individual with a latent infection. Further more skin reaction may not correlate with disease severity, and has been shown to decrease with disease severity.

The finding that we have also consistent in that, in those subjects who had low immune status with CD4 count below 350 cells/ mm^3, the skin test showed anergy to PPD. Therefore, tuberculin response in BCG vaccinated TB endemic area cannot be used as a diagnostic marker for active tuberculosis, particularly in advanced disease. Clients be screened by TST, which adds further time and expense and an additional step where patients are lost to follow up (25). Therefore one could argue that in countries where tuberculosis is highly prevalent and where there is anergy, tuberculin skin test is not necessary and INH should be given to all HIV infected persons after active tuberculosis is carefully excluded. Simplification in the enrollment procedures might improve participation in the PT program. But Ugandan preventive therapy study indicates that persons who are anergic are less likely to benefit from preventive therapy (26).

We tried to explore the correlation of CD4 count and TST by Pearson correlation analysis and we had found that there is statistically significant correlation. In contrary to this, in the study conducted in Burkinafaso they didn't found direct correlation between indurations size of reactions to the tuberculin skin test and CD4 T-lymphocytes count using linear regression analysis (27).

Provision of IPT

Several studies had proven efficacy of different regimens, INH, in Haiti 3R2Z26H2, Thailand 4RH12H, Uganda 3RH, 3RHZ, 6H (28). Preventive therapy using more than one drug allow a shorter duration of therapy and also results in superior adherence (29). But none of these studies was designed to be powerful enough to show that refampin-containing regimens were better than INH alone.

Contrary to all these, in the study conducted in Baltimore, Maryland (U.S.A), suggests that in areas, where the prevalence of anergy and the risk of active TB if anergic are important variable in determining the optimal preventive strategy. And said TB vaccine may be useful strategy to prevent TB among HIV infected persons in the developing world, but only in areas where the prevalence of anergy is at least 35% and if the candidate vaccines effectiveness in this patient population greatly exceeds that of BCG (30).

Even though 8 different regimens have been proven to reduce the risk of active tuberculosis, INH is the regimen recommended in developing countries (29). Therefore the project has given INH as a daily base self administered treatment for 9 months. And choice of regimen is likely to be influenced by cost, availability of drugs, adverse drug effect. There is also some evidence that HIV positive patient may malabsorb anti-tuberculosis drugs, particularly rifamicine if refampine is malabsorbed, drug concentration in tissue and blood may be considerably reduced if given to HIV positive patients on an intermittent basis (31).

Like regimen, duration of treatment varies, here the important question is the durability of preventive therapy in areas where continued exposure to infection occurs. In

low prevalence countries where re-exposure to infection is rare the protective effect of INH PT lasts for up to 19 years or may be life long. In the study conducted in Zambia by Mwinga et al showed that, IPT is effective during treatment and shortly there after. Limited duration of protective effect of IPT in high TB prevalence areas such as Lusaka or Nairobi raises the question of the possibility for life long PT or the need for re-prophylaxis (32,4). Therefore longer duration of therapy may provide additional benefit insufficient duration of therapy in an immuno-compromised host may also have reduced the protective effect of isoniazid in the infected group (33). Macrophage and lymphocyte function, which is deficient in HIV infection one might therefor expect that the longer period of preventive therapy may be required to sufficiently reduced or eradicate a population of latent bacilli in HIV infected individuals (34). Otherwise insufficient duration of INH in subjects relatively advanced disease increase susceptibility to new infection, and high rate of transmission may compromise the efficacy of preventive treatment.

IPT has not previously been used in Ethiopia for HIV positive patients, and no nation wide data are available. The Ethio-Netherland AIDS Research Project tried to implement IPT service in the two cohort sites and the project has considered these services in the context of integrated care, with benefit to control tuberculosis, HIV care and public health programs.

