Chapter 11
The MDR-TB Epidemic in China: The Changing Landscape, Cause Analysis, Government Response, Current Status, and Future Aspects

Hui Zhang, Mingting Chen, Renzhong Li, and Caihong Xu

11.1 Introduction

The problems of drug-resistant tuberculosis (DR-TB) appeared soon after the medical application of anti-TB drugs. The most severe DR-TB problem in recent years has been multidrug-resistant TB (MDR-TB), in which the TB pathogen has become resistant to at least two of the most effective anti-TB drugs: isoniazid (H) and rifampicin (R) (WHO 2006). MDR-TB makes the TB disease not only difficult to treat but also creates new primary infections with a MDR-TB strain, thus making it possible for a MDR-TB epidemic (Wang 2006). At present, DR-TB, especially MDR-TB, has become the most serious challenge in the global fight against TB (WHO 2006). This chapter uses China as a case study to discuss the current MDR-TB epidemic and its possible causes, the government's strategy and specific measures to combat the epidemic, the various challenges and problems, and the future aspects of the MDR-TB prevention and control.

11.2 Current MDR-TB Epidemic in China

The current MDR-TB epidemic in China, like in many other developing countries in the world, is a very worrisome problem. According to the World Health Organization (WHO), the number of new MDR-TB cases annually in the world was 440,000 and, of these, 22.7 % (about 100,000) were reported in China (WHO 2010a).

H. Zhang, Ph.D. (✉) • M. Chen, M.S. • R. Li, M.S. • C. Xu, M.S.
National Center for Tuberculosis Control and Prevention, Chinese Center for Disease Control and Prevention, 155 Changbai Street, Changping District, Beijing, China
e-mail: zhanghui@chinatb.org; chenmt@chinatb.org; lirenzhong@chinatb.org; xucaihong@chinatb.org

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The MDR-TB rate in China is higher than the world average (WHO 2010b). In 2007–2008, the Chinese Ministry of Health conducted a National Tuberculosis Drug Resistance Survey and found that 8.3 % of the smear-test positive pulmonary TB patients had MDR-TB. Among new cases, 5.7 % had MDR-TB. Among retreatment cases, 25.6 % had MDR-TB. Table 11.1 shows the resistance spectrum of the surveyed MDR-TB cases along with their frequencies. All the MDR-TB strains were resistant to the most widely used anti-TB drugs (R and H) which had been the most effective treatment tools in the fight against the disease (Ministry of Health of the People's Republic of China 2010). Considering the availability and accessibility of all of these anti-TB drugs, the wide spectrum of MDR-TB in China is indeed worrisome for public health policy makers and officials, as well as public health workers and clinicians in the field.

While there were more females than males in the smear-test positive pulmonary TB patients who developed MDR-TB after having received their first time anti-TB drug treatment ($x^2 = 10.215$, $p = 0.001$), no statistical difference was observed between different age groups or between different regions in the country. In the smear-test positive pulmonary MDR-TB patients who had been previously treated, there were more female than male patients ($x^2 = 12.966$, $p = 0$), and a statistical difference was reported between ages ($x^2 = 27.772$, $p = 0$), with the group of ages 20~39 showing the highest rate. No statistical difference was seen between regions (Ministry of Health of the People's Republic of China 2010).

However, different regions in China do report different degrees of MDR-TB problems. In a WHO sponsored nationwide TB control project, 13 of the 31 provinces, autonomous regions, and municipalities in the country have participated

Table 11.1 Spectrum of multidrug-resistant TB strains (Ministry of Health 2010)

Drug resistance	% of total MDR-TB strains
H + R	12.97
H + R + E	8.48
H + R + S	23.94
H + R + OFX	1.50
H + R + KM	0.50
H + R + E + S	21.95
H + R + E + OFX	3.24
H + R + E + KM	0.50
H + R + S + OFX	2.99
H + R + S + KM	1.50
H + R + OFX + KM	0.25
H + R + E + S + OFX	12.47
H + R + E + S + KM	2.74
H + R + S + OFX + KM	1.00
H + R + E + S + OFX + KM	5.99
Total	100

Abbreviations: *H* isoniazid, *R* rifampicin, *E* ethambutol, *S* streptomycin, *OFX* ofloxacin, *KM* kanamycin

the drug resistance surveillance study since 1996. Data collected from 11 provinces showed that MDR-TB prevalence ranged from 3.5 to 16.9 % among all reported TB cases, with rates of 2.1 to 10.8 % among new smear-positive cases and 11.7 to 41.9 % among previously treated cases (WHO 2008a).

