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The Impact of Poverty and Social Protection on Tuberculosis

A dissertation submitted in partial satisfaction of the requirements for the degree Doctor of Philosophy in Health Policy and Management

by

Andrew Siroka

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ABSTRACT OF THE DISSERTATION

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Doctor of Philosophy in Health Policy and Management

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Professor Ninez A. Ponce, Chair

Tuberculosis (TB) infects over 9 million people annually and is responsible for approximately 1.5 million deaths each year. Despite high treatment success rates, declines in incidence have averaged only 1.5% per year over the past decade. The newly adopted End TB Strategy sets a progressive agenda that moves beyond the medical sphere and includes a focus on upstream social determinants aimed at prevention. The strategy specifically calls for stronger poverty alleviation and social protection programs and policies. This dissertation sets out to support the need for social protection programs to combat TB, as well as attempting to answer the questions of who should be the recipients of such programs and in what form should they take.

Paper one uses country-level data to show that spending on social protection is associated with decreased TB prevalence, incidence, and mortality. This work has a global purview and

predicts a drop of 18 per 100,000 persons in TB prevalence rate from 1% increase in social protection spending. This is true even after adjusting for factors associated with TB rates such as level of economic development, the strength of the health system, and HIV burden.

The second paper examines the relationship between household poverty and TB disease. Using household asset and characteristic data, this work creates household socioeconomic quintiles and attempts to show the relationship between this measure and individual active TB disease. The work utilized eight national TB prevalence surveys; large household surveys with a rigorous diagnostic TB algorithm. Although this approach found lower risk of TB disease for individuals in the poorest quintiles in four countries, a dose-response relationship was not observed. This paper also created an absolute wealth estimate, a US dollar-based measure of household wealth, which allowed for comparability across settings and also pooled country models. This measure of household socio-economic level did not have a clear association with individual TB risk. This work suggests novel ways of assessing the relationship between poverty and TB at the individual level that have the potential to be more efficient and to further the field of the social determinants of TB.

The final paper of this dissertation focuses on a TB patient cost survey in Myanmar. This nationally representative survey includes 966 TB patients across the country and gathers information about their income and costs while seeking care. This survey is the first step in measuring the percentage of TB-affected households experiencing catastrophic costs due to the disease, defined as costs exceeding 20% of annual household income. This metric is one of the high level indicators in the End TB Strategy and will be measured by the World Health Organization and its partners in the majority of high burden countries in the coming years. The Myanmar survey found 65% of households experiencing catastrophic costs due to TB, with major cost drivers being patient’s time and additional food and/or nutritional supplements required because of the disease.

Together these three papers contribute to new knowledge in both measurement and content on the role of social protection, alongside appropriate and timely medical care, in order to reach the ambitious targets set forth by the End TB Strategy.

The dissertation of Andrew Siroka is approved.

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CHAPTER 1: Introduction

Tuberculosis (TB) is a major public health problem worldwide. Globally, an estimated 9 million people developed TB in 2014 and 1.5 million died from the disease.[1] This places TB as the number one infectious cause of death worldwide. TB is caused by the bacillus *Mycobacterium tuberculosis* and is spread through the air when those are sick with TB expel bacteria by sneezing or coughing.[2] A relatively small proportion (~10%) of people infected with *mycobacterium tuberculosis* develop active TB disease. However, this percentage jumps markedly for immune-suppressed individuals, such as those who are malnourished or infected with HIV/AIDS.

TB also has a massive economic cost to society. It has been estimated that TB accounts for approximately $12 billion to be lost from the global economy,[3] in large part because 75% of cases occur in working-aged (15 to 54) adults.[4] Beyond the fact that these weakened individuals are often unable to continue working, the burden of taking care of them usually falls to their family members, who in turn often forgo productive economic activity themselves. Furthermore, TB-related mortality has a large economic impact on low and middle-income countries, where 94% of TB cases and 98% of TB deaths occur.[5] The costs of TB, both in terms of lives and financial resources, are avoidable, as TB treatment is widely available and cost-effective.[6] In fact, TB treatment ranked as the fifth most desirable intervention, on the basis of costs and benefits in the Copenhagen Consensus, an analysis of nearly 40 proposals to confront global challenges.[7] This has led *The Economist* to include reducing TB on its list of "no brainers" that yield the greatest benefit per dollar spent.[8]

Policy Setting

The Millennium Development Goal (MDG) for TB was established in 2000 with a goal of halting and reversing TB incidence.[1] This goal (MDG Target 6.c) has been achieved at a global level since TB incidence has begun to decline. However, despite having treatments with high cure rates, global TB incidence fell at an average rate of only about 1.5% per year between 2000 and 2013.[1]

In 2015 the MDGs came to the end of their term and were replaced by the 2030 Sustainable Development Goals (SDGs). The SDGs are of unprecedented scope and go well beyond the MDGs covering a broad range of activities with 17 goals across three dimensions: economic, social, and environmental. While poverty eradication, health, and education, remain priorities, the SDGs also include economic, social, and environmental objectives. There is now widespread recognition that these goals are not just linked but interdependent. This view represents a new, more harmonized approach to development wherein vertical approaches are discouraged in lieu of more integrative programs and policies.

In alignment with the SDG agenda, the 67th session of the World Health Assembly (WHA) approved the post-2015 strategy ("End TB Strategy") on May 19, 2014.[9] This plan has a vision of zero deaths, disease, and suffering from tuberculosis and includes ambitious targets for 2025 and 2035, such as a 95% reduction in TB deaths and a 90% reduction in global incidence rates by 2035. The current rate of decline in TB incidence is insufficient to meet these ambitious goals. This has led to the World Health Organization (WHO), country officials, and TB advocates to look beyond medical interventions and increase their focus on the social determinants of TB. The TB community has drawn inspiration from witnessing the significant decrease in the global HIV/AIDS burden by focusing on that disease's social determinants. [10]

Pillar two of the End TB Strategy, “bold policies and supportive systems”, codifies the WHA’s emphasis on factors beyond medical interventions in TB care and control. This aspect of the strategy stresses the need for universal health coverage and social protection programs that aim to alleviate poverty. This focus on the social determinants of TB supports the need for policies and activities that affect poverty, food security, and living and working conditions for the most disadvantaged populations. Without progressive policies in these areas, achieving the ambitious goals set forth for TB by the End TB Strategy will be impossible.

Social protection and TB

There has been growing consensus that an increased emphasis on social protection programs that tackle the social determinants of tuberculosis is needed.[11] Social protection “consists of policies and programs designed to reduce poverty and vulnerability by promoting efficient labor markets, diminishing people's exposure to risks, and enhancing their capacity to manage economic and social risks, such as unemployment, exclusion, sickness, disability and old age”.[12] Examples of social protection, often called social insurance or social security programs, include cash transfers, subsidized health care, food rations, disability pay, maternity leave, and labor market protections such as mandated levels of minimum wage.

Leaders in this field have developed a conceptual framework showcasing strategic entry points for action outside of the health sector.[13] Nonetheless, there has been little work done on the link between social protection programs and tuberculosis disease. A recent study in *The Lancet Infectious Diseases* by Reeves et al. examined the relationship between social protection levels and national TB rates in Europe.[14]. The country-year analysis showed an inverse relationship between social protection spending and TB incidence and mortality rates in relatively wealthy nations with sizeable social protection systems and secure welfare mechanisms.

Tuberculosis and poverty

While TB is not exclusively a disease of the poor, poverty has been shown to increase the risks of infection and development of disease via more proximal risk factors.[15,16] For example, poverty can lead to overcrowded living/working conditions and poor ventilation, which increases the likelihood of individuals being exposed to mycobacterium tuberculosis. Poverty can also beget malnutrition, which affects the likelihood of the latent infection developing into active TB disease. Work by Lönnroth et al. estimates nearly half of the TB burden can be attributed to poverty-related risk factors of indoor air pollution and malnutrition.[17] Bolstering this estimate, a 2012 study by Oxlade and Murray found low BMI to be the strongest driver of all TB risk factors.[18]

Despite this relationship being taken as a given within the TB community, little work has been done showing the increased risk of TB of individuals with lower socioeconomic status. The majority of analyses showing direct links between poverty and TB has been ecological, linking poorer regions or countries to higher TB rates .A well-known example of this ecological analysis was Janssens and Rieder's work, which showed an inverse relationship between GDP per capita and TB prevalence.[19]

Catastrophic costs due to tuberculosis

Not only does TB tend to affect the most vulnerable individuals, but it also has the power to drive them further into poverty. This is due to the direct costs of care as well as the loss of wages to the individual and the household. This latter cost is particularly important as TB most commonly occurs in working age adults.[2] In fact, it has been estimated that lost wages account for 60% of the total costs incurred by a patient as a result of TB disease.[20]

One of the three high-level targets for the End-TB Strategy is that no patient or their household should face catastrophic costs due to TB (Figure 1.1). Catastrophic costs due to TB have been defined as costs that are in excess of 20% of annual household income. To monitor progress towards this target, countries will measure occurrence of catastrophic costs with cross-sectional patient cost surveys. Along with partners in country, WHO is planning to conduct at least 12 of these surveys in the coming two years. These surveys strive to improve on previous work done in the field of TB patient costs while imposing minimal burden on patients and national TB programs.

A review of patient cost studies in TB has shown that the majority of studies takes place in high income settings and suffer from low sample sizes.[21] Furthermore, many of these studies are done as part of cost-effectiveness analyses and do not measure the income of patients, therefore, are not designed to assess whether or not costs are catastrophic. Chapter four of this dissertation sets out to produce a reliable estimate for the percentage of TB-affected households facing catastrophic costs due to TB in Myanmar. The analysis includes 1000 nationally-representative TB patients interviewed in 2015. It will further describe the breakdown of costs and examine risk factors associated with incurring catastrophic costs due to TB.

Policy implications and contributions to the field

Together, the three papers of this dissertation aim to provide insight the complex relationships surrounding socioeconomic status, social protection, and TB. Each paper attempts to bolster the End TB Strategy's focus on increased social protection as a way of mitigating the social determinants of TB. Furthermore, this work utilizes new data sources and methods to contribute to the advancement of research in tuberculosis and beyond.

The first paper shows a relationship between social protection and TB burden at the country level. The second paper of this dissertation makes use of eight national TB prevalence surveys, which include strong individual-level data on asset ownership and bacteriologically confirmed TB, to examine the association between socioeconomic level and TB disease. In countries with greater TB disparities between the lowest and highest socioeconomic groups, one would expect greater gains in the fight against TB as a result of social protection programs that focus on the poor. This analysis uses a novel method that takes relative socioeconomic data, combined with aggregate national statistics, to produce absolute wealth estimates for households. This "absolute wealth estimate" method allows for the direct comparison of households from different countries and/or time periods.

This paper also utilizes a newly constructed database consisting of multiple TB prevalence surveys. This was part of an initiative by the WHO Global TB Programme to create an open microdata catalog of these data-rich surveys. The goal of this catalog is to enable researchers to freely access surveys from a multitude of countries to research associations beyond this reported in the individual prevalence survey reports.

The third paper uses individual surveys in Myanmar to investigate the cost faced by patients as a result of TB disease. As the End TB strategy calls for an end to catastrophic costs due to TB, this work will be an important first step in developing the methodology to track progress towards this goal. By delving deep into specific cost drivers, the findings from this analysis have the potential to guide specific types of social protection that target the costs faced by TB patients. It will also serve as a benchmark for future patient cost surveys.

Figure 1.1. The vision, goals, and targets of the End TB Strategy

STRATEGY

A WORLD FREE OF TB

ZERO deaths, disease, and suffering due to TB

END THE GLOBAL TB EPIDEMIC

	MILESTONES		TARGETS	
			SDG	END TB
	2020	2025	2030	2035
Reduction in number of TB deaths compared with 2015 (%)	35%	75%	90%	95%
Reduction in TB incidence rate compared with 2015 (%)	20%	50%	80%	90%
TB-affected families facing catastrophic costs due to TB (%)	0%	0%	0%	0%

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CHAPTER 2: Association between spending on social protection and tuberculosis burden: a global analysis

Abstract

Objective: The End TB Strategy places great emphasis on increasing social protection and poverty alleviation programmes. However, the role of social protection on controlling tuberculosis has not been examined fully. We analyzed the association between social protection spending and tuberculosis prevalence, incidence, and mortality globally.

Methods: We used publicly available data from WHO's Global Tuberculosis Programme for tuberculosis burden in terms of yearly incidence, prevalence, and mortality per 100 000 people, and social protection data from the International Labour Organization (ILO), expressed as the percentage of national gross domestic product (GDP) spent on social protection programmes (excluding health). Data from ILO were from 146 countries covering the years between 2000 and 2012. We used descriptive assessments to examine levels of social protection and tuberculosis burden for each country, then used these assessments to inform our fully adjusted multivariate regression models. Our models controlled for economic output, adult HIV prevalence, health expenditure, population density, the percentage of foreign-born residents, and the strength of the national tuberculosis treatment programme, and also incorporated a country-level fixed effect to adjust for clustering of data points within countries.

Findings: Overall, social protection spending levels were inversely associated with tuberculosis prevalence, incidence, and mortality. For a country spending 0% of their GDP on social protection, moving to spending 1% of their GDP was associated with a change of -18·33 per 100 000 people (95% CI -32·10 to -4·60; p=0·009) in prevalence, -8·16 per 100 000 people

(-16·00 to -0·27; p=0·043) in incidence, and -5·48 per 100 000 people (-9·34 to -1·62; p=0·006) in mortality. This association weakened at higher levels of social protection spending, and lost significance when more than 11% of GDP was spent.

Conclusion: Our findings suggest that investments in social protection could contribute to a reduced tuberculosis burden, especially in countries that are investing a small proportion of their GDP in this area. However, further research is needed to support these ecological associations.

Introduction

Tuberculosis (TB) is a major global health problem with over 9 million new cases and 1·5 million TB-related deaths annually.[1] The Stop TB Strategy 2006-2015 focused on six strategic areas with an aim to reduce TB prevalence and mortality by 50% relative to 1990 levels.[5] The centerpiece of this strategy was to expand and enhance access to quality TB diagnosis and treatment, addressing MDR-TB and TB/HIV coinfection, strengthening health systems, engaging public and private providers, empowering patients, and promoting research.

The ambitious goals set for 2006-2015 are within reach. The TB mortality rate fell by an estimated 45% between 1990 and 2013 and the TB prevalence fell by 41% during the same period.[1] Despite this progress, the decline in TB incidence has been very slow – with an estimated 1·5% per year decrease in global TB incidence during 2000 – 2013. This slow rate of decline has led to a greater focus on programmes and policies to expand the strategy to also include interventions outside of the traditional curative approach within the health care delivery sphere.

