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Economics and business statistics

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2020-03

Series editors Dr Nicholas Rohde and Dr Athula Naranpanawa **ISSN** 1837-7750

Department of Accounting, Finance and Economics

Explaining inequalities in COVID-19 mortality between U.S. States

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Abstract

The U.S. has the most confirmed cases of coronavirus in the world, and all the states have been affected in varying degrees, including the death rates. Washington, New York, Oklahoma, have COVID-19 deaths rates of over 4.5%, which is three times higher than Tennessee and Texas death rates, of 1.8%.[1] It is unknown whether such inequalities reflect differences between states in their population characteristics, socio-economics, health, and tobacco environmental or all of these. We used data from the COVID-19 data repository of the Johns Hopkins Center for Systems Science and Engineering (Baltimore, MD, USA) to examine state-by-state differences in COVID-19 mortality rates. We estimate regression models to determine the independent effect of pre-pandemic tuberculosis rate on COVID-19 death rates. We exploit differences in tobacco policy environment across states to build an instrument for our main variable of interest – pre-existing tuberculosis prevalence. We show that a significant proportion of the observed interstate variation can be traced back to pre-existing prevalence of tuberculosis. Our results imply that pre-existing tuberculosis rates are associated with an increase in COVID-19 mortality rates of 3.2 to 7.4 deaths per 100,000 population. Our findings point to the need for considering pre-existing tuberculosis context in designing interventions aimed at reducing pandemic transmission. Identifying heterogeneity in the state-by-state distribution of tuberculosis cases and characterising its drivers can help to inform targeted public health response and can benefit efforts to stop the spread of COVID-19.

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[1] Author's calculation.

INTRODUCTION

Why do some U.S. states have a higher COVID-19 fatality rate than others? The answer to this question can provide useful information for the design and implementation of policy interventions. In this paper, we show that a significant proportion of the observed interstate variation can be traced back to the pre-existing prevalence of tuberculosis. Tackling the tuberculosis pandemic is therefore likely to have positive externalities for COVID-19.

Geographical inequality in US adult mortality has been studied in the context of spatially patterned characteristics of the population and the socio-economic environment. These include social cohesion (e.g. inequality of income distribution, unemployment, incidence of violent crime) (Montez *et al*. 2016; Singh and Siahpush, 2014), economic opportunities (e.g. median household income, aggregate real income, educational expenditure, and education attainments) (Dunn et al., 2005; Kinding and Cheng, 2013; Morgan and Morgan, 2013; Montez *et al*. 2019), and racial and demographic factors (Ezzati *et al*. 2008; Bime *et al*. 2016). Interestingly, some recent analysis suggests that part of the variation due to race is explained by other characteristics, primarily education attainments and exposure to risk factors such as obesity and smoking (Elo *et al*. 2017).

While data are still preliminary, some evidence on factors affecting variation in COVID-19 mortality is starting to emerge. Studies emphasise several common characteristics shared by at-risk individuals, including older age (Diamond *et al.* 2020; Zhou *et al*. 2020), pre-existing conditions/comorbidities (e.g. other respiratory disease, hypertension, cardiovascular disease) (Cen *et al.* 2020; Wu *et al*. 2020a; Diamond *et al.* 2020; Ahmed *et al.* 2020), and obesity and smoking (Wu *et al.* 2020b, Wang *et al.* 2020). The availability of hospital beds in the relevant territorial administration is another relevant risk factor (Wu et al. 2020).

Our study joins these two strands of the literature to estimate the contribution of pre-existing tuberculosis prevalence to the observed variation in COVID-19 mortality in the U.S. Miller et al. (2020) identify a correlation between Bacille Calmette Guerin (BCG) immunization policy and reduced morbidity and mortality for COVID-19. However, other studies argue that this correlation is not significant (Li *et al.* 2020) or spurious (Fukui *et al*. 2020). We contribute to this debate in two ways. First, we look at tuberculosis prevalence directly, so to focus on the outcome of the policy intervention rather than the input. Second, we take advantage of significant differences in the tobacco policy environment across U.S. states to instrument our variable of interest.

