Articles

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

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Summary

Background 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 analysed 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 100000 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 datapoints within countries.



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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 $-18 \cdot 33$ per 100 000 people (95% CI $-32 \cdot 10$ to $-4 \cdot 60$; p= $0 \cdot 009$) in prevalence, $-8 \cdot 16$ per 100 000 people ($-16 \cdot 00$ to $-0 \cdot 27$; p= $0 \cdot 043$) in incidence, and $-5 \cdot 48$ per 100 000 people ($-9 \cdot 34$ to $-1 \cdot 62$; p= $0 \cdot 006$) in mortality. This association was mitigated at higher levels of social protection spending, and lost significance when more than 11% of GDP was spent.

Interpretation 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.

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Introduction

Tuberculosis is a major global health problem, with more than 9.6 million new cases and 1.5 million related deaths occurring annually.¹ WHO's Stop TB Strategy 2006–15 focused on six strategic areas with an aim to reduce tuberculosis prevalence and mortality by 50% relative to 1990 levels.² The centrepiece of this strategy was to expand and enhance access to quality diagnosis and treatment of tuberculosis, address multidrug-resistant (MDR) tuberculosis and tuberculosis–HIV co-infection, strengthen health systems, engage with public and private healthcare providers, empower patients, and promote research.

The target of the Millennium Development Goals to halt and reverse tuberculosis incidence has been achieved on a worldwide basis. Additionally, the ambitious targets of halving tuberculosis prevalence and mortality by 2015, relative to 1990 levels, have almost been reached. Since 1990, global tuberculosis prevalence has fallen by 42% and global mortality has fallen by 47%.¹Despite this progress, the fall in tuberculosis incidence has been very slow—with an estimated decrease of 1.5% per year in global incidence of tuberculosis during 2000–13. This slow decrease has led to a greater focus on programmes and policies outside 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 interventions needed to end the global tuberculosis epidemic by 2035.³ This strategy places a greater emphasis on prevention and care of tuberculosis through addressing the social determinants of the disease, including policies to alleviate poverty, and social protection programmes. The International Labour Organization (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".⁴ This definition covers protection against general poverty and social exclusion, and protection against a shortage of affordable access to health care, labour market protections, and work-related income. Examples of social-protection

Research in context

Evidence before this study

We searched PubMed for English-language articles published between 2005 and 2015 with the terms "social protection AND tuberculosis" or "tuberculosis AND poverty". Many studies assess the link between poverty and tuberculosis; however, we only identified a few publications that analysed the relation between social protection and the disease. Other than this literature search, we relied on the methods used by the study by Reeves and colleagues on social protection and tuberculosis rates in Europe. Furthermore, our conceptual model was heavily driven by previously reported research on the link between poverty, malnutrition, and overcrowding, and research into these conditions as risk factors for tuberculosis.

Added value of this study

This study shows that an inverse association exists between social protection spending and the prevalence, incidence, and

programmes are cash transfers (both conditional and unconditional), free or subsidised health care, food rations, disability pay, maternity leave, housing subsidies, and labour market protections.

To achieve long-term epidemiological goals, more emphasis is needed on interventions that reduce people's susceptibility to tuberculosis infection and progression from infection to active disease.⁵ Despite a call for further research, only a few studies have investigated the relation between social protection and tuberculosis burden, especially in developing countries that have the highest disease burden.

Results from a study reported in The Lancet Infectious Diseases by Reeves and colleagues6 examined the association between social protection levels and national tuberculosis control in 21 European countries. The investigators examined data from 1995 to 2012 using tuberculosis statistics from WHO and social protection data from the European Union (EU) database, EuroStat. The country-year analysis showed an inverse association between social protection spending and tuberculosis incidence (r=-0.65, p=0.0003) and mortality (r=-0.62, p=0.0104). Reeves and colleagues reported an association between social protection and tuberculosis in wealthy nations with large social protection systems and secure welfare mechanisms. Our study builds on this research by analysing this association with a global purview. We aimed to examine the association between levels of social protection, measured as the percentage of national gross domestic product (GDP) spent on social protection programmes (excluding health) and national tuberculosis estimates of prevalence, incidence, and mortality.

Methods

Data sources and study design

For this global analysis, we obtained social-protection data from the publicly available database of the ILO's mortality of tuberculosis. To our knowledge, ours is the first study to do so with a global perspective, and to comment particularly on the association between social protection spending and tuberculosis burden in settings with few social protection programmes in place.

