

EVIDENCE-STATEMENT: TUBERCULOSIS (Screening)

Why This Chapter is
Important for
Employers:
An Overview

- An estimated 3% to 5% of persons (or 9.8 to 15.1 million persons) residing in the United States have latent tuberculosis infection (LTBI),¹ a condition in which an individual is infected with *Mycobacterium tuberculosis* but does not currently have tuberculosis (TB) disease. Individuals who have LTBI have no signs or symptoms and cannot spread TB. Approximately 5% to 10% of persons with LTBI will develop clinical TB disease at some point in their lifetime.²⁻³ When active TB disease occurs, these persons may become infectious and then transmit the infection to others.
- The global TB burden is substantial and increasing. Immigration to the United States from areas of the world where TB is common is continually supplementing the pool of persons in the United States with TB and LTBI.
- Preventing TB involves preventing those with LTBI from *progressing* to TB disease. Therefore, testing and treatment for LTBI is recommended for those at high risk for TB disease, especially those from regions with high TB rates.
- Identifying and properly treating persons with TB disease early can prevent extensive transmission and costly contact investigations.
- Businesses that employ workers from countries or regions where TB is common or that are based in those countries may face a heightened risk of a TB outbreak. In addition, businesses that employ workers at high risk for TB (such as HIV-infected or other immunosuppressed persons or low-income minorities) or have clients who are at high risk for TB need to be aware and knowledgeable about TB and include prevention activities in their plans.

Clinical Preventive Service Recommendations

U.S. Preventive
Services Task Force
Recommendation

In 1996, the U.S. Preventive Services Task Force (USPSTF) recommended screening for LTBI with tuberculin skin testing (TST) for asymptomatic high risk persons.⁴

The USPSTF recognizes the importance of targeted screening for tuberculosis. However, the USPSTF has decided not to update its 1996 recommendation and rather defers to the guidelines of the Centers for Disease Control and Prevention (CDC) referenced below.

CDC
Recommendation

CDC has published guidelines on screening for LTBI,² preventing transmission in health-care settings,⁵ investigating contacts of infectious TB patients,⁶ treating TB disease,⁷ and controlling TB in the United States.⁸

The CDC recommends conducting targeted testing of persons at high risk for TB (see below) to identify LTBI and TB disease early and treating those who have TB and LTBI to prevent transmission and prevent progression of LTBI to disease.² Targeted testing programs should be conducted among groups at risk for recent infection with *M. tuberculosis* and those who, regardless of duration of infection, are at increased risk for progression to TB disease.

The CDC does not recommend targeted testing of persons at low risk for TB, with the exception of initial (baseline) testing of persons whose future activity will place them at increased risk of exposure, such as some healthcare workers who may require serial screening.

Evidence Rating:

Not Specified. Each of the referenced CDC guidelines describes the evidence basis for the recommendations, but not all provide ratings.

Information Sources

The recommendations and supporting information contained in this document came from several sources, including the:

- Centers for Disease Control and Prevention (CDC)
- Peer-reviewed research
- U.S. Preventive Services Task Force (USPSTF)

The background and supporting information contained in this document is a compilation of research findings. All information presented in this document should be attributed to its referenced source and should not be considered a reflection of other organizations cited in the text.

Condition/Disease Specific Information**Epidemiology of Condition/Disease**

Tuberculosis is a bacterial disease caused by *Mycobacterium tuberculosis*, which usually attacks the lungs (pulmonary TB) but can attack any part of the body, including the kidney, spine, and brain. Symptoms of TB disease include a productive cough lasting more than 2 to 3 weeks, chest pain, coughing up blood, fever, chills, night sweats, appetite loss, weight loss, and easy fatigue. A person who has developed infectious pulmonary or laryngeal TB disease can spread infection to others through coughing, sneezing, speaking, or singing.

When exposure to infectious TB occurs, the health department conducts a contact investigation.⁶ Studies of contact investigations in the United States reveal that 30% to 40% of close contacts of persons having infectious TB disease become infected with LTBI (as evidenced by a positive tuberculin skin test or “TST”) and identify an additional two percent with active TB disease.⁹⁻¹⁰ Approximately 5% to 10% of persons with LTBI will progress to clinically active TB disease at some point in their lives.²⁻³ About half of those who progress will do so in the first 2 years after initial infection (i.e., recent infection). Treatment of LTBI reduces the risk of developing TB disease by 70% to 90%.²

Populations at high risk for TB include persons who had recent close contact with an infectious TB patient, foreign-born persons from areas where TB is common, HIV-infected and other immunosuppressed persons, homeless persons, substance users (e.g., injection drug users, crack cocaine users, alcoholics), low-income minorities, young children exposed to high-risk adults, health care workers who serve high-risk clients, residents and employees of high-risk congregate settings such as homeless shelters, correctional institutions, nursing homes, or mental institutions.