DATA AND RESULTS

We used data from the COVID-19 data repository of the Johns Hopkins Center for Systems Science and Engineering (Baltimore, MD, USA) to examine state-by-state differences in COVID-19 mortality rates.[2] We estimate multivariate regressions that relate recent COVID-19 death rates to pre-pandemic tuberculosis rate (TB) across states.[3] The percentage of tuberculosis cases vary significantly by geographical location across the U.S. states. In 2018, among the U.S. states, the majority of TB cases continued to be reported from 4 states: California (23.2%), Texas (12.5%), New York (8.3%), and Florida (6.5%) (Centre for Disease Control and Prevention). Low-socioeconomic status and ethnic background continue disproportionally to bear the burden of tuberculosis among U.S. born individuals (Noppert *et al.* 2017).[4] The immune status that makes people vulnerable to tuberculosis could also make them susceptible to coronavirus infection and increase disease severity (Liu *et a.* 2020).

We estimate regression models to determine the independent effect of pre-pandemic tuberculosis rate on COVID-19 death rates.[5] We include state-level socioeconomic characteristics (gross state product per capita, percent of adults 25 years and older with a bachelor's degree, unemployment rates as percentage of the labor force, proportion of population above aged of 65, violent crime rate, number of hospital beds) and pre-existing health characteristics (hypertension and kidney prevalence). We account for omitted variable bias in an instrumental variable model by considering tobacco environment as a potential risk factor for tuberculosis infection and disease progression.[6] We use as instruments state-level controls for average cost per cigarette pack and state tax as percent of retail price of cigarette.[7] The exclusion restriction rests on the assumption that average cost per cigarette pack and state tax as percent of retail price of cigarette do not affect the COVID-19 outcome directly.

[2] Data of COVID-19 cases and death per state were obtained from John Hopkins University Coronavirus Resource Centre on 9th April 2020. Although there is no ideal geographic level for examining health inequalities, there is long and prominent tradition of focusing on states (e.g., Patel et al., 2014).

[3] Tuberculosis (TB) remains one of the major causes of infectious morbidity and mortality globally, claiming millions of lives every year. Approximately one-third of the world's population is estimated to be infected with *Mycobacterium tuberculosis*, giving rise to 10 million cases of active TB disease each year (WHO, 2019).

[4] The tuberculosis rates are higher among Hispanics, blacks or African Americans. In 2015, about 87% of the TB cases in the U.S. were in racial and ethnic minorities (Centres for Disease Control and Prevention).

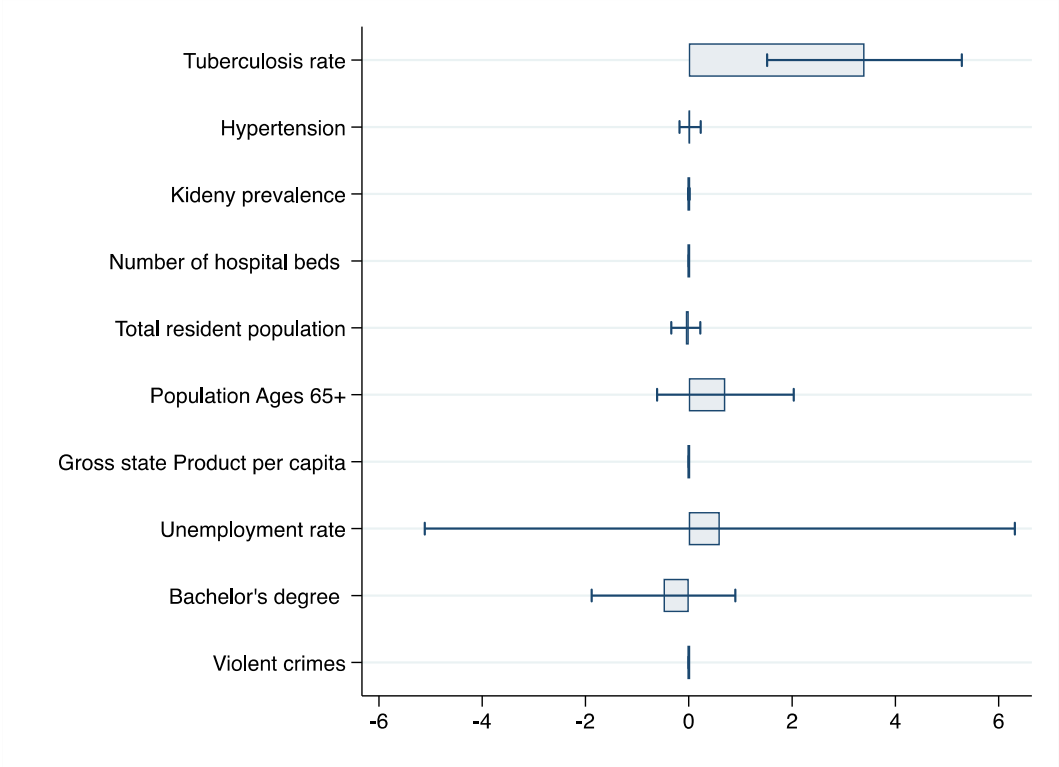
[5] Death rate refers to the number of people who die from coronavirus compared with the number of confirmed cases. According to John Hopkins University Coronavirus Resource Centre the global death rate is 4.5%.

