Lessons learned from two interventions designed to increase adherence to LTBI treatment in Latino youth

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A R T I C L E   I N F O

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A B S T R A C T

Effort is required to meet the Healthy People 2020 goal of tuberculosis (TB) disease reduction to 1 new case per 100,000 in the United States (US) and reduce burden among those disparately affected. Preventing new cases by reducing conversion from latent TB infection (LTBI) to infectious disease is one approach to reducing disease burden. This paper describes the outcome of a trial designed to determine if LTBI-positive youth prescribed daily Isoniazid with peer counseling would achieve higher adherence than attention control participants. The paper also compares adherence to a previous trial. 263 students age 15.9 years (SD = 1.2), 51.7% female, 96.2% Latino, 43.7% foreign-born were randomly assigned to condition. Adherence was measured by self-report validated by metabolite analysis. Outcome analyses used number of pills taken and proportion of youth consuming 80% of medication. There was no significant difference by condition for either analysis. Thirty-seven percent of adherence participants completed treatment versus 40% of controls. Without a usual-care control group we were unable to determine whether conditions were equally effective or ineffective. The study's inability to pay for treatment resulted in the intervention being tested in the context of compromised access to care. Still to be determined is whether same-age peers can influence adherence among Latino adolescents.

Trial registration: ClinicalTrials.gov Identifier NCT00233168.

1. Introduction

Despite progress in reducing global TB, latent Mycobacterium tuberculosis infection continues at pandemic levels, affecting approximately 33% of the world's population [1]. Disease propagation continues, as 5 to 15% of latently infected individuals progress to active TB, with higher conversion rates among immunocompromised individuals [2].

The US had a case rate of 2.9 per 100,000 in 2016 [3]. However, it is unlikely we will meet the Healthy People 2020 goal of 1 new case per 100,000 [4,5]. Foreign-born US immigrants bear the heaviest disease burden, with an active TB rate 13 times that of US-born persons in 2014, accounting for two-thirds of active TB cases [5]. Racial/ethnic disparities also exist. Asians have an active TB rate 29 times that of non-Hispanic whites; Hispanics and non-Hispanic blacks have rates eight times that of non-Hispanic whites [5]. TB disease rates also differ regionally, with California, Texas, Florida and New York accounting for 51% of US cases [5].

Obstacles to global and domestic reduction of TB include incomplete treatment, drug resistance, missed or delayed diagnoses, low rates of preventive therapy in HIV-infected individuals, and inadequate funding for detection, treatment, and prevention [5–7]. In the US, reactivation of LTBI accounts for over 80% of active TB cases [8]. While LTBI treatment may reduce the conversion rate by approximately 90%, treatment length raises concerns for adherence and hepatotoxicity [9]. Prescribed regimens are: 6 or 9 months of daily, or directly observed twice weekly, Isoniazid (INH); directly observed
12-dose once-weekly INH and Rifapentine; or 4 months of daily Rifampin [10]. Shorter courses of treatment have improved completion rates [6,8,11,12] with reduced adverse effects and costs [13]. These short course treatments are now listed as alternative treatment regimens in guidelines from the World Health Organization [14], the Centers for Disease Control and Prevention (CDC) [10], and California’s Department of Public Health [15]. However, intermittent regimens require direct observed therapy (DOT). The 9-month, daily INH regimen continues to be included as a recommended treatment [10,14,15], and efforts to increase completion rates for longer treatment regimens remain important. Completion rates vary from 19 to 96% across LTBI treatment studies. Among large-scale trials, INH completion rates range from 61 to 64% [9]. These treatment completion rates may be inadequate to lower rates of active TB.

Comparing intervention efficacy across LTBI treatment adherence trials is difficult due to varying definitions of adherence and sample heterogeneity. Studies often combine intervention strategies, such as incentives and DOT, making it difficult to identify which strategies are most efficacious. A review suggested that professional counseling, DOT, cash or non-cash incentives, and education, improved adherence, but also described inconsistency in efficacy for any specific intervention [11]. Cochrane reviews showed low evidence for improved adherence in adults from education, professional counseling, and incentives [16,17]. Among youth, DOT [18], professional counseling [16], lay counseling [19], and incentive-based programs [20] increased adherence.

Peer counseling has been shown to increase LTBI medication adherence among injection drug users [21], but not among homeless [22]. A quasi-experimental study of college students found an increase in medication adherence using peer advocates [23]. Another peer counseling study in adolescents showed no improvement in medication completion [24].

