# Screening Latino Adolescents for Latent Tuberculosis Infection (LTBI)

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# **SYNOPSIS**

**Objectives.** To investigate the rates of latent TB infection (LTBI) in a sample of young people in San Diego County and examine potential predictors of a positive tuberculin skin test (TST).

**Methods.** Latino and foreign-born students from ten public middle and high schools were invited to screenings along with a random 10% sample of all other students. After obtaining parental consent, Mantoux tests were placed (N=2,698) and read (n=2,667 [98.9%]) in 48–72 hours. A positive TST was defined as  $\geq$ 10 mm induration. The mean age of the sample was 14.34 years (SD=1.81); 50.1% were female (n=1,353); 78.5% were Latino (n=2,108); 35.7% were foreign-born (n=939); and 44.3% were uninsured (n=930).

**Results.** The positive TST rate for Latinos was 21.8% vs. 5.6% for non-Latinos, p<0.001. Foreign-born Latinos had the highest infection rate (31.3%), followed by foreign-born non-Latinos (20.4%), U.S.-born Latinos (15.4%), and U.S.-born non-Latinos (1.0%), p<0.001. Logistic regression was conducted to determine predictors of TST positivity. Being Latino (odds ratio [OR]=3.27), uninsured (OR=1.60), foreign-born (OR=3.90), and living in the south county region closest to the U.S./Mexico border (OR=2.72) were significant predictors.

**Conclusions.** Results suggest that Latino youth near the California/Mexico border are at high risk for infection, for remaining undiagnosed, and for being under-treated for LTBI.

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The global burden of tuberculosis (TB) remains enormous, with individuals born outside the United States making up an increasing proportion of U.S. and California morbidity from the disease. In 2001, new cases of *M. tuberculosis* (MTB) totaled over 8.7 million worldwide, including more than 3.8 million new cases of infectious pulmonary (smear-positive) disease. Eighty percent of all new TB cases were in 22 countries located in Asia, Africa, and Latin America. The global prevalence of cases was 16.2 million in 1997, with an estimated 1.87 million deaths from TB during that same year.

Travel and emigration to and from high-prevalence countries present challenges to TB control in the U.S. The 2010 national goal issued by the Centers for Disease Control and Prevention (CDC) and Advisory Council for the Elimination of Tuberculosis (ACET) calls for an overall case rate of less than 1/100,000,3 compared to 5.6/100,000 in 2001.4 Targeted goals for reducing the incidence of TB in the U.S. are especially far from being realized in ethnic minorities, particularly those who are born outside the United States.<sup>3</sup> In 2001, the TB case rate for foreign-born individuals in the U.S. was more than seven times (26.6 vs. 3.1) the case rate of those born in the U.S.4 The continuing high rate of TB in many parts of the world is of increasing interest to the U.S., as the proportion of U.S. TB cases represented by foreign-born individuals has increased steadily from 27% in 1992 to 50% in 2001.4

In 2001, Mexico accounted for 23% of the total foreign-born TB cases reported in the U.S., with the Philippines (12%) and Vietnam (8%) the next most common countries of origin. California's foreign-born TB cases represent a higher proportion (74%) of total state cases than is seen for the U.S. as a whole (49.2%). In California, Latinos represent more than 37% (37.6%) of all TB cases, with the majority of Latino TB cases (63%) being foreign-born in Mexico.

Incidence and prevalence of TB in California may be due in part to its proximity to the U.S. border with Mexico, a moderate TB-prevalence country. This may provide increased opportunity for TB transmission. This border crossing is the world's busiest; it is estimated that there are 290 million crossings each year into the U.S. from Mexico, with over 95 million crossings from Mexico into California, and 52 million crossing into San Diego.<sup>5</sup>

About one million border crossings into the U.S. from Mexico occur daily, with the San Diego-Tijuana and El Paso-Ciudad Juarez crossings accounting for 40% of these. A study published in 1994 reported that of the 521,000 individuals crossing into San Diego each month, 25% cross at least 20 times per month

and another 35% cross between four and 19 times per month. Mexican residents account for 56.5% of all crossings.<sup>7</sup>