The MDR-TB epidemic in China has grown in recent years. A nationwide review study reported that the percentages of identified MDR-TB cases among TB patients had increased 3.84 times from 1985 to 2005 (Yang et al. 2010).

11.3 Possible Causes for the Current MDR-TB Epidemic in China

There are multiple possible causes for an expanding MDR-TB epidemic in China, including fundamental microbiology, errors in medical practice, and poor patient compliance. Microbiological adaptations are the nature of the evolution of any living organism, including the bacterial pathogens and their human hosts, and are somewhat unavoidable. In contrast, human factors such as clinical practice and poor patient compliance can be improved and errors can be corrected and prevented in future.

From a medical science point of view, drug resistance (or multiple resistances) acquired by the pathogen results from specific genetic mutations that enable it to survive in the presence of certain drugs. From a social science point of view, if a patient is prescribed an inadequate drug regimen, or fails to comply with a proper drug treatment plan, it is possible for the TB pathogens that have acquired drug-resistant mutation to gradually replace the original drug-sensitive strains (WHO 2008b). Therefore, accessibility to effective chemotherapy and high-quality public health services have been identified as the most important factors in reducing the chances of MDR-TB epidemics (Wang 2006).

In 2000, the fourth Chinese national epidemiological sampling survey of TB showed that only 12 % of the pulmonary TB patients received anti-TB drug treatment for their illness and only 4.3 % of the suspected TB patients actually went to a local TB prevention and control station to seek medical treatment (Wang et al. 2002). This is in spite of the central government's effort to provide DOTS (Directly Observed Treatment Short Course) nationwide, which by 2005 had reached 100 % coverage of all counties in the country.

In addition to the lack of public awareness of proper TB treatment, the incorrect usage of the available anti-TB drugs also contributed significantly to the MDR-TB epidemic (WHO 2006; Wang 2006). The anti-TB drug providers, who might have limited understanding of chemotherapeutic principles of the TB treatment due to the lack of proper medical training, could have prescribed incorrect drug(s) to TB patients, thus causing MDR-TB to develop (Wang 2006). In a report published by He et al. (2011), a survey of six local hospitals that specialized in TB treatment showed that only 18 % of the new patients and 9 % of retreatment patients were given the correct standardized TB drug treatment as required by the published national TB treatment guidelines.

Lack of patient compliance to the TB drug treatment plan is another major contributor to the rise of MDR-TB cases. Such medical noncompliance usually resulted from the lack of knowledge about the TB disease by patients in general and the lack of proper medical counseling by the medical staff and service providers. In 2006, a national survey found that only 75 % of the TB patients participated in the survey had the general knowledge of the correct course of an anti-TB drug treatment (Center for Disease Control and Prevention and Ministry of Health of the People's Republic of China 2008). The patients' noncompliance could also be a result of economic factors. For example, despite the fact that anti-TB drugs are provided by the government free of cost, some pulmonary TB patients might have financial difficulties to pay for additional auxiliary clinical examinations and medical expenses to treat severe drug side effects. Additionally, the regimen of taking multiple drugs over a long period of time can be difficult for patients to maintain.

Furthermore, currently there are no effective public health measures, if any, to manage those TB patients whose infection becomes MDR while undergoing standard anti-TB treatment. These new MDR-TB patients may spread disease by infecting others with their new MDR-TB strain, which in turn leads to new TB patients who are initially infected with MDR-TB and have little or no hope of receiving effective free medical treatment provided by the government for the limited kinds of expensive second-line TB drugs.

11.4 Government Plans and Measures to Combat the MDR-TB Epidemic in the Context of the National TB Prevention and Control

One of the most important government actions to control the spread of the MDR-TB epidemic in China has been to continuously improve the quality of the ongoing national programs to modernize the standard anti-TB drug treatment, thus reducing the numbers of MDR-TB that resulted from incorrect drug prescription, lack of treatment counseling, and medical noncompliance as described above (Tu 2006; WHO 2008b). In this regard, China may serve as a helpful case study for other countries or regions.

