Prevalence and Treatment of Latent Tuberculosis Infection Among Newly Arrived Refugees in San Diego County, January 2010–October 2012

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Objectives. We determined the prevalence and treatment rates of latent tuberculosis infection (LTBI) in newly arrived refugees in San Diego County, California, and assessed demographic and clinical characteristics associated with these outcomes.

Methods. We analyzed data from LTBI screening results of 4280 refugees resettled in San Diego County between January 2010 and October 2012. Using multivariate logistic regression, we calculated the associations between demographic and clinical risk factors and the outcomes of LTBI diagnosis and LTBI treatment initiation.

Results. The prevalence of LTBI was highest among refugees from sub-Saharan Africa (43%) and was associated with current smoking and having a clinical comorbidity that increases the risk for active tuberculosis. Although refugees from sub-Saharan Africa had the highest prevalence of infection, they were significantly less likely to initiate treatment than refugees from the Middle East. Refugees with postsecondary education were significantly more likely to initiate LTBI treatment.

Conclusions. Public health strategies are needed to increase treatment rates among high-risk refugees with LTBI. Particular attention is required among refugees from sub-Saharan Africa and those with less education. (*Am J Public Health.* 2014;104:e95–e102. doi:10.2105/AJPH.2013.301637)

Tuberculosis (TB) in the United States is primarily a disease of foreign-born people. In 2011, approximately 62% of all incident TB cases within the United States occurred among foreign-born individuals, a proportion that has been increasing steadily since 2001.[1–3] Within the first few years after arrival in the United States, immigrants and refugees from countries in which TB is highly endemic have been found to develop active TB at rates more similar to incidence rates in their home countries than those of the United States, which has been documented to be largely because of reactivation of latent TB infection (LTBI) acquired abroad.[4–8] Among foreign-born people in the United States, the risk for active TB is particularly elevated for immigrants and refugees from sub-Saharan Africa and Southeast Asia.[2,3] A recent study found that the TB case rate among Africans in the United States was 3 times higher than that among other foreign-born people and 27 times higher than that among US-born people, a finding attributed to the large burden of LTBI in this population.[9]

Refugees resettling in the United States have typically originated from regions with high rates of active TB, including Southeast Asia and sub-Saharan Africa. In addition, previous studies have documented that refugees have higher rates of TB after resettlement in the United States than other foreign-born people.[10,11] Although active TB disease among refugees is usually diagnosed and treated before departure for the United States,[12] the treatment of LTBI before arrival in the United States is not mandated. To prevent the reactivation of LTBI after arrival to the United States, the Centers for Disease Control and Prevention currently recommends screening for and treating LTBI among all recently arrived refugees.[8,13]

Despite the Centers for Disease Control and Prevention's recommendation, there has been only limited assessment of the prevalence, epidemiology, and treatment rates of LTBI among newly arrived refugees in the United States. Previous studies of LTBI among refugees in the United States[14–17] were primarily conducted during the previous decade and do not reflect changes in the demographics of more recent refugee arrivals. Additionally, few reported LTBI treatment completion rates. The majority of these studies were also conducted before the introduction of interferon γ release assays, TB screening tests that provide a more accurate diagnosis of LTBI because of their higher specificity than the tuberculin skin test.[18,19]

Between 2010 and 2012, California received almost 10% of the 187 966 refugees settled in the United States, making it one of the largest resettlement regions in the country.[20–22] San Diego County, in Southern California, is a leading refugee resettlement site, and it also has one of the highest rates of active TB in the country, with an incidence rate of 8.4 cases per 100 000 people in 2011.[23,24] Assessment of LTBI prevalence and treatment among recently arrived refugees is needed to effectively address the control of TB, because untreated, reactivated LTBI in this population may be an important contributor to TB incidence in the United States.[8] This information is critical for public health departments that provide care for refugee populations, not only to ensure the health of individual refugees, but also to prioritize efforts to reduce the disproportionately high rate of active TB among foreign-born people in the United States. In this study, we investigated LTBI prevalence by birth region and clinical risk factors, and identified demographic and clinical factors associated with LTBI treatment initiation and completion among newly arrived refugees diagnosed with LTBI in San Diego County from January 1, 2010, through October 1, 2012.

METHODS

Refugees who enter San Diego County are eligible to receive a domestic medical screening examination within 90 days of arrival through the Refugee Health Assessment Program (RHAP), which is funded by the Office of Refugee Resettlement and administered by the County of San Diego Health and Human Services Agency. The RHAP includes testing for LTBI, hepatitis B and C, syphilis, HIV, and intestinal parasites.

