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Social and behavioral factors predicting beliefs about the use of traditional Chinese medicine for tuberculosis treatment in Myanmar and Yunnan, China.

By

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Rollins School of Public Health of Emory University
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2016

Abstract

Social and behavioral factors predicting beliefs about the use of traditional Chinese medicine for tuberculosis treatment in Myanmar and Yunnan, China.

By Mark Fajans

Tuberculosis (TB) is a major public health issue in both Myanmar and China; two countries listed as one of the 14 countries with high burden of TB, TB/HIV and MDR-TB. In low resource countries, where the ratio of patient to healthcare provider may not be enough to meet the healthcare needs of the country, traditional medicine is often a widely used alternative, including for suspected and active tuberculosis. However, using traditional medicine as a substitute for standard therapy can prevent initiation of effective treatment regimens and treatment non-adherence, resulting in increased opportunities for onward transmission. Using a validated questionnaire examining socio-demographic and knowledge about TB, 1473 participants were convenience sampled in Yunnan Province, China, and various regions in Myanmar. Of these 1473 participants, 1250 subjects (288 Chinese, 962 Burmese) were examined to investigate which factors predict whether a subject believed that traditional Chinese medicine (TCM) could cure TB. Multivariable logistic regression analysis was used to construct predictive models for each cohort. Comparing the Chinese and Burmese models highlighted the predictive power of education levels, knowing where to get tested, location of treatment for previous illness, and perception of time taken to cure TB. Marital status influenced predictive power only in the Chinese model, while being a manual laborer, believing that TB can be transmitted genetically and geographic area influenced predictive power in the Burmese model. These differences can potentially be attributed to regional variations in cultures, socioeconomic factors and attitudes towards TB. These findings provide potential targeting strategies for intervention development in order to increase efficacy in preventing TB transmission and mortality as a result of continued TCM use. Considering these types of variables may help to identify the community and presumptive patients/families who are most likely to believe that traditional medicine can cure TB. Educating these communities may improve uptake of TB treatment.

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1. Introduction

Tuberculosis (TB) is a respiratory disease primarily caused by bacterial infection by Mycobacterium tuberculosis, and is spread from person to person via expulsion of aerosol particles. In 2014, there were an estimated 9.6 million TB incident cases, including both active and latent cases, resulting in approximately 1.1 million deaths per year (W.H.O., 2015). TB is one of the greatest causes of death worldwide due to a single infectious agent, and is the leading cause of death in HIV infected people, causing one fourth of all HIV-related deaths. The occurrence of TB disease is influenced by a range of co-morbidities such as diabetes, suboptimal housing and living standards and social deprivation (Abubakar, Lipman, McHugh, & Fletcher, 2016).

TB is a major public health issue in Myanmar and China; both countries are classified as one of the 14 high burden countries for TB, TB/HIV and MDR-TB (W.H.O., 2015). In 2014, the prevalence rate in Myanmar of 457 cases per 100,000 population was nearly three times the average global rate, and one of the highest in Asia (W.H.O., 2015). Though China has a lower prevalence rate compared to Myanmar (89 cases vs 457 cases per 100,000 population), in 2014 there were an estimated 1,200,000 prevalent cases with 930,000 incident cases reported (W.H.O., 2015). Case detection varies greatly between the two countries, with an estimated range of 82-95% in China versus an estimated range of 64-78% in Myanmar (W.H.O., 2015). The difference in case detection can be attributed to a number of factors ranging from outreach programs, lack of diagnostic capabilities, and lack of knowledge about TB in the public.

During March and April of 2013, technical staff from FHI 360 identified barriers to TB diagnosis and treatment in Kunming City, China and multiple regions in Myanmar; two areas covered by the USAID Control and Prevention of Tuberculosis project (CAP-TB), which is implemented by FHI 360. The CAP-TB project aims to reduce incidence and mortality from TB and MDR-TB in Myanmar, China and Thailand (FHI360, 2015). In addition to a large proportion of the study population exhibiting poor TB knowledge, an alarmingly large amount were unsure or believed that TB could be cured with traditional herbal medicine. This belief has serious clinical implications, since improper treatment of active TB symptoms can lead to further infections of others in close proximity, as well as development of drug resistance due to discontinuation of treatment in favor of traditional medicines.

Delays in diagnosis and treatment initiation plays a major role in increasing the infectivity and sustaining transmission of TB (Madebo & Lindtjorn, 1999). People who have active TB disease are likely to transmit to others who they come into close contact to on a regular basis. Further consequences in delayed TB diagnosis include TB-related morbidity and increased mortality (Yoon et al., 2012). By actively seeking diagnosis once TB is suspected, patients can be quickly initiated on multidrug combination treatment consisting of isoniazid (INH), rifampin (RIF), ethambutol (EMB) and pyrazinamide (PZA) as recommended by the CDC (C.D.C., 2016). Prompt access to diagnosis and treatment is essential to promote disease cure and to reduce ongoing transmission (McNerney & Zumla, 2015). This is especially important in vulnerable populations such as those living in urban slums, which constitute low income and underserved sections of the community (Mistry et al., 2016). It is suggested that the infectiousness of patients with TB disease diminishes

