Latent Tuberculosis Infection Screening, Diagnosis, and Treatment at Jefferson Center for

Refugee Health: A Community-Informed Analysis

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#### Abstract

Latent tuberculosis infection (LTBI) affects approximately 11 million people in the United States and activation of LTBI accounts for 80% of active TB cases. Recent LTBI control guidelines have suggested utilizing models adapted to specific populations. This study contributes to the understanding of LTBI screening, diagnosis, and treatment processes for refugees by characterizing the process timeline and treatment completion rates as well as acquiring input from community stakeholders on barriers, enablers, and the LTBI screening and treatment process. A retrospective chart review was conducted of refugees (n = 1,244) resettled in Philadelphia between 2007 and 2014. After refugees arrive in the U.S., the LTBI screening, diagnosis, and treatment process at Jefferson Center for Refugee Health takes approximately 8 months with rifampin as treatment. Results indicate an overall increase in treatment completion rates over time with a 67.3% treatment completion rate in 2013. Key informant interviews (n =4) were also conducted. Key interview themes included: communication, patient motivation, resources, community relationships, standards of care, and access to health care. Identified barriers were patient and provider education, language barriers, and loss to follow up. Main enablers included: a collaborative model, Centers for Disease Control and Prevention (CDC) guidelines as standard of care, family member/community experiences, and healthcare staff advocating for patients. Key recommendations included: providing patients with documentation, implementing training modules, use of the CDC guidelines for primary care providers, and creation of an integrated patient registry. Treatment completion rates and the overall efficiency of the screening, diagnosis, and treatment process can be improved by promoting enablers and addressing these barriers.

# Latent Tuberculosis Infection Screening, Diagnosis, and Treatment at Jefferson Center for Refugee Health: A Community-Informed Analysis

One third of the world's population is infected with *Mycobacterium tuberculosis*, the etiologic agent that causes tuberculosis (TB) (Centers for Disease Control and Prevention [CDC], 2013) and approximately 1.7 million people die from TB every year (World Health Organization [WHO], 2014). Latent tuberculosis infection (LTBI) is a quiescent form of TB that is essentially suppressed, and individuals with LTBI do not have signs or symptoms of TB disease (WHO, 2015). Without treatment for LTBI, infected individuals have an estimated 5-10% risk of developing active TB in their lifetime (CDC, 2013). The risk of converting to active TB is even higher in select groups, such as individuals with compromised immune systems and children under five years of age who may have 5% per annum rate of conversion (WHO, 2015). Approximately 11 million people in the U.S. have LTBI (CDC, 2013) and LTBI activation accounts for approximately 80% of active TB cases in the United States (Cohn *et al.*, 2000). *Refugees and LTBI* 

In the U.S., LTBI disproportionately affects foreign-born individuals: incidence rates in foreign-born persons are 12 to 27 times higher than rates in US-born persons (CDC, 2014). Though individuals with LTBI are not infectious (WHO, 2015), preventing conversion to active TB is essential to preserving personal and public health. Many of the foreign-born individuals in the United States are refugees, arriving from regions with high prevalence of TB ( $\geq$ 75 cases per 100,000 population) (WHO, 2013). The 1951 Refugee Convention has defined a refugee as an individual who leaves a country where he or she faces a well-founded fear of persecution because of his or her race, religion, and other factors (United Nations, 1951). In 2013, 69,909 refugees were admitted into the U.S. and greater than 60% of these refugees arrived from Iraq,

Burma/Myanmar, and Bhutan as a result of major crises—such as ethnic cleansing—in their country of origin (U.S. Department of Homeland Security [DHS], 2014). Recently, an increase in refugees from the Democratic Republic of Congo and other nations has shifted the refugee population demographic (DHS, 2014).

In most cases, refugees are considered for resettlement outside of the U.S. (Burt & Batalova, 2014), a process that includes a health evaluation with TB screening and diagnosis. The CDC recommends that newly arrived refugees undergo screening, diagnosis, and treatment for LTBI in the U.S. in order to prevent conversion of LTBI to active TB (CDC, 2012).

#### LTBI Screening and Diagnosis

Screening can be conducted with one of two approved methods in the U.S.: the Mantoux tuberculin skin test (TST) or an interferon-gamma release assay (IGRA)-QuantiFERON®-TB Gold In-tube Test (OFT-GIT) and T-SPOT (CDC, 2012). Numerous studies have been conducted on the effectiveness of these screening tests, with several indicating that IGRAs may be more effective for high-risk adult populations (e.g. refugees) and in BCG-vaccinated populations (Diel et al., 2011; Pai et al., 2008; Orlando et al., 2010). In children age five and younger, TST appears to be the preferred method for diagnosing LTBI (Mandalakas et al., 2011; Machingaidze *et al.*, 2011). But studies on the effectiveness of the current screening methods have been highly inconsistent due to varying methodologies and lack of an LTBI diagnosis standard (Herrera et al., 2011). Though very few studies have been conducted in the refugee population, IGRAs appear to have several practical benefits for refugees compared to TST, including greater specificity in groups that have been BCG vaccinated and less testing (and thus less trips to the health care facility, lost time from work, etc.).

For individuals who have a positive IGRA or TST, the next step of the screening process involves a chest X-ray and sputum Acid-Fast Bacillus (AFB) smear and culture, which allow for a diagnosis of active TB (if positive) or LTBI (if negative). Individuals with an LTBI diagnosis undergo a treatment regimen specific to LTBI (WHO, 2015). After treatment completion, patients should be provided with documentation of their LTBI health status for future health care providers and employers (CDC, 2013).

#### LTBI Treatment

The current best practices suggested for LTBI treatment are six or nine months of isoniazid (INH), four months of rifampin (RIF), or three months of rifapentine and isoniazid (CDC, 2015). Nine months of INH preceded the four-month RIF treatment as a best practice and it has proven successful in preventing conversion to active TB (Cohn et al., 2000), but INH generally has very low completion rates—often less than 70% (Lobue & Moser, 2003; Sterling et al., 2011). These low rates have principally been attributed to the long treatment duration and the potential for serious adverse events, including hepatitis (Menzies et al., 2011). Another treatment, rifampin (RIF), has been used in instances of INH resistance, intolerance, or other difficulties with INH. For example, LTBI cases originating in countries with high prevalence of INH-resistant TB may be more effectively treated with RIF (Menzies et al., 2011). Countries in South Asia, such as Nepal, have demonstrated a significant prevalence of INH-resistant TB (Jenkins, Zignol, & Cohen, 2011), suggesting that RIF will be more effective in these countries and in individuals—such as refugees—whose country of origin has a high prevalence of INHresistant TB. In addition to circumventing resistance issues, treatment with RIF is only four months, and numerous studies have indicated substantially higher completion rates for four months of RIF compared to nine months of INH (Lardizabal et al., 2006; Page et al., 2006;

Menzies *et al.*, 2004). RIF also has significantly lower hepatotoxicity than INH (Page *et al.*, 2006) and is more cost-effective than the nine month INH treatment (Menzies *et al.*, 2004; Holland *et al.*, 2009). While nine months of INH has a protective treatment efficacy of 60-90%, the treatment efficacy of four months of RIF has not yet been determined (Sharma *et al.*, 2014). Studies have demonstrated that the type of treatment utilized to treat LTBI in refugee populations has a significant impact on completion rates (Hirsch-Moverman *et al.*, 2008).

#### Population Approach to the LTBI Process

Ultimately, LTBI treatment completion is the critical metric for public health. In the U.S., the national LTBI treatment completion rate (67.7%) is significantly lower than the Healthy People 2020 goal for treatment completion in contact investigation cases (79%) (U.S. Department of Health and Human Services [HHS], 2015). Various models for treatment regimens and for ensuring adherence to LTBI treatment have been proposed, but no standard national guidelines have been established except for HIV positive individuals and children under five years old (WHO, 2015). The LTBI CDC Guidelines for Primary Care Providers provides one set of recommendations for LTBI control but is not used as a standard across the nation. As a result of the lack of standard LTBI control guidelines, the WHO has published guidelines for LTBI treatment that encourage moving away from a standard guideline and toward models adapted for specific populations in a given context (WHO, 2015). The WHO recommendations are bolstered by a systematic review of LTBI treatment adherence, which confirms that a onesize-fits-all approach would not be successful in all settings and populations (Hirsch-Moverman et al., 2008). To address low treatment completion rates, the characteristics of a given setting and population must be assessed to determine best practices. Even within the refugee population,

factors such as culture and country of origin may render each refugee group unique as a result of different barriers and enablers.

Very little research has been done on LTBI treatment completion in specific groups of refugees (i.e. grouped based on country of origin). A prospective study of asylum seekers in Switzerland suggests that relatively high completion rates (80%) are possible with short treatment regimens (i.e., four months of RIF) and Directly Observed Therapy (DOT) for a population of individuals with stable housing (Sarivalasis *et al.*, 2013). In contrast, a review indicates that DOT is only equally as successful as self-administered therapy (SAT) (Volmink & Garner, 2007). DOT requires patients to take doses of their treatment under supervision of a selected health provider while SAT involves a greater role for the patient in completing treatment. Walters *et al.* suggests that LTBI treatment completion rates for refugee population (Lobue & Moser, 2003; Sterling *et al.*, 2011), suggesting that foreign-born persons in the U.S. face unique barriers that must be addressed to increase LTBI treatment completion rates. *Philadelphia's Refugee Population* 

To understand and ultimately improve LTBI treatment completion rates in the diverse refugee population resettled in the U.S., it is essential to take into consideration the specific characteristics (e.g., demographics) of individual refugee communities as well as barriers that these diverse groups, or the programs that serve these groups, might encounter. Pennsylvania has consistently been in the top ten states accepting the largest number of refugees (DHS, 2014): more than 2,000 refugees arrive in Pennsylvania every year from an average of thirty different countries (Pennsylvania Refugee Resettlement Program [PRRP], 2015). Philadelphia generally receives more refugees than any other county in Pennsylvania, and in recent years the majority of

these refugees have been arriving from Bhutan (via Nepal), Burma/Myanmar, and Iraq (PRRP, 2015).