In this particular study recruitment started when HIV positive individuals express interest in receiving preventive therapy. Therefore 132 HIV positive participants passed through the screening process. Among these individuals only 61(46.2%) with CD4 count below 350 cells/ mm^3, free from INH contra-indication and those who had excluded

current and recent TB history were invited for IPT. Except 3 participants who are delayed for screening and 5 individuals who are refused to participate in the study, the rest are excluded with different exclusion criteria. This strategy was in line with the WHO recommendation. Therefore initiation rate of IPT in the ENARP project is slightly lower. But this finding is similar to the proportion found in an ongoing study in northern Thailand which involves 5 HIV counseling and testing sits, where therapy started varies between 30% and 60% and almost similar and consistent with the finding in Uganda where only 51% were commenced therapy (35). This low rate of initiation of treatment might be explained in that, in order to maximize the utility of preventive therapy, selections of those who are benefited most were strictly screened.

In this ongoing study, therapy was completed by 57.4% of those who started IPT this level of adherence compare favorably with reports from northern Thailand where the proportion of those completed varies between 60% and 80% and low in comparison to Uganda studies (35) where therapy was completed by 76% of those who started. This finding should however be considered in view of that, there are some individuals who are still on treatment at the time of data collection that made the completion rate some how low.

An alternative explanation could be the problem of non-adherence, 25% of those who started failed to complete the course due to different reason. Poor adherence to therapy is major concern for the successful implementation of INH prophylaxis program. Therefore, the result that we have found in the project was better than Uganda's study, where 38% failed to collect 80% of their pills (18), in Thailand 31% failed to complete a 9 months INH regimens in a prospective cohort study, in the Nairobi efficacy study 31%

of subjects missed at least 5 weeks of tablets during the 6 months treatment period (19, 33)

Convincing patients who are essentially well to take medication for an extended period is difficult. This requires techniques to maximize adherence to therapy, like frequent health education, counseling on TB prophylaxis, creating conducive environment to take pills, minimize waiting time to collect, and to see medical doctors. These and other techniques were used persistently in the cohort sits. And more or less similar with the Italian study on acceptance of IPT by close contacts of TB cases where they tried to maximize completion rate by providing the patient's explanatory brochure, recalling defaulting patients by telephone and by mail (36). Further more by reducing frequent staff change improves patient's compliance with the follow-up schedule and treatment regimen due to the trust that developed. Utilization of the service increased to 31% in Uganda's study while participants had got support, encouragement given by enrolled persons to hesitant clients' (18).

Tracing of those who missed scheduled date of appointment should be considered as enhancing mechanism to achieve better adherence. Therefore the project has assigned social worker who actively traced and made work place visit of clients who missed appointment. Of 19 subjects who missed their date of appointment 16 of them were reminded by active tracing of social worker and this helps to achieve good compliance rate. Unfortunately this service is unlikely to be feasible if IPT were more broadly implemented.

Since IPT is effective in preventing active TB cases when adherence to treatment is assured, all efforts should be undertaken in order to provide patients with information

about the rationales and risk of treatment that they should take even when they fell well. Therefore it seems desirable to link education on tuberculosis risk and prevention to pre and post- test counseling for HIV testing. Efforts will be needed to educate the public that, preventive therapy may indeed improve the quality and duration of life if they are infected.

Though the finding don't make a big difference, other factors like knowledge of sero-status between partners. And knowledge of IPT plays important role in enhancing adherence to treatment. Furthermore many potential participants were probably discouraged by the fact that the project has come to its final closure date.

Adherence to treatment was assessed by records of missed date of appointment. Among those who successfully completed IPT 5 of them missed to collect drug for one day. Out of 7 who are still on treatment except one subject all are complaints. The INH metabolite test performed in 46 individuals of whom started IPT; in 37 (80.4%) of them the test result was positive. This figure is comparable with those observed in the Uganda study, where INH metabolites test were found positive in 88% overall. Therefor-principal measure of adherence scheduled attendance report, self-report for which pills were not taken, and urine testing produced similar and consistent results with the Uganda study and this reassuring us the reliability of our final adherence figures.