We significantly increased INH adherence in high-risk, middle and high school students, using college-age counselors [19], in a study based on the Behavioral Ecological Model (BEM) [25,26]. Over half (51.1%) of the counseled group completed treatment compared to 37.5% receiving usual care. Urine samples were collected at unscheduled visits to confirm medication adherence, increasing the accuracy of these reported adherence rates compared to unconfirmed reports in the literature [27].

A follow-on trial based on the BEM was conducted to determine if LTBI-positive high school youth prescribed daily INH medication with adherence counseling would achieve higher adherence rates compared to attention control participants. This paper describes the outcome [28,29] and compares adherence rates of the current study to our previous trial. Results provide insights regarding variance in medication adherence by age and group condition, within the context of economically strained conditions affecting families, providers, and investigators.

2. Methods

2.1. Design

From 2004 to 2007, LTBI-positive high school students who had not completed treatment for LTBI were recruited and randomly assigned to INH adherence counseling (n = 133) or a life skills counseling attention control (n = 130). Youth completed interviews at baseline, monthly during treatment, and upon treatment completion or 12 months post medication initiation. INH adherence was measured monthly during unannounced visits. Self-reported pill taking validated by urine analysis was used to assess adherence. Outcome analyses used cumulative number of pills taken and proportion of youth consuming 80% of prescribed medication. All procedures were approved by the San Diego State University Institutional Review Board.

2.2. Screening and recruitment

Seven high schools participated. With parental permission, Mantoux tuberculin skin tests were placed, and reactions read 48 to 72 h post-administration. Following CDC guidelines, students exhibiting reactions ≥ 10 mm of induration were classified as infected and referred for chest x-rays. None were active cases. Parents of LTBI-positive adolescents were invited to attend a meeting addressing test results, basic TB information, treatment, and the study’s description. All LTBI-positive adolescents were referred for treatment and screened for study eligibility. Eligibility criteria were: no plans to move within the year or receive LTBI treatment in Mexico; no physical limitations that would preclude participation in interviews or counseling; and the ability to communicate in English or Spanish.

2.3. Intervention

Following random assignment, participants were assigned to a peer counselor for 14, 30 to 40-min counseling sessions over 6 months: weekly for 8 weeks; bi-weekly for 2 months; and monthly for 2 months. Counseling sessions followed a standardized protocol in English or Spanish. For attendance, participants entered a raffle for cash prizes up to $100. Peer counselors (bilingual Latino students whenever possible) were recruited from participating schools. Counselors underwent 10 h of initial training to deliver either intervention. Counseling supervisors met twice monthly with peer counselors to discuss ongoing counseling methods and review participants’ cases.

2.3.1. Adherence counseling

Participants were informed about TB, LTBI, and LTBI treatment, including prescribed frequency and duration, potential side effects, and the importance of regimen completion. Counselors reviewed pill taking within the past week and since the last session; adherence strategies including calendars, pill dispensers, and cues for pill taking; and solutions for potential future adherence barriers. Counselors praised success and helped participants identify sources of social support for pill taking, including the establishment of a parent-delivered reward system.

2.3.2. Life skills counseling

Participants received counseling focused on developing life skills to enhance self-esteem. Topics included communication, goal setting, and time management. Life skills counselors were instructed not to counsel on medication adherence and to refer participants with questions about TB or treatment to their medical providers.

2.4. Measures

Research assistants were blind to participant conditions. Investigators and treating physicians were blind to outcome data until all measures were completed. “Intent-to-treat” procedures were employed.

2.4.1. Baseline and follow-up interviews

Baseline interviews were completed with adolescents and separately with their primary caregiver (79% mothers, 14% fathers, 6% others). Follow-up interviews occurred upon treatment completion or 12 months post-baseline. Parent interviews assessed demographics;
parenting strategies; social support; TB knowledge, attitudes, and exposure; and healthcare utilization. Adolescent interviews included questions about acculturation [30]; health and risk behaviors; past medication adherence; social support; TB knowledge and attitudes; and self-esteem. For interview completion, parents and adolescents each received $20 at baseline and $25 at follow-up.

