UNIVERSITY OF NAIROBI

IMPLEMENTATION OF ISONIAZID PREVENTIVE THERAPY AMONG HIV INFECTED CHILDREN IN THREE HEALTH FACILITIES IN NAIROBI COUNTY

A Dissertation Submitted in Part Fulfillment of the Requirements of the University of Nairobi for Award of the Degree of Master of Medicine in Paediatrics and Child Health

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DECLARATION

This dissertation is my original work and has not been presented for the award of a degree in any other university

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DEDICATION

To God Almighty who gives us strength, grace and victory.

To Pastor Dan Murage, your counsel and prayers will forever be appreciated.

To Mark, you are a great inspiration and blessing in my life.

To the wonderful caregivers, children and health workers who participated in this study.

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LIST OF ABBREVIATIONS

TB	Tuberculosis
PTB	Pulmonary Tuberculosis
IPT	Isoniazid Preventive Therapy
INH	Isoniazid
ICF	Intensified Case Finding
HIV	Human Immunodeficiency Syndrome
PLWHIV	People Living with HIV
PPD	Purified Protein Derivative
IGRA	Interferon Gamma Release Assay
WHO	World Health Organization
SPSS	Statistical Package for Social Sciences
KNH	Kenyatta National Hospital
UON	University of Nairobi
AIDS	Acquired immune deficiency disorder
IRIS	Immune reconstitution inflammatory syndrome
DLTLD	Division of Leprosy, Tuberculosis and Lung Disease
CSRI	Client Services Receipt Inventory

DEFINITION OF TERMS

Isoniazid preventive therapy: refers to taking a course of isoniazid treatment in order to prevent the development of tuberculosis.

Tuberculosis: a widespread contagious disease caused by various strains of mycobacteria, usually *mycobacteria tuberculosis*.

Latent tuberculosis: *Mycobacterium tuberculosis* bacteria are in the body but are inactive and cause no symptoms. Manifested by a positive mantoux test and or a positive interferon gamma release assay (IGRA)

Active tuberculosis: a disease that is caused by Mycobacterium tuberculosis in any part of the body and is in an active state as determined by either: radiographic, current clinical or laboratory evidence.

Infant: a child younger than one year of age.

Child: The law under the employment Act, 2007, and the children Act, defines a child in Kenya as a person below the age of 18 years.

Xpert MTB/RIF: a molecular test that detects *Mycobacterium tuberculosis* DNA as well as mutation that confer rifampicin resistance.

ABSTRACT

Background: Approximately 9 million new cases of tuberculosis (TB) occur in the world every year, 15% of these occur in children less than 15years. In Kenya, children comprise 11% of all tuberculosis cases. Kenya is position 15 of the 22 high tuberculosis burden countries. [1, 2] Human immunodeficiency virus (HIV) infection increases the risk of progression from latent tuberculosis to active disease by 20 to 37 fold.[1] HIV infected children have a much higher risk of active disease. Isoniazid preventive therapy has been shown to reduce tuberculosis related morbidity by 72% and mortality by 54%.[24] In 2013, only 21% of countries globally and 14 out of the 41 high TB/HIV burden countries reported provision of isoniazid preventive therapy (IPT) to people living with HIV.[1] Following the 2011 Kenyan policy, data is needed to inform IPT implementation and scale up in our local context.

Objectives: To determine the level of uptake of isoniazid preventive therapy among HIV infected children in care at Kenyatta National Hospital. To evaluate knowledge and practice of health workers at Kenyatta National Hospital, Mbagathi District Hospital and Langata Health Centre regarding isoniazid preventive therapy in HIV infected children.

Study Design: This was a mixed method research combining a cross-sectional survey with structured, in-depth, key informant interviews.

Methods

The study was carried out in paediatric wards, paediatric outpatient clinicsand paediatric comprehensive HIV care clinic (CCC) at Kenyatta National Hospital and Mbagathi District Hospital together with the paediatric outpatient clinics at Langata Health Centre.

We enrolled children aged 1 to 15 years with documented HIV infection receiving care in Kenyatta National Hospital and consenting health care workers (HCW) in the pediatric units at the three study facilities. We excluded children with active tuberculosis (TB) together with those found to have contraindications to isoniazid.

We carried out consecutive recruitment of all HIV infected children aged 1 to 15 years receiving care in the comprehensive care clinic and those admitted in the wards. A questionnaire was administered to eligible child-caregiver pairs to assess knowledge and

prior or current use of isoniazid for TB prevention. Each child was screened for TB using the WHO algorithm for TB screening followed by a complete physical examination and review of available relevant investigations. We approached all HCW in the paediatric units during the study period. A self-administered questionnaire was given to consenting HCW. We also conducted key informant interviews of HCW in the KNH CCC.

Data collected was entered into preformed Access database and analyzed using SPSS version 17.0.

Results: We enrolled 111 children with a median age of 8 (IQR 6.7- 9.6) years. Among the children in the study 58.6% were male and 106 (96%) were on ART. Baseline CD4was available for 104 children, 65% of these had a count of <500cells/µL. Majority (79%) had a current absolute count of>500cells/µL. We observed that IPT uptake was53.2% (95% CI 43.9% - 62.4%) among eligible children. The study demonstrates good completion (88%) of IPT once initiated. Caregiver education was found to be associated with better uptake of IPT. Additionally, children whose caregivers had a history of being on IPT had an increased likelihood of having received IPT ($p<0.001$, OR 27.50).Increase in baseline CD4 count of the child was associated with an increase in the probability of a child receiving IPT ($p = 0.007$).

Of the 66 HCW interviewed 77% were working at KNH, 16% at Mbagathi DH and 6% at Langata HC. The majority (47%) were postgraduate doctors working in the inpatient department. The median duration in the paediatric unit was 15 (IQR 3 – 30) months. Relatively few health workers expressed concern that isoniazid (INH) was not effective enough (2%) or that the side effects were too dangerous (28.8%). Half of the health workers had not prescribed INH within the previous year. Moreover, 19.7% indicate a preference to wait to see whether a patient develops active TB, which can then be treated.

Conclusion: This study demonstrated poor implementation of existing IPT guidelines and good completion (88%) of IPT once initiated. Half of the health workers had not prescribed INH within the previous year. There is a need to scale up and strengthen IPT services.

CHAPTER 1

1.0 INTRODUCTION

Tuberculosis (TB) in humans is caused by bacilli of the genus *Mycobacterium* and species *Mycobacterium tuberculosis* complex.[4,5]Tuberculosis is the single most prevalent cause of death in those with human immunodeficiency virus infection (HIV).[6, 7]

In 2013, an estimated 9 million people developed TB globally and 1.5 million died from the disease, 360,000 of whom were HIV co-infected. Among children there were an estimated 550,000 new cases. An estimate of TB mortality among HIV infected children is not yet available due to the difficulties arising from the miscoding of HIV deaths as TB deaths.[1]

The African region accounts for about four out of every five TB and HIV co-infected cases. The World Health Organization (WHO) global report 2014 ranks Kenya among the 22 high burden countries in the world and among the top 5 from Sub Saharan Africa. In 2013 Kenya reported a total of 89,796 of all forms of TB,6% of these were children aged less than 15 years.[1, 2]

The millennium Development Goal 6, target 6c was to halt and reverse the incidence of TB. The Stop TB partnership set targets that the incidence of TB should be falling and the mortality and prevalence should be halved by 2015 compared with 1990 levels. Globally the incidence of TB has been falling for about a decade.

Isoniazid preventive therapy (IPT) refers to taking a course of isoniazid treatment in order to prevent progression of latent tuberculosis to active disease. WHO recommends IPT (10mg/kg/day) for six months to all children living with HIV who are more than 12 months of age and in whom active TB has been ruled out through symptom based screening. Only 21% of countries globally and 14 out of the 41 high burden TB/HIV countries reported provision of IPT to people living with HIV in 2013.[1]This is despite clear evidence that IPT is safe and efficacious, evidence shows that it reduces TB related morbidity by 72% and mortality by 54% (as shown in table 1).[3]

A study done among adults attending HIV outpatient clinics in Kenya and Uganda showed that only 38% received IPT.[8] We aim to determine the proportion of HIV infected children in care and eligible for IPT, who received IPT and the level of adherence. We will also describe barriers to and facilitators of IPT implementation.

CHAPTER 2

2.0 BACKGROUND AND LITERATURE REVIEW

2.1 Epidemiology of Tuberculosis

In 2013, an estimated 1.1 million (13%) of the 9 million people who developed TB were HIV positive. The African region accounted for 78% of the estimated number of HIV positive incident TB cases.[1]Kenya is one of the 22 high burden countries and is ranked 15th according to the WHO global TB Report 2014.The case notification rate was 89,796/100,000. Children less than 15 years constituted 6% of all cases notified.[1,2]The major factor responsible for the large TB disease burden in Kenya is the concurrent HIV epidemic. According to the 2013 data 38% of TB patients had HIV co-infection. HIV testing among TB patients increased from 88% in 2009 to 94% in 2013.[1, 2,9]

Transmission

Transmission of *M. tuberculosis* is person to person, usually by airborne mucus droplet nuclei particles 1-5 micrometer in diameter that contain *M. tuberculosis*. Infectious droplet nuclei are generated when persons who have pulmonary or laryngeal TB disease cough, sneeze, shout or sing. These particles can remain suspended in the air for several hours. Transmission may rarely occur by direct contact with an infectious discharge or a contaminated fomite.[4,5,10]

The chance of transmission increases when the patient has a positive acid- fast smear of sputum, an extensive upper lobe infiltrate or cavity, copious production of thin sputum, and severe and forceful cough. The longer the duration of contact, the more frequent the contact, the closer the contact, the higher the risk of transmission. Poor ventilation and overcrowding also enhance transmission. Young children rarely infect others because they have paucibacillary disease, and cough is often absent or lacks the tussive force required to suspend infectious particles.[2,4,5, 10]

The risk for progression of latent tuberculosis infection to tuberculosis disease is increased in patients with HIV infection, age less than 2 years, infection with M. tuberculosis within the last 2 years, history of poorly treated previous TB and other immune suppressive conditions e.g malnutrition, malignancies and immunosuppressive therapy.[2, 4,5]

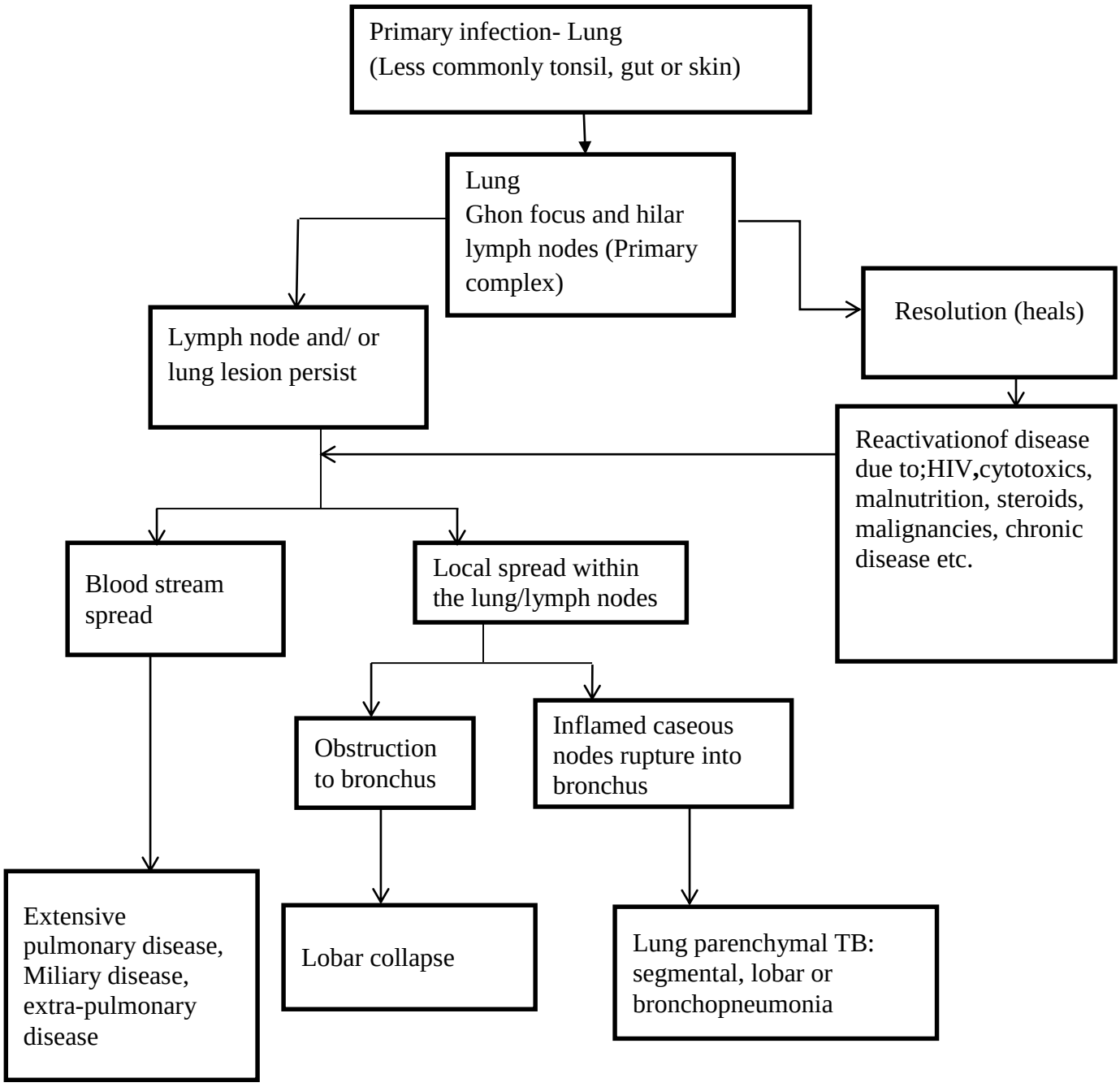


Figure 1: The Natural History of Tuberculosis

2.2 Pathogenesis and Diagnosis of Tuberculosis

The lung is the portal of entry in >98% of cases. The tubercle bacilli multiply within the alveoli, most of them are killed but some survive within non-activated macrophages and are carried to the regional lymph nodes (figure 1). After 2-12 weeks T lymphocytes induce cell mediated hypersensitivity. The parenchymal portion of the primary complex often heals completely by fibrosis or calcification. Occasionally this portion continues to enlarge, resulting in focal pneumonitis and pleuritis.

Healing is less complete in the regional lymph nodes and viable bacilli can persist for decades within these foci. Hilar and paratracheal nodes that enlarge significantly can encroach on a regional bronchus resulting in atelectasis or hyperinflation. During the development of the primary complex tubercle bacilli are carried to distant sites through blood and lymphatics. Disseminated TB occurs if the number of circulating bacilli is large and the host's cellular immune response is inadequate (figure 1).

Diagnosis

The diagnosis of TB in children relies on a careful history and a thorough physical examination (figure 2). The most common symptoms are cough, fever, wheezing and failure to gain weight.[11] Clinical symptoms are usually meager, crepitation and wheezes over the affected lung field are the most common. Signs and symptoms of extra pulmonary TB are referred to the involved organ.