The Chinese national government started to modernize "The TB Supervision Chemotherapy Guidelines" nationwide in 1978. By 2005, all of the counties and districts in the country had reportedly implemented the National Strategic Plan for TB Control and Prevention, including the new standardized diagnosis, treatment, and management measures for newly identified smear-test positive pulmonary TB patients. Consequently, the rates of case identification and successful treatment achieved 80 % and 94 %, respectively, nationwide (WHO 2007). In the context of this, the National Strategic Plan for TB Control and Prevention, the new public health measures of preventing MDR-TB mainly include the following steps.

11.4.1 Increasing the National Budget for the TB Control and Prevention

In recent years, the central government has been increasing the national budget for TB prevention and treatment programs. There have been three 10-year national strategic plans for the TB prevention and control from 1981 to 2010, including the critically important national guidelines on the "National Tuberculosis Control Program (2001–2010)," which outlined the new modernized TB control strategy nationwide (Xiao 2011). The central government continued to increase the national budget for the TB prevention and control with a 40 million RMB ($6.25 million) fund directly allocated annually from the central government budgets. These funds were used for the purchase of anti-TB drugs, training of medical staff in modernized treatment and prevention practices, supervision of treatment counseling, and various public health awareness works. In 2004, the central government's spending on the TB program totaled up to 270 million RMB (Xiao 2011). As more development works of the TB prevention and control were implemented annually, the national TB budget continued to increase, and by the year 2010, the central government's spending on various TB prevention and control programs had increased to 570 million RMB (see Table 11.2). In the 10-year period from 2001 to 2010, the central government spent total of 3100 million RMB on improving effectiveness of clinical diagnosis of pulmonary TB patients, providing free anti-TB drugs, standardizing treatment compliance management, patient information tracking, and monitoring epidemic and health promotion work. Local government funds also showed an increasing trend yearly (Xiao 2011).

Increased spending by the central government has resulted in significant improvement in various key areas of both national and local TB prevention and controls, which in turn contribute to the prevention and control of MDR-TB nationwide. These key areas included:

(a) The implementation of the new standardized clinical diagnostics for pulmonary TB ensures the correct diagnosis for patients. Better trained medical staff and bet-

Table 11.2 National budget for the TB prevention and control (Xiao 2011)

Year	Budget (in million RMB)
2001	4000
2002	4000
2003	4000
2004	26,947
2005	26,554
2006	35,877
2007	48,918
2008	51,790
2009	53,654
2010	57,635
Total	313,375

ter management of drug treatment plans, combined with the registration of patient treatment records for better compliance, provide more effective drug treatment.

(b) Once anti-TB treatments are started, compliance counseling is provided by local TB clinics. Registered pulmonary TB patients are monitored with a periodic sputum sample check to insure early detection of treatment ineffectiveness or severe drug side effects that might affect patient's compliance with the prescribed drug regimen.

(c) Ensuring high product quality of the anti-TB drug supplies by the Chinese Food and Drug Administration (SFDA) with mandatory Good Manufacturing Practices (GMP) compliance for the production of all anti-TB drugs.

(d) Establishing the national TB disease surveillance system as well as other important infectious diseases. In 1982, China began to set up the TB disease monitoring system. By 2005, all the provinces in the country joined the internet-based national infectious disease reporting system which requires a quarterly update of TB disease surveillance and treatment monitoring. In the same year, the National Tuberculosis Management Information System became operational. The system has been optimized gradually with the medical science expert supervision and administrative supervision systems in combination with the international partners.

11.4.2 Specific Measures to Control the MDR-TB Epidemic

China uses the same set of specific measures for the MDR-TB control that has been used elsewhere in the world, that is, "DOTS-PLUS." Such measures were first proposed by the WHO in 1998 specifically for the control of MDR-TB (WHO 2006). The Chinese central government has since incorporated these specific measures into its own new modernized TB control plan to combat the growing MDR-TB epidemic in the country. The following is a brief description of these specific measures:

(a) New national funds were specifically established, including the new medical insurance fund, the MDR-TB epidemic monitoring fund, and the relief policy on the diagnosis and treatment of patients with MDR-TB. These new funds have significantly improved the local public health systems nationwide and enabled them to establish the new TB control services. These services include the local general hospitals, the TB special clinics, and the TB prevention and control institutions, all of which have basic TB clinical laboratory capability and are part of the National Center for Disease Controls networks. The new national fund also made it possible to improve the national important infectious disease registration system. On the basis of the Tuberculosis Management Information System established by the central government, the online registration report modules now include the records of MDR-TB diagnosis and treatment histories (Huang et al. 2011). As described in the following sections, these new funds and new infrastructures are designed to play critical important roles in controlling the spread of MDR-TB in China.

