EClinicalMedicine
Published by THE LANCET

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RESEARCH PAPER | VOLUME 25, 100464, AUGUST 01, 2020

A country level analysis measuring the impact of government actions, country preparedness and socioeconomic factors on COVID-19 mortality and related health outcomes

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Open Access • Published: July 21, 2020 • DOI: https://doi.org/10.1016/j.eclinm.2020.100464

Abstract

Background

A country level exploratory analysis was conducted to assess the impact of timing and type of national health policy/actions undertaken towards COVID-19 mortality and related health outcomes.

Methods

Information on COVID-19 policies and health outcomes were extracted from websites and country specific sources. Data collection included the government's action, level of national preparedness, and country specific socioeconomic factors. Data was collected from the top 50 countries ranked by number of cases. Multivariable negative binomial regression was used to identify factors associated with COVID-19 mortality and related health outcomes.

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Increasing COVID-19 caseloads were associated with countries with higher obesity (adjusted rate ratio [RR]=1.06; 95%CI: 1.01–1.11), median population age (RR=1.10; 95%CI: 1.05–1.15) and longer time to border closures from the first reported case (RR=1.04; 95%CI: 1.01–1.08). Increased mortality per million was significantly associated with higher obesity prevalence (RR=1.12; 95%CI: 1.06–1.19) and per capita gross domestic product (GDP) (RR=1.03; 95%CI: 1.00–1.06). Reduced income dispersion reduced mortality (RR=0.88; 95%CI: 0.83–0.93) and the number of critical cases (RR=0.92; 95% CI: 0.87–0.97). Rapid border closures, full lockdowns, and wide-spread testing were not associated with COVID-19 mortality per million people. However, full lockdowns (RR=2.47: 95%CI: 1.08–5.64) and reduced country vulnerability to biological threats (i.e. high scores on the global health security scale for risk environment) (RR=1.55; 95%CI: 1.13–2.12) were significantly associated with increased patient recovery rates.

Interpretation

In this exploratory analysis, low levels of national preparedness, scale of testing and population characteristics were associated with increased national case load and overall mortality.

Funding

This study is non-funded.

Keywords

COVID-19 • Public health policies • Country-level analysis

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Research in context

Evidence before this study

In a matter of weeks after the World Health Organization (WHO) declaring a global pandemic for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), over 100 countries implemented varied levels of containment in order to reduce disease

ansmission. Some evidence suggested that strict social distancing measures ar ... er

terventions may limit spread of this novel pathogen, originating from individu countries or from jurisdictions within countries. To our knowledge, no published articles have used a country-level analysis, pooling data across multiple countries, to report the impact of population health interventions, country-specific socioeconomic factors, and healthcare capacity on overall COVID-19 cases (recovered or critical), and associated mortality.

Added value of this study

We built a country-level model, incorporating data from 50 different countries, to assess country-specific socioeconomic factors and healthcare capabilities on COVID-19-related outcomes such as new case burden, critical cases, and mortality. Our country-level model demonstrated that travel restrictions and containment measures put in place up till 01 May 2020 may have an impact on the total number of COVID-19 cases in a given country, but there was no observed association between public health policies and the number of critical cases or mortality. Importantly, low levels of national preparedness in early detection and reporting, limited health care capacity, and population characteristics such as advanced age, obesity and higher unemployment rates were key factors associated with increased viral spread and overall mortality.

Implications of all the available evidence

As governments consider partially or completely lifting travel restrictions and containment measures, understanding the roles of these policies in mitigating infection is imperative to minimize the impact of second and third waves of outbreaks. A careful consideration of epidemiological evidence can help governments identify socioeconomical and baseline population health factors that might indicate an added level of risk and additional challenges while trying to contain COVID-19.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing coronavirus disease 2019 (COVID-19), was declared a global pandemic on March 11, 2020 by the World Health Organization (WHO), affecting over 100 countries in a matter of weeks [1]. On April 1, 2020 the WHO reported that COVID-19 had been detected in more than 200 countries and territories, with approximately 823,626 confirmed cases and 40,598 deaths [2]. Countries have differed significantly in their individual approaches in the management of this pandemic. At the time of publication, there remains no widely available vaccine or widespread population immunity. An evidence-based strategy to assist governments and healthcare systems worldwide is imperative. While public health policies to limit exposure and manage population risk remain in place in many jurisdictions, governments continue to plan for a return to economic and social life. An understanding of factors at the national level associated with a higher population risk for more widespread infection, severity of illness, and mortality is critical. The impact of existing national policies, and the association of specific country-level factors with outcomes, is urgently required as many jurisdictions have begun the process of relaxing public health interventions – with an accompanying risk of subsequent waves of infection [3].