The new "End TB Strategy" was adopted in May 2014 by the World Health Assembly and sets out the required interventions to end the global TB epidemic by 2035.[9] This strategy places a greater emphasis on prevention and care of TB through addressing social determinants of TB, including poverty alleviation policies and social protection programs. The ILO describes social protection as "nationally defined sets of basic social security guarantees which secure protection aimed at preventing or alleviating poverty, vulnerability and social exclusion".[22] This definition covers protection against: general poverty and social exclusion, lack of affordable access to health care, lack of labor market protections, as well as a lack of work-related income.

Examples of social protection programmes are cash transfers (both conditional and unconditional), free or subsidized health care, food rations, disability pay, maternity leave, housing subsidies and labor market protections.

In order to achieve long-term epidemiological targets more emphasis is needed on interventions that reduce peoples' vulnerability for TB infection and for progressing from infection to active TB.[13] Despite a call for further research, there is a limited amount of work on the relationship between social protection and tuberculosis, especially in developing countries that have the highest disease burden.

A recent study in *The Lancet Infectious Diseases* by Reeves et al. examined the relationship between social protection levels and national TB rates.[14] The authors examined 21 European nations from 1995 to 2012 using TB statistics from WHO and social protection data from EuroStat. The country-year analysis showed an inverse relationship between social protection spending and TB incidence and mortality rates (r=-0·65 and r=-0·63 respectively). Reeves et al. showed the relationship between social protection and TB in relatively wealthy nations with sizeable social protection systems and secure welfare mechanisms. This paper builds upon this work by analyzing this association with a global purview.

Methods

We aim to show the association between levels of social protection, measured as the percentage of national GDP spent on social protection programmes (excluding health) and national tuberculosis estimates of prevalence, incidence, and mortality rates. Social protection data were obtained from the International Labour Organization (ILO) Social Protection Department's publicly available database.[23] In order to produce its World Social Protection

Report, ILO provides a global overview of social protection systems, their coverage, benefits, and public expenditures. The sources for this data are international organizations such as IMF, OECD, and EuroStat. The data covers the years 2000 – 2012 and includes over 190 countries. The measure of social protection spending is very broad including social assistance (cash transfers, subsidized health care, food rations etc.), social insurance (disability, maternity leave, health insurance), and labour market protection (unemployment compensation, severance pay, training subsidies). One limitation to this data source is that the number of observations per year is not consistent, with the years 2001-2004, 2006, and 2012 contributing a much smaller share of the data than other years. We chose to keep the social protection spending measure as a percentage of GDP rather than an absolute dollar amount as we felt this was more policy relevant to low and high income countries alike.

TB burden is expressed in terms of estimated annual incidence, mortality, as well as disease prevalence. These three outcome measures are expressed per 100,000 people. Estimates from the World Health Organization are derived from population-based national surveys of the prevalence of TB disease, time-series of TB case notification data, and mortality data from vital registration systems with standard coding of causes of death. Scarcity of data in some countries and incomplete coverage of surveillance are the primary reason for uncertainty in published estimates. In this paper, estimated TB mortality includes deaths due to TB as well as deaths attributed to the combination of TB/HIV, in cases where TB is ruled to be the more immediate cause of death. Estimated TB prevalence and incidence include all forms of TB. The Global TB database is publicly available on the WHO website and continuously updated when new data becomes available.[24] The method by which WHO estimates these statistics are described in detail in an online technical appendix and are reviewed annually by an expert panel.[25]

We first examined levels of social protection by each country (Figure 2.1) and then investigated the association between this level and TB rates, without adjusting for any other factors (Figure 2.2). These descriptive assessments were not stand-alone analyses but helped to inform our fully adjusted regression models. The multivariate regression analyses include national-level factors that were pre-specified and conceptually believed to influence TB rates. Besides our primary predictor of interest, social protection spending, the full models contain six covariates. These include 1) a measure of national economic strength measured by GDP per capita (in US$), 2) HIV rates (of those aged 15-49), and 3) the strength of the health system indicated as the percentage of GDP spent on health.[26,27] Further included control variables are 4) population density, 5) percentage of foreign-born residents, and 6) first-line TB treatment success rate among new cases. This last included measure represents the strength of the national TB treatment program. We did not include national measures of more proximal TB risk factors such as alcohol use, malnutrition, or overcrowding despite the evidence of their association with both TB and socio-economic status.[28-30] while important, we believe these putative risk factors to be downstream on the causal pathway from social protection to tuberculosis.

We were limited by the data availability of these covariates; however, the majority of countries that are excluded from the multivariate analyses are small island states that do not have a large TB burden. The 664 observations in the multivariate models include 146 countries, which accounted for over 98% of global TB notifications in 2013.

To account for the clustering of data points within countries over time we used a country-level fixed effects model. This is preferable to only using robust standard errors as it is able to purge omitted variable bias of time-invariant factors that are not included in the models such as the quality of health care delivery systems.

The relationship between social protection and TB rates was hypothesized to be curvilinear and thus a model with a squared social protection term was employed. Having a non-linear relationship allows for the marginal change resulting from a one percent of GDP increase in social protection to vary depending on the starting level of social protection in a particular country. This "U-shaped" relationship is helpful as it allows for interpretation of social protection level changes more accurately for individual countries.

We also conducted a sensitivity analysis to test the robustness of this relationship. In order to see if the level of social protection spending took time to affect TB burden rates we tried the same model specifications as described above but lagged (by one year) the measure of social protection levels. Analyses were done with STATA 13.

Results

Table 2.1 describes the average values of key covariates by World Bank income group. These statistics represent average values weighted by each country's population over the years 2000-2012. Figure 2.1 shows individual countries' social protection levels as a percent of national GDP. In general, high-income countries tend to allocate a greater proportion of their GDP to social protection programs. Western Europe is especially generous with several countries expending more than 20% of their GDP on social protection. On the other hand, low-income countries tend to spend very small amount (proportionally) on social protection. Some notable exceptions are Egypt and Brazil which both have notable cash transfer programs. The majority of high-burden TB countries, located in sub-Saharan Africa and South-east Asia, allocate less than 10% of their GDP on social protection.

Figure 2.2 presents the bivariate relationship between TB prevalence and social protection levels. The size of the country bubble is set to the square-root of 2013 case notifications. BRICS (Brazil, Russia, India, China, and South Africa) and some other countries of interest were labelled to highlight variations. The majority of the high–burden countries are grouped in the top-left quadrant with high prevalence and low levels of social protection. South Africa is a notable outlier, which strengthens the support that this data are best analyzed in a multivariable analysis that includes HIV rates. The figure highlights a strong inverse relationship between social protection levels and TB prevalence. The figure also shows that the relationship may not be linear, particularly at very low levels of social protection as shown by the curvilinear line of best fit and 95% confidence band.

In multivariate models, social protection levels were significantly inversely associated with all three measures of TB burden as shown in Table 2.2. This was formally tested using a joint significance test of social protection and its squared term. These significant associations were observed even when controlling for country-year level covariates and country level fixed effects.

Higher GDP was associated with lower TB prevalence, incidence, and mortality rates, although only statistically significant in the TB prevalence model. Country-year treatment success rates of new TB patients were inversely related to TB burden but only significant in the mortality model. The adult HIV rate had a positive significant association with higher TB rates. Within a country, a one per 1,000 persons drop in the adult HIV rate was associated with a 5.44 per 100,000 reduction in TB prevalence, while holding other factors in the model constant. The association with incidence is even greater with an equivalent decrease in HIV rate leading to an estimated 7.22 per 100,000 decrease on the rate of new TB cases.

Figure 2.3 examines the marginal effects of increased social protection level on TB. The greatest predicted impact comes at low levels of social protection. For example, if a country were currently spending 5% of their GDP on social protection spending (excluding health) we would expect their moving to 6% would result in a 12.7/100,000 drop in their TB prevalence [95% CI: (3.63, 21.8)]. This same increase in social protection is associated with 5.84 and 3.71 declines in TB incidence and mortality rates, respectively. However, this relationship is attenuated once a country reaches higher levels of social protection spending. At the 12% of GDP level, the marginal impact of a one percent of GDP increase on social protection spending is no longer significantly related to a lower TB prevalence, incidence, or mortality. Nevertheless, less than 8% of 2013 TB case notifications derive from countries at or above the social protection spending level of 12% of GDP.

Discussion

We found a clear ecological association between social protection spending (as a percentage of GDP) and TB prevalence, incidence, and mortality. This was especially true in setting with low levels of social protection spending.

Due to the ecological nature of this study we cannot show a causal relationship between social protection levels and TB rates. However, the association found in this analysis supports further research in this area. Bolstering this relationship is the vast amount of evidence on the more proximal poverty-driven risk factors of TB such as malnutrition, overcrowding, and air pollution, as well as poverty as a risk factor for TB itself.[18,29-32] We chose not to control for these measures because we believe them to be on the causal pathway between social protection and TB. To more conclusively explain this causal pathway, we recommend the inclusion of detailed social protection questions to be included in future national tuberculosis prevalence surveys as well as in stand-alone studies on tuberculosis prevention. Furthermore, there is a need for better national social protection data that not only provides overall levels of social protection but also breakdowns of these amounts by type of social protection program.

Incomplete longitudinal country-level data limited us in two ways. Primarily, it mitigated our ability to add more national-level measures related to TB to our models without sacrificing sample size. As our covariates were often derived from disparate sources, each additional merging of datasets resulted in the loss of observations and thus statistical power. This limited sample size also affected our abilities to include interaction terms to see if the association between social protection spending and TB burden differs in different settings. Nonetheless, we did run the models separately for both European nations only and all other nations. In the models excluding European nations, the inverse relationships were stronger than in the complete data models. No significance could be shown between social protection levels and TB burden in the Europe-only models due to a limited number of observations (Figure 2.A1).

Temporal ambiguity poses a threat to this analysis as perhaps social protection spending have a lagged impact on TB rates. However, additional lagged analyses showed minimal difference to the main models (Table 2.A1). Our country fixed effects specification addresses country-specific uniqueness that is not time varying. However, we acknowledge that the study may be threatened by ecological fallacy, which is that the inverse relationship that we detect in the whole sample cannot necessarily be applied to each country. Our country fixed effects specification addresses country-specific uniqueness that is not time varying. However, we acknowledge that the study may be threatened by ecological fallacy, which is that the inverse relationship that we detect in the whole sample cannot necessarily be applied to each country.

We were also concerned with the potential colinearity of GDP and levels of social protection in the models (r=0.55). GDP per capita is a significant predictor of social protection spending in an unadjusted regression model (Table A2). Including GDP in the model was an attempt to explore the effect of social protection spending after controlling for national wealth. However, we recognize that confounding is still a threat to this research. Nevertheless, all measures in the models have variance inflation factors below 2.5 and the coefficients of these two variables do not change markedly when one variable is excluded from the model. Furthermore, we performed a Karlson, Holm, Breen test which compares the coefficients of GDP per capita on TB burden outcomes from the "full model" (with social protection measure) and the "reduced model" (without social protection measure) to test whether social protection is a mediator of GDP.[33] This test shows that social protection significantly mediates the relationships between GDP per capita and TB burden (Table A3).

The outcomes of our models are WHO estimated TB prevalence, incidence and mortality rates. WHO derives estimates of TB disease from notifications as provided by the 202 national TB programmes in 2014, as well as from national TB prevalence survey results. The latest WHO estimates, used in this analysis, were revised retroactively to reflect the results of the latest TB prevalence surveys. We do acknowledge that some countries' current estimates are over- or under-estimates of the true burden of TB disease, however the true extent of this is not known. Under-estimates may arise from under-reporting or under-diagnosis of TB cases. Nonetheless, we believe the WHO estimates are the best TB burden data available.

Lastly, this analysis relies on the ILO's broad definition of social protection described above. It would be beneficial to split social protection spending into programmatic areas to investigate how each program's expenditures are associated with TB rates. This would both strengthen the analysis and provide information with higher policy relevance, guiding decisions on specific social protection investments. For example, social protection includes labor protections, which may not be as beneficial at reducing TB burden in countries with a large informal economy, compared to cash transfer programs. Such information was available in the work put forth by Reeves et al. as a result of more harmonized data in Eurostat, the European Union's statistical office.[14] A more refined measurement of social protection on a global scale would be helpful in determining which programmes or policies are best at reducing the morbidity and mortality burden associated with TB.

This work gives support to increased funding for upstream interventions that target the social determinants of tuberculosis, especially poverty alleviation. Although the main responsibility for social protection rests mainly outside the health sector, the Ministry of Health and the national tuberculosis control programmes, as well as their international technical partners should be proactively involved in the development of social protection policy and schemes and in the coordination of its implementation, in order to maximize health impact.

The benefits of increased social protection spending go well beyond tuberculosis and would likely affect rates of other communicable and non-communicable diseases, especially those with a well-documented association with tuberculosis and poverty. In fact, a study of Organisation for Economic Co-operation and Development (OECD) countries from 1995 to 2005 found that social expenditure was more closely tied to indicators of health than direct health services expenditure.[34] The authors also found that a higher ratio of social spending to health spending was predictive of improved infant mortality and life expectancy after controlling for GDP and the overall level of health expenditures.

Table 2.1. Mean values, overall and by world bank income groups (with standard deviations)*

	Overall	Low-income	Lower-middle-income	Upper-middle-income	High-income
TB prevalence (per 100,000)	199 (170)	393 (192)	311 (121)	128 (119)	42·1 (61·9)
TB incidence rate (per 100,000)	136 (127)	275 (125)	201 (81·5)	96·3 (125)	29·5 (40·4)
TB mortality rate (per 100,000)	25·8 (39·6)	71·6 (54·0)	41·6 (33·9)	10·8 (33·4)	3·57 (6·69)
Social protection, excluding health (percent of GDP)	5·81 (5·68)	1·03 (0·90)	2·39 (3·77)	5·37 (3·52)	12·96 (4·66)
GDP per capita (2014 US$, thousands)	8·28 (13·7)	0·50 (0·26)	1·30 (0·77)	4·28 (2·87)	32·0 (15·5)
Adult HIV rate (per 1,000 adults)	6·48 (20·4)	22·7 (35·2)	5·38 (13·9)	5·00 (23·0)	2·63 (2·06)
Health expenditure (percent of GDP)	5·96 (3·04)	5·04 (2·23)	4·34 (1·22)	5·40 (1·34)	10·3 (3·90)
Population density (persons per sq. km.)	195 (268)	320 (439)	273 (135)	108 (51·3)	168 (452)
Foreign-born (percent of population)	2·78 (4·80)	1·40 (1·43)	1·08 (2·08)	0·89 (2·25)	9·97 (5·92)
TB treatment success rate (percent of new cases)	81·9 (12·6)	82·6 (8·38)	81·3 (12·9)	86·7 (10·7)	73·0 (12·1)

*Averages across years 2000-2012, weighted by country population size.