sufficiently after 2 weeks of effective treatment such that transmission to contacts is unlikely (Yates et al., 2016). Factors which have been shown to contribute to delayed diagnosis of TB include patient delays, health system delays, and delays inherent to the conventional TB diagnostic process (Yoon et al., 2012). A review of published clinical trials found that, despite having access to rapid diagnostics, patients reported waiting over a week to access treatment due to health system delays (McNerney & Zumla, 2015). This is further confirmed in other studies, as patients reported that the largest contributor to delays in initiating treatment was the time spent on obtaining a diagnosis (Mistry et al., 2016). Even when initiated on treatment, transmission can still occur unless their active disease is controlled. Preventing transmission in indoor congregate settings is important in high burden settings. Workplaces have been shown to be key locations for adult transmission, and household public transport are important sites of transmission between age groups (Yates et al., 2016). By choosing traditional herbal medicine over modern treatments, patients with active disease continue to transmit TB in their community.

In low and middle income countries where the ratio of healthcare practitioners may not be enough to meet the health care needs of the country, traditional medicine (TM) is considered an important resource for population health. Compared to modern medicine, TM is perceived to be more affordable, accessible and acceptable to the communities in need, and those who used TM were more likely to be less socio-economically advantaged. (Oyebode, Kandala, Chilton, & Lilford, 2016). In China, traditional Chinese medicine (TCM) is a highly profitable and utilized industry, and a widespread belief that it works is part of the history, culture and politics of the country (Oyebode et al., 2016). Many

physicians have training in traditional medicine, and use medicinal herbs and remedies as part of their treatment recommendations.

In TCM theory, tuberculosis is explained as being caused by deficient yin, resulting from weak qi (vital energy) that is unable to defend the body against invasion from an external evil (Jiang, Xu, & Fu, 2015). TB belongs in the category of qi deficiencies and yin and yang imbalances (Jiang et al., 2015). TCM herbal formulas mainly consist of the following herbs: *Radix astragalus* (huangqi), *Radix conopsis* (dangshen), *Radix angelicae* (danggui), *Radix paeoniae* (chishao), *Radix ranunculi* (maozhuacao) and *Radix euphorbiae* (langdu) (Jiang et al., 2015). In addition, *Mahonia bealei* and *Mahonia fortunei* have been traditionally used for many years to treat TB, and have been shown to have antimicrobial activity in vitro (He & Mu, 2015). In a computational predictive model study, two computational models based on high throughput assays of Mycobacterium Tuberculosis using a database of molecular ingredients found in TCM identified 160 potential molecules that could potentially exhibit antimycobacterial properties. These 160 molecules passed all selection filters, were shown to be able to permeate the mycobacterial cell wall and have potential additional activity on drug tolerant and non-replicating M. Tuberculosis. Of these, previous literature demonstrated that the sources of these molecules have been used previously in treatment (Jamal & Scaria, 2014). In a meta-analysis conducted by Jiang et al, Chinese herbal medicine (CHM) combined with chemotherapy was associated with superiority in treatment compared to chemotherapy alone when treating MDR-TB ((Jiang et al., 2015). However, a separate meta-analysis could not confirm the beneficial effects of CHM since the majority of clinical trials were methodologically weak and had a high risk of bias (Wang, Guan, Chi, Robinson, & Liu, 2015). In addition, CHM was only shown to have

preliminary evidence of being effective as an adjuvant therapy to modern treatments, and not as a standalone treatment. No evidence existed of CHM being an effective alternative to modern treatment.

In our study, we use predictive modeling to identify which socioeconomic, cultural and behavioral factors are most influential in predicting whether a subject believes traditional Chinese medicine can cure TB.

2. Materials & Methods

2.1 Study Subjects & Data Collection

The study population included 1473 participants convenience-sampled in Kunming City, Yunnan Province, China and several townships in Yangon, Mandalay & Sagaing Myanmar during March and April of 2013. A total of 1473 participants (450 Chinese, 1023 Burmese) were interviewed by outreach workers using a pre-validated, cross-sectional questionnaire consisting of socio-demographic and socio-economic characteristics, knowledge about TB symptoms, transmission and treatment, health seeking behaviors, and barriers preventing from accessing healthcare. Our study sample was further restricted to 1250 total subjects (288 Chinese, 962 Burmese) based on inclusion/exclusion criteria. Subject responses for 27 questions were collected. Subjects were informed of their participation in the study, and data was de-identified prior to analysis. Exclusion criteria included missing values for the outcome and answering 'No' for having previously heard of TB. An analysis of the missing data was conducted to determine if selection bias was being introduced to our analysis.

2.2 Variable Selection

Of the 27 total questions, 16 questions of interest were selected for further analysis. Questions were selected for their relationship with our selected outcome of interest and for clinical significance based on previous literature. Our selected outcome of interest was

defined as whether a participant believed that traditional herbal treatments could cure TB. Selected measures consisted of demographic information and responses for TB knowledge.

