ORIGINAL ARTICLE

Overseas Screening for Tuberculosis in U.S.-Bound Immigrants and Refugees

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ABSTRACT

BACKGROUND

In 2007, a total of 57.8% of the 13,293 new cases of tuberculosis in the United States were diagnosed in foreign-born persons, and the tuberculosis rate among foreign-born persons was 9.8 times as high as that among U.S.-born persons (20.6 vs. 2.1 cases per 100,000 population). Annual arrivals of approximately 400,000 immigrants and 50,000 to 70,000 refugees from overseas are likely to contribute substantially to the tuberculosis burden among foreign-born persons in the United States.

METHODS

The Centers for Disease Control and Prevention (CDC) collects information on overseas screening for tuberculosis among U.S.-bound immigrants and refugees, along with follow-up evaluation after their arrival in the United States. We analyzed screening and follow-up data from the CDC to study the epidemiology of tuberculosis in these populations.

RESULTS

From 1999 through 2005, a total of 26,075 smear-negative cases of tuberculosis (i.e., cases in which a chest radiograph was suggestive of active tuberculosis but sputum smears were negative for acid-fast bacilli on 3 consecutive days) and 22,716 cases of inactive tuberculosis (i.e., cases in which a chest radiograph was suggestive of tuberculosis that was no longer clinically active) were diagnosed by overseas medical screening of 2,714,223 U.S.-bound immigrants, representing prevalences of 961 cases per 100,000 persons (95% confidence interval [CI], 949 to 973) and 837 cases per 100,000 persons (95% CI, 826 to 848), respectively. Among 378,506 U.S.-bound refugees, smear-negative tuberculosis was diagnosed in 3923 and inactive tuberculosis in 10,743, representing prevalences of 1036 cases per 100,000 persons (95% CI, 1004 to 1068) and 2838 cases per 100,000 persons (95% CI, 2785 to 2891), respectively. Active pulmonary tuberculosis was diagnosed in the United States in 7.0% of immigrants and refugees with an overseas diagnosis of smear-negative tuberculosis and in 1.6% of those with an overseas diagnosis of inactive tuberculosis.

CONCLUSIONS

Overseas screening for tuberculosis with follow-up evaluation after arrival in the United States is a high-yield intervention for identifying tuberculosis in U.S.-bound immigrants and refugees and could reduce the number of tuberculosis cases among foreign-born persons in the United States.

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Tuberculosis is the second most common cause of death from infectious diseases in the world.[1] During the period from 1990 through 2003, the incidence of tuberculosis increased globally.[2] The World Health Organization (WHO) has reported that Asia and sub-Saharan Africa accounted for 84.1% of the estimated 8.8 million new cases of tuberculosis worldwide in 2005.[3] Global migration has greatly affected the epidemiology of tuberculosis in developed countries. In 2007, foreign-born persons accounted for 57.8% of new cases of tuberculosis in the United States.[4] In that year, the tuberculosis rate in the United States was 20.6 cases and 2.1 cases per 100,000 population among foreign-born and U.S.-born persons, respectively.[4] Furthermore, 27.5% of tuberculosis cases among foreign-born persons are diagnosed within 2 years after the person's arrival in the United States.[5] Approximately 400,000 immigrants and 50,000 to 70,000 refugees arrive in the United States annually, many from countries with a high incidence of tuberculosis.[6] Therefore, these populations are likely to contribute substantially to the tuberculosis burden among foreign-born persons in United States.

To eliminate tuberculosis in the United States, it is essential to control and prevent tuberculosis in foreign-born persons.[7] Overseas tuberculosis screening of U.S.-bound immigrants and refugees, coupled with follow-up evaluation after their arrival in the United States, is considered to be one intervention that may decrease the incidence of tuberculosis in foreign-born persons in the United States.[8] Previous studies of this intervention have focused primarily on the follow-up evaluation at state and local levels,[9-17] although one recent study examined the efficacy of overseas screening for tuberculosis among U.S.-bound immigrants in Vietnam.[18] To understand the epidemiology of tuberculosis in U.S.-bound immigrants and refugees, we analyzed data from the Centers for Disease Control and Prevention (CDC) notification system for tuberculosis in immigrants and refugees.