Adverse drug reactions must be monitored carefully through out the period of TB preventive therapy. The major side effect of all three anti-tuberculosis drugs is hepato-toxicity. This is uncommon below the age of 35, but incidence increases with increasing age (37). Increases in liver function test of more than 3 times the base line value were considered to indicate a degree of abnormality of liver function. Even though the project

had given preventive treatment irrespective of the age of the participants none of them develop either liver or neurological problem, only 5(4.5%) mentioned other problem like dyspepsia.

Effect of IPT on TB incidence

IPT has been proven effective in reducing TB incidence, in different regimens, duration of treatment and in different level of immuno-suppression. However estimating effect of IPT is not the intention of this study, and this study was designed and limited only to evaluate the operational aspect of the program. But we were able to see some of the outcomes.

Among those who discontinued preventive treatment 3 of them develop tuberculosis and started to take anti-tuberculosis treatment, but while they were on treatment non-of them were seen INH resistant. Once preventive therapy is discontinued acquisition of new infection with rapid progression to active TB is possible (38). Among 15 individuals who discontinued preventive therapy three of them develop active TB. These subjects were protected from reactivation by INH, may have subsequently exposed and acquire new rapidly progressive infection.

Cost assessment

Our result might help in estimating the cost incurred by implementing IPT program in the existing VCT centers. But the model had not included personnel and health facility overhead costs. The cost of counseling and testing for HIV were taken based on the average payment requested by VCT centers in Addis Ababa to have HIV testing. So that 10 birr was taken as a cost for VCT. Even though anti TB drugs are

distributed freely in the country, the cost data we have used for the treatment was taken from Ministry of Health drug dispensing centers.

Our finding reveal that 93,7% of the over all cost of the program spent before the patient starts preventive therapy, for HIV testing and active TB screening, and this finding could be favorably compared with the study conducted in Zambia (39) where 81% spent before IPT initiation.

The model took in to consideration the number of additional infections of TB caused by one index case. And we tried to limit assessment only by 2 additional cases per index cases. But under certain condition where the index case comes in to contact with many others, one case can lead to very high numbers of new infections. Therefore, establishment of IPT should be considered for people whose work or living situation places them in close contact with large number of other people, including members of very large house hold (39). The average family size in our study was 4.7.

VII- Strength of the study

- Has operational and public health relevance
- No similar study sofar in our country, therefore this study Showed feasibility of IPT in our context
- Data collection supplemented with review of available data verify data validity

Limitation of the study

- Small sample size might decrease its internal and external validity.
- Lack of literature done in our country for comparison.
- Bias due to interviewers can not ruled out

VIII-Conclusion

- Screening for HIV and active tuberculosis was done according to the WHO guidelines
- Selecting the most benefited participants for IPT using CD4 count in our set up might not be feasible while IPT would start to utilize widely, due to cost, lack of skilled person and availability of the CD4 counter.
- Tuberculin skin test lack specificity in our country because of high prevalence of TB and the problem of anergy in our participants limited its use as a screening tool.
- The appropriateness of the cut of point used to select eligible participants for the prophylaxis seems correct but needs further evaluation with large sample size.
- Provision of IPT done as it was recommended by WHO, monthly supply and self administered treatment gives a chance to monitor adherence and side effect of the drug, therefore this should be strengthen.
- Techniques used to enhance adherence, like organizational support, good staff approach to the patient and minimum waiting time, created conducive environment to adhere to treatment.
- The benefit of prophylaxis treatment exceeded the cost of the program.
- The initiation and completion rate of IPT looks adequate and these reflected the strong capacity of the project in terms of organizational structure, finance and trained manpower and this particular study provides appropriate information on how to implement PT in other setup.

IX- Recommendation

- Mechanism used to identify those who are benefited most for IPT should be considered in terms of availability of CD4 counter, cost, and skilled manpower. Therefore it is appropriate to use serial absolute lymphocyte count instead of CD4 count and tuberculin skin test.
- Regarding the regimen of PT it seems appropriate but for how long should be PT given and its protection effect need further study.
- And the result of this study support that, where the problem of anergy is greater in HIV positive individuals and if we have found candidate vaccine effectiveness greatly exceed that of BCG we have to look this vaccine as an alternative strategy of preventing development of active TB.