2.3 Variable coding

City, township and region of location was simplified to rural versus urban based on urban and rural population percentages. Urban and rural population percentages were based on UNFPA's Myanmar 2014 population & housing census (UNFPA, 2014). Subjects located in urban areas that reported not being registered in their current district were classified as being from a rural location in order to account for the high frequency of rural to urban migration in these areas. Education was re-coded into three education levels, combining elementary school education with having not completed school, middle school education with high school education, and combining higher education with professional training. Income source was collapsed into 6 occupation types for analysis; unemployed, office worker, shopkeeper/merchant, manual labor, service based and retired. Marital status was coded as married versus unmarried, with unmarried including single, divorced and widowed. For responses to perceived time taken to treat TB, responses were coded as "<6 months", "6-12 months", "12+ months' and "Don't Know". Responses for reported location of last medical care visit were reclassified to combine "informal pharmacy" and "informal healer" due to their close similarities, in order to quantify the total visits to vendors who typically provide TCM. Subject's preferred treatment type was reclassified to combine 'combination therapy' with 'traditional therapy' due to sparse data, under the assumption that subjects preferring to take a treatment combination of both western and traditional medicine aren't completely certain about whether traditional herbal medicine can be used as an effective

treatment. For our outcome variable "believes that TCM can cure TB", participants who answered "Don't Know" were combined with those that answered "Yes" due to sparse data issues following our preliminary analysis. This decision was justified by response profile similarities between the two groups and by the fact that subjects that answered 'Don't Know' were more likely to seek traditional treatment options. For multivariable analysis, individual levels for multi-level variables were recoded to binary 'yes/no' outcomes in order to eliminate dummy variables and allow us to isolate the influence of sub-level factors predictive ability.

2.4 Statistical Analysis

Data were entered into Microsoft Access 2007 (Microsoft Corporation, Redmond, WA, USA). Analysis was conducted using SAS 9.4 (SAS Institute Inc, Cary, NC, USA). Descriptive data were presented as median and IQR due to their skewed distribution for continuous variables, and frequencies and percentages for categorical variables. Bivariate associations between predictor variables and our outcome of interest were examined using unconditional logistic regression to obtain a crude odds ratio and corresponding 95% confidence interval. Multivariable logistic regression using stepwise model selection was used to generate the combination of risk factors that produced the greatest predictive value and best fit. Interaction terms between rural location, education level and manual labor occupation were included due to clinical relevance. A p value of 0.1 was used as the level of significance for variable inclusion/exclusion. The selected models were used to assess the

risk factors with greatest influence to predict whether a person believed that TB could be cured using traditional herbal treatment by examining adjusted odds ratios and their corresponding confidence intervals. Assessment for collinearity demonstrated no issues between variables.

3. Results

3.1 Univariate Analysis

Of the 1473 participants surveyed, 1250 subjects were included in our analysis. 288 (23.0%) of subjects were Chinese, and 962 (77.0%) were Burmese (Table 1). Burmese participants were younger than Chinese participants (median age (IQR): 34.0 (20) vs 46.5 (27)) (Table 1). We observed a larger proportion of participants having no schooling, not completing school or only having a primary school education in our Burmese cohort compared to our Chinese cohort (40.2% vs 30.6%). A larger proportion of Chinese participants had a secondary/high school education compared to Burmese participants (58.0% vs 44.7%).

A larger proportion of Chinese participants believed that traditional herbal treatment could cure TB compared to Burmese participants (46.9% vs 27.3%), with a 50% of Burmese subjects reporting that they did not believe that it was an effective treatment for TB (Table 2). Most Burmese subjects reported that they did not know what their preferred type of treatment was (83.9%). A larger proportion of Burmese participants reported having been previously diagnosed with TB compared to their Chinese counterparts (11.5% vs 1.4%).

3.2 Bivariate analysis of predictor variables with outcome

Amongst Chinese participants, marital status, believed time needed to cure TB, preferred treatment type, knowing where to get tested and treatment location for previous sickness were significantly associated with our outcome when not controlling for other variables (Table 3). Subjects who were married were more likely to believe that TB can be cured using TCM (OR=2.49; 95% CI: 1.13-5.45). Participants who were unsure of how long it took to

effectively treat TB were more likely to believe that TB can be cured using TCM compared to those who correctly knew treatment duration was usually 6-12 months (OR=4.17; 95% CI: 1.33-13.13). Both subjects whose preferred treatment was a traditional/combination therapy regimen (OR=3.10; 95% CI: 1.36-7.05) and those who were unsure of their preferred treatment (OR=3.78; 95% CI: 0.48-29.61) were more likely to believe in TCM as an effective cure compared to subjects who chose western treatment regimens as their preferred treatments. Subjects who knew where to get tested were less likely to believe TCM could cure TB (OR=0.42; 95%: 0.20-0.89). Participants who were treated at public clinics/hospitals for their previous illness were less likely to believe in TCM as an effective cure compared to those who were treated at a private clinic/hospital (OR=0.33; 95% CI: 0.12-0.91).