METHODS

POPULATIONS OF U.S.-BOUND IMMIGRANTS AND REFUGEES

Demographic data for 2,714,223 immigrants who received a visa for permanent residence and who arrived in the United States during the period from 1999 through 2005 were obtained from the U.S. Department of Homeland Security. Demographic data for 378,506 refugees who arrived in the United States during the same period were obtained from the CDC's notification system for tuberculosis in immigrants and refugees, which collects information about overseas screening for tuberculosis and follow-up evaluation of immigrants and refugees after their arrival in the United States. The office of the Associate Director for Science, Division of Global Migration and Quarantine, CDC, determined that this analysis was considered to be part of the CDC's public health surveillance activities, not human-subjects research, and therefore approval by an institutional review board and informed consent were not required.

OVERSEAS SCREENING FOR TUBERCULOSIS

A medical examination performed overseas is required for U.S.-bound immigrants and refugees. The U.S. embassies and consulates appoint 400 to 800 licensed local physicians worldwide as panel physicians to perform the examinations.[7,8] The U.S. Department of State sponsors refugees, but immigrants are responsible for paying for their own examinations. Although there is no formal certification process, the CDC provides technical guidance and oversight to the panel physicians.[7,8,19] Screening for tuberculosis is a major component of the examination. During the period from 1999 through 2005, the tuberculosis screening algorithm, which was based on the 1991 Technical Instructions for Panel Physicians, consisted of a standard posteroanterior radiograph of the chest for persons 15 years of age or older; in the case of those with a chest radiograph suggestive of active tuberculosis or with symptoms of tuberculosis, sputum specimens were obtained on 3 consecutive days and stained for acid-fast bacilli.[19] Panel physicians made local arrangements for the radiologic and laboratory examinations required as part of the screening.[8] No mycobacterial cultures were obtained during the study period. Children younger than 15 years of age were required to undergo screening for tuberculosis only if they had a history of tuberculosis, signs or symptoms suggestive of tuberculosis, or close contact with someone who had tuberculosis.

Persons were classified as having smear-positive tuberculosis if the chest radiograph was sug-

gestive of active tuberculosis and one or more sputum smears were positive for acid-fast bacilli; smear-negative tuberculosis if the chest radiograph was suggestive of active tuberculosis and sputum smears were negative for acid-fast bacilli on 3 consecutive days; inactive tuberculosis if the chest radiograph was suggestive of tuberculosis that was not clinically active (e.g., showing fibrosis, scarring, pleural thickening, diaphragmatic tenting, or blunting of costophrenic angles); or no tuberculosis, if the chest radiograph was normal.[19] Persons with smear-positive tuberculosis had two options: either complete a course of tuberculosis therapy, administered over a specified period of time with documented smear negativity at the end of treatment, at which point they would be reclassified as having inactive tuberculosis, or receive tuberculosis treatment until sputum smears became negative and then apply for a medical immigration waiver.[7,8] Persons with immigration waivers were allowed to travel to the United States but were instructed to report to the U.S. jurisdictional public health agency for evaluation.[7,8] Persons with smear-negative or inactive tuberculosis were allowed to travel without restriction, although a voluntary evaluation visit to the U.S. jurisdictional health agency after their arrival in the United States was recommended.[7,8] Although aggregate national data are unavailable, previous studies indicate that the percentage of post-arrival follow-up evaluations that are completed varies widely among tuberculosis-control programs of state and local health departments, ranging from 63.6 to 97.3%.[8,10,13,14]

FOLLOW-UP EVALUATION AFTER ARRIVAL IN THE UNITED STATES

When immigrants and refugees with overseas diagnoses of tuberculosis arrive at U.S. ports of entry, their medical-examination forms (Department of State forms DS-2053, DS-3024, DS-3025, and DS-3026) are collected by the U.S. Citizenship and Immigration Services of the Department of Homeland Security and forwarded to the CDC Quarantine Station that has jurisdiction over the port of arrival.[7] The CDC notifies health departments of arriving immigrants and refugees in whom tuberculosis was diagnosed overseas. Health department physicians are asked to conduct a follow-up evaluation, assign a post-arrival tuberculosis diagnosis, and sign and return the follow-up evaluation form (CDC form 75.17) to the CDC. We categorized the status of these immigrants and refugees in the following way: follow-up completed, if the evaluation form included information about a tuberculosis diagnosis; follow-up not completed, if the evaluation form had other follow-up information but did not have information about a tuberculosis diagnosis; lost to follow-up, if the evaluation form had no follow-up information or indicated that the person had not been located; or follow-up form not received by the CDC. On the basis of results of chest radiography and sputum smears, health department physicians assigned one of the following post-arrival diagnoses for persons who completed the follow-up evaluation: active pulmonary tuberculosis; extrapulmonary tuberculosis; pulmonary tuberculosis, activity undetermined; inactive tuberculosis; or no tuberculosis.

