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# Increasing Follow-up in College Students with Latent Tuberculosis Infection

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Increasing Follow-up in College Students with Latent Tuberculosis Infection

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#### Abstract

Around 13 million people in the United States have latent tuberculosis infection (LTBI) with a 5-10% chance of developing active tuberculosis (TB) in their lifetime if not treated (Center for Disease Control, 2015). At a University Student Health Center (SHC), there is a matriculation requirement for TB testing for students that screen as high risk. Many students have these testing requirements performed at outside clinics, including foreign clinics, and follow-up regarding education about LTBI and treatment recommendations was often missing. The purpose of this evidence-based practice (EBP) project was to increase follow-up, education, and treatment options after diagnosis of LTBI. Students presenting with LTBI to the SHC received a standardized message through the secure patient-portal regarding their diagnosis, treatment options and education regarding LTBI. It asked them to follow-up with a message, telephone call or in-person appointment. Prior to the intervention, most students with LTBI received no follow-up, and after the intervention 100% of new cases received follow-up. A total of 42 students were sent a secure message, 31 read the secure message and 13 of those students contacted the health center or an outside provider for further follow-up. Out of those 13 students, 7 started treatment for LTBI. The goals of this study were to increase follow-up and education around LTBI, and increase the number of students choosing treatment, all of these outcomes were met. The secure message system was a reliable way to contact students regarding their diagnosis and education around LTBI.

*Keywords*: Latent tuberculosis, interferon-gamma release assay, tuberculin skin test, mycobacterium tuberculosis

#### Background

Latent tuberculosis infection (LTBI) is diagnosed when an individual has either a positive tuberculin skin test (TST) or interferon-gamma release assay (IGRA) blood test, negative chest x-ray (CXR) and is showing no signs or symptoms of active tuberculosis (TB) disease (Centers for Disease Control and Prevention (CDC), 2013). The TST or IGRA detects an individual that has been infected with mycobacterium TB and a CXR, along with a thorough history, rules out active disease. In certain circumstances, a sputum sample is sent as well. Individuals with LTBI are infected with mycobacterium TB, but it has not progressed to active disease, and during this latent stage they are not at risk of spreading the disease (Johnson, Moore, & Patterson-Johnson, 2017). It is estimated that around 13 million people in the United States have LTBI, with a 5-10% chance of developing active TB in their lifetime if not treated (CDC, 2013). While most people with LTBI develop active TB within the first five years of being infected, they are still at risk throughout their lifetime (World Health Organization (WHO), 2015). First-line therapy for LTBI is 9-months of isoniazid (INH) therapy, if these individuals receive treatment, their risk for developing active TB can decrease to 0.5-1% (CDC, 2013).

#### Problem

Hall and Elliott (2015) stated that TB kills more people annually than any other infectious disease besides HIV. Those with active TB are directly monitored and require an extensive medication regimen due to the severity of the disease and the contagious manner. Since LTBI is not contagious, it is sometimes overlooked, and evidence-based treatment is not discussed or started in these individuals. Belcher et al. (2012) stated that 59% of new TB cases in the United States were in foreign-born individuals, with Hispanics having the largest number of reported cases among all the groups. The University Student Health Center (SHC) is within 30 miles of

the Mexican-American border and has a very diverse population, including foreign-born students coming to the United States for their schooling. Based on the University's 2017 federal report 49.5% of students are Caucasian, 19% are Hispanic or Latino, 9% are international on a visa, 8.6% are Asian, 4% are African-American and <1% for American Indian or Pacific Islander (Race/Ethnicity of Fall 2017 Students: Federal Reports, 2017). To meet the matriculation requirement, students who screened high-risk for TB exposure, nursing students, volunteers and other entities are asked to submit TB testing. A positive IGRA blood test or TST require additional documentation of a negative chest x-ray. For students that received testing at an outside clinic, information about follow-up care including INH was requested but rarely obtained. Many of these students were international students coming from countries where it is not a typical practice to treat LTBI. Students that received their positive testing in the SHC were offered follow-up appointments to discuss INH but these appointments were rarely scheduled or kept. A chart review from 6/1/16-2/16/17 was performed and 68% of students with a new diagnosis of LTBI had no follow-up regarding INH.

