



UPTAKE OF ISONIAZID PREVENTIVE THERAPY AND PATIENT ASSOCIATED
FACTORS IN ADULT PLHIV ON CHRONIC HIV CARE AT SPHMMC ART CLINIC.
ADDIS ABABA, ETHIOPIA

INVESTIGATOR: LALISA CHALA (INTERNAL MEDICINE RESIDENT)

A THESIS PROPOSAL SUMMITTED TO SAINT PAUL'S HOSPITAL MILLINUM
MEDICAL COLLEGE DEPARTMENT OF INTERNAL MEDICINE FOR THE PARTIAL
FULFULLMENT OF CERTIFICATE IN INTERNAL MEDICINE SPECIALITY

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ADIVICERS: 1) DR. SAMUEL GIRMA (MD, INTERNIST, MPH)
2) MRS, FIREHIWOT WORKU (BSC, MPH)

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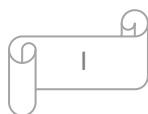
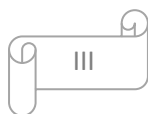


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LIST OF ACRONYMS

AIDS: Acquired Immune Deficiency Syndrome

AOR: Adjusted Odds Ratio

ART: Anti Retroviral Therapy

COR: Crudes Odds Ratio

FMOH: Federal Ministry of Health

HAART: Highly Reactive Antiretroviral Therapy

HIV: Human Immune Deficiency Virus

LITB: Latent Infection of TB

IPT: Isoniazid Preventive Therapy

MDR: Multi Drug Resistant

PLHIV: People Living with HIV

SPHMMC: Saint Paul's Hospital Millennium Medical College

SPSS: Statistical Package for the Social Sciences

TB: Tuberculosis

TB/HIV: Tuberculosis and HIV co-infection

THAC: TB/HIV Advisory Committee

TWG: Technical Working Group

WHO: World Health Organization

ABSTRACT

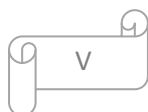
BACKGROUND: Management of latent tuberculosis (TB) infection (LTBI) is one of the globally recommended key strategies to end TB. Patients living with human immune deficiency virus (PLHIV) and under-five children were the two groups recommended to receive Isoniazid Preventive Therapy (IPT) according to the earlier versions of world health organization (WHO) guidelines, and most high burden countries adopted this recommendation. However, there is limited experience with translation of global recommendations into action at country levels. Ethiopia has adopted this policy in 2008 as a pilot that has since been rapidly rolled out nationally even though IPT uptake remains very low in the country.

OBJECTIVE: The overall aim of the study was to assess the uptake of IPT and patient associated factors among IPT-eligible PLHIV and on chronic HIV care follow up at Saint Paul's Millennium Medical College (SPHMMC) antiretroviral therapy (ART) clinic.

METHOD: Institution based Retrospective Descriptive study was conducted in this study. Data was extracted from 350 eligible patients living with human immune deficiency virus and on chronic HIV care at ART clinic from patient charts to calculate the proportion of IPT uptake among eligible PLHIV. Bivariate analysis, followed by simple binary and multivariable logistic regression analyses was used to identify patient associated factors with uptake of IPT. 95% Confidence intervals and $(p) < 0.05$ were used to measure significance of associations between uptakes of IPT versus independent variables.

RESULT: Proportion of eligible PLHIV who had been ever provided with IPT was 55 (16%). The clients within the age range of 30-39 years (AOR 17.07, 95% CI: 1.96-14.97) had significant higher IPT uptake rate compared to those age above 50. Clients living in Addis Ababa (AOR 52.90, 95% CI: 2.91-9.08) had significant higher uptake rates when compared to their counterparts from other towns. Clients with high level of education (AOR 23.43, 95% CI: 1.29-4.26) had higher uptake rate than those with low educational status. Clients who presented with early disease stage (AOR 15.27, 95% CI: 1.19-19.06) had higher IPT uptake rate when compared with their counterparts who presented at advanced stage of their disease. Clients less than three years since enrollment into HIV care (AOR 0.07, 95% CI: 0.01-0.46) and those with poor functional status at enrollment (AOR 0.03, 95% CI: 0.01-0.96) had significantly low IPT uptake in comparison with those who were enrolled for more than five years and with good functional status at enrollment respectively. IPT uptake was significantly lower among Clients who were on HAART for less than 6 months (AOR 0.04, 95% CI: 0.04-0.54) when compared with those on treatment for more than a year.

CONCLUSION AND RECOMMENDATION: In this study the IPT coverage at SPHMMC Chronic HIV Care Unit was considerably low. The uptake was significantly lower among the following patient variables: old age, clients living outside of Addis Ababa, low educational status, advanced disease stage (WHO stage 4) and clients with poor functional status, new to care clients as well as those on HAART for short duration. Another study of this nature with the objective to find out the reason behind low uptake in this group of clients is recommended.



CHAPTER ONE: INTRODUCTION

1.1 Background

Globally in 2017, there were an estimated 10 million people fell ill with TB including 1 million among 37million PLHIV. The risk of developing TB PLHIV was 20 times higher than the risk in the rest of the world population. HIV patients infected with TB have approximately a 5-10% annual risk of developing TB, compared to a 5-10% life time risk among seronegative individuals. The proportion of TB cases confected with HIV was highest in countries in the WHO African Region, exceeding 50% in parts of southern Africa .The 30 high TB burden countries accounted for 87% of all estimated incident cases worldwide, and eight of these countries accounted for two thirds of the global total. [1, 2, and 3].

TB is the tenth leading cause of death worldwide, and since 2011 it has been the leading cause of death from a single infectious agent, ranking above HIV and malaria [4]. There were an estimated 1.3 million deaths from TB among HIV-negative people in 2017 and an additional 0.3 million deaths from TB among HIV-positive people. About 82% of TB deaths among HIV-negative people occurred in the WHO African Region and the WHO South- East Asia Region in 2017; these regions accounted for 85% of the combined total of TB deaths in HIV-negative and HIV-positive people. Globally, the number of TB deaths among HIV-negative people per hundred thousand populations was 17 in 2017 and 21 when TB deaths among HIV-positive people were included [1].

