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US Postarrival Evaluation of Immigrant and Refugee Children with Latent Tuberculosis Infection Diagnosed Overseas, 2007–2019

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Abstract

Objective—To assess outcomes from the US postarrival evaluation of newly arrived immigrant and refugee children aged 2–14 years who were diagnosed with latent tuberculosis infection (LTBI) during a required overseas medical examination.

Study design—We compared overseas and US interferon-γ release assay (IGRA)/tuberculin skin test (TST) results and LTBI diagnosis; assessed postarrival LTBI treatment initiation and completion; and evaluated the impact of switching from TST to IGRA to detect *Mycobacterium tuberculosis* infection overseas.

Results—In total, 73 014 children were diagnosed with LTBI overseas and arrived in the US during 2007–2019. In the US, 45 939 (62.9%) completed, and 1985 (2.7%) initiated but did not complete a postarrival evaluation. Among these 47 924 children, 30 360 (63.4%) were retested for *M tuberculosis* infection. For 17 996 children with a positive overseas TST, 73.8% were negative when retested by IGRA. For 1051 children with a positive overseas IGRA, 58.0% were negative when retested by IGRA. Overall, among children who completed a postarrival evaluation, 18 544 (40.4%) were evaluated as having no evidence of TB infection, and 25 919 (56.4%) had their overseas LTBI diagnosis confirmed. Among the latter, 17 229 (66.5%) initiated and 9185 (35.4%) completed LTBI treatment.

Conclusions—Requiring IGRA testing overseas could more effectively identify children who will benefit from LTBI treatment. However, IGRA reversions may occur, highlighting the need for individualized assessment for risk of infection, progression, and poor outcome when making diagnostic and treatment decisions. Strategies are needed to increase the proportions receiving a postarrival evaluation and completing LTBI treatment.

The majority of tuberculosis (TB) cases in the US occur among non–US-born persons. In 2019, non–US-born persons accounted for 70.9% of the reported TB cases; TB incidence

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Data Statement

Data sharing statement available at www.jpeds.com.

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rate was 15.5 times greater than that among US-born persons.[1] Importantly, most (>75%) TB cases among non–US-born persons are believed to result from reactivation of latent tuberculosis infection (LTBI) that was likely acquired before coming to the US.[2,3] This phenomenon also is seen in other countries with low TB incidence, including many European countries, Australia, and Canada.[4] Improved diagnosis and effective treatment for LTBI among newly arrived individuals at risk are therefore a major focus for the control and elimination of TB in the US and other low-incidence countries.[1–5]

Diagnosis of LTBI (also referred to as TB infection, ie, infection with *Mycobacterium tuberculosis* [*Mtb*])[6,7] can be challenging, as it is currently not possible to directly detect *Mtb* in persons with LTBI, an asymptomatic condition defined by absence of evidence of TB disease.[8] LTBI is used here to distinguish infection that is not associated with extant or previously treated disease. There is no "gold standard" to confirm a diagnosis of LTBI.[9] The tuberculin skin test (TST) has been widely used for more than a century. A major drawback of TST is that TST antigens crossreact with *Mycobacterium bovis*–bacille Calmette-Guérin (BCG) vaccines and many environmental nontuberculous mycobacteria (NTM), leading to false-positive results for *Mtb* infection. Interferon-γ release assays (IGRAs) are ex vivo blood tests that detect T-lymphocyte release of interferon-γ after stimulation by antigens found on the *Mtb* complex. These antigens are not found on *M bovis*–BCG strains or most species of NTM. Therefore, IGRA is more specific than TST for diagnosis of LTBI among persons vaccinated with BCG or infected with NTM.[6–9]

TB screening, required for all US-bound immigrants and refugees, is a key component of the overseas medical examination conducted by overseas doctors appointed by the US Department of State. The US Centers for Disease Control and Prevention (CDC) provides Tuberculosis Technical Instructions (TB TIs) for this screening.[10,11] Before 2007, children were not actively screened for TB. According to the TB TIs, beginning in 2007, applicants aged 2–14 years living in countries with a World Health Organization–estimated TB incidence rate of ≥20 cases per 100 000 population are required to be tested for *Mtb* infection by TST or IGRA. If the test is positive, a chest radiograph is required. In 2018, the CDC released updated TB TIs specifying that IGRA must be performed, with TST only accepted in countries where IGRA is not licensed for use. Children who have a positive TST or IGRA but have a normal chest radiograph and no clinical findings of TB disease are classified as "Class B2 TB, LTBI Evaluation." Applicants aged ≥15 years are not required to test for *Mtb* infection; chest radiographs are required for all those aged ≥15years.TheCDCrecommendsthatUSstateand local health departments conduct a postarrival TB evaluation for immigrants and refugees with an overseas TB classification, including children with a Class B2 TB, LTBI Evaluation classification.[12] We assessed outcomes from the US postarrival evaluation of immigrant and refugee children aged 2–14 years who received a Class B2 TB, LTBI Evaluation classification overseas and arrived between 2007 and 2019. We also evaluated the impact of the 2018 TB TIs change from allowing TST to mandating IGRA in the overseas medical examination.

Methods

We conducted a retrospective analysis of newly arrived immigrant and refugee children aged 2–14 years who were diagnosed with LTBI during a required overseas medical examination and arrived in the US during 2007–2019.