Mantoux test uses purified protein derivative for detecting infection by *M. tuberculosis*. The reaction is measured as millimeters of induration after 48 to 72 hours. A positive result indicates TB exposure therefore additional tests are required to confirm TB disease. An induration of 5mm or more in immunosuppressed children and 10mm in other children is considered positive.[2]Mantoux may be negative despite the child having TB especially in HIV, malnutrition and severe disseminated TB.[12]

The initial step in detection and isolation of the mycobacterium is to obtain appropriate specimens for bacteriologic examination. Examination of sputum, gastric lavage, bronchoalveolar lavage, lung tissue, lymph node tissue, bone marrow, blood, liver, cerebral spinal fluid, urine and stool may be useful, depending on the location of the disease.[2]

Acid-fast bacilli (AFB) staining provides preliminary confirmation of the diagnosis. Conventional methods are Zielh-Neelsen staining method. With the use of fluorochrome stains such as auramine and rhodamine the acid fast material stands out against the dark, non-fluorescent background.[4,5] For reliably producing a positive result, smears require approximately10,000organisms/ml, in children with paucibacillary disease results may be negative. Fewer than 20% of children with pulmonary TB have a positive AFB smear of sputum or gastric aspirate.[13]

Culture of mycobacterium is the definitive method to detect bacilli. It is more sensitive than examination of the smear and allows specific species identification and testing for drug susceptibility patterns. However, because *M. tuberculosis* is a slow growing organism, a period of 6-8 weeks is required in conventional culture media. Conventional solid culture media include the Lowenstein-Jensen medium and Middlebrook. Rapid growth techniques include automated radiometric culture methods (e.g BACTEC) they allow growth within 9-16 days.[4,5,10]

Molecular methods detect species specific genes. Nucleic acid amplification technique allows direct identification of *M. tuberculosis* in clinical specimens. By using molecular techniques the time required for the identification of mycobacteria has been shortened (24-48hours), in comparison to the time required by microbiological tests. Nucleic acid amplification can detect as few as one M. tuberculosis organism per 100ml of specimen. Multiple commercial tests are available, Xpert MTB/RIF is recommended by WHO in resource limited countries.[1,14]

Evidence of pulmonary TB in chest radiographs varies, but usually radiographs show enlargement of hilar, mediastinal or subcarinal lymph nodes and lung parenchymal changes.[15] The most common findings are segmental hyperinflation then atelectasis, alveolar consolidation, interstitial densities, pleural effusion and rarely a focal mass. Cavitation is rare in young children but more common in adolescents. The clinical scoring systems although helpful have low sensitivity and specificity.[16]

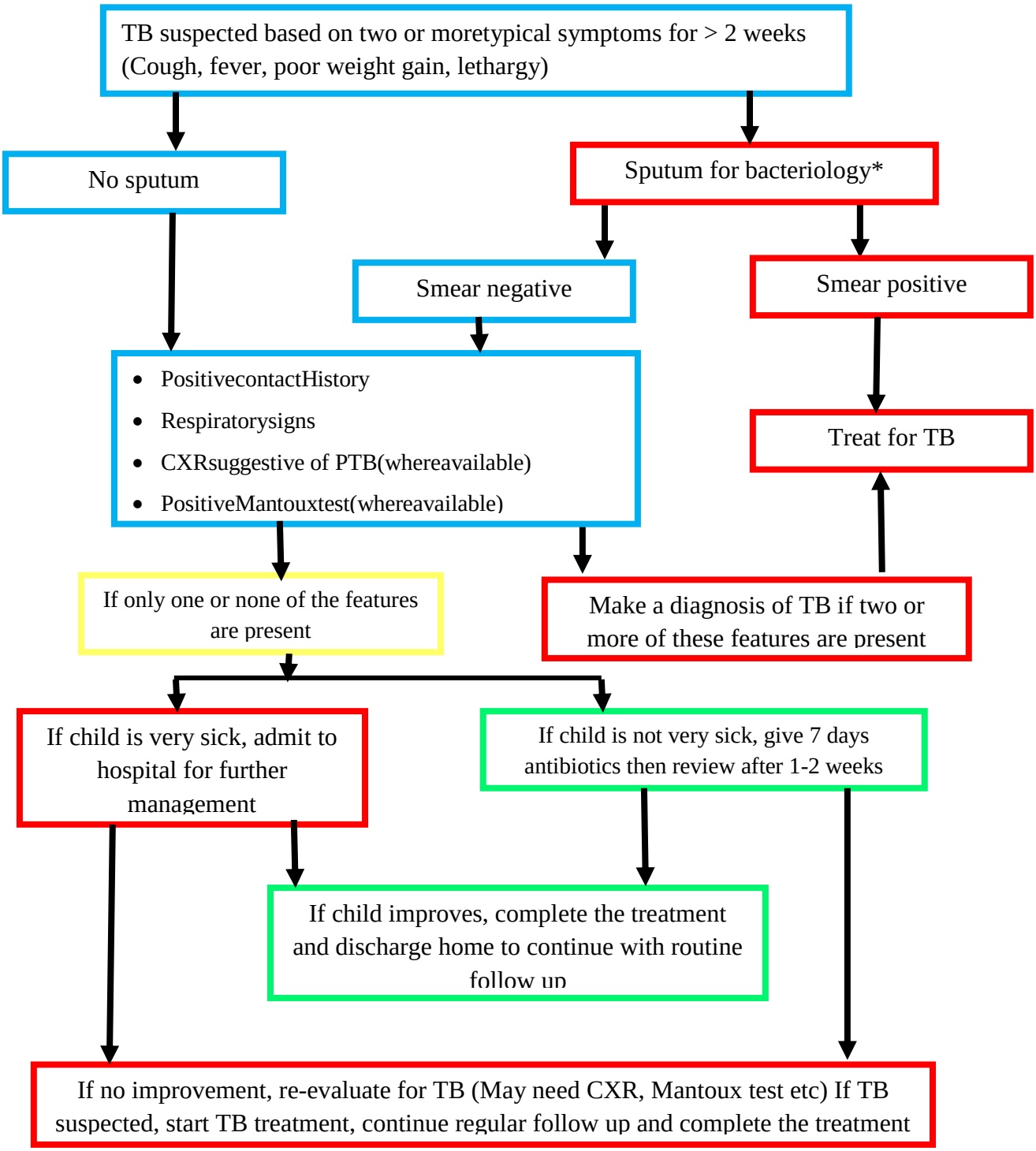


Figure 2: Kenya National Algorithm for Tuberculosis Diagnosis in Children

Source: National Guidelines on Management on Tuberculosis in Children, Ministry of Health 2013[2]

2.3 Tuberculosis and Human Immunodeficiency Virus Co-infection

Tuberculosis is an important cause of acute and chronic pneumonia in African children with HIV.[17]HIV infection is the most important predisposing factor for the development of active TB.[1, 2, 5]Risk of TB doubles within a year of infection with HIV[18]. Risk of developing active disease after infection approaches 100% in advanced HIV.[19]Annual risk of a person co-infected with the tubercle bacillus and HIV developing TB is around 50 times higher than in HIV negative person.[20]

Progression from infection to overt disease occurs in few months as opposed to several years in immune competent individuals.[21]The host immune response to TB infection enhances HIV replication and accelerates the immune suppression.[22]Diagnosis of TB in HIV infected children is more complex as many HIV related lung diseases can easily be confused with TB.[23] Microbiological diagnosis is not always feasible due to difficulties in obtaining sputum specimens and the fact that children are more likely to have paucibacillary disease. Skin test reactivity can be absent.[24]

Antiretroviral and anti-TB drugs have potentially significant drug-drug interactions as well as overlapping toxicities. Response to TB treatment may be slow. Rates of drug resistant TB tend to be higher in HIV infected adults and probably are also higher in HIV infected children.[25]

TB is the single most prevalent cause of death in those infected with HIV.[10, 18]In the pre-anti-retroviral therapy era approximately 30% of HIV positive smear positive TB patients died within 12 months of commencing treatment and about 25% of those who survived died during the subsequent months.[5] ART reduces the incidence of TB by around 80% but incidence remains higher than in those who are HIV negative.[26]

TB is associated with a greater frequency of serious (grade 3 or 4) adverse events in HIV co-infected individuals than in patients with TB alone (40% v 26%). [5]Rifamycins (such as rifampicin and rifapentine) used in the treatment of TB are potent inducers of CYP3A4 which metabolizes protease inhibitors and Non-Nucleoside Reverse transcriptase Inhibitors.[27,28] Rifampicin results in a 22-25% reduction in peak trough efavirenz

concentration, 20-58% reduction in nevirapine concentration and a >90% reduction in the concentration of unboosted protease inhibitors.[28,29]

TB, other mycobacterial infection and cryptococcal diseases account for about 60% of cases of immune reconstitution inflammatory syndrome (IRIS). Paradoxical TB IRIS affects approximately 15% of all HIV 1 infected patients. [30]Systematic review by Muller et al reported a mortality rate of 3% in patients with TB IRIS.

HIV infection does not induce multidrug resistant TB but fuels its spread by increasing susceptibility to infection and accelerating transmission.[31]Recurrence after treatment may be due to endogenous reactivation or exogenous reinfection. Recurrence rates have been observed at between 18 and 22 per 100 person years of observation.[32]

2.4 Isoniazid Preventive Therapy

IPT refers to taking a course of isoniazid treatment in order to prevent progression of latent TB infection to TB disease. There is a 10% lifetime risk of developing active TB if infected with M. tuberculosis alone. The annual risk of developing active TB if co-infected with HIV is 5-10%.[20,21]

There is an asymptomatic state in patients infected with M. tuberculosis prior to the development of active disease. The manifestation of this state is a positive PPD or IGRA. The bacterial load at this time is several orders of magnitude lower and the patient may be treated with a single agent.[3, 5]

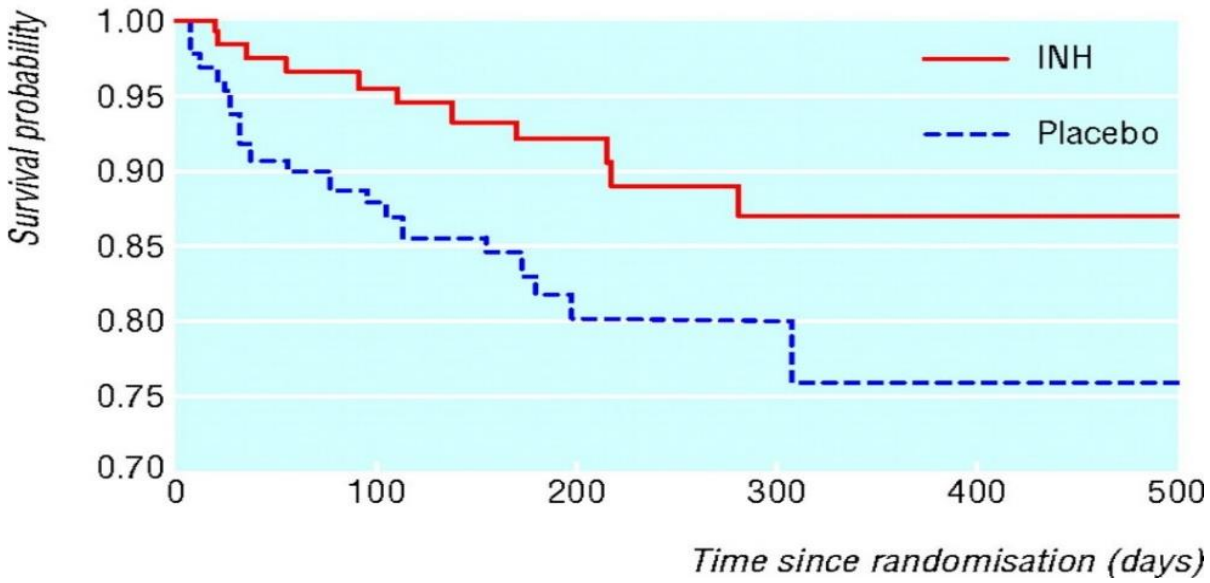


Figure 3: A graph comparing survival among HIV negative children ≥ 8 weeks with HIV on isoniazid or placebo in South Africa. Mortality was lower in the isoniazid group than in the placebo group. Source: Heather J Zar et al. 2007[3]

Isoniazid is associated with a 72% reduction in the chance of developing probable or definite TB. It also has a significant impact on all-cause mortality reducing the risk of death by 54% (table 1). The effect on survival is in addition to that provided by cotrimoxazole. Benefits apply across Centres for Disease Control clinical categories.[3] Studies have shown that isoniazid is superior to placebo in reducing mortality (as shown in figure 3).

Table 1: Efficacy of Isoniazid Preventive Therapy

Country, Author, Year	Study Design N=Sample Size	Study Population	Results
S. Africa Heather J Zar et al 2007	Randomized controlled trial N = 263	HIV infected children aged ≥ 8 weeks	• Mortality in the INH group 8%, placebo 16% • TB incidence in the INH group 3%,placebo group 9.9%
Ethiopia Kesebirhana et al 2007 to 2010	Retrospective Cohort N = 5,407	HIV+ individuals Children <15yrs accounted for 9% of the population	▪ ART only was associated with a 68% reduction in incidence of TB ▪ IPT only resulted in a 65% reduction in the incidence of TB ▪ ART+IPT was associated with an 80% reduction in incidence of TB
India, France, Kenya S. Africa, Mexico, Canada, United States James Ayieko et al 2013 **Brazil** Golub et al 2005-2011.	Meta-analysis of randomized controlled trials N = 10,320 Cluster randomized trial N = 11,026	Children aged ≤15 years regardless of HIV status HIV+ individuals on ART+INH	▪ IPT associated with a 59% reduction in the risk of TB ▪ 76% reduction in the incidence of TB ▪ Adverse events 1.2% ▪ Completion rates 85%.

2.4.1 How to Assess Factors Influencing Implementation of Isoniazid Preventive Therapy

Figure 4: World Health Organization Framework of Health Components (2000)

WHO defines health systems as all organizations, people and actions whose primary intent is to promote, restore or maintain health. The main goals of the health system are: good health for the citizens, responsiveness to the expectations of the population and financial risk pooling. Factors influencing IPT implementation can be assessed using tools devised to look into each component of the six system building blocks (figure 4) .

One study used the Client Services Receipt Inventory to assess availability of the HIV basic package (which includes IPT) in HIV clinics.[8] The CSRI is usually completed through interviews and it seeks to determine if the facility offers various specific components of care under the five domains of care: clinical, psychological, spiritual, social and preventive.

Factors influencing implementation can also be determined by in-depth interviews of health care workers on their personal perspectives to the medication and barriers and facilitators of IPT implementation. [34]

2.4.2 Factors Affecting Isoniazid Preventive Therapy Implementation

Despite IPT being recommended by WHO/UNAIDS for PLWHIV since 1993 uptake remains low (table 2).[28, 33-39]The fear of emerging isoniazid resistant TB was one of the reasons commonly cited among program managers and health care providers for limited scale up.[35, 36]However studies have shown there is no significant increased risk of isoniazid resistance.[37]

Difficulty with administration of tuberculin skin test has also been reported as a barrier by health care workers.[36] WHO has revised its guidelines on IPT and tuberculin skin test is not a requirement for initiating IPT. In addition studies reported that health care workers feared poor adherence to IPT among patients.[36, 34]On the other hand patient education is an effective strategy for increasing adherence. Other health work force related barriers include; concern for increased workload of health care worker, a feeling among some physicians that IPT is not beneficial and concerns about side effects of isoniazid. Unclear direction of the national policy and a notion that IPT did not provide a survival benefit were also cited as barriers. [36, 37]This is despite the fact that IPT has been shown to decrease the risk of death by 54%.[3]

A study in Thailand showed that the principal motivation for IPT implementation was healthcare worker knowledge that IPT can prevent tuberculosis**.** Second commonest reason was following of national guidelines on IPT. Other facilitators included; knowledge on IPT mortality benefit and support by research organizations.[36]

Table 2: Uptake of and Factors Affecting Isoniazid Preventive Therapy Implementation

Country, Author, Year	Study Design N=Sample Size	Findings
Uptake of Isoniazid Preventive Therapy		
Malawi R. Zacharia 2003	Cross sectional N= 239	▪ IPT uptake in passive group**17%** IPT uptake in the active group was 22%
Thailand Hirashunthikul et al 2005	cross sectional N= 300 physicians	**19.3%** of the physicians provided IPT
Global Haileyesus Getahun et al2010	Systematic review N = 6.6Million PLWHIV	▪ Only **1.3%** received IPT ▪ Most countries did not report IPT provision Countries with activity provided it for < **1%** of PLWHIV
S. India Shivaramakrishna et al Nov. 2012 - April 2013	Cross sectional 271 HIV negative children <6yrs	▪ Eligibility 96% ▪ Uptake **27%**
Factors Affecting Implementation of Isoniazid Preventive Therapy		
Addis Ababa Mesele Mindachew et al 2010	Qualitative study Sample population - Health care workers	▪ Barriers to IPT implementation ▪ Poor adherence 24.8% ▪ Fear of INH resistance 20.2% ▪ IPT not beneficial 6.2%

Thailand Saiyud M. et al 2013	Cross sectional N=89 public hospitals	▪ **20%** of the hospitals implemented IPT ▪ **Barriers** ,leadership and governance 97%, fear of INH resistance 52%, fear of poor adherence 30% ▪ **Motivation**: knowledge that IPT prevents TB 63%, following of national guidelines 34%, concern for TB prevention 32%.

2.4.3World Health Organization Policy Guidelines on Isoniazid Preventive Therapy

IPT has been recommended since 1998 by WHO, however its implementation was impeded by several barriers including lack of an accepted approach to exclude active TB and fear of developing drug resistance.[1] In January 2010, WHO conducted a global policy meeting to review evidence regarding IPT. The revised guidelines recommended the use of a simplified screening algorithm that relies on four clinical symptoms to identify those eligible for either IPT or further work up for TB and other conditions (figure 5). It also stated that a chest radiograph and a tuberculin skin test were not mandatory before starting IPT.[1]In 2009 IPT was introduced for the first time in the Kenya Ministry of health guidelines on management of leprosy and tuberculosis. It recommended that IPT be limited to controlled settings, for example prisons, among health care workers and in industrial medical clinics where client follow up and monitoring may be relatively easy.[9] The policy was revised in November 2011 and since then has been in-line with the WHO guidelines.[2]

Which child should receive isoniazid preventive therapy?