Ethiopia is among the 30 high TB, TB/HIV and multi drug resistant (MDR) TB burden countries with an estimated total (includes HIV+TB) incidence and prevalence rate of 200 and 207 per hundred thousand populations respectively. Incidence in PLHIV (HIV+TB only) is 12 per hundred thousand populations. Mortality in sero-negative patients (excludes HIV+TB) is 24 while mortality in PLHIV (HIV+TB only) is 3.5 per hundred thousand populations [1]. For this reason prevention of active TB disease by treatment of LTBI is a critical component of the WHO End TB Strategy and the efficacy of currently available treatment ranges from 60% to 90% [2, 6].

Despite evidence and strong recommendations underscoring the importance of IPT in reducing HIV associated morbidity and mortality, IPT coverage of PLHIV remains low in most high burden TB/HIV settings, including Ethiopia [2, 7]. Among people newly enrolled in HIV care during 2015, 10.6% were diagnosed with active TB and 40.6% initiated IPT, which leaves a 48.8% IPT gap and IPT coverage among newly enrolled HIV patients is estimated at 38% globally and 39% in the Africa Region according to WHO report [8].

In Ethiopia, TB/HIV collaborative activities were initiated in 2002 with establishment of a national coordinating body- The TB/HIV advisory committee (THAC). In 2004, pilot implementation was started in 9 selected sites. Building on the experience of the pilot implementation and as part of the effort to further strengthen the collaborative activities, the National TB/HIV Technical Working Group (TWG) was established in April 2007. The TWG, co-chaired by the TB and HIV programs on a yearly rotation basis started its functions by revising the national implementation guideline in 2008. This was followed by massive capacity building efforts for health workers. Between the year 2007 and 2008, major expansion of ART sites took place i.e. in terms of number, access (geographic coverage). In 2012, TB/HIV collaborative activity guideline got incorporated into comprehensive TBL & TB/HIV guideline. Recommendations from WHO's 2011 guidelines for intensified case finding and IPT were incorporated into the training materials [5].

To promote joint TB/HIV programming, to leverage resources for collaborative activities and to put together the planning process between the two programs, joint single TB/HIV concept note was developed in 2014. Despite the effort put to improve the uptake of IPT including massive expansion of HIV treatment sites providing IPT, there was significant decline in the proportion of PLHIV put on IPT. The main reasons for low provision and uptake of IPT were assessed as part of the national assessment of TB and TB/HIV services. According to the report, 72% of respondents reported INH supply interruption as the main reason while the remaining 28% reported lack of training, fear of acquiring further resistance in individual cases, difficulty of ruling out active TB (especially in children) because of lack of diagnostic capacity and fear of INH toxicity as reasons for the low uptake of IPT [9].

Based on the findings of the national assessment, an accelerated IPT implementation plan was developed and series of sensitization workshops were conducted for health care professionals nationwide which are believed to have contributed to increasing IPT uptake performance in 2015. Routine data from 2014-2015 showed that 96% of pre-antiretroviral (ART) patients were screened for TB during their initial visit. Among these 9.2% of were diagnosed with active TB and 18.2% of those with no clinical symptoms for TB received IPT (10). In our institution, Information on uptake rate of IPT and associated factors among PLHIV and on chronic HIV care was not studied and documented. Therefore, the aim of this study was to provide information on IPT uptake proportion and patient factors associated with IPT uptake and Identification of patient associated factors.

1.2. Statement of the Problem

The emergence of the HIV/AIDS epidemic has brought out new challenges in the fight against TB. The compromised immunity of PLHIV places them at greater risk for TB and both HIV and TB each accelerate the other's progression. Without proper host immune response, TB infection can easily progress to active disease and unlike other opportunistic infections, TB can occur at any level of immunodeficiency [1, 2, 3, 4]. Evidence has demonstrated that IPT significantly reduces the risk of TB in PLHIV [2, 5, and 6]. Management of latent TB has been part of the global recommendations for many years now. However, uptake of these services has been slow in many countries with only 38% of PLHIV newly enrolled in care having received INH preventive therapy in 2015 according to WHO's report [1].

The fundamental challenges of health systems in low income countries includes health care worker (HCW) shortage, interrupted supply of drug and commodities, as well as limited laboratory access also pose constraints on IPT implementation. Specific provider concerns in utilizing IPT have included ruling out active TB, toxicity of INH, side effects of INH, possible inducement of INH resistance, and maintaining patient adherence to the IPT regimen [11] At the patient level, a fear of stigmatization, lack of money for transport, competition with use of traditional medicine, and a reluctance to take medication in the absence of symptoms have all been barriers to achieving adherence. Negative side effects and pill burden have also been noted as challenges to IPT completion [12].

Although Ethiopia adopted an IPT policy shortly after the WHO recommendations were made, weak commitment from health authorities, poor mechanisms for program monitoring, and a lack of supervision still remain barriers to achieving IPT uptake goals in Ethiopia [13]. The main reasons for low provision and uptake of IPT were assessed as part of the national assessment of TB and TB/HIV services were mentioned earlier under the background information. However, our understanding of IPT implementation challenges remains limited. The objective of this study was to determine IPT uptake proportion and to identify patient factors associated with it among eligible PLHIV on Chronic HIV Care at SPHMMC ART Clinic.

1.3. Significance of the Study

TB remains the leading preventable cause of morbidity and mortality in PLHIV. IPT is internationally proven, effective treatment for TB prevention in PLHIV. Although TB represents a potential threat to the achievable benefits of HIV scale up care and treatment, IPT represents strong potential for reduction of mortality and morbidity in PLHIV. Despite its proven efficacy IPT uptake rate remains significantly low at countries level. IPT provision in Ethiopia is still much lower than expected.

No study has been conducted to so far to determine IPT uptake rate in SPHMMC Chronic HIV Care Service Unit. Therefore, this study attempted to present the status of IPT provision and also identifies patient factors associated with its uptake and the findings of this study would be helpful for the hospital to know its IPT uptake status and areas to be focused on to improve implementation of IPT. This study also provides a ground for further studies on IPT implementation in the future in our setup.

