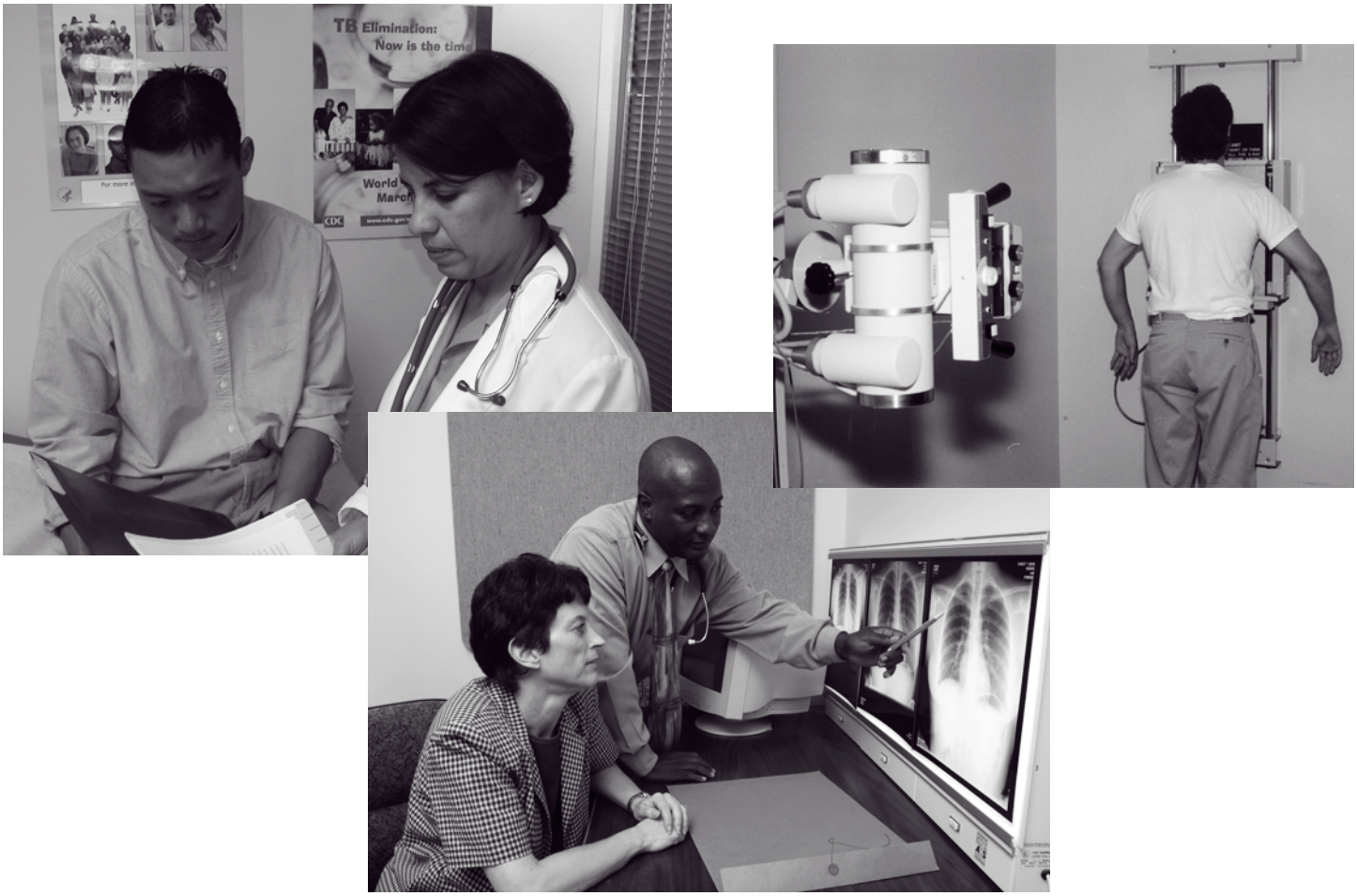
MMWR™

Morbidity and Mortality Weekly Report

Recommendations and Reports November 4, 2005 / Vol. 54 / No. RR-12

Controlling Tuberculosis in the United States

Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America



DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

The *MMWR* series of publications is published by the Coordinating Center for Health Information and Service, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30333.

SUGGESTED CITATION

Centers for Disease Control and Prevention. Controlling tuberculosis in the United States: recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America. MMWR 2005;54(No. RR-12): [inclusive page numbers].

Centers for Disease Control and Prevention

Julie L. Gerberding, MD, MPH
Director

Dixie E. Snider, MD, MPH
Chief Science Officer

Tanja Popovic, MD, PhD
Associate Director for Science

Coordinating Center for Health Information and Service

Steven L. Solomon, MD
Director

National Center for Health Marketing

Jay M. Bernhardt, PhD, MPH
Director

Division of Scientific Communications

Maria S. Parker
(*Acting*) *Director*

Mary Lou Lindegren, MD
Editor, MMWR *Series*

Suzanne M. Hewitt, MPA
Managing Editor, MMWR *Series*

Teresa F. Rutledge
(*Acting*) *Lead Technical Writer-Editor*

Jeffrey D. Sokolow, MA
Project Editor

Beverly J. Holland
Lead Visual Information Specialist

Lynda G. Cupell
Malbea A. LaPete
Visual Information Specialists

Quang M. Doan, MBA
Erica R. Shaver
Information Technology Specialists

CONTENTS

Introduction 1
Scientific Basis of TB Control 7
Principles and Practice of TB Control 14
Recommended Roles and Responsibilities for TB Control ... 20
Essential Components of TB Control in the United States .. 32
Control of TB Among Populations at Risk 42
Control of TB in Health-Care Facilities and Other High-Risk Environments 56
Research Needs to Enhance TB Control 59
Graded Recommendations for the Control and Prevention of Tuberculosis (TB) 60
Acknowledgments 69
References 69

Controlling Tuberculosis in the United States

Recommendations from the American Thoracic Society, CDC, and the Infectious Diseases Society of America

Summary

During 1993–2003, incidence of tuberculosis (TB) in the United States decreased 44% and is now occurring at a historic low level (14,874 cases in 2003). The Advisory Council for the Elimination of Tuberculosis has called for a renewed commitment to eliminating TB in the United States, and the Institute of Medicine has published a detailed plan for achieving that goal. In this statement, the American Thoracic Society (ATS), CDC, and the Infectious Diseases Society of America (IDSA) propose recommendations to improve the control and prevention of TB in the United States and to progress toward its elimination.

This statement is one in a series issued periodically by the sponsoring organizations to guide the diagnosis, treatment, control, and prevention of TB. This statement supersedes the previous statement by ATS and CDC, which was also supported by IDSA and the American Academy of Pediatrics (AAP). This statement was drafted, after an evidence-based review of the subject, by a panel of representatives of the three sponsoring organizations. AAP, the National Tuberculosis Controllers Association, and the Canadian Thoracic Society were also represented on the panel.

This statement integrates recent scientific advances with current epidemiologic data, other recent guidelines from this series, and other sources into a coherent and practical approach to the control of TB in the United States. Although drafted to apply to TB control activities in the United States, this statement might be of use in other countries in which persons with TB generally have access to medical and public health services and resources necessary to make a precise diagnosis of the disease; achieve curative medical treatment; and otherwise provide substantial science-based protection of the population against TB.

This statement is aimed at all persons who advocate, plan, and work at controlling and preventing TB in the United States, including persons who formulate public health policy and make decisions about allocation of resources for disease control and health maintenance and directors and staff members of state, county, and local public health agencies throughout the United States charged with control of TB. The audience also includes the full range of medical practitioners, organizations, and institutions involved in the health care of persons in the United States who are at risk for TB.

Introduction

During 1993–2003, incidence of tuberculosis (TB) in the United States decreased 44% and is now occurring at a historic low level (14,874 cases in 2003). The Advisory Council for the Elimination of Tuberculosis (ACET) (*1*) has called for a renewed commitment to eliminating TB in the United States, and the Institute of Medicine (IOM) (*2*) has published a detailed plan for achieving that goal. In this statement, the American Thoracic Society (ATS), CDC, and the Infectious Diseases Society of America (IDSA) propose recommendations to improve the control and prevention of TB in the United States and to progress toward its elimination.

This statement is one in a series issued periodically by the sponsoring organizations to guide the diagnosis, treatment, control, and prevention of TB (*3–5*). This statement supersedes one published in 1992 by ATS and CDC, which also was supported by IDSA and the American Academy of Pediatrics (AAP) (*6*). This statement was drafted, after an evidence-based review of the subject, by a panel of representatives of the three sponsoring organizations. AAP, the National Tuberculosis Controllers Association (NTCA), and the Canadian Thoracic Society were also represented on the panel. The recommendations contained in this statement (see Graded Recommendations for the Control and Prevention of Tuberculosis) were rated for their strength by use of a letter grade and for the quality of the evidence on which they were based by use of a Roman numeral (Table 1) (*7*). No rating was assigned to recommendations that are considered to be standard practice (i.e., medical or administrative practices conducted routinely by qualified persons who are experienced in their fields).

This statement integrates recent scientific advances with current epidemiologic data, other recent guidelines from this series (*3–5*), and other sources (*2,8–10*) into a coherent and practical approach to the control of TB in the United States.

Corresponding preparers: Zachary Taylor, MD, National Center for HIV, STD, and TB Prevention, CDC; Charles M. Nolan, MD, Seattle-King County Department of Public Health, Seattle, Washington; Henry M. Blumberg, MD, Emory University School of Medicine, Atlanta, Georgia.

TABLE 1. Grading system for ranking recommendations in this statement

Strength of recommendation	Criteria
A	Highly recommended in all circumstances
B	Recommended; implementation might be dependent on resource availability
C	Might be considered under exceptional circumstances
Quality of evidence	
I	Evidence from at least one randomized, controlled trial
II	Evidence from 1) at least one well-designed clinical trial, without randomization; 2) cohort or case-controlled analytic studies; 3) multiple time-series; or 4) dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities, on the basis of cumulative public health experience, descriptive studies, or reports of expert committees

SOURCE: Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001;32:851–4 (modified).

Although drafted to apply to TB control activities in the United States, this statement might be of use in other countries in which persons with TB generally have access to medical and public health services and resources necessary to make a precise diagnosis of the disease; achieve curative medical treatment; and otherwise provide substantial science-based protection of the population against TB.

This statement is aimed at all persons who advocate, plan, and work at controlling and preventing TB in the United States, including persons who formulate public health policy and make decisions about allocation of resources for disease control and health maintenance and directors and staff members of state, county, and local public health agencies throughout the United States charged with control of TB. The audience also includes the full range of medical practitioners, organizations, and institutions involved in the health care of persons in the United States who are at risk for TB.

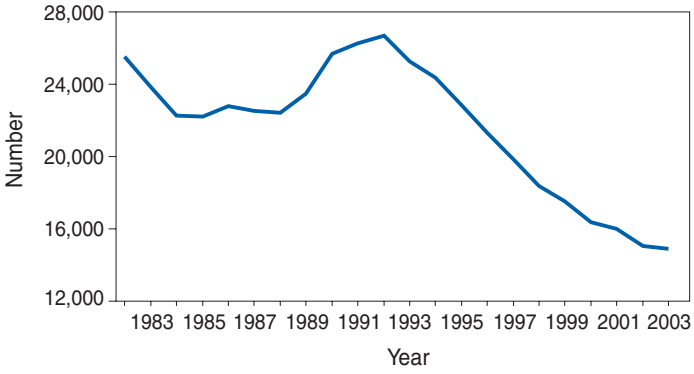
Throughout this document, the terms latent TB infection (LTBI), TB, TB disease, and infectious TB disease are used. LTBI is used to designate a condition in which an individual is infected with *Mycobacterium tuberculosis* but does not currently have active disease. Such patients are at risk for progressing to tuberculosis disease. Treatment of LTBI (previously called preventive therapy or chemoprophylaxis) is indicated for those at increased risk for progression as described in the text. Persons with LTBI are asymptomatic and have a negative chest radiograph. TB, TB disease, and infectious TB indicate that the disease caused by *M. tuberculosis* is clinically active; patients with TB are generally symptomatic for disease. Positive culture results for *M. tuberculosis* complex are an indication of TB disease. Infectious TB refers to TB disease of the lungs or larynx; persons with infectious TB have the potential to transmit *M. tuberculosis* to other persons.

Progress Toward TB Elimination

A strategic plan for the elimination of TB in the United States was published in 1989 (*11*), when the United States was experiencing a resurgence of TB (Figure 1). The TB resurgence was attributable to the expansion of HIV infection, nosocomial transmission of *M. tuberculosis*, multidrug-resistant TB, and increasing immigration from counties with a high incidence of TB. Decision makers also realized that the U.S. infrastructure for TB control had deteriorated (*12*); this problem was corrected by a substantial infusion of resources at the national, state, and local levels (*13*). As a result, the increasing incidence of TB was arrested; during 1993–2003, an uninterrupted 44% decline in incidence occurred, and in 2003, TB incidence reached a historic low level. This success in responding to the first resurgence of TB in decades indicates that a coherent national strategy; coordination of local, state, and federal action; and availability of adequate resources can result in dramatic declines in TB incidence. This success also raised again the possible elimination of TB, and in 1999, ACET reaffirmed the goal of tuberculosis elimination in the United States (*1*).

The prospect of eliminating tuberculosis was critically analyzed in an independent study published by IOM in 2000 (*2*). The IOM study concluded that TB could ultimately be eliminated but that at the present rate of decline, elimination would take ≥70 years. Calling for greater levels of effort and resources than were then available, the IOM report proposed a comprehensive plan to 1) adjust control measures to the declining incidence of disease; 2) accelerate the decline in incidence by increasing targeted testing and treatment of LTBI; 3) develop new tools for diagnosis, treatment, and prevention; 4) increase U.S. involvement in global control of TB;

FIGURE 1. Number of reported cases of tuberculosis, by year of diagnosis — United States, 1982–2003



and 5) mobilize and sustain public support for TB elimination. The report also noted the cyclical nature of the U.S. response to TB and warned against allowing another "cycle of neglect" to occur, similar to that which caused the 1985–1992 resurgence.

As noted, the 44% decrease in incidence of TB in the United States during 1993–2003 (*14,15*) has been attributed to the development of effective interventions enabled by increased resources at the national, state, and local levels (*1,2,16*). Whereas institutional resources targeted specific problems such as transmission of TB in health-care facilities, public resources were earmarked largely for public health agencies, which used them to rebuild the TB-control infrastructure (*13,17*). A primary objective of these efforts was to increase the rate of completion of therapy among persons with TB, which was achieved by innovative case-management strategies, including greater use of directly observed therapy (DOT). During 1993–2000, the percentage of persons with reported TB who received DOT alone or in combination with self-supervised treatment increased from 38% to 78%, and the proportion of persons who completed therapy in <1 year after receiving a diagnosis increased from 63% to 80% (*14*). Continued progress in the control of TB in the United States will require consolidation of the gains made through improved cure rates and implementation of new strategies to further reduce incidence of TB.

Challenges to Progress Toward TB Elimination

The development of optimal strategies to guide continuing efforts in TB control depends on understanding the challenges confronting the effort. The five most important challenges to successful control of TB in the United States are 1) prevalence of TB among foreign-born persons residing in the United States; 2) delays in detecting and reporting cases of pulmonary TB; 3) deficiencies in protecting contacts of persons with infectious TB and in preventing and responding to TB outbreaks; 4) persistence of a substantial population of persons living in the United States with LTBI who are at risk for progression to TB disease; and 5) maintaining clinical and public health expertise in an era of declining TB incidence. These five concerns (Box 1) serve as the focal point for the recommendations made in this statement to control and prevent TB in the United States.

BOX 1. Major challenges to successful control of tuberculosis (TB)

- Pravalence of TB among foreign-born persons residing in the United States
- Delays in detecting and reporting cases of pulmonary TB
- Deficiencies in protecting contacts of persons with infectious cases of TB and in preventing and responding to TB outbreaks
- Presence of a substantial population of persons living in the United States with latent TB infection who are at risk for progression to TB disease
- Maintaining clinical and public health expertise in an era of declining TB incidence

Prevalence of TB Among Foreign-Born Persons Residing in the United States

Once a disease that predominately affected U.S.-born persons, TB now affects a comparable number of foreign-born persons who reside in the United States permanently or temporarily, although such persons make up only 11% of the U.S. population (*14*). During 1993–2003, as TB incidence in the United States declined sharply, incidence among foreign-born persons changed little (*14*). Lack of access to medical services because of cultural, linguistic, financial, or legal barriers results in delays in diagnosis and treatment of TB among foreign-born persons and in ongoing transmission of the disease (*18–21*). Successful control of TB in the United States and progress toward its elimination depend on the development of effective strategies to control and prevent the disease among foreign-born persons.

Delays in Detection and Reporting of Cases of Pulmonary TB

New cases of infectious TB should be diagnosed and reported as early as possible in the course of the illness so curative treatment can be initiated, transmission interrupted, and public health responses (e.g., contact investigation and case-management services) promptly arranged. However, delays in case detection and reporting continue to occur; these delays are attributed to medical errors (*22–26*) and to patient factors (e.g., lack of understanding about TB, fear of the authorities, and lack of access to medical services) (*18–20*). In addition, genotyping studies have revealed evidence of persistent transmission of *M. tuberculosis* in communities that have implemented highly successful control measures (*27–29*), suggesting that such transmission occurred before a diagnosis was received. Improvements in the detection of TB cases, leading to earlier diagnosis and treatment, would bring substantial benefits to affected patients and their contacts, decrease TB among children, and prevent outbreaks.

Deficiencies in Protecting Contacts of Person with Infectious TB and in Preventing and Responding to TB Outbreaks

Although following up contacts is among the highest public health priorities in responding to a case of TB, problems in conducting contact investigations have been reported (*30–32*). Approaches to contact investigations vary widely from program to program, and traditional investigative methods are not well adapted to certain populations at high risk. Only half of at-risk contacts complete a course of treatment for LTBI (*32*). Reducing the risk of TB among contacts through the development of better methods of identification, evaluation, and management would lead to substantial personal and public health benefits and facilitate progress toward eliminating TB in the United States.

Delayed detection of TB cases and suboptimal contact investigation can lead to TB outbreaks, which are increasingly reported (*26,33–38*). Persistent social problems such as crowding in homeless shelters and detention facilities are contributing factors to the upsurge in TB outbreaks. The majority of jurisdictions lack the expertise and resources needed to conduct surveillance for TB outbreaks and to respond effectively when they occur. Outbreaks have become an important element in the epidemiology of TB, and measures to detect, manage, and prevent them are needed.

Persistence of a Substantial Population of Persons Living in the United States with LTBI Who Are at Risk for Progression to TB Disease

An estimated 9.6–14.9 million persons residing in the United States have LTBI (*39*). This pool of persons with latent infection is continually supplemented by immigration from areas of the world with a high incidence of TB and by ongoing person-to-person transmission among certain populations at high risk. For TB disease to be prevented among persons with LTBI, those at highest risk must be identified and receive curative treatment (*4*). Progress toward the elimination of TB in the United States requires the development of new cost-effective strategies for targeted testing and treatment of persons with LTBI (*17,40*).

Maintaining Clinical and Public Health Expertise in an Era of Declining TB Incidence

Detecting a TB case, curing a person with TB, and protecting contacts of such persons requires that clinicians and the staff members of public health agencies responsible for TB have specific expertise. However, as TB becomes less common, maintaining such expertise throughout the loosely coordinated TB-control system is challenging. As noted previously, medical errors associated with the detection of TB cases are common, and deficiencies exist in important public health responsibilities such as contact investigations and outbreak response. Errors in the treatment and management of TB patients continue to occur (*41,42*). Innovative approaches to education of medical practitioners, new models for organizing TB services (*2*), and a clear understanding and acceptance of roles and responsibilities by an expanded group of participants in TB control will be needed to ensure that the clinical and public health expertise necessary to progress toward the elimination of TB are maintained.

Meeting the Challenges to TB Elimination

Further improvements in the control and prevention of TB in the United States will require a continued strong public health infrastructure and involvement of a range of health professionals outside the public health sector. The traditional model of TB control in the United States, in which planning and execution reside almost exclusively with the public health sector (*17*), is no longer the optimal approach during a sustained drive toward the elimination of TB. This statement emphasizes that success in controlling TB and progressing toward its elimination in the United States will depend on the integrated activities of professionals from different fields in the health sciences. This statement proposes specific measures to enhance TB control so as to meet the most important challenges; affirms the essential role of the public health sector in planning, coordinating, and evaluating the effort (*43*); proposes roles and responsibilities for the full range of participants; and introduces new approaches to the detection of TB cases, contact investigations, and targeted testing and treatment of persons with LTBI.

The plan to reduce the incidence of TB in the United States must be viewed in the larger context of the global effort to control TB. The global TB burden is substantial and increasing. In 2000, an estimated 8.3 million (7.9–9.2 million) new cases of TB occurred, and 1.84 million (1.59–2.22 million) persons died from TB; during 1997–2000, the worldwide TB case rate increased 1.8%/year (*44*). TB is increasing worldwide as a result of inadequate local resources and the global epidemic of HIV infection. In sub-Saharan Africa, the rate of TB cases is increasing 6.4%/year (*44*). ACET (*1*), IOM (*2*), and other public health authorities (*45,46*) have acknowledged that TB will not be eliminated in the United States until the global epidemic is brought under control, and they have called for greater U.S. involvement in global control efforts. In response, CDC and ATS have become active participants in a

multinational partnership (Stop TB Partnership) that was formed to guide the global efforts against TB. U.S. public and private entities also have provided assistance to countries with a high burden of TB and funding for research to develop new, improved tools for diagnosis, treatment, and prevention, including an effective vaccine.

Despite the global TB epidemic, substantial gains can be made toward elimination of TB in the United States by focusing on improvements in existing clinical and public health practices (*47–49*). However, the drive toward TB elimination in the United States will be resource-intensive (*1,12*). Public health agencies that plan and coordinate TB-control efforts in states and communities need sufficient strength in terms of personnel, facilities, and training to discharge their responsibilities successfully, and the growing number of nonpublic health contributors to TB control, all pursuing diverse individual and institutional goals, should receive value for their contributions. Continued progress toward TB elimination in the United States will require strengthening the nation's public health infrastructure rather than reducing it (*1,50*).

Basic Principles of TB Control in the United States

Four prioritized strategies exist to prevent and control TB in the United States (*17*), as follows:

- The first strategy is to promptly detect and report persons who have contracted TB. Because the majority of persons with TB receive a diagnosis when they seek medical care for symptoms caused by progression of the disease, health-care providers, particularly those providing primary health care to populations at high risk, are key contributors to the detection of TB cases and to case reporting to the jurisdictional public health agency for surveillance purposes and for facilitating a treatment plan and case-management services.
- The second strategy is to protect close contacts of patients with contagious TB from contracting TB infection and disease. Contact evaluation not only identifies persons in the early stages of LTBI, when the risk for disease is greatest (*30–32*), but is also an important tool to detect further cases of TB disease.
- The third strategy is to take concerted action to prevent TB among the substantial population of U.S. residents with LTBI. This is accomplished by identifying those at highest risk for progression from latent infection to active TB through targeted testing and administration of a curative course of treatment (*4*). Two approaches exist for increasing targeted testing and treatment of LTBI. The first approach is to encourage clinic-based testing of persons who are under a clinician's care for a medical condition, such as human immunodeficiency virus (HIV) infection or diabetes mellitus, who are at risk for progressing from LTBI to active TB (*4*). The second approach is to establish specific programs to reach persons who have an increased prevalence of LTBI, an increased risk for developing active disease if LTBI is present, or both (*51*).
- The fourth strategy is to reduce the rising burden of TB from recent transmission of *M. tuberculosis* by identifying settings at high risk for transmission and applying effective infection-control measures to reduce the risk. This strategy was used during the 1985–1992 TB resurgence, when disease attributable to recent transmission was an important component of the increase in TB incidence (*52–54*). TB morbidity attributable to recent spread of *M. tuberculosis* continues to be a prominent part of the epidemiology of the disease in the United States. Data collected by CDC's National Tuberculosis Genotyping and Surveillance Network at seven sentinel surveillance sites indicate that 44% of *M. tuberculosis* isolates from persons with newly diagnosed cases of TB were clustered with at least one other intrasite isolate, often representing TB disease associated with recent spread of *M. tuberculosis* (*55*). TB outbreaks are also being reported with greater frequency in correctional facilities (*37*), homeless shelters (*33*), bars (*27*), and newly recognized social settings (e.g., among persons in an East Coast network of gay, transvestite, and transsexual HIV-infected men [*34*]; persons frequenting an abandoned junkyard building used for illicit drug use and prostitution [*26*]; and dancers in adult entertainment clubs and their contacts, including children [*38*]).

  Institutional infection-control measures developed in the 1990s in response to the 1985–1992 resurgence in transmission of *M. tuberculosis* in the United States (*10*) have been highly successful in health-care facilities (*56*). However, newly recognized high-risk environments (*26,27,33,34,37,38*) present challenges to the implementation of effective infection-control measures. Further attention is required to control the transmission of *M. tuberculosis* in these environments.

Structure of this Statement

This statement provides comprehensive guidelines for the full spectrum of activities involved in controlling and preventing TB in the United States. The remainder of this statement is structured in eight sections, as follows:

- **Scientific Basis of TB Control.** This section reviews the base of knowledge of how TB is transmitted and how

the disease is distributed in the U.S. population, including new information based on genotyping studies. It provides basic background information as a review for current workers in the field and orients health-care professionals who become new participants in TB-control efforts.

- **Principles and Practice of TB Control.** This section makes the transition from the scientific knowledge base to clinical and public health practice by discussing the goal of TB control in the United States, which is to reduce the morbidity and mortality caused by TB by preventing transmission of *M. tuberculosis* from persons with contagious forms of the disease to uninfected persons and preventing progression from LTBI to TB disease among persons who have contracted *M. tuberculosis* infection. This section also provides basic background information as a review for current workers in the field and serves as an orientation for health-care professionals who become new participants in TB-control efforts.
- **Recommended Roles and Responsibilities for TB Control.** This section outlines roles and responsibilities for the spectrum of participants in the diverse clinical and public health activities that lead to the control and prevention of TB. The paramount role of the public health sector is reviewed, followed by proposed responsibilities for nine prominent nonpublic health partners in tuberculosis control: medical practitioners, civil surgeons, community health centers, hospitals, academic institutions, medical professional organizations, community-based organizations, correctional facilities and the pharmaceutical and biotechnology industries. Because responsibilities for the nonpublic health sector have not been specified previously, this information also should be useful to policy makers and advocates for strengthened TB control.
- **Essential Components of TB Control in the United States.** This section gives detailed recommendations for enhancing the core elements of TB control: case detection and management, contact investigations, and targeted testing and treatment of LTBI. Recommendations are provided for targeted public education to neutralize the stigma of TB and facilitate earlier care-seeking behavior among patients and for education of health-care professionals from whom patients with TB seek care. A set of five clinical scenarios is presented in which a diagnosis of TB should be undertaken in primary medical practice, and guidelines are presented for activities among certain populations to detect TB among persons who have not sought medical care. Guidelines are provided for a conducting a systematic, step-by-step contact investigation. All jurisdictional TB-control programs are urged to develop written policies and procedures on the basis of these guidelines. Recommended procedures are also outlined for conducting surveillance for TB outbreaks and for developing an outbreak response plan. In addition, a framework is presented for identifying and prioritizing subpopulations and settings within a community that are at high risk for TB and that should receive targeted testing and treatment for LTBI. Priorities for high-risk populations should be established on the basis of the expected impact and efficacy of the intervention. Persons who are readily accessible and have preexisting access to health-care services (e.g., prisoners, patients receiving ongoing clinic-based care for HIV infection, and immigrants and refugees with abnormalities on preimmigration chest radiographs) should receive the highest priority. An approach is also presented to reach members of new immigrant and refugee communities, who often exist on the margin of U.S. society.
- **Control of TB Among Populations at High Risk.** On the basis of the epidemiology of TB in the United States, this section provides specific recommendations for controlling and preventing TB among five populations: 1) children; 2) foreign-born persons; 3) HIV-infected persons; 4) homeless persons; and 5) detainees and prisoners in correctional facilities. Each population is readily identifiable and has been demonstrated to be at risk for TB exposure or progression from exposure to disease, or both. Surveillance and surveys from throughout the United States indicate that certain epidemiologic patterns of TB are consistently observed among these populations, suggesting that the recommended control measures are generalizable.
- **Control of TB in Health-Care Facilities and Other High-Risk Environments.** This section recommends infection-control measures to prevent the transmission of *M. tuberculosis* in high-risk settings. The approach to control of TB that was developed for health-care facilities continues to be the most successful model and is discussed in detail. The recommendations in this section have been updated with respect to the assessment of institutional risk for TB. Three levels of risk (low, medium, and potential ongoing transmission) are outlined on the basis of community and institutional experience with TB. An associated recommendation is that the frequency of testing of employees for LTBI should be based on the institution's risk category. Recommendations also are provided for control of transmission of *M. tuberculosis* in correctional facilities, homeless shelters, and other newly identified high-risk environments.

- **Research Needs To Enhance TB Control.** This section defines gaps in knowledge and deficiencies in technology that limit current efforts to control and prevent TB. Additional research is needed in these areas to produce the evidence base and the tools for optimal diagnosis, treatment, and prevention of TB. This section should be useful to persons who formulate U.S. public health policy and research priorities and members of academic professions interested in contributing to enhanced TB control, both in the United States and throughout the world.
- **Graded Recommendations for Control and Prevention of TB.** This section groups detailed graded recommendations for each area discussed in this report.

Scientific Basis of TB Control

Transmission of TB

M. tuberculosis is nearly always transmitted through an airborne route, with the infecting organisms being carried in droplets of secretions (droplet nuclei) that are expelled into the surrounding air when a person with pulmonary TB coughs, talks, sings, or sneezes. Person-to-person transmission of *M. tuberculosis* is determined by certain characteristics of the source-case and of the person exposed to the source-person and by the environment in which the exposure takes place (Box 2). The virulence of the infecting strain of *M. tuberculosis* might also be a determining factor for transmission.

BOX 2. Factors determining transmission of *Mycobacterium tuberculosis*

Characteristics of the source case
- Concentration of organisms in sputum
- Presence of cavitary disease on chest radiograph
- Frequency and strength of cough

Characteristics of the exposed person
- Previous *M. tuberculosis* infection
- Innate resistance to *M. tuberculosis* infection
- Genetic susceptibility to *M. tuberculosis* infection or disease or both

Characteristics of the exposure
- Frequency and duration of exposure
- Dilution effect (i.e., the volume of air containing infectious droplet nuclei)
- Ventilation (i.e., the turnover of air in a space)
- Exposure to ultraviolet light, including sunlight

Virulence of the infecting strain of *M. tuberculosis*

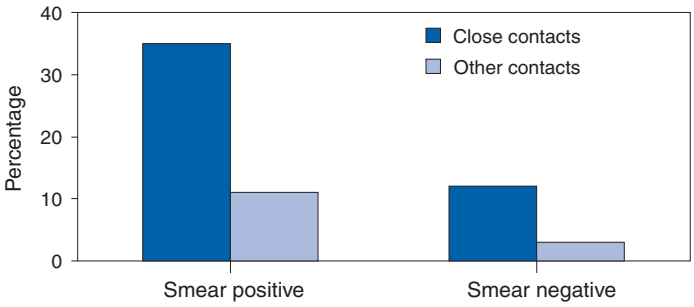
Characteristics of the Source-Case

By the time persons with pulmonary TB come to medical attention, 30%–40% of persons identified as their close personal contacts have evidence of LTBI (*30*). The highest rate of infection among contacts follows intense exposure to patients whose sputum smears are positive for acid-fast bacilli (AFB) (*31,57–59*) (Figure 2). Because patients with cavitary pulmonary TB are more likely than those without pulmonary cavities to be sputum AFB smear-positive (*60*), patients with cavitary pulmonary disease have greater potential to transmit TB. Such persons also have a greater frequency of cough, so the triad of cavitary pulmonary disease, sputum AFB smear-positivity, and frequency of cough are likely related causal factors for infectivity. AFB smear-negative TB patients also transmit TB, but with lower potential than smear-positive patients. Patients with sputum AFB smear-negative pulmonary TB account for approximately 17% of TB transmission (*61*).

Characteristics of the Exposed Person

A study of elderly nursing home residents indicated that persons with initially positive tuberculin skin test results during periods of endemic exposure to TB had a much lower risk for TB than those whose skin test results were initially negative (*62,63*). This finding suggests that preexisting LTBI confers protection against becoming infected upon subsequent exposure and progression to active disease. Similarly, having prior disease caused by *M. tuberculosis* had been assumed to confer protection against reinfection with a new strain of *M. tuberculosis*. However, molecular typing of paired isolates of *M. tuberculosis* from patients with recurrent episodes of TB disease has demonstrated that reinfection does occur among immunocompetent and immunocompromised persons (*64,65*).

FIGURE 2. Percentage of persons infected with *Mycobacterium tuberculosis*, by bacteriologic status of and proximity to the source case — British Columbia and Saskatchewan, 1966–1971



SOURCE: Grzybowski S, Barnett GD, Styblo K. Contacts of cases of active pulmonary tuberculosis. Bull Int Union Tuberc 1975;50:90–106.

The classic means of protecting persons exposed to infectious diseases is vaccination. Because of its proven efficacy in protecting infants and young children from meningeal and miliary TB (*66*), vaccination against TB with *Mycobacterium bovis bacillus Calmette-Guerín* (BCG) is used worldwide (although not in the United States). This protective effect against the disseminated forms of TB in infants and children is likely based on the ability of BCG to prevent progression of the primary infection when administered at that stage of life (*67*). Epidemiologic evidence suggests that BCG immunization does not protect against the development of infection with *M. tuberculosis* upon exposure (*68*), and use of BCG has not had an impact on the global epidemiology of TB. One recent retrospective study found that BCG protective efficacy can persist for 50–60 years, indicating that a single dose might have a long duration of effect (*69*). A meta-analysis indicated that overall BCG reduced the risk for TB 50% (*66*); however, another meta-analysis that examined protection over time demonstrated a decrease in efficacy of 5%–14% in seven randomized controlled trials and an increase of 18% in three others (*70*). An effective vaccine against *M. tuberculosis* is needed for global TB control to be achieved.

Because only 30%–40% of persons with close exposure to a patient with pulmonary TB become infected (*30,31*), innate immunity might protect certain persons from infection (*71*). The innate mechanisms that protect against the development of infection are largely uncharacterized (*71*). Although immunocompromised persons (e.g., those with HIV infection) are at increased risk for progression to TB disease after infection with *M. tuberculosis,* no definitive evidence exists that immunocompromised persons, including those with HIV infection, have increased susceptibility to infection upon exposure.

Observational studies suggest that population-based variability in susceptibility to TB might be related to the length of time a population has lived in the presence of *M. tuberculosis* and has thus developed resistance to infection through natural selection (*72–74*). However, the genetic basis for susceptibility or resistance to TB is not well understood (*72,75*).

Characteristics of the Exposure

Studies that have stratified contacts of persons with pulmonary TB according to time spent with the infected person indicate that the risk for becoming infected with *M. tuberculosis* is in part determined by the frequency and duration of exposure (*60*). In a given environment shared by a patient with pulmonary TB and a contact, the risk for transmitting the infection varies with the density of infectious droplet nuclei in the air and how long the air is inhaled. Indoors, tubercle bacilli are expelled into a finite volume of air, and, unless effective ventilation exists, droplet nuclei containing *M. tuberculosis* might remain suspended in ambient air (*76*). Exposures in confined air systems with little or no ventilation pose a major risk for transmission of TB; this has been demonstrated in homes, ships, trains, office buildings, and health-care institutions (*77–80*). When contact occurs outdoors, TB bacilli expelled from the respiratory tract of an infectious person are rapidly dispersed and are quickly rendered nonviable by sunlight (*77*). The risk for transmission during such encounters is very limited.

Considerable attention has been given to transmission of *M. tuberculosis* during air travel. Investigations have demonstrated that the risk for transmission from an infectious person to others on an airplane is greater on long flights (>8 hours) and that the risk for contracting *M. tuberculosis* infection is highest for passengers and flight crew members sitting or working near an infectious person (*81,82*). However, the overall public health importance of such events is negligible (*77,81*).

Virulence of the Infecting Strain of *M. tuberculosis*

Although much is known about factors that contribute to the risk for transmission of *M. tuberculosis* from person to person, the role of the organism itself is only beginning to be understood (*83*). Genetic variability is believed to affect the capability of *M. tuberculosis* strains to be transmitted or to cause disease once transmitted, or both. The *M. tuberculosis* W-strain family, a member of the globally spread Beijing family (*84*), is a group of clonally related multidrug-resistant organisms of *M. tuberculosis* that caused nosocomial outbreaks involving HIV-infected persons in New York City (NYC) during 1991–1994 (*85,86*). W-family organisms, which have also been associated with TB outbreaks worldwide, are believed to have evolved from a single strain of *M. tuberculosis* that developed resistance-conferring mutations in multiple genes. The growth of W-family organisms in human macrophages is four- to eightfold higher than that of strains that cause few or no secondary cases of TB; this enhanced ability to replicate in human macrophages might contribute to the organism's potential for enhanced transmission (*87*).

Whether *M. tuberculosis* loses pathogenicity as it acquires resistance to drugs is not known. Isoniazid-resistant *M. tuberculosis* strains are less virulent than drug-susceptible isolates in guinea pigs (*88*), and genotyping studies from San Francisco, California, and from the Netherlands indicated that isoniazid-resistant strains are much less likely to be associated with clusters of TB cases than drug-susceptible strains (*89,90*). Nevertheless, because person-to-person spread has been demonstrated repeatedly, persons with TB with drug-resistant

isolates should receive the same public health attention at the programmatic level as those with drug-susceptible isolates (*91,92*).

Effect of Chemotherapy on Infectiousness

Patients with drug-susceptible pulmonary and other forms of infectious TB rapidly become noninfectious after institution of effective multiple-drug chemotherapy. This principle has been established by studies demonstrating that household contacts of persons with infectious pulmonary TB who were treated at home after a brief period of hospitalization for institution of therapy developed LTBI at a frequency no greater than that of persons with pulmonary TB who were hospitalized for 1 year (*93*) or until sputum cultures became negative (*94*). This potent effect of chemotherapy on infectiousness is likely attributable, at least in part, to the rapid elimination of viable *M. tuberculosis* from sputum (*95*) and to reduction in cough frequency (*96*). The ability of chemotherapy to eliminate infectivity is one reason why detecting infectious cases and promptly instituting multiple-drug therapy is the primary means of interrupting the spread of TB in the United States.

The effect of chemotherapy to eliminate infectiousness was once thought to occur rapidly, and patients on chemotherapy were thought not to be infectious (*97,98*). However, no ideal test exists to assess the infective potential of a TB patient on treatment, and infectivity is unlikely to disappear immediately after multidrug therapy is started. Quantitative bacteriologic studies indicate that the concentration of viable *M. tuberculosis* in sputum of persons with cavitary sputum AFB smear-positive pulmonary TB at the time of diagnosis, which averaged 10^6–10^7 organisms/ml, decreased >90% (10-fold) during the first 2 days of treatment, an effect attributable primarily to administration of isoniazid (*99*), and >99% (100-fold) by day 14–21, an effect attributable primarily to administration of rifampin and pyrazinamide (*100*). Thus, if no factor other than the elimination of viable *M. tuberculosis* from sputum were to account for the loss of infectivity during treatment, the majority of patients (at least those with infection attributable to isolates susceptible to isoniazid) who have received treatment for as few as 2 days with the standard regimen (i.e., isoniazid, rifampin, ethambutol, and pyrazinamide) could be assumed to have an infective potential that averages 10% of that at the time of diagnosis. After 14–21 days of treatment, infectiousness averages <1% of the pretreatment level.

This statement presents general guidelines on elimination of infectivity with treatment (Box 3). However, decisions about infectiousness of a person on treatment for TB should always be individualized on the basis of 1) the extent of illness; 2) the presence of cavitary pulmonary disease; 3) the degree of positivity of sputum AFB smear results; 4) the frequency and strength of cough; 5) the likelihood of infection with multidrug-resistant organisms; and 6) the nature and circumstances of the contact between the infected person and exposed contacts (*101*). Patients who remain in hospitals or reside either temporarily or permanently in congregate settings (e.g., shelters and correctional facilities) are subject to different criteria for infectiousness. In such congregate settings, identification and protection of close contacts is not possible during the

BOX 3. Criteria for determining when during therapy a patient with pulmonary tuberculosis (TB) has become noninfectious*

- Patient has negligible likelihood of multidrug-resistant TB (no known exposure to multidrug-resistant tuberculosis and no history of prior episodes of TB with poor compliance during treatment).
- Patient has received standard multidrug anti-TB therapy for 2–3 weeks. (For patients with sputum acid-fast bacilli [AFB] smear results that are negative or rarely positive, threshold for treatment is 5–7 days.)
- Patient has demonstrated complete adherence to treatment (e.g., is receiving directly observed therapy).
- Patient has demonstrated evidence of clinical improvement (e.g., reduction in the frequency of cough or reduction of the grade of the sputum AFB smear result).
- All close contacts of patients have been identified, evaluated, advised, and, if indicated, started on treatment for latent TB infection. This criterion is critical, especially for children aged <4 years and persons of any age with immunocompromising health conditions (e.g., HIV infection).
- While in hospital for any reason, patients with pulmonary TB should remain in airborne infection isolation until they 1) are receiving standard multidrug anti-TB therapy; 2) have demonstrated clinical improvement; and 3) have had three consecutive AFB-negative smear results of sputum specimens collected 8–24 hours apart, with at least one being an early morning specimen. Hospitalized patients returning to a congregate setting (e.g., a homeless shelter or detention facility) should have three consecutive AFB-negative smear results of sputum specimens collected >8 hours apart before being considered noninfectious.

* These criteria for absence of infectivity with treatment should be considered general guidelines. Decisions about infectivity of a person on treatment for TB should depend on the extent of illness and the specific nature and circumstances of the contact between the patient and exposed persons.

early phase of treatment, and more stringent criteria for determining absence of infectivity (i.e., three consecutive AFB-negative sputum smears) should be followed (*10*). All patients with suspected or proven multidrug resistant TB should be subjected to these more stringent criteria for absence of infectivity (*10*).

Progression from LTBI to TB Disease

Although the human immune response is highly effective in controlling primary infection resulting from exposure to *M. tuberculosis* among the majority of immunocompetent persons, all viable organisms might not be eliminated. *M. tuberculosis* is thus able to establish latency, a period during which the infected person is asymptomatic but harbors *M. tuberculosis* organisms that might cause disease later (*4,71*). The mechanisms involved in latency and persistence are not completely understood (*71,72*).

For the majority of persons, the only evidence of LTBI is an immune response against mycobacterial antigens, which is demonstrated by a positive test result, either a tuberculin skin test (*3*) or, in certain circumstances, a whole blood antigen-stimulated interferon-γ release assay result (e.g., QuantiFERON®-TB Gold test [QFT-G] [Cellestis Limited, Carnegie, Victoria, Australia]). The tuberculin skin test measures delayed-type hypersensitivity; QFT-G, an ex vivo test for detecting latent *M. tuberculosis* infection, measures a component of cell-mediated immune response (*102*). QFT-G is approved by the Food and Drug Administration (FDA), and CDC will publish guidelines on its use. CDC had previously published guidelines for use of QuantiFERON®-TB, an earlier version of the test that is no longer available (*103*). T SPOT-TB,® an enzyme-linked immunospot assay for IFN-γ, is marketed in Europe along with QFT-G but is not FDA-approved for use in the United States. Although approved by FDA, the Tine Test® is not recommended for the diagnosis of *M. tuberculosis* infection. Tests available in other countries to diagnose *M. tuberculosis* infection (e.g., T SPOT-TB and Heaf test) are not recommended for clinical use in the United States.

Once a person has contracted LTBI, the risk for progression to TB disease varies. The greatest risk for progression to disease occurs within the first 2 years after infection, when approximately half of the 5%–10% lifetime risk occurs (*4,104*). Multiple clinical conditions also are associated with increased risk for progression from LTBI to TB disease. HIV infection is the strongest known risk factor (*4*). Other key risk factors because of their prevalence in the U.S. population are diabetes mellitus (*105*), acquisition of LTBI in infancy or early childhood, and apical fibro-nodular changes on chest radiograph (*106*).

A recent addition to the known risk factors for progression from LTBI to TB disease is the use of therapeutic agents that antagonize the effect of cytokine tumor necrosis factor alpha (TNF-α) and have been proven to be highly effective treating autoimmune-related conditions (e.g., Crohn's disease and rheumatoid arthritis) (*107*). Cases of TB have been reported among patients receiving all three licensed TNF-α antagonists (i.e., infliximab, etanercept, and adalimimab) (*108*). CDC has published interim guidelines for preventing TB when these agents are used (*109*).

Epidemiology of TB in the United States

Surveillance (i.e., the systematic collection, analysis, and dissemination of data) is a critical component of successful TB control, providing essential information needed to 1) determine patterns and trends of the disease; 2) identify populations and settings at high risk; and 3) establish priorities for control and prevention activities. Surveillance is also essential for quality-assurance purposes, program evaluation, and measurement of progress toward TB elimination. In addition to providing the epidemiologic profile of TB in a given jurisdiction, state and local surveillance are essential to national TB surveillance.

CDC's national TB surveillance system publishes epidemiologic analyses of reported TB cases in the United States (*110*). Data for the national TB surveillance system are reported by state health departments in accordance with standard TB case-definition and case-report formats (*110,111*). The system tracked the reversal of the declining trend in TB incidence in the United States in the mid-1980s, the peak of the resurgence in 1992 (with a 20% increase in cases reported during 1985–1992), and the subsequent 44% decline to an all-time low number (14,871) and rate (5.1 cases/100,000 population) of TB cases in 2003 (*14,15*) (Figure 1).