(b) To detect MDR-TB early by using the newly acquired clinical laboratory capacities nationwide such as the high-quality standard sputum culture system combined with the sensitive in vitro drug-resistant assays. Once a TB patient is diagnosed with MDR-TB, he or she can receive a second-line anti-TB drug regimen with special care, thus reducing further spread of MDR-TB. If necessary, some of these patients can be hospitalized and even isolated for better protection of his or her families and close communities. In regions with sufficient resources, all the smear-test positive TB patients diagnosed in general hospitals or TB special clinics are required to be screened for MDR-TB (Mi et al. 2011). Such MDR-TB screening is especially important for chronic pulmonary TB patients with bacterial discharge or close contacts with known MDR-TB patients. Smear-test positive pulmonary TB patients who are being retreated with anti-TB drug treatment and the first time TB patients remaining smear-test positive after 3 months of anti-TB drug treatment are also required to be tested for the presence of MDR-TB.
(c) To provide a more effective second-line anti-TB drug regimen to treat MDR-TB based on the results of drug-sensitive tests. For TB patients who have developed severe side effects that could result in noncompliance with the standard anti-TB drug treatment for the first time, alternative drug regimens should be considered. In order to ensure the qualities of the anti-TB drugs, the drug manufacturers are required to follow strict regulatory guidelines as issued by the Chinese FDA.
(d) To strictly follow the DOT protocols in all inpatient and outpatient treatments for MDR-TB. Regular medical counseling, including psychological counseling, is required to help the patients to complete their prescribed course of treatment with self-confidence, thus improving patients' compliance and reducing the probability of developing more severe forms of MDR-TB.
(e) To protect medical professionals and public health workers from being infected by MDR-TB patients in hospitals, TB clinics, and TB prevention and control stations. Identified MDR-TB patients are required to be assigned to separate hospital wards with a strict set of environmental disinfection procedures such as proper ventilation of the rooms, disinfection by ultraviolet irradiation, and periodic surface disinfections.

11.5 Current Status of the MDR-TB Control in China

China is a huge country with more than one billion people who reside in 22 provinces, 5 autonomous regions, and 4 municipalities. The differences between these provinces, regions, and municipalities are very significant in their cultures, living standards, disease burdens, social economic status, and other factors. These differences readily affect the MDR-TB control efforts and obviously make any national disease control program very difficult to manage successfully. The following sections describe various problems and challenges facing the national MDR-TB program.

11.5.1 Implement the International Standard MDR-TB Surveillance and Registry System Nationwide

In 1996, China began to implement the global TB drug resistance surveillance project as directed and supported by WHO and The International Union Against Tuberculosis and Lung Disease (The Union), which included the monitoring of MDR-TB in different provinces. To date, the project has been carried out in several of the 31 provinces, autonomous regions, and municipalities in the country. These include the provinces of Guangdong, Henan, Hubei, Liaoning, Shandong, Zhejiang, Hunan, and Heilongjiang; the autonomous regions of Inner Mongolia and Xinjiang; and the municipalities of Chongqing, Beijing, and Shanghai. Fund-raising efforts to set up the MDR-TB monitoring projects are actively carried out in the six additional provinces of Yunnan, Shaanxi, Jilin, Fujian, Guangxi, and Sichuan. This leaves 12 provinces (autonomous regions or municipalities) in the country where an international standard MDR-TB monitoring system needs to be established.

The Chinese Ministry of Health conducted a national baseline survey of TB drug resistance in 2007–2008. This survey included 70 survey stations distributed in all 31 provinces, autonomous regions, and municipalities in the country, which covered an estimated population of 47 million out of the 1.3 billion Chinese at that time. The survey collected sputum samples from a total of 4600 cases of the smear-test positive TB patients using the stratified cluster sampling method, including 3514 cases of the first time smear-test positive patients and 1086 cases of TB patients for retreatment (Ministry of Health of the People's Republic of China 2010). This national survey revealed the Chinese TB drug resistance baseline information, including the rates of drug resistance and drug resistance spectrum, resistance causes, and provided a scientific basis for the formulation and implementation of Chinese TB-resistant control strategies and measures (Ministry of Health of the People's Republic of China 2010).

