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Evaluating the costs associated with tuberculosis (TB)-related treatment, care, and services among low-income individuals in rural Guangxi, China

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Abstract

Evaluating the costs associated with tuberculosis (TB)-related treatment, care, and services among low-income individuals in rural Guangxi, China

By Parneet Kaur Ghuman

Introduction: China has the third highest prevalence of tuberculosis (TB) in the world. The burden of TB is especially high in the south-central province of Guangxi, which is considered to be a rural area where many low-income farmers reside. While TB treatment is advertised to be free for patients with health insurance in China, many individuals diagnosed with TB report that they still pay high costs to manage their TB disease. There is very little research that exists on the economic burden of seeking TB treatment, care, and services (both direct and indirect costs) among these poor and rural populations in Guangxi.

Methods: Two counties were identified in Guangxi (County A and County B) to have a high burden of TB among poor and rural residents, most of who were farmers. In each county, a data collection form was administered through in-home visits or telephone interviews to patients at least 18 years of age who were listed in the 2013 TB registry (n=128 in County A and n=79 in County B). Patients were asked about their demographic information, TB diagnosis, hospital expenses, and access to transportation.

Results: Our final response rate in County A was 76.6% (n=98) and 74.7% in County B (n=59). The top drivers for total expenditures incurred by TB patients in County A are the patient's injection fee (r=0.94567, p<0.0001), drug fee (r=0.94189, p<0.0001), and laboratory fee (r=0.88779, p<0.0001). In County B, these variables are the patient's injection fee (r=0.88118, p<0.0001), drug fee (r=0.85564, p<0.0001), and lodging fee (r=0.82617, p<0.0001).

Discussion: Patients in both counties reported incurring high hospitalization costs while being treated for TB. Many patients do not seek treatment until their TB symptoms become worse and are hospitalized longer, which results in higher costs associated with TB treatment and services. As most patients are rural sustenance farmers and generate little income, it is difficult to manage their total hospital expenditures that are not covered by insurance. The results of this study should be used to urge Chinese health authorities to reform the current insurance system to consider special subsidized funding in low socioeconomic areas.

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I. Introduction

Tuberculosis (TB) is one the most prevalent infectious diseases in the world. In 2014, TB infected 9.6 million people and killed 1.5 million, 0.4 million (26.7%) of whom were HIV-positive [1, 2]. Among the number of individuals newly diagnosed with TB during that year, 5.4 million were men, 3.2 million were women, and 1 million were children. Although the global TB prevalence in 2015 was 42% lower than in 1990, TB still remains as a prominent health issue among several under-resourced countries abroad [2]. Despite the vast presence of the disease worldwide, low and middle-income nations take on about 95% of global cases [3]. Specifically, 58% of new cases in 2014 occurred in Southeast Asia and Western Pacific regions. Africa as a whole accounted for 28% of the world's cases with a burden of 281 cases per 100,000 people, which is double the global average of 133 cases per 100,000 people [2].

TB is caused by a bacterium called *Mycobacterium tuberculosis*, which most commonly attacks the lungs of the infected person. TB is an airborne infection that is transmitted from person-to-person when someone with TB disease of the respiratory system coughs, sneezes, speaks, spits, or sings [4]. Most persons who become infected with *M. tuberculosis* will remain asymptomatic, and deemed to harbor latent TB infection. However, immunocompromising conditions, malnutrition, and several co-morbid health conditions (such as HIV infection and diabetes mellitus) have been associated with risk of disease progression. Symptoms of active pulmonary TB disease include cough with sputum and/or blood, chest pains, weakness, weight loss, fever, and night sweats [3]. In most countries of the globe, TB disease is a notifiable (i.e., reportable) infectious disease. Although TB incidence declined in post-World War II developed countries, the rise of HIV in the 1980s was also coupled with an increase in TB infections [5]. Compared with someone not infected with HIV, an individual who is HIV-infected is 20 to 30 times more likely to develop active TB, with the risk being even greater in the presence of other co-morbid health conditions [3].

M. tuberculosis transmission is hugely impacted by several factors, such as environmental conditions that increase the concentration of infectious droplet nuclei in the air. Such conditions include: prolonged exposure in small and enclosed spaces; lack of ventilation and poor air circulation; improper laboratory handling of clinical specimens; and positive air pressure in an infectious TB patient's room [6]. Social environmental conditions involve overcrowding and dense populations in confined spaces; urbanization and homelessness; low socioeconomic status (SES) and limited access to healthcare services; migration of infected persons to different geographic regions; the prevalence of the disease among some racial/ethnic subpopulations. In addition, health conditions have been associated with disease progression in people with latent TB. These include HIV co-infection; the presence of other co-morbidities (such as silicosis, diabetes mellitus, tobacco smoking, alcohol and drug abuse, underlying malignancies); poor nutritional status; and exposure to indoor air pollution. Some investigators have also implicated genetic factors on host susceptibility to infection with *M. tuberculosis* [7, 8].

According to 2014 data from the WHO, China has the third highest prevalence of TB in the world behind India and Indonesia. China also has the second highest prevalence of multi-drug resistant (MDR) TB in the world [1]. Overall, China accounts for approximately 10% of the global total of TB cases. The WHO estimated that 38,000 individuals died from TB, 1.2 million people were living with the disease, and 930,000 people became new cases in 2014 in China. About 5.7% of TB cases were MDR, while 43,000 of these MDR cases were pulmonary TB cases. Out of the 343,515 TB patients with known HIV status, approximately 5,300 (1.5%) of these individuals were HIV-positive [2]. Despite the efforts initiated by China's Ministry of Health to implement a TB control network and the WHO's program to expand its WHO's Stop TB Strategy across the country, the TB situation in China still faces immense challenges for controlling, preventing, and reducing the transmission and incidence of TB [9].

In 1992, China launched a wide-scale implementation of the Directly-observed therapy short-course (DOTS) strategy to standardize the diagnosis and treatment of TB, in which half of the country participated. As a result, the TB treatment success rate increased above the global target of 85% [10]. In addition, surveys done in 1990 and 2000 indicate a 32% decrease of the prevalence rate of all forms of TB in areas where DOTS was implemented [11]. China has also made achievements in the prevention and control of TB through health systems strengthening by improving case reporting through web-based reporting. However, *M. tuberculosis* transmission continues as a result of delays in diagnosing and treating active and infectious cases of TB. The DOTS program can therefore be rendered less effective if there is a delay between diagnosis and treatment among individuals with TB disease [8]. Despite these successes, the TB-case detection rate is relatively low because it relies on passive detection of TB cases among persons who seek medical attention. In addition, a relatively small proportion of patients who are confirmed with a diagnosis of TB while receiving care in hospitals do not visit the China Centers for Disease Control and Prevention (CCDC) facilities to enroll in the DOTS program [10]. Furthermore, hospitals mostly rely on chest X-rays to diagnose TB, and refer patients to obtain further follow-up at the CCDC where a sputum examination and microbiologic confirmation can occur [10].

China also has a high population of migrant workers who travel from the countryside to major cities to find employment. These workers generally hail from low-income backgrounds and end up becoming involved in high-risk industries and labor-intensive jobs, such as mining.

In these settings, many individuals are at an increased risk for *M. tuberculosis* infection due to poor working environments, poor and unsanitary living conditions, limited access to healthcare, and inadequate nutritional status [12]. In addition, migrants may engage in unsafe sexual practices, which place them at a high risk for becoming infected with HIV, which also increases the risk for TB disease progression. Migrants who develop TB disease often cannot obtain treatment in the cities as their social welfare benefits only apply to the location where they were registered at birth. Unfortunately, migrant workers cannot update their registration to become urban residents and access TB services in the city due to barriers of the rural healthcare system [13].

Poverty and lack of health insurance are two major factors that contribute to high incidence of TB disease in rural areas. Since 2005, China’s TB services have been decentralized to township hospitals in poor, rural regions. This type of community-based TB program facilitates access to health services by residents of these remote areas, such as the Guangxi Autonomous Region [14]. Located in the South Central region of China, Guangxi is home to an estimated 52 million people, 12 native ethnic groups, 14 cities, and 84 counties [16]. The province is also known for its extremely high prevalence of TB, relative to other provinces in the country. In 2000, the estimated TB disease prevalence rate in Guangxi was 650 per 100,000 people while the smear-positive rate was 127 per 100,000 people [15, 16]. In 2012, the TB case notification rate was about 81 per 100,000 people while the smear-positive case rate was about 24 per 100,000 people. In terms of the age distribution of TB in Guangxi, nearly 40% of all TB patients in 2014 were aged 45 to 64 years while individuals aged 15 to 34 years accounted for about 25% of the TB cases that year [16].

Guangxi is also a region that has incorporated DOTS into its TB control and prevention strategy. In 2004, DOTS expanded to 100% coverage of all counties in Guangxi as a result of government-backed financing; case detection with quality-assured bacteriology measures; supervised delivery of standardized treatment and increased patient support; an effective drug supply and management system; and a monitoring and evaluation system with impact measurement [16]. In rural areas, individuals displaying signs of TB infection first visit a village doctor who treats symptoms and then are generally referred to township hospitals to receive formal diagnostic and treatment services [14].

During my time in China (May 9th- July 6th 2015), I worked for the National Tuberculosis Program (NTP) at the Guangxi Province CCDC, where I participated in a broader project to evaluate the expenses associated with TB in inpatient and outpatient settings, given that China has high levels of poverty across all of its provinces. The introduction of the NTP in 2002 was also a breakthrough for addressing new TB cases, which resulted in the treatment of more than 400,000 active TB patients in Guangxi [16]. The Guangxi province in particular is generally very poor and rural, whose poverty poses an issue for TB patients who are not financially capable of managing their disease. My field supervisor, Dr. Zhigang Zheng, was a 2012-2013 Humphrey Fellow at Emory University Rollins School of Public Health, and held the position of the Deputy Director of the NTP at the Guangxi CCDC during the time of my practicum.

One of China's major public health insurance schemes is the New Rural Cooperative Medical Scheme (NRCMS), which covers about 850 million rural farmers living in the country. Under this plan, households pay a small amount of the premium while the government pays the rest of the cost. NRCMS aims to cover catastrophic illnesses and has high reimbursement rates for inpatient care but low rates for outpatient services. China's central government acts as the primary financer for premiums in both the district and county level, while the city and provincial sectors pay approximately 30% of costs at both levels. Although the NTP has paved the way for some major breakthroughs in TB control in Guangxi, it still faces several obstacles. The burden of TB disease remains very high in the province and there remain major discrepancies with case detection and reporting. Another major setback occurred in 2013 when financial support provided by the Bill and Melinda Gates Foundation ended, thereby cutting the TB funding budget in half [16].

There are currently two main models for controlling TB in Guangxi. The most prevalent model of TB practice in China is the dispensary model, in which general hospitals are responsible for referring TB patients to CCDC-operated TB dispensaries where patients can receive free treatment that covers the costs of medication, laboratory tests, and X-ray examinations. As a result, most TB cases are diagnosed and treated in these dispensaries. With the launch of the new integrated model in 2011, TB clinics have started shifting from CCDC dispensaries to hospital clinics where cases can be diagnosed and treatment plans can immediately be initiated for patients. However hospital providers are known prescribe more assistant drugs (i.e. liver protection drugs) and complete more screening and diagnostic tests that are otherwise unavailable in TB clinics. This practice increases the reliance on hospitalization and associated expenses. Additionally, TB patients face difficulties paying out-of-pocket hospitalization fees and more than half of families are impacted by TB faced significant out-of-pocket costs [16].

It is important to study each of these models in order to determine which is more convenient and economical for hospitals, public health clinics, and convenient for patients. Most TB cases in Guangxi hail from rural villages. In 2014, nearly 80% of TB cases were poor farmers [16]. Gathering evidence-based information about the financial burden of TB is critical for informing reforms in insurance plans and creating government subsidies for TB patients living in poverty. Unfortunately there is a very limited amount of published literature and statistics regarding the burden of TB in Guangxi. Most studies that have been completed regarding TB in the region focus on HIV/TB co-infection.