Historically, LTBI treatment completion rates in Pennsylvania (42% in 2003) have been far below the Healthy People 2020 goal (Philadelphia Department of Health [PDPH], n.d). Few statistics are available on LTBI completion rates in Philadelphia and its medical facilities despite the fact that the city has a higher incidence of TB cases than Pennsylvania as a whole (PDPH, 2014b). A study conducted in Philadelphia refugee populations indicates that LTBI treatment completion rates are 75% (Subedi, 2015). This research was unable to find studies in which refugee populations from Iraq, Burma/Myanmar, and Bhutan (via Nepal) were studied in the context of LTBI treatment completion rates and barriers and enablers to treatment completion. To best serve this unique population's needs and address LTBI in Philadelphia, this study seeks first to characterize the LTBI screening, diagnosis, and treatment process at the single largest clinical site serving refugees—Thomas Jefferson University's Center for Refugee Health—and then identify barriers, enablers, and recommendations for improvement of the process.

### Barriers to LTBI Treatment Completion

Studies have discerned several barriers that inhibit the completion of LTBI treatment, though very few of these studies have focused on refugees. Hirsch-Moverman *et al.* identified various potential barriers to LTBI treatment completion including patient-related factors such as patient perceived susceptibility and severity, BCG vaccination, unemployment, and drug use; clinical characteristics or adherence interventions such as using case managers; and treatment characteristics such as adverse drug effects (Hirsch-Moverman *et al*, 2008). Much like Munro *et al.* in their discussions of barriers and facilitators of TB treatment, it is suspect that patients' interpretations of their condition, knowledge and attitudes about treatment, immigration, personal characteristics, side effects, and family and community influence are all themes associated with LTBI treatment completion (Munro *et al.*, 2007). Because TB and LTBI treatment regimens have similar characteristics, these findings may provide some insight into LTBI treatment as well.

#### Enablers to LTBI Treatment Completion

Hirsch-Moverman *et al.* identified various clinical characteristics that act as enablers to LTBI treatment completion, including shorter treatment regimens, DOT, incentives, education programs, case managers, professional counseling, and peer support. Patient-related factors such as social support structures and higher education have been shown to promote LTBI treatment adherence. In addition, higher perceived risk and susceptibility to developing active TB are associated with increased LTBI treatment adherence (Hirsch-Moverman *et al.*, 2008).

While studies have identified general predictors of adherence and non-adherence to LTBI treatment completion, few studies were found focusing on the predictors, barriers, and enablers in the refugee population, and even fewer on specific refugee groups, such as Iraqi, Bhutanese/Nepali, and Burmese. The literature also lacks studies that have acquired community stakeholders' expert input as a source of information regarding the LTBI screening, diagnosis, and treatment process in specific refugee populations.

#### Value of Community Stakeholders

To identify barriers and enablers to the completion of these steps in the process, this study will rely on input from community stakeholders to supplement Electronic Health Record [EHR] data. Community stakeholders are individuals in the community who have an interest in what is being studied and have knowledge of—in this case—the LTBI screening, diagnosis, and treatment process for refugees (Kammi, 1999). Community stakeholders are experts in their field and can be instrumental in both providing information and affecting change. Best practices suggest that community stakeholders are not only important as sources of information and input on a public health concern but also as integrated partners, who can increase trust, collaboration, and information flow while promoting sustainable changes in the community (Barnett, 2012). These partners help in understanding a public health phenomenon in the context of social and cultural factors in the community, which is essential when considering the diversity of the refugee population. They provide multiple perspectives and understand agencies involved in a public health concern, which has proved useful in numerous interventions and program evaluations (Gilliam *et al.*, 2002). Finally, community stakeholders are important for applying findings to the community setting to make changes and improve public health (Israel *et al.*, 1998). Their holistic perceptions of the process can provide invaluable information to supplement quantitative characterization of the LTBI screening, diagnosis, and treatment process.

#### Community Stakeholders' Perceptions of Barriers and Enablers

In order to understand what barriers and enablers exist in the LTBI screening, diagnosis, and treatment process in Philadelphia, this study has sought out the perceptions of community stakeholders from a refugee resettlement agency, primary care office, pharmacy, and public health department. A modified socio-ecological model is a conceptual framework that allows for an extensive understanding of this public health issue across multiple levels ranging from the individual level to the societal level (McLeroy *et al.*, 1998; Magaziner, Miller, & Resnick, 2007). The individual level of the socio-ecological model involves knowledge, attitudes, beliefs, performance, and physical status of individuals (Magaziner, Miller, & Resnick, 2007) and how these factors impact a particular behavior or activity. The interpersonal level incorporates the

relationships between family, friends, peers, and staff that affect a behavior (Magaziner, Miller, & Resnick, 2007). The institutional/organizational level consists of rules, policies, norms, and practices that affect the behavior, while the policy level examines local, state, and federal policies (Magaziner, Miller, & Resnick, 2007). The socio-ecological model (Appendix B) is ideal for identifying a wide range of factors influencing an area of public health concern; information from the model can inform comprehensive changes. This study utilizes a mixed methods approach to characterize the LTBI screening, diagnosis, and treatment process within the recently resettled refugee population living in Philadelphia and to provide recommendations for improvement in the framework of the socio-ecological model.

# Methods

#### Setting

In 2007, the Philadelphia Refugee Health Collaborative (PRHC) was established as a model that initially brought together the refugee resettlement agency Nationalities Service Center (NSC) and Thomas Jefferson University's Department of Family and Community Medicine. The PRHC aimed to more efficiently help refugees through the health evaluation process. The refugee clinic model and partnership has now expanded to include seven additional primary care health clinics and two additional resettlement agencies serving Philadelphia. The model facilitates greater communication between the resettlement agency and medical providers and improves refugee access to health care (Philadelphia Refugee Health Collaborative [PRHC], 2014). Along the steps of the resettlement process and health evaluation, refugees interact with numerous community stakeholders including resettlement agency workers, health care providers, pharmacists, and the Philadelphia Department of Public Health (PDPH). The resettlement agencies NSC, Hebrew Immigrant Aid Society – Philadelphia (HIAS), and Lutheran Children

and Family Service in Pennsylvania (LCFS) provide social, educational, and legal services as well as direct refugees to health services (Nationalities Service Center, 2015).

Pennsylvania accepts more than 2,000 refugees annually on an ongoing basis (PRRP, 2015). An average of 700 refugees enter Philadelphia each year (PRRP, 2015), and approximately one third of the refugees entering Philadelphia receive health evaluations from Jefferson's Center for Refugee Health (JCRH). Thomas Jefferson University's (TJU) Department of Family and Community Medicine (DFCM) is a large academic, urban primary care practice located in Philadelphia, Pennsylvania. DFCM runs the Center for Refugee Health.

Refugees are provided with a "medical home" at one of the participating health centers, where they receive health screenings, including for TB. JCRH has provided health assessments for over 1,500 newly arrived refugees. DFCM's refugee LTBI screening, diagnosis, and treatment process (Figure 1) resembles WHO's recommended model (WHO, 2015) but consists of a largely pharmacy-run treatment tracking process.

#### Study Population

The three largest groups of refugees receiving their health evaluations from Thomas Jefferson University's Department of Family & Community Medicine between 2007 and 2014 come from Bhutan (via Nepali refugee camps), Burma/Myanmar (via Thailand refugee camps or urban centers in Malaysia) and Iraq (Table 1).

The community stakeholders interviewed for this study perform various roles in the refugee LTBI screening, diagnosis, and treatment process. Demographics and roles of the participants are summarized in Table 3.

Quantitative and Qualitative Data Collection: Electronic Health Record

A retrospective chart review of Electronic Health Records (EHR) was conducted at JCRH. The quantitative data collected were as follows: date of PPD and/or date of IGRA, TB screening results, Chest X-ray date(s) and result(s), AFB sputum date(s) and result(s), time to the first treatment non-adherence event, and treatment start and completion dates. Qualitative data collected included reasons for an incomplete diagnosis, not receiving treatment, not adhering to treatment, and not completing treatment as determined by health care provider notes. Data were collected through review of individual patient EHRs and these data were added to the established Jefferson Longitudinal Refugee Health Patient Registry (2014), an Excel database. Patients were considered eligible if they were refugees resettled in Philadelphia between 2007 and 2014 who had a medical visit to JCRH as documented in the Jefferson Longitudinal Refugee Health Patient Registry (2014).

#### Qualitative Data Collection: Key Informant Interviews

Qualitative data collection involved interviews with key community stakeholders who were selected based on their role in the refugee community. Stakeholders were recruited via email. The stakeholders interviewed in this study include officials from the Philadelphia Department of Public Health, medical providers and pharmacists from Jefferson's Department of Family and Community Medicine, and officials at refugee resettlement agencies. Stakeholders were invited to participate in interviews, which were conducted by phone or at stakeholders' offices. Two interviewers carried out key informant interviews: one interviewer asked questions and another interviewer recorded participant input via field notes (hand-written or typed notes). Interviews were carried out between June and August of 2015. Four community stakeholders participated and responded to the same semi-structured interview script as well as to questions unique to their role in the refugee LTBI process. The interviews lasted approximately 30 minutes.