Amongst Burmese participants, sex, being a manual laborer, education, being able to correctly identify effective TB treatments, believed time needed to cure TB, preferred treatment type, knowing where to get tested and treatment location for previous illness were significantly associated with our outcome when not controlling for other variables. Females were less likely to believe that TB can be cured using TCM (OR=0.76; 95% CI: 0.59-0.98). Participants who identified as manual laborers were less likely to believe that TB can be cured using traditional herbal treatment compared to those who did not identify as manual laborers (OR=2.01; 95% CI: 1.52-2.65). Both participants who completed secondary/high school (OR=0.75; 95% CI: 0.57-0.98) and participants with a university/graduate/professional level education (OR=0.46; 95% CI: 0.31-0.68) were less likely to believe that TB can be cured using traditional herbal treatment. Participants who

were unable to correctly identify effective treatments for TB were more likely to believe that TB can be cured using traditional herbal treatment (OR=3.13; 95% CI: 1.72-5.70). Participants who were unsure about treatment duration were more likely to believe that TB can be cured using TCM compared to participants who believed that it took 6-12 months to treat TB (OR=3.56; 95% CI: 2.01-6.31). Participants who were unsure of their preferred treatment type were less likely to believe that TB can be cured using TCM compared to participants who preferred western treatment regimens (OR=0.03; 95% CI: 0.01-0.1). Participants who knew where to get screened for TB were less likely to believe that TB can be cured using traditional herbal treatment (OR=0.25; 95% CI: 0.18-0.35). Participants who were treated at a pharmacy for their last major illness were less likely to believe that TB can be cured using traditional herbal treatment compared to those that were treated at a private clinic/hospital (95% CI: 0.29-0.70).

3.3 Multivariable Analysis

3.3.1 Chinese Cohort

The two multivariable models were selected based on the lowest values for Aikake's Information Criterion (AIC), which indicates the relative quality of a model. Though model 2 offers a slightly better measure of relative quality compared to model 1(AIC: 195.0 vs 196.6), keeping the variable concerning whether a subject is a manual laborer offers no increase in predictive accuracy (AUC: 0.79 vs 0.79). Both models offer approximately equal measures for goodness of fit to observed data points. Therefore, the model taking into account whether the subject knows where to get screened for TB, marital status, being treated at either at a public clinic/hospital or at an 'other' location for their previous major

illness, having a university/graduate/professional education and preferring western treatment provides the most predictive power. When adjusting for other covariates, marital status (aOR=3.10; 95% CI: 1.22-7.89), being treated at a public clinic/hospital for their last major illness (aOR=0.32; 95% CI: 0.13-0.77), having a university/graduate/professional education (aOR=0.25; 95% CI: 0.08-0.77) and preferring western treatment (aOR=0.25; 95% CI: 0.01-0.65) were significantly associated with believing that traditional herbal treatment can cure TB.

3.3.2 Burmese Cohort

The two multivariable models were selected based on the lowest values for AIC. Though model 2 offers slightly better relative model quality compared to model 1(AIC: 879.9 vs 881.2), removing the covariate concerning whether a subject has been previously diagnosed with TB does not result in a decrease in predictive accuracy (AUC: 0.78 vs 0.78). Model 1 offers slightly better goodness of fit compared to Model 2 (HL X^2 (*p*-value): 7.51 (0.46) vs 9.46 (0.30)). Due to the fact that the addition of the covariate affiliated with being previously diagnosed with TB not offer a major increase in predictive accuracy, model 2 is the preferable model. Model 2 includes covariates accounting for whether the participant is a manual laborer, knows where to get to screened for TB, has a high school/secondary school education, has a university/graduate/professional education, believes TB can be transmitted genetically, lives in a rural area, was treated at a public clinic/hospital for their last major illness, was treated at a pharmacy for their last major illness, was treated at a traditional pharmacy/healer for their last major illness, is unsure of the time taken to treat TB, believes that the time taken to treat TB is ≤6 months, unsure of preferred treatment, and the

interaction between living in a rural area and having a high school/secondary school education. When adjusting for other covariates, knowing where to get screened for TB (aOR=0.40; 95% CI: 0.27-0.60), believing that TB can be transmitted genetically (aOR=1.82; 95% CI: 1.14-2.91), living in a rural area (aOR=0.33; 95% CI: 0.21-0.54), being treated at a traditional pharmacy/healer (aOR=0.35; 95% CI:0.14-0.83), being unsure of preferred treatment type (aOR=0.04; 95% CI: 0.02-0.10), and the interaction between living in a rural area with having a high school/secondary school education (aOR=2.09; 95% CI: 1.07-4.11) were all significantly associated with believing that traditional herbal treatment can effectively treat TB.

4. **Discussion**

To prevent community transmission of TB, it is essential to be able to identify socio-economic, cultural and behavioral barriers preventing people from accessing screening and treatment for TB. Collecting data consisting of demographic, socio-economic, attitudes and beliefs concerning TB offers critical information to help us explore which factors are most likely to prevent people from seeking diagnosis or treatment. Though some studies show that traditional herbal medicine can be useful as an adjuvant therapy in combination with standard treatment, relying solely on TCM prevents effective treatment of TB disease and sustains opportunities for infection. By fitting predictive models to our data from both countries, we can begin to determine which characteristics are most influential in predicting if someone believes that TM can cure TB. This might help guide implementation strategy for field interventions. In addition, we can compare models from both countries to see whether they share common factors of predictive influence, which might be useful in identifying which factors can be targeted in multi-contextual settings.

In our Chinese subjects, a troubling 46.9% of participants believed that TCM was an effective treatment for TB, with an additional 36.9% reporting that they were unsure if TCM could be used to cure TB. The fact that such a large proportion of our study population held such beliefs is alarming, and raises concerns about treatment adherence and onward transmission in this population. When controlling for other variables, being married, having been treated at a public clinic/hospital for their last major illness, being treated at a non-listed treatment center for their last major illness, having a university/graduate/professional level education, and preferring western treatment were all shown to be significant predictors

of whether someone believes traditional medicine can cure TB. Subjects who were married were more likely to believe, while those who were treated at a public clinic/hospital, having a university/graduate/professional level education and preferring western treatment were less likely to believe that traditional medicine is an effective treatment.