[6] Smoking is a leading cause of preventable disease, disability, and death in the United States (HHS, 2014).

[7] The instrumental variable method allows us to estimate the coefficient of interest (pre-pandemic tuberculosis rate) consistently and free from asymptotic bias from omitted variables, without actually having data on the omitted variables or even knowing what they are (Angrist and Krueger, 2001).

We find a significant association between the pre-existing tuberculosis rates and COVID-19 mortality rates. In a most parsimonious specification, while only controlling for the proportion of elderly individuals (+65), our results imply that pre-existing tuberculosis rates are associated with an increase in COVID-19 mortality rates of 2.7 deaths per 100,000 population.[8] Controlling for socioeconomic and pre-existing health conditions increases slightly the magnitude of the main coefficient of interest, and we find a statistically significant increase in COVID-19 mortality rates of 3.2 deaths per 100,000 population (see Fig. 1). We see no significant predictive effect of the pre-existing hypertension and kidney health conditions, and socio-economic characteristics. To assess the robustness of our results to potential outliers we repeat the analysis excluding New York state.[9] Our results remain robust to this sample exclusion.

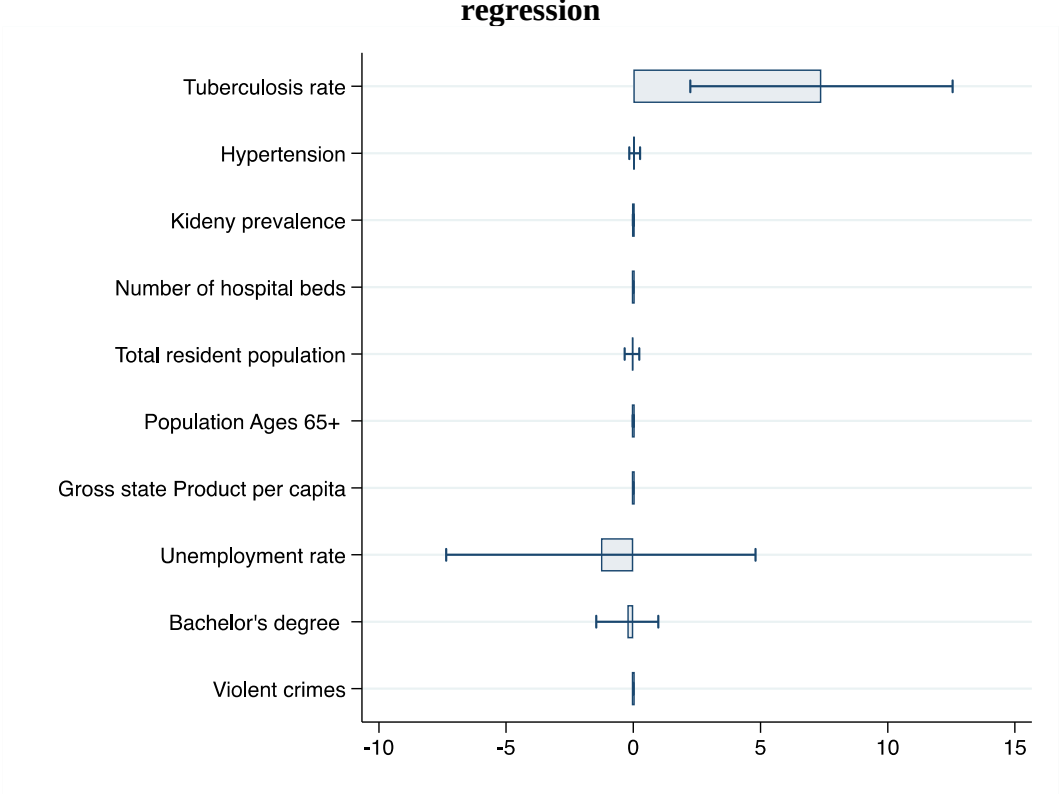
Figure 1 COVID-19 and pre-existing tuberculosis rate for the 50 U.S. states – OLS regression