11.5.2 Improve the Existing National TB Registry Information Management Systems by Gradually Adding Routine Monitoring of MDR-TB

In 2005, the Chinese Center for Disease Control and Prevention (China CDC) started to add the current TB disease registry information management system on the basis of the previously established national network of reporting systems for infectious diseases. This important addition has enabled all of the TB hospitals and clinics nationwide to manage their local and regional TB prevention and control activities and new disease information electronically using Internet. Through the establishment of this new system, real-time monitoring of the TB epidemic nationwide became possible, and patient registration and treatment prognosis could be reached in a timely manner. However, such existing TB registry information

management system was created to deal with regular TB (not MDR-TB), patient registration, anti-TB drug treatment follow-up, and the treatment management and planning activities for the national and local CDC.

Therefore, there had been an urgent need for a similar real-time registry information management system to monitor the spread of MDR-TB epidemic in the country, On April 1, 2011, an internet-based MDR-TB disease information management system was launched nationwide. This included MDR data collection, quality control, and statistical analysis reports. Using this system, local and regional MDR-TB disease information can also be quickly transmitted among the local TB prevention stations, community TB treatment clinics, and regional TB hospitals between neighboring counties, different provinces, and with the central government in Beijing. This nationwide disease information sharing network makes it possible to track the spread of MDR-TB and manage and follow the treatment of the identified MDR-TB patients.

11.5.3 Launch the Pilot Projects on MDR-TB Control That Can Be Followed by Nationwide Expansions

Dealing with MDR-TB is much more demanding than drug sensitive TB with respect to accurate clinical laboratory diagnosis, appropriate drug regimen selection for treatment, and patient compliance with the entire course of a specifically chosen treatment. Identifying and treating MDR-TB patients also demands much higher quality medical care provided by medical staff and public health workers at all levels, which of course in turn demands much more financial funding to make this possible. Considering all these potential difficulties and obstacles, the 2001–2010 National TB Control Program requested that the national and local CDC launch pilot studies for annual implementation on the new MDR-TB control projects between 2006 and 2010. These pilot projects are collectively named as "Multidrug Resistant Tuberculosis Treatment Management and its Gradual Promotion" program (Ministry of Health of the People's Republic of China 2011).

One of these pilot projects was the Chinese Fifth Round Global Fund TB Project, which focuses on dealing with the challenges of identifying and treating pulmonary MDR-TB patients, the spread of TB in the increasing migrating labor population in the country, and the TB/HIV co-infections. In October 2006, this pilot study was initiated in the city of Wuhan in Hubei province and in the city of Shenzhen of Guangdong Province.

Throughout this pilot project, a new disease control operational policy was put in test. The new policy calls for the "City to Declare, Province to Evaluate and Recommend, and the Nation to Inspect and Approve" of a proposed MDR-TB treatment management plan. Such a new policy laid a structural foundation for a regional MDR-TB control work, in which a city acts as a control information management center, a county acts as a drug treatment and information management hub, and an individual community acts as a base unit to perform all the functions. It also built up

a cooperation mechanism for all local TB clinics, regional TB hospitals, and different levels of CDC stations to carry out all necessary inpatient and outpatient drug treatment combination therapies in compliance with DOT. During the pilot study, the classical drug sensitivity tests were used for screening the TB patients with chronic TB symptoms, or with close contacts with a known MDR-TB patient, or tested as the smear-test positives after receiving the standard anti-TB drug treatment at the end of 3 months. The newly diagnosed MDR-TB patients were then treated with the proposed standard second-line anti-TB drug regimens: a 6-month treatment of Pyrazinamide (Z), Kanamycin (Km), Levofloxacin (Lfx), Prothionamide (Pto), and P-aminosalicylic acid (PAS), then 18 months of PAS (6 Z Km LfxPto PAS/18 PAS). All the second-line drugs were imported through the Global Drug Facility (GDF) and were freely provided to the confirmed MDR-TB cases. Once a second-line drug treatment for MDR-TB is started, the pilot model system provides the patient with a follow-up management plan. This plan may include hospitalization for inpatient clinical care, outpatient management with DOT and other community services, or a combined approach of inpatient and outpatient treatments. Patients are treated in a designated TB special hospital for the first 2 months, then return to their own residential communities for outpatient treatment care in TB clinics with DOT services, and finally return to the TB special hospitals where the treatment started for the follow-up treatment evaluation. The evaluation is performed in compliance with the regulations by the national MDR-TB control plan.