As expected, participants with a higher level of education and a preference for western treatment tended to be less likely to believe in the effectiveness of herbal medicine. However, it is interesting to see that married participants were more likely to believe in herbal treatment. We would have expected to see married participants more likely to have better access to health information, especially since young, single men are notoriously difficult to convince to access treatment for what they would perceive as non-life threatening ailments (Tudiver & Talbot, 1999). In addition, it is interesting to see that subjects who were treated at public clinics/hospitals were less likely to believe in the effectiveness of traditional medicine compared to subjects who sought treatment at private clinics/hospitals. We would have expected subjects being treated at private healthcare facilities to have a higher socioeconomic status and higher education, and thus being less likely to believe in using traditional medicine. However, this could be explained by the fact that public healthcare facilities are required to follow W.H.O. guidelines for treatment, while physicians at private hospitals may be more inclined to customize treatment and regimen duration. It is also interesting to see that when we control for other variables, not knowing how long it takes to cure TB no longer is associated with our outcome. Reasons for these results being different from expectation may be due to social and contextual factors affected by regional influences.

When all considered together, our predictive model offers fairly accurate predictive power (AUC=0.788). This signifies that when we have data for all the characteristics listed, there is a 78.8% chance that our predictive model is able to discriminate correctly between a person who believes and a person who does not believe that traditional medicine can cure TB.

Unlike in China, the belief that TCM can cure TB is not as widespread in Myanmar. Only 27.3% of Burmese participants believed that TCM could cure TB, with 22.7% reporting they were unsure. However, this still remains an issue of concern with regards to chances of transmission. When controlling for other variables, knowing where to get tested for TB, believing that TB can be transmitted genetically, living in a rural area, being treated at a traditional pharmacy/healer for their last major illness, being unsure of which treatment type they would prefer and being both from a rural area and having a high school/secondary school education were all shown to be significant predictors of whether someone believes traditional medicine can cure TB. Subjects who believed that TB can be transmitted genetically, as well as subjects who were both from a rural area but had a high school/secondary school education were more likely to believe that herbal treatments could cure TB, while subjects who knew where to get tested for TB, were from a rural area, were treated at a traditional pharmacy/healer for their last major illness and were unsure of their preferred treatment type were less likely to believe that TB can be cured using traditional treatment.

While we would expect knowing where to get tested for TB would reduce the likelihood of believing that TCM can cure TB, it is very surprising that living in a rural area,

being treated at a traditional pharmacy/healer for their last major illness as well as being unsure of preferred treatment type resulted in a decrease in the likelihood of believing herbal treatments are effective in treating TB. Due to less opportunities for education as well as access to health information, we would have expected to living in a rural area to be more likely to result in a subject believing in TM. This reduction in probability could perhaps be explained by equally difficult access to education for people living in urban slums, or social taboos preventing people from actively seeking out further information regarding TB treatment.

What is most surprising though that when we only look at the association between living in a rural area with our outcome, living in a rural area is associated with an increased probability of believing traditional medicine can cure TB as expected. However, when we adjust for other variables in our predictive model the effect is inversed. Though we would have expected subjects who were unsure what their preferred treatment was to rely on the more traditional treatment regimens that they are familiar with, this might not be the case in Myanmar. It is also important to note the significance of the interaction term between living in a rural area and having a high school/secondary school education. This signifies that there is a difference in attitudes towards TB between subjects living in rural versus urban areas who have a high school/secondary school education. This could be due to variations in the quality of education between these two areas, or could be more likely that people living in urban areas are more familiar with TB. It is also interesting to note that manual labor, though strongly associated with our outcome of interest when compared in bivariate analysis, no longer offers predictive value when adjusting for other predictors.

We would have also expected subjects that were treated at traditional pharmacies/healers for their last major illness to be more likely to believe that herbal medicine can cure TB. However, this reduction in likelihood could be explained by the fact that they are answering post-visit, signifying that their previous illness might not have been cured using TCM. It would be interesting to examine how many of these subjects' previous illness was active TB disease, how many were attempting to treat their TB by visiting a traditional healer, and how many subjects' illnesses were not cured as a result of taking traditional herbal treatments. We would then be able to determine if these subjects no longer believed traditional herbal treatments are effective in curing TB as a result of this visit.

By comparing the selected predictive model for our Chinese cohort and the predictive model for our Burmese cohort, we observe a number of shared variables. It is important to note that Yunnan province borders Myanmar, and that Kunming city lies relatively close to the border. There are a number of cultural and social similarities between Yunnan & Myanmar, which might explain a number of these shared characteristics. However, there a number of differences in influential factors between the two cohorts. First of all, being married is a significant predictor in China, while not in Myanmar. This could be due to the fact that gender is directly associated with our outcome in our Burmese cohort, with females being less likely to believe that TB can be cured using TCM. This is not the case in China, and could explain why married individuals are more likely to believe so, as they could be persuaded by their spouse. In addition, manual labor was a significant predictor in our Burmese model but not in our Chinese model. This could be due to the fact

that a large proportion of manual laborers in Myanmar were young construction workers, who are typically young men with low levels of education originally from rural areas. Though manual laborers in China also consisted of construction workers, farmers made up a larger proportion compared to in Myanmar. This further confirms that socio-economic and cultural differences between the two areas account for differences in our two models.

