Summary and Policy Options 1

Tuberculosis (TB) is a contagious disease that has killed millions of people worldwide over the centuries. The lack of a reliable cure prior to this century and TB's perceived randomness made it a common theme in literature and a metaphor for larger social and political ills (84,299). Today, TB continues to be a public health threat in the United States. After decreasing in the country as a whole for many decades, rates of TB disease are again on the rise. In some communities, particularly among economically disadvantaged groups, TB rates have consistently remained high.

Recent trends in the incidence of TB have been linked, in part, to decreases in public health investment over the last two decades (45,46,176). Other factors associated with the resurgence of TB include the human immunodeficiency virus (HIV) epidemic, foreign birth, substance abuse, poverty, and hopelessness. An important complication is the emergence of TB strains resistant to the most commonly used anti-TB drugs.

Unchecked, these recent trends in TB represent a serious threat to communities already saddled with poor health, poverty, and other social problems. Furthermore, this disease could become a additional major burden to the Nation's health care system.

Unlike the TB of past centuries, however, today's TB is amenable to human intervention, We know how it is spread. We know how to cure it, and we know how to prevent it. Although the primary governmental responsibility for controlling TB in the

NOTE: Because of the large amount of material synthesized to produce this report, most citations to the literature underlying this summary chapter are omitted. However, the detailed analysis presented in subsequent chapters is fully referenced, and the summary in this chapter closely follows the organization of the subsequent chapters. References to ideas that are found only in this chapter are given where they occur.

United States falls to State and local authorities, the Federal Government has had, and continues to have, a substantial role in eliminating this disease. This report synthesizes scientific understanding of TB in the United States in 1993 and considers the Federal role in its control.

SCOPE OF THE OTA REPORT

Three congressional committees requested this report: the Subcommittee on Health and the Environment of the House Committee on Energy and Commerce, the Subcommittee on Human Resources and Intergovernmental Relations of the House Committee on Government Relations, and the Senate Committee on Labor and Human Resources. The report provides information on the problems posed by TB that Congress can use in considering alternative Federal policy responses. Although the report gives an overview of the direction and magnitude of Federal involvement in TB control and considers options for Congress, the report does not evaluate in detail the effectiveness of specific programs in individual communities or Federal agencies. Another congressional research agency, the General Accounting Office (GAO), is currently evaluating the effectiveness of efforts to control TB in several communities hit hard by the disease (183).

One-third of the world's population is infected with the organism that causes TB. With significant migration to the United States by people horn countries with high levels of TB, foreign birth is a risk factor for the disease in this country. Hence, controlling TB abroad could have some impact on levels of TB in the United States. Although this report briefly considers the Federal Governrnent's support of international organizations involved in TB control in developing countries, it focuses on TB as it occurs in the United States.

Tuberculosis, Health Care Reform, and Public Health Investments

As policymakers focus on health care reform, the analysis in this report indicates that TB will not disappear with improved access and better cost control of health care services alone. Even with universal access to medical services, a change in the organization and financing of health care will not, in and of itself, eliminate the need for Federal funding and coordination of the infrastructure to conduct education, surveillance, screening, diagnosis, research, and even treatment.

Furthermore, TB control is an exercise in vigilance. With an estimated one-third of the world's population infected with TB and the relative mobility of people in and out of the United States through immigration and tourism, the complete eradication of tuberculosis from this country is unlikely in the foreseeable future. In addition, people infected with the organism that causes TB now may progress to active disease many years in the fiture, after the current epidemic is brought under control. Nevertheless, TB control measures can lower disease rates and minimize the public health threat posed by the disease. Achieving such a goal will require a properly targeted and sustained effort. Once this goal is achieved, continued investment to identify treat, and prevent TB will be necessary to maintain low disease rates. The current resurgence in TB is evidence that this last lesson was not learned in the past. Even in the last year, the Centers for Disease Control and Prevention (CDC) noted its own failure to implement recent TB control recommendations, due largely to a lack of resources (337).

What Is TB?

In 1882, the German scientist Robert Koch identified a species of bacteria, ***Mycobacterium tuberculosis (M.tb.*** or tubercle bacilli) as the

cause of TB. There are two general stages of the disease: tuberculous infection (or "latent TB") and active tuberculosis. Individuals with tuberculous infection are asymptomatic and not contagious, whereas individuals with active TB can be symptomatic and contagious. Tuberculous infection is necessary to develop TB, but overall only 10 percent of those with the infection ever develop active TB. Risk is higher for children and for people with HIV and other disorders that impair immunity. In immunocompetent individuals, the immune system is usually able to contain most tuberculous infections. A tuberculin skin test, which uses a substance known as purified protein derivative (PPD), is used to detect tuberculous infection. In most immunocompetent people with the infection, this test produces a small raised area on the skin within 48 to 72 hours of administration.

While active TB can attack various parts of the body, pulmonary TB is the most common and leads to the destruction of lung tissue and frequently death if untreated. Symptoms include weakness, fever, chest pain, cough, and when a small blood vessel is eroded, bloody sputum. Active TB can also occur in other parts of the body, with the brain (TB meningitis) being the most serious. TB outside the lungs is more likely to occur among children and people with HIV.

What Is the Risk of TB Infection?

People with TB are contagious when they expel airborne particles containing viable tubercle bacilli through, for example, coughing, singing, speaking, or sneezing. The likelihood of infection depends mainly on the:

- Probability of coming into contact with someone with contagious, active TB;
- Closeness or intimacy of the contact;
- Duration of the contact;
- Number of viable bacilli present in the air;
- Susceptibility of the uninfected case; and
- Environmental conditions (e.g., volume of airspace, ventilation with outside air, relative humidity, presence of sunlight).

Health care workers (HCWS) are at increased risk of infection, particularly if they perform cough-inducing medical procedures on patients with active pulmonary TB and if they work in environments with inadequate infection control measures.

Casual contact with an infectious person—i.e. with active, untreated TB—in a public place such as a movie theater or subway is unlikely to lead to infection, although the risk is not zero. Although infection occurs at a specific point in time when an infectious particle is inhaled, the longer the exposure, the greater the likelihood an infectious particle will be inhaled. Hence, exposure to an infectious person over a period of months is usually necessary for transmission to occur.

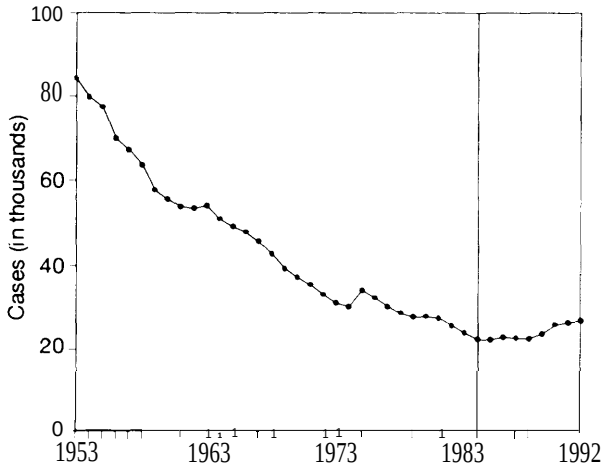
In general, less than 30 percent of household members become infected while living with an infectious person, but the risk is highly variable. Under extraordinary circumstances (when the concentration of airborne infectious particles is unusually high), exposures as brief as 2 hours have reportedly led to infection.

Adequate anti-microbial or anti-tuberculosis treatment can reduce the infectiousness of drug-susceptible TB within days. Although the exact amount of time needed to eliminate the infection completely varies by patient, it is about 6 months or longer. While there is no evidence that drug-resistant TB is more contagious than drug-susceptible TB, delays in diagnosis and treatment allow patients to remain infectious for a longer period of time, thus increasing chances of infecting others.

Trends in the Incidence of Active TB

Between 1953, when the Public Health Service (PHS) first implemented a national reporting system for active TB cases, and 1984, the number of annually reported cases declined 74 percent horn 84,304 (53 per 100,000 population) to

Figure I-l—Reported Tuberculosis Cases in the United States, 1953-92



SOURCE: Office of Technology Assessment, 1993, based on data from U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, 1992.

22,255 (9.4 per 100,000). Beginning in 1985, this decline slowed and then reversed (figure l-l). The number of new cases reported in 1992 was 26,673 (10.5 per 100,000), a 20 percent increase over 1985.

The Changing Demographics of TB

Over the years, TB has gradually shifted from a disease broadly distributed over the whole population to one that is more narrowly concentrated among certain portions of the population. Although the rapid increase in the overall number of new cases suggests a potential threat to the population as a whole, the current concentrations of the disease offer TB-control experts and policymakers a guide in targeting resources for controlling TB. Groups with particularly high rates of TB can be described according to geography, race, ethnicity, and factors causally related to the disease.

Heavy Concentrations in Certain Parts of the Country

The most populous States have the largest number of cases. In 1991, over half of all TB cases came from California, New York, Texas, Florida and Illinois. Urban areas with populations over 250,000 contained 18 percent of the country's population but 43 percent of its new TB cases in that year. The number of new TB cases per 100,000 of population in the South has always been above the national average, although New York, Hawaii, and California have the highest rates. Among cities, Atlanta (76.4 per 100,000), Newark (71.8 per 100,000), New York (50.3 per 100,000), Miami (48.5 per 100,000), and San Francisco (46.0 per 100,000) had the highest case rates[1] during 1991.

