Completion of Latent Tuberculosis Therapy in Children: Impact of Country of Origin and Neighborhood Clinics

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Background. Successful treatment of latent tuberculosis infection (LTBI) is an important objective in the United States’ strategy for tuberculosis (TB) control. We review the impact of demographic variables and community treatment upon completion of medical therapy of LTBI in a large pediatric cohort.

Methods. We performed a retrospective analysis of prospectively collected data from children referred for evaluation and treatment of LTBI. Children were followed in the main hospital TB clinic or in 1 of 2 hospital-run neighborhood clinics. Those completing and not completing medical treatment were compared based on demographic and history variables, clinic location, and distance to clinic. Propensity score techniques were used to match children treated at the main hospital and neighborhood clinics on collected demographic and history variables.

Results. Of 1516 children evaluated, 1184 (78.1%) initiated medical therapy and returned for at least 1 visit. Of these, treatment was completed by 89.2% (166 of 186) of children in the neighborhood clinics versus 83.2% (830 of 998) of children in the main hospital TB clinic (P < .037). Neighborhood and main hospital clinic children did not differ in rates of completion when propensity score-matched groups were compared. Country of origin was the most important factor in determining both initiation and completion of therapy.

Conclusions. Obstacles remain for successful initiation and treatment of children from identified geographic regions. Most of the dropout occurs early in treatment, and use of neighborhood clinics does not provide an obvious advantage when similar patient groups are compared. Emphasis upon initial education and early non-clinic follow-up may be useful in enhancing therapy completion.
PATIENTS AND METHODS

This is a retrospective analysis of prospectively collected data for 1516 children ≤19 years of age referred to Nationwide Children’s Hospital (NCH) with presumed LTBI (tuberculin skin test [TST] of ≥10 mm of induration and a negative chest radiograph) between July 1, 2006 and December 31, 2009. The NCH TB clinic is the designated site for treatment of children with active and latent TB in Franklin County and surrounding areas. All children referred to the clinic who met the above-stated criteria for LTBI were included in the analyses. Signs or symptoms of active TB were evaluated by both the referral source and during the initial evaluation in the NCH TB clinic. For analysis, the countries of birth were grouped into 8 major geographic regions: the Caribbean; Central Asia; Eastern Europe; Mexico, Central and South America; North Africa and the Middle East; North America and Western Europe; Pacific Asia; and Sub-Saharan Africa. Children were generally either from a TB-endemic country and required to complete TB screening prior to school entry, or they had another risk factor necessitating initial TST placement such as exposure to an active pulmonary TB case. Most children were referred to the NCH TB clinic for further evaluation and management within 2 weeks of identification of a positive TST placed by nurses in the Columbus Public Schools foreign-born screening clinic or the Columbus Public Health department.

Children were all initially evaluated in the NCH TB clinic by a physician or certified pediatric nurse practitioner (CPNP) and started on a 9-month course of INH therapy. For children with parents or legal guardians who were non-fluent in English, an interpreter was present during the initial encounter and all subsequent clinic visits. Handouts explaining LTBI, the need and rationale for medication, and possible medication side effects were provided in English, Spanish, and Somali, the most common languages spoken within this patient cohort. After the initial visit at the NCH TB clinic, children were subsequently followed on a monthly basis by the CPNP and were offered the choice to be followed in the NCH TB clinic or in 1 of 2 NCH-run neighborhood clinics closer to his or her home. The same LTBI follow-up clinic protocol was used at all 3 sites. The CPNP performed an examination, questioned for possible drug events, performed a pill count, and prescribed the next month’s supply of medication. Children who did not return for a scheduled monthly visit were contacted by telephone or mail (if unable to be reached by telephone). Children who failed to return to clinic for 3 consecutive months were classified as not completing therapy.

Completion of therapy was defined as 270 doses of INH within a 12-month period. Children who missed ≥3 consecutive months of therapy but eventually returned to the clinic were restarted on the full course of therapy; no credit was given for previous doses taken.