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Anex-1

Process evaluation of the INH prophylaxis program for HIV positive patient in the ENARP site

Questionnaire to be administered to the study population

Part 1 socio-demographic characteristics of the respondent

No	Questionnaire	Coding characteristics	
001	Study site	1=akaki 2=wonje	
002	Are you willing to give Answer to the question I am going to ask you	1=yes 2=no	
003	Respondent ID	F0000(akaki) W0000(wonje)	
004	Respondent age at enrolment	00(in year)	
005	Respondent sex	1=male 2=female	
006	Education status	1=unable to read and write 2=read and write 3=grade 2-6 4=grade 7-12 5=12^{+}	
007	Marital status	1=married 2=divorced 3=widow 4=separated with out divorce 5=not married	
008	Number of family	00	-------
009	Number of children	00	-------
010	Monthly income (in Birr)	0000	-------
Part 2	Questionnaire on set up and organization of the necessary resource	Coding characteristics	
001	Do you get medical support From the project	1=only clinical 2=clinical including lab 3=all including drug 4=nothing	
002	Do you ever attend health Education, if no go to Q-8	1=yes only counseling session 2=yes all type of session 3=no	

003	Do you ever heard of TB Prophylaxis	1=yes 2=no	
004	The regimen explained	1=yes 2=no	
005	The need to take IPT regularly	1=yes 2=no	
006	The danger of taking IPT irregularly	1=yes 2=no	
007	Possible side effect and when To seek medical care	1=yes 2=no	
000	How can you describe staff Approach to the patient give your Response by saying agree or disagree		
008	Greets clients	1=agree 2=disagree	
009	Listens actively	1=agree 2=disagree	
010	Is supportive	1=agree 2=disagree	
011	Give information in clear And simple terms	1=agree 2=disagree	
012	Talks about sensitive issues Appropriately to the culture	1=agree 2=disagree	
013	Did you feel comfortable With the ENARP staff	1=yes 2=sometimes 3=no	
014	Was there enough privacy During your counseling	1=yes 2=no	
015	How much time did you spend a)getting your first appointment b)waiting for your HIV test result c)waiting to see your doctor	 ---------- ---------- ----------	 ------- ------- -------
016	Would you recommend using This service to a friend or family member	1=yes 2=no 3=I don't know	
017	Did you had close contact with TB patient before.	1=yes in my family 2=yes in my work place 3=no	
018	Have you ever been treated For TB ,If yes when	1=yes before 2 years 2=yes with in this 2 years 3=no	
Part 3	Questionnaire on willingness and knowledge on IPT	Coding characteristics	
001	Did you agree if you were asked	1=yes	

	to take IPT (If no go to Q-003)	2=no	
002	If yes, tell me why you agree to take IPT and then go to Q-004	1=I know TB is serious 2=friend died of TB 3=familly pressure 4=had close contact with TB patient 5=advised by doctors 6=other	
003	If no, what is your reason not to take IPT	1=I am not convinced of the benefit of the drug 2=Taking drugs daily will make me suspicious to my partner and others 3=I don't know where to keep the drug at home 4=I am afraid to collect the drug because it is not convenient to me 5=I am not advised by doctor 6=other	
004	What will happen to you if you don't take IPT	1=I may develop TB 2=I don't know 3= other	
Part 4	Questionnaire on drug administration and adverse reaction	Coding characteristics	
001	Tell me your habit of drug administration	1=At scheduled time 2= some time I missed to take 3= I will take when some body remind me	
002	Are you on IPT at the moment If, your answer is not on IPT **go to part 5**	1=Yes 2=no 3=completed 4= quite to take	
003	How do you get taking tablet for 9 month	1=Difficult 2=some times difficult 3=its ok	
004	Have you ever missed collecting drug on your date of appointment (if no go toQ-009)	1=Yes 2=No 3=some times	