In recent years, the increasing TB control funds from the central, regional, and local governments together with the international funds from The Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund), the above-described pilot projects for MDR-TB control have been gradually expanding to more and more cities in China. By 2011, similar projects had been started in 41 cities in 12 different provinces nationwide. By 2012, the pilot projects expanded to 67 cities in 24 provinces. In 2013, the pilot projects were expanded to a total of 81 cities in 24 provinces.

While the geographic areas for the MDR-TB patient treatment have been gradually expanding, the qualities of the medical services for the MDR-TB treatment have also been continuously improving. The specific goals for the proposed quality improvement include (a) to provide the MDR-TB clinical laboratory tests for all the smear-test positive pulmonary TB patients in the covered areas; (b) to provide frequent drug resistance monitoring services to all the patients receiving the second-line drug treatment for MDR-TB in the areas; (c) to provide necessary TB special hospital beds, transportation assistance to the needy outpatients, essential nutritional aids, and psychological counseling support services for all the diagnosed MDR-TB patients in the areas; (d) to offer special helps to HIV-infected pulmonary TB patients who are tested negative for smear-tests but need to be tested with more expansive sputum culture tests and the possible follow-up drug-resistant tests if tested positive by the culture tests; and finally, (e) to introduce the new diagnostic testing tools into local hospitals and clinics by setting up the “demonstration laboratories for MDR-TB diagnosis and treatment” in each province in the project covered areas and undertaking the initial provincial hospital laboratory testing demonstrations and the city-level clinical treatment provider demonstrations.

11.5.4 Combat the MDR-TB Epidemic with Advanced Medical Researches with New Diagnosis and Treatment Tools

In order to effectively control the growing MDR-TB epidemic in China, TB clinicians and public health workers in the country should have access to the most advanced clinical diagnosis tools as well as the best available second-line anti-TB drugs. From the government point of view, it is essential not only to provide the necessary financial resource and coordinated national disease control policies to combat MDR-TB but also all the best advanced biomedical tools to ensure the success. For instance, the traditional practice for MDR-TB diagnosis, which has been used commonly in China until very recently, involves patient's sputum collecting and culturing, followed by drug resistance assays or direct sequencing of the TB pathogen isolated from the sputum samples. If a second-line drug treatment is considered, additional drug sensitivity tests may be required, too. Such a lengthy series of clinical laboratory procedures usually takes about 6–8 weeks or longer. In 2010, the Chinese FDA approved two new TB diagnostic products, the Tuberculosis Drug Resistance Detection Array Kit and the Mycobacteria Identification Array Kit (both from CapitolBio, Beijing), that significantly reduce the time requirement to achieve a confirmed test result. Both products are based on advanced DNA microarray methods and were developed by the National Engineering Research Center for Beijing Biochip Center with the direct financial support from the Ministry of Health and the Ministry of Science & Technologies (Wang et al. 2010). These new TB diagnostic products are much faster and have a much higher throughput than the traditional detection methods, thus allowing rapid identification of various drug resistance TB strains, including the 17 MDR-TB strains that had been most commonly reported in China. Available data from the independent clinical evaluation studies showed that the MDR-TB clinical diagnosis time has been shortened to 6 h and the assay specificity can be clinically confirmed with as high as 99 % accuracy in 1700 clinical samples (Chinese Medicine Biological Technology Association of Biological Chip Branch 2011). In these studies, the DNA microarray-based new TB diagnosis products shortened the detection time for the rifampicin and isoniazid resistance from 8 weeks to 6 h. A clinical trial performed by an independent third party showed 100 % consistency with the old time-consuming method of DNA sequencing. The sequencing results of the isolated MDR-TB strains confirmed 92 % of these rapid tests for the rifampicin resistance and 78 % of the isoniazid resistant (Guo et al. 2009). Larger scale of applications of these new products may significantly improve the effectiveness of the current MDR-TB control projects nationwide.