Table 2.2. Country-level fixed effects regression models predicting tuberculosis prevalence, incidence, and mortality rates (N=664; with 95% confidence intervals)

	Prevalence (per 100,000)	Incidence rate (per 100,000)	Mortality rate (per 100,000)
	β	β	β
Social protection, excluding health (percent of GDP)	-18·3** (-32·1, -4·60) p= 0·009	-8·16* (-16·0, -0·27) p= 0·043	-5·48** (-9·34, -1·62) p= 0·006
Social protection, excluding health (percent of GDP)^2	0·56* (0·00, 1·12) p= 0·049	0·23 (-0·09, 0·55) p= 0·156	0·18* (0·02, 0·34) p= 0·027
GDP per capita (2014 US$, thousands)	-1·75* (-3·37, -0·13) p= 0·034	-0·90 (-1·83, 0·03) p= 0·058	-0·17 (-0·62, 0·29) p= 0·469
Adult HIV rate (per 1,000 adults)	5·54*** (3·52, 7·57) p< 0·001	7·22*** (6·06, 8·39) p< 0·001	3·47*** (2·90, 4·03) p< 0·001
Health expenditure (percent of GDP)	-2·51 (-11·7, 6·71) p= 0·593	-1·87 (-7·16, 3·42) p= 0·488	-1·15 (-3·74, 1·44) p= 0·384
Population density (persons per sq. km.)	-0·016 (-0·16, 0·13) p= 0·831	-0·001 (-0·08, 0·08) p= 0·981	0·007 (-0·03, 0·05) p= 0·731
Foreign-born (percent of population)	12·3 (-1·17, 25·7) p= 0·074	5·55 (-2·17, 13·3) p= 0·159	0·51 (-3·27, 4·30) p= 0·789
TB treatment success rate (percent of new cases)	-0·70 (-1·60, 0·21) p= 0·131	-0·15 (-0·67, 0·38) p= 0·584	-0·28* (-0·54, -0·03) p= 0·031

Notes: *p<0·05, ** p<0·01, *** p<0·001. Social protection and its squared term are jointly significant at the .05 level in all three models with p-values of 0·024, 0·049, 0·004 for prevalence, incidence rate, and mortality rate models, respectively.

Figure 2.1. Levels of social protection (excluding health) spending as a percentage of national GDP

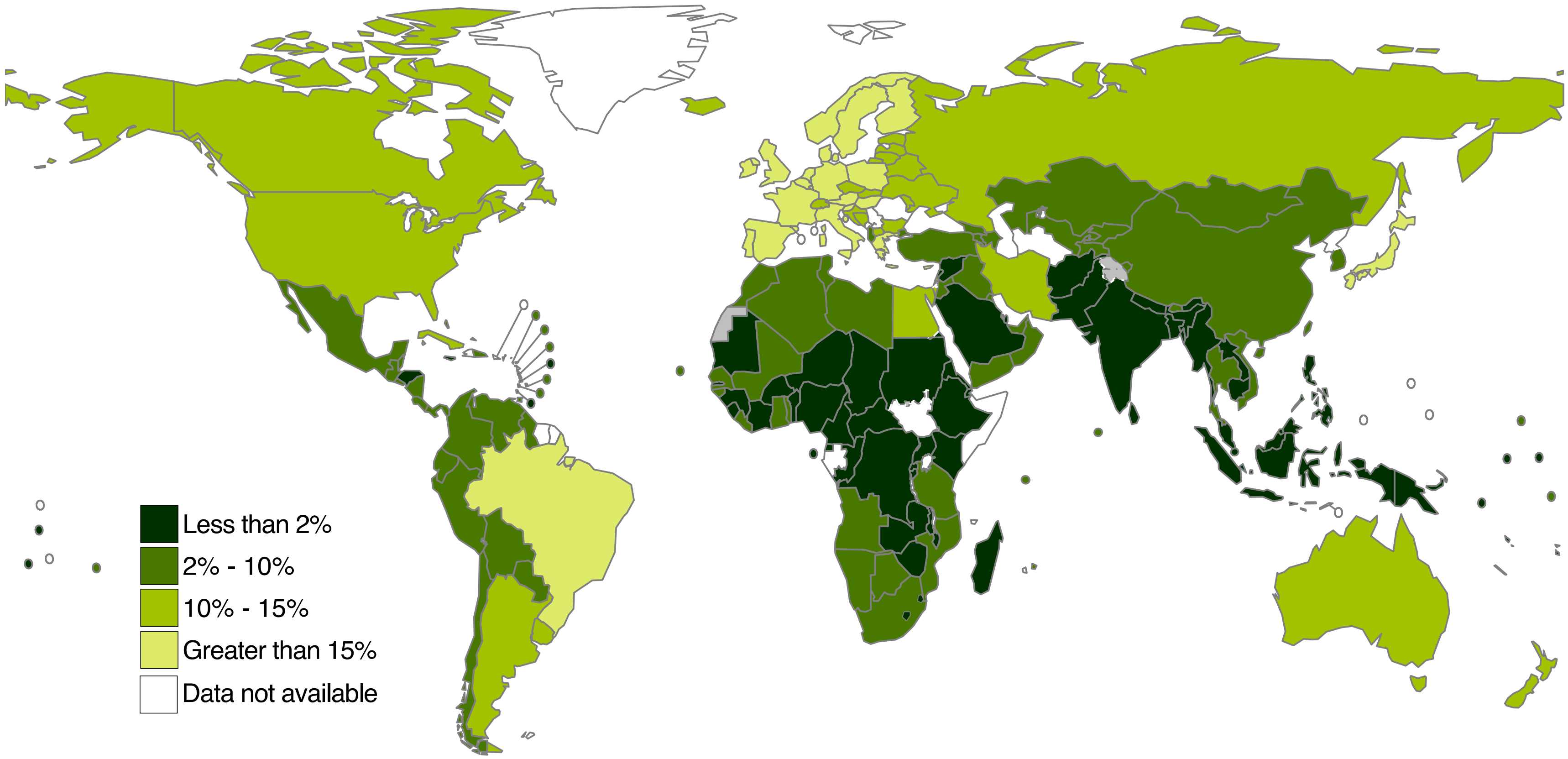
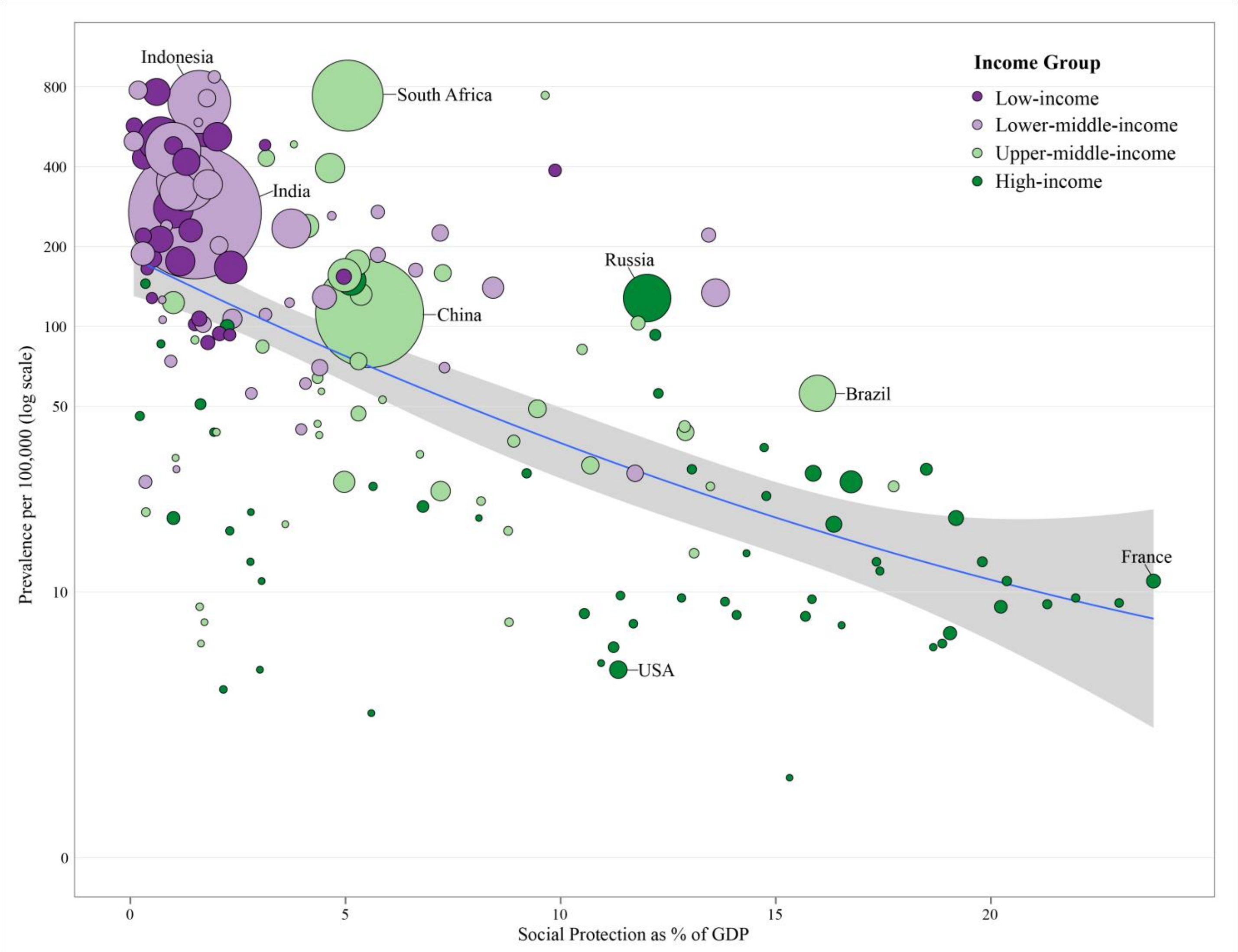
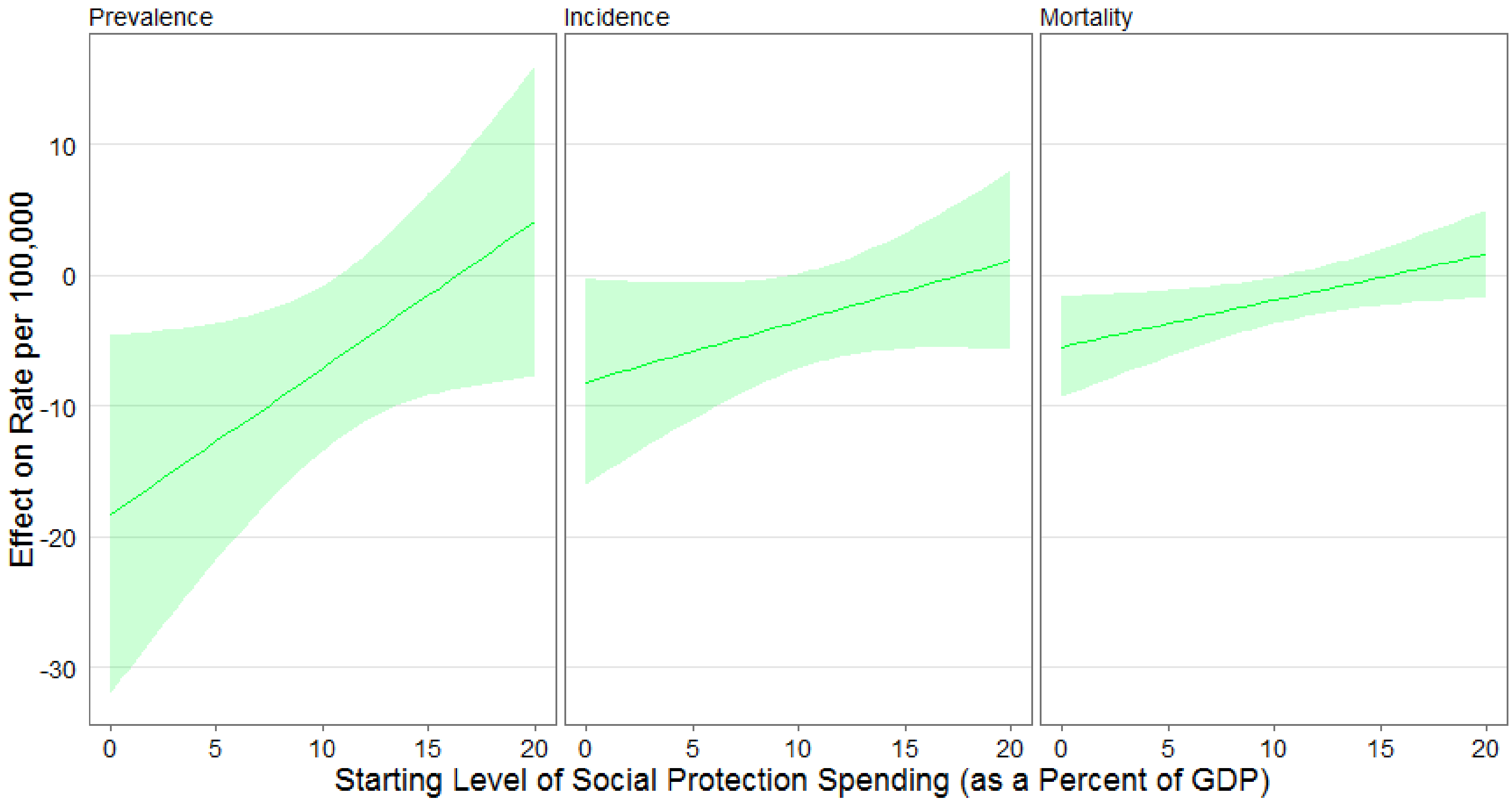


Figure 2.2. Bivariate relationship between social protection and TB prevalence*



* Color represents World Bank income group and bubble size represents the square root of the number of 2013 notified TB cases. The latest year of available data was used for each country.

Figure 2.3. Estimated effect of a one percent of GDP increase in social protection spending with 95% confidence bands (N=664)*



*Models adjusted for GDP per capita, levels of health expenditure, adult HIV rate, percent of population foreign-born, population density, TB treatment success rate, and country-level fixed effects.