2.4.2. Monthly interviews

Medication adherence was reported during unscheduled monthly interviews, until treatment completion or 12 months post-baseline. Unscheduled interviews were used to avoid changes in pill taking prompted by scheduled appointments. Participants reported pill consumption over the past 8 and 30 days. Monthly totals were summed to determine total pills consumed. Interviews assessed alcohol use, potential and perceived side effects, pill-taking barriers, and adherence aids used. Adolescents received $4 for completion of the first monthly interview, with a $1 increase for each subsequent interview. Cash prizes up to $100 were offered via raffles.

2.4.3. Urine assays

Accompanying monthly interviews, interviewers attempted urine collection. Urine samples were collected for 78% of completed interviews and analyzed for INH metabolites using the Arkansas method [31,32]. Detection of INH metabolite in urine indicated INH consumption within 72 h and was used to validate adolescent reports of recent pill taking [33]. The ability of the assay to detect and verify INH consumption was described to participants during the consent process to improve validity of reported pill taking [27].

2.5. Reliability and validity

Comparison of 8-day and 30-day recall measures provided a reliability check for monthly measures. Logarithmic transformations were conducted to adjust skewed distributions. Pearson correlation coefficients of log transformed 8-day and 30-day pill counts were significant (p < .001) and ranged from 0.64 to 0.99, with 11 of 12 monthly values greater than 0.80. Validity tests comparing monthly log-transformed 8-day and 30-day pill counts to the urine assay were significant (p < .01). Point biserial coefficients ranged from 0.49 to 0.76 for the 8-day recall, with 8 of 12 monthly values greater than 0.60, and from 0.34 to 0.72 for the 30-day recall, with 9 of 12 monthly values greater than 0.50.

2.6. Statistical analyses

Analyses were performed using SPSS version 22 (IBM, Inc, Armonk, NY). Composite scores of Self-Reported Risk Behaviors and Parental Involvement were created to facilitate regression analyses. Ran out of Medication summed monthly reports of missing pills because the participant ran out of medication and Alcohol summed the number of months participants reported using alcohol. The degree of family encouragement to take TB medication was measured monthly on a 5-point scale from “not at all” to “a great deal” and a sum score was created to assess the amount of Family Encouragement participants reported across 12 months.

The alcohol use, risk behaviors, and self-efficacy regarding taking daily TB medication variables were skewed, and either square root or logarithmic transformations were applied as appropriate to achieve normality. All analyses involving these variables were conducted using both the transformed and untransformed variables and as all results were essentially identical, the original untransformed variables were used to facilitate interpretation.

T-tests and analysis of variance (ANOVA) were used to compare baseline characteristics and treatment completion by group. Pearson’s correlation coefficients were used for bivariate analyses. Ordinary Least Squares multivariate regression analysis was used to test the strength of association of variables found significantly related to pill taking in bivariate screening, excluding number of sessions which was highly correlated with time spent in sessions, controlling for condition.

3. Results

3.1. Participants

Of 14,457 students invited for screening, 2792 had a test placed, read, and results recorded. Of these, 452 (16.2%) presented induration reactions ≥ 10 mm; 413 of these were eligible for the study. An additional 127 of 156 adolescents that had not completed treatment after a prior positive skin test were also eligible. Out of 540 eligible adolescents, 285 (52.8%) were recruited and 263 (92.3%) retained for analyses (see Fig. 1). Reasons for discontinued study participation included failure to initiate daily INH, physician refusing treatment, runaway, pregnancy, or refusal.

The mean age of the 263 adolescents retained for analyses was 15.9 years (SD = 1.2), 48.3% male, 96.2% Latino, 43.7% foreign-born, and 64.3% bicultural. Forty-one percent reported having medical insurance. Median parental level of education was between 7th and 11th grade. There were no significant baseline group differences in demographics, medication adherence history, or TB exposure, suggesting successful random assignment (see Table 1).

3.2. Potential and perceived side effects

Potential and perceived side effects were assessed monthly during the trial. Over the course of 12 months, there were reports of nausea (12.2% [3]), vomiting (9.9% [26]), yellow eyes (1.9% [5]), and yellow skin (1.1% [3]), but no one was diagnosed with hepatotoxicity during the study. One participant who experienced nausea and vomiting was switched to Rifampin for the remainder of a 9-month treatment regimen after having taken INH for approximately 6 months.

3.3. Intervention

The mean number of counseling sessions completed was 10.3 (SD = 4.1; Range = 0–14). There were no significant differences in mean number of sessions completed (Adherence = 10.8; Life Skills = 9.9). Mean length of intervention was 219 days (SD = 90.0), and also not significantly different.