Geographic Distribution of TB

Wide disparities exist in the geographic distribution of TB cases in the United States. In 2003, six states (California, Florida, Georgia, Illinois, New York, and Texas) each reported ≥500 cases and accounted for 57% of the national total (*14*). These states along with New Jersey accounted for approximately 75% of the overall decrease in cases since 1992. The highest rates and numbers of TB cases are reported from urban areas; >75% of cases reported in 2003 were from areas with ≥500,000 population (*14*). In 2003, a total of 24 states (48%) had incidence of ≤3.5 cases of TB/100,000 population, the rate established as the year 2000 interim target for the United States in the 1989 strategic plan for eliminating TB (*11*).

Demographic Distribution of TB

In 2003, adults aged 15–64 years accounted for 73.6% of reported TB cases. Incidence of TB was highest (8.4 cases/100,000 population) among adults aged >65 years, who accounted for 20.2% of cases. Children aged <14 years accounted for 6.2% of reported cases and had the lowest incidence of TB; 61.3% of reported cases occurred among men, and case rates among men were at least double those of women in mid- and older-adult age groups. In 2003, the white, non-Hispanic population accounted for only 19% of reported cases of TB, and TB incidence among the four other racial/ethnic populations for which data were available was 5.7–21.0 times that of non-Hispanic whites (Table 2). Foreign-born persons accounted for 94% of TB cases among Asians and 74% of cases among Hispanics, whereas 74% of cases among non-Hispanic blacks occurred among persons born in the United States (*15*).

Distribution of TB by Socioeconomic and Employment Status

Socioeconomic status (SES). Low SES is associated with an increased risk for TB. An analysis of national surveillance data that assigned socioeconomic indicator values on the basis of residence zip code indicated that the risk for TB increased with lower SES for six indicators (crowding, education, income, poverty, public assistance, and unemployment), with crowding having the greatest impact (*112*). Risk for TB increased uniformly between socioeconomic quartile for each indicator, similar to other socioeconomic health gradients for other chronic diseases, except for crowding, for which risk was concentrated in the lowest quartile. Adjusting for SES accounted for approximately half of the increased risk for TB associated with race/ethnicity among U.S.-born blacks, Hispanics, and American Indians (*112*).

Occupation. Increased incidence of TB among persons with certain occupations is attributable to exposure in the work environment and to an increased likelihood that workers will have other risk factors unrelated to occupation, such as foreign birth. A 29-state study of patients with clinically active TB reported during 1984–1985 indicated that increased incidence was independent of occupation. An association between general SES groupings of occupations and risk for TB also was demonstrated in that study (*113*). Chronically unemployed persons had high incidence of TB; this finding is consistent with surveillance data indicating that >50% of TB patients were unemployed during the 2 years before diagnosis (*14*).

TB among health-care workers (HCWs). Because transmission of *M. tuberculosis* in health-care institutions was a contributing factor to the resurgence of TB during 1985–1992, recommendations were developed to prevent transmission in these settings (*10*). In 2003, persons reported to have been HCWs in the 2 years before receiving their diagnoses accounted for 3.1% of reported TB cases nationwide (*14*). However, the elevated risk among HCWs might be attributable to other factors (e.g., birth in a country with a high incidence of TB) (*114*). A multistate occupational survey indicated that the majority of HCWs did not have a higher risk for TB than the general population; respiratory therapists, however, did appear to be at greater risk (*113*).

TABLE 2. Tuberculosis (TB) incidence* among five racial/ethnic populations — United States, 2003

Race/Ethnicity	Rate†	
White, non-Hispanic	1.4	
American Indian/Alaska Native	8.0	(5.7)
Hispanic	10.5	(7.5)
Black, non-Hispanic	11.5	(8.2)
Asian/Pacific Islander	29.4	(21.0)

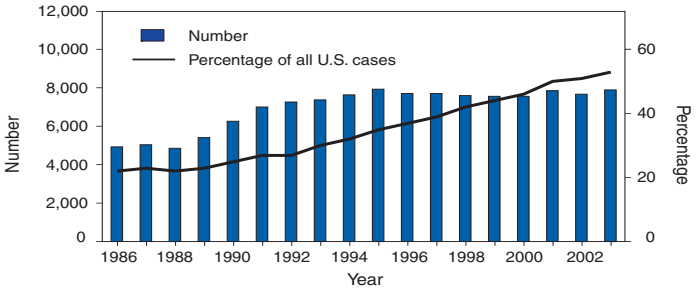
SOURCE: CDC. Trends in tuberculosis—United States, 1998–2003. MMWR 2004;53:209–14.
* Per 100,000 population.
† Numbers in parentheses represent risk for TB compared with white non-Hispanics.

Identification of Populations at High Risk for TB

Contacts of infectious persons. A high prevalence of TB disease and LTBI has been documented among close contacts of persons with infectious pulmonary TB (*31*). A study of approximately 1,000 persons from urban sites with pulmonary AFB sputum smear-positive TB indicated that more than one third of their contacts had positive tuberculin skin tests and that 2% of all close contacts had active TB. Contacts identified with TB disease were more likely to be household members or children aged <6 years (*31*).

Foreign-born persons. The proportion of TB cases in the United States occurring among foreign-born persons increased progressively during the 1990s; in 2003, persons born outside the United States accounted for 53% of reported cases (*14*) (Figure 3). Although foreign-born persons who received a diagnosis of TB in 2002 were born in >150 countries worldwide, as in each of the 6 previous years, five countries of origin accounted for the greatest number of foreign-born persons with TB: China (5%), India (8%), Mexico (26%), the Philippines (12%), and Vietnam (8%). During 1992–2003, the number of states in which ≥50% of the total reported cases occurred among foreign-born persons increased from four (8%) in 1992 to 24 (48%) in 2003 (*15*). Among states and cities, however, this profile can change rapidly, reflecting changes in patterns of immigration and refugee settlement (*21*).

FIGURE 3. Number and percentage of cases of tuberculosis among foreign-born persons, by year of diagnosis — United States, 1986–2003



Surveillance data indicate that incidence of TB among foreign-born persons is approximately 23 cases/100,000 population (*14*). Incidence varied by county of origin, appearing to reflect incidence of TB in the country of birth (*21,115,116*). In 2003, approximately 47% of foreign-born persons with TB received their diagnoses within 5 years of their arrival in the United States, and 19% received their diagnoses within 1 year of arrival. Among foreign-born persons, TB case rates decreased with longer duration of residence in the United States. TB rates were nearly four times higher among persons residing in the United States for <5 years than in those who were residents for ≥5 years (*115,116*).

HIV-infected persons. Because reporting of HIV infection among persons with TB is not complete, the exact prevalence of HIV infection among such persons is unknown. During 1993–2001, the prevalence of reported HIV infection occurring among persons also reported with TB decreased from 15% to 8% (*14*); this decrease has been attributed, in part, to reduced transmission of TB among HIV-infected persons (*16*). According to a recent worldwide epidemiologic assessment, however, 26% of adult TB cases in the United States are attributable to HIV infection (*44*).

Homeless persons. In 2003, persons known to have been homeless in the year before receiving a diagnosis accounted for 6.3% of cases of TB nationwide. On the basis of available population estimates (*117*), incidence of TB among homeless persons is approximately 30–40/100,000 population, more than five times the national case rate. However, a prospective study of a cohort of approximately 3,000 homeless persons in San Francisco documented an annual incidence of >250 cases/100,000 population (*118*). In addition, outbreaks of TB linked to overnight shelters continue to occur among homeless persons and likely contribute to the increased incidence of TB among that population (*119,120*).

Other populations at high risk. In 2003, persons known to have injected drugs in the year before receiving a diagnosis accounted for 2.2% of reported cases of TB, and noninjection drug use was reported by 7.3% of persons with TB. In certain U.S. communities, injection drug use is sufficiently prevalent so as to constitute a high risk for epidemiologic importance rather than simply an individual risk factor, especially when overlap exists between injection drug use and HIV infection (*121,122*).

TB Among Detainees and Prisoners in Correctional Facilities

The proportion of cases of TB occurring among inmates of prisons and jails has remained stable at approximately 3%–4% since data began to be collected in 1993; it was 3.2% in 2003 (*14*). Inmates also have high incidence of TB, with rates often >200/100,000 population (*123*), and they have a disproportionately greater number of risk factors for TB (e.g., low SES, HIV infection, and substance abuse) compared with the general population (*124,125*). TB transmission in correctional facilities contributes to the greater risk among those populations, presumably because of the difficulties in detecting cases of infectious TB and in identifying, evaluating, and treating contacts in these settings (*37,126*).

TB outbreaks occur in both prison and jail settings. Dedicated housing units for prison inmates with HIV infection were sites of transmission in California in 1995 (*126*) and South Carolina in 1999 and in South Carolina in 1999 (*37*). In the South Carolina outbreak, delayed diagnosis and isolation of an inmate who apparently had active TB after entering the facility led to >15 outbreak cases. Transmission leading to TB infection in the community also was documented in an outbreak that occurred in a jail in Tennessee during 1995–1997 (*127,128*) that involved approximately 40 inmates; contact investigations were incomplete because of brief jail terms and frequent movement of inmates. During the same period, 43% of patients with TB in the surrounding community had previously been incarcerated in that jail (*127*), and, after 2 years, the jail outbreak strain was more prevalent in the community than it was during the jail outbreak. Genotyping studies indicated that the outbreak strain accounted for approximately 25% of TB cases in the community, including those among patients with no history of incarceration (*128*).

Contributions of Genotyping of *M. tuberculosis*

M. tuberculosis genotyping refers to procedures developed to identify *M. tuberculosis* isolates that are identical in specific parts of the genome (*83*). To date, *M. tuberculosis*

genotyping has been based on polymorphisms in the number and genomic location of mycobacterial repetitive elements. The most widely used genotyping test for *M. tuberculosis* is restriction fragment length polymorphism (RFLP) analysis of the distribution of the insertion sequence IS6110 (*129*). However, genotyping tests based on polymorphisms in three additional mycobacterial repetitive elements (i.e., polymorphic guanine cytosine–rich repetitive sequences, direct repeats [e.g., spoligotyping], and mycobacterial interspersed repetitive units [MIRU]) have also been developed (*83*). *M. tuberculosis* isolates with identical DNA patterns in an established genotyping test often have been linked through recent transmission among the persons from whom they were isolated.

When coupled with traditional epidemiologic investigations, analyses of the genotype of *M. tuberculosis* strains have confirmed suspected transmission and identified unsuspected transmission of *M. tuberculosis*. These analyses have also identified risk factors for recent infection with rapid progression to disease, demonstrated exogenous reinfection with different strains, identified weaknesses in conventional contact investigations, and documented the existence of laboratory cross-contamination. Genotyping has become an increasingly useful tool for studying the pathogenesis, epidemiology, and transmission of TB.

Epidemiology of TB Among Contacts in Outbreak Settings

Conventional contact investigations have used the concentric circles approach to collect information and screen household contacts, coworkers, and increasingly distant contacts for TB infection and disease (*17*). The concentric circles model has been described previously (*130*). However, this method might not always be adequate in out-of-household settings. In community-based studies from San Francisco (*131*), Zurich (*132*), and Amsterdam (*133*), only 5%–10% of persons with clustered IS6110-based genotyping patterns were identified as contacts by the source-person in the cluster. This finding indicates that either 1) transmission of *M. tuberculosis* might occur more commonly than suspected and is not easily detected by conventional contact tracing investigations or 2) genotype clustering does not necessarily represent recent transmission (*55*). Because genotyping studies discover only missed or mismanaged contacts (i.e., those that subsequently receive a diagnosis of TB), such studies cannot explain the successes of the process or the number of cases that were prevented.

Certain populations (e.g., the urban homeless) present specific challenges to conducting conventional contact investigations. Genotyping studies have provided information about chains of transmission in these populations (*118,119*). In a prospective study of TB transmission in Los Angeles, the degree of homelessness and use of daytime services at three shelters were factors that were independently associated with genotype clustering (*119*). Additional studies support the idea that specific locations can be associated with recent or ongoing transmission of *M. tuberculosis* among homeless persons. Two studies among predominantly HIV-infected men have demonstrated evidence of transmission at specific bars in the community (*134,135*).

Genotyping techniques have confirmed TB transmission in HIV residential facilities (*136*), crack houses (i.e., settings in which crack cocaine is sold or used) (*137*), hospitals and clinics (*54*), and prisons (*138,139*). TB transmission also has been demonstrated among church choirs (*140*) and renal transplant patients (*141*) and in association with processing of contaminated medical waste (*142*) and with bronchoscopy (*143,144*).

Communitywide Epidemiology of TB

TB might arise because of rapid progression from a recently acquired *M. tuberculosis* infection, from progression of LTBI to TB disease, or occasionally from exogenous reinfection (*145*). The majority of genotyping studies have assumed that clustered isolates in a population-based survey reflect recent transmission of *M. tuberculosis*. Certain studies have identified epidemiologic links between clustered TB cases, inferring that the clustered cases are part of a chain of transmission from a single common source or from multiple common sources (*131,146*).

The number and proportion of population-based cases of TB that occur in clusters representing recent or ongoing transmission of *M. tuberculosis* have varied from study to study; frequency of clustering has varied from 17%–18% (in Vancouver, Canada) to 30%–40% (in U.S. urban areas) (*131,147,148*). Youth, being a member of a racial or ethnic minority population, homelessness, substance abuse, and HIV infection have been associated with clustering (*131,133, 148,149*).

The increasing incidence of TB among foreign-born persons underscores the need to understand transmission dynamics among this population. In San Francisco, two parallel TB epidemics have been described (*150,151*), one among foreign-born persons that was characterized by a low rate of genotype clustering and the other among U.S-born persons that was characterized by a high rate of genotype clustering. In a recent study from NYC, being born outside the United States, being aged ≥60 years, and receiving a diagnosis after 1993 were factors independently associated with being infected with a strain not matched with any other,

whereas homelessness was associated with genotype clustering and recent transmission (*152*). Among foreign-born persons, clustered strains were more likely to be found among patients with HIV infection (*152*).

Other Contributions of Genotyping

Genotyping can determine whether a patient with a recurrent episode of TB has relapsed with the original strain of *M. tuberculosis* or has developed exogenous reinfection with a new strain (*64,153*). In Cape Town, South Africa, where incidence of TB is high and considerable ongoing transmission exists, 16 (2.3%) of 698 patients had more than one episode of TB disease. In 12 (75%) of the 16 recurrent cases, the pairs of *M. tuberculosis* isolates had different IS6110-based genotyping patterns, indicating exogenous reinfection (*154*). However, in areas with a low incidence of TB, episodes of exogenous reinfection are uncommon (*153*). Because TB incidence in the majority of areas of the United States is low and decreasing, reinfection is unlikely to be a major cause of TB recurrence.

Genotyping has greatly facilitated the identification of false-positive cultures for *M. tuberculosis* resulting from laboratory cross-contamination of specimens. Previously, false-positive cultures (which might lead to unnecessary treatment for patients, unnecessary work for public health programs in investigating cases and pseudo-outbreaks, and unnecessary costs to the health-care system) were difficult to substantiate (*155*). Because of its capability to determine clonality among *M. tuberculosis* strains, genotyping has been applied extensively to verify suspected false-positive cultures (*156–158*) and to study the causes and prevalence of laboratory cross-contamination (*159,160*).

The Role of Genotyping of *M. tuberculosis* in TB-Control Programs

In 2004, CDC established the Tuberculosis Genotyping Program (TBGP) to enable rapid genotyping of isolates from every patient in the United States with culture-positive TB (*161*). State TB programs may submit one *M. tuberculosis* isolate from each culture-positive case within their jurisdictions to a contracted genotyping laboratory. A detailed manual describing this program, including information on how to interpret genotyping test results and how to integrate genotyping into TB-control activities, has been published (*162*).

Genotyping information is essential to optimal TB control in two settings. First, genotyping is integral to the detection and control of TB outbreaks, including ruling a suspected outbreak in or out and pinpointing involved cases and the site or sites of transmission (*54,136–144*). Second, genotyping is essential to detect errors in handling and processing of *M. tuberculosis* isolates (including laboratory cross-contamination) that lead to reports of false-positive cultures for *M. tuberculosis* (*156,158–160,163*).

More extensive use of *M. tuberculosis* genotyping for TB control depends on the availability of sufficient program resources to compare results with information from traditional epidemiologic investigative techniques. Time-framed genotyping surveys and good fieldwork can unravel uncertainties in the epidemiology of TB in problematic populations at high risk (*150–152,164*). Genotyping surveys and epidemiologic investigations also can be used as a program monitoring tool to determine the adequacy of contact investigations (*29,119,132–134,164–166*) and evaluate the success of control measures designed to interrupt transmission of *M. tuberculosis* among certain populations or settings (*167*).

Programs that use genotyping for surveillance of all of the jurisdiction's *M. tuberculosis* isolates should work closely on an ongoing basis with the genotyping laboratory and commit sufficient resources to compare genotyping results with those of traditional epidemiologic investigations. Information from both sources is needed for optimum interpretation of the complex epidemiologic patterns of TB in the United States (*84,168*).

Principles and Practice of TB Control

Basic Principles of TB Control

The goal of TB control in the United States is to reduce morbidity and mortality caused by TB by 1) preventing transmission of *M. tuberculosis* from persons with contagious forms of the disease to uninfected persons and 2) preventing progression from LTBI to TB disease among persons who have contracted *M. tuberculosis* infection. Four fundamental strategies are used to achieve this goal (Box 4) (*17,169*), as follows:

- **Early and accurate detection, diagnosis, and reporting of TB cases leading to initiation and completion of treatment.** Detecting and reporting suspected cases of TB is the key step in stopping transmission of *M. tuberculosis* because it leads to prompt initiation of effective multiple-drug treatment, which rapidly reduces infectiousness (Box 3). Completion of a full course of standard therapy is essential to prevent treatment failure, relapse, and the acquisition of drug resistance (*5*). TB is commonly diagnosed when a person seeks medical attention for symptoms caused by the disease or a concomitant medical condition. Thus, health-care providers, particularly those providing primary health-care

BOX 4. Strategies to achieve the goal of reduction of tuberculosis (TB) morbidity and mortality

- Early and accurate detection, diagnosis, and reporting of TB cases leading to initiation and completion of treatment
- Identification of contacts of patients with infectious TB and treatment of those at risk with an effective drug regimen
- Identification of other persons with latent TB infection at risk for progression to TB disease and treatment of those persons with an effective drug regimen
- Identification of settings in which a high risk exists for transmission of *Mycobacterium tuberculosis* and application of effective infection-control measures

to populations at high risk, are key contributors to TB case detection. A suspected or confirmed case of TB should be reported immediately to the jurisdictional public health agency. Reporting of new cases is essential to initiate public health responses, including institution of a treatment plan, case-management services, and evaluation of contacts, and for surveillance purposes. This statement contains detailed recommendations for improving detection of TB cases. Treatment of TB is the subject of another statement in this series from ATS, CDC, and IDSA (*5*).

- **Identification of contacts of patients with infectious TB and treatment of those at risk with an effective drug regimen.** The evaluation of contacts of cases of infectious TB is one of the most productive methods of identifying adults and children with LTBI at high risk for progression to TB disease and persons in the early stages of TB disease (*30,31*). Contact investigations therefore serve as an important means of detecting tuberculosis cases and at the same time identify persons in the early stage of LTBI, when the risk for progression to TB disease is high and the benefit of treatment is greatest (*4*).
- **Identification of other persons with LTBI at risk for progression to TB disease and treatment of those persons with an effective drug regimen.** Targeted testing is intended to identify persons other than TB contacts who have an increased risk for acquiring TB and to offer such persons diagnostic testing for *M. tuberculosis* infection and treatment, if indicated, to prevent subsequent progression to TB disease (*4*). This approach is critical to the eventual elimination of TB in the United States, because it is the only means of preventing TB in the substantial pool of persons with LTBI at high risk for progression to TB disease. Targeted testing and treatment of LTBI is also a primary means of controlling TB among foreign-born persons at high risk residing in the United States because genotyping surveys have consistently demonstrated that the majority of TB cases in that population are attributable to progression from LTBI (*150–152*). Targeted testing and treatment of LTBI is best accomplished through cost-effective programs aimed at patients and populations identified on the basis of local surveillance data as being at increased risk for TB (*51*). Guidelines for this activity have been published (*4*). This statement includes recommendations for organizing and conducting programs for targeted testing and treatment of LTBI.
- **Identification of settings in which a high risk exists for transmission of *M. tuberculosis* and application of effective infection-control measures.** For the rising burden of TB from recent transmission of *M. tuberculosis* to be reduced, settings at high risk for transmission should be identified, and effective infection-control measures should be taken to reduce the risk. In the 1980s, the majority of cases of TB in the United States were believed to arise through activation of LTBI, and few cases were believed to occur as a consequence of recent transmission of *M. tuberculosis* (*6*). During the 1985–1992 TB resurgence, however, disease caused by recent transmission was a critical component of the increase in TB incidence. TB outbreaks associated with person-to-person spread occurred in different venues, most prominently in health-care facilities (*52–54,170*). TB morbidity caused by recent spread of *M. tuberculosis* has continued to be a prominent part of the epidemiology of the disease in the United States. During 1996–2000, when incidence of TB was in constant decline, a survey involving 10,883 *M. tuberculosis* isolates collected from persons with newly diagnosed cases from seven NTGSN sentinel surveillance sites indicated that 52% were clustered with at least one other isolate (average genotype cluster size: six isolates), frequently representing cases of TB disease associated with recent spread of *M. tuberculosis* (*171*). Outbreaks of TB are also being reported with greater frequency (*33,34,172,173*). Institutional infection-control measures have been highly successful in health-care facilities (*56*), but other high-risk settings (e.g., correctional facilities [*37*], homeless shelters [*33*], bars [*27*]), and social settings that extend beyond single venues [*26,34,38,172*]) present challenges to effective infection control (*172*).

Vaccination with BCG is not recommended as a means to control TB in the United States because of the unproved efficacy of the vaccine in the U.S. population (*174,175*), its effect of confounding the results of tuberculin skin

testing (*176*) and the success of other measures in reducing incidence of TB (*16*). During the 1985–1992 TB resurgence, the documented spread of TB, including multidrug-resistant TB, in health-care institutions and in the community (*52–54,177,178*) stimulated interest in the potential use of BCG to protect HCWs and others from exposure to *M. tuberculosis*. In 1996, a statement from ACET and the Advisory Committee on Immunization Practices (*179*) recommended vaccination with BCG for 1) infants and children with exposure to *M. tuberculosis* in settings in which other protective measures are either inaccessible or proven to be ineffective and 2) HCWs when likelihood of exposure to multidrug-resistant TB is high and recommended control measures have not been successful. With improved TB control in the United States and the decline of multidrug-resistant TB (*13*), use of BCG for protection against TB has declined. An improved vaccine, particularly one that protects adults with LTBI against acquiring TB disease, would accelerate progress toward TB elimination in the United States (*180*).

Deficiencies in TB Control

Because TB control is a complex undertaking that involves multiple participants and processes, mistakes often occur, with adverse consequences. Common errors include 1) delays among persons with active TB obtaining health care; 2) delayed detection and diagnosis of active TB; 3) failed or delayed reporting of TB; 4) failure to complete an effective course of treatment for TB; 5) missed opportunities to prevent TB among children; and 6) deficiencies in conducting contact investigations and in recognizing and responding to outbreaks.

Delays in Obtaining Health Care

Homeless patients with TB symptoms often delay seeking care or experience delays in gaining access to care (*181*), and fear of immigration authorities has been associated with patient delay among foreign-born persons (*19*). Patients who speak languages other than English or who are aged 55–64 years are more likely than others to delay seeking care (*20*).

Cultural factors that might affect health-seeking behavior by foreign-born persons include misinterpretation or minimization of symptoms, self-care by using over-the-counter or folk medicines, and the social stigma associated with TB (*18*). In certain societies, women with TB are less likely to take advantage of health-care services, perhaps because of stigma associated with the diagnosis, including a lower likelihood of marriage (*182,183*). Even in areas with open access to public health clinical services, persons at risk for TB might not seek evaluation and treatment because they are not aware that these resources are available for persons with limited financial means (*118,184–186*).

Delayed Detection and Diagnosis of Active TB

Delayed detection of a case of TB and resulting delays in initiation of treatment can occur if the clinician does not suspect the diagnosis. A survey conducted in NYC in 1994 found that the median delay within the health-care system (defined as the time from first contact to initiation of treatment for active TB) was 15 days (range: 0–430 days) (*20*). Asians and homeless persons were more likely to encounter delays in receiving a diagnosis than non-Asians and persons with stable housing. Persons without cough who had AFB smear-negative TB or who did not have a chest radiograph at their initial visit also experienced delays. In London, England, delays in diagnosis occurred among whites and among women of all racial/ethnic populations (*187*).

Regardless of the reason, the consequences of delays in diagnosis and initiation of effective therapy can be serious. In Maine, a shipyard worker aged 32 years who was a TB contact and who was untreated despite having symptoms of active TB, repeated medical visits, and a chest radiograph consistent with active TB did not receive a diagnosis of TB until 8 months after he became ill (*188*), and 21 additional cases of TB occurred among his contacts. Of 9,898 persons who were investigated as contacts, 697 (7.0%) persons received diagnoses of new LTBIs. A high school student in California was symptomatic for >1 year before TB was diagnosed (*177*). Subsequently, 12 additional TB cases among fellow students were linked to the source-case, and 292 (23%) of 1,263 students tested had positive tuberculin skin tests.

Other instances of delayed or missed diagnoses of TB have been reported that have resulted in extended periods of infectiousness and deaths (*22,24,178*). These problems reflect the increasing difficulty in maintaining clinical expertise in the recognition of TB in the face of declining disease incidence (*41*). Recognition of TB among patients with AFB-negative sputum smear results is a challenge for practitioners and has been associated with delays in reporting and treatment (*22,189,190*).

Delayed Reporting of TB

Failure to promptly report a new TB case delays public health responses (e.g., institution of a treatment plan, case-management services, and protection of contacts). Although TB cases in the United States rarely remain unreported, timeliness of reporting varies (median: 7–38 days) (*190*).

Failure to Receive and Complete a Standard Course of Treatment for Active TB

Failure to receive and complete a standard course of treatment for TB has adverse consequences, including treatment failure, relapse, increased TB transmission, and the emergence of drug-resistant TB (*191–193*). At least two reasons exist for failure to complete standard treatment. Patients frequently fail to adhere to the lengthy course of treatment (*188*). Poor adherence to treatment regimens might result from difficulties with access to the health-care system, cultural factors, homelessness, substance abuse, lack of social support, rapid clearing of symptoms, or forgetfulness (*18,194*). Also, as TB has become less common, clinicians might fail to use current treatment regimens (*48*). These adverse outcomes are preventable by case-management strategies provided by TB-control programs, including use of DOT (*13,195,196*).

Missed Opportunities To Prevent TB Among Children

The absence of TB infection and disease among children is a key indicator of a community's success in interrupting the transmission of TB (*197*). The 1985–1992 TB resurgence included a reversal of the long-term decline in the incidence of TB among children, which indicated a failure of the public health system to prevent disease transmission (*197*). A study of 165 children reported with TB in California in 1994 found that for 59 (37%), an adult source-case was identified (*198*). Factors that contributed to transmission to children included delayed reporting, delayed initiation of contact investigations, and poor management of adult source-cases. Improvements in contact investigations might have prevented 17 (10%) of those cases (*198*).

Deficiencies in Conducting Contact Investigations and in Recognizing and Responding to Outbreaks

Deficiencies in contact investigations and failure to recognize and respond to TB outbreaks are among the most important challenges to optimal control of TB in the United States. These topics are discussed in detail in this statement along with the other essential components of TB control.

Importance of TB Training and Education

The 1985–1992 TB resurgence led ACET to call for a renewed focus on training and education as an integral part of strategies for TB control, prevention, and elimination (*1*). Factors indicating a need for this focus include the following:

- **Deficiencies in clinical knowledge and practice.** Errors have been documented on the part of medical practitioners and TB-control staff in the diagnosis, reporting, treatment, and follow-up of TB cases. These deficiencies indicate a broad need for training and education throughout the TB-control system, among both public health and nonpublic health participants.
- **Staffing and workforce concerns.** Ongoing education and training within TB-control programs are required to inform staff members about programmatic and patient management issues. For example, implementation of DOT for treatment of TB disease or LTBI or the integration of a new category of HCWs (e.g., outreach workers) might have substantial training requirements. Changes in the state or local epidemiology of TB and the emergence of new populations or settings of high risk also might necessitate additional training or retraining of staff members.
- **New guidelines and recommendations.** TB guidelines and recommendations are regularly published and updated (*3–5*). However, the promulgation of guidelines alone does not necessarily improve provider practices (*42,199*). Guidelines are more effective when supplemented with targeted education (*42*).
- **Education of new contributors to TB control.** TB elimination will require that new categories of health professionals, not previously identified as contributors to TB control in the community, take on expanded responsibilities. Education strategies for these new partners will be needed. For example, clinicians should understand the local epidemiology of TB sufficiently to know if their practice includes patients at high risk. They should know how to identify and treat patients at high risk who have LTBI. They should be able to recognize the signs and symptoms of TB disease and understand how to evaluate and treat persons with suspected cases. They should understand the public health aspects of TB, including the need for prompt reporting and the facilitating role of the jurisdictional health agency in case management. In particular, strategies are needed to maintain TB knowledge and expertise among clinicians in areas of low TB incidence (*48*).
- **Diminished teaching about TB in medical and nursing schools.** As TB case rates declined in the United States, schools of medicine and nursing gradually reduced their emphasis on TB education. With the resurgence of TB in the United States during 1985–1992 and recognition of the extent of the global epidemic, clinicians and public health programs have been faced with the challenges of learning to diagnose, manage, and control TB

as if it were a new disease (*42,200,201*). Education is essential to the future control of TB in the United States and globally (*2*), and creating interest in TB among students of the health professions is critical to generating the competent workforce needed to eliminate TB in the United States and contribute human resources to fighting the global TB epidemic.

Educating Patients and Communities at High Risk

Education of patients by clinicians, TB program staff, and trusted community members promotes acceptance and adherence to authoritative advice about controlling and preventing TB. Such education can influence patients' decision-making about whether to accept and complete treatment for LTBI (*202*).

Because cultural and health beliefs might act as barriers to effective control of TB (*18,19*), an increasing need exists for education targeted at populations at high risk (*19*). TB-control programs should enlist community-based organizations and other key informants to discover the health beliefs, norms, and values of communities at high risk in their jurisdictions (*202,203*). Professional associations and academic institutions (including schools of medicine, public health, and nursing) will be valuable partners in developing an understanding of the health perceptions of these populations. Education materials should be developed with input from the target audience to ensure that they are culturally and linguistically appropriate (*203,204*).

The Strategic Plan for TB Training and Education

In 1997, CDC funded a project to develop a Strategic Plan for Tuberculosis Training and Education (the Strategic Plan) that provided guidance to agencies and organizations in the United States that offer TB training and education for public- and private-sector providers. The Strategic Plan specified critical areas requiring attention, including 1) the need for culturally competent programs and materials, 2) effective methods and technologies, 3) collaboration and cooperation among training and education partners outside TB-control programs, and 4) adequate funding for training and education efforts.

Other Resources for TB Training and Education

Substantial progress has been made in developing and disseminating resources for TB training and education. CDC and national TB centers, NTCA, regional controllers associations (e.g., the Northeast Tuberculosis Training Consortium), state and local health departments, and the National Laboratory Training Network have all conducted education programs or developed training and education materials. In 2001, as stipulated by the Strategic Plan, the Tuberculosis Education and Training Network was established. The network is coordinated by CDC and includes educators in local, state, and territorial health agencies. CDC has also developed the Tuberculosis Information CD-ROM, Version 3, and the Tuberculosis Education and Training Resource Guide; these products are designed to enhance awareness and accessibility of resources (available at http://www.cdc.gov/nchstp/tb/default.htm) for TB education and training. The establishment in 2004 of the National Tuberculosis Curriculum Coordinating Center at the University of California at San Diego by the National Heart Lung and Blood Institute signals a commitment by the National Institutes of Health (NIH) to provide basic TB education for health-care students and providers.

Professional societies and specialty boards are means for reaching private medical providers. Including TB as a subject in state medical society programs, hospital grand rounds, and medical specialty board examinations would be a valuable resource for providers serving populations at low risk. New linkages should be established to reach providers serving populations at high risk (e.g., foreign-born, homeless, and HIV-infected persons). For example, the AIDS Education and Training Centers funded by the Health Resources and Services Administration are a resource for reaching HIV/AIDS providers, and foreign physicians' associations and community-based organizations are potential partners for reaching international medical graduates and health-care providers of foreign-born persons.

Laboratory Services for Optimal TB Control

The diagnosis of TB, management of patients with the disease, and public health control services rely on accurate laboratory tests. Laboratory services are an essential component of effective TB control, providing key information to clinicians (for patient care) and public health agencies (for control services).

Up to 80% of all initial TB-related laboratory work (e.g., smear and culture inoculation) is performed in hospitals, clinics, and independent laboratories outside the public health system, whereas >50% of species identification and drug susceptibility testing is performed in public health laboratories (*205*). Thus, effective TB control requires a network of public and private laboratories to optimize laboratory testing and the flow of information. Public health laboratorians, as a

component of the public health sector with a mandate for TB control, should take a leadership role in developing laboratory networks and in facilitating communication among laboratorians, clinicians, and TB controllers.

Role of Public Health Laboratories

Public health laboratories should ensure that clinicians and public health agencies within their jurisdictions have ready access to reliable laboratory tests for diagnosis and treatment of TB (*206*). Specific tasks to ensure the availability, accessibility, and quality of essential laboratory services are 1) assessment of the cost and availability of TB laboratory services and 2) development of strategic plans to implement and maintain a systems approach to TB testing (*207*). In this process, public health laboratories should assess and monitor the competence of laboratories that perform any testing related to the diagnosis, management, and control of TB within their jurisdictions; develop guidelines for reporting and tracking of laboratory results; and educate laboratory staff members, health-care providers, and public health officials about available laboratory tests, new technologies, and indications for their use. For example, public health laboratories should lead the discussion on the costs, logistics requirements (e.g., collection and transport of clinical specimens within the required time), and quality assurance issues associated with the use of QFT-G, the new test for latent *M. tuberculosis* infection (*103*). The process of coordinating TB laboratory services is usually best organized at the state level (*208*), and the Association of Public Health Laboratories has compiled descriptions of successful organizational models for integrated laboratory services (*207*).

Role of Clinical Laboratories

Because the majority of initial TB laboratory work related to diagnosis of TB is conducted in hospitals, clinics, and independent laboratories (*205*), clinicians and public health agencies are increasingly dependent on the laboratory sector for the confirmation of reported cases, and public health laboratories are similarly dependent for referral of specimens for confirmatory testing and archiving. However, as a result of laboratory consolidation at the regional or national level (*206*), private laboratories are experiencing more difficulties in fulfilling this function. In certain instances, consolidation has resulted in poor communication among laboratory personnel, clinicians, and public health agencies (*206,209*). Problems also have been identified in specimen transport, test result reporting, and quality control (*206,209,210*). In response, certain states (e.g., Wisconsin*) have adopted laws and regulations that mandate essential clinical laboratory services for TB control (e.g., drug susceptibility testing and reporting of the first *M. tuberculosis* isolate from each patient and submission of isolates to the state public health laboratory).

The clinical laboratory sector should accept the responsibilities that accompany its emergence as a provider of essential TB testing (*209*). This statement provides recommendations to guide turnaround times for essential tests, reporting to clinicians and jurisdictional public health agencies, and referral of specimens to public health laboratories or their designees.

Essential Laboratory Tests

Six tests performed in clinical microbiologic laboratories are recommended for optimal TB control services (Table 3). These laboratory tests should be available to every clinician involved in TB diagnosis and management and to jurisdictional public health agencies charged with TB control. In addition, other tests that are useful in the diagnosis and management of selected patients and for specific TB control activities include *M. tuberculosis* genotyping, serum drug levels, tests used for monitoring for drug toxicity, and QFT-G for diagnosis of latent *M. tuberculosis* infection (*5,103,162*). Access to these specialized tests should be provided as needed.

For suspected cases of pulmonary TB, sputum smears for AFB provide a reliable indication of potential infectiousness; and for AFB smear-positive pulmonary cases, a nucleic acid amplification assay (NAA) provides rapid confirmation that the infecting mycobacteria are from the *M. tuberculosis*

* Wisconsin Department of Health and Family Services. HFS 145. Control of Communicable Diseases. Available at http://www.legis.state.wi.us/rsb/code/hfs/hfs145.pdf.

TABLE 3. Essential laboratory tests for tuberculosis control

Test	Maximum turnaround time
Microscopy for acid-fast bacilli	≤24 hours from specimen collection or, if test is performed offsite, ≤24 hours from receipt in laboratory; if latter, time from specimen collection to laboratory receipt should be ≤24 hours
Nucleic acid amplification assay	≤48 hours from date of specimen collection
Mycobacterial growth detection by culture	≤14 days from date of specimen collection
Identification of cultured mycobacteria	≤21 days from date of specimen collection
Drug susceptibility testing	≤30 days from date of specimen collection
Drug susceptibility testing of second-line drugs	≤4 weeks from date of request

complex. These two tests, which should be available with rapid turnaround times from specimen collection, facilitate decisions about initiating treatment for TB or a non-TB pulmonary infection, and, if TB is diagnosed, for reporting the case and establishing priority to the contact investigation.

Growth detection and identification of *M. tuberculosis* by culture of sputum and other affected tissue is essential for confirmation of the identity of the organism and for subsequent drug susceptibility testing, which is recommended on all initial isolates for each patient. Cultures also remain the cornerstone for the diagnosis of TB in smear-negative pulmonary and extrapulmonary cases and, along with sputum smears for AFB, provide the basis for monitoring a patient's response to treatment, for release from isolation, and for diagnosing treatment failure and relapse (*5*). The use of liquid media systems, which can provide information in less time than solid media (in certain cases, 7 days), should be available in all laboratories that perform culture for mycobacteria. Detailed descriptions of these recommended laboratory tests; recommendations for their correct use; and methods for collecting, handling, and transporting specimens have been published (*3,211*).

Recommended Roles and Responsibilities for TB Control

This section delineates organizational and operational responsibilities of the public health sector that are essential to achieve the goals of TB control in the United States. However, a central premise of this statement is that continuing progress toward elimination of TB in the United States will require the collaborative efforts of a broad range of persons, organizations, and institutions in addition to the public health sector, which has responsibility for the enterprise. For example, clinicians who provide primary health care and other specialized health services to patients at high risk for TB, academic medical centers that educate and train them, hospitals in which they practice, and professional organizations that serve their interests can all make meaningful contributions to improve the detection of TB cases, one of the most important obstacles to continuing progress (Box 1). Similarly, important roles exist for such entities as community-based organizations representing populations at risk for TB and the pharmaceutical industry, which takes academic advances and develops the tools for diagnosis, treatment, and prevention of TB. This section discusses the importance to the TB elimination effort of participants outside the public health sector and proposes specific roles and responsibilities that each could fulfill toward that goal. The sponsoring organizations intend for these proposals to serve as the basis for discussion and consensus building on the important roles and responsibilities of the nonpublic health sector in continuing progress toward the elimination of TB in the United States.

Public Health Sector

The infrastructure for TB control has been discussed extensively in recent years. An analysis of contributing factors to the rise in the number of TB cases during 1985–1992 concluded that the resurgence never would have occurred had the public health infrastructure been left in place and supported appropriately (*212*). The need to maintain the TB-control infrastructure has been expressed repeatedly (*1,2,13,213,214*).

Public health activities have been described as consisting of four interrelated components: mission/purpose, structural capacity, processes, and outcomes (*215*). Among these four components, structural capacity (i.e., persons who do the work of public health, their skills and capacities, the places where they work, the way they are organized, the equipment and systems available to them, and the fiscal resources they command) represents the public health infrastructure for TB control.

The responsibility for TB control and prevention in the United States rests with the public health system through federal, state, county, and local public health agencies. Programs conducted by these agencies were critical to the progress that has been made in TB control, and the deterioration of those programs following the loss of categoric federal funding contributed to the resurgence of TB in the United States during 1985–1992 (*1,2,13,212–214*). Since 1992, as a result of increased funding for TB-control programs, national incidence of TB disease has declined. In 2004, $147 million in federal funds were dedicated to domestic TB control, compared with $6.6 million in 1989, during the resurgence. These funds have been used to rebuild public health–based TB-control systems, and the success achieved highlights the critical role of the public health system in TB control.

TB control in the United States has traditionally been conducted through categoric programs established to address the medical aspects of the disease and the specific interventions required for its successful prevention and management (*17,216*). CDC's Division of TB Elimination, in partnership with other CDC entities that conduct TB-related work, provides guidance and oversight to state and local jurisdictions by conducting nationwide surveillance; developing national policies, priorities, and guidelines; and

providing funding, direct assistance, education, and program evaluation. Setting the national agenda for support of basic and clinical research is also a critical function of federal health agencies, including NIH and CDC, with support from nongovernment organizations such as ATS and IDSA.

To meet the priorities of basic TB control (Box 4), state and local public health agencies with responsibility for TB control should provide or ensure the provision of a core group of functions (Box 5). Jurisdictional public health agencies should ensure that competent services providing these core elements function adequately within their jurisdictions and are available with minimal barriers to all residents.

How the core components of TB control are organized differs among jurisdictions, depending on the local burden of disease, the overall approach to public health services within the jurisdiction, budgetary considerations, the availability of services within and outside the public health sector, and the relationships among potential participants. Certain jurisdictions provide core program components themselves, whereas other jurisdictions contract with others to provide them. In the majority of cases, the organization includes a mix in which the public health agency provides certain services, contracts for others, and works collaboratively with partners and stakeholders to accomplish the remainder (*48*). Sharing of direct services, including patient management, increases the importance of the public health sector, which retains responsibility for success of the process. This evolving role of the public health sector in TB control is consistent with the widely accepted concept of the three core functions of public health that IOM proposed in 1988: assessment, policy development, and assurance (*43*).

BOX 5. Core responsibilities for control of tuberculosis (TB) by a jurisdictional public health agency

- Assessment of the extent and characteristics of TB in the jurisdiction through collection and analysis of epidemiologic and other data
- Development of policies and procedures and of a plan for controlling TB, on the basis of the assessment of the problem
- Assurance of diagnostic, clinical, and preventive services needed to implement the plan for controlling TB
- Monitoring and evaluating the effectiveness of the plan for controlling TB
- Providing information and education to policy makers, health-care professionals, and the public regarding control of TB in the jurisdiction

Health Insurance Portability and Accountability Act

The Health Insurance Portability and Accountability Act (HIPAA) of 1996 included provisions to protect the privacy of individually identifiable health information. To implement these privacy protections, the U.S. Department of Health and Human Services has issued a ruling on how health-care providers may use and disclose personally identifiable health information about their patients; these regulations provide the first national standards for requirements regarding the privacy of health information (*217*).

HIPAA also recognizes the legitimate need for public health authorities and others responsible for ensuring the public's health and safety to have access to personal health information to conduct their missions and the importance of public health disease reporting by health-care providers. HIPAA permits disclosure of personal health information to public health authorities legally authorized to collect and receive the information for specified public health purposes. Such information may be disclosed without written authorization from the patient. Disclosures required by state and local public health or other laws are also permitted. Thus, HIPAA should not be a barrier to the reporting of suspected and verified TB cases by health-care providers, including health-care institutions. Additional information about HIPAA is available at http://www.hhs.gov/ocr/hipaa.

Roles and Responsibilities of Federal Public Health Agencies

- **Establishment of standards and guidelines.** Federal agencies should take a leadership role in developing and promulgating standards of public health and clinical practice for TB, in collaboration with professional medical societies, state and local TB-control programs, and other organizations. These partnerships have served the medical and public health communities and should be continued and strengthened.
- **Financial and technical support for TB control and elimination.** Federal agencies should continue to provide financial and technical support for TB control and elimination within their own institutions and jurisdictions and provide direct support to state and local TB-control programs through CDC cooperative agreements. In addition, CDC should continue to provide technical assistance through the assignment of medical and administrative staff to state and local TB-control programs and by responding to requests for assistance with TB outbreaks. In relation to these responsibilities, CDC should determine the level of necessary

financial support from the federal government needed to control and prevent TB in the United States.

- **National reporting, surveillance, and analysis.** Federal agencies should continue to support the collection, aggregation, and distribution of national surveillance data through cooperative agreements with state and local TB programs. Consultation and technical support from federal resources are also essential to maintain the state and local network of surveillance throughout the United States.
- **Program oversight and monitoring.** Federal agencies should facilitate development of quality improvement programs and establishment of quality indicators for state and local TB-control programs.
- **Education and training.** Although multiple participants in TB control are responsible for education and training of patients and health-care providers, federal agencies should take the lead in developing training and education materials to facilitate TB control at the state and local levels.
- **Public health research.** Federal agencies should plan, conduct, and support basic, clinical, and public health research leading to improvements in TB diagnosis, treatment, and prevention.
- **Evaluation of immigrants and refugees outside the United States.** Federal agencies are responsible for ensuring that legal immigrants and refugees are evaluated appropriately for TB before their arrival in the United States and for notifying state and local TB-control programs of the arrival in their jurisdictions of immigrants and refugees with suspected TB. Agencies involved in evaluating and reporting arriving immigrants and refugees should ensure the quality and timeliness of those processes.
- **Coordination of interstate TB-control efforts.** Federal agencies should take the lead in resolving interstate TB-control issues, including movement of TB patients across state lines and multistate TB outbreaks.