The purpose of this study was to assess the economic burden of TB on affected individuals and families in Guangxi. As Guangxi is a province with a very high prevalence rate of TB and given that there is virtually no literature that highlights the financial difficulties in obtaining TB-related treatment and care, it is important to investigate this issue so that Chinese government officials and health authorities can make appropriately informed policy revisions and/or accommodations for those impacted or at a high risk for the disease.

I worked with the NTP to design two data collection forms to evaluate the burden of TB-related expenses on township hospitals and patients. Our team traveled to two rural counties in Guangxi, hereby designated as County A and County B. In both counties we identified consecutive TB cases reported in 2013 to conduct interviews aimed at capturing health and demographic information, and direct/indirect expenditure information incurred as a result of TB diagnosis and treatment. During the interviews, many patients living in these rural villages expressed that they had travelled to larger cities for employment prospects and returned to their homes with TB disease. Often times these patients would transmit their infection to others in close contact, such as family members. Despite the lack of studies regarding the economic impact of TB on rural patients in this province, our discussions with patients and hospital staff suggested that affordability and access to transportation were two critical barriers to receiving appropriate and timely care.

II. Literature Review

In the province of Guangxi, the burden of TB remains high. Unfortunately, there is a relative paucity of studies to assess the economic burden of disease in this province. The main purpose of this literature review is to describe previous research efforts that have investigated the economic burden of TB among rural patients in Guangxi. However, this section will also discuss research studies that have investigated the costs incurred on individuals and patients affected by TB in other parts of China with similar demographic, socioeconomic (SES), and geographical features to Guangxi. While there is limited information of the type of research studies that have been done exclusively in Guangxi, strategies and interventions implemented in other countries with economic and healthcare systems similar to rural China can be valuable for addressing the issue in Guangxi. This review will explore the current literature available regarding the TB situation in China and other countries, their approaches for confronting the economic burden of TB, how their most effective strategies for addressing this issue can be applied in Guangxi, and identify further research that needs to be done in this field.

Description of decentralized health services for TB diagnosis and treatment

As Guangxi is located in a very rural area in China, members of the province face a number of challenges traveling directly to and from health facilities. According to one study, more than 50% of individuals who display clinical signs suggestive of TB visit the local village doctor first to receive treatment for their symptoms [17]. Only 20% of village doctors will recommend that patients visit a general hospital for formal diagnosis and treatment. Guangxi is a relatively poor province in which most of its residents are farmers and have low annual incomes [17]. Since the majority of patients who display TB symptoms are aware that they should visit local hospitals for formal treatment and services, this suggests there are financial barriers that prohibit individuals from seeking this appropriate care. This may include, but is not limited to, lacking personal means of transportation, inability to afford public transportation costs, not being able to afford hospitalization expenses, or the fear of income or job loss from taking time to travel to the health site [17]. Furthermore, the decentralization of TB services from the county to township levels could shorten care-seeking pathways and decrease the delay of TB diagnosis for patients.

TB expenses are not limited to costs associated with a patient going to a general hospital, but can also include referrals between general hospitals and CCDC dispensaries. One study explored the barriers between the TB programme (CCDC) and general hospitals in China in the provinces of Zhejiang and Guangxi [18]. Although Zhejiang is a more affluent province compared to Guangxi, researchers found that there were discrepancies in TB reporting and referrals by the hospitals to the dispensaries were in both counties. The referral process is fraught with potential conflicts of interest, such as doctors and hospitals making extra profits by retaining uncomplicated TB patients instead of directly referring them to TB dispensary clinics [18]. Patients who are hospitalized usually have significantly greater medical costs for the diagnosis and treatment of TB, as hospitalization is not free under the current National TB Program. Although hospitals claim that hospitalization is a measure for precaution, one report suggests that doctors tend to hospitalize patients and prescribe them more drugs than necessary in order to increase their salaries [19]. Such inconsistencies in referral patterns and provision of health care likely contribute to the financial expenses incurred by the patients for extra hospitalization and examination costs.

Types of models

One of the major issues in addressing the burden of TB in China is within the type of TB healthcare model that is used in certain hospitals. Researchers who investigated the quality of TB care between the integrated and dispensary models in the Zhejiang province found that the overall medical expenditures in the integrated hospitals were slightly lower than in the hospitals following the dispensary model [20, 21]. The integrated model also has the potential to shorten health-seeking pathways for the TB patients as patients do not need to obtain referrals from village doctors and general hospitals to visit dispensary clinics for TB care [21]. Furthermore, a study that compared patient care-seeking pathways in four different provinces (Shandong, Zhejiang, Guangxi, and Shanghai) between the dispensary, integrated, and specialist models found that among the three, TB patients were treated more promptly and experienced shorter treatment delays with the integrated approach [22].

Although the majority of China involves hospitals referring patients to CCDC sites, there are select areas in the country that have undergone the transition from the dispensary to the integrated approach. Changning, Shanghai and Nanning, Guangxi are two such examples [23]. CCDC staff from both locations reported that before the reorganization of healthcare delivery, limitations in technology, equipment, and staff made it difficult to treat TB complications at the dispensaries, while hospitals had a greater capacity to treat TB patients. Only after the private and public sectors had merged could the CCDC then focus its attention on health systems management and health education for TB patients.

Although China has a free-service policy for TB patients, many patients end up paying a great amount of their income for medical care [24]. The expenses generally come from out-of-pocket costs that stem from costs associated with diagnostic tests, the intake of commonly prescribed “liver protective” drugs, X-ray examinations, and additional second-line drugs (drugs used for drug-resistant TB). Abuse of second-line drugs increases the probably of MDR-TB and consequently increases TB costs [24]. Most patients also report being prescribed liver protection drugs in the absence of any medical rationale in TB dispensaries [25]. Under the NRCMS, households pay a small premium cost and the local government finances the insurance premium. In a study that measured the proportion of TB patients who received reimbursements for medical costs, patients did not have to pay anything for anti-TB medications but were required to pay high costs for extra examinations and auxiliary traditional medications used to “protect liver function” [26]. Although insurance for rural families is designed to cover basic TB costs, several aspects of TB care are not covered for patients, which intensifies the economic burden of the disease for patients who rely on rural farming to provide for themselves and their family members.

Economic burden for patients diagnosed with TB

Although there are a limited number of studies that were completed in Guangxi regarding this topic, there are studies that also investigate the economic burden of TB treatment and services among low-income individuals and families in similar Chinese provinces. A study completed in Jiangsu, a province that is comparable to Guangxi in that it is rural and most of its residents are farmers, researchers surveyed patients who had already completed their anti-TB treatment regimen regarding their total costs of TB diagnosis and treatment and found that patients only sought care due to severe symptoms, such as chest pain or a persistent cough. They were commonly given a high quantity of medications, and experienced a delay in receiving their TB diagnosis [19]. These findings suggest that although a patient’s health status may become more severe if they do not seek care until their symptoms worsen, doctors and hospital staff also contribute to diagnostic delays and to additional cost expenditures incurred by the patients.

While TB health services are advertised to be free of cost to the community, the perceived costs of TB expenses have been substantial among community members [27]. Hospitalization fees and the cost of supplemental “liver protection drugs” are not covered by health insurance, resulting in most patients living in rural areas paying more for services than initially anticipated. Without being able to afford “liver protection drugs” that are commonly prescribed with anti-TB medications, patients may stop their anti-TB regimen altogether [27]. Treatment interruption can lead to complications in a patient’s TB disease, and increase the likelihood of developing drug resistance. Drug resistance, especially multidrug-resistant (MDR) TB (defined as resistance to at least isoniazid and rifampin) would render the subsequent use of routinely prescribed treatment regimens for TB ineffective. While patients are ultimately responsible for making health decisions regarding adherence to prescribed treatment regimens needed for at least six months, many report not receiving adequate health education from healthcare providers regarding the consequences of not keeping up with the recommended anti-TB regimen [27].

Although one of the major barriers that TB patients encounter in receiving TB care involves the affordability of medical services, the accessibility of such resources remains a large issue in rural China. Low-income groups are less likely to seek care, as they may not have the appropriate financial means for transportation in addition to the fact that traveling to hospitals may be limited, complex, and very time-consuming [28]. Moreover, those who visit the hospitals and are diagnosed with TB may not be able to continue to make daily visits to the health sites to complete the DOTS program, in which the regimen would typically be required for a minimum of six months [28].

In other instances, high treatment expenditures may result from the patient's lack of awareness about TB services available free of charge located at the township hospitals. A patient may spend a lot of money during the early stages of diagnosis and treatment, but later discontinue the treatment regimen once sources of income have been exhausted. Alternatively, patients may try to avoid defaulting on their treatment progress by borrowing money or selling property for additional income [28, 29]. In both examples, patients who already have low incomes, either because they are farmers or are self-employed, would face worse financial conditions and could potentially exacerbate their health outcomes should they abandon treatment altogether.

Intervention strategies

In addition to health system reform, there have been a number of trial programs that have been launched in order reduce the burden of TB in China. One program, the Health X Project, determined which strategies were affordable for TB control compared to similar strategies in other countries. The major initiatives of this program were to support the diagnosis and treatment of TB with first-line drugs. Another strategy involved scaling up the DOTS implementation. Findings from this project demonstrated that these measures were not only cost-effective for the health system, but for the patients as well [30]. Another project involved the implementation of a drug susceptibility test (DST), Genechip, which is a system for rapid diagnosis of resistance to first-line drugs, rifampin and isoniazid. The cost effectiveness of Genechip was better compared to the gold standard DST. The report suggested that a fast-acting test such as Genechip would be more widely used if it were less expensive [31]. Both of these projects are examples of successful intervention strategies for strengthening the TB health system and reducing the financial burden of TB on patients.

Although China has adopted the Stop TB Strategy in which DOTS serves as the main method for TB control among known TB patients, this approach does not bear a significant presence in rural provinces. Rural patients report several difficulties traveling to clinics to complete their treatment regimen, which is problematic for controlling their TB. However, studies have found that regular home visits and supervision by township and village health workers contributed to better treatment outcomes. This strategy served as the main source of health education and management and required more financial and human resources to carry on a long-term community impact [32]. DOTS is ultimately a cost-effective tool for both patients and health facilities and is an especially good control strategy for smear-positive TB [33].

Migrant populations

In addition to the burden of TB in rural areas, health systems problems cause barriers for migrants to access TB care [34]. Due to the “hukou” system, in which individuals can only receive local medical insurance from the cities where they have local household registration, migrants are not eligible to receive subsidized TB care in cities where they are temporarily residing for employment purposes. Migrants working in Shanghai, for example, who contract TB often cannot continue working due to their illness and would sometimes lose their jobs [34]. As a result, migrants often face high medical costs with little to no income, which can be especially devastating as living costs are much more expensive in major cities than in their respective home provinces. Many report being treated for TB for a long time at general hospitals and eventually being drained of their financial resources in the middle of their anti-TB treatment regimens [34]. Furthermore, migrants report being prescribed additional drugs and may end up spending three to five times the amount of their annual incomes for TB treatment. Due to financial difficulties of keeping up with the anti-TB regimens, migrants face an especially high risk for defaulting on treatment [34].

Economic burden of TB in other countries

While TB remains a challenging health issue in China, it is important to consider how other developing nations with high rates of TB and decentralized health systems are addressing the economic burden of the disease among low-income individuals. By exploring similar research studies in other countries with high rates of poverty and widespread transmission of TB, such findings and intervention strategies could potentially be generalizable to rural areas in China such as Guangxi.

India has the highest burden of TB in the entire world, with an estimated 40% of the population infected with latent or active TB [35]. Past research demonstrates that although smear tests and first-line drugs are free for patients, the diagnosis and treatment of TB impact the direct and indirect cost burden on patients. While the DOTS program plays a huge role in TB control in India, patients report losing income traveling to and from health sites for pill collection [36]. However, another study done in district Tamilnadu, India, suggests that when the DOTS program is expanded such that decentralized services for diagnosis and treatment are close to patients' homes in rural areas, travel costs are significantly lower and treatment outcomes had improved overall [37]. This example from India suggests that the DOTS program is most effective if services are offered close to patients' homes, therefore minimizing transportation expenditures.