3.4. Treatment completion and primary test of intervention

Defining treatment completion as consumption of 80% of CDC’s prescribed regimen of 270 pills in 12 months, recommended at the time the study was conducted [34], 37% of the Adherence group and 40% of the Life Skills group completed treatment. Defining treatment completion at the 80% level using the former CDC recommendation of 180 pills in 9 months [34], 74% of Adherence and 75% of Life Skills completed treatment. Neither of these comparisons was statistically significant. ANOVA revealed no significant group difference in total number of pills taken. Over 12 months, the mean for the Adherence group was 181.3 pills (SD = 66.4) and 184.4 pills (SD = 69.0) for Life Skills.
3.5. Exploratory analyses

To explain the variance in pill taking, demographic, family, behavioral, and peer-related variables hypothesized to influence pill taking were analyzed. Bivariate analyses revealed that running out of medication ($r = -0.38$, $p < .001$), alcohol use ($r = -0.17$, $p < .01$), risk behaviors ($r = -0.20$, $p = .001$), and age ($r = -0.14$, $p < .05$) were significantly negatively correlated with pill taking. Family encouragement ($r = 0.45$, $p < .001$), total time spent in counseling sessions ($r = 0.26$, $p < .001$), number of counseling sessions ($r = 0.17$, $p < .05$), parental involvement ($r = 0.20$, $p = .001$), and self-efficacy ($r = 0.14$, $p < .05$), were significantly positively correlated with pill taking. Group assignment, gender, household income, having medical insurance, country of origin, acculturation, grades in school, parent education, parental strictness, agreement with parental rules, pill taking tools used, barriers to taking INH, potential and perceived side effects, perceived peer adherence, and perceived consequence of not taking INH did not correlate significantly with pill taking. An Ordinary Least Squares multivariate regression model significantly explained 34% of the variance in pills taken over 12 months ($F_{9,246} = 15.665$, adjusted $R^2 = 0.34$, $p < .001$) (see Table 2).
## Table 1
Demographic characteristics by group.

| Characteristics                  | Total (n=263) | Adherence Group (n=133) | Life-Skills Group (n=130) |
|----------------------------------|---------------|-------------------------|---------------------------|
| Agea                            | 15.9 (1.2)    | 15.9 (1.3)              | 15.9 (1.1)                |
| Range                           | 13-19         | 13-19                   | 13-19                     |
| Gender                          |               |                         |                           |
| Female                          | 136 (52%)     | 70 (53%)                | 66 (51%)                  |
| Male                            | 127 (48%)     | 63 (47%)                | 64 (49%)                  |
| Latino                          | 253 (96%)     | 131 (99%)               | 122 (94%)                 |
| Place of Birth                  |               |                         |                           |
| US                              | 148 (56%)     | 71 (53%)                | 77 (59%)                  |
| Mexico                          | 105 (40%)     | 58 (44%)                | 47 (36%)                  |
| Other                           | 10 (4%)       | 4 (3%)                  | 6 (5%)                    |
| Acculturation Level             |               |                         |                           |
| Hispanic                        | 70 (27%)      | 37 (28%)                | 33 (25%)                  |
| Bicultural                      | 169 (64%)     | 82 (62%)                | 87 (67%)                  |
| American                        | 24 (9%)       | 14 (11%)                | 10 (8%)                   |
| Parent Educationb               |               |                         |                           |
| 7th-11th grade                  |               |                         |                           |
| Insurance                       |               |                         |                           |
| None                            | 111 (42%)     | 61 (46%)                | 50 (39%)                  |
| Medi-Cal                        | 43 (16%)      | 16 (12%)                | 27 (21%)                  |
| Private                         | 35 (13%)      | 18 (14%)                | 17 (13%)                  |
| Healthy Families                | 29 (11%)      | 17 (13%)                | 12 (9%)                   |
| Other                           | 3 (1%)        | 2 (2%)                  | 1 (1%)                    |
| Don't Know                       | 41 (16%)      | 19 (14%)                | 22 (17%)                  |

*mean (standard deviation)

Table 2
Multivariate regression of pill taking over 12 months (n = 256).