Estimated global prevalence of MTB infection is 32%,² and an estimated 10 to 15 million people in the U.S. (or about 5%) have LTBI.<sup>8</sup> Rates among high-risk populations are two to five times higher.<sup>9</sup> As of 1999, an estimated 10% of Californians, or 3.4 million people, had LTBI.<sup>10</sup> A 1998 study of two high schools with high-risk populations in San Diego County reported positive TST rates (for both schools combined) of 40.2% for non-U.S.-born students and 4.1% for U.S.-born students.<sup>11</sup> The purpose of the current study was to explore TST positivity rates among Latino and non-Latino students attending public middle and high schools in San Diego County, and explore the possible predictors of LTBI among young Latinos.

### **METHODS**

This study was part of a larger National Heart, Lung, and Blood Institute (NHLBI)-funded clinical trial designed to determine if counseling/coaching could sustain adherence to isoniazid (INH) in Latino adolescents with LTBI in San Diego County. The screening process described in this article was conducted in order to recruit 13- to 18-year-old TST-positive Latino participants to the trial.

School districts within San Diego County were targeted for screening if they contained public middle or high schools with student bodies that were at least 40% Latino. Project staff presented information on the screening at a school staff meeting to educate teachers and request their support in promoting the screening and education of the students.

Selection of students to be invited was designed to over-sample Latinos for the trial. To promote support for the screening, all Latino and foreign-born students, and 1,729 other students (10% of all other students, selected at random) were invited by a letter to the parents from the principal. Students who were not invited could request and receive screening.

The letter and consent forms were in English and Spanish, and at one school also in Aramaic. Letters were mailed about four weeks prior to the screening. The letter explained the importance of TB screening and therapy, the need to be screened even if vaccinated with BCG, the process and dates of the screening, the incentive for returning the consent forms by the deadline, the follow-up care to be offered to TST-positive students, and an explanation of a positive result. Parents were encouraged to contact the school nurse with questions.

The letter was accompanied by a parental consent form to accept or decline screening; it also obtained the following information: name; age; gender; ethnicity; address; phone number; history of TB skin testing; history of BCG (added after first five screenings); history of LTBI or active disease treatment; medical provider's name, address and phone number; and current insurance information. Adolescents who had previously tested positive were requested to complete the form to better describe the prevalence and treatment of TB infection in this population. Those with documentation of a past positive TST were not retested; however, those who did not complete treatment were invited to receive care as offered to those screened by this project and invited to participate in the trial if a new complete course of treatment was indicated.

Project staff members were designated as school volunteers, and the schools provided the project with the phone numbers of all invited Latino students. A few days after the mailing, project staff phoned parents to encourage the return of the consent forms and to answer any questions about the screening.

As time permitted, staff members contacted parents to clarify incomplete or ambiguous information on the submitted consent forms, and to provide additional education to parents who initially refused. The week prior to each screening, students attended an assembly about TB and the purpose and procedures of the screening.

Students who returned a parental consent form, whether accepting or refusing the screening, were entered in a raffle for gift certificates worth \$50 (two from a popular clothing store) or \$25 (four from a music store). Parent educational meetings were also held, providing the same information that the students received at their assembly. Initially, these meetings were held prior to screening, with very limited turnout. However, after four screenings, modified meetings were held after the screening for families of TST-positive students only, with greatly improved attendance.

Each screening was completed during a one-week period, with the first two days dedicated to test placement and the remainder of the week dedicated to reading results at 48 to 72 hours. Areas were screened off to allow privacy. Snacks were provided for participating students. Nurses from the San Diego County TB Control Program and skin test personnel from the University of California, San Diego Medical Center placed and read the tests. Students who were absent for the reading were called at home and brought in by parents whenever possible.

At the time of TST reading, students who tested

positive had one-on-one counseling with project staff. Induration of ≥10mm was considered positive, based on California standards. 12 Written and verbal information was provided regarding the meaning of the test, the importance of a chest x-ray and evaluation for therapy, and how to obtain low-cost follow-up care. Students who completed screening received a written copy of their results. Students with a 5 to 9 mm result were advised to have immediate follow-up if they were immune-compromised. Parents of students with positive results were phoned and invited to the parent meeting, and given follow-up treatment recommendations.