Table 2.A1. Regression models predicting tuberculosis prevalence, incidence, and mortality rates using lagged social protection spending (N=664; with 95% confidence intervals)

	Prevalence (per 100,000)	Incidence rate (per 100,000)	Mortality rate (per 100,000)
	β	**β**	**β**
Lagged (one year) social protection, excluding health (percent of GDP)	-14·0* (-27·3, -0·76) p= 0·038	-6·90 (-15·0, 1·22) p= 0·096	-4·84* (-8·87, -0·81) p= 0·019
Lagged (one year) social protection, excluding health (percent of GDP)^2	0·43 (-0·10, 0·96) p= 0·111	0·19 (-0·13, 0·51) p= 0·249	0·15 (-0·008, 0·31) p= 0·062
GDP per capita (2014 US$, thousands)	-1·37 (-2·87, 0·13) p= 0·074	-0·75 (-1·67, 0·16) p= 0·108	-0·16 (-0·61, 0·30) p= 0·493
Adult HIV rate (per 1,000 adults)	6·94*** (4·83, 9·04) p< 0·001	7·88*** (6·60, 9·17) p< 0·001	3·99*** (3·35, 4·63) p< 0·001
Health expenditure (percent of GDP)	-7·48 (-16·2, 1·27) p= 0·093	-4·47 (-9·82, 0·88) p= 0·101	-1·91 (-4·56, 0·75) p= 0·159
Population density (persons per sq. km.)	-0·01 (-0·14, 0·11) p= 0·861	-0·005 (-0·07, 0·08) p= 0·894	0·004 (-0·03, 0·04) p= 0·837
Foreign-born (percent of population)	13·1* (0·23, 25·9) p= 0·046	5·78 (-2·07, 13·6) p= 0·148	1·17 (-2·73, 5·07) p= 0·555
TB treatment success rate (percent of new cases)	-0·69 (-1·43, 0·05) p= 0·069	-0·25 (-0·70, 0·21) p= 0·284	-0·20 (-0·42, 0·03) p= 0·084

Notes: *p<0·05, ** p<0·01, *** p<0·001.

Figure 2.A1. Effect of a one percent of GDP increase in social protection spending with 95% confidence bands (Europe only; N=230)

Table 2.A2. Regression model of GDP per capita predicting social protection spending

	Social protection spending (percent of GDP)
	B
GDP per capita (2014 US$, thousands)	0·19*** (0·18, 0·22)

Notes: *** p<0·001.

Table 2.A3. Karlson-Holm-Breen test comparing coefficients of GDP per capita with and without social protection spending in the models, adjusted for full set of covariates

	Prevalence (per 100,000)	Incidence rate (per 100,000)	Mortality rate (per 100,000)
	β	**B**	**β**
GDP per capita coefficient in reduced model	-3·39*** (-4·60, -2·20) p< 0·001	-1·99*** (-2·74, -1·24) p< 0·001	-0·40** (-0·68, -0·12) p= 0·005
GDP per capita coefficient in full model	-1·61* (-2·94, -0·29) p= 0·017	-1·22** (-2·05, -0·39) p= 0·004	-0·18 (-0·48, 0·13) p= 0·267
Difference	-1·79*** (-2·42, -1·15) p< 0·001	-0·76*** (-1·14, -0·39) p< 0·001	-0·22** (-0·36, -0·09) p= 0·001

Notes: *p<0·05, ** p<0·01, *** p<0·001.

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CHAPTER 3: The effect of household poverty on tuberculosis

Abstract

Objective: The study aims to assess the relationship between household socioeconomic level, both relative position within a country and a household's absolute level of wealth, and individual TB disease.

Methods: We analyzed national TB prevalence household surveys from eight countries individually and in pooled multi-country analyses. Socioeconomic level was measured both in terms of relative household position and absolute wealth. These measures were derived from principal component analyses of household characteristics and asset ownership. The outcome of interest was whether or not an individual had TB disease, measured using a rigorous diagnostic algorithm. Logistic regression models were utilized, which controlled for putative risk factors of TB disease such as age, sex, and previous treatment history.

Findings: Overall, a strong association between household socioeconomic level and individual TB disease could not be shown. This was true for both relative and absolute measures of socioeconomic level in pooled analyses. Limited significance was found in the individual country models, with the lowest socioeconomic quintile being associated with higher risk in four countries: Mongolia, Myanmar, UR Tanzania, and Viet Nam.

Conclusion: Despite strong data quality, results were not as expected and in general the models were unable to show an association between household socioeconomic level and individual TB disease. We suggest alternative methods of examining this association that bypass estimating the socioeconomic level of thousands of individuals without disease. Recommended alternatives

include measuring the socioeconomic level of individuals in a nested case-control study within the prevalence survey or exclusively for TB patients in facilities once treatment is sought.

Introduction

The newly adopted End TB Strategy has an increased emphasis on the social determinants of tuberculosis (TB).[1] It calls for bold policies in the realms of universal health coverage, social protection, and poverty alleviation. It furthermore sets a goal for zero TB-affected families facing catastrophic costs due to TB. As attention shifts to interventions outside the medical sphere it becomes increasingly important to understand how poverty differentially affects TB risk in different countries. A country with great TB disparities between individuals in higher and lower socioeconomic groups may want to increase their focus on activities that target the most vulnerable populations such as an active case finding program in slums. Such an activity may yield greater benefit than in a country that has relatively equal TB risk across their socioeconomic continuum.

There is a vast amount of literature showing that socioeconomic position (SEP) is associated with TB burden. However, much of this literature relies on ecological data and does not include control variables for well-known risk factors. Spence et al. analyzed 33 districts in the United Kingdom and found a strong correlation between rates of poverty and prevalence rates of TB.[2] Similar findings have been observed in census tracts in California and São José do Rio Preto, Brazil, as well as in administrative districts in Cambodia.[3-5] In 2008, Janssens and Rieder found a significant inverse relationship between gross domestic product and incidence of TB incidence using data from 171 countries, but were limited to one year of data (2005) and did not control for other confounding factors.[6]

Many studies that analyze data at the individual level only focus on patients who are already on TB treatment. Belo and colleagues examined how TB treatment success rates were associated with SEP among TB patients on treatment in Duque de Caxias, Brazil.[7] They found those from the lowest socioeconomic group had over four times the odds of having an unsuccessful treatment outcome as those in the highest socioeconomic group. A Zambian case-control study used 52 cases and 318 controls to explore the causal pathway from SEP to TB disease.[8] The authors found people living in lower SEP households had over six times the prevalence of those from higher SEP households. However, when the authors looked at TB infection in the same population, as opposed to disease, they observed counterintuitive findings – that high socioeconomic level was associated with a greater risk of TB infection. The authors explain this surprising result by citing research that those in higher social positions have more human interaction and thus a greater chance of infection.[9] Nationally representative, individual level analyses have investigated the relationship between socioeconomic position and TB using Demographic and Health Surveys from South Africa and India.[10,11] These studies found the lowest quintile to have approximately 5 and 12 times the odds of recent TB infection, respectively, relative to the wealthiest quintile after controlling for other risk factors. One major limitation to these works was that they utilized self-reported recent TB infection.

This is the first study to our knowledge to combine individual-level data from several countries to examine the relationship between household socioeconomic level and TB. Our objective is to show the association between household socioeconomic level, both relative and absolute, and bacteriologically-confirmed TB disease at the individual level. The conceptual framework for this work has been adapted from a model of determinants of TB developed by Lönnroth et al.[12] In this model, poverty does not directly relate to TB, but does so through increasing vulnerability. This analysis represents a reduced-form model as the main poverty-driven risk factors, malnutrition and overcrowding, are not being directly measured. The rationale for this model is that an individual living in a less impoverished household will have better living conditions, nutrition, and other unmeasured risk factors making them less susceptible to TB exposure and/or progression to TB disease.

This work improves upon previous research by using a more rigorous diagnostic algorithm for TB disease that includes chest X-rays, sputum smear microscopy, and bacteriological cultures, as well as looking at nationally representative pools of individuals. Furthermore, we include analyses of not only socioeconomic position within a country and TB risk but also how the overall level of household wealth affects TB risk. Our findings may be useful for country TB treatment programmes and policy makers as it allows them to allocate resources to best meet their country's specific TB burden.

Methods

Data sources

TB prevalence surveys (TBPS) are nationally representative community-based surveys that aim to estimate the prevalence of bacteriologically-confirmed pulmonary TB disease among adults 15 years and older. Methods that incorporate systematic screening of all participants by symptom questionnaire and chest X-ray, followed by case confirmation with at least culture have been standardized since 2009.[13] As TB is a relatively rare disease, prevalence surveys often evaluate up to 90 000 individuals to ensure enough bacteriologically-confirmed TB cases are detected to produce reliable burden estimates. In addition, these surveys collect vast amounts of individual-level data that include demographics, TB-related symptoms, health-seeking behavior and socioeconomic status. Between 2007 and 2014, there have been 20 completed prevalence surveys using standardized methodology of which eight had available individual-level socioeconomic data. These countries include Malawi, Mongolia, Myanmar, the Philippines, Rwanda, United Republic of Tanzania, Viet Nam and Zambia. The Mongolia prevalence survey data only include urban clusters and are thus not nationally representative.

As TB is a relatively rare disease, prevalence surveys often evaluate upwards of 50,000 individuals to ensure enough bacteriologically confirmed cases are detected to produce reliable burden estimates. TB prevalence surveys usually take between 12-18 months to complete and cost an average of US$ 1.5 million in Asia and US$ 3 million in Africa. The data from these surveys are often under-utilized as there are limited funds available to conduct analyses beyond the primary goal of producing epidemiologic estimates of TB prevalence and incidence. Further limiting the use of these surveys for research is that, until now, there has not been a central data repository where researchers could request access to these data. Building the database required permissions from numerous ministries of health, who are the owners of their national TB prevalence survey data. Country NTP managers have begun uploading TBPS survey data, codebooks, and data collection forms to an online data repository hosted by WHO (https://extranet.who.int/tb-prevalence-surveys/index.php/catalog). This database will continue to grow and be available to researchers who wish to work with household level data with a strong measure of TB disease.

Analyses

Socioeconomic position was measured using household asset questions on the TBPS, which typically ask for the presence of durable goods, the quality and materials used for housing construction, and types of water access and sanitation facilities. Principal component analysis

(PCA) was used to create household poverty scores from these items. This approach to poverty measurement has been gaining popularity recently as the Demographic and Health Surveys (DHS) and World Bank have favored this approach.[13] Furthermore, several studies have shown a correlation between household asset score and directly measured household expenditure.[13,14] Once the household asset scores were derived, households were classified into five wealth quintiles within the survey. The lists of items used to create the poverty score in each country are shown in the appendix. It is worth noting that household asset scores only represent the relative wealth within a particular country in a particular survey year. Although the survey is nationally representative, asset scores or quintiles based on asset scores are not comparable across countries or time periods. For this reason, we also explore a measure of absolute wealth as described below.

Each survey was analyzed separately using the logistic regression equation: $Y_{ij}=\beta_0+\beta_1(SEP_j)+\beta_2(Age_{ij})+\beta_3(Sex_{ij})+\beta_4(\text{Previous Treatment}_{ij})+\beta_5(Urban_j)$ where Y represents the log-odds of TB, SEP is the household's socioeconomic position quintile, and i, and j represent individual and household respectively. These models will describe the role of relative socioeconomic position on TB within a given country at the time the prevalence survey was conducted. The highest quintile of the socioeconomic position will serve as the reference group. Due to the rarity of TB disease, odds ratios will approximate risk ratios.[15]

Beyond these models, pooled multi-country analyses that use an absolute wealth estimate (AWE) in constant U.S. dollars for each household were used. This novel metric utilizes the ranking of each household's asset score within a country as well as information on the country's gross domestic product per capita and Gini coefficient, a well-known measure of inequality. The method, previously documented in the Bulletin of the World Health Organization, has been validated against World Bank poverty indicators as well as nutritional status indicators known to be linked to poverty.[16] The AWE allows for examining the effect of absolute household wealth, and not only relative socioeconomic position, on the risk of TB disease. Since all absolute wealth estimates are given in 2014-constant U.S. dollars with purchasing power parity, the wealth of households from different countries or time periods are comparable. Mongolia data were excluded from these models because at the time of this work the survey was not nationally representative but only included the urban portion of the country. Therefore, we could not provide accurate inputs to produce absolute wealth estimates for these Mongolian households. In regression models, AWE was transformed into hundreds of dollars as the effect of one additional dollar was thought to be too small.

Numerous sensitivity analyses were undertaken to determine if model structure or variable creation greatly affected the main results. The creation of wealth quintiles may be splitting the cases across too many strata. Therefore, wealth tertiles were created as well as a comparison between the bottom quintile and remaining four quintiles. Furthermore, asset scores were used as a continuous measure to predict the risk of TB disease. Although this continuous measure yields a difficult to interpret coefficient, it would hint at the potential significance of the primary relationship of interest. Models that excluded people who were previously treated for TB were also tested. The logic behind this was that if socioeconomic position were to affect TB risk then including previously treated patients would introduce additional endogeneity in the models. Stata 13 (StataCorp. College Station, TX) was used for all analyses. The free and informed consent of all subjects or their legal guardians was obtained and this work was exempt from review by the University of California, Los Angeles (CA, USA) institutional review board.

Results

For eight surveys, the number of participants ranged from 30 667 to 87 413 (table 1). In general, most participants were female and from rural areas. The proportion of respondents who were previously treated for TB varied substantially across the surveys, ranging from 0.7% in Zambia to 3.3% in the Philippines. The number of TB cases identified for each survey is quite small relative to the number of those that were not diagnosed with TB (non-cases). Myanmar, with 311 cases, had the highest proportion of TB cases of its participants (0.61%), and Rwanda had the lowest (0.08%).