Roles and Responsibilities of Jurisdictional Public Health Agencies

Planning and policy development. The blueprint for TB control for a given area is a responsibility of the jurisdictional public health agency. Policies and plans should be based on a thorough understanding of local epidemiologic data and on the capabilities and capacities of clinical and support services for clients, the fiscal resources available for TB control, and ongoing indicators of program performance. Open collaboration is essential among public health officials and community stakeholders, experts in medical and nonmedical TB management, laboratory directors, and professional organizations, all of whom provide practical perspectives to the content of state and local TB-control policy. Policies and procedures should reflect national and local standards of care and should offer guidance in the management of TB disease and LTBI.

A written TB control plan that is updated regularly should be distributed widely to all interested and involved parties. The plan should assign specific roles and responsibilities; define essential pathways of communication between providers, laboratories, and the public health system; and assign sufficient resources, both human and financial, to ensure its implementation, including a responsible case manager for each suspected and verified case of TB. The plan should include the provision of expert consultation and oversight for TB-related matters to clinicians, institutions, and communities. It should provide special guidance to local laboratories that process TB-related samples, assist local authorities in conducting contact or outbreak investigations and DOT, and provide culturally appropriate information to the community. Systems to minimize or eliminate financial and cultural barriers to TB control should be integral to the plan, and persons with TB and persons at high risk with TB infection should receive culturally appropriate education about TB and clinical services, including treatment, with no consideration for their ability to pay. Finally, the plan should be consistent with current legal statutes related to TB control. Relevant laws and regulations should be reviewed periodically and updated as necessary to ensure consistency with currently recommended clinical and public health practice (e.g., mandatory reporting laws, institutional infection-control procedures, hospital and correctional system discharge planning, and involuntary confinement laws) (*218*).

Collection and analysis of epidemiologic and other data. The development of policies and plans for the control of TB within a jurisdiction requires a detailed understanding of the epidemiology of TB within the jurisdiction. Mandatory and timely case reporting from community sources (e.g., providers, laboratories, hospitals, and pharmacies) should be enforced and evaluated regularly. To facilitate the reporting process and data analyses, jurisdictions should modify systems as necessary to accommodate local needs and evolving technologies. State and local TB-control programs should have the capability to monitor trends in TB disease and LTBI in populations at high risk and to detect new patterns of disease and possible outbreaks. Populations at high risk should be identified and targeted for active surveillance and prevention, including targeted testing and treatment of LTBI (*4*).

Timely and accurate reporting of suspected and confirmed TB cases is essential for public health planning and assessment at all levels. Analyses of these data should be performed at least annually to determine morbidity, demographic characteristics, and trends so that opportunities for targeted screening for disease or infection can be identified. Regular reviews of clinical data (e.g., collaborative formal case presentations and cohort analyses of treatment outcomes; completeness, timeliness and effectiveness of contact investigations; and treatment of LTBI) may be used as indicators of program performance.

Data should be collected and maintained in a secure, computerized data system that contains up-to-date clinical information on persons with suspected and confirmed cases and on other persons at high risk. Each case should be reviewed at least once monthly by the case manager and by field or outreach staff to identify problems that require attention. The TB-case registry should ensure that laboratory data, including data on sputum culture conversion and drug susceptibility testing of clinical isolates, are promptly reported, if applicable, to the health-care provider so any needed modifications in management can be made. This requires a communications protocol for case managers, providers, and the public health and private laboratory systems that will transmit information in a timely fashion. Aggregate program data should be available to the health-care community and to community groups and organizations with specific interests in public health to support education and advocacy and to facilitate their collaboration in the planning process.

Clinical and diagnostic services for patients with TB and their contacts. TB-control programs should ensure that patients with suspected or confirmed TB have ready access to diagnostic and treatment services that meet national standards (*3,5*). These services are often provided by state- or city-supported TB specialty clinics and staffed by health department personnel or by contracted service providers; however, persons may seek medical care for TB infection or disease in the private medical sector. Regardless of where a person receives medical care, the primary responsibility for ensuring the quality and completeness of all TB-related services rests with the jurisdictional health agency, and health departments should develop and maintain close working relations with local laboratories, pharmacies, and health-care providers to ensure that standards of care, including those for reporting, are met.

Clinical services provided by the health department, contracted vendors, or private clinicians should be competent, accessible, and acceptable to members of the community served by the jurisdiction. Hours of clinic operation should be convenient, and waiting intervals between referral and appointments should be kept to a minimum. Persons with symptoms of TB should be accommodated immediately (i.e., on a walk-in basis). Staff, including providers, should reflect the cultural and ethnic composition of the community to the extent that this is possible, and competent clinical interpreter services should be available to those patients who do not speak English. All clinical services, including diagnostic evaluation, medications, clinical monitoring, and transportation, should be available without consideration of the patient's ability to pay and without placing undue stress on the patient that might impair completion of treatment.

Clinical facilities should provide diagnostic, monitoring, and screening tests, including radiology services. Health-care providers, including nurses, clinicians, pharmacists, laboratory staff members, and public health officials, should be educated about the use and interpretation of diagnostic tests for TB infection and disease. Clinics and providers should monitor patients receiving TB medications at least monthly for drug toxicity and for treatment response, according to prevailing standards of care (*5*). Counseling and voluntary testing for HIV infection should be offered to all persons with suspected and proven TB and to certain persons with LTBI, with referral for HIV treatment services when necessary. A case manager, usually a health department employee, should be assigned to each patient suspected or proven to have TB to ensure that adequate education is provided about TB and its management, standard therapy is administered continuously, and identified contacts are evaluated for infection and disease.

A treatment plan for persons with TB should be developed immediately on report of the case. This plan should be reviewed periodically by the case manager and the treating clinician and modified as necessary as new data become available (*219*). The treatment plan should include details about the medical regimen used, how and where treatment is to be administered, monitoring of adherence, drug toxicity, and clinical and bacteriologic responses. Social and behavioral factors that might interfere with successful completion of treatment also should be addressed.

Patient-specific strategies for promoting adherence to treatment should take into account each patient's clinical and social circumstances and needs (*5*). Such strategies might include the provision of incentives or enablers (e.g., monetary payment, public transportation passes, food, housing, child care, or transportation to the clinic for visits). Whether the patient's care is managed by a public health clinic or in the private sector, the initial strategy used should emphasize direct observation of medication

ingestion by an HCW. Patient input into this process (e.g., regarding medications to be taken or the location of DOT) is often useful as it can minimize the burden of treatment and provide the patient a degree of control over an anticipated lengthy course of therapy.

Expert medical consultation in TB should be available to the health-care community, especially for patients who have drug-resistant disease or medical diagnoses that might affect the course or the outcome of treatment. Consultants may be employees of the health department or clinicians with expertise who are under contract with the health department.

Inpatient care should be available to all persons with suspected or proven TB, regardless of the person's ability to pay. Hospitalized patients with suspected proven TB should have access to expert medical and nursing care, essential diagnostic services, medications, and clinical monitoring to ensure that diagnostic and treatment standards are met. Inpatient facilities that manage persons who are at risk for TB should have infection-control policies and procedures in place to minimize the risk for nosocomial spread of infection. Facilities should report persons with suspected or confirmed TB to the health department and arrange for discharge planning as required by statute.

Public health agencies should have legal authority and adequate facilities to ensure that patients with infectious TB are isolated from the community until they are no longer infectious. This authority should include the ability to enforce legal confinement of patients who are unwilling or unable to adhere to medical advice (*218,220*). This authority also should apply to nonadherent patients who no longer are infectious but who are at risk for becoming infectious again or becoming drug resistant.

TB-control programs should serve as sources of information and expert consultation to the health-care community regarding airborne infection and appropriate infection-control practice. A TB program's presence raises overall provider awareness of TB and facilitates timely diagnosis, reporting, and treatment. Collaboration with local health-care facilities to design and assist in periodic staff education and screening is often a health department function. Expertise in airborne infections by TB-control personnel may be shared with biologic terrorism programs to assist in the design and implementation of local protocols.

Contact investigation, including education and evaluation of contacts of persons with infectious TB, is a key component of the public health mandate for TB control. Often the primary responsibility of the case manager, contact investigation should proceed as quickly and as thoroughly as indicated by the characteristics of the specific case and by those of the exposed contact (e.g., young children or immunocompromised persons). This statement includes recommendations on organizing and conducting contact investigations. TB-control programs that are prepared to implement enhanced TB-control strategies should initiate or facilitate implementation by other medical providers of programs for targeted testing and treatment of persons with LTBI on the basis of local epidemiologic data that identify populations at high risk. A public health approach to this activity is presented in this statement (see Essential Components of TB Control in the United States).

Liaison with communities at high risk is critical to the success of TB control in any jurisdiction. TB-control programs should develop strong lines of communication with local community groups and organizations and their health-care providers to understand local priorities and beliefs about TB. Trusted community members can facilitate the design and implementation of strategies to improve TB diagnosis and prevention. Community-based clinical services that use local providers who are educated in TB treatment and prevention and who have a connection with the TB-control program can improve community acceptance of prevention and treatment of TB (*221*).

Training and education. TB-control programs should provide education and training in the clinical and public health aspects of TB to all program staff. Staff members should receive appropriate education at regular intervals on the basis of their particular responsibilities in the program and should demonstrate proficiency in those areas when tested. Public health TB programs also should educate health-care providers (both public and private), community members, public health officials, and policy makers on the basis of local epidemiology and needs. To ensure the availability of a competent workforce for TB that understands and meets the needs of its community, state TB programs should use resources from CDC-funded national TB centers, NIH-supported TB curriculum centers, NTCA, and other national and local agencies to create and implement education activities in coordination with schools of medicine, nursing, pharmacy, dentistry, and public health; community-based organizations and their constituents; local health-care providers; and health-care institutions (*222*). A Strategic Plan for Public Health Work Force Development (*223*) and a Strategic Plan for Tuberculosis Training and Education have been developed.

Information management. Information-management systems are key factors in medical safety and quality improvement (*224,225*) and should be prioritized by all TB-control programs. Information technology can improve care of patients with TB through standardized collection of data; tracking of test results and details of treatment, including administration of DOT; and prediction of

interactions among medications. Information technology can also facilitate analysis and rapid distribution of epidemiologic data and the management of individualized treatment plans (*5*) and support ongoing program performance analyses. Barriers to successful implementation of information technology include costs and resistance to change.

Monitoring and evaluation. The systematic monitoring and analysis of program activities is a critical factor in enhancing program performance. Evaluation techniques provide TB programs with an evidence-based approach to assess and improve their TB-control strategies by understanding what causes good or bad program performance. Evaluation can also be used for program advocacy, assessing staffing needs, training and capacity building, directing limited resources to the most productive activities, accounting for available resources, generating additional resources, and recognizing achievement (*226*).

Each public health agency should develop its own priorities for program evaluation on the basis of the nature and dimensions of the TB problem in its jurisdiction and the way that services are organized. In general, the first priority for evaluation efforts should be to focus on those activities and outcomes that relate most directly to the key strategies of TB control: detecting patients with infectious TB and administering a complete course of treatment; finding contacts and other persons at high risk with LTBI and treating them; and interrupting transmission of *M. tuberculosis* in high-risk settings (Box 4).

Targets for program performance have been established by CDC (*227*) to assist public health agencies in treating TB patients, protecting their contacts, and improving the quality of case reporting for national surveillance (Table 4). These national objectives for program performance provide a starting point for state and local TB-control programs to use for program evaluation, but each TB-control program should establish methods to evaluate its performance.

TB case management has typically been evaluated by reviewing individual charts and case conferences. However, cohort analysis, a systematic evaluation of the treatment outcomes of all TB cases during a stipulated period of time, is the preferred means of determining the number and percentage of cases that complete a course of treatment in ≤12 months. Cohort analyses should be a cornerstone of evaluation by all TB-control programs. A guide to cohort analysis and other evaluation tools has been published (*228*). National objectives have been set for completing treatment for LTBI among contacts of infectious cases of TB (Table 4). Other program areas that should be monitored through formal evaluation methods include timeliness and completeness of reporting of TB cases and suspected cases, frequency of use of a recommended treatment regimen for patients with TB and LTBI, and quality of the program's databases for surveillance and case management.

TABLE 4. National performance measures and objectives for tuberculosis (TB) control

Performance measure	Objective (2005)	Performance (yr*)	
Increase the percentage of TB patients who complete a course of curative TB treatment in ≤12 months after initiation of treatment (certain patients require >12 months)	90%	80%	2000
Increase the percentage of TB patients with initial cultures who also have drug susceptibility results	95%	93%	2002
Increase the percentage of contacts of persons with infectious (acid-fast bacilli sputum smear-positive) TB who are placed on treatment for latent TB infection and complete a treatment regimen	61%	57%	2000
For TB case reports sent to CDC from states, increase the percentage in which ≥90% of core data items are complete	95%	73%	2002

SOURCE: CDC. Final FY 2005 performance plan. Atlanta, GA: US Department of Health and Human Services, CDC; 2005. Available at http://www.cdc.gov/od/perfplan/index.htm.
* Most recent year for which data to determine performance are available.

To respond to the need for improved and standardized program evaluation activities, CDC and six state TB-control programs have established an Evaluation Working Group whose goal is to improve the capacity of TB-control programs to routinely conduct self-evaluations and use the findings to improve and enhance their programs. The group is developing indicators for program performance and an inventory of evaluation tools, including data collection instruments, data analysis methods, and evaluation training materials. During the next 2 years, a draft set of these materials will be tested in three TB-control programs for utility, feasibility, and accuracy. Ultimately, this package of evaluation materials and resources will be made available to all TB-control programs.

Public Health Workforce

No single model exists for staffing public health TB-control programs. Approaches to TB control should be flexible and adaptable to local needs and circumstances. Two components of the public health workforce, public health nurses and community outreach workers, merit specific attention.

Public health nurses. Public health nurses are registered nurses with a Bachelor of Science degree who are employed or whose services are contracted for by health departments. Certain states require certification for additional competencies before being hired as a public health nurse. Public

health nurses traditionally have played a prominent role in TB control in the United States. Their training, including that in nonmedical aspects of disease, has provided nurses with the special skills needed to manage or coordinate the medical and the social-behavioral concerns associated with the prevention and treatment of TB (*229*). Their training includes 1) designing contact and source-case investigations; 2) educating patients, contacts, and families; 3) identifying ineffective drug therapy regimens and drug toxicities; 4) recognizing patient behaviors that might lead to poor adherence; and 5) developing strategies to encourage completion of therapy. As health departments adapt to changing health-care environments, the role of public health nurses working to control TB also is evolving to accommodate the varied mechanisms by which services are delivered. Standards of practice for TB nursing are being updated by the National Tuberculosis Nurse Consultant Coalition, a section of NTCA, to guide jurisdictions in creating and maintaining a specialized nursing resource for TB control and prevention.

Community outreach workers. Community outreach workers are staff members who provide services, such as DOT, to patients outside of the clinic. They may also be classified as disease investigation specialists or community health educators. Because TB has become concentrated in specific populations (e.g., foreign-born and homeless persons) in the United States, outreach workers have assumed a key role in TB control. Often members of the communities they serve, outreach workers connect the health-care system with populations at high risk, ensuring that the principles and processes of TB control are communicated to and understood by those populations. Outreach workers' functions include facilitating treatment for patients and contacts; providing DOT; educating patients, their families, workplace personnel, and communities; and participating in contact investigations. In each case, outreach workers form a bridge between patients and health-care providers to achieve common understandings and acceptance of plans for diagnoses and treatment. Clinicians with specialized expertise, including nurse-case managers, should supervise outreach workers.

Clinicians

Clinicians in medical practice in the nonpublic health sector play a vital role in TB control throughout the United States. Hospital- or clinic-based medical practitioners, including those working in emergency departments (EDs), are usually the first source of medical care for persons with TB (*230–232*); they also may provide ongoing management for TB patients (*48*). The role of medical practitioners in TB control will increase as TB morbidity in the United States decreases and jurisdictions reduce or even eliminate public health clinical services for TB.

Medical practitioners are often not sufficiently knowledgeable about TB (*233*), and clinicians in private practice frequently do not follow recommended guidelines and make errors in prescribing anti-TB therapy (*231,234,235*). The failure of public health and private practitioners to interact effectively is a weak link in global TB control (*236*). Successful models exist for acknowledging and facilitating the work of private medical practitioners in the complex process of diagnosing and treating persons with TB. For example, for each reported TB case in New Mexico, a collaborative case-management strategy is used that includes treating clinicians and pharmacists from the private sector in addition to public health case managers (*48*). Another model of effective private-public partnerships was employed in NYC during the 1985–1992 TB resurgence, with health department case management and DOT for patients under private care (*13*).

As TB elimination efforts continue, the role of medical practitioners will further expand because they provide access to populations that have been targeted for testing and treatment of LTBI. Greater participation by the nonpublic health sector in preventive intervention has been advocated (*2,51*), and clinical standards have been published to guide medical practitioners in managing patients with TB disease and LTBI (*8*).

Roles and Responsibilities of Clinicians

- Private medical practitioners should
  - — understand prevalent medical conditions, including those with public health implications, of populations within their practice;
  - — understand applicable state laws and regulations for reporting diseases and the need to report cases;
  - — understand the range of responsibilities, statutory and otherwise, that arise when TB is suspected in a patient under medical evaluation, including 1) the need for prompt establishment of diagnosis; 2) use of consultants and hospitalization if indicated; 3) reporting the suspected case to the jurisdictional public health agency and cooperating with subsequent public health activities; and 4) developing, in partnership with the public health agency, a treatment plan that optimizes the likelihood that the patient will complete the recommended course of therapy;
  - — incorporate current recommendations for diagnosis (*3*), standard treatment of TB (*5*), and targeted testing and treatment of LTBI (*4*); and
  - — be able to place and read tuberculin skin tests, rule out suspected TB disease (by clinical examination,

history, and chest radiograph), and treat and monitor treatment for LTBI.

- Providers of medical care for children and adolescents should also
  - — use a questionnaire to screen all new patients for risk factors for LTBI and give those with risk factors a tuberculin skin test to be interpreted by a trained health-care provider (*237*), and
  - — place and interpret tuberculin skin tests of family members of children with LTBI when this service is not otherwise accessible.
- Clinicians who administer treatment that can suppress the immune system should administer a questionnaire about risk factors for TB. If risk factors are present, a tuberculin skin test should be administered and the result obtained before or commensurate with starting immunosuppressive therapy.

Civil Surgeons

Civil surgeons are licensed physicians who are certified by the U.S. Citizenship and Immigration Service (CIS) to conduct a required health screening examination, including testing for LTBI and active TB disease, on foreign-born persons living in the United States who apply for permanent residency. In 2002, approximately 679,000 foreign-born persons applied for permanent residency and were screened by civil surgeons, compared with 245,000 such persons in 1995 (*238*). CDC has responsibility for providing guidance on screening and treatment but has no regulatory role in monitoring the quality or outcomes of these examinations.

Because of their access to foreign-born persons at high risk, civil surgeons are a critical component of TB control. U.S.-based immigration screening can identify foreign-born persons with LTBI for whom treatment is indicated (*239*). Although civil surgeons receive immigration-focused training, little information is available on the knowledge, attitudes, and practices of civil surgeons. A recent survey indicated that among 491 physicians serving as civil surgeons in California, Massachusetts, and New York, the majority were graduates of U.S. medical schools; 75% were primary care practitioners; and 47% were board certified in their specialty. Among 5,739 foreign-born applicants examined by these civil surgeons, 1,449 (25%) received nonstandard screening (*240*). As a result of these findings, efforts are under way to develop guidance documents and training materials for physicians who screen immigrants for TB infection and disease.

Roles and Responsibilities of Civil Surgeons

- Civil surgeons should
  - — understand current guidelines for the diagnosis (*3*) and treatment of TB (*5*) and LTBI (*4*),
  - — establish a working relationship with the jurisdictional health agency and report suspected and confirmed cases of TB, and
  - — develop a referral mechanism for evaluation for TB disease and LTBI of persons seeking adjustment of immigration status.

Community Health Centers

Community health centers typically provide primary health-care services to populations that encounter barriers to receiving those services at other sites in the health-care system, such as low-income working persons and their families, immigrants and refugees, uninsured persons, homeless persons, the frail elderly, and poor women and children. Patients at high risk for TB often receive primary and emergency health care in community health centers (*51*). For example, community health centers in certain inner-city areas might serve primarily a clientele of homeless persons, whereas centers in neighborhoods in which certain racial and ethnic populations are concentrated might become predominant health-care providers for immigrants and refugees. Newly arriving refugee families are frequently directed to community health centers to receive federally supported health-screening services, which might include targeted testing and treatment for LTBI. Persons with symptoms of TB might go first for evaluation and care to a community health center. For these reasons, community health centers are a critical part of efforts to control and prevent TB.

Roles and Responsibilities of Community Health Centers

- Community health centers should
  - — provide their medical staff with the skills and knowledge needed to conduct a TB risk assessment of their clients, diagnose and initiate treatment for TB disease, and diagnose and treat LTBI (*241*);
  - — develop close working relationships with consultant physicians, hospitals, and clinical laboratories and with the public health agency that serves their jurisdiction;
  - — arrange for reporting patients with suspected TB, ensuring availability of diagnostic services (e.g., sputum smears for AFB, cultures for *M. tuberculosis*, and chest radiographs), and providing consultation and referral of patients for diagnosis, treatment, and hospitalization, as indicated);

— understand federal and state programs that support screening, diagnostic, and treatment services for patients at high risk and make prevention, diagnosis, and treatment of TB a high priority;
— work with public health agencies to educate patients about the personal and public health implications of TB and LTBI and motivate them to accept prevention services; and
— establish recommended infection-control practices (*10*) to protect patients and staff.

Hospitals

Hospitals provide multiple services that are instrumental to the diagnosis, treatment, and control of TB. Hospitals with active outpatient and EDs often serve as sites of acute and primary medical care for homeless persons, inner-city residents, immigrants and refugees, and other persons at high risk for TB. Also, hospital staff members often provide medical consultation services for the diagnosis and management of TB by public health and community clinicians. Laboratory services provided by hospitals for community-based medical care providers might include key diagnostic tests for TB.

TB cases often are detected during hospitalization at acute-care hospitals (*230,242*). In a prospective cohort study at 10 sites in the United States, 678 (45%) of 1,493 patients reported with TB received their diagnosis during hospitalization (*230*). Hospital-based health professionals evaluate patients for TB, establish the diagnosis, and initiate treatment regimens and reporting of cases to public health departments. Instances of delayed recognition, diagnosis, and treatment for TB among hospitalized patients subsequently found to have TB have been reported (*24,178*), indicating a need for more effective training and education of hospital medical staff members.

Because 25%–45% of patients with TB receive their diagnostic evaluation while in a hospital (*230,242*), hospitals have an opportunity to provide patient-based teaching on TB for their own staff members and for health professionals from the community served by the hospital. Venues such as staff conferences and medical grand rounds, conducted regularly by hospitals, can be sources of training and education on clinical, laboratory, and public health concerns that arise during evaluation and initial medical management of hospitalized patients with TB.

Hospitals should protect their patients, staff, and visitors from exposure to *M. tuberculosis*. The importance of effective TB infection control was emphasized during the 1985–1992 TB resurgence in the United States, when hospitals were identified as sites of transmission of multidrug-resistant TB (*243*). Implementation of effective infection-control guidelines has been effective in reducing transmission of TB in hospitals (*56,244,245*).

Roles and Responsibilities of Hospitals

- Hospitals that deliver inpatient care for TB should develop policies that ensure that patients suspected to have contagious forms of the disease are isolated and that effective infection-control measures are implemented. Such hospitals should provide recommended TB-related diagnostic testing and should ensure that patients receive a standard treatment regimen (*245*).
- Hospitals should promptly report any patient with a suspected or confirmed diagnosis of TB to the jurisdictional public health agency. A written policy for discharging patients with TB, developed in collaboration with the public health agency, should be prepared. Certain states have regulations stipulating that the jurisdictional public health agency should approve discharge from hospital of patients with TB. Patients with TB should be discharged on a standard anti-TB regimen, and advance arrangements should be made to ensure follow-up after discharge. Close coordination between the hospital and the jurisdictional public health agency can enhance patient follow-up after discharge (*5,56*).
- Hospitals should develop a written policy and plan for prevention of the nosocomial transmission of TB. Recommendations have been published to guide the development of an infection-control plan (*10*) and are reviewed in this statement. New guidelines for prevention of transmission of *M. tuberculosis* in health-care settings will be published by CDC in 2005.
- Hospitals should take responsibility for the training and ongoing medical education of their medical and house staff in the prevailing diseases of the populations to which they provide care. When appropriate, education should include the local epidemiologic profile of TB, the best current diagnostic tests and recommended treatment regimens, appropriate infection-control measures, and case management responsibilities (i.e., reporting, protection of contacts, importance of treatment until cure, and the concept of public health case management).

Academic Institutions

Academic institutions (including schools of medicine, public health, and nursing) have an opportunity to contribute to TB control in the United States and worldwide. Students from diverse disciplines, including the clinical and laboratory sciences, nursing, epidemiology, and health services should be introduced to applicable concepts of

public health in general and, because TB is a major cause of preventable illness and death in developing countries (*44*), to TB in particular. During the resurgence of TB in the United States during 1985–1992, expertise in TB was limited. Federal funding for programs (e.g., the NIH National Heart Lung Blood Institute's Tuberculosis Academic Award program) helped provide funding to incorporate teaching of TB more fully into medical school curricula. Researchers at academic institutions are critical to efforts to improve the prevention, management, and control of TB because of their efforts to develop new tools, including new diagnostic tests, new drugs, better means of identifying and treating LTBI, and basic research to create a vaccine for TB (*180,246,247*).

As with hospitals, academic institutions can provide benefits to other participants in TB control. Conferences, grand rounds, and other presentations are a source of continuing education for private medical practitioners and other community-based HCWs. As well-trained specialists, researchers at academic institutions can provide clinical, radiographic, and epidemiologic consultation to medical practitioners and public health agencies. A majority of academic institutions manage university-based hospitals, which often serve populations at high risk. University hospitals can become models for TB risk assessment of patients, inpatient care, and infection-control practice, and they can serve as tertiary care sites for an entire community or region.

Partnerships between academic institutions and public health agencies are mutually beneficial (*248*). In certain cases, health departments and public health TB clinics are staffed or managed by faculty physicians from academic institutions. This partnership facilitates use of these clinics for graduate medical training for physicians in subspecialty areas (e.g., pulmonary and infectious diseases), enhances training for clinic staff, and provides opportunities for clinical and operational research.

Roles and Responsibilities of Academic Institutions

- Academic institutions (including schools of medicine, public health, and nursing) should incorporate TB education into their curricula. Training and teaching programs should include the routine applications of TB risk assessment. Students and trainees in all medical disciplines should understand and appreciate the importance and roles of the primary and specialty medical care providers and public health, including the necessary collaboration between academic institutions and local, state, and federal public health agencies.
- Academic institutions should serve as repositories of expertise in the treatment and management of TB and as a resource for public health and community-based clinicians and other HCWs.
- Academic institutions should partner with public health agencies to improve TB control. Partnerships are mutually beneficial. For academic institutions, partnerships provide additional sites for education and training, opportunities for clinical research, and, for patients with TB, a systematic transition from hospital to outpatient care, including DOT. Public health agencies gain exposure to students and trainees, a ready source of referral for consultation and management of complex medical problems, and research opportunities.
- Academic institutions should provide leadership in conducting research in diagnostics, drugs, and vaccines for TB.

Medical Professional Organizations

Because they are involved with medical practice, research, education, advocacy, and public health, medical professional organizations are critical partners in TB control efforts. Greater participation of the nonpublic health medical sector is needed to maintain clinical expertise in the diagnosis and management of TB in an era of declining incidence. Organizations whose memberships include primary care medical practitioners can make significant contributions to the control, prevention, and elimination of TB by including TB in their training and education agendas.

ATS and IDSA both support TB control efforts in the United States. With a membership of approximately 14,000 health professionals, including clinicians trained in pulmonary diseases, ATS conducts research, education, patient care, and advocacy to prevent respiratory diseases worldwide. IDSA promotes and recognizes excellence in patient care, education, research, public health, and the prevention of infectious diseases. In recent years, IDSA has joined ATS in focusing education and advocacy activities on TB through its annual meetings, publications, and sponsorship of this series of statements.

Other medical professional organizations also can support TB control efforts. Medical professional organizations can 1) provide TB education to their members through meetings, symposia, statements, and web sites; 2) serve as venues for better communication between the private medical and public health sectors; 3) promote the TB research agenda locally and nationally; and 4) advocate for resources for strong TB control globally and in the United States.

Roles and Responsibilities of Medical Professional Organizations

- Medical professional organizations should train and educate their members and other health professionals (e.g., private medical practitioners, nurses, epidemiologists, laboratory specialists, or program administrators) regarding the clinical and public health aspects of the risk assessment, diagnosis, treatment, control, and prevention of TB. Training and education can be provided in traditional venues, such as scientific meetings and symposiums, and electronically through web sites. As continuing medical and nursing education is now a prerequisite to licensure, medical professional organizations are a convenient education resource for the private medical community.
- Medical professional organizations should provide professional leadership on clinical practice and control of TB by participating in the development or endorsement of guidelines, influencing professional school curricula, and establishing and supporting fellowship training programs as applicable.
- Medical professional organizations should provide advocacy for adequate funding for TB control and research through public education campaigns.
- Medical professional organizations should advocate the importance of greater U.S. involvement in global control of TB by linking U.S. health professionals with those from other parts of the world at meetings and symposia, including information on global TB in statements and education materials, providing their members with opportunities to serve as technical consultants, and participating in special projects to support or improve TB control in other regions of the world.

Community-Based Organizations

Involvement of community groups in TB control has long been encouraged (*17*). The critical importance of such involvement is underscored by the trend in the United States for TB to be limited to certain populations at high risk (e.g., contacts of persons with active cases, persons born outside the United States, homeless persons, incarcerated persons, and persons with HIV infection). Programs for education and targeted testing and treatment of LTBI should be organized for these populations.

The public health sector frequently experiences difficulty in gaining access to persons in populations of high risk (*51*). Such persons might be socially marginalized, as in the case of new refugees, or they might be suspicious of persons representing government agencies, as in the case of undocumented aliens. Furthermore, the target population's own view of its health-care priorities, often best articulated by community-based organizations that represent them, should be considered in the design of public health interventions (*249*). Social, political, religious, and health-related organizations that have arisen from grassroots efforts to meet community needs often can facilitate access to public health programs (*221*).

Community-based organizations can be particularly effective in providing information and education on TB to their constituencies. As part of the communities they serve, such organizations are often highly regarded in their communities, and their messages might be accepted more positively than those delivered by the jurisdictional health department.

Roles and Responsibilities of Community-Based Organizations

- Community-based organizations should be aware of their constituents' health risks. Organizations providing services to populations at risk for TB should partner with the jurisdictional public health TB program and medical care providers from the community to facilitate access to diagnostic, treatment, and prevention services for the target population. As resources allow, organizations should provide assistance for treatment services to their constituency (e.g., DOT, incentives and enablers, and other outreach services).
- When serving a population at risk for TB, community-based organizations should become involved in advocacy initiatives, such as state and local TB advisory committees and coalitions.
- Community organizations serving populations at high risk should work with public health agencies and educational institutions to develop education materials that are tailored culturally and linguistically to their populations.

Correctional Facilities

Correctional facilities are common sites of TB transmission and propagation (*250,251*). Incidence of TB and of LTBI are substantially higher in prisons and jails than in the general population (*252,253*). TB is believed to be the leading cause of death for prisoners worldwide (*254*).

Targeted testing for and treatment of LTBI in correctional facilities have been demonstrated to have a substantial public health impact (*124*). Testing and treatment for LTBI is carried out more easily in prisons (*255*) because the length of stay is generally sufficient to permit completion of a course of treatment. Jails have proved convenient sites for targeted

testing, but subsequent treatment of LTBI has proved challenging (*256*). Innovative methods for assuring completion of treatment for LTBI in jail detainees have been proposed (*257*).

Because of their communal living arrangements, correctional facilities, like health-care facilities, have the responsibility to limit the transmission of TB within the institution and to protect their inhabitants and staff from exposure. This is a particular challenge in jails because of the short lengths of stay for the majority of detainees. Even in prison systems, abrupt and unexpected transfers of detainees among institutions might occur, with little consideration for health issues. Prisons and jails frequently house HIV-infected persons in separate facilities to ensure adequate health care. However, recent publications describing outbreaks of TB in such settings have emphasized the hazard of this strategy (*35,126*).

Roles and Responsibilities of Correctional Facilities

- Correctional facilities should work with the jurisdictional public health agency to develop and maintain an accurate epidemiologic profile of the risk for TB in the inmate population.
- On the basis of the local epidemiology of TB, correctional facilities should develop written policies to establish effective programs to screen for active TB, respond promptly when cases occur within the facility, provide targeted testing and treatment programs for inhabitants and detainees with LTBI, and provide ongoing, competency-based education of all staff members.
- Correctional facilities should establish ongoing working relations with public health agencies, hospitals, and other community partners for policy development, consultation and referral.
- Correctional facilities should develop firm linkages for referral of persons under treatment for TB disease and LTBI.
- Correctional facilities, following requirements of the Occupational Safety and Health Administration and other regulatory agencies, should develop infection-control programs to protect inhabitants, detainees, staff, and visitors from exposure to TB (*258*). Correctional facilities should continually evaluate the effectiveness of the institutional TB-control program to eliminate transmission within the facility.

Pharmaceutical and Biotechnology Industries

Because of their essential role in developing new diagnostics, drugs, and vaccines, the pharmaceutical and biotechnology industries are partners in TB control. Although development of new tools for diagnosis, treatment, and prevention of TB has been deemed essential to the effort to combat the disease globally and to continue to make progress toward its elimination in the United States and other developed countries (*1,2,45,259*), progress in these fields has been slow. Slow progress in this field has been attributed to private industry's perception that such products are not needed in developed countries and do not offer profit opportunities in resource-poor countries (*246,260*). However, new public-private partnerships are emerging to facilitate the development of essential new tools (*261*), including three partnerships established with support from the Bill and Melinda Gates Foundation: the Global Alliance for Tuberculosis Drug Development (http://www.tballiance.org), the Aeras Global Tuberculosis Vaccine Foundation (http://www.aeras.org), and the Foundation for Innovative New Diagnostics (http://www.finddiagnostics.org). These organizations have provided venues to identify and address obstacles to developing new tools for TB among private industry, public and academic researchers, and philanthropic organizations. These organizations also receive support from the private sector.

The pharmaceutical industry has also contributed to the global TB control effort by assisting in making drugs for TB, including second-line drugs for patients with multidrug-resistant TB, more affordable (*262,263*). Such actions can enable pharmaceutical companies to become leaders in efforts to improve TB control and prevention.

Roles and Responsibilities of the Pharmaceutical and Biotechnology Industries

- The pharmaceutical and biotechnology industries should
  - — understand the dimensions of the global TB epidemic and realize their key role in developing the necessary tools for diagnosis, treatment, and prevention of TB;
  - — respond to the current surge of interest in TB globally by reexamining the costs of new product development and by considering potential new public and private funding and the markets for such products in developing countries;
  - — contribute their perspectives and become involved in coalitions such as NCET, the Global Partnership to Stop Tuberculosis, the Global Alliance for Tuberculosis Drug Development, and the Foundation for Innovative New Diagnostics; and
  - — work with other stakeholders to ensure access of essential products to those whose lives are at stake.

Essential Components of TB Control in the United States

Case Detection and Management

Case detection and case management include the range of activities that begin when a diagnosis of TB is first suspected and end with the completion of a course of treatment for the illness. TB case management describes the activities undertaken by the jurisdictional public health agency and its partners to ensure successful completion of TB treatment and cure of the patient. The rationale and methodology of TB case management have been described previously (*5*). Organizational aspects of case management from the viewpoint of the jurisdictional public health agency are also discussed in this statement.

Case detection includes the processes that lead to the presentation, evaluation, receipt of diagnosis, and reporting of persons with active TB. Case detection involves patients with active TB who seek medical care for symptoms associated with TB, their access to health care, their health-care providers, the consultants and clinical laboratories used by those health-care providers, and the responsible public health agency. Although steadily increasing treatment completion rates (*14*) indicate that progress has been made in the management of TB patients, TB case detection is still problematic. Delays in diagnosis and report of TB cases continue to be common. Also, despite the 44% reduction in TB incidence in the United States since 1992, the proportion of pulmonary cases that are sputum smear-positive at diagnosis has changed little, accounting for >60% of all reported cases (*14*). The majority of pulmonary TB cases continue to be diagnosed at an advanced stage. Earlier diagnosis would result in less individual morbidity and death, greater success in treatment, less transmission to contacts, and fewer outbreaks of TB. Improvement in the detection of TB cases is essential to progress toward elimination of TB in the United States (Box 1).

The first step in improving TB case detection is to remove barriers in access to medical services that are often encountered by persons in high-risk categories. Such barriers might be patient-related, such as cultural stigmas associated with the diagnosis of TB, which might lead foreign-born persons to deny or hide symptoms (*264,265*), or fear of being reported to immigration authorities if medical care is accessed (*19*). Foreign-born persons, particularly recently arrived immigrants, refugees, and other persons of low SES might not have access to primary health services because they do not have health insurance or they are not familiar with the U.S. medical care system (*20,118,266*).

Removing patient-related barriers to health care is particularly difficult. Improved patient education about TB is needed (*18*). Continuing immigration from countries at high risk, often including persons with strong cultural views about TB, underscores the need for patient education. As with other interventions to enhance TB control and prevention, local public health action should be based on the local pattern of disease. In developing education messages and outreach strategies, public health authorities should work with organizations that serve communities at high risk to gain community input (*203*). This statement provides recommendations on working with community-based organizations, key informants, and academic institutions to gain ethnographic information, learn about the health beliefs and values of populations at high risk within the community, and develop targeted interventions that will be most effective.

The majority of TB cases are detected during the medical evaluation of symptomatic illnesses (*19,267*). Persons experiencing symptoms ultimately attributable to TB usually seek care not at a public health TB clinic but rather from other medical practitioners and health-care settings. In 18 California counties with the highest TB morbidity of persons during 1996–1997, initial points of entry into the health-care system for persons who received a diagnosis of TB were hospital inpatient evaluations (45%), private outpatient offices or clinic evaluations (32%), TB clinic evaluations (12%), and other sites (11%), including a non-TB clinic in a health department and correctional facilities (California Tuberculosis Controllers Association, unpublished data, 2003). A similar pattern was observed in Washington state. In Seattle and its suburban areas in 1997, primary care practitioners or clinics reported 48% of TB cases during evaluations of outpatients with symptoms and 32% during hospital evaluations; only 2% of cases were diagnosed during a public health TB clinic evaluation for a symptomatic illness (Seattle-King County Department of Public Health, unpublished data, 1998).

These data indicate that the professionals in the primary health-care sector, including hospital and ED clinicians, should be trained to recognize patients with symptoms consistent with TB. Dramatic reductions in TB were recorded in NYC (*13*) and Baltimore (*195*) in association with extensive education campaigns for health-care providers in the community. These studies indicate the need to maintain clinical expertise for the diagnosis and treatment of TB (*24,41*).

Because pulmonary disease among adults is most frequently associated with the spread of TB, the following discussion and recommendations regarding TB case detection are limited to considerations of pulmonary TB among

adults. A classic set of historic features, signs, symptoms, and radiographic findings occurring among adults should raise a suspicion of pulmonary TB and prompt a diagnostic investigation (*3,189,267–271*). Historic features include exposure to TB, a positive test result for *M. tuberculosis* infection, and the presence of risk factors such as immigration from a high-prevalence area, HIV infection, homelessness, or previous incarceration. Signs and symptoms typical of TB include prolonged coughing with production of sputum that might be bloody, fever, night sweats, and weight loss. On a chest radiograph, the classical findings of TB in immunocompetent patients are upper-lobe infiltrates, frequently with evidence of contraction fibrosis and cavitation (*270*). However, these features are not specific for TB, and, for every person in whom pulmonary TB is diagnosed, an estimated 10–100 persons are suspected on the basis of clinical criteria and must be evaluated (*272,273*).

The clinical presentation of TB varies considerably as a result of the extent of disease and the host response. In addition, variation in clinical symptoms and signs of TB is associated with underlying illnesses (e.g., HIV infection, chronic renal failure, alcoholism, drug abuse, and diabetes mellitus). The signs of TB are also associated with race and ethnicity and are attributed to unknown factors (*3,267,270*). The chest radiograph among persons with advanced HIV infection and pulmonary TB, for example, might have lower-lobe and lobar infiltrates, hilar adenopathy, or interstitial infiltrates (*274*). TB should be suspected in any patient who has persistent cough for ≥2–3 weeks or other compatible signs and symptoms as noted previously (*10,267,275*).

In the drive toward TB elimination in the United States, effective TB case detection is essential, and medical practitioners should recognize patients in their practice who are at increased risk for TB and be aware of the possibility of diagnosing TB if they observe compatible symptoms. Guidelines have been provided for the initial steps of TB case detection in five clinical scenarios encountered by providers of primary health care, including those serving in medical EDs (Table 5). In these settings, evidence exists to support proceeding with a diagnostic evaluation for pulmonary TB. The subsequent management of suspected cases in these scenarios depends on the judgment of the medical practitioner, in consultation with specialists in internal medicine, pulmonary diseases, or infectious diseases if necessary (*5*). These recommendations do not cover the spectrum of clinical presentations of pulmonary TB in adults and are not meant to substitute for sound clinical judgment.

Cases of pulmonary TB also are detected through directed public health activities designed to detect TB disease among certain persons who have not sought medical care. Compared with persons whose cases were detected passively by medical practitioners among patients who have sought medical care, persons whose cases are detected actively are usually in a less advanced stage of pulmonary disease, as manifested by the absence of symptoms and by negative sputum AFB smear results. Although no supporting literature exists, cases detected in that stage of disease might be less advanced and easier to cure.

TABLE 5. Guidelines for the evaluation of pulmonary tuberculosis (TB) in adults in five clinical scenarios

Patient and setting	Recommended evaluation	Evidence rating
Any patient with a cough of ≥2–3 weeks' duration, with at least one additional symptom, including fever, night sweats, weight loss, or hemoptysis	Chest radiograph: if suggestive of TB*, collect three sputum specimens for acid-fast bacilli (AFB) smear microscopy and culture	AII
Any patient at high risk for TB† with an unexplained illness, including respiratory symptoms, of ≥2–3 weeks' duration	Chest radiograph: if suggestive of TB, collect three sputum specimens for AFB smear microscopy and culture	AIII
Any patient with HIV infection and unexplained cough and fever	Chest radiograph, and collect three sputum specimens for AFB smear microscopy and culture	AII
Any patient at high risk for TB with a diagnosis of community-acquired pneumonia who has not improved after 7 days of treatment	Chest radiograph, and collect three sputum specimens for AFB smear microscopy and culture	AIII
Any patient at high risk for TB with incidental findings on chest radiograph suggestive of TB even if symptoms are minimal or absent§	Review of previous chest radiographs if available, three sputum specimens for AFB smear microscopy and culture	AII

* Infiltrates with or without cavitation in the upper lobes or the superior segments of the lower lobes. **SOURCE:** Daley CL, Gotway MB, Jasmer RM. Radiographic manifestations of tuberculosis: a primer for clinicians. San Francisco, CA: Francis J. Curry National Tuberculosis Center; 2003:1–30.

† Patients with one of the following characteristics: recent exposure to a person with a case of infectious TB; history of a positive test result for *Mycobacterium tuberculosis* infection; HIV infection; injection or noninjection drug use; foreign birth and immigration in ≤5 years from a region in which incidence is high; residents and employees of high-risk congregate settings; membership in a medically underserved, low-income population; or a medical risk factor for TB (including diabetes mellitus, conditions requiring prolonged corticosteroid and other immunosuppressive therapy, chronic renal failure, certain hematological malignancies and carcinomas, weight >10% below ideal body weight, silicosis, gastrectomy, or jejunoileal bypass).

§ Chest radiograph performed for any reason, including targeted testing for latent TB infection and screening for TB disease.

Active efforts to detect cases of TB among persons who have not sought medical care are routinely made during evaluation of contacts of patients with pulmonary TB (*30,31,276*) and of other persons with newly diagnosed infection with *M. tuberculosis* (*4*). Screening for TB also is performed during evaluation of immigrants and refugees with Class B1 or Class B2 TB notification status (*277–279*), during evaluations of persons involved in TB outbreaks (*34,35,136,172,280,281*), and occasionally in working with populations with a known high incidence of TB (*167,185*). Screening for TB disease is indicated when the risk for TB in the population is high and when the consequences of an undiagnosed case of TB are severe (*282*), such as in jails and prisons (*253,283*).

Screening for TB disease (i.e., active case finding) might contribute substantially to overall TB case detection. A population-based study from Los Angeles indicated that 30% of reported TB cases during the period of study were detected through screening activities (*267*). During 1998–2001, of 356 TB cases reported by the Seattle-King County TB Program, 40 (11%) were detected through active case detection in contact investigation and evaluations of immigrants and refugees with Class B1 and B2 TB notification status.

The clinical settings in which TB has been effectively detected among persons without symptoms, the methodology of testing, and outcomes of the screening process have been described (Table 6). On the basis of its very high yield of detecting TB cases, domestic follow-up evaluation of immigrants and refugees with Class B1 and B2 TB notification status should be given highest priority by all TB-control programs. The yield of detecting TB cases during screening at homeless shelters increased sharply in an outbreak setting (Table 6). Although prevalence data from individual studies are not available, investigations undertaken to control TB outbreaks that involved diverse settings and groups of immunocompetent and immunocompromised persons have consistently been productive in detecting TB cases and high rates of LTBI among exposed persons (*34,35,136,173,280,281*). Outbreak investigations should be counted among the settings in which screening for active TB is recommended.