The process involved a semi-structured interview guide (Appendix A) that facilitated flexible conversation regarding the barriers and enablers of the LTBI screening, diagnosis, and treatment process. The interview explored what community stakeholders perceived as barriers and enablers existing at the individual, interpersonal, institutional/organizational, and policy levels of a modified socio-ecological model (McLeroy *et al.*, 1998; Magaziner, Miller, & Resnick, 2007). Participants were also asked to impart any recommendations for improvement of the process. Community stakeholders were provided with a paper or electronic sample of the socio-ecological model (Appendix B) and a flowchart of the LTBI screening, diagnosis, and treatment process (Figure 1) to reference throughout the interview. The stakeholders were asked open-ended questions encouraging discussion and if necessary, prompted with additional questions to further explore perceptions. These factors were utilized to establish potential solutions and improvements to the process at each level of the socio-ecological model. The Thomas Jefferson University Institutional Review Board approved both quantitative and qualitative aspects of the study.

#### Statistical Design and Analysis

### Quantitative Data Analysis

For quantitative assessment, descriptive information including means and standard deviations were computed for continuous variables, and frequencies were calculated for categorical variables using Excel PivotTables (Excel Version 15.16). Continuous variables included demographics (i.e. age), and the number of days between arrival in the United States, TB screening, diagnosis, and treatment. The time between steps in the refugee LTBI screening, diagnosis, and treatment process were calculated using Excel formulas and average times were computed using Excel PivotTables.

Categorical variables included patient demographics (gender and country of origin), initiation and completion of treatment regimens (yes or no), screening results (positive or negative), result of chest X-ray (positive or negative), status of sputum/culture (done, not done, incomplete), and diagnosis (no TB, LTBI, active TB, incomplete). Frequencies were computed for these categorical variables using Excel. The frequency of TB and LTBI diagnoses was determined overall and stratified by country of origin, year, and for Burmese refugees only by transit country. Treatment completion rates were calculated for the total population and for subgroups stratified by age, gender, country of origin, treatment regimen, and year. Statistical significance of completion rates was determined using a two-sample t-test in Excel. For the patients who did not adhere to their treatment, the time to their first non-adherence event was recorded and assessed as interval data (0.25 months, 0.50 months, 1 month, 2 months, 3 months, or 4 months) and the frequency for each time to non-adherence was determined using Excel PivotTables.

#### Qualitative Data Analysis

For qualitative assessment, three researchers independently coded interview notes and identified categories and themes from key informant interviews through a thematic content analysis process outlined by Braun and Clark (Braun & Clark, 2006) and based on a modified grounded theory approach to data analysis (Strauss & Corbin, 1990).

Qualitative data on reasons for not completing treatment were reported after organization into categories including lost to follow-up/moved/not asked in follow-up appointments, comorbidities/side effects, insurance, near completed, unknown, and other. Reasons for not adhering to treatment were categorized into no refill/prescription pick-up, comorbidities/side effects, insurance, taking treatment regimen incorrectly, unknown, and other. The most common reasons for not completing treatment and not adhering to treatment were determined through quantitative analysis by calculating the percent of patients with non-adherence associated with each of the reasons.

Categories and themes identified from EHRs and key informant interviews were utilized to propose and distribute solutions and improvements for the screening, diagnosis, and treatment steps of the refugee LTBI process in the framework of the socio-ecological model. Recommendations, findings, and process changes will be disseminated to community stakeholders involved in the refugee resettlement process in order to strengthen relationships and foster ongoing dialogue.

#### Results

#### *Refugee Demographics*

There were 1,244 refugees resettled in Philadelphia between 2007 and 2014 and who received health evaluations at JCRH as documented in the Jefferson Center for Refugee Health Patient Registry (2014). The population of refugees studied in this study excluded U.S. born individuals (n = 10). Approximately half of the refugees were male (n = 676, 53.8%). The majority of refugees were adults ages 19 to 45 (65.4%). Children ages 0 to 5 (7.6%) and 6 to 18 (8.2%) (Table 1) were also included in the study. The most common country of origin was Bhutan/Nepal (n = 377, 30.3%), followed by Iraq (n = 352, 28.3%), Burma/Myanmar (n = 214, 17.2%) and Eritrea/Ethiopia (n = 80, 6.4%). Thirty-three other countries of origin were combined (n = 221, 17.8%) to protect patient confidentiality due to the limited number of refugees resettled from each of these country individually.

Stratification of the number of refugees recorded in the Jefferson Center for Refugee Health Patient Registry (2014) as receiving health evaluations at JCRH by year indicated that 9 refugees were seen in 2007, 74 in 2008, 104 in 2009, 171 in 2010, 233 in 2011, 242 in both 2012 and 2013, and 169 in 2014. Data from 2014 includes data collected up to September 30, 2014. *LTBI Screening and Diagnosis Completion* 

Of the 1,244 refugees that received health evaluations at JCRH, the majority completed TB screening with either QFT-GIT or TST (97.7%), with a relatively small proportion not completing screening (2.3%) due to loss to follow up, moving out of Philadelphia, or unknown reasons. There were 1,206 refugees who had a diagnosis of LTBI, no TB, or Previous Medical History (PMH) TB (99.2%) after completing screening, while 10 had incomplete diagnoses (0.8%) (Figure 2) due to no screening completion or results. Diagnosis was determined by chest X-ray and, in relatively few cases when refugees presented with concerning symptoms such as cough or weight loss, an AFB sputum and culture was also considered (n = 32). No patients had a positive sputum result, 40.6% had a negative AFB sputum and culture, and 59.4% of AFB sputum and culture results were incomplete (i.e. three sputum samples were not collected in three consecutive days).

The majority of refugees diagnosed had no TB (n = 885), followed by LTBI (n = 285), PMH TB (n = 37), and active TB (n = 1). When stratified by year of health evaluation at JCRH, the largest number of LTBI diagnoses occurred in 2013 (n = 60), in 2011 (n = 57), and in 2012 (n = 54) (Figure 3).

Diagnoses of LTBI and PMH TB were stratified by country of origin (Table 2). The greatest number of LTBI cases (n = 104) and PMH TB (n = 22) were diagnosed in

Bhutanese/Nepali refugees (n = 104). Iraqi refugees had the second highest number of LTBI cases (n = 56), followed by refugees from Burma/Myanmar (n = 54).

Burmese refugees are one of the largest populations of refugees cared for at JCRH (Table 1), and they constitute the largest population of refugees passing through transit countries of Malaysia and Thailand (87.4%). Malaysia and Thailand have a high prevalence of TB (Stop TB Partnership, 2012). The number of Burmese refugees diagnosed with LTBI was similar for refugees passing through each transit country.

#### LTBI Treatment Completion

There were 288 refugees that required treatment after diagnosis was completed. This included patients with a diagnosis of LTBI, active TB, or PMH TB (Appendix C). Of those patients requiring treatment, 235 (81.6%) had a start date for the treatment, while 53 (18.4%) did not initiate treatment mainly due to a loss to follow up or failure to pick up their prescription as documented in EHRs and by pharmacy. The majority of patients that initiated treatment for LTBI at JCRH started RIF for four months (n = 199, 85.0%) and a small proportion of patients started INH for nine months (n = 35, 15.0%). Patients who started one treatment regimen but switched to another treatment that they then finished were categorized based on the drug that was completed. Four patients were followed by other health care facilities or the Philadelphia Department of Public Health for treatment (and the treatment regimen was not specified). The treatment regimen was stratified by year that a refugee arrived at JCRH and showed that INH for nine months was the primary treatment regimen prior to 2010, with greater than 75% of treatment regimens as INH. The majority of refugees who arrived in 2010 or later and required treatment were given RIF for four months (83% in 2010 and reaching 96% in 2014).

There were 141 refugees who initiated treatment between 2007 and 2014 and had a treatment completion date recorded and therefore had completed (60.0%) treatment. In contrast, 94 refugees did not complete treatment (40.0%). Of those who initiated treatment and did not complete treatment, the top four reasons for not completing treatment included loss to follow up/moved/not asked in follow up appointments (n = 64), unknown reasons (n = 10), comorbidities/side effects (n = 9), and insurance (n = 4).

Treatment completion after initiation was stratified by year to determine completion rates per year of refugee arrival at JCRH (Figure 4). Only one refugee arriving in 2007 initiated treatment, and this patient did not complete treatment (0.0% completion in 2007). Refugees arriving in 2008 and initiating treatment had a 33.3% completion rate, which more than doubled for those arriving in 2009 (69.2%). The percent completion for 2010 was 65.5%, followed by 59.3% for 2011, 61.4% in 2012, and 67.3% in 2013. The largest increases in completion rate occurred between 2008 and 2009 (35.9%) followed by 2011 to 2013 (8.0%). Refugees arriving in 2014 and initiating treatment had a 50.0% treatment completion rate when considering only the available data up to September 30, 2014.

