Article title: Statistical Modeling of deaths due to COVID-19 influenced by social isolation in Latin American countries

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Number of figures: 2
Number of tables: 1
Number of words: 1.786

Abstract

Social isolation is extremely important to minimize the effects of a pandemic. Latin American (LA) countries have similar socioeconomic characteristics and health system infrastructures. These countries face difficulties to deal with the COVID-19 pandemic and some of them had very high death rates. Government stringency index (GSI) of twelve LA countries was gathered from the Oxford COVID-19 Government Response Tracker (OxCGRT) project. GSI was calculated considering nine metrics such as school and work closures, stay-at-home requirements, among others types of social distancing and isolation measures. Population data from the United Nations Population Fund and number of deaths data was collected from the dashboard of the World Health Organization (WHO). We performed an analysis of the period March-December using a mixed linear model approach. Peru, Brazil, Chile, Bolivia, Colombia, Argentina and Ecuador had the highest death rates with an increasing trend over time, while Suriname, Venezuela, Uruguay, Paraguay and Guyana had the lowest ones, which remained steady. GSI in most countries followed the same pattern during the analyzed months. i.e., high indices at the beginning of the pandemic and lower ones in the last evaluated months, while the number of deaths increased over the whole period. Almost no country kept its GSI high for much time, especially from October to December. Time and GSI as well as their interaction were highly significant. As their interaction increases, death rate decreases. In conclusion, our statistical model explains and substantiates the need for maintaining social distancing and isolation measures over time during the pandemic.

Keywords: COVID-19, SARS-CoV-2, Coronavirus, Latin American countries, Social isolation, Government stringency index

Introduction

The COVID-19 pandemic has affected healthcare systems and caused collapses across the globe. In Latin America (LA), the first case of SARS-CoV-2 infection was recorded on
February 25th in the City of São Paulo. In less than a month after the first case, all LA countries had confirmed cases of COVID-19.\(^1\,^2\).

The LA region has several obstacles that make it difficult for countries to take action against the spread of the virus. Precarious conditions, such as poverty, lack of hospital infrastructure, low sanitary conditions, high prevalence of chronic diseases and government’s tardy responses are factors that make it difficult to prevent contamination by the virus, so that they facilitate transmission and directly impact the hospital system.\(^3\,^5\). Through predictive models' studies, it has been suggested that the virus could spread aggressively through LA.\(^6\,^7\).

Moreover, analyses of the initial cases of the COVID-19 pandemic in LA estimated an unfavorable scenario for the countries, and also evidenced aggressive dynamics of the disease outbreak in Brazil and Ecuador compared to Italy and Spain.\(^7\). Above all, among the LA countries, Brazil was considered a major epicenter of the disease.\(^8\).

Although there are measures aimed at reducing the spread of the new coronavirus such as social distancing, school closures, cancellation of public events and, sometimes, severe methods such as lockdown, these measures have been relaxed, in addition to noncompliance by the population and poor governmental management.\(^9\). Considering that social distancing and isolation are important protective measures for the containment of SARS-CoV-2 infection, and that there is lack of studies demonstrating the relationship between the social isolation and death rate due to COVID-19, based on the Government Stringency Index (GSI) from The Coronavirus Government Response Tracker (OxCGRT)\(^10\), the objective of this work was to analyze the relationship between GSI and time, and the death rate from COVID-19 in 12 LA countries, using a mixed linear model approach. Through this model, the need for maintaining social distancing and isolation measures over time during the pandemic is explained and substantiated.

### Material and Methods

#### Data Sources

Government stringency index of twelve LA countries was developed by the Oxford University and gathered from the platform Policy Responses to the Coronavirus Pandemic on the website (https://ourworldindata.org/policy-responses-covid). This index represents the strictness of government policies and was calculated considering nine metrics of social distancing and isolation, such as school and work closures, stay-at-home requirements, transport restrictions, restrictions on public gatherings, cancellation of public events, public information campaigns; restrictions on internal movements; and international travel controls. The index on any given day is calculated as the mean score of nine policy measures, each taking a value between 0 and 100. The detailed methodology for calculating indices is described elsewhere (https://github.com/OxCGRT/covid-policy tracker/blob/master/documentation/index_methodology.md). To use that data, we first calculated the mean of the GSI for each month. The number of cumulative monthly deaths data was collected from the dashboard of the World Health Organization (WHO). Population data were obtained from the United Nations Population Fund available on (https://www.unfpa.org/about-us) and used to calculate the proportion of the number of deaths for each country. This data was collected from the first day of March until the last day of December of 2020.