The proportion of TB cases in the United States occurring among foreign-born persons increased progressively during the 1990s; in 2004, persons born outside the United States accounted for 54% of reported cases.¹¹ Although foreign-born persons who received a diagnosis of TB in 2004 were born in approximately 150 countries worldwide, 5 countries of origin accounted for over half of foreign-born persons with TB: Mexico (25%), the Philippines (11%), Vietnam (8%), India (7%), and China (5%). The number of states in which greater than 50% of the total reported cases occurred among foreign-born persons increased from 5 (10%) in 1992 to 22 (44%) in 2004.¹¹ Among U.S. states and cities, this profile can change rapidly, reflecting changes in patterns of immigration and refugee settlement.¹² Globally, half of new TB cases each year occur in India, China, Indonesia, Bangladesh, and Pakistan.¹³

In the United States, the majority of healthcare workers do not have a high risk for TB, but some, such as respiratory therapists, appear to be at greater risk.^{5,14} Persons who work in, or are served by, clinics or community health organizations providing care to HIV-infected persons are considered a priority population for targeted testing and treatment of TB and LTBI because of the risk of transmission to this highly vulnerable population.⁸

Condition/Disease Risk Factors

An individual at high risk for TB has one or more of the following characteristics: recent exposure to a person having infectious TB; history of previous TB disease or positive tuberculin skin test or QuantiFERON-TB Gold result; HIV infection or other immunosuppressive medical condition; being a young child with contact to a high-risk adult; history of injection or non-injection drug use; birth outside the United States in a region where TB is common; being a resident or employee of a high-risk congregate setting; being a member of a low-income minority population; or being a health care worker who serves high-risk persons. However, TB should be suspected in any patient who has had a persistent cough for more than 2 to 3 weeks, with at least one additional symptom, including fever, night sweats (sufficient to require changing of bed clothes or sheets), weight loss, or hemoptysis (coughing up blood).

Value of Prevention

Economic Burden of Condition/Disease

From the late 1980s through the early 1990s, outbreaks of TB among HIV-infected persons in the United States contributed to a surge in TB, reversing a steadily declining trend. Billings or charges for inpatient TB care increased 3.2-fold from 1985 through 1990.¹⁵ During that period, an estimated 77,700 TB hospitalizations resulted in about 1.1 million days of care. The total direct medical expenditures for TB in a 1991 study of TB outpatient treatment, screening, and treatment for LTBI, contact investigation, and surveillance were estimated at \$703 million and TB costs were estimated at \$574 million (in year 1991 dollars.) In addition, 20,803 TB hospitalizations resulting in 413,980 days of inpatient care occurred.¹⁶ Extrapolating from a 1996 study at 10 mostly urban sites, an estimated 12,631 TB hospitalizations and approximately 270,650 days of inpatient care occurred in the United States in 1996.¹⁷ A study in 2000 estimated that there were over 11,000 TB hospitalizations resulting in more than 160,000 inpatient days.¹⁸ Approximately half of TB patients are hospitalized,

which adds approximately \$19,000 to the cost of treatment.¹⁷ While it appears that there might be a slight downward trend in TB hospitalizations as management practices have improved and the total number of TB patients declines each year, TB still places a substantial burden on the U.S. economy.

More recently, direct medical TB costs have been estimated (and updated to 2004 dollars) from several studies¹⁷⁻²¹ with the costs varying according to the kinds of treatment needed. Direct medical costs of LTBI screening and treatment caused by exposure to strains susceptible to normally-used drugs were approximately \$208 to \$311 per person without directly observed treatment (DOT).¹⁹ DOT improves the likelihood of completion of a full course of treatment. If drug susceptible TB disease is diagnosed, outpatient treatment costs are approximately \$4,000 under daily DOT.²⁰

Costs associated with MDR TB are likely to be much higher than for drug-susceptible tuberculosis due to longer hospitalization, longer and more complex treatment with more expensive and toxic medications, and higher mortality. Direct medical costs associated with MDR TB hospitalization range from \$15,000 to \$137,000 per case.²¹ In-patient MDR TB costs average \$30,740 per person and \$1,232 per person-day of hospitalization. Outpatient costs average \$22,625, or \$52 a day per person. Direct medical costs for both inpatient and outpatient MDR TB care average approximately \$53,000 per person. For each infected contact of a patient with multidrug-resistant (MDR) TB in California, the cost of two years of follow-up and treatment to prevent the development of MDR TB was estimated to be \$11,125.²²

These direct medical costs are underestimates because they exclude the additional public health program costs of providing culturally appropriate outreach, interpreters, and transportation services. Also, in areas where the cost-of-living is much higher, such as San Francisco and New York City, medical costs may be 80% to 95% higher.²³ Additional costs to society include the productivity losses associated with TB deaths and productivity losses for the 6 months of treatment when patients are unable to work.