Addresses of the cases from each of the 3 clinics, as well as the clinic addresses, were batch geocoded. Additional data cleaning and manual geocoding were performed for cases that were unmatched, matched to street name only, or matched to zip code only. After data cleaning and manual geocoding, a match rate of 98.6% was obtained for children attending the main hospital LTBI clinic, 98.6% for children attending neighborhood clinic A, and 98.0% for children attending neighborhood clinic B. Euclidean (straight line) distances between cases and their respective clinics were determined. In addition, street network distance was calculated for each case to the respective clinic to take into account linear impedances and the actual probable routes of travel. All geocoding and Euclidean distance calculations were performed using ESRI ArcGIS 10 (Environmental Systems Research Institute, Redlands, CA). Street network distance calculations were performed using the ESRI Network Analyst extension for ArcGIS.

Variables examined in relation to completion of therapy included clinic location, age, sex, foreign or US born, region of birth, duration in the United States, history of TB exposure, size of TST reaction, availability of handouts in primary language, and distance from the patient’s residence to the follow-up clinic. The χ² and t tests were used to evaluate categorical and continuous variables, respectively, in univariate analyses. Logistic regression was performed, including all variables significant at the 0.05 level of significance on univariate testing without additional interaction or higher order terms.

Because clinic location was not randomly assigned, the propensity score matching (PSM) method was used to decrease the bias of clinic selection by the patient [12]. This technique allows for matching of children seen in the neighborhood clinics with similar children, as determined by measured variables, followed in the hospital-based clinic. The probability that a patient would be followed at an offsite clinic location was estimated using the demographic and history variables noted above, with and without inclusion of distance from patient’s home to the clinic, in a multivariate logistic regression model with clinic location as the dependent variable. This propensity score was used to match controls (ie, children followed in
the main TB clinic) with each patient treated at a neighborhood clinic. This matching was performed to the nearest neighbor (1:1) with a propensity score within 0.001 units. Those neighborhood clinic children who could not be matched with a corresponding patient from the main hospital clinic were eliminated from the PSM analysis. Univariate testing on the model variables was performed (using either $\chi^2$ or $t$ tests as appropriate) to evaluate the effectiveness of the matching. The primary outcome in the PSM analysis was percentage of children who completed therapy. The $\chi^2$ test was used to compare children followed in the offsite locations with propensity score-matched children followed in the main TB clinic.

Data were prospectively collected and stored in a Microsoft Access database (Microsoft Corporation, Redmond, WA). Statistical analyses were performed using Stata (version 10.0; StataCorp, College Station, TX) as well as the PSMATCH2 module developed by Leuven and Sianesi [13]. This study was approved by the Institutional Review Board of Nationwide Children’s Hospital.

RESULTS

There were 1516 children referred to NCH for treatment of LTBI between July 1, 2006 and December 31, 2009 (mean age 10.9 years, median age 11.4 years). Children were mostly foreign born (90.5%), representing 91 different birth countries. Fifty percent of these children were from 1 of the following 4 countries: Mexico (278, 18.3%), Somalia (221, 14.6%), Kenya (186, 12.3%), and Ethiopia (80, 5.3%). One hundred thirty-two (8.7%) children had known contact with an individual with active TB.

The overall completion rate, including all children referred for LTBI evaluation, was 65.7% (996 of 1516). Medical treatment was refused by 138 (9.1%) of these children (Figure 1). The main variable determining whether children refused INH therapy was region of birth. Only children from countries in Pacific Asia (47.6%), Eastern Europe (38.9%), and North Africa and the Middle East (19.0%) had greater than 10% rate of treatment refusal.