Contact Investigation and Outbreak Control

Contact investigation is an essential function of TB control in the United States (Box 4) (*1,17*). The investigation

TABLE 6. Settings, methodologies, and outcomes for detecting tuberculosis (TB) in persons without symptoms

Setting	Methodology*	Cases detected/ Persons screened (%)
Correctional facility intake screening	3	0.07, 0.17†
Shelter-based screening of homeless men (routine setting)	1,2	0.18, 0.36§
Inner-city residents seeking social services	1,2	0.52¶
Contact investigations	1,2	1.0–3.0**
Shelter-based screening of homeless men (outbreak setting)	1,2,4	3.1, 4.3††
U.S.-based screening of immigrants and refugees with Class B1 and B2-TB notification status¶¶	1,2,3	3.0–14.0§§

* 1 = patients were screened with questionnaire for symptoms of TB; if present, a chest radiograph was obtained; if radiograph was suggestive of TB, sputum specimens were obtained for acid-fast bacilli (AFB) microscopy and culture; 2 = patients were screened with tuberculin skin test; if positive, chest radiograph was obtained; if radiograph was suggestive of TB, sputum specimens were obtained for AFB microscopy and culture; 3 = patients were screened with chest radiography; if radiograph was suggestive of TB, sputum specimens were obtained for AFB microscopy culture; and 4 = patients were screened by obtaining sputum specimens for AFB microscopy and culture.

† **SOURCES:** Puisis M, Feinglass J, Lidow E, Mansour M. Radiographic screening for tuberculosis in a large urban county jail. Public Health Rep 1996;111:330–4; Jones TF, Schaffner W. Miniature chest radiograph screening for tuberculosis in jails: a cost-effectiveness analysis. Am J Respir Crit Care Med 2001;164:77–81.

§ **SOURCES:** Moss AR, Hahn JA, Tulsky JP, Daley CL, Small PM, Hopewell PC. Tuberculosis in the homeless. A prospective study. Am J Respir Crit Care Med 2000;162(2 Pt 1):460–4; Kong PM, Tapy J, Calixto P, et al. Skin-test screening and tuberculosis transmission among the homeless. Emerg Infect Dis 2002;8:1280–4.

¶ **SOURCES:** Schluger NW, Huberman R, Holzman R, Rom WN, Cohen DI. Screening for infection and disease as a tuberculosis control measure among indigents in New York City, 1994–1997. Int J Tuberc Lung Dis 1999;3:281–6.

** **SOURCES:** Reichler MR, Reves R, Bur S, et al. Evaluation of investigations conducted to detect and prevent transmission of tuberculosis. JAMA 2002;287:991–5; Marks SM, Taylor Z, Qualls NL, Shrestha-Kuwahara RJ, Wilce MA, Nguyen CH. Outcomes of contact investigations of infectious tuberculosis patients. Am J Respir Crit Care Med 2000;162:2033–8; Dasgupta K, Schwartzman K, Marchand R, Tennenbaum TN, Brassard P, Menzies D. Comparison of cost-effectiveness of tuberculosis screening of close contacts and foreign-born populations. Am J Respir Crit Care Med 2000;162:2079–86.

†† **SOURCES:** Nolan CM, Elarth AM, Barr H, Saeed AM, Risser DR. An outbreak of tuberculosis in a shelter for homeless men. A description of its evolution and control. Am Rev Respir Dis 1991;143:257–61; Kimerling ME, Shakes CF, Carlisle R, Lok KH, Benjamin WH, Dunlap NE. Spot sputum screening: evaluation of an intervention in two homeless shelters. Int J Tuberc Lung Dis 1999;3:613–9.

§§ **SOURCES:** Sciortino S, Mohle-Boetani J, Royce SE, Will D, Chin DP. B notifications and the detection of tuberculosis among foreign-born recent arrivals in California. Int J Tuberc Lung Dis 1999;3:778–85; CDC. Recommendations for prevention and control of tuberculosis among foreign-born persons: report of the Working Group on Tuberculosis Among Foreign-Born Persons. MMWR 1998;47(No. RR-16):1–29; Zuber PL, Knowles LS, Binkin NJ, Tipple MA, Davidson PT. Tuberculosis among foreign-born persons in Los Angeles County, 1992–1994. Tubercle Lung Disease 1996;77:524–30.

¶¶ Persons with TB disease are classified as having suspected active noninfectious (Class B1) or inactive (Class B2) TB notification status.

of a case of TB results in identifying approximately 10 contacts (*284*). Among close contacts, approximately 30% have LTBI, and 1%–3% have progressed to TB disease (*30,284*). Without intervention, approximately 5% of contacts with newly acquired LTBI progress to TB disease within 2 years of the exposure (*285*). The prevalence of TB among close contacts is approximately 1,000/100,000 population (>100-fold higher than in the general population) (*285*). Examination of contacts is therefore one of the most important activities for identifying persons with disease and those with LTBI who have a high risk for acquiring TB disease.

Transmission of *M. tuberculosis* has occurred in healthcare facilities (*286,287*), bars (*134,288*), doctors' offices (*289*), airplanes (*290*), crack houses (*291*), respite facilities that provide care for HIV-infected persons (*136*), drug rehabilitation methadone centers (*36*), navy ships (*292*), homeless shelters (*120*), schools (*173*), church choirs (*140*), and renal transplant units (*141*). The utility and importance of contact investigations in those settings and also for populations at high risk (e.g., foreign-born persons [*293*], children [*294–297*], and persons exposed to multidrug-resistant TB cases [*91,298*]) has also been documented.

In the United States, state and local public health agencies perform 90% of contact investigations as part of the public health mandate for TB control (Box 5) (*2*). Public health TB-control programs are responsible for ensuring that contact investigations are conducted effectively and that all exposed contacts are identified, provided with access to adequate care, and followed to completion of therapy. For health agencies to fully discharge this responsibility, adequate funding and political commitment are required.

Health agencies use a general epidemiologic framework for contact investigations (*299*). However, this approach alone might have limited effectiveness because of factors such as initial diagnostic delays and failure to ensure completion of therapy for LTBI. Consequently, programs have recognized the necessity of widening traditional contact investigation sites to include nonhousehold locations (e.g., homeless shelters, correctional facilities, nursing homes, and hospices that serve HIV-infected persons) and households. Genotyping studies have documented that traditional contact investigation methods have failed to identify contacts or detect transmission of *M. tuberculosis* (*28,33,34,151,172*). As a result, IOM (*2*) and ACET (*1*) have called for the development and implementation of enhanced techniques for contact investigation.

The primary goal of a contact investigation is to identify persons who were exposed to infectious *M. tuberculosis* and ensure that they are tested for *M. tuberculosis* infection, screened for TB disease, are followed up, and complete a standard course of treatment, if indicated. Secondary goals are to stop transmission of *M. tuberculosis* by identifying undetected patients with infectious TB and to determine whether a TB outbreak has occurred. In that case, an expanded outbreak investigation should ensue.

Steps of a Contact Investigation

State and local public health agencies, often represented by TB-control programs, are responsible for initiating and conducting contact investigations and evaluating their outcomes to ensure their effectiveness. A contact investigation has 14 steps, as follows:

1. **Setting priorities.** A contact investigation is considered once a suspected or confirmed case of TB comes to the attention of the jurisdictional TB-control program. At that time, a decision should be made about the priority of that investigation among other TB-control activities. Not all cases of TB require a contact investigation, and certain investigations will have greater priority than others. Priorities should be decided on the basis of the characteristics of the source-case, of the environment of the place(s) of exposure, and of the contacts. The three most important categories of information used to establish priorities for cases for contact investigations are 1) the site of disease, 2) the results of sputum AFB smears and NAA testing, and 3) the findings on the chest radiograph. In general, patients with pulmonary TB, positive sputum AFB smear results, and cavitation noted on a chest radiograph are more infectious and therefore have a higher priority for contact investigation. The use of an NAA test is helpful in rapidly differentiating between pulmonary disease caused by *M. tuberculosis* and nontuberculous mycobacteria, thus avoiding unnecessary contact investigations. Persons with pulmonary TB who have negative sputum AFB smear results tend to be less infectious, and their contacts should be investigated, but with lower priority.

   Contacts of patients with extrapulmonary TB should be evaluated if the patient has concurrent pulmonary or laryngeal disease, the contacts are at increased risk for acquiring TB disease (e.g., children aged <5 years and HIV-infected persons), or the patient has pleural TB (*300*). Pleural TB is a manifestation of primary TB and often occurs among persons who have been recently infected. In addition, persons with pleural TB can have positive sputum AFB smear results. Children aged <5 years with TB, regardless of the site of disease, should have a contact investigation to identify the source-case.

2. **Defining the beginning and end of the period of infectiousness.** Before a contact investigation can be started, the period of infectiousness of the index case should be determined. This period sets the limits for the investigation, allows for setting priorities for contacts within the designated timeframe, and determines the scheduling for follow-up tests. Exactly when a patient becomes infectious is unknown; the usual assumption is that the patient becomes infectious approximately 3 months before diagnosis; however, it might be longer, depending on the history of signs and symptoms, particularly cough and the extent of disease. The end of the period is defined as the time when contact with the index case is broken or when all of the criteria for determining when during therapy a patient with pulmonary TB has become noninfectious (Box 3) are met. Patients with multidrug-resistant TB who are on inadequate therapy or who have persistently positive sputum AFB smear or culture results might remain infectious for a prolonged period of time. Those patients, if not in effective isolation, should be reassessed for new contacts as long as they remain infectious.
3. **Medical record review.** For potential transmission risk and infectiousness of a case to be assessed, all currently available information about the reported case or suspect is obtained through case medical record reviews, conversations with the health-care provider or other reporting source, and laboratory report reviews. This information can be disclosed by covered entities for public health activities as provided by the Privacy Rule of HIPAA (*217*).
4. **Case interview and reinterview.** The patient interview may be conducted in the hospital, at the patient's home, or wherever convenient and conducive to establishing trust and rapport. The ability to conduct an effective interview might determine the success or failure of the contact investigation. All persons with whom the patient has been in close contact and the locations that the patient commonly frequents should be identified. Good interviewing skills can elicit vital information that otherwise might not be forthcoming. For different reasons (e.g., stigmatization, embarrassment, or involvement in illegal activities), patients might be reluctant to identify contacts or places they frequent. Developing an ability to interview patients effectively so as to elicit contacts requires training and periodic review by supervisors, and only trained personnel should interview patients. A patient should be interviewed as soon as possible after notification and reinterviewed 1–2 weeks later to clarify data or obtain missing data. When possible, the second interview should be conducted at the patient's primary residence. Also, all interviews should be conducted in the patient's primary language and with sensitivity to the patient's culture.
5. **Field investigation.** Field investigations enable investigators to 1) interview or reinterview identified contacts and obtain an adequate medical history to evaluate previous exposure to TB, existence of prior *M. tuberculosis* infection, existence of disease and treatment, risk factors for acquiring TB, and symptoms; 2) obtain locator information; 3) apply a tuberculin skin test to identified contacts (the role of QFT-G in the assessment of contacts has not been determined); 4) observe contacts for any signs or symptoms suggestive of TB; 5) schedule subsequent medical evaluations and collect sputum samples from any contact who is symptomatic; 6) identify sources of health care and make referrals; 7) identify additional contacts who might also need follow-up; 8) educate contacts about the purpose of the investigation and the basics of TB pathogenesis and transmission; 9) observe the contact's environment for possible transmission factors (e.g., crowding and poor ventilation); 10) assess contacts' psychosocial needs and other factors that might influence compliance with medical recommendations; and 11) reinforce confidentiality. Visits to the exposure site(s) should be conducted as soon as possible. Contacts at higher risk for disease progression and more severe disease (e.g., young children and HIV-infected persons) require the most rapid follow-up.

   Transmission sites might involve social networks not customarily considered in traditional contact investigations. For example, in certain TB cases reported separately in different communities, participation in a church choir was identified as a common factor (*140*). The contact investigation failed to identify the source-patient's choir contacts, resulting in secondary cases of TB. In an outbreak associated with a floating card game, the outbreak was propagated because a network of persons engaged in illegal activities was not identified (*172*). These examples demonstrate the importance of congregate activities beyond work and socially defined high-risk contacts.
6. **Clinical evaluation of contacts.** All close contacts of patients with pulmonary or laryngeal TB and a positive culture result for *M. tuberculosis* or a positive sputum AFB smear result should receive a tuberculin skin test unless they have documentation of a previously

positive test. Highest priority for tuberculin skin testing and follow-up evaluation should be given to 1) contacts identified as being at highest risk for recent infection on the basis of their history of exposure to the case-patient and risk for transmission and 2) those at high risk for progression from *M. tuberculosis* infection to TB disease (e.g., infants, young children, HIV-infected persons, and other persons whose medical conditions predispose them to progress from infection to disease). Among children and infants, children aged <3 years are at greatest risk for rapid progression and should receive the highest priority for all preventive interventions for contacts. For the greatest level of protection of children exposed to TB to be ensured, all children aged <5 years should be considered to be high-risk contacts.

Regardless of where the tuberculin skin test is performed (e.g., field visit, TB clinic, or referral site), arrangements should be made to ensure that the skin test is read within 48–72 hours. Contacts who have tuberculin skin test reactions ≥5 mm and who have no history of a prior positive result are considered at risk for newly acquired *M. tuberculosis* infection. Those persons should receive a chest radiograph and medical evaluation for TB disease. Adults and children aged ≥5 years should receive a single posterior-anterior radiograph (*4*); children aged <5 years should receive both posterior-anterior and lateral TB radiographs (*4*). The following contacts should have a chest radiograph regardless of skin test result: 1) persons with symptoms of TB; 2) persons who are immunosuppressed or who have other risk factors for progression from *M. tuberculosis* infection to TB disease; and 3) children aged <5 years.

The presence of HIV coinfection might affect decisions about subsequent management of contacts (e.g., prescribing prophylactic treatment and completing treatment for LTBI regardless of results of a tuberculin skin test). An HIV-infected contact also should be effectively counseled about the substantial risk for disease progression and the need to accept and adhere to a course of treatment for LTBI. Although contacts of HIV-infected persons with TB have substantial risk for HIV infection themselves, contacts of TB cases without HIV infection have low rates of HIV infection (*301*), suggesting that offering HIV testing to all contacts might not be cost-effective. The decision should be based on local data demonstrating that contacts of TB cases are at high risk for HIV infection (i.e., the contacts have a prevalence of HIV infection of ≥1% [*302*]). The local epidemiology of TB, HIV infection, and TB/HIV coinfection also may be used as a basis for the decision. If resources are limited, and if local data indicate that HIV infection contributes only minimally to the TB problem (i.e., the HIV seroprevalence of contacts is likely to approach 0.1% of the general U.S. population), then the highest priority for voluntary HIV counseling and testing should be assigned to contacts of HIV-infected persons with TB and those who have identified risk factors for HIV (*303*).

Contacts who have a documented prior positive tuberculin skin test and who are not known or likely to be immunocompromised generally do not require further evaluation unless they have symptoms suggestive of TB disease. However, candidates for treatment of LTBI on the basis of other criteria (*4*) should first receive a medical evaluation, including a chest radiograph, to exclude TB. Contacts with a negative tuberculin skin test should be retested approximately 8–12 weeks after the first test unless the initial skin test was performed >8 weeks after the contact's last exposure to the index patient. Every 3 months, all contacts with negative skin test results who remain in close contact with an infectious patient should receive a repeat tuberculin skin test and, if symptoms of TB disease are present, a chest radiograph. A contact whose repeated test is positive (≥5mm) should receive a chest radiograph if one has not been taken recently. If the radiograph is normal, the contact should be evaluated for treatment of LTBI; if it is abnormal, the patient should be evaluated for TB disease or other cause of the abnormality.

TB-control programs should find and evaluate all persons who have had sufficient contact with an infectious TB patient to become infected. Contacts at high risk (e.g., infants, young children, and HIV-infected persons) should be identified and evaluated rapidly to prevent the onset of serious, potentially life-threatening complications (e.g., TB meningitis). In certain jurisdictions, legal measures have been put in place to ensure that contact evaluation and follow-up occurs (*304*). The use of existing communicable disease laws should be considered for contacts that fail to comply with the examination requirements. All contacts should be assessed routinely for obstacles to their participation in the evaluation process. Any structural barrier that impedes the ability of the patient to access services (e.g., inconvenient clinic hours or location, work or family obligations, and lack of transportation) should be addressed.

7. **Treatment of contacts with LTBI.** Contacts with LTBI should be treated unless compelling contraindications exist. For completion of therapy to be ensured, contacts should be placed on DOT whenever possible. If resources do not allow that all infected contacts receive DOT, priority should be assigned to 1) children aged <5 years; 2) contacts with HIV infection; 3) other contacts with risk factors for progression to TB disease (*4*); 4) contacts with documented skin test conversion; and 5) contacts of patients with positive sputum AFB smear results and cavities on chest radiography. Contacts on self-administered therapy should be monitored monthly by personal interview for adverse effects and adherence until treatment is completed.
8. **Primary prophylaxis of high-risk contacts.** Because tuberculin skin test results might take 8–10 weeks to become positive after infection with *M. tuberculosis*, a contact's initial skin test result might be negative even if the person is infected. A second test should be placed 8–12 weeks after the contact's last exposure to the infectious patient, so the possibility of LTBI for those persons can be better evaluated. During the 8–12 week window period between a first and second skin test, the following contacts with initially negative tuberculin skin test results should receive treatment for LTBI after TB disease has been ruled out by clinical examination and chest radiograph: 1) contacts aged <5 years (with highest priority given to those aged <3 years) and 2) contacts with HIV infection or who are otherwise immunocompromised (*4*). If the second skin test result is negative (<5 mm), the contact is immunocompetent (including immunocompetent young children) and no longer exposed to infectious TB, treatment for LTBI may be discontinued, and further follow-up is unnecessary. If the second skin test is negative but the contact is immunocompromised (e.g., with HIV infection), a course of therapy for LTBI should be completed. If the second skin test result is negative but the person remains in close contact with an infectious patient, treatment for LTBI should be continued if the contact is 1) aged <5 years; 2) aged 5–15 years, at the clinician's discretion; or 3) HIV-seropositive or otherwise immunocompromised.
9. **Expanding the contact investigation.** Defining the extent of the contact investigation is the responsibility of the investigating TB-control program. Once testing of high-priority contacts is completed, the extent of transmission of *M. tuberculosis* should be evaluated. Consideration can then be given to expanding the investigation to include contacts at lower risk for infection. In general, the contact investigation need be expanded only if excessive transmission is detected, on the basis of the following criteria: 1) secondary cases of TB are identified in contacts; 2) documented skin test conversions exist; and 3) comparison of skin test positivity among contacts with available data on the baseline prevalence of skin test positivity in the population indicates the probability of transmission. When a contact investigation is expanded, resources should continue to be directed to persons identified as being at greatest risk. In any case, the total contact-tracing process should be completed ≤3 months after initiation of the investigation, unless evidence of transmission requires further expansion of testing.
10. **Data management and use in decision-making.** Maintenance of data is crucial to all aspects of the contact investigation. Protocols should be developed to maximize the efficiency of the process, given available resources. Data should be collected for cases and contacts by using standardized forms (paper or electronic) with standard definitions and formats, according to national guidelines (*305*). Data elements should mirror those collected by the states and CDC, but individual jurisdictions may elect to expand the data elements.
11. **Evaluation.** Contact investigation steps should be adequately documented, so the process can be monitored and evaluated. National performance measures for TB control stipulate that programs should complete treatment of LTBI among 61% of contacts of infectious TB cases (Table 4). Additional parameters should also be tracked and evaluated. Programs should determine whether the indications given previously for conducting a contact investigation are applied to all reported cases. In addition, for each TB case that is investigated, the number of contacts identified should be recorded. For each contact identified, outcomes to monitor include 1) whether the contact evaluation took place (including placing and reading the first and second tuberculin skin tests, if applicable) and was completed and 2) whether the recommended protective interventions (including screening for TB disease, treatment for LTBI, and prophylaxis within the window period) were offered, accepted, started, and completed. Results of the evaluation should be aggregated and recorded for stipulated intervals of time, as follows: 1) among identified contacts, the number and percentage that were referred for evaluation; 2) among those referred, the number and

percentage that completed evaluation; 3) among those evaluated, the number and percentage eligible for treatment of LTBI; and 4) among those eligible, the number and percentage that started and completed treatment.

Surveillance of individual contacts is not conducted routinely in the United States. However, CDC collects aggregate data on the outcomes of contact investigations from state and local TB control programs through the Aggregate Report for Program Evaluation. Routine collection and review of these data can provide the basis for evaluation of contact investigations for TB control programs.

12. **Education and training for contact investigations.** The education needs for all aspects of the investigation process (including medical abstraction, patient interviewing, cultural competency, maintaining patient confidentiality, and how to perform tuberculin skin testing) should be continuously assessed. All involved staff should receive ongoing training. CDC-funded regional training centers offer training courses in contact investigation and interviewing skills.
13. **Confidentiality.** Maintaining confidentiality is a critical component of the contact investigation process. Guidelines for release of confidential information related to conducting contact investigations should be developed. An example of appropriate release of confidential medical information is the release of an index case patient's drug susceptibility test results to a clinician caring for a contact with LTBI or one who has progressed to active TB.
14. **Contact investigations among special populations.** Contact investigations often are conducted among special populations or locations (e.g., homeless shelters, correctional facilities, HIV residential facilities, schools, worksites, health-care facilities, active drug users, and living along the U.S.–Mexico border). Guidelines offering specific recommendations for contact investigations under these circumstances have been published (*305*).

Outbreak Investigations

Failure to recognize an increase in the occurrence of TB (*162*) or to expand a contact investigation when needed can result in continued transmission of TB. Missed epidemiologic links among patients with TB can have severe consequences as evidenced in an outbreak associated with a floating card game in the rural south (*172*) and an outbreak in Kansas among exotic dancers and their close contacts that occurred during a 7-year period (*38*).

When TB occurs with high incidence, clusters of cases that have epidemiologic links likely occur constantly but tend to blend into the generally high morbidity (*306*). In a low-incidence setting, however, clusters of linked TB cases can be identified more readily. Three criteria have been established to determine that a TB outbreak is occurring (*162*): 1) an increase has occurred above the expected number of TB cases; 2) transmission is continuing despite adequate control efforts by the TB-control program; and 3) contact investigations associated with the increased cases require additional outside help.

TB outbreaks have occurred in low-incidence areas in which expertise and experience in dealing with such outbreaks might be lacking. Such outbreaks have occurred among different populations and settings, including a young foreign-born child in North Dakota (*25*); exotic dancers and their contacts in Kansas (*38*), homeless persons in Syracuse, New York (*120*); factory workers in Maine (*188*); and limited, seemingly unrelated clusters of cases that were the cause over time of perpetuating transmission in Alabama (*307*).

For an increase in the expected number of TB cases (the first criterion of an outbreak) to be identified, the local epidemiology of TB should be understood. Detection of a TB outbreak in an area in which prevalence is low might depend on a combination of factors, including recognition of sentinel events, routine genotype cluster analysis of surveillance data, and analysis of *M. tuberculosis* drug-resistance and genotyping patterns.

When an outbreak is identified, short-term investigation activities should follow the same principles as those for the epidemiologic part of the contact investigation (i.e., defining the infectious period, settings, risk groups, mode of transmission, contact identification, and follow-up). However, long-term activities require continued active surveillance, *M. tuberculosis* genotyping, additional contact investigations and related follow-up for additional cases, and continuing education of providers, staff, and patients. Consequently, a plan for long-term support should exist from the outset of the investigation.

A written protocol should be developed. At a minimum, the protocol should outline the outbreak response plan, including indications for initiating the plan, notification procedures, composition of the response team, sources of staffing, plan for follow-up and treatment of contacts, indications for requesting CDC assistance, and a process for evaluation of the outbreak response. The outbreak response plan should also include information on how to work strategically with the media during the public health emergency. CDC offers training packages to assist public HCWs in media communications, including emergency and crisis communication.

This training emphasizes prevent planning, event response activities, and post-event follow-up. Information on public health communication programs is available at http://www.cdc.gov/communication/cdcynergy.htm.

Targeted Testing and Treatment of LTBI

An estimated 9.5–14.7 million persons in the United States have LTBI (*39*). Continued progress toward eliminating TB in the United States and reducing TB among foreign-born persons will be impossible without devising effective strategies to meet this challenge. Guidelines on targeted testing and treatment of LTBI have been published (*4*) and revised (*308*). Those guidelines include recommendations for diagnosing LTBI and treating infected persons, limiting the possibility of treatment-associated hepatotoxicity, and identifying persons and populations to target for testing. A new diagnostic test for LTBI, QFT-G, has been approved by FDA, and guidelines for its use will be published by CDC. This section outlines a recommended approach to planning and implementing programs for targeted testing and treatment of LTBI to create an effective public health tool for communitywide prevention of TB.

Targeted testing and treatment of persons with LTBI is not a new concept for the prevention of TB in the United States (*309*). The effectiveness of treating LTBI among populations at high risk has been established in clinical trials (*285*), but this intervention has not been proven to have an impact on the incidence of TB in the United States. Theoretically, the epidemiologic impact would be considerable if cases of TB in a population were largely the result of progression of LTBI and if all persons at high risk with latent infection could be identified and treated successfully. Practically, those circumstances rarely exist. In the United States, the effectiveness of targeted testing and treatment of LTBI as a public health measure has been limited by concern for the side effects of treatment (notably hepatotoxocity) (*310*), poor acceptance of the intervention among health professionals (*311*), and poor adherence among patients to the lengthy course of treatment (*45,312*).

Two approaches exist to increasing targeted testing and treatment of LTBI. One is to promote clinic-based testing of persons who are under a clinician's care for a medical condition (e.g., HIV infection or diabetes mellitus) that also confers a risk for acquiring TB. This approach, which depends on a person's risk profile for TB and not on the local epidemiology of the disease, requires education of health-care providers and depends ultimately on their initiative. Although difficulties exist in quantifying and evaluating its effectiveness, this approach could conceivably become a useful tool to reduce the incidence of TB among foreign-born and other persons at high risk because they can be accessed conveniently where they receive primary health-care services. The other approach is to establish specific programs that target a subpopulation of persons who have a high prevalence of LTBI or who are at high risk for acquiring TB disease if they have LTBI, or both. This approach presumes that the jurisdictional TB-control agency has identified the pockets of high TB risk within its jurisdiction through epidemiologic analysis and profiling (*313–316*). Those high-risk pockets might consist of foreign-born, homeless, or HIV-infected persons, or they might be geographic regions (e.g., a neighborhood within a city or town) or specific sites (e.g., a homeless shelter or an HIV-housing facility).

The epidemiologic profile should include an assessment of the risk for TB in the population or at the site, the ease of access to the population or site, and the likelihood of acceptance of and adherence to targeted testing and treatment. For this assessment to be facilitated, populations at high risk may be separated into three tiers (Box 6). Assignment of groups to these three tiers is based on six criteria: 1) incidence of TB; 2) prevalence of LTBI; 3) risk for acquiring TB disease if the person is infected with *M. tuberculosis*; 4) likelihood of accepting treatment for LTBI

BOX 6. Priority population subpopulations and sites for targeted testing and treatment of latent tuberculosis (TB) infection

Tier 1
- Persons working in or served by clinics or community health organizations providing care to HIV-infected persons
- Prisoners
- Legal immigrants and refugees with Class B1 and B2 TB notification status
- Recently-arrived refugees
- Other well-defined groups in congregate living facilities
- Persons enrolled in substance abuse treatment programs*

Tier 2
- Jail detainees
- Persons working or living in homeless shelters
- Immigrants reporting for adjustment of status

Tier 3
- Other foreign-born persons at high risk (i.e., those that immigrated ≤5 years from countries with a high incidence of TB)

* Persons enrolled in substance abuse treatment programs should be considered a transition group between Tier 1 and Tier 2, depending on the local epidemiology of tuberculosis.

and adhering to it; 5) ease of access to the population; and 6) in a congregate setting, the consequence of transmission of *M. tuberculosis*.

Tier 1 is made up of well-defined populations at high risk that can also be conveniently accessed and followed, either in locations such as clinics or community health centers, prisons, or other congregate living sites or through mandatory registration. Persons in this tier often have a high prevalence of TB and LTBI (immigrants and refugees with Class B TB notification status), an increased risk for TB disease if infected with *M. tuberculosis* (persons with HIV infection), or both (certain homeless and detained populations). The consequences of the spread of TB in congregate settings increase the necessity of preventive action. Location-based, high-risk communities in Tier 1 are, for the most part, readily identifiable and easily accessible; often have their own resources; and generally include the probability of access for a long enough period to permit completion of treatment for LTBI. These populations should be the first priority for targeted testing programs.

Persons enrolled in substance-abuse treatment centers may be considered transitional between Tier 1 and Tier 2, depending on local epidemiologic and demographic factors. Substance abusers might have a high prevalence of LTBI. Injection drug users also might have an increased risk for acquiring TB if they are infected with *M. tuberculosis* and at increased risk for HIV infection (*317*). Access and factors related to acceptance and completion of therapy also might vary by location. Typically, substance abuse treatment centers that include long-term inpatient treatment or regularly scheduled appointments (e.g., methadone treatment centers) are the best choices for intervention because ease of ongoing access allows sufficient time for completion of therapy. Voluntary HIV counseling and testing should be offered routinely as part of any targeted testing program among this population.

Populations in Tier 2 also include identifiable and accessible populations made up of persons at high risk, but the distinguishing characteristic is that obtaining satisfactory rates of completion of treatment for LTBI might be difficult because of dispersal of the population throughout a larger community or a brief duration of residency in congregate settings. For example, in Atlanta, Georgia, after local epidemiology of TB was analyzed, community sites for targeted testing and treatment of LTBI of residents of high-risk inner-city areas were identified (*184*). Sites of access included outpatient areas of the public hospital, the city jail, clinics serving homeless persons, and neighborhoods frequented by substance abusers. Although 65% of the targeted population that had a tuberculin skin test placed returned to have the skin test read, only 20% of those with an indication for treatment of LTBI completed a course of therapy; this represented 1% of persons who underwent targeted testing.

Tier 3 consists of persons born in countries with a high incidence of TB or U.S.-born persons in racial/ethnic minority populations with high prevalence of LTBI who do not necessarily have an increased risk for progressing to TB disease. Eventually, the control of TB among foreign-born persons and progress toward elimination of TB in the United States depends on achieving greater success in preventing TB among populations at high risk by widespread targeted testing and treatment of LTBI in the public and private medical sectors. However, establishing successful targeted testing and treatment programs for foreign-born persons who are not found in Tier 1 or Tier 2 settings is challenging. Obstacles include the limitations of the tuberculin skin test to differentiate between reactions attributable to BCG or infection with *M. tuberculosis*, the prevalent belief among a substantial number of foreign-born persons that BCG vaccination is the cause of a positive test for *M. tuberculosis* infection and is also protective against TB disease, language and cultural barriers, barriers in access to medical care, and difficulties in providing outreach and education.

Typical Tier 3 populations are new refugee and immigrant groups that are not yet assimilated into U.S. society. Such populations might be ignorant of their TB risk, usually lack ready access to health-care services, and might have strong cultural understandings about TB that are at variance with those that guide TB-control activities in the United States. TB-prevention activities in this kind of community are highly cost-intensive (*221*). Engaging such communities is a challenging task.

Community-based TB prevention for Tier 3 populations requires a partnership between the jurisdictional health department and the affected community. The community should gain an understanding of the TB problem as it relates to them and should participate in the design of the intervention. Community education is essential for this approach to succeed. The target population should be involved in the design and implementation phases of the intervention, interventions should be developed within the cultural context of the targeted population, and intermediate goals or benchmarks should show the population that program activities are achieving success. For example, in Los Angeles, California, the public health TB program contracted with community-based organizations to screen and provide treatment for LTBI to persons at risk in Latino and Asian neighborhoods and at schools teaching English as a second language (*249*). In Cambridge, Massachusetts, a coalition of

Haitian community groups identified TB education as an issue for their community; strategies to achieve this goal included development of a videotape written and produced for viewing in Haitian barbershops and beauty salons in the community, a lottery, and measures for evaluation in terms of knowledge and future access to care (S. Etkind, Massachusetts Department of Health, personal communication, 2002).

For communities in Tier 3, TB is only one (and often not the most important) of multiple medical and public health needs. A broad approach should be adopted that includes TB prevention with other activities to improve health status. Certain Tier 3 populations have achieved sufficient self-identity and development to establish access to health care through a community health center, individual medical providers, or clinics. Those communities that have an already established route of access to health care have an infrastructure in place to establish programs for targeted testing and treatment of LTBI. Obstacles to overcome often include lack of medications and chest radiographs, the need for a system to track patients who do not return for monthly appointments, and the capacity to evaluate the program.

Programs for population-based targeted testing and treatment for LTBI often have been conducted by public health agencies through TB-control programs. However, recent studies have also described the establishment of such programs in nonpublic health venues. Promising results, in terms of access to persons at high risk and completion of treatment of LTBI, have been achieved from nontraditional sites, including syringe exchanges (*318*), jails (*256*), neighborhood health clinics (*319*), homeless shelters (*320*), and schools (*321,322*). This trend indicates a widening interest in this means of preventing TB and is possibly influenced by the emergence of community-oriented primary care (*241,323*), which places primacy on interventions for specific patients that help prevent disease and preserve the health of the entire population from which these patients are drawn.

As programs move from Tier 1 to Tier 2 and Tier 3 populations, the complexity of the effort and the cost of the program will increase. Also, because persons in Tier 3 populations generally have a lower risk for progression from LTBI to TB disease, the effectiveness and impact of a program will be less than efforts directed to Tier 1 and Tier 2 populations. Whatever population is selected or strategy is employed for the targeted testing project, programs should systematically evaluate the activity to ensure the efficient use of resources. Process, outcome, and impact indicators should be selected and routinely monitored by the program.

For purposes of monitoring and evaluation, activities associated with targeted testing and treatment for *M. tuberculosis* infection can be divided into three phases: the testing itself, the medical evaluation of persons with positive test results, and the treatment of those persons with LTBI. Performance indicators should be selected for each phase. For the testing phase, indicators include the number of persons at high risk identified and the number and proportion of those that were actually tested. Among those tested, the number and proportion that had a positive result for *M. tuberculosis* infection should be tracked. Useful indicators for the medical evaluation phase include the proportion of persons with a positive test result who completed a medical evaluation and the number and proportion that were determined to have TB disease. Indicators for the treatment phase include the proportion of eligible persons starting treatment for LTBI and the number and proportion that completed treatment. Reasons for failure to complete treatment (e.g., adverse drug effects, loss of interest, and loss to follow-up) should be monitored. Costs should be measured for each phase of the project. The cost per person with LTBI completing treatment provides a measure of the relative efficiency of the program. Finally, the impact of the program can be estimated by estimating the number of cases of TB prevented, which is dependent on the number of persons completing treatment and the estimated risk for progressing to TB disease.

Surveillance of persons with LTBI does not routinely occur in the United States. However, CDC has recently developed a national surveillance system to record serious adverse events (i.e., hospitalization or death) associated with treatment of LTBI. Surveillance of these events will provide data to evaluate the safety of treatment regimens recommended in current guidelines (*4,324*).

Control of TB Among Populations at Risk

This section contains recommendations for measures to control and prevent TB in five populations (children, foreign-born persons, HIV-infected persons, homeless persons, and detainees and prisoners in correctional facilities). Each of these populations occupies an important niche in the epidemiology of TB in the United States. Individual members of each population have been demonstrated, on the basis of their membership in the population, to be at higher risk for exposure to *M. tuberculosis* or for progression from exposure to disease, or both. Furthermore, nationwide surveillance and surveys (*27,118–120,127,136,139,150,198,295,315,325,326*)

indicate that the epidemiology of TB in these populations is similar from community to community, which suggests that the recommended control measures are subject to generalization and can be applied more or less uniformly throughout the United States.

Children, foreign-born persons, HIV-infected persons, homeless persons, and detainees and prisoners should not be assumed to be the only populations at high risk for TB, nor are homeless shelters and detention facilities the only settings in need of enhanced TB-control strategies. Local surveillance and surveys frequently have identified populations and settings of high TB risk and transmission that required the formulation of specific control measures (*122,137,152,313,315,316,327,328*). This is the primary reason why state and local surveillance should be conducted to develop a clear understanding of the epidemiology of TB at the jurisdictional level.

Most important, the concept of identifying and targeting populations and settings at high risk should be viewed as a dynamic rather than as a static process. Such populations emerge and recede in importance at the local, state, and national levels. For example, foreign-born persons received little attention in the 1992 edition of this statement (*6*). A population whose risk for TB is now being recognized and delineated is U.S.-born non-Hispanic blacks, who account for approximately 25% of TB morbidity in the United States and who have TB rates approximately eight times those of whites (*329,330*) (Table 2). CDC and collaborating public health agencies in Chicago, Illinois and the states of Georgia and South Carolina are exploring new strategies to address this problem (*331*).

Control of TB Among Children and Adolescents

The occurrence of TB among infants and young children indicates recent transmission of *M. tuberculosis* and often the presence in the community of an unidentified adult with infectious TB. Thus, a case of TB in a child is a sentinel health event that signals a public health breakdown (*197*). Also, certain features of TB among children mandate special considerations in case detection and case management, contact investigations, and targeted testing and treatment of LTBI. For example, if LTBI results from exposure to TB in infancy and early childhood, a substantial risk exists for rapid progression to TB disease, including the development of potentially lethal forms of TB (*198,294,325*). The recommendations in this statement for control of TB among children and adolescents should receive high priority in all state and community TB-control plans.

Basis for Recommendations for TB Control Among Children and Adolescents

Case detection and primary prevention strategy: contact investigation of adults with pulmonary TB. The majority of infants and children who acquire TB disease do so within 3–12 months of contracting *M. tuberculosis* infection. Infants and toddlers aged <3 years are especially prone to the rapid progression from infection to disease, and they often acquire severe forms of TB, including meningitis and disseminated disease. The most important step to detect and prevent TB among children is the timely identification and effective treatment of adults with active TB. The cornerstone of TB prevention among children is high-quality contact investigations of suspected cases of pulmonary TB in adults, because 20%–40% of pediatric cases of TB could have been prevented if contact investigation had been more timely and thorough (*198,293,325*).

Contact investigation of adult pulmonary TB cases is crucial to the detection, control, and prevention of pediatric TB and its complications (*332,333*). The yield of detection of TB and LTBI is high, with an average of 50% of childhood household contacts having LTBI or TB disease (*31,60*). Because ≤50% of cases of TB among children are asymptomatic despite abnormal radiographic findings, contact investigation leads to earlier discovery of TB among children, better treatment outcomes, and fewer complications (*326*). Also, children with LTBI or TB disease identified through contact investigation are more likely to receive DOT at the same time as the source-case, which increases adherence to therapy.

Another benefit of contact investigations is the ability to identify and treat infants and young children who have been exposed to a person with a contagious case of TB and who might be infected but nevertheless have a negative tuberculin skin test (the role of QFT-G for diagnosis of LTBI in children aged <17 years has not been determined). A tuberculin skin test might take 2–3 months after infection to become positive in an infant or toddler. However, the incubation period for severe TB, including meningitis and disseminated disease, might be only 4–6 weeks. Failure to give empiric treatment for LTBI to exposed infants and young children with negative tuberculin skin test results, particularly those aged <3 years, might therefore result in rapid acquisition of disease (*295,325*).

Case management. The record for adherence to treatment for TB is no better for children than it is for adults (*333*). Children with TB might live in socially disorganized or disadvantaged homes and receive care from multiple adults. A chaotic environment can lead to a poor understanding of TB and its treatment and decreased adherence. DOT is effective in TB treatment for children

and adolescents. However, almost 10% of children receiving DOT experience gaps in treatment that require extensions of therapy (*326*). Intensive-case management, including use of incentives and enablers, is a crucial element of a TB-treatment plan for children.

Contact investigation of cases of TB among children and adolescents. Contact investigations for children with suspected TB are generally conducted to identify the adult source-case. Identifying a source-case serves to establish the diagnosis of TB in the majority of children and, if the source-case is culture-positive for *M. tuberculosis*, to determine the likely drug susceptibility pattern of the infecting strain of *M. tuberculosis* in the child.

Even with optimal medical evaluation, *M. tuberculosis* can be isolated from <50% of children with clinically suspected TB. While microbiologic testing determines the diagnosis of TB for the majority of adults, positive culture results often are lacking for children. In the majority of cases, the diagnosis of pediatric TB is established by the triad of 1) a positive tuberculin skin test result, 2) either an abnormal chest radiograph or physical examination or both, and 3) discovery of a link to a known or suspected case of contagious pulmonary TB. Because culture yields from children with TB are low, determining the drug susceptibility pattern from the source-case isolate often is the only way to determine optimal treatment for children with either LTBI or TB disease (*334,335*).

Because TB among infants and young children usually occurs within weeks to months of contracting infection with *M. tuberculosis*, having a child with disease is a marker of recent transmission from someone in the child's environment. The source-case, often a parent or other caregiver (*336–338*), might not have been identified as having TB by the time the child becomes ill. Consequently, parents and other adults who are close contacts of children hospitalized with TB should be evaluated themselves for TB disease as soon as possible to serve as a case-detection tool and to prevent nosocomial transmission of *M. tuberculosis* (*339*). A chest radiograph should be performed on these family members to exclude pulmonary TB; certain centers have implemented this recommendation by requiring that adults who accompany a child have a chest radiograph performed and interpreted immediately while at the health-care facility (*339*). Other adult family members or friends also should be required to show evidence of a normal chest radiograph, performed by the health department or other provider, before being allowed to visit the child. Because TB in the child, not LTBI, is the reliable marker of recent infection, chest radiograph screening of accompanying adults is not necessary if the child has LTBI without TB disease.

Associate investigations (i.e., efforts to identify and evaluate household contacts of a child with LTBI to identify the infectious person responsible for the child's infection) are often performed as part of the evaluation of a child with LTBI (*5,17,340–343*). The usefulness of this approach depends on the criteria for placing skin tests on children. If testing of children at low risk is undertaken, associate investigations will be costly, have a low yield, and divert TB-control resources from more important activities. Associate investigations of children at high risk, however, usually detect a limited number of persons with TB but do identify substantial numbers of other persons with LTBI who are candidates for treatment (*341–343*).

Targeted testing and treatment of LTBI. In the 1950s and 1960s, child-centered TB control activities were based on periodic testing of all children for LTBI (*344*). However, as the number of TB cases dropped, the disease became concentrated among persons at high risk in particular subpopulations. Consequently, the majority of U.S. children have negligible risk for acquiring LTBI. Among children at low risk, the majority of positive tuberculin skin test results are false positives caused by nonspecific reactivity or exposure to nontuberculous mycobacteria in the environment (*344*). False-positive results lead to unnecessary health-care expenditures and anxiety for the child, family, school, and HCWs (*345*). Thus, while the testing of children with an expected high prevalence of LTBI is desirable, mass testing of children with a low prevalence of LTBI is counterproductive and should not be undertaken.

The optimal approach is to perform tuberculin skin testing only on those children with specific risk factors for LTBI. A questionnaire that assesses risk factors for TB can be used successfully in clinics and private offices to identify children at risk for LTBI (*237,346–348*); this approach can also be used to identify at-risk college students (*349*). The screening tool is the questionnaire; only those children whose answers indicate that they are at risk for LTBI should receive a tuberculin skin test. Use of a questionnaire can also address issues related to discrimination; all children in a setting such as a school or child-care center can be screened easily, but only those with identified risk factors for LTBI should receive a tuberculin skin test, thereby diminishing the number of false-positive results.

No single questionnaire has been validated for use in all settings and for all ages of children. Factors that have correlated highly with risk for LTBI among children in more than one study include 1) previous positive tuberculin skin test result; 2) birth in a foreign country with high prevalence; 3) nontourist travel to a high-prevalence country for >1 week; 4) contact with person with TB; and 5) presence in the

household of another person with LTBI. Questions pertaining to a locally identified population with a high rate of TB should be included in a questionnaire, but validation of these questions is difficult.

In certain treatment programs for LTBI among children in the United States, the completion rate associated with 6–9 months of self-supervised isoniazid therapy is only 30%–50%. As LTBI among young children might progress rapidly to TB disease, DOT is recommended. Children with LTBI, who are most likely to benefit from DOT because of their high risk for rapid progression of infection to disease, include contacts of persons with recently diagnosed cases of pulmonary TB, infants and young children, and children with immunologic deficiencies, especially HIV infection.

Control of TB Among Foreign-Born Persons

TB among foreign-born persons is of increasing importance. During 1992–2003, the number of TB cases decreased 64% among U.S.-born persons but increased 8% among persons born outside the United States (*14,15*). During 1992–2003, the percentage of TB cases in the United States that occurred among foreign-born persons increased from 27% in 1992 to 53.3% in 2003 (*15*), and the number of states in which >50% of reported cases of TB occurred among foreign-born persons increased from four (8%) in 1992 to 25 (50%) in 2003 (*15*). In 2003, eight states (California, Florida, Illinois, Massachusetts, New Jersey, New York, Texas, and Virginia) accounted for 71% of cases among foreign-born persons. Foreign-born persons with TB have been more likely than U.S.-born persons to harbor drug-resistant strains of *M. tuberculosis*; in 2003, 10.6% of foreign-born persons with TB had TB with primary isoniazid resistance, compared with 4.6% of U.S.-born persons with TB (*14*).

The increase in cases of TB among foreign-born persons has been attributed to at least three factors (*350*). First, the number of persons entering the United States from other countries in which TB occurs with high incidence (*44*) now accounts for >75% of the immigrant flow (*116,278*); during 1994–2003, an estimated 80%–86% of immigrants admitted to the United States came from high-incidence countries (*351*). Second, foreign-born persons are subject to cultural and linguistic barriers that might affect health-seeking behavior and access to medical care, resulting in delays in diagnosis and difficulty in understanding and completing treatment (*18,19,194,325*). Third, these barriers, which have implications for the treatment, control, and prevention of TB among foreign-born persons, have not been sufficiently appreciated and addressed in TB-control program planning in the United States.