In the single country analyses, SEP quintile was not predictive of TB disease in the majority of country surveys after adjusting for other putative risk factors (table 2). Viet Nam and Myanmar are exceptional in that there is a pattern of higher risk among lower quintile households. In Viet Nam, an individual residing in a lowest quintile household had approximately double the risk (OR=1.94; 95% CI= 1.21, 3.11) of TB disease as someone residing in the highest quintile household. This same OR was 1.52 (95% CI= 1.03, 2.25) in Myanmar. Despite the significant findings in these two settings, the odds ratios did not align with the socioeconomic gradient consistently. For example, the Myanmar model predicts higher associated TB risk with residing in a second quintile home relative to a household in the lowest quintile (OR of 1.75 vs. 1.52). In fact, none of the models show consistently decreasing odds ratios when moving up the socioeconomic gradient. There are several other quintiles that are associated with significantly higher risk relative to the wealthiest quintile: the lowest quintiles in Mongolia and Tanzania, as well as the fourth quintile in Zambia. The pattern of these significant results did not substantially differ with the use of asset scores as continuous measures, wealth tertiles, or when comparing the bottom quintiles to the upper four quintile groups within each country. Results were not significantly different when the analytic sample excluded previously treated patients from regression models. Other risk factors included in the models were significantly associated with increased risk of TB diseases across country settings. Previous TB treatment was strongly associated with TB risk with odds ratios ranging from 2.85 (the Philippines) to 8.07 (Zambia). Males were more likely to have TB in all settings, with OR ranging from 1.31 (Malawi) to 4.89 (Viet Nam). Lastly, an additional year of age was significantly associated with increased TB risk with an additional risk of 2-4% per year.

When using a logged scale of absolute wealth estimates (AWE) for households within each survey, the distributions appear approximately normally distributed with several being skewed to the right (Figure 3.1). These distributional tails represent a small percentage of households who are better off than their peers. The AWE were used in pooled multi-country analyses of socioeconomic level on TB risk (table 3.3). The first two models in table 3.3 show that when data are pooled together, socioeconomic position quintiles are not predictive of TB disease, with or without country-level dummy indicators, with an exception for the lowest quintile. Models three and four show a similar lack of significance between AWE and TB disease, indicating an additional dollar of household wealth has no association with TB. Quintiles of AWE across all countries were also created and tested; however, this did not change the lack of significant findings. Furthermore, neither SEP quintile nor absolute wealth was associated with decreased TB risk in separate models when no other variables were included in these analyses (result not shown).

Discussion

This study set out to document the relationship between TB and socioeconomic status. In general, such a relationship was not found, contrary to our hypotheses and previous research. The relationship between a household's lower socioeconomic position, relative to other households, was significant in four out of the eight countries studied, but this association did not exhibit a dose-response relationship as expected. Further, when assessing absolute wealth in multi-country pooled analyses, no relationship was found except for the lowest quintile.

Despite these results, we caution that the absence of consistent findings found here should not be taken to mean that household socioeconomic level is unrelated to TB risk. There are a number of reasons why such a relationship may not have been detected. First, the relationship between socioeconomic status and TB may actually differ among countries, based on the presence and level of a range of other confounding factors, such as population density, effectiveness of national TB control programs, and the ways that households in different country contexts experience poverty. Potential policy implications of these findings are that the lack of association between relative socioeconomic position and TB in some countries may warrant national TB policies that reach households across the entire socioeconomic spectrum. For other countries, such as Viet Nam, Myanmar, Tanzania, and Mongolia, there does seem to be some justification to allocate policy action to the lower SEP groups. However, the lack of consistently significant findings and several other limitations limit our ability to make strong recommendations.

Due to the relatively low prevalence of TB in the general population, among the 387 515 individuals across the eight prevalence surveys there were only 1399 cases of bacteriologically-confirmed TB. This creates an issue of statistical power due to the small number of cases in certain strata. As a result, it may be true that individuals residing in lower SEP households are at a greater risk of TB but we are unable to show this relationship without more cases. This is one of the main arguments against using TB prevalence surveys to identify risk factors. Nevertheless, the risk factors of age, sex, and previous treatment history were very clearly associated with TB disease across the surveys, as well as in the pooled analysis.

This study is also unable to measure SEP prior to an individual's participation in the survey. Estimating the causal impact of SEP on TB using cross-sectional prevalence surveys is subject to endogeneity bias as it has been established that TB can lead to poverty.[16] TB often strikes in the prime of an individual's earning years and it has been estimated that up to 60% of the cost of TB can be attributed to lost wages.[17] However, the decision to use assets as the main measure of SEP minimizes this concern as assets are considered to be "slow moving".[13] It has been shown that even important changes in the household socioeconomic level may not affect the ownership of assets in the medium-term.[18] Furthermore, this analysis represents the reduced form model, which does not measure more proximal risk factors associated with both poverty and TB such as undernutrition or crowding. One potential explanation for the lack of significant is that the complex causal pathway from low household socioeconomic level to increased vulnerability and eventual TB disease is not fully understood.

Policy makers across the globe need better population-based evidence to guide allocation of resources beyond the healthcare sphere to maximise the impact of TB control programmes. This analysis was an attempt to provide that evidence by identifying the TB risk differential for the most impoverished households. Despite a robust measure of TB disease and large, individual-level datasets, this analysis showed limited evidence for an increased risk of TB among individuals residing in households of lower socioeconomic level.

If the goal is to assess whether household poverty is a risk factor for TB, collecting household asset data from all participants in TB prevalence surveys may not be an efficient use of resources. These analyses may be underpowered even in the context of these large surveys. The resources freed up by not asking all respondents about household socioeconomic level could be used to conduct a nested case-control study within the TB prevalence survey. This smaller analysis would allow for a more in-depth investigation as to the social risk factors associated with TB disease. Coker et al employed this design in the Russian Federation and found a strong link between household asset ownership and TB risk.[19] Another alternative would be to routinely collect information on the household socioeconomic level of patients in TB treatment centers. This information could be used in conjunction with national household surveys that place more emphasis on socioeconomic level (e.g. DHS). The socioeconomic level of households from the national survey would serve as a comparator group to TB patients and allow for a stronger method of exploring the association between household socioeconomic level and TB.

Table 3.1. Characteristics of analyzed national TB prevalence surveys

Country		Malawi	Mongolia (urban)	Myanmar	Philippines	Rwanda	U.R. Tanzania	Viet Nam	Zambia
Main year of survey		2013	2014	2009	2007	2012	2012	2007	2014
Number of participants		31 579	46 785	51 367	30 667	43 128	50 477	87 413	46 099
Sex									
	Male	18 480 (58.52%)	21 065 (45.03%)	22 394 (43.60%)	15 549 (50.70%)	18 195 (42.19%)	20 735 (41.10%)	39 654 (45.36%)	19 457 (42.21%)
	Female	13 099 (41.48%)	25 720 (54.97%)	28 973 (56.40%)	15 118 (49.30%)	24 933 (57.81%)	29 701 (58.88%)	47 759 (54.64%)	26 642 (57.79%)
Setting									
	Urban	2889 (9.15%)	-	11 254 (21.91%)	14 745 (48.08%)	-	19 588 (38.77%)	24 400 (27.91%)	30 042 (65.17%)
	Rural	28 690 (90.85%)	-	40 113 (78.09%)	15 922 (51.92%)	-	30 889 (61.23%)	63 013 (72.09%)	16 057 (34.83%)
Previous TB Treatment									
	Yes	250 (0.79%)	1 268 (2. 71%)	1463 (2.85%)	999 (3.26%)	559 (1.30%)	790 (1.57%)	1558 (1.79%)	644 (1.40%)
	No	31 329 (99.21%)	45 517 (97.29%)	49 904 (97.15%)	29 668 (96.74%)	42 569 (98. 70%)	49 657 (98.43%)	85 292 (98.21%)	45 455 (98.60%)
Age in years (standard deviation)		34.65 (16.86)	31.26 (19.37)	38.87 (16.46)	25.73 (19.84)	35.55 (16.59)	38.14 (17.83)	40.11 (17.41)	36.09 (16.96)
TB status									
	Cases	132 (0.42%)	142 (0.30%)	311 (0.61%)	136 (0.44%)	40 (0.09%)	155 (0.31%)	250 (0.29%)	265 (0.27%)
	Non-cases	31 447 (99.58%)	46 643 (99.73%)	51 056 (99.39%)	30 531 (99.56%)	43 088 (99.91%)	50 292 (99.69%)	87 163 (99.71%)	45 834 (99.43%)

Table 3.2. Odds ratio of TB case with separate model for each country (95% confidence intervals)

Country	Malawi	Mongolia	Myanmar	Philippines	Rwanda	U.R. Tanzania	Viet Nam	Zambia
Socioeconomic position quintile [a]								
1	1.03 (0.55, 1.93)	1.95^{*} (1.05, 3.59)	1.52^{*} (1.03, 2.25)	1.09 (0.61, 1.95)	1.22 (0.54, 2.74)	1.88^{*} (1.05, 3.39)	1.94^{**} (1.21, 3.11)	1.02 (0.61, 1.72)
2	1.67 (0.96, 2.91)	0.74 (0.35, 1.56)	1.75^{*} (1.18, 2.60)	1.48 (0.89, 2.49)	0.52 (0.19, 1.41)	1.37 (0.73, 2.57)	2.15^{**} (1.37, 3.37)	0.85 (0.51, 1.40)
3	1.61 (0.91, 2.84)	0.87 (0.42, 1.78)	1.33 (0.89, 1.98)	0.93 (0.53, 1.65)	0.43 (0.14, 1.34)	1.26 (0.67, 2.36)	1.75^{*} (1.11, 2.76)	1.21 (0.79, 1.86)
4	0.9 (0.49, 1.67)	1.02 (0.52, 2.03)	1.63^{*} (1.11, 2.39)	0.98 (0.56, 1.71)	0.59 (0.22, 1.62)	0.90 (0.46, 1.77)	1.37 (0.85, 2.19)	1.47^{*} (1.03, 2.11)
5	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Sex								
Male	1.31 (0.93, 1.85)	2.30^{***} (1.48, 3.55)	2.60^{***} (2.04, 3.32)	2.65^{***} (1.81, 3.86)	4.01^{***} (1.95, 8.22)	2.04^{***} (1.40, 2.97)	4.89^{***} (3.55, 6.70)	1.87^{***} (1.44, 2.43)
Female	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Urban setting	3.36^{***} (2.12, 5.71)	-	1.52^{**} (1.18, 1.96)	1.06 (0.74, 1.51)	-	1.28 (0.87, 1.89)	0.96 (0.70, 1.30)	1.83^{***} (1.30, 2.58)
Previous TB Treatment	6.95^{***} (3.62, 13.4)	4.77^{***} (2.56, 8.90)	5.00^{***} (3.64, 6.86)	2.85^{***} (1.78, 4.54)	7.11^{***} (2.79, 18.7)	5.37^{***} (2.97, 9.72)	4.85^{***} (3.29, 7.15)	8.07^{***} (5.50, 11.8)
Age (years)	1.04^{***} (1.03, 1.05)	1.02^{***} (1.01, 1.03)	1.03^{***} (1.03, 1.04)	1.04^{***} (1.03, 1.05)	1.02^{**} (1.01, 1.04)	1.03^{***} (1.02, 1.04)	1.04^{***} (1.03, 1.05)	1.02^{***} (1.01, 1.02)

Notes: Quintiles 1 and 5 are the lowest and highest ranked socioeconomic position, respectively. $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$

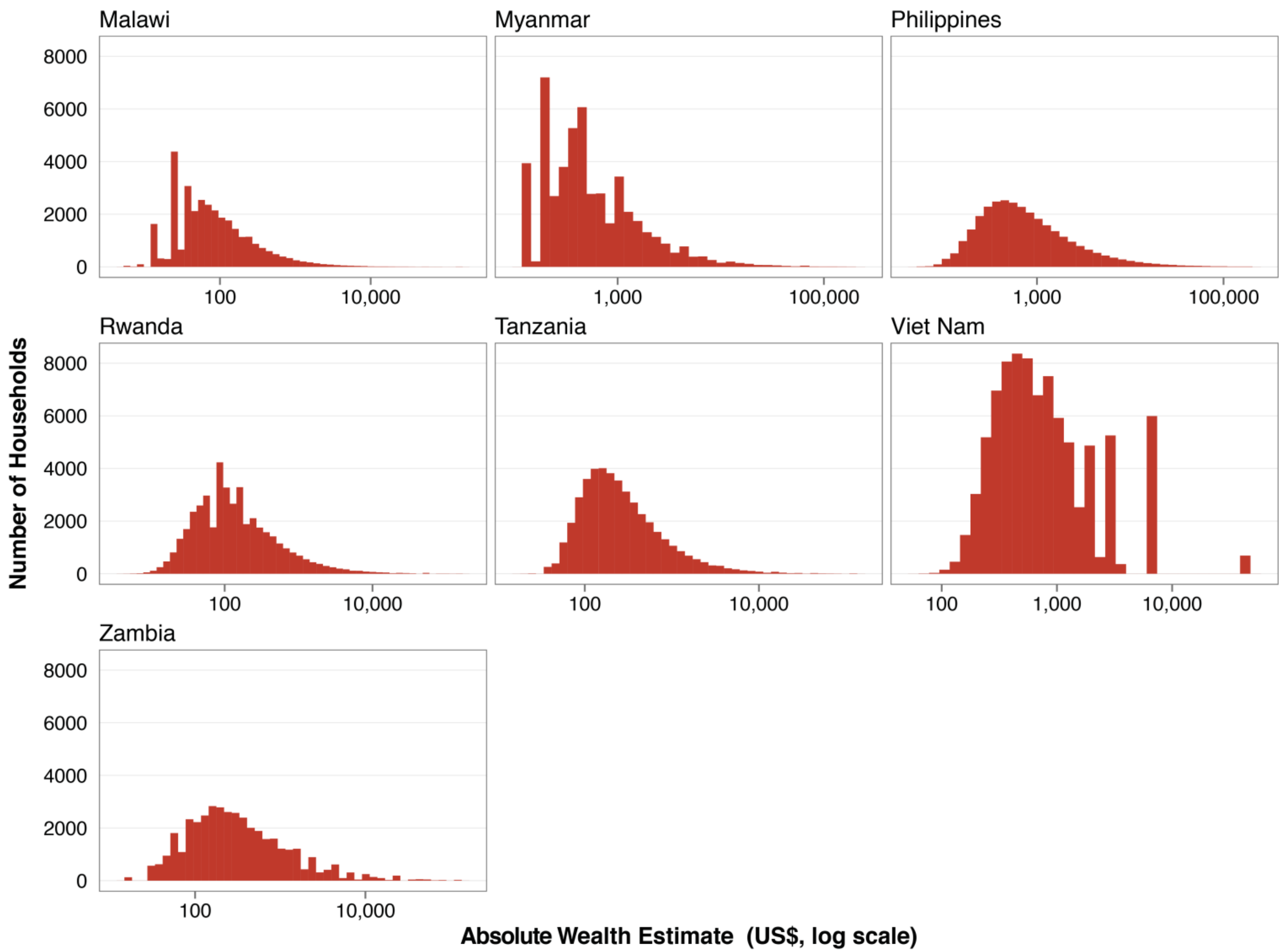
Table 3.3. Odds ratios of TB disease using pooled multi-country models (95% confidence intervals)

	Model 1 Wealth quintiles [a]	Model 2 Wealth quintiles with country-level dummy variables [a]	Model 3 Absolute wealth estimate (AWE) [b]	Model 4 AWE with country-level dummy variables [b]
Socioeconomic position quintile [c]				
1	1.21* (1.02, 1.44)	1.18 (0.99, 1.41)	-	-
2	1.17 (0.98, 1.40)	1.17 (0.98, 1.40)	-	-
3	1.09 (0.91, 1.31)	1.08 (0.90, 1.30)	-	-
4	1.15 (0.96, 1.37)	1.14 (0.96, 1.37)	-	-
5	Reference	Reference	-	-
Absolute Wealth Estimate (2014 U.S. dollars, hundreds)	-	-	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
Sex				
Male	2.43*** (2.17, 2.73)	2.42*** (2.16, 2.72)	2.43*** (2.16, 2.75)	2.43*** (2.15, 2.74)
Female	Reference	Reference	Reference	Reference
Previous TB Treatment	5.70*** (4.85, 6.71)	5.36*** (4.55, 6.32)	5.76*** (4.87, 6.82)	5.38*** (4.54, 6.38)
Age (years)	1.03*** (1.03, 1.03)	1.03*** (1.03, 1.03)	1.03*** (1.03, 1.03)	1.03*** (1.03, 1.03)

Notes:
*p <0.05, ***p <0.001

a. N= 356 943
b. N= 326 329; Mongolia was excluded from AWE estimation because this survey only included urban clusters and was therefore not nationally representative.
c. Quintile 1 and 5 are the lowest and highest ranked socioeconomic position, respectively.