We extracted data for the current study from the Refugee Health Electronic Information System (RHEIS) database, an electronic database that was established in 2000 by the California Department of Public Health and contains data from refugee medical screening programs in 9 of the largest refugee resettlement programs in the state, including the San Diego County RHAP.

Beginning in August 2008, refugees in San Diego County aged 13 years and older received the QuantiFERON-TB Gold In-Tube (QFT-GIT) to screen for latent TB infection. Refugees aged younger than 13 years received the TST as the screening test for TB. In November 2011, use of the QFT-GIT was expanded to include all refugees aged 2 years and older, with refugees younger than 2 years being tested with the TST. All refugees with a positive QFT-GIT (≥ 0.35 IU) or TST (≥ 10 mm) received a chest x-ray to evaluate for active TB. Refugees with a positive screening test and a normal chest x-ray and physical examination were diagnosed with LTBI, and those with a positive screening test and abnormal chest x-ray or physical examination were referred to the public health department to rule out active TB. Refugees aged between 6 and 49 years without comorbid medical conditions (e.g., chronic liver disease, alcoholism) that required laboratory monitoring of liver function tests while on isoniazid (INH) were offered treatment of LTBI through the San Diego County RHAP clinic. In accordance with current Centers for Disease Control and Prevention LTBI treatment guidelines, we considered treatment complete after 6 to 9 months of daily INH was completed. Refugees aged 50 years and older were not offered treatment at the RHAP clinic because of the increased risk of INH-induced hepatotoxicity in older adults, which requires a higher level of clinical complexity and laboratory monitoring than can be provided at the RHAP clinic. Because of their increased risk for progression to active TB, refugees aged 50 years and older with an additional risk factor for progression to active TB (e.g., diabetes, current smoking) were referred to their primary care providers in the community for consideration of LTBI treatment depending on risk–benefit ratios.

Study Population

All primary refugees aged 13 years or older who were evaluated through the San Diego County RHAP and received the QFT-GIT between January 1, 2010, and October 1, 2012, were included in this study. We chose arrival age of 13 years or older to restrict the analysis to only those refugees who received the QFT-GIT test for TB screening. Secondary-to-state refugees were excluded from the study given that they had resided in the United States for a longer period of time. We also excluded refugees with missing or incomplete QFT-GIT results.

Clinical and Demographic Data

The primary outcome of interest was the diagnosis of LTBI. The secondary outcomes studied were LTBI treatment initiation and treatment completion. Clinical variables extracted from the RHEIS database included QFT-GIT result (positive or negative; quantitative QFT-GIT values were not available), chest radiograph result, comorbid medical conditions that had previously been reported to increase the risk of TB reactivation (diabetes, HIV infection, end-stage renal disease [ESRD], and malignancy), and current tobacco smoking. Demographic variables extracted included arrival age (≥ 13 years), gender, birth country, and years of education. We coded chest radiograph results as "normal," "abnormal and consistent with TB," "abnormal but not consistent with TB disease," and "not done" and defined latent tuberculosis diagnosis as a positive QFT-GIT with a normal chest radiograph. Refugees with a positive QFT-GIT and abnormal chest radiograph or no chest radiograph results were excluded from the final analysis. We coded LTBI treatment initiation and completion status as "yes" or "no" and included the reason for not initiating or completing treatment. Smoking status, years of education, and comorbid medical conditions, except HIV status, were based on self-report. In the final analysis, we combined comorbid medical conditions including HIV, ESRD, and malignancy into 1 variable because of small numbers. Birth country was recoded into the following regions: the Middle East (including North Africa), sub-Saharan Africa, Asia, and other. Reflecting important age cut-offs for LTBI treatment initiation, we categorized age into 4 age groups: 13 to 17 years, 18 to 34 years, 35 to 49 years, and 50 years or older. Education was categorized as primary (0–6 years), secondary (7–12 years), and postsecondary (> 12 years).

To ensure the accuracy of the RHEIS database, we completed a random subsample chart review before data analysis.

