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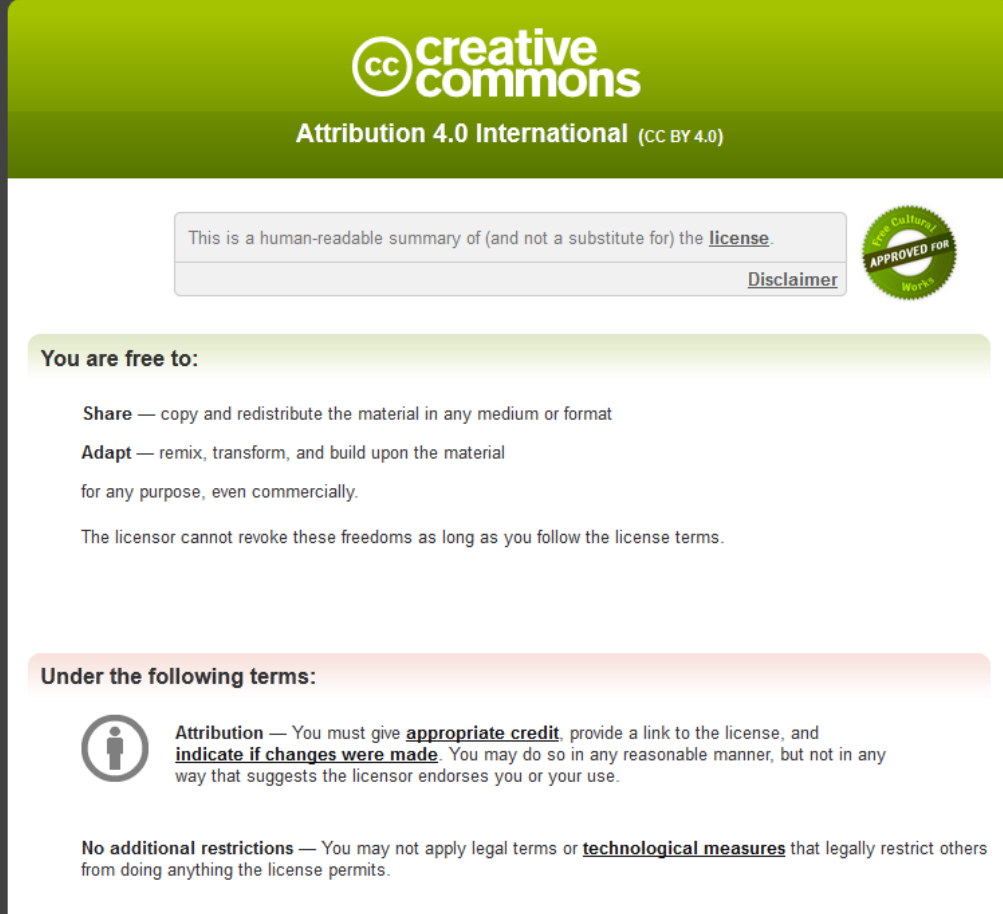
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## Tuberculosis Control in Jiangsu Province, China

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### Introduction

Tuberculosis (TB) has been a major health problem for thousands of years [1-3]. It took almost 200 years after the discovery of the disease in early 1689 to identify the causative pathogen, namely *Mycobacterium tuberculosis*, by Robert Koch who was awarded a Nobel Prize in physiology or medicine in 1905 for his work in this area. Currently, TB is a global pandemic that outranks HIV-AIDS and malaria as the leading cause of death by infectious disease [4,5]. In 1993 the World Health Organization declared TB a global health emergency. At the turn of the century the United Nations set the ambitious Millennium Development Goal (MDG) of reducing the prevalence and mortality rates of TB to 50% of those observed in 1990 by the 2015 deadline [6]. It can be argued that the policies and programs that were put into place have had an impact on TB control as the rates of new cases and mortality have reduced over the last decade to within reach of the 2015 target. In contrast, the prevalence of drug resistant infections is increasing [7]. Both single drug resistant TB and multidrug-resistant TB (MDR-TB) need to be addressed as a public health crisis in order to achieve the ambitious MDG target of complete elimination of TB as a public health concern by 2050 [4,7].

China is a key player in the global fight against TB. It is estimated that China has 1 million new cases of TB every year [8]. The overall disease burden is being controlled in China as the incidence has declined by 3.4% since 1990. The overall prevalence rate per 100,000 population fell from 215 in 1990 to 108 in 2010 [8]. In 2010, China achieved its MDG for TB control 5 years ahead of the initial target date. This is indeed welcome news, and the authorities should be recognized for this significant achievement. However, the rise of multidrug resistant infections threatens to undo the good work of the past 25 years. It is estimated that 6.3% of the 1 million new cases of TB in China each year are now due to multidrug resistant tuberculosis (MDR-TB). MDR-TB infections are a major concern for healthcare providers, as they do not respond to front line antibiotics isoniazid and rifampicin. Instead these infections require more expensive and potentially more toxic second line drugs. These treatments often require extended courses of treatment with the associated cost. Whilst new shorter treatment regimens are available that substitute isoniazid with moxifloxacin, these have not been widely adopted in China as clinical efficacy has not been proven to be superior to the existing regimen.

### Jiangsu Province

Jiangsu province in the south-east of the country is a microcosm

of modern China. Home to 79.6 million people, Jiangsu is one of the more prosperous provinces in the country with GDP per capita of \$US12,000 (compared with \$7,590 for all of China). Additionally, the province enjoys higher average life expectancy and lower maternal and infant mortality rates than the rest of the country. There is also a high level of urbanization of the population (66% in Jiangsu vs 55% for the rest of China). This is important as the prevalence of active TB in rural China is nearly double that of the urban population (307 cases per 100,000 urban vs. 569 per 100,000 rural). There is also a high level of migration into the province, which introduces an estimated 5,000 new TB patients each year.

