

## Case 3

# Controlling Tuberculosis in China

**Geographic area:** China

**Health condition:** Tuberculosis (TB) is the leading cause of death from infectious disease among adults in China. Every year, 1.4 million people develop active TB. In 1990, 360,000 people in China died from the disease.

**Global importance of the health condition today:** TB currently ranks as the third leading cause of death and disability among adults in the world, and nearly one third of the world's population is infected with the tuberculosis bacillus. Of these cases, more than 9 million people become sick with TB when their immune system is weakened, and 1.76 million die each year.

**Intervention or program:** In 1991, China revitalized its ineffective tuberculosis program and launched the 10-year Infectious and Endemic Disease Control project to curb its TB epidemic in 13 of its 31 mainland provinces. The program adopted the WHO-recommended TB control strategy, DOTS, through which trained health workers watched patients take their treatment at local TB county dispensaries. Information on each treatment was sent to the county TB dispensary, and treatment outcomes were sent in quarterly reports to the National Tuberculosis Project Office.

**Cost and cost-effectiveness:** The program cost \$130 million in total. The World Bank and the WHO estimated that successful treatment was achieved at less than \$100 per person. One healthy life was saved for an estimated \$15 to \$20, with an economic rate of return of \$60 for each dollar invested. The World Bank ranks DOTS as one of the most cost-effective of all health interventions.

**Impact:** China achieved a 95 percent cure rate for new cases within two years of adopting DOTS, and a cure rate of 90 percent for those who had previously undergone unsuccessful treatment. The number of people with TB declined by over 37 percent in project areas between 1990 and 2000, and 30,000 TB deaths have been prevented each year. More than 1.5 million patients have been treated, leading to the elimination of 836,000 cases of pulmonary TB.

**A**t any given time, nearly one third of the world's population is infected with tuberculosis bacillus, and every second a new person becomes infected. Of those ill in 2004, an estimated 9 million people became sick with TB disease. Although Asia accounts for over half of all TB patients, the highest rates of TB occur in sub-Saharan Africa.<sup>1</sup> TB kills an estimated 1.7 million people each year and ranks

as the third leading cause of death and disease burden among adults aged 15 to 59.<sup>1,2</sup> And there are few signs that the epidemic is subsiding: The global incidence of TB is growing at approximately 0.6 percent per year and at much faster rates in sub-Saharan Africa, where as much as 4 percent growth in incidence has followed rising HIV rates.<sup>1</sup>

Over the last decade, China, one of the countries most profoundly affected by TB, has demonstrated the po-

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The first draft of this case was prepared by Jane Seymour.

tential for large-scale deployment of DOTS, the WHO-recommended TB control strategy. DOTS is a public health approach focused on the early detection of TB patients via smear microscopy and with a standardized directly observed 6-month treatment in dispensaries or in the community until cure.<sup>a</sup> This strategy was developed primarily to prevent the early dropout from treatment, which can result in the development of bacteria that are resistant to available drugs. China has shown how a combination of adequate funding, leadership, and a sound technical approach, delivered through a relatively strong health system, can dramatically reduce TB over a short period. In the process, China has averted hundreds of thousands of deaths and paved the way for future wins in the battle against TB.

## How TB Kills

TB is caused by the bacteria *Mycobacterium tuberculosis* and is contracted by inhaling infected air droplets spread by active TB carriers when they cough, sneeze, or talk. The majority of the people who come into contact with the bacteria can fight the progression of the disease, and the bacteria then lie dormant in the body without the development of any symptoms. Carriers of latent TB cannot spread the infection to others but are still at risk of developing the disease at some point in their lives if their immune system becomes depressed.

Between 5 percent and 10 percent of those infected with TB will fall ill.<sup>3</sup> TB occurs when a weakened immune system allows the bacteria to multiply and active disease to develop. TB in the lungs, or pulmonary TB, is the most common form, although the bacilli can cause the disease in any part of the body. The main symptom of pulmonary TB is a persistent worsening cough. If left untreated, night sweats, malaise, weight loss, blood in sputum, and shortness of breath take hold as the lungs are slowly destroyed.