005	For how long you missed treatment If, you are on IPT	1=For days 2= for weeks 3= for months	
006	At what time you miss treatment	1=With in the first week 2=between 1-2 months 3= between 3-4 months 4=above 5 months	
007	What would you do ,if you accidentally missed taking tablet	1=I will take double the next day 2=I will take doses of that day only	
008	Who remind you to recollect treatment again	1=ENARP staff 2=by my self 3=other	
009	Are you experienced any sickness after you take IPT(if no go to part 5)	1=Yes 2=no 3=NA	
010	If yes, what was your problem	1=Neurological 2=liver 3=seizures 4=other	
Part 5	Questionnaire on reason for missed scheduled appointment	Coded characteristics	
000	What do you think, why someone missed treatment Give your response by saying agree or disagree with the statement.		
001	If he or she feel well	1=agree 2=disagree	
002	If he or she taught that not have TB	1=agree 2=disagree	
003	Presumed side effect	1=agree 2=disagree	
	Luck of information		
004	If busy,	1=agree 2=disagree	
005	no interest,	1=agree 2=disagree	
006	discourage due to inconvenience	1=agree 2=disagree	
007	Denial, had no accepted HIV disease	1=agree 2=disagree	
000	luck of motivation		

008	Moved far away	1=agree 2=disagree	
009	Family problem	1=agree 2=disagree	
010	Too sick	1=agree 2=disagree	
011	Discourage by relatives	1=agree 2=disagree	
000	Luck of support		
Part 6	Questionnaire on sero-status	Coded characteristics	
001	Do you live with partner	1=Yes 2=no	
002	Did your partner know your sero-status	1=Yes 2=no 3=I don't want to tell to my partner	
003	Have you ever face difficulty to take tablet in front of your partner	1=Yes 2=no 3=I will not do that in front of my partner	
004	Would you advice some one like you to go for IPT	1=Yes 2=no 3=I don't know	

Process evaluation of the INH prophylaxis program for HIV positive patient in the ENARP site

Questionnaire to be filled by data collectors' part 7

No	Questionnaire	Coded characteristics	
001	BCG scare presence	1=Yes 2 =No	
002	Tuberculin skin test result	1=Non reactive 2= 1-5mm 3=>5mm	
003	AFB result	1=Positive 2=negative 3=not done	
004	c-x- ray result	1=Yes with active TB finding 2= no active TB finding 3=No pathological finding	
005	Liver function test	1=Yes with liver problem 2=no liver problem	
006	Attendance on scheduled date	1=Yes 2=No	
007	Urine INH metabolite test	1=Positive 2=negative 3=not done	
008	Mean CD4 count	1=Before IPT 000 2=after IPT 000	-------- - -------- -
009	Mean viral load	1=Before IPT 00000 2=After IPT 00000	-------- - --------
010	Mean body weight	1=before IPT in Kg 00 2=After IPT in Kg 00	-------- --------

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ቁጥር	መጠይቅ	ኮድ	
001	የጥናት ቦታ	1 አቃቂ 2 ወንጂ	
002	የሚጠየቁትን ጥያቄ ለመመለስ ፈቃደኛ ነዎት ወይ	1 አዎ 2 የለም	
003	የመላሹ መለያ ቁጥር	F=00000 አቃቂ W= 00000 ወንጂ	
004	የተሳታፊው ዕድሜ በፕሮጀክቱ ተሣታፊ መሆን ሲጀምር	00	
005	የተሣታፊው ፆታ	1 ወንድ 2 ሴት	
006	የትምህርት ደረጃ	1 ማንበብ መፃፍ የማይችል 2. ማንበብና መፃፍ የሚችል 3. ከ2 እስከ 6 ክፍል 4. ከ7-12 ክፍል 5. ከ12 በላይ	
007	የጋብቻ ሁኔታ	1. ያገባ 2. የተፋታ 3. የሞተባት /የሞተችበት/ 4. ሳይፋታ የተለያየ 5. ያላገባ	
008	የቤተሰብ ብዛት	00	
009	የልጆች ብዛት በቤት ውስጥ	00	
010	የወር ገቢ	0000	