The following children should be given IPT provided they have no evidence of active TB on symptom based screening; all HIV infected children above one year of age, all HIV infected children less than 12 months of age with recent contact with a TB case and all

children below 5 years who have had recent exposure to an adult or adolescent with PTB or suspected PTB irrespective of their HIV status.[1, 2]

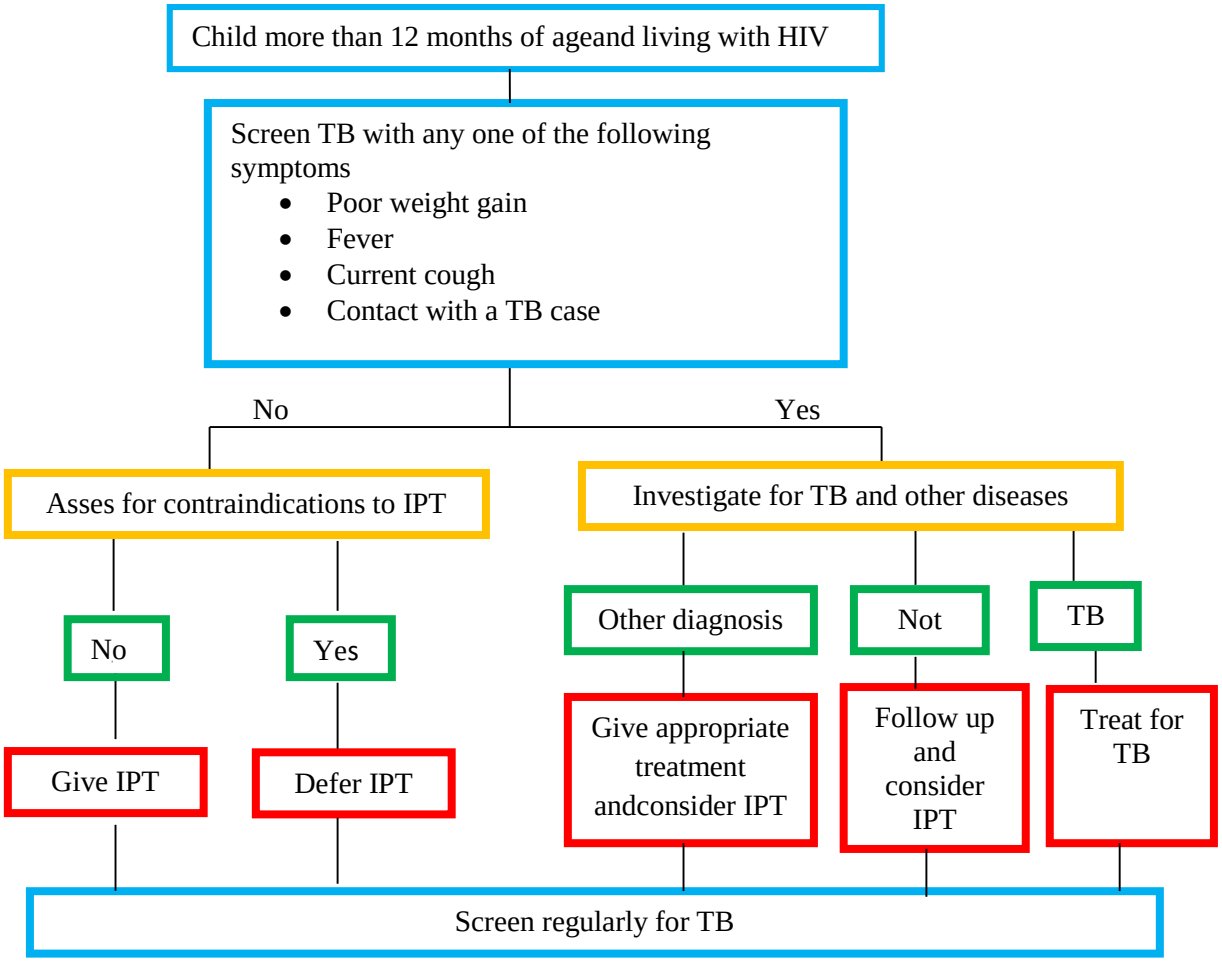


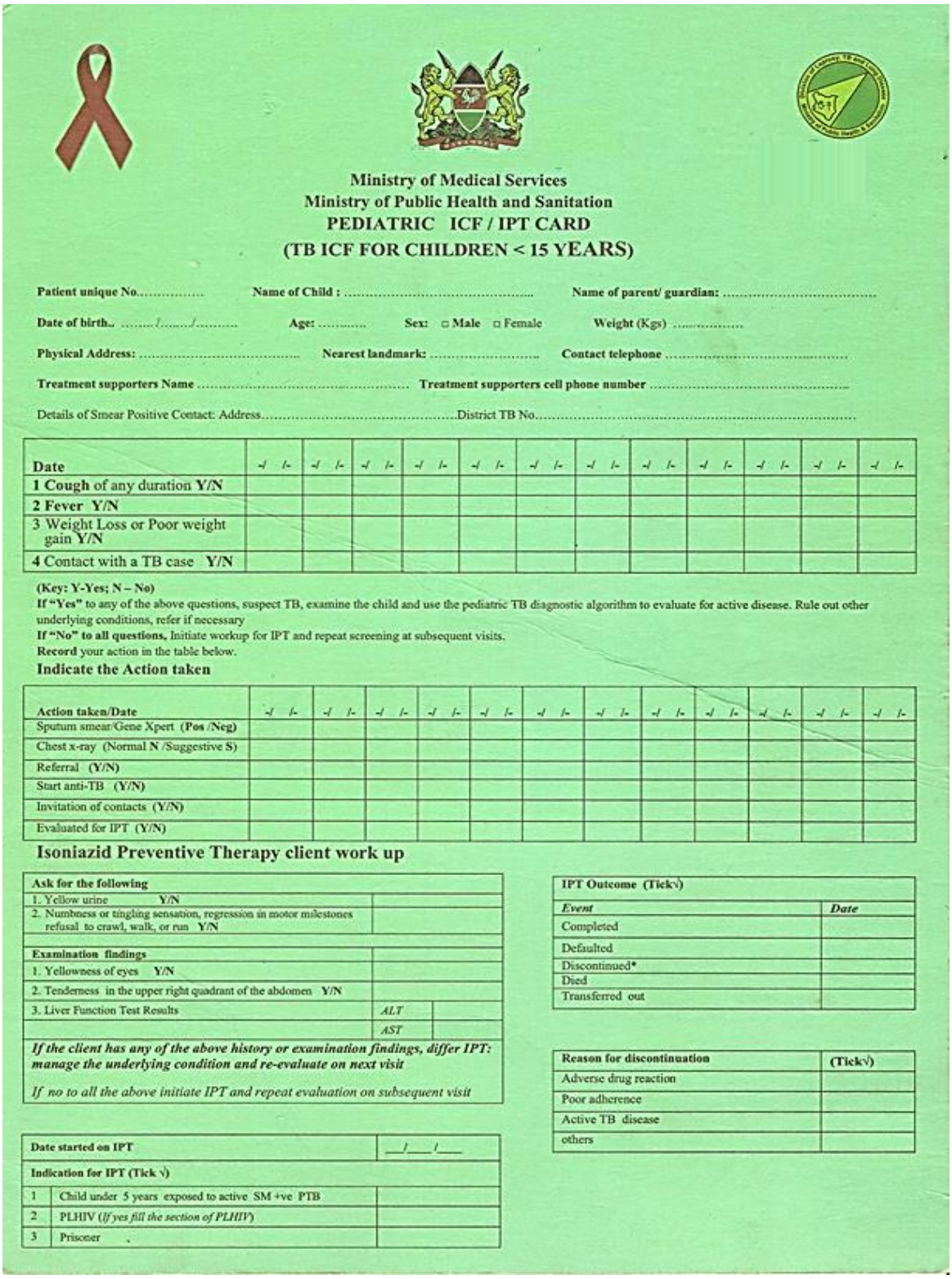
Figure 5*:* World Health Organization Algorithm for Tuberculosis Screening and Isoniazid Preventive Therapy in Human Immunodeficiency Virus infected children above Age 1 year of age

Isoniazid is given at a dose of 10 milligrams per kilogram per day (mg/kg/day) with a maximum dose of 300mg/day in combination with pyridoxine at 1 to 2mg/kg/day to a maximum of 50mg daily for 6 months. Patients on IPT should be reviewed every 28 days. Clinic appointments for INH review should be harmonized with routine HIV care. During the visit the patients should be screened for TB using the standard ICF tool, be evaluated clinically to rule out hepatitis, peripheral neuropathy and assessed for adherence.[1, 2]

Pediatric Intensified Case Finding/ Isoniazid Preventive Therapy (ICF/IPT) Card depicted in figure 6 was introduced by the Ministry of Medical Services and Public Health Kenya in 2013 for use in children less than 15years. It has four parts: the first part contains the patient's bio data and demographic data, the second part enquires on history of cough of any duration, fever, weight loss/poor weight gain or contact with a TB case, the third part enquires on the action taken if the symptom screen was positive and the final parts includes examination for signs of hepatitis, review of liver function tests, date of IPT initiation and outcome. The ICF/IPT card should be filled at each visit.

IPT is contraindicated in patients with active TB as this would lead to isoniazid resistant TB. Since the most frequent major toxic effect of isoniazid is hepatitis, IPT is contraindicated in patients with pre-existing active hepatitis as it would exacerbate the condition. Peripheral neuropathy is observed in 10-20% of patients given dosages greater than 5 mg/kg/d of isoniazid, even though this is reversed by administration of pyridoxine, Most guidelines recommend avoiding IPT in patients with existing signs and symptoms of peripheral neuropathy.[1,2,9]

In patients with poor adherence to cotrimoxazole preventive therapy despite adherence counseling, IPT should be deferred until this is fully addressed. Active substance abuse in an older child or the primary caregiver may result in poor adherence or increase the risk of adverse drug reaction such as hepatitis in alcoholics.[1,2,29]



Ministry of Medical Services
Ministry of Public Health and Sanitation
PEDIATRIC ICF / IPT CARD
(TB ICF FOR CHILDREN < 15 YEARS)

Patient unique No..... **Name of Child :** ..... **Name of parent/ guardian:** .....

Date of birth.. ...../...../..... **Age:** ..... **Sex:** □ **Male** □ Female **Weight (Kgs)** .....

Physical Address: ..... **Nearest landmark:** ..... **Contact telephone** .....

Treatment supporters Name ..... **Treatment supporters cell phone number** .....

Details of Smear Positive Contact: Address.....District TB No.....

Date	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-
1 Cough of any duration **Y/N**												
2 Fever Y/N												
3 Weight Loss or Poor weight gain **Y/N**												
4 Contact with a TB case **Y/N**												

(Key: Y-Yes; N – No)
If "Yes" to any of the above questions, suspect TB, examine the child and use the pediatric TB diagnostic algorithm to evaluate for active disease. Rule out other underlying conditions, refer if necessary
If "No" to all questions, Initiate workup for IPT and repeat screening at subsequent visits.
Record your action in the table below.

Indicate the Action taken

Action taken/Date	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-	-/ /-
Sputum smear/Gene Xpert **(Pos /Neg)**												
Chest x-ray (Normal N /Suggestive S)												
Referral **(Y/N)**												
Start anti-TB **(Y/N)**												
Invitation of contacts **(Y/N)**												
Evaluated for IPT **(Y/N)**												

Isoniazid Preventive Therapy client work up

Ask for the following	
1. Yellow urine Y/N	
2. Numbness or tingling sensation, regression in motor milestones refusal to crawl, walk, or run **Y/N**	
Examination findings	
1. Yellowness of eyes **Y/N**	
2. Tenderness in the upper right quadrant of the abdomen **Y/N**	
3. Liver Function Test Results	*ALT*
	AST

If the client has any of the above history or examination findings, differ IPT: manage the underlying condition and re-evaluate on next visit

If no to all the above initiate IPT and repeat evaluation on subsequent visit

IPT Outcome (Tick√)	
Event	***Date***
Completed	
Defaulted	
Discontinued*	
Died	
Transferred out	

Reason for discontinuation	**(Tick√)**
Adverse drug reaction	
Poor adherence	
Active TB disease	
others	

Date started on IPT		___/___/___
Indication for IPT (Tick √)		
1	Child under 5 years exposed to active SM +ve PTB	
2	PLHIV (*If yes fill the section of PLHIV*)	
3	Prisoner	

Figure 6: Patients Intensified Case Finding/ Isoniazid Preventive Therapy charts (Ministry of Medical Services, Ministry of Public Health and Sanitation)

2.5 Study Justification and Utility

Kenya is among the top 20 high TB burden countries globally with a reported annual incidence of 283/100,000 among children in 2013.[1] TB is a major cause of illness and death in people living with HIV, even in those taking antiretroviral therapy. TB can be prevented in millions of people infected with both HIV and TB through IPT; this is especially true among HIV infected children in whom IPT has been shown to reduce incidence and mortality by as much as 72% and 54% respectively.[3] IPT should be part of the package of care delivered by HIV and TB service providers for PLWHIV. IPT is one of the key interventions recommended by WHO in 1998 to reduce the burden of TB in PLWHIV; yet implementation of IPT has been very low.[33, 35-38]Evidence from local research conducted among HIV infected adults indicates a low level of uptake[8] and there is no published research on IPT uptake among children in Kenya. We set out to evaluate the level of IPT uptake among HIV infected children at a tertiary level hospital, a level 5 hospital, and a health centre in Nairobi as well the health worker knowledge and practice regarding IPT. The information obtained from this study will be useful to inform strategies for implementation of TB preventive therapy among HIV infected children.

CHAPTER 3

3.0 RESEARCH QUESTION

What is the level of isoniazid preventive therapy uptake among HIV infected children aged 1 to 15 years in care at Kenyatta National hospital? What is the knowledge and practice of health workers at Kenyatta National Hospital, Mbagathi District Hospital and Langata Health Centre regarding isoniazid preventive therapy in HIV infected children?

3.1 Primary Objective

1. To determine the proportion of HIV infected children in care at Kenyatta National Hospital who have received isoniazid preventive therapy within the preceding 2 years.
2. To evaluate knowledge and practice of health workers at Kenyatta National Hospital, Mbagathi District Hospital and Langata Health Centre regarding isoniazid preventive therapy in HIV infected children.

3.2 Secondary Objective

1. To determine the level of adherence to therapy among children initiated on isoniazid preventive therapy within the preceding 2 years in Kenyatta National Hospital.
2. To describe factors associated with uptake of isoniazid preventive therapy among HIV infected children in care at Kenyatta National Hospital.

CHAPTER 4

4.0 METHODOLOGY

4.1 Study Design

Cross-sectional study design as it allows one to compare many different variables at the same time in this case IPT uptake, adherence and factors associated with uptake. Both quantitative and qualitative methods were used to provide a comprehensive picture of health worker knowledge and practice regarding IPT.

4.2 Study Area

The child-caregiver survey was conducted at Kenyatta National Hospital, while the health worker survey was conducted at Kenyatta National Hospital, Mbagathi District Hospital and Langata health centre in Nairobi County. Purposive sampling was used to select the three study facilities. Nairobi is the capital city of Kenya and East Africa's most populous city (4.0 million). The city and its surrounding also form Nairobi County.

*Kenyatta National hospital(KNH)*is situated in Nairobi Upper Hill area. It is categorized as a level 6hospital (the highest level in provision of preventive and curative services). KNH is the National Referral and Teaching Hospital in Kenya. It has a catchment of 4 million in Nairobi only but being one of only two National referral hospitals in Kenya it receives patients from all over the country. KNH has six inpatient pediatric wards, an outpatient pediatric department and six specialty clinics. A multidisciplinary team provides specialized HIV care. In September 2015, 1996 children were on follow up in the comprehensive HIV care clinic (CCC), 68% of whom are on ART. HIV infected children with life threatening conditions are admitted to the general pediatric wards. The staff in the pediatric CCC include; one pediatrician, two clinical officers and one pharmaceutical technician who is responsible for dispensing medications.

Mbagathi District Hospital (MDH) is a level 5 hospital situated in Kenyatta Golf Course Location, Dagoretti Constituency, Nairobi. The main catchment area for the hospital is from Dagoretti Constituency, but also sees clients from all over Nairobi and the outskirts of Nairobi. The patients are mostly of middle to low socioeconomic status, largely from

nearby slums. It has a pediatric inpatient ward, pediatric outpatient department and a pediatric HIV clinic. A total of 320 children aged 1-15years are enrolled in the CCC, 98% of whom are on ART. It offers a comprehensive and coordinated HIV primary care services to HIV positive children in Nairobi County and its environs. HIV positive children have access to both the pediatric HIV outpatient clinic and the pediatric wards for those requiring admissions. The CCC staff include; one medical officer, seven clinical officers, a pharmacist and several pharmaceutical technicians. They attend to both children and adults.

Health Centre (HC) are medium sized units which cater for a population of about 80,000 people. They provide a range of services, such basic curative and preventive services for adults and children, as well as reproductive health services. They augment their service coverage with outreach services, and refer severe and complicated conditions to the appropriate level, such as the level 5 hospitals. Atypical health centre is staffed by at least a clinical officer, nurses, health administration officer, medical technologist, pharmaceutical technologist, health information officer, public health officer, nutritionist, driver, housekeeper and supporting staff.

According to the health management information system report, there were a total of 634 health centres in Kenya in 2004. We also carried out the study in Langata HC which is located in Nairobi's Langata Constituency. It serves decanting, Gatweekera, Kianda, Southlands and Soweto. Services offered in the two facilities include immunization, family planning, antiretroviral therapy, HIV testing and counseling and curative in-patient services. Langata HC operates 5 days a week, HIV infected children 5 years old and below are seen by a clinical officer in the MCH. HIV infected children above 5 years are seen by three clinical officers in the out-patient clinic which also attends to adults.

4.3 Study Population

Children

Inclusion criteria

- Documented HIV infection
- Aged 1 to 15years
- Receiving care at the study facility
- Informed consent

Exclusion criteria

- Active TB disease
- On current treatment for active TB disease
- Contraindications to isoniazid (active hepatitis, peripheral neuropathy)

Health workers

Inclusion

- Health worker prescribing INH to eligible children
- Health workers involved in ordering/procuring and dispensing INH
- Informed consent

Study Period

The study was conducted from 1st October 2015 to January 31st2016.

4.4 Case Definition

HIV infection: infection with the human immunodeficiency virus as evidenced by:

- In a patient age > 18months a documented positive HIV antibody test
- In a patient age < 18months a documented positive HIV antigen test (DNA or RNA PCR).

Determination of age: Ascertaining the duration or the measure of time elapsed since a person's birth.

TB symptom screen: children with HIV who have poor weight gain, fever, current cough or contact history with a TB case, may have TB and should be evaluated for TB and other conditions.[1,2]

Poor weight gain: is defined as[1,2]

- Reported weight loss
- Weight for age < -2 Z-score
- Confirmed weight loss (> 5%) since the last visit
- Growth curve flattening.

Adherence to IPT was defined as consumption of ≥ 90% of doses in the preceding two weeks[43]

Poor adherence to IPT: consumption of less than 90% of doses in the preceding 2 weeks.