At present, public health policies across countries have varied considerably with respect to the restrictiveness of interventions, the acceptance of widespread implementation, and presumed effectiveness in reducing disease transmission. Measures such as the detection and isolation of infected individuals, contact-tracing, quarantine measures, physical distancing, and closure of non-essential businesses have become major components of public health guidance, aiming to reduce the spread of further infection, and prevent health system strain [4]. Although containment measures implemented in countries like China, South Korea, and Taiwan have reduced new cases by more than 90%, this has not been the case in many other countries such as Italy, Spain, and the United States [5,6]. Despite appropriate public health guidance, less than optimal population compliance in western democracies may be an important contributing factor to variation in outcomes among the various countries. In addition, the timing of implementation of public health measures [7], pre-existing socioeconomic characteristics of the country, baseline healthcare capacity, and other health-related population features (i.e. smoking prevalence, obesity rate, and global health indices) may be contributing factors to disparities in outcomes between countries.

In this exploratory analysis, our objective was to examine country-specific public health ...entions to contain the virus spread. Knowing the most effective interventions in ...ning COVID-19 caseloads (recovered or critical) and reducing overall m... ity assist health policy makers in resource allocation decisions, provide evidence regarding the effectiveness of population health measures, and assist countries with internal geographic disparities in mitigating risk with more informed resource planning.

We accessed publicly available COVID-19 surveillance data from the top 50 countries in terms of reported cases to assess the impact of population health interventions (e.g. containment measures such as lockdowns, border closings), country-specific socioeconomic factors, and healthcare capacity on overall COVID-19 cases (recovered or critical) and deaths.

2. Methods

2.1 Data extraction

Publicly available information on COVID-19 related national policies and health outcomes consisting of the total number of cases, recovered cases, critical cases and overall mortality (expressed per million population) were extracted from websites such as the John Hopkins University – Center for Science and Engineering (JHU-CSSE) [8], the World Health organization (WHO) [9], the Centers for Disease Control and Prevention (CDC) [10] and the Worldometer Coronavirus Statistics website [11]. The first reported case in China was set as 31 December 2019, based on when it was reported to the WHO [12]. The first reported COVID-19 case for each index country was obtained from the WHO Situation Reports [9]. The COVID-19 status of each country from JHU-CSSE included the total and recovered number of COVID-19 cases and the associated mortality. Since the data was continuously evolving, 01 May 2020 was set as the final data capture timeline as many countries began relaxing more restrictive public health policies around this time. Only data for the top 50 countries as of April 01, 2020 by number of case counts were included in the current analysis (listed in electronic-supplementary Table-1). However, data on the number of critical cases were only available as of April 01, 2020.

Data for public health policies for each country was captured through various sources. These included types of travel restrictions: (1) no measures implemented; (2) partial border closures, i.e. limited to either certain areas or limited to travelers from certain high-risk countries; (3) complete border closure, i.e. closure to all travelers except returning citizens of the index country. Similarly, data for containment measures was also collected: (1) no measures implemented; (2) partial lockdown, i.e. physical cing measures only; (3) complete lockdown, i.e. enhanced containme asi ing suspension of all non-essential services; (4) and curfew implemen ə. s at-home orders limited to specific hours. Implementation dates of these policies were used to determine the time from the first reported case to implementation (in days) in each country.