We used the data in the CDC's Electronic Disease Notification (EDN) system.[13] Overseas medical examination data were first entered into the US Department of State official forms by panel physicians and later electronically transferred or manually entered into EDN. State and local health departments entered their postarrival evaluation data directly into EDN through the EDN TB Follow-Up Worksheet (OMB Control No. 0920–1238). We also used data extracted from the US Department of State's Worldwide Refugee Admissions Processing System to determine nationality for refugee children.

Definitions

We defined "overseas LTBI diagnosis" as a child receiving a Class B2 TB, LTBI Evaluation classification during his or her overseas medical examination. We defined US diagnoses, evaluation status, and LTBI treatment status based on the data recorded on the EDN TB Follow-Up Worksheet (Table I; available at www.jpeds.com).[14] We considered an overseas LTBI diagnosis as confirmed domestically if a child received a diagnosis of LTBI domestically with or without additional testing. We defined arrival as arrival at a US port of entry. We used country of birth as country of origin for immigrant children, and country of nationality as country of origin for refugee children (51% were born in their countries of asylum).

Testing for *Mtb* Infection

The 2007 TB TIs allowed panel physicians to use QuantiFERON®-TB Gold (QFT-G), QuantiFERON®-TB Gold In Tube (QFT-GIT), or T-SPOT. The 2018 TB TIs allowed the use of QIAGEN QuantiFERON® (any iteration approved by the Food and Drug Administration) or Oxford Immunotec T-SPOT®.TB (Oxford Immunotec Ltd). The IGRA brand names and quantitative test results from overseas medical examination and US postarrival evaluation were not collected systematically. Both the 2007 and 2018 TB TIs required panel physicians to follow the manufacturers' written instructions for performing tests and interpreting test results. For the overseas and US IGRA results, we used the clinician's interpretation (positive/negative) as reported to EDN. We excluded indeterminate results (0.3% of overseas IGRA results and 0.9% of US retesting IGRA results). For the overseas and US TST results, a cutoff of TST ≥5 mm was positive for known TB contacts or immunosuppressed persons, and ≥10 mm was positive for all others.[11,12] A "reversion" was defined as a positive result overseas and a negative result in the US if the same child was tested both by TST or both by IGRA.

Data Analyses

We calculated the proportions of children who initiated or completed a postarrival evaluation, received an LTBI diagnosis, and initiated or completed LTBI treatment. We compared overseas and US testing methods, diagnoses, and postarrival LTBI treatment

initiation and completion under the 2007 TB TIs and under the 2018 TB TIs. We compared overseas and US retesting IGRA and TST results.

Because test specificity is greater for IGRAs than TSTs, we hypothesized that the proportion of persons who tested positive for *Mtb* infection by IGRA may be lower than that by TST. To assess this assumption, we used SAS PROC STDRATE (SAS Institute Inc) to calculate the nationality standardized ratio of the proportion positive by IGRA vs positive by TST overseas. For this calculation, refugee children aged 2–14 years originating from Burma, Democratic Republic of the Congo (DRC), or Iraq were the only nationalities with sufficient numbers of children tested by IGRA. To assess whether sex, age, examination country, and immigrant vs refugee status were associated with the reversions of overseas IGRA on US retesting with IGRA, we performed univariate and multivariate logistic regressions. All 2-way interaction terms between the independent variables (sex, age, examination country, and visa type) were evaluated and no significant ($P < .05$) interactions were detected. We conducted data analysis using SAS software, version 9.4, by the SAS Institute Inc.

Ethical Review

This project was proposed, reviewed and approved in accordance with CDC institutional review policies and procedures. Because it received a nonresearch determination, review by an institutional review board was not required.

Results

Demographics

A total of 73 014 children were diagnosed with LTBI during their overseas medical examination and arrived in the US during 2007–2019. Among these children, 86.2% were immigrants and 13.8% were refugees; 50.2% were male; and 74.3% came from 5 countries of origin: Philippines (42.8%), Mexico (17.3%), Dominican Republic (5.0%), Vietnam (4.8%), and Burma (4.5%) (Table II).

US Postarrival Diagnoses and LTBI Treatment

Among all 73 014 children diagnosed with LTBI overseas, 45 939 (62.9%) ever had documentation of a completed postarrival evaluation. Among them, 18 544 (40.4%) were evaluated as having no evidence of TB infection; 25 919 (56.4%) had their overseas LTBI diagnosis confirmed domestically; 125 (0.3%) were diagnosed with TB disease; and 1351 (2.9%) were diagnosed with inactive TB. Among children whose overseas LTBI diagnosis was confirmed domestically, 19 429 (75.0%) were recommended for LTBI treatment; 17 229 (66.5%) accepted and started treatment; and 9185 (35.4%) completed treatment (Table II).

Comparison of Results before and after Implementation of 2018 TB TIs

The 2018 TB TIs require that overseas testing for *Mtb* infection is performed by IGRA. For the 71 028 (97.3%) of children whose overseas medical examination was conducted before the implementation of the 2018 TB TIs, 67 589 (95.2%) were tested overseas by TST and 2307 (3.2%) by IGRA; domestically, 44 852 (63.1%) completed a postarrival evaluation. Of these, 18 183 (40.5%) were evaluated as having no evidence of TB infection, and 25

208 (56.2%) had their overseas LTBI diagnosis confirmed domestically. For the 1986 (2.7%) of children whose overseas medical examination was conducted after the implementation of 2018 TB TIs, 58 (2.9%) were tested overseas by TST and 1883 (94.8%) by IGRA; domestically, 1087 (54.7%) completed a postarrival evaluation. Of these, 361 (33.2%) were evaluated as having no evidence of TB infection, and 711 (65.4%) had their overseas LTBI diagnosis confirmed domestically (Figure, A).