Our study has several limitations. First, participants were selected using convenience sampling by outreach location, rather than by random sampling. The subjects were participants that came into contact with outreach workers and who consented to participating in the survey. If participants were selected using convenience sampling, we are unable to make inferential conclusions concerning our study population, as our selection of subjects is not random. However, our data was obtained via implementation programs in low resource areas; settings in which standard epidemiologic studies are difficult to conduct with limited funds. Though convenience sampling does not provide us with a perfect representation of the overall population, drawing inference from data obtained by quick, inexpensive and effective methods offers us extremely useful information for future strategies for program implementation.

Second, the study suffered from sparse data, especially in our Chinese cohort. Following subject inclusion/exclusion, having only 288 subjects resulted in small counts for responses once stratified upon our outcome. Having limited answers prevented us from calculating odds ratios comparing the difference in likelihood of our outcome for participants who were unable to correctly identify symptoms of TB, as well as subjects who reported being treated at a pharmacy for their previous illness. This could have had a major

effect upon our model selection, resulting in a biased process of variable addition/elimination. As seen in Table 1, all of our odds ratios had an extremely wide confidence interval, which is driven by sparse data in comparison groups. As a result, the association between a number of variables and our outcome were shown to be statistically insignificant despite having a fairly large measure of effect. Examples include being treated at an 'other' location for previous illness (OR=0.28; 95% CI: 0.07-1.08) as well as having a university/graduate/professional level education (OR=0.45; 95% CI: 0.16-1.23), which both had large effect sizes but were statistically insignificant when not controlling for other variables. During model selection, both variables were included in the final predictive models due to their influence on predictive power. Having such inaccurate confidence intervals could possibly lead to the presence of multiple cases of type 2 error when selecting which factors are shown to influence the predictive ability of our models.

Third, a source of error could be due to assumptions that were required to make when reclassifying variables and creating our inclusion/exclusion criteria, which could have resulted in overestimating or underestimating the effect size of certain factors. Due to sparse data found especially in multi-level variables, reclassification of certain categories was necessary. Though categories that were combined were done so after evaluating clinical and demographic similarities, there is the possibility that this has either diluted the effect size or introduced associations that do not actually exist. Our original outcome variable was a 3-level variable ("Yes", "No" and "Don't Know"). Instead of using a polytomous logistic regression analysis, we decided to convert our outcome into a binomial outcome due to sparse data and use a regular logistic regression analysis. We chose to combine the answers 'Yes' with 'Don't Know', under the assumption that someone who was unsure if TB can be

cured using traditional medicine would more likely believe that it could be or at least use a combination therapy of western and traditional medicine. During the creation of our rural vs urban variable, subjects living in an urban area who were not registered in their district were classified as rural to account for rural to urban migration. Though this is a well-documented indicator for whether someone is originally from a rural area but temporarily living and working in an urban environment, this might not be the case for every subject that we classified as rural. In order to address this issue, the addition of a question in our outreach survey addressing this issue would be necessary.

Finally, our study lacked an internal validation step when evaluating the predictive ability of our selected models. Ideally, we would have liked to split our dataset into a model selection and validation set, where we build our models using one and validate our models in another to see if they accurately reflect the data. Due to the sparse data and rare outcome issues presented, we encountered high variability of selected variables when this internal validation step was attempted. Therefore, to confirm the predictive power of our models, we would ideally like to use an external validation database to confirm that our models are effective outside of our selected context. Regional variations in cultures, socioeconomic factors and attitudes towards TB have the potential to greatly reduce the predictive power of our models. Therefore, an external validation would be useful in determining whether our predictive model remains effective in multi contextual settings.

5. Conclusion

The use of TCM as a treatment for active TB remains an issue in preventing onward transmission and adherence to treatment, especially in low resource areas with a high burden of TB. By fitting predictive models to data collected on Chinese & Burmese participants, we provide potential characteristics and behaviors to help identify who is most likely to believe, and use, TCM to cure their TB. This will provide with useful targeting strategies for intervention development in order to increase efficacy in preventing TB transmission and mortality as a result of continued TCM use. It is important to consider the influence of the local cultural and socio-economical context on determining what strategies should be adopted in which situations. Considering these types of variables may help to educate the community and presumptive patients/families and may improve access to TB treatment.