Accounting for 14 percent of the total number of new TB cases reported in the United States during 1991 and with a TB case rate five times the national average, New York City alone has a significant, concentrated portion of the Nation's entire TB problem. In one part of the city, Central Harlem, the case rate was 169.2 per 100,000 in 1989 and has never dipped below 52 during the 40 years that data have been kept (45).

Heavy Concentrations Among Minorities and the Young

Within a given geographic area, certain demographic groups are more likely than others to produce new cases of TB. In 1991, 71 percent of new cases occurred in racial and ethnic minorities. Hispanic Americans, Black Americans, and Americans of Asian or Pacific Island[2] origin showed relatively large increases in TB during the 1985-91 period. Although the risk of TB in adults increased with age, this pattern was not consistent across different racial and ethnic groups. Among white, non-Hispanic Americans, most TB cases occurred among elderly people, while among

[1] A "case rate" is defined as the number of cases of active TB diagnosed in a given year per 100,000 population.

[2] Terms used to describe these demographic groups are those used in the original studies from which the epidemiologic findings are drawn.

Black and Hispanic Americans, the bulk occurred in the 25 to 44 year-old age group.

Rates of increase have been disproportionately high among children; this trend is also concentrated among racial and ethnic minorities, who accounted for 86 percent of all childhood cases in 1991. Childhood cases of TB are strong evidence of recent transmission of the disease, suggesting contact with other infectious individuals in the community and possibly more, undetected cases of infection. High rates of TB among immigrants and increases in TB among parents in the 25 to 44 age group may account for the observed increases among children. Furthermore, children infected now could suffer active disease years in the future.

High Rates *Among Immigrants, Prisoners, Drug Users, Migrant Workers, and Homeless People*

Being born outside the United States, being homeless, a substance abuser, being incarcerated, or being a migrant worker is a risk factor for tuberculous infection. In addition, being confected with HIV increases one's risk of progressing from infection to active disease. The overlap among these groups reinforces the concentration of TB within the United States population and the particular risk for members of these groups.

Given the high prevalence of TB infection in many other parts of the world (171), a large percentage of new TB cases in the United States occur among individuals born elsewhere (27 percent in 1991). Among homeless populations, several studies have found latent TB infection to be as high as 50 percent. Impaired immunity due to poor overall health, substance abuse, or HIV infection may cause homeless people with tuberCUIOUS infection to progress to active disease. In addition, homeless shelters can generate new transmissions, due to crowding and poor ventilation. Twenty percent of newly diagnosed TB cases in New York City in 1991 were homeless.

Substance-abusing populations overlap with other groups at high risk of TB, especially with homeless and HIV-infected people.

The prevalence of TB in prisons is related to the close living quarters, poor ventilation, and other risk factors that inmates may possess. In some States, epidemiologists have estimated that TB may be as much as 6 to 11 times more prevalent among prisoners than among the general population. Prison populations comprise other groups at high risk of TB--drug users, HIV-infected people, and individuals homeless prior to incarceration. Persons with active TB in prisons cannot only spread the disease among other prisoners, but they also place at-risk prison staff and family or friends with whom they have close contact upon their release.

Among migrant workers, lack of access to health services and lack of adequate working and housing conditions are believed to contribute to the heightened risk of TB as noted among some limited recent studies, Many members of this group are also poor, minorities, foreign born, or former homeless shelter residents.

People With HIV Have High TB Rates

HIV is the pathogen that causes acquired immunodefiency syndrome (AIDS). Because HIV-related immunosuppression impairs the body's ability to fight a tuberculous infection, individuals infected with both tubercle bacilli and HIV are estimated to have a risk of as high as 8 percent per year of progressing rapidly to active TB disease, compared with a 10 percent lifetime risk for HIV-negative individuals.

Epidemiologic evidence has consistently shown a higher prevalence of TB among individuals with AIDS compared with the general population, even after adjustment for age, race, and sex. In addition, more than one-half of deaths with TB in

individuals 20 to 49 years old appear to occur in people who also have AIDS.[3]

Multidrug-Resistant Tuberculosis

When a patient takes TB medication erratically or when an inadequate combination of drugs is prescribed, active, infectious TB can recur in a form resistant to one or more of the drugs used in the original treatment.[4] As described later in this chapter and in detail in chapter 4, cases of MDR-TB are far more difficult and costly to treat than drug-sensitive TB, and can be fatal despite the best available treatment. CDC began regularly collecting drug susceptibility data on each reported case of TB in 1993, a practice done periodically with surveys prior to 1986.

Preliminary data from a 1991 CDC survey indicate that drug resistant TB cases have been reported in all regions of the country, but are most heavily concentrated in a few States. Cases resistant to at least one drug were found in 36 States and to two or more drugs in 13 States. Of the cases found to be resistant to the two most commonly used drugs, isoniazid (lNH) and rifampin (RW), over half were in New York City. In a separate study, 33 percent of the 466 TB cases reported in New York City during April 1991 were resistant to one or more drugs, and 19 percent were resistant to both INH and RIF.

Since 1990, there have been at least 9 outbreaks of MDR-TB among 297 individuals in prisons and hospitals. Most of these people were HIV-infected. As many as 89 percent of those with MDR-TB (including 6 health care workers and 1 prison guard) have died from their TB.[5] Delayed or inadequate infection control measures, premature discontinuation of patient isolation, delayed reporting of drug resistance, and lack of isolation facilities were major factors in the spread of MDR-TB in these institutions.

Three Strategies for TB Prevention

Under public policy discussion are three strategies for preventing the spread of T'B-infection control, finding and offering preventive treatment to infected high-risk populations, and bacillus Calmette-Gu&in (BCG) vaccination.

Infect/on Control

Although tuberculous infection has long been known as an occupational hazard for health care workers, and although there is some evidence that HCWS in some jobs (e.g. pulmonary medicine) are at greater risk than other HCWS, the actual magnitude of the risks have not been well documented in recent years.

CDC updated its guidelines for preventing TB transmission within hospitals in 1990 and is expected to do so again in the near future (79). The guidelines call for a' 'hierarchy of controls,' including limiting exposure to the source of infection (through identification, respiratory isolation, and prompt treatment of infectious patients), implementing environmental measures, and using individual protective devices. None of these measures are believed to have been widely adopted by hospitals or other institutions.

Although implementing combinations of these measures appears to have been effective in ending the recent outbreaks, there are few data on the effectiveness of individual measures under conditions of actual use ***(79).***[6] ***In*** practice, decisions

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[3] Despite the prevalence of TB among those with HIV, *M.tb.* may represent only 10 percent of mycobacterial infections in this patient group. Non-tuberculous mycobacteria (e.g., *M.avium*) is very common among AIDS patients; these infections occur in later stages of AIDS (when CD4 cell counts are below 100/mm^3), are untreatable, and maybe fataL

[4] Strains of TB treatable with available anti-TB medications are called 'drug sensitive. " Strains resistant to at least one anti-TB medication are called "drug-resistant."According to the CDC, strains resistant to, at least, isoniazid and rifampin are referred to as MDR-TB.

[5] It is unknown whether the high rate of mortality observed in these outbreaks applies to other HIV-infected populations or to HIV-negative individuals.

[6] CDC currently has some such research underway with plans to begin more in the future (see chapter 7).

about the adoption of individual measures depend not just on their efficacy in controlled experiments, but also on their feasibility given the physical characteristics of the relevant facility, the patient population, and available resources.

Another basic component of CDC'S guidelines is achieving adequate ventilation, which can be difficult in modern facilities designed for energy conservation or in older buildings without central air circulation. New devices are under development to filter and recirculate air within individual rooms. Also, germicidal ultraviolet-C (W-C) light has been advocated as an adjunct to ventilation controls, as have masks designed to fit tightly around the mouth and nose (called disposable particulate respirators); but ***data on the effectiveness of each under actual conditions of use are lacking.***

In 1992, the National Institute of Occupational Safety and Health (NIOSH), a part of the CDC, recommended that HCWS who come in contact with infectious TB patients should wear ''powered air purifying respirators" (PAPRs), devices commonly employed in industrial settings to protect workers from toxic fumes and other substances. Other TB experts at CDC criticized the NIOSH recommendation, arguing that PAPRs are unnecessary and interfere with the provision of clinical care. TB experts outside of CDC report that these contradictory recommendations have caused confusion among HCWS, patients, and those charged with controlling infection in facilities with TB patients (304). The divergent recommendations may reflect the different missions of NIOSH and the rest of CDC. While NIOSH is mandated to seek zero occupational risk, the position of the others at CDC on PAPRs reflects an attempt to balance worker safety with the provision of feasible effective treatment to patients (79). Whatever the intent or impact of these recommendations, however, there is currently no evidence on the effectiveness of PAPRs.

Skin Testing and Preventive Treatment

For several decades, it has been theoretically possible to prevent most new cases of TB with available diagnostic and preventive treatment methods. As TB has retreated from the general population and become more concentrated among subset populations, such targeted efforts should have become more feasible. Indeed, CDC has long recommended screening for tuberculous infection among groups with high rates of TB, with HIV, or with other risk factors for developing active disease and INH preventive treatment (IPT) for those found to be infected. ***The ability to implement these recommendations has been limited largely by the availability of funding, other resources, and knowledge about the most cost-effective methods of providing these services to high-risk groups.***

In order to prescribe IPT, one must first detect a TB infection, usually with the PPD tuberculin skin test. For otherwise healthy people, the test detects an existing infection about 95 percent of the time with a variable false positive rate. For people with HIV and other immune deficiencies, the test is much less likely to detect tuberculous infection (due to a condition called anergy), reducing its effectiveness as a screening tool in these populations and thus limiting the use of IPT.