The Ministry of Health had closely collaborated with the Bill & Melinda Gates Foundation to promote wider clinical applications of new MDR-TB diagnostic products in China. The central government has promoted scientific collaborations on MDR-TB control between TB researchers in medical research institutions, clinicians in TB special hospitals, and public health workers in the local CDC stations. Other national research areas also involve the health care insurance companies,

Table 11.3 Some ongoing national studies on MDR-TB

Research topic	Institution
Multiple Drug Resistant Pulmonary Tuberculosis Epidemic and Treatment Strategies	National Center for TB Control and Prevention, China CDC
A Retrospective Study of the Cause and Outcome of Multiple Drug Resistant Tuberculosis	National Center for TB Control and Prevention, China CDC
The Investigation of Second-line Anti-tuberculosis Drug Usage and Drug Sensitivity Testing	National Center for TB Control and Prevention, China CDC
The Infection Status and Influential Factors for MDR-TB Close Family Contacts	National Center for TB Control and Prevention, China CDC
The Study for Comprehensive Treatment of Multidrug-resistant Tuberculosis	Guang Dong provincial TB dispensary
The Study of a Clinical Occurrence Warning Model for Drug Resistant Tuberculosis Research	National Center for TB Control and Prevention, China CDC
New Technology Platform Research for Tuberculosis Infection Control	National Center for TB Control and Prevention, China CDC

government funding agencies, alternative fund-raising mechanisms, and the use of third parties for supervision and payment of detecting and treating MDR-TB.

Some of the ongoing national studies on MDR-TB are listed in Table 11.3. These studies are expected to further improve the central government's ability to control the MDR-TB in the country.

11.5.5 Provide the National Guidelines for MDR-TB Control Policies and Medical Practices

As the first-line anti-TB drugs are still the most powerful tool in the prevention and control of the current TB pandemic in China, it is very important for clinicians as well as TB patients to use these drugs correctly in order to maintain their effectiveness and prevent the appearance of MDR-TB. The China CDC in 2008 joined with the Chinese National TB Prevention Association and the Chinese Medical Association to publish the "Handbook for the Use of Anti-tuberculosis Drugs" (Chinese Center for Disease Control et al. 2008) which described the characteristics, principles, methods, and adverse reactions of each anti-TB drug, as well as how to make the best combination to reach the best treatment effect.

Then "The Handbook of Chinese Tuberculosis Control and Prevention" was subsequently published in 2010, which elaborated on the TB prevention and control, especially in the different environments and populations. The handbook also outlined TB prevention and control in China from the governmental point of view, thus providing detailed guidelines on the organizational management structure, management measures, working environmental and engineering controls for public health workers' personal protections. The handbook was specially designed to be applicable for all levels of governmental agencies on TB prevention and treatment institutions,

hospitals, and health organizations. The book offered guidelines for management personnel, the medical personnel of the medical and health institutions on how to control the TB infection within medical institutions, the crowd gathering places, public places, and family environments with pulmonary TB patients (Wang et al. 2010).

The first national guidelines dealing specifically with MDR-TB for public health workers and TB clinicians in the country was the "Multidrug-resistant Tuberculosis Chemotherapy Views (for Trial Implementation)" written and published by the Chinese National TB prevention Association in 2002. Then in 2009, with the new knowledge and lessons learned during the previous trial period, the book was revised and renamed "Treatment Guidelines for Drug resistant Tuberculosis Medicine," which included the contents from the "Drug-resistant Tuberculosis Planning Guide—2008 Update Edition" and elaborated on the determination and adjustment of then commonly used MDR-TB drug treatment schemes and how to deal with adverse reactions to the treatments (Chinese Antituberculosis Association 2010).

Then in 2010, the National Bureau of Disease Control & Prevention and the Department of Medicine of the Chinese Ministry of Health, together with the China CDC, issued the current national policy document, "The Management Guideline of Multi-drug Resistant Pulmonary Tuberculosis." The new national guideline is not only in consistent with "The Management Guideline of Drug Resistant Tuberculosis" as produced by WHO in 2006, it also includes the special experiences and lessons from all of the pilot projects during the previous trial years in China, thus becoming a practically useful guidebook to all TB clinicians and public health workers at all levels of the government agencies involved in the country's fight against MDR-TB.