Medical treatment was initiated by 1378 children (mean age = 10.9 years, median = 11.5 years) and completed by 996 (72.3%). Children who completed treatment differed significantly from those not completing treatment on 6 of the 10 variables collected: clinic location, age, foreign or US born, duration in the United States, region of birth, and distance from home to clinic (Table 1). No statistically significant findings were seen for sex, history of TB exposure, size of TST reaction, or availability of handouts in primary language. Logistic regression including the 6 significant variables resulted in 3 independent predictors: age, region of birth, and clinic location. Those who completed therapy were younger (mean age 10.7 years, range 6 months to 19.9 years) than those who did not (mean age 11.3 years, range 3 months to 19.9 years), and increasing age was associated with decreasing likelihood of therapy completion. Children from Mexico, Central and South America (256 of 330, 77.6%), Central Asia (40 of 52, 76.9%), and Sub-Saharan Africa (507 of 675, 75.1%) were most likely to complete treatment. Only 45.4% (10 of 22) of those from Eastern Europe completed treatment.

The location of treatment had a strong impact on completion of therapy. Those treated in an offsite, neighborhood clinic were more likely to complete treatment (166 of 186, 89.2%) compared to those treated at the main hospital clinic (830 of 1192, 69.6%).

Although 1378 children agreed to medical therapy and received prescription for INH at the initial visit, 194 (14.1%) of these children did not return for a subsequent visit. Completion rate for the 1184 children having ≥2 clinic visits was 84.1% (996 of 1184). Of these 1184 children, those who completed treatment differed significantly from those not completing treatment on 4 of the 10 variables collected: clinic location, foreign or US born, duration in the United States, and region of birth (Table 2). No statistically significant findings were seen for age, sex, history of TB exposure, size of TST reaction, availability of handouts in primary language, or driving distance to clinic. Logistic regression including the 4 significant variables resulted in 2 independent predictors: region of birth and clinic location. As noted previously, children from Mexico, Central and South America (256 of 298, 85.9%),

Figure 1. Summary of clinic visits and latent tuberculosis infection treatment completion. Abbreviation: LTBI, latent tuberculosis infection.
In matching 183 of the 186 children seen in the various clinic sites, we performed PSM, which resulted in 83.0% (969 of 1175) of the sample being propensity score-matched to the main hospital clinic. As seen in Table 3, there were no significant differences noted in these 2 groups on demographic and history variables after matching, except for distance from home to the clinic. This contrasts to differences noted for region of birth, foreign or US born status, and driving distance for the unmatched groups. In contrast to the findings from multivariate logistic regression analysis using the entire treated sample, the propensity score-matched groups did not differ significantly in percentage completing therapy, with 89.1% of those seen in the offsite, neighborhood clinics successfully completing therapy compared with 84.2% of those seen in the main hospital clinic.