Data collection also included country level statistics and indices such as GDP per capita based on purchasing power parity (2019) [13], total population (2019) [13], median population age (2020) [14], gender distribution of population (%) [15], population density (people per km^2) [11], unemployment rate (% of total labor force) [13], Corruption Perceptions Index score (2019) [16], and family income dispersion measured by the Gini index [17]. The Gini index is a measure of dispersion intended to represent the income or wealth distribution of a nation's residents. It is the most commonly used measurement of wealth inequality [18]. The Gini index ranges from 0, indicating perfect equality (where everyone receives an equal share), to 100, perfect inequality (where only one recipient or group of recipients receives all the income) [17]. Our interest in including the Gini Index was to see if high levels of systemic corruption in the flow of goods and services within a nation impact the risk of COVID-19 related death and other clinical outcomes. Other country level statistics consisted of the Corruption Perceptions Index, which is published annually, ranks 180 countries by their perceived levels of public sector corruption, as determined by expert assessments and opinion surveys. It is expressed as a scale from 100 (very clean) to 0 (highly corrupt) [16]. Similarly, the global health security (GHS) index score was also obtained for each country [19]. The GHS Index is a comprehensive assessment of health security and related capabilities across the 195 countries, which grades the state of preparedness upon the emergence of a pandemic [19]. The index is subdivided into six categories, with scores ranging from 0 to 100: Prevention of the emergence or release of pathogens; Early detection and reporting of epidemics of potential international concern; Rapid response to and mitigating the spread of an epidemic; Sufficient and robust health system to treat the sick and protect health workers; Compliance with international norms; Overall risk environment and country vulnerability to biological threats. Higher scores in each of the categories indicate a greater level of national preparedness [19].

Data on healthcare capacity was also collected for each country and consisted of the number of hospital beds[20], number of ICU beds[21,22], number of physicians, and the number of nurses per million of population[23]. The current health expenditure of each country per capita ($US) was also obtained and included in the analysis [13]. Population fitness levels and comorbidities that may be contributing factors towards COVID-19 outcomes were abstracted from public sources and consisted of smoking ence (% of adults)[24], diabetes prevalence (% of adults) [25], obesity le defined as body mass index ≥ 30 (% of adults) [23], adult mortality risk (i.e. risk of dying between ages 18 and 65)[23] as well as the Bloomberg Global Health index score (GHI) [26]. The GHI ranks 163 countries based on variables such as life expectancy, environmental factors, and health risks including malnutrition, high blood pressure, and tobacco use with a score from 100 (healthiest) to 0 (most unhealthy) [26].

2.2 Statistical analysis

The unit of analysis was each individual country, and baseline information on each nation was presented descriptively as medians, means and proportions, with 95% confidence intervals (95%CI). 95%CIs were also presented for medians, which represent the 2.5% and 97.5% percentiles. Event rates as descriptive measures were calculated by dividing the number of COVID-19 related events by the total number of reported cases. The outcome variables of interest were the total number of cases, recovered cases, critical cases, and overall mortality, all expressed per million population (as of May 01, 2020).

Poisson regression modeling (PRM) is typically used to evaluate count data. However, overdispersion, which occurs when the conditional variance exceeds the conditional mean, must be assessed. Negative binomial regression modeling (NBRM) can be used for over-dispersed count data. If the dependent variable is over-dispersed, the confidence intervals for the coefficients of NBRM are likely to be narrower relative to those generated from PRM. In the current analysis, each model was assessed for overdispersion using the Likelihood ratio test, which compares the Log likelihood generated from a Poisson and Negative binomial regression model. The difference in 2 x ($\ln L_{NBRM} - \ln L_{PRM}$) is equal to a chi square with one degree of freedom. A statistically significant difference is consistent with the presence of overdispersion.

An initial assessment of the data indicated considerable over-dispersion, precluding the use of Poisson regression for count data. Therefore, a series of main effects multivariable negative binomial regression models were built to identify the factors significantly associated with COVID-19 mortality as well as the other health outcomes (a total of 4 models). The main exposure variable for each model, which is amount of time an observation was at risk, was the duration of virus exposure in days, from the first reported case in the reference country until May 01, 2020. Given the limited sample size (n = 50 countries), which increases the risk of overfitting in regression analysis, the potential predictors (independent variables) for model inclusion were first identified by a ...iable screening process with a pre-set p = 0.25. This is a recommended approa... ...noving weak predictors so that a more manageable set of predictor va...es ...