For those with tuberculous infection the preventive use of the anti-TB drug isoniazid (INH) has been shown in large, randomized clinical trials to be as much as 90 percent effective in eliminating the bacilli from the body and preventing subsequent development of active disease. Between 2 and 3 percent of adults over age 50 receiving INH develop liver inflammation that can lead to hepatitis if the drug is not stopped when blood tests reveal the condition.

BCG Vaccination

Since the early 1950s, the World Health Organization (WHO) has advocated widespread vaccination with BCG as a preventive measure against TB in countries with a high prevalence of

the disease. Currently, about 70 percent of the world's children receive BCG. However, BCG has never been widely used in the United States due, in part, to controversy over its efficacy and low expected utility in populations in which the rate of TB transmission is relatively low.

BCG refers to several strains of bovine tubercle bacilli derived from a single strain produced about 70 years ago in France. One form of BCG is currently manufactured and sold with Food and Drug Administration (FDA) approval in the United States, Instead of preventing initial TB infection, BCG is believed to enhance the body's immune response to the infection and prevent the multiplication and dissemination of bacilli to various parts of the body.

Several studies, including randomized clinical trials, have produced estimates of the preventive efficacy of BCG that range from zero (or negative) to 80 percent. It is also unclear how long BCG might enhance immunity and whether HIV-related irnmunodeficiency inhibits the vaccines' usefulness. Attempts to interpret the existing data and understand the differing results continue. Some research does suggest that BCG may be more effective in preventing the more serious extrapulmonary forms of TB among children than in preventing the pulmonary forms of the disease. Although side effects are rare and data are insufficient to make actual risk estimates, there have been published case reports of BCG complications among HIV-infected individuals.

BCG vaccination may itself cause subsequent tuberculin skin tests to show up as positive for 3 to 5 years, thereby complicating public health efforts to detect actual infections and offer preventive treatment. ***Framed as a policy choice among alternative strategies for prevention"on, Federal policy in the United States has long favored strong infection control, skin testing, and preventive treatment. However, CDC does recommend selected use of the vaccine in high -tisk infants and children for whom preventive treatment is infeasible or culturally unacceptable.***

Diagnosis of Active TB

At present, diagnosis of active TB is based on a combination of clinical symptoms, laboratory tests, and chest x-ray findings. Although these technologies have been generally adequate, their deficiencies have grown in the face of rising drug resistance and the need to prevent the rapid spread of TB among patients who have HIV or who live in congregate settings.

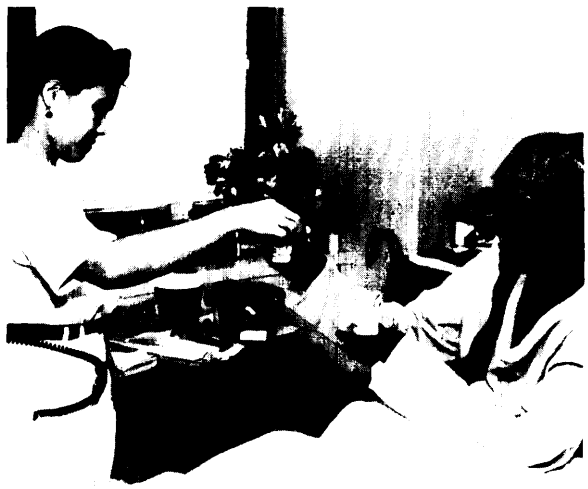
The TB skin test used for detecting tuberculous infection is considered inadequate for diagnosing active disease, partly because of its unreliability with imrnunocompromised and other sick people and with the minimum of ***48*** hours required for results. The initial diagnostic laboratory test is the sputum smear in which a sample of the patient sputum is stained with a dye for acid fast bacilli (AFB) and is examined under a light microscope. However, only 50 to 80 percent of patients with active TB have positive sputum smears, and the rate may be even lower for people with HIV. Hence, negative smears cannot be used to rule out TB. Chest x-rays are also used to detect signs of the presence of TB in the lungs or the damage caused by the disease.

Definitive diagnosis of TB has been traditionally based on culturing and identifying tubercle bacilli from a patient's sputum, body fluids, or tissue in the laboratory. This test takes 3 to 6 weeks given the bacilli's slow rate of growth. A relatively new, automated, radiometric device (known by the trade name of BACTEC™) reduces testing time to about 10 days by measuring carbon dioxide given off by the tubercle bacilli. Other diagnostic technologies are under development.

Effective treatment depends on determining the susceptibility of a patient's TB to antituberculosis drugs. Delayed diagnosis and drug susceptibility testing were considered to be one of the main factors contributing to the recent outbreaks of MDR-TB and continue to represent a major impediment in the control of TB. Conventional methods of drug susceptibility testing

typically require 8 to 12 weeks. Newer radiometric techniques used with direct testing can determine susceptibility to the five first-line drugs within 3 weeks, although these tests are relatively expensive and not yet widely available.

Newer diagnostic technologies under study include a genetic technique called polymerase chain reaction (PCR) to amplify the amount of deoxyribonucelic acid (DNA) material specific to tubercle bacilli. PCR-based diagnosis has reportedly produced results in research conditions within 48 hours. However, PCR techniques currently carry a high risk of operator error, and TB diagnosis using this technology is not yet available for nonexperimental use (29,30).[7] A recently reported method uses the light-producing enzyme from fireflies to distinguish drug-resistant and drug-sensitive tubercule bacilli in 2 to 3 days. However, this technology has not yet been adapted for clinical use. Other quick diagnostic technologies are in various stages of development.



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Treatment of drug-susceptible TB involves taking three or four drugs together on a daily, two-, or three-time a week basis for 6 months. However, hospitalization is usually not necessary after a few weeks of treatment renders the patient noninfectious. Treatment of drug-resistant TB can involve more drugs for a longer period of time and potentially longer hospital stays.

Treatment of Active TB

The introduction of antibiotic drug treatment in the 1940s dramatically changed the practice and outcome of TB treatment. Over the past 20 years, no new drugs have replaced or supplemented the five main frost-line drugs-INH, RF, pyrazinamide (PZA), ethambutol (EMB), and streptomycin (SM)--although other drugs of lesser effectiveness and greater toxicity are available as second-line drugs. In addition, clinical research has permitted abetter understanding of how drugs eliminate TB from the body as well as the refinement of drug treatment regimens.

Combinations of antimicrobial drugs with overlapping functions are used in current treatment regimens to attack tubercle bacilli in the body. Anti-tuberculous drugs are generally classified as bactericidal (producing rapid killing of bacilli) or sterilizing (killing the last surviving, slowly metabolizing bacilli over the long-term), INH is the major bactericidal drug. RIF and PZA are the most potent sterilizing drugs.

Current regimens usually consist of two phases and can, if taken fully, produce cure rates of 98 percent with relapses among less than 3 percent. During an initial 2-month bactericidal phase, the daily use of INH, RIF, PZA, and SM or EMB is intended to eliminate quickly the bulk of tubercle bacilli. During the second 4 to 5 month sterilizing phase, patients take INH and RIF on a daily schedule or a two- to three-time a week schedule to eliminate remaining bacilli. These drugs can cause side effects, the most serious of which is hepatitis, an inflammation of the liver.

By comparison, treatment of MDR-TB is longer, potentially more toxic, less effective, and significantly more costly. Drug regimens for MDR-TB are determined on a case-by-case basis using information on the patient's prior drug therapy, drug-susceptibility testing of the pa-

[7] One manufacturer, Hoffman LaRoche, offers this test as a service for laboratories that provide it with patient tissue samples; however, the cost is approximately $175 per specimen, making it relatively expensive (29,30).

tient's bacilli, and the patient's tolerance of adverse effects. Cases resistant to two or more of the first-line drugs would be treated with combinations of drugs selected from among the first- and second-line drugs, often for 18 to 24 months or longer.

The arsenal of second-line TB drugs includes: capreomycin, kanamycin, ethionarnide, cycloserine, and p-aminosalicyclic acid. Reliable data to judge the effectiveness of these second-line drugs are lacking, but anecdotal experience suggests that they are much less effective and more likely to lead to serious toxic effects. Adjunctive surgery to remove heavily infected tissue (usually in the lung) is sometimes used as a last resort when drug treatment is inadequate in patients with localized pulmonary TB.

Current evidence suggests that drug-sensitive TB is curable in many individuals with HIV, even some with advanced stages of immunodeficieny. Most documented cases of treatment failure in patients with HIV have been linked with incomplete treatment or poor absorption of antituberculosis drugs. The major problems in treating TB in HIV-infected people are drug side effects and interactions with other treatments or conditions.

Recently, the FDA has worked with drug manufacturers to rectify shortages of some drugs. Public health officials have also expressed concern over increases in the price of antituberculosis drug treatments. Table 1-1 shows the results of a recent CDC survey of the prices paid by State and local health departments for drugs they purchase for two common TB drug regimens. Table 1-1 suggests drug price increases of about 9 percent per year on average between 1986 and 1992 for treating an uncomplicated case and about 12 percent per year for treating a patient resistant to INH and RIF.