#### Review of the Literature

A review of the literature was performed using multiple nursing and health science search engines. This included: PubMed, CINAHL, Medline, and the Cochrane library including Cochrane central register of controlled trials and Cochrane database of systematic reviews.

MeSH terms included: "Latent Tuberculosis", "interferon-gamma release assay", "tuberculin skin test", "mycobacterium tuberculosis". Inclusion criteria included: English language, adolescents and adults, and studies within the past ten years. After review of multiple articles, four studies were chosen for the project based on relevance, strength and quality of evidence.

Getahun et al., (2015) developed guidelines for management of LTBI, in hopes to reduce TB by 90% by 2035 as part of the WHO End TB Strategy. A systematic review of the evidence was performed using a structured approach, and this provided the framework for the LTBI guidelines and algorithms for WHO. Testing for LTBI should be performed on those at high-risk or with certain clinical indications, and a thorough history/symptoms should be performed before testing (Getahun et al., 2015). A TST or IGRA are both appropriate tests and either can be used. Getahun et al., (2015) recommended anyone with a positive TST or IGRA should then receive a CXR to rule-out active TB. After LTBI is diagnosed, treatment should begin immediately. Getahun et al., (2015) recommended a few LTBI treatment options: 6 to 9-months of INH therapy, weekly INH plus rifapentine for 3 months, daily INH plus rifampicin for 3-4 months, or daily rifampicin for 3-4 months.

The CDC (2013) stated that TB testing is routinely performed on low-risk individuals to meet legal or administrative requirements which is discouraged. In low-risk individuals, a TST reaction of >15mm is considered positive where as a high-risk is >5mm and moderate risk is >10mm to be considered positive. Testing requirements for those who received the bacilli Calmette-Guerin (BCG) vaccination is different than those who did not receive the vaccine. The BCG vaccination is not recommended in the United States but is given in some high-risk TB countries to prevent TB infection. A TST can produce false-positive results in those individuals who received a BCG vaccine. However, CDC (2015) stated that the TST reactivity should fade overtime, so if a BCG vaccine was given early in life it should not affect TST results. The IGRA blood test will have no false-positives in relation to the BCG vaccine, so the CDC (2013) recommended that those who received the BCG vaccine should receive an IGRA blood test as the preferred TB testing method. CDC (2015) recommended three treatment regimens that could

be used to treat LTBI: an INH regimen, a directly observed regimen of INH plus rifapentine or a rifampin only regimen. The 9-month INH regimen was proven to be the gold standard with minimal side effects.

In a study by Belcher et al., (2012) a partnership was made between a university and a public health department (PHD) to improve follow-up and compliance of LTBI. There were many shortages at the PHD, so follow-up for patients with LTBI became non-existent and this partnership was formed to help increase the task force. The PHD identified 280 individuals with LTBI that had not received any follow-up. Belcher et al., 2012 included any individual with a positive TST or a positive TST and a negative CXR. The purpose was to identify a way to follow-up with all 280 individuals and discuss LTBI and treatment options. Methods included using a standardized letter and/or telephone script with hopes to make direct contact with the patient or have them contact the PHD after receiving the notification (Belcher et al., 2012). For patients with just a positive TST, a CXR was recommended and then continued follow-up after receiving results of the CXR. For the patients with a positive TST and negative CXR, preventative treatment was discussed. Nine-months of INH therapy is the recommended treatment for those with LTBI and was offered to the individuals in this study at no cost (Belcher et al., 2012). An "active" file was started for each person to track the follow-up and where each person was in the process. A telephone call was made, if no response, then a letter was sent, and if still no response a house-visit was made. If after three attempts reaching the patient was unsuccessful, then the file was closed (Belcher et al., 2012). Out of the 280 individuals, 14 started treatment and 40 never responded. Limitations to this project included language barriers, inaccurate patient information and inability to leave detailed information on a personal telephone messaging system.