HIV/AIDS and TB are a particularly deadly combination. Because HIV weakens the immune system, it raises the likelihood of latent TB becoming active.

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a In 2006, WHO launched the Stop TB Strategy, a new strategy for TB control. In addition to the expansion and enhancement of DOTS, the strategy recommends the adoption of TB/HIV collaborative activities as well as MDR-TB treatment as key elements to an integrated approach to TB control.

Consequently, TB is the leading cause of death among HIV-infected persons and accounts for approximately 11 percent of all AIDS deaths worldwide. As the number of people infected with HIV has increased so has the number of active TB cases.<sup>3</sup> Unfortunately, the diagnostic tools, which were developed some 100 years ago, often fail to accurately detect TB in HIV-positive individuals.

The spread of HIV has fueled the TB epidemic, but it is not the only reason TB persists as a major global health problem. TB is both a cause and consequence of poverty. Untreated TB spreads quickly in dense populations, and urbanization and migration accelerate its transmission. Refugees and displaced persons are at an especially high risk because they are usually in crowded refugee camps or shelters and frequently relocate, making compliance with a 6-month treatment regimen extremely difficult. The TB epidemic also is closely associated with the breakdown of financing and infrastructure for public health systems, particularly in the former Soviet Union and in Africa, where access to effective detection and treatment services is limited.

## Treatment and the Age of DOTS

For more than half a century, antibiotics have been available to cure standard cases of TB, but their effectiveness depends on strict patient adherence. The drugs must be taken for at least six months, but many patients discontinue use once their coughing subsides, when they suffer from side effects such as vomiting, jaundice, and confusion, or can no longer afford or access treatment. Patients who are only “half-cured” can still transmit TB, which poses a serious public health problem by enabling multidrug-resistant TB (MDR-TB)<sup>b</sup> to develop, rendering first-line drugs ineffective in MDR-TB patients.

In the 1970s, Dr. Karel Styblo of the International Union Against Tuberculosis and Lung Disease pioneered a new approach to TB treatment with the ministries of health of Tanzania, Malawi, and Mozambique. The new strategy promoted the integration of TB diagnosis, treat-

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b MDR-TB refers to TB infection that is resistant to at least two of the primary drugs used to treat TB. MDR-TB is the result of improper treatment and is caused most often when patients stop taking TB medicines too early.

ment, and follow-up with an existing health unit. This approach eventually evolved into the DOTS strategy, through which health workers or lay people encourage compliance by watching patients take their medicine. The essential elements of DOTS include the following:

- Government commitment to sustaining TB control activities
- Case detection by microscopic examination of a sputum sample among symptomatic patients who seek health services
- Standardized treatment regimen of six to eight months for at least all patients with positive sputum exams, using DOTS for at least the initial two months
- A regular, uninterrupted supply of all essential anti-TB drugs
- A standardized recording and reporting system that allows assessment of treatment results for each patient and of the TB control program as a whole

In the absence of HIV/AIDS or multidrug resistance, DOTS cure rates reach near or over the 2005 target of 85 percent, even in the poorest countries. DOTS has been ranked as one of the most cost-effective of all health interventions.<sup>4</sup> In some countries, the drugs used in DOTS cost as little as \$16 per patient for a 6-month supply.<sup>1</sup>

The WHO first endorsed and recommended DOTS in 1993 when it also declared TB a global health emergency. As of 2004, 183 countries had adopted the strategy, representing 83 percent of the global population.<sup>1</sup> An estimated 22 million infectious patients were successfully treated under the DOTS programs since 1995, with a reported average cure rate of approximately 82 percent.<sup>5</sup> In 2004, some 53 percent of new smear-positive cases were detected under DOTS, and this figure was closer to 60 percent in 2005.<sup>5</sup> The WHO aims to detect 70 percent of new infectious TB cases and to cure 85 percent of those detected.