Over the past decade TB control in Jiangsu province has outperformed the wider Chinese community. Jiangsu province has 5% of the TB burden of China, with approximately 40,000 new patients every year. Since 2005 the number of TB notifications has noticeably decreased from 77 cases per 100,000 population to 42 cases per 100,000 in 2014. In contrast, the number of notifications in China has decreased from 96 per 100,000 in 2005 to 65 per 100,000 in 2014. This is again welcome news in the global fight against TB and provides evidence that political commitment is essential for success. This commitment is now required to address MDR-TB.

### Political Commitment

At a federal level, the management of TB lies with the National Health and Family Planning Commission. The Commission provides national leadership by establishing the "Guidelines for the implementation of tuberculosis prevention and treatment planning in China". However, service delivery and cost recovery are delegated to the provinces. Funding for surveillance and treatment comes from three main sources, namely the provincial governments, individual patients and private medical insurers. The amount of funding contributed by the three parties is not controlled by the Commission, so individual provinces are left to devise policies to support service delivery. Jiangsu province has set the overall cost to MDR-TB patients at 10 – 30%, making out of pocket expenses one of the lowest in the country. This policy consideration is important as patients should not be discouraged from seeking clinical assistance for financial reasons.

In 2004 the Jiangsu provincial government established a co-ordinate committee for the prevention and control of important infectious disease, which included TB and AIDS. The TB control project is reviewed by the Jiangsu provincial government every 5 years. A network for TB control has been established that incorporates provincial, prefecture, county, township and village diagnostic and

clinical agencies. A key objective is to strengthen the capabilities of the network by 1) enhancing human resource development, 2) increase the number of technical staff at all levels and 3) strengthen training at all levels with an emphasis on doctors in urban districts and rural townships.

## Laboratory Network

An important resource in the fight against MDR-TB is the pathology laboratories that play essential roles in rapid diagnosis and TB surveillance. The data generated by these laboratories ultimately direct patient care and government policy. At the heart of the operation is the provincial laboratory run by the Department of Chronic Infectious Disease under the supervision of the Center for Disease Control and Prevention. The negative pressure laboratory is BSL-2 certified and has the capability to perform microbiological analysis such as TB sputum smear, culturing strain identification and drug susceptibility testing using the BACTEC™ MGIT™ 960 Mycobacterial Detection System. It also has access to molecular detection techniques such as HAINs, GeneXpert and Genechip to detect drug-resistance markers in clinical isolates. These rapid molecular techniques can provide information for clinicians within hours and are faster than traditional microbiological techniques that require long culturing times. Under the provincial laboratory are 13 prefecture TB laboratories, all of which have microbiological and molecular diagnostic capabilities. Also in the network are 73 county TB laboratories that all perform TB sputum smear and culturing assays, with 26 having molecular diagnostic capability. The aim here is to rapidly diagnose all TB patients and to prioritize those with MDR-TB.

## Disease Reporting

An internet based Communicable Disease Reporting System has been established. This includes a TB management information system that stores individualized data of cases. The database has fast case searching and provides accurate statistic reporting. The data also facilitates timely assessment of government programmes.

## DOTS-plus Strategy for MDR-TB

The WHO recommends the Directly Observed Treatment, Short-course (DOTS) strategy of policy, diagnosis, treatment and management of TB. DOTS is a five-point programme to: 1) secure political commitment and sustained funding; 2) ensure early case detection and diagnosis; 3) provide standardized treatment; 4) ensure effective drug stewardship and supply and 5) monitor and evaluate performance and impact. Management of MDR-TB is guided by DOTS-plus. DOTS-plus is developed on the basis of the DOTS strategy, but includes timely diagnosis and rational use of second-line anti TB drug treatment strategies. All suspected MDR-TB cases are confirmed by microbiology culture and molecular testing methods. Free MDR testing is also performed for five kinds of suspected patients, namely 1) chronic bacteria discharge/retreatment failure patients; 2) close contact to MDR patients with pulmonary tuberculosis of smear positive tuberculosis patients; 3) initial treatment failure patients; 4) recurrence and return patients and 5) smear positive patients after 3 months treatment. All MDR-TB patients are treated by MDR-TB hospitals, are included in medical insurance policies and 70-90% of the medical fee can be claimed for reimbursement.

## Key Challenges Ahead

As described earlier, initiatives to reduce TB burden are having an impact to drive down the global burden of TB. However, there will be a need for continued and diligent adherence to policies and revisions of goals in the decades to come. This will require ongoing political commitment to ensure sufficient and sustainable funding is available. Several imminent threats require ongoing monitoring and already place further strain on existing resources. The growing number of patients with HIV and those with TB - HIV co-infection are a significant concern. It is estimated that in 2011 China had 13,000 HIV positive TB cases. Co-infected patients are treated

with expensive multi-drug regimens, and for those with MDR-TB infection the number of drugs that can be administered becomes restrictive. Furthermore, migrants entering new communities that carry new TB strains are a continued threat. In Jiangsu, 5,000 new migrants harboring a TB infection enter the province each year. To maintain momentum in TB control authorities must improve the quality of DOTS and DOTS-plus implementation. TB control will also need to better integrate migrants and HIV patients. Jiangsu has proven itself ready to deal with the challenge and serves as a model for other countries with high TB burden. The province also highlights what can be achieved with sufficient resourcing and political will.

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