A retrospective study performed by Chang, Polesky, and Bhatia (2013) used home-based follow-up to increase adherence in LTBI. Instead of monthly clinic visits that required patients to leave their homes, a home-based follow-up program was designed. Chang, Polesky, and Bhatia (2013) stated that the better the patient adherence, the better outcomes for not developing active TB. LTBI education, assessment of compliance, language translation and monitoring of patients was done without them coming into the office. There were 3918 patients in the study and 986 were assigned to the home-based follow-up group, while the other 2932 remained in the normal clinic follow-up group. Chang, Polesky, and Bhatia (2013) study showed that home-based follow-up had 21% better probability of adherence versus the in-clinic group and was a greater indicator of INH treatment completion.

#### Intervention

The purpose of this evidence-based practice (EBP) project was to increase follow-up after diagnosis of LTBI, increase education around LTBI and treatment options and increase the number of students choosing treatment. A report was produced monthly that included all students who had gotten a CXR from April 2017 to October 2017. The medical assistant at the SHC would also notify the provider of any new positive TB results on a daily basis. Anyone who had a history of a positive TB test, positive test results done at the clinic, or documentation of a positive TST or IGRA from an outside clinic was required to get a CXR. The monthly report included students who had TB testing at the SHC and those who had testing elsewhere. Using this list and their TB records/results, students with LTBI were identified. LTBI was added to their medical history and all these students received a standardized message through the secure patient-portal. This message entailed the student's diagnosis, why they received the message, education around LTBI and treatment options. It asked them to follow-up with a secure message,

telephone call or in-person appointment to discuss these results. The students who followed-up to the first message received further information and education on LTBI. This included a thorough history, what LTBI means, their risk of developing active TB, treatment options and the risks/benefits of treatment vs no treatment. Nine-months of INH therapy was offered to all students who received follow-up. For those students who did not follow-up to the first message, a second secure message was sent. This message had a brief version of the first message and included a short survey as to why they had not followed-up with the SHC. If there was no response after the second secure message, then the student's file was closed.

#### **Ethical Considerations**

The Institutional Review Board of the University of San Diego approved project implementation and dissemination of the findings. After being deemed an evidence-based practice project, implementation was approved by the supervising physician at the University Student Health Center. Permission was granted for publication and presentations using any data collected for the project. All data was cleansed of patient, student or institutional identifiers.

#### Results of Outreach to College Students with LTBI 45 40 42 29 35 30 13 34 25 8 20 Yes 21 21 15 No 10 5 13 2 5 8 Sent secure Read Student **Treatment** Sent 2nd Read Student **Treatment** responded received secure responded received message message: message Initial message education received Phase 1 Phase 2

#### **Evaluation of Results**

Figure 1. Response rates after a secure message was sent to students with LTBI

The main outcome of this EBP project was to increase follow-up for students with LTBI. In phase 1 of Figure 1, 100% of students with LTBI were sent a secure message about their diagnosis and education regarding LTBI. Of those 42 students, 29 students read the message and 8 students responded to the message. In phase 1, out of the 8 students who responded, 2 students began treatment for LTBI.

In Phase 2 of Figure 1, a second secure message was sent to those students who did not read the first message or read the first message but did not respond. Thirty-four students were sent a secure message in phase 2. Thirteen students read the second message, 5 students responded, and all of those 5 students started treatment.