CHAPTER TWO: LITERATURE REVIEW

2.1 TB Chemoprophylaxis and Its Effect on TB Incidence and Mortality

Several studies have previously demonstrated the effects of using chemoprophylaxis among adults and children without HIV to reduce the burden of TB on them. A community-wide randomized controlled trial in Alaska during the 1960s first identified the effectiveness of INH, observing a 55% reduction TB incidence during a period of 6 years [14]. IPT has also been associated with reduced mortality among HIV positive individuals. In a study done by Churchyard et al, IPT resulted in a 26% reduction in mortality among patients with a positive tuberculin test, as compared with the placebo arm [15]. Two large scale cohort studies in Brazil and South Africa observed a 76-89% TB risk reduction among PLHIV receiving both ART and IPT simultaneously [16,17].

A systematic review of 12 randomized controlled trials (RCTs) of 8578 PLHIV found that preventive treatment reduced the overall risk for TB by 33% (relative effect [RR] 0.67, 95% CI 0.51;0.87) PLHIV. For those who were tuberculin skin test (TST) positive, the reduction increased to 64% (RR 0.36, 95% CI 0.22; 0.61). Although not statistically significant, the reduction was 14% among TST-negative people (RR 0.86, 95% CI 0.59; 1.26) and those of unknown TST status (RR 0.86, 95% CI 0.48; 1.52) [18]. A double-blind RCT of 1329 people living with HIV and receiving ART indicated that those on ART with negative TST benefited more from IPT than those who were TST or IGRA positive [19]. An RCT of 2056 PLHIV [20] and follow-up data showed additive benefits of preventive treatment plus ART in reducing both TB incidence and overall mortality. The protective effect lasted for more than 5 years [21].

In Ethiopia, a study carried out in the Southern Nations, Nationalities and People's Region (SNNPR) observed an 80% reduction in TB incidence among ART patients taking IPT, and a 65% reduction in TB incidence among pre-ART patients taking IPT [22]. Another two studies done in Ethiopia have shown that IPT had significant contributions to reduce the burden of TB in ART patients than non-IPT group. Hospital-based retrospective study carried out in Arbaminch hospital ART clinics on a total of 271 study participants have shown that TB-infected ART patients were higher among non-IPT group (37 [27.8%]) compared to IPT group (12 [8.7%]). The finding showed that IPT prophylaxis significantly reduces acquiring TB with the relative risk =0.31 (95% confidence interval =0.122- 0.49) in ART patients of this study site where the TB prevalence is prominent.

Another study done at Jimma hospital in which a total of 588 patients on pre-ART care (294 IPT and 294 non-IPT group) was followed retrospectively for a median duration of 24.1 months showed that during the follow up period, 49 individuals were diagnosed with tuberculosis, giving an overall incidence of 3.78 cases per 100 person year (PY). The incidence rate of TB was 5.06 per 100 PY in non-IPT group and 2.22 per 100 PY in IPT user group.

Predictors of higher TB risk were: being on clinical WHO stage III/IV (adjusted hazard ratio (AHR) = 3.05, 95% confidence interval (CI): 1.61, 5.81); non-IPT user (AHR = 2.02, 95% CI: 1.04, 3.92); having CD4 + cell count less than 350 cells/ μ l (AHR = 3.16, 95% CI: 1.04, 3.92) and between 350–499 cells/ μ l, (AHR = 2.87; 95% CI: 1.37 - 6.03) and having episode of opportunistic infection (OI) in the past (AHR = 2.41, 95% CI: 1.33-4.34).

2.2 Uptake of IPT

In northern Ethiopia, one study found the coverage of IPT among eligible PLHIV to be 19.6%. INH stock out, fear of creating INH resistance, problems in patient acceptance, and lack of commitment of health managers to scale up the program were indicated by health providers as the main barriers hindering implementation of IPT. There was a wide variation in uptake, although not statistically significant, when hospitals were compared with other smaller facilities (hospitals had higher uptake); as well as when the authors compared early implementers to the late adopters of IPT. It is also worth noting that for the 19.6% that were initiated on IPT, a third did not complete their course. [13] Two studies conducted in Addis Ababa have shown the overall proportion of PLHIV who had ever uptake of IPT was **32%** in one study and **28.5** in the other study [27, 28]

In a cross-sectional study done at one hospital in Kenya of adults that had been on treatment and care services for at least six months an uptake of IPT of 77% was noted, a very modest figure compared to the Ethiopian studies. Three variables were found to independently affect initiation on IPT, these were- fear of acquiring TB, having received IPT-associated health education, as well as having a good relationship with the healthcare worker (HCW) [29] A clinical trial in Botswana setting out to describe reasons from exclusion from IPT, as well as to describe outcomes of PLHIV after six months of IPT, found that 68% of those that had TB excluded via two-stage TB screening process were initiated on IPT. It also found that being on ART was significantly associated with greater adherence to IPT, even after multivariate analysis [30].

One study in northern Thailand found that only 20% of health facilities that should have been offering IPT actually were providing this service. Among the 80% majority of non implementers, they further found that the main barriers were the unclear direction of national policy (60%), fear of emerging INH resistant TB (52%), as well as fear of poor adherence (30%) once patients were initiated. Among implementers the motivating factors were by the knowledge that IPT can prevent TB (63%), adhering to national guideline (34%), and concern for TB prevention even after the expansion of access to ART (32%) [11].

2.3 Adherence to IPT and Rates of Completion of IPT

Uptake of IPT can be thought of as a process indicator for monitoring incidence of TB among PLHIV. Further downstream, indicators such as adherence to IPT, completion rates of IPT among PLHIV initiated on ART, as well as the incidence of TB among PLHIV can also be monitored.