IPT completion was defined as having received and consumed INH for a total of 6 months.[43]

4.5 Outcome Measures

i. Receipt of IPT within the preceding 2 years
ii. Adherence to IPT
iii. Caregiver and child factors associated with IPT uptake
iv. Health worker knowledge and practices
    i. Correct knowledge- Correct dosage of INH for weight 10mg/kg/d with a maximum of 300mg, correct frequency of once a day, and correct duration of six months
    ii. Practice- we looked at whether the health worker had ever started a patient on IPT and if they had started at least one patient on INH in the twelve months preceding the survey.

4.6 Sample Size and Sampling Methods

Sample size calculation for Children to determine proportion on IPT

The calculation was as follows using Fisher's formula:

$$N_0 = \frac{Z^2 P (1-P)}{d^2}$$

N_0 = minimum sample size

Z = the value from the standard normal distribution corresponding to the desired confidence level (Z= 1.96 or 95% CI)

P = We used an estimate of 50% as no local data exists regarding IPT uptake in children

d= degree of precision (10%)

$$N_0 = \frac{(1.96)^2\ 0.5\ (1-0.5)}{0.10^2}$$

$N_0 = 96$

Assuming 10% loss to follow up = 106 minimum required sample size shall be 106 children

We carried out consecutive recruitment of all HIV infected children aged 1 to 15 years receiving care in the comprehensive care clinic and those admitted in the wards. We included eligible children who presented to the CCC every day between 8am and 8pm until sample size was achieved.

Health Care Workers

Sample Size Determination

The calculation is as follows using Fisher's formula:

$$n_0 = \frac{z^2\ p\ (1-p)}{d^2}$$

= Minimum required sample size

Z = the value from the standard normal distribution corresponding to the desired confidence level (Z= 1.96 or 95% CI)

P = We shall use an estimate of 50% as no local data exists regarding knowledge and practice of health workers in regarding IPT in HIV infected children

d= degree of precision (10%)

$$n_0 = \frac{(1.96)^2\ 0.5\ (1-0.5)}{0.10^2}$$

$n_0 = 96.2$

The sample size (n_0) was adjusted for finite population using **Equation II.**

$$n = \frac{n_0}{1 + \frac{(n_0 - 1)}{N}}$$ .....**Equation II**

Where n is the final minimum required sample size and N is the population size.

Thus, $n = \frac{96.2}{1+\frac{96.2-1}{144}}$ = 57.9

The minimum required sample size for the study is 58 health care workers.
We approached health workers involved in prescribing, dispensing or procuring IPT to HIV infected children in CCC or paediatric wards and relevant pharmacies.

4.7 Study Tools

The child-caregiver pair questionnaire was structured to include, socio-demographic data, a TB symptoms screen, history of drug allergy, TB treatment at the time of the study, history of isoniazid preventive therapy and a physical examination for clinical features of active TB (Appendix D and E).

Information was abstracted from the IPT registers, ward treatment sheets of enrolled in patients and from drug prescriptions containing IPT at the pharmacy for enrolled outpatients at KNH. The data was abstracted into the questionnaire.

A self-administered questionnaire (Appendix G) was given to the health workers working in the paediatric units to assess their knowledge and practice with regards to IPT among HIV infected children. An interviewer guide (Appendix H) was used to conduct in-depth interviews of key informant health workers in the peadiatric units to obtain information on knowledge, attitude and practice in regards to IPT.

IPT registers were available at the MDH CCC and Langata HC pharmacy. We went through them to identify HIV infected children aged 1-15 years initiated on IPT. We visited the pharmacy in all the three health facilities to enquire on the availability of INH and pyridoxine.

4.8 Study Procedures

Recruitment of child- caregiver pairs was done at the paediatric wards and the paediatric comprehensive HIV care clinic (CCC) at the KNH with the help of two research assistants trained by the principal investigator on the scope of the study, use of the study tools and

clinical features of TB. Both research assistants were registered clinical officer with experience working in the CCC.

Paediatric Comprehensive HIV Care Clinic in KNH

We identified potential eligible subjects with documented HIV infection from the triage nurse (Flowchart 7). Guardians who gave informed consent (Appendix A and B) were requested to respond to the questionnaire (Appendix D and E).We also sought assent(Appendix C) for children more than 8 years. In a study done by Weithorn L et al children as young as 9 years of age were shown to be able to participate meaningfully in personal health-care decision making.

The WHO algorithm for TB screening and IPT in HIV infected children more than 1 year (figure 3) was used to screen for TB.[1] The patients were examined for findings suggestive of TB such as wasting, lymphadenopathy, respiratory signs, abdominal distention with ascites or a gibbus. Available relevant investigations such as sputum smears, chest radiographs, mantoux and GeneXpert were reviewed. Those found with positive symptom screen or suggestive findings were referred to the clinician for investigation and management. All children who had not received IPT without evidence of active TB were referred to the clinician for a prescription.

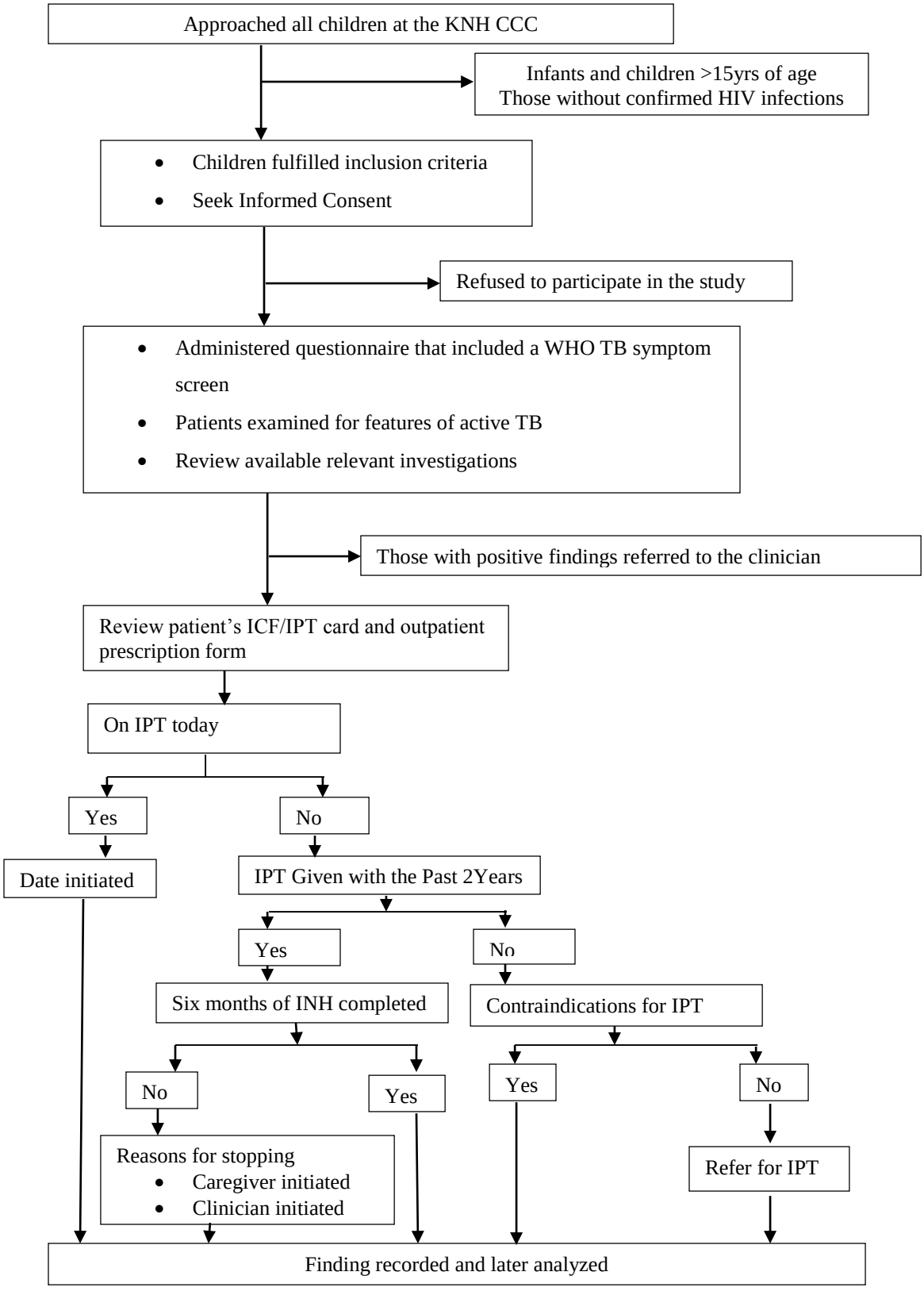
Finally we viewed pharmacy records to determine whether the drugs were dispensed upon prescription and refills where indicated were issued appropriately for the patients who were on IPT during the study period (Flowchart 7).

Paediatric Wards

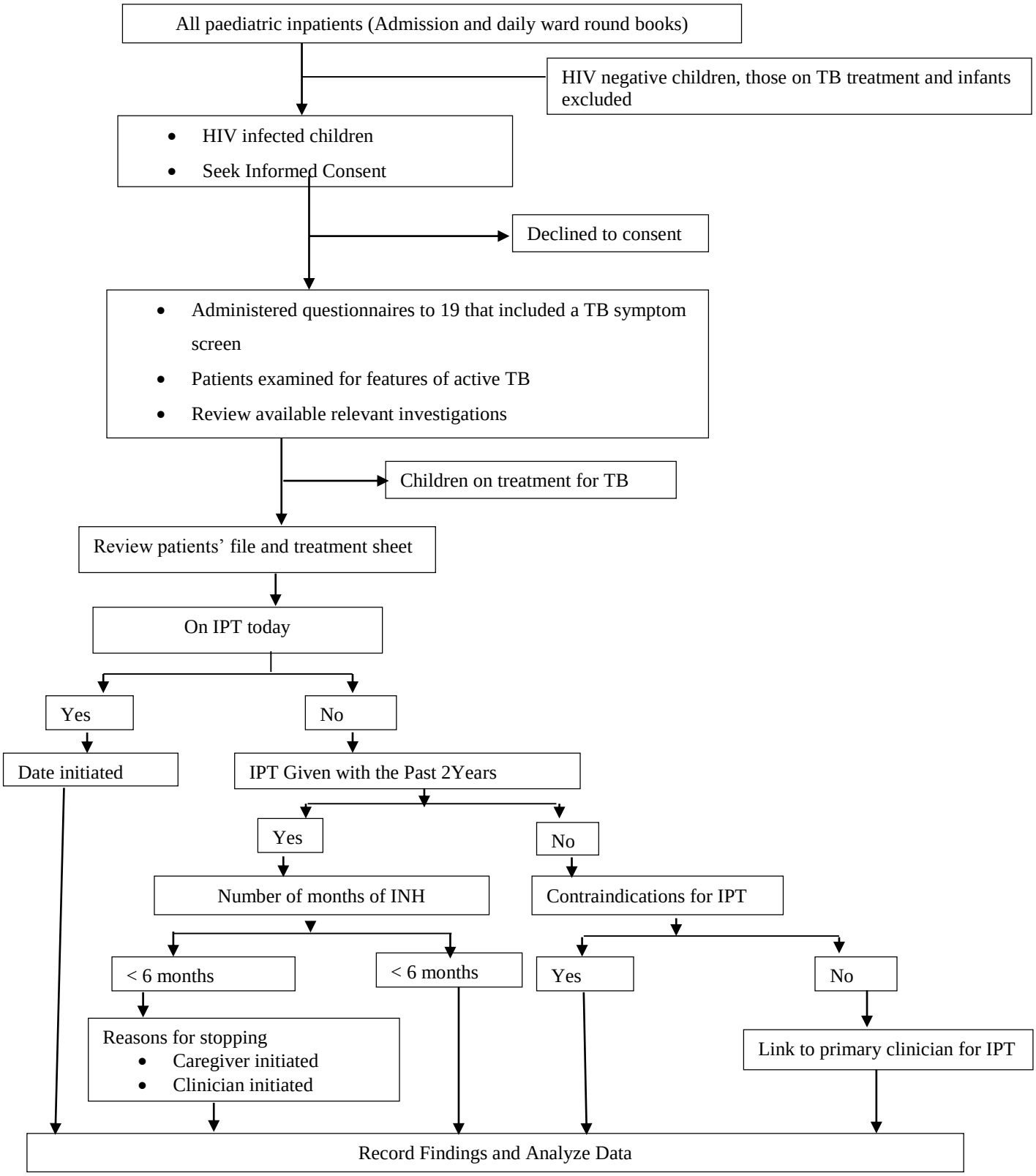
Both the admission and the ward round books; were used to identify potential eligible children with documented HIV infection (Flowchart 8). Questionnaires were administered to consenting caregivers. For children more than 8 years we also sought assent.

The WHO algorithm for TB screening and IPT in HIV infected children more than 1 year (figure 3) was used to screen for TB. The patient was examined for findings suggestive of TB such as wasting, lymphadenopathy, respiratory signs, abdominal distention with ascites or a gibbus. Available relevant investigations such as sputum smears, chest radiographs, mantoux and GeneXpert were reviewed. All children who had not received IPT without

evidence of active TB were referred to the clinician for a prescription. Treatment sheets were reviewed to determine whether IPT was prescribed, appropriate INH dosing for weight, correct duration and frequency.



Flowchart 7: Procedure for Patient Enrolment and Data Collection in the KNH CCC



Flowchart 8: Procedure for Patient Enrolment and Data Collection at KNH Paediatric Wards

Health worker Survey Procedures

The HCW questionnaire was structured to include a section on knowledge and another on practice (Appendix G) with regards to IPT among HIV infected children. Recruitment of HCW was done in the paediatric wards, CCC and out-patient clinics at KNH and MDH. We also enrolled HCW in the out-patient clinic and Maternal and Child clinic at LHC. Consent was sought from all health workers who were to be interviewed. A self-administered questionnaire was given to them to assess their knowledge and practice. The five-point Likert scale responses provided, by the study participants, for the set of statements used to evaluate the attitude of the healthcare workers were scored. The scores per statement ranging from zero to four. A composite score was then computed based on the aggregation of scores for the attitude assessment statements and expressed as a percentage.

We also conducted in-depth key informant interviews at the KNH CCC with the aid of an interviewer guide (Appendix H). We interviewed all the health workers working at the KNH pediatric CCC. Areas covered during the interview included knowledge, attitude and practice pertaining IPT among HIV infected children. The interviews were tape recorded and transcribed verbatim.

4.9 Data Management and Analysis

Data was collected using standardized questionnaires and entered into a password protected Microsoft access database. The entered data was then compared with hard copy forms to assess for completeness and accuracy. During this period, all hard copy data forms were stored in a secured cabinet accessible only to the researcher and statistician. Exploratory data analysis was conducted in order to determine inconsistent data and identify outliers.

Descriptive statistics of the children and their caregivers were determined as follows: For continuous variables, we determined the medians and the interquartile range (IQR). Where appropriate the continuous variables were converted into categories.

To determine objective 1 “To determine the proportion of HIV infected children in care Kenyatta National Hospital, who have received isoniazid preventive therapy in the past 2

years to date". We determined the numbers and the corresponding proportions and the 95% confidence intervals for the appropriate categories.

To determine objective 3 " the level of adherence to isoniazid preventive therapy course among children initiated on isoniazid preventive therapy within the preceding two years at KNH" We determined the numbers and the corresponding proportions and the 95% confidence intervals for the appropriate categories.

To determine objective 4 'To describe factors associated with uptake of isoniazid preventive therapy among HIV infected children in care at KNH'. Univariate analysis was carried out. The analysis involved chi square tests where categorical variable were involved while Mann Whitney U test was used in comparisons of continuous variables whose distributions deviated from normality. We also conducted a multivariate analysis(binary logistic regression) to test associations between the dependent variable and the independent variables found significant at the univariate analysis stage. The resultant adjusted odds ratios, the corresponding 95% confidence intervals and the respective p-values were reported. The threshold for statistical significance in all tests was set at $p<0.05$.

To determine the IPT knowledge (objective 4) as well as attitudes and practice of healthcare workers the five-point Likert scale responses provide for the set of test statements were scored. The scores per statement ranged from zero to four. A composite score was then computed based on the aggregation of scores for the assessment statements and expressed as a percentage. Categorical variables such as gender, and correct practice and knowledge were summarized as numbers and corresponding proportions using frequency tables whereas continuous variables such as age, duration of follow up, duration of IPT use were summarized using measures of central tendency and dispersion mainly median and IQR. Raw qualitative data from the in-depth interviews was transcribed, then themes analysed manually.

Minimization of Bias

Measures to avoid the various types of bias included:

Double entry: to prevent erroneous copying of data from questionnaire to the data base and thus minimized measurement and transcription error. The questionnaires were pre-tested to ensure that it gathered the required data (face validity). To minimize sampling bias only those who met the eligibility criteria were included. Familiarization of the researcher and research assistants on the information to be collected prior to the implementation of the study and training of the research assistants was done to minimize information bias. To avoid recall bias information collected from the care givers and health workers was verified using medical records.

4.10 Ethical Considerations

Permission was sought and obtained from the ethics and research committee in KNH/UON before starting the study. We also obtained permission from the Nairobi County and KNH research committees. Copies of this Protocol, the Informed Consent Form as well as any subsequent modification to either document was presented to the above named committee for written approval prior to commencing the study. The purpose of the study was carefully explained to the health workers and caregivers with a view to obtaining written consent prior to enrolling into the study.

Benefits that participants accrued from the study included receiving education regarding TB prevention in HIV infected children. Children who qualified for IPT and had not received it were referred to the clinician for initiation of the same. Feedback was given to health workers in the facilities where IPT was not being implemented. Strict confidentiality was observed throughout the entire study period, held in trust by participating investigators, research staff and the study institutions. The study participants were given study identification codes and no personal identification data was recorded on the questionnaire. No information concerning the individual study findings was released to any unauthorized third party.