be utilized with multivariable techniques [27]. The Likelihood ratio test was then used in a backwards elimination process ($p < 0.05$ to retain) to select the final set of independent variables for retention in the COVID-19 outcome models. Special data handling methods were not be employed for dealing with missing data for the predictor or outcome variables. All outcomes of the regression analysis were reported as rate ratios (RR), where a value less than one suggests a decreased likelihood and a value of greater than one an increased likelihood of the event under investigation. Model goodness of fit and evaluation of outliers were assessed by the Akaike information criterion (AIC), the Bayesian information criterion (BIC) and McFadden's pseudo R-squared statistic. Individual models were assessed with and without potential outliers to evaluate their impact on the results. All of the statistical analyses were performed using Stata, release 16.0 (Stata Corp., College Station, Texas, USA).

Role of Funding Source: Not applicable

3. Results

3.1 Characteristics of selected countries

Socioeconomic and health capacity related characteristics of the 50 countries with the highest COVID-19 cases as of May 01, 2020 are summarized in Table 1 (reported as medians and 95% CI). The median population size of the country sample was 32.6 million (11.1, 55.1) and the population density per km^2 was 101 (69.4137). In the year 2020, the projected median age from the entire sample was 40 years (36,42) and the percent females was 50.4% (50.2%, 50.7%). Among the sample of 50 countries, the median GDP per capita ($US) was $23,122, of which $1914 ($45, $10,246) was allocated for health care spending. The median percentage of the population recorded as unemployed was 5.2% (4.2%, 5.9%) and the overall Gini coefficient and corruption index scores were 35.4 (30.8, 41.4) and 58.5 (46.1, 69.0), respectively (Table 1). Furthermore, the prevalence of obesity, smoking and diabetes (types 1 and 2) was 22.1% (20.2%, 23.1%), 34.0% (29.1%, 39.9%), and 6.75% (5.85%, 7.65%), respectively. The median rate of adult mortality per 1000 people was 74 (65.7, 93.7), and the median GHI score was 84.8 (82.6, 87.0). The median number of hospital and ICU beds per million population of selected countries was 3092 (2662, 4243) and 87 (65.5, 112), while the number of physicians and nurses were 2866 (2311, 3521) and 6235 (5379, 8343) per million population, respectively (Table 1). Finally, the overall GSH score of included countries was 58.4 (53.6, 60.6).

Table 1 Socioeconomic and health related characteristics of selected countries.

Characteristic (median; 95%CI)[1]	Outcome (*n* = 50)
Population in millions	32.6 (11.1 to 55.1)
Median population age in 2020	40 (36 to 42)
Percent females within the population	50.4% (50.2 to 50.7%)
Population density (people per km^2)	101 (69.4 to 137)
Socioeconomic characteristics	
Per capita GDP ($US)	$23,122 ($13,777 to $41.370)
Health care spending per capita ($US)	$1914 ($45 to $10,246)
Percent unemployment	5.2% (4.2 to 5.9%)
Income dispersion within the nation[2]	35.4 (30.8 to 41.4)
Level of corruption within the nation[3]	58.5 (46.1 to 69.0)

Abbreviations: GDP = gross domestic product, ICU = intensive care unit.

1 Missing data due to unavailability was present for the number of physicians per million population (36% missing) and GHI score (32% missing).

2 Income dispersion is measured by the Gini coefficient, which is presented on a scale from 0 to 100. Countries with a more uniform dispersion of wealth have higher scores.

3 Corruption within a country is measured by the Corruption Perceptions Index, which is presented on a scale from 0 to 100. Countries with less systemic corruption in their institutions have higher scores.

4 Probability of dying between 15 and 60 years per 1000 population.

5 Measured on a scale from 0 to 100, the GHI score grades countries on variables such as life ancy, overall fitness and imposes penalties on health risks such as tobacco use and . It also takes into consideration environmental factors such as access to cl ate

sanitation.

6 Measured on a scale from 0 to 100 and presents a country's overall preparedness in the event of a global pandemic. Higher scores indicate a greater level of national preparedness.