Treatment completion after initiation was stratified by country of origin (Table 2). The Bhutanese/Nepali refugees that initiated treatment had the highest completion rate (80.8%) compared to Iraqis (45.2%), Burmese (39.5%), Eritrean/Ethiopians (50.0%) and others (48.5%). The difference between Bhutanese/Nepali and Iraqi completion rates and the difference between Bhutanese/Nepali and Burmese completion rates were statistically significant with p<0.05. The treatment regimen undergone had a statistically significant affect on completion rates. Though substantially less refugees used INH between 2007 and 2014 (n = 15, 10.6%) compared to RIF (n = 126, 89.4%), the completion rate for refugees who underwent RIF four-month treatment

(63.6%) was significantly higher than the completion rate for refugees who underwent INH ninemonth treatment (44.1%).

When stratified by age range, treatment completion after initiation was highest for ages 46 to 64 (74.4%) and lowest for ages 6 to 17 (33.3%), though very few refugees ages 6 to 17 initiated treatment (n = 9). The age range with the largest number of refugees initiating treatment was 18 to 45 (n = 162) and this age range had a treatment completion rate of 57.4%. Males and females had a statistically significant difference in their completion rates, with females more likely to complete treatment (67.7% completion) than males (54.9%).

#### LTBI Treatment Non-Adherence

A total of 57 refugees who initiated treatment were reported to have a non-adherence event during the course of their treatment. Most patients that did not adhere to their initiated LTBI treatment had their first non-adherence event after one month of treatment (n = 30, 52.6%). The next most common time to non-adherence was after two months of treatment (n = 10,17.5%), followed by three months of treatment (n = 6, 10.5%) and one week (n = 5, 8.8%). The top three reasons for non-adherence as reported in the EHR were no refill/prescription pick-up (n = 35), comorbidities/side effects (n = 12), and insurance (n = 4).

#### Confirmation of Treatment Completion

Of the 141 refugees who completed their treatment after initiating, 61 were confirmed by pharmacy through EHR or data provided by the DFCM pharmacy. The pharmacy began collecting data on LTBI treatment completion in 2012. There were 79 patients who were seen after 2012 at JCRH and completed treatment and 17 of these patients had dual confirmation of their completion (i.e. patient and pharmacy independently confirmed).

#### Documentation Provided to Refugee Upon Completion

There were four patients who were provided documentation regarding the completion of their LTBI treatment of the 141 who completed their treatment. A substantial number of refugees who completed their treatment were not provided with documentation (n = 137, 97.2%). *LTBI Screening, Diagnosis and Treatment Timeline* 

The overall time for a refugee to move through the LTBI screening, diagnosis, and treatment process at JCRH varied depending on the treatment regimen. For patients undergoing RIF for four months, the average cumulative time from arrival to treatment completion was 207.9 days or approximately 6.9 months. A patient undergoing INH for nine months took an average cumulative time of 356.4 days or 11.9 months to complete the screening, diagnosis, and treatment process after arrival. Three patients were excluded from all timeline calculations because of an active TB diagnosis or because their first screen was negative or indeterminate and a subsequent TB screen years later was positive.

The mean or median time between each of the steps in the LTBI screening, diagnosis, and treatment process is summarized in Figure 5. The mean time between a refugee's arrival in the U.S. and their first TB screen at JCRH was 38.9 days (SD = 103.1) or approximately 1.25 months, and the median time was 16 days (0.5 months). Four patients were excluded from this calculation due to screening conducted abroad before arrival and not repeated in the health evaluation (one outlier warranted the use of the median in cumulative calculations). There were 901 patients used for this calculation (of the 1,216 screened in the U.S.) due to unknown arrival dates for 315 patients. The mean time to diagnosis (determined by the date of chest X-ray) after the initial positive TB screen was 35.0 days (SD = 55.7) or approximately one month. The cumulative time to a complete diagnosis was approximately 1.7 months (51.0 days) after arrival in the U.S. Patients took an average of 31.4 days (SD = 56.4) or approximately one month to

initiate LTBI treatment after their diagnosis. Ten patients were excluded from this calculation because they did not receive a chest X-ray or had an unknown chest X-ray date but received a diagnosis that required treatment. The cumulative time to treatment initiation was 82.4 days or approximately 2.7 months after arrival. Patients who initiated treatment with the four-month RIF treatment regimen had a median time to treatment completion of 125.5 days and a mean time of 181.8 days (SD = 144.13). The total time for a patient to complete screening, diagnosis, and treatment given that they took RIF for four months was 6.9 months. There were 126 patients who initiated and completed the RIF treatment. Completion of the nine-month INH treatment regimen took an average of 272.1 days (SD = 32.3) or approximately nine months with a median time of 274 days. Patients undergoing a nine-month INH treatment took approximately 11.9 months to complete screening, diagnosis, and treatment.

#### Key Informant Interviews

Interviews were conducted with four community stakeholders representing Jefferson pharmacy, Jefferson providers, the Philadelphia Department of Public Health, and a resettlement agency. The interviewers included both males and females ranging from 3 to 12 years of experience with TB and/or refugee work in Philadelphia. Key informant roles in the community are summarized in Table 3. The interviews ranged from 27 to 55 minutes (Mean = 38, SD = 12) and were conducted between May 2015 and August 2015.

Interviews elicited descriptive responses to the semi-structured interview questions based on the community stakeholders' professional experiences interacting with refugees and facilitating various steps of the resettlement process and LTBI screening, diagnosis, and treatment. Their responses reflect the steps of the modified socio-ecological model and include barriers, enablers, and recommendations affecting patients and providers. A full summary of responses is presented in Tables 4,5, and 6. Key themes included communication, patient motivation, resources, community relationships, standards of care, and access to health care and the barriers and enablers categorized under these themes are presented in Table 7.

#### Barriers at the Individual Level

Community stakeholders identified a variety of patient-related factors at the individual level that affect the LTBI screening, diagnosis, and treatment process. Understanding and navigating the health care system was the most common barrier identified for newly resettled agencies. This includes understanding the prescription refill process, which Jefferson providers and pharmacy cited as a barrier. Two community stakeholders also suggested that taking off work for health care (i.e. appointments and follow-ups) is also a significant barrier for refugees as they undergo the LTBI screening, diagnosis, and treatment process. Community stakeholders also cited other patient-related barriers including patient comorbidities, low health literacy, low perceived severity and susceptibility, length of the treatment, and language barriers, patients moving away, and patients changing their phone numbers (i.e. leading to loss to follow up).

In addition to factors directly affecting the patient, several factors were identified as barriers at the individual level that health care providers encounter as they participate in the LTBI screening, diagnosis, and treatment process for refugees. These barriers included provider lack of knowledge of the health care system, communicating the health care process to refugees, and cultural literacy.

#### Barriers at the Interpersonal Level

Barriers at the interpersonal level included those related to interactions between refugees and interpreters, family members, community, and health care providers. Community

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stakeholders cited poor interpreter quality, interpreter input, lack of community or family knowledge of the TB treatment process, and excessive trust in the provider as barriers facing the patients at the interpersonal level. When refugees are resettled in Philadelphia, an established community of refugees with similar background and ethnic origin were cited as helpful in refugees maneuvering the health care system, but lack of this community is a barrier. As one community stakeholder explained, "refugee communities are always waxing and waning" and when refugees arrive from a country of origin with no community settled in Philadelphia, they face barriers in understanding and maneuvering through the health care system, including the LTBI screening, diagnosis, and treatment process. One community stakeholder also indicated that lack of health care provider (including pharmacy) communication acts as a barrier in the LTBI screening, diagnosis, and treatment process.

#### Barriers at the Organizational/Institutional Level

Community stakeholders consistently identified waiting times for appointments as a barrier to the LTBI screening, diagnosis, and treatment process. In addition, both Jefferson pharmacy and the Philadelphia Department of Public Health indicated that a large number of patients are seen for TB evaluation, generating a great deal of data and unearthing the need for more staff and funding. Other barriers include the lack of available staff and primary care providers, the lack of funding, the limited physical space available at pharmacies, the lack of a voicemail system for patients with question about their medications, lack of nurses at schools to administer DOT for children taking TB medication, drug shortages (occur infrequently), and the loss of a key community engagement and coordinating member and role. The absence of the latter role in the public health department and in the community results in a "challenge for the

health department to maintain the same level of engagement in this particularly vulnerable population."

#### Barriers at the Policy Level

Responses to the policy level barriers were not as numerous compared to other levels. However, there was consistency among interviews with a Jefferson provider, pharmacy, and the resettlement agency, which indicated that insurance is a barrier to the LTBI screening, diagnosis, and treatment process. In particular, three community stakeholders described Jefferson's current limit on accepting patients with Keystone medical assistance as a significant issue for incoming refugees undergoing the LTBI evaluation (or receiving any health care services) at JCRH. For public health departments, the lack of resources and the fact that LTBI is not a reportable condition lead to weak LTBI surveillance, all of which were identified as barriers. Resources were consistently described as an area of concern in LTBI control. The public health departments were described as "resource-starved" and in need of both funding and greater number of staff members. One stakeholder described a "state and federal absenteeism," in which the state or federal level provide CDC guidelines for LTBI control and ask the local level to "make it happen" without financial or staff support.

In regards to potentially implementing DOT for LTBI treatment in adults, community stakeholders did not have consistent responses. Lack of DOT was considered to be a barrier to two of the community stakeholders, while two others consider DOT to be an expensive, cumbersome, or "paternalistic" method of ensuring compliance, which would not be feasible. *Enablers at the Individual Level* 

Community stakeholders identified fewer enablers than barriers. Two community stakeholders indicated that patients are highly cooperative and motivated to access healthcare

and complete treatment. Other enablers include patients' health literacy, shorter treatment length (i.e. RIF compared to INH), and appointment notifications provided for patients to present to employers. There was consistency among all community stakeholders regarding the efficacy of JCRH's LTBI screening, diagnosis, and treatment process and the providers and pharmacists aiding in the process: upon examining the LTBI process at JCRH (Figure 1), all stakeholders identified JCRH providers' advocacy for patients as a major enabler. Those participating in refugee care are seen as "a health care team dedicated to going above and beyond [for the refugee patients]." Overall, community stakeholders were highly pleased with the work JCRH does, including provider devotion to patients and JCRH adherence to LTBI screening, diagnosis, and treatment CDC guidelines.