An institution-based prospective cross-sectional study which was conducted from March 10 to June 11, 2016 in Gondar town has shown the adherence level to IPT was 90.3% for the last 7 days of the study. Respondents who had received an explanation about IPT were 83% times more likely to be adherent compared to those who had not received it (95% CI, AOR: 0.266 [0.23–3.127]). Respondents who had taken IPT for 5 months were more likely to be adherent than those who had taken it for 1–2 months [95% CI, COR: 1.484]. On the other hand, respondents who experienced side effects were 36% less likely to be adherent compared to those who did not experience any. Among the predictors reported, carelessness and/or forgetfulness, side effects, and absence from home were the major factors identified for being non adherent. [31]

A facility based cross-sectional study which was conducted in Addis Ababa, the capital city of Ethiopia from December 2010 to February 2011 the level of self-reported adherence rate of IPT is found to be 89.5% with 95% CI (86.1–92.3). In this study, patients who were taking antiretroviral drug were more likely to be adherent [95% CI, COR = 1.97 (1.01–3.84)] than patients who were on Pre-ART with $P < 0.05$. Respondents who reported to take their pills in the range of 1–11 hrs before the interview were more likely to be adherent than those who did not remember when they took their last dose [95% CI, COR = 3.79 (1.49–9.64)]. Respondents who have taken IPT for ≥ 5 months were more likely to be adherent than those who took for 1-2 months [95% CI, COR 3.86 (1.24–12.00)]. Individuals who were explained about the reasons for taking IPT by their doctors/nurses were found to be more likely to be adherent than those who did not have information why they are taking IPT [95% CI, COR 6.83 (1.47–31.70)].[32]

In terms of IPT completion rates, a similarly heterogeneous picture is found. A randomized control trial found a 65% IPT completion rate in Brazil [33]. One study done in Ethiopia also found similar rates with a completion rate of 68% [13]. Another study among PLHIV that were ART-naïve at being initiated on IPT found completion rates as high as 78% however. Completion rates seem to be higher among the ART-naïve demographic compared to their counterparts on ART. Further, the authors found that the ART-naïve group that was subsequently put on ART while on IPT had lower completion rates. This is somewhat baffling as being on ART was identified by several authors to have a positive effect on adherence, as noted earlier. Being on ART could however have an adverse effect on treatment completion compared to adherence through a separate mechanism.

This remains to be explored and needs to be studied urgently in light of its programmatic implications. To support this, the authors note that the commonest reason for not completing IPT among those that ended up with concomitant ART was drug toxicity, while the commonest reason among those that were ART-naïve until end of IPT was being lost to follow-up [34].

In a retrospective cohort study carried out in seven pilot sites in Zimbabwe, it was found that 81% of PLHIV on IPT completed their course, a notably high figure. This is potentially confounded by the fact that these pilot sites started IPT implementation much earlier than the other 627 IPT-implementing facilities, and have since matured through any teething issues and therefore do not reflect the performance of the facilities that started to implement more recently. This study further noted that over 90% of those that failed to complete IPT were due to three reasons only- being lost to follow up, undocumented reasons, as well as drug toxicity. Finally, the authors note that in the study being currently on ART, and receiving a two month supply of INH at the start of treatment as being associated with a lower risk of not completing IPT; while missing clinic visits prior to starting IPT was associated with a higher risk of non-completion.[35]

2.4 WHO Progress of IPT Implementation Guidelines

The efficacy of TB Preventive therapy was first recognized in a 1993 policy statement by the WHO and the International Union against Tuberculosis and Lung Disease (IUATLD) [23]. In 1998, the WHO recommended a joint approach to tackling TB and HIV, with six months of IPT outlined as part of the essential package of care for PLHIV in whom active TB was safely excluded [24]. Since 1998, a number of additional important global TB HIV policy statements and guidelines have continued to push forward IPT as a key part of TB as well as HIV control.

Advocacy for the roll-out of IPT as a public health intervention for people with HIV continued to grow during the WHO “3 I’s Meeting: Intensified case finding, IPT, and TB infection control for people living with HIV” in 2008, where the WHO urged that “national policies should be strengthened to include IPT and a standardized screening tool as part of national HIV/AIDS policy and program guidance” [25]. In efforts to advance intensified case finding and IPT uptake, the WHO recommended a new TB screening algorithm for PLHIV among resource limited settings in 2011. This algorithm outlined provider-initiated TB screening based on 4 symptoms for ruling out active TB in PLHIV- the absence of any cough, fever, night sweats, or weight loss [5].

This provided a simplified and cost-effective way for providers to identify HIV patients eligible for IPT and those who needed further TB evaluation. In 2013 and 2015 the WHO put forth recommendations and operational guidelines about systematic screening for active tuberculosis, emphasizing the importance of routine symptom based TB screening of PLHIV every initial and follow up visit [26].

CHAPTER THREE: -OBJECTIVES

3.1. General Objective

- The aim of the study is to assess IPT uptake among IPT-eligible PLHIV in Adult Patients on Chronic HIV Care at SPHMMC ART Clinic and identifies patient factors associated with its uptake.

3.2. Specific Objectives

1. To assess uptake of IPT among eligible PLHIV in Adult Patients on Chronic HIV Care at SPHMMC ART Clinic
2. Identify patient factors associated with uptake of IPT in Adult Patients on Chronic HIV Care at SPHMMC ART Clinic

CHAPTER FOUR : METHDOLOGY

4.1 Study Area and Study Period

4.1.1 Study Area

This study was conducted in SPHMMC Adult Chronic HIV Care Service Unit. St. Paul's hospital is one of the largest tertiary referral public hospitals in the capital under the Federal Ministry of Health. The hospital is located in Gullele Sub city at Swaziland Street, Addis Ababa, Ethiopia. Established by Emperor Haile Selassie in 1961, the hospital primarily gives service to those unable to afford care elsewhere. It has over 1200 clinical and non-clinical staff. The hospital added a medical college in 2007 G.C. The hospital has different units in it: internal medicine, pediatrics, gynecology/obstetrics, surgery, dentistry, psychiatry, ophthalmology, maxillofacial, hospital pharmacy, dermatology and the Chronic HIV Care Service Unit.

4.1.2 Study Period

From January 1, 2017 to December 31, 2018 GC.

4.2 Study Design

A Retrospective Descriptive Study Design was used

4.3. Population

4.3.1 Source Population

All HIV positive patients who have been enrolled to chronic HIV care at ART clinic

4.3.2 Study Population

All HIV positive clients who visited the clinic during the study period specified

4.3.3 Study Unit

Adult PLHIV and eligible for IPT who were getting ART services during the specified study period

4.4. Inclusion and Exclusion Criteria

4.4.1 Inclusion Criteria

- Confirmed adult PLHIV on follow up seen at least once in ART clinic during review period
- Active TB disease ruled out through TB Screening
- Seen between the 01st January 2017 and the 31st December 2018GC

4.4.2 Exclusion Criteria

- Age < 18 years.
- Hypersensitivity/ allergy to INH.
- Clients with active hepatitis.
- PLHIV with active tuberculosis on treatment or tuberculosis suspected.
- Those treated for tuberculosis within the last three years.
- Those who took IPT previously.