## Tackling TB in China

In China, where 400 million people are infected with TB, the burden is especially heavy. TB ranks as the leading cause of death from infectious disease, with 1.4 million people developing active TB each year. A national tuberculosis program was first established in 1981 to reform control efforts, and to expand the reporting system and treatment. Inadequate financial support, however, hampered the program's human resource and technical capacity in many areas, particularly in poorer provinces with the weakest primary health care infrastructure.

Although some important progress was achieved during the 1980s, the program was plagued by poor treatment compliance, a deficient network of diagnostic laboratories, and an inadequate system of reporting and evaluating cases. Furthermore, the treatment offered at urban hospitals was too expensive for many victims of the disease, and patients often abstained from treatment altogether or abandoned the drug regimen early.

As a result, a third nationwide TB random sample survey in 1990 revealed only a slight improvement in TB prevalence compared with rates in 1979 and 1985. In 1990, according to vital registration data, 360,000 people died from TB, making it the leading cause of death among adults. As is typical with TB, the poorest communities were most acutely affected.

Recognizing that the widespread incidence of the disease served as an obstacle to its ambitious social and economic goals, the government of China decided to formally evaluate its TB control program with assistance from the World Bank and the WHO. The analysis highlighted the need for a more effective and efficient method of TB surveillance and treatment of infected patients.

In 1991, with \$58 million in financial support from the World Bank, China embarked on a 10-year Infectious and Endemic Disease Control (IEDC) project to help curb its TB epidemic in 13 of its 31 mainland provinces.<sup>6</sup> The project adopted the DOTS strategy and short-course chemotherapy. It set out to improve findings of new smear-positive cases from 35 percent to 70 percent and increase the cure rate from less than 50 percent to

more than 90 percent of these cases by 2005. Accomplishing these goals would avoid an estimated 100,000 deaths each year and slash TB prevalence in half by 2015 in provinces covered by the program.

## A Rapid Rollout of DOTS

The IEDC program was the largest natural experiment in TB control in history. Starting with a pilot project in five counties in Hebei province in April 1991, the program was quickly expanded first to 65 counties and then to approximately half of China's counties. By 1994, the IEDC project in China involved 1,208 counties in 12 provinces and a population of 573 million people. With this expansion of services, China's health system bolstered its TB control support and management services with logistic systems, provincial and township supervision, and monitoring and reporting systems.

Individuals demonstrating symptoms such as a persistent cough for at least three weeks, productive sputum in cough, shortness of breath, night sweats, and fatigue were referred to TB county dispensaries—local TB clinics that are part of the public health system. Free diagnosis was offered, and patients' lungs were examined with chest fluoroscopy. If results gave cause for concern, three sputum samples were taken and a chest X-ray was ordered if appropriate. Patients with positive-testing sputum have the most active and thus infectious TB and are the main targets for observed treatment. In suspect cases, where bacilli do not show up under the microscope, culturing the sputum or a subsequent X-ray may later reveal TB.

From 1991 to 2000, the DOTS program in China evaluated nearly 8 million people in the TB dispensaries, with 3.53 million having sputum smear tests carried out. Of those, 1.3 million had smear-positive results, and more than a half million more people with smear-negative results were later diagnosed with TB. At the start of the project, just over 70 percent of the smear-positive cases were new cases; this figure increased to a plateau of around 80 percent after seven years as case-finding improved and fully cured cases did not return for retreatment.

New patients with smear-positive pulmonary TB were started on a course of directly observed treatment of antibiotics, every other day for at least two months and up to six months. Treatment was free, an important feature of the program because fewer than 20 percent of patients had health insurance and 80 percent to 90 percent paid medical expenses out of pocket.<sup>7</sup> Health care workers watched patients every day, or three times a week, depending on the drug regimen, as the patients swallowed their prescribed drugs—the direct observation element.