#### Enablers at the Interpersonal Level

All community stakeholders identified family member experiences as an enabler to completion of the LTBI screening, diagnosis, and treatment process. Family members who have completed treatment or understand the health care process because of personal experience can guide newly settled refugees or aid in alleviating any fears or concerns with treatment (e.g. urine changing color with RIF treatment). The presence of a community of refugees who can provide further guidance about the health care system also enables patients to successfully maneuver through the LTBI and healthcare process. Finally, interpreter access and the high quality and general approval of interpreters were identified as enablers for patients.

#### Enablers at the Organizational/Institutional Level

The organizational/institutional level includes various enablers specific to different players in refugee resettlement and health care evaluation and different steps in the LTBI screening, diagnosis, and treatment process. In the Jefferson pharmacy, face-to-face pharmacy counseling, cooperation with local pharmacies, and various aids for understanding treatment (e.g. pictograms) enable patients to initiate and complete LTBI treatment. The resettlement agencies' clinical case manager role ensures that patients are provided with an individual who understands their specific situation and guides them through every step of health care (including non-TB related health care). Having a primary care clinic (i.e. JCRH) carrying out all of these health functions in one place was also cited as an enabler, and one community stakeholder discussed how as a primary care clinic, JCRH serves as a "long term primary care home" for refugees much like the other primary care clinics in associated with PRHC.

For the public health department, patient-related enablers include the Flick Clinic, which provides DOT and free TB and LTBI medications, transportation tokens, food in the clinic, and resources in many languages. In Philadelphia schools, DOT is provided to children taking TB medication and the public health department relationship with schools acts as an enabler. For providers, enablers include what a community stakeholder identified as the "standard of care" for LTBI control: the CDC Guidelines for Primary Care Providers. In addition, providers have access to established refugee resources and community relationships through the PRHC. *Enablers at the Policy Level* 

Community stakeholders identified few policy level enablers. These enablers include IOM screening abroad and tracking through the Electronic Disease Notification System and Secure Access Management Services, strong relationships between the Nationalities Services Center and the public health department, and the PRHC relationship with the public health department.

#### Recommendations

Recommendations for improvement of the LTBI screening, diagnosis, and treatment process were limited but generally addressed the top two or three most significant factors that community stakeholders perceived as barriers that requiring attention. Two stakeholders described the need to distribute documentation of treatment completion (or their progress in the screening, diagnosis, and treatment process) to refugees. All community stakeholders consistently reported that health care provider training needed to be improved or instituted. Other recommendations included improving Electronic Medical Record tracking of LTBI, improving resources for public health, utilizing in person interpreters (not considered essential to all stakeholders but suggested to improve communication), increasing the number of clinical liaisons working at resettlement agencies, improving access to health care, and solving issues concerning access to health care due to insurance.

#### Discussion

The LTBI screening, diagnosis, and treatment process that refugees undergo upon arrival in the U.S. is an integral part of TB control. In Philadelphia, the PRHC entities—particularly the resettlement agencies—play an instrumental role in connecting newly arrived refugees to health services and screening, thus initiating the LTBI screening, diagnosis, and treatment process. At JCRH, refugees pass through an LTBI evaluation process that had not been characterized in terms of timeline and completion rates. Moreover, the diversity of the refugee population in Philadelphia suggests that specific enablers and barriers to completion of the process must be identified in order to provide suggestions for improvement and best practices. This study has described the length and completion rates for the LTBI screening, diagnosis, and treatment process as well as demographics, completion rates and barriers and enablers to this process perceived by community stakeholders. The LTBI screening, diagnosis, and treatment process at JCRH closely follows the WHO recommendations for LTBI control (WHO, 2015) and the CDC Guidelines for Primary Care Providers (CDC, 2012), which public health departments have identified as the "standard of care" for LTBI. To initiate the LTBI evaluation process, refugees at JCRH are screened with IGRA QFT-GIT if they are an adult, or TST if they are children. Those with a positive IGRA or TST must then undergo a chest X-ray and possibly an AFB sputum and culture (Figure 1) to receive a diagnosis. JCRH utilizes a four-month RIF treatment regimen as the standard treatment for LTBI for adults, in part due to the better treatment completion rates for four month RIF but also because of high rates of INH resistance in South East Asia (Menzies *et al.*, 2011), from which many of the refugees receiving treatment at JCRH have arrived. Children are generally given INH for nine months as recommended by the CDC (CDC, 2012) through the school system or Philadelphia Department of Health. Though very few refugees in this study underwent INH treatment, it is likely that the use of a shorter treatment regimen is positively influencing treatment completion rates.

Refugees arriving in Philadelphia are provided with eight months of health insurance through Medicaid after which they are required to find alternative healthcare. This process is generally facilitated by a resettlement agency, but may result in an interruption in healthcare. Because LTBI treatment is lengthy, it is essential that the screening, diagnosis, and treatment process function efficiently and within this eight-month period to prevent premature cessation of treatment. The screening, diagnosis, and treatment process at JCRH takes an average of 7.7 months when the RIF treatment is provided, which indicates that many patients complete the treatment regimen within the eight-month period of Medicaid insurance and many do not. The treatment step appears to be the limiting step and is often slowed by non-adherence events such as patient lack of knowledge regarding the refill system. However, other steps are also likely amenable to intervention. Improvements in the timeline must focus on reasons for non-adherence which occurs most often after the first month of treatment when patients must come in for the first refill (i.e. the top reason for non-adherence documented in the EHR was no refill/prescription pick-up). Because patients often lack knowledge about the U.S. healthcare system as a whole, including the refill process, better patient and staff education is recommended regarding pharmacy procedures and treatment guidelines. As one community stakeholder described: "Navigating the healthcare system is difficult…even if you are born in the U.S. The system is bizarre to [refugees] and to us. You need to have an appointment, referrals, and sometimes copays. It is very challenging." Community stakeholders recommended training modules for local pharmacies and residents, which could include training on patient education and cultural competency.

#### Screening and Diagnosis

The screening and diagnosis steps are highly effective in terms of completion, reflecting an effective aspect of the LTBI evaluation process for refugees at JCRH. Almost all refugees were screened (97.7%) and diagnosed (99.2%) between 2007 and 2014, indicating that JCRH is able to effectively reach refugees arriving for health evaluations and is committed to consistent LTBI screening and diagnosis. While screening and diagnosis completion rates are very high at JCRH, the quality or effectiveness of the tests was not evaluated in this study. There is some debate over the effectiveness of IGRAs compared to TSTs, particularly in children, but studies have generally demonstrated that QFT-GIT is preferable in high-risk adult groups and in BCGvaccinated groups (CDC, 2012). Because most JCRH refugees come from high-incidence TB regions of the world, they are considered high-risk groups and some are BCG vaccinated, suggesting that the use of QFT-GIT as the primary screening test for adults at JCRH is ideal. However, further studies must be conducted to evaluate how well these tests are capturing LTBI cases in the refugee population, and greater research is needed to determine the effectiveness of using IGRA versus TST to screen refugee children.

#### Recommendations for Improvement of Treatment Initiation

Treatment initiation and completion represent an opportunity for improvement of the LTBI screening, diagnosis, and treatment process. Approximately one fifth of patients requiring LTBI treatment did not initiate a treatment regimen. Because patients initiate treatment approximately one month after receiving a diagnosis (i.e. at their next appointment), several factors may be affecting patients' desire or ability to initiate treatment; this study demonstrated that loss to follow up and failure to pick up prescriptions (documented as non-adherence at month zero) were the most common reasons for these initiation rates and reflect a need for community and healthcare provider collaboration. Patients might move away or change their phone number, leading to discontinued care and loss of contact with the patient. To update electronic health records and refugee information, JCRH can strengthen methods of receiving information from refugee resettlement agencies regarding the status of refugees through an integrated surveillance registry.

Failure to pick up prescriptions may be the result of several underlying causes including patient lack of understanding the refill process, lack of knowledge of the healthcare system, and poor healthcare provider communication of the prescription process. To improve access and rates of filling prescriptions, patient education should be targeted through training modules and standardized resident training of the pharmacy process and patient LTBI education. In addition, language barriers and low patient health literacy may also prevent patient understanding of the treatment regimen. Local pharmacies in Philadelphia currently lack interpreter lines for some languages and dialects spoken by recently resettled refugees, which is a potential target for patient education improvement and thus treatment completion rates. *Recommendations for Improvement of Treatment Completion* 

LTBI treatment completion rates represent another opportunity for improvement of the LTBI screening, diagnosis, and treatment process. Healthy People 2020 goals for LTBI treatment among contact cases is 79%, a value that can be used as a standard for individual institutions. Despite a great increase in treatment completion between 2008 and 2009 (Figure 4), JCRH's treatment completion rate in 2013 (67.3%) was still significantly lower than the national goal. Data from 2014 is likely to indicate similar completion rates, since no significant systems changes have occurred.