ክፍል ሁለት

001	የህክምና እርዳታ ከፕሮጀክቱ ያገኛሉ ወይ	1. አዎ የሀኪም ምርመራ ብቻ 2. የሀኪምና የላቦራቶሪ አገልግሎት 3. ሁሉንም ተጨማሪ የመድኃኒት አገልግሎት 4. ምንም አላገኝም	
002	የጤና ትምህርት በፕሮጀክቱ ውስጥ ተከታትለው ያውቃሉ	1. አዎ የምክር አገልግሎት 2. አዎ የምክርና ሌላም ትምህርት 3. ተሰጥቶኝ አያውቅም	
003	የሣንባን ነቀርሣን እንዴት መከላከል እንደሚቻል ሰምተው ያውቃሉ	1. አዎ 2. የለም	
004	ስለመከላከያው መድኃኒት አጠቃቀም ተገልፆልዎታል	1. አዎ 2. የለም	
005	መከላከያ መድኃኒቱን በትክክል መውሰድ እንደሚያስፈልግ	1. አዎ 2. የለም	
006	መድኃኒቱን በትክክል ባለመውሰድ ስለሚፈጠረው ችግርስ	1. አዎ 2. የለም	
007	ስለመድኃኒቱ ተጓዳኝ ችግሮችስ መቼ ሀኪምዎን ማማከር እንዳለብዎት	1. አዎ 2. የለም	
000	የፕሮጀክቱ የጤና ባለሙያዎች ለበሽተኛ ያላቸውን አስተያየት እንዴት ይገልፁታል መልስዎን እስማማለሁ ወይም አልስማማም በማለት ይመልሱ		
008	ተሣታፊውን ያመሰግናሉ	1. እስማማለሁ 2. አልስማማም	
009	በጥሞና ያዳምጣሉ	1. እስማማለሁ 2. አልስማማም	
010	በሁሉም ነገር ይረዳሉ	1. እስማማለሁ 2. አልስማማም	
011	በቀላሉ መረጃን ይሰጣሉ	1 እስማማለሁ 2 አልስማማም	
012	ገለፃቸው ባህልን የተመረኮዘ ነው	1 እስማማለሁ 2 አልስማማም	
013	ከጤና ባለሙያዎቹ ጋር መነጋገር ምቾት ይሰማዎታል	1. አዎ 2. አልፎ አልፎ 3. የለም	
014	በምክር አገልግሎት ወቅት ደህንነትዎ ይጠበቅልዎታል	1. አዎ 2. የለም	
015	ምን ያህል ሰዓት ጠበቁ የመጀመሪያ ቀጠሮ ለመውሰድ የደም ውጤት ለመስማት ሀኪምዎን ለማግኘት	---------- ---------- ----------	
016	ይሄንን አገልግሎት ለሌላ ለቤተሰብዎ አባል ተጠቃሚ እንዲሆን ይፈልጋሉ	1. አዎ 2. የለም 3. አላውቅም	
017	ከሣንባ ነቀርሣ በሽተኛ ጋር ጥብቅ ቁርኝት ኖሮዎት ያውቃሉ ወይ	1. አዎ ቤተሰብ ውስጥ 2. አዎ ስራ ቦታ 3. የለም	
018	የሣንባ ነቀርሣ ህክምና ወስደው ያውቃሉ ከወሰዱ መቼ	1. አዎ ከሁለት ዓመት በፊት 2. አዎ ባለፉት ሁለት ዓመት ውስጥ 3. የለም	