6. Tables

Table 1. Descriptive statistics for subjects surveyed concerning barriers preventing from accessing diagnosis and treatment in Myanmar & China		Overall N= 1250
Characteristic	**China (n=288)**	**Myanmar (n=962)**
Age (years), *Median (IQR)*	46.5 (27)	34.0 (20)
**12 missing values*		
Gender, *N (%)*		
Male	134 (46.5)	452 (47.4)
Female	154 (53.5)	502 (52.6)
**8 missing values*		
Income Source, *N (%)*		
Unemployed	36 (12.5)	150 (15.7)
Manual Labor	25 (8.7)	300 (31.5)
Office Worker	30 (10.4)	197 (20.7)
Service Industry	39 (13.5)	24 (2.5)
Shop Owner/Merchant/Broker	64 (22.2)	236 (24.7)
Retired	76 (26.4)	28 (2.9)
Other	18 (6.3)	19 (2.0)
**8 missing values*		
Education, *N (%)*		
No school/Did not complete/Primary School	88 (30.6)	383 (40.2)
Secondary/High School	167 (58.0)	426 (44.7)
University/Graduate/Professional	33 (11.5)	144 (15.1)
**9 missing values*		
Marital Status, *N (%)*		
Single/Divorced/Widowed	45 (15.6)	341 (35.8)
Married	243 (84.4)	611 (64.2)
**10 missing values*		
Geographic Area, *N (%)*		
Urban	128 (44.4)	370 (38.7)
Rural	160 (55.6)	585 (61.3)
**7 missing values*		

Table 2. Subject responses concerning beliefs related to tuberculosis symptoms & treatments in Myanmar & China		Overall N= 1250
Characteristic	**China (n=288)**	**Myanmar (n=962)**
Believes Traditional Herbal Treatment Can Cure TB		
Yes	135 (46.9)	263 (27.3)
No	39 (13.5)	481 (50.0)
Don't Know	114 (39.6)	218 (22.7)
Answered 'Don't Know' for knowledge of TB symptoms, *N (%)*	16 (5.6)	73 (7.6)
Answered 'Don't Know' for knowledge of TB transmission, *N (%)*	36 (12.5)	77 (9.0)
Answered 'Don't Know' for knowledge of TB treatment, *N (%)*	35 (12.2)	59 (6.1)
Believes TB can be transmitted genetically, *N (%)*	32 (11.1)	128 (13.3)
Believed time taken to cure TB, *N (%)*		
<6 months	125 (43.4)	504 (52.4)
6-12 months	45 (15.6)	276 (28.7)
12+ months	37 (12.9)	106 (11.2)
Don't Know	78 (27.1)	75 (7.8)
**4 missing values*		
Preferred type of treatment, *N (%)*		
Traditional/Combination	113 (39.2)	75 (7.8)
Western	157 (54.5)	72 (7.5)
Don't Know	17 (5.9)	807 (83.9)
**9 missing values*		
Knows where to get tested for TB, *N (%)*	162 (56.3)	611 (63.5)
**125 missing values*		
Previously Diagnosed with TB, *N (%)*	4 (1.4)	111 (11.5)
**3 missing values*		
Treatment location for previous sickness, *N (%)*		
Private Clinic/Hospital	69 (24.0)	643 (66.8)
Public Clinic/Hospital	120 (41.7)	127 (13.2)
Pharmacy (Formal)	3 (1.0)	101 (10.5)
Traditional Pharmacy/Healer	72 (25.0)	42 (4.4)
Other	23 (8.0)	4 (0.4)
**46 missing values*		

Table 3. Measure of effects between predictor variables and outcome variable "Believes Traditional Herbal Treatment Can Cure TB"		Overall N= 1250
Variable	**China** OR (95% CI)	**Myanmar** OR (95% CI)
Age (per 5 years)	1.06 (0.95-1.18)	0.99 (0.94-1.04)
Sex		
Male	Ref	Ref
Female	1.25 (0.63-2.45)	0.76 (0.59-0.98)
Income Source		
Office Worker	Ref	Ref
Manual Labor	0.58 (0.12-2.90)	2.08 (1.44-2.99)
Unemployed	0.90 (0.18-4.33)	1.10 (0.72-1.69)
Service Industry	0.43 (0.10-1.79)	0.92 (0.39-2.18)
Shop Owner/Merchant/Broker	0.91 (0.22-3.77)	1.13 (0.77-1.65)
Retired	0.83 (0.21-3.29)	0.61 (0.26-1.42)
Other	0.39 (0.08-1.99)	0.75 (0.28-1.99)
Manual Laborer		
No	Ref	-Ref
Yes	0.81 (0.0.26-2.49)	2.01 (1.52-2.65)
Education		
No school/Did not complete/Primary School	Ref	Ref
Secondary/High School	1.05 (0.48-2.30)	0.75 (0.57-0.98)
University/Graduate/Professional	0.45 (0.16-1.23)	0.46 (0.31-0.68)
Marital Status		
Single/Widowed/Separated	Ref	Ref
Married	2.49 (1.13-5.45)	0.78 (0.60-1.02)
Geographic Area		
Urban	Ref	Ref
Rural	1.55 (0.79-3.05)	1.19 (0.92-1.54)
Correctly identified TB symptoms		
Yes	Ref	Ref
No	NA*	2.16 (1.30-3.58)
Correctly identified modes of TB transmission		
Yes	Ref	Ref
No	2.92 (0.67-12.69)	1.54 (0.96-2.47)
Correctly identified effective TB treatment		
Yes	Ref	Ref
No	1.77 (0.52-6.08)	3.13 (1.72-5.70)
Believes TB can be transmitted genetically		
No	Ref	Ref
Yes	1.58 (0.46-5.47)	1.24 (0.86-1.81)
Believed time needed to cure TB		
<6 months	2.10 (0.86-5.08)	1.21 (0.90-1.62)
6-12 months	Ref	Ref