In 2014, there were about 180,000 people living with TB in Vietnam [28]. In light of the high burden of TB among impoverished individuals, Vietnam's NTP has made several initiatives to make TB-related services more accessible and affordable to the community [39]. One strategy the NTP is pursuing is to involve the private sector in public-private-mix activities that would minimize travel expenses as well as accommodation and hospitalization costs for TB patients and family members. In response to the difficulties that patients have encountered with completing their anti-TB treatment regimen, the NTP has also decided to reduce the anti-TB treatment regimen from 8 to 6 months in order to alleviate treatment time and transportation costs for patients. The NTP is also moving forward with providing TB services at provincial, public, and private hospitals and is planning to provide social and economic support to TB patients in each district [39].

Research that focuses on the economic burden of TB among rural patients in Guangxi is an area that is significantly understudied. The current study aims to provide meaningful information and insight into the costs incurred by people diagnosed with TB disease and can hopefully inform evidence-based policy makers and federal health authorizes to make actionable changes for poor TB patients in Guangxi.

III. Methods

Introduction

The purpose of this research project is to assess the financial burden of TB patients and their ability to afford TB-related treatment, care, and services. Our team developed two data collection forms to gather information regarding the township hospital's information of TB cases in the county as well as what is expensive and what is affordable to the patient in terms of accessibility to TB treatment, services, and care. Within this data collection instrument, there is an outpatient cost survey to determine the percentage of TB treatment costs that is covered by insurance and the patient's household income. The data collected from this survey will determine what could possibly lower the financial burden of patients for affording TB treatments, identify ways to mitigate this burden, and inform policies to subsidize the cost of managing TB among poor households and effectively strengthen TB control strategies in the community.

Population and Sample

The target population for our study included all persons who were diagnosed with pulmonary TB in calendar year 2013, were at least 18 years of age, listed in the registry of two township hospitals (in County A and County B, respectively), and resided in the Guangxi province. Patients who had extra-pulmonary TB or multidrug-resistant (MDR) TB were excluded from our sample. Our research specifically focused on individuals who live in rural villages in the province. The population almost exclusively includes farmers who do not generate much monetary income and primarily rely on their crops as sustenance for themselves and their families. Most of these families live in cluttered and unsanitary (multi-person, single room dwellings; dirt floors; lack of potable water; reliance on latrines) home environments that may enable the spread and communication of *M. tuberculosis* infection.

The two counties that were chosen by the Guangxi CCDC for this study have been designated County A and County B. Both counties have rural and underdeveloped environments are reported to have a high burden of TB. County A is one of the western-most counties located in Guangxi and is also a border town to Vietnam. County B is located in the eastern region of the province and is slightly more developed than County A.

Research Design

We designed a cross-sectional survey questionnaire that was interviewer-administered to selected patients in Chinese Mandarin, which is the native language in both counties. The interviewers received instructions before conducting the interviews. Seventy percent of the data were collected through telephone interviews and 30% through home-visit interviews. Completed telephone interviews and home-visit interviews were sent via mail to our office in Nanning, Guangxi. Our team conducted telephone and home-visit interviews between the hours of 9am and 6pm over the time period of two weeks.

Procedures

My site supervisor and I traveled from Nanning, Guangxi to each county on two separate occasions. The Guangxi CCDC arranged for a car and driver to take us to each county. The township hospitals in County A and County B each provided our team with a TB registry of patients who were diagnosed with TB in 2013. In County A, there were 1001 active patients in the 2013 TB registry list. An interval-sampling method was used in which every 5th patient was selected, resulting in a sample of 200 patients. After matching this list of 200 patients with the hospitalization list of 506 patients, we ended up with 128 patients who had reimbursement records in the insurance system. In County B, we followed an identical sampling approach to County A. There were 391 patients on the 2013 TB registry in County B and we selected every 5th name from the list using interval-sampling methods to obtain a sample of 79 patients. The County A and County B 2013 TB lists from which we selected names through interval-sampling methods only included patients who were over the age of 18 years. Each township hospital was able to provide additional expense information regarding testing and other hospitalization fees. Therefore, we did not ask patients about these expenses.

For each county, our sample list was divided such that 70% of patients would be interviewed through the telephone and 30% would be interviewed during a home-visit. All responses collected from participants were recorded in hard-copy data collection forms.

Telephone Interviews

A group of five to ten healthcare workers from each county conducted telephone-interviews using a scripted standardized questionnaire at the township hospital locations (See Appendix A, page 45). These healthcare workers were employees of the hospital and were asked by our CCDC office to serve as interviewers for our study. For both the home-visit and telephone interviews, the interviewers did not receive any additional training. If the patient answered the phone, the worker introduced him or herself and described the broad purpose of the study and the role of the patient for our study. The patient would then provide his or her verbal consent to participate. Every patient that answered the phone provided his or her consent to become a part of the study. The worker would then proceed to administer the survey to the patient over the phone.

If a patient did not answer or was unavailable, he or she was called up to six or seven more times. Patients who were temporarily unavailable at the time of the call were contacted again during a more convenient time. If the patient still did not answer, they were deemed non-respondent.

In-person Interviews

Approximately three to five healthcare workers accompanied my site supervisor and me to the villages where we would conduct in-person interviews at patients' homes. Each county provided our team with in-kind transportation services for the home visits. We arrived at each household without providing prior notice to the patient. At times, we had to ask neighbors where we could find the patient's home. Those who we asked would give us directions to the home. Once the patient's home was located, we would knock on the door and ask to survey the patient. Patients who were at home welcomed us into their homes and were willing to provide us with the information necessary for our surveys. On average, each home interview lasted about 20 minutes. Interviews were usually conducted on the front porch of the home or inside of the living room. Family members were usually present during the interviews.

We began each visit by explaining our purpose of the interview and describing the importance of the study. If the patient agreed to participate, they signed a consent form. We would then administer the questionnaire verbally to each patient in the local language, Mandarin Chinese. The interviewer would record the responses on the data collection form. When available, patients would produce financial statements that contained information needed for the survey. If no such statements were available, the patient would be asked to provide an estimate based on memory and best recall. During the some interviews, patients would discuss the responses of certain survey questions with family members in order to recall particular events or financial expenditures.

Survey Instruments

We designed two data collection forms. In both forms, the currency reported was in Chinese Yuan (¥)[1]. One form was designed for our participants to provide demographic information and their indirect/direct costs incurred as a result of their TB diagnosis (See Appendix B, page 48). The second form was designed for township hospitals to report how many cases they had seen in the past year and the costs associated with TB cases (we will exclude from this report the data collected from this second form). The data from this form will be collected and analyzed by the CCDC office.

The patient data collection form contained three sections. Patients were firsts asked to provide their basic demographic information such as their date of birth, ethnic group, occupation, highest level of education, and health insurance type. This part also included questions on the patient's date of diagnosis and treatment start/end, and approximate costs of TB diagnosis. The second section of the survey focused on the dates of each TB hospitalization, complications that may have developed as a result of the hospital visit, and whether or not relatives accompanied the patient during the hospitalization. In the third section, patients reported the direct costs such

[1] For all costs reported in Chinese Yuan, the costs will also be reported in U.S. dollars. The conversion rate between the Yuan and the U.S. Dollar at the time of study was 6.14 Yuan = 1 U.S. Dollar.

as insurance and out-of-pocket expenses. Patients were also asked about additional testing fees and indirect costs such as food and lodging.

All forms (including IRB consent forms) were translated into Chinese Mandarin.

Data Analysis

In both counties, my supervisor and I were present for about five to seven home interviews. This range accounts for a different number of homes visited in each county. The rest of the home visits were completed during a period lasting two-to-three weeks. The telephone interviews were also continued for the same time period. Once the in-person and telephone interviews were completed, the hard-copy surveys were sent to our office in the Guangxi CCDC for data entry and analysis.

Data were collected and transcribed electronically by me. Data were entered into EpiInfo 7 and analyzed using SAS 9.4. Statistical analyses were performed to identify the factors associated with patients' TB-related direct and indirect expenses.

Ethical Considerations

In compliance with the Emory University Institutional Review Board (IRB), I submitted my protocol and research instruments to IRB as my research included human subjects and their personal health information. Expedited approval was granted on May 6th, 2015.

Statistics Analysis Plan

This plan outlines the procedure for determining the statistical findings of the data collected from County A and County B. Only those variables with at least 90% of data will be considered in all analyses. Variables with observations coded as "Don't know" or "Other" will be re-coded as missing values for analysis purposes. For all statistical tests, an alpha value of 0.05 will be used. All statistical tests are two-sided.

We will be introducing two derived variables to our dataset. The first variable is the difference of incomes before and during diagnosis. We asked patients to report their annual incomes the year before their TB diagnosis and the year of their TB diagnosis. We created a new variable in which we subtracted the income from the year before from the income from the year of the patient's diagnosis.

The second derived variable is the total expenditures by each patient during hospitalization, which is the outcome variable. The total expenditures variable is derived from other fee variables in the data set. In County A, those variables are the lodging fee, examination fee, B ultra fee, chest X-ray (CXR) fee, Chinese medicine fee, drug fee, laboratory fee, oxygen fee, nursing fee, materials fee, and treatment fee. In County B, those variables are the same as listed for County A, but with the addition of the electrocardiograph (ECG) fee, operation fee, test fee, Color B ultra fee, computed tomography (CT) fee, blood fee, ambulance fee, encephalogram fee, magnetic resonance imaging (MRI) fee, and other fees. Since we are interested in learning about the economic burden of TB on patients, we decided the most effective way to measure this was to assess the total costs incurred by patients during hospitalization.

Before data collection, we considered collapsing information for County A and County B. Following data collection, we found that SES and other collected variables statistically differed by county. Therefore we conducted stratified analyses for each county to identify significant associations with total expenditure (Table 2a and Table 2b). Furthermore, County B has additional variables absent for County A, therefore Tables 2a and 2b consider each county separately for the analyses. The County B township hospital provided us with more patient data than the County A township hospital.

In Table 1a, we aim to determine the statistical differences of each categorical variable between County A and County B. The variables with more than 10% missing data for at least one county are TB confirmation type and HIV status. The number of observations in each variable and its respective levels will be reported. P-values will be reported from either a chi-square test or the Fisher's Exact test. The parametric statistical test that would be used for the comparison of each categorical variable by county type is the chi-square test of independence. The Chi-square test requires that 80% of cells have an expected counts ≥5 [40]. For categorical variables that do not meet this requirement, the Fisher's Exact test statistic will be used, which is a nonparametric alternative to the chi-square test [40].

In Table 1b, we aim to determine the statistical differences of each continuous variable between County A and County B. The variables with more than 10% missing data for at least one county are treatment period and loss of wages. The number of observations, mean, standard deviation, median, 1st quartile (Q1), and 2nd quartile (Q3) for each variable would be reported in the table. These descriptive statistics will show similarities or differences for each variable across both counties. P-values will be reported from either the Two-Sample independent t-test or the Wilcoxon Rank-Sum test. The two-sample t-test compares the population means by comparing two independent normally distributed samples [41]. The Wilcoxon Rank-Sum test is based on the sum of the two sample's observations of the combined sample and is a nonparametric alternative to the two-sample t-test that is used for continuous variables that are not normally distributed [42]. The variables EC fee, operation fee, other fee, test fee, color B ultra fee, CT fee, blood fee, ambulance fee, encephalogram fee, and MRI fee will not be included in statistical analysis because these data for these variables were only available for patients in County B.

In Table 2a, a univariate analysis will be performed to determine the Spearman correlation, which would be used to assess the association between each continuous variable and the continuous outcome variable, the total expenditure during hospitalization. A Spearman correlation coefficient is a nonparametric version of the Pearson correlation coefficient that determines a non-normal variable's strength and direction in association with the outcome variable [40]. The correlation value, r, can vary from -1 to +1: -1 indicates a perfect negative correlation, 0 indicates no correlation, and +1 indicates a perfect positive correlation [43]. P-values for the Spearman correlation will also be reported to show if there is a statistically significant correlation between a continuous variable and the total expenditures outcome variable. For the purposes of this study, the cutoff point for a "very weak" correlation value is 0.01-0.19; a "weak" correlation value is 0.20-0.39; a "moderate" correlation value is 0.40-0.59; a "strong" correlation value is 0.60 to 0.79; and a "very strong" correlation value is 0.80-1.0 [44].