### Table 1. Demographics by Treatment Completion: Children Initiating Treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Completed Treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n)</td>
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<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>No (1175)</td>
<td></td>
</tr>
<tr>
<td>Mean, median</td>
<td>10.7, 11.4</td>
<td>.02&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Range (mo–y)</td>
<td>6–19.9</td>
<td></td>
</tr>
<tr>
<td>TST size (mean mm)</td>
<td>16.2</td>
<td>.23</td>
</tr>
<tr>
<td>Driving distance (median miles)</td>
<td>7.25</td>
<td>.001&lt;sup&gt;a,c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Birth region (n [%])</td>
<td>Sub-Saharan Africa (673)</td>
<td>507 [75.1] 168 [24.9]</td>
</tr>
<tr>
<td>Central Asia (44)</td>
<td>256 [77.6]</td>
<td>74 [22.4]</td>
</tr>
<tr>
<td>North America and Western Europe (140)</td>
<td>85 [60.7] 55 [39.3]</td>
<td></td>
</tr>
<tr>
<td>North Africa and Middle East (81)</td>
<td>61 [67.3] 31 [38.3]</td>
<td></td>
</tr>
<tr>
<td>Pacific Asia (44)</td>
<td>26 [59.1]</td>
<td>18 [40.9]</td>
</tr>
<tr>
<td>Central Asia (52)</td>
<td>40 [76.9]</td>
<td>12 [23.1]</td>
</tr>
<tr>
<td>Caribbean (34)</td>
<td>22 [64.7]</td>
<td>12 [35.3]</td>
</tr>
<tr>
<td>Sex (n [%])</td>
<td>Female (621)</td>
<td>441 [71.0] 180 [29.0]</td>
</tr>
<tr>
<td>Male (757)</td>
<td>555 [73.3]</td>
<td>202 [26.7]</td>
</tr>
<tr>
<td>Duration in US (n [%])&lt;sup&gt;d&lt;/sup&gt;</td>
<td>&lt;1 year (683) 496 [72.6] 187 [27.4]</td>
<td>&lt;.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>1–5 years (370)</td>
<td>296 [80.0]</td>
<td>74 [20.0]</td>
</tr>
<tr>
<td>&gt;5 years (152)</td>
<td>105 [69.1]</td>
<td>47 [30.9]</td>
</tr>
<tr>
<td>Foreign born (n [%])&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Yes (1247) 918 [73.6] 329 [26.4]</td>
<td>.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>No (131)</td>
<td>78 [59.5]</td>
<td>53 [40.4]</td>
</tr>
<tr>
<td>TB exposure (n [%])&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Yes (129) 100 [77.5] 29 [22.5]</td>
<td>.16</td>
</tr>
<tr>
<td>No (1249)</td>
<td>896 [71.7]</td>
<td>353 [28.3]</td>
</tr>
<tr>
<td>Handouts in primary language (n [%])</td>
<td>Yes (684) 506 [74.0] 178 [26.0]</td>
<td>.16</td>
</tr>
<tr>
<td>No (694)</td>
<td>490 [70.6]</td>
<td>204 [29.4]</td>
</tr>
<tr>
<td>Offsite clinic (n [%])&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Yes (187) 166 [88.8] 21 [11.2]</td>
<td>&lt;.001&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>No (1191)</td>
<td>830 [69.7]</td>
<td>361 [30.3]</td>
</tr>
</tbody>
</table>

### Table 2. Demographics by Treatment Completion: Children With ≥2 Visits

<table>
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<tr>
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<th>Completed Treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n)</td>
<td>Yes (996)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>No (188)</td>
<td></td>
</tr>
<tr>
<td>Mean, median</td>
<td>10.7, 11.4</td>
<td>.06&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Range (mo–y)</td>
<td>6–19.9</td>
<td></td>
</tr>
<tr>
<td>TST size (mean mm)</td>
<td>15.8</td>
<td>.86</td>
</tr>
<tr>
<td>Driving distance (median miles)</td>
<td>7.25</td>
<td>.61&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Birth region (n [%])&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Sub-Saharan Africa (383)</td>
<td>507 [87.0] 76 [13.0]</td>
</tr>
<tr>
<td>Mexico, Central and South America (298)</td>
<td>256 [85.9] 42 [14.1]</td>
<td></td>
</tr>
<tr>
<td>North America and Western Europe (113)</td>
<td>85 [75.2] 28 [24.8]</td>
<td></td>
</tr>
<tr>
<td>North Africa and Middle East (63)</td>
<td>50 [79.4] 13 [20.6]</td>
<td></td>
</tr>
<tr>
<td>Pacific Asia (39)</td>
<td>26 [66.7]</td>
<td>13 [33.3]</td>
</tr>
<tr>
<td>Central Asia (45)</td>
<td>40 [88.9]</td>
<td>5 [11.1]</td>
</tr>
<tr>
<td>Eastern Europe (14)</td>
<td>10 [71.4]</td>
<td>4 [28.6]</td>
</tr>
<tr>
<td>Caribbean (29)</td>
<td>22 [75.9]</td>
<td>7 [24.1]</td>
</tr>
<tr>
<td>Sex (n [%])</td>
<td>Female (531)</td>
<td>441 [83.0] 90 [16.9]</td>
</tr>
<tr>
<td>Male (653)</td>
<td>555 [85.0]</td>
<td>98 [15.0]</td>
</tr>
<tr>
<td>Duration in US (n [%])&lt;sup&gt;d&lt;/sup&gt;</td>
<td>&lt;1 year (585) 496 [84.8] 89 [15.2]</td>
<td>.002&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>1–5 years (330)</td>
<td>296 [89.7]</td>
<td>34 [10.3]</td>
</tr>
<tr>
<td>&gt;5 years (133)</td>
<td>105 [78.9]</td>
<td>28 [21.0]</td>
</tr>
<tr>
<td>Foreign born (n [%])&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Yes (1078) 918 [85.2] 160 [14.8]</td>
<td>.002&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>No (106)</td>
<td>78 [73.6]</td>
<td>28 [26.4]</td>
</tr>
<tr>
<td>TB exposure (n [%])&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Yes (115) 100 [87.0] 15 [13.0]</td>
<td>.38</td>
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<td>No (1069)</td>
<td>896 [83.8]</td>
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<td>Handouts in primary language (n [%])</td>
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<td>.38</td>
</tr>
<tr>
<td>No (589)</td>
<td>490 [83.2]</td>
<td>99 [16.8]</td>
</tr>
<tr>
<td>Offsite clinic (n [%])&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Yes (186) 166 [89.2] 20 [10.8]</td>
<td>.04&lt;sup&gt;c,e&lt;/sup&gt;</td>
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<tr>
<td>No (998)</td>
<td>830 [83.2]</td>
<td>168 [16.8]</td>
</tr>
</tbody>
</table>