Current research is focused on developing new drugs, shorter regimens, and better methods of drug delivery. A number of individual drugs are being investigated for anti-TB activity, but so far there is limited or no data about their efficacy and safety from controlled clinical trials. Among such drugs not yet approved for TB treatment in the United States are clofazamine and the classes of drugs known as quinolones, rifamycin derivatives, and phenazines.

Combination tablets containing INH and RIF (known by the trade name Rifamate™) are approved by the FDA but not widely used in the United States. In 1993, the FDA received an application to market Rifater™, a combination of INH, RIF, and PZA, in the United States. Implantable devices containing anti-TB drugs for slow release similar to the contraceptive NorPlant™ are not yet ready for clinical evaluation. Irnmunotherapeutic approaches to treating TB are also under investigation.

Delivering TB Treatment

Because current TB treatment involves taking multiple drugs over many months, complete, appropriate treatment can be hard to achieve. Hence, the delivery of treatment is as important for TB control as is the arsenal of available drugs themselves. Current programs to deliver treatment and other TB services are heterogeneous and can vary across and with communities.

Data based on samples of TB case reports suggest that about 75 percent of U.S. patients being treated for TB complete treatment within a year and that 80 percent take their medication on a continuous basis. However, these national averages obscure wide variation among different areas of the country. For example, in the late 1980s, cities such as Chicago, New York, and the District of Columbia reported completion rates ranging from 54 to 60 percent, while Dallas, San Francisco, and El Paso had rates above 94 percent.

While much public discussion has focused on patient behavior as the cause of treatment failure, evidence suggests that the availability and quality of TB control services as well as prescription of optimal treatment regimens may be equally important in determining whether patients are cured.

Table I-l—Trends in Drug Costs for Treating Tuberculosis in a 165 lb (75 kg) Patient, 1986-92: An Uncomplicated Case Versus a Case Resistant to INH and RIF[a]

Uncomplicated case: Drug	Daily dose	Duration	1986 cost	1990 cost	1992 cost
Isonizaid	300 mg	180 days	$ 5.04	$ 6.50	$ 8.50
Rifampin	600 mg	180 days	106.20	159.30	165.30
Pyrazinamide	25 mg/kg	60 days	98.00	160.00	179.20
			$209.24	$325.80	$353.00
Average annual percentage increase in cost, 1986-92: 9.1 Yo					
A case resistant to INH and RIF: Drug	Daily dose	Duration	1986 cost	1990 cost	1992 cost
Pyrazinamide	25 mglkg	540 days	$882.00	$1,440.00	$1,613.00
Ethambutol	15 mgfkg	540 days	690.00	1,246.00	1,610.00
Streptomycin	15 mgfkg	120 days	138.00	192.00	206,00
Ethionamide	20 mg/kg	540 days	890.00	1,458.00	1,691.00
Ciprofloxacin	1500 mg	540 days	NA	3,000,00	3,600.00
			$2,600.00	$7,338.00	$8720.00'
Average annual percentage increase in cost, 1986-92 (without Ciprofloxacin): 12.0%					
*Add ofloxacin=$4,080 .00					
Add amikacin=$27,648 .00					
Add clofazimine=$71 .00					

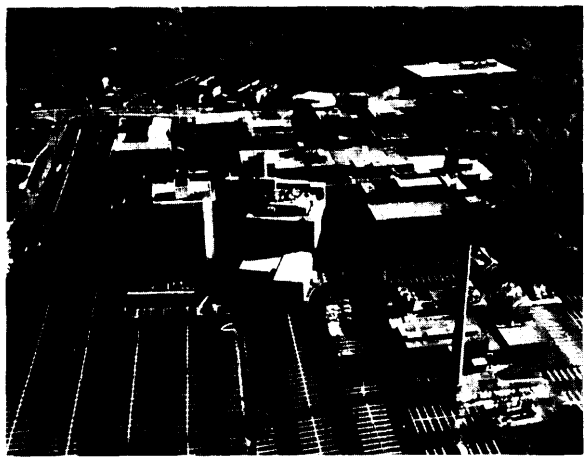
KEY: NA - not available.
a Treatment costs based on median prices given **in table 5-1. Costs are for an entire recommended treatment CYde. Estimates include drug casts only.**

SOURCE: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, Division of Tuberculosis Elimination, 1993.

State statutes authorize State and local health agencies to control TB and other communicable diseases. Most of these agencies, in turn, contract with local hospitals and clinics to provide TB services. It is widely held, though infrequently documented, that these public health services have generally not kept pace with health problems in recent years, resulting in part from dwindling funds, lack of expertise, and outdated technologies. In addition, long waiting times, an inhospitable environment for personal care, and lack of flexible service hours in many public health clinics may also contribute to inadequate treatment.

As many specialized TB facilities closed during the 1960s and 1970s, much of the job of TB diagnosis and treatment has shifted to private primary care physicians, many of whom are unaccustomed to seeing patients with active TB or MDR-TB. These physicians maybe less likely to suspect TB, diagnose it quickly, and prescribe the most efficacious treatment regimen. Recently collected data suggest that as many as 40 percent of physicians would unknowingly prescribe an inappropriate TB regimen, an error which could lead to treatment failure and emergence of drug resistance.

Even when an optimal drug regimen is prescribed, available, and feasible, patients do not always complete treatment. A very small percentage of patients do refuse or are mentally unable to follow treatment. Still, available evidence suggests that most patients would complete treatment if it were feasible to do so or if encouraged to do so through incentives and progressively more stringent measures as allowed by law to protect the public health.



The Centers for Disease Control and Prevention, headquartered in Altanta, has primary responsibility within the Federal Government for TB control.

A central issue in treatment delivery concerns the degree to which supervision by HCWS is necessary to bring about higher rates of treatment completion. One form of supervised treatment is directly observed treatment (DOT), which CDC defines as observation of the patient by a health care provider or other responsible person who has frequent contact with the patient as the patient ingests anti-TB medications. Although the concept of DOT is often proposed in policy and clinical discussions, often as an alternative to more restrictive forms of ensuring treatment completion, DOT can take many forms. Some programs limit DOT to health care facilities, while others send workers to patients' homes or other places. All DOT programs are labor-intensive and require skill, diligence, perseverance, and funds.

While some groups, including CDC and ALA, have recommended DOT be considered for every patient, others have argued that its use for most patients is wasteful and needlessly restrictive since they would complete therapy anyway. Most of the existing literature of different treatment delivery strategies are only descriptive in nature. ***Little systematic research has been done on the effectiveness or cost effectiveness of individual DOT strategies or of DOT compared to less supervised treatment for different patient populations. A more complete assessment of costs and outcomes is needed to generate useful information for public policy.***

Federal Involvement in TB Control

Primary responsibility for designing and carrying out TB control services rests with State and local health departments, not the Federal Government. Still, the Federal Government does provide the major funding, other resources, leadership, and coordination to the Nation's TB control efforts through several agencies. Only a few of these agencies are able to estimate spending for TB as distinct from funds for other responsibilities.

Public Health Activities

The Centers for Disease Control and Prevention make up the lead Federal agency for TB control. Out of its $79 million TB budget for fiscal year 1993, CDC gave $34.3 million in grants to State and local health departments. Another $39.2 million constituted emergency funds that Congress separately appropriated for TB control in six States and seven cities most heavily affected by TB. The remaining $5.2 million supported TB program operations at CDC itself. CDC also used $25.4 million designated for HIV activities for HIV-related TB efforts. Table 1-2 breaks down CDC'S TB spending for fiscal year 1993 by function. These appropriations represented a major increase in TB funds over previous years (see figure 1-2). In addition, the President's fiscal year 1994 budget request includes $50 million over fiscal year 1993.

Following a drastic scaleback in Federal TB funding in the 1960s and 1970s, CDC restarted many of its activities in the early 1980s and developed a comprehensive "Strategic Plan for the Elimination of Tubeculosis in the United States' with the goal of lowering the incidence to 3.5 per 100,000 by the year 2000 and 0.1 per

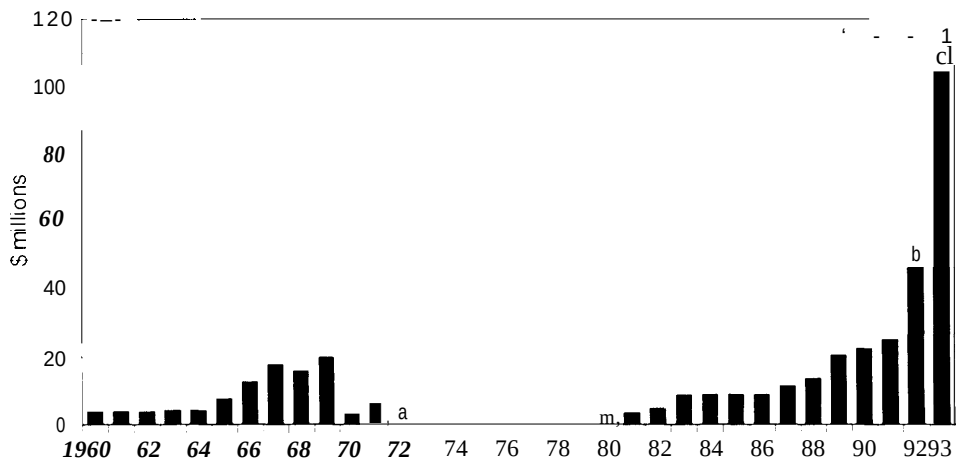
Table 1-2—U.S. Centers for Disease Control and Prevention Spending for Tuberculosis by Function, Fiscal Year 1993

	Dollars ($ millions)	Percent Of budget
Community-based control programs (screening, treatment, prevention, infection control)	$36.9	35!40
Outreach and service linkage (implementation of directly observed therapy)	36.7	35
Research and demonstration	9.8	9
Surveillance, epidemiology and data systems	7,0	7
Laboratory services	4.8	5
Public education and information	4.4	4
Professional competence assurance (training for service providers, physicians, researchers, and laboratory personnel)	2.2	2
Leadership and administration (technical assistance to improve management of State and local TB control programs)	2.2	2
Community protecition/regulatory programs	NA	NA
Total	$104.0	100?40'

NA = not available.
a Component percentages do not add up to 100 percent due to rounding error.