Implications of all the available evidence

National tuberculosis programmes should consider proactive dialogue and interaction with national social protection programmes run by other divisions of government than ministries of health, and with non-governmental organisations. This research gives evidence for tuberculosis-funding donors, such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria, to support the funding of social protection interventions outside the medical sphere in an effort to control tuberculosis.

Social Protection Department.7 To produce its World Social Protection Report, ILO provides a global overview of social protection systems, their coverage, benefits, and public expenditures. The underlying sources for these data are international organisations such as the International Monetary Fund, Organisation for Economic Co-operation and Development (OECD), and EuroStat. The data cover the years 2000–12 from 146 countries. The measure of social protection spending is very broad, and includes social assistance (cash transfers, free health care, food rations, etc), social insurance (disability, maternity leave, and health insurance), and labour market protections (unemployment compensation, severance pay, and training subsidies). One limitation to this data source is that the volume of data per year is not consistent-the years 2001-04, 2006, and 2012 contributed a much smaller share of the data than other years. We chose to keep this measure as a percentage of GDP rather than an absolute dollar amount because we believed this method was more relevant to the policies of both low-income and high-income countries.

Tuberculosis burden is expressed in terms of estimated annual incidence, mortality, and disease prevalence. These three outcome measures are reported per 100000 people. Estimates from WHO are derived from population-based national surveys of the prevalence of tuberculosis, time series of case notifications, 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 main reasons for uncertainty about published estimates. In our study, estimated tuberculosis mortality includes deaths due to tuberculosis alone and deaths attributed to the combination of tuberculosis and HIV, in cases for which tuberculosis was judged to be the more immediate cause of death. Estimated prevalence and incidence of tuberculosis included data for all forms of

the disease. The Global Tuberculosis database⁸ is publicly available on WHO's website and continuously updated when new data become available. The method by which WHO estimates these statistics is described online⁹ and are reviewed annually by an expert panel.

Procedures

We first examined levels of social protection by country and then investigated the association between this level and tuberculosis prevalence, incidence, and mortality, without adjusting for any other factors. 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 prespecified and believed to affect the burden of tuberculosis. Besides our main predictor of interest—social-protection spending-the full models contain six covariates: (1) measure of national economic strength measured by GDP per person (in US\$),10 (2) HIV (prevalence in people aged 15-49 years),11 (3) strength of the health system using the percentage of GDP spent on health as a proxy,¹⁰ (4) population density,¹⁰ (5) percentage of foreign-born residents,10 and (6) success of first-line tuberculosis treatment in new cases.8 Success of treatment is meant to represent the strength of the national tuberculosis treatment programme for each country in a specific year (country-year). We did not include national measures of more proximal tuberculosis risk factors such as alcohol use, malnutrition, or overcrowding, despite the evidence of their association with both tuberculosis and socioeconomic status.¹²⁻¹⁴ We believe these putative risk factors to be partly on the causal pathway from social protection to tuberculosis.

| | Overall | Low-income | Lower middle-income | Upper middle-income | High-income |
|--|--------------|--------------|------------------------|------------------------|---------------|
| Prevalence (per 100 000) | 199 (170) | 393 (192) | 311 (121) | 128 (119) | 42.1 (61.9) |
| Incidence (per 100 000) | 136 (127) | 275 (125) | 201 (81.5) | 96-3 (125) | 29.5 (40.4) |
| Mortality (per 100 000) | 25.80 (39.6) | 71.60 (54.0) | 41·60 (33·9) | 10.80 (33.4) | 3.57 (6.69) |
| Social protection excluding health (percentage of GDP) | 5.81% (5.68) | 1.03% (0.90) | 2·39% (3·77) | 5·37% (3·52) | 12.96% (4.66) |
| GDP per person (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 prevalence (per 1000 adults) | 6.48 (20.4) | 22.7 (35.2) | 5.38 (13.9) | 5.00 (23.0) | 2.63 (2.06) |
| Health expenditure (percentage of GDP) | 5.96% (3.04) | 5.04% (2.23) | 4·34% (1·22) | 5·40% (1·34) | 10.30% (3.90) |
| Population density (individuals per km²) | 195 (268) | 320 (439) | 273 (135) | 108 (51·3) | 168 (452) |
| Foreign-born (percentage of population) | 2.78% (4.80) | 1.40% (1.43) | 1.08% (2.08) | 0.89% (2.25) | 9.97% (5.92) |
| Treatment success rate (percentage of new cases) | 81.9% (12.6) | 82.6% (8.38) | 81·3% (12·9) | 86·7% (10·7) | 73·0% (12·1) |
| | | | | | |

Data are mean (SD). Data calculated across years 2000-12, weighted by the population size of each country. GDP=gross domestic product.