**Abbreviations:** TB, tuberculosis; TST, tuberculin skin test; US, United States.

<sup>a</sup>Significant in multivariate logistic regression.

<sup>b</sup>Data skewed, non-parametric test performed; values are medians.

<sup>c</sup>Statistically significant at <.05; noted in bold text.

<sup>d</sup>Data skewed, non-parametric test performed; values are medians.

<sup>e</sup>Among foreign born (n = 1078).
Additional PSM was performed including distance from home to the clinic as a predictor variable along with the variables noted above. With this greater restriction, 86 of the 186 children seen in the offsite clinics could be matched with children followed in the main hospital TB clinic. As anticipated, there were no significant differences noted in these 2 groups on demographic and history variables, including distance from home to the clinic. Again, the propensity score-matched groups did not differ significantly in percentage completing therapy, with 90.7% of those followed in the offsite, neighborhood clinics successfully completing therapy compared to 84.9% of those seen in the main hospital clinic.

DISCUSSION

In a previous review of results from our TB clinic, an overall completion rate of 54.4% was found among 545 children evaluated [11]. This rate included those who refused to initiate medical therapy. The major predictive factor was birth region. Despite implementation of several recommendations of the Pediatric Tuberculosis Collaborative Group [14], including minimizing delay between time of screening and onset of therapy, providing dedicated consistent staff for follow-up and medication monitoring, offering incentives (eg, movie tickets), and supplying interpreters and language-specific educational materials for the most common languages in the clinic (ie, English, Spanish, Somali), overall rate of completion was poor. The overall completion rate in the current study, including all children referred for LTBI evaluation, was 65.7%.

Two studies involving children and using a 6-month INH protocol reported completion rates of 28% and 74%, respectively [6, 7]. In a Canadian study with intervention based on school-based screening, overall 62% of children started on therapy complied with a 9-month INH regimen. Successful adherence was related only to having ≥2 family members screened for TB [8]. In a more recently published study out of Canada, completion rate was 61.3% among those who initiated therapy. Poor adherence was related to older age (>16 years), delay between TST and TB clinic visit, and presence of adult relatives in the household [9].