Precise information is lacking to assist in the identification of foreign-born persons who have an elevated risk for acquiring TB during residence in the United States. Immigrants entering either Canada or the United States have a risk for TB during their early years of residence that approximates that of residents of the country of birth (*115,352,353*). Over time, the risk declines and approaches that of residents of the host country. Consequently, recent guidelines have designated immigrants from countries with a high prevalence of TB who have resided in the United States <5 years as foreign-born persons at high risk (*4*).

Criteria for characterizing countries as having a high prevalence of TB have not been developed, and no consensus exists on which countries should be designated as having a high prevalence of TB. In rank order, the 14 countries listed most frequently as country of origin of foreign-born persons with reported TB in the United States are Mexico, the Philippines, Vietnam, India, China, Haiti, South Korea, Somalia, Guatemala, Ecuador, Ethiopia, Peru, El Salvador, and Honduras), and these 14 countries accounted for 76% of cases among foreign-born persons during 1999–2002 (*14*). Estimated incidence rates of TB in these countries in 2002 ranged from 33/100,000 population (Mexico) to 406/100,000 population (Somalia) (*354*). However, the country of origin of foreign-born persons with TB can vary substantially among localities within a state and between states and regions across the United States.

State and local TB control programs should develop their own profiles of risk for TB among foreign-born persons as part of the jurisdiction's overall epidemiologic analysis of TB and then define which immigrant and foreign-born populations in their areas should be considered as being at high risk for TB. Data sources for TB programs to use in making this determination include 1) WHO data on the estimated incidence of TB in countries of origin (*354*); 2) local epidemiologic and surveillance data (*151,152,313–316,355*); 3) published guidelines (*4,279*), and other sources of data (*115,116*); 4) qualitative information on refugee and immigrant movement into the jurisdiction; and 5) availability of resources to establish control and prevention measures targeted toward the foreign-born population. The principles and priorities of TB control among foreign-born persons at high risk are not different from those for control of TB among U.S.-born persons (Box 4). However, for the reasons given previously, TB control among foreign-born persons at high risk might present challenges requiring targeted strategies specific to that population (*152,356*).

How Foreign-Born Persons Enter the United States

Foreign-born persons enter the United States legally through different official channels (Table 7). As a condition of entry, persons migrating as immigrants, refugees, and asylees are required to be screened for diseases of public health significance, including TB. Persons entering in the nonimmigrant category do not require preentry screening. Persons who enter the country without legal documentation are referred to as unauthorized aliens.

During 1992–2002, an estimated 380,000–536,000 persons entered the United States annually as immigrants, refugees, or asylees (Table 8). In 2002, among the estimated 516,000 persons in those categories, 86.6% were from countries with high incidence of TB. Immigrants, refugees, and asylees constitute only a fraction of foreign-born persons who enter the United States each year; the majority (20–35 million persons) enter in one of the nonimmigrant subcategories (Table 8). The majority of entering nonimmigrants are tourists or business travelers who spend only a short time in the United States. However, an estimated 850,000–1.9 million workers, students, and other visitors and their families might reside in the United States for multiple years (Table 8).

A nonimmigrant, refugee, or asylee residing in the United States who meets the eligibility requirements and applies for a change in visa status to that of a lawful permanent resident should undergo required health screening assessment by a civil surgeon. During 2002, of the 679,305 persons who adjusted their immigration status under this program, 536,995 (79%) were from countries with high incidence of TB (*238*). In addition, an estimated 7 million unauthorized aliens resided in the United States in January 2000, and during 1990–1999, the unauthorized alien population increased annually by approximately 350,000 persons (*357*).

TABLE 7. U.S. Citizenship and Immigration Services immigration categories, by tuberculosis (TB) screening mandate

Category	Definition	TB screening mandated as condition of entry
Immigrant	An alien* admitted to the United States as a lawful permanent resident	Yes
Refugee/Asylee	A person outside his or her country of nationality (refugee) or at a point of entry to the United States (asylee) who is unable or unwilling to return because of a well-founded fear or persecution	Yes
Nonimmigrant	An alien granted temporary entry to the United States for a specific purpose (most common visa classifications for nonimmigrants are visitors for pleasure, visitors for business, temporary workers, students, and visitors)	No
Unauthorized alien	An alien residing in the United States in an unlawful status	NA†

SOURCE: US Citizenship and Immigration Service. Glossary & acronyms. Washington, DC: US Citizenship and Immigration Service; 2004. Available at http://uscis.gov/graphics/glossary.htm.
* A persons who is not a U.S. citizen.
† Not applicable.

TABLE 8. Numbers of foreign-born persons who entered the United States, by immigration category — United States, 2002

Category	No. (in 1,000s)	
Immigrants	384	(380–536)*
Refugees/Asylees†	132	(43–132)
Nonimmigrants	27,907	(20,910–33,690)
Temporary visa: pleasure	19,967	(16,441–24,104)
Temporary visa: business	4,377	(2,788–4,593)
Temporary visa: worker	723	(216–755)
Students§	687	(400–740)
Visitors§	370	(230–388)

SOURCE: US Citizenship and Immigration Services. Statistical yearbook. Available at http://uscis.gov/graphics/shared/aboutus/statistics/ybpage.htm.
* Numbers in parentheses are the 1992–2002 range.
† Includes parolees (i.e., persons allowed to enter the U.S. for urgent humanitarian reasons).
§ Includes family members.

Current Requirements for TB Screening of Immigrants

U.S. immigration law mandates screening outside the United States for applicants designated as immigrants who are applying for permanent residence status and for applicants designated as refugees or asylees (Table 7). The purpose of mandated screening is to deny entry to persons who have either communicable diseases of public health import or physical or mental disorders associated with harmful behavior, abuse drugs or are addicted to drugs, or are likely to become wards of the state. The current list of infectious diseases of public health significance that are grounds for exclusion include infectious TB, HIV infection, leprosy, and certain sexually transmitted diseases (*358*). Worldwide, approximately 400 licensed local physicians, designated as "panel physicians," perform these medical examinations. Panel physicians are appointed by U.S. embassies and consulates that issue visas. CDC is responsible for monitoring the quality of these examinations and for providing technical guidance and consultation for TB diagnosis and treatment.

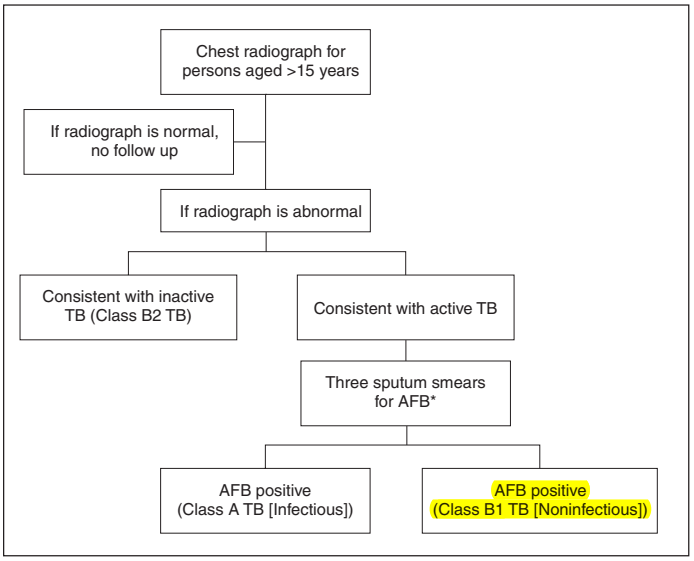
The TB screening process is a program for active TB case detection designed to deny entry to persons with infectious

Please note: An erratum has been published for this issue. To view the erratum, please click here.

pulmonary TB (identified by positive sputum AFB smear results). For persons aged ≥15 years, a brief medical history and a chest radiograph are obtained (Figure 4). If the chest radiograph is considered compatible with pulmonary TB, three sputum specimens are obtained and examined for AFB. Although procedures vary from site to site, smears are usually performed by Ziehl-Neelsen staining and examined with light microscopy. Cultures for *M. tuberculosis* are not required and are not routinely performed. Persons aged <15 years are evaluated only if they have symptoms that are consistent with TB or are a contact of person with infectious TB. A test for *M. tuberculosis* infection is performed, and a chest radiograph is obtained if the test is positive or if the child is suspected to have TB.

Persons with abnormal chest radiographs suggestive of TB and with AFB-positive sputum smear results are classified as having Class A TB, which is an excludable condition for entry into the United States (*358*). Persons so designated have two options: 1) to complete a course of treatment for TB, including documented negative sputum AFB smears at the end of treatment, at which point they are classified according to their chest radiograph results and may enter the United States; or 2) to receive TB treatment until sputum smear results for AFB convert from positive to negative and then apply for an immigration waiver. A U.S. health-care provider who agrees to assume responsibility for the completion of TB treatment after a person's arrival in the United States should sign the waiver. The waiver is countersigned by a representative of the jurisdictional public health agency of the person's intended U.S. destination. An applicant whose chest radiograph is compatible with active TB but whose sputum AFB smear results are negative is classified as having Class B1 status and may enter the United States. If the chest radiograph is compatible with inactive TB, no sputum specimens are required, and the applicant enters the country with Class B2 status (*358*).

FIGURE 4. Tuberculosis (TB) screening process for immigrants and refugees conducted outside the United States



* Acid-fast bacilli.

Immigrants with a Class A waiver or with Class B1 or B2 status are identified at ports of entry to the United States by CIS on entry to the United States and reported to CDC's Division of Global Migration and Quarantine (DGMQ). DGMQ notifies state and local health departments of refugees and immigrants with TB classifications who are moving to their jurisdiction and need follow-up evaluations. Persons with a Class A waiver are required to report to the jurisdictional public health agency for evaluation or risk deportation. For persons with Class B1 and B2 status, however, the stipulated evaluation visits to the health agency are voluntary.

Persons Seeking Adjustment of Status After Arrival

Persons seeking to adjust their immigration status after residing in the United States with nonimmigrant visa status should undergo a medical evaluation by one of the approximately 3,000 U.S. medical practitioners designated by DGMQ as civil surgeons. TB screening by civil surgeons is based on tuberculin skin testing; QFT-G is also approved for detecting LTBI. If an applicant seeking adjustment of status has a tuberculin skin test reading of ≥5 mm, a chest radiograph is required. If the radiograph is compatible with active TB, the person is referred to the jurisdictional public health agency for further evaluation (*358*). Civil surgeons are also advised that persons with a positive tuberculin test result and no signs or symptoms of TB disease should be referred to public health agencies for evaluation for treatment of LTBI, following ATS/CDC/IDSA guidelines (*4,324*).

Because data on the outcomes of TB screening of persons seeking to adjust their immigration status are not aggregated or analyzed, only limited information is available. In an evaluation of the screening practices in five U.S. Immigration and Naturalization Service jurisdictions, among 5,739 applicants eligible for screening through tuberculin skin testing, 4,290 (75%) were considered to have been screened appropriately (*240*). In Denver, Colorado, where health department physicians serve as civil surgeons, 7,573 persons were evaluated for adjustment of status during May 1987–December 1988 (*239*). Applicants were screened with tuberculin skin testing, chest radiographs, or both. Among 4,840 applicants that had a tuberculin skin test

placed, 2,039 (42%) had a reaction ≥10 mm. Sixteen persons (0.7%) were sputum culture-positive for *M. tuberculosis*. Therapy with isoniazid was recommended for 1,029 applicants, of whom 716 (70%) completed 6 months of treatment.

Immigration Status of Foreign-Born Persons with TB

Studies have sought to identify the initial immigration status of foreign-born persons with reported TB. During 1992–1993 in Hawaii, 78% of TB cases occurred among immigrants, 4% among student nonimmigrants, and 4% among nonimmigrant tourists (*350*); in 14% of cases, the immigration status could not be determined. During 1992–1994 in Seattle, Washington, 58% of TB cases among foreign-born persons who had resided in the United States for <1 year occurred among immigrants or refugees (*293*); immigration status was not determined among the remaining foreign-born persons. During 1998–2000, a total of 59% of foreign-born persons with TB in Tarrant County, Texas, were immigrants or refugees, 24% were unauthorized immigrants, and 17% were nonimmigrant students and workers (*316*).

Assessment of TB Screening Requirements for Immigrants

The priority for immigration screening efforts is to detect cases of pulmonary TB among persons applying for permanent residence in the United States and to prevent the most infectious persons from entering the United States. However, requirements for screening outside the United States do not apply to the majority of foreign-born persons entering the United States because those classified as nonimmigrants and unauthorized immigrants do not undergo screening (Table 7) (*277*).

Furthermore, a significant proportion of immigrants with Class B1 (4%–14%) and B2 (0.4%–4%) status allowed to enter the United States with abnormal chest radiographs because of having AFB-negative sputum smears on screening outside the United States are later discovered (on the basis of follow-up evaluations by U.S. public health agencies) to have active TB at the time of entry (*350*). This finding has great importance for TB-control activities in certain U.S. jurisdictions.

IOM, NTCA, and CDC have suggested changes in the screening procedures for immigrants, as follows:

- IOM has recommended that testing for *M. tuberculosis* infection be added as a requirement to the medical evaluation for immigrant visa applicants from countries with high incidence of TB (*2*).
- IOM has recommended that 1) a Class B4 TB designation be created for persons with normal chest radiographs and positive tuberculin skin tests and that 2) immigrants with B4 status be required to undergo an evaluation for TB and, when indicated, complete an approved course of treatment for LTBI before receiving a permanent residency card.
- CDC has proposed enhancing training and oversight of panel physicians outside the United States and of civil surgeons in the United States to improve the quality of immigration screening (*359*). CDC is also working to develop an electronic system for notifying jurisdictional public health agencies about the arrival of Class B immigrants.
- NTCA has called for 1) clarification of legal and fiscal issues associated with domestic evaluation and treatment of immigrants; 2) efforts to educate immigrants with Class B1 and B2 status about their responsibilities for follow-up; and 3) operational research to address the cost effectiveness of screening additional categories of immigrants.
- Consideration also should be given to broadening the scope of medical evaluations for immigrants. The costs and benefits of extending the requirement for screening to all visa applicants planning to reside in the United States for >6 months should be examined. Consideration is being given to adding sputum cultures to the sputum AFB smear evaluation of visa applicants who, on the basis of an abnormal chest radiograph, are suspected to have pulmonary TB or who, at least for persons with smear-positive TB cases, are from countries with known high rates of drug resistance.

TB Control at the U.S.-Mexican Border

The U.S.-Mexican border presents specific challenges to TB control. Four U.S. states (California, Arizona, New Mexico, and Texas) and six Mexican states (Baja California Norte, Sonora, Chihuahua, Coahuila, Nuevo León, and Tamaulipas) comprise the U.S.-Mexican border, and an estimated 1 million persons cross the border daily. In the six Mexican border states, estimated annual TB incidence is 27.1 cases/100,000 population, compared with 5.1 cases/100,000 population in the United States (*359*). In 1999, Mexico was the country of origin for 23% of foreign-born persons in the United States with reported TB, and 75% of those cases were reported from the four U.S. border states. In 1996, those same states reported 83% of TB cases among foreign-born Hispanics (*360*). The high rate of TB at the border, the substantial number of border crossings, the substantial geographic area involved, and the prevalent cultural and linguistic barriers make TB control a challenge in this region.

Recommendations to improve TB control at the U.S.-Mexican border have been published (*361*). These recommendations include use of a binational case definition and development of a binational registry of TB cases, improvements in clinical care of binational TB patients and close contacts by cross-border case-management strategies, development of performance indicators for these activities, and setting research priorities (*361*).

Basis for Recommendations on TB Control Among Foreign-Born Persons

Surveillance. The inability to distinguish imported TB present at the time of entry of foreign-born persons into the United States from domestically occurring disease obscures the progress that certain states and cities have made in TB control. Standardized reporting of new TB cases does not allow separating TB among foreign-born persons that is present at the time of entry from cases that arise during residence in the United States. This is more than a semantic distinction because cases of TB that occur among short-term visitors and workers, students, and unauthorized aliens are counted as U.S. incident cases even though a substantial number are imported (*115*). Surveys using sputum cultures indicate that 4%–13% of immigrants and refugees with Class B1 status have TB disease at the time of entry (*279*). TB present at the time of entry is likely to contribute to the higher incidence rates of TB noted among foreign-born persons in the first 2 years after arrival (*115*). The importance of imported cases and the need to distinguish them from domestic cases has also been demonstrated in the smallpox, polio, and measles eradication efforts in North America.

Case detection. Multiple factors common to the experience of foreign-born persons in the United States might lead to delays in the detection of TB. Preexisting culturally derived beliefs about TB might serve as a disincentive to seek health care when symptoms of TB are experienced (*18,279*). Also, foreign-born persons wishing to receive a medical evaluation might encounter financial, linguistic, or other barriers to access (*19*). Once medical services are sought, foreign-born persons are likely to receive their evaluation from certain kinds of health-care providers (e.g., foreign-born physicians or those working in community health centers or hospital EDs) rather than from TB clinics conducted by public health agencies. These challenges to optimal case detection among foreign-born persons will require 1) targeted public education for foreign-born populations at high risk to explain that TB is a treatable, curable disease; 2) better access to medical services, especially for recently arrived immigrants and refugees; and 3) maintenance of clinical expertise in the diagnosis and management of TB among medical practitioners (Box 1).

The TB-screening process for visa applicants (i.e., identification of persons with abnormal chest radiographs) has provided opportunities for active case detection in follow-up evaluations in the United States. Data derived from programs that have sought to identify active TB cases on the basis of positive sputum cultures for *M. tuberculosis* among immigrants with Class B notification status indicate that 3%–14% of the approximately 6,000 immigrants with Class B1 status who enter the United States each year and 0.4%–4.5% of the 12,000 immigrants with Class B2 status have TB at the time of entry (*279*). In San Francisco, California, during July 1992–December 1993, of 182 immigrants with Class B1 status who received follow-up evaluations, 27 (14.8%) had active TB, and 134 (73.3%) had inactive TB (*362*). Among 547 immigrants with Class B2 status, 24 (4.3%) had active TB, and 301 (54.5%) had inactive TB. In California, 3.5% of all persons with a Class B notification status who arrived during January 1992–September 1995 were reported to have active TB ≤1 year of arrival (*277*). Recent arrivals with Class B notification status accounted for 38% of all foreign-born persons with TB reported ≤1 year of arrival. Among 124 immigrants and refugees in Hawaii who were reported during 1992–1993 to have TB ≤1 year of arrival, 78 (63%) had been classified as having Class B1 status and 17 (14%) as having Class B2 status (*350*). However, a study from Los Angeles suggested that the visa application process was more effective in identifying cases among persons recently arrived from Southeast Asia than among those from Mexico and Central America (*363*).

An active Class B1/B2 follow-up program can be relatively cost effective. During October 1995–June 1996, in Santa Clara County, California, 87% of immigrants with Class B status responded to letters inviting them to receive a follow-up evaluation, resulting in a cost of $9.90 to locate one immigrant with Class B1/B2 status and $175.88 to locate one person with TB (*364*).

Case management. As with case detection, cultural and linguistic differences might impede successful treatment outcomes among foreign-born persons. Case management of persons whose primary language is not English depends on reliable and competent medical translation. Providers and agencies that work with foreign-born patients at high risk should ensure that adequate translation and interpretation services are available. In jurisdictions in which the majority of the cases occur among foreign-born person, providing these services can be costly. For example, in 2000, the Tarrant County Health Department TB Program (Fort Worth, Texas), spent

approximately $24,000 on professional translation services (*365*). Ideally, professional services should be used for translation rather than relatives or family friends (*365*).

Culturally derived attitudes and beliefs about TB and its treatment can also be impediments to the management of TB among foreign-born persons. Each culture has its own knowledge, attitudes, and beliefs about TB and how it should be treated. For example, in a study that used focus groups to evaluate attitudes regarding TB among Filipino immigrants, participants expressed a belief that TB was extremely contagious (*264*) and mentioned the associated social stigma and isolation. Although all participants agreed that medical therapy was necessary, participants also trusted the effectiveness of traditional treatments. As more of the burden of TB in the United States is borne by foreign-born persons, the need for health-care providers to understand cultural attitudes toward TB will increase.

Case management is particularly difficult at the U.S.-Mexico border where, until recently, tracking systems for persons who migrated between the two countries were not in place. A new binational system has been established to ensure continuity of care and completion of TB treatment for patients who migrate between the United States and Mexico and to coordinate the referral of patients between the health systems of both countries. The project is now being tested in four U.S.-Mexican jurisdictions (San Diego, California, and Tijuana, Baja California; El Paso, Texas–Las Cruces, New Mexico, and Ciudad Juarez, Chihuahua; Webb and Cameron Counties, Texas, and Matamoros, Tamaulipas; and Arizona and Sonora). If the pilot project proves successful, this binational TB patient referral and information system will likely be expanded to other parts of the United States and Mexico.

Contact investigation. Contact investigations have a particularly high yield when conducted on foreign-born patients. In Seattle, for example, contacts of foreign-born persons with TB were more numerous (6.0 versus 3.4 per case) and substantially more likely to be have positive tuberculin skin test results (50% versus 18%) and to be started on treatment for LTBI (40% versus 23%) than were contacts of U.S.-born persons with TB (*293*). A multicenter survey from around the United States demonstrated that the tuberculin skin test was positive among 71% of foreign-born contacts compared with 32% of all close contacts (*31*). Although not all foreign-born contacts identified during a contact investigation are recently infected, the majority would nevertheless be considered candidates for treatment of LTBI under current guidelines (*4*). In addition, a Canadian study indicated that contact investigations were more cost effective than preimmigration screening and postarrival surveillance (*276*).

Targeted testing and treatment of LTBI. Surveys using molecular epidemiologic methods have consistently demonstrated that less clustering of *M. tuberculosis* isolates occurs from foreign-born patients than from U.S.-born patients; this has been interpreted as evidence that less person-to-person spread of TB occurs among foreign-born persons in the United States and that the majority of cases of TB among foreign-born persons occur as a result of activation of a latent infection (*150–152,356*). In fact, one reason for the lack of progress in reducing TB among foreign-born persons might be that insufficient attention has been given to targeted testing and treatment (*152*), which should be the most applicable prevention strategy for this population, in which TB disease occurs mainly by progression from LTBI.

The success of programs for targeted testing and treatment of LTBI among populations at high risk in the United States has been thwarted by poor interest in the intervention on the part of medical practitioners and poor adherence by patients (*51*). Among foreign-born persons, these problems are magnified by the lack of access to care and by cultural and linguistic obstacles. Successful models for administering targeted testing and treatment of LTBI among refugees have been published; these models are resource-intensive and require a commitment to working within the population's cultural contexts (*202,221*). In addition, the use of DOT increases treatment completion rates (*366*).

Other opportunities to conveniently access foreign-born persons for targeted testing programs include school-based testing of foreign-born students. The majority of persons residing as students in the United States remain long enough to receive targeted testing for LTBI and, if TB is diagnosed, to complete a course of treatment. Screening for TB is required by 61% of colleges and universities: for all students in 26%, for all international students in 8%, and for students in specific academic programs in 47% (*367*). School-based screening also has been evaluated among younger students (*150,322,345*). In California, widespread TB screening of kindergarten and high school students yielded a low prevalence of skin test reactors and a limited number of cases of TB, but foreign-born students were >30 times more likely than U.S.-born students to have the infection (*345*). In a cost-benefit analysis, screening all students would be expected to prevent 14.9 cases/10,000 children screened, whereas targeted testing would prevent 84.9 cases/10,000 screened and would be less costly (*345*).

Control of TB Among Persons with HIV Infection

HIV and *M. tuberculosis* interact in ways that tend to worsen both diseases among coinfected persons (*368*).

When a person with HIV infection is exposed to a patient with infectious TB, the risk for acquiring TB disease soon after that exposure is markedly increased (*369*). In outbreaks in which the start of exposure could be determined, HIV-infected persons acquired active TB in as little as a month after exposure to a person with infectious TB (*136*). HIV coinfection is also a highly potent risk factor for progression from LTBI to TB (*44,46,370*). Persons with LTBI and HIV coinfection have a risk for progressing to TB disease of approximately 10%/year (*317,371,372*), which is 113–170 times greater than the risk for a person with LTBI who is HIV-seronegative and has no other risk factors (*4,44*).

On a global level, HIV infection has had a substantial effect on the epidemiology of TB. Areas of the world most heavily affected by the global epidemic of HIV/AIDS (e.g., sub-Saharan Africa) have also sustained increases in the incidence of TB (*44,46,373*). TB is the most common infectious complication and the most common cause of death among persons with HIV/AIDS in places where the incidence of both diseases is high (*374*). In the United States, HIV infection has been associated with TB outbreaks in institutional settings, including health-care facilities (*53*), correctional facilities (*37*), and homeless shelters (*33*).

Before the advent of highly active antiretroviral therapy (HAART) in the early 1990s, HIV infection caused a progressive decline in immune competence and death. However, the use of HAART using combination therapy plus protease inhibitors has prolonged the survival among persons with HIV infection (*375–377*). The introduction of HAART has also decreased the incidence of TB among HIV-infected persons: an 80% decrease in risk for TB has been demonstrated among HIV-infected persons receiving HAART (*378*).

With the declining incidence of TB in the United States since 1992, the incidence of HIV infection among persons with TB also has decreased. This is likely attributable to increased understanding of the biologic interactions between the two pathogens, leading to more targeted TB-control efforts and to the introduction of HAART. Another factor is improved TB infection control in health-care facilities, because HIV- infected persons were particularly affected by health-care–associated transmission of *M. tuberculosis* (*53*).

HIV infection was a prominent cause of the 1985–1992 TB resurgence in the United States, especially the incursion of health-care–associated TB (including multidrug-resistant disease). That fact, along with the knowledge that the global epidemics of HIV infection and TB are continuing unabated (*44*), dictates a high degree of respect and vigilance for the adverse consequences that HIV infection could impose on the epidemiology of TB in the United States.

Basis for Recommendations of Control of TB Among Persons with HIV Infection

HIV counseling and testing. Knowledge of the presence of HIV infection among patients with TB is useful for surveillance purposes to ensure that an optimal drug regimen is chosen for treatment (*5*), refer persons for HIV primary care if the case is newly detected, and guide decisions about contact investigations. TB is frequently the first illness that brings a person who has not previously received a diagnosis of HIV infection into the health-care system.

Voluntary counseling and testing for HIV is recommended for all patients with TB (*5*), but this recommendation has not been fully implemented, and reporting of HIV among persons with TB is incomplete (*14*). In 2003, HIV testing was performed for <50% of patients reported with TB in the United States, and only 63% of persons in the age group at greatest risk (persons aged 25–44 years) were tested (*14*). HIV counseling and testing has also been recommended for contacts of persons with TB (*302*). However, recent data indicate that contacts of HIV-infected persons with TB have a high rate of HIV infection but that contacts of persons with TB without HIV infection do not (*301*). HIV testing for other persons with LTBI should be limited to those who have clinical or behavioral risk factors for HIV infection.

Case detection. HIV coinfection affects the clinical and radiographic manifestations of TB. HIV-infected patients are more likely than persons without HIV infection to have extrapulmonary and miliary TB (*379,380*), and those who have pulmonary TB tend to have atypical findings (e.g., they are less likely to have apical cavities and are more likely to have lower lobe or instititial infiltrates and mediastinal or paratracheal lymphadenopathy). These atypical features are heavily dependent on the patient's CD4 cell count; those with CD4 cell counts >300 cells/μL usually have manifestations, such as upper lobe cavitary infiltrates (*274*). Persons with HIV infection might also have pulmonary TB despite a normal chest radiograph (*274,379*).

HIV-infected patients are also vulnerable to other pulmonary and systemic infections such as *Pneumocystis carinii* and pneumococcal pneumonias and disseminated *M. avium* complex disease. Although the symptoms and signs of TB are usually different to the trained clinician from those caused by other prevalent invasive pathogens (*273,381*), HIV co-infection often results in delay in the diagnosis of TB as a result of altered clinical and radiographic manifestations (*23*).

Undetected transmission of *M. tuberculosis* to HIV-infected persons can have serious sequelae (*136*). A substantial outbreak of TB in a prison in South Carolina in 1999

demonstrated the widespread consequences of an unrecognized TB case in a congregate setting with a substantial number of HIV-infected persons (*37*). In that outbreak, 32 TB cases and 96 tuberculin skin test conversions resulted from a single unrecognized case. Similar outbreaks have occurred in hospitals (*53,244*), HIV-living facilities and day-treatment programs (*136*), and homeless shelters (*33*). Such outbreaks underscore the importance of aggressive TB screening and treatment in settings in which HIV-infected persons congregate. Screening for TB in those settings has been successfully conducted by using symptom checklists, tuberculin skin testing, and chest radiographs (*37,118,136*).

Case management. Management of TB among persons with HIV infection is complex. Drugs used to treat TB and those employed in combination antiretroviral therapy have overlapping toxicities and potentially dangerous drug interactions (*382*). Paradoxical responses to TB therapy are more common among HIV-infected persons (*383*). Use of multiple potentially toxic medications also provides further challenge to adherence with TB treatment. Therefore, integration of management of both HIV infection and TB is critical to the success of management of both. Comprehensive case management, including DOT, is particularly important (*5*). Among HIV-infected TB patients, more favorable outcomes and survival have been associated with DOT than with self-administered therapy (*384*). ATS/CDC/IDSA guidelines should be consulted for recommendations on length and mode of treatment and selection of drug regimens (*5*). Finally, patients with HIV and TB bear the brunt of two conditions that are associated with clinical and social complexities that can be personally overwhelming. Both HIV infection and TB are associated with stigmatization, and patients with these concomitant conditions often suffer from isolation and a lack of social support.

Contact investigation. Despite controversy as to whether HIV-coinfected patients with TB are more or less infectious than HIV-seronegative patients (*385,386*), they are clearly capable of transmitting *M. tuberculosis*; contacts of the two populations of patients have comparable rates of LTBI (*369,387*). The higher risk for progressing rapidly from exposure to *M. tuberculosis* to TB disease means that all of the medical and public health interventions (case detection and reporting, initiation of an effective drug regimen, and identification and evaluation of contacts) are more urgent when working to control HIV-associated TB (*388*).

Although offering HIV counseling and testing to all contacts of persons with infectious TB has been recommended (*302*), this undertaking would be resource-intensive. Whereas prevalence of HIV infection among contacts of HIV-infected persons is high, prevalence among contacts of persons with TB without HIV infection or with undetermined status is negligible (*301*).

Targeted testing and treatment of LTBI. HIV coinfection is the most important known risk factor for persons with LTBI acquiring active TB (*317,371,372*). Treatment of LTBI is effective in reducing the risk for progression to TB disease among HIV coinfected persons (*372,389*). Thus, all possible efforts should be made to ensure that HIV-infected persons are tested for *M. tuberculosis* infection and that those found to have latent infection receive and complete a course of treatment. In addition, knowledge of the HIV status of persons being evaluated for LTBI is desirable 1) in interpreting the tuberculin skin test result (e.g., ≥5 mm of induration is considered a positive test among persons with HIV infection [*4*]) and 2) in counseling persons with positive skin test results about the risks and benefits of treatment for LTBI (the role of QFT-G for testing persons with HIV infection for LTBI has not been determined). According to current guidelines (*302*), persons being evaluated for LTBI should also be screened for HIV infection by using self-reported clinical and behavioral risk factors.

Institutional infection control. Infection-control measures recommended to prevent transmission of *M. tuberculosis* have been effective in limiting exposure of HIV-infected persons, including patients, visitors, and staff members, to *M. tuberculosis* in hospitals, extended care facilities, and correctional facilities (*9,244*). Nevertheless, the risk for rapid progression from exposure to TB disease means that HIV-infected persons should continue to be advised of any potential sites of institutional exposure so an informed choice regarding employment or volunteering can be made.

Control of TB Among Homeless Persons

The persistence of TB among homeless persons in the United States is a major public health problem. The homeless population is not insubstantial; in 1995, an estimated 5 million persons (2.5% of adult U.S. residents) either were or had recently been homeless, living in streets or shelters, or marginally housed (e.g., living on public support in residential hotels) (*390*). TB incidence is high among homeless persons, and evidence exists of considerable transmission of *M. tuberculosis*. Among 2,774 homeless persons enrolled during 1990–1994 in San Francisco, California, 25 incident cases were identified for 1992–1996, for an annual rate of 270 cases/100,00 population (*118*). Among 20 *M. tuberculosis* isolates from incident cases that were subjected to genotyping study, 15 (75%) were clustered,

indicating chains of transmission in the population. Other molecular epidemiology studies also have identified homelessness as an important risk factor for clustering of *M. tuberculosis* isolates (*33,119,391,392*).

Shelters are key sites of TB transmission among homeless persons throughout the United States (*27,33,118–120,166, 391–393*). In Los Angeles, California during March 1994–May 1997, three homeless shelters were sites of TB transmission for 55 (70%) of 79 homeless patients (*33*). In Fort Worth, Texas during 1995–1996, clusters of cases among homeless persons occurred simultaneously in four homeless shelters (*27*). In Alabama, genotyping of isolates from TB cases reported in 1994-98 revealed an undetected statewide outbreak of TB that was traced to transmission in a correctional facility and in two homeless shelters (*166*). In an outbreak in a shelter in Syracuse, New York, during 1997–1998, a shelter resident was probably infectious for 10 months before receiving a diagnosis; ventilation in the shelter was poor, and the population included vulnerable persons with risk factors that included HIV infection, substance abuse, and malnutrition (*120*).

Multiple barriers to the control of TB among homeless persons have been identified. Delays in detection of infectious cases have been reported (*20*); in a computer simulation study that modeled multiple strategies for TB control among homeless persons, a 10% improvement in access to treatment led to greater declines in disease and death after 10 years than comparable improvements in treatment programs (*394*). Traditional methods of conducting contact investigations often fail to identify contacts of homeless persons with TB (*30,119,120*). Difficulties also have been encountered in completing treatment for homeless patients with active TB (*395*) and LTBI (*167,184*).

Basis for Recommendations for Control of TB Among Homeless Persons

Surveillance and case detection. Delays in diagnosis and treatment of TB among homeless persons might occur as a result of delays in seeking medical care (*181*) and to the failure of medical providers to detect TB among those seeking care (*20*). Homeless persons with TB are disproportionately likely to receive care in hospital EDs and other urgent care clinics (*232*). For example, during 1994–1996, homeless persons in Atlanta, Georgia, were more likely than other patients to receive a diagnosis in a hospital ED (*184*). On the basis of sputum AFB smear results and radiologic findings, homeless persons had more advanced disease at the time of diagnosis, another indication that they received diagnoses later in the course of their disease (*184*).

Shelters have proved to be effective sites for case detection by use of screening procedures among homeless persons. During May 1996–February 1997, among 127 homeless persons in Alabama for whom shelter-based screening was conducted by using symptom evaluation, sputum culture, and chest radiographs as the screening package, four (3.1%) persons had TB disease (*281*). Symptom evaluation alone was not proven to be useful. In a similar study from London, United Kingdom, that employed symptom evaluation, tuberculin skin testing, and chest radiography, 1.5% of homeless persons were determined to have TB (*396*).

On the basis of findings of a high prevalence of TB in shelter-using homeless populations, certain communities have implemented compulsory screening of shelter residents based on symptom evaluation or tuberculin skin testing with radiographs for those with positive tests. One such program in Portland, Oregon, initiated in 1985, was associated with an 89% reduction in TB morbidity in the geographic area served by participating shelters during 1980–1995 (*397*). The implementation of a similar screening program in shelters in Denver, Colorado, in 1995 led to lower rates of active TB and reduced transmission of TB disease, as demonstrated by less genotype clustering by DNA fingerprinting (*167*). Both screening programs were based on symptom evaluation, tuberculin skin testing, and chest radiography. The decrease in TB morbidity in both these studies was attributed to shelter-based case detection through screening activities.

Case management. Completion of treatment for active TB is more difficult for homeless persons, particularly those who report substance abuse, including alcohol abuse (*395*). Homeless persons with active TB are at high risk for poor adherence even with enhanced DOT and are more likely to default and move from the area of initial diagnosis. They are also more likely to have legal action taken in the form of court-ordered treatment or detention. Comprehensive case management that includes a variety of incentives and enablers, including food, temporary housing, transportation vouchers, and treatment for substance abuse and mental illness has improved rates of treatment completion in this population.

Costs for homeless persons who are hospitalized for initial treatment of active TB have been $2,000 more than costs for persons who were not homeless (*398*). Excess hospital utilization could be attributable to social considerations, clinical indications (especially the need to render a patient noninfectious before discharge to a congregate living setting), or concerns about adherence to the plan of treatment. In San Diego, California, a novel housing program that used hostels facilitated the completion of treatment of TB in homeless persons (*399*). Completion rates of 84%–100% were achieved for persons housed at a designated hostel in 1995. Certain TB-control programs in

cities with substantial homeless populations routinely provide temporary or longer-term housing in attempts to improve completion of treatment. The California Department of Health allots funds for temporary housing of persons with TB to each of its county and local jurisdictions. The U.S. Department of Housing and Urban Development also provides funding for housing patients with TB.

The beneficial impact on treatment outcomes of an integrated approach to managing homeless patients with TB has been emphasized (*394*). For example, a social care and health follow-up program among homeless patients in Spain was associated with a decrease in TB rates from 32.4/100,000 in 1987 to 19.8 cases/100,000 in 1992, and better completion rates and reduced costs for hospitalizations were also documented (*400*). In Massachusetts, 58 (34.5%) of 214 persons hospitalized in a dedicated inpatient unit for difficult TB patients during 1990–1995 were homeless (*401*). Regardless of the case-management plan that is chosen, all such interventions should take into consideration the importance of addressing major gaps in knowledge, attitudes, and beliefs about TB among homeless persons (*181*).

Contact investigation. Contact investigations for cases of TB among homeless persons are particularly challenging. Homeless patients with TB often fail to identify contacts during routine investigation (*30*). Completing a contact evaluation in identified contacts and completing treatment for LTBI among contacts that are homeless are often difficult (*320,391,402*). Interpretation of the results of tuberculin skin testing of contacts of homeless cases is problematic because the background prevalence of positive tuberculin skin tests in the population is usually higher than that of the general population. As with contact investigations among other populations at high risk, discerning when a contact investigation has become a targeted testing program is often difficult. A proposed alternative approach to conducting contact investigations of homeless persons is to focus on possible sites or locations of exposure, such as shelters (*391,393*).

Targeted testing for and treatment of LTBI. When homeless persons are identified as a population at high risk on the basis of the local epidemiology of TB, targeted testing and treatment protocols tailored to local circumstances should be developed. However, low rates of completion of therapy for LTBI are commonly observed (*167,184,402*). For example, among 7,232 inner city residents (including homeless persons) screened for LTBI during 1994–1996 in Atlanta, Georgia, 4,701 (65%) completed tuberculin skin testing; of 809 (17%) who had a positive test, 409 (50%) were candidates for isoniazid therapy, and 84 (20%) completed treatment (*184*). In another study conducted in San Francisco, California, during 1991–1994 that was designed to improve adherence, two novel interventions (biweekly preventive DOT with either a $5 incentive or a peer health adviser) were compared with the usual method of self-supervised treatment (*402*). Even though completion of treatment was not high for any of the three groups, multivariate analysis indicated that independent predictors of completion were being offered the monetary incentive and residence in a hotel or other stable housing at entry into the study. That report confirmed an earlier finding that advocated offering monetary incentives (*320*).

Institutional and environmental controls. Efforts have been made to reduce transmission of TB in shelters for homeless persons by enhancing institutional control measures. These efforts have included reducing shelter size (*13*), improving ventilation systems, and using germicidal ultraviolet light (*280*).

Control of TB Among Detainees and Prisoners

Correctional facilities in the United States include jails and prisons, which serve different but complementary functions. Jails serve as pretrial detention centers and house persons (detainees) awaiting trial and those sentenced to <1 year of incarceration. Local and county governments operate the majority of jails. Jails are characterized by rapid turnover of detainees with short lengths of stay. Prisons serve as sites of detention for persons (prisoners) who have been sentenced and will be incarcerated for a known length of time, generally >1 year. State governments, the federal government, and the military all operate prison systems. On any given day, approximately 2 million persons in the United States are incarcerated; 1.4 million of those are imprisoned, and the remainder are detained in jails. Approximately 6 million persons are incarcerated in jails or prisons each year for variable lengths of time (*124,125*).

Detainees and prisoners represent the poorest and most medically underserved segments of the U.S. population, the same population segments at risk for LTBI and TB disease (*124,252,253*). Persons entering prisons have usually spent time in jail, and detainees and prisoners eventually reenter the community. Consequently, TB outbreaks among detainees, prisoners, and the general population of a geographic area are interrelated (*127,403*), and close coordination of TB-control activities is needed between health programs in correctional facilities and jurisdictional public health agencies.

Prisons have long been identified as sites of transmission of *M. tuberculosis* to other inmates and workers (*38,139,404–408*), including those with HIV infection

(*38,139,405,408*). In addition, time spent in jail is a risk factor for subsequent acquisition of TB (*127,250,256*), an indication that jails often are also sites of transmission. Correctional facilities are among the most important sites of transmission of *M. tuberculosis* in the United States.

Failure to detect TB in correctional facilities results in TB outbreaks, which have been well documented (*37,139,404–408*). Outbreaks of multidrug-resistant TB involving inmates and staff, including HIV-infected persons, were a prominent component of the 1985–1992 TB resurgence in the United States (*404,405,409–411*). However, outbreaks have continued to occur (*37,139*), even though TB control, including control of *M. tuberculosis* transmission, in the United States has improved.

Basis for Recommendations on Control of TB Among Detainees and Prisoners

Case detection and case management. Despite the importance of jails and prisons in sustaining and amplifying the reservoir of TB in the United States (*127,405,407*), little is known about the optimal means of case detection of TB among detainees and prisoners. The majority of prisons have adopted a case-detection strategy that is based on a survey of TB symptoms obtained on admission, in which all entrants are tested for *M. tuberculosis* infection ≤14 days of admission; universal chest radiographs of all entrants are rarely offered (*410*). No data have been published supporting the effectiveness of symptom surveys and testing for *M. tuberculosis* infection for detecting cases of TB and preventing transmission within jail systems, although screening by tuberculin skin testing was effective in controlling TB in one prison system (*411*). Certain substantial urban jails perform chest radiographs on all persons entering the institution in an attempt to minimize transmission of TB (*283,412*), and data indicate that this approach is cost effective (*412*). Because nearly all prison entrants have first been detained in a jail system, effective TB case-detection programs in jails will substantially decrease the probability that persons with undetected active TB will be admitted to prison.

Once cases are detected, strategies similar to those used in the community have led to high rates of successful treatment completion (*413*). A particular problem for case management in a jail setting is the unanticipated release of detainees, which often precludes the development of an effective discharge plan. Strategies to better coordinate discharges with public health authorities should be promoted.

Contact investigation. Continuing outbreaks of TB in correctional facilities (*37,139*) underscore the importance of prompt and thorough contact investigations in jails and prisons. Contact investigations in correctional facilities involve two steps: 1) identifying and evaluating persons exposed before the source-case was incarcerated, and 2) identifying and evaluating persons exposed during incarceration of the source-case. Effective case detection is important to limit the size of the latter group. Contact investigations often need to be conducted broadly, among more than one facility, because of the movement of detainees within the correctional system (*414*).

Conducting contact investigations based on the concentric circle method is difficult in correctional institutions. Frequently, a single infected person can expose up to several hundred persons both before and after incarceration. Cases involving persons who were exposed before incarceration should be managed by the jurisdictional public health agency for the community in which the person lived before arrest. For the jurisdictional public health agency to carry out those contact investigations effectively, prompt notification and case reporting by the detention facility is necessary. Guidelines for conducting contact investigations in jails have been published (*258*).

Targeted testing and treatment of LTBI. Targeted testing and treatment of latent TB among detainees and prisoners has been described in detail (*415–417*). Because of the high risk for transmission of *M. tuberculosis* in correctional facilities, inmates incarcerated for >14 days usually receive a test for *M. tuberculosis* infection as part of TB case detection. Detainees and prisoners with LTBI often are considered to be candidates for treatment of latent TB (*124,252,253*). Prisons often are an ideal setting for effective treatment of LTBI because of known location of the patient, length of stay, prohibition of illicit drugs and alcohol, and a predictable diet. Nevertheless, achieving high rates of completion of treatment for LTBI in prisons or jails has been difficult (*257,416,417*).

The majority of jail detainees are released in ≤14 days of entry. If treatment for LTBI is started in the jail setting, community follow-up after release from jail is essential. Without specific interventions to assure such follow-up, the probability of completion of treatment might be <10% (*256,257,418*). Recent developments in short-course treatment of latent TB with a combination of rifampin and pyrazinamide for 2 months offered promise in improving treatment completion rates (*419*). However, the toxicity of this regimen precludes its routine use (*324*), and this combination should generally not be used for the treatment of LTBI in correctional settings because the rates of toxicity have been similar to those observed in the wider community. In addition, detainees and prisoners have high rates of hepatitis C infection, making them especially prone to serious hepatotoxicity.

Institutional infection control. Correctional institutions have been sites of virulent outbreaks of TB, including multidrug-resistant TB, that have involved HIV-infected inmates and staff (*37,139,405,408*). Common findings in these outbreaks have included the failure to isolate persons with active TB quickly. Another common finding has been disease associated with rapid transmission of *M. tuberculosis* when immunosuppressed detainees and prisoners are housed together. An effective infection-control program can decrease the likelihood of TB transmission in correctional institutions (*420*). Guidelines to assist correctional institutions in developing effective infection-control programs have been published (*258*).

Control of TB in Health-Care Facilities and Other High-Risk Environments

During the 1985–1992 TB resurgence in the United States, TB cases resulted from transmission of *M. tuberculosis* in settings where patients with infectious TB congregated closely with susceptible persons (*52–54,170,421*). This epidemiologic disease pattern had not been recognized in the United States since the development of effective drugs against TB starting in the 1950s. Hospitals and other health-care facilities were the primary, but not the only, sites of transmission (*405,406,408*), and HIV-infected persons were prominent among those who contracted *M. tuberculosis* infection and rapidly acquired TB disease (*52–54,170,406,408*). Although incidence of TB in health-care facilities has been markedly reduced because of the development and deployment of effective infection-control measures (*56,422–424*) and decreasing incidence of TB in different communities, TB disease attributable to recent transmission of *M. tuberculosis* in other settings has not only persisted but has been recognized in a wide variety of sites and settings and become an established epidemiologic pattern.