|                         | B   | SE  | 95% CI          | p-value |
|-------------------------|-----|-----|-----------------|---------|
| Group                   | -1.475 | 0.011 | -6.992 (-15.248, 12.297) | 0.833 |
| Age                     | -1.620 | 0.029 | 2.942 (-7.415, 2.417) | 0.582 |
| Ran out of medication   | -9.594 | 0.312 | 1.611 (-12.768, -6.420) | **0.000** |
| Time spent in sessions  | 3.502 | 0.149 | 1.227 (1.084, 5.919) | **0.005** |
| Family encouragement to take INH | 1.922 | 0.356 | 0.297 (1.338, 2.506) | **0.000** |
| Alcohol                 | -0.193 | 0.007 | 1.507 (-3.161, 2.774) | 0.898 |
| Self-efficacy           | 6.498 | 0.784 | 4.342 (-2.055, 15.050) | 0.136 |
| Parental involvement    | 2.156 | 0.064 | 1.823 (-1.436, 5.747) | 0.238 |
| Risk behaviors          | -4.768 | 0.068 | 3.991 (-12.628, 3.092) | 0.233 |

B = unstandardized regression coefficients
β = standardized regression coefficients
SE = standard error
95% CI = 95% confidence intervals for the unstandardized regression coefficients (B)
Bolded p-values indicate statistically significant correlates

### 3.6. Comparison to earlier cohort

Our previous study using college-aged counselors to coach high school and middle school-aged youth on INH adherence showed a significant difference in pill taking between adherence, attention control, and usual care conditions [19]. To explore possible reasons for differences across studies, we evaluated pill taking among the high school-aged subset of the first study compared to the current study. There were 201 high school-aged youth (mean age 16.5 years (SD = 1.2)) in the first study, conducted between 1996 and 2000 when LTBI treatment guidelines called for either 6 or 9 months of INH [35]. To control for the potential difference in prescribed treatment length, we compared treatment completion between the two cohorts at the 6-month time point.
ANOVs revealed a near-significant difference between experimental conditions for the high school sample from the prior study at 6 months (p = .08), while the current study remained non-significant (p = .83). Of note, the high school-aged youth in the adherence group from the earlier cohort took a mean of 119.9 pills at 6 months, while high school-aged youth in the adherence group from the current study took a significantly greater mean of 135.7 pills (p = .04). In addition, middle school-aged youth in the adherence group from the earlier cohort took a mean of 150.7 pills at 6 months, significantly more than high school-aged youth from the same cohort (p < .01), but not significantly different from the current high school-aged cohort (p = .21) (see Table 3).

### 4. Discussion

Peer counseling conducted by high school-aged peers did not significantly increase INH adherence compared to controls. Multivariate regression analyses were conducted to explore explained variance in pill taking. The strongest significant positive correlate of pill taking, which also had the highest ranking (largest beta) amongst all correlates, was family encouragement to take INH. As greater family support was associated with higher medication adherence, future studies could emphasize engineering social contingencies of reinforcement from family for medication adherence. Theoretically, an individual with a network of support including family, friends, and clinicians should demonstrate improved medication adherence [16,19,23,25,26].

Regardless of group assignment, total time spent in counseling sessions was also significantly positively associated with medication adherence in the model, suggesting that both conditions affected medication adherence. Alternately, youth that spend more time in counseling sessions may be more likely to exhibit medication compliance.

Running out of medication was a strong significant negative correlate of pill taking in the regression results. Medical services and cost of care systems need improvement to reduce barriers to pill acquisition and medical supervision to enhance adherence. Provider-level barriers to LTBI treatment discovered during this trial included: a demonstrated lack of basic TB knowledge on written tests and in practice; relaying misinformation; inappropriate dosing; not scheduling monthly visits; inappropriate length of treatment regimens; poorly constructed methods of obtaining medical histories of possible INH side effects; and problems dispensing prescribed refills [36]. It is not likely that counseling of any kind can compensate for systems that fail to provide appropriate care or medication.

Strengths of the study include the assessment of LTBI rates in foreign-born and non-foreign-born Latino adolescents in the San Diego border region (35% and 15%, respectively, compared to 2% for US-born non-Latinos). These rates are comparable to prior assessments [37]. This study targeted an important group, with elevated LTBI rates, greater ability to tolerate INH treatment due to their age, and offered more protected years conferred by treatment completion. The study sample also faced health care disparities; over two-thirds had either no medical insurance or publicly-funded health care. Additional strengths included the use of unannounced urine collection visits, reliable and valid measures of medication adherence, and high rates of retention and measures completion.