Table 2b will examine the association of each categorical variable within County A and County B. If necessary, levels may be collapsed in order to have an adequate number of observations for each level of a categorical variable. A one-way analysis of variance (ANOVA) is a parametric test that assesses the differences among three or more independently sampled levels in a normally distributed continuous variable. The Kruskal-Wallis test is a nonparametric version of the one-way ANOVA that will be used to determine if there are any statistically significant differences between more than two levels in the non-normal continuous outcome variable. For non-normal outcome associations with a categorical variable with two levels, the p-value for the Wilcoxon Rank-Sum Test or the Two-Sample independent t-test statistic would be reported [45]. Hence if total expenditure is normally distributed, t-test or ANOVA tests will be utilized. If total expenditure is not normally distributed, Wilcoxon Rank-Sum and Kruskal-Wallis tests will be conducted.

IV. Results

At the end of our data collection period, we had interviewed a total of 100 patients from County A, for a response rate of 80.5%. However, there were two patients who reported having MDR-TB. Since we were considering patients who only had pulmonary TB, we had to exclude these two patients from our sample. Therefore, our response rate dropped to 76.6% (n=98). After conducting in-person and telephone interviews, we had collected data from 59 patients, for a 74.7% response rate in County B.

In County A, 28 patients from our sample list could not be reached because they did not answer their telephones if they were in the telephone-interview group or because they were not home if they were in the in-person interview group. In County B, 20 patients from our sample list were not reached for the same reasons as observed in County A.

Table 1a: Categorical Variables between County A and County B

Variable	County A (N=98) n (%)	County B (N=59) n (%)	County A vs. County B p-value
Gender	98	58	0.818
Male	71 (72.4)	43 (74.1)	
Female	27 (27.6)	15 (25.9)	
Occupation	96	58	0.001
Farmer	74 (77.1)	44 (75.9)	
Farmer worker	17 (17.7)	0 (0)	
Housekeeper	0 (0)	0 (0)	
Retired staff	1 (1.04)	3 (5.17)	
Student	2 (2.08)	8 (13.8)	
Government employee	0 (0)	3 (5.2)	
Factory worker	0 (0)	0 (0)	
Education	98	59	0.044
No formal schooling	19 (19.4)	3 (5.1)	
Elementary school	36 (36.7)	13 (22.0)	
Middle school	29 (29.6)	30 (50.8)	
High school	11 (11.2)	11 (18.6)	
Junior college	1 (1.02)	1 (1.7)	
Bachelor's degree	2 (2.04)	1 (1.7)	
Graduate or professional degree	0 (0)	0 (0)	
Insurance	95	59	0.004
New Rural	90 (94.7)	47 (79.7)	
Cooperative Medical urban worker	5 (5.3)	12 (20.3)	
Commercial insurance	0 (0)	0 (0)	
No insurance	0 (0)	0 (0)	
Place of residence	97	49	<0.0001
Plain area	1 (1)	4 (8.2)	
Hill area	0 (0)	34 (69.4)	
Mountain area	96 (99)	11 (22.4)	
TB bacterial confirmation type	98	---	---
Smear (+)	25 (25.5)	---	
Smear (-)	49 (45.9)	---	
Culture (+) and Smear (-)	0 (0)	---	
No smear result	24 (24.4)	---	

In this table, all differences in variables are statistically significant with regard to county type, except for gender (p=0.818). In County A, the population comprised of 72.9% males and 27.6% females versus 74.1% males and 25.9% females in County B. Place of residence differed significantly between County A and County B (p<0.0001). In County A, 98.9% of patients lived in mountain areas compared to 22.4% of patients residing in mountain areas in County B. Furthermore, the majority of patients (69.4%) in County B report living in hill areas versus no patients in County A. Educational level differed moderately, with County A residents being more likely to have no formal schooling (19.4%) than those in county B (5.1%), alpha level p=0.044. County B data for TB bacterial confirmation type had an "n" less than 90% and therefore was excluded from analysis.

Table 1b: Statistical Differences of Continuous Variables between County A and County B

	County A (N=98)			County B (N=59)			County A vs. County B
Variable	n (%)	Mean (SD)	Median (Q1, Q3)	n (%)	Mean (SD)	Median (Q1, Q3)	p-value
Total expenditure (Yuan)	97 (99.0)	7198 (4104)	6198 (4390, 8812)	59 (100)	10611 (8509)	8885 (669, 13626)	0.006
Income during year before diagnosis (Yuan)	98 (100)	29117 (26137)	20000 (8000, 45000)	59 (100)	25915 (15420)	25000 (15000, 30000)	0.466
Income during year of diagnosis (Yuan)	98 (100)	17841 (17976)	12000 (5000, 25000)	59 (100)	20441 (11500)	19000 (12000, 25000)	0.008
Difference of incomes before and during diagnosis (Yuan)	98 (100)	11275 (14064)	3750 (2000, 20000)	59 (100)	5474 (5893)	5000 (2000, 5000)	0.916
Age (years)	98 (100)	49.599 (16.247)	46.984 (39.016,61.775)	59 (100)	54.833 (16.922)	57.466 (43.688, 68.307)	0.059
Distance (km)	98 (100)	34.837 (17.648)	33.000 (20.000, 51.000)	59 (100)	27.619 (18.953)	30.000 (10.000, 45.000)	0.024
Average number of days relatives accompanied patient during hospitalization	98 (100)	9.913 (8.444)	9.500 (4.000, 14.000)	58 (98.3)	11.207 (4.862)	11.000 (7.000, 15.000)	0.053
Average number of visits to TB clinic in one month	94 (95.9)	0.766 (0.406)	1.000 (0.500,1.000)	58 (98.3)	0.966 (0.373)	1.000 (1.000, 1.000)	0.003
Cost of transportation from home to TB clinic (Yuan)	97 (99.0)	20.845 (11.995)	20.000 (12.000, 30.000)	59 (100)	14.814 (8.080)	15.000 (8.000, 20.000)	0.003
*Amount of wages lost per month (Yuan)**	---	---	---	59 (100)	791 (753)	500 (400, 1000)	---
Lodging fees (Yuan)	97 (99.0)	306 (177)	255 (180, 360)	59 (100)	279 (241)	227 (88.000, 393)	0.131
Examination fee (Yuan)	97 (99.0)	78.889 (36.306)	72.000 (54.000, 93.000)	59 (100)	227 (169)	212 (76.800, 323)	<0.0001
B Ultra fee (Yuan)	97 (99.0)	261 (232)	196 (87.500, 371)	59 (100)	50.088 (99.548)	0.000 (0.000, 26.000)	<0.0001
CXR fee (Yuan)	97 (99.0)	613 (398)	668 (334, 668)	59 (100)	45.865 (60.471)	0.000 (0.000, 82.000)	<0.0001
Chinese medicine fee (Yuan)	97 (99.0)	294 (419)	130 (57.000, 358)	59 (100)	355 (610)	95.940 (0.000, 410)	0.187
Drug fee (Yuan)	97 (99.0)	2665 (2061)	2087 (1380, 3095)	59 (100)	3713 (2720)	2793 (1197, 5979)	0.037
Laboratory fee (Yuan)	97 (99.0)	1704 (616)	1555 (1316, 2009)	59 (100)	1851 (995)	1680 (1293, 2320)	0.254
Injection fee (Yuan)	97 (99.0)	247 (169)	192 (140, 313)	59 (100)	357 (253)	291 (136, 523)	0.014
Oxygen fee (Yuan)	97 (99.0)	150 (356)	0.000 (0.000, 0.000)	59 (100)	975 (6325)	17.200 (0.000, 259)	0.001

Nursing fee (Yuan)	97 (99.0)	459 (270)	384 (280, 565)	59 (100)	313 (313)	208 (93.700, 416)	<0.0001
Materials fee (Yuan)	97 (99.0)	218 (195)	138 (94.000, 245)	59 (100)	584 (1864)	218 (116, 475)	0.026
Treatment fee (Yuan)	97 (99.0)	112 (339)	0.000 (0.000, 22.600)	59 (100)	536 (423)	442 (193, 804)	<0.0001
*ECG fee (Yuan)***	---	---	---	59 (100)	32.534 (28.361)	22.000 (22.000, 26.500)	---
*Operation fee (Yuan)***	---	---	---	59 (100)	81.678 (333)	0.000 (0.000, 22.000)	---
*Other fee (Yuan)***	---	---	---	59 (100)	8.566 (63.356)	0.000 (-0.030, 0.030)	---
*Test fee (Yuan)***	---	---	---	59 (100)	352 (731)	68.000 (0.000, 323)	---
*Color B Ultra fee (Yuan)***	---	---	---	59 (100)	173 (168)	105 (87.500, 252)	---
*CT fee (Yuan)***	---	---	---	59 (100)	608 (513)	403 (403, 806)	---
*Blood fee (Yuan)***	---	---	---	59 (100)	28.729 (141)	0.000 (0.000, 0.000)	---
*Ambulance fee (Yuan)***	---	---	---	59 (100)	9.432 (35.928)	0.000 (0.000, 0.000)	---
*Encephalogram fee (Yuan)***	---	---	---	59 (100)	1.203 (9.243)	0.000 (0.000, 0.000)	---
*MRI fee (Yuan)***	---	---	---	59 (100)	10.983 (59.137)	0.000 (0.000, 0.000)	---

*At least 10% of data were missing for "*Amount of wages lost per month (Yuan)"* in County A
** Data for these variables available only in County B

In Table 1b, the variables that statistically significant differed by county were distance (p=0.024), average number of visits to TB clinic in one month (p=0.003), cost of transportation from home to TB clinic (p=0.003), examination fee (p<0.0001), B ultra fee (p<0.0001), CXR fee (p<0.0001), Chinese medicine fee (p<0.0001), drug fee (p=0.037), injection fee (p=0.014), oxygen fee (0.001), nursing fee (<0.0001), materials fee (p=0.026), and treatment fee (p<0.0001).

In County A, the variables whose median values are "0" are oxygen fee and treatment fee. In County B the median values for these variables are ¥17.2 ($2.80) and ¥442 ($71.99), respectively, which explains the observed statistical difference in oxygen fee and treatment fee. In County B, those variables with median values of "0" are B ultra fee, CXR fee, operation fee, other fee, blood fee, ambulance fee, encephalogram fee, and MRI fee. In County A, the median values for B ultra fee and CXR fee are ¥196 ($31.92) and ¥668 ($108.79), respectively, and explain why these two variables are highly significant between both counties. Data for EC fee, operation fee, other fee, test fee, color B ultra fee, CT fee, blood fee, ambulance fee, encephalogram fee, and MRI fee were not available in County A. These "0" values have been verified to be authentic values and not missing values.

In County A, the annual net income of rural households was ¥4,786 ($779.48) while the annual net income of urban residents was ¥18,356 ($2,989.58) in 2013 (Z. Zheng, personal communication, February 14, 2016). In this sample, patients reported a median income of ¥20,000 ($3,257.33). The year during their diagnosis, the reported median annual income dropped to ¥12,000 ($1,954.40).

In 2013, the annual net income of rural households in County B was ¥7,994 ($1,301.95) while among urban residents this figure was ¥21,084 ($3,433.88). Patients reported a median annual income of ¥25,000 ($4,071.66) the year before TB diagnosis. During the year of diagnosis, the reported median annual income for patients was ¥19,000 ($3,094.46). Urban households in this county were reported to have an annual net income of ¥21,084 ($3,433.88) in 2013 (Z. Zheng, personal communication, February 14, 2016).

The comparison of incomes before diagnosis between both counties was not significant (p=0.466), however the comparison of incomes during diagnosis was significant (p=0.008).