Figure 3.1: Distribution of household average wealth estimate



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CHAPTER 4: Catastrophic costs due to tuberculosis in Myanmar

Abstract

Objective: To produce a baseline measure for the percentage of TB-affected households experiencing catastrophic costs due to TB in Myanmar. The study has a secondary objective of validating the methodology for future patient cost surveys, particularly the use of dissaving strategies as a proxy measure for catastrophic costs.

Methods: Across Myanmar, a nationally representative survey was administered to 996 eligible TB patients in health facilities from December 2015 to February 2016. The cross-sectional survey focused on costs of TB treatment, direct and indirect, as well as household income and dissaving strategies. We estimate a total cost for each household by extrapolating reported costs and comparing this to household income. If the proportion of total costs exceeds 20% of annual household income, the TB-affected household was deemed to have faced catastrophic costs.

Findings: 65% of TB-affected households face catastrophic costs in Myanmar .On average, total spending was $1178 and the largest proportion of this total was accounted for by patient time (49%) followed by nutritional supplement costs (25%). Being on MDR-TB treatment and household wealth quintile were both significant predictors of facing catastrophic costs. Dissaving strategies were not sensitive enough to be used as a proxy measure for facing catastrophic costs due to TB.

Conclusion: The high proportion of TB-affected households experiencing catastrophic costs bolsters the need for TB-sensitive social protection programs alongside effective, patient-centered medical care. The large proportion of total spending attributable to lost wages and

food/nutritional supplements suggest that income replacement programs and/or packages may ameliorate the burdensome costs faced by patients and their families.

Introduction

Tuberculosis (TB) kills approximately 1.5 million people per year.[1] Beyond being the deadliest infectious disease, TB often imparts large costs on affected households. The economic burden of illness due to TB can be devastating. In low- and middle-income countries, TB patients face costs that, on average, amount to half of their annual income.[2] Although, in many countries TB diagnosis and drugs are provided for free, this has been shown to be insufficient in protecting TB-affected households.[3] The reason for this is that TB costs go beyond direct medical expenditure and include payments for transport, accommodation and food expenses, as well as income loss from illness and care seeking. Failure to reduce these economic barriers can mean access to care is inhibited, diagnosis and treatment are delayed or foregone, and TB transmission in the community is exacerbated.

In 2014, the World Health Assembly approved a new WHO strategy, known as the End TB Strategy that aims to end the global TB epidemic. The targets for 2035 are to reduce deaths by 95% and incidence by 90% compared with 2015 levels. The End TB Strategy also has a goal of zero TB-affected families suffering from catastrophic costs due to the disease. This target is in line with policy efforts to move health systems closer to universal health coverage (UHC) as well as the broader SDG agenda, which recognizes the intrinsic link between poverty and health. This goal is being operationalized at the country level with an increased focus on social protection and poverty alleviation, as well as recognition for the need of more rigorous measurement of patient costs.

There has been previous work on measuring patient costs in the field of TB, including in Myanmar.[4-13] However, a literature review on TB patient costs found the majority of studies were outdated, conducted in high income settings, suffered from small sample sizes, and had inconsistent methodology.[14] Furthermore, many of these studies did not assess costs alongside patient or household income, therefore not allowing for a measure on the financial repercussions to TB-affected individuals.

In March 2015, a WHO Global TB Programme Task Force Meeting on catastrophic cost measurement was held in Geneva to agree on standardized methodology for this work and produce a questionnaire and protocol that can be adapted by countries. Myanmar is the first country to utilize the tools and methodology that were created by the task force. Myanmar is a lower-middle income country and one of the top 30 high TB burden countries with 141,957 notified TB patients in 2014. This Myanmar patient costs survey improves on past work by utilizing a large, nationally representative survey of patient costs that includes not only disaggregated cost data but also a set of measures of individual and household income. It aims to set a standard for the methods and measurement of the End TB Strategy indicator of zero TB-affected families undergoing catastrophic costs, which can be used in future TB patient cost surveys.

Methods

A nationally-representative cluster sample was conducted in Myanmar in late 2015. Twenty five facilities throughout the country were sampled based on a probability proportional to size (PPS) approach, wherein each facility's chance of being selected as a cluster was relative to the number of TB patients notified at that facility in 2014.[4] Within each selected facility, each patient who gave consent was interviewed about their TB-related spending, treatment history, household income, social consequences of the disease, and other key concepts. Patients were excluded if they were within the first two weeks of either their intensive of continuation phase of

TB treatment because we believed they would not have provided enough cost information to obtain an accurate estimate for their entire TB episode.

The target sample size was 40 patients at each of 25 facilities. The respondent sample has been weighted to reflect the actually number of patients who completed a questionnaire at each facility. For example, a patient who was interviewed at a facility that completed 35 interviews would be assigned a weight of 40/35. Questionnaires employ skip patterns based on the type of patient (new or retreatment) responding and what phase of treatment they are in. This information is obtained from each patient's treatment card, which is held at the health facility, by the interviewer prior to informed consent and interview processes.

Patient Costs

In this analysis, total costs include direct costs, both medical (e.g. drugs) and non-medical (e.g. transport), as well as indirect costs, which represent the value of a patient's time spent seeking care. Direct medical costs are net of any reimbursements a patient receives from health insurance, if applicable. Less easily estimated are the indirect costs of TB disease. These are particularly important as it has been shown that lost earnings exceeded direct medical costs by nearly a factor of three in Uganda and South Africa.[16,17] Further, a systematic literature review estimates 60% of the total costs incurred by a patient is the loss of income as result of TB disease.[2] Indirect costs are defined as the difference in pre and post-disease household annual income. As a sensitivity analysis, a second measure of indirect costs was examined using the human capital approach. In the human capital approach, an individual's time is valued based on their reported income prior to disease. This involves multiplying the number of hours a patient spends seeking and receiving care by an hourly wage rate. Each survey respondent is assigned an hourly wage rate based on income/asset questions in the survey, as described below. Asset questions were validated using, the Myanmar Household Income and Expenditure Survey (HIES). This survey allowed for a determination as to which of many household asset questions served as the strongest predictors of household annual income. This human capital approach may be conservative as it focuses on the reported time spent seeking and receiving care, but does not value the productivity lost due to the disease when not actively pursuing care.

Additionally, many individuals seek care from traditional healers prior to arriving at a facility within the National Tuberculosis Program (NTP) network. A study of tuberculosis patients in Malawi found that almost 40% had done so before arriving at a government facility.[18] This indirect treatment pathway can lead to a large amount of cost incurred before TB disease is correctly diagnosed. This was highlighted in work by Croft and Croft that analyzed data of Bangladeshi TB patient costs and found they spent an average of $130 before reaching the TB clinic.[5] To put this in perspective, the GDP per capita of Bangladesh during the year of the study was $396. As a result, the questionnaire includes items pertaining to the entire diagnostic pathway as well as items about previous TB treatment history, which may be part of the same TB episode. In the instance where more than one household member is currently suffering from TB, we tried to interview that patient as well and include their TB-related costs in the numerator of our catastrophic cost definition. If they could not be reached, we assumed they incurred the same costs as their already interviewed household member.

Assessing Income

The primary measure is self-reported individual and household annual income. For individuals who are not part of the formal economy and/or cannot accurately report annual wages, income needed to be estimated. Therefore, in addition to asking for personal and household income, the questionnaire also inquired about household asset ownership and dwelling characteristics. Using these items, we were able to estimate each household's annual income by utilizing the relationship between them and income for those who had complete data on these items.

Regression coefficients from the model predicting income with the asset ownership/dwelling characteristic items were used to predict household annual income. From this point, we ascribe a portion of the household's annual income to the individual patient based on the average proportion of total income reported as individual by other patients who answered these items. This individual income estimate is used in conjunction with reported hours worked per week to estimate individual hourly wages. Children were given an hourly wage of zero, although the time value of their caregiver(s) was estimated.

Extrapolation of resource utilization

The questionnaire was cross-sectional, meaning that each patient was interviewed only once after starting their TB treatment. Each patient was only asked about their current treatment phase in an attempt to minimize recall bias. To further minimize recall bias, respondents were asked about the costs incurred during their last visit; per period costs were then calculated by multiplying the cost per visit against the number of visits reported during that period.

As a result, each patient's cost and time spent for the entire TB episode were estimated using a combination of their reported cost and time and the responses of other patients. We hypothesized that patients' resource utilization differed greatly in the two treatment phases: intensive and continuation. For this reason, within a treatment phase (either intensive or continuation) it was assumed that a patient's costs were constant per day. For example, if a patient incurred $300 of costs after completing half of their intensive phase treatment, we assign them a total intensive phase cost of $600. To estimate the direct costs for the treatment phase the patient is not currently in, we assign them the median direct cost of respondents in that phase. The same methods were used for the amount of time a patient spends seeking treatment. However, to estimate the indirect cost of that phase the patient is not in, we use each patient's hourly wage estimate in conjunction with this median time of others. Medians were calculated and assigned separately for drug-susceptible and MDR-TB patients due to their hypothesized differences in resource utilization. Median values of costs and time were seen as more conservative than means due to the skewed distributions of both costs and time spent seeking care. A sensitivity analysis was done in which future cost and income was discounted using an annual rate of 3%.

Defining Catastrophic Costs

The definition of whether or not a household incurred catastrophic costs was if the total costs were more than 20% of the total household income (pre-disease). This cut-off point is based upon a study done by Wingfield et al. wherein patients who had costs greater than 20% of their household income had inferior treatment outcomes.[20] Each TB-affected household is defined as either exceeding this threshold or not. In sensitivity analyses, this original threshold is varied to see how it affects the final percentage of households incurring TB-related catastrophic costs.

We also examine whether or not the TB-affected household had to undergo any kind of dissaving as a result of TB. This includes using savings, selling assets, or borrowing to cope with the costs of the disease. The term highlights a reduction of financial strength of a household, in the same way that saving increases a household's resilience to financial shocks. Previous work has shown an association between dissaving and costs, both total and relative to income, for TB patients in India.[21]

Analyses

Descriptive statistics of those included in the survey. We report total costs by type (direct-medical, direct non-medical, and indirect) as well as with and without the cost of caregiver time included. By disaggregating total costs into its components we hope to target programs or policies to the Myanmar context. For example, if the majority of costs are being incurred before diagnosis this would support an active case finding (ACF) program in which individuals with TB are actively sought out, usually among high risk groups such as refugees, rather than waiting for them to seek care.

The three measures of catastrophic costs were compared for agreement: 1) total costs as a percentage of household income using the human capital approach, 2) total costs as a percentage of household income using output approach, and 3) any dissaving. We further look at different types of dissaving (selling assets, borrowing, and use of savings) and how each relates to experiencing catastrophic costs to check the validity of this more simplified measure.

Risk factors that were thought to be conceptually linked to incurring catastrophic costs were tested using multivariable logistic regressions. These predictors included demographics, health-seeking behaviour, household income, drug resistance status, insurance status, and reported social protection benefits. Costs were converted to United States Dollars (US$) using the average annual exchange rate during study enrolment of US$1 = 1282.65 Myanmar kyat (oanda.com). All analyses were conducted in Stata 13 (StataCorp, College Station, TX).

Results

Table 4.1 shows descriptive statistics for the study population of 966 survey participants with some form of income data (either self-reported income or estimated income from household assets). Only two patients did not agree to participate in the survey and 65 patients were being treated for MDR-TB at the time of the survey. 50 households did not report data and had to have income estimated using household assets. On average, patients reported annual household income of US$ 2184. 288 new patients who were in the intensive phase of treatment reported on average a 6.85 week delay from onset of symptoms before diagnosis. However, this length of time varied greatly from 0 to 72 weeks.

On average, patients incurred US$ 1178 as a result of their TB disease. These costs include $185.39 of direct medical expenditure, $394.35 of direct non-medical spending, and $597.93 of lost income due to the disease (Table 4.2). Of the direct non-medical spending, additional food and/or nutritional supplements made up for the largest portion of total spending. Figure 4.2 shows that spending on nutritional supplements and/or food outside the patient's normal diet accounted for approximately one quarter of total spending, on average.

Figure 4.1 shows the change in distribution of income of households before their TB diagnosis and at the time of the survey. There is a marked, statistically significant, shift in incomes and this difference served as a proxy for indirect costs in the output approach. Under this output approach, 65% (628/966) of TB-affected households experienced catastrophic costs due to TB at the 20% threshold. This result was fairly consistent between the two approaches of patient time valuation. Under the human capital approach, 59% of TB-affected households (574/966) faced catastrophic costs. The methods agreed on whether or not a TB-affected household faced catastrophic costs over 75% of the time (Table 4.3).

The median percentage of household income spent on TB was 36.5% with a mean of 65.9%. Again there was a wide range in the mean measure with the percentage ranging from 1% of annual household income to over 15 times annual household income. Unsurprisingly, as the percentage of household income threshold is increased, the resulting percentage of households deemed to be facing catastrophic costs decreases (Figure 4.4). Strikingly, at a threshold of 100% of annual household income, 20.2% of households surveyed would be deemed as confronting catastrophic costs due to TB.