Smear-positive patients continued to receive free treatment for up to an additional six months, while smear-negative patients were required to pay for their treatment. Sputum specimens were collected after two months of treatment and at regular intervals thereafter to document sputum conversion and cure.<sup>6,8</sup>

## Down to the Village

The success of the IEDC project depended largely on the involvement of village doctors with basic health training, who played an essential role in patient diagnosis, treatment, and surveillance. In the 1980s, most Chinese doctors had become private practitioners because they were not receiving a salary from the local government. The reliance on payments from patients for services and drugs made free TB care problematic, even with free drugs from the government. To engage doctors in the program and to increase the number of TB patients diagnosed and treated, an incentive scheme was created. Village doctors received \$1 for each patient enrolled in the treatment program, an additional \$2 for each smear examination carried out at two months in the county TB dispensary, and \$4 for each patient who completed his or her treatment.<sup>6</sup>

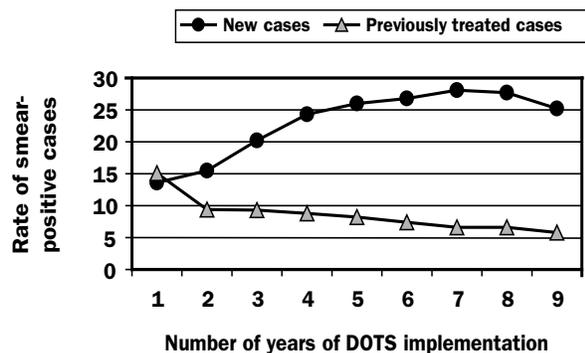
To monitor the TB epidemic, all infectious TB patients were registered with the county TB dispensary and issued a TB treatment and identity card. A copy of the treatment card was sent to the village doctor to record each dose of treatment. If a patient did not return for treatment, a village doctor visited the patient at home and then reported back to the county TB dispensary.

Furthermore, efforts were made to strengthen the institutions involved. A National Tuberculosis Project Office and a Tuberculosis Control Centre were established. The program worked to strengthen the management and finance of local TB dispensaries and bring them in line with the new DOTS framework. Operational research on management, economic, social, and epidemiological factors was encouraged to improve TB control and establish a basis for future health programs.

Quarterly reports summarizing the case findings, treatment outcomes, and other program activities were submitted from each county to the province, the central government, and the newly formed National Tuberculosis Project Office, allowing for consistent monitoring of the project. Involvement of all levels of the government also helped maintain the program's quality.<sup>9</sup>

Careful attention was paid to the implementation of necessary administrative, managerial, and financial changes. Training and supervision was extensive; more than 60 demonstration and training centers were established, which trained tens of thousands of staff from TB dispensaries. Quality was checked through random visits by TB staff to patients' homes, through review of the registry system, and through random examination of smear slides.

**Figure 3-1**  
**Rates of new and previously treated smear-positive cases among all smear-positive cases by number of years of DOTS implementation.**



## Impressive and Fast Results

The DOTS strategy proved powerful (Figure 3-1). The global target of curing 85 percent of identified patients was quickly achieved—overall, the cure rate was 95 percent for new cases. This 95 percent cure rate is the highest for any country undertaking a large-scale TB control program and compares with a rate of just 52 percent before DOTS was launched in 1991. About two thirds of that improvement happened within the first two years of DOTS implementation.