For children whose overseas LTBI diagnosis was confirmed domestically, a greater proportion of children whose overseas medical examination conducted after vs before implementation of the 2018 TB TIs were recommended for LTBI treatment (96.1% vs 74.4%), accepted and started treatment (77.9% vs 66.1%), and completed treatment (57.8% vs 34.8%) (Figure, B).[15,16] All comparisons were statistically significant ($P<.0001$) by χ^2 analysis.

US Postarrival Retesting Proportions, Results, and Impact on Postarrival LTBI Treatment Initiation

Overall, among children whose postarrival evaluation was completed or initiated but not completed, 30 360 (63.4%) were retested (Figure, A). Among 2444 children with a positive overseas IGRA and a documented US postarrival evaluation, 1198 (49.0%) were retested, whereas among 44 571 children with a positive overseas TST and a documented US postarrival evaluation, 28 568 (64.1%) were retested (Table III).

During postarrival evaluation, among 1051 children with a positive overseas IGRA, 610 (58.0%) were negative on US retest with IGRA; among 17 996 children with a positive overseas TST, 13 274 (73.8%) were negative on US retest with IGRA; among 158 children with a positive overseas IGRA, 87 (55.1%) were negative on US retest with TST; and among 11 580 children with a positive overseas TST, 4335 (37.4%) were negative on US retest with TST (Table IV).

There were different approaches to postarrival LTBI treatment initiation according to overseas and postarrival US retest IGRA and TST results. Among the IGRA-positive children overseas who were retested in the US, if children retested as IGRA-positive, 76.9% initiated LTBI treatment; if children retested as TST-positive, 59.3% initiated LTBI treatment; and if children retested IGRA-negative, just 3.9% initiated LTBI treatment. Among the TST-positive children overseas who were retested in the US, if children retested as IGRA-positive, 76.0% initiated LTBI treatment; if children retested as TST-positive, 61.0% initiated LTBI treatment; and if children retested as IGRA-negative, just 2.2% initiated LTBI treatment (Table III).

Nationality Standardized Ratio of Proportion Positive by IGRA vs Positive by TST Overseas

The ratio of the proportion positive by IGRA vs positive by TST was calculated for refugee children aged 2–14 years originating from Burma, DRC, or Iraq who were tested by IGRA and/or TST during their overseas medical examination and who arrived in the US during 2014–2019. Overall, when tested overseas by IGRA, 3.4% were positive, and when tested by TST, 6.6% were positive (ratio = 0.5, 95% CI 0.4–0.6).

Factors Associated with Reversion of Positive Overseas IGRA Retested with IGRA during US Postarrival Evaluation

Both univariate and multivariate logistic regressions showed sex was not significantly associated with IGRA reversion. Age was significantly associated with IGRA reversion in both univariate and multivariate logistic regressions. Compared with children aged 2–4 years, odds of IGRA reversion for children aged 5–9 years were 50% lower (aOR 0.5, 95% CI 0.3–0.8), and for children aged 10–14 years were 70% lower (Aor 0.3, 95% CI 0.2–0.5). Association of examination country with IGRA reversion varied, and results of univariate and multivariate logistic regressions were similar. Compared with children whose medical examination was conducted in Mexico, children whose medical examination was conducted in China had approximately 5 times greater odds of IGRA reversion (aOR 5.3, 95% CI 2.7–10.4); children whose medical examination was conducted in other high-volume examination countries had no significant difference in odds of IGRA reversion. Univariate logistic regressions showed refugee children were more likely to have IGRA reversion than immigrant children (OR 2.4, 95% CI 1.9–3.1), but the difference was not statistically significant after adjusting for sex, age and examination country (aOR 1.4, 95% CI 1.0–1.9) (Table V; available at www.jpeds.com).

Discussion

Our results demonstrated that the 2018 TB TIs requirement for testing for *Mtb* infection by IGRA in the overseas medical examination was implemented effectively. Among children diagnosed with LTBI overseas, the majority (95%) of overseas tests were IGRAs after the implementation, whereas 95% were TSTs before the implementation.

Overseas testing for *Mtb* infection by TST had disadvantages. Consistent with findings from many previous studies comparing TST and IGRA performance in BCG vaccinated children and adolescents,[17–22] and studies in assessing IGRA performance in patients with NTM disease or infection,[23,24] we found that TST likely yielded many false-positive results in US-bound immigrant and refugee children aged 2–14 years likely due to the high coverage of BCG vaccination,[21,25] and prevalence of NTM infections in their countries of origin.[26,27] The majority (63%) of children diagnosed with LTBI overseas were retested during their postarrival evaluation. Among children with a positive overseas TST, when retested by IGRA, a high proportion (74%) were negative. When retested positive by IGRA, a greater proportion initiated postarrival LTBI treatment than retested positive by TST (76% vs 61%); and when retested negative by IGRA, a very low proportion (2%) initiated treatment. Such findings, first seen in unpublished internal analyses, along with evolving US clinical guidelines[7] in favor of IGRA over TST, led CDC to switch in the 2018 TB TIs from TST to IGRA to detect *Mtb* infection in the overseas medical examination.