#### Statistical analysis

We evaluated the relationship between GSI and time, and the death rates from COVID-19. Since we analyzed repeated measures over a period of time (time was uniformly measured across all countries), this is a longitudinal analysis requiring a mixed linear model approach,

\[
y_{ij} = \mu + X_{ij}^T\beta + Zy + \epsilon_{ij},
\]

where

\[
y_{ij} = \frac{\text{N}^0 \text{ of deaths related to } COVID - 19 \times 1000000}{\text{N}^0 \text{ of inhabitants in the country}}
\]
\( \mu \) = mean of the death ratio adjusted by total population for each million inhabitants, 

\[ X_{ij} = \text{vector of covariates}, \beta = \text{vector of the regression parameters for the covariates}. Z = \text{matrix of covariates}, \gamma = \text{vector of random effects and } \varepsilon_{ij} = \text{vector of random errors}. \gamma \text{ and } \varepsilon \text{ are uncorrelated.} \]

In the model, the variables time (month) and GSI were considered both as fixed. In addition, the country was included as a random effect. All statistical analysis was performed under the most commonly used significance levels (1%, 5% and 10%) using the RStudio statistical software v.3.6.

**Results**

We analyzed data of deaths related to COVID-19 in twelve LA countries in order to evaluate the relationship between death rates, government stringency index and time progression. In this context, time and isolation index are useful to explain the dispersion of the data. Figure 1a displays death rates from March to December. Peru, Brazil, Chile, Bolivia, Colombia, Argentina and Ecuador have high death rates, with an increasing trend over time, while Suriname, Venezuela, Uruguay, Paraguay and Guyana presented low death rates, which remained stable. Figure 1b displays GSI from March to December. It is noticeable that there was much fluctuation in the GSI for most countries, but with a large decrease from October to December. The only country whose GSI was maintained high for the whole period was Venezuela.

Also, in Figure 1a, it is possible to observe the asymmetry of the data, so a skew-t distribution was adopted for the model’s error. Since the model presents a variable dispersion, we used a linear regression model for the dispersion.

\[
y_{ij} \mid \text{time}_{i}, \text{country}_{j}, \text{GSI}_{ij} \sim ST(\mu_{ij}, \sigma_{ij}, v, \tau) \\
\mu_{ij}^{-1} = \beta_0 + \beta_1 \text{time}_{i} + \beta_2 \text{GSI}_{ij} + \beta_3 \text{time}_{i} \times \text{GSI}_{ij} + \gamma_0 + \gamma_1 \text{country}_{j} \\
\log(\sigma_{ij}) = \alpha_0 + \alpha_1 \text{time}_{i} + \alpha_2 \text{GSI}_{ij}.
\]

where \( i = 1, \ldots, 10 \) represents each of the months, starting from March, and \( j = 1, \ldots, 12 \) corresponds to each of the countries. \( \text{time}_{i} \) represents the \( i \)-th month, \( \text{country}_{j} \) represents the \( j \)-th country, \( \text{GSI}_{ij} \) represents the GSI in the \( i \)-th month in the \( j \)-th country. \( \sigma_{ij} \) corresponds to the standard deviation in the \( i \)-th month in the \( j \)-th country, with its corresponding parameters \( \alpha \).

Table 1 displays the coefficient estimates of the mixed linear model and the dispersion model. Time and GSI, as well as their interaction, were highly significant to explain the rate death under all assumed significance levels. As time progresses, the death rate per million inhabitants increases. In addition, as the interaction of time and GSI increases, the death rate decreases.

In Figure 2a, the QQ-plot envelope shows there is no evidence that the skew-t distribution is inappropriate to explain the death rate for each million inhabitants. Other aspects of the model were analyzed by the quantile residuals (Figure 2b), such as the correct specification of the model’s dispersion and distribution. We can conclude from these graphs that the model satisfies the assumptions so that the model specification is appropriate.

**Discussion**

In the COVID-19 pandemic, prolonged periods of social isolation were adopted across the globe, as recommended by the WHO. Social isolation can have a dual impact. It has been observed that, in this period, there is an increase in the rate of suicides, mental disorders, and depression, which are explained by human hyper sociability. In addition, it can trigger physical effects that impact children, young people and the elderly. In contrast, we know that social
isolation is extremely important to decrease the spread of the SARS-CoV-2 virus. It is important
to note that, during the pandemic caused by Influenza A (H1N1), social isolation was also
adopted\(^3\). Mortality from influenza and pneumonia during the 1918-1919 pandemic was lower
in civilians in rural areas when compared to those in urban areas. These observations have led to
the planning of strategies for pandemics, suggesting that social distancing interventions have a
potential effect on mortality by reducing the number of deaths\(^14\). In addition to social distancing
and isolation, large-scale testing is fundamental to fight against the pandemic. However,
addressing the influence of this factor on death rates remains a big challenge because countries
publish their testing data at different time points: some provide daily updates, while others
provide only on a weekly-basis, and some only publish figures on an ad-hoc basis at longer
intervals.