The IEDC program demonstrated extraordinary cure rates of not only new cases but also of relapsed and retreatment cases. The cure rate for people treated with DOTS who had previously undergone unsuccessful treatment for TB was 90 percent. These successes have contributed to an MDR-TB rate three times lower in the 12 provinces covered by DOTS than in non-DOTS provinces.<sup>10</sup> Considering China's status as the country with the highest MDR-TB cases in the world—approximately 30 percent—the success of the IEDC program in reducing MDR-TB cases provides hope to the rest of the world.<sup>11</sup>

From 1990 to 2000, the number of people with TB in the DOTS area declined by 36.1 percent, about 4.1 percent each year, compared with a decline of 3.1 percent in non-DOTS areas. In western China, for example, where five provinces implemented DOTS and seven provinces did not, the prevalence in the DOTS area decreased by 33.3 percent while the prevalence in the non-DOTS area decreased by just 11.7 percent.<sup>8</sup> The magnitude of this difference in TB prevalence between DOTS and non-DOTS provinces may also have been influenced by factors other than the DOTS program, such as socioeconomic differences.<sup>12</sup>

Since DOTS was introduced in China, more than 1.5 million patients have been treated, and approximately 30,000 TB deaths have been prevented each year. DOTS is now available to 96 percent of the population with a 94 percent treatment success rate.<sup>1</sup> A national TB prevalence survey carried out in 2000 estimated that the program eliminated 836,000 cases of pulmonary TB disease, 382,000 cases of culture-positive disease, and 280,000 cases of smear-positive disease.<sup>13</sup>

## BOX 3–1

### Stop TB: The Quest to Curb MDR-TB

Despite the successes achieved by DOTS programs in China and elsewhere, multidrug-resistant tuberculosis (MDR-TB) is on the rise. MDR-TB is a more dangerous and difficult to treat form of TB that is resistant to two or more of the most powerful anti-TB drugs currently available. It can arise when patients fail to complete the standard TB treatment regimen for economic or health reasons, or receive improper treatment. Other people they infect will have the same drug-resistant strain.

More than 400,000 MDR-TB cases emerge each year globally, with hotspots in parts of China, India, and the Russian Federation.<sup>1</sup> First-line drugs typically used to control TB are ineffective against MDR-TB, and although new second-line TB drugs for MDR-TB exist, they are particularly toxic and can cost local purchasers 1,000 to 3,000 times as much as first-line drugs, making them largely inaccessible to most MDR-TB patients.

For a long time, these were major barriers in the treatment and control of the highly pernicious MDR-TB, but after a long and hard-won battle, WHO created DOTS-Plus. This new program was initiated in 1999 to curb MDR-TB by preventing the development of new cases through the introduction of second-line drugs, and preventing the spread of resistant strains through adequate laboratory support. The program benefited from the previous work of a joint global program for anti-TB drug resistance surveillance that had been in place since the mid-1990s.

Another critical tool in combating MDR-TB is the Green Light Committee, established in 2000 by the international Stop TB Partnership to promote access to second-line drugs at reduced prices. By defining the market, consolidating various sources of demand, and negotiating prices with pharmaceutical companies, the Green Light Committee and the Stop TB Working Group on MDR-TB were able to reduce the price of high-quality MDR-TB medicines by up to 90 percent.<sup>16</sup> Thanks in large part to their efforts, MDR-TB detection and treatment can be feasible and cost-effective, even in resource-limited settings. With the expansion of MDR-TB treatment projects, it is estimated that 142,000 deaths from MDR-TB will be prevented between 2006 and 2015.<sup>17</sup>

### The Price Tag

Funding for China's IEDC project came from the Chinese government at both national and local levels and was supplemented by a World Bank loan. Originally budgeted at \$102.5 million, the total cost amounted to nearly \$130 million in the end. Most of the resources were devoted to improving case detection and management. Savings were made on the cost of drugs because China bought in bulk and utilized other procurement schemes.