We observed positive changes after the implementation of the 2018 TB TIs. Compared with before the implementation, the proportion of children retested in postarrival evaluation fell by 8%; concordance between overseas and US LTBI diagnosis increased by 9%; the proportions of LTBI treatment initiation and completion for children whose overseas LTBI diagnosis was confirmed domestically increased by 12% and 23%, respectively. The increase in the proportions initiating and completing LTBI treatment are consistent with calls

and efforts to better address LTBI in people at high risk of reactivated TB in the US[5]; it may also reflect greater confidence in a positive IGRA, leading more US providers to initiate treatment and improving patient acceptance and adherence to treatment.

We expected switching from TST to IGRA in the overseas medical examination to substantially reduce positive test results overseas. As expected, when we calculated the nationality-standardized ratio of the proportion positive by IGRA vs positive by TST overseas for refugee children aged 2–14 years originating in Burma, DRC, or Iraq, we found an overall risk ratio of 0.5 (95% CI 0.4–0.6), suggesting a 50% reduction in number of positive results if testing by IGRA instead of TST in these 3 nationalities. Given the large numbers of US-bound immigrant and refugee children screened for *Mtb* infection during their overseas medical examination globally, such a reduction could translate to substantially fewer children requiring a postarrival TB follow-up evaluation in the US.

We found in our analysis that among children who were IGRA-positive overseas and retested domestically, the reversion proportion was high at 58%. Discordant IGRA results are not uncommon, and have been reported by previous studies on serial testing of healthcare workers[28,29] with reversion rates being consistently greater than conversion rates (range 22%−71% vs 1%−14%),[29] and on repeated testing among TB contacts.[30] Although there have been a few findings,[31–33] discordant results in repeated IGRA testing in children and adolescents have not been well characterized. Studies on QFT-GIT testing in TB contacts aged 5–9 years (<5 years not retested) in Indonesia[32] found that 20% of children reverted to negative at 3-month follow-up; in aged 0–15 years in Venezuela[33] found that 62% of children reverted to negative or indeterminate at 12-month follow-up.

Our analysis showed that compared with children aged 2–4 years, children aged 5–9 years and 10–14 years had 50% and 70% lower odds of IGRA reversion, respectively. Odds of IGRA reversion were approximately 5 times greater for children whose medical examination was conducted in China than children whose medical examination was conducted in Mexico. Difference in children's age distribution could be a potential explanation. Comparing Mexico with China, the proportion of children aged 10–14 years among all children retested was 68% and 49%, respectively. Our findings are consistent with previous studies.[34–36] The study[34] on domestic evaluation of immigrants 2–14 years old who arrived in California with a classification of TB infection found that the proportion with positive IGRA increased significantly with age (years): 2–4 (11%), 5–9 (19%), 10–14 (28%), $P < .0001$; was lowest among arrivers from China (6%) and greatest among arrivers from Mexico (48%). The study[35] comparing the performance of TST and IGRA in children aged 2–14 years applying to immigrate to the US from Mexico, Philippines, and Vietnam reported that Mexican children aged 10–14 years old were 13 times as likely to be QFT-positive compared with those 2–5 years old (relative risks 12.7; 95% CI 1.76–91.0). It is expected that positive IGRA results are associated with older age because of cumulative exposure to TB over time.

IGRA reversion should not lead to a conclusion that no treatment is necessary without a thorough assessment. The CDC-updated guidelines for using IGRA state that for discordant test results (ie, one positive and the other negative), decisions about medical or public health management require individualized judgment, and find it reasonable to take a positive result

from either of the 2 tests as evidence of infection if the risk for infection, progression, and a poor clinical outcome (eg, meningitis, disseminated disease, or death) are increased.[9] The current CDC guidance for screening for TB infection and disease during the domestic medical examination for newly arrived refugees recommends that treatment for LTBI should be considered after TB disease is ruled out for those with positive IGRA results, unless TB disease or LTBI treatment was completed before arrival.[12]

Non–US-born children and adolescents from countries with high TB incidence are at greater risk for TB disease than US-born children and adolescents.[37,38] In this analysis, 65% of children were from countries of origin with a World Health Organization–estimated TB incidence rate of ≥100 cases per 100 000 population. Furthermore, young children and adolescents in general are at greater risk of progressing to TB disease once infected, and younger children are at greater risk of developing severe disease (TB meningitis, miliary TB), whereas adolescents frequently progress to adult-type disease.[39,40] Early effective diagnosis and treatment reduce disease burden and transmission.

Our results showed that postarrival evaluation, LTBI treatment initiation and completion for immigrant and refugee children aged 2–14 years who were diagnosed with LTBI overseas and arrived in the US during 2007–2019 were not optimal. The proportion of children who had completed a postarrival evaluation remained low (range 35%−68%, 63% overall). For children whose overseas LTBI diagnosis was confirmed domestically, the overall proportions of LTBI treatment initiation and completion were 67% and 35%, respectively. Lower treatment completion proportions were seen for children from some countries with large numbers of US-bound immigrants (eg, Mexico, 29%; Philippines, 30%). Despite the improvement in the proportions of children initiating and completing LTBI treatment after the implementation of the 2018 TB TIs, LTBI treatment initiation proportion (78%) and completion proportion (58%) remain suboptimal. A framework to better address LTBI in at-risk populations in the US, including immigrants and refugees, has been put forth; its components include systems to monitor progress, scale-up of targeted LTBI testing, scaleup of short-course treatment regimens and development of even shorter-course regimens, engagement of affected communities and their medical providers, and increased public health staffing for implementation and oversight.[5]