4.5 Sampling

4.5.1 Sample Size Determination

The required sample size is determined by using single population proportion formula

$$n = \frac{(Z_{\alpha/2})^2 P (1-p)}{d^2}$$

The following assumptions were considered: proportion (P) of uptake of IPT 32% and 44% for the associated factors (the highest being educational level) from the study which was done in Addis Ababa in 2008 GC, 95% confidence level ($Z_{\alpha/2}$), and 0.05 margin of error (D). The calculated total sample size (N) was 324 for uptake of IPT and 350 for associated factors. The largest sample size was taken. A total of 350 study participants' available information such as demographic data, IPT status, WHO Clinical Stage, duration of enrolment into care, duration on HAART, functional Status as well as other variables were collected from patient charts to establish the uptake of IPT among eligible PLHIV and assessing patient associated factors.

4.5.2. Sampling Procedure

This process began after all the necessary permissions from the head unit of the ART Clinic. Information data from Smart Care was obtained with the assistance of the data clerk personnel for all PLHIV who were on follow up during the study period specified. The data obtained had information on patients ID number, age, sex, Tb screening status and Tb treatment status, previous IPT treatment history and baseline LFT as transferred in and out patients record. The data extraction processing performed to obtain eligible PLHIV for IPT before the actual sample data collection was presented below.

4.5.2.1 Abstraction of Records from the Smart Care

3649(net cohort) records of PLHIV was abstracted from the Smart Care database and exported to excel spreadsheet which was processed for assessment of eligibility of PLHIV for IPT provision. Data representing an individual client, in the form of an individual row on the Excel spreadsheets with the required information described in the preceding chapter was then processed as described below.

Out of the total 3649 records 204 records clients who were transferred in, 150 records of clients age less than 18 years old, 800 records with no documented Tb screening status, 429 patients with documented Tb treatment history in the last three preceding years, 180 patients on Tb treatment at the time of the study period, 133 patients with documented previous history of IPT treatment and 118 patients with deranged liver function test at any point were excluded. The numbers of files that fit this description and were removed are shown with flow chart below. The remaining 1,630 records were checked for duplication and duplicates were not identified through this process. Finally, while the records were still in the form of an individual row on the Excel spreadsheets, they were numbered to be used as a sampling frame from which systematic sampling was done to draw the sample.

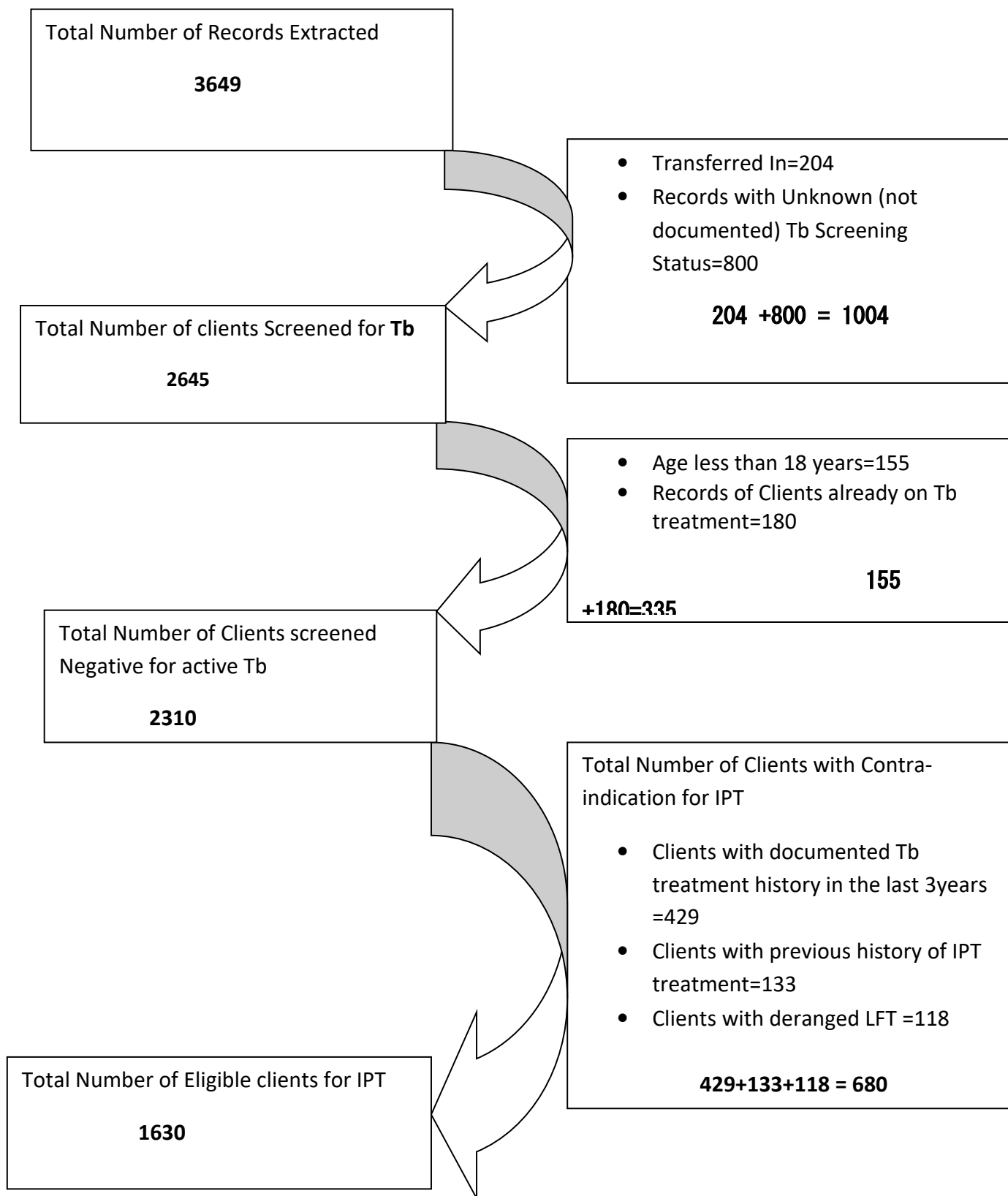


Figure1: Flow Diagram Summarizing the Selection Process of the Study Population before Drawing Samples