TB patients in Myanmar are also undertaking burdensome coping strategies with approximately two-thirds using savings, borrowing, or selling assets to help pay for care (Table 4.4). Furthermore, over one quarter of the sample reported that TB had either a “serious” or “very serious” financial impact on the household. Figure 4.3 show the cost, as a percentage of annual income, incurred due to TB broken down by whether or not the household was forced to employ one of the three coping strategies included in the survey. Households taking a loan, selling assets, or undertaking at least one of the three activities had significantly higher costs (as a percentage of their income) than those that did not. Although average costs were higher for those who experienced dissavings, the difference on this coping strategy was not statistically significant.

Table 4.5 shows odds ratios for facing catastrophic costs and undertaking at least one coping strategy resulting from univariate logistic regressions. Measures with significant relationships with these outcomes are whether or not a patient is undergoing treatment for MDR-TB and the income quintile of the household. Patients from the poorest quintile have between 4.76 and 15 times the odds of those in the wealthiest quintile of experiencing catastrophic costs or coping. Using the output approach, MDR-TB patients have 37.5 (95% CI: 5.28, 276.92) times the odds of experiencing catastrophic costs, relative to drug-susceptible patients. This odds ratio increases to 49.1 under the human capital approach, showing how these methods diverge in the case of long treatment regimens, such as the 20 month treatment recommendation for MDR-TB patients in Myanmar.

Limitations

This study was limited to patients who were treated in NTP facilities. This excludes both TB-affected individuals who do not seek care altogether as well as those who rely on the private sector. The reason for this limitation is that patients who are treated elsewhere are rarely notified and registered, and thus not reachable for a survey. Despite higher costs, TB patients in Myanmar often utilize the private sector because of perceived higher quality care and/or shorter waiting times. Surprisingly, previous work has shown that in urban parts of Myanmar, TB patients who seek care in the private sector are poorer than those in the general population.[22] If this assumption holds true, the exclusion of private sector patients may lead to an underestimate of the percentage of patient households that experience catastrophic costs due to TB.

A major threat to the estimation of total patient costs incurred is recall bias- patients not accurately remembering the amount of time or money they spent in seeking care for their TB diagnosis and treatment. We attempted to minimize this bias by only asking patients about their current treatment phase. However, scaling up the cost of a patient's treatment phase depending on the amount of treatment remaining in that phase ignores how patients may adapt over time. Admittedly, the extrapolation of costs are second-best approaches to measurement, however, it was infeasible to continually follow patients to gather costs as they occurred. Furthermore, this study assumes all patients continue and successfully finish treatment. It is unclear whether this leads to an over or under-estimate of costs as some patients who fail treatment never return and others restart treatment from the beginning. The sensitivity analysis of discounting costs and income at 3% made no difference into the categorization as to whether or not a TB-affected household faced catastrophic costs.

Moreover, indirect costs of TB for the patient and the household can extend well beyond the treatment period, also for people who are declared cured from TB. People may be left with short- or long-term sequelae of the disease. Effects of coping mechanisms, such as selling household assets or taking children out of school can impair household economy for years. For the documentation of long-term need of social and economic support for TB-affected households, measures of costs need to have a longer term time-window than the present indicator.

Discussion

The relevance and importance of this work are clear: reducing these direct and indirect costs related to TB care will contribute to improvements in treatment adherence and in financial protection. Thus, the assessment of the magnitude of patient costs and identifying the main cost drivers can be used to monitor financial barriers to adherence and inform related health and social policy changes to improve TB control.

Despite policies of free public sector TB care in Myanmar, many TB-affected households are experiencing catastrophic costs due to TB. This is true regardless of which of the two methods of patient time valuation is used. Even under the most conservative approach, wherein patient costs are not counted, over 40% of households are estimated to be facing catastrophic costs due to TB (not shown). This national estimate will serve as a baseline measure for the End

TB Strategy target of zero TB-affected families experiencing catastrophic costs. Myanmar should periodically monitor patient costs to track their progress towards this goal.

As direct medical expenditure accounted for only 15% of total costs, it is unlikely that universal health coverage will have a major impact on the percentage of TB-affected household facing catastrophic costs. The largest components of total costs were patient's time and food or nutritional supplements outside the patient's normal diet, accounting for 49% and 25% of total costs respectively. This supports the need for social protection programs or policies aimed at income replacement and improving nutrition for TB patients. For example, food packages for those starting treatment would likely mitigate a large portion of total costs faced by TB patients. Apart from ensuring that healthcare services are fairly financed and delivered in a way that minimizes direct and indirect costs, there is a need to ensure that TB patients and affected families receive appropriate income replacement and other social protection interventions.

Table 4.1. Descriptive statistics of survey sample, by MDR status and overall

	MDR-TB (N=65)	Drug-susceptible TB (N=901)	All (N=966)
Sex			
Male	39 (60%)	557 (61.8%)	596 (61.7%)
Female	26 (40%)	344 (38.2%)	370 (38.3%)
Age in years (SD)	36.2 (13.4)	34.6 (20.7)	34.8 (20.3)
Phase			
Intensive	29 (44.6%)	348 (38.6%)	377 (39.0%)
Continuation	36 (55.4%)	553 (61.4%)	589 (61.0%)
HIV Status			
Positive	6 (9.23%)	53 (5.88%)	59 (6.10%)
Negative	40 (61.5%)	674 (74.8%)	714 (73.9%)
Unknown	19 (29.2%)	174 (19.3%)	193 (20.0%)
Retreatment status			
New	14 (21.5%)	791 (87.8%)	805 (83.3%)
Retreatment/Relapse	51 (78.5%)	110 (12.2%)	161 (16.7%)
Monthly household income in US$ (SD)	212.8 (163.8)	179.8 (150.3)	182.0 (151.4)
Diagnosis delay in weeks (SD)*	6.63 (6.21)	6.86 (8.93)	6.85 (8.86)

*Only assessed for 277 new patients in intensive phase

Table 4.2. Summary of detailed costs in 2015 US$

	Median	Mean
Before diagnosis		
Medical	$12.47	$25.83
Non-medical	$5.07	$9.87
Patient time	$2.25	$9.74
After diagnosis		
Medical	$81.08	$159.56
Travel	$5.98	$89.91
Accommodation	$0.0	$8.21
Food/Nutritional support	$151.02	$286.36
Patient's time	$99.55	$583.36
Caregiver time	$0.0	$4.83
Grand Total	$431.24	$1177.67

Table 4.3. Counts of TB-affected households classified as facing catastrophic costs under the two methods of indirect cost calculation

		Human Capital Approach		
		Not Catastrophic	Catastrophic	
Output Approach	Not Catastrophic	242	92	334
	Catastrophic	150	482	632
		392	574	966

Table 4.4. Coping mechanisms and social consequences

	Income Quintiles					
	Poorest (N=199)	Less Poor (N=201)	Average (N=181)	Less Wealthy (N=222)	Wealthiest (N=163)	Overall (N=966)
Coping Strategies						
Loan	84 (42.2%)	84 (41.8%)	55 (30.4%)	61 (27.5%)	30 (18.4%)	314 (32.5%)
Use of savings	68 (34.2%)	72 (35.8%)	68 (37.6%)	85 (38.3%)	63 (38.7%)	356 (36.8%)
Sale of assets	60 (30.2%)	63 (31.3%)	39 (21.6%)	42 (18.9%)	25 (15.3%)	230 (23.8%)
Any of the three above	149 (74.9%)	141 (70.2%)	114 (63.0%)	127 (57.1%)	91 (55.8%)	623 (64.4%)
Food insecurity	6 (3.0%)	5 (2.5%)	3 (1.7%)	1 (0.5%)	0 (0.0%)	15 (1.6%)
Divorce or separated from spouse/partner	2 (1.0%)	0 (0.0%)	1 (0.6%)	2 (0.9%)	0 (0.0%)	5 (0.5%)
Loss of job	3 (1.5%)	3 (1.5%)	2 (1.1%)	6 (2.7%)	4 (2.5%)	18 (1.9%)
Child interrupted schooling	12 (6.0%)	4 (2.0%)	8 (4.4%)	3 (1.4%)	6 (3.7%)	33 (3.4%)
Social exclusion	12 (6.0%)	13 (6.5%)	6 (3.3%)	11 (5.0%)	5 (3.1%)	47 (4.9%)
Any days of work lost	99 (49.8%)	119 (59.2%)	114 (63.0%)	124 (55.9%)	94 (57.8%)	551 (57.0%)
How big of a financial impact did TB have on your household?						
No impact	40 (20.1%)	27 (13.4%)	37 (20.4%)	52 (23.4%)	49 (30.1%)	205 (21.2%)
Little impact	49 (24.6%)	65 (32.3%)	56 (30.9%)	67 (30.2%)	42 (25.8%)	279 (28.9%)
Moderate impact	49 (24.6%)	57 (28.4%)	43 (23.8%)	49 (22.1%)	39 (23.9%)	238 (24.6%)
Serious impact	47 (23.6%)	45 (22.4%)	35 (19.3%)	39 (17.6%)	25 (15.3%)	191 (19.8%)
Very serious impact	14 (7.0%)	6 (3.0%)	10 (5.6%)	15 (6.8%)	7 (4.3%)	52 (5.4%)

Table 4.5. Odds ratios of experiencing catastrophic costs under the two indirect cost methods and for engaging in any coping strategies [a,b]

	Catastrophic cost incurred (Output approach)	Catastrophic cost incurred (Human capital approach)	Any of the three coping strategies
Age	1.02*** (1.01, 1.02)	1.01 (1.00, 1.01)	1.00 (1.00, 1.01)
Sex			
Male	1.29 (0.98, 1.69)	1.33* (1.02, 1.73)	1.07 (0.81, 1.40)
Female	Reference	Reference	Reference
MDR-TB	37.5*** (5.18, 271.7)	49.1*** (6.78, 355.2)	1.61 (0.91, 2.84)
Long delay (> 4 weeks before diagnosis)[c]	1.39 (0.84, 2.29)	1.25 (0.74, 2.11)	1.61 (0.98, 2.84)
HIV	2.08* (1.09, 4.00)	0.91 (0.53, 1.56)	1.18 (0.66, 2.10)
Income Quintile			
Poorest	4.76*** (2.88, 7.84)	15.0*** (8.65, 25.9)	2.36*** (1.51, 3.68)
Less Poor	1.66* (1.08, 2.54)	3.98*** (2.57, 6.17)	1.86** (1.21, 2.87)
Average	1.23 (0.80, 1.89)	2.63*** (1.70, 4.07)	1.35 (0.87, 2.07)
Less wealthy	1.10 (0.73, 1.66)	1.44 (0.95, 2.19)	1.06 (0.70, 1.59)
Wealthiest (Reference)	Reference	Reference	Reference

a. * < 0.05, ** <0.01, *** <0.001
b. All results are from univariate models
c. Only assessed for 277 new patients in intensive phase

Figure 4.1 Distribution of annual household income pre-TB diagnosis and at time of survey, in 2015 US$

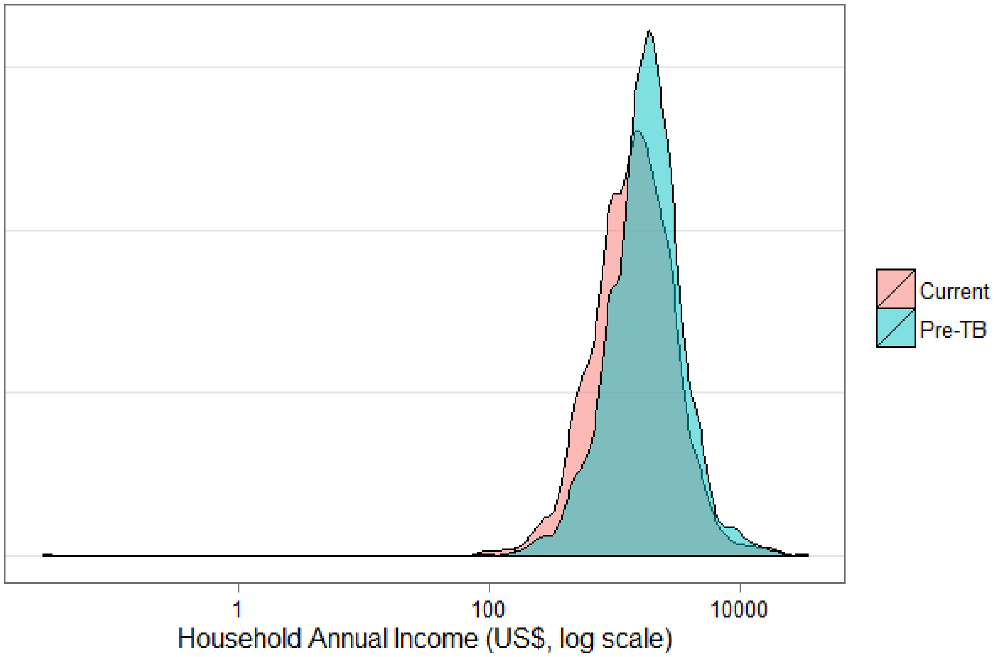


Figure 4.2 Average breakdown of cost categories both pre and post-TB diagnosis

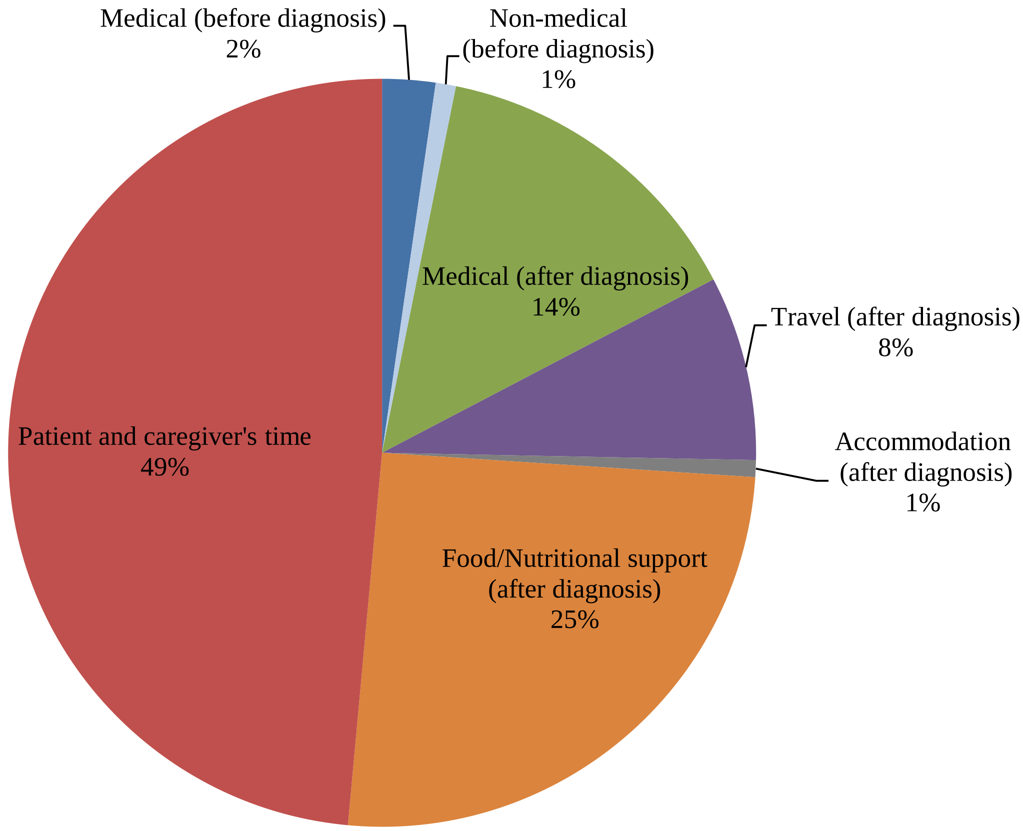


Figure 4.3 Comparison of costs incurred due to TB, as a percentage of annual household income, for households that did and did not undertake coping strategies