CHAPTER 5

5.0 RESULTS

Section A: Child-Caregiver Survey

5.1 Characteristics of the Study Participants

Profile of the Caregivers

We enrolled 111 (92% from CCC) child-caregiver pairs visiting KNH between the month of October 2015 and January 2016. The median (interquartile range (IQR)) age of the caregivers was 36.0 (30.5 to 41.0) years. Most of the caregivers were female (77.3%), married (62.5%), HIV positive (85.4%) and were mothers to the children who took part in the study (69.1%). Analysis of the caregivers' level of education showed that 29.2%, 36.5% and 33.3% had attained, respectively, primary, secondary and college levels of education. Four caregivers (4.2%) were either on TB treatment at the time of the study or had completed the treatment within a period of 6 months from the time the study was undertaken. Most of the respondents were employed (75.0%) constituted by 22.9% and 52.1% of the respondents who were engaged in formal employment and self-employment respectively (Table 3).

Table 3: Profile of the Enrolled Caregivers

Characteristic	Frequency	Percentage
Age (years) (n=77)		
< 25	6	7.8
≥ 25	71	92.2
Gender (n=97)		
Male	22	22.7
Relationship to the child (n=97)		
Mother	67	69.1
Other	30	30.9
Marital status (n=96)		
Married	60	62.5
Education (n=96)		
No formal education	1	1.0
Primary	28	29.2
Secondary	35	36.5
College	32	33.3
Employment status (n=96)		
Employed	*72*	*75.0*
Unemployed	*24*	*25.0*
HIV status of caregiver (n=96)		
Negative	14	14.6
Positive	82	85.4
Currently on TB treatment or completed in the past 6 months (n=96)		
Yes	4	4.2

5.2 Socio-demographic Characteristics of Enrolled Children at KNH

The median (IQR) age of the enrolled children was 8.0 (9.7 to 12.6) years with those aged less than five years being 8.1% while those aged above five years but not more than ten years were 44.1%. Majority of the children were male (58.6%). Enquiries on the number of habitable rooms in the places of residence where the enrolled children hailed from revealed that 33.3%, 28.8% and 18.0% of the children lived in houses with one, two and three habitable rooms respectively. Moreover, 25.2%, 23.4% and 15.3% of the children lived in houses where the numbers of residents were, respectively, four, five or more than

five. Analysis of the household density (number of people per room) showed that median (IQR) was 2.00 (1.25 – 3.00) (Table 4).

Of the 111 children 106 (95.5%) were on ART, of these 35.8% had been on therapy for less than five years and 56.6% for five to ten years. On the frequency of clinic visits, appointment interval was 1 month for 7.2%, 2 months for 6.3%, 3 months for 60.4% and 4 months for 25.2% of children (Table 4).

Table 4: Socio-demographic and Clinical Characteristics of the HIV Infected Children at KNH

Characteristic	**Frequency (n=111)**	**Percentage**
Age (years)		
1 - <5	9	8.1
5 - <10	49	44.1
10 - <13	29	26.1
13 – 15	24	21.6
Gender		
Male	65	58.6
Female	46	41.4
Number of rooms in the house		
1	37	33.3
2	32	28.8
3	20	18.0
≥4	22	19.8
Household density	**Median**	**IQR**
No. of persons/room	2.00	1.25 – 3.00
Child on ART (n=111)		
Yes	106	95.5
No	5	4.5
Duration (years) on ART (n=106)		
1 to <5	38	35.8
5 to 10	60	56.6
>10 to 15	8	7.5
Clinic visits intervals (months) (n=111)		
1	9	8.1
2	7	6.3
3	67	60.4
4	28	25.2

The baseline CD4 count and percentage was available for 104 children. The baseline median (IQR) CD4 counts for the children less than five years were 790.0 (496.5-1731.0) cells/µL, five to ten years756.5 (473.8-1177.0) cells/µL and more than ten years of age

566.0(284.0-906.5) cells/µ. The corresponding median (IQR) baseline CD4 percentage for the three age groups were 19.4 (9.5-23.5) %, 21.0(9-32) % and 19.0(9.1-32) % (Table 7).

The median (IQR) CD4 percentage at the last visit for the children less than five years were 29.3(15.0-31.9) %, five to ten years 35 (29.4-40.1) % and more than ten years of age 27.7(14.8 – 85.5)%. The corresponding median (IQR) CD4 count for the three age groups on the latest data available at the time of the study were 964 (764.8-1232.6), 1000.0(615.8-1265.8) and 678.0(482.0-855.5) cells/µL (Table 5).

Table 5: Child CD4 Count at Baseline and At Last Visit

Age (years)	**Baseline CD4 count [Median(IQR)]**	**Latest CD4 count [Median(IQR)]**	**Number of Children(%)**
CD4 Count (cells/µL)			
1 to <5yrs	790 (496.5 - 1731)	964 (764.8-1232.6)	11(10)
5 to 10yrs	756.5 (473.8 - 1177)	1000 (615.8-1265.8)	23(21)
>10 to 15yrs	566 (284.0-906.5)	678 (482 -855.5)	7(63)
All children	**679 (435 - 1063.5)**	**769.6 (542.8 - 1055.1)**	**111(100)**
Baseline CD4 % [Median(IQR)]		**Latest CD4 % [Median(IQR)]**	
1 to <5yrs	19.4(9.5-23.5)	29.3(15.0-31.9)	11(10)
5 to 10yrs	21 (9 -32)	35.0(29.4-40.1)	23(21)
>10 to 15yrs	19 (9.1-32)	27.7(14.8 - 85.5)	7(63)
All children	**20 (9.8 - 32)**	**31.4 (25.9 - 38.2)**	**111(100)**

Table 6: Uptake of Isoniazid Preventive Therapy among Children in Care at KNH

Characteristic (n=111)	**Number**	**Percentage**
Currently on IPT	34	30.6
Received and completed 6 months of IPT	22	19.8
Received and interrupted IPT	3	2.7
Never received IPT	52	46.8
Overall uptake (ever received IPT)	**59**	**53.2**

Out of the 111 children who were eligible for IPT, 59 were found to be, either, on isoniazid at the time of the study or had received it within the two years preceding the survey (Figure

9). The overall uptake of IPT was thus 53.2% (95% confidence interval 43.9% - 62.4%). In particular, 34 (30.6%) of the children who participated in the study were taking isoniazid at the time of the study while 25 (22.5%) of the children had been on isoniziad during the two year period prior to the time of undertaking the study (table 8). All the children who were on once daily isoniazid (30.6%) at the time of the study were also taking pyridoxine (Table 6).

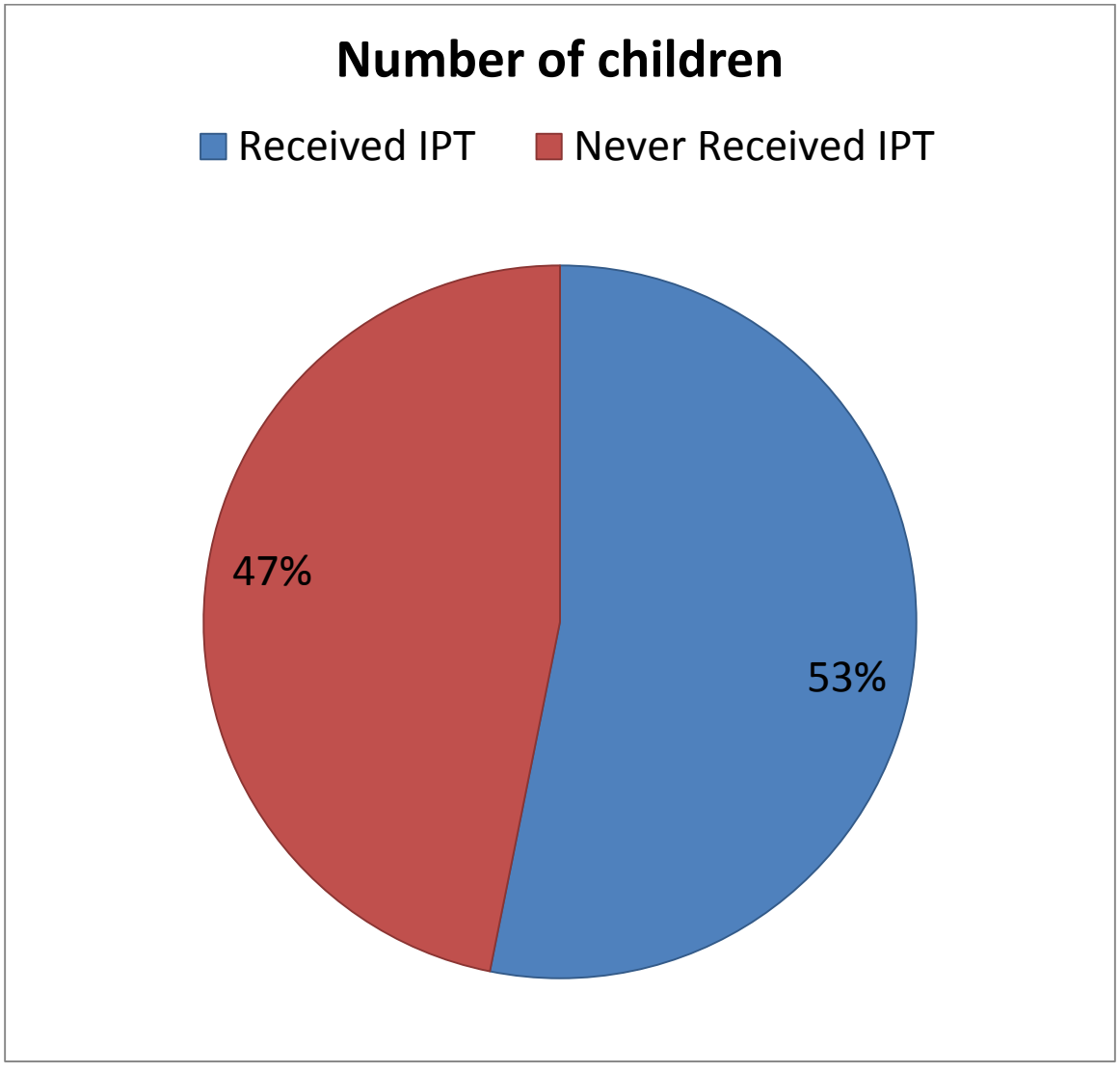


Figure 9: Proportion of HIV infected children who have received isoniazid preventive therapy within the preceding two years (n=111)

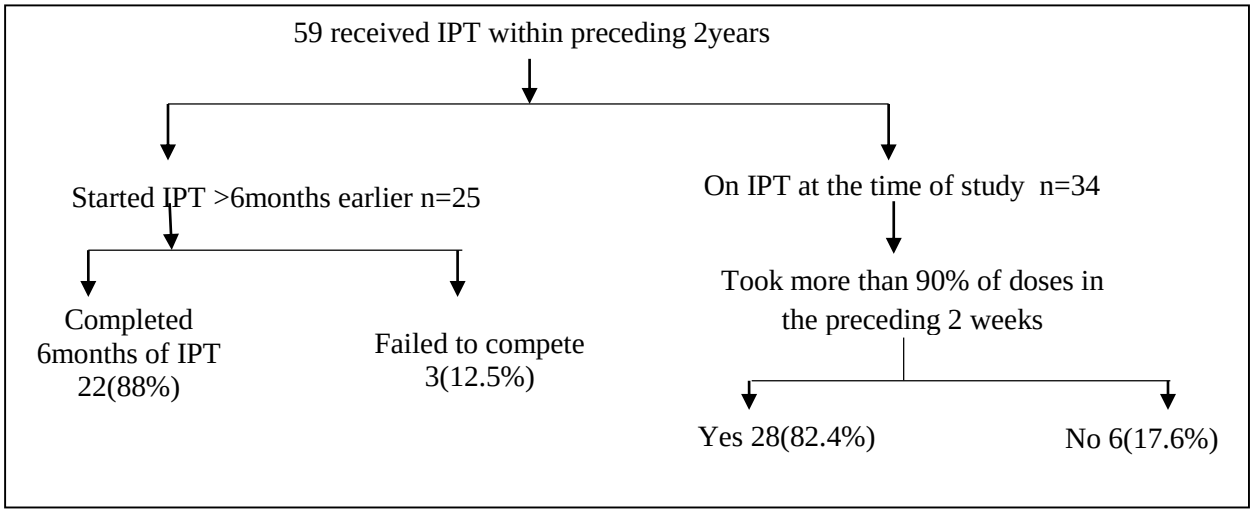


Figure 10: Level of Adherence among 59 children who ever received Isoniazid Preventive Therapy

5.3 Adherence among 59 Children who ever Received Isoniazid Preventive Therapy

Among children who started IPT more than 6 months before the study date, adherence was defined as completing 6 months of IPT. We found that 22(88.0%) of those who had a history of having been on isoniazid had completed the required six month treatment course. For those who had not completed the six month treatment course (12.0%), reasons for non-completion revealed that, in one case, the caregiver initiated the cessation of the treatment due to the immense pill burden. The second case of IPT non- completion, was instigated by the health care provider due to poor treatment adherence while there was no information provided for the third case of IPT non-completion (Table 7 and Figure 10).

Among participants, who were on isoniazid at the time of the survey, adherence was defined as consumption of ≥ 90% of doses in the preceding two weeks. We found that 27 (79.4%) had not missed a dose for the entire period under consideration. The rest (20.6%) were found to have missed at least one dose of isoniazid in the two weeks preceding the time the study. Specific numbers of doses missed by 7 participants were as follows: one dose-1 child, 3doses-1 child, 5 doses -3 children, 3 doses- 1 child, 5 doses– 3 children and 14 doses- 2 children. Study participants who had taken at least 90% of the prescribed doses were classified as adherent, else non-adherent. The proportion of the participants who were categorized as adherent was 82.4% (Table 7 and Figure 10).

Table 7: Adherence to Isoniazid Preventive Therapy within the Preceding 2weeks

Characteristic	Frequency (n=34)	Percentage
Missed a dose preceding 2 weeks		
Yes	7	20.6
No	27	79.4
Number of doses missed		
0	27	79.4
1	1	2.9
3	1	2.9
5	3	8.8
14	2	5.9
Good adherence (took ≥ 90% doses)		
Yes	28	82.4
No	6	17.6

Knowledge and Awareness of Isoniazid Preventive Therapy among Caregivers

Enquiries into the awareness of isoniazid preventive therapy (IPT) among the caregivers revealed that 66.7% were aware of it. Their source(s) of information included health care providers (85.1%), peer mentors (2.7%) and friends (2.7%). Most of the respondents who were aware of IPT also knew that its role was to prevent TB (90.5%). Furthermore, 54.1% of the respondents reported having ever used IPT (Table 8).

Table 8: Caregivers Knowledge and Awareness of Isoniazid Preventive Therapy

Characteristic	Frequency	Percentage
Aware of isoniazid preventive therapy (n=111)		
Yes	**74**	66.7
No	22	19.8
Missing	15	13.5
HIV Positive Caregivers (n=82)		
Aware of IPT	67	82.7
Not aware of IPT	14	17.3
Missing	1	
HIV Negative Caregivers (n=14)		
Aware of IPT	7	50.0
Not aware of IPT	7	50.0

Source of information (n=74)		
Health care provider	63	85.1
Peer mentor	8	10.8
Friends	2	2.7
Sister	1	1.4
Role of IPT (n=74)		
Prevent TB	67	90.5
Treat TB	4	5.4
Not sure	3	4.1

5.4 Factors Associated with Uptake of Isoniazid Preventive Therapy

Evaluation of the Association between Caregiver's Characteristics and IPT uptake

The current study also sought to determine the factors associated to IPT uptake in children. The median (IQR) ages of the caregivers whose children had ever received IPT (uptake group) and for the children who had not received IPT (no uptake group) were 38.5 (34.0-43.0) and 35.0 (30.0-42.0) years respectively. Comparisons of the two groups using Wilcoxon-Mann-Whitney test revealed no statistically significant differences in the distributions of the ages of caregivers ($z = -1.361$, $p = 0.191$). The findings are presented in Table 9 and Table 10. Education of the caregiver was partially associated with IPT uptake. Children of caregivers who had attained secondary level education were 70% less likely to having been on IPT as compared to their counterparts whose caregivers had no formal education or had reported primary school as the highest level of education achieved (odds ratio (OR) 0.300 (95% confidence interval (CI) 0.106-0.847), p=0.021). On the other hand, having post-secondary qualifications among the caregivers had no association with IPT uptake (p=0.081). The rest of the attributes failed to show any statistically significant relationship with the uptake of IPT in children.