### Table 3. Demographics and Treatment Completion by Clinic Location for Unmatched and Propensity Matched Groups (Without Driving Distance)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Offsite Clinic</th>
<th>Propensity Matched*</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(Unmatched)</td>
<td>(Propensity Matched)*</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
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<td>(186)</td>
<td>(998)</td>
</tr>
<tr>
<td>Age (mean years)</td>
<td>10.8</td>
<td>10.8</td>
</tr>
<tr>
<td>TST size (mean mm)</td>
<td>15.9</td>
<td>15.8</td>
</tr>
<tr>
<td>Driving distance (median miles)</td>
<td>2.82</td>
<td>7.95</td>
</tr>
<tr>
<td>Birth region (n [%])</td>
<td>Sub-Saharan Africa (583)</td>
<td>125 [21.4]</td>
</tr>
<tr>
<td></td>
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<tr>
<td>TB exposure (n [%])</td>
<td>Yes (115)</td>
<td>11 [9.6]</td>
</tr>
</tbody>
</table>

Abbreviations: TB, tuberculosis; TST, tuberculin skin test; US, United States.

*Propensity-matched age, sex, region of birth, duration in the US, TB exposure history, size of TST reaction.

Data skewed, non-parametric test performed; values are medians.

Statistically significant at <.05; noted in bold text.
a recent study from Houston, of the children starting LTBI therapy, 186 of 248 (75%) completed therapy. The highest rate of completion (120 of 129, 93%) was seen in a population non-randomly selected to receive directly observed therapy twice weekly for the duration of the treatment [10].

Difficulties with clinic access have been noted as a predictor of poor treatment adherence [9]. Attempts have been made to improve access through use of school-based programs for screening and treatment [8, 9]. At our facility, a change in LTBI treatment was made allowing children to be followed in neighborhood clinics closer to their homes. Although 89.2% of children followed in the offsite, neighborhood TB clinics completed therapy, the corresponding rate was 83.2% in the main hospital clinic among those children who returned for at least 1 visit after initiation of medical therapy. This rate of treatment completion among patients followed at the hospital clinic is encouraging and suggests that stable clinic providers and inducements for follow-up visits can be effective if patients have initial understanding of the importance of, and commitment to, treatment. Rates of completion did not differ between neighborhood and main hospital clinics among children matched on measured history and demographic variables, regardless of inclusion of distance from home to the clinic. Rates of completion were high in both settings.

Table 4. Demographics and Treatment Completion by Clinic Location for Unmatched and Propensity-Matched Groups (With Driving Distance)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Offsite Clinic (Unmatched)</th>
<th>Offsite Clinic (Propensity Matched)*</th>
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<tr>
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<td>Yes (n)</td>
<td>No (n)</td>
</tr>
<tr>
<td>(n)</td>
<td>(186)</td>
<td>(998)</td>
</tr>
<tr>
<td>Age (mean years)</td>
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<td>10.8</td>
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<tr>
<td>TST size (mean mm)</td>
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<td>2.82</td>
<td>7.95</td>
</tr>
<tr>
<td>Birth region (n [%])</td>
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<tr>
<td>Sub-Saharan Africa (583)</td>
<td>125 [21.4]</td>
<td>458 [78.6]</td>
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<td>Mexico, Central and South America (298)</td>
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<td>264 [88.6]</td>
</tr>
<tr>
<td>North America and Western Europe (113)</td>
<td>3 [2.6]</td>
<td>110 [97.3]</td>
</tr>
<tr>
<td>North Africa and Middle East (63)</td>
<td>14 [22.2]</td>
<td>49 [77.8]</td>
</tr>
<tr>
<td>Pacific Asia (39)</td>
<td>2 [5.1]</td>
<td>37 [94.9]</td>
</tr>
<tr>
<td>Central Asia (45)</td>
<td>2 [4.4]</td>
<td>43 [95.6]</td>
</tr>
<tr>
<td>Eastern Europe (14)</td>
<td>2 [14.3]</td>
<td>12 [85.7]</td>
</tr>
<tr>
<td>Caribbean (29)</td>
<td>4 [13.8]</td>
<td>25 [86.2]</td>
</tr>
<tr>
<td>Sex (n [%])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (531)</td>
<td>84 [15.8]</td>
<td>447 [84.2]</td>
</tr>
<tr>
<td>Male (653)</td>
<td>102 [15.6]</td>
<td>551 [84.4]</td>
</tr>
<tr>
<td>Duration in US (n [%])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1 year (585)</td>
<td>96 [16.4]</td>
<td>489 [83.6]</td>
</tr>
<tr>
<td>1–5 years (330)</td>
<td>67 [20.3]</td>
<td>263 [79.7]</td>
</tr>
<tr>
<td>&gt;5 years (133)</td>
<td>18 [13.5]</td>
<td>115 [86.5]</td>
</tr>
<tr>
<td>Unknown (30)</td>
<td>2 [6.7]</td>
<td>28 [93.3]</td>
</tr>
<tr>
<td>TB exposure (n [%])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (115)</td>
<td>11 [9.6]</td>
<td>104 [90.4]</td>
</tr>
<tr>
<td>Completed therapy (n [%])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes (996)</td>
<td>166 [16.7]</td>
<td>830 [83.3]</td>
</tr>
<tr>
<td>No (188)</td>
<td>20 [10.6]</td>
<td>168 [89.4]</td>
</tr>
</tbody>
</table>