The percentage of post-arrival follow-up evaluations that were completed could not be calculated, since some evaluation forms were not received by the CDC. We therefore estimated a lower percentage and a higher percentage. The lower estimate was based on the assumption that immigrants and refugees did not complete the follow-up evaluation if their evaluation forms were not received by the CDC. The higher estimate was based on the assumption that they completed the follow-up evaluation even though their evaluation forms were not received by the CDC.

STATISTICAL ANALYSIS

In this analysis, we focused on smear-negative and inactive tuberculosis. We calculated the prevalence of smear-negative and inactive tuberculosis among immigrants and refugees, examined time trends for the prevalence of these conditions, and analyzed the results of the post-arrival follow-up evaluation. The WHO regions used in the analysis were the African region, the region of the Americas, the Eastern Mediterranean region, the European region, the Southeast Asian region, and the Western Pacific region.[3] The chi-square test or Fisher's exact test was used to compare proportions. The Cochran–Armitage test was used to analyze time trends for prevalence and to generate associated P values.[20,21] The time-trend statistic was computed on the basis of actual yearly data. All analyses were performed with the use of SAS software, version 9.13 (SAS Institute). All reported P values are two-sided and have not been adjusted for multiple testing.

RESULTS

RATES OF TUBERCULOSIS IN U.S.-BOUND IMMIGRANTS AND REFUGEES

During the period from 1999 through 2005, among 2,714,223 U.S.-bound immigrants screened overseas, smear-negative tuberculosis was diagnosed in 26,075 and inactive tuberculosis in 22,716, representing prevalences of 961 cases per 100,000 persons (95% confidence interval [CI], 949 to 973) and 837 cases per 100,000 persons (95% CI, 826 to 848), respectively (Table 1). Among 378,506

Table 1. Prevalences of Smear-Negative and Inactive Tuberculosis among U.S.-Bound Immigrants, 1999–2005.

Variable	All Immigrants	Immigrants with Smear-Negative Tuberculosis		Immigrants with Inactive Tuberculosis	
	no. (%)	*no. (%)*	*no./100,000 persons (95% CI)*	*no. (%)*	*no./100,000 persons (95% CI)*
Total	2,714,223 (100.0)	26,075 (100.0)	961 (949–973)	22,716 (100.0)	837 (826–848)
Sex					
Male	1,203,271 (44.3)	13,175 (50.5)	1095 (1076–1114)	11,146 (49.1)	926 (909–943)
Female	1,510,952 (55.7)	12,900 (49.5)	854 (839–869)	11,570 (50.9)	766 (752–780)
Age					
0–14 yr	676,821 (24.9)	2,024 (7.8)	299 (286–312)	412 (1.8)	61 (55–67)
15–24 yr	535,218 (19.7)	1,077 (4.1)	201 (189–213)	1,183 (5.2)	221 (208–234)
25–44 yr	821,394 (30.3)	5,422 (20.8)	660 (642–678)	4,881 (21.5)	594 (577–611)
45–64 yr	500,072 (18.4)	10,643 (40.8)	2128 (2088–2168)	9,683 (42.6)	1936 (1898–1974)
≥65 yr	180,718 (6.7)	6,909 (26.5)	3823 (3734–3912)	6,557 (28.9)	3628 (3542–3714)
World Health Organization region of birth					
African	148,095 (5.5)	41 (0.2)	28 (19–37)	159 (0.7)	107 (90–124)
The Americas	1,029,503 (37.9)	1,491 (5.7)	145 (138–152)	3,249 (14.3)	316 (305–327)
Eastern Mediterranean	220,672 (8.1)	41 (0.2)	19 (13–25)	268 (1.2)	121 (106–136)
European	370,071 (13.6)	298 (1.1)	81 (72–90)	1,169 (5.1)	316 (298–334)
Southeast Asian	250,988 (9.2)	444 (1.7)	177 (160–194)	1,885 (8.3)	751 (717–785)
Western Pacific	694,894 (25.6)	23,760 (91.1)	3419 (3376–3462)	15,986 (70.4)	2300 (2265–2335)
Country of birth*					
Philippines	216,508 (8.0)	15,106 (57.9)	6977 (6869–7085)	7,346 (32.3)	3393 (3317–3469)
Vietnam	114,764 (4.2)	6,980 (26.8)	6082 (5943–6221)	1,721 (7.6)	1500 (1429–1571)
China†	202,395 (7.5)	1,383 (5.3)	683 (647–719)	3,600 (15.8)	1779 (1721–1837)
Mexico	389,408 (14.3)	991 (3.8)	254 (238–270)	1,200 (5.3)	308 (290–326)
India	181,735 (6.7)	357 (1.4)	196 (175–217)	1,438 (6.3)	791 (750–832)
Other	1,609,413 (59.3)	1,258 (4.8)	78 (74–82)	7,411 (32.6)	460 (450–470)
Prevalence of tuberculosis in birth country‡					
0–9 cases/100,000	170,727 (6.3)	17 (0.1)	10 (5–15)	97 (0.4)	57 (45–69)
10–19 cases/100,000	110,148 (4.1)	10 (<0.1)	9 (3–15)	148 (0.7)	134 (112–156)
20–49 cases/100,000	629,895 (23.2)	1,029 (3.9)	163 (153–173)	1,665 (7.3)	264 (251–277)
50–99 cases/100,000	229,260 (8.4)	103 (0.4)	45 (36–54)	1,843 (8.1)	804 (767–841)
100–149 cases/100,000	334,288 (12.3)	460 (1.8)	138 (125–151)	2,085 (9.2)	624 (597–651)
≥150 cases/100,000	1,207,380 (44.5)	24,385 (93.5)	2020 (1995–2045)	16,165 (71.2)	1339 (1318–1360)
No estimate	32,525 (1.2)	71 (0.3)	218 (166–270)	713 (3.1)	2192 (2031–2353)