At the national public health policy level, the prevention and control of MDR-TB had been written into the "National TB Control Program (2001–2010)" for the first time. It was subsequently issued again at the national level as the 2006–2010 implementation plan. The other policy-oriented documents and technical supporting papers issued by the central government also include the following (Ministry of Health of the People's Republic of China 2011):

(a) Developing framework and implementation planning of national MDR-TB prevention and control work
(b) Performing a pilot study on MDR-TB treatment management
(c) Developing TB drug resistance surveillance
(d) Strengthening TB laboratory biosafety management; improving laboratory working conditions; and gradually meeting the required biological safety standards
(e) Taking a step-by-step approach to initiate the new modernized sputum culturing technologies or to replace the old methodology gradually with the new one
(f) Expanding the clinical laboratory testing capacities to include the best available TB drug sensitivity experiments

At present, the China CDC has drafted a new policy document named "The Framework of the Nationwide MDR-TB Prevention and Control." Its main contents include preventing the occurrence of drug resistant TB, strengthening the new TB clinical laboratory network construct, identifying and monitoring MDR-TB,

developing the new functional roles of TB special hospitals and local clinics in administering the new standardized second-line drug treatment for MDR-TB patients, promoting public health awareness campaigns about prevention of the spread of MDR-TB, and other related new public measures.

11.6 The Future Prospect for MDR-TB Prevention and Control in China

In recent years and at present, the problem of having to deal with drug-resistant TB in China has become increasingly prominent. If not effectively controlled, the current MDR-TB epidemic will certainly be growing significantly in the coming years and will make the TB prevention and control task even more challenging.

The Chinese Leadership has been taking the threat of MDR-TB very seriously. In April 2009, public health ministers around the world from countries with the greatest burden of drug-resistant TB gathered in Beijing and endorsed a Call for Action on the prevention and control of MDR-TB and Extreme Drug-Resistant TB (XDR-TB; WHO 2009). A month later, the 62nd World Health Assemblies in Geneva passed a similar resolution sponsored by the Chinese delegation. During the 2009 Beijing Ministerial Conference on MDR-TB, the current Chinese Premier Li Keqiang, then the vice premier in charge of the national health, together with the WHO director and the president of the Gates Foundation, declared that the Chinese government will work closely with the international community to strengthen the prevention and control of MDR-TB in China in the coming years (Chen 2009). The details of this plan focused on achieving the following specific goals:

(a) By 2015, more than 80 % of the national TB clinical laboratories should be able to carry out the new sputum cultivation works, and 100 % of the regional TB clinical laboratories should be able to conduct the TB drug sensitivity tests. By then, all of the provincial clinical TB laboratories should also be able to meet the rapid TB strain identification requirements and each major city in the country should have established a centralized clinical laboratory unit to be capable of providing MDR-TB clinical diagnosis.
(b) By 2015, up to 60 % of the identified MDR-TB patients in the country should be able to have access to drug-sensitive tests, second-line anti-TB drug treatment in compliance with DOTS, and the standardized follow-up medical services, If successful, these measures should reduce the MDR-TB incidences, death rate, and the disease transmission in the country.
(c) Domestic anti-TB drug manufacturers should receive more support in order for them to supply the country with the high quality first-line and second-line anti-TB drugs. In order to support other countries in need, these qualified Chinese drug manufacturers should also acquire all the necessary international quality certifications. More specifically in the near future, cycloserine and p-aminosalicylic acid granules should become available in order to enrich the

current second-line anti-TB drug choices. The development, assessment, and promotion of new diagnostic tools should be actively promoted.

(d) By 2015, the medical staff should be trained on detecting and treating MDR-TB in order to train personnel and build up a steady TB prevention and control team. MDR-TB prevention and control demands higher technical requirements and a longer course of treatment. In order to achieve a complete cure, the staff needs to be highly responsible and devoted to anti-TB work. In the control process, especially during the treatment, changing staff often will affect the patient's treatment and lead to new multidrug-resistant patients. The human resources should be strengthened on diagnosis, treatment, and prevention of laboratory management, and gradually form an anti-TB diagnosis, treatment, and prevention management team)

(e) There have been no new anti-TB drugs since the 1960s in China. The development of new first and second-line anti-TB drugs or regimens, with a shorter course of treatment and easy for a patient to take regularly, with fewer and milder side effects, will become more and more desirable for the fight against MDR-TB. As the issue of cost effectiveness of treating MDR-TB will certainly become more and more important for the government, local communities, and patients, new research and development of new effective prophylactic vaccines will continue to be the hope of a new era of controlling MDR-TB in China and in the rest of the world.

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