Table 1: Tuberculosis burden and key covariates broken down by World Bank income groups



Figure 1: Levels of social-protection spending as a percentage of national gross domestic product Levels of social protection exclude health spending. The latest year of available data was used for each country.



For the **interactive version of figure 2** see https://asiroka. shinyapps.io/LID_figure2

Figure 2: Bivariate association between social protection and tuberculosis prevalence, incidence, and mortality

Colours represent World Bank income group and the size of the circle for each country is set to the square root of 2013 case notifications of tuberculosis. Brazil, Russia, India, China, South Africa, France, USA, and Indonesia are labelled to emphasise variations. The latest year of available data was used for each country. GDP=gross domestic product.

In fully adjusted regression models, we were limited by the data availability of these covariates; however, most countries that were excluded from the multivariate analyses are small island states that do not have a large tuberculosis burden. This study was given an ethics review waiver from the University of California, Los Angeles (CA, USA) institutional review board.

Statistical analysis

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

We postulated that the association between social protection and tuberculosis occurrence would be curvilinear and thus we used a model with a squared social protection term. Having a non-linear association allows the marginal change resulting from an increase of one percentage point of GDP in social protection to vary depending on the current level of social protection spending in a particular country. This U-shaped relation is helpful because it enables changes in social protection levels to be interpreted more accurately for individual countries. We ran the models separately for European nations only and then all other nations. To see if the level of social protection spending took time to affect tuberculosis burden, we tried the same model specifications as described earlier but lagged (by 1 year) the measure of social protection spending. Additionally, to test for endogeneity, we did a Karlson-Holm-Breen test¹⁵ that compares the coefficients of GDP per person on tuberculosis burden outcomes from the full model (with social protection measures) with those from the reduced model (without social protection measures). We did all analyses with STATA version 13.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

The mean values of key covariates by World Bank income group were weighted by each country's population over the years 2000–12 (table 1). Generally, high-income countries tended to allocate a greater proportion of their GDP to social-protection programmes than low-income countries (figure 1). Several countries in western Europe expended more than 20% of their GDP on social protection. Low-income and middle-income countries tended to spend proportionally less on social protection, but two exceptions were Egypt and Brazil, which both have large cash-transfer programmes. Most countries with a high burden of tuberculosis allocated less than 10% of their GDP on social protection.

Results from bivariate analyses showed a strong inverse association between social protection spending and tuberculosis prevalence, incidence, and mortality, and also suggested that the relation might not be linear, especially at very low levels of social protection (as shown by the curvilinear line of best fit and 95% CI band; figure 2). South Africa is a notable outlier, which strengthens the notion that these data are best analysed in a multivariable analysis that includes HIV rates.

In multivariate models, social-protection levels were significantly inversely associated with all three measures of tuberculosis burden. When we formally tested this association using a joint significance test of social protection and its squared term, these significant associations were noted even when controlling for country-year level covariates and country-level fixed effects. Social protection and its squared term were jointly significant at the 0.05 level in all three models with p values of 0.024 for prevalence, 0.049 for incidence, and 0.004 for mortality. The 664 observations in the multivariate models were from 146 countries, which accounted for more than 98% of global tuberculosis notifications in 2013. Higher GDP was significantly associated with lower tuberculosis prevalence only (table 2). Country-year treatment success rates of new patients with tuberculosis were significantly inversely associated with mortality.

The adult HIV prevalence had a positive significant association with higher tuberculosis rates: within a country, a fall of one per 1000 adults with HIV was associated with reductions of 5.54 (95% CI 3.52-7.57; p<0.0001) per 100000 individuals in tuberculosis prevalence, 7.22 (6.06-8.39; p<0.0001) in incidence, and 3.47 (2.90-4.03; p<0.0001) in mortality, while holding other factors in the model constant. Heath expenditure, population density, percentage foreign-born, and tuberculosis treatment success were not significantly associated with disease burden (table 2).