Table 2a: Univariate Spearman Correlation between Continuous Variables and Total Expenditures within Each County

	County A (N=98)		County B (N=59)	
Total Expenditure vs. Variable	r	p-value	r	p-value
Income during year before diagnosis (Yuan)	-0.15096	0.1399	-0.06171	0.6424
Income during year of diagnosis (Yuan)	-0.19451	0.0562	-0.03398	0.7983
Difference of incomes before and during diagnosis (Yuan)	0.00797	0.9382	-0.08124	0.5407
Age (years)	-0.12082	0.2385	0.16458	0.2129
Distance (km)	0.24661	0.0149	-0.13837	0.2960
Average number of days relatives accompanied patient during hospitalization	0.35890	0.0003	0.18982	0.1535
Average number of visits to TB clinic in one month	-0.02052	0.8452	0.11557	0.3877
Cost of transportation from home to TB clinic (Yuan)	0.26661	0.0086	-0.18653	0.1572
Lodging fees (Yuan)	0.75915	<0.0001	0.82617	<0.0001
Examination fee (Yuan)	0.86260	<0.0001	0.80199	<0.0001
B Ultra fee (Yuan)	0.35110	0.0004	0.23494	0.0733
CXR fee (Yuan)	0.59503	<0.0001	-0.04097	0.7580
Chinese medicine fee (Yuan)	0.45437	<0.0001	0.28219	0.0304
Drug fee (Yuan)	0.94189	<0.0001	0.85564	<0.0001
Laboratory fee (Yuan)	0.88779	<0.0001	0.79642	<0.0001
Injection fee (Yuan)	0.94567	<0.0001	0.88118	<0.0001
Oxygen fee (Yuan)	0.46428	<0.0001	0.29231	0.0247
Nursing fee (Yuan)	0.80832	<0.0001	0.76092	<0.0001

Materials fee (Yuan)	0.78373	<0.0001	0.75465	<0.0001
Treatment fee (Yuan)	---	---	0.74823	<0.0001
*ECG fee (Yuan)***	---	---	0.23864	0.0687
*Operation fee (Yuan)***	---	---	0.40127	0.0016
*Other fee (Yuan)***	---	---	0.13188	0.3194
*Test fee (Yuan)***	---	---	0.11603	0.3815
*Color B Ultra fee (Yuan)***	---	---	0.24828	0.0579
*CT fee (Yuan)***	---	---	0.54806	<0.0001
*Blood fee (Yuan)***	---	---	0.31463	0.0152
*Ambulance fee (Yuan)***	---	---	-0.14761	0.2646
*Encephalogram fee (Yuan)***	---	---	-0.13108	0.3224
*MRI fee (Yuan)***	---	---	0.12100	0.3613

County A

In County A, the variables that are statistically significantly correlated with total expenditures included distance (r=0.24661, p=0.0149), number of days relatives accompanied patient (r=0.35890, p=0.0003), cost of transportation (r=0.26661, p=0.0086), lodging fee (r=0.75915, p<0.0001), examination fee (r=0.86260, p<0.0001), B ultra fee (r=0.35110, p=0.0004), CXR fee (r=0.59503, p<0.0001), Chinese medicine fee (r=0.45437, p<0.0001), drug fee (r=0.94189, p<0.0001), laboratory fee (r=0.88779, p<0.0001), injection fee (r=0.94567, p<0.0001), oxygen fee (r=0.46428, p<0.0001), nursing fee (r=0.80832, p<0.0001), materials fee (r=0.78373, p<0.0001). These variables each share a positive correlation with the total expenditures during hospitalization.

The variables with “strong” to “very strong” positive correlation values are lodging fee, examination fee, drug fee, laboratory fee, injection fee, nursing fee, and materials fee. Variables with negative correlation values in this county are income during year before diagnosis (-0.15096), income during year of diagnosis (-0.19451) age (-0.12082) and average visit per month

(-0.02052), both of which have “very weak” strength. Two variables that have “weak” to “moderate” positive correlation values and are statistically significant are CXR fee and cost of transportation.

County B

In County B, the variables that were statistically significantly correlated with total expenditures included lodging fee (r=0.82617, p<0.0001), examination fee (r=0.80199, p<0.0001), Chinese medicine fee (r=0.28219, p<0.0001), drug fee (r=0.85564, p<0.0001), laboratory fee (r=0.79642, p<0.0001), injection fee (r=0.88118, p<0.0001), oxygen fee (r=0.29231, p=0.0247), nursing fee (r=0.76092, p<0.0001), materials fee (r=0.75465, p<0.0001), treatment fee (r=0.74823, p<0.0001), operations fee (r=0.40127, p=0.0016), CT fee (r=0.54806, p<0.0001), and blood fee (r=0.31463, p=0.0152). These variables are all positively correlated with the outcome variable.

The variables with “strong” to “very strong” positive correlation values are lodging fee, examination fee, drug fee, laboratory fee, injection fee, nursing fee, materials fee, and treatment fee. The variables in this county with negative correlation values are income during year before diagnosis (-0.06171), income during year of diagnosis (-0.03398), difference in incomes (-0.08124), distance (-0.13837), cost of transportation (-0.18653), CXR fee (-0.04097), ambulance fee (-0.14761), and encephalogram fee (-0.13108). All of these variables have correlation values that are “very weak” to “weak”.

Table 2b: Wilcoxon Rank-Sum Tests/ Kruskal-Wallis (K-W) for Association with Total Expenditures within Each County

Variable	County A			County B		
	Mean (SD)	Median (Q1, Q3)	Wilcoxon or K-W p-value	Mean (SD)	Median (Q1, Q3)	Wilcoxon or K-W p-value
Gender			0.7422			0.3417
Male	7366 (4426)	6268 (4488, 9335)		9859 (6656)	8885 (4754, 13626)	
Female	6740 (3085)	5736 (4360, 8575)		13398 (12271)	11200 (6693, 14230)	
Occupation			0.0140			0.2966
Farmer/farmer worker	7437 (4152)	6352 (4610, 8957)		9978 (8379)	8139 (4669, 13192)	
All other occupations	4128 (1395)	4196 (3217, 5311)		12469 (8910)	12178 (5810, 14704)	
Education			0.5158			0.3054
No formal schooling	6774 (3785)	6210 (4069, 8542)		5350 (976)	5506 (4305, 6239)	
Grade level education	7381 (4234)	6198 (4650, 9335)		10730 (8584)	10254 (5342, 13626)	
College and above	5329 (2853)	4169 (3217, 8575)		15296 (12854)	15296 (6207, 24385)	
Insurance			0.3742			0.1551
New Rural	7320 (4219)	6210 (4390, 8955)		9848 (8153)	7876 (4754, 13103)	
Cooperative Medical urban worker	5389 (1392)	5310 (4689, 5740)		13601 (9570)	12669 (8505, 16348)	
Place of residence			0.1522			0.4055
Plain area	13153 (--)	13153 (13153,13153)		8765 (10670)	4770 (1991, 15539)	
Hill area	--	--		10045 (4986)	9486 (6207, 13626)	
Mountain area	7160 (4094)	6198 (4360, 8812)		11577 (14443)	7665 (2891, 13280)	
TB bacterial confirmation type			0.2136			--
Smear (+)	8063 (3993)	7523 (5311, 9842)		--	--	
Smear (-)	7307 (4654)	5772 (4270, 8766)		--	--	
No smear result	6079 (2694)	5218 (4278, 7363)		--	--	

County A

In County A, only occupation was statistically significantly associated with total expenditures (p=0.0140). A standard deviation for the "Plain Area" group in place of residence in County A could not be obtained as there was only one observation in these levels.

County B

In County B, no variables were statistically associated with total expenditures.

V. Discussion

In each county, there were particular variables that were the top drivers for total expenditures incurred by TB patients. Based on our findings reported in Table 2a, in County A these variables are the patient's injection fee (r=0.94567, p<0.0001), drug fee (r=0.94189, p<0.0001), and laboratory fee (r=0.88779, p<0.0001). In County B, these variables are the patient's injection fee (r=0.88118, p<0.0001), drug fee (r=0.85564, p<0.0001), and lodging fee (r=0.82617, p<0.0001).

It is not surprising to see that the drug, laboratory, and injection fees make up the biggest burden of expenditures for TB patients in County A. We speculated that the burden of disease and therefore the cost of the disease are highest in this county since most of the patients are farmers living in rural mountain areas and would only seek TB care after their symptoms have become severe. Therefore, physicians are likely to prescribe to the patient anti-TB medications and other drugs to alleviate extensive symptoms. In addition, a patient who is hospitalized for a longer period of time would be prescribed more medications (mean= ¥2,665 ($434.04), 37% of total cost), undergo more laboratory tests (mean= ¥1,704 ($277.52), 24% of total cost), and be prescribed injections (mean= ¥357 ($58.14), 3.4% of total cost) for treatment purposes. Although County B is slightly more developed and patients spend less on drug (mean= ¥3,713 ($604.72), 35% of total cost) and laboratory fees fee (mean= ¥1,851 ($301.47), 17% of total cost) than in County A, these two costs are also the main drivers for total expenditures in County B. Patients in this county are mostly farmers and live in hill areas. Based on our interviews, these patients reported seeking care only when symptoms have worsened. Since County B is less rural than County A, finding affordable lodging for family members who accompany patients during hospitalization may be a reason for a strong association with total expenditures (mean= ¥279 ($45.44), 2.6% of total cost).

In Table 1b, we are surprised to find that the oxygen fee is high in County B (mean= ¥975 ($158.79), 9% of total cost) but not in County A (mean= ¥150 ($24.43), 2% of total cost). If oxygen fees account for 9% of the total costs in County B, then we would expect this fee in County A to be in the same range, if not higher. One potential reason could be that because

County A hospitals may have limited oxygen equipment available for TB patients, or alternatively reflect differences in prescribing practices with medical providers in County B being more likely than providers in County A to use oxygen for the management of symptoms of persons with TB disease.

One intriguing observation is that the reported rural annual incomes in County A and County B are far greater than the 2013 annual incomes reported by the Guangxi CCDC for rural households in both counties. There is approximately a difference of ¥15,000 ($2,443) between the median rural income figures the figures reported by patients in County A. In County B, this difference is about ¥18,000 ($2,931.60). It is also feasible that local and federal authorities in Guangxi rely on different criteria for determining the annual incomes for homes in these counties. Another speculation is that households that were remotely located or difficult to reach were not considered in these annual figures, or perhaps patients over-estimated their income during our study by including sources of income that they did not report to the government. It is possible that the homes we visited were classified as urban and not rural. The reason for these stark differences in income is not clear.

Another surprising finding is that in County B, the distance from the patient's home to the hospital and the cost of transportation to travel from home to the hospital have a negative correlation with the total expenditure while in County A, the correlation values for these variables are positive. We would assume that these variables and the outcome variable shared a direct relationship, meaning that if any of these variables had a large value, then the value for the outcome variable would increase. In addition, all of these correlation values have "weak" associations with the total expenditure.

We had assumed that the distance between a patient's home and the hospital would have a direct relationship with the outcome variable. Therefore, it's interesting to observe that the distance variable had a negative correlation (r= -0.13837) with the outcome variable in County B but not in County A. Although distance is positively correlated with the outcome variable in County A, its correlation value is also weak (r=0.24661). Regardless of the county type, we would have thought distance to have a correlation value closer to +1 with the total expenditure. Patients who are ill with TB and live far away from a health facility may be less inclined to seek care right away. This means that a patient would be more likely to obtain healthcare services once TB symptoms have become more severe, which could result in more drugs prescribed to the patient and/or a longer length of stay in the hospital [19].

In County A, this variable has a "weak" relationship with the outcome, however it is statistically significant (p=0.0149), suggesting that the distance traveled to the hospital is associated with the total cost of TB expenditures. This county is very rural and most of the population lives in the mountains, which suggests that most patients live farther away from hospitals than do patients in County B. As reported in Table 1b, the mean distance for patients in County A is 34.837 km, while in County B it is 27.619 km. In addition, the difference between both counties is statistically significant (p=0.024). Another explanation for the distance being correlated with total expenditures is that the geographic area of County A is mountainous and patients may have to travel to a bus stop that is outside of their village.