Data Analysis

We calculated univariate descriptive statistics with frequencies for each demographic and clinical variable and conducted bivariate associations using the χ^2 test and 95% confidence intervals (CIs) to assess the unadjusted association of each independent variable with the primary and secondary outcomes. We used Fisher exact *P* values for cell sizes less than 5 in the bivariate analysis. For LTBI treatment initiation, the analysis included only refugees who were offered treatment at the San Diego County RHAP clinic; refugees with LTBI were not offered treatment at the RHAP if they were aged 50 years or older, were currently pregnant, had a medical contraindication, or had prior adequate treatment. We performed multivariate logistic regression modeling to calculate adjusted odds ratios (AORs) and 95% CIs for the demographic and clinical variables associated with a diagnosis of LTBI and LTBI treatment initiation. We included independent variables in the logistic regression models if they were associated with the outcomes at $P \leq .15$ in bivariate analyses. Effect modification by region of birth for the demographic variables of age, gender, and level of education was tested using interaction terms in the final models using $P \leq .05$ as indication of significance. We did not conduct multivariate logistic regression for the outcome of LTBI treatment completion because the sample size was too small. All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

RESULTS

A total of 4365 primary refugees were screened through the San Diego County RHAP between January 1, 2010, and October 1, 2012. Of the refugees, 85 had missing QFT-GIT results, which resulted in a final study sample of 4280 refugees (98%; Table 1). The majority of refugees were born in the Middle East (86.8%); Iraq was the most common birth country (n = 3558), followed by Burma (n = 245) and Somalia (n = 155). The median age of refugees was 31 years; 43.4% of refugees were aged between 18 and 34 years. The study population was approximately half female (49.7%) and half male (50.3%); 47.8% of refugees had between 7 and 12 years of education. Comorbid medical conditions reported among refugees included diabetes mellitus (n = 182, 4.3%), malignancy (n = 15, 0.4%), HIV infection (n = 3, 0.07%), and ESRD (n = 1, 0.02%). A total of 663, or 15.5%, of refugees reported being current tobacco smokers.

TABLE 1—Demographic and Clinical Characteristics of Newly Arrived Refugees: San Diego County, CA; January 2010–October 2012

Characteristic	No. (%)
Birth region	
Middle East[a]	3713 (86.8)
Asia[b]	302 (7.1)
Sub-Saharan Africa[c]	248 (5.8)
Other[d]	17 (0.40)
Age group, y	
13–17	548 (12.8)
18–34	1856 (43.4)
35–49	1009 (23.6)
≥ 50	867 (20.3)
Gender	
Male	2154 (50.3)
Female	2126 (49.7)
Education, y	
0–6	1160 (27.1)
7–12	2044 (47.8)
> 12	1076 (25.1)
Comorbid medical condition (that increases risk for progression to active TB)	
Diabetes mellitus	182 (4.3)
Malignancy	15 (0.44)
HIV-positive	3 (0.07)
End-stage renal disease	1 (0.02)
None	4079 (95.3)
Tobacco smoking	
Yes	663 (15.5)
No	3617 (84.5)
QFT-GIT result	
Positive (≥ 0.35 IU)	916 (21.4)
Negative	3364 (78.6)