A weakness of the study was the lack of a usual care control group, partially based on limited study funds. Consequently, we were unable to determine whether both experimental conditions were equally effective or ineffective in improving medication adherence. The inclusion of the attention control condition to equalize reactivity to counseling attention [38] may have inadvertently made the conditions too similar to result in differentiation.

Additionally, the medication adherence condition may not have been of sufficient quality to exceed reactivity effects. In contrast to our earlier study, this study used high school-aged peer counselors, who may have lacked the required skills or resources to help their peers overcome barriers to medication adherence, including transportation, medical costs, and access to care [36].

The inability of the study to pay for medication or physician visits resulted in the intervention being tested in the context of compromised access to medication and care [36]. Most participants were from low-income, uninsured families and paid for care out of pocket, which possibly contributed to low adherence. Funds for LTBI care were largely unavailable due to concurrent CDC funding reductions for TB control. During the first study, public funds were available from County resources for LTBI treatment at County or community clinics. While limited funding and barriers to medical care due to costs were potential study limitations, these conditions could be considered a strength, since they demonstrate the reality of what occurs during LTBI treatment in the community. Research studies testing compliance to LTBI treatment under ideal conditions, with limited barriers, report levels of compliance that are not reproducible under real world conditions.

Despite economic hardship, youth in the current study consumed more pills than in our earlier adherence trial [19]. Youth in both conditions took about 16 more pills over 6 months than high school-aged youth in the adherence group from the first study, and about 30 more pills than high school-aged youth in attention control or usual care conditions from the first study. The improvement in pill taking between trials may be attributable to the medication adherence and life skills interventions or to other unknown factors.

Neither group within the current trial had a treatment completion rate > 75%. Results fell within the 51% to 92% adherence range found in past adolescent LTBI adherence studies. But significant variance in

### Table 3

| Current Study | Prior Study High School Group | Prior Study Middle School Group |
|---------------|-------------------------------|---------------------------------|
| Adherence     | Life Skills                   | Adherence | Attention Control | Usual Care | Adherence | Attention Control | Usual Care |
| (n=133)       | (n=130)                       | (n=64)    | (n=74)            | (n=63)     | (n=28)    | (n=33)         |           |
| **Duration**  |                               |           |                   |           |           |               |           |
| 6 months      | 135.73                        | 136.95    | 119.91            | 105.73    | 102.35    | 150.68        | 135.91    | 133.61 |
| (44.32)       | (44.80)                       | (42.97)   | (46.81)           | (50.93)   | (27.05)   | (42.08)       | (45.99)   |       |
| 9 months      | 177.49                        | 178.15    | 166.50            | 147.65    | 130.67    | 210.64        | 183.35    | 189.76 |
| (64.38)       | (65.11)                       | (57.73)   | (69.90)           | (67.76)   | (42.13)   | (64.54)       | (69.91)   |       |
| 12 months     | 181.30                        | 184.41    | -                 | -         | -         | -             | -         |       |
| (66.34)       | (69.02)                       |           |                   |           |           |               |           |       |

SD = Standard Deviation

**Table 3**

Cumulative mean pill count (SD) by cohort, school age and group.
adherence measures and definitions of adherence still leave valid comparisons difficult [18,19,24,39,40,41]. Apparent from adolescent INH adherence study results is that dates to be more intensive interventions are required to protect LTBI-positive adolescents from active TB. The findings from this study suggest that this appears to be particularly true for youth with less family support and those who have difficulty regularly obtaining INH medication. Increased clinical oversight, which frequently failed to meet CDC guidelines in this study, may be important for medication refills and boosting adherence rates [36].

5. Conclusions

Still to be determined is whether same-age peers can effectively influence medication adherence among Latino adolescents. Future research including a usual care condition can make this determination more definitively. Payment for treatment or provision of medication should be established to remove lack of access to medication as a potential reason for intervention failure. Continued efforts in the area of TB control are required to achieve unmet key goals [4,7], particularly for low-income populations in border regions, in communities with large immigrant populations, and among groups with the highest rates of LTBI and the lowest medication adherence.

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Competing interests

The authors have no competing interests to declare. The National Heart, Lung, and Blood Institute of the National Institutes of Health was not involved in the study design; collection, analysis, and interpretation of the data; writing of this manuscript; or in the decision to submit this manuscript for publication.

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