Abbreviations: TB, tuberculosis; TST, tuberculin skin test; US, United States.
*Propensity-matched on age, sex, region of birth, duration in the US, TB exposure history, size of TST reaction, driving distance to clinic.
*bData skewed, non-parametric test performed; values are medians.
*cStatistically significant at <.05; noted in bold text.

Although there was a small effect of clinic location on treatment completion among those initiating therapy, this was not an independent predictor in the context of other measured variables, regardless of inclusion of distance from home to the clinic. Although perceived clinic access may influence initiation of therapy, we were unable to evaluate this given that all initial visits occurred at the main hospital clinic and...
treatment location was only determined based on location of subsequent visits.

Medical treatment was refused by 9.1% of children who were screened and had positive TST results. Like treatment completion, a prominent factor in this decision was region of birth. Children from Pacific Asia (47.6%), Eastern Europe (38.9%), and North Africa and the Middle East (19.0%) were especially likely to refuse therapy. As noted in our previous report, this refusal appeared to be a result of a belief in the impact of Bacillus Calmette-Guérin (BCG) vaccine upon TST and a perception of low likelihood of conversion to active TB.

Although the majority (90.9%) of referred children agreed to initiate therapy for latent TB, 14.1% of these children (194 of 1378) did not return after the initial visit and start of therapy. In addition, the 6.2% (73 of 1184) who did return did so for only 1 visit. That is, of those children who stated agreement with medication treatment, 19.4% (267 of 1378) returned for 0–1 visits. This result suggests that an early and more intensive focus on LTBI education and possible obstacles to treatment, as well as more active engagement and early non-clinic follow-up, might lead to more successful outcomes when referred children as a whole are considered (Figure 2). In the recent study from Houston noted previously, completion rate for treatment of pediatric LTBI was improved with monthly visits and weekly telephone contact with the local health department [10].

There are several limitations to the current work. For example, data were obtained prospectively but reviewed retrospectively. We did not have information available regarding patient perceptions of treatment or access or other personal or motivational factors that may have affected treatment initiation, selection of clinic location for follow-up, and treatment persistence. In addition, our measure of completion was based upon return to clinic for follow-up and reported medication adherence, which may not reflect actual medication use. Furthermore, although propensity score methods provide an intuitive method for comparison of children receiving treatment at the main hospital and neighborhood clinics, they are limited to measured variables and does not eliminate the impact of potential non-measured confounders such as motivation for treatment.

In summary, although increased accessibility to clinic follow-up may improve treatment completion, obstacles remain to the initiation of therapy and completion of treatment, especially for children from identified geographic regions. Improved acceptance of LTBI diagnosis by confirmation of infection with interferon-γ release assays may prove useful with those individuals or groups who doubt the diagnosis based upon receipt of BCG or other factors. Effective shorter courses of therapy are also needed, although our data suggest that most dropout occurs early and not in the latter stages of treatment. Early active engagement in therapy through education and other interventions appear to be critical in achieving the goal of successful treatment of LTBI.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References