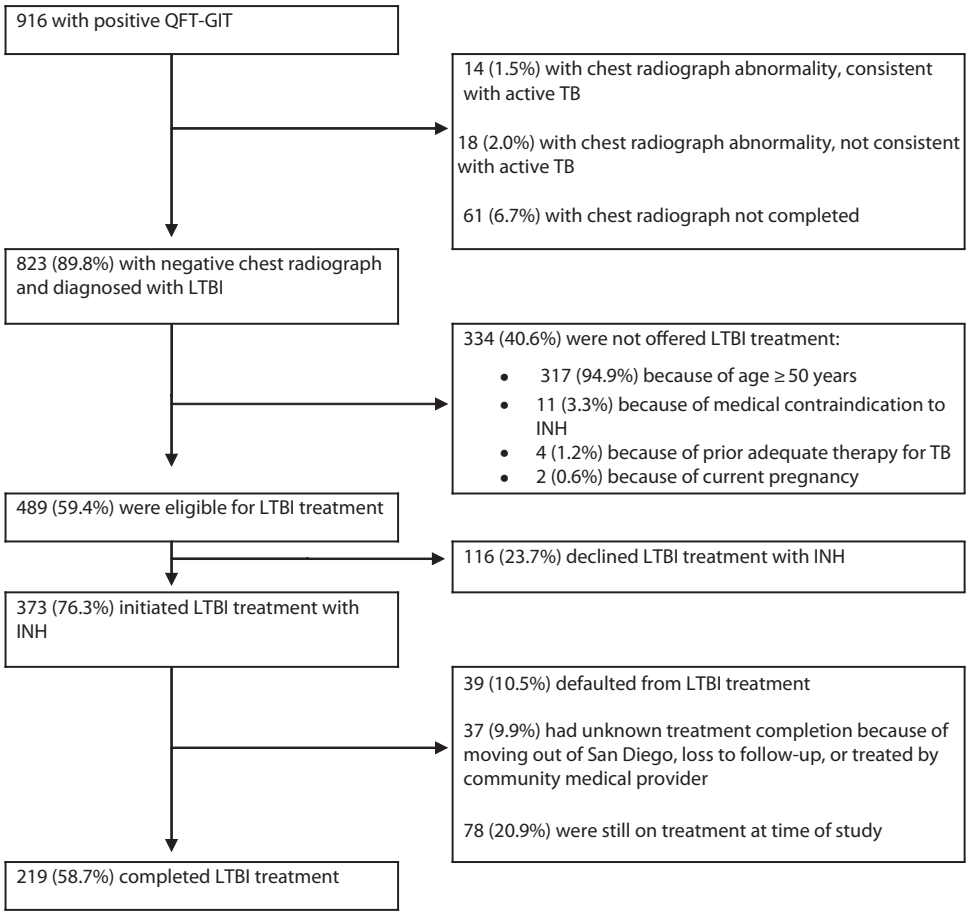
Note. QFT-GIT = QuantiFERON-TB Gold In-Tube; TB = tuberculosis. The sample size was n = 4280.
[a]Iraq, Iran, Afghanistan, Uzbekistan, Syria, Kuwait, Lebanon, Jordan, and Egypt.
[b]Burma, Bhutan, Thailand, Vietnam, India, China, and Taiwan.
[c]Somalia, Ethiopia, Democratic Republic of Congo, Sudan, Eritrea, Uganda, and Kenya.
[d]Cuba, Guatemala, Haiti, Colombia, and unknown.

The quality control chart review found no errors in QFT-GIT result, chest x-ray, treatment status, or clinical risk factors but found that arrival age in RHEIS was occasionally incorrect by 1 to 2 years from the actual arrival age in refugees' paper charts.

Diagnosis of Latent Tuberculosis Infection

Nine hundred sixteen refugees (21.4%) in the study had a positive QFT-GIT result (Table 1). Of those, 823 (89.8%) had a normal chest radiograph and were diagnosed with LTBI (Figure 1). Sixty-one (6.7%) did not receive a chest radiograph; 14 (1.5%) had an abnormal result that was consistent with active TB; and 18 (2.0%) had an abnormal result that was not consistent with active TB. The prevalence of LTBI was highest among refugees from sub-Saharan Africa—43.1% compared with a prevalence of 18.3% among refugees from the Middle East and 19.0% among refugees from Asia.

In the final multivariate logistic regression model, refugees with LTBI were significantly more likely to be from sub-Saharan Africa (adjusted odds ratio [AOR] = 5.3; 95% confidence interval [CI] = 3.9, 7.2), male gender (AOR = 1.7; 95% CI = 1.4, 2.0), current tobacco smokers (AOR = 1.6; 95% CI = 1.3, 2.0), and diabetic (AOR = 1.6; 95% CI = 1.1, 2.2) and to have a comorbid medical condition of HIV, malignancy, or ESRD (AOR = 2.8; 95% CI = 1.1, 7.3) than were refugees with a negative QFT-GIT result (Table 2). Increasing age conferred a higher odds of LTBI; primary refugees aged 35 to 49 years were more than 2 times as likely to have LTBI than refugees aged 13 to 17 years (AOR = 2.9; 95% CI = 2.0, 4.0), whereas refugees aged 50 years and older were approximately 6 times as likely to have LTBI than refugees aged 13 to 17 years (AOR = 6.5; 95% CI = 4.6, 9.2). Higher education level was significantly associated with a lower odds of LTBI; compared with refugees with 6 years of education or less, refugees with 7 to 12 years of education had 0.8 times lower odds of LTBI (AOR = 0.8; 95% CI = 0.7, 0.9), whereas refugees with more than 12 years of education had 0.7 times lower odds of LTBI (AOR = 0.7; 95% CI = 0.6, 0.9). Interaction terms for region of birth by age, gender, and education level tested individually in the final model were not statistically significant.



Note. INH = isoniazid; QFT-GIT = QuantiFERON-TB Gold In-Tube; TB = tuberculosis.

FIGURE 1—Number and percentage of newly arrived refugees with latent tuberculosis infection (LTBI): outcomes of treatment initiation and treatment completion assessment; San Diego County, CA; January 2010–October 2012.