ክፍል 3

001	የሣንባ ነቀርሣ መድኃኒት እንዲወስዱ በሀኪም ቢጠየቁ ፈቃደኛ ነዎትን (ካልሆነ ወደ ጥያቄ 003 ይተላለፉ)	1. አዎ 2. የለም	
002	መልስዎ አዎን ከሆነ መከላከያውን ለመውሰድ ለምን ተስማሙ	1. የሣንባ ነቀርሣ አደገኛ በሽታ ስለሆነ 2. ጓደኛዬ በሣንባ ነቀርሣ ስለሞተ 3. የቤተሰብ ግፊት ስላለ 4. ከሣንባ ነቀርሣ በሽተኛ ጋ የቅርብ ግንኙነት ስላለኝ 5. ሀኪም ካዘዘኝ 6. ሌላ	
003	መልስዎ የለም ከሆነ መከላከያውን ላለመውሰድ ምክንያትዎን ይንገሩን	1. በመከላከያው ጥቅም እምነት ስለሌለኝ 2. መድኃኒት በየቀኑ መውሰድ ስለሚያስጠረጥረኝ 3. መድኃኒቱን ቤቱ ውስጥ የት ማስቀመጥ እንዳለብኝ ስለማላውቅ 4. መድኃኒቱን ለመውሰድ ስለምፈራና ስለማያመቸኝ 5. ሀኪም ስላላዘዘኝ 6. ሌላ	
004	መከላከያውን ባይወስዱ ችግር ይገጥመኛ ል ብለው ያስባሉ	1. ሣንባ ነቀርሣ ይይዘኝ ይሆናል 2. አላውቅም 3. ሌላ	

ክፍል 4 የመድኃኒት አጠቃቀምና ተጓዳኝ ችግሮች

001	የመድኃኒት አወሳሰድ ልምድዎን ይንገሩን	1. በተባልኩ ጊዜና ሰዓት እወስዳለሁ 2. አልፎ አልፎ ልረሣ እችላለሁ 3. ሰው ሲያስታውሰኝ እወስዳለሁ	
002	በአሁኑ ሰዓት የሣንባ ነቀርሣ መከላከያ ይወስዳሉን መድኃኒት የማይወስዱ ከሆነ ወደ ጥያቄ ክፍል 5 ይተላለፉ	1. አዎ 2. የለም 3. ጨርሻለሁ 4. አቋርጫለሁ	
003	መከላከያውን ለ9 ወር መውሰድ እንዴት ያዩታል	1. ያስቸግራል 2. አልፎ አልፎ ያስቸግራል 3. ችግር የለውም	
004	በቀጠሮ መድኃኒት ሳይወስዱ የቀሩበት ጊዜ አለ	1. አዎ 2. የለም 3. አልፎ አልፎ	
005	ለምን ያህል ጊዜ አቋረጡ	1. ለቀኖች 2. ለሣምንት 3. ለወሮች	
006	መቼ ነበር ያቋረጡት	1. በመጀመሪያው ሣምንቶች ውስጥ 2. በመጀመሪያው ከ1-2 ወሮች ውስጥ 3. በመጀመሪያው ከ3-4 ወሮች ውስጥ 4. ከአምስተኛው ወር በኋላ	
007	መድኃኒቱን ሳይወስዱ ቢቀሩ ምን ያደርጋሉ	1. በሚቀጥለው ቀን ጨምሬ እወስዳለሁ 2. በቀኑ መውሰድ የሚገባኝን ብቻ እወስዳለሁ	
008	የረሱትን መድኃኒት እንዲወስዱ ማን ያስታውስዎታል	1. የፕሮጀክቱ የጤና ባለሙያዎች 2. እራሴ አስታውሼ እወስዳለሁ 3. ሌላ	
009	መድኃኒቱን ሲወስዱ ያጋጠመዎት የጤና ችግር አለ	1. አዎ 2. የለም 3. መድኃኒት አልወስድም	
010	መልሱ አዎን ከሆነ ምን የጤና ችግር ገጠመዎ	1. ከነርቭ ጋር የተያያዘ 2. የጉበት ችግር 3. የማንቀጥቀጥ 4. ሌላ	