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3.2 COVID-19 infection characteristics as of May 01, 2020

The characteristics of COVID-19 infections among the top 50 countries with the most cases as of May 01, 2020, along with government responses are summarized in Table 2 (as medians and 95%CI). When expressed per million population, the median number of cases was 1032 (670, 1598), recovered cases 201 (123, 480), critical cases 7 (2.85,14.6), and deaths at 33 (16, 53). Furthermore, the median number of COVID-19 tested population was 10,657 (5709, 22,809) per million. Finally, the overall reported rates for mortality, critical cases and recovered cases were 4.20% (3.14%, 5.69%), 2.47% (1.92%, 3.70%), and 40.2% (26.8%, 54.2%), respectively.

Table 2 COVID-19 infection characteristic and government responses.

Characteristic as of May 01, 2020 (median; 95%CI)[1]	Outcome (*n* = 50)
Number of cases	17,054 (10,674 to 25,809)
Number of recovered cases	4522 (2992 to 10,359)
Number of critical cases[2]	83 (50 to 148)
Number of deaths	620 (245 to 1194)
Total number of tests done	186,561 (106,385 to 275,848)
Testing per million population	10,657 (5709 to 22,809)
Cases per million population	1032 (670 to 1598)
Recovered cases per million population	201 (123 to 480)
Critical cases per million population[2]	7 (2.8 to 14.6)
Deaths per million population	33 (16 to 53)

1 Missing data due to unavailability occurred for total number of tests done (20% missing).

2 Data were only available until April 1, 2020.

3 Calculated by dividing the number of events by the total number of reported cases.

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Among the 50 countries included in the analysis, 38 (76%) had a complete border closures, while 10 (20%) had only partial border closures by April 01, 2020. The median time to any border closure from the first reported case in China was 78 days (77, 80), or 23 days (18, 44) from the first case in each country. Of the 50 countries, 40 (80%) had implemented a complete lockdown by the reference date (May 01, 2020), while a partial lockdown or a curfew was applied by 5 (10%) countries. The median time to any ...wn from first reported case in China or from first case in the reference ... try ... ays (76, 81) and 23 days (19, 32), respectively (Table 2).

3.3 Factors affecting COVID-19 spread and recovery

The findings of the multivariable regression analyses to identify factors associated with COVID-19 total case rates and recovered cases (per million) are presented in Table 3. Predictors significantly associated with the total number of reported cases per million were days to any lockdown (i.e. full or partial), median age of population, prevalence of obesity, days to any border closure and number of tests performed per million population (Table 3). There was a negative association between the number of days to any lockdown (RR=0.94; 95%CI:0.91–0.98) and the total number of reported cases per million, where a longer time prior to implementation of any lockdown was associated with a lower number of detected cases per million. In contrast, those countries with a higher median population age (RR=1.10; 95%CI:1.05–1.15), prevalence of obesity (RR=1.06; 95%CI:1.01–1.11) and a longer number of days to any border closure (RR=1.04; 95%CI 1.01–1.08) had significantly higher caseloads. When the analysis was continued on the outcome variable 'recovered cases per million'; a full lockdown (versus partial/curfew only; RR=2.47; 95%CI:1.08–5.64); and a higher GHS risk environment (RR=1.55; 95%CI:1.13–2.12) were positively associated with an increased number of recovered cases (Table 3).

Table 3 Multivariable negative binomial regression analysis on COVID-19 case diagnosis and successful resolution of disease.

Variable[1]	RR	SE	(95%CI)
Cases per million[2]			
Significant independent variables[3]			
Days to any lockdown[4]	0.94	0.08	(0.91 to 0.98)
Days to any border closure[5]	1.04	0.02	(1.01 to 1.08)
Tests per million population	1.001	(< 0.001)	(1.000 to 1.001)
Median age of population	1.10	0.03	(1.05 to 1.15)
Obesity prevalence (%)	1.06	0.027	(1.01 to 1.11)
McFadden's Pseudo R^2[6]	0.091		
Variable[7]	**RR**	**SE**	**(95%CI)**
Recovered cases per million			

Abbreviations: RR = rate ratios, SE = standard error, GHS = Global Health Security.