Latent Tuberculosis Infection Treatment Initiation

Of the 823 refugees diagnosed with LTBI, 334 (40.6%) were not offered treatment at the RHAP clinic, most because they were aged 50 years or older (Figure 1). Among refugees with an increased risk for progression to active TB, only 7 refugees with diabetes and 110 refugees who currently smoked were eligible for LTBI treatment at the RHAP clinic. The remainder of refugees with diabetes and refugees who smoked were not offered treatment because they were aged 50 years or older. Treatment outcomes for these refugees referred to community medical providers for consideration of treatment and closer clinical monitoring were unknown.

Of the 489 refugees with LTBI who were offered treatment, 373 (76.3%) initiated LTBI treatment. After controlling for age, refugees who initiated treatment of LTBI were significantly less likely to be from Africa (AOR = 0.5; 95% CI = 0.3, 0.8) and significantly more likely to have more than 12 years of education (AOR = 2.5; 95% CI = 1.3, 4.8) than were those who did not initiate treatment (Table 3). No other variables were significantly associated with LTBI treatment initiation. Interaction terms for region of birth by age and education level were not statistically significant.

Latent Tuberculosis Infection Treatment Completion

Among the 373 refugees who initiated treatment, 78 (20.9%) were still on treatment at the time of analysis, 219 (58.7%) had completed treatment, and 39 (10.5%) defaulted from treatment (Figure 1). The most common documented reason for defaulting from treatment was that the patient chose to stop (n = 16; Table A, available as a supplement to this article at http://www.ajph.org). Treatment completion status was unknown for 37 (9.9%) refugees who started treatment; among these refugees, the majority (n = 28) had moved out of San Diego County before treatment completion. In the bivariate analysis, refugees with 7 to 12 years of education were significantly more likely to complete treatment than were refugees with 6 or fewer years of education (OR = 2.5; 95% CI = 1.1, 5.6; Table B; available as a supplement to this article at http://www.ajph.org). We found no other significant associations. Refugees from sub-Saharan

TABLE 2—Demographic and Clinical Characteristics Associated With LTBI on the Basis of Positive QFT-GIT and Negative Chest Radiograph Among Newly Arrived Refugees: San Diego County, CA; January 2010–October 2012

Characteristic	Prevalence of LTBI,[a] No. (%)	OR (95% CI)	AOR (95% CI)
Birth region			
Middle East[b] (Ref)	670/3664 (18.3)	1.00	1.00
Asia[c]	54/284 (19.0)	1.05 (0.77, 1.42)	1.37 (0.99, 1.90)
Sub-Saharan Africa[d]	97/225 (43.1)	3.39*** (2.57, 4.47)	5.33*** (3.94, 7.20)
Other[e]	2/14 (14.3)	0.74 (0.17, 3.33)	0.73 (0.16, 3.44)
Age group, y			
13–17 (Ref)	53/546 (9.7)	1.00	1.00
18–34	251/1826 (13.7)	1.48* (1.08, 2.03)	1.60** (1.15, 2.23)
35–49	207/982 (21.1)	2.48*** (1.80, 3.43)	2.85*** (2.02, 4.03)
≥ 50	312/833 (37.5)	5.57*** (4.06, 7.64)	6.50*** (4.58, 9.23)
Gender			
Female (Ref)	327/2072 (15.8)	1.00	1.00
Male	496/2115 (23.5)	1.63*** (1.40, 1.91)	1.67*** (1.39, 2.00)
Education, y			
0–6 (Ref)	275/1119 (24.6)	1.00	1.00
7–12	351/2009 (17.5)	0.65*** (0.54, 0.78)	0.82* (0.68, 0.99)
> 12	197/1059 (18.6)	0.70*** (0.57, 0.86)	0.74** (0.59, 0.92)
Diabetes mellitus			
No (Ref)	747/4011 (18.6)	1.00	1.00
Yes	76/176 (43.2)	3.32*** (2.44, 4.52)	1.58** (1.13, 2.20)
Comorbid condition[f]			
No (Ref)	814/4168 (19.5)	1.00	1.00
Yes	9/19 (47.4)	3.71* (1.50, 9.16)	2.77* (1.06, 7.25)
Tobacco smoking			
No (Ref)	625/3540 (17.7)	1.00	1.00
Yes	198/647 (30.6)	2.06*** (1.71, 2.48)	1.62*** (1.31, 2.01)