Workplace Burden of Condition/Disease

The workplace burden of TB includes lost productivity, absenteeism, high hospitalization costs, and disease transmission to other employees. Hospitalization burdens include not only direct medical costs, but also the lost productivity of workers during hospitalization days. Outpatient care involves workers' lost productivity due to clinic visits or fatigue and other effects of the illness. In fact, productivity losses may last for months or longer if permanent physical effects are experienced.²⁴ Disease transmission may result in a costly contact investigation as well as stigmatization and disruption of business. However, the risk of TB transmission in the workplace is highly variable, depending on factors such as the TB risk of clients served, the activities conducted by the business, and the TB risk posed by coworkers.⁵

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| <p>Economic Benefit of Preventive Intervention</p> | <p>Successfully completing a treatment regimen for LTBI and thereby eliminating the preventable direct medical cost of illness due to TB disease saves \$4,000 per case.²⁰ Benefits rise if the case of disease that is prevented would have required hospitalization (\$19,000 benefit) and even more if that case would have required treatment of a multi-drug-resistant strain (\$15,000 to \$137,000 benefit).^{17, 21} Additional benefits include the reduction of worker productivity losses due to illness and the avoidance of stigmatization or work disruption that often follows a TB outbreak in a worksite.</p> <p>Early identification of TB disease can also be expected to substantially reduce the costs of contact investigations, which would be less extensive than if the patient were undiagnosed for a long period, and costs of secondary TB cases among contacts, which would be fewer than for contacts of later diagnosed cases.</p> |
| <p>Estimated Cost of Preventive Intervention</p> | <p>In 2004, the private-sector cost of tuberculosis screening averaged \$22; approximately 95% of all paid claims fell within the range of \$0 to \$49 per screen.²⁵</p> |
| <p>Estimated Cost of Treatment</p> | <p>Direct medical costs of LTBI screening <i>and</i> treatment (without DOT) for infection by presumed <i>M. tuberculosis</i> strains that can be treated by first-line drugs are approximately \$208 to \$311 per person.¹⁹ If employees miss work for the screening and treatment, productivity losses for the standard 9 months of treatment might also occur. The direct medical cost of illness due to TB disease is approximately \$4,000 per case of drug susceptible TB disease treated by DOT.²⁰ Costs rise if the case of disease requires hospitalization (\$19,000) and even more for treatment of a multi-drug-resistant strain (\$15,000 to \$137,000).^{17, 21}</p> |
| <p>Cost-Effectiveness and/or Cost-Benefit Analysis of Preventive Intervention</p> | <p>For individuals at high risk for TB, the benefits of screening for LTBI and completion of treatment outweigh the costs if treatment reduces the risk of — and costs associated with — TB disease and hospitalization.²⁶ Reducing the risk of medication-induced adverse events and any potential productivity losses associated with LTBI treatment would add to the benefit.</p> |

Preventive Intervention Information

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| <p>Preventive Intervention: Purpose of Screening</p> | <p>Screening/testing individuals at high risk for TB allows clinicians to identify affected persons and begin treatment. Early identification and treatment of TB disease improves outcomes and reduces the risk of transmission. Identification of LTBI and completion of LTBI treatment reduces an individual's risk of developing TB disease by 70% to 90%.²</p> |
| <p>Benefits and Risks of Intervention</p> | <p>Clinicians should individualize their decision to conduct targeted testing and treatment for TB and LTBI to the specific patient's risks and environment. Routine testing for TB or LTBI is not recommended for persons who are not at high risk for TB. The TST is subject to variability like all medical tests, but many of the inherent variations in administering and reading tests can be avoided by careful attention to details and the clinical provider should be aware of these details. Interferon gamma release assays (IGRA), such as the QuantiFERON-TB®</p> |

(QFT) Gold blood test can be used instead of the TST for LTBI screening. CDC has published guidelines for the use of approved IGRAs,²⁷ and will do so for additional tests as they become available. For individuals at high risk for TB, the benefits of LTBI screening and completion of treatment outweigh the costs.²⁶

Screening high-risk populations for TB disease by asking about the major TB symptom, a cough of 2 to 3 weeks duration, has been shown to be effective,²⁸ and is likely to be cost-effective over routine screening using chest radiographs. This intervention is simple, inexpensive, and is potentially cost-effective in many settings.