We had also expected the cost of transportation from a patient's home to the hospital to have a positive correlation with the total expenditure in both counties. Similar to distance, if a patient travels a long distance to a hospital, he or she would have to spend more money on his or her transportation fare [17]. Therefore, if it is costly and also time-consuming to travel to a clinic, a patient may only seek health services if he or she is experiencing severe TB signs or symptoms. Just as with the variable distance, a complicated or severe diagnosis of TB may result in more drugs being prescribed, more tests being done, and a longer length of stay in the hospital- all of which can contribute to a higher overall expenditures during hospitalization. Furthermore, if family members are accompanying the TB patient to the hospital, indirect expenses would be incurred, adding to the total costs associated with hospitalization. A negative correlation value of -0.18653 for distance indicates both a negative and “very weak” relationship with the outcome variable.

In County A, the cost of transportation has a positive but “weak” correlation with the outcome variable. However, it shares a statistically significant association (p= 0.0086) with the patient’s total expenditures in that county. Patients in County A, the majority of whom are farmers, live in more poor and rural living conditions than patients in County B. As a result, fewer families in County A own a bicycle or automobile and would rely on public transportation to access healthcare services. On the other hand, there is no statistical significance (p=0.1572) between cost of transportation and total expenditures in County B. As this county is a bit more developed than County A, patients may have access to personal means of transportation and thus incur fewer travel fees.

In Table 2b, the only variable whose levels had statistically significant differences in County A was occupation (p=0.0140). According to Table 1a, farmers and farmer workers make up the majority of occupational levels in County A (77.1% and 17.7%, respectively). Patients in this county who identified as either a farmer or a farmer worker on average spent ¥7,437 ($1,211.24) compared to ¥4,128 ($672.31) among patients in all other occupations. This may be because those who do farm work may be more hesitant to seek TB care as they do not generate much income and for the most part subsist on their own crops. Aside from having a very low annual income, farmers and/or farmer workers might be worried that becoming hospitalized could mean that their land would not be properly maintained and that their crops would go to waste. Therefore, he or she may be hesitant to visit a doctor. On the other hand, we cannot make this assumption for occupation type in County B as the association is non-significant. One speculation is that the occupational demographics are different and that there are fewer farmers in this county than in County A.

In Table 1a, the educational level of patients between both counties is moderately significant at p=0.044. In County A, the majority of patients have an elementary school education (36.7%) while in County B the majority of patients have a middle school education (50.8%). As County B is more urbanized and there are other employment opportunities, in addition to agricultural work, compared to County A, education may be more accessible and/or regarded as valuable. Therefore, one could speculate that those who are more educated would have greater knowledge about maintaining a more sanitary home environment and keeping a distance from those who are infected with TB- all of which are strategies that could reduce the transmission of TB [4]. Furthermore, those with more education than none might be more inclined to seek healthcare soon after the onset of TB symptoms instead of waiting for the disease to become worse and therefore end up incurring fewer expenditures during hospitalization.

However as we observe in Table 2b, in County B education level does not appear to have any significant effect on the total amount of money a patient would pay during hospitalization. Although one would assume that someone with at least some formal schooling might have more knowledge about TB or even the importance of adhering to a doctor's recommendation, it could be that education does not significantly influence a patient's decision to complete his or her anti-

TB treatment regimen. If a patient stops taking medication, his or her illness might become worse or even develop multi-drug resistant, resulting in increased visits to the hospital and incurring more health expenses. The rationale behind this observation is unclear.

What is interesting to note is that the mean total expenditure for a patient with no formal schooling is ¥6,774 ($1,103.26), ¥7,381 ($1,202.12) for a patient with grade level education, and ¥5,329 ($867.92) for a patient who has at least attended college in County A. The fact that the total cost is lower in the completely uneducated group than the group with grade level education is unclear, however one conjecture is that a patient without any education might have a much lower income and would not have enough money to travel to the hospital each day to complete their DOTS regimen. Someone with at least a college level education may have a lower overall cost if they seek care upon displaying signs and symptoms of TB instead of waiting until their illness becomes worse to seek care. On the other hand in County B, the total expenses appear to increase with a greater educational background.

One reason why the other variables in both counties were non-significant might be because in Table 2a, we collapsed the levels within each variable in order to have a more even distribution for each category. Since the number of observations is spread among the levels, this might explain why there are no significant differences between the levels in each county.

Study Limitations

Although our research team had collected ample data from each county, there were several limitations to this study. With regard to the in-person interviews, inclement weather affected our ability to visit some homes. During some days of our data collection, periods of heavy rain made traveling on the unpaved village roads difficult. Some roads were inaccessible and we called patients to ask if they could meet us at a closer location. In at least three cases, we could not interview the patient at all due to unfavorable weather conditions.

Another limitation included diagnostic misclassification: some patients on our initial list later had a diagnosis other than TB and had to be excluded from the analysis. They appeared in the TB registry because they presented with signs and symptoms consistent with TB of the lungs, however they were later deemed to have a different medical condition.

Although we recorded data collected from TB financial registries, County A and County B both had different data available in their respective registries. Not all data were available for certain cost breakdowns. In fact, a section of our original survey that contained questions about TB patients' outpatient costs had been excluded/omitted. The Guangxi CCDC decided to focus only inpatient costs for this particular study. As a result, we may be missing important associations regarding economic burden of TB on low-income rural patients.

During the interviews, questions were sometimes asked out of sequence. For example, if the patient had receipts from their hospitalization or clinic visits, interviewers might have skipped certain questions to write information from those documents first, and would then go back to the other questions. The fact that questions were asked non-sequentially during the interviews may have resulted in different responses from patients. For example, a patient who is asked about his or her HIV status or annual income much earlier on in the survey may not yet feel comfortable with answering a sensitive question and could therefore refuse to answer.

Another limitation encountered during both the telephone and in-person interview process was recall bias. Patients were not consistently asked to provide written documentation of their expenses in writing, but frequently had to rely on estimates. As many patients were subsistence farmers, they did not generate much income. Therefore, annual income estimates may not be consistently estimated. Most patients no longer had their financial statements available and recited financial figures from memory. We had also encountered at least three homes in which a patient on our list had already passed away. When the patient was deceased, we instead interviewed family members who may not been aware of that person's TB disease and income. The type of recall bias may result in under or over-estimates of the patient's financial expenditures. If our team had the opportunity to make additions to questionnaire, we would have included a variable that determined whether the interview took place in the patient's home or via the telephone. We would have also included a variable that accounted for if a patient reported his or her hospitalization costs from memory or from hospital bills.

Data Analysis Limitations

One limitation was that we were not able to perform data analysis on certain variables if more than 10% of data were missing. This was problematic if there were data missing for one county but not the other, meaning that we could observe any potential statistical differences between both counties. Another limitation was that hospital staff in County B provided our team with data that were not provided by County A. Therefore, we could not make any meaningful comparisons for those particular variables between both counties.

VI. Implications/Recommendations

Although the local and federal health authorities have made efforts to reduce the impact of TB in poor and rural regions in Guangxi by reforming insurance policies and providing certain treatment options at no cost to patients, the burden of the disease is still remarkably high. Accessibility to township hospitals where patients can receive TB treatment and services is still a huge obstacle for impoverished patients to seek care. Furthermore, a lack of patient education provided by healthcare workers may hinder a patient from understanding the importance for completing his or her anti-TB regimen on schedule.

One of the biggest challenges for revising the TB control and prevention strategy in this province is that there have been very few published studies that provide evidence for creating effective interventions in Guangxi. Moreover, there are even fewer studies that have investigated the economic burden of TB among rural patients by looking at the total expenditures during hospitalization. Although it is obvious that there is a TB problem, a strong research foundation needs to be built in Guangxi that can effectively identify the financial hardships of individuals and families affected by TB. Once a patient is hospitalized for TB, there are a number of different services provided to the patient that are not covered by his or her insurance. We recommend that the reimbursement system should be revised such that patients do not pay all hospitalization costs out-of-pocket first as it is challenging for poor patients to afford to pay a lump sum initial payment.

During our research visits to rural villages in Guangxi, several households reported that a family member, in all cases a young male, contracted TB while seeking employment in a larger city. This suggests that it is not uncommon for individuals to travel from rural Guangxi to urban areas in search of work and return to the province with TB, potentially spreading the infection to household members. Although making TB services to migrants more affordable poses a challenge to the existing “hukou” system, there are other potential alternatives to improve treatment completion among this group. For example, offering treatment incentives to poor migrants who have TB disease could be a cost-effective tool for alleviating financial hardships associated with receiving TB-related services [34].

With regard to intervention-based practices, it is critical that doctors only prescribe anti-TB and liver protection drugs if necessary. As only the costs of basic anti-TB drugs are subsidized, patients have to pay out of pocket for any additional prescribed medications.

Therefore, it is essential that doctors only prescribe medications according to the severity of TB diagnosis in order to minimize the financial impact of TB for patients. In addition, healthcare professionals in both county hospitals should provide more in-depth education and counseling to TB patients. During interviews, patients reported that they voluntarily stop taking TB medications because they perceived their symptoms to either be at the same or a worse level as before they started their treatment regimen. Patients should be informed that they need to complete their anti-TB treatment regimen and if they have any concerns, they should consult their healthcare provider immediately.

In an effort to create a simple pathway for patients to get care, it is essential for the Chinese government to consider shifting access to TB care from the dispensaries to the hospitals, especially in rural areas such as Guangxi. While shifting to an integrated approach would drastically improve China's TB care system, there are many challenges in order to achieve this goal with regard to motivation for integration within the CCDCs, resource allocation, management coordination, providing incentives to staff, and training hospital and CCDC staff to work together. The health sector itself would need to undergo massive reformation and its success would require a great deal of support, funding, and resources from the government [23]. However, the implementation of an integrated approach would be a meaningful step toward simplifying TB services and delivery to patients, however the healthcare system itself in China adds to the issues that many low-income patients face for getting care.

We hope that with the data that we have collected, we have demonstrated a strong evidence-based need for a new TB policy implementation and reformation. In fact, our research is also in line with the WHO's Global TB Strategy, which is one of the highlighted milestones for the year 2025 to reduce the number of affected families facing catastrophic costs due to TB to

0 [46]. According to WHO, Catastrophic costs occur when individuals have to pay healthcare fees and co-payments that are comparatively higher in relation to their household income [47]. We have examined most of the fees that an average TB patient in Guangxi would encounter during his or her hospitalization. The analysis of this information is helpful for ascertaining which particular individual fees are top drivers for the total expenditures incurred by a TB patient. However, we still hope that the research and the recommendations that we have presented will serve as a platform for improving the economic burden of TB in Guangxi province.

VII. Appendix

Appendix A. Telephone Script.

If calling the potential participant:

Tentative Phone Script

"May I speak to (name)? This is __________________ from the Guangxi Center for Disease Control and Prevention's National Tuberculosis Program. I am a Principal Investigator working with a study in which we will determine the impact of TB-related expenses on patients living in the Guangxi province. The [name of the hospital in County ___] permitted our study team access to list of recent TB patients at their site. I am calling to see if you would be willing to participate in our study. It will involve scheduling a time to visit the site for an in-person interview in which you will be surveyed about the affordability of managing TB-related costs. The interview will take about 60 minutes. Would you be willing to participate?"

- If yes: "Great! May I first ask you some screening questions to verify that you qualify to participate in this study? The screening process will take no more than five minutes and your answers will be confidential. *If yes, ask screening questions* [to be finalized].
    - If passes screening test: "Great! Would you be available to come in [list upcoming times and dates and location]? *If yes, proceed with scheduling their interview time and provide directions to hospital site, if necessary.*
    - If no: Thank the subject and end the phone call.
- If no: Thank the subject and end the phone call.

If leaving message on voicemail:

Sample Voicemail Script

"Hello, this message is for [name]. It is [date] at [time]. My name is ____________ from the Guangxi Center for Disease Control and Prevention's National Tuberculosis Program.

I am a Principal Investigator working with a study in which we will determine the impact of TB-related expenses on patients living in the Guangxi province. The [name of the hospital in County ___] permitted our study team access to list of recent TB patients at their site. I am calling to see if you would be willing to participate in our study. It will involve scheduling a time to visit the site for an in-person interview in which you will be surveyed about the affordability of managing TB-related costs. The interview will take about 60 minutes. Please contact us at [phone number] if you are interested in participating. Thank you and we hope to hear from you soon.