1 The model exposure variable, required for negative binomial regression analysis of this type, was the duration of virus exposure in days, from the first reported case in the reference country to May 1, 2020.

2 Dependent variable: cases per million population.

3 These were the final variables that were retained following the application of the Likelihood ratio test (*p* < 0.05 to retain) in a backwards elimination process. An RR of less than one means lower risk and greater than one and increased number of events. All continuous independent variables were centered on the mean.

4 Time to any lockdown from first case in reference country.

5 Time to any border from first case in reference country.

6 McFadden's pseudo R-squared is calculated as 1 – LR (full model)/LR (null model). Negative ... al regression does not have an equivalent to the R-squared measure found ... ina ... quares (OLS) regression. Hence, this statistic does not mean what R-square ... in

regression, which is the proportion of variance for the dependent that is variable explained by the predictor variables. Therefore, the statistic should be interpreted with caution.
7 Dependent variable: recovered cases per million population.
9 Probability of dying between 15 and 60 years per 1000 population.
10 Measured on a scale from 0 to 100 and presents a country's overall risk environment and vulnerability to biological threats. Higher scores indicate reduced vulnerability.

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3.4 Factors affecting COVID-19 critical cases rates and mortality

The next series of analyses focused on the number of critical cases and deaths per million. Socioeconomic variables positively associated with an increased number of critical cases per million for any given country were: a higher percent unemployment rate (RR=1.18; 95%CI:1.07–1.30) and per capita GDP (RR=1.02; 95%CI 1.01–1.4). In contrast, lower income dispersion scores (RR=0.92; 95%CI:0.87–0.97) and a higher prevalence of smoking within a population (RR=0.96; 95%CI:0.93–0.99) were associated with a reduction in the number of critical cases (Table 4).

Table 4 Multivariable negative binomial regression analysis on COVID-19 mortality and critical illness.

Variable[1]	RR	SE	(95%CI)
Critical cases per million[2]			
Significant independent variables[3]			
Income dispersion within the nation[4]	0.92	0.02	(0.87 to 0.97)
Unemployment rate (%)	1.18	0.06	(1.07 to 1.30)
Smoking prevalence (%)	0.96	0.01	(0.93 to 0.99)
Per capita GDP[5]	1.02	0.01	(1.01 to 1.4)
McFadden's Pseudo R^2[6]	0.073		
Variable[4]	**RR**	**SE**	**(95%CI)**
Deaths per million[7]			
Significant independent variables[3]			

Abbreviations: RR = rate ratios, SE = standard error, GDP = gross domestic product.

1 The model exposure variable, required for negative binomial regression analysis of this type, was the duration of virus exposure in days, from the first reported case in the reference country to May 1, 2020.

2 Dependent variable: critical cases per million population. Data were only available until April 1, 2020.

3 These are the final variables that were retained following the application of the Likelihood ratio test (*p* < 0.05 to retain) in a backwards elimination process. An RR of less than 1.0 means lower risk and greater than one and increased number of events. All continuous independent variables were centered on the mean.

4 Income dispersion is measured by the Gini coefficient, which is measured on a scale from 0 to 100. Countries with a more uniform dispersion of wealth have higher scores.

very thousand dollars increase in per capita GDP.

dden's pseudo R-squared is calculated as 1 – LR (full model)/LR (null model ati

binomial regression does not have an equivalent to the R-squared measure found in ordinary least squares (OLS) regression. Hence, this statistic does not mean what R-square means in OLS regression, which is the proportion of variance for the dependent that is variable explained by the predictor variables. Therefore, the statistic should be interpreted with caution.
7 Dependent variable: deaths per million population.

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When COVID-19 mortality was assessed, variables significantly associated with an increased death rate per million were population prevalence of obesity and per capita GDP (Table 4). In contrast, variables that was negatively associated with increased COVID-19 mortality were reduced income dispersion within the nation, smoking prevalence, and the number of nurses per million population (Table 4). Indeed, more nurses within a given health care system was associated with reduced mortality (Fig. 1). Mortality rates were also higher in those counties with an older population upon univariate analysis, but age as a factor was not retained in multivariable analysis (Fig. 2). Lastly, government actions such as border closures, full lockdowns, and a high rate of COVID-19 testing were not associated with statistically significant reductions in the number of critical cases or overall mortality.