* Countries are listed in descending order, according to the total number of persons with smear-negative and inactive tuberculosis.
† The values for China do not include those for Taiwan, Hong Kong, or Macau.
‡ Values are World Health Organization estimates for 2005.

U.S.-bound refugees, smear-negative tuberculosis was diagnosed in 3923 and inactive tuberculosis in 10,743, representing prevalences of 1036 cases per 100,000 persons (95% CI, 1004 to 1068) and 2838 cases per 100,000 persons (95% CI, 2785 to 2891), respectively (Table 2). The prevalence of smear-negative tuberculosis among refugees was slightly higher than that among immigrants, but

Table 2. Prevalences of Smear-Negative and Inactive Tuberculosis among U.S.-Bound Refugees, 1999–2005.

Variable	All Refugees	Refugees with Smear-Negative Tuberculosis		Refugees with Inactive Tuberculosis	
	no. (%)	*no. (%)*	*no./100,000 persons (95% CI)*	*no. (%)*	*no./100,000 persons (95% CI)*
Total	378,506 (100.0)	3923 (100.0)	1036 (1004–1068)	10,743 (100.0)	2,838 (2,785–2,891)
Sex					
Male	194,197 (51.3)	2276 (58.0)	1172 (1124–1220)	6,488 (60.4)	3,341 (3,261–3,421)
Female	184,309 (48.7)	1647 (42.0)	894 (851–937)	4,255 (39.6)	2,309 (2,240–2,378)
Age					
0–14 yr	117,752 (31.1)	86 (2.2)	73 (57–89)	143 (1.3)	121 (101–141)
15–24 yr	86,996 (23.0)	445 (11.3)	512 (464–560)	2,127 (19.8)	2,445 (2,342–2,548)
25–44 yr	113,357 (29.9)	1309 (33.4)	1155 (1092–1218)	2,913 (27.1)	2,570 (2,477–2,663)
45–64 yr	45,775 (12.1)	1136 (29.0)	2482 (2338–2626)	3,243 (30.2)	7,085 (6,849–7,321)
≥65 yr	14,626 (3.9)	947 (24.1)	6475 (6073–6877)	2,317 (21.6)	15,842 (15,247–16,437)
World Health Organization region of birth					
African	58,286 (15.4)	339 (8.6)	582 (519–645)	739 (6.9)	1,268 (1,176–1,360)
The Americas	22,612 (6.0)	3 (0.1)	13 (0–30)	46 (0.4)	203 (142–264)
Eastern Mediterranean	91,426 (24.2)	443 (11.3)	485 (439–531)	3,165 (29.5)	3,462 (3,343–3,581)
European	162,744 (43.0)	1396 (35.6)	858 (813–903)	5,428 (50.5)	3,335 (3,247–3,423)
Southeast Asian	14,605 (3.9)	150 (3.8)	1027 (860–1194)	75 (0.7)	514 (395–633)
Western Pacific	28,833 (7.6)	1592 (40.6)	5521 (5256–5786)	1,290 (12.0)	4,474 (4,234–4,714)
Country of birth*					
Ukraine	37,955 (10.0)	620 (15.8)	1634 (1505–1763)	2,071 (19.3)	5,456 (5,226–5,686)
Vietnam	24,059 (6.4)	1155 (29.4)	4801 (4529–5073)	1,190 (11.1)	4,946 (4,670–5,222)
Somalia	32,434 (8.6)	271 (6.9)	836 (735–937)	1,930 (18.0)	5,951 (5,692–6,210)
Bosnia and Herzegovina	56,644 (15.0)	137 (3.5)	242 (201–283)	1,202 (11.2)	2,122 (2,002–2,242)
Sudan	18,486 (4.9)	112 (2.9)	606 (491–721)	1,029 (9.6)	5,566 (5,233–5,899)
Other	208,928 (55.2)	1628 (41.5)	779 (741–817)	3,321 (30.9)	1,590 (1,536–1,644)
Prevalence of tuberculosis in birth country†					
0–9 cases/100,000	3,380 (0.9)	0	0 (0–15)	7 (0.1)	207 (39–375)
10–19 cases/100,000	20,501 (5.4)	3 (0.1)	15 (0–34)	37 (0.3)	180 (120–240)
20–49 cases/100,000	37,068 (9.8)	75 (1.9)	202 (155–249)	307 (2.9)	828 (734–922)
