

**EPI Fact Sheet 1: Primary, Secondary, and Tertiary Prevention Fact Sheet –  
TB Examples**

**LEARNING OBJECTIVES**

After reviewing this Fact Sheet, participants should be able to:

- Distinguish among primary, secondary, and tertiary prevention activities
- Provide examples of primary, secondary, and tertiary prevention activities related to the prevention and control of *M. tuberculosis*

**ASPH DISCIPLINE-SPECIFIC COMPETENCIES ADDRESSED IN THIS FACT SHEET**

C.6. Apply the basic terminology and definitions of epidemiology

C.8. Communicate epidemiologic information to lay and professional audiences

**ASPH INTERDISCIPLINARY/CROSS-CUTTING COMPETENCIES ADDRESSED IN THIS  
FACT SHEET**

I.8. [Public Health Biology] Apply biological principles to development and implementation of disease prevention, control, or management programs

L.1. [Systems Thinking] Identify characteristics of a system

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## **Introduction**

Epidemiology is an important part of tuberculosis (TB) control efforts because the information on patterns of infection and disease can assist in identifying people or groups of people at risk for TB, understanding how the disease is transmitted, prioritizing cases, and planning appropriate use of staff and resources.<sup>1</sup>

The objectives of epidemiology are to:

- Identify the cause of disease or risk for disease
- Determine the burden of disease in a community
- Study the natural history and prognosis of disease
- Evaluate both existing and new preventive and therapeutic measures and modes of health care delivery
- Provide the foundation for developing public policy and regulatory decisions relating to environmental problems<sup>2</sup>

In a community or group with a high burden of disease, it is the responsibility of public health officials, knowing its cause and biologic implications, to put in place preventive measures to alleviate the burden. There are three prevention approaches that are crucial in decreasing mortality and morbidity of a disease: primary, secondary, and tertiary prevention. These levels of prevention were first described by Leavell and Clark<sup>3</sup> and continue to provide a useful framework to describe the spectrum of prevention activities.

## **Primary Prevention**

“Primary prevention denotes action taken to prevent the development of a disease in a person who is well and does not have the disease in question” (page 6).<sup>2</sup> These activities include health promotion as well as disease prevention activities. Health promotion activities can be as simple as using appropriate hand washing techniques or can be more sophisticated such as vaccination to prevent disease occurrence.

### **1. Vaccines**

The only vaccination for TB on the market is the bacille Calmette-Guérin (BCG) vaccine; however, its use is rarely indicated in the United States. Before putting a vaccine on the market in the United States, the Centers for Disease Control and Prevention (CDC) along with the US Food and Drug Administration and other government agencies, must evaluate the vaccines efficacy, safety, contraindications, utility, and cost effectiveness.

Two controlled prospective community trials before 1955 and studies done in 1947, 1950, and after 1975 using different BCG strains, found poor efficacy ranging from 0% to 80%.<sup>4,5</sup> In addition to poor efficacy, the BCG vaccine is not indicated in the United States because secondary prevention techniques are greatly hindered by the BCG vaccine, which can interfere with the management of persons who are possibly infected with *M. tuberculosis*.

Safety is another concern when evaluating a vaccine. High rates of local reaction and infection often leave a permanent scar at the site of a BCG vaccine. Also, the estimated risk of a complication from a subcutaneous abscess is 387 per 1 million vaccinations, 0.39-0.89 per 1 million from a musculoskeletal lesion, and 0.19-1.56 per 1 million fatalities from disseminated lesions.<sup>6</sup>

Since the resurgence of TB in the early 1990s, the BCG vaccine was again evaluated for use in the United States. Since then, the CDC has made the following recommendations<sup>6</sup>: 1) BCG is considered for children in the United States who have a negative tuberculin skin test (TST) and are continually exposed to an untreated or ineffectively treated patient who has infectious TB and/or drug-resistant TB and cannot be isolated from the patient; 2) BCG is also considered on a case-by-case basis for health care workers in high-risk settings. Currently, new vaccines for the prevention of TB are in the development phase.<sup>7</sup>

## 2. Environmental controls

Another form of primary prevention for TB is environmental control, such as ultraviolet lights and ventilation; however, these measures are taken mostly at hospitals and cannot be practically implemented at places where most TB transmission exists (e.g., nursing homes, prisons, in the community, etc.).<sup>8</sup> However, programs aimed at decreasing overcrowding can also be considered primary prevention measures for TB.

## Secondary Prevention

“Secondary prevention denotes the identification of people who have already developed a disease, at an early stage in the disease’s natural history, through screening and early intervention.” “The rationale for secondary prevention is that if we can identify disease earlier in its natural history, intervention measures will be more effective. Perhaps we can prevent mortality or complications of the disease and use less invasive or less costly treatment to do so”.<sup>2</sup> (page 6)

### 1. Detection of latent TB infection (LTBI)

The CDC recommends a strategy to identify those who have LTBI and, if indicated, the use of chemotherapy to **prevent the latent infection from progressing to active TB disease**. There are two tests that can be used to help detect LTBI.

