Tuberculosis Among Foreign-Born Persons in the United States

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Tuberculosis Among Foreign-Born Persons in the United States

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Stephen R. Benoit, MD
Carla A. Winston, PhD
William R. MacKenzie, MD


The main goals of TB control in the United States are (1) to find and treat individuals with TB disease early to minimize transmission to others; and (2) to use tuberculin skin testing or other assays for Mycobacterium tuberculosis to find and treat individuals with latent TB infection (LTBI) (not transmissible) to prevent TB disease. Limitation of transmission of TB to others has mainly been achieved through early diagnosis and treatment of individuals with TB disease and screening of close contacts of these patients for TB disease and LTBI. These measures for interrupting TB transmission are widely practiced in the United States. Outside of contact investigations, testing for LTBI among foreign-born persons who are at high risk for TB disease is recommended, but is not widely implemented in the United States. Studies of TB genotypes in the United States suggest that TB among foreign-born persons is typically due to activation of LTBI, for which infection was likely acquired before US arrival. Since the most widely implemented TB control strategies in the United States focus on interrupting recent transmission of disease, it is understandable why current TB control strategies have limited success in a large subset of foreign-born populations that enter the United States with high rates of LTBI.

As long as TB is a major problem globally, additional strategies will need to be implemented to improve TB control in the US foreign-born population. There are 3 such strategies that can presently be implemented. First, we could enhance overseas premigration screening of immigrants and refugees for TB disease by adding TB cul-

See also Patient Page.
ture to current screening practices. Currently, chest radiography is performed overseas for all US-bound immigrants and refugees older than 15 years of age, and a sputum-smear microscopy for acid-fast bacilli is obtained from individuals with an abnormal chest radiograph or symptoms of TB disease. Individuals entering the United States who are not immigrants or refugees, such as students, workers, and visitors, along with undocumented migrants, are not routinely screened. Approximately 30% of all foreign-born persons in the United States fall into one of these unscreened categories. Second, we could find and treat cases of LTBI among foreign-born persons, including those already living in the United States, and newly arriving migrants at elevated risk for TB could be tested and treated for LTBI after arrival to the United States or prior to US entry. Third, we could make financial and technical investments in global TB control.

The potential effects of these strategies is not currently known. More than 37 million foreign-born persons are currently living in the United States. In 2006, there were nearly 500,000 newly arriving legal immigrants and refugees to the United States from more than 75 countries. The rates of TB range widely in these nations. To date, data have been insufficient to describe which populations of foreign-born persons in the United States would benefit most from LTBI testing and treatment, or identify the populations that need enhanced overseas TB screening prior to US entry. Practical guidance is needed to target LTBI testing and treatment for the highest-risk groups of foreign-born persons in the United States. Population-based data are needed to guide the approach to finding and preventing TB in this population.

**METHODS**

We analyzed data from the US National TB Surveillance System database for TB cases reported from 2001 through 2006. These data are compiled from reports of TB cases submitted to the Centers for Disease Control and Prevention by the 50 states and the District of Columbia using a standardized case report form. The TB case reports include information on each reported individual’s country of birth, month and year of US entry, along with demographic and clinical characteristics. Consistent with US Census Bureau definitions, an individual is classified as a US-born person if he or she was born in the United States or associated jurisdictions or was born in a foreign country but at least 1 parent was a US citizen. All other individuals are classified as foreign-born.

We used the public-use microdata sample files from the 2001-2006 American Community Survey (ACS) to derive population denominators for reported TB cases to calculate case rates. These data were derived from annual surveys of approximately 800,000 to 1.3 million US households and include each reported individual’s country of birth and arrival year in the United States. The ACS does not consider immigration status when surveying households (thus, undocumented migrants are counted) and, along with the TB Surveillance System, did not report data on immigration status. Therefore, our analysis includes data on all foreign-born persons living in the United States and does not consider immigration status. Case rates are reported as the annual number of cases per 100,000 persons. When we report that case rates are stratified, the rate reported is a stratum-specific rate. For selected countries from which there are few individuals living in the United States, the ACS combines countries into groups and provides population data for the group. We compared TB rates with respect to each reported individual’s country of origin, age at arrival to the United States, and time between US entry and TB diagnosis. For instances in which the ACS combined data for countries, we combined TB case data into groups inclusive of the same countries and applied the TB rate calculated for the group to all countries included in that group. Details of how the ACS groups selected countries are available at the US Census Bureau Web site.