50–99 cases/100,000	81,891 (21.6)	313 (8.0)	382 (339–425)	1,751 (16.3)	2,138 (2,038–2,238)
100–149 cases/100,000	70,540 (18.6)	1007 (25.7)	1428 (1340–1516)	3,372 (31.4)	4,780 (4,622–4,938)
≥150 cases/100,000	165,002 (43.6)	2525 (64.4)	1530 (1470–1590)	5,268 (49.0)	3,193 (3,108–3,278)
No estimate	124 (<0.1)	0	0 (0–403)	1 (<0.1)	806 (0–2,783)

* Countries are listed in descending order, according to the total number of persons with smear-negative and inactive tuberculosis.
† Values are World Health Organization estimates for 2005.

the prevalence of inactive tuberculosis among refugees was 3.4 times as high as that among immigrants (Tables 1 and 2). During the same period, 31 immigrants and 16 refugees with smear-positive tuberculosis were granted immigration waivers.

GEOGRAPHIC VARIATION

Table 1 shows the results of overseas screening of immigrants from 1999 through 2005 according to geographic region. Immigrants born in the Western Pacific region had the highest prevalences of smear-negative and inactive tuberculosis. Only 25.6% of U.S.-bound immigrants were born in the Western Pacific region, but they accounted for 91.1% of the cases of smear-negative tuberculosis and 70.4% of the cases of inactive tuberculosis among immigrants. The top five birth countries of immigrants with overseas diagnoses of tuberculosis (the Philippines, Vietnam, China, Mexico, and India) accounted for 40.7% of U.S.-bound immigrants but for 95.2% of the cases of smear-negative tuberculosis and 67.4% of the cases of inactive tuberculosis among immigrants.

Table 2 shows the results of overseas screening of refugees from 1999 through 2005 according to geographic region. Refugees born in the Western Pacific region had the highest prevalence of smear-negative and inactive tuberculosis. Only 7.6% of U.S.-bound refugees were born in the Western Pacific region, but they accounted for 40.6% of the cases of smear-negative tuberculosis and 12.0% of the cases of inactive tuberculosis among refugees. The top five birth countries of refugees with overseas diagnoses of tuberculosis (Ukraine, Vietnam, Somalia, Bosnia and Herzegovina, and Sudan) accounted for 44.8% of U.S.-bound refugees but for 58.5% of the cases of smear-negative tuberculosis and 69.1% of the cases of inactive tuberculosis among refugees.

BIRTH COUNTRIES WITH A HIGH PREVALENCE OF TUBERCULOSIS

During the 1999–2005 period, 56.8% of U.S.-bound immigrants and 62.2% of U.S.-bound refugees were born in countries that had a tuberculosis prevalence of 100 or more cases per 100,000 population per year, as estimated by the WHO, but they accounted for 95.3% of the cases of smear-negative tuberculosis and 80.4% of the cases of inactive tuberculosis among immigrants as well as 90.1% of the cases of smear-negative tuberculosis and 80.4% of the cases of inactive tuberculosis among refugees (Tables 1 and 2).