<u>If the potential subject calls back, proceed with the following</u>:

Thank you for calling us back. We would like to see if you would be interested in participating in this research study about determining the impact of TB-related expenses on patients living in the Guangxi province being conducted by the Guangxi Center for Disease Control and Prevention's National Tuberculosis Program. It will involve an interview in which we will administer a survey to you that will take about 60 minutes. Would you be willing to participate?

- If yes: "Great! May I first ask you some screening questions to verify that you qualify to participate in this study? The screening process will take no more than five minutes and your answers will be confidential. *If yes, ask screening questions* [to be finalized].
    - If passes screening test: "Great! Would you be available to come in [list upcoming times and dates and location]? *If yes, proceed with scheduling their interview time and provide directions to hospital site, if necessary.*

  - If no: Thank the subject and end the phone call.

- If no: Thank the subject and end the phone call.

Appendix B. Data Collection Form #1.

Questionnaire 1: Interview on TB diagnosis and treatment expenditure and reimbursement in _____________________ county, Guangxi province, Southern China

A. TB patient general information

A.1)	What is your patient code (6 digit county code + 2 digit case code)?	*Please write code:* __ __ __ __ __ __ - __ __
A.2)	What is your TB Notification Number?	*Please write notification number:* __ __ __ __ __ __ __ __ __ __
A.3)	What is your date of birth?	*Please write date of birth:* __ __ __ __ Y __ __ M __ __ D
A.4)	What is your gender?	*Please select one (1) response:* [ ] Male ……………………………………………...…...1 [ ] Female ………………………………………….2
A.5)	What is your ethnic group?	*Please select one (1) response:* [ ] Han ……………………………………..…….1 [ ] Zhuang ……………………………………….2 [ ] Miao ………………………………......................3 [ ] Yao …………………………………………….4 [ ] Dong ………………………………...………..5 [ ] Mulao …………………………….…………6 [ ] Other (please specify): ……………………..…...7 ______________________________
A.6)	What is your occupation?	*Please select one (1) response:* [ ] Farmer ………………….………………….…...1 [ ] Farmer worker ....2 [ ] Housekeeper ………….…………………………3 [ ] Retired staff ……………………………………..4 [ ] Student …………………………………………..5 [ ] Factory worker …………………………………6 [ ] Government employee ……..…………………...7 [ ] Other (please specify): ………..………………99 ______________________________

A.7)	What is your highest level of education?	*Please select one (1) response:* [ ] No formal schooling ……………….……………………1 [ ] Elementary school ………………..……………..2 [ ] Middle school ………………………………….....3 [ ] High school …………………………………….4 [ ] Junior college ……………………………….....5 [ ] Bachelor's degree …………………………….6 [ ] Graduate or Professional degree ………………..7
A.8)	What type of health insurance do you have?	*Please select one (1) response:* [ ] New Rural ……………………..…………….1 [ ] Cooperative Medical urban worker …..………...2 [ ] Commercial insurance …………………….……3 [ ] No insurance ………………………………….4 [ ] Other (please specify): …………..…………….99 ____________________________
A.9)	Where is your place of residence?	*Please select one (1) response:* [ ] Plain area ……………………………………1 [ ] Hill area ……………………………..……...2 [ ] Mountain area ……………………………..……3 [ ] Other (please specify): ………………………..99 ____________________________
A.10)	How many kilometers is your home from the local TB clinic?	*Please write number of kilometers:* __ __ __ __ Kilometers
A.11)	When was the date of your: a. Active TB diagnosis? b. Anti-TB treatment initiation? c. Anti-TB treatment termination?	*Please write date:* __ __ __ __ Y __ __ M __ __ D __ __ __ __ Y __ __ M __ __ D __ __ __ __ Y __ __ M __ __ D
A.12)	What is your TB bacterial confirmation type?	*Please select one (1) response:* [ ] Smear (+) ……………………………………1

	[ ] Smear (-) ……………………………………….2 [ ] Culture (+) and Smear (-) ………….………..3 [ ] Culture (-) and Smear (-) ………….………...4 [ ] No smear result ……………………….………..5 [ ] Other (please specify): ……………..…………..6 ______________________________
A.13) What is your HIV status?	*Please select one (1) response:* [ ] Positive …………………………...…………1 [ ] Negative ……………………………………..2 [ ] Don't know …………………...……………..3
A.14) Which co-morbidities (other medical conditions) do you have?	*Please check all that apply:* [ ] Chronic Obstructive Pulmonary Disease (COPD) ……………………………………………1 [ ] Diabetes ……………………………………..2 [ ] Smoking …………………………...………...3 [ ] Cancer ………………………………………4 [ ] I do not have any co-morbidities ……………....5 [ ] Other (please specify): …………………..……99 ______________________________
A.15) How much was your approximate (or estimated) income during the year before your TB diagnosis?	*Please write the cost:* __ __ __ __ __ __ __ Yuan
A.16) How much was your approximate (or estimated) income during the year that you were diagnosed with TB?	*Please write the cost:* __ __ __ __ __ __ __ Yuan

B. TB hospitalization

B.1)	On average, how many times do you visit the TB clinic in one month?	*Please write the number of times:* __ __ Times per month
B.2)	How long were your hospitalized during your: a. First time?	*Please write the dates or number of days:* Start: __ __ __ __ Y __ __ M __ __ D End: __ __ __ __ Y __ __ M __ __ D - or - Number of days of hospitalization: __ __ __
	b. Second time (if applicable)?	*Please write the dates or number of days:* Start: __ __ __ __ Y __ __ M __ __ D End: __ __ __ __ Y __ __ M __ __ D - or - Number of days of hospitalization: __ __ __
	c. Third time (if applicable)?	*Please write the dates or number of days:* Start: __ __ __ __ Y __ __ M __ __ D End: __ __ __ __ Y __ __ M __ __ D - or - Number of days of hospitalization: __ __ __
B.3)	Have you been hospitalized more than three times?	*Please select one (1) response:* [ ] Yes ……………………………...………1 [ ] No ………………………………..…….2

B.4)	Have you developed other complications during any of your hospitalizations?	*Please select one (1) response:* [ ] Yes ………………………………...…………1 [ ] No …………………………………..………2
B.5)	If "Yes", what is the complication?	*Please check all that apply:* [ ] Hemoptysis ………………………………1 [ ] Diabetes …………………………………..2 [ ] Pneumothorax ……………………….……3 [ ] Emphysema ………………………………4 [ ] Difficulty Breathing ……………………....5 [ ] Liver damage ……………………………..6 [ ] Other (please specify): …………………..99 ____________________________________
B.6)	How many of your relatives accompanied you during your initial hospitalization?	*Please write the number of relatives:* __ __
B.7)	What is the average number of days that each relative accompanied you during your initial hospitalization?	*Please write the average number of days:* __ __

C. TB diagnosis and treatment expenditures during hospitalization

C.1) What was your TB consultation fee?	*Please write the cost:* __ __ __ __ Yuan
C.2) How much did you pay for insurance fees?	__ __ __ __ __ __ Yuan
C.3) How much did you pay for out-of-pocket fees?	__ __ __ __ __ __ Yuan
C.4) How much was your total expenditure during TB hospitalization?	*Please write the costs:* __ __ __ __ __ __ Yuan
C.5) Among the total expenditure, how much did you pay for: a. Lodging fees? b. Cost of food? c. Operation fees? d. Cost of drugs? e. Testing fees? f. Aid therapy fees? g. Nursing and injection fees? h. Materials fees? i. Other expenses?	*Please write the costs:* __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan

C.6)	Among total drugs costs, how much did you pay for: a. Anti-TB drugs? b. Assistant drugs? c. Other drugs?	*Please write the costs:* __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan __ __ __ __ __ __ Yuan
C.7)	Among total testing fee, how many times were you tested and how much did you pay for: a. CXR testing? b. DR testing? c. CR testing? d. CT testing? e. Liver function testing? f. Sputum smear? g. Sputum culture?	*Please write the costs:* Number of times tested: __ __ Cost: __ __ __ __ __ __ Yuan Number of times tested: __ __ Cost: __ __ __ __ __ __ Yuan Number of times tested: __ __ Cost: __ __ __ __ __ __ Yuan Number of times tested: __ __ Cost: __ __ __ __ __ __ Yuan Number of times tested: __ __ Cost: __ __ __ __ __ __ Yuan Number of times tested: __ __ Cost: __ __ __ __ __ __ Yuan Number of times tested: __ __ Cost: __ __ __ __ __ __ Yuan
C.8)	What is the cost of transportation from your home to the TB clinic?	*Please write the cost:* __ __ __ Yuan
C.9)	Did your income suffer as a result of your hospitalization?	*Please select one (1) response:* [ ] Yes ……………………..……………………….….1 [ ] No ……………………..……………………….2

C.10) If yes, then how much did you lose in wages per month?	*Please write the cost:* __ __ __ __ __ __ Yuan
C.11) Did you lose your occupation as a result of your hospitalization?	*Please select one (1) response:* [ ] Yes ……………………...…………………...…1 [ ] No ……………………..…………………….2 [ ] I am self-employed …………….……………………3

Investigator：________ Investigation time：__ __ __ __ Y __ __ M __ __

Appendix C. Description of Variables and Codes.

Variable	Description
Gender	Male or female
Occupation	Current occupation: farmer, farmer worker, housekeeper, retired staff, student, factory worker, or government employee
Education	Highest level of education: no formal school, elementary school, middle school, high school, junior college, Bachelor's degree, graduate or professional degree
Insurance	Type of health insurance: New Rural Cooperative Medical Scheme, Cooperative Medical urban worker, commercial insurance, or no insurance
Place of residence	Residence in plain area, hill area, or mountain area
Total expenditure (Yuan)	Total expenditures during hospitalization
Income during year before diagnosis (Yuan)	Annual household income in 2012
Income during year of diagnosis (Yuan)	Annual household income in 2013
Difference of incomes before and during diagnosis (Yuan)	The difference between the annual household income in 2012 and the annual household income in 2013
Age (years)	Age in years
Distance (km)	Kilometers from home to TB clinic
Average number of days relatives accompanied patient during hospitalization	Average number of days relatives accompanied patient during hospitalization
Average number of visits to TB clinic in one month	Average number of visits to TB clinic in one month
Cost of transportation from home to TB clinic (Yuan)	Cost of transportation from home to TB clinic
Amount of wages lost per month (Yuan)	Amount of wages lost per month as a result of TB hospitalization
Lodging fees (Yuan)	Cost of lodging during hospitalization
Examination fee (Yuan)	Cost of examination tests during hospitalization
B Ultra fee (Yuan)	Cost of B ultra test during hospitalization. The B ultra test is a tool that uses ultrasonic wave scanning to examine organs such as the liver. The results are in black and white.
CXR fee (Yuan)	Cost of chest X-ray during hospitalization
Chinese medicine fee (Yuan)	Cost of Chinese medicine fees during hospitalization
Drug fee (Yuan)	Cost of anti-TB drugs during hospitalization
Laboratory fee (Yuan)	Cost of laboratory tests during hospitalization

Injection fee (Yuan)	Cost of injections during hospitalization
Oxygen fee (Yuan)	Cost of oxygen treatment during hospitalization
Nursing fee (Yuan)	Cost of nursing services during hospitalization
Materials fee (Yuan)	Cost of materials during hospitalization
Treatment fee (Yuan)	Cost of treatment services during hospitalization
ECG fee (Yuan)	Cost of electrocardiograph test. This test is used to scan the heart.
Operation fee (Yuan)	Cost of operation during hospitalization
Other fee (Yuan)	Fees that are incurred during hospitalization but not listed in the hospital database
Test fee (Yuan)	Cost of additional tests completed during hospitalization
Color B Ultra fee (Yuan)	Cost of Color B ultra test during hospitalization. The Color B ultra test is a tool that uses ultrasonic wave scanning to examine organs such as the liver. The results are in color.
CT fee (Yuan)	Cost of Computed Tomography (CT) test. The CT test is used to scan the lungs of a TB patient. This test is used as a secondary exam if the CXR image is not clear enough to make a diagnosis.
Blood fee (Yuan)	Cost of blood test during hospitalization
Ambulance fee (Yuan)	Cost of ambulatory services during hospitalization
Encephalogram fee (Yuan)	Cost of encephalogram test during hospitalization
MRI fee (Yuan)	Cost of Magnetic Resonance Imaging (MRI) test during hospitalization

VIII. References

1. Kanabus, A. (2015). TB statistics: global, regional, high burden, and MDR. Retrieved from: <http://www.tbfacts.org/tb-statistics/>

2. World Health Organization (2015). Global Tuberculosis Report. Retrieved from: <http://apps.who.int/iris/bitstream/10665/191102/1/9789241565059_eng.pdf?ua=1>

3. World Health Organization (2015). Tuberculosis. Retrieved from: <http://www.who.int/mediacentre/factsheets/fs104/en/>

4. Centers for Disease Control and Prevention (2012). Tuberculosis. Retrieved from: <http://www.cdc.gov/tb/topic/basics/default.htm>

5. Mayo Clinic (2014). Tuberculosis: definition. Retrieved from: <http://www.mayoclinic.org/diseases-conditions/tuberculosis/basics/definition/con-20021761>

6. Centers for Disease Control and Prevention (n. d.) Chapter 2: transmission and pathogenesis of tuberculosis. Retrieved from: <http://www.cdc.gov/tb/education/corecurr/pdf/chapter2.pdf>

7. Lienhardt, C. (2001). From exposure to disease: the role of environmental factors in susceptibility to and development of tuberculosis. *Epidemiol Rev*, *23*(2).