For some analyses, we dichotomized time after the individual’s US entry and defined as a recent entrant any person who entered the United States 2 years or less before receiving a TB diagnosis, and any person who entered the United States more than 2 years before receiving a TB diagnosis as a nonrecent entrant. We used 2 years as the cutoff because TB rates are known to decline rapidly 1 to 5 years after US entry and because risk of activation to TB disease is highest in the first 2 years after being infected. While time of infection is not known, time of entry is the time at which exposure to endemic TB ended. For TB cases, time since US entry was calculated by subtracting the month and year of US entry from month and year of the case report date. For instances in which the month of US entry was missing, we set it equal to June. Individuals without year-of-arrival data were excluded from further analysis. Details of the use of ACS data for determining the population denominators were previously reported.

We assessed drug-resistance patterns for isolates from TB patients from the 15 most common foreign countries of origin that contributed cases to the US National TB Surveillance System. We reported results of initial drug susceptibility testing for new TB patients who were culture-positive at the time of TB diagnosis. We defined patients with any resistance to isoniazid as isoniazid-resistant and patients with resistance to both isoniazid and rifampin as having multidrug-resistant TB.

To understand the burden of potentially imported TB disease and therefore the potential impact of enhanced pre-entry overseas TB screening, we analyzed data for foreign-born persons diagnosed with TB less than 3 months after US entry and less than 6 months after US entry. We characterized the epidemiology of these patients according to results of each patient’s chest radiography, sputum smear, and sputum culture results at the time of their TB diagnosis, along with
their country of origin. Because neither the TB case data nor the ACS data report the immigration status of individuals, it was not possible to determine what type of preimmigration screening was actually required for each individual.

Ethical Review
The protocol for this project was reviewed by the Centers for Disease Control and Prevention and found to be public health surveillance and not human subjects research, which requires oversight by an institutional review board and informed consent.

RESULTS
From 2001 through 2006, 46 998 TB cases were reported among foreign-born persons of which 28 were excluded because the country of origin was missing. Of the 46 970 remaining cases, 12 928 (28%) were recent entrants compared with 32 337 (69%) nonrecent entrants; duration of residence was unknown for 1705 (4%) patients. Case rates were highest among foreign-born persons who had entered the United States most recently. However, even foreign-born persons who had lived in the United States for more than 20 years had annual TB case rates of more than 10 per 100 000 persons, which was greater than 4 times the rate among US-born persons in 2006 (Figure 1).

![Figure 1. Number of TB Cases and Annual Case Rates Among Foreign-Born Persons in the United States, Years Since US Entry 2001-2006](image)

Reflects 46 970 reported cases of tuberculosis (TB); 1705 cases are not shown because years since US entry were unknown.

Table 1. Annual TB Case Rates and Drug Resistance Among Foreign-Born Persons by Country of Birth, 2001-2006

<table>
<thead>
<tr>
<th>15 Most Commonly Reported Countries of Birth</th>
<th>Annual TB Case Rates in the United States/100 000 Persons</th>
<th>Drug Resistance Among Foreign-Born Persons in the United States With Culture-Positive TB</th>
<th>US Entry ≤2 y (n = 8708)</th>
<th>US Entry &gt;2 y (n = 24 325)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mexico</td>
<td>52 14</td>
<td>2008[171(9)] 31(2)</td>
<td>6052(455) 53(1)</td>
<td></td>
</tr>
<tr>
<td>Philippines</td>
<td>283 38</td>
<td>956[158(17)] 16(2)</td>
<td>393(15) 32(1)</td>
<td></td>
</tr>
<tr>
<td>Vietnam</td>
<td>319 47</td>
<td>505[100(20)] 11(2)</td>
<td>354(16) 24(1)</td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>106 33</td>
<td>755[86(11)] 21(3)</td>
<td>205(11) 28(2)</td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>74 26</td>
<td>305[48(16)] 17(6)</td>
<td>120(10) 14(1)</td>
<td></td>
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<tr>
<td>Haiti</td>
<td>189 40</td>
<td>229[22(10)] 1(&lt;1)</td>
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<tr>
<td>North and South Koreaa</td>
<td>40 19</td>
<td>156[21(13)] 6(4)</td>
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</tr>
<tr>
<td>Guatemala</td>
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<td>306[22(7)] 2(1)</td>
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<td>Ecuador</td>
<td>194 31</td>
<td>224[11(5)] 3(1)</td>
<td>32(7) 4(1)</td>
<td></td>
</tr>
<tr>
<td>Peru</td>
<td>159 32</td>
<td>235[42(18)] 15(6)</td>
<td>67(14) 15(3)</td>
<td></td>
</tr>
<tr>
<td>Ethiopia and Eritrea</td>
<td>562 82</td>
<td>292[34(12)] 4(1)</td>
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<td></td>
</tr>
<tr>
<td>Somalia</td>
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<td>294[36(12)] 5(2)</td>
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<td></td>
</tr>
<tr>
<td>El Salvador</td>
<td>73 11</td>
<td>164[10(6)] 1(1)</td>
<td>27(6) 2(&lt;1)</td>
<td></td>
</tr>
<tr>
<td>Honduras</td>
<td>177 28</td>
<td>222[12(5)] 0</td>
<td>37(4) 0</td>
<td></td>
</tr>
<tr>
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<td>307 65</td>
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</tr>
<tr>
<td>All others</td>
<td>2011 197(10) 37(2)</td>
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Abbreviations: MDR, multidrug resistant; TB, tuberculosis.