4.6 Variables

4.6.1 Dependent Variable

- Uptake of IPT

4.6.2 Independent variables

- Socio-demographic characteristics (Age, Sex, Residence, Educational status, Marital status)
- WHO Clinical Stage for RVI
- Duration of stay on HAART
- Functional Status
- Duration of enrolment into care

4.7 Operational Definition

- IPT is the use of INH drug to sterilize latent TB infection.
- Uptake is the use of INH drug by people at high risk of developing active tuberculosis

4.8 Data Collection

This process began after all the necessary permissions from the department and chart record unit was obtained. Information data was collected from clients' chart.

4.8.1 Instrument

Well-structured check list

4.8.2 Data Collection Procedure

Two nurses were deployed as data collector. Data was extracted from patients chart.

4.9 Data Quality Management

The data was collected using well-structured check lists that was prepared in English. The data collectors were trained on how to use the data collection check list format and appropriate data recording and pre test was done before the actual data collection. The collected data was checked for completeness, clarity and consistency by the investigator during the data collection process.

4.10 Data Analysis and Presentation

Data entry was done using EPI info version 7.2.2.6. Data clean up was performed to check for accuracy, consistencies and values. Data analysis was performed using SPSS 25 statistical packages. Descriptive statistics was employed for socio demographic characteristics, for uptake of IPT among eligible PLHIV. Both descriptive and inferential statistics were used for presenting the findings. Bivariate and multivariate logistic regressions were used. 95% Confidence intervals and $(p) < 0.05$ were used to measure significance of associations between uptakes of IPT versus independent variables.

4.11 Ethical Consideration

Approval request paper was submitted to Internal Medicine Department to undertake the study. Confidentiality of the data was assured by keeping information that would have revealed patient's identity strictly hidden in a locked drawer and patients' name was not revealed in the check list; instead ID number was used.

CHAPTERFIVE: - RESULT

5.3 Background Characteristics of Participants

As can be seen on Table one below among the study clients, there were 126 male and 224 female clients with female to male distribution of 64:36. The median age of the clients was 42 years (IQR 37-48). In terms of residential areas 43% (152) of clients on follow up were from Addis Ababa followed by 24%(84) from Burayu. Nearly half, 51 %(179), of the clients were married. Majority of the clients 62 %(217)) were graduated from college.

In terms of WHO clinical stage at enrolment, nearly one third 136 %(126) were having stage three diseases respectively. Regarding functional status of the clients at the time of enrollment into care, majority of them 159 (45 %).With respect to the duration of enrollment into chronic HIV care, almost half 165 (47 %) of the clients were less than three years since enrolled while the remaining half 185 (53 %) were enrolled for more than three years. Clients who were on HAART for less than six months accounted for about one third 108(31 %) while the remaining two third 242(69 %) were on treatment for more than six months.

Table: 1 Socio-demographic Characteristics of IPT Eligible PLHIV on chronic HIV Care, from January, 2017 GC up to December, 2018 GC

Characteristics	Number of IPT Eligible Clients	Percent	No. Missed Data (%)
Sex			
Male	126	36	0
Female	224	64	
Age			
18-29	16	4.6	0
30-39	75	21	
40-49	175	50	
>=50	84	24	
Residence			
Addis Ababa	152	43	0
Burayu	83	24	
Sululta	58	17	
Sebeta	19	5	
Others	38	11	
Marital Status			
Married	179	51	12(4)
Single	137	39	
Divorced	22	6	

Educational Status			
Certificate and Above	217	62	9(3)
Secondary	77	22	
Primary/ illiterate	47	13	
WHO Clinical Stage			
Stage One	90	26	1(0.3)
Stage Two	79	23	
Stage three	126	36	
Stage Four	55	16	
Functional Status			
Working	159	45	4(1)
Schooling	13	4	
Ambulatory	133	38	
Bed Ridden	41	12	
Duration of Enrollment			
<3 Years	165	47	0
3-5 Years	102	29	
>5 Years	83	24	
Duration on HAART			
< 6 Months	108	31	0
6Months - 1 Year	119	34	
>1 Year	123	35	

The bar chart below depicts the overall IPT Uptake Status of the study clients. Among the total clients studied, only 55(16%) were taking IPT while the majority of eligible clients were not on IPT.

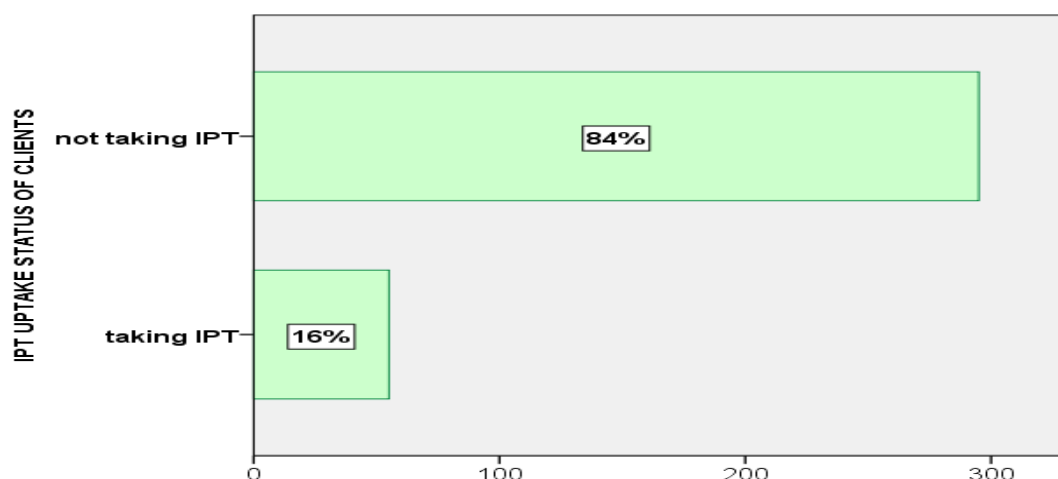


Figure Two: Bar Charts: IPT Uptake Status of Eligible Clients on Follow Up at SPHMMC Chronic HIV Care Unit from January 2017 TO December 2018 GC