Project staff negotiated reduced treatment charges with one or more community clinics near each school, and referred students without a provider to these clinics. X-rays were taken at reduced rates or provided by the county TB Program.

School nurses assisted with follow-up of TST-positive students. Students who attended community clinics or the county TB Program and otherwise met recruitment criteria for the project were then invited to participate in the adherence trial.

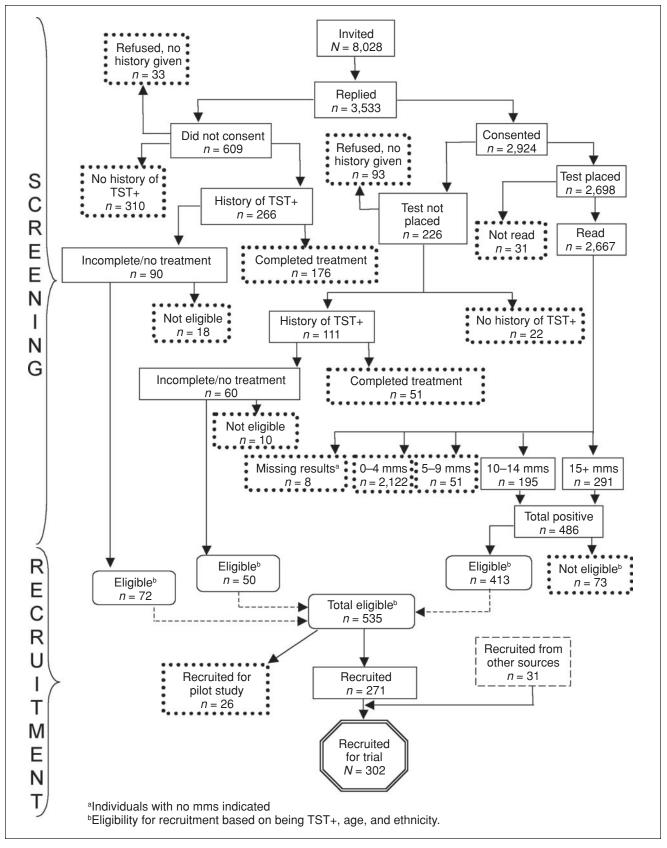
Figure 1 presents a flowchart describing the components of the screening process from the initial mailing of invitations to be screened through the recruitment of participants into the adherence trial. Project staff attempted to contact as many nonrespondents as possible. Some parents could not be reached due to language limitations or disconnected, nonexistent, or inaccurate phone numbers. Of those invited, 4,495 (56%) did not respond (i.e., did not return the screening consent form to the school nurse).

All students who responded to the invitation are accounted for in one of the boxes following the one labeled "Replied" in the flowchart. The boxes outlined with dots designate students who were not eligible for recruitment into the trial. In general, these students lacked proof of being TST-positive, had previously completed treatment, did not meet the trial's eligibility criteria for age and ethnicity, or were treated by a private practitioner instead of a clinic. In addition to those students identified through project screenings, a total of 31 students were recruited into the trial after being identified through other sources (i.e., schools, community clinics, and relatives participating in the trial).

### Statistical analyses

Statistical analyses were performed using the SPSS 6.1.3 for Windows software package.<sup>13</sup> Frequencies of descriptive variables were conducted, and chi-square tests were used to examine the relationship between ethnicity and testing positive as well as the relation-

Figure. Screening and recruitment outcomes



ship between testing positive and the interaction of ethnicity/foreign-born status. A logistic regression model was used to determine predictors of having LTBI.