Our findings should be interpreted within the context of the limitations of our data. The link between test results and initiation of LTBI treatment we observed does not account for information in addition to a TST or IGRA result that clinicians may have considered when making the treatment decisions. Postarrival evaluation, LTBI treatment initiation, and LTBI treatment completion may still be ongoing for immigrants and refugees who arrived in 2019, and state and local health departments may not enter all these data into EDN. In addition, the postarrival TB evaluation itself is only recommended, not required, for children diagnosed with LTBI overseas. The dramatic shift from TST to IGRA in testing for *Mtb* infection overseas after the implementation of 2018 TB TIs that we demonstrated in Figure, A represented only children who were tested for *Mtb* infection and diagnosed with LTBI overseas and, therefore, might not be representative of all children who were tested for *Mtb* infection overseas. Similarly, when calculating nationality standardized ratio of the proportion positive by IGRA vs positive by TST overseas, we could not include

all nationalities in our study population because of inadequate numbers of immigrant and refugee children tested by IGRA. In addition, we used country of origin to categorize TB incidence, because 51% refugee children that we analyzed were born in their countries of asylum, if risk of acquiring LTBI was substantially different in country of origin from that in refugee camps and in country of asylum, inaccurate categorizing could happen. Finally, additional time may be needed to determine the full impact of the 2018 TB TIs as, at the time of this analysis, postimplementation data were only available for people who were examined after September 2018 and arrived during 2018–2019.

Our results showed that overseas testing for *Mtb* infection by TST for this population had disadvantages, including a high proportion of retesting in the US, a high proportion negative on US retest with IGRA, and a low proportion of postarrival LTBI treatment initiation when children retested negative by IGRA. Our findings demonstrated that mandating IGRA testing for all overseas medical examinations could substantially reduce the proportion of children tested positive for *Mtb* infection overseas, thus reduce the number of children who need chest radiograph and postarrival evaluation, and more effectively identify children who will benefit from LTBI treatment. However, a high US retest proportion, a high reversion proportion, and a low proportion of postarrival LTBI treatment initiation when children retested negative by IGRA were observed for children with a positive overseas IGRA, although to a lesser extent. Given that immigrant and refugee children from TB-endemic countries are at high risk for *Mtb* infection, disease progression, and a poor clinical outcome, it is imperative that US programs consider LTBI treatment, after TB disease is excluded, for children who have a positive IGRA overseas. Our results also showed postarrival evaluation, LTBI treatment initiation, and completion in this high-risk population had remained suboptimal. Strategies are needed to increase the proportions receiving a postarrival evaluation and completing LTBI treatment.

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The findings and conclusions of this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC). References in this article to any specific commercial products, process, service, manufacturer, or company do not constitute endorsement or recommendation by the U.S. Government or CDC.

Glossary

BCG	Bacille Calmette-Guérin
CDC	Centers for Disease Control and Prevention
DRC	Democratic Republic of the Congo

EDN	Electronic Disease Notification
IGRA	Interferon-γ release assay
LTBI	Latent tuberculosis infection
Mtb	*Mycobacterium tuberculosis*
NTM	Nontuberculous mycobacteria
TB	Tuberculosis
TB TIs	Tuberculosis Technical Instructions
TST	Tuberculin skin test

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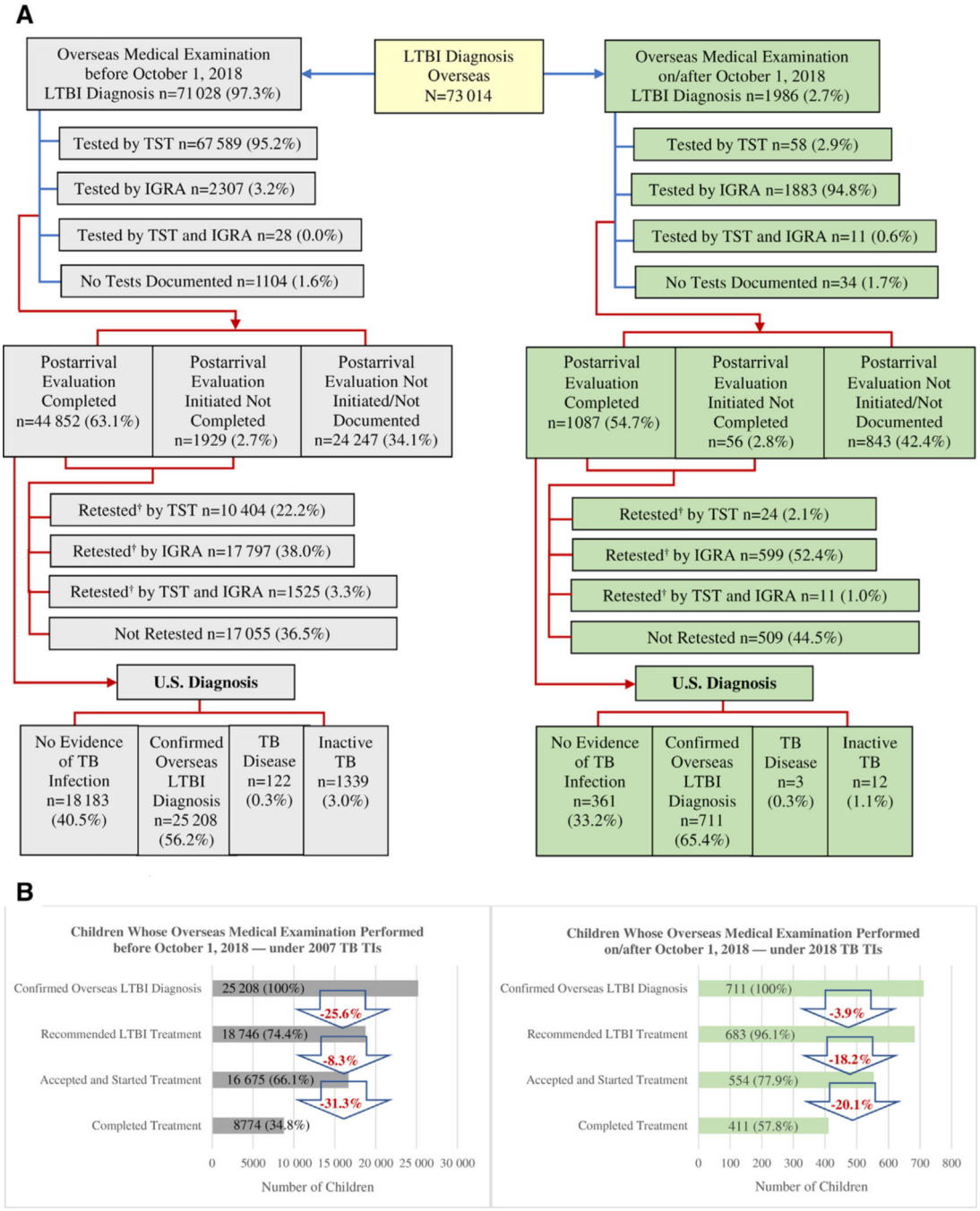