SOURCE: Office of Technology Assessment, 1993, based on data from C. Bozzi, Assistant to the Director for Tuberculosis Coordination, Division of Tuberculosis Elimination, Public Health Service, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, Atlanta, GA, personal communication, July 9, 1993.

Figure 1 -2—Tuberculosis Funding, U.S. Centers for Disease Control and Prevention, Fiscal Years 1960-93



a Fiscal years 1972 through 1982 categorical grants ceased, funds to states were in block grants not specific for TB.
b Fiscal year 1992 includes $26 million in human immunodeficiency virus (HIV) funds, used for HIV-related TB activities.
C Fiscal year 1993 includes $25 million in HIV funds used for HIV-related TB activities.

SOURCE: Office of Technology Assessment, 1993, based on data from the U.S. Centers for Disease Control.

100,000 by 2010. In 1992, CDC headed a task force of Federal agencies and other public health groups that issued a complementary "National Action Plan to Combat MDR-TB. " The task force plan, which targets all forms of TB, not just drug-resistant forms, details an exhaustive array of government and private responsibilities in TB control and research.

CDC estimates that Congress would need to increase CDC'S budget for TB control by $380 million for fiscal year 1994 to implement fully CDC'S responsibilities under the MDR-TB Action Plan. This amount is $330 million more than the amount actually requested in the President's 1994 budget. Estimates of money necessary for other agencies to implement their responsibilities under the action plan are not currently available.

Other Federal agencies run health care facilities that provide TB treatment. These agencies include the Department of Veterans Affairs, the Indian Health Service, and the Federal Bureau of Prisons. In addition to supporting some anti-TB drug research and the development of educational materials on TB for health professionals, the Department of Health and Human Services' (U.S. DHHS) Health Resources and Services Administration (HRSA) funds TB services through State and locally run clinics that serve disadvantaged and underserved populations. The U.S. Agency for International Development (U.S. AID) gave over $8 million for TB control in developing countries, most of which supported BCG vaccination of children. Other agencies with roles in TB control include the U.S. DHHS Substance Abuse and Mental Services Administration (SAMHSA), Department of State's consular offices and embassies abroad, the Department of Justice's Immigration and Naturalization Service (INS), and the Department of Labor's Occupational Safety and Health Administration (OSHA).

Research and Development

Most Federal TB-related research and development R&D is conducted or funded by the National Institutes of Health (NIH). Its spending for TB research has increased dramatically from $4.2 million in fiscal year 1991 to $35.9 million in fiscal year 1993, with an additional $10 million requested by the President in his fiscal year 1994 budget proposal.[8] The bulk of NIH's funding (57 percent) for fiscal year 1993 is administered by the National Institute of Allergy and Infectious Disease (NIAID), although a total of 17 NIH institutes and centers within NIH report ongoing TB research.

NIAID estimates that fill finding of those activities in the MDR-TB National Action Plan that fall within NIAID's purview would cost $45.6 million in fiscal year 1994, $20.6 million above NIAID's spending in fiscal year 1993. In spring 1993, an NIH Executive Committee identified and prioritized new TB research opportunities for all of NIH. Fully funding this research agenda would cost an estimated $102 million above fiscal year 1993 funding.

Areas of NIH research include development of new diagnostic tools, drugs, and vaccines as well as behavioral issues on prevention of transmission and adherence to treatment. NIH is also spending $2.3 million to convert an existing building into a containment laboratory that allows for the safe handling of drug-resistant strains of tubercle bacilli. Too few containment laboratories at NIH and other research institutions limit the amount of TB research scientists can conduct (29,30).

The Office of Technology Assessment (OTA) found a lack of systematic research on the effectiveness or cost-effectiveness of individual interventions to control TB infection in hospitals or to ensure that patients in different communities or treatment settings complete anti-TB therapy. In addition, little effort in health services and health

[8] The 1993 budget includes $14.1 million also counted as HIV spending and $4.8 in one-time funds transferred by the NIH director from her discretionary budget.

economics research has been devoted to understanding variation in the use of hospitalization and costs of treating TB, especially during the disease's acute, infectious period.

Although CDC and some institutes at NIH are conducting studies on the effectiveness and appropriateness of TB services, U.S. DHHS'S Agency for Health Care Policy and Research (AHCPR) takes the lead in conducting and supporting federally sponsored health services, health economics, and medical care effectiveness research. AHCPR'S main efforts so far on TB were its participation in developing the MDR-TB National Action Plan and a 1993 workshop for judges on HIV and TB.

Regulation of TB Technology

The Food and Drug Administration ensures the safety and effectiveness of drugs used to treat TB. It also regulates and approves BCG and other vaccines, tuberculin skin tests, other diagnostic reagents used to detect *M.tb.* or to deterrnin e drug susceptibility, and devices used to prevent the spread of the disease. In recent years, FDA's role in TB control has focused on alleviating shortages of some TB drugs and expediting the approval of new TB drugs. The FDA recently helped make available an interim supply of SM and PAS for MDR-TB patients through CDC when adequate amounts of the drug could not be obtained privately. The FDA is also working with companies to encourage development of combination drugs and new technologies such as implantable, slow-release formulations.

Federal Disability Programs

The Social Security Administration (SSA) administers two programs for people unable to work due to disability-the Disability Insurance (DI) program for those who have paid the requisite social security taxes over the course of their careers, and the Supplemental Security Income (SS1) program for very low-income individuals. While SS1 pays a set amount each month and can begin once the beneficiary is forced to stop work, DI benefits depend on the amount of social security taxes paid by the beneficiary; DI has a 5-month waiting period after the onset of disability.

By law, both programs require that an applicant be unable to work due to a physical or mental impairment expected to result in death or to last at least a year. SS1 and DI are not available for most patients with drug-susceptible TB because they are usually able to work once a few weeks of treatment renders them noncontagious. However, TB patients can quilify for SSI or DI if they also have concurrent HIV or if they have some other disabling condition.

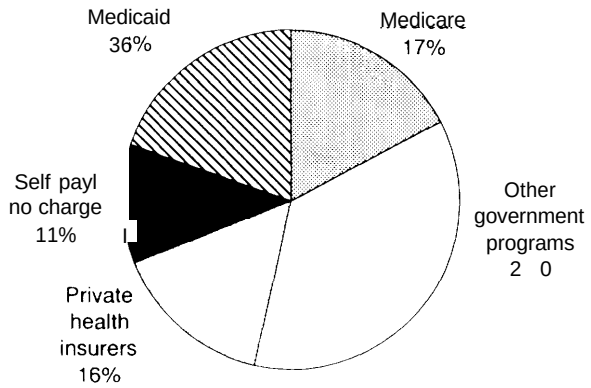
Medicaid and Medicare

While many medical services for people with active TB are provided directly in outpatient clinics through State and local programs that do not necessarily charge patients, third-party health insurers also pay for some TB services for their beneficiaries. Little if any systematic research has been done on the role of insurance in financing care for TB. However, indirect evidence does suggest a significant role for Federal insurance programs. Figure 1-3, which breaks down all hospitalizations for TB in 16 States in 1990 according to payer, shows that Medicaid was the single most likely payer (36 percent), with Medicare paying for another 17 percent. In total, government pays for almost three-quarters of TB hospitalizations in these States.[9]

Medicaid, aState-administered program funded jointly by the Federal and State governments, provides health insurance to certain categories of low-income individuals, including recipients of SS1, many poor women and children, and, in some States, people whose high medical bills make them poor or almost poor. The minimum set of

9 Although not necessarily representative of the entire country, the States presented do include several with the highest TB burdens, most notably New York and California.

Figure 1-3-Hospital Admissions With a Diagnosis of Tuberculosis in *16* States[a] by Payer, 1990



a States ar, Arizona, California, Colorado, Florida, Massachusetts, Maine, New Hampshire, New Jersey, Nevada, New York, Oregon, Pennsylvania, South Carolina, Vermont, Washington, and Wisconsin.

SOURCE: Office of Technology Assessment, 1993 based on data derived from State hospital discharge abstracts covering 100 percent of acute short-stay hospitals and U.S. Department of Veterans Affairs hospitals. Data prepared by Codman Research Group, Inc., Lebanon, New Hampshire.

benefits provided under Medicaid covers inpatient, outpatient, laboratory, and other services for TB patients at approved facilities.