As a consequence of the changed epidemiology of TB in the United States, the primary strategies now required to control the disease include measures for its prevention in settings in which a risk for transmission of *M. tuberculosis* exists (Box 4). Recommendations for infection-control measures in high-risk settings are provided in this statement. The approach to control of TB and other airborne infections that was developed for health-care facilities (*10*) is the most successful model and is outlined in detail in this statement. Recommendations are also provided for control of transmission of *M. tuberculosis* in extended care facilities, correctional facilities, homeless shelters and other high-risk settings.

Control of TB in Health-Care Facilities

Strategies for control of TB in health-care facilities, which also are applicable for other settings in which high-risk persons congregate, are based on comprehensive guidelines issued by CDC in 1994 (*10*). New CDC guidelines for preventing transmission of *M. tuberculosis* in health-care facilities will be published in 2005. A draft[†] of these guidelines has been published in the Federal Register. In the assessment of institutional risk for TB, three levels of risk (low, medium, and potential ongoing transmission) are recommended, based on the recent experience with TB in the institution and in the community it serves. The recommended frequency of testing of employees for *M. tuberculosis* infection varies, depending on the institution's level of risk. The tuberculin skin test is recommended for testing HCWs and other employees with a risk for exposure to *M. tuberculosis*. QFT-G is also approved for detecting LTBI; guidelines for the use of QFT-G will be published in the *MMWR*.

The risk for TB associated with health-care facilities is related to the incidence of TB in the community served by the facility and to the efficacy of infection-control measures (*422*). Implementation of infection-control guidelines (*10*) has markedly reduced risk for exposure to TB in health-care facilities during the past decade (*56,422–424*) and has also contributed to the decreasing numbers of TB cases. Implementation of effective infection-control measures in the medical workplace is thus an important element of broader national and international strategies to prevent transmission of TB (*244*).

Epidemiologic investigations of the early outbreaks of TB in health-care facilities, including those involving multidrug-resistant cases, indicated that transmission usually occurred because of failure to identify and isolate patients with infectious forms of TB. In certain instances, diagnosis of TB was delayed as a result of the atypical presentation of TB among patients with HIV infection, especially those with low CD4 counts. Transmission was also facilitated by 1) the intermingling of patients with undiagnosed TB with patients who were highly susceptible; 2) inadequate laboratory facilities or delayed laboratory reporting; and 3) delayed institution of effective therapy. Other factors facilitating transmission included a lack of negative pressure respiratory isolation rooms, recirculation of air from respiratory isolation rooms

[†] Draft Guidelines for Preventing the Transmission of *Mycobacterium tuberculosis* in Health-Care Settings. Federal Register 2004;69:70457–8.

to other parts of the hospital, failure to isolate patients until they were no longer infectious, allowing isolated patients to leave their rooms without wearing a mask, and leaving respiratory isolation room doors open (*52–54,170,421,425,426*).

CDC guidelines recommend a hierarchy of TB infection-control measures (*10*). In order of importance, these measures are administrative controls, engineering controls, and personal respiratory protection (PRP) (Box 7). Administrative controls consist of measures to reduce the risk for exposure to persons with infectious TB, including screening of patients for symptoms and signs of TB at the time of admission, isolating those with suspected disease, establishing a diagnosis, and promptly initiating standard therapy (*5*). Engineering control measures are designed to reduce dissemination of droplet nuclei containing *M. tuberculosis* from infectious patients and include the use of airborne infection isolation rooms. The third level (and the lowest on the hierarchy of controls) is the use of PRP devices such as N-95 respirators. Respirator usage for the prevention of TB is regulated by the Occupational and Health Safety Administration under the general industry standard for respiratory protection[§].

In implementing a comprehensive infection control program for TB, institutions should first conduct a risk assessment to determine what measures are applicable. Risk for transmission of *M. tuberculosis* varies widely, and procedures that are appropriate for an institution in an area of high TB incidence (e.g., an inner-city hospital or homeless shelter in a metropolitan high-incidence area) differ from those applicable to an institution located in a low incidence area that is rarely used by patients with TB. The jurisdictional public health TB-control program should assist in the development of the assessment, which should include data on the epidemiology of TB in the community served by the institution and the number of TB patients receiving evaluation and care.

The institutional risk for TB can be stratified according to the size of the institution and the number of patients with TB as low risk, medium risk, or potential ongoing transmission. Hospitals with ≥200 beds that provided care for fewer than six patients with TB during the previous year are categorized as low risk whereas those that cared for six or more patients are categorized as medium risk. For hospitals with <200 beds, those with fewer than three TB patients in the previous year are considered low risk, and those with three or more cases are considered medium risk. Outpatient clinics, outreach programs, or home health

[§] Personal Protective Equipment, 29 C.F.R. Sect. 1910.134 (2003).

BOX 7. Principles of control and prevention of tuberculosis (TB) in health-care facilities, by strength of recommendation and quality of evidence*

- A TB infection control program should be established in all health-care settings (sites that provide care to patients with TB and sites that refer such patients to other facilities) to prevent transmission of *Mycobacterium tuberculosis*. A hierarchy of controls (i.e., administrative, engineering, respiratory protection) should be implemented (AII).
- A risk assessment should be implemented to determine the appropriate level of controls to implement. The risk assessment will also determine the frequency of testing of health-care workers for latent TB infection (AIII).
- Administrative controls, designed to ensure the prompt recognition, isolation, diagnosis, and treatment of patients with infectious TB, are the most important elements of an infection control program (AII).
- A high index of suspicion for TB should be maintained by health-care providers. Airborne infection isolation should be implemented for patients as soon as TB is suspected, whether during emergency care, during hospital evaluation, or in a clinic setting (AIII).
- When indicated, standard therapy for TB should be promptly initiated, and the diagnosis confirmed or excluded as soon as possible (AII).
- Surveillance should be conducted to ensure that rooms for airborne infection isolation are functioning properly. A risk assessment should determine the number of rooms for airborne infection isolation that are needed (AIII).
- Institutions that do not provide care to persons with TB should have a plan for isolation and prompt transfer of suspected patients to other facilities (AIII).
- Patients with infectious TB should be discharged from hospital only when arrangements have been made to prevent contact with susceptible persons[†] (AIII).
- Health-care facilities should cooperate closely with public health agencies to ensure that patients with TB receive adequate planning for outpatient management to ensure that treatment is continued until a complete course of curative therapy has been administered (AIII).
- All health-care workers should undergo baseline testing for latent TB infection. The frequency of subsequent testing should be based on results of the risk assessment. Employees with latent TB infection should be encouraged to start and complete treatment, if indicated. Surveillance and analysis of results of serial testing of employees for *M. tuberculosis* infection should be conducted (AIII).
- Employees should regularly receive education on TB (AIII).

SOURCE: CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care facilities, 1994. MMWR 1994;43(No. RR-13):1–132.

* See Table 1.

† See Box 3.

settings that provide care for fewer than three patients with TB per year are considered low risk, and those that care for three or more patients are considered medium risk. TB clinics, outreach programs, and other settings in which HCWs are responsible for the care of persons with TB are classified as medium risk. Any institution, clinic, or setting with evidence of recent patient-to-patient or patient-to-employee transmission of *M. tuberculosis* or of ongoing or unresolved transmission should be classified as having potential ongoing transmission until effective control measures have been implemented and transmission is interrupted. Potential ongoing transmission is a temporary classification.

When transmission of *M. tuberculosis* is suspected at a facility, an immediate investigation should be undertaken that includes consultation with public health officials or experts in hospital epidemiology and infection control. Evidence of potential transmission of *M. tuberculosis* includes clusters of conversions of tests for *M. tuberculosis* infection among employees from negative to positive, increased rates of positive tests for *M. tuberculosis* infection among employees, an employee with potentially infectious TB, unrecognized TB among patients or employees, and recognition of identical strains on genotyping of *M. tuberculosis* isolates from patients or employees.

How often employees at health-care facilities and other at-risk sites for *M. tuberculosis* infection are tested depends on the risk assessment. The positive predictive value of the tuberculin skin test is low when populations with a low prevalence of infection with *M. tuberculosis* are tested (*424,427*). Consequently, frequent testing by using that method in low-incidence, low-risk settings is discouraged. In addition, false-positive tests have been reported when institutions changed brands of Purified Protein Derivative (PPD) reagent, for example from Tubersol® to Aplisol® (*427*).

At the time of employment, all HCWs should undergo baseline testing (with two-step testing if the tuberculin skin test is used and no testing was performed during the preceding year) (*10*). Those in medium-risk settings should be tested annually. Follow-up testing is recommended for workers in low-risk settings only if exposure to a patient with infectious TB (i.e., a patient not initially isolated but later found to have laryngeal or pulmonary TB) has occurred. Institutions in which ongoing transmission of *M. tuberculosis* is documented should carry out testing for *M. tuberculosis* infection of HCWs at risk every 3 months until transmission has been terminated.

Employees testing positive for *M. tuberculosis* infection should receive a chest radiograph to exclude TB disease and should be evaluated for the treatment of LTBI based on current recommendations (*4,324*). Compliance with therapy for LTBI among HCWs, including clinicians, has historically been poor (*428–430*). Employee health clinics and infection-control departments should emphasize to HCWs the importance of completion of therapy for LTBI. In a comprehensive infection-control program that encourages HCWs to complete treatment for LTBI, higher completion rates have been reported (*431,432*).

Control of Transmission of *M. tuberculosis* in Other High-Risk Settings

Extended Care facilities. Elderly persons residing in a nursing home are almost twice as likely to acquire TB as those living in the community (*252,433,434*). Certain considerations for control of TB in hospitals apply also to extended care facilities, including 1) maintaining a high index of suspicion for the disease; 2) promptly detecting cases and diagnosing disease; 3) isolating infectious persons and initiating standard therapy; 4) identifying and evaluating contacts; and 5) conducting contact investigations when indicated. The value of treating LTBI in elderly residents of nursing homes so as to prevent future outbreaks has been documented (*435*).

In 1990, CDC published recommendations for TB control in extended care facilities (*433*). Those long-term care facilities that do not have airborne-infection-isolation rooms should transfer patients suspected to have infectious TB to other facilities (including acute-care hospitals) until the disease is ruled in or out and treatment is started if indicated and continued until the patient is noninfectious (*10*). The risk assessment and frequency of testing for LTBI for employees at long-term care facilities are similar to those described previously. Residents should be tested on admission to the facility and should provide a history and undergo physical examination to identify symptoms and signs of TB. Residents with LTBI should be offered treatment according to current recommendations (*4,324*), with careful monitoring for drug toxicity.

Correctional facilities. Common findings in outbreaks of TB in correctional facilities were the failure to recognize and isolate patients with TB and rapid progression of outbreaks when immunosuppressed detainees were housed together (*405,406,408*). Because of the substantial numbers of cases of TB infection and disease that might result from outbreaks at correctional facilities and the natural movement of inmates from incarceration to the general population, correctional facilities should be viewed as being among the most important sites of transmission of *M. tuberculosis* in the United States (*128,436*).

Guidelines for control of TB transmission in correctional facilities (*123*) have emphasized that the infection-control

principles developed for health-care facilities (*10*) are also applicable to correctional facilities. In prisons and jails, the most important activity in TB infection control is efficient detection of infectious TB cases, including those that are prevalent among persons entering the facility and those that arise during detention. A prompt diagnostic evaluation, respiratory isolation (including transfer out of the facility if airborne-infection-isolation rooms are not available), and institution of a standard treatment regimen are urgent priorities when suspected cases are encountered. If this process is delayed, a substantial number of persons might be exposed as a result of the congregate living arrangements that characterize correctional facilities.

Because of crowded conditions that favor the spread of *M. tuberculosis* (*420*) and the high prevalence of HIV infection among prisoners (*255*), contact investigations should be undertaken immediately once a case of TB has occurred at a facility. In a study conducted in the Maryland state correctional system, prisons that conducted programs for targeted testing and treatment of LTBI among inmates experienced lower rates of tuberculin skin test conversions, an indication that this measure can contribute to successful infection control (*420*). A template is now available to assist jails in instituting an effective infection-control program (*258*).

Shelters for homeless persons. As with correctional facilities, homeless shelters are important sites of transmission of *M. tuberculosis* and an important cause of the continuing high incidence of TB among the homeless population (*33,118*). Effective infection-control strategies in those venues are use of *M. tuberculosis* genotyping for rapid identification of clustered cases and sites of transmission (*27,33*), screening shelter users for TB disease, wide-ranging contact investigations, and engineering controls, including ultraviolet germicidal irradiation (*437*). A systematic shelter-based program for targeted testing and treatment of LTBI in Denver was also demonstrated to decrease incidence of TB in the homeless population (*167*).

Because crowding and poor ventilation are often prevalent in shelters, infection-control efforts should also include engineering modifications to decrease exposure to *M. tuberculosis*. A guide to assist shelters in improving the safety of their environment through modifications in ventilation, air filtration, and the introduction of ultraviolet germicidal irradiation has been published (*438*).

Other high-risk settings. As the incidence of TB has receded in recent years, new patterns of transmission have become evident. Epidemiologic investigations prompted by an increase in the incidence in TB in a community or state or by the identification of clusters of cases with identical *M. tuberculosis* genotype patterns have detected transmission in such venues as crack houses (*137*) and bars (*27*). In addition, transmission has been identified in association with certain social activities that are not typically considered in routine contact investigations; a church choir (*140*), a floating card game (*172*), exotic dancers and their contacts (*38*), a transgender social network (*34*), and persons who drink together in multiple drinking establishments (*439*).

Although special techniques have been developed for exploring chains of transmission of *M. tuberculosis* in complex social networks (*439*), transmission of *M. tuberculosis* in such settings is not amenable to prevention by available infection-control strategies. These newly identified patterns of transmission of *M. tuberculosis* might be too complex to be detected and controlled by traditional approaches, and real-time *M. tuberculosis* genotyping capable of identifying unsuspected linkages among incident cases might be increasingly useful (*131*).

This new TB threat, transmission in previously unknown settings, has emerged at a time when local TB-control programs often are not prepared to respond. As TB morbidity decreases in the United States and TB-control programs necessarily contract, new approaches will emerge, particularly in low-incidence areas. One model envisions that local public HCWs who do not work exclusively on TB are served by regional TB supervisors, who in turn are supported by statewide consultants and CDC specialists (*172*).

Research Needs to Enhance TB Control

Implementation of the recommendations contained in this statement will likely improve TB control and allow progress to be made toward eliminating TB in the United States. However, achieving TB elimination as defined by ACET (i.e., one annual case of TB per one million population [*11*]) will require substantial advancements in the technology of diagnosis, treatment, and prevention of the disease. IOM has estimated that at the current rate of decline, approximately 6% annually, eliminating TB in the United States would take >70 years (*2*). New tools are needed for the diagnosis, treatment, and prevention of TB to accelerate the decline in TB incidence and reach the elimination threshold sooner (*1,2,45*). In addition, improved tests for the diagnosis of TB and LTBI and more effective drugs to treat them are needed to reduce the substantial worldwide burden of disease and death resulting from TB (*44*).

AFB smear microscopy and the tuberculin skin test, the most commonly used tests for the diagnosis of TB and latent infection respectively, derive from technology developed in the 19th Century; the only available vaccine against TB, BCG, dates from the early 20th Century; and rifampin, the most recent novel compound for treatment of TB, was introduced in 1963. In the long term, the development of a new and effective vaccine would have the greatest impact on the global epidemic of TB, and the United States should lead the research and advocacy efforts to develop such a vaccine (*180,440*). However, other advances in TB diagnosis and treatment might substantially improve the control of TB in the United States. Better means to diagnose and treat LTBI are needed immediately. Breakthrough diagnostics and drugs that would facilitate the more effective usage of this therapeutic intervention to prevent TB would have an immediate and lasting effect on the incidence of the disease in the United States by affecting at least three of the major challenges to TB control in the United States: the substantial pool of persons with LTBI, TB among foreign-born persons, and TB among contacts of persons with infectious TB (Box 1).

Public health interventions to control TB should be based on practices that have been demonstrated to be effective. Because an established scientific basis is lacking for certain fundamental principles of TB control, including certain recommendations contained in this statement, logic, experience, and expert opinion have been used to guide clinical and public health practice to control TB. In the preparation of these recommendations for TB control, deficiencies in evidence were frequently noted. Better understanding is needed of which persons among the millions of foreign-born persons that enter the United States each year (Table 8) are at sufficient additional risk for TB to warrant public health intervention. The approaches recommended for the development of programs for targeted testing of LTBI need additional verification. The new concepts of identifying contacts of infectious TB cases (*439*) require refinement. The optimal method of reducing the concentration of *M. tuberculosis* in ambient air in venues such as homeless shelters is not yet defined (*438*). Methods to monitor and evaluate TB control programs, and in particular, new activities such outbreak surveillance and response (*441*), should be delineated and standardized.

The epidemiology of TB in the United States is constantly changing. Recent examples, as noted throughout this statement, are the increase in TB among foreign-born persons, the upsurge in reports of TB outbreaks, and the persistent high incidence of the disease among U.S.-born non-Hispanic blacks. Epidemiologic studies, including economic analyses, are needed to augment surveillance data and facilitate decisions about allocation of effort and resources to address newly identified facets of the epidemiology of TB.

As new diagnostics are introduced to TB control, operational, economic, and behavioral studies will be needed to determine their most effective use. For example, QFT, a new diagnostic test for LTBI, was licensed in 2001, and early research indicated that this new test might have advantages over the tuberculin skin test in distinguishing between latent *M. tuberculosis* infection and infection with nontuberculous mycobacteria or vaccination with BCG (*102*). However, guidelines on testing for LTBI recommended that QFT should not be used in the evaluation of contacts of infectious cases of TB, for children aged <17 years, for pregnant women, or for patients with immunocompromising conditions, including HIV infection, because of a lack of data from studies in those populations (*103*). A newer version of the test, QFT-G, was licensed in 2004. The role of this new test in these populations has not been determined Thus, considerable research remains to be done to delineate the advantages this new test can bring to TB control.

Despite the best efforts of national, state, and local TB programs, nonadherence to prescribed treatment for TB and latent infection remains a major barrier to TB elimination. As evidence of the importance of that intervention, completion of a course of treatment is the first national performance standard for TB (Table 4). For the outcome of TB treatment to be improved, both patient and health-care provider behaviors related to adherence to TB treatment must be understood, and that understanding should be used to design and implement methods for improving adherence. Although considerable research has been conducted in this field, no comprehensive effort has been undertaken to examine and compile the results and identify best practices. Gaps in knowledge remain, and the need exists to develop and implement a comprehensive behavioral and social science research agenda to address these deficiencies.

Graded Recommendations for the Control and Prevention of Tuberculosis (TB)

Recommendations for TB Laboratory Services

- Laboratorians, clinicians, and public health officials should work together to develop an integrated system that ensures timely laboratory testing and flow of information among laboratorians, clinicians, and TB controllers (AIII).

- Public health laboratorians should take a leadership role to develop the laboratory system and assure that essential laboratory tests for TB control are available, accessible, standardized, reproducible, and with high sensitivity and specificity (AII).
- Public health laboratories should educate laboratory staffs, health-care providers, and public health officials about the most effective uses of clinical microbiologic laboratory services. Such activities might include education programs, development of web-based or written materials, or direct consultation (standard practice [SP]).
- All microbiology laboratories should subscribe to specified turnaround times (Box 2) from date of specimen collection to date when the following results are reported:
  — acid-fast microscopy: ≤24 hours;
  — growth detection of mycobacteria in culture: ≤14 days;
  — identification of *M. tuberculosis* complex: ≤21 days; and
  — drug susceptibility testing: ≤30 days (AII).
- The following laboratory results should be reported immediately (preferably by electronic or fax transmission) by the testing laboratory to the responsible clinician and to the jurisdictional TB control program:
  — a positive smear for AFB and the subsequent growth detection (culture) result of that specimen;
  — identification of *M. tuberculosis* complex in any specimen; and
  — drug susceptibility test results, especially when isolates are drug resistant (AII); and
- Clinical microbiologic laboratories should include, as part of quality improvement, a plan for identification and review of possible false-positive results. Any false-positive result should trigger an inquiry and a plan of correction (*155*) (SP).

Recommendations for TB Case Detection

- Steps recommended by IOM (*2*) to improve public knowledge and awareness about the risk factors for TB, symptoms of TB, and the implications of the diagnosis of latent infection should be undertaken by TB-control programs, community-based organizations representing populations at high risk, and academic health sciences institutions. Targeted education of populations at high risk might be particularly effective in neutralizing the stigma associated with TB among foreign-born populations on the basis of cultural beliefs in their country of origin. Programs for patient education should always be designed with input from the targeted community (AII).
- Because nonpublic health medical practitioners most often conduct the initial evaluation on persons who have symptoms related to TB, health departments, academic institutions, and medical professional organizations should provide continuing education about TB to their constituent health-care providers. These efforts should be focused on clinicians serving populations at high risk for TB on the basis of local or regional trends in TB epidemiology (AIII).
- Jurisdictional public health agencies should ensure that clinicians who evaluate persons with suspected TB have access to current, accurate, and timely diagnostic services (SP).
- Guidelines for detection of TB cases in clinical settings should be followed by primary care, ED, and hospital-based practitioners (Table 5).
- Screening for TB cases during contact and outbreak investigations and during the evaluation of immigrants and refugees with Class A/B1/B2 TB notification status has a high yield of finding cases (Table 6) and should be given high priority as a method for TB case detection (AII).
- Public health programs should identify other opportunities for screening for TB disease on the basis of the local epidemiology of TB, such as in congregate settings, homeless shelters, and correctional facilities in which the consequences of an undiagnosed case are severe. All case detection activities should be evaluated periodically to determine their usefulness (AII).

Recommendations for Contact Investigations and for Outbreak Prevention and Response

- Contact investigations are a critical component of TB control, following only TB case detection and treatment in priority (AIII).
- State and local health departments should establish a comprehensive contact investigation program to ensure that contacts of infectious TB cases are identified, access to adequate care is provided, and therapy is completed (AIII).
- TB-control programs should develop a protocol for conducting contact investigations that identifies persons responsible for each step of the investigation and outline processes to maximize the efficiency of the process within the framework of available resources (AIII).
- TB-control programs should have procedures for voluntary HIV counseling and testing of contacts. Those procedures should set priorities for HIV counseling and testing of contacts on the basis of locally derived data on the risk for HIV infection among contacts or, alternatively, on the local epidemiology of TB and HIV infection (BIII).

- Tuberculin skin testing of contacts should establish as first priorities those contacts who are at highest risk for progressing from LTBI to TB disease on the basis of transmission risk assessment and the presence in contacts of risk factors for progression (e.g., age <5 years, HIV infection, and other immunocompromising conditions (*4*) (AII).
- DOT for LTBI should be considered for all contacts. High risk contacts should receive highest priority for directly observed treatment (AIII).
- TB-control programs should apply existing communicable disease laws that protect the health of the community to contacts who fail to comply with the examination requirements (BIII).
- TB-control programs should develop guidelines, in conjunction with the program legal office and in compliance with HIPAA rule, for release of confidential information related to conducting contact investigations (BIII).
- TB-control programs should evaluate the effectiveness and impact of contact investigations and develop interventions to improve performance when indicated (BIII).
- TB-control programs should develop outbreak response plans for their jurisdictions. These plans should include indications for initiating the plan, notification procedures, composition of the response team, source of staffing, plan for follow-up and treatment of contacts, indications for requesting assistance from CDC, and a plan for evaluating the outbreak response (BIII).

Recommendations for the Public Health Aspects of Targeted Testing and Treatment of LTBI

- When a TB-control program is prepared to develop strategies for targeted testing and treatment of LTBI (i.e., the program satisfies national objectives for management of TB cases and contacts [Table 4]), it should begin by identifying populations and communities at high risk for LTBI within its jurisdiction and establish priorities for intervention (AIII).
- Populations and communities should be categorized on the basis of the expected impact and efficacy of targeted testing in the setting. Tier 1 groups (Box 6) should receive the highest priority, followed by groups in Tier 2 and Tier 3 (AII).
- Once the targeted population or community has been identified, strategic and operational decisions should be made on how best to establish the targeted testing and treatment program. Questions to decide include where to locate the program, how to identify and allocate resources, what training is needed for practitioners and patients, and what data-management needs exist. Focus groups, influential community leaders, associations and community action agencies, religious organizations, coalitions, block organizations, and informal community groups all can contribute to these decisions (AII).
- Public health agencies that establish targeted testing and treatment programs should maximize patient convenience and acceptance through strategies such as employing, when possible, staff members from the populations being served, medical translation, cultural awareness and sensitivity, flexible clinic hours, outreach services for patient transport, and the use of incentives and enablers. All services should be free of cost to patients (AII).
- Targeted testing programs established in the community (e.g., at community health centers, schools, prisons, jails, substance abuse centers, and homeless shelters) should receive full support from the jurisdictional public health agency. Such support might be decisive in the success of nonpublic health targeted testing and treatment programs. Types of support should include training and education of providers, patient education materials, provisions of medication, radiographs and other laboratory services, clinical consultation, and design of tracking and data management systems (AII).
- Targeted testing programs should be routinely and systematically evaluated for their effectiveness, efficiency and impact. Programs that are not effective should be improved or discontinued (AIII).

Recommendations for TB Control Among Children and Adolescents

Case Detection and Primary Prevention Strategy

- Timely reporting of suspected cases of infectious TB is crucial to the prevention of TB among children (AII).
- Contact investigation of adults with infectious TB is the most important activity for early detection of TB among children, identification of children with LTBI who are at high risk for progressing to primary TB and its sequellae, and determination of the drug susceptibility pattern of the *M. tuberculosis* isolate causing TB disease or LTBI in a child. Contact investigations should be timely and thorough, and adequate resources for them should be made available. This should be one of the highest priority goals of any TB-control program (AII).

- Children aged <5 years who have been identified as contacts of persons with infectious TB should receive a clinical evaluation, including a tuberculin skin test and chest radiograph, to rule out active TB. Once active TB has been ruled out, children with positive tuberculin skin test results should receive a full course of treatment for LTBI. Those who have negative skin test results should also receive treatment for presumed LTBI. This intervention is especially critical for infants and toddlers aged <3 years but is recommended for all children aged <5 years. A second tuberculin test is then placed at least 3 months after exposure to infectious TB has ended. If the second test result is positive, treatment should be continued for a full course of treatment for LTBI. If the second test result is negative, treatment may be stopped (AII).

Case Management

- DOT should be the standard of care for treatment of TB disease among children and adolescents (AII).
- As adherence to treatment is no better for children than for adults, all efforts should be made to support children and families through treatment of TB through comprehensive case management (AIII).

Contact Investigation

- Infants and younger children with primary TB disease are rarely if ever contagious. They do not need to be excluded from activities or isolated in health-care settings (AII).
- Children and adolescents of any age with characteristics of adult-type TB (i.e., productive cough and cavitary or extensive upper lobe lesions on chest radiograph) should be considered potentially contagious at the time of diagnosis (AII).
- Infants with suspected or proven congenital pulmonary TB should be considered contagious and effective infection-control measures should be undertaken (AII).
- Adults who accompany and visit children with TB in health-care settings should be evaluated for TB disease as soon as possible to exclude the possibility that they are the source case for the child. These adults should have a chest radiograph to rule out pulmonary TB and to prevent the possibility of transmission within the health-care setting (AII).
- Testing of the contacts of children aged <4 years with LTBI is recommended for persons sharing a residence with the child or those with equally close contact. Such investigations may be performed by public health agencies or primary health-care providers (BII).

Targeted Testing and Treatment of LTBI

- Contact investigations of adults with TB and targeted tuberculin skin testing of foreign-born children from countries with a high incidence of TB are the best and most efficient methods for finding children with LTBI (AII).
- Because foreign birth in a country with a high prevalence of TB is the greatest attributable risk factor for LTBI, children born in or with extensive travel to such countries should be targeted for testing for LTBI. This includes foreign-born adopted children. Testing for LTBI among children with low risk for infection should be avoided (AII).
- A risk assessment questionnaire can be used to identify children with risk factors for LTBI who should undergo a tuberculin skin test (AI).
- A decision to place a tuberculin skin test is a commitment to arrange evaluation and treatment for LTBI (SP).
- A tuberculin skin test should always be placed, read, and interpreted by specifically trained persons (SP).
- In general, foreign-born children with LTBI should be treated with isoniazid unless information exists linking them to a specific case of isoniazid-resistant TB (AIII).
- DOT should be considered strongly as the means of treatment for newborns and infants, contacts of persons with recent cases, and immune-compromised children and adolescents with LTBI because they are at greatest risk for progression to TB disease (AIII).

Recommendations for TB Control Among Foreign-Born Persons

Surveillance

- Public health agencies in states and communities with a substantial number of TB cases among foreign-born persons should develop enhanced surveillance methods in order to gain a detailed understanding of the local epidemiology of TB among foreign-born persons. This is important for program planning and to ensure that recently arrived immigrants, refugees, and other foreign-born persons at high risk have access to medical and public health services (AIII).
- Imported cases of TB present at the time of entry should be distinguished from incident cases, i.e., those that arise during residence in the United States (AIII).
- Cases of TB among persons granted temporary entry to the United States as visitors, students, and temporary workers and unauthorized aliens (Table 7) should be distinguished from those among foreign-born permanent residents (AIII).

- Cases identified as a result of targeted testing activities should be distinguished from those identified by noting symptoms of active TB (AIII).
- For TB control along the U.S.-Mexico border to be facilitated, a binational TB case definition and TB registry system should be adopted and evaluated (AIII).

Case Detection

- Jurisdictional public health agencies responsible for TB control should undertake or engage community groups to undertake education campaigns for foreign-born persons at high risk. These campaigns should communicate the importance of TB as a personal and public health threat, the symptoms to look for, how to access diagnostic and targeted testing services in the community, and the concept of LTBI. The purpose of this education is to destigmatize the infection, acquaint the population with available medical and public health services, and explain the approaches used to treat, prevent, and control TB (AIII).
- Public health agencies conducting TB-control programs should establish liaisons with primary care physicians, community health centers, hospital EDs, and other organizations that provide health care for foreign-born populations at high risk to provide TB publications and guidelines and education about the local epidemiology of TB (AIII).
- Public health agencies conducting TB-control programs should establish liaisons with civil surgeons within their jurisdictions. They should also ensure that civil surgeons have access to recent TB publications and guidelines and that they promptly report all suspected cases of TB (AIII).
- CDC should provide standardized education and training programs with a formal certification process for panel physicians and civil surgeons. As part of the certification, continuing education programs should be required (AIII).
- Federal, state and local public health agencies should assign high priority to the follow-up of immigrants with a Class A TB waiver and Class B1 and B2 TB notification status (AII).

Case Management

- Culturally appropriate case management should be instituted, including readily available professional translation and interpretation services, for all foreign-born persons. If possible, outreach workers should be from the patient's own cultural background (AII).

Contact Investigation

- Local and state jurisdictions should assign high priority to contact investigations of foreign-born persons with TB because of the high likelihood of identifying persons with LTBI as well as secondary TB cases (AII).
- Culturally sensitive and appropriate contact investigation protocols should be established (AIII).

Targeted Testing and Treatment of LTBI

- In jurisdictions where foreign-born persons constitute a major proportion of the TB burden, targeted testing and treatment of LTBI for foreign-born persons at high risk (*4*) should be implemented as a primary means of preventing TB in the community. The tiered approach (Box 6), which is based on access to the target populations and likelihood of implementing a successful program, should be employed (AII).
- In developing the plan for targeted testing and treatment of LTBI among foreign-born persons at high risk, TB-control programs should collaborate with health-care providers, neighborhood health centers, and community advocacy groups that serve and work with the target populations (AII).
- The testing of immigrants and refugees with a Class A TB waiver and Class B1 and B2 TB notification status for LTBI as well as for active TB should always be prioritized (AII).
- Targeted testing and treatment of foreign-born children at high risk aged <15 years should be a priority (SP).
- When resources permit, DOT for LTBI should be used to ensure high completion rates (BII).
- Jurisdictional public health agencies should work with local colleges and universities to develop targeted testing protocols for foreign-born students at high risk and assist with treatment of LTBI (BIII).

Recommendations for TB Control Among HIV-Infected Persons

HIV Counseling and Testing

- Voluntary HIV counseling and testing is recommended for all patients with TB and should be considered the standard of care. In extreme circumstances, if establishing priorities is necessary as a result of resource constraints, patients aged 25–44 years should receive highest priority (SP).
- Clinic staff members at sites where patients with TB are followed should receive up-to-date education and training on the most current concepts and methodology of voluntary HIV counseling, testing, and referral. If on-site HIV

testing is not feasible, TB facilities should have well-established arrangements for referral to other testing sites (SP).

- Voluntary HIV counseling and testing should be offered routinely to contacts of HIV-infected TB cases (AII).
- Voluntary HIV counseling and testing should be offered to all contacts that are members of populations with a prevalence of HIV infection ≥1% (*302*). In other communities and settings, the decision of whether to routinely offer voluntary HIV counseling and testing to contacts of persons with infectious TB should be based on the local epidemiology of HIV infection and TB. In communities or settings where populations at risk for TB are also known to have high rates of HIV infection (e.g., injection drug users (IDUs) in inner cities [*317*]), all contacts should be routinely offered voluntary HIV counseling and testing. In communities and settings in which the HIV seroprevalence likely approaches that of the general U.S. population (<0.1%), a risk-factor assessment for HIV infection should be included in the evaluation of contacts of infectious cases, and contacts with clinical or behavioral risk factors for HIV infection (*302*) should receive voluntary HIV counseling and testing (AII).
- Persons with LTBI who are members of populations with a prevalence of HIV infection ≥1% should be routinely offered voluntary HIV counseling and testing (*302*). Otherwise the decision of whether to routinely offer HIV counseling and testing to persons with LTBI should based on the local epidemiology of HIV infection and TB. In communities or settings where populations at risk for TB are also known to have high rates of HIV infection (e.g., IDUs in inner cities [*317*]), routine counseling and testing among patients with LTBI is indicated. In other communities and settings the HIV seroprevalence is likely to approach that of the general U.S. population (<0.1%), a risk-factor assessment for HIV infection should be included as a standard part of the initial evaluation for all persons diagnosed with LTBI. Persons with clinical or behavioral risk factors (*302*) should receive HIV counseling and testing (AII).
- Routine periodic cross-matches of jurisdictional HIV and TB case registries should be conducted to ensure completeness of reporting of both diseases (SP).

Case Detection

- Physicians who provide primary care to persons with HIV infection or populations at increased risk for HIV infection should maintain a high index of suspicion for TB. Every patient in whom HIV infection has been newly diagnosed should be assessed for the presence of TB or LTBI. This should include a history for symptoms compatible with TB (e.g., cough of ≥2–3 weeks' duration, fever, night sweats, weight loss, or hemoptysis, or unexplained cough and fever [Table 5]) and of exposure to persons with TB. Physical examination should include examination of extrapulmonary sites such as lymph nodes, and a chest radiograph should be taken to check for findings of current or previous TB. Testing for *M. tuberculosis* infection by using the tuberculin skin test should be conducted, and patients with ≥5 mm of induration be considered to have a positive test and should receive, in addition to chest radiography, a clinical evaluation to rule out TB (*4*) (SP).
- Public health agencies conducting TB-control activities should maintain close contact with HIV control programs, medical practitioners and clinics, community-based organizations, homeless shelters, correctional facilities, and housing facilities that serve persons with HIV infection to ensure that a high index of awareness of TB is maintained by persons who provide services at those sites and by their HIV-infected patients (AIII).
- Health-care facilities, social service agencies, and work sites that serve patients with HIV infection should establish firm lines of referral for patients with respiratory symptoms (AIII).

Case Management

- Public health agencies conducting TB-control activities should have access to consultants with expertise in managing HIV related TB (SP).
- Management of TB and HIV infection should be effectively integrated and should include a multidisciplinary team of providers and supportive care (AIII).
- Comprehensive case management, including DOT, is strongly recommended for persons with HIV infection who have TB (AII).
- HIV-infected patients with TB and a CD4 count <100 cells/μL should receive DOT daily or three times per week (A1).

Contact Investigation

- Contact investigations of persons with TB and known or suspected HIV infection and those conducted in any circumstance in which HIV-infected persons could have been exposed to a person with infectious TB should have the highest priority and be completed without delay (AII).
- Persons with known or suspected HIV infection who have contact with a patient with infectious pulmonary TB should be offered a full course of treatment for LTBI regardless of the initial result of tuberculin skin testing once active TB has been ruled out (AII).

Targeted Testing and Treatment of LTBI

- Targeted testing and treatment for LTBI are strongly recommended at the time the diagnosis of HIV infection is established (AII).
- For HIV-infected persons whose initial tuberculin skin test is negative, repetitive testing is recommended (at least yearly) if the local epidemiologic setting indicates an ongoing risk for exposure to TB (AII).
- An HIV-infected patient who is severely immunocompromised and whose initial tuberculin skin test result is negative should be retested after the initiation of antiretroviral therapy and immune reconstitution, when CD4 cell counts are greater than 200 cells/μL) (AII).
- HIV-infected persons who receive a diagnosis of LTBI should receive high priority for DOT (BIII).

Institutional Infection Control

- HIV-infected persons should be advised that certain occupations and activities increase the likelihood of exposure to TB. These include employment and volunteer work in certain health-care facilities, correctional institutions, and shelters for the homeless, as well as in other high-risk settings identified by jurisdictional health authorities. The decision about continuing employment or volunteer activities in a high-risk setting should be made in consultation with a health-care professional and be based on factors such as the person's specific duties in the workplace, prevalence of TB in the community, and the degree to which precautions are taken to prevent TB transmission in the workplace (AIII).

Recommendations for TB Control Among Homeless Persons

Surveillance and Case Detection

- Information on whether the person is homeless should be included for each reported TB case to determine the importance of homelessness in the TB morbidity in the state or community. This is particularly important for communities that provide shelters or other congregate living facilities that are conducive to the transmission of TB (AII).
- In designing programs for control and prevention of TB in homeless persons, public health agencies should work closely with providers of shelter, housing, primary health care, treatment for alcoholism or substance abuse, and social services to ensure a comprehensive approach to improving the health and welfare of this population (AIII).
- Public health agencies should closely monitor the location, mode (i.e., screening or symptomatic presentation), and timeliness of diagnosis of TB in homeless persons in their community and use such data to develop more effective control strategies (AIII).
- Public health agencies should identify providers of medical care for homeless persons and facilities that serve homeless persons (e.g., hospital EDs and correctional institutions) to ensure that practices and procedures are implemented to readily detect and report suspected cases of TB (AIII).
- Providers of primary health care for homeless persons should be knowledgeable about how to diagnose (Table 5), isolate, and report suspected cases of TB (AIII).
- Public health agencies should have ready access to an inpatient facility for the isolation and induction phase of therapy of homeless patients with infectious TB (AII).
- Public health agencies should be prepared to conduct activities to detect TB among persons without symptoms and enhance TB case detection as part of a plan for TB control among homeless persons (Table 6). Indications for screening for TB disease include 1) a documented outbreak, 2) an increase in incidence of TB in the homeless population, and 3) evidence of current transmission of TB in the population. Shelters should always be suspected as sites of transmission (AII).

Case Management

- Case management for homeless persons with TB should be structured to encourage adherence to treatment regimens by making TB treatment a major priority for the patient. It should include provision of housing, at least on a temporary basis; an increasing number of models have demonstrated the importance of a housing incentive in successful treatment of TB in homeless persons. Case management should also include establishing linkages with providers of alcohol and substance treatment services, mental health services, and social services (AII).

Contact Investigation

- Health departments should regularly evaluate their methods for contact investigation for cases of TB among homeless persons to identify barriers and develop alternative strategies, such as shelter- or other location-based contact investigations oriented to possible sites of transmission. Factors to evaluate should include timeliness of completing contact investigations, number of contacts identified and evaluated per case, proportion of evaluated contacts with LTBI and TB disease, and completion of treatment of LTBI among contacts (AII).

Targeted Testing and Treatment of LTBI

- Targeted testing and treatment of LTBI should be a priority for homeless populations because studies from throughout the United States have demonstrated high rates of transmission of *M. tuberculosis* in this group. This epidemiologic situation, causing a high ongoing risk for acquiring LTBI and TB disease, might necessitate repetitive testing for *M. tuberculosis* infection among homeless persons (AII).
- When high rates of transmission of *M. tuberculosis* are documented among homeless persons, those with a positive test for *M. tuberculosis* infection should be presumed to be recently infected and treated for LTBI (AIII).

Institutional and Environmental Controls

- Organizations that provide shelter and other types of emergency housing for homeless persons should develop institutional TB-control plans. Guidelines to facilitate this process are available from CDC (*9*) and the Francis J. Curry National TB Center (*403*) (AII).

Recommendations for TB Control Among Detainees and Prisoners

Case Detection and Case Management

- All jails and prisons should conduct a TB case detection program for detainees and prisoners entering the facility as well as for those who become ill during incarceration to ensure prompt isolation of contagious cases of TB (AII).
- Strategies for case detection for incoming detainees and prisoners include symptom surveys (BIII), testing for *M. tuberculosis* infection followed by chest radiography (BIII) for those with a positive test, and universal chest radiography in jails (BII). In each setting, the adopted strategy should receive ongoing evaluation.
- Each correctional facility's health-care program for inmates and staff should ensure that training in the clinical and public health aspects of TB and other diseases of public health significance is provided in an ongoing manner (SP).
- Detainees and prisoners with signs and symptoms of TB should be placed in respiratory isolation on-site or off-site until infectious TB is ruled out (SP).
- Case-management strategies including DOT and incentives should be used to assure completion of therapy of detainees and prisoners with TB (BII).
- When detainees and prisoners receiving therapy for TB are transferred to another facility or released from detention, responsibility for continuation of the treatment plan should be transferred to the appropriate facility or agency, and the jurisdictional TB-control program should be notified (SP).

Contact Investigation

- Contact investigations of infectious TB cases in corrections facilities should receive equal priority as effective case detection as the primary means of aborting TB outbreaks. Facilities should have written procedures for contact investigations and have adequate staff to ensure prompt and thorough contact investigations. They should also consult with the jurisdictional public health TB-control program (AII).

Targeted Testing and Treatment of LTBI

- Prisons should implement a treatment program for prisoners with LTBI as part of the effort to prevent the transmission of *M. tuberculosis* within their walls and to contribute to the overall goal of TB elimination (AII).
- Treatment programs for LTBI in jail detainees should be undertaken only if it is possible to develop a successful plan for community follow-up of released persons on treatment (AII).
- Reducing the length of treatment for LTBI is more likely to lead to completion of treatment in correctional facilities; 4 months of rifampin is recommended as an alternative for the treatment of LTBI (*4,324*). Correctional health providers need to consider the costs and benefits of this regimen compared with the standard 9-month course of isoniazid in each individual case (BIII).

Institutional Infection Control

- Jails and prisons should implement effective infection-control programs including risk assessment, staff training, screening and treatment of LTBI, isolation of inmates with infectious forms of TB, treatment and discharge planning, and contact investigation (AII).
- HIV-infected detainees and prisoners should not be housed together in a separate facility unless institutional control programs following current guidelines have been established and proved to be effective in preventing the transmission of *M. tuberculosis* (AIII).

Recommendations for TB Control in Health-Care Facilities and Other High-Risk Settings

- All health-care institutions and other sites at high risk for transmission of *M. tuberculosis* should have in place a TB infection control program; they should implement and enforce procedures to promptly identify,

isolate, and either manage or refer persons with suspected and confirmed infectious TB (AII).

- All health-care institutions that care for persons with TB and other sites that are at risk for transmission should implement TB infection-control measures based on a hierarchy of administrative controls, engineering controls, and respiratory protection. Administrative controls and early recognition of persons with TB are the most important parts of an airborne infection control program for TB (AII).
- Employees who have first contact with patients in settings that serve populations at high risk for TB should be trained to detect persons who could have infectious TB. Patients should be routinely asked about exposure to *M. tuberculosis*, previous TB infection or disease, current symptoms suggestive of TB, and medical conditions that increase the risk for TB. The medical evaluation should include an interview conducted in the patient's primary language, with the assistance of a medical interpreter if necessary (AIII).
- The index of suspicion for TB should be very high in health-care settings located in geographic areas where TB is prevalent and those serving patients at high risk for TB. Guidelines exist for conducting an evaluation for suspected pulmonary TB in adults at high risk (Table 5) (AIII).
- Among persons suspected of having TB, arrangements should be available for the diagnosis to be promptly established and standard therapy initiated (AII).
- HCWs and employees in other high-risk settings should be tested for *M. tuberculosis* infection upon employment. Subsequent testing should be based on risk assessment (AIII).
- Health-care facilities and other high-risk institutions should conduct a risk assessment to determine the frequency of testing for *M. tuberculosis* infection among employees, as a component of the proper level of TB infection control measures (AIII).
- For HCWs and employees in other high-risk settings with no other risk factors for TB, a cut-off of 15 mm of induration (rather than 10 mm) on the tuberculin skin test should be used to define a positive baseline test at the time of initial employment. An increase of $\geq$10 mm in reaction size is generally accepted as a positive test result on subsequent testing unless the worker is a contact of a TB case or has HIV infection or is otherwise immunocompromised, in which case a result of $\geq$5 mm is considered positive (AIII).
- Employees with *M. tuberculosis* infection should have a chest radiograph performed to exclude TB disease and should be evaluated for treatment of LTBI, based on current recommendations (AII).
- HCWs and employees in other high risk settings with an indication for treatment of LTBI should be encouraged to initiate and complete treatment (AII).
- Residents admitted to long-term care facilities should be tested for *M. tuberculosis* infection upon admission (with a two-step test if using tuberculin skin testing) and should receive a history and physical examination to detect symptoms and signs of TB. Residents with *M. tuberculosis* infection should be offered treatment if indicated (*4,324*), with careful monitoring for drug toxicity (BII).
- Jails and prisons should develop and implement effective infection-control programs including risk assessment, staff training, screening for TB among incoming detainees and prisoners, isolation of inmates with infectious forms of TB, treatment and discharge planning and prompt and thorough contact investigations (AII).
- In jails and prisons, HIV-infected inmates should not be housed together in a separate housing unit unless institutional control programs following current guidelines have been established and proved to be effective in preventing the transmission of *M. tuberculosis* (AII).
- Organizations that provide shelter and other types of emergency housing for homeless persons should develop institutional TB-control plans. Guidelines to facilitate this process are available from the Francis J. Curry National TB Center (*403*) (AII).
- TB-control programs should remain aware of the possibility of TB disease as a result of current transmission when conducting epidemiologic surveillance and contact investigations. *M. tuberculosis* genotyping should be immediately available to any program that is investigating possible transmission of *M. tuberculosis* (AII).
- In an era of declining rates of TB in the United States, expertise in the recognition, diagnosis and treatment of TB is likely to decline, especially in areas in which incidence is low (*48*). Because the risk for spread of *M. tuberculosis* increases when the diagnosis is not promptly made, institutional education programs for HCWs, including physicians in training, should be made a continuing priority (AIII).