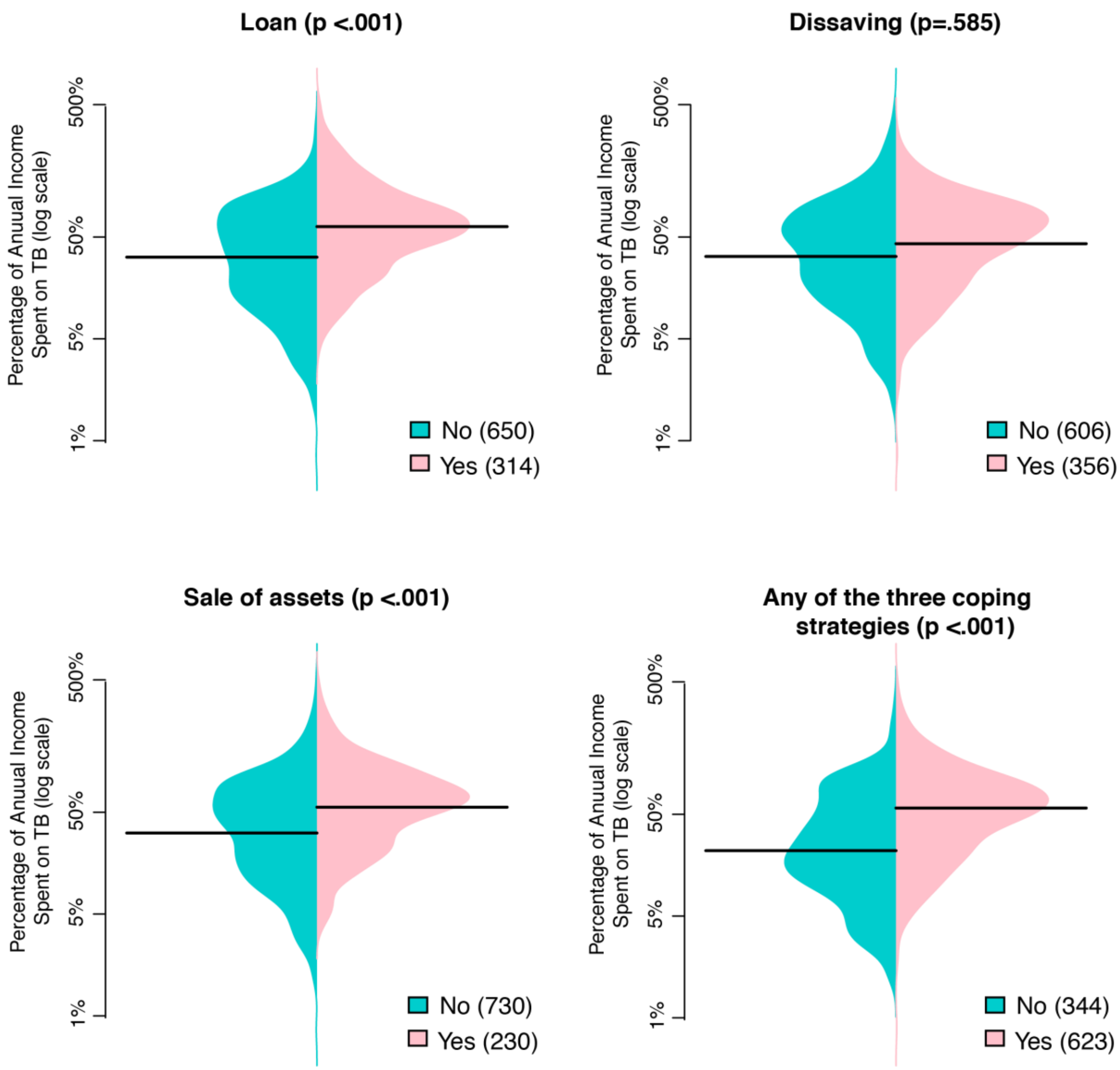
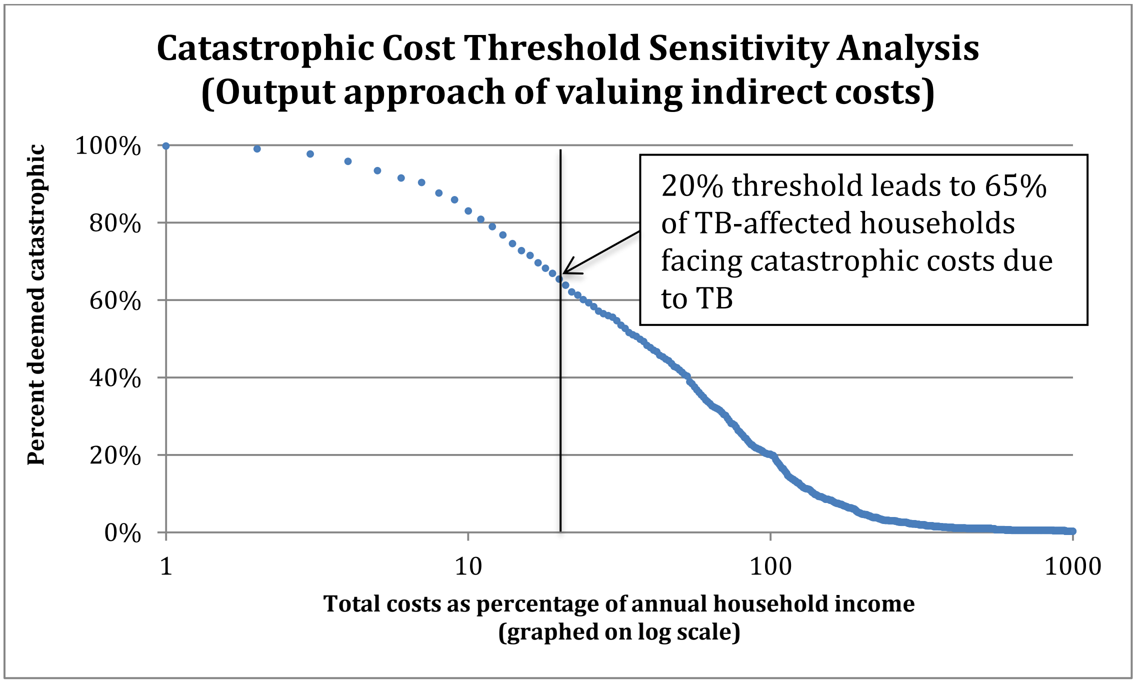


Figure 4.4 Sensitivity analysis of threshold used for determining catastrophic costs



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CHAPTER 5: Conclusion

This dissertation advances the existing literature on how tuberculosis fits in with programs and policies beyond the medical sphere. It does so at a vital time as countries and funders need guidance on how to operationalize the new End TB Strategy. The first paper, entitled "Association between spending on social protection and tuberculosis burden: a global analysis", shows that social protection, alongside effective medical treatment, can reduce TB burden especially in settings that currently offer little in the way of social support. This analysis was shown to be robust to multivariate models as well as numerous sensitivity analyses and endogeneity checks. The first paper also shows the sizeable magnitude of decline one might expect from a one percent of GDP increase in social protection spending. This relative amount was thought to be within reason for all TB-endemic countries. This paper was limited by its ecological design and data limitations. Stronger data on social protection, specifically spending disaggregated by type, would shed more light on the complex pathway from decreased poverty to lower TB burden. Furthermore, individual level data on this relationship could be examined to further strengthen the literature on the beneficial health effects of increased social protection. One example of such work could be to track the health, including tuberculosis status, of recipients of large-scale social protection programs, such as Brazil's Bolsa Familia program.

A commentary published alongside this work, recently published, states, "*The results of Siroka and colleagues' important study support recent changes in global tuberculosis policy, and show that governments should invest not only in diagnosing, treating, and supporting people living with tuberculosis, but also in fighting poverty through social protection to prevent the* *disease. Such approaches have the capacity to transform tuberculosis control, support other public health priorities, and ultimately contribute to sustainable development.*"[1]

Lastly, this paper also provides potential inputs to TB dynamic transmission models, which model the long-term population-level effects of program or policy changes. These models are especially useful when conducting controlled studies are not feasible or ethical. There has been a dearth of dynamic models that have attempted to show how a change in social determinants affect TB burden due to a lack of input.[2] TB modelling needs to start including social and structural determinants to remain a useful tool for policy discussions. The first paper of this dissertation can help by providing some basic inputs to these mathematical models in scenarios of increased social protection spending.

The second paper of this dissertation examined the relationship between household poverty, as measured by an asset score, and individual level active TB disease. One of the great strengths of this work was the use of eight national TB prevalence surveys that rigorously diagnose TB with bacteriological diagnostic tests. Even with this strong measure of TB disease, the relationship between TB and household socioeconomic level could not be found consistently. This was true in most individual country models as well as in pooled analyses using an absolute wealth estimate of households. However, there was limited significance of socioeconomic level found in this paper and, as a result, several countries now have evidence to prioritize lower socioeconomic households as a high risk group for TB. Furthermore, as part of this work, a database of national TB prevalence surveys was developed to facilitate other researchers using these data-rich sources of information.

The relationship between poverty and TB is complex and this study was unable to directly measure poverty-driven risk factors, such as malnutrition and overcrowding, which are known to be linked to TB infection and disease activation. Studies which can measure these intermediate steps on the proposed causal pathway from low socioeconomic level to TB disease may be able to more fully explain this relationship, and offer insights on interventions. Furthermore, the great imbalance of TB cases to non-cases may have limited the ability of these analyses to detect a significant risk differential between low and high socioeconomic level households. However, other risk factors such as being older, male, and having been previously diagnosed with TB were significant risk factors across all models. Although these relationships were not the focus of the study, this paper represents an exhaustive investigation into these three characteristics as risk factors for TB.

Rather than surveying every participant within a TB prevalence survey, this paper recommends alternative ways of investigating poverty as a risk factor for TB. One of these alternatives is to conduct nested case-control studies within TB prevalence surveys. The resources freed up by not asking all prevalence survey participants would allow for more in-depth questioning as to socioeconomic level including household assets, income, and expenditure. This would mitigate the argument that a few household asset questions are not able to properly classify households into socioeconomic quintiles. This work also suggests routinely collecting socioeconomic data of TB patients as they seek treatment at a health care facility. As this method would not collect data on controls, a second data source that also collected data on socioeconomic level would be needed. Fortunately, many of these surveys are already taking place in high TB burden settings such as the Demographic Health Surveys (DHS) and the World Bank's Living Standards and Measurement Survey (LSMS).

The third paper illuminated the burdensome costs faced by TB patients in Myanmar. 65% of TB-affected households face catastrophic costs at a threshold of 20% of household annual income. The majority of these costs draw from the patient's time/lost income and food/nutritional supplement beyond a patient's normal diet. The relatively low proportion (15%) of direct medical costs shows that universal health coverage alone will not be enough to protect against catastrophic costs due to TB. Social protection will be needed in Myanmar to substantially reduce the economic burden on patients and their families. The main cost drivers from this analysis can help guide the types of social protection programs that could be of greatest benefit to TB-affected households, specifically food packages and compensation for lost income. Furthermore, the analysis of risk factors of catastrophic costs shows that those being treated for MDR-TB and those in the poorest socioeconomic groups are at greatest risk. With scarce resources available for social protection for TB patients, these patients should be at the forefront of any program aimed at meeting the target of zero TB-affected households facing catastrophic costs due to TB.

Furthermore, this work sets methodological precedent by attempting to validate and standardize methods to measure catastrophic costs in all countries. Specifically, there is robust work on cost and income estimation despite cross-sectional data collection, as well as an attempt to validate coping strategies as a proxy for facing catastrophic costs. The data from Myanmar hint that using coping strategies as a proxy is too crude a measure of whether or not a TB-affected household experienced catastrophic costs, but further research is needed in this area.

Patient cost surveys have the potential to spur more in-depth qualitative research, which could beget a better understanding of patient cost drivers and shape social protection programs to be most effective at mitigating these costs. In Myanmar, qualitative research could shed light on why patients are spending such a great deal on nutritional supplements and the types of additional food and supplements they are buying. This could lead to tailored nutritional packages for TB patients or perhaps a greater emphasis on educating TB patients on their dietary needs while on treatment. Lastly, repeat surveys within a country could monitor progress towards the End TB strategy goal of zero households facing catastrophic costs and could also serve to monitor the efficacy of UHC and social protection programs.

Social protection can and should be a valuable tool in the fight against TB. However, it should not be viewed as "disease-specific", nor should its benefits be evaluated separately for diseases. To do this is to risk underestimating the beneficial effect these programs may bring to many areas of health, development, and beyond. Advocating for these programs and policies should be undertaken by a coalition of partners, from a multitude of disciplines. This may not be easy as global health work is often done in vertical silos and diseases are often seen as competing with one another for resources rather than working together. This dissertation contributes to the growing evidence that seriously considering upstream social determinants of health, with a non-siloed approach, is necessary to end tuberculosis and mitigate the burden of other poverty/driven diseases.

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