### **RESULTS**

### **Participants**

Figure 1 also describes screening outcomes. Out of 8,028 invited students; 3,533 responded (44% of those invited); 2,924 consented (82.8% of respondents); 2,698 were placed (92.2% of consented); and 2,667 were read (98.9% of placed). Table 1 presents demographic information and medical history variables for the 2,698 students who had a test placed. The mean age of the sample was 14.34 (SD=1.81) with a range of 12–21. Of the sample, 2,108 (78.5%) were Latino, 305 (11.4%) were white, 163 (6.0%) were Asian/Pacific Islander, 64 (2.4%) were black, and 44 (1.6%) were other. U.S.-born numbered 1,691 (64.3%), 780 (28.7%) were born in Mexico, and 159 (6.0%) were born in other countries (see Table 1 for additional sample characteristics).

### Rates of LTBI

Of the 2,698 individuals who had a test placed, test results were available for 2,659. Of these, 2,173 (81.7%) were 0–9 mm and 486 (18.2%) were ≥10 mm (positive). The range of mm induration for individuals with test results was 0-35.

Of Latinos with test results, 21.8% were positive; the positive rate for non-Latinos with a test read was 5.6%,  $\chi^2$  (1, n=2,645) = 77.31, p<0.001 (see Table 2). A chi-square test was also used to determine differences in patterns of being infected among interaction groups depicting Latino vs. non-Latino and foreignvs. U.S.-born,  $\chi^2$  (3, n=2,582) = 181.67, p<0.001 (see Table 2). Foreign-born Latinos had the highest rate of

Table 1. Characteristics of participants who had a test placed (N=2698)

Age		Sex		
Mean	14.34 (1.81)	Male	1,345 (49.9%)	
Median	14	Female	1,353 (50.1%)	
Range	12–21			
Reg	gion	Current gra	de in school	
East	744 (27.6%)	Mean	8.97	
North	754 (27.9%)	Median	9	
South/Central	1,200 (44.5%)	Range	6–12	
		No response	58	
Ethr	nicity	Country of birth		
White	305 (11.4%)	U.S.	1,691 (64.3%)	
Black	64 (2.4%)	Mexico	780 (28.7%)	
Latino	2,108 (78.5%)	Other	159 (6.0%)	
Asian/Pacific Islander	163 (6.0%)	Don't know	2	
Other	44 (1.6%)	No response	68	
No response	14	·		
ВС	CG <sup>a</sup>	Child ever had	a TB skin test?	
Yes	482 (47.4%)	Yes	1,650 (70.8%)	
No	535 (52.6%)	No	682 (29.2%)	
Don't know	594	Don't know	305	
No response	1,087	No response	61	
Doctor/health	Doctor/health care provider Medical insurar		insurance	
Yes	1,460 (83.6%)	Yes	1,168 (55.7%)	
No	286 (16.4%)	No	930 (44.3%)	
Don't know	1	Don't know	7	
No response	951	No response	593	

BCG history was not added until after the first five screenings, so only 65.5% of students screened were asked this question.

Table 2. TST Positive rates for various subgroups

Ethnicity						
MMS induration	Latinos	Non-Latinos	Row total			
≤9	n=1,626	n=535	n=2,161			
Row percent	75.2	24.8	81.7			
Column percent	78.2	94.4				
Total percent	61.5	20.2				
≥10	n=452	n=32	n= 484			
Row percent	93.4	6.6	18.3			
Column percent	21.8	5.6				
Total percent	17.1	1.2				
Column	n=2,078	n=567	n=2,645			
Total	78.6	21.4	100.0			

Ethnicity/birthplace interaction groups					
MMS induration	Foreign-born Latinos	U.Sborn Latinos	Foreign-born non-Latinos	U.Sborn non-Latinos	Row total
≤9	n=541	n=1,049	n=109	n=413	n=2,112
Row percent	25.6	49.7	5.2	19.6	81.8
Column percent	68.7	84.6	79.6	99.0	
Total percent	21.0	40.6	4.2	16.0	
≥10	n=247	n=191	n=28	n=4	n=470
Row percent	52.6	40.6	6.0	0.9	18.2
Column percent	31.3	15.4	20.4	1.0	
Total percent	9.6	7.4	1.1	0.2	
Column	n=788	n=1,240	n=137	n=417	n=2,582
Total	30.5	48.0	5.3	16.2	100.0

infection (31.3%), followed by foreign-born non-Latinos (20.4%), U.S.-born Latinos (15.4%), and U.S.-born non-Latinos (1.0%).