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Abbreviations: MDR, multidrug resistant; TB, tuberculosis.

aIncludes only patients with no previous history of TB and excludes culture-positive patients without drug-susceptibility testing results (n = 279).
bIncludes only patients with no previous history of TB and excludes culture-positive patients without drug-susceptibility testing results (n = 771).
cCountries were combined for consistency with American Community Survey data, which combined them for part of the study period.
When stratified by country of birth, recent entrants consistently had case rates 3 to 7 times higher than nonrecent entrants (Table 1). Rates varied substantially by country and region of origin. Individuals born in most countries of sub-Saharan Africa had annual case rates of greater than 250 per 100,000 persons during the first 2 years after US entry, while individuals born in Central America, Eastern Europe, the Pacific Islands, and South, East, and Central Asia had annual case rates of greater than 100 per 100,000 persons in the first 2 years. Risk was low among individuals born in Western Europe, Japan, Canada, Australia, and New Zealand, all of which had annual case rates of less than 10 per 100,000 persons (Figure 2). The pattern was similar for nonrecent entrants, but the rates were lower (Table 1).

In total, an average of 4035 TB cases per year were reported among individuals born in high-risk countries (populations with annual case rates of 100 or greater per 100,000 persons among recent entrants; Figure 2). Individuals born in these countries account for 53% of the total annual number of cases among foreign-born persons, but comprised just 22% of the total US foreign-born population (Table 2). Consequently, TB case rates varied by age at US entry for recent and nonrecent entrants. Annual case rates for recent entrants were 25 to 30 per 100,000 persons for individuals younger than 5 years of age at arrival in the United States and increased to exceed 100 per 100,000 persons for those aged 50 years or older at the time of US entry. Annual case rates for nonrecent entrants also rose with age at entry, ranging from less than 5 per 100,000 persons for individuals younger than 5 years of age at arrival in the United States to greater than 60 per 100,000 persons for those aged 60 years or older at US entry. While most cases among foreign-born persons occurred in individuals aged 15 to 40 years at US entry, case rates continued to rise with increasing age at arrival (Figure 3). For individuals arriving in the United States at aged 40 years or older, TB case rates among nonrecent entrants do not decrease with increasing time in the United States. Individuals between 60 and 80 years of age at arrival in the United States had annual TB rates of greater than 65 cases per 100,000 persons (Figure 4).

Table 2. Number and Proportion of TB Cases and Total Foreign-Born Population by Country of Birth Risk Category, 2001-2006

<table>
<thead>
<tr>
<th>Risk Category, Annual TB Case Rate/100,000 Persons</th>
<th>Total No. (%)</th>
<th>Annual No. of TB Cases</th>
<th>Average Annual Foreign-Born Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥250</td>
<td>2267 (30)</td>
<td>33660000 (9)</td>
<td></td>
</tr>
<tr>
<td>100-249</td>
<td>1768 (23)</td>
<td>44840000 (12)</td>
<td></td>
</tr>
<tr>
<td>10-99</td>
<td>3375 (45)</td>
<td>22182000 (61)</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>134 (2)</td>
<td>6058000 (17)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>7544</td>
<td>36090000</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: TB, tuberculosis.

*Risk category refers to populations from specific countries of birth as shown in Figure 2.
Drug resistance was more common among foreign-born than among US-born persons, and there were differences in drug resistance patterns across countries. While just 4.4% of US-born persons with TB had isolates resistant to isoniazid, resistance was found in 11% of recent entrants and in 10% of nonrecent entrants overall. Among recent entrants who were culture-positive, isoniazid resistance was found in 20% from Vietnam, 18% from Peru, 17% from the Philippines, and 16% from China. Resistance was less common in Latin America (other than Peru). Isoniazid resistance was generally more common among recent entrants than among nonrecent entrants (Table 1).