Fig. 1

Fig. 1 **Mean deaths per million by number of nurses per million population, as of May 1, 2020 (*p* = 0.10 via one-way ANOVA, but *p* < 0.001 by multivariable analysis).**

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Fig. 2

Fig. 2 **Mean deaths per million by median age of country population, as of May 1, 2020 (*p* = 0.017 via one way ANOVA).**

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4. Discussion

An exploratory country level analysis using publicly available sources of data was conducted to examine factors associated with COVID-19 related health outcomes. Predictors evaluated consisted of government policies/actions for COVID-19 containment, scale of testing, country specific socioeconomic parameters, health care capacity, degree of preparedness, and population comorbidities. Consistent with reported COVID-19 outcome data from Europe, the United States, and China, higher caseloads and overall mortality were associated with comorbidities such as obesity [28], and advanced population age[29]. In contrast, a lower income dispersion within the nation reduced overall mortality and critical cases. Of all the GHS subscales evaluated, the index for risk environment had the most profound association with recovered cases per million. Countries that were the least vulnerable to biological threats (as indicated by higher scores) had the highest number of recovered cases. Indeed, for every ten-unit increase in the GHS score for risk environment, the relative rate of recovered cases increased by 55%.

There were a series of predictors with significant associations with the outcome variables that require careful interpretation. An increased scale of national testing was not associated with the number of critical cases, or deaths per million. The government policy of full lockdowns (vs. partial or curfews only) was strongly associated with recovery rates (RR=2.47; 95%CI: 1.08–5.64). Similarly, the number of days to any border closure was associated with the number of cases per million (RR=1.04; 95%CI: 1.01–1.08). This suggests that full lockdowns and early border closures may lessen the peak of transmission, and thus prevent health system overcapacity, which would facilitate increased recovery rates.

The final two variables significantly associated to poorer outcomes were per capita GDP and smoking prevalence. Countries with a higher per capita GDP had an increased number of reported critical cases and deaths per million population. This may reflect more widespread testing in those countries, greater transparency with reporting and better national surveillance systems. Other potential putative reasons for the association might include increase accessibility to air travel and international holidays in wealthier countries, as travel was identified as an important factor contributing to international viral spread [9]. The final unexpected finding was the lower frequency of critical cases and deaths in countries with a higher smoking prevalence. This finding requires further investigation, as the literature is inconsistent [30,31]. However, there was an interesting observation from a recently published paper describing 393 critical patients

COVID-19 admitted to two hospitals in New York City. The analysis revealed that only 5.1% of the patient sample were current smokers [32], compared to the 15.6% smoking incidence in United States reported by the CDC [33]. The finding of relatively lower smoking rates amongst critical ill COVID-19 patients is due in part due to their increased age distribution, since countries with a lower median age have higher smoking rates [33,34]. Hence, the potentially lower median age amongst countries with higher smoking prevalence in our model may be driving the observed association of low COVID-19 critical cases and deaths with high smoking prevalence. A potential protective effect of smoking was identified in a recent evaluation of 17 million adult patients within the National Health Service of the United Kingdom, with 5683 COVID related deaths [31]. In their analysis, current smokers were associated with a reduced risk of COVID-19 related mortality (adjusted HR = 0.88; 95%CI: 0.79–0.99) [31]. Notwithstanding these findings, more study is needed.

Several other studies have examined the impact of public health measures on local transmission of COVID-19, but the evidence was primarily from modeling evaluations [35, 36, 37]. However in a recent study, Cowling et al., evaluated a range of public health interventions (e.g. social distancing, border restrictions, quarantine and isolation) undertaken in Hong Kong to reduce the spread of COVID-19 [38]. The investigators used laboratory-confirmed COVID-19 case data to estimate the daily effective reproduction number (Rt), along with telephone surveys to assess population behavior changes for containing viral spread. It was determined that viral transmission declined when social distancing and other measures were implemented. In our study, an increasing number of days to border closures was associated with a higher caseload, and more restrictive public health measures (such as a full lockdown compared to partial or curfew only measures) were associated with an increase in the number of recovered cases per million population. These findings suggest that more restrictive public health practices may indeed be associated with less transmission and better outcomes. However, in our analysis, full lockdowns and wide-spread COVID-19 testing were not associated with reductions in the number of critical cases or overall mortality.