### Predictors of testing TST positive

Table 3 describes the results of a logistic regression conducted for the entire sample (i.e., Latinos and non-Latinos combined) to determine factors associated with being TST-positive. Being Latino (OR=3.27, confidence interval [CI] 1.95, 5.47), uninsured (OR=1.60, CI 1.19, 2.16), foreign born (OR=3.90, CI 2.90, 5.24), and living closest to the U.S.-Mexico border (OR=2.72, CI 1.83, 4.04) were significant predictors of testing positive for LTBI.

## **DISCUSSION**

The CDC recommends targeting LTBI screening to high-risk groups to improve test accuracy and resource effectiveness.<sup>14</sup> However, it is left for local areas to define *high risk* in their communities. Communities in the U.S.-Mexico border region have unique character-

istics that may represent higher TB risk than for the U.S. as a whole, and may also require unique screening strategies for the identification and treatment of those at highest risk. Although Mexico is a moderate TB-rate country with TB prevalence 2.5 times that of the U.S., the proximity to the U.S. and ongoing frequent mixing of U.S. and Mexican populations, particularly Latino populations, increases the importance of achieving TB control in the U.S., particularly in border communities.<sup>15</sup>

However, it is because of the high volume of nonimmigrant visitors received by communities on both sides of the border on a daily basis that TB screening of this population is not feasible. Whereas most immigrants are considered at highest risk for active TB within five years of immigration (most often from activation of LTBI)<sup>16</sup> the regular visits to and from Mexico to visit family and friends may prolong the risk for acquiring active TB in Mexican-American immigrant populations, and may extend the increased risk to subsequent U.S.-born generations.

TB screening of foreign-born individuals is currently

Table 3. Predictors of being TST Positive (n=1752)

					95% CI	
Variable	В	Standard error	Sig.	Exp (B)	Lower	Upper
Latino	1.1844	0.2630	0.0000	3.2688	1.9523	5.4730
Past skin test	0.1157	0.1492	0.4381	1.1227	0.8380	1.5041
Gender	-0.2277	0.1344	0.0902	0.7963	0.6119	1.0363
No medical insurance	0.4722	0.1523	0.0019	1.6035	1.1897	2.1611
Foreign-born	1.3611	0.1509	0.0000	3.9005	2.9021	5.2424
North	0.0422	0.2097	0.8405	1.0431	0.6915	1.5734
South	1.0010	0.2018	0.0000	2.7211	1.8323	4.0410
Age	-0.1972	0.2165	0.3624	0.8210	0.5371	1.2550
Constant	-3.5170	0.3866	0.0000			

B = Logit coefficients (unstandardized logistic regression coefficients)

Sig. = significance level of the individual coefficients

Exp(B) = odds ratios of the individual coefficients

CI = confidence interval of Exp (B)

required for: (a) immigrants and refugees applying for permanent legal status, and (b) individuals of foreign birth in the U.S. who are applying for legal permanent resident status. The Institute of Medicine's Committee on the Elimination of Tuberculosis in the U.S. recommends TB control in foreign-born populations by screening nonpermanent residents and providing post-immigration treatment for permanent residents who arrive from high-incidence countries. Even if applied, these measures would not adequately address the TB control needs in the U.S.-Mexico border region. Effective screening programs should target frequent border crossers as well as those who come in contact with immigrants from countries with moderate to high TB rates.

The results presented here were generated from screenings conducted as part of an NHLBI trial specifically targeting Latino adolescents. While these screenings were not designed to establish population rates of LTBI for San Diego County, important patterns emerged that may inform methods for targeting TB screening approaches in this community and others in the U.S.-Mexico border region.