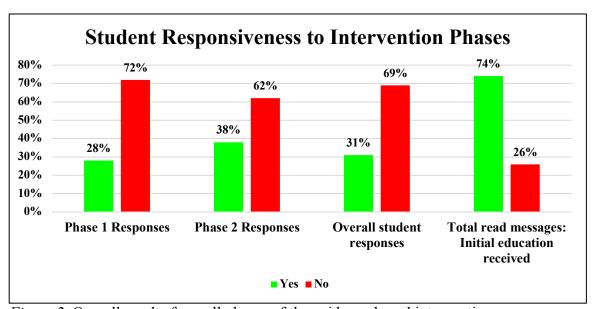


Figure 2. Overall results from all phases of the evidence-based intervention

Figure 2 represents the responsiveness of the students during each phase of the EBP project. In phase 1, of the 29 students who read the message, 28% of them responded. In phase 2, a total of 38% of students who read the secure message responded. Overall, 31% responded who read the secure message.

Thirty-one of 42 students received and read the secure message, which means they got follow-up and education around LTBI. Seven of the 42 students received treatment for LTBI. In total, 74% of students received LTBI education and 17% of those students started treatment for LTBI.

#### Cost Benefit Analysis

There were no extra costs spent prior to or during implementation of this EBP project. Using the secure messaging system, the provider was able to send a message quickly to students regarding LTBI. It was an efficient way to relay education and promote follow-up in those students who may be hard to reach by phone or in-person. A secure message only takes minutes to send where as a phone-call or office-visit follow-up may last >15 minutes per patient. By using the secure messaging system ,no extra visits or hours is taken out of the providers schedule.

Every student with LTBI who is educated and treated decreases their chance of converting to active TB in their lifetime. Guo et al., 2008, stated that the average cost of treatment for LTBI is \$75 to \$100 while treatment of active TB can range anywhere from \$5,000 to \$50,000. Seven students began LTBI treatment which could save anywhere from \$35,000 to \$350,000. By treating LTBI, the financial burden active TB has on a society will be decreased.

#### Summary

Secure messaging proved to be effective in relaying information and education to college students with LTBI. There was no follow-up in the past for students with LTBI and during this EBP project, 100% of students with LTBI received follow-up. While the response and treatment rates were low, 31 of the 42 students were reached and read the secure message related to education and treatment options for LTBI. This means that 74% of the college students with

LTBI have had a seed planted on their diagnosis, what LTBI is and treatment options. While most students did not chosen treatment at this time, maybe they will choose it in the future, or at least be aware of active TB symptoms if the LTBI progresses in their lifetime.

During phase 2 of the EBP project, a survey was completed asking students why they did not respond to the secure message. All the students who completed the survey had sought care and treatment with another provider after the initial secure message regarding their LTBI. This survey was not sent during phase 1, so there could have been a lot more students who had received treatment or followed-up with an outside provider. Opportunities in the future would include this survey in both phases of the EBP project.

#### Limitations

Many students in the EBP project were from foreign countries where the BCG vaccine was given. The CDC, 2013, stated that IGRA testing is preferred over a skin TST for those who have received the BCG vaccine, as there will be no potential for a false-positive result. The BCG status of most of these students was not available, so the validity of their TST results could be uncertain. It would be important to determine any false-positive TB results to ensure a correct diagnosis and that INH therapy is not being started for those who do not need it.

Other limitations in this study include the unique population of college students. Interacting with this population has many challenges and barriers, especially within the realm of increased technology, social media and smartphones. Most studies on LTBI are related to the general population or high-risk groups but none directly related to college students. These studies are also directed more at treatment compliance versus the follow-up after initial diagnosis of LTBI. Using technology and telehealth could show great improvement in the diagnosis and management of LTBI moving forward.

#### Conclusions

TB is a public health issue and LTBI needs to be addressed by providers treating these patients and managing the results of their TB tests. LTBI can be safely managed in the primary care setting using the evidence-based practice guidelines placed by WHO and CDC.

Further studies could be done on the barriers related to follow-up and reasons why students did not respond. While the secure message system was effective, other methods such as telephone calls, written mail letters or an in-person visit could be evaluated.

Sustainability of this EBP project is possible with the help of the medical assistants and providers at the SHC. If every patient with LTBI is sent the secure message at the time of diagnosis, then students will not be lost to follow-up in the future.

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