5.5 Bivariate Analysis of Patient Factors Affecting IPT Uptake

As all the variables are categorical variables, including the outcome itself, bivariate analysis was carried out using the chi-square analysis to identify variables that are associated with uptake of IPT. All the variables were analyzed. As can be seen on Table two below, when age, residence, educational status, WHO clinical stage, functional status ,duration of enrollment into care and duration on HAART are considered, the extremely low p-value shows that there is, in fact, a statistically significant association between these indicator variables and uptake of IPT. Sex and marital status do not seem to be associated with the uptake of IPT

Table Two: Bivariate Analysis Between Study Variables and Uptake of IPT Using the Chi-Square Method.

Characteristics	IPT Uptake Status				Chi-Square	Degree of freedom	P-value
	Taking	Percent	Not Taking	Percent			
Sex							
Male	18	14	108	86	0.73	1	0.45
Female	37	16	187	84			
Age							
18-29	9	56	7	44	20.99	3	<0.01**
30-39	20	28	55	72			
40-49	19	11	156	89			
>=50	9	11	75	89			
Residence							
Addis Ababa	34	22	118	78	10.90	4	0.03*
Burayu	12	15	71	85			
Sululta	5	9	53	91			
Sebeta	2	10	17	90			
Others	2	5	36	95			
Marital Status							
Married	35	20	144	80	3.782	2	0.15
Single	17	12	120	88			
Divorced	2	9	20	91			
Educational Status							
Certificate and Above	51	24	166	76	24.05	2	<0.01**
Secondary	3	4	74	96			
Primary/ illiterate	1	2	46	98			
WHO Clinical Stage							

Stage One	40	44	50	56	78.23	3	<0.01**
Stage Two	9	11	70	89			
Stage three	4	3	122	87			
Stage Four	2	4	55	96			
Functional Status							
Working	48	30	111	70	88.86	3	<0.01**
Schooling	3	23	10	77			
Ambulatory	3	2	130	98			
Bed Ridden	1	2	40	98			
Duration of Enrollment							
<3 Years	6	4	159	96	47.79	2	<0.01**
3-5 Years	18	18	84	82			
>5 Years	31	37	52	63			
Duration on HAART							
< 6 Months	2	2	106	98	47.35	2	<0.01**
6Months - 1 Year	12	10	107	90			
>1 Year	41	33	82	68			

* P value< 0.05

**P value< 0.01

5.6 Multivariable Logistic Regression Analysis of IPT Uptake

Bivariate analysis had already shown that IPT uptake was associated with age using the chi-square method. Multivariable logistic regression further strengthen this and show that clients with age 30-39 years (AOR 17.07, 95% CI: 1.96-14.97) had significantly higher uptake of IPT when compared to their greater than 50 years old counterparts after adjusting for potential confounding.

With regard to residential area, clients from Addis Ababa (AOR, 52.90 95% CI: 2.91-9.08) had significant higher IPT uptake when compared to those from towns other than Oromia 'Liyu Zones' and from rural areas after adjusting for potential confounding.

In terms of clinical picture at care enrollment (WHO clinical staging), clients enrolled before developing symptoms suggestive of significant immune suppression (stage one) (AOR 15.27, 95% CI: 1.19-16.07)) had significantly higher uptake of IPT when compared to clients who presented with stage four disease at enrollment even after multivariate logistic regression.

Participants who were on HAART for less than six months (AOR 0.044, 95% CI: 0.04-0.54) had significantly lower IPT uptake when compared with those on HAART for greater than one year counterparts even after adjustment with other variables .

Using the chi-square method bivariate analysis had already shown that IPT uptake was significantly associated with duration of enrollment into HIV care. Multivariable logistic regression signify this further and show that participants who were enrolled for less than three years (AOR 0.069, 95% CI: 0.01-0.46) had significantly lower IPT uptake when compared with those who were enrolled for more than five years.

When functional status of the participants was analyzed, bed ridden patients (AOR 0.027, 95% CI: 0.01-0.96) had significantly lower uptake of IPT in comparison to patients who were working with multivariate logistic regression modeling.

This study also showed that clients with high level of education (AOR 23.43, 95% CI: (1.29-4.26) had significantly higher IPT uptake rate when compared with those of low level of education. Sex of the clients and marital status were not associated with IPT uptake status of clients in this study

TABLE Three: Out Come of Multivariate Logistic Regression for IPT Uptake

Characteristics	Number Eligible	Number taking (%)	Crude OR	P-value	Adjusted OR	P-value
Sex						
Male	126	18(14)	1.55(0.76-3.18)	0.23	0.74(0.16-3.46)	0.71
Female	224	37(16)	1		1	
Age						
18-29	16	9(56)	6.48(1.94-21.64)	0.002	3.03(0.17-55.56)	0.45
30-39	75	20(28)	3.03(1.28-7.16)	0.012	17.07(1.96-14.97)	0.01**
40-49	175	19(11)	1.02(0.44-2.35)	0.97	1.66(0.26-10.59)	0.59
>=50	84	9(11)	1		1	
Residence						
Addis Ababa	152	34(22)	3.89(0.86-17.47)	0.08	52.90(2.91-9.08)	0.01**
Burayu	83	12(15)	1.86 (0.37-9.36)	0.45	4.50(0.27-73.65)	0.29
Sululta	58	2(10)	1.55(0.28-8.57)	0.62	1.02(0.04-25.78)	0.10
Sebeta	19	5(9)	2.00 (0.25-15.85)	0.51	11.98(0.34-424.51)	0.17
Others	38	2(5)	1		1	
Marital Status						
Married	179	35(20)	1.58(0.34-7.42)	0.56	0.12(0.01-2.25)	0.16
Single	137	17(12)	0.97(0.20-4.81)	0.97	0.04(0.002-1.02)	0.042
Divorced	22	2(9)	1		1	
Educational Status						
Certificate and Above	217	51(24)	12.26(1.63-9.16)	0.02	23.43(1.29-4.26)	0.03*
Secondary	77	3(4)	1.36(0.12-15.50)	0.81	2.56(0.09-7.86)	0.58
Primary/illiterate	47	1(2)	1		1	