Note. AOR = adjusted odds ratio; CI = confidence interval; LTBI = latent tuberculosis infection; OR = odds ratio; QFT-GIT = QuantiFERON-TB Gold In-Tube.
[a]Number of QFT-GIT positive, chest x-ray–negative refugees in cohort (n = 823)/total number in cohort (n = 4187); refugees with a positive QFT-GIT but abnormal or incomplete chest x-ray were excluded from the denominator.
[b]Iraq, Iran, Afghanistan, Uzbekistan, Syria, Kuwait, Lebanon, Jordan, and Egypt.
[c]Burma, Bhutan, Thailand, Vietnam, India, China, and Taiwan.
[d]Somalia, Ethiopia, Democratic Republic of Congo, Sudan, Eritrea, Uganda, and Kenya.
[e]Cuba, Guatemala, Haiti, Colombia, and unknown.
[f]Malignancy, HIV infection, and end-stage renal disease combined because of limited numbers.
*$P \leq .05$. **$P \leq .01$. ***$P \leq .001$.

Africa had slightly lower LTBI treatment completion rates (71.4%) than refugees from the Middle East (86.2%) and Asia (81.5%), although this difference was not statistically significant.

DISCUSSION

In this study of LTBI prevalence based on interferon γ release assays and LTBI treatment among refugees resettling in San Diego County between 2010 and 2012, refugees from sub-Saharan Africa had the highest prevalence of LTBI (43.1%) compared with refugees from the Middle East (18.3%) and Asia (19.0%). Despite the significantly higher odds of LTBI among refugees from sub-Saharan Africa, LTBI treatment initiation was significantly lower among these refugees than among refugees from the Middle East (60.5% and 78.6%, respectively; $P \leq .001$). This is concerning because it reveals a missed opportunity to decrease the risk of progression to active TB among this high-risk group of refugees resettling in the United States. Treatment completion analysis was limited by small numbers but suggested that refugees from sub-Saharan Africa may also have lower treatment completion rates than refugees from the Middle East (71.4% and 86.2%, respectively; $P = .51$), although this was not statistically significant. Only a very small proportion (1.5%) of refugees had chest x-ray findings consistent with active TB. This is likely, in part, because of the rigorous overseas medical screening designed to prevent the importation of active, infectious TB before departure to the United States.[12,25–27]

Consistent with previous studies with newly arrived refugees,[14,15,28,29] we found that the diagnosis of LTBI was significantly associated with male gender, older age, and African origin. Specifically, the prevalence of LTBI among refugees from sub-Saharan Africa documented in this study is consistent with that found in previous studies of LTBI that used the TST for LTBI screening in African refugees, in which the prevalence has ranged from 38% to 54.5%.[11,14,15,17] Increasing age likely confers a higher risk of LTBI among refugees as a result of longer time spent living in a TB-endemic region. Furthermore, it has been hypothesized that men are more likely to be exposed to *Mycobacterium tuberculosis* and thus acquire TB infection because of behavioral factors associated with increased mobility and social crowding.[8,13,14]

To our knowledge, this study is the first to assess clinical risk factors that increase the risk for progression to active TB among refugees resettled in the United States who are diagnosed with LTBI. Our results reveal that resettled refugees with LTBI have a high prevalence of clinical risk factors for active TB, especially diabetes and current smoking. In addition, though the total number of refugees with a comorbid condition including HIV infection, malignancy, and ESRD was small, this group of refugees was also more likely to be diagnosed with LTBI than refugees without a comorbid medical condition, even after controlling for potential confounding variables.

Recent studies have provided evidence that smoking is an independent risk factor associated with both LTBI and active TB disease.[30–32] Refugees in our study who reported smoking

TABLE 3—Demographic and Clinical Characteristics Associated With LTBI Treatment Initiation Among Newly Arrived Refugees Diagnosed With LTBI Who Were Eligible for and Initiated Treatment of LTBI: San Diego County, CA; January 2010-October 2012