[8] Table A 2. shows four specifications in which variables were added sequentially. The first specification includes proportion of elderly individuals (+65), and column (2) adds in addition health conditions, such as hypertension and kidney prevalence. In columns (3) and (4) we expand the regression model by controlling for total resident population, gross state product per capita, and number of hospital beds, unemployment rate and percent of adults 25 years and older with a bachelor's degree, respectively.
[9] New York state has experienced the most severe COVID-19 outbreak and we anticipate that it may influence our analysis.

The instrumental variable estimates are twice as large - other things equal. Our results imply that pre-existing tuberculosis rates are associated with an increase in the COVID-19 mortality rates of 7.4 deaths per 100,000 population (see Fig. 2). The first-stage result indicates that the coefficients for the average cost per cigarette pack and state tax as percent of the retail cigarette price are highly significant, indicating that the two instruments are strong predictors for the prevalence of tuberculosis. Previous systematic reviews and meta-analyses of observational studies have shown a strong association between the global epidemics of tuberculosis and smoking, exposure to tobacco smoke having been associated with tuberculosis infection, active tuberculosis, and tuberculosis-related mortality (Bates *et al.*, 2017). Other things equal, we demonstrate that higher average cost per pack and the state taxation are reducing significantly the incidence of tuberculosis (see Table A 2).

Figure 2: COVID-19 and pre-existing tuberculosis rate for the 50 U.S. states – IV regression



This study has several limitations. The present analysis cannot approximate relationships at the individual level; instead relationships between state aggregate characteristics are described. Although we have done considerable exploration of alternative factors, this article does not demonstrate causality as the analysis is limited by data availability. Individual level data from across the U.S. and other countries about deaths by age, underlying medical conditions,

medications being taken at time of death, and other factors could help us understand how the COVID-19 behaves at both a population and individual level. While we have tried to address a range of factors identified as important in mortality context, including tobacco policy environment, our analysis may not capture all of the factors that contributed to the COVID-19 mortality. In particular, our analysis does not account for local state interventions in response to the pandemic that could have influenced the variation in the COVID-19 death rates across states.

DISCUSSION

"The current pandemic is not COVID-19 but tuberculosis. It is worth comparing the COVID-19 and tuberculosis pandemics to ensure that, while we focus on the former, we do not forget the latter" (Wingfield, et al., 2020). Our findings support the view that tackling the tuberculosis pandemic generates positive externalities for the COVID-19 pandemic. While we do not establish a direct casual effect between the Bacille Calmette-Guerin (BCG) vaccine and COVID-19 mortality, our results indicate that a policy aimed at preventing the spread of tuberculosis will likely reduce mortality from COVID-19. A second important corollary finding of our analysis is that the tobacco policy environment, through its impact on the prevalence of tuberculosis, can also contribute to reducing COVID-19 mortality. Future work should extend the analysis towards the estimation of a more structural set of relationships, whereby the determinants of tuberculosis prevalence and its effect on COVID-19 are jointly estimated.