Initiation, Cessation, and Interval of Screening

TB and LTBI testing programs should be conducted among groups at high risk for recent infection with *M. tuberculosis* and those who, regardless of duration of infection, are at increased risk for progressing to TB disease (e.g., HIV-infected or other immunosuppressed persons with certain medical conditions, injection drug users, those with a history of inadequately treated TB disease).

Workers in health-care settings who have face-to-face contact with patients with suspected or confirmed TB disease or clinical TB specimens should be included in a screening program.⁵ In settings where routine screening is mandated but classified as low risk for TB exposure (where persons with TB disease are not expected to be encountered), workers should receive baseline testing using a two-step TST or an IGRA upon hiring (with appropriate follow-up evaluation for those found to have positive TST or IGRA results); additional screening is not necessary unless TB exposure occurs. In settings classified as medium risk (where workers will or will possibly be exposed to persons with TB disease or TB clinical specimens), workers should receive baseline two-step TST and annual screening for TB symptoms; workers who are TST-negative at baseline should also receive annual TST. If the setting has potential ongoing TB transmission, more frequent TST may be needed until infection control lapses have been corrected.⁵

Intervention Process

For the majority of infected persons, the only evidence of LTBI is an immune response to mycobacterial antigens, demonstrated by a positive TST or IGRA result. In the United States, the preferred skin test for LTBI is the intradermal, or Mantoux method, injection of 0.1 ml (5 TU) of purified protein derivative (PPD). Tests should be read by a trained professional 48 to 72 hours after the skin test has been applied. Multiple puncture tests (e.g., Tine and Heaf) and PPD strengths of 1 TU and 250 TU should not be used.²

IGRAs have been shown to have a lower likelihood of giving false-positive readings.²⁷ IGRAs provide significant advantages in delivery (e.g., no patient return for test reading) that may actually make them more cost-effective than the TST in populations that are likely to have high rates of false-positive TST results because of prior vaccination with the Bacille Calmette-Gerlin (BCG). However, data on IGRA performance in high-risk populations are being evaluated.

Screening high-risk populations for TB disease by asking about the major TB symptom, a cough of 2 to 3 weeks duration, is simple, inexpensive, and is potentially cost-effective in many settings.

Treatment
Information

Health benefits should include provisions for follow-up and treatment services.

A daily 9-month regimen of isoniazid (300 mg for adults, 10 to 15 mg/kg up to 300 mg for children) is recommended for treatment of LTBI caused by isoniazid-susceptible strains of *M. tuberculosis*. Completion of 270 doses within a 12-month period is optimal.² Twice-weekly dosing is an acceptable alternative (76 doses within 12 months).² A daily regimen of rifampin (10 to 20 mg/kg, 600 mg maximum) for 4 months is also an acceptable alternative and is the recommended choice for contacts to isoniazid-resistant TB patients; completion is considered optimal with 120 doses taken within 6 months.² Directly-observed treatment (DOT) improves the outcome of TB disease treatment and is therefore recommended over self-administered therapy (SAT), and has been shown to be cost-effective to prevent the development of drug resistant TB disease.²⁹ DOT is also recommended for LTBI treatment of vulnerable populations, such as HIV-infected persons or young children.

Strength of Evidence for the Clinical Preventive Service

The strength of evidence for the recommendations contained in this chapter is described below.

Recommended Guidance:

Centers for Disease Control and Prevention (CDC)

Strength of Evidence: Not Specified. Each of the referenced CDC guidelines describes the evidence basis for the recommendations, but not all provide ratings.

- The CDC recommends conducting targeted testing of persons at high risk for TB and treating those who have TB and LTBI to identify TB disease early, prevent transmission, and prevent progression of LTBI to disease.²
- The CDC recommends, if routine TB screening is mandated in low-risk settings, the provision of baseline LTBI testing upon hiring, with the addition of annual screening for TB symptoms in medium-risk settings.⁵

Authored by:

Marks S. Tuberculosis evidence-statement: screening. In: Campbell KP, Lanza A, Dixon R, Chattopadhyay S, Molinari N, Finch RA, editors. *A Purchaser's Guide to Clinical Preventive Services: Moving Science into Coverage*. Washington, DC: National Business Group on Health; 2006.

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