#### a. The Tuberculin Skin Test (TST)

The first is a skin test in which testing material, called tuberculin, is injected intradermally into the individual and in 2 to 3 days, the patient returns to the health care worker who checks to see if there is a reaction to the test.<sup>8</sup>

#### b. QuantiFERON-TB Gold (QFT-G)

The second test used to identify LTBI is QFT-G, a blood test that measures how a person’s system reacts to the bacteria that causes TB.<sup>9</sup>

As mentioned previously, secondary control methods for TB are greatly hindered by the BCG vaccine. Post-vaccination BCG-induced tuberculin reactivity ranges from no induration to an induration of 19 mm at the skin-test site. Tuberculin reactivity caused by BCG vaccination wanes with time and is unlikely to persist >10 years after vaccination in the absence of *M. tuberculosis* exposure and infection. Recent studies have suggested that the QFT-G is more sensitive than the TST.<sup>10</sup> Another recent study that compared TST and QFT-G found that the QFT-G test was highly specific and unaffected by BCG vaccination status, a major cause of false-positive TST responses.<sup>10</sup> Since there is no gold standard for screening tests to determine if someone has TB disease, other specialized tests such as chest X-ray and a sample of sputum may be needed. Table I is a summary of evidence comparing TST to QFT-G, a type of interferon-gamma assay.

Performance and Operational Characteristics	TST	RD1-based IFN- $\gamma$ Assays
Estimated sensitivity (in patients with active TB)	75–90 % (lower in immunocompromised populations)	80–95 % (inadequate data in immunocompromised populations)
Estimated specificity (in healthy individuals with no known TB disease/exposure)	70–95 % (lower in BCG vaccinated)	95–100 % (unchanged with BCG)
Cross-reactivity with BCG	Yes	Less likely
Cross-reactivity with nontuberculous mycobacteria	Yes	Less likely
Association between test-positivity and subsequent risk of active TB during follow-up	Moderate to strong positive association	Insufficient evidence
Correlation with <i>M. tuberculosis</i> exposure	Yes	Yes (correlated better with exposure than TST in some head-to-head comparisons)
Benefits of treating test-positives (based on randomized controlled trials)	Yes	No evidence
Reliability (reproducibility)	Moderate	Limited evidence but may be high
Boosting phenomenon	Yes	No
Adverse reactions	Rare	Rare
Material costs	Low	Moderate to high
Patient visits	Two	One
Laboratory infrastructure required	No	Yes
Time to obtain a result	2–3 d	1–2 d, but longer if run as batches
Trained personnel required	Yes	Yes

*Definition of abbreviations:* BCG = bacillus Calmette-Guérin; TB = tuberculosis; TST = tuberculin skin test.  
Adapted by permission from Reference 7.

\* In December 2005, the United States Centers for Disease Control and Prevention recommended that the QuantiFERON-TB Gold assay may be used in all circumstances in which the TST is currently used. <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5415a4.html>.

Advances in the diagnosis and treatment of tuberculosis. Nahid P, Pai M, Hopewell PC. *Am Thorac Soc.* 2006;3:103-110. (permission pending)

Secondary prevention of TB involves the identification and testing of targets groups of people and communities with greater likelihood of being infected. "Targeted tuberculin testing for LTBI is a strategic component of tuberculosis (TB) control that identifies persons at high risk for developing TB who would benefit by treatment of LTBI, if detected".<sup>8</sup>

Some of these high risk groups are:

- Health care workers who work with patients at risk of TB
- Those who have lived or traveled extensively in areas where TB is endemic
- Immunocompromised individuals
- Those who have had a recent positive conversion of a skin test
- Persons who live in a congregant setting (e.g. jails and nursing homes)
- Homeless persons

Another type of secondary prevention measure is called a contact investigation. During a contact investigation a public health worker interviews patients with active TB disease in order to identify “contacts” or people who may have been exposed to that person. Once identified the contacts will be evaluated for LTBI and TB disease and provided with appropriate treatment, when necessary.

## 2. Treatment of LTBI

Patients who are identified as being infected with TB should be evaluated for active TB disease, by receiving a chest X-ray, and a focused clinical evaluation. Once active disease is excluded, one of the following treatments listed in Table 2 is indicated.

**Table: Drug Regimens for the Treatment of LTBI**

<b>Drugs</b>	<b>Duration (months)</b>	<b>Interval</b>	<b>Minimum doses</b>
Isoniazid	9	Daily	270
		Twice weekly*	76
Isoniazid	6	Daily	180
		Twice weekly*	52
Rifampin	4	Daily	120
* Directly observed therapy (DOT) is mandatory for patients on twice weekly (intermittent) therapy			

Table source: modified version of CDC table available at: <http://www.cdc.gov/TB/pubs/tbfactsheets/treatmentLTBI.htm>. Accessed March 19, 2008. Centers for Disease Control and Prevention. TB fact sheet.

Directly observed therapy (DOT) is suggested for patients with LTBI at high risk of not adhering to the prescribed therapy, and mandatory for those on twice weekly regimens. For

DOT, a health care worker or other trained person who is not a family member watches as the patient swallows antituberculosis medicines for at least the first 2 months of treatment. DOT thus shifts the responsibility for cure from the patient to the health care system.

### **Tertiary Prevention<sup>11</sup>**

The treatment of people who have already developed a disease is often described as tertiary prevention. The final strategy used for preventing and controlling TB in the United States is identifying and treating patients with active TB. Each person with infectious TB has the potential to infect many others; however, the site of the infection is important in determining its capability to spread. For example, the lungs and larynx are two common organs where TB may be highly infectious. If instead, the TB infection is localized to areas such as lymph nodes or outside the lung, treatment is necessary, yet it is not transmissible and, therefore, is not a major public health concern.

The treatments used for people with active TB will vary depending on whether the TB is resistant to some of the standard TB medications. Treatment can take 6 months or longer. Some of the most common drugs used to treat TB are:

- isoniazid (INH)
- rifampin (RIF)
- ethambutol
- pyrazinamide

DOT is used to be sure that patients who have active disease to remember to take their TB medications.

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