The greatest predicted effect of increased social protection on tuberculosis burden comes at low levels of social protection (figure 3)—ie, the association is strongest if a country is currently spending 0% of their GDP on social protection and increases this spending to 1% of their GDP. For example, if a country allocated 5% of its GDP to social-protection spending (excluding health), we would expect that an increase of this allocation to 6% would be associated with a decrease in prevalence of 12.7 per 100000 individuals (95% CI 3.63-21.8) in their tuberculosis prevalence. This same increase in social protection would be associated with a decrease of 5.84 (95% CI -11.10 to -0.62) in tuberculosis incidence and a decrease of 3.71 $(-6 \cdot 26 \text{ to } -1 \cdot 15)$ in mortality. However, the association gets weaker as the initial percentage of GDP spent on social protection gets larger. At the 11% of GDP level, the marginal effect of an increase by 1% of GDP on socialprotection spending is no longer significantly related to a lower prevalence, incidence, or mortality. Nevertheless, fewer than 10% of the tuberculosis case notifications in 2013 derived from countries at or above the social protection spending level of 11% of their GDP.

We were concerned with the potential co-linearity of GDP and levels of social protection in the models (r=0.55).

| | for prevalence (per 100 000) | coefficients for incidence (per 100 000) | coefficients for mortality (per 100 000) |
|---|---------------------------------|--|--|
| Social protection excluding health, as percentage of GDP | -18·33 (-32·1 to -4·60); | -8·16 (-16·0 to -0·27); | -5·48 (-9·34 to -1·62); |
| | p=0·009 | p=0·043 | p=0·006 |
| (Social protection, excluding health, as percentage of GDP) squared | 0·56 (0·00 to 1·12); p=0·049 | 0·23 (-0·09 to 0·55); p=0·156 | 0·18 (0·02 to 0·34); p=0·027 |
| GDP per person (2014 US\$, | -1·75 (-3·37 to -0·13); | -0·90 (-1·83 to 0·03); | -0·17 (-0·62 to 0·29); |
| thousands) | p=0·034 | p=0·058 | p=0·469 |
| Adult HIV rate per 1000 adults | 5·54 (3·52 to 7·57); | 7·22 (6·06 to 8·39); | 3·47 (2·90 o 4·03); |
| | p<0·0001 | p<0·0001 | p<0·0001 |
| Health expenditure as | -2·51 (-11·7 to 6·71); | –1·87 (–7·16 to 3·42); | -1·15 (-3·74 to 1·44); |
| percentage of GDP | p=0·593 | p=0·488 | p=0·384 |
| Population density (individuals per km²) | -0·016 (-0·16 to 0·13); | -0.001 (-0.08 to 0.08); | 0·007 (-0·03 to 0·05); |
| | p=0·831 | p=0.981 | p=0·731 |
| Foreign-born percentage of | 12·3 (–1·17to 25·7); | 5·55 (–2·17 to 13·3); | 0·51 (-3·27 to 4·30); |
| population | p=0·074 | p=0·159 | p= 0·789 |
| Treatment success rate as | -0·70 (-1·60 to 0·21); | -0·15 (-0·67 to 0·38); | -0·28 (-0·54 to -0·03); |
| percentage of new cases | p=0·131 | p=0·584 | p=0·031 |
| All data are β values (95% CIs) calcul | ated from multivariate regre | ssions estimated from 664 | country-years. |

Table 2: Effect of social protection and covariates on tuberculosis prevalence, incidence, and mortality

This led to a Karlson-Holm-Breen test, the findings from which showed that social protection significantly mediated the association between GDP per person and disease burden (appendix). When we ran the models separately See online for appendix excluding European nations, the inverse associations were stronger than in the complete data models (appendix). No significance could be shown between social protection levels and tuberculosis burden in the Europe-only models because of too few data points (appendix).

Discussion

Our findings show a clear ecological association between social protection spending (as a percentage of GDP) and tuberculosis prevalence, incidence, and mortality. This was especially true in settings with low levels of social protection spending.