Figure.

A, Testing* for *Mtb* infection and outcomes of US postarrival evaluation of immigrant and refugee children aged 2–14 years who were diagnosed with LTBI during the overseas medical examination under 2007 TB TIs and under 2018 TB TIs (went into effect October 1, 2018) and arrived in the US during 2007–2019. *Chest radiograph, culture, or smear tests performed during the overseas medical examination and US postarrival evaluation were not shown. †Among children whose postarrival evaluation was completed or initiated but not completed, 29 726 (63.5%) were retested under 2007 TB TIs and 634 (55.5%) were retested

under 2018 TB TIs. The overall number of children retested and percent of children whose postarrival evaluation was completed or initiated but not completed were 30 360 (63.4%). **B,** LTBI cascade of care for children aged 2–14 years whose overseas LTBI diagnosis was confirmed during their US postarrival evaluation, 2007–2019. For the concept of LTBI cascade of care, refer to the references.[15,16]

Table I.

US postarrival evaluation diagnosis, evaluation status, and LTBI treatment status of immigrant and refugee children aged 2–14 years who were diagnosed with LTBI during the overseas medical examination and arrived in the US during 2007–2019

Variables	Category	Definition*
Evaluation diagnosis	No evidence of TB infection	Received a classification of Class 0†: no TB exposure, not infected or Class 1†: TB exposure, no evidence of infection
	Confirmed overseas LTBI diagnosis	Received a classification of Class 2†: TB infection, no disease
	TB disease	Received a classification of Class 3†: TB, TB disease
	Inactive TB	Received a classification of Class 4†: TB, inactive disease
Evaluation status	Completed	An evaluation diagnosis was recorded
	Initiated not completed	An evaluation diagnosis was not recorded, and evaluation disposition was “completed evaluation,” or “initiated evaluation/not completed,” or US TST/IGRA testing or US LTBI/TB treatment was recorded
	Not initiated/not documented	An evaluation diagnosis was not recorded, and evaluation disposition was “did not initiate evaluation,” or was missing
LTBI treatment status	Recommended LTBI treatment	“Completed evaluation” and LTBI treatment being recommended were recorded in evaluation disposition section, or “completed evaluation” and treatment being recommended were recorded in evaluation disposition section and LTBI treatment initiation was recorded in US treatment section (for the oldest version of the Worksheet)
	Accepted and started treatment	LTBI treatment initiation was recorded in US treatment section
	Completed treatment	LTBI treatment completion was recorded in US treatment section

*Used the data recorded on the CDC’s Electronic Disease Notification Tuberculosis Follow-Up Worksheet for Newly-Arrived Persons with Overseas Tuberculosis Classifications (EDN TB Follow-Up Worksheet, [OMB Control No. 0920–1238]).

†For the postarrival TB evaluation, newly arrived immigrants and refugees were classified according to the classification of persons exposed to and/or infected with *Mycobacterium tuberculosis* of the American Thoracic Society (ATS)[14] as collected on the EDN TB Follow-Up Worksheet.

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Table II.

Arrivals, characteristics, and outcomes of US postarrival evaluation of immigrant and refugee children aged 2–14 years who were diagnosed with LTBI during the overseas medical examination and arrived in the US during 2007–2019