With approval from the Federal Health Care Financing Administration (HCFA) that administers Medicaid and Medicare, New York's Medicaid program pays for directly observed therapy for Medicaid-eligible TB patients with reimbursement amounts dependent on the intensity of effort necessary to provide and supervise therapy. No other State has yet attempted innovative approaches to providing TB services with Medicaid funding. HCFA estimates that in 1991, the Federal Government' sportion of Medicaid spending for TB totaled $45 million, while the States' portion totaled $30 million.

Medicare provides health insurance to individuals who are over age 65, who have end-stage renal disease, or who have received Social Security DI benefits for 2 years. Medicare pays for inpatient services provided in short-stay hospitals and ambulatory services provided in an office or clinic under a physician's supervision. Although Medicare does contain some limited home health care benefits and long-term care and skilled nursing services in certain types of approved facilities, DOT in the home and long-term care facilities dedicated to TB care would most likely not qualify for Medicare reimbursement. HCFA estimates that Medicare spending for TB totaled $65 million in 1991.

Policy Options for Congress

Through its analysis, OTA has identified 11 options for congressional consideration (box l-A). Each option has the underlying goal of improving TB control capabilities in the United States. They fall into three categories that affect:

- The public health infrastructure for combating TB;
- The research, development, and availability of technologies for combating TB; and
- The financial security and financial access to health care services for persons with, or at risk of, TB.

The focus of this discussion is on potential actions of the Federal Government in providing leadership and resources for the Nation's TB control activities, rather than on potential actions of the State, local, and private authorities that carry out many of the programs to fight this disease. A fuller discussion of these options and their potential implications follows.

Options That Affect the Public Health Infrastructure for Comating TB

OPTION 1. *Fully fired the public health activities identified in the CDC'S 1992 National Action Plan to Combat Multidrug-Resistant Tuberculosis.*

CDC estimates that full implementation of all activities in its 1992 National Action Plan to combat MDR-TB (described in box 7-B) for which it would be responsible would require appropriations of $380 million during the first year over and above the $105 million appropriated in fiscal year 1993. This estimate includes

Box I-A—Policy Options for Congressional Consideration

option 1. Fund fully the public health activities identified in the CDC'S 1992 National Action Plan to Combat Multidrug-Resistant Tuberculosis.

Option 2. Establish a mechanism for direct Federal intervention in cities and other jurisdictions with extraordinarily high levels of active tuberculosis, multidrug-resistant TB, or HIV and TB confection.

option 3. Require universal directly observed treatment (DOT) through legislation, regulation, or as a condition of receiving Federal TB control funds.

option 4. Require periodic TB skin testing, active case finding (by chest x-ray), and preventive treatment in Federal hospitals, prisons, and other facilities.

option 5. Purchase directly anti-TB drugs and distribute them to State and local authorities.

Option 5a. Purchase directly anti-TB drugs with State and local authorities reimbursing the Federal Government.

option 6. Increase support for international TB control activities.

Option 7. Make a concerted effort to develop health Services research relevant to the fight against TB.

Option 8. Fully fund basic and clinical TB research as outlined in the CDC'S 1992 National Action Plan to Combat Multidrug-Resistant tuberculosis and NIH's 1993 Tuberculosis Research Opportunities.

Option 9. Support the creation of additional regional "centers of excellence" for TB treatment and research.

Option 10. Expand the Federal Government's definition of disability to include active TB as a disabling condition for the purposes of Supplemental Security Income (SSI) and Disability Insurance (DI) benefits.

option 11. Provide States with the option to expand categorical Medicaid coverage to persons without other forms of health insurance who have tuberculous infection or active TB.

Option ha. Limit the option of expanding categorical Medicaid eligibility to those with active disease only.

Option llb. Limit categorical Medicaid eligibility to TB-related services only.

SOURCE: Office of Technology Assessment 1993.

$62 million in R&D expenditures, with the remainder allocated toward various forms of public health activities. Although CDC currently has no estimates of amounts that would be required for subsequent years, the $380 million increase would include some one-year-only spending as well as some spending that would be continued subsequently (35). No estimates currently exist of the cost of fully implementing activities in the National Action Plan that are the responsibility of other Federal agencies.

OTA found that CDC and other TB experts agreed on the need for increased Federal involvement and resources. However, some of the options that follow in this section highlight major policy questions that would need answers to fully implement the CDC plan. In addition, because CDC has given only rough indicators of priority among all of the actions it recommends, Congress and other policymakers cannot evaluate in detail how CDC and other Federal agencies would propose to allocate funding increases if Congress

appropriated less than the amount required for full implementation.

Immediate full funding of the plan may not be more effective or more efficient than a more incremental phase-in. On the one hand, such a dramatic increase in funding would alert the country to the threat of TB to affected communities and the value the Federal Government places on TB control.

On the other hand, the public health and research system may not be able to absorb such a large influx of cash as efficiently as it could if the increases came more gradually. In the course of OTA'S analysis, public health officials pointed out the highly regulated and slow process some State and local governments face in hiring qualified individuals to administer TB therapy and to perform other public health functions (29,30). Additional Federal grants would not immediately increase the supply of qualified public health workers or speed up local governmental hiring processes. Also, this report highlights the lack of information about the relative effectiveness of individual infection control procedures. Without frost developing better experimental data on these technologies, some money devoted to retrofitting hospital rooms and other facilities to serve active TB patients would probably be spent inefficiently or unnecessarily. In an era of limited Federal resources and many competing public health needs, policymakers may wish to weigh the value for spending some TB control dollars better in the future against the value of providing maximum resources for TB now.

OPTION 2. *Establish a mechanism for direct Federal intervention in cities and other jurisdictions with extraordinarily high levels of active TB, MDR-TB, or HIV and TB confection.*

Support for this option would rest on the assumption that TB can pose a significant enough threat in some communities that State and local authorities alone are unable to respond quickly and sufficiently, even with Federal financial support. One TB expert suggested to OTA that the magnitude of drug resistance, HIV dual infection, substance abuse, hopelessness, and incomplete TB treatment is great enough in New York City to warrant the formation of a Federal task force to supply personnel and expertise from elsewhere on a short-term, emergency basis (29,30).[11] Such a plan would extend the technical expertise that CDC routinely provides to State and local health authorities. Federal personnel would help provide TB treatment, find cases of TB in facilities that public health officials suspect to harbor the disease, and perform other TB services needed in the community.

This option raises several questions. First, by what criteria would the Federal Government decide to intervene? Given that most legal authority to protect the public health has been traditionally vested in State and local governments (125), any Federal intervention would almost certainly, at a minimum, require a request from the relevant local governments. Second, Federal officials would need to develop epidemiologic or other criteria for judging that TB has reached levels high enough to justify this Federal action. These criteria would need to be measurable and perhaps flexible. Inclusion of TB and HIV confection rates or numbers of foreign-born residents, if measurable, could make this option available for communities with low rates of existing TB but the potential for high rates in the future. The emphasis of Federal intervention in these communities may be on screening high-risk groups and preventive treatment, rather than on providing resources for treating active disease.

Decisionmakers would also want to question whether Federal Government intervention would actually be more effective than the local governments and private organizations acting alone. As noted, the ability to bring in Federal persomel

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10 The initiation of such research is itself includedin the Action Plan.

11 This suggestion was not made by an official of the New YorkState or City governments.

may offer a significant advantage for State and local governments that face limitations in hiring, although the Federal Government may also face hiring restrictions. Reassignment of professionals from the Commissioned Public Health Service Corps would mean these individuals would be unable to continue to fulfill their current responsibilities,

The cost of hiring additional Federal personnel on a short-term basis would depend on the number hired, their qualifications, the duration of their employment, and perhaps whether they currently reside in the targeted community or must relocate. Another possibility would be to make voluntary service on such task forces one means of paying back government loans for health professional education and training as was done in greater numbers during the 1970s and 1980s under the National Health Service Corps. There is also precedent for providing special visas for qualified foreign medical personnel to fill positions in undeserved areas.

OPTION 3. *Require universal directly observed treatment (DOT) through legislation, regulation, or as a condition of receiving Federal TB control funds.*

The American Lung Association recently recommended DOT for all persons with active TB (244). In contrast, CDC has recommended that DOT be considered for active cases,

Supporters of universal DOT point to the practical difficulty of predicting *a priori* which patients will complete treatment without supervision. These supporters argue that human nature should lead health professionals to expect that patients will forget to take medication without reminders. Universal DOT proponents also argue that some health authorities may be more likely to assume that homeless individuals, drug users, and people without access to regular health care would be less likely than other TB patients to complete therapy. These groups may be subjected to more restrictive treatment measures without a strong medical or public health rationale. Requiring universal DOT helps insure that all TB patients are treated in an equitable manner.

Opponents of requiring universal DOT point out that despite the difficulties in predicting who is unlikely to complete treatment, between 1976 and 1990, over 80 percent of persons with active TB in the United States completed treatment without DOT (9). One estimate for New York City suggests that DOT costs may fall between $2,000 and $3,000 per person excluding the cost of drugs (29,30). Opponents argue that universal DOT is a wasteful use of limited resources and needlessly intrusive for most patients.

In addition, Federal policymakers would need to define exactly what State and local governments would have to do to conform to the Federal requirement. DOT can take many different forms and degrees of restrictiveness, require varying intensities of resources, and be combined with a variety of complementary programs such as incentives or inducements to complete therapy.