Table 9: Assessment of caregiver's socio-demographic characteristics and Isoniazid Preventive Therapy uptake

Factor	Total	IPT uptake		OR† (95% CI§)	P-value
		Yes	No		
Gender					
Male	22	9(40.9)	13(59.1)	0.574(0.219-1.505)	0.256
Female	75	41(54.7)	34(45.3)	Reference	
Total	97	50(51.5)	47(48.5)		
Marital status					
Married	60	31(51.7)	29(48.3)	1.069(0.468-2.443)	0.874
Other	36	18(50.0)	18(50.0)	Reference	
Total	96	49(51.0)	47(49.0)		
Education					
Post-secondary	32	15(46.9)	17(53.1)	0.397(0.139-1.134)	0.081
Secondary	35	14(40.0)	21(60.0)	0.300(0.106-0.847)	0.021
No formal Education/Primary	29	20(69.0)	9(31.0)	Reference	
Total	96	49(51.0)	47(49.0)		
Relationship between caregiver and child					
Mother	67	37(55.2)	30(44.8)	2.158(0.577-8.075)	0.333
Father	19	9(47.4)	10(52.6)	1.575(0.343-7.224)	0.708
Other	11	4(36.4)	7(63.6)	Reference	
Total	97	50(51.5)	47(48.5)		
Employment status					
(Self) Employed	72	37(51.4)	35(48.6)	1.057(0.420-2.663)	0.906
Other	24	12(50.0)	12(50.0)	Reference	
Total	96	49(51.0)	47(49.0)		

†Odds ratio §Confidence interval

A lower proportion of uptake of IPT was observed in children caregivers whose serostatus was negative when compared with those of caregivers who were seropositive. However this association was not significant (28.6% versus 54.9% respectively, p=0.087). Further, being on TB treatment at the time of the study or having completed the treatment showed no association with IPT uptake in children (p=0.999). Being aware of IPT was associated with seven-fold increment in the likelihood

of uptake of IPT in a child (OR 7.393 (95%CI 2.270-24.080), p <0.001). Moreover, having been on IPT among the caregivers was associated with increased probability of uptake of IPT (OR 19.500 (95% CI 6.372-59.672), p<0.001). There was no significant difference in IPT uptake between those who reported having challenges in visiting the hospital and those who reported that they had not experienced any challenges in the visiting the hospital (41.0% compared to 55.6%, p=0.144).

Table 10: Assessment of caregiver's health-related attributes and IPT uptake

Factor	Total	IPT uptake		OR (95% CI)	P-value
		Yes	No		
HIV Status					
Negative	14	4(28.6)	10(71.4)	0.329(0.095-1.135)	0.087
Positive	82	45(54.9)	37(45.1)	Reference	
Total	96	49(51.0)	47(49.0)		
Completed/Currently on TB treatment					
Yes	4	2(50.0)	2(50.0)	0.957(0.129-7.090)	0.999
No	92	47(51.1)	45(48.9)	Reference	
Total	96	49(51.0)	47(49.0)		
Aware of IPT					
Yes	74	46(62.2)	28(37.8)	7.393(2.270-24.080)	<0.001
No	22	4(18.2)	18(81.8)	Reference	
Total	96	50(52.1)	46(47.9)		
History of IPT use					
Yes	40	35(87.5)	5(12.5)	19.500(6.372-59.672)	<0.001
No	53	14(26.4)	39(73.6)	Reference	
Total	93	49(52.7)	44(47.3)		

Children's Characteristics and Uptake of Isoniazid Preventive Therapy

The median (IQR) ages of the children had ever received IPT (uptake group) and those who had not were, respectively, 10.0 (8.0-12.0) years and 10.5 (8.3-13.0) years. No statistically significant differences were observed between the ages of the two groups after carrying out Wilcoxon-Mann-Whitney test (z = -0.617, p = 0.537). Duration/period a child had been on ART was also not associated with uptake of IPT (z = -0.154, p = 0.878).Uptake of Isoniazid Preventive Therapy was significantly associated with higher Baseline CD4 counts (790 (493-1409.5) and542(309-859) median (IQR) absolute CD4 cells/µL in

children who had ever received IPT and those who had never received IPT respectively, z = -2. 705, p = 0.007). Additionally, significantly higher current median (IQR) CD4 counts (852.0(606.5-1235.1) absolute cells/µL were observed in the children who had ever received IPT as compared to their counterparts who had not received IPT (733.8(470.4-935.2) absolute cells/µL), z = -2. 263, p = 0.024). The gender of the child and frequent of clinic visits were not associated with IPT uptake as shown in Table 11.

Table 11:Children's Characteristics and Uptake of Isoniazid Preventive Therapy

Characteristic	Total	IPT uptake		OR (95% CI)	P-value
		Yes	**No**		
Gender					
Male	65	33(50.8)	32(49.2)	0.793(0.371-1.695)	0.550
Female	46	26(56.5)	20(43.5)	Reference	
Total	111	59(53.2)	52(53.2)		
Frequent of clinic visits					
<Q	39	18(46.2)	21(53.8)	0.621(0.282-1.370)	0.237
Quarterly	69	40(58.0)	29(42.0)	Reference	
Total	108	58(53.7)	50(46.3)		
		Median (IQR)	**Median (IQR)**		
Age (years)		10.0 (8.0-12.0)	10.5 (8.3-13.0)		0.537
Duration/period on ART (months)		72(33-96)	60(24-96)		0.878
Baseline CD4, absolute cells/µL		790 (493-1409.5)	542(309-859)		0.007
Current CD4, absolute cells/µL		852.0(606.5-1235.1)	733.8(470.4-935.2)		0.024

Multivaraiate analysis: Caregivers' Characteristics and Uptake of IPT

The association between caregivers' characteristics and uptake of IPT was evaluated using binary logistic regression and the outputs are presented in Table 12. Age of the caregiver, though not associated with IPT uptake after univariate analysis, was included in the multivariate analysis due its potential confounding effect. Overall, education was found to be associated with uptake of IPT (p=0.047). In particular, children whose caregivers had

attained secondary school level of education were found to be 87% less likely to have received IPT when compared with those of caregivers who had no formal education or had achieved Primary school as the highest level of education (adjusted odds ratio (aOR) 0.131; 95% confidence interval (CI) 0.026-0.665, p=0.014). Additionally, children whose caregivers had a history of being on IPT had an increased likelihood of having received IPT (aOR 27.497; 95%CI 5.390-140.283, p<0.001). Analysis of the ages of caregivers showed that a unit increase in age resulted in about 8% increment in the probability of IPT uptake in children. However, this relationship failed to attain statistical significance (aOR 1.076; 95%CI 0.989-1.169, p=0.088).

Table 12: Multivariate Analysis Outputs: Caregivers' Characteristics and IPT Uptake

Variable	aOR†	95% CI§		P-value
		Lower	Upper	
Age (years)	1.076	0.989	1.169	0.088
Education (REF: None/Primary)				0.047
Post-secondary	0.281	0.057	1.386	0.119
Secondary	0.131	0.026	0.665	0.014
Aware of IPT {Yes vs. No}	1.678	0.333	8.455	0.531
History of IPT {Yes vs. No}	27.497	5.390	140.283	<0.001

£Beta co-efficient; #Standard error; †Adjusted odds ratio; †Confidence interval

Section B: Healthcare Workers Survey

5.5 Characteristics of Interviewed Healthcare Workers

We interviewed a total of 66 healthcare workers from three health facilities, this included all the health workers at Mbagathi DH (n=11) and Langata HC (n=4) at the time of the study together with a further 51 at KNH to reach the target sample size. The characteristics of the healthcare workers are outlined in Table 13. Overall, most of the healthcare workers worked in the Paediatric Inpatient Department (65.1%). In Langata Health Centre, all the healthcare workers interviewed were working in the Paediatric out-patient.

Table 13 shows the distribution of minimum required sample size by the participating health facilities.

Table 13: Distribution of Health Workers across Health Facilities

Department	Facility			Total
	KNH	Langata H/C	Mbagathi D/H	
Paediatric CCC	5(9.8%)	3(75%)	4(36.4%)	12(18.2%)
Paediatric inpatient	38(74.5%)	N/A	5(45.4%)	43(65.1%)
Paediatric outpatient	8(15.7%)	N/A	2(18.2%)	10(15.2%)
MCH	N/A	1(25%)	N/A	1(1.5%)
Total	**51**	**4**	**11**	**66**

Most of the participants were female (65.2%). Postgraduate doctors constituted 47.0% and Registered Clinical Officers 28.8% of the enrolled healthcare workers and were working at the Paediatric inpatient department (69.0%). Additionally, 9.1% of the respondents were Medical Officer Interns and 12.1% Clinical Officer Interns.

The median (IQR) duration in the paediatric unit was 15 (3 to 30) months with 33.3% having served in the unit for a period not exceeding twelve months, 28.8% one to two years and 47.0% more than two years (Table 14).

Table 14: Characteristics of the Healthcare Workers Interviewed

Facility/Position	Number	%
KNH (n=51)		
MO intern	1	2.0
CO intern	8	15.7
RCO	10	19.6
Postgraduate doctors	31	60.8
MO	1	2.0
Langata H/C (n=4)		
RCO	4	100.0
Mbagathi D/H (n=11)		
MO intern	5	45.5
RCO	5	45.5
MO	1	9.1

5.6 Health Worker Knowledge on Isoniazid Preventive Therapy

Table 16 outlines the results of the evaluation of knowledge on IPT amongst the HCWs. Out of the 66 healthcare workers interviewed, 61(92.4%) responded "*yes*" on being asked if TB is preventable. Of these, 59 (96.7%) and 2 (3.3%) HCWs reported that isoniazid and BCG vaccine could be used to prevent TB. Further, the 47 out of 61 HCWs (77.0%) stated that the IPT dosage is 10 mg/kg/day, while 59 HCWs (96.7%) reported that the drug is administered once daily. Fifty HCWs (85.2%) knew that isoniazid is given over a period of six months. A probe into the sources of information provided by the study participants showed that both pre-service and in-service trainings (77.0%), colleagues (13.1%), Guidelines/Booklets (11.5%) and media (6.6%) were some of the key sources of information (Table 15). Majority of the respondents (80.3%) either disagreed or strongly disagreed with the statement '*It's preferable to wait until a patient gets TB and then treat rather than administer prophylaxis'.*

Table 15: Assessment of IPT knowledge

Knowledge question	**Frequency (%)**
TB can be prevented (n=66)	
Yes	61(92.4)
No	5(7.6)
Drug used to prevent TB (n=61)	
Isoniazid	59(96.7)
BCG vaccine	2(3.3)
Isoniazid/rifampicin/ RZHE	2(3.3)
Dose for children (n=61)	
10mg/kg/day	47 (77.0)
3mg/kg/day	1(1.6)
5mg/kg/day	1(1.6)
15g/kg/day	1(1.6)
20mg/kg/day	1(1.6)
Don't know/Not sure	3(4.9)
No response	6(9.8)
Frequency of administration (n=61)	
Once daily	59(96.7)
Not sure	1(1.6)
No response	1(1.6)
Length of time drug is administered (n=61)	

6 months	52(85.2)
3 months	5(8.2)
No response	3(4.9)
Not sure	1(1.6)
Source of information (n=61)	
Training	47(77.0)
Colleague	8(13.1)
Media	4(6.6)
Guidelines/Booklets (MoH, NASCOP etc)	7(11.5)
Other*	2(3.2)
It's preferable to wait until a patient gets TB and then treat rather than administer prophylaxis (n=61)	
Strongly agree	3 (4.5)
Agree	6(9.1)
Not sure	4(6.1)
Disagree	38(57.6)
Strongly disagree	15(22.7)

5.7 Assessment of Attitude and Practices in Regards to Isoniazid Preventive Therapy

The study participants' attitude towards IPT was also assessed and the outcome is presented in Table 16. A vast majority of the study participants (97.0%) rated IPT as either effective or very effective. Those who reported that they were comfortable or very comfortable with administering IPT were 80.3% while 50.0% rated the side effects of IPT as mild or very mild. Ease of following IPT guidelines was rated as either easy or very easy by 84.8% of the respondents.

The five-point Likert scale responses provided, by the study participants, for the set of statements used to evaluate the attitude of the healthcare workers were scored. The scores per statement ranging from zero to four. A composite score was then computed based on the aggregation of scores for the attitude assessment statements and expressed as a percentage. The composite scores per respondent ranged from 37.5% to 93.8% with the mean ± standard deviation score being 70.5% ± 12.5%. Respondents were dichotomized into those with favourable attitude towards IPT (>60%) and those with unfavourable attitude towards IPT (≤60%). Based on this criterion, 81.8% of the interviewed healthcare

workers who took part in the current study were considered to have a favourable attitude towards IPT (Table 16).

Asked if they had ever started a patient on isoniazid, 68.2% of the study participants responded in the affirmative. Moreover, 50.0% of the respondents reported that they had started at least one patient on isoniazid in the twelve months preceding the survey. Additionally, 36.4% reported having ever renewed an isoniazid prescription while 31.8% of respondents stated that they had prescribed it in the one year period preceding the time the study

Table 16: Assessment of the Attitude and Practices in Regards to Isoniazid Prevention Therapy

Item		Frequency (n=66)	%
Rate your comfort in giving IPT			
Comfortable or very comfortable		53	80.3
Uncomfortable or very uncomfortable		6	9.1
Not sure		7	10.6
Rate effectiveness of IPT			
Effective or very effective		64	97.0
Ineffective or very ineffective		2	3.0
Rate side effects of IPT			
Dangerous or very dangerous		19	28.8
Mild or Very mild		33	50.0
Not sure		14	21.2
Rate ease of following IPT guidelines			
Easy or very easy		56	84.8
Difficult or very difficult		4	6.1
Not sure		6	9.1
Rating of overall attitude			
Favourable		54	81.8
Unfavourable		12	18.2
Practice			
Started a patient on IPT			
Over the past 1 year	Yes	33	50.0
	No	33	50.0
Ever started	Yes	45	68.2
	No	21	31.8
Renewed a patient's IPT prescription			
Over the past 1 year	Yes	21	31.8
	No	45	68.2
Ever renewed	Yes	24	36.4
	No	42	63.6

Considerations by Health Worker during Screening and IPT Initiation

Asked to state the considerations they make during screening and IPT initiation respondents gave more than one answer. Some of the most commonly mentioned considerations during screening and IPT initiation were risk of exposure (42.2%), ruling out active TB in the patients (72.1%), liver function tests (22.2%) and HIV status of the client (31.1%). Health workers who reported that they had ever renewed a prescription reported the following as key considerations when executing that task; adherence (41.7%), adverse effects (33.3%), absence of PTB (25.0%) and the weight of the child (16.7%), among others as shown in Table 17.

Table 17: Considerations by HCWs during Screening, IPT Initiation and Renewal of INH Prescription

Consideration	**During screening & IPT initiation Frequency (%) [n=45]**	**During IPT follow-up/IPT Renewal Frequency (%) [n=24]**
Exposure to adult with TB		
Risk of exposure	19(42.2)	0(0.0)
Time from exposure	17(37.8)	0(0.0)
Ruling out TB/TB diagnosis in child prior to giving IPT And Tests/preparing for IPT start		
Rule out TB	32(72.1)	6(25.0)
Gastric aspirates	1(2.6)	0(0.0)
ESR	2(4.4)	0(0.0)
Scoring (TB symptom score)	16(35.6)	0(0.0)
LFT	10(22.2)	2(8.3)
Renal	3(6.7)	0(0.0)
Age of the child	7(15.6)	0(0.0)
Evaluate child for concurrent illnesses prior to starting IPT		
HIV status (history)	12(26.7)	
Diagnosis of HIV status (HIV test)	14(31.1)	1(4.2)
CD4 count	4(8.9)	2(8.3)
Use of other drugs	11(24.4)	4(16.7)
Adherence	0(0.0)	10(41.7)
Weight of the child	3(6.7)	4(16.7)
Adverse Effects	0(0.0)	8(33.3)

5.8 Health Worker Key Informant Interviews

I conducted in depth interviews in the KNH CCC so as to gain more insight into the health worker knowledge and practice with regards to IPT. Those interviewed included all the health workers at the KNH pediatric CCC;

- The paediatrician in charge of the paediatric CCC care and management at KNH
- The pharmacy technician in charge of the paediatric CCC pharmacy
- Two clinical officers attached to the CCC whose daily duties includes attending to all the children and adolescents presenting to the clinic under the supervision of the paediatrician

The paediatrician in charge reported that all children seen at the CCC are screened for TB using the ICF tool and IPT is initiated if TB is ruled out. She reported that the clinicians were aware of the IPT guidelines "Sensitization was done to all the clinicians in April2015 and we did a repeat three months later we have continued to do so everybody is aware and we also have morning patient education at the waiting bay." Measures that had been put in place to ensure adherence to guidelines included; a mandatory form in the electronic medical records, routine data edits to check for missed opportunities and SOPS for the clinicians to follow. On being asked to comment on IPT uptake in the CCC her response was "we actively started prescribing IPT from October 2015 and by the end of the year we were half way …….. Our target is by the end of March 2016 72% coverage and by September 100%." She highlighted some of the facilitators to IPT uptake as follows; "the national programme has been very supportive together with our partners, they have ensured we now have consistent commodities, the uptake has been widely accepted and also the clients are accepting." The challenges mentioned included; absence of an electronic IPT register and transfer of patients from other facilities without clear medical records.

The pharmacy technician who had been working at the CCC pharmacy for 7 years reported that there was adequate stocks of INH (both the 100mg and 300mg tablets) and pyridoxine. He was aware of the correct dosage, frequency and duration of INH and pyridoxine together with their side effects. He reported that he had received some training on IPT in 2015. He had both a soft copy and hard copy of the National TB guidelines. He felt that IPT was effective and that INH side effects were uncommon. He was concerned that INH

was only available in tablet form making dosing for smaller children difficult. He pointed out that with proper projections and timely procurement stocks outs can be.

We interviewed two clinical officers, both genders were represented; one of them had worked in his current position for 8 months while the other had been working for 6 years. They both reported that they routinely screened all patients for TB using the WHO symptom screen and initiated those without TB on IPT. They were aware of the correct dosage and duration of INH and pyridoxine for IPT. One of them reported that he had not received any training on IPT; "I have been here for eight months and there is none actually which I have ever heard about." He however stated that he had a hard copy of the National TB guidelines. His colleague however reported that they had received two sessions of continuous medical education (CME) on IPT in 2015. They were also able to list the side effects associated with IPT. One of them reported that the side effects were not common while the other stated that "I have discontinued a number because of side effects." They felt that IPT was effective because they had not come across cases of TB among patients who had received IPT. Some of the barriers to IPT that emerged include; some patients refusing to take IPT because of pill burden and long duration of treatment "….half a year scares them." The clinicians also felt that counseling patients on IPT would increase the waiting time "I know the IPT is okay but whenever a patient comes in I start the health talk from the word zero..... I will be comprising the services for others" They were also concerned about the pill burden "There are some patients who....actually you yourself as the clinician you feel the burden of the patient." They also reported that other health workers receiving care at the CCC had a negative attitude towards IPT and were discouraging other patients from taking IPT "……if you get a staff they will never take IPT, so it is like they have negative attitude towards the IPT so even if it is a child's staff, you cannot initiate."