Recommendations on Research for Progress Toward Elimination of TB

- A comprehensive TB research plan for the United States should be developed that identifies the major areas of need and the most effective research approaches to meet those needs. CDC and NIH should convene a broadly-based group of experts and stakeholders to develop this plan (AIII).

- The availability of improved diagnostic tests and therapies for LTBI would have an immediate and lasting impact on the incidence of TB in the United States, and research in those fields should be a priority (AIII).
- Research leading to a new and effective TB vaccine is one of the most important contributions that the United States can make to the global TB epidemic and should be a priority (AIII).
- The CDC-funded Tuberculosis Epidemiological Studies Consortium and Tuberculosis Trials Consortium represent excellent new models for bringing resources from the Federal government, public health agencies, and academia together to plan and implement research for the assessment of new diagnostics and drugs and epidemiologic and operational research on TB. These initiatives should be a priority (AIII).
- Because a substantial number of recommendations for TB control are based on logic, anecdotal experience, and expert opinion, additional research, including clinical, operational, behavioral, and economic research should focus on unanswered questions relating to the basic elements of TB control (AIII).

Acknowledgments

The following persons provided constructive and helpful insights: WJ Burman, MD, Denver Public Health, Denver, Colorado. EP Desmond, MD, California Department of Health Services, Richmond; PC Hopewell, MD, San Francisco General Hospital, University of California, San Francisco; A Green Rush, Francis J. Curry National Tuberculosis Center, San Francisco, California. RJ O'Brien, MD, Foundation for Innovative New Diagnostics, Geneva, Switzerland. T Oemig, Wisconsin Division of Public Health, Madison, Wisconsin. PM Small, MD, The Bill and Melinda Gates Foundation, Seattle; G Wang, MD, Puget Sound Neighborhood Health Centers, Seattle, Washington. KG Castro, MD, MF Iademarco, MD, L Nelson, MD, TR Navin, MD, T Shinnick, MD, Div of TB Elimination, National Center for HIV, STD, & TB Prevention, Coordinating Center for Infectious Diseases, CDC. A Lipavsky and B Nodell also assisted in the preparation of this report.

References

1. CDC. Tuberculosis elimination revisited: obstacles, opportunities, and a renewed commitment—Advisory Council for the Elimination of Tuberculosis (ACET). MMWR 1999;48(No. RR-9):1–13.
2. Institute of Medicine. Ending neglect: the elimination of tuberculosis in the United States. Washington, DC: Institute of Medicine, National Academy Press; 2000.
3. American Thoracic Society, CDC, Infectious Diseases Society of America. Diagnostic standards and classification of tuberculosis in adults and children. Am J Respir Crit Care Med 2000;161(4 Pt 1):1376–95.
4. American Thoracic Society, CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. Am J Respir Crit Care Med 2000;161(4 Pt 2):S221–47.
5. American Thoracic Society, CDC, Infectious Diseases Society of America. Treatment of tuberculosis. Am J Respir Crit Care Med 2003;167:603–62.
6. American Thoracic Society, CDC, Infectious Diseases Society of America. Control of tuberculosis in the United States. Am Rev Respir Dis 1992;146:1623–33.
7. Kish MA; Infectious Diseases Society of America. Guide to development of practice guidelines. Clin Infect Dis 2001;32:851–4.
8. Horsburgh CR Jr., Feldman S, Ridzon R; Infectious Diseases Society of America. Practice guidelines for the treatment of tuberculosis. Clin Infect Dis 2000;31:633–9.
9. CDC. Guidelines for preventing opportunistic infections among HIV-infected persons—2002: recommendations of the U.S. Public Health Service and the Infectious Diseases Society of America. MMWR 2002;51(No. RR-8):1–52.
10. CDC. Guidelines for preventing the transmission of *Mycobacterium tuberculosis* in health-care facilities, 1994. MMWR 1994;43(No. RR-13): 1–132.
11. CDC. A strategic plan for the elimination of tuberculosis in the United States. MMWR 1989;38:269–72.
12. National Coalition for the Elimination of Tuberculosis. Tuberculosis elimination: the federal funding gap. Washington, DC: National Coalition for the Elimination of Tuberculosis; 2002.
13. Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City—turning the tide. N Engl J Med 1995;333:229–33.
14. CDC. Reported tuberculosis in the United States, 2003. Atlanta, GA; US Department of Health and Human Services, CDC; 2004.
15. CDC. Trends in tuberculosis—United States, 1998–2003. MMWR 2004;53:209–14.
16. McKenna MT, McCray E, Jones JL, Onorato IM, Castro KG. The fall after the rise: tuberculosis in the United States, 1991 through 1994. Am J Public Health 1998;88:1059–63.
17. CDC. Essential components of a tuberculosis prevention and control program: recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR 1995;44(No. RR-11):1–16.
18. Rubel AJ, Garro LC. Social and cultural factors in the successful control of tuberculosis. Public Health Rep 1992;107:626–36.
19. Asch S, Leake B, Gelberg L. Does fear of immigration authorities deter tuberculosis patients from seeking care? West J Med 1994;161:373–6.
20. Sherman LF, Fujiwara PI, Cook SV, Bazerman LB, Frieden TR. Patient and health care system delays in the diagnosis and treatment of tuberculosis. Int J Tuberc Lung Dis 1999;3:1088–95.
21. Talbot EA, Moore M, McCray E, Binkin NJ. Tuberculosis among foreign-born persons in the United States, 1993–1998. JAMA 2000;284:2894–900.
22. DeRiemer K, Rudoy I, Schecter GF, Hopewell PC, Daley CL. The epidemiology of tuberculosis diagnosed after death in San Francisco, 1986–1995. Int J Tuberc Lung Dis 1999;3:488–93.
23. Kramer F, Modilevsky T, Waliany AR, Leedom JM, Barnes PF. Delayed diagnosis of tuberculosis in patients with human immunodeficiency virus infection. Am J Med 1990;89:451–6.
24. Rao VK, Iademarco EP, Fraser VJ, Kollef MH. Delays in the suspicion and treatment of tuberculosis among hospitalized patients. Ann Intern Med 1999;130:404–11.
25. Curtis AB, Ridzon R, Vogel R, et al. Extensive transmission of *Mycobacterium tuberculosis* from a child. N Engl J Med 1999;341:1491–5.

26. Fitzpatrick LK, Hardacker JA, Heirendt W, et al. A preventable outbreak of tuberculosis investigated through an intricate social network. Clin Infect Dis 2001;33:1801–6.
27. Weis SE, Pogoda JM, Yang Z, et al. Transmission dynamics of tuberculosis in Tarrant County, Texas. Am J Respir Crit Care Med 2002;166:36–42.
28. Bishai WR, Graham NM, Harrington S, et al. Molecular and geographic patterns of tuberculosis transmission after 15 years of directly observed therapy. JAMA 1998;280:1679–84.
29. Chin DP, Crane CM, Diul MY, et al. Spread of *Mycobacterium tuberculosis* in a community implementing recommended elements of tuberculosis control. JAMA 2000;283:2968–74.
30. Reichler MR, Reves R, Bur S, et al. Evaluation of investigations conducted to detect and prevent transmission of tuberculosis. JAMA 2002;287:991–5.
31. Marks SM, Taylor Z, Qualls NL, Shrestha-Kuwahara RJ, Wilce MA, Nguyen CH. Outcomes of contact investigations of infectious tuberculosis patients. Am J Respir Crit Care Med 2000;162:2033–8.
32. Reichler MR, Reves R, Bur S, et al.; Contact Investigation Study Group. Treatment of latent tuberculosis infection in contacts of new tuberculosis cases in the United States. South Med J 2002;95:414–20.
33. Barnes PF, Yang Z, Pogoda JM, et al. Foci of tuberculosis transmission in central Los Angeles. Am J Respir Crit Care Med 1999;159 (4 Pt 1):1081–6.
34. Sterling TR, Thompson D, Stanley RL, et al. A multi-state outbreak of tuberculosis among members of a highly mobile social network: implications for tuberculosis elimination. Int J Tuberc Lung Dis 2000;4:1066–73.
35. CDC. Drug-susceptible tuberculosis outbreak in a state correctional facility housing HIV-infected inmates—South Carolina, 1999–2000. MMWR 2000;49:1041–4.
36. Conover C, Ridzon R, Valway S, et al. Outbreak of multidrug-resistant tuberculosis at a methadone treatment program. Int J Tuberc Lung Dis 2001;5:59–64.
37. McLaughlin SI, Spradling P, Drociuk D, Ridzon R, Pozsik CJ, Onorato I. Extensive transmission of *Mycobacterium tuberculosis* among congregated, HIV-infected prison inmates in South Carolina, United States. Int J Tuberc Lung Dis 2003;7:665–72.
38. CDC. Cluster of tuberculosis cases among exotic dancers and their close contacts—Kansas, 1994–2000. MMWR 2001;50:291–3.
39. Bennett DE, Courval JM, Onorato IM, et al. Prevalence of TB infection in the US population, 1999–2000 [Abstract 67921]. In: Program and abstracts, 131st annual meeting of the American Public Health Association; San Francisco, California, November 15–19, 2003.
40. Chaulk CP, Grady M. Evaluating tuberculosis control programs: strategies, tools and models. Int J Tuberc Lung Dis 2000;4(2 Suppl 1):S55–60.
41. Nardell EA. Needles in haystacks: diagnosing tuberculosis under low prevalence conditions. Tuber Lung Dis 1996;77:389–90.
42. Mahmoudi A, Iseman MD. Pitfalls in the care of patients with tuberculosis. Common errors and their association with the acquisition of drug resistance. JAMA 1993;270:65–8.
43. Institute of Medicine. The future of public health. Washington, DC: Institute of Medicine, National Academy Press; 1988.
44. Corbett EL, Watt CJ, Walker N, et al. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. Arch Intern Med 2003;163:1009–21.
45. Miller B, Castro KG. Sharpen available tools for tuberculosis control, but new tools needed for elimination. JAMA 1996;276:1916–7.
46. Frieden TR, Sterling TR, Munsiff SS, Watt CJ, Dye C. Tuberculosis. Lancet 2003;362(9387):887–99.
47. Cantwell MF, Snider DE Jr., Cauthen GM, Onorato IM. Epidemiology of tuberculosis in the United States, 1985 through 1992. JAMA 1994;272:535–9.
48. CDC. Progressing toward tuberculosis elimination in low-incidence areas of the United States: recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR 2002;51 (No. RR-5):1–16.
49. Hopewell PC. Targeting tuberculosis prevention. Am J Respir Crit Care Med 2000;162:2017–8.
50. Desonia R. Running on empty: the state budget crisis worsens. National Health Policy Forum Issue Brief 2002(783):1–19.
51. Nolan CM. Community-wide implementation of targeted testing for and treatment of latent tuberculosis infection. Clin Infect Dis 1999;29:880–7.
52. Fischl MA, Uttamchandani RB, Daikos GL, et al. An outbreak of tuberculosis caused by multiple-drug-resistant tubercle bacilli among patients with HIV infection. Ann Intern Med 1992;117:177–83.
53. Beck-Sague C, Dooley SW, Hutton MD, et al. Hospital outbreak of multidrug-resistant *Mycobacterium tuberculosis* infections. Factors in transmission to staff and HIV-infected patients. JAMA 1992; 268:1280–6.
54. Edlin BR, Tokars JI, Grieco MH, et al. An outbreak of multidrug-resistant tuberculosis among hospitalized patients with the acquired immunodeficiency syndrome. N Engl J Med 1992;326:1514–21.
55. Ellis BA, Crawford JT, Braden CR, McNabb SJ, Moore M, Kammerer S; National Tuberculosis Genotyping and Surveillance Network Work Group. Molecular epidemiology of tuberculosis in a sentinel surveillance population. Emerg Infect Dis 2002;8:1197–209.
56. Blumberg HM, Watkins DL, Berschling JD, et al. Preventing the nosocomial transmission of tuberculosis. Ann Intern Med 1995; 122:658–63.
57. Grzybowski S, Barnett GD, Styblo K. Contacts of cases of active pulmonary tuberculosis. Bull Int Union Tuberc 1975;50:90–106.
58. Shaw JB, Wynn-Williams N. Infectivity of pulmonary tuberculosis in relation to sputum status. Am Rev Tuberc 1954;69:724–32.
59. van Geuns HA, Meijer J, Styblo K. Results of contact examination in Rotterdam, 1967–1969. Bull Int Union Tuberc 1975;50:107–21.
60. Bailey WC, Gerald LB, Kimerling ME, et al. Predictive model to identify positive tuberculosis skin test results during contact investigations. JAMA 2002;287:996–1002.
61. Behr MA, Warren SA, Salamon H, et al. Transmission of *Mycobacterium tuberculosis* from patients smear-negative for acid-fast bacilli. Lancet 1999;353(9151):444–9.
62. Stead WW, Lofgren JP, Warren E, Thomas C. Tuberculosis as an endemic and nosocomial infection among the elderly in nursing homes. N Engl J Med 1985;312:1483–7.
63. Stead WW, To T. The significance of the tuberculin skin test in elderly persons. Ann Intern Med 1987;107:837–42.
64. Small PM, Shafer RW, Hopewell PC, et al. Exogenous reinfection with multidrug-resistant *Mycobacterium tuberculosis* in patients with advanced HIV infection. N Engl J Med 1993;328:1137–44.
65. Godfrey-Faussett P, Sonnenberg P, Shearer SC, et al. Tuberculosis control and molecular epidemiology in a South African gold-mining community. Lancet 2000;356(9235):1066–71.

66. Colditz GA, Brewer TF, Berkey CS, et al. Efficacy of BCG vaccine in the prevention of tuberculosis. Meta-analysis of the published literature. JAMA 1994;271:698–702.
67. Fine PE. BCG: the challenge continues. Scand J Infect Dis 2001;33:243–5.
68. Styblo K, Meijer J. Impact of BCG vaccination programmes in children and young adults on the tuberculosis problem. Tubercle 1976;57:17–43.
69. Aronson NE, Santosham M, Comstock GW, et al. Long-term efficacy of BCG vaccine in American Indians and Alaska Natives: a 60-year follow-up study. JAMA 2004;291:2086–91.
70. Sterne JA, Rodrigues LC, Guedes IN. Does the efficacy of BCG decline with time since vaccination? Int J Tuberc Lung Dis 1998;2:200–7.
71. Flynn JL, Chan J. Tuberculosis: latency and reactivation. Infect Immun 2001;69:4195–201.
72. Schluger NW. Recent advances in our understanding of human host responses to tuberculosis. Respir Res 2001;2:157–63.
73. Stead WW. Genetics and resistance to tuberculosis. Could resistance be enhanced by genetic engineering? Ann Intern Med 1992;116:937–41.
74. Sousa AO, Salem JI, Lee FK, et al. An epidemic of tuberculosis with a high rate of tuberculin anergy among a population previously unexposed to tuberculosis, the Yanomami Indians of the Brazilian Amazon. Proc Natl Acad Sci U S A 1997;94:13227–32.
75. Boom WH, Canaday DH, Fulton SA, Gehring AJ, Rojas RE, Torres M. Human immunity to *M. tuberculosis*: T cell subsets and antigen processing. Tuberculosis (Edinb) 2003;83:98–106.
76. Nardell EA, Keegan J, Cheney SA, Etkind SC. Airborne infection. Theoretical limits of protection achievable by building ventilation. Am Rev Respir Dis 1991;144:302–6.
77. Rieder HL. Risk of travel-associated tuberculosis. Clin Infect Dis 2001;33:1393–6.
78. Houk VN, Baker JH, Sorensen K, Kent DC. The epidemiology of tuberculosis infection in a closed environment. Arch Environ Health 1968;16:26–35.
79. Houk VH, Kent DC, Baker JH, Sorensen K, Hanzel GD. The Byrd study. In-depth analysis of a micro-outbreak of tuberculosis in a closed environment. Arch Environ Health 1968;16:4–6.
80. Suzuki S, Nakabayashi K, Ohkouchi H, et al. Tuberculosis in the crew of a submarine [Japanese]. Nihon Kyobu Shikkan Gakkai Zasshi 1997;35:61–6.
81. World Health Organization. Tuberculosis and air travel: guidelines for prevention and control. Geneva, Switzerland: World Health Organization; 1998.
82. CDC. Exposure of passengers and flight crew to *Mycobacterium tuberculosis* on commercial aircraft, 1992–1995. MMWR 1995; 44:137–40.
83. Kato-Maeda M, Bifani PJ, Kreiswirth BN, Small PM. The nature and consequence of genetic variability within *Mycobacterium tuberculosis*. J Clin Invest 2001;107:533–7.
84. Barnes PF, Cave MD. Molecular epidemiology of tuberculosis. N Engl J Med 2003;349:1149–56.
85. Bifani PJ, Mathema B, Liu Z, et al. Identification of a W variant outbreak of *Mycobacterium tuberculosis* via population-based molecular epidemiology. JAMA 1999;282:2321–7.
86. Munsiff SS, Nivin B, Sacajiu G, Mathema B, Bifani P, Kreiswirth BN. Persistence of a highly resistant strain of tuberculosis in New York City during 1990–1999. J Infect Dis 2003;188:356–63.
87. Zhang M, Gong J, Yang Z, Samten B, Cave MD, Barnes PF. Enhanced capacity of a widespread strain of *Mycobacterium tuberculosis* to grow in human macrophages. J Infect Dis 1999;179:1213–7.
88. Middlebrook G, Cohn ML. Some observations on the pathogenicity of isoniazid-resistant variants of tubercle bacilli. Science 1953;118 (3063):297–9.
89. Burgos M, DeRiemer K, Small PM, Hopewell PC, Daley CL. Effect of drug resistance on the generation of secondary cases of tuberculosis. J Infect Dis 2003;188:1878–84.
90. van Soolingen D, Borgdorff MW, de Haas PE, et al. Molecular epidemiology of tuberculosis in the Netherlands: a nationwide study from 1993 through 1997. J Infect Dis 1999;180:726–36.
91. Snider DE Jr., Kelly GD, Cauthen GM, Thompson NJ, Kilburn JO. Infection and disease among contacts of tuberculosis cases with drug-resistant and drug-susceptible bacilli. Am Rev Respir Dis 1985; 132:125–32.
92. Frieden TR, Sherman LF, Maw KL, et al. A multi-institutional outbreak of highly drug-resistant tuberculosis: epidemiology and clinical outcomes. JAMA 1996;276:1229–35.
93. Kamat SR, Dawson JJ, Devadatta S, et al. A controlled study of the influence of segregation of tuberculous patients for one year on the attack rate of tuberculosis in a 5-year period in close family contacts in South India. Bull World Health Organ 1966;34:517–32.
94. Gunnels JJ, Bates JH, Swindoll H. Infectivity of sputum-positive tuberculous patients on chemotherapy. Am Rev Respir Dis 1974; 109:323–30.
95. Brindle R, Odhiambo J, Mitchison D. Serial counts of *Mycobacterium tuberculosis* in sputum as surrogate markers of the sterilising activity of rifampicin and pyrazinamide in treating pulmonary tuberculosis. BMC Pulm Med 2001;1:2.
96. Loudon RG, Spohn SK. Cough frequency and infectivity in patients with pulmonary tuberculosis. Am Rev Respir Dis 1969;99:109–11.
97. Goodwin RA Jr. Pulmonary tuberculosis. In: Wyngaarden JB, Smith LH Jr., eds. Cecil textbook of medicine. Vol 2. 16th ed. Philadelphia, PA: W.B. Saunders Company; 1982:1542–8.
98. Hopewell PC. Mycobacterial diseases. In: Murray JF, Nadel JA, eds. Textbook of respiratory medicine. Philadelphia, PA: W.B. Saunders Company; 1988:856–915.
99. Jindani A, Aber VR, Edwards EA, Mitchison DA. The early bactericidal activity of drugs in patients with pulmonary tuberculosis. Am Rev Respir Dis 1980;121:939–49.
100. Jindani A, Dore CJ, Mitchison DA. Bactericidal and sterilizing activities of antituberculosis drugs during the first 14 days. Am J Respir Crit Care Med 2003;167:1348–54.
101. Earnest MA, Sbarbaro JA. Defining the issues: returning patients with tuberculosis to institutional settings. Clin Infect Dis 1995;20:497–500.
102. Mazurek GH, LoBue PA, Daley CL, et al. Comparison of a whole-blood interferon gamma assay with tuberculin skin testing for detecting latent *Mycobacterium tuberculosis* infection. JAMA 2001;286:1740–7.
103. CDC. Guidelines for using the QuantiFERON-TB test for diagnosing latent *Mycobacterium tuberculosis* infection. MMWR 2003;52 (No. RR-2):15–8.
104. Ferebee SH. Controlled chemoprophylaxis trials in tuberculosis. A general review. Bibl Tuberc 1970;26:28–106.
105. Boucot KR, Dillon ES, Cooper DA, Meier P, Richardson R. Tuberculosis among diabetics: the Philadelphia survey. Am Rev Tuberc 1952;65:1–50.

106. International Union Against Tuberculosis Committee of Prophylaxis. Efficacy of various durations of isoniazid preventive therapy for tuberculosis: five years of follow-up in the IUAT trial. Bull World Health Organ 1982;60:555–64.
107. Gardam MA, Keystone EC, Menzies R, et al. Anti-tumour necrosis factor agents and tuberculosis risk: mechanisms of action and clinical management. Lancet Infect Dis 2003;3:148–55.
108. Ellerin T, Rubin RH, Weinblatt ME. Infections and anti-tumor necrosis factor alpha therapy. Arthritis Rheum 2003;48:3013–22.
109. CDC. Tuberculosis associated with blocking agents against tumor necrosis factor-alpha—California, 2002–2003. MMWR 2004; 53:683–6.
110. CDC. Case definitions for infectious conditions under public health surveillance. MMWR 1997;46(No. RR-10):1–55.
111. CDC. Surveillance Appendix I. Tuberculosis Information Management System (TIMS) user's guide. Version 1.10. Atlanta, GA: US Department of Health and Human Services, CDC; 2001.
112. Cantwell MF, McKenna MT, McCray E, Onorato IM. Tuberculosis and race/ethnicity in the United States: impact of socioeconomic status. Am J Respir Crit Care Med 1998;157(4 Pt 1):1016–20.
113. McKenna MT, Hutton M, Cauthen G, Onorato IM. The association between occupation and tuberculosis. A population-based survey. Am J Respir Crit Care Med 1996;154(3 Pt 1):587–93.
114. Panlilio AL, Burwen DR, Curtis AB, et al. Tuberculin skin testing surveillance of health care personnel. Clin Infect Dis 2002;35:219–27.
115. Zuber PL, McKenna MT, Binkin NJ, Onorato IM, Castro KG. Long-term risk of tuberculosis among foreign-born persons in the United States. JAMA 1997;278:304–7.
116. McKenna MT, McCray E, Onorato I. The epidemiology of tuberculosis among foreign-born persons in the United States, 1986 to 1993. N Engl J Med 1995;332:1071–6.
117. Burt MR, Aron LY, Douglas T, Valente J, Lee E, Iwen B; the Urban Institute. Homelessness: programs and the people they serve. Findings of the National Survey of Homeless Assistance Providers and Clients. Washington, DC: US Department of Housing and Urban Development; 1999. Available at http://www.huduser.org/publications/homeless/homeless_tech.html.
118. Moss AR, Hahn JA, Tulsky JP, Daley CL, Small PM, Hopewell PC. Tuberculosis in the homeless. A prospective study. Am J Respir Crit Care Med 2000;162(2 Pt 1):460–4.
119. Barnes PF, el-Hajj H, Preston-Martin S, et al. Transmission of tuberculosis among the urban homeless. JAMA 1996;275:305–7.
120. Curtis AB, Ridzon R, Novick LF, et al. Analysis of *Mycobacterium tuberculosis* transmission patterns in a homeless shelter outbreak. Int J Tuberc Lung Dis 2000;4:308–13.
121. Zolopa AR, Hahn JA, Gorter R, et al. HIV and tuberculosis infection in San Francisco's homeless adults. Prevalence and risk factors in a representative sample. JAMA 1994;272:455–61.
122. Selwyn PA, Sckell BM, Alcabes P, Friedland GH, Klein RS, Schoenbaum EE. High risk of active tuberculosis in HIV-infected drug users with cutaneous anergy. JAMA 1992;268:504–9.
123. CDC. Prevention and control of tuberculosis in correctional facilities: recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR 1996;45(No. RR-8):1–27.
124. Glaser JB, Greifinger RB. Correctional health care: a public health opportunity. Ann Intern Med 1993;118:139–45.
125. US Department of Justice. Profile of jail inmates, 1996. Washington, DC: US Department of Justice, Bureau of Justice Statistics; 1998.
126. CDC. Tuberculosis outbreaks in prison housing units for HIV-infected inmates—California, 1995–1996. MMWR 1999; 48:79–82.
127. Jones TF, Craig AS, Valway SE, Woodley CL, Schaffner W. Transmission of tuberculosis in a jail. Ann Intern Med 1999;131:557–63.
128. Jones TF, Woodley CL, Fountain FF, Schaffner W. Increased incidence of the outbreak strain of *Mycobacterium tuberculosis* in the surrounding community after an outbreak in a jail. South Med J 2003;96:155–7.
129. Cave MD, Eisenach KD, McDermott PF, Bates JH, Crawford JT. IS6110: conservation of sequence in the *Mycobacterium tuberculosis* complex and its utilization in DNA fingerprinting. Mol Cell Probes 1991;5:73–80.
130. Etkind SC, Veen J. Contact follow-up in high- and low-prevalence countries. In: Reichman LB, Hershfield ES, eds. Tuberculosis. A comprehensive international approach. 2nd ed. New York, New York: Marcel Dekker; 2000:275–89.
131. Small PM, Hopewell PC, Singh SP, et al. The epidemiology of tuberculosis in San Francisco. A population-based study using conventional and molecular methods. N Engl J Med 1994;330:1703–9.
132. Pfyffer GE, Strassle A, Rose N, Wirth R, Brandli O, Shang H. Transmission of tuberculosis in the metropolitan area of Zurich: a 3 year survey based on DNA fingerprinting. Eur Respir J 1998;11:804–8.
133. van Deutekom H, Gerritsen JJ, van Soolingen D, van Ameijden EJ, van Embden JD, Coutinho RA. A molecular epidemiological approach to studying the transmission of tuberculosis in Amsterdam. Clin Infect Dis 1997;25:1071–7.
134. Yaganehdoost A, Graviss EA, Ross MW, et al. Complex transmission dynamics of clonally related virulent *Mycobacterium tuberculosis* associated with barhopping by predominantly human immunodeficiency virus-positive gay men. J Infect Dis 1999;180:1245–51.
135. Tabet SR, Goldbaum GM, Hooton TM, Eisenach KD, Cave MD, Nolan CM. Restriction fragment length polymorphism analysis detecting a community-based tuberculosis outbreak among persons infected with human immunodeficiency virus. J Infect Dis 1994; 169:189–92.
136. Daley CL, Small PM, Schecter GF, et al. An outbreak of tuberculosis with accelerated progression among persons infected with the human immunodeficiency virus. An analysis using restriction-fragment-length polymorphisms. N Engl J Med 1992;326:231–5.
137. Leonhardt KK, Gentile F, Gilbert BP, Aiken M. A cluster of tuberculosis among crack house contacts in San Mateo County, California. Am J Public Health 1994;84:1834–6.
138. March F, Coll P, Guerrero RA, Busquets E, Cayla JA, Prats G. Predictors of tuberculosis transmission in prisons: an analysis using conventional and molecular methods. AIDS 2000;14:525–35.
139. Mohle-Boetani JC, Miguelino V, Dewsnup DH, et al. Tuberculosis outbreak in a housing unit for human immunodeficiency virus-infected patients in a correctional facility: transmission risk factors and effective outbreak control. Clin Infect Dis 2002;34:668–76.
140. Mangura BT, Napolitano EC, Passannante MR, McDonald RJ, Reichman LB. *Mycobacterium tuberculosis* miniepidemic in a church gospel choir. Chest 1998;113:234–7.
141. Jereb JA, Burwen DR, Dooley SW, et al. Nosocomial outbreak of tuberculosis in a renal transplant unit: application of a new technique for restriction fragment length polymorphism analysis of *Mycobacterium tuberculosis* isolates. J Infect Dis 1993;168:1219–24.
142. Johnson KR, Braden CR, Cairns KL, et al. Transmission of *Mycobacterium tuberculosis* from medical waste. JAMA 2000;284:1683–8.

143. Agerton T, Valway S, Gore B, et al. Transmission of a highly drug-resistant strain (strain W1) of *Mycobacterium tuberculosis*. Community outbreak and nosocomial transmission via a contaminated bronchoscope. JAMA 1997;278:1073–7.
144. Michele TM, Cronin WA, Graham NM, et al. Transmission of *Mycobacterium tuberculosis* by a fiberoptic bronchoscope. Identification by DNA fingerprinting. JAMA 1997;278:1093–5.
145. Small PM, Fujiwara PI. Management of tuberculosis in the United States. N Engl J Med 2001;345:189–200.
146. Genewein A, Telenti A, Bernasconi C, et al. Molecular approach to identifying route of transmission of tuberculosis in the community. Lancet 1993;342(8875):841–4.
147. Hernandez-Garduno E, Kunimoto D, Wang L, et al. Predictors of clustering of tuberculosis in Greater Vancouver: a molecular epidemiologic study. CMAJ 2002;167:349–52.
148. Barnes PF, Yang Z, Preston-Martin S, et al. Patterns of tuberculosis transmission in Central Los Angeles. JAMA 1997;278:1159–63.
149. Alland D, Kalkut GE, Moss AR, et al. Transmission of tuberculosis in New York City. An analysis by DNA fingerprinting and conventional epidemiologic methods. N Engl J Med 1994;330:1710–6.
150. Chin DP, DeRiemer K, Small PM, et al. Differences in contributing factors to tuberculosis incidence in U.S.-born and foreign-born persons. Am J Respir Crit Care Med 1998;158:1797–803.
151. Jasmer RM, Hahn JA, Small PM, et al. A molecular epidemiologic analysis of tuberculosis trends in San Francisco, 1991–1997. Ann Intern Med 1999;130:971–8.
152. Geng E, Kreiswirth B, Driver C, et al. Changes in the transmission of tuberculosis in New York City from 1990 to 1999. N Engl J Med 2002;346:1453–8.
153. Bandera A, Gori A, Catozzi L, et al. Molecular epidemiology study of exogenous reinfection in an area with a low incidence of tuberculosis. J Clin Microbiol 2001;39:2213–8.
154. van Rie A, Warren R, Richardson M, et al. Exogenous reinfection as a cause of recurrent tuberculosis after curative treatment. N Engl J Med 1999;341:1174–9.
155. Maurer JR, Desmond EP, Lesser MD, Jones WD Jr. False-positive cultures of *Mycobacterium tuberculosis*. Chest 1984;86:439–43.
156. Burman WJ, Reves RR. Review of false-positive cultures for *Mycobacterium tuberculosis* and recommendations for avoiding unnecessary treatment. Clin Infect Dis 2000;31:1390–5.
157. Bruchfeld J, Aderaye G, Palme IB, Bjorvatn B, Kallenius G, Lindquist L. Sputum concentration improves diagnosis of tuberculosis in a setting with a high prevalence of HIV. Trans R Soc Trop Med Hyg 2000;94:677–80.
158. Small PM, McClenny NB, Singh SP, Schoolnik GK, Tompkins LS, Mickelsen PA. Molecular strain typing of *Mycobacterium tuberculosis* to confirm cross-contamination in the mycobacteriology laboratory and modification of procedures to minimize occurrence of false-positive cultures. J Clin Microbiol 1993;31:1677–82.
159. Burman WJ, Stone BL, Reves RR, et al. The incidence of false-positive cultures for *Mycobacterium tuberculosis*. Am J Respir Crit Care Med 1997;155:321–6.
160. Jasmer RM, Roemer M, Hamilton J, et al. A prospective, multicenter study of laboratory cross-contamination of *Mycobacterium tuberculosis* cultures. Emerg Infect Dis 2002;8:1260–3.
161. CDC. New CDC program for rapid genotyping of *Mycobacterium tuberculosis* isolates. MMWR 2005;54:47.
162. National Tuberculosis Controllers Association, CDC Advisory Group on Tuberculosis Genotyping. Guide to the application of genotyping to tuberculosis prevention and control. Atlanta, GA: US Department of Health and Human Services, CDC; 2004.
163. Northrup JM, Miller AC, Nardell E, et al. Estimated costs of false laboratory diagnoses of tuberculosis in three patients. Emerg Infect Dis 2002;8:1264–70.
164. McNabb SJ, Braden CR, Navin TR. DNA fingerprinting of *Mycobacterium tuberculosis*: lessons learned and implications for the future. Emerg Infect Dis 2002;8:1314–9.
165. Kimerling ME, Benjamin WH, Lok KH, Curtis G, Dunlap NE. Restriction fragment length polymorphism screening of *Mycobacterium tuberculosis* isolates: population surveillance for targeting disease transmission in a community. Int J Tuberc Lung Dis 1998; 2:655–62.
166. Dobbs KG, Lok KH, Bruce F, Mulcahy D, Benjamin WH, Dunlap NE. Value of *Mycobacterium tuberculosis* fingerprinting as a tool in a rural state surveillance program. Chest 2001;120:1877–82.
167. Kong PM, Tapy J, Calixto P, et al. Skin-test screening and tuberculosis transmission among the homeless. Emerg Infect Dis 2002;8:1280–4.
168. Miller AC, Sharnprapai S, Suruki R, et al. Impact of genotyping of *Mycobacterium tuberculosis* on public health practice in Massachusetts. Emerg Infect Dis 2002;8:1285–9.
169. Etkind SC. The role of the public health department in tuberculosis. Med Clin North Am 1993;77:1303–14.
170. Dooley SW, Villarino ME, Lawrence M, et al. Nosocomial transmission of tuberculosis in a hospital unit for HIV-infected patients. JAMA 1992;267:2632–4.
171. Cowan LS, Crawford JT. Genotype analysis of *Mycobacterium tuberculosis* isolates from a sentinel surveillance population. Emerg Infect Dis 2002;8:1294–302.
172. Bock NN, Mallory JP, Mobley N, DeVoe B, Taylor BB. Outbreak of tuberculosis associated with a floating card game in the rural south: lessons for tuberculosis contact investigations. Clin Infect Dis 1998;27:1221–6.
173. Washko R, Robinson E, Fehrs LJ, Frieden TR. Tuberculosis transmission in a high school choir. J Sch Health 1998;68:256–9.
174. Comstock GW, Woolpert SF, Livesay VT. Tuberculosis studies in Muscogee County, Georgia. Twenty-year evaluation of a community trial of BCG vaccination. Public Health Rep 1976;91:276–80.
175. Comstock GW, Livesay VT, Woolpert SF. Evaluation of BCG vaccination among Puerto Rican children. Am J Public Health 1974;64:283–91.
176. Menzies D. What does tuberculin reactivity after bacille Calmette-Guerin vaccination tell us? Clin Infect Dis 2000;31 Suppl 3:S71–4.
177. Ridzon R, Kent JH, Valway S, et al. Outbreak of drug-resistant tuberculosis with second-generation transmission in a high school in California. J Pediatr 1997;131:863–8.
178. Greenaway C, Menzies D, Fanning A, Grewal R, Yuan L, FitzGerald JM; Canadian Collaborative Group in Nosocomial Transmission of Tuberculosis. Delay in diagnosis among hospitalized patients with active tuberculosis—predictors and outcomes. Am J Respir Crit Care Med 2002;165:927–33.
179. CDC. The role of BCG vaccine in the prevention and control of tuberculosis in the United States: a joint statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices. MMWR 1996;45(No. RR-4):1–18.

180. CDC. Development of new vaccines for tuberculosis: recommendations of the Advisory Council for the Elimination of Tuberculosis (ACET). MMWR 1998;47(No. RR-13):1–6.
181. Peterson Tulsky J, Castle White M, Young JA, Meakin R, Moss AR. Street talk: knowledge and attitudes about tuberculosis and tuberculosis control among homeless adults. Int J Tuberc Lung Dis 1999;3:528–33.
182. Liefooghe R, Michiels N, Habib S, Moran MB, De Muynck A. Perception and social consequences of tuberculosis: a focus group study of tuberculosis patients in Sialkot, Pakistan. Soc Sci Med 1995;41:1685–92.
183. Nair DM, George A, Chacko KT. Tuberculosis in Bombay: new insights from poor urban patients. Health Policy Plan 1997;12:77–85.
184. Bock NN, Metzger BS, Tapia JR, Blumberg HM. A tuberculin screening and isoniazid preventive therapy program in an inner-city population. Am J Respir Crit Care Med 1999;159:295–300.
185. Schluger NW, Huberman R, Holzman R, Rom WN, Cohen DI. Screening for infection and disease as a tuberculosis control measure among indigents in New York City, 1994–1997. Int J Tuberc Lung Dis 1999;3:281–6.
186. Shrestha-Kuwahara R, Wilce M, DeLuca N, Taylor Z. Factors associated with identifying tuberculosis contacts. Int J Tuberc Lung Dis 2003;7(12 Suppl 3):S510–6.
187. Rodger A, Jaffar S, Paynter S, Hayward A, Carless J, Maguire H. Delay in the diagnosis of pulmonary tuberculosis, London, 1998–2000: analysis of surveillance data. BMJ 2003;326(7395):909–10.
188. Allos BM, Genshelmer KF, Bloch AB, et al. Management of an outbreak of tuberculosis in a small community. Ann Intern Med 1996;125:114–7.
189. Kanaya AM, Glidden DV, Chambers HF. Identifying pulmonary tuberculosis in patients with negative sputum smear results. Chest 2001;120:349–55.
190. Curtis AB, McCray E, McKenna M, Onorato IM. Completeness and timeliness of tuberculosis case reporting. A multistate study. Am J Prev Med 2001;20:108–12.
191. Frieden TR, Sterling T, Pablos-Mendez A, Kilburn JO, Cauthen GM, Dooley SW. The emergence of drug-resistant tuberculosis in New York City. N Engl J Med 1993;328:521–6.
192. Weis SE, Slocum PC, Blais FX, et al. The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. N Engl J Med 1994;330:1179–84.
193. Mitchison DA. How drug resistance emerges as a result of poor compliance during short course chemotherapy for tuberculosis. Int J Tuberc Lung Dis 1998;2:10–5.
194. Sumartojo E. When tuberculosis treatment fails. A social behavioral account of patient adherence. Am Rev Respir Dis 1993;147:1311–20.
195. Chaulk CP, Moore-Rice K, Rizzo R, Chaisson RE. Eleven years of community-based directly observed therapy for tuberculosis. JAMA 1995;274:945–51.
196. Chaulk CP, Kazandjian VA. Directly observed therapy for treatment completion of pulmonary tuberculosis: consensus statement of the Public Health Tuberculosis Guidelines Panel. JAMA 1998;279:943–8.
197. Bloch AB, Snider DE Jr. How much tuberculosis in children must we accept? Am J Public Health 1986;76:14–5.
198. Lobato MN, Mohle-Boetani JC, Royce SE. Missed opportunities for preventing tuberculosis among children younger than five years of age. Pediatrics 2000;106:E75.
199. DeRiemer K, Daley CL, Reingold AL. Preventing tuberculosis among HIV-infected persons: a survey of physicians' knowledge and practices. Prev Med 1999;28:437–44.
200. Bloom BR, Murray CJ. Tuberculosis: commentary on a reemergent killer. Science 1992;257(5073):1055–64.
201. Snider DE Jr., Roper WL. The new tuberculosis. N Engl J Med 1992;326:703–5.
202. Hovell MF, Sipan CL, Blumberg EJ, et al. Increasing Latino adolescents' adherence to treatment for latent tuberculosis infection: a controlled trial. Am J Public Health 2003;93:1871–7.
203. Houston HR, Harada N, Makinodan T. Development of a culturally sensitive educational intervention program to reduce the high incidence of tuberculosis among foreign-born Vietnamese. Ethn Health 2002;7:255–65.
204. Morisky DE, Malotte CK, Ebin V, et al. Behavioral interventions for the control of tuberculosis among adolescents. Public Health Rep 2001;116:568–74.
205. Tokars JI, Rudnick JR, Kroc K, et al. U.S. hospital mycobacteriology laboratories: status and comparison with state public health department laboratories. J Clin Microbiol 1996;34:680–5.
206. Peterson LR, Hamilton JD, Baron EJ, et al. Role of clinical microbiology laboratories in the management and control of infectious diseases and the delivery of health care. Clin Infect Dis 2001;32:605–11.
207. Association of Public Health Laboratories. The future of TB laboratory services: a framework for integration, collaboration and leadership. Washington, DC: Association of Public Health Laboratories; 2004.
208. CDC. Core functions and capabilities of state public health laboratories: a report of the Association of Public Health Laboratories. MMWR 2002;51(No. RR-14):1–8.
209. Infectious Diseases Society of America. Policy statement on consolidation of clinical microbiology laboratories. Clin Infect Dis 2001;32:604.
210. Pascopella L, Kellam S, Ridderhof J, et al. Laboratory reporting of tuberculosis test results and patient treatment initiation in California. J Clin Microbiol 2004;42:4209–13.
211. National Committee for Clinical Laboratory Standards. Susceptibility testing of mycobacteria, nocardiae, and other aerobic actinomycetes; approved standard [Document no. M24-A]. Wayne, PA: National Committee for Clinical Laboratory Standards; 2003.
212. Reichman LB. How to ensure the continued resurgence of tuberculosis. Lancet 1996;347(8995):175–7.
213. The American Lung Association Conference on re-establishing control of tuberculosis in the United States. Washington, DC, March 11–13, 1994. Am J Respir Crit Care Med 1996;154:251–62.
214. Hopewell PC. The baby and the bath water. The case for retaining categorical services for tuberculosis control in a reformed health care system. Am J Respir Crit Care Med 1994;150:895.
215. Handler A, Issel M, Turnock B. A conceptual framework to measure performance of the public health system. Am J Public Health 2001;91:1235–9.
216. Binkin NJ, Vernon AA, Simone PM, et al. Tuberculosis prevention and control activities in the United States: an overview of the organization of tuberculosis services. Int J Tuberc Lung Dis 1999;3:663–74.
217. CDC. HIPAA privacy rule and public health: guidance from CDC and the U.S. Department of Health and Human Services. MMWR 2003;52 Suppl:1–20.
218. CDC. Tuberculosis control laws—United States, 1993: recommendations of the Advisory Council for the Elimination of Tuberculosis (ACET). MMWR 1993;42(No. RR-15):1–28.
219. Hale YM, Pfyffer GE, Salfinger M. Laboratory diagnosis of mycobacterial infections: new tools and lessons learned. Clin Infect Dis 2001;33:834–46.