Multidrug-resistant TB was most common among individuals from Peru and China, with 6% of isolates from recent entrants resistant to isoniazid and rifampin, compared with just 0.6% among US-born persons. The proportion of individuals from other countries with multidrug-resistant TB was generally 4% or less. Multidrug-resistant TB was more common among recent entrants compared with nonrecent entrants (Table 1).

New preentry screening procedures for immigrants and refugees outlined in 2007 and currently implemented in select countries\(^{17}\) direct that cultures be obtained from individuals with an abnormal chest radiograph and negative sputum smears. We found that a total of 4499 foreign-born persons were reported with TB disease within 3 months of US entry, of whom 4104 (91%) had pulmonary disease. Of these, 1211 individuals (30%) had findings of an abnormal chest radiograph and a positive sputum smear and thus, if eligible, could likely have had TB detected through preentry screening procedures in place before 2007 (818 individuals [68%] were from countries other than Mexico).\(^{18}\)

An additional 1502 individuals (37%) during this 6-year period had an abnormal chest radiograph and a negative sputum smear, but a positive sputum culture. Thus, 1502 cases, approximately 250 per year on average, represent the maximum number of additional cases that could have been detected if all foreign-born persons were screened prior to US entry using the new screening procedures (Table 3). Of these smear-negative cases, 46% were from individuals from Vietnam or the Philippines. If we include any individual diagnosed with TB within 6 months of US entry, a maximum of 2066 additional cases could potentially have been detected from 2001 through 2006 if all foreign-born persons were screened prior to entry and if those with an abnormal radiograph reading had been screened with TB culture (Table 3).
With more than 37 million foreign-born persons currently living in the United States, it is not possible to find and test all foreign-born persons for LTBI. This study assists in targeting LTBI screening efforts by examining risk of TB disease among subgroups of foreign-born populations. Finding and treating LTBI among some specific groups of foreign-born persons living in the United States is likely to provide high yield relative to some other TB control strategies. Given current immigration patterns, the impact of culture-enhanced overseas screening of immigrants and refugees is likely to be greatest in the Philippines and Vietnam, but may have limited yield for most other countries of birth.

Among all foreign-born populations, rates are highest in the first 2 years after US entry. Rates are especially high (>250/100,000 persons annually) among recent entrants from many countries of sub-Saharan Africa and Southeast Asia (Figure 2). With such high annual rates, more than 0.5% of all migrants from these countries will develop TB within 2 years of US entry. Annual rates are as high as 889 per 100,000 persons for individuals from Somalia and 562 per 100,000 persons for individuals from Ethiopia and Eritrea. Thus, 1.8% of all migrants from Somalia and 1.1% from Ethiopia and Eritrea develop TB within 2 years after US entry. These rates are comparable to those among close contacts of TB patient cases in the United States. Since 20% to 30% of TB patient case contacts will be found to have LTBI,19 and approximately 5% of individuals with recently acquired LTBI will develop TB within 2 years,16 1.0% to 1.5% of TB contacts will develop TB disease. These high rates would suggest that LTBI testing and treatment among recent entrants from the highest-risk countries (those with annual rates of 250 or greater per 100,000 persons among recent entrants; Figure 2) should be a high priority, similar to that of TB contact investigations. Likewise, a health care worker’s suspicion of TB should be as high for a recent entrant from one of these areas as it would be for a patient presenting with reported recent contact with infectious pulmonary TB.

While TB rates generally decrease after foreign-born persons have lived in the United States for more than 2 years, the rates can still be markedly higher than among rates of US-born persons. Since 69% of TB cases among foreign-born persons in the United States occur among individuals who have lived in the United States for more than 2 years, this burden clearly must be addressed to control and eliminate TB. Populations with the highest rates of TB disease within the first 2 years after US entry typically have the highest rates beyond 2 years as well.

Over half of all TB cases in foreign-born persons occurred in the 22% of the foreign-born population born in sub-Saharan Africa and Southeast Asia. In contrast, individuals in the United States who were born in Canada, Australia, New Zealand, countries of Western Europe, and Japan have very low annual rates of TB disease (<10/100,000). Since rates are low and individuals from these countries account for 17% of the population but only 2% of TB cases among foreign-born individuals, these populations should not be routinely targeted for LTBI testing and treatment unless other TB risk factors are present.2 Clinicians should consider LTBI testing for any foreign-born patient other than these. When resource constraints do not permit testing all foreign-born persons, as is often the case in health departments and community outreach programs, LTBI screening activities should be as high yield as possible. Such programs should prioritize screening to target as many individuals from the highest-risk countries of birth as resources allow (Figure 2).