HIV AND TUBERCULOSIS COINFECTIONS

Among 179 immigrants infected with the human immunodeficiency virus (HIV), 4 (2.2%) had smear-positive, smear-negative, or inactive tuberculosis. The proportion of immigrants with overseas diagnoses of tuberculosis did not differ significantly between those who were infected with HIV and those who were not (2.2% and 1.8%, respectively; P=0.57). Among 1343 refugees infected with HIV, 112 (8.3%) had smear-positive, smear-negative, or inactive tuberculosis. The proportion of refugees with overseas diagnoses of tuberculosis was significantly higher among those who were infected with HIV than among those who were not (8.3% vs. 3.9%, P<0.001).

TEMPORAL VARIATION

Figure 1 shows the prevalences of smear-negative tuberculosis and inactive tuberculosis among immigrants and refugees from 1999 through 2005. There was a trend toward an overall increase in the prevalence of smear-negative tuberculosis among both immigrants and refugees (P<0.001 for both tests for time trends). However, the prevalence of smear-negative tuberculosis increased by only 1.9% among immigrants, as compared with an increase of 158.9% among refugees between 1999–2002 and 2003–2005. There was a trend toward a decrease in the prevalence of inactive tuberculosis among immigrants and among refugees (P<0.001 for both tests for time trends). The preva-

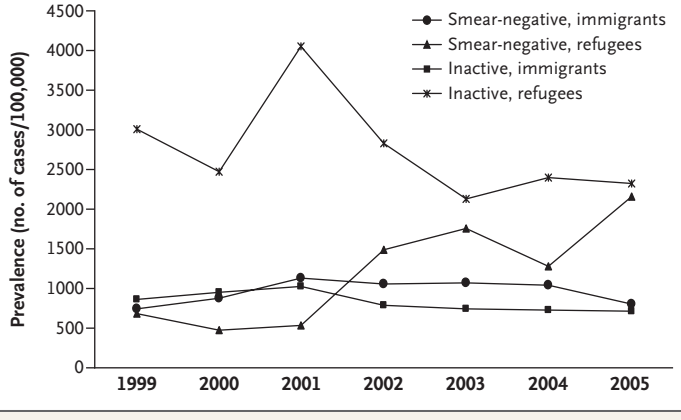

Figure 1. Prevalences of Smear-Negative and Inactive Tuberculosis among U.S.-Bound Immigrants and Refugees, 1999–2005.

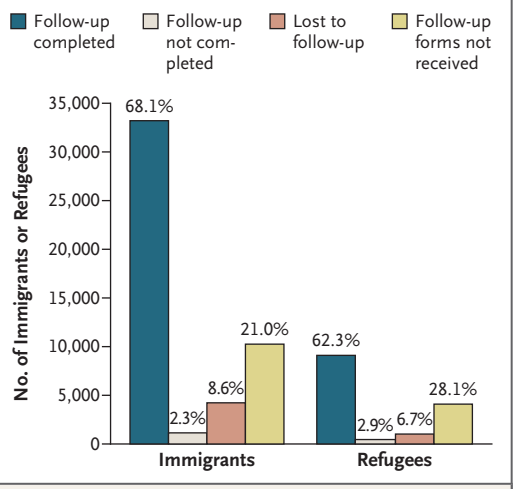

Figure 2. Rates of Follow-up Evaluation in the United States among Newly Arrived Immigrants and Refugees in Whom Smear-Negative or Inactive Tuberculosis Had Been Diagnosed Overseas, 1999–2005.

lence of inactive tuberculosis decreased by 19.9% among immigrants and by 25.8% among refugees between 1999–2002 and 2003–2005.

FOLLOW-UP EVALUATION AFTER ARRIVAL IN THE UNITED STATES

Figure 2 shows the estimated rates of completed follow-up evaluations in the United States among newly arrived immigrants and refugees with overseas diagnoses of tuberculosis, for the period from 1999 through 2005. For immigrants, the lower estimate (based on the assumption that the follow-up evaluation was not completed if an evaluation form was not received by the CDC) was 68.1%, and the higher estimate (based on the assumption that the evaluation was completed even though the form was not received by the CDC) was 89.1%; the lower and upper estimates for refugees were 62.3% and 90.4%, respectively.