Characteristic	Prevalence of LTBI Treatment Initiation,[a] No. (%)	OR (95% CI)	AOR (95% CI)
Birth region			
Middle East[b] (Ref)	286/364 (78.6)	1.00	1.00
Asia[c]	38/43 (88.3)	2.07 (0.79, 5.44)	2.36 (0.87, 6.38)
Sub-Saharan Africa[d]	49/81 (60.5)	0.42*** (0.25, 0.69)	0.46** (0.27, 0.81)
Other[e]	0/1	. . .	. . .
Age group,[f] y			
13–17 (Ref)	38/52 (73.1)	1.00	1.00
18–34	195/243 (80.2)	1.50 (0.75, 2.98)	1.30 (0.63, 2.68)
35–49	139/193 (72.0)	0.99 (0.49, 1.97)	0.74 (0.35, 1.58)
Gender			
Female (Ref)	142/189 (75.1)	1.00	
Male	231/300 (77.0)	1.11 (0.72, 1.70)	. . .
Education, y			
0–6 (Ref)	102/150 (68.0)	1.00	1.00
7–12	177/228 (77.6)	1.63* (1.03, 2.59)	1.56 (0.95, 2.57)
> 12	94/111 (84.7)	2.60** (1.40, 4.84)	2.46** (1.27, 4.77)
Diabetes mellitus			
No (Ref)	368/482 (76.3)	1.00	
Yes	5/7 (71.4)	0.77 (0.15, 4.05)	. . .
Comorbid condition[g]			
No (Ref)	373/486 (76.7)	1.00	
Yes	0/3[h]	. . .	. . .
Tobacco smoking			
No (Ref)	286/379 (75.5)	1.00	
Yes	87/110 (79.1)	1.23 (0.73, 2.06)	. . .

Note. AOR = adjusted odds ratio; CI = confidence interval; ESRD = end-stage renal disease; LTBI = latent tuberculosis infection; OR = odds ratio; QFT-GIT = QuantiFERON-TB Gold In-Tube.
[a]Number of refugees with LTBI who initiated treatment in cohort (n = 373)/total number with LTBI eligible for treatment in cohort (n = 489)
[b]Iraq, Iran, Afghanistan, Uzbekistan, Syria, Kuwait, Lebanon, Jordan, and Egypt.
[c]Burma, Bhutan, Thailand, Vietnam, India, China, and Taiwan.
[d]Somalia, Ethiopia, Democratic Republic of Congo, Sudan, Eritrea, Uganda, and Kenya.
[e]Cuba, Guatemala, Haiti, Colombia, and unknown.
[f]Age limited to < 50 y because ≥ 50 y is a contraindication for treatment at the San Diego County Refugee Health Assessment Program LTBI clinic. One refugee aged ≥ 50 y was coded as initiating treatment and was excluded from the analysis.
[g]Malignancy, HIV infection, and ESRD combined because of limited numbers.
[h]Three refugees with HIV infection and LTBI were eligible for treatment; their treatment initiation status was unknown because they were referred to infectious disease physicians because of their diagnosis of HIV; 6 refugees with malignancy/ESRD and LTBI were not eligible because of their age (≥ 50 y) but were referred to their community medical providers for consideration of treatment.
*$P \leq .05$. **$P \leq .01$. ***$P \leq .001$.

tobacco had almost twice the odds of LTBI as refugee nonsmokers (AOR = 1.6; 95% CI = 1.3, 2.0); this magnitude of association is similar to that found in a recent meta-analysis by Bates et al.[32] on smoking and TB. Because smoking is a preventable risk factor for TB, efforts to decrease smoking among newly arrived refugees could have important implications for the control of reactivation TB in this population. Furthermore, initiating LTBI treatment of refugees who smoke should be a high priority for medical providers who care for newly arrived refugees.

Our finding that refugees with diabetes were significantly more likely to be diagnosed with LTBI than nondiabetic refugees (AOR = 1.6; 95% CI = 1.1, 2.2) is important because of the rising prevalence of diabetes worldwide. In particular, there has been a large influx of refugees from Iraq in the past decade, and studies on resettled Iraqi refugees have documented high rates of both obesity (a risk factor for diabetes) and diabetes.[29,33,34] Because diabetes is a strong risk factor for the development of active TB,[13,34,35] special attention to Iraqi refugees with diabetes and LTBI is warranted.

Despite the increased risk of LTBI among diabetic refugees and refugees who smoked in our study, it is difficult to draw conclusions regarding LTBI treatment initiation and completion rates among these high-risk refugees because the majority were not offered treatment at the RHAP clinic because of their age and the inability to provide close clinical and laboratory monitoring at the RHAP clinic. Because public health departments are largely responsible for TB prevention and limited research has been done on LTBI treatment rates among refugees treated by private clinicians, additional resources for local health departments to provide treatment to more clinically complex refugees may improve LTBI treatment rates and thus prove to be cost-effective.