Age at arrival into the United States is an important factor to consider when assessing risk of TB disease among foreign-born persons. While the majority of TB cases were reported among individuals who were aged 15 to 40 years at US entry, TB disease rates increased with increasing age at US entry. We also found that for individuals who had been in the United States for more than 2 years, case rates for those 40 years of age or older were similar for all non-recent year spans after US entry. Several factors may influence the rising rates of disease with increasing age of US arrival, including (1) increased time of exposure to a high burden of TB in the country of origin, which may be reflected by higher LTBI prevalence; and (2) among individuals with LTBI, diminishing immune function with advanced age makes activation to TB disease more common.15,20,21 Given the increasing risk of disease with increasing age at US entry, older individuals should not be excluded from LTBI

### Table 3. Reported TB Cases Among Foreign-Born Persons in the United States Less Than 3 Months and Less Than 6 Months, 2001-2006

<table>
<thead>
<tr>
<th>Time Since US Entry, mo</th>
<th>No. of TB Cases, 2001-2006</th>
<th>Pulmonary Cases</th>
<th>Abnormal Radiograph</th>
<th>Normal or No Radiograph</th>
<th>Negative Sputum Smear, Culture-Positive</th>
<th>Negative Sputum Smear, Culture-Positive</th>
<th>Negative Sputum Smear, Culture-Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>4499</td>
<td>4104 (91)</td>
<td>1211 (30)</td>
<td>1502 (37)</td>
<td>31 (1)</td>
<td>101 (2)</td>
<td>1259 (31)</td>
</tr>
<tr>
<td>&lt;6</td>
<td>6835</td>
<td>6036 (88)</td>
<td>1924 (32)</td>
<td>2066 (34)</td>
<td>40 (1)</td>
<td>133 (2)</td>
<td>1873 (32)</td>
</tr>
</tbody>
</table>

Abbreviation: TB, tuberculosis.

aIncludes patients with pulmonary TB only and patients with both pulmonary and extrapulmonary TB.
screening and treatment on the basis of age alone. In spite of increased risk of toxicity with LTBI treatment with increasing age, treatment remains cost-effective regardless of age.22-25

Finding foreign-born persons with LTBI is in itself insufficient. Steps are needed, including culturally sensitive approaches, to ensure high rates of safe LTBI treatment initiation and completion.6-31 As with all medications, LTBI treatment should be given according to guidelines for adverse event monitoring.4-22 If appropriate monitoring cannot be provided, treatment should not be started.

Increasing levels of drug resistance complicate TB treatment. Drug resistance is especially common in individuals from Asia. Given that isoniazid treatment is favored even in the presence of high levels of resistance,33 however, alternative LTBI treatment is available, such as with use of rifampin. Further studies are needed to determine the most appropriate choice for LTBI treatment for populations with high rates of resistance to isoniazid, rifampin, or both.

We found that the potential impact of adding mycobacterial culture to overseas TB screening among foreign-born persons will likely be limited. Performing TB culture on every foreign-born person prior to US entry would have prevented importation of approximately 250 TB cases per year during that 5-year period. The true number of imported cases prevented by enhanced overseas screening would be smaller than this because (1) some of these patients may have developed TB disease after arrival or had negative spu
tum culture results at the time of screening; and (2) only immigrants and refugees are screened prior to US entry, not all foreign-born persons.34 Since we do not know the visa status of the patients with TB, we do not know what proportion of the individuals diagnosed with TB would have been subjects to screening before US entry. Adding culture to screening in Vietnam and the Philippines first would provide the highest yield. The 2007 technical instructions for overseas screening have added culture to the screening process and are currently being implemented in select countries.35 The impact of culture-enhanced screening should be evaluated to monitor progress in controlling and eliminating TB among foreign-born persons.

Current strategies for TB control, as presently implemented, are not adequate for achieving TB elimination in the near future. TB control and elimination among foreign-born persons in the United States will require a multifaceted approach.9 In the future, preventing TB disease among legal immigrants to the United States might best be accomplished through overseas diagnosis and treatment of LTBI prior to immigration. The present use of a 9-month regimen for LTBI treatment makes this strategy impractical. This strategy may be both feasible and high yield when shorter, effective treatment regimens for LTBI become available. Increased investment in global TB control could also result in decreases in US TB rates. One study suggests investment in TB control may be more cost effective than other strategies in the 3 countries studied: Mexico, Haiti, and the Dominican Republic.31

Substantial improvements in TB control among foreign-born persons in the United States can be made now. LTBI testing and treatment among foreign-born persons needs to be more widely implemented, but even when it cannot be fully implemented, its yield can be higher by focusing on the highest-risk populations of foreign-born persons first.

Author Contributions: Dr Cain had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Acquisition of data: Cain.

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Drafting of the manuscript: Cain, Benoit.

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