Treatment completion rates have historically been a challenge for TB control, with national LTBI treatment completion rates continuing to fall below the Healthy People 2020 goals (HHS, 2015). Numerous studies have been conducted to understand factors affecting treatment completion, and a systematic review identified barriers including patient-related factors such as patient perceived susceptibility and severity, BCG vaccination, unemployment, and drug use; clinical characteristics or adherence interventions such as using case managers; and treatment characteristics such as adverse drug effects (Hirsch-Moverman *et al*, 2008). Another study cited family and community influence as predictors of TB treatment completion (Munro *et al.*, 2007). Many of these barriers overlap with those identified in this study; however, as recommended by the WHO (WHO, 2015), this study sought to identify barriers and enablers specific to the population of interest. Community stakeholders were invaluable in identifying these barriers and
enablers because their role in the community and interaction with the healthcare system provided them with an overarching perspective of the LTBI screening, diagnosis, and treatment process. Their input allowed for the identification of numerous barriers (Table 4), of which patient and provider education, language barriers, and loss to follow up appear to be the most susceptible to change.

This study also demonstrated that treatment completion rates for Bhutanese/Nepali refugees was greater than all other countries of origin, suggesting that lessons may be drawn from this population and that greater attention must be paid to treatment completion in Iraqi, Burmese, Eritrean/Ethiopian, and other refugees. Future studies could explore cultural factors and community organization in the resettlement city to understand the reason for these lower treatment completion rates and identify methods for improvement. In addition, this study has demonstrated that females are more likely than males to complete treatment, providing another area for future research.

On the other hand, treatment completion rates have greatly benefited from the use of RIF four-month treatment compared to INH for nine months. Recently, the CDC, ATS, and Infectious Diseases Society of America (IDSA) have recommended a new LTBI treatment regimen: isoniazid and rifapentine (INH-RPT) for three months, once a week under Directly Observed Therapy (DOT) (CDC, 2011). This treatment appears to be equally as effective as nine months of INH in preventing active TB, and completion rates for INH-RPT (82.1%) are superior to INH for nine months (self-administered) (69%) (Sterling *et al.*, 2011). CDC guidelines suggest that this treatment is not ideal for patients at risk of having INH-resistant TB, which constitutes a large majority of the refugees currently seen at JCRH due to their country of origin. As refugee population demographics change over time, the shorter INH-RPT treatment may be considered

for certain populations. While several treatment options are available, more research is required to determine the treatment best practices for specific populations and the efficacy of these tests. *General Recommendations for the LTBI Screening, Diagnosis, and Treatment Process* 

In considering community stakeholder perspectives on barriers and enablers, there are several recommendations and policy implications for improvement of the JCRH LTBI screening, diagnosis, and treatment process. In terms of training and education, local pharmacies can receive training modules delineating how best to approach language barriers, work with refugees, and standardize LTBI treatment administration/consultation. Physician training (particularly for emergency department physicians who may often be the first to see TB cases) can be improved and standardized such that physicians are aware of both TB and LTBI concerns and best practices particularly in refugee populations. Use of the CDC Guidelines for Primary Care Providers should be encouraged in order to standardize LTBI control. The CDC guidelines should also be followed in regards to the use of an AFB smear/sputum for diagnosis. Current sputum checks at JCRH are not standardized and are often not carried out with sufficient time in between collections of sputum, leading to numerous "incomplete" sputum/smears.

LTBI surveillance efforts can be improved by creating a systematic and coordinated workflow between providers and pharmacy. Recent efforts have been made to create an integrated registry so that participating entities have an up to date status on the patients diagnosed with LTBI. To follow patient adherence, routine pharmacy follow-up calls should be continued. Because RIF results in bodily fluids taking on an orange hue, future improvements in adherence follow-ups might include monitoring urine color in patients to determine if treatment has been discontinued. The relationships fostered among PRHC appear to be positively influencing refugee health and collaboration among various players in the resettlement process. This relationship could be beneficial for health clinic follow up with refugees. Clinic communication with resettlement agencies can identify refugees that have been lost to follow up or who have moved away and would allow for more complete EHR. Expanding the number of clinical liaisons functioning between resettlement agencies and clinics would allow for easier transitions for refugees as well as better care, as demonstrated by studies suggesting that case workers play a significant role in treatment adherence and completion (Hirsch-Moverman *et al*, 2008).

JCRH guidelines for LTBI screening, diagnosis, and treatment should include standard distribution of documentation of treatment completion. Once patients have completed LTBI treatment, the CDC recommends that documentation be provided, which includes information on the screening results, chest X-ray results (if applicable), names and dosages of medication, and the duration of the treatment (CDC, 2012). This is essential for patients to present in situations where TB testing is required for work, other hospital visits, etc. JCRH currently does not have a standardized documentation providing process—a barrier than can be eliminated by creating a packet of information that can be given to patients upon treatment completion.

The Philadelphia Department of Public Health's TB Control program is a comprehensive department that controls both LTBI and TB and runs the Flick TB Clinic. Despite significant success at controlling TB, the public health department requires greater resources to carry out TB and LTBI control and improve LTBI treatment completion rates. These resources can range from monetary to staffing and would lead to improved surveillance of LTBI in Philadelphia as well as greater ability to control and monitor both LTBI and TB. Finally, because LTBI is not a reportable disease, it may not be identified as a pressing public health concern requiring

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increased funding or attention. Advocating to make LTBI a reportable disease has benefits and drawbacks, but it is one option for improving LTBI control and surveillance and ultimately increasing LTBI treatment completion rates.

Understanding the barriers and enablers that refugees face as they move through the LTBI screening, diagnosis, and treatment process is essential to improving treatment completion rates. Refugees face a multitude of difficulties as they adjust, and enablers at both the healthcare system and community level can aid not only in adjustment but also maintaining health. With the success of PRHC, it is apparent that collaboration and communication are paramount in achieving this goal and improving all levels of the LTBI screening, diagnosis, and treatment process. This study identifies barriers and enablers and presents recommendations for improvements and further studies are important to examine best practices and to implement changes. As a result of the research conducted in this study, gaps in providing documentation have been identified and are being prioritized, there is a greater focus on integrating and expanding educational efforts for staff as well as improving follow-up and confirmation of treatment completion by pharmacists, and greater emphasis has been placed on implementing programs to educate residents and resettlement partners on LTBI treatment factors (such as free LTBI medication without insurance).

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Table 1

Refugee Characteristics	N = 1244 (100%)	
Male	676 (53.8%)	
Age group (years)		
0-5	94 (7.5%)	
6-18	119 (9.6%)	
19-45	797 (64.1%)	
46-64	164 (13.2%)	
≥65	70 (5.6%)	
Country of Origin		
Bhutan/Nepal	377 (30.3%)	
Iraq	352 (28.3%)	
Burma/Myanmar	214 (17.2%)	
Eritrea/Ethiopia	80 (6.4%)	
Other*	221 (17.8%)	

Demographics of Refugees Receiving Health Evaluations at Jefferson Center for Refugee Health between 2007 and 2014

Notes. \*Other countries of origin include Afghanistan, Chad, Cuba, Democratic Republic of
Congo, Egypt, Gabon, Guinea, Haiti, Indonesia, Iran, Israel, Ivory Coast, Jamaica, Jordan,
Kuwait, Lebanon, Liberia, Malaysia, Oman, Philippines, Republic of Moldova, Romania,
Russian Federation, Senegal, Sierra Leone, Sri Lanka, Sudan, Syria, Thailand, Tunisia, Ukraine,
Uzbekistan, and Vietnam.

				C	ountry of Ori	igin	
				Bhutan/	Burma/	Eritrea/	
		Total	Iraq	Nepal	Myanmar	Ethiopia	Other
Diagnosis	LTBI	285	56	104	54	20	51
Diagnosis	PMH TB*	37	0	22	11	3	1
	Completed	141	19	80	17	9	16
Treatment	Not Completed	94	23	19	26	9	17
	Percent Completed		45.2%	$80.8\%^\dagger$	39.5%	50.0%	48.5%

Table 2LTBI Diagnosis and Treatment Completion by Country of Origin

*Notes.* \*PMH TB diagnosis was determined from the International Organization for Migration form uploaded into the JCRH Electronic Health Records.

<sup>†</sup>The differences between completion rates (i.e. percent completed) based on country of origin were statistically significant at p < .05 for Iraq and Bhutan and Burma and Bhutan. Other and Eritrea/Ethiopia were not considered in completion rate comparisons.