CHAPTER 6
6.0 DISCUSSION

We evaluated IPT uptake among HIV infected children aged 1-15 years receiving care at Kenyatta National Hospital. We also evaluated the knowledge and practice of health workers at Kenyatta National Hospital, Mbagathi District Hospital and Langata Health Centre regarding isoniazid preventive therapy in HIV infected children.

In this study, we determined that IPT uptake among HIV infected children was 53.2%. A half of the health workers had not prescribed IPT within the previous year. We also determined that 77% of the health workers knew the correct dosage, while 96.7% knew the correct frequency and 50% were aware of the correct duration.

The World Health Organization (WHO) recommends the use of Isoniazid preventive therapy (IPT) as one of the strategies to reduce the TB burden among people living with HIV infection.[1] However, its uptake in countries with high TB burden has been poor.[33-3535]Our analysis demonstrated that IPT uptake (53.2%)is poor despite the Kenyan National IPT guidelines that have been available since November 2013[2]and subsequently rolled out in April 2015. A study in Uganda among HIV infected children reported similar results with IPT uptake at 52.9%.[47] However, the uptake of IPT in this population was higher than the 17% and 27% reported in previous studies done in Malawi (Zacharia et al) and India (Shivaramakrishna et al).[33, 38]The different rates may be due to differences in study design, study population and settings. The higher level of IPT uptake in this study could be due to the revised WHO guidelines on IPT, previously a chest radiograph and a mantoux test were mandatory before IPT initiation but this is no longer the case. Similarly, low uptake of IPT was reported in Ethiopia where 39% of people living with HIV were initiated on IPT, use of ART increased the chances of receiving IPT in this study.[40]One study showed that the patients who had contracted TB were less likely to be using IPT (15% uptake) compared to 35% uptake in those who were TB-free.[47]

Several factors have been highlighted in previous studies to be associated IPT uptake. This study found out that uptake of IPT among children was high if their caregivers had themselves used IPT. This can be attributed to the fact that caregivers who had received

IPT were aware of its benefits and were therefore more likely to accept IPT initiation for their children, on the other hand they might have requested the health worker to initiate IPT for their children. We also assessed the association between the characteristics of the enrolled children and uptake of IPT. High baseline CD4 count was associated with an increase in the probability of a child receiving IPT. This may be attributed to fact that these children were likely to be clinically stable as opposed to a child with a low CD4 count who is likely to be having opportunistic infections with the possibly of being on multiple medications. Children whose caregivers had attained secondary school level of education were less likely to have received IPT when compared with those of caregivers who had no or lower level of education. In-depth interviews of health workers indicated that more educated caregivers were more likely to decline IPT initiation for their children citing pill burden as one of the reasons, those who were less educated were reported to follow the health worker instructions. No statistically significant differences were observed between the ages of the children who had received IPT and those who had not. Gender and frequency of clinic visits were not associated with IPT uptake; neither were caregiver's HIV status or TB treatment. In Uganda, poor adherence to ART, poor attendance to periodic HIV follow-ups and pill burden were reported as the three main reasons to delay IPT.[47]

Notably, our study found out that two of the three facilities where the study was conducted were not administering IPT to HIV infected children demonstrating the disparity in implementation of guidelines across facilities. The observed IPT uptake in KNH was supported by increased clinical updates, assurance of INH supplies, supportive supervision and quarterly audits within the CCC.

Among children who started IPT more than 6 months before the study date, adherence was defined as completing 6 months of IPT. The study demonstrates good completion (88%) of IPT once initiated. The low non-completion rate we found can partly be explained by the high percentage of anti-retroviral drug treatment (95.5%) in our study group. Patients had an incentive to come to the clinic already that was independent of IPT therapy thus removing any additional travel and time burden related to acquiring IPT medication. Lower completion rate was reported in Ethiopia where 24% of the patients were documented to

have completed treatment.[40]The study in Ethiopia did not explore the reasons for the low completion rate.

Among participants, who were on isoniazid at the time of the survey, adherence was defined as consumption of≥ 90% of doses in the preceding two weeks. The proportion of the participants who were categorized as adherent was 82.4%.Good adherence might have been a result of patients acting in the accordance to the directives to take isoniazid daily. Studies elsewhere have reported high adherence levels of IPT with average of 98.6% in Uganda; children reporting significantly lower (92%) adherence than adults.[43]The lower adherence level among children in Uganda could be explained by the fact that children those who were above 10 years of age had been informed about their HIV status and were taking their medications independent of their guardians. Our findings on adherence revealed the available opportunity of effectively increasing coverage of IPT among HIV infected children. However, our study indicated the contribution the care givers and health workers have in IPT initiation or lack of it.

The following were the reasons we found for non-completion of IPT: in one case was reported to be due to the caregiver initiating the cessation of the treatment due to the immense pill burden. The second case of IPT non-completion was instigated by the healthcare provider due to poor treatment adherence while there was no information provided for the third case of IPT non-completion. In Tanzania where the dropout rate was reported at 13%, non-completion was physician initiated in 33% (due to active TB or side effect), patient initiated in 52% (due to self-cessation/ loss to follow up) and due to death in 8% (unrelated to IPT).[45]However, this rate is substantially higher than the non-completion rate of 2.2% in a Dar es Salaam study.[43] The higher completion rate in the Dar es Salaam study could be explained by the high percentage of anti-retroviral drug treatment. Therefore, though not tested in this study, adherence to ART could influence IPT uptake and adherence. IPT adherence has been the focus of recent studies hence the testing of models of interventions such as the use of lay health workers, patient education and counseling, incentives and enablers.

The study population of the health workers comprised those working in the paediatric units of Kenyatta National Hospital, Mbagathi District Hospital and Langata Health Centre. We observed that in this study majority of the clinicians had correct knowledge with regards to IPT. There being no local study on the prevalence of correct knowledge and practice with regards to IPT this serves as baseline information for their level of correct knowledge.

A half of the health workers at the time of this study had not prescribed INH within the previous year. This is similar to a study carried out in Georgia County (Miles et al) in which less had prescribed IPT within the previous year. We found that 68.2% of health workers had ever started a patient on IPT whereas Miles et al reported that only 54% of health workers interviewed reported ever having started a patient on IPT. The different rates may be due to differences in study design and study population. The study by Miles looked at primary care physicians and non-primary care physicians, a vast majority of the later reported that they didn't consider prescribing IPT because they believed the practice to be outside their medical specialty.

Relatively few health workers expressed concern that isoniazid INH was not effective enough (2%) or that the side effects were too dangerous (28.8%).Majority of the respondents (80.3%) did not think it was preferable to wait until a patient gets TB and then treat rather than administer prophylaxis.Our findings frame the issues similar with the study by M. Miles in which 4% of responders indicated that INH was not effective enough and that the side effects of INH made it too dangerous to prescribe. Moreover, fewer than 1% indicated a preference to wait to see whether an infected patient develop active TB, which can then be treated.[44]Attitude of the healthcare workers was assessed and 81.8% of the interviewed workers had favorable attitude towards IPT.

Having a policy set of guidelines for IPT, but experiencing a lack of implementation, is common in many countries. A cross-sectional email survey by WHO reported that only 28% of countries with a national policy for IPT had achieved nationwide implementation (Date et al, .2010). Lowas and coworkers had written that guidelines for practice may predispose physicians to consider changing their behavior, but unless there are other incentives or disincentives are removed, guidelines may be unlikely to effect rapid change in actual practices.[46]

Some of the barriers to IPT implementation that emerged include; among the health workers pill burden and long waiting time because of the time required to educate each patient on IPT. The caregivers were also concerned about the pill burden and the long duration of IPT. A study done in Thailand had highlighted the following barriers; fear of INH resistance, lack of clear guidelines and fear of poor adherence.[39] However studies have shown there is no significant increased risk of INH resistance associated with IPT.[37] In the study by Miles et al physicians who had not prescribed IPT within the previous year gave as a reason the belief that many patients don't like taking isoniazid.

In this study, we can conclude that majority of the health workers have good knowledge on IPT because of the availability of clear National Guidelines together with the recent Nationwide IPT roll out. There is however a gap in health worker practices with regards to IPT. We also found that adherence among children initiated on IPT was good with high completion rate.

STUDY STRENGTHS AND LIMITATION

The strengths of this study are that it was able to review the practice of a diverse group of people in Nairobi County. We also reviewed multiple steps in IPT implementation from identification of eligible children, to screening, initiation and completion of IPT. To maximize our response rate the health worker questionnaire was brief. We also combined qualitative and quantitative methods to shed light on health worker knowledge and practices relative to TB prevention recommendations.

These findings may not be generalizable to other counties considering that the study was based in an urban setting. The patients were enrolled from a single hospital and thus the proportion of eligible children in Mbagathi District Hospital and Langata Health Centre cannot be reported. Reporting bias may also have been present with some health workers reporting prescription of isoniazid. Since we were using questionnaires for both the health worker and child-caregiver survey there was a problem of nonresponse. The in-depth interviews were only carried out at Kenyatta National Hospital and therefore we might have missed out on some important information from the other health facilities.

CONCLUSION

1. IPT uptake was low at 53.2% in this cohort of HIV infected children
2. Completion of IPT for those initiated was satisfactory while adherence among those on IPT at the time of the study was suboptimal.
3. Uptake of IPT was higher among children whose caregivers had a history of being on IPT or had no formal education or had reported primary school as the highest level of education as well as among children with a higher CD4 count at enrolment
4. HCWS have the requisite knowledge for provision of IPT
5. A half of the health workers at the time of this study had not prescribed isoniazid within the previous year.

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RECOMMENDATIONS

1. There is a urgent need to scale up isoniazid preventive therapy
2. The scale up plan should include strategies to address the concerns identified among health workers
3. Provision of supportive supervision and mentorship for health workers may accelerate isoniazid preventive therapy implementation.
4. Continued public education on the different modalities available for tuberculosis prevention
5. Continuous medical education sessions to reinforce knowledge and practice in regards to HIV management and the essential care package of people living with HIV of which isoniazid features prominently.

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APPENDICES

Appendix A

Implementation of Isoniazid Preventive Therapy in two Hospitals and one Health Centre in Nairobi County

Child-Caregiver Pairs Information and Consent Form- English

Investigator: Dr. Peninah Muthoni Mwangi

Telephone number: 0719892169

Supervisors: Professor Elizabeth Maleche Obimbo, Associate Professor Dalton Wamalwa, Dr. Diana Marangu, University of Nairobi

Investigators statement: We are requesting you and your child to kindly participate in this research study. The purpose of this consent form is to provide you with information you will need to help you decide whether to participate in the study. The process is called informed consent. Please read this consent information carefully and ask questions or seek clarification on any matter concerning the study with which you are uncertain.

Introduction: HIV infection is the most important risk factor for the development of active tuberculosis. Tuberculosis is the single most prevalent cause of death in those infected with HIV. Isoniazid preventive therapy has been shown to be effective in decreasing incidence and deaths due to tuberculosis. This study seeks to establish if your child has received isoniazid preventive therapy and establish any barriers to its implementation.

Inclusion Criteria: The study subjects shall be drawn from children aged 1 to 15 years with documented HIV infection receiving care in the inpatient and outpatient departments of Kenyatta National Hospital, Mbagathi District Hospital Langata and Kangemi health centre.

*Study procedure***:** We are kindly requesting for 15minutes of your time during which a questionnaire will be administered, the researcher will ask the questions and fill the answers appropriately. Participants, who are literate and opt to, will fill on their own. The researcher will then examine the child and review relevant medical records.

Benefits: If your child is eligible for isoniazid preventive therapy and has not received it, arrangements will be made to avail it. Those children who will be found to have active tuberculosis will be initiated on treatment. The results of the research will be used by heath

workers, policy makers and program managers in this county and other counties to inform isoniazid preventive therapy implementation.

Risks: There will be no risks to you or your child during the study. There will be no invasive procedure carried out during the study that may harm your child. Refusal to participate will not jeopardize the care of your child in any way.

Voluntariness: The study will be fully voluntary. There will be no financial rewards to you for participating in the study. One is free to participate or withdraw from the study at any point. Refusal to participate will not compromise your child's care in any way.

Confidentiality: The information obtained about you and your child will be kept in strict confidentiality. No specific information will be released to any person without your permission. We will however, discuss general overall findings regarding all children enrolled but nothing specific will be discussed regarding your child. We will not reveal your identity or that of your child in these discussions.

Problems or questions: If you have any questions about the study or about the use of the results you can contact the principle investigator, Dr. Peninah Mwangi by calling 07198922169.

If you have any questions on your rights as a research participant you can contact Kenyatta National Hospital Ethics and Research Committee (KNH-ESRC) BY CALLING +2542726300-19 or email uonknh-erc@uonbi.ac.ke.

To indicate that you understand the conditions of this study and that you consent to participate in it, please sign or put your thumb print in the space provided below.

I, _____ confirm that the study has been fully explained to me and I give full consent to participate in it.

Care giver' signature/thumb print: _____

Investigators signature: _____

Date: ____/_____/ 2015

Appendix B

Utekelezaji wa Isoniazid njia ya Kuzuia katika Hospitali mbili katika Kata ya Nairobi

Habari ya Muhusika na Fomu ya Idhini - Kiswahili

Mpelelezi: Dkt. Peninah Mwangi

Tel: 0719892169

Wasimamizi: Prof Maleche-Obimbo, Prof Dalton Wamalwa, Dkt. Diana Marangu, Chuo Kikuu cha Nairobi, Idara ya Paediatrics na Afya ya Mtoto

Kumbusho ya mpelelezi: Asante sana kwa kukubali kusoma fomu hii. Inatoa habari kuhusu utafiti huu ambayo itasaidia kuamua kama utashiriki katika utafiti huu au la. Tafsiri sahihi itatekelezwa katika lugha ambayo uko na starehe zaidi**.**

Utangulizi: Maambukizi ya HIV ni muhimu sana kwa sababu ya adhari ya maendeleo ya kifua kikuu kinachoendelea. Kifua kikuu ni moja wapo ya magonjwa inayosababisha vifo kwa wale walioambukizwa na HIV. Tiba ya kuzuia Isoniazid imekuwa ikionyesha kuwa inafanya kazi kwa kupunguza matukio na vifo kutokana na kifua kikuu. Utafiti huu unataka kujua kama mtoto wako amepokea tiba ya kuzuia isoniazid na kuangalia vikwazo vyovyote vya utekelezaji wake.

Taratibu za Utafiti: Maswali itaulizwa kutumia fomu kwa walezi wa watoto waliohitimu kuingia. Mtafiti atuuliza maswali na kujaza majibu ipasavyo. Washiriki, ambao wanajua kusoma na kuandika na wanachague, watajaza wao wenyewe. Mtafiti kisha atachunguza mtoto na kuangalia kumbukumbu zinazohusika kwa matibabu.

Faida: Kama mtoto wako amehitimu kupata tiba ya kuzuia isoniazid na hajapata, mipango itafanywa apate yake. Wale watoto ambao watapatikana kuwa na kifua kikuu kinachoendlea wataanzishwa matibabu.. Matokeo ya utafiti itatumiwa na mfanyakazi wa afya, watunga sera na wasimamizi wa orodha katika kata hii na kata nyingine kuwajulisha kuhusu tiba ya kuzuia isoniazid na utekelezaji.

Hatari: Hakutakuwa na hakuna hatari kwako au mtoto wako wakati wa utafiti huu. Hakutakuwa na kundugwa wakati wa utafiti huu , ambayo inaweza kuleta madhara kwa mtoto wako. Kukataa kushiriki haitahatarisha huduma ya mtoto wako kwa njia yoyote.

Kujitolea: Utafiti huu utakuwa kikamilifu kwa hiari yako. Hakutakuwa na zawadi za fedha kwa ajili ya kushiriki katika utafiti. Uko na huru wa kushiriki au kutoshiriki na utafiti katika hatua yoyote. Kukataa kushiriki haitazuia huduma ya motto wako kwa njia yoyote.

Siri: kama utakubali kushiriki kwa utafiti huu, hakuna taarifa maalum ya mshirika yoyote itakuwa wazi kwa mtu yeyote bila idhini yake kwa mwandishi.

Matatizo au maswali: Ukiwa una maswali yoyote kuhusu utafiti au kuhusu matatizo ya matokeo unaweza kuwasiliana na mpelelezi mkuu kutumia mawasiliano hapa chini:

Dkt: Peninah Mwangi Tel: 0719892169

Ukiwa na maswali au matatizoziada kuhusu utafiti huu, unaweza kuwasiliana na mmoja wa wasimamizi wangu, **Prof. Wamalwa 0721239493** au unaweza kuwasiliana moja kwa moja na KNH/UON Maadili na Utafiti wa kamatikwa nambari ya simu **+2542736300-19** au barua pepe **uonknh-erc@uonbi.ac.ke.**

Kuonyesha kwamba unaelewa hali ya utafiti huu na kwamba ridhaa ya kushiriki katika hayo, tafadhali tia ishara au uweke kidole chako katika nafasi iliyotolewa hapa chini.

Mimi,_____ nathibitisha kwamba nimeelezwa kuhusu utafiti na ninatoa kibali ya kushiriki katika utafiti huu.