ክፍል 5 በቀጠሮ ያለመምጣት የሚቀርቡ ምክንያቶች

በቀጠሮ መቶ መድኃኒት ባለመውሰድ የሚሰጡ መልሶችን

አዎ እስማማለሁ ወይም አልስማማም በማለት ይመልሱ

001	ጤንነት ከተሰማኝ	1. እስማማለሁ 2. አልስማማም	
002	የሣንባ ነቀርሣ የለብኝም ብለው ካሰቡ	1. እስማማለሁ 2. አልስማማም	
003	ተጓዳኝ የመድኃኒቱን ችግር በመፍራት	1. እስማማለሁ 2. አልስማማም	
000	በአጠቃላይ የመረጃ ማጣት		
004	ጊዜ ማጣት	1. እስማማለሁ 2. አልስማማም	
005	የፍላጐት አለመኖር	1. እስማማለሁ 2. አልስማማም	
006	መድኃኒቱን ለመውሰድ ስለማይመች	1. እስማማለሁ 2. አልስማማም	
007	ክህደት ኤች አይ ቪ የለብኝም በሚል	1. እስማማለሁ 2. አልስማማም	
000	ባጠቃላይ ተነሳሽነት ያለመኖር	1. እስማማለሁ 2. አልስማማም	
008	ሌላ ቦታ ርቆ በመሄድ	1. እስማማለሁ 2. አልስማማም	
009	የቤተሰብ ችግር	1. እስማማለሁ 2. አልስማማም	
010	በጠና መታመም ምክንያት	1. እስማማለሁ 2. አልስማማም	
011	የቤተሰብ ማጣጣል	1. እስማማለሁ 2. አልስማማም	
000	ባጠቃላይ ረዳት ማጣት	1. እስማማለሁ 2. አልስማማም	

ክፍል 6 የደም ውጤትን በተመለከተ መጠይቅ

001	ከጓደኛዎ ጋር ነው የሚኖሩት	1. አዎ 2. የለም	
002	ጓደኛዎ የርስዎን የደም ውጤት ያውቃሉ	1. አዎ 2. የለም 3. ለመንገር ፈቃደኛ አይደለሁም	
003	በጓደኛዎ ፊት መድኃኒት መውሰድ ይቸገራሉ	1. አዎ 2. የለም 3. በጓደኛዬ ፊት መድኃኒት አልወስድም	
004	ከርስዎ ጋር ተመሳሳይ ችግር ላለበት ሰው መድኃኒቱን መውሰድ እንዳለበት ይመክራሉን	1. አዎ 2. የለም 3. አላውቅም	

<u>ክፍል 7.</u> የተሳታፊውን የክትትል መዝገብ በማየት በጠያቂው የሚሞላ

001	የሣንባ ነቀርሣ ክትባት	1. አዎ አለ 2. የለውም	
002	PPD ክትባት ውጤት	1. ውጤት የለም 2. ከ1-5 ሚ.ሚ ጥጥር አለው 3. ከ5-10 ሚ.ሚ ጥጥር አለው 4. ከ10 በላይ ሚ.ሚ ጥጥር አለው	
003	የአክታ ምርመራ ውጤት	1. አለው 2. የለውም 3. አልተሰራም	
004	የራጅ ምርመራ ውጤት	1. አዎ አክቲቭ የሣንባ ነቀርሣ ምልክት 2. አክቲቭ የሆነ የሣንባ ነቀርሣ ምልክት የለም 3. ነፃ ነው	
005	የጉበት ምርመራ ውጤት	1. የጉበት ችግር አለው 2. የጉበት ችግር የለውም	
006	በቀጠሮ ይገኛል	1. አዎ 2. የለም	
007	የሽንት ምርመራ ውጤት ለ INH	1. ፖዝቲቭ 2. ኔጋቲቭ 3. አልተሰራም	
008	CD 4 ቁጥር ልክ	1. ከመከላከያው በፊት 2. ከመከላከያው በኋላ	
009	የቫይረሱ ቁጥር መጠን	1. ከመከላከያው በፊት 2. ከመከላከያው በኋላ	
010	የተሣታፊው አማካይ ክብደት	1. ከመከላከያው በፊት 2. ከመከላከያው በኋላ	