Key hijoin	ium Demog	srupnies				
				Range of		
	Range of			years in	Range of	
	length of			TB or	years in	
Interviews	interview	Interview		refugee	position in	
conducted	(min)	location	Gender	position	Philadelphia	Position description
4	27-55	In-person	Female	3-12	3-12	Academic/clinical
		(n = 2)	(n = 2)			pharmacist,
						attending physician,
		Phone	Male			member of public
		(n = 2)	(n = 2)			health department,
			. ,			member of
						resettlement agency

# Table 3Kev Informant Demographics

# Table 4Barriers Identified by Key Informants

Individual Level	
Lack of knowledge of healthcare system*	Refugees are not aware of the way the healthcare system is set up and how they must navigate through the process
Lack of knowledge of insurance*	Patients may not have an understanding of how insurance works to cover their prescriptions for LTBI treatment and their general health care
Low health literacy	Refugees may not understand medical jargon or have limited knowledge of human body/function
Language barriers*	Low English proficiency or illiteracy (even in own language)
Low perceived severity	Patients with LTBI may not understand why they need to take medication (esp. with side effects) when they have no symptoms
Low perceived susceptibility	Patients may not believe their chances of getting active TB are high when they have LTBI
Length of treatment	Four months of RIF can be difficult for patients to complete
Comorbidities	Patients have other diseases or are pregnant, which prevents them from safely taking LTBI treatment. Generally recommended that they discontinue or defer treatment to a later time
Drug toxicity	Patients may fear the toxicity of the drugs or they may experience negative side effects which deter them from taking medication
Missing appointments (unknown reason)*	Patients may miss their appointments without a clear reason noted and therefore prolong their treatment course or fail to complete
Lack of insurance	Current situation: JCRH not able to accept Medicaid so refugees not entering system

Work schedule*	Patients may not be able to get time off to go to health appointments
Taking off work	Loss of income from taking off work either full or half days (esp. since refugees just arrived and began work)
Patients move away	Patients move or are lost to follow up
Patients change phone number	Patients change the phone number which is the main form of communication
Stigma (identified as a low impact barrier due to few cases noted)	Employers and others "outside" of the refugee populations may misunderstand the meaning of having LTBI and mistake it for having active TB, leading to fear and a potential stigma against patients with LTBI in their records
Lack of knowledge of healthcare system*	Providers may not understand the process that refugees must maneuver through
Communicating the healthcare system to refugees*	Providers may not be able to effectively communicate the process that refugees are undergoing, particularly with LTBI screening, diagnosis, and treatment
Cultural literacy*	Providers may not be aware of the cultural background of patients and therefore communicate less effectively

# LTBI AT JCRH: A COMMUNITY-INFORMED ANALYSIS

Interpersonal	
Trust in provider*	Refugees' trust in provider can be a barrier, as they simply agree to provider recommendations rather than actively participating in their care
Family/friend knowledge	Patients may encounter family and friends with negative experiences with LTBI treatment and therefore be less inclined to take LTBI medications
Lack of community knowledge	Incoming refugees may not have access to a community of similar culture/background who have gone through the LTBI process and can help guide them or provide insights
Interpreter quality*	Few negative interactions occur with interpreters but their competency may impact provider interaction with patients
Interpreter input*	Interpreters may input their own opinion or tone into the conversation, influencing the patient (not
Family member interpreting*	Family members may not be effective interpreters, and may not be comfortable discussing family member health. This is not a best practice.
Lack of staff communication*	Providers failing to communicate with each other because there are inter-professional "siloes" with no overlap between students, hospital staff, residents, pharmacy, etc.

# LTBI AT JCRH: A COMMUNITY-INFORMED ANALYSIS

Organizational/Institutional	
Volume of patients	A large volume of patients requiring pharmacy services can overwhelm the services
Lack of pharmacy staffing	Pharmacy is understaffed (see above); relies on students and residents
Lack of pharmacy funding	Pharmacy lacks funding to staff and include more resources (e.g. space and more language lines)
Lack of primary care practice*	More primary care physicians are required to deal with the large number of refugees
Lack of voicemail for patients*	Patients cannot always leave a voicemail for their providers because a voicemail system is not in place; if voicemail is in place, they may not be able to understand the language
Time consuming LTBI process*	The LTBI process is long and requires multiple appointments and refills, which can prove a barrier to completion
Waiting times	Waiting times may dissuade patients from attending appointments
Transportation to appointments*	Transportation to appointments (including those at Flick Center) may be difficult for refugees who are newly arrived, whether due to financial reasons or because they are less aware of how transportation works
Lack of physical space*	The size of the pharmacy and health care facilities limits the physical space available to see patients
Limited availability*	Lack of staff and providers due to funding thus lack of staff availability to see patients
Large volumes of data*	TB control programs have more data than they can deal with
Less nurses in schools to administer DOT to children	Lack of nurses limits effectiveness of DOT administration and leaves untrained staff with this role
Drug shortages (occurs infrequently)	Drug shortages have occurred in the past when

	there has been a lack of TB drug supply
Loss of community engagement member*	This role was important for maintaining community engagement and continuity with the public health department
Policy	
Lack of DOT	Directly Observed Therapy has been shown to be effective in some studies as a means of ensuring treatment completion
DOT	DOT is expensive, cumbersome, and paternalistic
LTBI not a reportable condition*	LTBI is not a CDC reportable condition so surveillance is very weak
Lack of public health department resources*	Financial limitations
JFMA inability to enroll new patients	JFMA is not able to enroll new patients with Medicaid, which includes refugees
State/federal absenteeism*	Lack of financial support and leave local institutions to take care of LTBI control
Public health department only tracks contact cases*	Lack of strong surveillance
Home isolation (occurs infrequently) *	Home isolation may interfere with individual freedom

*Notes.* \*Affects more than one step of the process

Responses have been organized to depict barriers directly related to patients (light blue highlight) and directly related to providers, medical care, and all other non-patient factors (white highlight).

# Table 5

Enablers Identified by Key Informants

Individual	
Health education	Patients are educated on the way to take their medications, what LTBI is, etc. in order
Health literacy	Patients are provided with materials that are easier to follow: in language of choice and simpler language/visual aides
Shorter treatment length (RIF vs. INH)	RIF has a shorter treatment length, which improves treatment completion rates
Cooperative patients*	Patients are willing to work with providers and are motivated with their healthcare
Motivation to access healthcare*	Patients are motivated to utilize the health care provided
Motivation to complete treatment (for Greencard status)	Patients are motivated to complete treatment so they can apply for Greencard after one year
Appointment notification for employers	Patients are able to take appointment notifications to their employers to be excused from work for LTBI appointments
Advocate for Patients*	Providers and other staff are devoted to the refugees and truly advocate for their patients' well-being

Interpersonal	
Trust in provider*	Trust in providers facilitates better communication with providers
Family member experiences*	Family members with TB experiences can aid patients in the LTBI screening, diagnosis, and treatment process and reassure if any concerns arise
Interpreter Access*	JCRH has ready access to interpreters and language lines which facilitate conversation with patients
Interpreter Quality*	Interpreters are certified and are seen as very positive influences on the patient-provider relationship
Community knowledge*	Incoming refugees have access to a community of similar culture/background who have gone through the LTBI process and can help guide or provide insights

Organizational/Institutional	
Face to face pharmacy counseling	Patients benefit from in-person counseling with the pharmacy regarding their TB treatment regimen
Proactive care*	Pharmacy commitment to care
Pictograms for education	Pharmacy provides pictograms for TB treatment regimen, which delineate how to take the medications (circumvents language barrier)
Local pharmacies cooperative	Relationship between the pharmacy at TJU and the local pharmacy is strong, allowing for communication and surveillance of TB treatment completion (through refills)
Flick Clinic (for TB DOT)	Flick Clinic provides free TB drugs and DOT
Free TB medication	Circumvents financial barriers
Transportation tokens to Flick Clinic	Circumvents transportation issues
Food provided to patients in Flick Clinic	Incentive for DOT
DOT in school for children	Ensures that this high risk group (i.e. children) complete TB treatment, which they are provided by nurses at their school
Resources available in many languages	Multiple languages allows for materials to be readable by refugees of various backgrounds
Advocate for patients*	The organization and institutions actively advocate for their patients
CDC guidelines*	CDC LTBI Guidelines for Primary Care Providers presents a standard of care for LTBI recommended by the public health department (CDC, 2013)
PRHC*	The Philadelphia Refugee Health Collaborative effectively ties together the resettlement agencies, health care settings, and refugees ( <u>http://philarefugeehealth.org</u> )
Primary care offices that facilitate all aspects of LTBI care*	Primary care offices, like JCRH, provide comprehensive health care and facilitate all aspects of the LTBI screening, diagnosis, and

	treatment process
	-
Clinical case managers/Clinic Liaison roles*	Liaison guides refugees through the health care
	process including the ITBI screening
	diagnosis and treatment process; lisison
	diagnosis, and treatment process, naison
	connects the healthcare system/providers with
	the resettlement agencies
Policy	
IOM Seveening abread and treaking vie	Initial acrossing conducted chroad and wall
TOW Screening abroad and tracking via	
EDN/SAMS	tracked/documented for providers – encourages
	continuity of care
Institution adherence to LTBI process	All health care settings follow the LTBI
I I I I I I I I I I I I I I I I I I I	nrocess in Figure 1
	process in rigure r
Desettlement exercise have strong	Department a convergence in with
Resettlement agencies have strong	Resettlement agency communication with
relationship with public health department	public health department
PRHC relationship with public health	PRHC communication with public health
department	department
DOT	DOT has been shown to promote LTBI
	treatment completion

Notes. \*Affects more than one step of the process

Responses have been organized to depict barriers directly related to patients (light blue highlight)

and directly related to providers, medical care, and all other non-patient factors (white highlight).