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Appendix

Table A 1. State contextual characteristics, data sources, and years of coverage

Characteristic (data source in brackets)	Year
Economic Environment	
1. Real gross state product per capita	2018
2. Education expenditures per capita	2017
3. % of adults aged 25+ years with a bachelor's degree or higher	2018
Health conditions	
4. Tuberculosis rate	2018
5. Hypertension	2018
6. Kidney prevalence	2018
Social Cohesion and population	
7. Gini coefficient of household income inequality	2018
8. Unemployment rate	2019
9. Total resident population	2019
10. Population ages 65+	2018
11. Violent crime rate	2008
Tobacco Environment	
12. State tax as percent of retail price of cigarettes	2018
13. Average cost per cigarette pack	2018

References

[1] U.S. Bureau of Economic Analysis.
[2] Urban Institute & Brookings Institution.
[3] U.S. Census Bureau.
[4] Centers for Disease Control and Prevention.
[5] Hypertension Hospitalization Rate per 1,000 Medicare Beneficiaries.
[6] Kidney prevalence per million state residents. Centers for Disease Control and Prevention. Chronic Kidney Disease Surveillance System.
[7] U.S. Census Bureau. *Income. Gini ratios by state.*
[8] U.S. Bureau of Labor Statistics. Unemployment Rates shown are a percentage of the labor force.
[9] U.S. Census Bureau.
[10] U.S. Census Bureau. Vintage 2018 Population Estimates.
[11] U.S. Violent Department of Justice, Federal Bureau of Investigation, Crime in the United States, annual.
[12] *State Tobacco Activities Tracking and Evaluation (STATE) System.*
[13] *State Tobacco Activities Tracking and Evaluation (STATE) System.*

Table A 2. OLS and IV regressions with state COVID-19 as a function of pre-existing tuberculosis

	OLS				First-stage	IV
	(1)	(2)	(3)	(4)	(5)	(6)
Pre-pandemic Tuberculosis rate	2.776***	3.173***	3.629***	3.194***	-	7.393***
	(0.643)	(0.739)	(0.736)	(1.021)		(2.631)
Population ages 65+	-0.001	-0.002	-0.002	-0.008	-0.001	-0.002
	(0.001)	(0.001)	(0.001)	(0.013)	(0.001)	(0.013)
Hypertension	-	0.070	0.053	0.018	-0.006	0.051
		(0.089)	(0.093)	(0.115)	(0.010)	(0.108)
Kidney prevalence	-	0.004	0.004	0.001	0.000	0.005
		(0.006)	(0.007)	(0.008)	(0.001)	(0.009)
Total resident population	-	-	-0.077	-0.039	0.002	-0.000
			(0.140)	(0.146)	(0.014)	(0.000)
Real GDP per capita	-	-	-0.000	-0.000	0.000	-0.000
			(0.000)	(0.000)	(0.000)	(0.000)
Number of hospital beds	-	-	-	0.000	0.000	0.000
				(0.001)	(0.000)	(0.001)
Unemployment rate	-	-	-	0.863	0.172	1.274
				(2.902)	(0.289)	(3.102)
Bachelor's degree	-	-	-	-0.318	-0.024	-0.239
				(0.718)	(0.064)	(0.622)
Violence crime	-	-	-	-0.000	0.000	-0.000
				(0.000)	(0.000)	(0.000)
Average cost per cigarette pack	-	-	-		-1.896***	
					(0.494)	
State tax as % of retail cigarette price	-	-	-	-	-1.927***	-
					(0.603)	
First- stage *F-statistics*	-	-	-	-	13.96	-
Sargan statistics p-value					0.9045	
Durbin-Wu-Hausman test p-value						0.0366
N	50	50	50	50	50	50
R_2	0.103	0.141	0.170	0.195		0.138

Notes: Standard Errors clustered at state level are in parentheses. *p< 0.1, **p<0.05, ***p<0.01. The The first–stage *F–statistics* on the excluded instruments compare favourably with the Stock and Yogo (2005) rule-of-thumb threshold. The Sargan test of the overidentifying restriction (*p*-value) implies that the overidentifying restrictions are valid and cannot be rejected, thus confirming that the two instruments are well determined. Endogeneity test corresponds to Durbin-Wu-Hausman (DWH) test (*p*-values).