220. Gostin LO, Burris S, Lazzarini Z. The law and the public's health: a study of infectious disease law in the United States. Columbia Law Rev 1999;99:59–128.
221. Goldberg SV, Wallace J, Jackson JC, Chaulk CP, Nolan CM. Cultural case management of latent tuberculosis infection. Int J Tuberc Lung Dis 2004;8:76–82.
222. Gebbie KM. The public health workforce: key to public health infrastructure. Am J Public Health 1999;89:660–1.
223. Brown CK, Roddy C; Joint Council of State and Local Health Officials. Joint Council of State and Local Health Officials: workforce development—principles for action. J Public Health Manag Pract 2001;7:55–9.
224. Jha AK, Perlin JB, Kizer KW, Dudley RA. Effect of the transformation of the Veterans Affairs Health Care System on the quality of care. N Engl J Med 2003;348:2218–27.
225. Bates DW, Gawande AA. Improving safety with information technology. N Engl J Med 2003;348:2526–34.
226. CDC. Framework for program evaluation in public health. MMWR 1999;48(No. RR-11):1–40.
227. CDC. Final FY 2005 performance plan. Atlanta, GA: US Department of Health and Human Services, CDC; 2004. Available at http://www.cdc.gov/od/perfplan/index.htm.
228. Francis J. Curry National Tuberculosis Center. Quality improvement for TB case management: an online course. San Francisco, CA: Francis J. Curry National Tuberculosis Center; 2004. Available at http://ww.nationaltbcenter.edu/catalogue/online_courses.cfm.
229. Berroa J. Case management: a nursing point of view. Int J Tuberc Lung Dis 1998;2(9 Suppl 1):S53–6.
230. Taylor Z, Marks SM, Rios Burrows NM, Weis SE, Stricof RL, Miller B. Causes and costs of hospitalization of tuberculosis patients in the United States. Int J Tuberc Lung Dis 2000;4:931–9.
231. Liu Z, Shilkret KL, Finelli L. Initial drug regimens for the treatment of tuberculosis: evaluation of physician prescribing practices in New Jersey, 1994 to 1995. Chest 1998;113:1446–51.
232. Asch S, Leake B, Knowles L, Gelberg L. Tuberculosis in homeless patients: potential for case finding in public emergency departments. Ann Emerg Med 1998;32:144–7.
233. Sumartojo EM, Geiter LJ, Miller B, Hale BE. Can physicians treat tuberculosis? Report on a national survey of physician practices. Am J Public Health 1997;87:2008–11.
234. Rao SN, Mookerjee AL, Obasanjo OO, Chaisson RE. Errors in the treatment of tuberculosis in Baltimore. Chest 2000;117:734–7.
235. LoBue PA, Moser K, Catanzaro A. Management of tuberculosis in San Diego County: a survey of physicians' knowledge, attitudes and practices. Int J Tuberc Lung Dis 2001;5:933–8.
236. Uplekar M, Pathania V, Raviglione M. Private practitioners and public health: weak links in tuberculosis control. Lancet 2001;358(9285):912–6.
237. Ozuah PO, Ozuah TP, Stein RE, Burton W, Mulvihill M. Evaluation of a risk assessment questionnaire used to target tuberculin skin testing in children. JAMA 2001;285:451–3.
238. US Citizenship and Immigration Service. 2002 yearbook of immigration statistics. Washington, DC: US Department of Homeland Security, US Citizenship and Immigration Service, Office of Immigration Statistics; 2003. Available at http://uscis.gov/graphics/shared/aboutus/statistics/Yearbook2002.pdf.
239. Blum RN, Polish LB, Tapy JM, Catlin BJ, Cohn DL. Results of screening for tuberculosis in foreign-born persons applying for adjustment of immigration status. Chest 1993;103:1670–4.
240. Saraiya M, Cookson ST, Tribble P, et al. Tuberculosis screening among foreign-born persons applying for permanent US residence. Am J Public Health 2002;92:826–9.
241. Brown TM, Fee E. "Palliatives will no longer do": the deep roots and continuing dynamic of community-oriented primary care. Am J Public Health 2002;92:1711–2.
242. Sotir MJ, Parrott P, Metchock B, et al. Tuberculosis in the inner city: impact of a continuing epidemic in the 1990s. Clin Infect Dis 1999;29:1138–44.
243. Moss AR, Alland D, Telzak E, et al. A city-wide outbreak of a multiple-drug-resistant strain of *Mycobacterium tuberculosis* in New York. Int J Tuberc Lung Dis 1997;1:115–121.
244. Institute of Medicine, Committee on Regulating Occupational Exposure to Tuberculosis. In: Field MJ, ed. Tuberculosis in the workplace. Washington, DC: National Academy Press; 2001.
245. Blumberg HM. tuberculosis infection control. In: Reichman LB, Hershield E, eds. Tuberculosis: a comprehensive international approach. New York, NY: Marcel-Dekker, Inc.; 2000:609–43.
246. O'Brien RJ, Nunn PP. The need for new drugs against tuberculosis. Obstacles, opportunities, and next steps. Am J Respir Crit Care Med 2001;163:1055–8.
247. Perkins MD. New diagnostic tools for tuberculosis. Int J Tuberc Lung Dis 2000;4(12 Suppl 2):S182–8.
248. D'Lugoff MI, Jones W, Kub J, et al. Tuberculosis screening in an at-risk immigrant Hispanic population in Baltimore city: an academic health center/local health department partnership. J Cult Divers 2002;9:79–85.
249. Ashkar BE. Applying advances to the clinic and health care delivery: putting the strategies to work. Int J Tuberc Lung Dis 2000;4 (2 Suppl 1):S41–4.
250. Bellin EY, Fletcher DD, Safyer SM. Association of tuberculosis infection with increased time in or admission to the New York City jail system. JAMA 1993;269:2228–31.
251. Nardell EA. Tuberculosis in homeless, residential care facilities, prisons, nursing homes, and other close communities. Semin Respir Infect 1989;4:206–15.
252. Hutton MD, Cauthen GM, Bloch AB. Results of a 29-state survey of tuberculosis in nursing homes and correctional facilities. Public Health Rep 1993;108:305–14.
253. White MC, Tulsky JP, Portillo CJ, Menendez E, Cruz E, Goldenson J. Tuberculosis prevalence in an urban jail: 1994 and 1998. Int J Tuberc Lung Dis 2001;5:400–4.
254. Levy MH, Reyes H, Coninx R. Overwhelming consumption in prisons: human rights and tuberculosis control. Health Hum Rights 1999;4:166–91.
255. Lobato MN, Leary LS, Simone PM. Treatment for latent TB in correctional facilities: a challenge for TB elimination. Am J Prev Med 2003;24:249–53.
256. Tulsky JP, White MC, Dawson C, Hoynes TM, Goldenson J, Schecter G. Screening for tuberculosis in jail and clinic follow-up after release. Am J Public Health 1998;88:223–6.
257. White MC, Tulsky JP, Reilly P, McIntosh HW, Hoynes TM, Goldenson J. A clinical trial of a financial incentive to go to the tuberculosis clinic for isoniazid after release from jail. Int J Tuberc Lung Dis 1998;2:506–12.
258. Francis J. Curry National Tuberculosis Center. Tuberculosis infection control plan template for jails. San Francisco, CA: Francis J. Curry National Tuberculosis Center; 2002. Available at http://www.nationaltbcenter.edu.

259. Broekmans JF, Migliori GB, Rieder HL, et al.; World Health Organization, International Union Against Tuberculosis and Lung Disease, Royal Netherlands Tuberculosis Association Working Group. European framework for tuberculosis control and elimination in countries with a low incidence. Recommendations of the World Health Organization (WHO), International Union Against Tuberculosis and Lung Disease (IUATLD) and Royal Netherlands Tuberculosis Association (KNCV) Working Group. Eur Respir J 2002;19:765–75.
260. Mabey D, Peelin RW, Ustianowsk A, Perkin MD. Tropical infectious diseases: diagnostics for the developing world. Nat Rev Microbiol 2004;2:231–40.
261. Wheeler C, Berkley S. Initial lessons from public-private partnerships in drug and vaccine development. Bull World Health Organ 2001;79:728–34.
262. Gupta R, Kim JY, Espinal MA, et al. Public health. Responding to market failures in tuberculosis control. Science 2001;293 (5532):1049–51.
263. Kumaresan J, Smith I, Arnold V, Evans P. The global TB drug facility: innovative global procurement. Int J Tuberc Lung Dis 2004; 8:130–8.
264. Yamada S, Caballero J, Matsunaga DS, Agustin G, Magana M. Attitudes regarding tuberculosis in immigrants from the Philippines to the United States. Fam Med 1999;31:477–82.
265. Carey JW, Oxtoby MJ, Nguyen LP, Huynh V, Morgan M, Jeffery M. Tuberculosis beliefs among recent Vietnamese refugees in New York State. Public Health Rep 1997;112:66–72.
266. Bock NN, McGowan JE Jr., Blumberg HM. Few opportunities found for tuberculosis prevention among the urban poor. Int J Tuberc Lung Dis 1998;2:124–9.
267. Miller LG, Asch SM, Yu EI, Knowles L, Gelberg L, Davidson P. A population-based survey of tuberculosis symptoms: how atypical are atypical presentations? Clin Infect Dis 2000;30:293–9.
268. Tattevin P, Casalino E, Fleury L, Egmann G, Ruel M, Bouvet E. The validity of medical history, classic symptoms, and chest radiographs in predicting pulmonary tuberculosis: derivation of a pulmonary tuberculosis prediction model. Chest 1999;115:1248–53.
269. Catanzaro A, Perry S, Clarridge JE, et al. The role of clinical suspicion in evaluating a new diagnostic test for active tuberculosis: results of a multicenter prospective trial. JAMA 2000;283:639–45.
270. Daley CL, Gotway MB, Jasmer RM. Radiographic manifestations of tuberculosis: a primer for clinicians. San Francisco, CA: Francis J. Curry National Tuberculosis Center; 2003:1–30.
271. Cohen R, Muzaffar S, Capellan J, Azar H, Chinikamwala M. The validity of classic symptoms and chest radiographic configuration in predicting pulmonary tuberculosis. Chest 1996;109:420–3.
272. Scott B, Schmid M, Nettleman MD. Early identification and isolation of inpatients at high risk for tuberculosis. Arch Intern Med 1994;154:326–30.
273. Long R. Smear-negative pulmonary tuberculosis in industrialized countries. Chest 2001;120:330–4.
274. Perlman DC, el-Sadr WM, Nelson ET, et al. Variation of chest radiographic patterns in pulmonary tuberculosis by degree of human immunodeficiency virus-related immunosuppression. The Terry Beirn Community Programs for Clinical Research on AIDS (CPCRA). The AIDS Clinical Trials Group (ACTG). Clin Infect Dis 1997;25:242–6.
275. Mandell LA, Bartlett JG, Dowell SF, File TM Jr., Musher DM, Whitney C; Infectious Diseases Society of America. Update of practice guidelines for the management of community-acquired pneumonia in immunocompetent adults. Clin Infect Dis 2003;37: 1405–33.
276. Dasgupta K, Schwartzman K, Marchand R, Tennenbaum TN, Brassard P, Menzies D. Comparison of cost-effectiveness of tuberculosis screening of close contacts and foreign-born populations. Am J Respir Crit Care Med 2000;162:2079–86.
277. Sciortino S, Mohle-Boetani J, Royce SE, Will D, Chin DP. B notifications and the detection of tuberculosis among foreign-born recent arrivals in California. Int J Tuberc Lung Dis 1999;3:778–85.
278. Zuber PL, Binkin NJ, Ignacio AC, et al. Tuberculosis screening for immigrants and refugees. Diagnostic outcomes in the state of Hawaii. Am J Respir Crit Care Med 1996;154:151–5.
279. CDC. Recommendations for prevention and control of tuberculosis among foreign-born persons: report of the Working Group on Tuberculosis Among Foreign-Born Persons. MMWR 1998;47 (No. RR-16):1–29.
280. Nolan CM, Elarth AM, Barr H, Saeed AM, Risser DR. An outbreak of tuberculosis in a shelter for homeless men. A description of its evolution and control. Am Rev Respir Dis 1991;143:257–61.
281. Kimerling ME, Shakes CF, Carlisle R, Lok KH, Benjamin WH, Dunlap NE. Spot sputum screening: evaluation of an intervention in two homeless shelters. Int J Tuberc Lung Dis 1999;3:613–9.
282. CDC. Screening for tuberculosis and tuberculosis infection in populations at high risk. Recommendations of the Advisory Council for the Elimination of Tuberculosis. MMWR 1995;44(No. RR-11):19–34.
283. Puisis M, Feinglass J, Lidow E, Mansour M. Radiographic screening for tuberculosis in a large urban county jail. Public Health Rep 1996;111:330–4.
284. Jereb J, Etkind SC, Joglar OT, Moore M, Taylor Z. Tuberculosis contact investigations: outcomes in selected areas of the United States, 1999. Int J Tuberc Lung Dis 2003;7(12 Suppl 3):S384–90.
285. Ferebee SH. Controlled chemoprophylaxis trials in tuberculosis. A general review. Bibl Tuberc 1970;26:28–106.
286. Nivin B, Nicholas P, Gayer M, Frieden TR, Fujiwara PI. A continuing outbreak of multidrug-resistant tuberculosis, with transmission in a hospital nursery. Clin Infect Dis 1998;26:303–7.
287. Hennessey KA, Schulte JM, Valway SE, et al. Using DNA fingerprinting to detect transmission of *Mycobacterium tuberculosis* among AIDS patients in two health-care facilities in Puerto Rico. South Med J 2000;93:777–82.
288. Garcia-Garcia ML, Jimenez-Corona ME, Ponce-de-Leon A, et al. *Mycobacterium tuberculosis* drug resistance in a suburban community in southern Mexico. Int J Tuberc Lung Dis 2000;4(12 Suppl 2):S168–70.
289. Askew GL, Finelli L, Hutton M, et al. *Mycobacterium tuberculosis* transmission from a pediatrician to patients. Pediatrics 1997;100:19–23.
290. Kenyon TA, Valway SE, Ihle WW, Onorato IM, Castro KG. Transmission of multidrug-resistant *Mycobacterium tuberculosis* during a long airplane flight. N Engl J Med 1996;334:933–8.
291. CDC. Crack cocaine use among persons with tuberculosis—Contra Costa County, California, 1987–1990. MMWR 1991;40:485–9.
292. DiStasio AJ 2nd, Trump DH. The investigation of a tuberculosis outbreak in the closed environment of a U.S. Navy ship, 1987. Mil Med 1990;155:347–51.

293. Wells CD, Zuber PL, Nolan CM, Binkin NJ, Goldberg SV. Tuberculosis prevention among foreign-born persons in Seattle-King County, Washington. Am J Respir Crit Care Med 1997;156(2 Pt 1):573–7.
294. Goldman JM, Teale C, Cundall DB, Pearson SB. Childhood tuberculosis in Leeds, 1982–90: social and ethnic factors and the role of the contact clinic in diagnosis. Thorax 1994;49:184–5.
295. Mehta JB, Bentley S. Prevention of tuberculosis in children: missed opportunities. Am J Prev Med 1992;8:283–6.
296. Rubilar M, Brochwicz-Lewinski MJ, Anderson M, Leitch AG. The outcome of contact procedures for tuberculosis in Edinburgh, Scotland 1982–1991. Respir Med 1995;89:113–20.
297. Topley JM, Maher D, Mbewe LN. Transmission of tuberculosis to contacts of sputum positive adults in Malawi. Arch Dis Child 1996;74:140–3.
298. CDC. Multi-drug-resistant tuberculosis—North Carolina. MMWR 1987;35:785–7.
299. Etkind SC. Contact tracing in tuberculosis. In: Reichman L, Herschfield E, eds. Tuberculosis: a comprehensive international approach. New York, NY: Marcel Dekker, Inc.; 1993:275–89.
300. Ong A, Creasman J, Hopewell PC, et al. A molecular epidemiological assessment of extrapulmonary tuberculosis in San Francisco. Clin Infect Dis 2004;38:25–31.
301. Reichler MR, Bur S, Reves R, et al. Results of testing for human immunodeficiency virus infection among recent contacts of infectious tuberculosis cases in the United States. Int J Tuberc Lung Dis 2003;7(12 Suppl 3):S471–8.
302. CDC. Revised guidelines for HIV counseling, testing, and referral. MMWR 2001;50(No. RR-19):1–57.
303. Long R, Houston S, Hershfield E; Canadian Tuberculosis Committee of Centre for Infectious Disease Prevention and Control, Population and Public Health Branch, Health Canada. Recommendations for screening and prevention of tuberculosis in patients with HIV and for screening for HIV in patients with tuberculosis and their contacts. CMAJ 2003;169:789–91.
304. California Department of Health Services, California Tuberculosis Controllers Association. Joint guidelines for tuberculosis treatment and control in California. Berkeley, CA: California Department of Health Services, California Tuberculosis Controllers Association; 1998. Available at http://www.ctca.org/publications/guidelines/index.htm.
305. CDC. Guidelines for the investigation of contacts to infectious tuberculosis patients. Atlanta, GA: National Tuberculosis Controllers Association; US Department of Health and Human Services, CDC. In press 2005.
306. Veen J. Microepidemics of tuberculosis: the stone-in-the-pond principle. Tuber Lung Dis 1992;73:73–6.
307. Dunlap NE. The use of RFLP as a tool for tuberculosis control: utility or futility? Int J Tuberc Lung Dis 2000;4(12 Suppl 2):S134–8.
308. CDC. Fatal and severe liver injuries associated with rifampin and pyrazinamide for latent tuberculosis infection, and revisions in American Thoracic Society/CDC recommendations—United States, 2001. MMWR 2001;50:733–5.
309. American Thoracic Society. Preventive treatment in tuberculosis; a statement by the Committee on Therapy. American Thoracic Society. Am Rev Respir Dis 1965;91:297–8.
310. Mitchell JR, Zimmerman HJ, Ishak KG, et al. Isoniazid liver injury: clinical spectrum, pathology, and probable pathogenesis. Ann Intern Med 1976;84:181–92.
311. Glassroth J, Bailey WC, Hopewell PC, Schecter G, Harden JW. Why tuberculosis is not prevented. Am Rev Respir Dis 1990;141 (5 Pt 1):1236–40.
312. CDC. Transmission of *Mycobacterium tuberculosis* associated with failed completion of treatment for latent tuberculosis infection—Chickasaw County, Mississippi, June 1999–March 2002. MMWR 2003;52:222–4.
313. Granich RM, Zuber PL, McMillan M, et al. Tuberculosis among foreign-born residents of southern Florida, 1995. Public Health Rep 1998;113:552–6.
314. Liu Z, Shilkret KL, Tranotti J, Freund CG, Finelli L. Distinct trends in tuberculosis morbidity among foreign-born and US-born persons in New Jersey, 1986 through 1995. Am J Public Health 1998; 88:1064–7. Comment in: Horsburgh CR Jr. What it takes to control tuberculosis. Am J Public Health 1998;88:1015–6.
315. El Sahly HM, Adams GJ, Soini H, Teeter L, Musser JM, Graviss EA. Epidemiologic differences between United States- and foreign-born tuberculosis patients in Houston, Texas. J Infect Dis 2001;183:461–8.
316. Weis SE, Moonan PK, Pogoda JM, et al. Tuberculosis in the foreign-born population of Tarrant county, Texas by immigration status. Am J Respir Crit Care Med 2001;164:953–7.
317. Selwyn PA, Hartel D, Lewis VA, et al. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. N Engl J Med 1989;320:545–50.
318. Perlman DC, Perkins MP, Solomon N, Kochems L, Des Jarlais DC, Paone D. Tuberculosis screening at a syringe exchange program. Am J Public Health 1997;87:862–3.
319. Nelson KR, Bui H, Samet JH. Screening in special populations: a "case study" of recent Vietnamese immigrants. Am J Med 1997; 102:435–40.
320. Pilote L, Tulsky JP, Zolopa AR, Hahn JA, Schecter GF, Moss AR. Tuberculosis prophylaxis in the homeless. A trial to improve adherence to referral. Arch Intern Med 1996;156:161–5.
321. Kohn MR, Arden MR, Vasilakis J, Shenker IR. Directly observed preventive therapy. Turning the tide against tuberculosis. Arch Pediatr Adolesc Med 1996;150:727–9.
322. Chang S, Wheeler LS, Farrell KP. Public health impact of targeted tuberculosis screening in public schools. Am J Public Health 2002;92:1942–5.
323. Geiger HJ. Community-oriented primary care: a path to community development. Am J Public Health 2002;92:1713–6.
324. CDC. Adverse event data and revised American Thoracic Society/CDC recommendations against the use of rifampin and pyrazinamide for treatment of latent tuberculosis infection—United States, 2003. MMWR 2003;52:735–9.
325. Nolan RJ Jr. Childhood tuberculosis in North Carolina: a study of the opportunities for intervention in the transmission of tuberculosis to children. Am J Public Health 1986;76:26–30.
326. Al-Dossary FS, Ong LT, Correa AG, Starke JR. Treatment of childhood tuberculosis with a six month directly observed regimen of only two weeks of daily therapy. Pediatr Infect Dis J 2002;21:91–7.
327. CDC. HIV-related tuberculosis in a transgender network—Baltimore, Maryland, and New York City area, 1998–2000. MMWR 2000;49: 317–20.
328. CDC. Increase in African immigrants and refugees with tuberculosis—Seattle-King County, Washington, 1998–2001. MMWR 2002;51:882–3. Erratum in: MMWR 2002;51:919.

329. CDC. Trends in tuberculosis morbidity—United States, 1992–2002. MMWR 2003;52:217–22.
330. CDC. Racial disparities in tuberculosis—selected southeastern states, 1991–2002. MMWR 2004;53:556–9.
331. CDC. Trends in tuberculosis—United States, 2004. MMWR 2005;54:245–9.
332. Hsu KH. Contact investigation: a practical approach to tuberculosis eradication. Am J Public Health Nations Health 1963;53:1761–9.
333. Perry S, Starke JR. Adherence to prescribed treatment and public health aspects of tuberculosis in children. Semin Pediatr Infect Dis 1993;4:291–8.
334. Teixeira L, Perkins MD, Johnson JL, et al. Infection and disease among household contacts of patients with multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 2001;5:321–8.
335. Schaaf HS, Van Rie A, Gie RP, et al. Transmission of multidrug-resistant tuberculosis. Pediatr Infect Dis J 2000;19:695–9.
336. George RH, Gully PR, Gill ON, Innes JA, Bakhshi SS, Connolly M. An outbreak of tuberculosis in a children's hospital. J Hosp Infect 1986;8:129–42.
337. Weinstein JW, Barrett CR, Baltimore RS, Hierholzer WJ Jr. Nosocomial transmission of tuberculosis from a hospital visitor on a pediatrics ward. Pediatr Infect Dis J 1995;14:232–4.
338. Aznar J, Safi H, Romero J, Alejo A, Gracia A, Palomares JC. Nosocomial transmission of tuberculosis infection in pediatrics wards. Pediatr Infect Dis J 1995;14:44–8.
339. Munoz FM, Ong LT, Seavy D, Medina D, Correa A, Starke JR. Tuberculosis among adult visitors of children with suspected tuberculosis and employees at a children's hospital. Infect Control Hosp Epidemiol 2002;23:568–72.
340. American Academy of Pediatrics. Tuberculosis. In: Pickering LK, ed. 2000 red book: report of the Committee on Infectious Diseases. 26th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2003:658.
341. Soren K, Saiman L, Irigoyen M, Gomez-Duarte C, Levison MJ, McMahon DJ. Evaluation of household contacts of children with positive tuberculin skin tests. Pediatr Infect Dis J 1999;18:949–55.
342. Driver CR, Cordova IM, Munsiff SS. Targeting tuberculosis testing: the yield of source case investigations for young children with reactive tuberculin skin tests. Public Health Rep 2002;117:366–72.
343. Sullam PM, Slutkin G, Hopewell PC. The benefits of evaluating close associates of child tuberculin reactors from a high prevalence group. Am J Public Health 1986;76:1109–11.
344. Starke JR. Universal screening for tuberculosis infection. School's out! JAMA 1995;274:652–3.
345. Mohle-Boetani JC, Miller B, Halpern M, et al. School-based screening for tuberculous infection. A cost-benefit analysis. JAMA 1995;274:613–9.
346. Lobato MN, Hopewell PC. *Mycobacterium tuberculosis* infection after travel to or contact with visitors from countries with a high prevalence of tuberculosis. Am J Respir Crit Care Med 1998;158:1871–5.
347. Froehlich H, Ackerson LM, Morozumi PA; Pediatric Tuberculosis Study Group of Kaiser Pernamente, Northern California. Targeted testing of children for tuberculosis: validation of a risk assessment questionnaire. Pediatrics 2001;107:E54.
348. Saiman L, San Gabriel P, Schulte J, Vargas MP, Kenyon T, Onorato I. Risk factors for latent tuberculosis infection among children in New York City. Pediatrics 2001;107:999–1003.
349. Koppaka VR, Harvey E, Mertz B, Johnson BA. Risk factors associated with tuberculin skin test positivity among university students and the use of such factors in the development of a targeted screening program. Clin Infect Dis 2003;36:599–607.
350. Binkin NJ, Zuber PL, Wells CD, Tipple MA, Castro KG. Overseas screening for tuberculosis in immigrants and refugees to the United States: current status. Clin Infect Dis 1996;23:1226–32.
351. US Department of Homeland Security. Yearbook of Immigration Statistics, 2003. Washington, DC: US Government Printing Office; 2004:16–9. Available at http://uscis.gov/graphics/shared/statistics/yearbook/index.htm.
352. Enarson D, Ashley MJ, Grzybowski S. Tuberculosis in immigrants to Canada. A study of present-day patterns in relation to immigration trends and birthplace. Am Rev Respir Dis 1979;119:11–8.
353. Nolan CM, Elarth AM. tuberculosis in a cohort of Southeast Asian Refugees. A five-year surveillance study. Am Rev Respir Dis 1988;137:805–9.
354. World Health Organization. Global tuberculosis control—surveillance, planning, financing. Geneva, Switzerland: World Health Organization. Available at http://www.who.int/tb/publications/global_report/2004/en.
355. Sharnprapai S, Miller AC, Suruki R, et al. Genotyping analyses of tuberculosis cases in U.S.- and foreign-born Massachusetts residents. Emerg Infect Dis 2002;8:1239–45.
356. Borgdorff MW, Behr MA, Nagelkerke NJ, Hopewell PC, Small PM. Transmission of tuberculosis in San Francisco and its association with immigration and ethnicity. Int J Tuberc Lung Dis 2000;4:287–94.
357. US Immigration and Naturalization Service. Estimates of the unauthorized immigrant population residing in the United States: 1990 to 2000. Washington, DC: US Immigration and Naturalization Service, Office of Policy and Planning; 2003. Available at http://uscis.gov/graphics/shared/aboutus/statistics/Ill_Report_1211.pdf.
358. CDC. Technical instructions for panel physicians. Atlanta, GA: US Department of Health and Human Services, CDC; 2002. Available at http://www.cdc.gov/ncidod/dq/panel.htm.
359. CDC. CDC's response to ending neglect: the elimination of tuberculosis in the United States. Atlanta, GA: US Department of Health and Human Services, CDC; 2002. Available athttp://www.cdc.gov/nchstp/tb/pubs/iom/iomresponse/iomresponse.pdf.
360. Wells CD, Ocana M, Moser K, Bergmire-Sweat D, Mohle-Boetani JC, Binkin NJ. A study of tuberculosis among foreign-born Hispanic persons in the U.S. states bordering Mexico. Am J Respir Crit Care Med 1999;159:834–7.
361. CDC. Preventing and controlling tuberculosis along the U.S.-Mexico border. MMWR 2001;50(No. RR-1):1–27.
362. DeRiemer K, Chin DP, Schecter GF, Reingold AL. Tuberculosis among immigrants and refugees. Arch Intern Med 1998;158:753–60.
363. Zuber PL, Knowles LS, Binkin NJ, Tipple MA, Davidson PT. Tuberculosis among foreign-born persons in Los Angeles County, 1992–1994. Tubercle Lung Disease 1996;77:524–30.
364. Catlos EK, Cantwell MF, Bhatia G, Gedin S, Lewis J, Mohle-Boetani JC. Public health interventions to encourage TB class A/B1/B2 immigrants to present for TB screening. Am J Respir Crit Care Med 1998;158:1037–41.
365. Weis SE, Burgess G. Tuberculosis control in a border state. Treatment of the foreign-born. Infect Dis Clin North Am 2002;16:59–71.
366. White MC, Gournis E, Kawamura M, Menendez E, Tulsky JP. Effect of directly observed preventive therapy for latent tuberculosis infection in San Francisco. Int J Tuberc Lung Dis 2003;7:30–5.

367. Hennessey KA, Schulte JM, Cook L, Collins M, Onorato IM, Valway SE. Tuberculin skin test screening practices among US colleges and universities. JAMA 1998;280:2008–12.
368. Whalen CC, Nsubuga P, Okwera A, et al. Impact of pulmonary tuberculosis on survival of HIV-infected adults: a prospective epidemiologic study in Uganda. AIDS 2000;14:1219–28.
369. Havlir DV, Barnes PF. Tuberculosis in patients with human immunodeficiency virus infection. N Engl J Med 1999;340:367–73.
370. Bucher HC, Griffith LE, Guyatt GH, et al. Isoniazid prophylaxis for tuberculosis in HIV infection: a meta-analysis of randomized controlled trials. AIDS 1999;13:501–7.
371. Markowitz N, Hansen NI, Hopewell PC, et al. Incidence of tuberculosis in the United States among HIV-infected persons. The Pulmonary Complications of HIV Infection Study Group. Ann Intern Med 1997;126:123–32.
372. Pape JW, Jean SS, Ho JL, Hafner A, Johnson WD Jr. Effect of isoniazid prophylaxis on incidence of active tuberculosis and progression of HIV infection. Lancet 1993;342(8866):268–72.
373. Mukadi YD, Maher D, Harries A. Tuberculosis case fatality rates in high HIV prevalence populations in sub-Saharan Africa. AIDS 2001;15:143–52.
374. Joint United Nations Programme on HIV/AIDS (UNAIDS). UNAIDS 2002 report on the global HIV/AIDS epidemic; Geneva, Switzerland: Joint United Nations Programme on HIV/AIDS; 2002.
375. Mocroft A, Vella S, Benfield TL, et al. Changing patterns of mortality across Europe in patients infected with HIV-1. EuroSIDA Study Group. Lancet 1998;352(9142):1725–30.
376. Palella FJ Jr., Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. N Engl J Med 1998;338:853–60.
377. Detels R, Munoz A, McFarlane G, et al. Effectiveness of potent antiretroviral therapy on time to AIDS and death in men with known HIV infection duration. Multicenter AIDS Cohort Study Investigators. JAMA 1998;280:1497–503.
378. Jones JL, Hanson DL, Dworkin MS, et al. Surveillance for AIDS-defining opportunistic illnesses, 1992–1997. In: CDC Surveillance Summaries, April 16, 1999. MMWR 1999;48(No. SS-2):1–22.
379. Barnes PF, Bloch AB, Davidson PT, Snider DE Jr. Tuberculosis in patients with human immunodeficiency virus infection. N Engl J Med 1991;324:1644–50.
380. Shafer RW, Edlin BR. Tuberculosis in patients infected with human immunodeficiency virus: perspective on the past decade. Clin Infect Dis 1996;22:683–704.
381. Selwyn PA, Pumerantz AS, Durante A, et al. Clinical predictors of *Pneumocystis carinii* pneumonia, bacterial pneumonia and tuberculosis in HIV-infected patients. AIDS 1998;12:885–93.
382. Burman WJ, Jones BE. Treatment of HIV-related tuberculosis in the era of effective antiretroviral therapy. Am J Respir Crit Care Med 2001;164:7–12.
383. Narita M, Ashkin D, Hollender ES, Pitchenik AE. Paradoxical worsening of tuberculosis following antiretroviral therapy in patients with AIDS. Am J Respir Crit Care Med 1998;158:157–61.
384. Alwood K, Keruly J, Moore-Rice K, Stanton DL, Chaulk CP, Chaisson RE. Effectiveness of supervised, intermittent therapy for tuberculosis in HIV-infected patients. AIDS 1994;8:1103–8.
385. Espinal MA, Perez EN, Baez J, et al. Infectiousness of *Mycobacterium tuberculosis* in HIV-1-infected patients with tuberculosis: a prospective study. Lancet 2000;355(9200):275–80.
386. Carvalho AC, DeRiemer K, Nunes ZB, Martins M, Comelli M, Marinoni A. Transmission of *Mycobacterium tuberculosis* to contacts of HIV-infected tuberculosis patients. Am J Respir Crit Care Med 2001;164:2166–71.
387. Cruciani M, Malena M, Bosco O, Gatti G, Serpelloni G. The impact of human immunodeficiency virus type 1 on infectiousness of tuberculosis: a meta-analysis. Clin Infect Dis 2001;33:1922–30.
388. CDC. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. MMWR 1998;47(No. RR-20):1–58.
389. Gordin F, Chaisson RE, Matts JP, et al. Rifampin and pyrazinamide vs isoniazid for prevention of tuberculosis in HIV-infected persons: an international randomized trial. Terry Beirn Community Programs for Clinical Research on AIDS, the Adult AIDS Clinical Trials Group, the Pan American Health Organization, and the CDC Study Group. JAMA 2000;283:1445–50.
390. Link B, Phelan J, Bresnahan M, Stueve A, Moore R, Susser E. Lifetime and five-year prevalence of homelessness in the United States: new evidence on an old debate. Am J Orthopsychiatry 1995;65:347–54.
391. Kearns AM, Barrett A, Marshall C, et al. Epidemiology and molecular typing of an outbreak of tuberculosis in a hostel for homeless men. J Clin Pathol 2000;53:122–4.
392. McElroy PD, Southwick KL, Fortenberry ER, et al. Outbreak of tuberculosis among homeless persons coinfected with human immunodeficiency virus. Clin Infect Dis 2003;36:1305–12.
393. Barnes PF. Tuberculosis among the inner city poor. Int J Tuberc Lung Dis 1998;2(9 Suppl 1):S41–5.
394. Brewer TF, Heymann SJ, Krumplitsch SM, Wilson ME, Colditz GA, Fineberg HV. Strategies to decrease tuberculosis in US homeless populations: a computer simulation model. JAMA 2001;286:834–42.
395. Burman WJ, Cohn DL, Rietmeijer CA, Judson FN, Sbarbaro JA, Reves RR. Noncompliance with directly observed therapy for tuberculosis. Epidemiology and effect on the outcome of treatment. Chest 1997;111:1168–73.
396. Southern A, Premaratne N, English M, Balazs J, O'Sullivan D. Tuberculosis among homeless people in London: an effective model of screening and treatment. Int J Tuberc Lung Dis 1999;3:1001–8.
397. Rendleman NJ. Mandated tuberculosis screening in a community of homeless people. Am J Prev Med 1999;17:108–13.
398. Marks SM, Taylor Z, Burrows NR, Qayad MG, Miller B. Hospitalization of homeless persons with tuberculosis in the United States. Am J Public Health 2000;90:435–8.
399. LoBue PA, Cass R, Lobo D, Moser K, Catanzaro A. Development of housing programs to aid in the treatment of tuberculosis in homeless individuals: a pilot study. Chest 1999;115:218–23.
400. Diez E, Claveria J, Serra T, et al. Evaluation of a social health intervention among homeless tuberculosis patients. Tuber Lung Dis 1996;77:420–4.
401. Singleton L, Turner M, Haskal R, Etkind S, Tricarico M, Nardell E. Long-term hospitalization for tuberculosis control. Experience with a medical-psychosocial inpatient unit. JAMA 1997;278:838–42.
402. Tulsky JP, Pilote L, Hahn JA, et al. Adherence to isoniazid prophylaxis in the homeless: a randomized controlled trial. Arch Intern Med 2000;160:697–702.
403. Hammett TM, Harmon MP, Rhodes W. The burden of infectious disease among inmates of and releasees from US correctional facilities, 1997. Am J Public Health 2002;92:1789–94.
404. Steenland K, Levine AJ, Sieber K, Schulte P, Aziz D. Incidence of tuberculosis infection among New York State prison employees. Am J Public Health 1997;87:2012–4.

405. Valway SE, Richards SB, Kovacovich J, Greifinger RB, Crawford JT, Dooley SW. Outbreak of multi-drug-resistant tuberculosis in a New York State prison, 1991. Am J Epidemiol 1994;140:113–22.
406. CDC. Probable transmission of multidrug-resistant tuberculosis in a correctional facility—California. MMWR 1993;42:48–51.
407. Pelletier AR, DiFerdinando GT Jr., Greenberg AJ, et al. Tuberculosis in a correctional facility. Arch Intern Med 1993;153:2692–5.
408. Valway SE, Greifinger RB, Papania M, et al. Multidrug-resistant tuberculosis in the New York State prison system, 1990–1991. J Infect Dis 1994;170:151–6.
409. CDC. Outbreak of multidrug-resistant tuberculosis at a hospital—New York City, 1991. MMWR 1993;42:427–34.
410. Bock NN, Reeves M, LaMarre M, DeVoe B. Tuberculosis case detection in a state prison system. Public Health Rep 1998;113:359–64.
411. Anderson KM, Keith EP, Norsted SW. Tuberculosis screening in Washington state male correctional facilities. Chest 1986;89:817–21.
412. Jones TF, Schaffner W. Miniature chest radiograph screening for tuberculosis in jails: a cost-effectiveness analysis. Am J Respir Crit Care Med 2001;164:77–81.
413. Klopf LC. Tuberculosis control in the New York State Department of Correctional Services: a case management approach. Am J Infect Control 1998;26:534–7.
414. Johnsen C. Tuberculosis contact investigation: two years of experience in New York City correctional facilities. Am J Infect Control 1993;21:1–4.
415. Kendig N. Tuberculosis control in prisons. Int J Tuberc Lung Dis 1998;2(9 Suppl 1):S57–63.
416. Alcabes P, Vossenas P, Cohen R, Braslow C, Michaels D, Zoloth S. Compliance with isoniazid prophylaxis in jail. Am Rev Respir Dis 1989;140:1194–7.
417. CDC. Tuberculosis prevention in drug-treatment centers and correctional facilities—selected U.S. sites, 1990–1991. MMWR 1993; 42:210–3.
418. Reichard AA, Lobato MN, Roberts CA, Bazerman LB, Hammett TM. Assessment of tuberculosis screening and management practices of large jail systems. Public Health Rep 2003;118:500–7.
419. Bock NN, Rogers T, Tapia JR, Herron GD, DeVoe B, Geiter LJ. Acceptability of short-course rifampin and pyrazinamide treatment of latent tuberculosis infection among jail inmates. Chest 2001;119:833–7.
420. MacIntyre CR, Kendig N, Kummer L, Birago S, Graham NM. Impact of tuberculosis control measures and crowding on the incidence of tuberculous infection in Maryland prisons. Clin Infect Dis 1997;24:1060–7.
421. Zaza S, Blumberg HM, Beck-Sague C, et al. Nosocomial transmission of *Mycobacterium tuberculosis*: role of health care workers in outbreak propagation. J Infect Dis 1995;172:1542–9.
422. McGowan JE Jr. Nosocomial tuberculosis: new progress in control and prevention. Clin Infect Dis 1995;21:489–505.
423. Wenger PN, Otten J, Breeden A, Orfas D, Beck-Sague CM, Jarvis WR. Control of nosocomial transmission of multidrug-resistant *Mycobacterium tuberculosis* among healthcare workers and HIV-infected patients. Lancet 1995;345(8944):235–40.
424. Maloney SA, Pearson ML, Gordon MT, Del Castillo R, Boyle JF, Jarvis WR. Efficacy of control measures in preventing nosocomial transmission of multidrug-resistant tuberculosis to patients and health care workers. Ann Intern Med 1995;122:90–5.
425. Jarvis WR. Nosocomial transmission of multidrug-resistant *Mycobacterium tuberculosis*. Am J Infect Control 1995;23:146–51.
426. Kenyon TA, Ridzon R, Luskin-Hawk R, et al. A nosocomial outbreak of multidrug-resistant tuberculosis. Ann Intern Med 1997;127:32–6.
427. Blumberg HM, White N, Parrott P, Gordon W, Hunter M, Ray S. False-positive tuberculin skin test results among health care workers. JAMA 2000;283:2793.
428. Barrett-Connor E. The epidemiology of tuberculosis in physicians. JAMA 1979;241:33–8.
429. Fraser VJ, Kilo CM, Bailey TC, Medoff G, Dunagan WC. Screening of physicians for tuberculosis. Infect Control Hosp Epidemiol 1994;15:95–100.
430. Geiseler PJ, Nelson KE, Crispen RG. Tuberculosis in physicians. Compliance with preventive measures. Am Rev Respir Dis 1987; 135:3–9.
431. Camins BC, Bock N, Watkins DL, Blumberg HM. Acceptance of isoniazid preventive therapy by health care workers after tuberculin skin test conversion. JAMA 1996;275:1013–5.
432. Shukla SJ, Warren DK, Woeltje KF, Gruber CA, Fraser VJ. Factors associated with the treatment of latent tuberculosis infection among health-care workers at a midwestern teaching hospital. Chest 2002;122:1609–14.
433. CDC. Prevention and control of tuberculosis in facilities providing long-term care to the elderly: recommendations of the Advisory Committee for Elimination of Tuberculosis. MMWR 1990;39 (No. RR-10):7–20.
434. Ijaz K, Dillaha JA, Yang Z, Cave MD, Bates JH. Unrecognized tuberculosis in a nursing home causing death with spread of tuberculosis to the community. J Am Geriatr Soc 2002;50:1213–8.
435. Stead WW. Tuberculosis among elderly persons, as observed among nursing home residents. Int J Tuberc Lung Dis 1998;2(9 Suppl 1):S64–70.
436. Ijaz K, Yang Z, Templeton G, Stead WW, Bates JH, Cave MD. Persistence of a strain of *Mycobacterium tuberculosis* in a prison system. Int J Tuberc Lung Dis 2004;8:994–1000.
437. Nardell EA. Environmental infection control of tuberculosis. Semin Respir Infect 2003;18:307–19.
438. Francis J. Curry National Tuberculosis Center, Institutional Consultation Services, California Department of Health Services. Tuberculosis in homeless shelters: reducing the risk through ventilation, filters, and UV. San Francisco, CA: Francis J. Curry National Tuberculosis Center; 2000 Available at http://www.nationaltbcenter.edu/catalogue/downloads/tbhomelessshelters.pdf.
439. Klovdahl AS, Graviss EA, Yaganehdoost A, et al. Networks and tuberculosis: an undetected community outbreak involving public places. Soc Sci Med 2001;52:681–94.
440. Ginsberg AM. A proposed national strategy for tuberculosis vaccine development. Clin Infect Dis 2000;30(Suppl 3):S233–42.
441. CDC. Framework for evaluating public health surveillance systems for early detection of outbreaks: recommendations from the CDC Working Group. MMWR 2004;53(No. RR-5):1–11.

Terms and Abbreviations Used in This Report

AAP	American Academy of Pediatrics
ACET	Advisory Council for the Elimination of Tuberculosis
AFB	acid-fast bacilli
ATS	American Thoracic Society
BCG	*Mycobacterium bovis bacillus Calmette-Guerín*
CIS	U.S. Citizenship and Immigration Service
DGMQ	CDC's Division of Global Migration and Quarantine
DOT	directly observed therapy
EDs	emergency departments
FDA	Food and Drug Administration
HAART	highly active antiretroviral therapy
HCWs	health-care workers
HIPPA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
IDSA	Infectious Diseases Society of America
IOM	Institute of Medicine
LTBI	latent tuberculosis infection
NAA	nucleic acid amplification assay
NCTA	National Tuberculosis Controllers Association
NIH	National Institutes of Health
NTCA	National Tuberculosis Controllers Association
NTGSN	National Tuberculosis Genotyping and Surveillance Network
NYC	New York City
PRP	personal respiratory protection
QFT	QuantiFERON®-TB test
QFT-G	QFT gold test
RFLP	restriction fragment length polymorphism
SES	socioeconomic status
TB	tuberculosis
TBGP	Tuberculosis Genotyping Program
TNF-α	cycotine tumor necrosis factor alpha
WHO	World Health Organization

Joint Subcommittee of the American Thoracic Society (ATS), the Infectious Diseases Society of America (ISDA), and CDC

Membership List, November 2004

Chair: Charles M. Nolan, MD, Seattle-King County Department of Public Health, Seattle, Washington (American Thoracic Society).

Co-chairs: Henry M. Blumberg, MD, Emory University School of Medicine, Atlanta, Georgia (Infectious Diseases Society of America), Zachary Taylor, MD, National Center for HIV, STD, and TB Prevention, CDC, Atlanta, Georgia.

Members: John Bernardo, MD, Boston University School of Medicine, Boston, Massachusetts; Patrick J. Brennan, MD, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania; Nancy E. Dunlap, MD, PhD, University of Alabama at Birmingham, Birmingham, Alabama; Charles L. Daley, MD, National Jewish Medical and Research Center, Denver, Colorado; Wafaa M. El-Sadr, MD, Harlem Hospital and Columbia University, New York City, New York; Sue Etkind, MS, Massachusetts Department of Public Health, Jamaica Plain, Massachusetts; Mark FitzGerald, MD, University of British Columbia, Vancouver, British Columbia, Canada; James B. McAuley, MD, Rush Medical College, Chicago, Illinois; Marisa Moore, MD, Centers for Disease Control and Prevention, Atlanta, Georgia; Noreen L. Qualls, DrPH, Centers for Disease Control and Prevention, Atlanta, Georgia; Randall R. Reves, MD, Denver Public Health, Denver, Colorado; Sarah E. Royce, MD, California Department of Health Services, Berkeley, California; Max Salfinger, MD, Wadsworth Center, New York State Department of Health, Albany, New York; Jeffrey R. Starke, MD, Texas Children's Hospital and Baylor College of Medicine, Houston, Texas; Wanda Walton, PhD, Centers for Disease Control and Prevention, Atlanta, Georgia; Stephen E. Weis, DO, University of North Texas Health Science Center at Fort Worth, Fort Worth, Texas; and Jan Young, MS, California Department of Health Services, Berkeley, California.

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format and on a paid subscription basis for paper copy. To receive an electronic copy each week, send an e-mail message to *listserv@listserv.cdc.gov*. The body content should read *SUBscribe mmwr-toc*. Electronic copy also is available from CDC's World-Wide Web server at *http://www.cdc.gov/mmwr* or from CDC's file transfer protocol server at *ftp://ftp.cdc.gov/pub/publications/mmwr*. To subscribe for paper copy, contact Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone 202-512-1800.

Data in the weekly *MMWR* are provisional, based on weekly reports to CDC by state health departments. The reporting week concludes at close of business on Friday; compiled data on a national basis are officially released to the public on the following Friday. Address inquiries about the *MMWR* Series, including material to be considered for publication, to Editor, *MMWR* Series, Mailstop K-95, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30333; telephone 888-232-3228.

All material in the *MMWR* Series is in the public domain and may be used and reprinted without permission; citation as to source, however, is appreciated.

All *MMWR* references are available on the Internet at http://www.cdc.gov/mmwr. Use the search function to find specific articles.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

References to non-CDC sites on the Internet are provided as a service to *MMWR* readers and do not constitute or imply endorsement of these organizations or their programs by CDC or the U.S. Department of Health and Human Services. CDC is not responsible for the content of these sites. URL addresses listed in *MMWR* were current as of the date of publication.

☆U.S. Government Printing Office: 2006-523-142/00120 Region IV ISSN: 1057-5987