A study conducted by the Ministry of Health and the Shanghai Medical University found that each case detected cost approximately \$83 and that the cost per new

smear-positive cured was \$537. The World Bank and WHO estimated that successful treatment was achieved at less than \$100 per person. One life-year was saved for an estimated \$15 to \$20, with an economic rate of return of \$60 for each dollar.<sup>14</sup>

### The Project's Limitations

Despite China's success in curing TB, the project achieved lower than hoped for rates of case detection. The case detection rate is the number of notified cases divided by the estimated number of TB cases in the population. The estimated case detection rate in 1998 of 53.5 percent fell short of the 2005 target rate of 70 per-

cent.<sup>9</sup> The WHO estimated a much lower case detection rate of 30 percent for the same year.<sup>7</sup>

One of the main contributing factors to the low case detection rate was inadequate referral of suspected TB cases from hospitals to the TB dispensaries.<sup>9</sup> The 2000 National TB Prevalence Survey reported that just 12 percent of TB patients received their diagnosis from a TB dispensary. Because hospitals can charge for TB treatment and diagnosis, they have little economic incentive to direct patients to the dispensaries. As a result, despite the existence of regulations requiring referrals to dispensaries, most TB patients are diagnosed in hospitals where treatment is often abandoned prematurely.

## Lessons for the Future

Several lessons can be drawn from both the outstanding success and the limitations of the Chinese national TB program.

- **DOTS can be rapidly scaled up, while simultaneously achieving high coverage rates.** In less than five years, DOTS coverage increased from 0 percent to 90 percent in the program areas.<sup>9</sup> Under rapid expansion, such programs face the risk of sacrificing treatment quality and case management unless adequate levels of training, supervision, and quality control are maintained. In such a scenario, drug resistance could increase. China's experience, however, demonstrated that it is possible to increase the cure rate and lower the treatment failure rate under rapid scale-up and expansion.
- **Political commitment is essential.** Strong political commitment at various levels of government in China contributed to the program's success. Project-leading groups led by the vice-governor or vice-mayor were established at each government level to supervise the program.
- **Creative incentives work.** The provision of incentives to both patients and providers proved essential to the success of the IEDC project. Free diagnosis and treatment for TB patients helped dramatically increase treatment rates over the previous program, and incentives provided to doctors to diagnose and treat patients also contributed to

the program's success. The resistance from hospitals to refer patients to TB dispensaries exposed a weakness of the program and created the need for further innovative incentives to address this shortcoming.

## Maintaining and Expanding the Success

Despite the success of the IEDC project, which concluded in 2001, TB remains a deadly threat in China. More than 300 million people are infected, and 10 percent of these people will develop TB during their lifetime.<sup>15</sup> The government of China now faces the dual challenge of maintaining high cure rates in the provinces covered by the IEDC project and scaling up the DOTS program to the remaining half of the population. The latter endeavor carries a number of challenges, particularly the need to marshal political support at the local level, increase the numbers of trained staff at the central and provincial levels, increase access to TB dispensaries in the 20 percent of counties where no dispensary exists, and address increasing drug resistance and TB-HIV coinfection issues.<sup>1,7</sup>

Important progress has been made in recent years. To continue and increase the success of the IEDC project, the State Council of China released a 10-year National Plan for the Prevention and Control of TB (2001–2010), and the Ministry of Health completed a 4-year implementation plan (2002–2005) and a work plan (2002). While keeping the same high level of treatment success, these projects have been successful in expanding DOTS coverage to 90 percent of the country and reaching a case detection rate of more than 70 percent. In line with the new Stop TB Strategy, China is also beginning to tackle MDR-TB.<sup>18</sup>

The World Bank; the Department for International Development of the United Kingdom; the government of Japan through the Japan International Cooperation Agency; the Damien Foundation Belgium; the Global Fund to Fight AIDS, TB, and Malaria; and other organizations have all contributed funds to the projects, and the central government of China continues to financially support the fight against TB. The WHO, the International Union Against TB and Lung Disease, the Royal

Netherlands TB Association, and others are providing expertise to identify new ways for hospitals to work with TB dispensaries to increase case detection rates.<sup>7</sup> With this international financial commitment and technical cooperation, China can achieve its goals and significantly reduce the health burden due to TB.

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