12+ months	1.04 (0.36-2.97)	0.96 (0.61-1.51)
Don't Know	4.17 (1.33-13.13)	3.56 (2.01-6.31)
Preferred Treatment Type		
Traditional/Combination	3.10 (1.36-7.05)	0.5 (0.12-2.08)
Western	Ref	Ref
Don't Know	3.78 (0.48-29.61)	0.03 (0.01-0.10)
Knows where to get tested		
No	Ref	Ref
Yes	0.42 (0.20-0.89)	0.25 (0.18-0.35)
Previously diagnosed with TB		
No	Ref	Ref
Yes	0.15 (0.02-1.11)	0.68 (0.45-1.01)
Treatment location for previous sickness		
Private Clinic/Hospital	Ref	Ref
Public Clinic/Hospital	0.33 (0.12-0.91)	1.18 (0.81-1.73)
Pharmacy (Formal)	NA*	0.45 (0.29-0.70)
Traditional Pharmacy/Healer	1.05 (0.29-3.79)	0.53 (0.28-1.02)
Other	0.28 (0.07-1.08)	0.32 (0.03-3.10)

* Unable to calculate OR due to sparse data

Table 4. Multivariable models for prediction of outcome "Believes Traditional Herbal Treatment Can Cure TB" in Chinese cohort			Overall N=288
Variable	**Crude OR (95% CI)**	**Model 2 aOR (95% CI)**	**Model 1 aOR (95% CI)**
Knows where to get tested for TB	0.42 (0.20-0.89)	0.53 (0.21-1.36)	0.56 (0.22-1.40)
Married	2.49 (1.13-5.45)	3.09 (1.21-7.91)	3.10 (1.22-7.89)
Treated at a public clinic/hospital for last major illness	0.42 (0.20-0.84)	0.32 (0.13-0.77)	0.32 (0.13-0.77)
Treated at 'other' location for last major illness	0.51 (0.18-1.48)	0.28 (0.08-1.03)	0.29 (0.08-1.06)
Unsure of time taken to cure TB	2.77 (1.04-7.37)	1.96 (0.64-6.00)	2.04 (0.67-6.23)
University/Graduate/Professional Education	0.43 (0.18-1.04)	0.25 (0.08-0.78)	0.25 (0.08-0.77)
Preferred Treatment Type: Western Treatment	0.32 (0.14-0.69)	0.24 (0.09-0.63)	0.25 (0.01-0.65)
Manual Laborer	0.81 (0.26-2.49)	0.62 (0.14-2.70)	-
AIC	NA	196.6	195.0
AUC	NA	0.791	0.788
Hosmer-Lemeshow Goodness of Fit Test (*p*-value)	NA	4.16 (0.84)	3.44 (0.84)
N	NA	277	277

Table 5. Multivariate models for prediction of outcome "Believes Traditional Herbal Treatment Can Cure TB" in Burmese cohort			Overall N=1250
Variable	**Crude OR (95% CI)**	**Model 1 aOR (95% CI)**	**Model 2 aOR (95%CI)**
Manual Laborer	2.01 (1.52-2.65)	1.36 (0.92-2.00)	1.35 (0.92-1.99)
Knows where to get tested for TB	0.25 (0.18-0.35)	0.39 (0.26-0.58)	0.40 (0.27-0.60)
High School/Secondary School Education	0.92 (0.71-1.19)	0.68 (0.41-1.12)	0.69 (0.41-1.13)
University/Graduate/Professional Education	0.53 (0.37-0.77)	0.68 (0.40-1.17)	0.69 (0.40-1.18)
Believes TB can be transmitted genetically	1.24 (0.86-1.81)	1.85 (1.15-2.96)	1.82 (1.14-2.91)
Geographic area (rural)	1.19 (0.92-1.54)	0.34 (0.21-0.54)	0.33 (0.21-0.54)
Treated at a public clinic/hospital for last major illness	1.35 (0.93-1.97)	1.53 (0.96-2.44)	1.54 (0.97-2.46)
Treated at a pharmacy for last major illness	0.45 (0.29-0.70)	0.62 (0.36-1.07)	0.60 (0.35-1.04)
Treated at a traditional pharmacy/healer for last major illness	0.53 (0.28-1.02)	0.36 (0.15-0.86)	0.35 (0.14-0.83)
Unsure of time taken to cure TB	3.21 (1.88-5.49)	2.16 (1.00-4.68)	2.09 (0.97-4.49)
Believes ≤6 months of treatment required to cure TB	1.00 (0.78-1.29)	1.31 (0.91-1.90)	1.28 (0.89-1.84)
Previously Diagnosed with TB	0.68 (0.45-1.01)	1.24 (0.76-2.05)	-
Unsure of preferred treatment type	0.05 (0.02-0.09)	0.04 (0.02-0.10)	0.04 (0.02-0.10)
Interaction: Rural Area x High School/Secondary School Education	1.34 (0.64-2.83)	2.09 (1.07-4.11)	2.09 (1.07-4.11)
AIC	NA	881.2	879.9
AUC	NA	0.782	0.780
Hosmer-Lemeshow Goodness of Fit Test (*p*-value)	NA	7.51 (0.4625)	9.46 (0.3049)
N		783	783

* aOR= Adjusted Odds Ratio; AIC= Aikake's Index Criterion; AUC= ROC Area under curve

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