Overall, LTBI treatment initiation and completion rates among refugees of Middle Eastern and Asian origin were higher in this study than previously reported in the limited literature on LTBI treatment among refugees. Studies on treatment initiation among refugees in the United States, Canada, and Australia have documented initiation rates from 49% to 76%,[14,28,36] whereas completion rates have consistently been lower than initiation rates and varied from 29% to 69%.[14,28,36–38] Although comparison between studies is difficult because the countries of origin, study design, and sample sizes differ, results from our study highlight local success in preventing active TB specifically among refugees from the Middle East and Asia.

Our finding in the multivariate analysis that refugees born in sub-Saharan Africa were almost half as likely to initiate treatment of LTBI as refugees from the Middle East highlights a priority area for further research and intervention. Possible reasons for this disparity include cultural and communication barriers and clinic-related barriers to care, such as

lack of transportation and the required frequency of clinic visits.

After controlling for birth region, higher education level was positively associated with LTBI treatment initiation; refugees with more than 12 years of education were approximately twice as likely to initiate treatment as refugees with less than 6 years of education (AOR = 2.5; 95% CI = 1.3, 4.8). Furthermore, among refugees initiating treatment of LTBI, we found that refugees with secondary education were more likely to complete treatment than refugees with primary education (OR = 2.5; 95% CI = 1.1, 5.6), though this finding is limited to bivariate analysis only. For public health departments that provide LTBI screening and treatment of recently arrived refugees, results from our study provide evidence that enhanced efforts to provide culturally appropriate health education during the screening process are needed.

Finally, though treatment completion rates did not vary significantly by birth region, it is important to note that this portion of the analysis was limited by the large number of refugees whose treatment completion status was unknown because they moved out of San Diego County (secondary migration) after starting LTBI treatment. This finding suggests that recently resettled refugees are mobile; efforts to improve follow-up for refugees who undergo secondary migration while receiving LTBI treatment could enhance our understanding of completion rates.

Limitations

Our study has several limitations. Refugees self-reported data on smoking, diabetes, malignancy, ESRD, and education. As a result, information bias may have limited the accuracy of these variables; however, self-reporting most likely results in underreporting, because of either perceived stigma (e.g., in the case of reporting smoking behavior to medical professionals) or a previously undiagnosed medical condition (e.g., in the case of diabetes). Misclassification of the arrival age variable as a result of data entry errors in RHEIS could also have been a problem in this study. Given that this was a nondifferential misclassification bias, we are confident it did not affect the study results. Finally, this study is limited to refugees resettling in San Diego County and may not be representative of newly arrived refugees in other health departments in the United States.

Conclusions

Our findings suggest that newly arrived refugees with LTBI have a considerable burden of clinical risk factors that increase their risk for reactivation of TB, which may contribute to the increased proportion of active TB among foreign-born populations in the United States if not prioritized for LTBI treatment. Efforts to ensure adequate LTBI treatment among high-risk refugees such as those documented in this study should be a public health priority. The low treatment initiation among refugees from sub-Saharan Africa in this study is particularly alarming because refugees from this region of the world have been resettling in the United States since 1980.[39] Although there is likely no single factor that accounts for the low treatment rates among this group of refugees, future research using focus groups among African refugees with LTBI could help understand the reasons for this disparity. In addition, public health departments that provide LTBI services to refugees with documented low treatment rates should consider programmatic changes to improve treatment acceptance.

One approach to potentially increase treatment initiation is to offer the 12-week LTBI treatment regimen with weekly INH and rifapentine via directly observed therapy.[40,41] Research is currently under way in the United States to explore the cost-effectiveness of this regimen[42] and evaluate LTBI treatment rates with rifapentine via weekly, directly observed therapy among high-risk groups in Southern California, including newly arrived refugees. Although a shorter course of therapy may not address all treatment barriers among refugees, it provides an opportunity to eliminate the long duration of therapy required with daily INH, which is a known barrier to treatment acceptance and completion[38,43,44] and may also be a barrier to refugees who secondarily migrate after initial resettlement. Among refugees from different cultural backgrounds, weekly, directly observed therapy may also provide an opportunity for enhanced culturally appropriate educational efforts regarding the long-term risk and public health significance of reactivation TB attributable to LTBI. ■

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Contributors

R. J. Bennett was responsible for the data analysis. All authors originated the study design. T. C. Rodwell had ultimate oversight for the study, including the study design, data analysis, and interpretation, and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed equally to the data interpretation and writing of the article.

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Human Participant Protection

This study was reviewed and approved by the institutional review boards of the University of California, San Diego; San Diego State University; and San Diego County Health and Human Services Agency.

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