	Diagnosed with LTBI overseas		Postarrival evaluation completed		Confirmed overseas LTBI diagnosis during postarrival evaluation*		Recommended postarrival LTBI treatment†		Accepted and started postarrival LTBI treatment†		Completed postarrival LTBI treatment	
Variables	No.	(%)	No.	% of children diagnosed with LTBI overseas	No.	% of children for whom postarrival evaluation completed	No.	% of children with overseas LTBI diagnosis confirmed during postarrival evaluation‡	No.	% of children with overseas LTBI diagnosis confirmed during postarrival evaluation‡	No.	% of children with overseas LTBI diagnosis confirmed during postarrival evaluation‡
Arrival year												
2007	23	(0.0)	8	(34.8)	7	(87.5)	6	(85.7)	6	(85.7)	5	(71.4)
2008	1262	(1.7)	627	(49.7)	439	(70.0)	267	(60.8)	272	(62.0)	102	(23.2)
2009	7359	(10.1)	4373	(59.4)	2877	(65.8)	1965	(68.3)	2029	(70.5)	939	(32.6)
2010	8529	(11.7)	5720	(67.1)	3599	(62.9)	2364	(65.7)	2436	(67.7)	1015	(28.2)
2011	7584	(10.4)	5159	(68.0)	3294	(63.8)	2105	(63.9)	2156	(65.5)	883	(26.8)
2012	8340	(11.4)	5628	(67.5)	3260	(57.9)	2065	(63.3)	2115	(64.9)	1061	(32.5)
2013	6766	(9.3)	4468	(66.0)	2604	(58.3)	1579	(60.6)	1610	(61.8)	842	(32.3)
2014	6661	(9.1)	4107	(61.7)	2165	(52.7)	1978	(91.4)	1451	(67.0)	806	(37.2)
2015	7531	(10.3)	4505	(59.8)	2237	(49.7)	2048	(91.6)	1425	(63.7)	917	(41.0)
2016	7941	(10.9)	4860	(61.2)	2332	(48.0)	2154	(92.4)	1564	(67.1)	1067	(45.8)
2017	5492	(7.5)	3260	(59.4)	1417	(43.5)	1296	(91.5)	928	(65.5)	664	(46.9)
2018	3499	(4.8)	2100	(60.0)	982	(46.8)	925	(94.2)	687	(70.0)	478	(48.7)
2019	2027	(2.8)	1124	(55.5)	706	(62.8)	677	(95.9)	550	(77.9)	406	(57.5)
Sex												
Male	36 635	(50.2)	23 139	(63.2)	13 138	(56.8)	9896	(75.3)	8748	(66.6)	4682	(35.6)
Female	36 379	(49.8)	22 800	(62.7)	12 781	(56.1)	9533	(74.6)	8481	(66.4)	4503	(35.2)
Age, y, at arrival												
2–4	9902	(13.6)	6399	(64.6)	3544	(55.4)	2633	(74.3)	2271	(64.1)	1228	(34.7)
5–9	23 783	(32.6)	14 939	(62.8)	7961	(53.3)	5902	(74.1)	5131	(64.5)	2719	(34.2)

Variables	Diagnosed with LTBI overseas		Postarrival evaluation completed		Confirmed overseas LTBI diagnosis during postarrival evaluation*		Recommended postarrival LTBI treatment†		Accepted and started postarrival LTBI treatment†		Completed postarrival LTBI treatment	
	No.	(%)	No.	% of children diagnosed with LTBI overseas	No.	% of children for whom postarrival evaluation completed	No.	% of children with overseas LTBI diagnosis confirmed during postarrival evaluation‡	No.	% of children with overseas LTBI diagnosis confirmed during postarrival evaluation‡	No.	% of children with overseas LTBI diagnosis confirmed during postarrival evaluation‡
10–14	39 329	(53.9)	24 601	(62.6)	14 414	(58.6)	10894	(75.6)	9827	(68.2)	5238	(36.3)
Country of origin												
Philippines	31 220	(42.8)	20 484	(65.6)	9832	(48.0)	6577	(66.9)	5571	(56.7)	2964	(30.1)
Mexico	12 617	(17.3)	6778	(53.7)	4611	(68.0)	3459	(75.0)	3163	(68.6)	1348	(29.2)
Dominican Republic	3611	(5.0)	2356	(65.2)	1727	(73.3)	1505	(87.1)	1511	(87.5)	929	(53.8)
Vietnam	3513	(4.8)	2242	(63.8)	1313	(58.6)	1016	(77.4)	926	(70.5)	445	(33.9)
Burma	3290	(4.5)	2350	(71.4)	1527	(65.0)	1250	(81.9)	1206	(79.0)	737	(48.3)
Other	18 756	(25.7)	11 725	(62.5)	6906	(58.9)	5619	(81.4)	4849	(70.2)	2760	(40.0)
Unknown	7	(0.0)	4	(57.1)	3	(75.0)	3	(100.0)	3	(100.0)	2	(66.7)
Visa type												
Immigrants	62 967	(86.2)	38 795	(61.6)	21 472	(55.3)	15 641	(72.8)	13 775	(64.2)	7196	(33.5)
Refugees	10 047	(13.8)	7144	(71.1)	4447	(62.2)	3788	(85.2)	3454	(77.7)	1989	(44.7)
TB incidence in country of origin§												
0–19	786	(1.1)	464	(59.0)	246	(53.0)	3788	(85.2)	120	(48.8)	64	(26.0)
20–99	24 785	(34.0)	14 002	(56.5)	8714	(62.2)	6767	(77.7)	6072	(69.7)	3042	(34.9)
≥100	47 399	(64.9)	31 445	(66.3)	16 946	(53.9)	12 518	(73.9)	11 032	(65.1)	6075	(35.8)
No estimate	44	(0.1)	28	(63.6)	13	(46.4)	8	(61.5)	5	(38.5)	4	(30.8)
Total	73 014	(100.0)	45 939	(62.9)	25 919	(56.4)	19 429	(75.0)	17 229	(66.5)	9185	(35.4)

*Other diagnoses among children who completed a postarrival evaluation were no evidence of TB infection = 18 544 (40.4%), TB disease = 125 (0.3%), inactive TB = 1351 (2.9%).

†Data quality being suboptimal for early years of EDN data could contribute to the discrepancy between recommended postarrival LTBI treatment and accepted and started postarrival LTBI treatment.