The median time from overseas screening to arrival in the United States was 83 days (interquartile range, 47 to 141) for immigrants and 111 days (interquartile range, 63 to 174) for refugees. The median time from arrival in the United States to the follow-up evaluation was 53 days (interquartile range, 26 to 103) for immigrants and 47 days (interquartile range, 26 to 86) for refugees.

On follow-up evaluation, active pulmonary tuberculosis was diagnosed in 6.9% of immigrants and 7.7% of refugees who had received an overseas diagnosis of smear-negative tuberculosis and in 1.4% of immigrants and 1.8% of refugees who had received an overseas diagnosis of inactive tuberculosis (Table 3). Two HIV-infected immigrants who had received an overseas diagnosis of smear-negative tuberculosis completed the follow-up evaluation, and active pulmonary tuberculosis was not diagnosed in either of them. Active pulmonary tuberculosis was diagnosed in 5 (17.9%) of the 28 HIV-infected refugees who had received an overseas diagnosis of smear-negative tuberculosis and in 3 (9.1%) of the 33 HIV-infected refugees who had received an overseas diagnosis of inactive tuberculosis.

DISCUSSION

One objective of overseas screening for tuberculosis is to identify active tuberculosis in U.S.-bound immigrants and refugees before their arrival in the United States. Another objective is to allow appropriate follow-up of newly arrived immigrants and refugees who are at high risk for tuberculosis. Overseas screening also provides a unique opportunity to offer preventive therapy for latent tuberculosis infection, since the majority of immigrants and refugees with overseas diagnoses of tuberculosis have a positive tuberculin skin test.[11] From 1999 through 2005, an average of 4285 immigrants and refugees with smear-negative tuberculosis and 4480 with inactive tuberculosis arrived annually in the United States. During that period, only 47 immigrants and refugees with smear-positive tuberculosis were granted immigration waivers. The number of cases of smear-positive tuberculosis diagnosed by overseas screening was unavailable, although a previous study has reported that 7.0% of adults with a chest radiograph suggestive of active tuberculosis have positive smears.[18]

The algorithm for tuberculosis screening put forth in the 1991 Technical Instructions for Panel Physicians[19] could not identify persons who had tuberculosis that was smear-negative but culture-positive. The limitations of this algorithm have been confirmed by a previous study, which showed that 10.9% of persons with smear-negative tuberculosis have positive culture results.[18] To address these limitations, the CDC released the 2007 Technical Instructions for Tuberculosis Screening and Treatment for Panel Physicians, which require a mycobacterial culture and drug-susceptibility testing for persons with suspected tuberculosis.[22,23]

Our findings indicate that overseas screening

Table 3. Results of Follow-up Evaluation in the United States of Newly Arrived Immigrants and Refugees with an Overseas Diagnosis of Smear-Negative Tuberculosis or Inactive Tuberculosis, 1999–2005.

Group and Follow-up Diagnosis	Overseas Diagnosis		
	Total	Smear-Negative Tuberculosis	Inactive Tuberculosis
		number (percent)	
Immigrants	33,238 (100.0)	18,245 (100.0)	14,993 (100.0)
Active pulmonary tuberculosis	1,481 (4.5)	1,267 (6.9)	214 (1.4)
Extrapulmonary tuberculosis	94 (0.3)	42 (0.2)	52 (0.3)
Pulmonary tuberculosis — activity undetermined	3,873 (11.7)	2,472 (13.5)	1,401 (9.3)
Inactive tuberculosis	18,035 (54.3)	9,836 (53.9)	8,199 (54.7)
No tuberculosis	9,755 (29.3)	4,628 (25.4)	5,127 (34.2)
Refugees	9,132 (100.0)	2,365 (100.0)	6,767 (100.0)
Active pulmonary tuberculosis	306 (3.4)	182 (7.7)	124 (1.8)
Extrapulmonary tuberculosis	42 (0.5)	14 (0.6)	28 (0.4)
Pulmonary tuberculosis — activity undetermined	661 (7.2)	259 (11.0)	402 (5.9)
Inactive tuberculosis	4,490 (49.2)	1,106 (46.8)	3,384 (50.0)
No tuberculosis	3,633 (39.8)	804 (34.0)	2,829 (41.8)
Immigrants and refugees	42,370 (100.0)	20,610 (100.0)	21,760 (100.0)
Active pulmonary tuberculosis	1,787 (4.2)	1,449 (7.0)	338 (1.6)
Extrapulmonary tuberculosis	136 (0.3)	56 (0.3)	80 (0.4)
Pulmonary tuberculosis — activity undetermined	4,534 (10.7)	2,731 (13.3)	1,803 (8.3)
Inactive tuberculosis	22,525 (53.2)	10,942 (53.1)	11,583 (53.2)
No tuberculosis	13,388 (31.6)	5,432 (26.4)	7,956 (36.6)