Because of the ecological nature of this study, we cannot show a causal association between socialprotection spending and tuberculosis burden. However, the inverse association shown in this analysis supports further research in this area. Bolstering this relation is the large amount of evidence for the more proximal, poverty-driven risk factors of the disease, such as malnutrition, overcrowding, and air pollution, as well as poverty itself.^{13,14,16–18} We chose not to control for these measures because we believe them to be on the causal pathway between social protection and tuberculosis. To more conclusively explain this pathway, we recommend the inclusion of detailed social protection questions in both future national tuberculosis prevalence surveys and stand-alone studies of tuberculosis prevention. Furthermore, better national social-protection data are needed that provide not only information about overall levels of social protection, but also breakdowns of these



Figure 3. Estimated effect of an increase of one percentage point of GDP in social protection spending on tuberculosis prevalence, incidence, and mortality at different levels

Estimates are changes after an increase in social protection spending of 1% of GDP (95% CI bands); n=664 country-years. Models adjusted for GDP per person, levels of health expenditure, adult HIV prevalence, percentage foreign-born, population density, tuberculosis treatment success, and country-level fixed GDP effects. GDP=gross domestic product.

amounts by the type of social-protection programme.

Incomplete longitudinal country-level data restricted our study in two ways. First, they mitigated our ability to add more national-level measures related to tuberculosis to our models without sacrificing sample size. Because our covariates were often derived from disparate sources, each additional merging of datasets resulted in the loss of datapoints and thus statistical power. This issue affected our ability to include interaction terms to see if the association between social protection spending and tuberculosis burden differs in different settings.

Social protection spending might not have an immediate effect on tuberculosis burden; however, results from additional lagged analyses showed few differences from the main models (appendix). Our country fixed-effects specification addresses countryspecific uniqueness that does not vary by time. However, we acknowledge that the study might be threatened by ecological fallacy—ie, the inverse relation that we detected might not necessarily be applicable on an individual level.

GDP per person is a significant predictor of social protection spending in an unadjusted regression model (appendix). We included GDP per person in the model in an attempt to explore the effect of social-protection spending after controlling for national wealth. However, we recognise that confounding is still a threat to this research. Nevertheless, all measures in the models have variance inflation factors less than 2.5 and the coefficients of these two variables do not change markedly when one variable is excluded from the models.

The outcomes of our models are WHO estimates of tuberculosis prevalence, incidence, and mortality. WHO derives these estimates from notifications provided by the 202 national tuberculosis programmes in 2014, and results of national tuberculosis prevalence surveys. The latest WHO estimates, used in this analysis, were retroactively revised to include the results of the latest prevalence surveys. We acknowledge that some countries provide overestimates or underestimates of the true burden of tuberculosis; however, the extent of these inaccuracies is not known. Underestimates might arise from under-reporting or underdiagnosis of cases. Nonetheless, we believe WHO estimates are the best data available for tuberculosis burden.

Last, this analysis relies on the ILO's broad definition of social protection. Splitting social protection spending into programmatic areas would be beneficial to investigate how each programme's expenditures are associated with tuberculosis incidence, prevalence, and mortality. These results would both strengthen the analysis and provide information with higher policy relevance, guiding decisions about specific social protection investments. For example, social protection includes labour protections, which might not be as beneficial at reducing the burden of tuberculosis in countries with a large informal economy, compared with cash-transfer programmes. Such information was available in the study by Reeves and colleagues⁶ as a result of more harmonised data in Eurostat. A more refined measurement of social protection on a global scale would be helpful to determine which programmes or policies are best at reducing the morbidity and mortality associated with tuberculosis.

The results from this study support the notion that funding should be increased for upstream interventions that target the social determinants of tuberculosis, especially poverty alleviation. Although the main responsibility for social protection rests outside the health sector, ministries of health, and national tuberculosis-control programmes and their international technical partners should be proactively involved in the development of social-protection policies and schemes and coordination of their implementation, to maximise the positive effects on health.

The benefits of increased social protection spending go beyond tuberculosis and would be likely to affect the burden of other communicable and non-communicable diseases, especially those with a well documented association with poverty. In fact, results from a study of OECD countries from 1995 to 200519 showed that social expenditure was more closely tied to indicators of health than direct health-services expenditure. The investigators of this study also noted 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. Our findings suggest that investments in social protection could contribute to a reduced tuberculosis burden. However, further research is needed to provide more evidence of these ecological associations.

Contributors

AS and KL conceived the idea for the study. AS did the literature review, obtained, cleaned, and analysed the data, and led the report writing and data interpretation. KL assisted with the literature review, data interpretation, and writing of the report. NAP assisted in guiding the conceptual design, technical specifications of the models, and contributed to revisions of the report.

Declaration of interests

KL and AS are employed by WHO's Global TB Programme. NAP declares no competing interests.

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