‡In accordance with LTBI cascade of care shown in Figure, B, percentage was calculated with the denominator being children with overseas LTBI diagnosis confirmed during postarrival evaluation.

§2016 World Health Organization–estimated TB incidence (cases per 100 000 population) for country of origin.

Table III.

Initiation of LTBI treatment according to overseas and US postarrival IGRA and TST test results, 2007–2019

	Initial testing in overseas medical examination					
	Positive overseas IGRA			Positive overseas TST		
	Total[†]	Initiated postarrival LTBI treatment		Total[‡]	Initiated postarrival LTBI treatment	
Retesting in US postarrival evaluation[*]	N	No.	(%)	N	No.	(%)
US test result known						
Positive IGRA and/or TST						
IGRA+ and TST+	11	6	(54.5)	348	274	(78.7)
IGRA+ and TST unknown[§]	428	329	(76.9)	4355	3308	(76.0)
IGRA+ and TST–	2	1	(50.0)	19	13	(68.4)
TST+ and IGRA unknown[§]	59	35	(59.3)	6092	3715	(61.0)
TST+ and IGRA–	1	0	(0.0)	805	81	(10.1)
No positive IGRA and/or TST						
IGRA– and TST unknown[§]	591	23	(3.9)	12 232	270	(2.2)
TST– and IGRA unknown[§]	67	8	(11.9)	4080	88	(2.2)
IGRA– and TST–	18	0	(0.0)	236	2	(0.8)
US test unknown/not done						
Results inconclusive or not recorded	21	9	(42.9)	401	116	(28.9)
Not retested	1246	875	(70.2)	16 003	8353	(52.2)
No postarrival evaluation	1724	0	(0.0)	22 798	0	(0.0)

[*] Excludes immigrant and refugee children for whom retesting in US postarrival evaluation was performed but none of their overseas IGRA/TST tests were documented, or all their overseas IGRA/TST results were negative, or inconclusive, or not recorded.

[†] A total of 2444 children with a positive overseas IGRA had a documented US postarrival evaluation. Among them, 1198 (49.0%) were retested (including those with inconclusive or unknown US test results), and 1246 (51.0%) were not retested.

[‡] A total of 44 571children with a positive overseas TST had a documented US postarrival evaluation. Among them, 28 568 (64.1%) were retested (including those with inconclusive or unknown US test results), and 16 003 (35.9%) were not retested.

[§] Unknown includes immigrant and refugee children for whom either US retesting IGRA or TST was not performed, or retesting IGRA or TST result was inconclusive, or result was not recorded.

Table IV.

Overseas and postarrival IGRA/TST results among children who were documented positive overseas and retested after US arrival, 2007–2019

	Initial testing in overseas medical examination			
	Positive overseas IGRA		Positive overseas TST	
Retesting in US postarrival evaluation	No.	(%)	No.	(%)
US IGRA *				
IGRA +	441	(42.0)	4722	(26.2)
IGRA –	610	(58.0)	13 274	(73.8)
US TST *				
TST +	71	(44.9)	7245	(62.6)
TST –	87	(55.1)	4335	(37.4)

* Excludes immigrant and refugee children for whom retesting in US postarrival evaluation was performed but none of their overseas IGRA/TST tests were documented, or all their overseas IGRA/TST results were negative, or inconclusive, or not recorded, or all their US retesting IGRA/TST results were inconclusive or not recorded.

Table V.

Factors associated with reversion of positive overseas IGRA among children who were retested by IGRA after US arrival, 2007–2019

	US Retesting IGRA on positive overseas IGRA (N = 1051)									
	Children retested		Reverted on retesting		Not reverted on retesting		Univariate		Multivariate	
Variables	No.	(%)	No.	(%)	No.	(%)	Crude OR (95% CI)		aOR (95% CI)	
Sex										
Male	552	(52.5)	322	(58.3)	230	(41.7)	Reference		Reference	
Female	499	(47.5)	288	(57.7)	211	(42.3)	1.0	(0.8–1.2)	1.0	(0.8–1.3)
Age, y, at arrival										
2–4	169	(16.1)	133	(78.7)	36	(21.3)	Reference		Reference	
5–9	347	(33.0)	217	(62.5)	130	(37.5)	0.5	(0.3–0.7)	0.5	(0.3–0.8)
10–14	535	(50.9)	260	(48.6)	275	(51.4)	0.3	(0.2–0.4)	0.3	(0.2–0.5)
Examination country										
Mexico	73	(7.0)	21	(28.8)	52	(71.2)	Reference		Reference	
China	109	(10.4)	77	(70.6)	32	(29.4)	6.0	(3.1–11.5)	5.3	(2.7–10.4)
Dominican Republic	132	(12.6)	53	(40.2)	79	(59.9)	1.7	(0.9–3.1)	1.7	(0.9–3.1)
Philippines	62	(5.9)	14	(22.6)	48	(77.4)	0.7	(0.3–1.6)	0.8	(0.3–1.7)
Vietnam	18	(1.7)	3	(16.7)	15	(83.3)	0.5	(0.1–1.9)	0.5	(0.1–1.9)
Other	657	(62.5)	442	(67.3)	215	(32.7)	5.1	(3.0–8.7)	3.7	(2.1–6.7)
Visa type										
Immigrant	610	(58.0)	301	(49.3)	309	(50.7)	Reference		Reference	
Refugee	441	(42.0)	309	(70.1)	132	(29.9)	2.4	(1.9–3.1)	1.4	(1.0–1.9)