is a relatively high-yield intervention for identifying cases of active tuberculosis in U.S.-bound immigrants and refugees. We found that among immigrants and refugees who underwent follow-up evaluation after their arrival in the United States, active pulmonary tuberculosis was diagnosed in 7.0% of those who had received an overseas diagnosis of smear-negative tuberculosis and in 1.6% of those who had received an overseas diagnosis of inactive tuberculosis. Our findings are consistent with those of previous studies, in which active tuberculosis was diagnosed in 3.3 to 14.8% of immigrants and refugees who had received an overseas diagnosis of smear-negative tuberculosis and in 0.4 to 4.3% of immigrants and refugees who had received an overseas diagnosis of inactive tuberculosis.[8-15] In comparison, active tuberculosis is identified in 0.7 to 2.4% of persons who have close contact with patients with infectious tuberculosis.[24-26]

Our analyses show that during the period from 1999 through 2005, the majority of cases of tuberculosis diagnosed overseas among U.S.-bound immigrants and refugees were among persons born in the Philippines, Vietnam, China, Mexico, and India. Previous studies in which data from the CDC's National Tuberculosis Surveillance System were used have shown that these five countries also account for the majority of cases of tuberculosis diagnosed in foreign-born persons in the United States.[4,5,27,28] In addition, our study showed a trend toward an increasing prevalence of smear-negative tuberculosis among immigrants and refugees. These findings highlight the need to target and enhance overseas screening, treatment, and control activities for tuberculosis among U.S.-bound immigrants and refugees from countries with a high incidence of tuberculosis.

We found an association between tuberculosis and HIV infection among refugees but not among immigrants. This finding was not unexpected, since during the study period, restrictions were placed on the admission of HIV-infected immigrants to the United States, restrictions that did not apply to HIV-infected refugees. Despite the elevated prevalence of tuberculosis among HIV-infected refugees, cases in this subgroup did not contribute substantially to the number of

overseas diagnoses of tuberculosis among U.S.-bound refugees.

During the 1999–2005 period, 10.9 to 31.9% of immigrants and 9.6 to 37.7% of refugees with overseas diagnoses of tuberculosis may not have completed the follow-up evaluation. State and local health departments may improve the rate of follow-up evaluation if they can institute active outreach policies.[8,13]

Our findings should be interpreted in the context of the limitations of the data used in this study. Misclassifications of tuberculosis cases are likely to have occurred during overseas screening and post-arrival follow-up evaluation. We could not examine the effects of misclassification owing to a lack of detailed case information. On post-arrival follow-up evaluation, no tuberculosis was diagnosed in 26.4% of the immigrants and refugees who had received an overseas diagnosis of smear-negative tuberculosis and in 36.6% of those who had received an overseas diagnosis of inactive tuberculosis, suggesting that tuberculosis may have been overdiagnosed overseas. Although the CDC has developed technical instructions for panel physicians, accurate diagnosis of tuberculosis still depends on many factors, including the professional training of the examining physician and the quality of laboratory testing. In addition, we lacked follow-up data for 31.9% of the immigrants and 37.7% of the refugees with overseas diagnoses of tuberculosis. Finally, we are likely to have underestimated tuberculosis cases in children, since the screening algorithm in use during the study period did not require a routine chest radiograph for children younger than 15 years of age.

Overseas screening for tuberculosis, with follow-up evaluation in the United States, is a high-yield intervention for identifying tuberculosis in U.S.-bound immigrants and refugees and could reduce the number of tuberculosis cases among foreign-born persons in the United States. Improvements such as overseas use of mycobacterial culture, drug-susceptibility testing, directly observed therapy, tuberculin skin testing for children 2 to 14 years of age, and a shorter interval between screening and departure for the United States, as well as use of the CDC's Electronic Disease Notification system for data exchange among the CDC, state and local health departments, and international partners, should increase the effectiveness of this intervention.[22,23] To further reduce and prevent tuberculosis, diagnosis and treatment of latent tuberculosis infection among U.S.-bound immigrants and refugees may be considered in the future, particularly if shortened treatment regimens for latent tuberculosis infection are proved to be effective.

No potential conflict of interest relevant to this article was reported.

The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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