WHO Clinical Stage						
Stage One	90	40(44)	16.73(3.75-74.66)	<0.001	15.27(1.19-19.06)	0.04*
Stage Two	79	9(11)	3.46(0.70 -17.15)	0.13	1.56(0.11-22.12)	0.74
Stage three	126	4(3)	1.02 (0.18-5.80)	1	0.87(0.06-12.91)	0.92
Stage Four	55	2(4)	1		1	
Functional Status						
Working	159	48(30)	1		1	
Schooling	13	3(23)	14.44(1.90-11.70)	0.01	1.31(0.07-23.51)	0.86
Ambulatory	133	3(2)	12.00(1.10-13.24)	0.04	0.63(0.01-31.55)	0.82
Bed Ridden	41	1(2)	0.65(0.06-7.37)	0.73	0.03(0.01-0.96)	0.04*
Duration of Enrollment						
<3 Years	165	6(4)	0.09(0.03-0.24)	<0.001	0.07(0.01-0.46)	0.01
3-5 Years	102	18(18)	0.40(0.19-0.86)	0.02	0.64(0.14-2.88)	0.56
>5 Years	83	31(37)	1		1	
Duration on HAART						
< 6 Months	108	2(2)	0.06(0.01-0.24)	<0.001	0.04(0.04-0.54)	0.02*
6Months - 1 Year	119	12(10)	0.35(0.17-0.74)	0.01	0.69(0.15-3.22)	0.63
>1 Year	123	41(33)	1		1	

* P value< 0.05

**P value< 0.01

CHAPTER SIX: DISCUSSION

5.1 IPT Coverage and Patient Associated Factors

The study found an uptake of IPT among eligible PLHIV of 16%. This is almost similar with Report on National TB/HIV Sentinel Surveillance from April 2010 - June 2015 (18%)[10] but lower than the reported IPT coverage of 28.7 % for Addis Ababa in 2011 and 32% in 2008 [27,28]. This is a less than ideal coverage of a preventive service proven to reduce especially morbidity and to a lesser extent mortality related to TB among PLHIV. This could be as a result of INH supply interruption which was found to be the main reason for low IPT provision in the country [9].

Seven of the Variables studied were found to predict IPT uptake independently in this study.

In these study clients with age 30-39 years had statistically significant higher uptake of IPT when compared to their greater than 50 year's old counterparts. Regarding coverage of life saving services to reduce Disability-Adjusted Life Years (DALYs) related to TB and HIV, studies have shown that pediatric age groups and relatively younger patients receive less than those older than 30 years [37] which is also the case here but the lower uptake in those age greater than 50 years in this study was not reflected in other studies.

When looking into clients' residential area, this study found that clients from Addis Ababa had significant higher IPT uptake when compared to those from other towns and rural areas, however, other studies have not incorporated clients residential areas but geographical location of facilities providing medical services as a general has higher uptake of new formulations of several medicines among urban populations than with rural populations [39]. To speculate the finding in this study clients who could not return to the facility every month with liver function test to check for presence of INH toxicity might not be initiated on IPT.

Education level has been shown to be an important factor in the uptake of preventive health services in different studies [38]. This study also showed that clients with high level of education had significantly higher IPT uptake rate when compared with those of low level of education.

Clients that had been in care for longer period had demonstrated higher uptake of IPT when compared to those enrolled into care for short period of time. One study that was done in Zimbabwe in 2017 has shown similar result [36].

In this study, clients enrolled before developing symptoms suggestive of significant immune suppression (stage one) and those with good functional status at enrollment had significantly higher uptake of IPT when compared to clients who presented with stage four diseases at enrollment and with those having poor functional status at enrollment. This goes with the finding of the study which was done in Zimbabwe [36].

The phenomenon of high IPT uptake demonstrated by longer stay on HAART in this study was not studied in other literatures and insights into this could be provided with further studies.

5.2 Limitation of the Study

1. The confidence with which the effect estimate is made remains weak due to wide interval as a result of small size of clients who were on IPT
2. Due to the nature of the study design, health workers and facility related factors were not assessed as this information could not be from secondary data sources.
3. The study is limited in terms of any inferences. It was carried out at one institution and this will limit its external validity.

5.3 Conclusion and Recommendation

In this study the IPT coverage at SPHMMC Chronic HIV Care Unit is considerably low. This is quite less than the recommended IPT coverage even though not far from the nationally reported IPT coverage. Policy makers and concerned bodies should enforce its implementation. The uptake was significantly lower among the following patient variables- patients living outside of Addis Ababa, low educational status, advanced disease stage (WHO stage 4) and patients with poor functional status, new to care patients as well as those on HAART for short duration. Another study of this nature with the objective to find out the reason behind low uptake in this group of clients is recommended. As the low uptake of IPT in those recently enrolled into care and those with low educational status might be due to lack of awareness of the benefit of the drug counseling should focus on these group.

6. REFERENCES

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7. APPENDIX

7.1 ANNEX: - QUESTIONNAIRES

1) Age

18-29 ☐ 30-37 ☐ 40-49 ☐ above 50 ☐

2) Sex

Male ☐ Female ☐

3) Marital status

Single ☐ Married ☐ Divorced ☐ data missed/not documented ☐

4) Educational status

Illiterate ☐ Primary ☐ Secondary ☐ Certificate and above ☐

Data missed/not documented ☐

5) Uptake of IPT

Taking ☐ Not Taking ☐ data missed/not documented ☐

6) WHO clinical stage at enrollment

Stage 1 ☐ Stage 2 ☐ stage 3 ☐ Stage 4 ☐ data missed/ not documented ☐

7) Duration on HAART

Less than six months ☐ Six month to one year ☐

Greater than one year ☐ data missed/ not documented ☐

8) Duration since enrolled in to chronic HIV care

<3 years ☐ 3-5 years ☐ >5 years ☐ data missed/ not documented ☐

9) Functional status

Working ☐ School ☐ Ambulatory and bedridden ☐ data missed/ not documented ☐