Tal	bl	e	6
		-	-

Recommendations of Key Informants

Clinical

Letters to employers confirming LTBI treatment completion Train emergency department doctors regarding TB Improve EHR tracking and keep charts up to date Clear signage for the Flick TB Clinic Earlier messaging of the need to complete treatment for Greencard status (where applicable) In person interpreters Improve resident training on LTBI Standardize resident training on LTBI Use urine color change for adherence Every 3 months, check patients to make sure LTBI requirements have been met Continue commitment to care/patient home

#### Policies

Training modules for local pharmacies regarding LTBI treatment and refugees Language lines for local pharmacy

Pharmacy

More resources for public health departments Make LTBI a reportable disease Provide patients with documentation of treatment completion Utilize CDC Guidelines for Primary Care Providers (e.g., standardize sputum guidelines)

Resettlement

Communicate with resettlement agency for loss to follow up and secondary migration information More clinical liaisons

Table 7	
Key Informant Interview Themes	
Communication	
Barriers	Leals of staff communication
	Lack of staff communication
	Interpreter quality
	Interpreter input
	Family member interpreting
	Trust in provider
	Cultural literacy
	Low health literacy
	Language barriers
	Lack of voicemail for patients calling
	Patients move away
	Patients change phone number
Enablers	
	Trust in provider
	Health literacy
	Face to face pharmacy counseling
	Interpreter access
	Interpreter quality
	Pictograms for education
	Resources available in many languages
	Clinical case managers/Clinic liaison role
	IOM Screening abroad and tracking via EDN/SAMS
Resources	
Banners	Lack of public health resources
	State/federal absenteeism
	Large volumes of data
	Large volume of patients
	Lack of pharmacy staffing
	Lack of pharmacy funding
	Lack of primary care practice
	Lack of physical space
	Limited availability
	Less nurses in schools to administer
	DOT in children
	Drug shortages (occurs infrequently)
Patient Motivation	
Barriers	

Low perceived severity Low perceived susceptibility Family/friend knowledge Missing appointments (unknown reason)

	Lack of knowledge of healthcare system (providers)
Enablers	
	Health education
	Motivation to access healthcare
	Family member experiences
	Community knowledge
	Motivation to complete treatment (for Greencard status)
•	Cooperative patients
Access	
Barriers	Lask of knowledge of health are greater
	Lack of knowledge of healthcare system
	WORK Schedule
	Taking off work
	Walting times Transportation to appointments
	ICRH not accenting Keystone First
	Jerri not decepting Reystone 1 ist
Enablers	
Lindolers	Transportation tokens to Flick Clinic
	Appointment notification for employers
Community Relatio	nships
Barriers	
F 11	Loss of current community engagement member
Enablers	Desattlement agancies strong relationship with public health department
	<b>DPHC</b> relationship with public health department
	I ocal pharmacies cooperative
Standards of Care	
Barriers	
Darriers	Home isolation (occurs infrequently)
	DOT
	Length of treatment
	Drug toxicity
	Comorbidities
Enablers	
	CDC guidelines
	Institution adherence to LTBI process
	Primary care offices that facilitate all aspects of LTBI care
	DOT in school for children
	Free TB medication
	Flick Clinic (for TB DOT)
	DOT
	Shorter treatment length (RIF vs. INH)







Health



*Figure 2.* LTBI screening, diagnosis, and treatment process completion rates for refugees receiving health evaluations at Jefferson Center for Refugee Health



*Figure 3*. The number of refugees diagnosed with LTBI, previous medical history of TB (Appendix C), and no LTBI each year.



*Figure 4*. The percent completion of LTBI treatment after treatment initiation in refugees by annual cohort.

\*More data in process

LTBI AT JCRH: A COMMUNITY-INFORMED ANALYSIS



*Figure 5*. Mean time (in days) between arrival, screening, diagnosis, and treatment of LTBI and cumulative time in process.

#### Appendix A: Key Informant Interview Guide

# Community Stakeholders' Perceptions of Barriers and Enablers to LTBI Screening, Diagnosis, and Treatment across the Socio-Ecological Model Community Stakeholders—Key Informant Interview Guide

#### I. GREETING

Hello and thank you for taking the time to share some of your thoughts with me. My name is Neda Bionghi and I am an Master of Public Health student at Thomas Jefferson University. I am interested in learning more about your thoughts on the refugee latent tuberculosis infection or LTBI screening, diagnosis, and treatment process. I am looking to interview experts in the field and so would like to hear your thoughts on the LTBI process for refugees in Philadelphia. This interview should take about 30 minutes. If you would like to stop at any time, please let me know. Thank you and let's start the interview.

# **II. INTRODUCTION & STAKEHOLDER ROLE**

- 1) Please tell me about your role in the refugee resettlement and/or health evaluation process.
  - a) Prompt: How long have you been in this role? How long have you held this role in Philadelphia?
- 2) What do you think about the current refugee LTBI screening, diagnosis, and/or treatment process?

I would now like to ask you about barriers and enablers in the process at the individual, interpersonal, institutional, and policy levels.

# III. INDIVIDUAL LEVEL

- 1) What **barriers** have you observed that influence a refugee's likelihood of getting screened, being diagnosed, or initiating and completing treatment for LTBI?
- 2) What **enablers** have you observed that influence a refugee's likelihood of getting screened, being diagnosed, or initiating and completing treatment for LTBI?

Prompts: How have the following influenced refugees getting screened, diagnosed with LTBI, and completing LTBI treatment: Education? Transportation? Comorbidities/physical factors? Disability? Language/health literacy? Religion? Gender? Age? Country of origin/ethnicity? Feelings and perceptions (e.g. fear, shame, etc.)? Stigma? Clinical/biological (e.g. BCG vaccination, PMH TB)? Treatment length? Medication side effects? Perceived severity? Perceived susceptibility?

# IV. INTERPERSONAL LEVEL

- 1) What **barriers** have you observed that influence a refugee's likelihood of getting screened, being diagnosed, or initiating and completing treatment for LTBI?
- 2) What **enablers** have you observed that influence a refugee's likelihood of getting screened, being diagnosed, or initiating and completing treatment for LTBI?

Prompts: How have the following influenced refugees getting screened, diagnosed with LTBI, and completing LTBI treatment: Family members? Interpreters? Health care providers (i.e. pharmacists, nurses, doctors, others)?

# V. ORGANIZATIONAL/INSTITUTIONAL LEVEL

- 1) What **barriers** have you observed that influence a refugee's likelihood of getting screened, being diagnosed, or initiating and completing treatment for LTBI?
- 2) What **enablers** have you observed that influence a refugee's likelihood of getting screened, being diagnosed, or initiating and completing treatment for LTBI?

Prompts: How have the following influenced refugees getting screened, diagnosed with LTBI, and completing LTBI treatment: Waiting times? Screening standards/requirements? Length of process? Insurance? Institutional adherence with LTBI guidelines? Pharmacy follow up? Clarity of refill process? Clarity of follow up procedures? School system? Work? Support from work (i.e. time off to return for testing, accommodations, etc.)? Resettlement agencies? Communication among the PRHC entities?

#### VI. POLICY LEVEL

- 1) What **barriers** have you observed that influence a refugee's likelihood of getting screened, being diagnosed, or initiating and completing treatment for LTBI?
- 2) What **enablers** have you observed that influence a refugee's likelihood of getting screened, being diagnosed, or initiating and completing treatment for LTBI?

Prompts: How have the following influenced refugees getting screened, diagnosed with LTBI, and completing LTBI treatment: Screening standards/requirements? Screening result interpretation? Definition of LTBI? DOT (or lack thereof)? Medication accessibility?

#### VII. CONCLUSION & RECOMMENDATIONS

- 1) Do you have any recommendations for how to improve the refugee TB process?
- 2) Is there anything else you would like to add?

I really appreciate the time that you took to share your expertise on this health topic. Your interview will help me to answer the question of what barriers and enablers exist in the LTBI screening, diagnosis, and treatment process. Thank you very much for your participation. If you think of anything later that you would like to add of if you have any questions, please feel free to follow up with me.



# Appendix B: Socio-Ecological Model for Key Informant Interviews

#### Appendix C: Definitions of Measures

#### Latent tuberculosis infection

Indicated by a positive TB screening test (IGRA or TST), exposure to and infection by

Mycobacterium tuberculosis, negative chest X-ray and no symptoms of active TB.

#### Active tuberculosis

A case of tuberculosis in which a patient presents with symptoms of tuberculosis (such as coughing, fever, weight loss) and tests positive in a TB screening and chest X-ray.

Previous medical history of tuberculosis (PMH TB)

A case in which a patient has previously been diagnosed with TB and potentially been treated, but they present with a positive TB screening.

#### Treatment completion

Treatment completion was defined by pharmacy as taking greater than 80% of a four-month rifampin or nine month isoniazid treatment. Completion was measured through one or more of the following: filling and picking up four prescriptions of rifampin or nine prescriptions of isoniazid as recorded by local pharmacies, pill counts, patient report of taking four months of RIF or nine months of INH, and/or physician record of patient completion of the aforementioned treatments.

#### Medication refill

A refill of medication was defined as when a patient pharmacy automatically fills a prescription request for a subsequent month of treatment (i.e. second, third, etc. months of treatment), providing the patient with another 30 pills which he or she must pick up from the pharmacy. *Treatment non-adherence*
Non-adherence to LTBI treatment was defined as when a patient fails to take their LTBI pills for any number of days and therefore misses doses of their LTBI treatment. Treatment nonadherence was utilized for the purpose of indicating the time to the first incident of nonadherence (i.e. a patient missing doses).

# Time to screening

A patient's time to screening was defined as the time (in days) between their arrival into the United States and their first TB screening test (IGRA or TST).

### Time to diagnosis

Time to diagnosis was defined as the time (in days) between a patient's first TB screening test (IGRA or TST) and their first chest X-ray result for TB diagnosis.

### Time to treatment initiation

Time to treatment initiation was defined as the time (in days) between a patient's initial TB screening (IGRA or TST) and initiation of LTBI treatment regimen.

# Directly Observed Therapy (DOT)

DOT was defined as treatment regimens supervised by a selected professional (i.e. not a family member or friend) who ensures that patients take prescribed doses (Hirsch-Moverman, 2008).

# Self-administered treatment (SAT)

SAT was defined as patients self-administering prescribed doses of LTBI treatment (Hirsch-Moverman, 2008).