8. Padmanesan Narasimhan, James Wood, Chandini Raina MacIntyre, and Dilip Mathai, “Risk Factors for Tuberculosis,” Pulmonary Medicine, vol. 2013, Article ID 828939, 11 pages, 2013. doi:10.1155/2013/828939

9. World Health Organization. (2015). Tuberculosis in China. Retrieved from: <http://www.wpro.who.int/china/mediacentre/factsheets/tuberculosis/en/>

10. Wan, L., Cheng, S., Chin, D. P. (2007). A new disease reporting system increases TB case detection in China. Retrieved from: <http://www.who.int/bulletin/volumes/85/5/06-036376/en/>

11. Dye C, Floyd K. Tuberculosis. In: Jamison DT, Breman JG, Measham AR, et al., editors. Disease Control Priorities in Developing Countries. 2nd edition. Washington (DC): World Bank; 2006. Chapter 16.

12. Tobe, R. G., Xu, L., Song, P., & Huang, Y. (2011). The rural-to-urban migrant population in China: gloomy prospects for tuberculosis control. *Bioscience trends*, *5*(6), 226-230.

13. Chelala, C. (2014). TB in China: a new epidemic of an old disease. Retrieved from: <http://www.theglobalist.com/tb-in-china-a-new-epidemic-of-an-old-disease/>

14. Wei, X. L., Liang, X. Y., Walley, J. D., Liu, F. Y., & Dong, B. Q. (2009). Analysis of care-seeking pathways of tuberculosis patients in Guangxi, China, with and without decentralised tuberculosis services. *The International Journal of Tuberculosis and Lung Disease*, *13*(4), 514-520.

15. Wang, L., Liu, W., Wang, L., Wang, Y., & Wu, Z. (2010). HIV prevalence among pulmonary tuberculosis patients in Guangxi, China. *Journal of acquired immune deficiency syndromes (1999)*, *53*(Suppl 1), S61.

16. Zheng, Zhigang (2015). NTP Surveillance, new TB diagnosis and treatment system and New Rural Cooperative Medical Scheme in Guangxi, Southern China [PowerPoint slides].

17. Wei XL, Liang XY, Walley JD, Liu FY, Dong BQ. Analysis of care-seeking pathways of tuberculosis patients in Guangxi, China, with and without decentralised tuberculosis services. Int J Tuberc Lung Dis. 2009 Apr;13(4):514-20. PubMed PMID: 19335959.

18. Zou, G., King, R., Walley, J., Yin, J., Sun, Q., & Wei, X. (2015). Barriers to hospital and tuberculosis programme collaboration in China: context matters.*Global health action*, *8*.

19. Pan HQ, Bele S, Feng Y, Qiu SS, Lü JQ, Tang SW, Shen HB, Wang JM, Zhu LM. Analysis of the economic burden of diagnosis and treatment of tuberculosis patients in rural China. Int J Tuberc Lung Dis. 2013 Dec;17(12):1575-80. doi: 10.5588/ijtld.13.0144. PubMed PMID: 24200271.

20. Sun Q, Yin J, Yin X, Zou G, Liang M, Zhong J, Walley J, Wei X. Does the integration of TB medical services in the general hospital improve the quality of TB care? Evidence from a case study in China. J Public Health (Oxf). 2013 Jun;35(2):322-8. doi: 10.1093/pubmed/fds089. Epub 2012 Oct 26. PubMed PMID: 23104893.

21. Wei X, Yin J, Zou G, Walley J, Zhong J, Chen S, Sun Q, Wang X. Patient care pathways under the model of integrating tuberculosis service with general hospitals in China. Trop Med Int Health. 2013 Nov;18(11):1392-9. doi: 10.1111/tmi.12197. Epub 2013 Oct 8. PubMed PMID: 24107010.

22. Wei X, Zou G, Yin J, Walley J, Sun Q. Comparing patient care seeking pathways in three models of hospital and TB programme collaboration in China. BMC Infect Dis. 2013 Feb 20;13:93. doi: 10.1186/1471-2334-13-93. PubMed PMID: 23425261; PubMed Central PMCID: PMC3598790.

23. Zou, G., Wei, X., Walley, J. D., Yin, J., & Sun, Q. (2012). Factors influencing integration of TB services in general hospitals in two regions of China: a qualitative study. *BMC health services research*, *12*(1), 21.

24. Qiu S, Pan H, Zhang S, Peng X, Zheng X, Xu G, Wang M, Wang J, Lu H. Is tuberculosis treatment really free in China? A study comparing two areas with different management models. PLoS One. 2015 May 20;10(5):e0126770. doi: 10.1371/journal.pone.0126770. eCollection 2015. PubMed PMID: 25993411; PubMed Central PMCID: PMC4439067.

25. Liu Q, Smith H, Wang Y, Tang S, Wang Q, Garner P. Tuberculosis patient expenditure on drugs and tests in subsidised, public services in China: a descriptive study. Trop Med Int Health. 2010 Jan;15(1):26-32. doi: 10.1111/j.1365-3156.2009.02427.x. Epub 2009 Nov 16. PubMed PMID: 19917035.

26. Wei X, Zou G, Yin J, Walley J, Zhang X, Li R, Sun Q. Effective reimbursement rates of the rural health insurance among uncomplicated tuberculosis patients in China. Trop Med Int Health. 2015 Mar;20(3):304-11. doi: 10.1111/tmi.12438. Epub 2014 Dec 29. PubMed PMID: 25430477.

27. Liu X, Thomson R, Gong Y, Zhao F, Squire SB, Tolhurst R, Zhao X, Yan F, Tang S. How affordable are tuberculosis diagnosis and treatment in rural China? An analysis from community and tuberculosis patient perspectives. Trop Med Int Health. 2007 Dec;12(12):1464-71. PubMed PMID: 18076553.

28. Zhang T, Tang S, Jun G, Whitehead M. Persistent problems of access to appropriate, affordable TB services in rural China: experiences of different socio-economic groups. BMC Public Health. 2007 Feb 8;7:19. PubMed PMID: 17288593; PubMed Central PMCID: PMC1805429.

29. Chen, S., Zhang, H., Pan, Y., Long, Q., Xiang, L., Yao, L., & Lucas, H. (2015). Are free anti-tuberculosis drugs enough? An empirical study from three cities in China. *Infectious diseases of poverty*, *4*(1), 1-10.

30. Wang WB, Zhang H, Petzold M, Zhao Q, Xu B, Zhao GM. Cost-effectiveness of the Health X Project for tuberculosis control in China. Int J Tuberc Lung Dis. 2014 Aug;18(8):939-45. doi: 10.5588/ijtld.13.0131. PubMed PMID: 25199008.

31. Pang Y, Li Q, Ou X, Sohn H, Zhang Z, Li J, Xia H, Kam KM, O'Brien RJ, Chi J, Huan S, Chin DP, Zhao YL. Cost-effectiveness comparison of Genechip and conventional drug susceptibility test for detecting multidrug-resistant tuberculosis in China. PLoS One. 2013 Jul 23;8(7):e69267. doi: 10.1371/journal.pone.0069267. Print 2013. PubMed PMID: 23935970; PubMed Central PMCID: PMC3720587.

32. Xu L, Gai R, Wang X, Liu Z, Cheng J, Zhou C, Liu J, Zhang H, Li H, Tang W. Socio-economic factors affecting the success of tuberculosis treatment in six counties of Shandong Province, China. Int J Tuberc Lung Dis. 2010 Apr;14(4):440-6. PubMed PMID: 20202302.

33. Xu Q, Jin SG, Zhang LX. Cost effectiveness of DOTS and non-DOTS strategies for smear-positive pulmonary tuberculosis in Beijing. Biomed Environ Sci. 2000 Dec;13(4):307-13. PubMed PMID: 11351865.

34. Wei X, Chen J, Chen P, Newell JN, Li H, Sun C, Mei J, Walley JD. Barriers to TB care for rural-to-urban migrant TB patients in Shanghai: a qualitative study. Trop Med Int Health. 2009 Jul;14(7):754-60. doi: 10.1111/j.1365-3156.2009.02286.x. Epub 2009 Apr 17. PubMed PMID: 19392747.

35. Kanabus, A. (2013). TB statistics for India- National and state statistics. <Retrieved from: http://www.tbfacts.org/tb-statistics-india/>

36. John, K. R., Daley, P., Kincler, N., Oxlade, O., & Menzies, D. (2009). Costs incurred by patients with pulmonary tuberculosis in rural India. *The International Journal of Tuberculosis and Lung Disease*, *13*(10), 1281-1287.

37. Muniyandi, M., Ramachandran, R., & Balasubramanian, R. (2005). Costs to patients with Tuberculosis treated under DOTS Programme.

38. Kanabus, A. (2015). TB statistics: global, regional, high burden, and MDR. <Retrieved from: http://www.tbfacts.org/tb-statistics/>

39. Mauch, V., Bonsu, F., Gyapong, M., Awini, E., Suarez, P., Marcelino, B., ... & Klinkenberg, E. (2013). Free tuberculosis diagnosis and treatment are not enough: patient cost evidence from three continents. *The International Journal of Tuberculosis and Lung Disease*, *17*(3), 381-387.

40. Winters, R., Winters, A., & Amedee, R. G. (2010). Statistics: a brief overview. *The Ochsner Journal*, *10*(3), 213-216.

41. Two sample t-test with SAS. 2010. Retrieved from: <http://www.stat.purdue.edu/~tqin/system101/method/method_two_t_sas.htm>

42. The Wilcoxon Rank-Sum Test. (n.d) Retrieved from: <https://www.stat.auckland.ac.nz/~wild/ChanceEnc/Ch10.wilcoxon.pdf>

43. Mukaka, M. M. (2012). A guide to appropriate use of Correlation coefficient in medical research. *Malawi Medical Journal*, *24*(3), 69-71.

44. Pearson's correlation. (n.d). Retrieved from: <http://www.statstutor.ac.uk/resources/uploaded/pearsons.pdf>

45. McKight, P. E., & Najab, J. (2010). Kruskal- Wallis Test. *Corsini Encyclopedia of Psychology*.

46. World Health Organization (2015). End TB Strategy. Retrieved from: <http://www.who.int/tb/strategy/End_TB_Strategy.pdf?ua=1>

47. World Health Organization (2005). Technical briefs for policy makers. Retrieved from: <http://www.who.int/health_financing/documents/pb_e_05_2-cata_sys.pdf>