Based on relative LTBI rates among the various subpopulations represented, screening results support categorizing Latino adolescents and foreign-born adolescents as high-risk populations for TB in San Diego County who should be targeted in future screening efforts. In this sample, Latino adolescents were four times as likely to be infected as non-Latino adolescents. Young, foreign-born non-Latinos were 20 times more likely to be infected than young, U.S.-born non-

Latinos. Moreover, foreign-born Latino adolescents were over 30 times as likely as U.S.-born non-Latino adolescents to be infected. Although rates were high among non-Latino foreign-born adolescents (20.4%), they were not as high as those found among foreign-born Latinos (31.3%). In this context, it is important to note that due to the demographics of the schools selected for screening, we did not have access to sufficient numbers of adolescents from high TB-rate countries to analyze.

Although the sample size was relatively large, with 2,698 students having TSTs placed and 2,667 students having tests read, 2,698 accounts for only 34% of the total of 8,028 students who were initially invited to participate in the screening. This might have introduced a responder bias that may actually underestimate the true infection rates. As the proportion of students tested increases, the sample would include more students from the very difficult to reach cohort, who would tend to have higher risk profiles. Future studies should use even more aggressive procedures than those employed in the present study to capture the higher-risk individuals.

When we explored possible predictors of LTBI in this group of screened adolescents, being foreign-born, Latino, living in the south county region nearest the Mexican border, and not having medical insurance emerged as significant predictors. These results indicate that foreign-born Latino adolescents, and even U.S.-born Latino adolescents, are at a substantially elevated risk of LTBI. This further suggests that ethnicity, foreign-born status, and residence in proximity to

Mexico should be considered as characteristics denoting LTBI risk among adolescents in this, and perhaps other, border counties. This increased risk may represent exposure due to contact with active cases either residing in or visiting from Mexico, which may occur either when visitors come to the U.S. or when the young people visit Mexico. These specific groups of students may constitute an important population to target for episodic screening to identify and treat LTBI, in addition to other "traditional" high-risk groups, i.e., those who are foreign born, institutionalized, immune compromised, and known contacts of active cases. Moreover, the importance of conducting screenings that deliberately access young people who do not have medical insurance was apparent in that being uninsured was a predictor of being TST-positive. This suggests that not only are these young people less likely to be screened through other mechanisms, but they would also be less likely to access LTBI treatment in the absence of a system that provides low-cost treatment for TST-positive students.

One of the challenges of TB control through targeted screening and LTBI treatment is to design screenings that are feasible and cost-effective, and at the same time conducted in a manner that does not promote discrimination against specific groups of individuals. It is particularly important not to foster antiimmigrant sentiments, either in the conduct of the screenings or the reporting of results. The screenings described here included features to diminish perceptions of singling out specific ethnicities and immigrants. This was accomplished by not publicly stating the criteria for invitation to screening, inviting a 10% sample of non-foreign born, non-Latino students, and allowing uninvited students to be screened upon request. Pre-screening school staff meetings and student assemblies were used to identify and address the methodology of the screening; concerns expressed by school staff or students about discrimination were addressed by project staff and the school administration, as needed. There were no complaints of discrimination or stigmatization as a result of any of the ten school screenings.

Targeting high-risk adolescents through schools makes it possible to find them in large numbers, identify those who have demographic characteristics predictive of LTBI risk, and provide an organizational base from which to conduct screenings and monitor follow-up treatment. This strategy follows the recommendation of the Working Group on Tuberculosis among Foreign-Born Persons that selective screening should be conducted among populations who are at highest risk for TB infection and disease, accessible

for screening, and likely to complete preventive therapy.<sup>16</sup>

Targeting young people also provides treatment for a subpopulation for which side effects (particularly INH-induced hepatitis) are the least severe and frequent, and the years of protected life the greatest. Another benefit of the screenings described here was the ability to identify students who had tested positive in the past but had not completed treatment. This screening served as a means of identifying these young people in the community, who could now be recaptured for treatment completion.

The experience described here suggests that specific subpopulations of students attending middle and high schools in border areas may represent an easily identifiable and accessible high-risk group suitable for episodic, targeted TB screening. Without such screenings, many eligible young people would miss the opportunity to receive LTBI treatment at an age that renders the greatest risk/benefit ratio. However, targeted screening and treatment of LTBI should be limited to areas where completion of therapy for active cases and contact tracing activities are currently adequate. <sup>16</sup>

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