There are important limitations with our data, including the fact that at or prior to May 1, 2020, many countries included in our dataset were not yet in the “plateau” or downslope phase of their individual epidemiologic curves, with border restrictions having been introduced only very recently. In the context of COVID-19, it is thought that public health interventions typically require from 2 to 3 weeks to affect outcomes, hence the impact of pread border restrictions may not have yet been detected in our dataset [38,39]. onally, the relative difference in the number of cases in neighboring cc es likely to have a significant impact on whether border closures are effective. Two countries with similar epidemiologic curves and effective social distancing policies may not see a major impact from border closures, whereas two countries with very disparate epidemiologic curves may be more likely to see a significant impact from travel restrictions. In the case of full lockdowns, such a government policy may only be effective in those countries where it can be easily implemented and enforced. For example, the United States has had challenges enforcing lockdowns, with citizens in several states publicly protesting public health measures to limit viral transmission, and encouraging open revolt [40]. There was missing data for the number of physicians per million population (36% missing), the GHI score (32% missing), and the total number of tests performed (20% missing). This may introduce important unintended bias in our results. With only 50 countries, our dataset is somewhat limited, and our results may not be generalizable across other countries not included in this dataset. Furthermore, this was an exploratory study utilizing publicly available data which was not audited for accuracy or confirmed with individual public health units. Additionally, the case definitions between countries may have varied, and indeed the case definitions have been known to vary in the past. Notwithstanding these limitations, our findings propose avenues for further debate, research, and exploration, and do not support a definitive judgement on the effectiveness of various public health interventions implemented across different countries.

The findings of this country level analysis on COVID-19 related health outcomes suggest that low levels of national preparedness, scale of testing, as well as population characteristics such as obesity, advanced age and higher per capita GDP are associated with increased national case load and mortality.

Author Contributions

Rabail Chaudhry MD: This author helped design the study, collect the data, interpret the data, and write the manuscript. George Dranitsaris PhD: This author helped design the study, collect the data, perform the data analysis, interpret the data, and write the manuscript. Talha Mubashir MD: This author helped collect the data, interpret the data, and write the manuscript. Justyna Bartoszko MD: This author helped interpret the data and write the manuscript. Sheila Riazi MD: This author helped design the study, collect the data, interpret the data, and write the manuscript. This author had full access to all ta in the study and had final responsibility for the decision to submit f ation.

Data sharing statement

The authors declare that the data collected for the study was gathered from publicly available databases and is available upon request.

Funding

This study is non-funded.

Declaration of Competing Interest

Rabail Chaudhry MD, MSc: This author declares no financial interests.

George Dranitsaris PhD: This author declares no financial interests.

Talha Mubashir MD: This author declares no financial interests.

Justyna Bartoszko MD, MSc: This author declares no financial interests.

Sheila Riazi MD: This author declares no financial interests.

Appendix. Supplementary materials

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...le Info

Publication History

Published: July 21, 2020

Accepted: July 2, 2020

Received in revised form: July 1, 2020

Received: May 5, 2020

Identification

DOI: https://doi.org/10.1016/j.eclinm.2020.100464

ScienceDirect

Access this article on ScienceDirect

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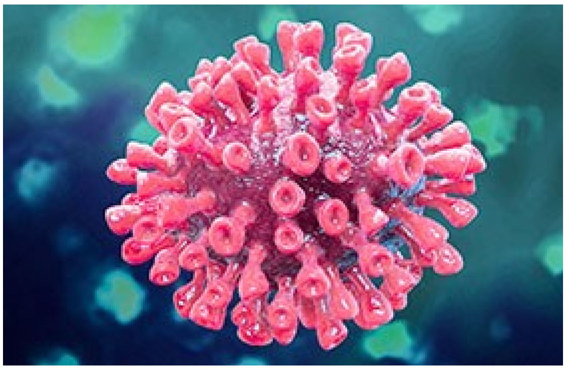

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