As suggested in chapter 6, there are more options available to policymakers than just requiring DOT for everybody or trying to predict *a priori* which TB patients will not complete therapy. One alternative, used in some communities, is to monitor all patients' therapy, but allow their behaviors to be indicators of the need for more intensive supervision of therapy. Only when patients do not show up for medical appointments or give other evidence that they might not complete therapy would public health officials require patients to be observed taking their medications. Although this alternative to universal DOT requires that public health authorities have the resources to track down missing patients quickly, a potentially difficult and labor-intensive task, particularly for homeless or other difficult-locate patients, it may be less expensive and as effective in some communities.

OPTION 4. *Require periodic TB skin testing, active case finding (by chest x-ray) and preventive treatment in Federal hospitals, prisons, and other facilities.*

Epidemiological evidence indicates that hospitals, prisons, and other facilities housing people in congregate settings may be appropriate targets for TB prevention because institutions house many individuals at high risk of progressing to active disease. Identifying infected residents and workers at high risk of developing active TB, as well as those who already have active TB, offers an opportunity to prevent the potential spread of the disease to others with whom the active cases have close contact. Immigrants, currently screened for active disease for legal entry into the United States, are another high-risk group that the Federal Government may wish to consider for screening and preventive treatment if found to have tuberculous infection.

Positive skin tests would help identify candidates for preventive treatment, although health officials would have to consider the problem of false negative among immunocompromised individuals with tuberculous infection. In addition, officials would need to consider the best way to use chest x-ray technology in order to identify active disease.

By requiring screening and preventive treatment programs in its own facilities, the Federal Government would be setting a standard that could encourage State and local authorities to adopt voluntarily for their own congregate institutions. However, there are some potential drawbacks to a Federal policy. The Federal agencies charged with administering each type of institution may not correctly identify groups at high enough risk of active disease to warrant screening and follow-up preventive treatment.

For example, many patients admitted to Veterans Administration or other Federal hospitals for short periods of time may be at very low risk of developing active TB if infected. In addition, nonfederal institutions attempting to follow the Federal Government's lead might also establish screening programs where they are likeIy to yield little benefit. Workplace screening in low-risk settings such as a factory are unlikely to have much effect on the spread of much TB. Analysis in this report suggests that research into the most cost-effective ways of running screening and preventive treatment programs may not be available to guide the implementation of this option.

Funding for screening and prevention in Federal institutions would presumably come from the budgets of the agencies charged with administering them as do most current TB control efforts. The Department of Veterans Affairs (U.S. DVA) currently pays for TB control in its own hospitals, the Bureau of Prisons in Federal prisons, and so on. This decentralized administration of Federal facilities raises the further problem of ensuring compliance with a screening and prevention requirement. Current Bureau of Prisons policy already requires chest x-rays for new inmates and tuberculin skin testing every 2 years, but no data are available on the extent to which such testing is actually carried out. Adoption of screening requirements would require mechanisms to ensure they are carried out as well as sufficient resources to ensure appropriate diagnostic fol-Iowup and treatment; this includes not just money, but trained personnel as well.

OPTION 5. *Directly purchase anti-TB drugs and distribute them to State and local authorities.*

The rationale behind universal TB drug purchase is that the Federal Government, acting as a single, large-volume buyer should get the needed pharmaceuticals at a lower cost than can individual States or local health departments. The same considerations could apply to universal purchase of PPD skin testing kits.

The Federal Government already purchases some childhood vaccines under contract at prices substantially below retail. The CDC'S recent survey of trends in anti-TB drug prices revealed that the price paid for the same form and dose of a drug can vary greatly from State to State. In addition, if the Federal Government were to take

on the function of paying for all TB drugs, State and local governments could use the money that would have gone to pharmaceutical purchase for other purposes.

CDC currently has the statutory authority to take on this activity; it requires only the appropriations to do so. CDC estimates that in 1993, the cost of purchasing all anti-TB drugs used at the State and local levels would total $80 million. This figure is included in the CDC'S estimates of fully implementing its National Action Plan for the elimination of TB.

However, this amount of money would cover only the cost of the drugs themselves and does not include the cost of administering the drug purchase program or distributing the pharmaceuticals. CDC currently has no estimates of the costs of these functions. It is also not clear whether the Federal Government would take on the function of distributing the drugs to the States or whether that function would continue to be done by the drug suppliers. U.S. DVA currently purchases drugs in bulk for use in its own hospitals, but does so with a highly centralized distribution system, thus minimizing the distribution costs borne by the pharmaceutical suppliers. The willingness of suppliers to give discounts for bulk purchasing may be partially dependent on whether the Federal Government took on responsibility for distributing the drugs since the suppliers' costs would be lower.

CDC has not indicated the assumptions that went into its $80 million estimate. Not only is it not clear what prices the government would expect to pay for each pharmaceutical, but also CDC has not shown how improved case finding might increase drug costs in subsequent years or how decreases in TB rates would ultimately decrease funds necessary to purchase drugs.

The final price negotiated for these drugs could also depend on the number of manufacturers for a drug. Some of the more expensive drugs are still covered by patents and hence only have one manufacturer. When manufacturers do not face competition, they may not see an incentive to give significant discounts in order to sell their products. In other cases, there may be only one manufacturer of a drug or its active ingredient even though it is no longer covered by a patent (121,152). These manufacturers may also be reluctant to give significant discounts. Finally, the pharmaceutical industry has suggested that centralized purchase would provide an added disincentive for firms to invest in research to develop new drugs as discussed in option 8 below (286).

OPTION 5a. *Directly purchase anti-TB drugs with State and local authorities reimbursing the Federal Government.*

This option would be identical to Option 5 except that the Federal Government would not bear the $80 million estimated to be necessary for the purchase of the pharmaceuticals themselves. Instead, State and local governments would continue to pay for drugs, but would reap any cost savings the Federal Government can realize by purchasing on their behalf. Such cost savings might not be spread evenly among the States. The CDC survey indicates that some States, presumably those purchasing large quantities of drugs, already receive a discount through negotiated contracts with drug suppliers. These States would likely benefit less per unit of drug purchased than would areas of the country paying higher retail prices for their TB drugs.

OPTION 6. *Increase support for international TB control activities.*

The American Lung Association, among others, advocates greater support of the World Health Organization's TB programs, greater CDC provision of its technical staff to international organizations, and selected nations, more support for TB research in developing countries through ND-I, and greater involvement of AID in tuberculosis control as well as in bilateral programs with other countries and through WHO (85). As noted in chapter 7, the Federal Government supports each

of these activities to a certain extent, although the vast bulk of current and expected TB spending is targeted to the United States.

If Congress decided to increase TB control efforts in less developed countries, it could decide to do so purely on humanitarian grounds. However, even if Congress sought only to protect this nation's health, controlling TB abroad could lower TB incidence of the disease here given the mobility of foreign born people to the United States. Research oriented toward developing countries could also have benefits at home; for example, a fast, definitive diagnostic test designed for developing countries that do not have easy access to sophisticated clinical laboratories could be of great use in many urban and rural areas of the United States as well.

A potential danger of increasing United States support of TB efforts abroad is that it might divert resources from domestic TB control activities. The Federal Government has already laid out an ambitious domestic agenda to control TB for which there may not be sufficient funds to fully implement in the short-run. If money for expanded TB control efforts outside the United States would come from appropriations that would otherwise go to domestic public health and research activities, Congress may need to weigh the value of supporting efforts abroad against the impact that money would have on the health of people with TB at home.

Options That Affect the Research, Development, and Availability of Technologies for Combating TB

OPTION 7. *Make a concerted effort to develop health services research relevant to the fight against tuberculosis and to disseminate research results to policyrnakers and health professionals.*

Several areas of this report suggest that better health services and economic research results could help policymakers target TB control efforts more efficiently. Through legislation or through direction of U.S. DHHS, relevant agencies such as the CDC, AHCPR, HCFA, NIH, and HRSA could publicize TB health services research as a priority in various types of extramural funding programs. Several of these agencies have said they intend to expand their efforts in this area. Two sample questions suggested by OTA'S analysis that might be answered by health services and health economics research are:

- What are the effectiveness and cost-effectiveness of various forms of DOT and how do these measures vary among different parts of the country and different groups of patients?
- What sources of income do TB patients have and what impact do government benefits have on the identification, treatment, and control of TB such as through SS1, Aid to Families with Dependent Children, housing programs, and food stamps?

This option could include efforts to disseminate to policymakers and health professionals the results of both health services and clinic research to improve the delivery of health services and to ensure appropriate clinical treatment for TB.

One drawback of this such research is that it could draw resources away from direct TB control. Data on the effectiveness and cost-effectiveness of treatment strategies such as DOT are best gained through randomized clinical trials, which are expensive. In addition, the size of such studies increases as one wants to learn more about differences in effectiveness among different sociodemographic groups or according to other ways that differentiate TB patients. Policymakers would also want to consider health services research already being undertaken by State and local governments and private groups such as foundations to assess its quality and to avoid duplication.

CDC'S estimates of funds necessary to implement its responsibilities under the 1992 National Action Plan include funds for the health services and health economics it hopes to carry out. Estimates of funds needed for new health sources research that other Federal agencies would support are not available.