Sahihi/kidole: _____

Tarehe:_____/_____/_____

Appendix C

Implementation of Isoniazid Preventive Therapy in two Hospitals and one Health Centre in Nairobi County

Assent Form for Children 8 to 15 Years of Age - English

Investigator: Dr. Peninah Muthoni Mwangi

Telephone number: 0719892169

Supervisors: Professor Elizabeth Maleche Obimbo, Associate Professor Dalton Wamalwa, Dr. Diana Marangu, University of Nairobi

Investigators statement: We are requesting you to kindly participate in this research study. The purpose of this assent form is to provide you with information you will need to help you decide whether to participate in the study. You can ask questions at any time.

Introduction: This study seeks to establish if you have received isoniazid a drug used for tuberculosis prevention.

*Study procedure***:** The researcher will perform a physical examination on you. We will also look at your past doctor visits and use information about your care.

Benefits: If you are eligible for isoniazid preventive therapy and have not received it, arrangements will be made to avail it. The results of the research will be used by heath workers, policy makers and program managers in this county and other counties to help other children.

Risks: There will be no risks to you during the study. There will be no invasive procedure carried out during the study that may harm you. If you object the research will be terminated and you will not be punished or scolded.

Voluntariness: The study will be fully voluntary. You would not be paid too be in the study. It is also okay to say 'yes' and change your mind later. You can stop being in the research at any time. We will still take good care of you no matter what you decide.

Confidentiality: The information obtained about you and your child will be kept in strict confidentiality.

Problems or questions: Ask us any questions you have. Take the time you need to make your choice.

If you want to be in the research after we talk, please write your name below. We will write our name too. This shows we talked about the research and you want to take par

Name of the participant: _____

Name of the investigator: _____

Investigators signature: _____

Date: ____/_____/ 2015

Appendix D

Implementation of Isoniazid Preventive Therapy in two Hospitals and one Health Centre in Nairobi County

Questionnaire for Child-Caregiver Pairs – English:

Thank you for participating in this study

CAREGIVERS BIO DATA

Study number _____

Date _____/_____/_____

Date of Birth ____/_____/_____ Sex Male [ ] Female [ ]

Relationship to the child

Mother [ ] Father [ ] Aunt [ ] Uncle [ ] Grandmother [ ] Sister [ ] Other (if other, specify) _____

Marital status

Single [ ] Married [ ] Separated/divorced [ ] Other [ ] If other specify _____

Level of Education of Caregiver

_____

Employment of Caregiver

Unemployed [ ] Employed [ ] Retired [ ] Student [ ] Self employed [ ]

Other (specify)

_____

HIV status of the care giver

Negative [ ] Positive [ ] [ ] Unknown[ ] Declined to disclose

Are you currently on treatment for TB/ have you completed TB treatment in the past 6 months

Yes [ ] No [ ]

Are you aware of isoniazid preventive therapy Yes [ ] No [ ]

b.If yes where did they get the information(tick one)

- Health provider
- Peer mentor
- Social media
- Friends
- Others (specify) _____

In your understanding what is the role of isoniazid preventive therapy?

[ ] Prevent TB [ ] Treat TB [ ] Not sure

[ ]Other please specify

Have you ever used isoniazid preventive therapy?

Yes [ ] No [ ]

CHILD'S BIO DATA

Study number _____

Date _____/_____/_____

Date of birth _____/_____/_____

Sex Male [ ] Female [ ]

SOCIO- DEMOGRAPHICS

1. Did you have challenges coming to the hospital Yes [ ] No [ ]
2. If yes what kind of a challenge (tick)
    - Financial
    - Family related
    - Work related
    - Other (specify)_____
3. Number of habitable rooms in your house? _____
4. How many people live in that house? _____

CHILD'S CLINICAL INFORMATION

1. a. HIV status of the child (confirm with the patient's file)

   [ ] Negative [ ] Positive [ ] [ ] Unknown

   b.When was the diagnosis made; Age _____ Years _____Months Date_____/ _____ /___
2. Weigh_____. _____ Kilograms
3. Height ____ _____. ___ cm, Weight for height Z-score _____
4. Date enrolled into comprehensive care clinic_____/_____/_____
5. Current history of ;
    a. Cough Yes[ ] No[ ] If yes duration _____
    b. Persistent fever and/ night sweats Yes[ ] No[ ] Duration _____
    c. Weight loss or poor weight gain Yes [ ] No [ ]
    d. Fatigue, reduce playfulness, less active Yes [ ] No [ ] Duration _____
6. a) Abnormal respiratory signs Yes [ ] No [ ] If yes please tick
        - Increased respiratory rate
        - Respiratory distress
        - Stony dull percussion note
        - Added breath sound (wheezing, crackles, bronchial breathing)

- Other (please specify) _____

b) Diagnosis

- Pneumonia
- Effusion
- Airway obstruction
- Other 9specify)

7. CXR suggestive of PTB (where available) Yes [ ] No [ ] If yes specify
   - Focal lung opacification
   - Enlarged hilar or subcarinal lymph nodes
   - Miliary pattern
   - Pleural effusion
   - Upper lobe opacification
   - Other (please specify) _____
8. Mantoux test done Yes [ ] No [ ] If yes, result _____ mm
9. a) Exposure to an adult/adolescent with pulmonary tuberculosis

   Yes [ ] No [ ]

   b) If yes please tick

   - Living in the same household as index case with PTB
   - In frequent contact with (child minder, school staff) index case with PTB

   c) Conclusion [ ] Close contact [ ] No contact

10. Principal investigator/ research assistant conclusion [ ] Confirmed TB

    [ ] Suspected TB [ ] No TB

11. a. Is the child on antiretroviral therapy Yes[ ] No[ ]

b. If yes for how long have they been on ART _____

12. How frequent are your visits to the clinic? Every _____ months
13. a. Is the child currently on isoniazid monotherapy Yes [ ] No [ ]

(**As you show the care giver a tablet of isoniazid, if no skip to number 13**)

b. If yes how much did you give _____

c. How many times in a day did you give it? _____ times

d. Did you receive any instructions on how to give it Yes [ ] No [ ]

e. Is the child taking pyridoxine Yes [ ] No [ ]

f. Within the past two weeks how many doses has the child missed _____ doses

12. Could you please show me the isoniazid pills you currently have (count remaining pills)

_____ pills

13 a. History of isoniazid monotherapy use in the past 2 years Yes [ ] No [ ]

(**If no skip to number 15**)

b. If yes when was it started ____/_____/_____

c. For how many months did the child take the isoniazid _____ months

14. If IPT was not completed what was the reason for non-completion

a) Health care worker initiated due to [ ] Confirmed TB [ ] Suspected TB [ ] side effects [ ] Poor adherence
[ ] Others specify _____
b) Caregiver initiated due to [ ] Side effects[ ] Pill burden [ ] Loss to follow-up
[ ] Others, please specify)_____

MEDICAL RECORD

The following information will be retrieved from the patient's records (i.e. ICF/IPT card, file, pharmacy records, IPT register)

15. Baseline CD4, absolute _____ cells/micro liter CD4 % _____
    Total lymphocyte count _____ x 10^9/ L
16. Most recent CD4, absolute _____ cells/ml CD4 % _____
    Total lymphocyte count _____
17. a. Date of IPT initiation _____
    b. Prescribed dosage _____mg/tablets _____times/day (from treatment sheet/out-patient prescription form/file)
18. How many pills of isoniazid were dispensed in the last visit _____ pills(pharmacy records)
19. Reasons for not initiating IPT

[ ] Hepatitis [ ] Peripheral neuropathy [ ] Isoniazid out of stock

[ ] Not documented [ ] Declined IPT

[ ] Other (please specify)_____

Appendix E

Questionnaire for Child-Caregiver Pairs- Kiswahili

Utekelezaji wa Isoniazid njia ya Kuzuia katika Hospitali mbili katika Kata ya Nairobi

Asante kwa kushiriki katika utafiti huu.

HABARI ZA MTOTO

Nambari ya Utafiti _____

Terehe _____

Miaka kati ya 1-2 _____ Miaka 3-5 _____ Miaka 6-15 _____

Mume [ ] Kike [ ]

Uzito _____. _____ Ratili

HABARI ZA KIDEMOGRAPHIA

1. Je ulipata changamoto kuja hospitalini Ndio [ ] La [ ]
2. Kama ndiyo ni aina gani ya changamoto (Jibu moja)
    - Fedha
    - Inahusiana na familia
    - Inahusiana na kazi
    - Nyingine (Taja)_____
3. Idadi ya vyumba katika nyumba yako? _____
4. Watu wangapi wanaishi katika nyumba hiyo? _____

HABARI YA KLINIKI YA MTOTO

1. Historia ya kisasa ;
    a. Kukohoa Ndio [ ] La [ ]
    b. Njoto Ndio [ ] La [ ]
    c. Kupoteza kilo Ndio [ ] La [ ]
    d. Wazi kwa watu wazima/vijana kwa kifua kikuu cha mapafu
    Ndio [ ] La [ ]
2. Je mtoto ako kwa tiba ya kifua kikuu wakati huu? Ndio [ ] La [ ]

3. Je mtoto ako kwa tiba ya kupigana na makali ? Ndio [ ] La [ ]

3b. Kama ndio kwa mda gani _____

4. Je mlezi anajua kuhusu tiba ya kuzuia isoniazid Ndio [ ] La [ ]

4b.Kama ndio walipata wapi habari hizi? (Jibu moja)

- Muhudumu wa afya
- Vyombo vya habari
- Marafiki
- Nyingine(Taja) _____

5. Umbali wa siku za kutembelea kliniki _____

6. Je mtoto anapata isoniazid Ndio [ ] La [ ]
   (Onyesha mhudu wa afya tebe ya isoniazid, kama hakuna ruka hadi 7)

6b. Kama ndio onyesha unampa ngapi _____

6c. Mara ngapi kwa siku unampa? _____ Mara

6d. Je ulipata maelezo jinsi ya kumpa Ndio [ ] La [ ]

6e. Je mtoto anakunywa pyridoxine Ndio [ ] La [ ]

7. Hitoria ya matumizi ya isoniazid kwa miaka 2 iliyopita Ndio [ ] La [ ]

7b.Kama ndio mtoto amekunywa kwa mda gani_____

8. Kama kuna historia ya madhara kwa isoniazid kwa mtoto wako Ndio [ ] La [ ]
9. Je unafikiri kama isoniazid inaweza zuia TB? Ndio [ ] La [ ]

REKODI YA MATIBABU

Habari ya ifuatayo itatolewa kwa rekodi za mgonjwa (Kwa mfano kadi ICF/IPT, Faili na rekodi za madawa)

1. Siku ya kuandikishwa kwa huduma _____
2. Kuandikiwa kwa IPT Ndio [ ] La [ ]

2b.Kama ndio ulipatiwa Ndio [ ] La [ ]

2c.Kama ndio siku ya mwisho kupata Isoniazid _____

3. Kifua kikuu kinacho julikana Ndio [ ] La [ ]

3b. Kama ndio tarehe ilipojulikana _____

Appendix F

Implementation of Isoniazid Preventive Therapy in two Hospitals and one Health Centre in Nairobi County

Health Worker Information and Consent Form

Investigator: Dr. Peninah Muthoni Mwangi

Telephone number: 0719892169

Supervisors: Professor Elizabeth Maleche Obimbo, Professor Dalton Wamalwa,

Dr. Diana Marangu, University of Nairobi

Investigator Note: Thank you for agreeing to read this form. It offers information about this study which will help you decide if you will take part in this study or not.

Introduction: HIV infection is the most important risk factor for the development of active tuberculosis. Tuberculosis is the single most prevalent cause of death in those infected with HIV. Isoniazid preventive therapy has been shown to be effective in decreasing incidence and deaths due to tuberculosis. This study seeks to establish proportion of children who received isoniazid preventive therapy and establish any barriers to its implementation.

Eligibility Criteria: We are seeking to interview consultant pediatricians, medical officers, medical officer interns, clinical offices, and clinical officer interns working in the pediatric wards or comprehensive HIV care clinic. Pharmacists, pharmacy technologists dispensing medication to HIV infected children and nurses maintaining the IPT register in your facility.

Procedure: If you agree to be part of this study, I will ask you questions on your practices with regards to IPT, availability of isoniazid in your hospital and barriers/facilitators of IPT implementation. To do this we will require 15 minutes of your time.

Benefits: Findings of this study will be interpreted to you, the hospital management team and the University of Nairobi. This will help those involved in hospital policy making to improve practice within the hospital as we try to reduce TB/HIV confection and deaths.

Risks: There will be no risks to you during the study.

Voluntariness: The study will be fully voluntary. There will be no financial rewards to you for participating in the study. One is free to participate or withdraw from the study at any point. Refusal to participate will not compromise your child's care in any way.

Confidentiality: if you agree to be part of this study, the information you give will be held in strict confidence and only used for the purpose of the study. No specific information of any participant will be revealed to any person without their permission in writing.

Problems or questions: If you have any questions about the study or about the use of the results you can contact the principle investigator, Dr. Peninah Mwangi by calling 07198922169.

If you have any questions on your rights as a research participant you can contact Kenyatta National Hospital Ethics and Research Committee (KNH-ESRC) BY CALLING +2542726300-19 or email uonknh-erc@uonbi.ac.ke.

To indicate that you understand the conditions of this study and that you consent to participate in it, please sign or put your thumb print in the space provided below.

I, _____ confirm that the study has been fully explained to me and I give full consent to participate in it.

Health Worker's signature/thumb print: _____

Investigators signature: _____

Date: ____/_____/ 2015

Appendix G

Implementation of Isoniazid Preventive Therapy in two Hospitals and one Health Centre in Nairobi County

Health Worker Questionnaire

Thank you for participating in this study

DEMOGRAPHICS

A. Date _____ B. Sex _____

B. Department
   - Paediatric comprehensive care clinic
   - Paediatric inpatient department
   - Paediatric outpatient clinic

C. Current position held
   - Medical Officer Intern
   - Clinical Officer Intern
   - Registered Clinical Officer
   - Consultant Paediatrician
   - Postgraduate doctors
   - Other (please specify) _____

D. Duration in the paediatric unit _____

1. a) Can TB be prevented using medicine Yes [ ] No [ ]
   b) If yes state which medicine _____
2. Who should be given the drug
   _____
3. What is the dose for children _____
4. How many times should the drug be administered in a day _____ daily
5. For how long should the drug be administered _____ months
6. Where did you get this information
   - Training
   - Colleague

- Media
- Other _____

7. a) Are you aware of any guidelines on prevention of TB [ ] Yes [ ] No
   b) If yes which ones [ ] WHO [ ] Kenya MOH [ ] Other_____
8. a) How comfortable are you giving IPT Very comfortable [ ]
   Comfortable [ ] Not sure [ ] Uncomfortable [ ] Very uncomfortable [ ]
9. How effective is IPT?
   Very effective [ ] Effective [ ] Not sure [ ] Ineffective [ ] Very ineffective [ ]
10. Rate the side effects of IPT
    Very dangerous [ ] Dangerous [ ] Not sure [ ] Mild [ ] Very mild [ ]
11. How easy is it to follow IPT guidelines
    Very easy [ ] Easy [ ] Not sure [ ] Difficult [ ] Very difficult
12. It is preferable to wait until a patient gets TB and then treat rather than administer prophylaxis
    Very easy Easy Not sure Difficult Very difficult
13. Have you ever started a patient on INH Yes [ ] No [ ]
14. Have you started a patient on INH in the previous year Yes [ ] No [ ]
15. If you have ever started a patient on INH prophylaxis what did you consider during screening and IPT initiation?

    _____

    _____

    _____

16. Have you ever renewed an INH prescription Yes [ ] No [ ]
17. Have you renewed an INH prescription in the previous year Yes [ ] No [ ]
18. If you have ever renewed an INH prescription what were your primary considerations?

    _____

    _____

    _____

Appendix H

Implementation of Isoniazid Preventive Therapy in two Hospitals and two Health Centers in Nairobi County

Interviewer Guide for Health Workers

Thank you for participating in this study

DEMOGRAPHICS

E. Date _____ B. Sex _____

F. Department
   - Paediatric comprehensive care clinic
   - Paediatric inpatient department
   - Paediatric outpatient clinic

G. Current position held
   - Medical Officer Intern
   - Clinical Officer Intern
   - Registered Clinical Officer
   - Consultant Paediatrician
   - Postgraduate doctors
   - Other (please specify) _____

H. Duration in the paediatric unit _____

19. a) Can TB be prevented using medicine Yes [ ] No [ ]
    c) If yes state which medicine _____
20. Who should be given the drug

_____

21. What is the dose for children _____
22. How many times should the drug be administered in a day _____ daily
23. For how long should the drug be administered _____ months
24. Where did you get this information
    - Training
    - Colleague

- Media
- Other _____

25. a) Are you aware of any guidelines on prevention of TB [ ] Yes [ ] No

    c) If yes which ones [ ] WHO [ ] Kenya MOH [ ] Other_____

26. How do you feel about giving IPT?

    What makes you feel that way?

27. How effective is IPT?

28. Rate the side effects of IPT

29. How easy is it to follow IPT guidelines

30. It is preferable to wait until a patient gets TB and then treat rather than administer prophylaxis

31. Have you ever started a patient on INH

32. Have you started a patient on INH in the previous year

33. If you have ever started a patient on INH prophylaxis what did you consider during screening and IPT initiation?

    _____

    _____

    _____

34. Have you ever renewed an INH prescription?

35. Have you renewed an INH prescription in the previous year

36. If you have ever renewed an INH prescription what were your primary considerations?

Appendix I: Kenyatta National Hospital Ethics and Research Committee Approval

Appendix J: Nairobi County Services Approval Form