OPTION 8. *Fullyfund basic and clinical TB research as outlined in the CDC'S 1992 National Action Plan to Combat Multidrug-Resistant Tuberculosis and NIH's 1993 Tuberculosis Research Opportunities.*

CDC estimates that its research under the 1992 National Action Plan would cost $62 million in the first year above fiscal year 1993 spending. NIH estimates that new TB research would cost **$102** million over several years. These research activities include not only basic research on the TB organism and its behavior in the human body, but also clinical investigations of new forms of prophylaxis, diagnosis, and treatment; the experimental study of environmental infection control technologies; and relevant human behavioral research.

On the rate of funding increases, the same considerations for policymakers described under Option 1 apply here. The ability of the scientific infrastructure to absorb funding for certain types of TB research include a limited number of researchers and clinicians trained to perform work in this area and a limited number of biomedical laboratories with sufficient containment facilities to prevent accidental infection of laboratory staff and others, On the other hand, some researchers have suggested that increases in funding will naturally lead to an increased capacity to do research (152).

As with Option 1, clarification of funding priorities for R&D activities would help Congress and other policymakers understand better the implications of partial or phased-in funding of the CDC National Action Plan. NIH has provided detailed priorities for research projects in its plan. In addition, analysis in this report suggests several areas of relatively high priority: development of faster and definitive diagnostic and drug susceptibility testing techniques, development of new anti-tuberculosis drugs, and the development of easier-to-use dosage forms of the treatments, such as combinations of commonly used drugs and slowly released, implantable formulations, and new research to bolster our understanding of the TB bacilli and its manifestations in the human body.

The area of drug development raises a few additional issues for the Federal Government. The FDA indicates that some drug companies have been reluctant to develop a drug for both TB and non-TB uses for fear that many physicians would reserve the drug for TB treatment only rather than using it for more common infections. The companies fear that these implicit restrictions of the drugs' use would limit the revenue they generate and their ability to recoup the manufacturers' initial R&D costs. In addition, the pharmaceutical industry is concerned about disincentives to engage in research should the Federal Government attempt to force discounts for TB drugs as discussed in Option 5 (120).[12]

This situation suggests that there are important constraints other than funding and resources in making new therapies available. Congress, executive branch agencies, and groups outside of government may wish to examine new ways to encourage drug industry participation in TB drug development beyond those that the FDA has already tried. New ideas could run the gamut of measures, from focusing public attention on the need for new treatments, to clarifying the applicability of orphan drug subsidies to this area,[13] and to offering new, more direct financial incentives.

OPTION 9. *Support the creation of additional regional ''centers of excellence" for TB treatment and research.*

Several centers that specialize in the treatment of drug-susceptible and more complicated cases

12 The FDA cites the classes of drugs known as qunolones and macrolides as potential examples.

13 To encourage the development of new treatments for conditions that affect fewer than 200,000 persons in the United States, the Orphan Drug Law (Public Law 97-414) provides incentives including a 7-year market exclusivity as well as grants and tax credits to support clinical research. Currently, active TB fits the definition of an orphan condition.

of TB already exist.[14] One TB expert has suggested establishing a total of 6 to 12 centers funded at a cost of about $5 million each per year (29,30). In addition to treating difficult cases and training TB clinicians and researchers who would pursue future work on this disease, these centers would provide an opportunity to study and disseminate new technologies for the diagnosis and treatment of TB. Not only would researchers be able to study the technologies under relatively controlled conditions, but also the centers could train clinicians and technicians in their use.

The main question for policymakers is whether establishing additional centers is the most efficient public policy to treat difficult patients, train TB professionals, and bring together TB research interests. Even if it were an efficient approach to TB care, research, and training, it is not clear whether 6 to 12 centers (or any other suggested number) are commensurate with the threat posed by TB. It is also not clear how sick patients would be before they would have to be transferred to the centers for treatment. Policymakers would want to consider the number of patients in need of such specialized services in deterrnining how many centers the country needs. The existence of such centers might encourage their use for some patients that could be treated in institutions closer to their homes. Furthermore, once the current epidemic is brought under control, the country might not need as many such centers.

Pollicymakers may want to understand better whether there would be cost or other advantages to treating patients in centers instead of other institutions. They may also want to consider whether existing institutions could be modified for less than the cost of establishing a new center to conduct biomedical TB research. Similarly, it might be possible to train clinicians and other professionals sufficiently in existing institutions for less money.

Another issue that would need to be examined is how centers would be reimbursed for the care of patients from a separate jurisdiction if the cost of such care would usually be borne by the health department or Medicaid program where the patient currently usually lives. The centers would also require trained personnel who may only be available in sufficient numbers over time.

Options That Affect the Financial Security and Financial Access to Housing and Health Care Services for Persons with or at Risk of TB

OPTION 10. *Expand the Federal Government's definition of disability to include active TB as a disabling condition for the purposes of Supplemental Security Income and Disability Insurance benefits.*

Underlying this proposal is the observation that many people with active TB are in precarious financial situations. Their poverty may interfere with their ability to receive treatment and to prevent transmission of the disease to others. Many TB patients are homeless. For disabled individuals without other sources of income, SSI provides a very basic subsistence and categorical eligibility for Medicaid health insurance. In the case of substance abusers, many residential treatment programs have been successful in receiving SSI to cover some of the costs of those patients in treatment may last more than a year.

As described in Chapter 7, most individuals with TB alone are not considered disabled because their condition does not prevent them from working for a year or longer. Changing this rule in order to make active TB patients eligible for SSI would require congressional legislation to amend the Social Security Act. In passing such legislation, Congress would also need to decide whether this exception applies only to the SS1 program or whether it would also apply to the DI

14 These include National Jewish Hospital in Denver, Colorado, the University of Medicine and Dentistry of New Jersey in Newark, New Jersey and Bellevue Hospital in New York City.

program as well since both currently rely on the same definition and processes for determining disability.

A new law would establish a significant exception to one of the most basic tenets of current disability policy. A major drawback of this option is that it would use a disability program to provide financial benefits to a group of people who are not disabled according to the way Congress has defined disability over the history of the SS1 and DI programs. In adopting this option, Congress could be opening a Pandora's box of requests to use disability programs as a means of providing income to other groups of individuals who are not currently considered disabled.

A proposal to revise the SSA'S disability definition to include TB may reflect two other problems perceived by proponents of this option: 1) a perceived lack of coordination of all public benefits for which TB patients may currently be eligible, and 2) a lack of resources to provide housing for many TB patients in some areas of the country,

To the extent these two perceived problems are real, the Federal Government, along with State and local authorities, may wish to consider other options for coordination of relevant Federal benefits for each case of active TB and directly to consider other ways the Federal Government could help alleviate TB patients' need for housing. Dealing with these policy problems directly may be preferable to setting a precedent of using disability programs in ways they were not designed. Specific actions to provide housing are not included in the CDC'S 1992 National Action Plan.

One alternative action for policymakers that would not require a change in statute would be to educate patients and their caregivers to make sure TB patients currently eligible for SS1 already because of HIV, substance abuse, or protracted TB treatment actually apply for the program.

OPTION 11. *Provide States with the option to expand categorical Medicaid coverage to persons without other forms of health insurance who have tuberculous infection or active TB.*

Over the years, Congress has expanded categorical Medicaid eligibility, especially for certain groups of women and children. Congress offers States the option of extending eligibility to all persons with tuberculous infection or active disease with the usual mix of Federal and State funds. The added cost of this option to State or Federal Medicaid budgets is uncertain. For the State government, the cost largely depends on the prevalence of TB in the State. For the Federal Government, it depends on how many and which States decide to adopt the option. In addition, to the extent that patients with TB have other medical problems but were not previously covered by Medicaid, the costs of expanding Medicaid eligibility would be more than just those costs associated with TB care.

This option would transfer some share of the burden for TB services from public health department budgets to the Medicaid program at both the Federal and State levels. The option would also reinforce the trend toward the ''privatization' of TB services (noted in chapter 6), shifting the focus of TB control from public health activities to individual, reimbursable health services. Another impact of this option would be to add to the administrative costs of State Medicaid programs in processing applications for eligibility and claims reimbursement. Finally, as noted in chapter 6, financial access is not the only factor in ensuring that patients receive and complete treatment; expanding Medicaid eligibility does not guarantee that there will be enough trained professionals to provide and supervise appropriate therapy.

OPTION 11a. Limit the option of expanding categorical Medicaid eligibility to those with active disease only.

Although limiting Medicaid coverage to active disease cases only would reduce the cost of this

option, it would also exclude from Medicaid reimbursment any diagnostic services and preventive therapy for people with qtuberculous infection (unless the infected patients were eligible for Medicaid through some other provision in the Medicaid statutes).

OPTION 1 lb. *Limit categorical Medicaid eligibility to TB-related services only.*

This option would also save money by limiting the reimbursement to services related to TB only. Under this option, Congress could cover all people with tuberculous infection or limit coverage to those with active TB Only.[15] This option has the disadvantage of excluding treatments for other conditions the individual may have, such as HIV. Treatment for these other conditions not only affects the individual's overall health, but can affect his or her ability to recover from TB itself. However, some portion of patients with both TB and other conditions like HIV would qualify for full Medicaid eligibility through other provisions in the Medicaid statutes.

15 While this report was in its final publishing stages, Congress adopted a version of this option (P.L.103-66) giving States the opportunity to use Medicaid funds to pay for TB services only for low income individuals with either tuberculous infection or active disease who do not otherwise qualify for Medicaid.