Based on GSI data extracted from the OxCGRT project\(^10\), it is possible to propose
statistical models to evaluate how closely these variables are related to time. Herein, the model
shows that the relationship between time and GSI is highly significant. When analyzing time
and GSI together, it was observed that, as the interaction of these two variables increases, a drop
in the death rate is detected. For instance, according to this model, with a GSI set to 0 in March
and a GSI set to 80 in April, i.e. a 80% increase in the strictness of government policies, we
could have observed a reduction of approximately 32 deaths per million inhabitants. In Brazil,
whose population is near 212 million, that would represent 6,784 lives that could have been
saved at the beginning of the pandemic. This figure would be even higher in other months
within the analyzed period. Furthermore, once these two variables were analyzed separately, as
time increases, the rate of deaths per million inhabitants increases as well. Surprisingly, the
same happens with the GSI reported by the countries. In light of these observations, we can
make two hypotheses: 1) GSI alone may not entirely represent the reality regarding social
isolation and the death rate from COVID-19, since this condition depends on other factors, such
as the infrastructure of the countries’ public hospitals, government management, and the
population's compliance with the rules. 2) Restriction policies as measured by GSI do not have
immediate effects and must be maintained over longer periods in order to decrease death rates
by COVID-19. Hence, the problem is complex and deserves to be studied in detail taking into
account other aspects that may be influencing the death rates.

LA countries present problematic issues, such as social inequality and less access to
healthcare. However, complying with social isolation is difficult for individuals when work is
the only source of income\(^1\). In our analyses, countries such as Peru, Brazil, Chile, Bolivia,
Colombia, Argentina and Ecuador have the highest death rates. Peru presents low conditions to
face a pandemic and even in lockdown at the beginning of the pandemic\(^2\), it presented high
death rates. In a prediction study with data from the first 10 days of the pandemic, it was
estimated that Peru had the lowest effective reproductive number (\(R_t\)), parameter used to keep
track of epidemics\(^7\), therefore, the country had these numbers accentuated during the pandemic
period.

Brazil was the first LA country to report cases of COVID-19\(^16\)–\(^18\). Since it presents
favorable conditions to face a pandemic when compared to other LA countries, it was expected
to have lower rates. However, in the present study, Brazil and Chile presented higher death
rates, followed by Peru. It is important to consider that, although Peru’s president has played a
germane role helping to control the number of deaths from COVID-19, there has not been
neither a national strategic plan to guide communication and educational health policies nor a
large-scale awareness campaign to stimulate people to protect their health and abide to the
protective measures. This lack of policies is also a current problem in Brazil\(^7\). For instance,
through GSI e and COVID-19 Community Mobility Reports from Google, daily new cases and
real time \(R_t\) were calculated, showing that Brazil is not doing very well regarding its response to
COVID-19 pandemic\(^19\). Although Brazil presents a robust public health system and reasonable
GSI, the high death rates may be deeply connected to inadequate policy management that has
received several criticisms\(^3\),\(^15\). In comparison to Brazil, Suriname had a similar GSI but a low
death rate, remaining stable over time. Except for Venezuela, no other country kept a high GSI
for longer periods. Particularly, GSI decreased in the end of the year (October-December) in
most countries, while death rates increased. On the other hand, isolation in Venezuela was
maintained even in December (an atypical month because of Christmas and holiday season), and
its death rates were low and remained unchanged over time.

According to the present analysis, Uruguay followed a relatively lower GSI than other
LA countries but showed low death rates. Uruguay was a country that acted quickly, closing its
borders and schools, with insertion of screening tests, reducing SARS-CoV-2 infections and
controlling the outbreak very efficiently\textsuperscript{20}. In contrast, Ecuador started with high social
isolation, but a decrease in the isolation rate was observed later. On the other hand, Ecuador had
a high mortality rate, which is accentuated over time even with the adoption of lockdown. In
addition, it should be noted that this country had poor conditions of public health infrastructure
at the beginning of the pandemic\textsuperscript{2}. At the beginning of the COVID-19 pandemic, it had been
already suggested that closing public transportation, work places and schools is particularly
effective in reducing COVID-19 transmission\textsuperscript{21}.

The rapidly evolving pandemic in LA countries is worthy of especial attention,
considering their often weak and low stringency responses to the current sanitary crisis. In this
study, GSI varies considerably in all LA countries over time. This variation can partially explain
why these countries have been differently impacted by COVID-19. In spite of not specifically
addressing and discussing the government policies adopted by each country, in this
investigation, we successfully show that social distancing and isolation measured by GSI
influences death rates from COVID-19 over time. For instance, the interaction between GSI and
time can decrease the number of deaths, which demonstrates the importance of maintaining
social distancing and isolation measures for longer periods, as opposed to what most LA
countries did. Almost no country kept its GSI high for much time, especially from October to
December.

Our results have significant implications; however, some limiting aspects must be
considered. 1) The GSI was extracted from the OxCGRT project. The curators of this database
emphasized how challenging the collection of information on the exact data was due to the
nature and extent of the policies of the different governments. This complex data set can
obscure the qualitative differences in each of the nine metrics GSI measures across countries. In
addition, many local and cultural factors can affect the implementation of interventions. 2) Our
data provide a general interpretation of the influence of time and GSI on death rates in LA.
Therefore, future studies can deepen the search for more specific interpretations for each
country, taking into account local aspects and other metrics not covered here. 3) The numbers of
deaths from COVID-19 can be easily underreported\textsuperscript{22,23}, this is due to limited testing, problems
in determining the cause of death and the way in which COVID-19 deaths are recorded. Hence,
we cannot define the real impact of the GSI on death rates with perfect precision. 4) We know
that the differences in population size between countries are often large, and the COVID-19
death count in more populous countries tends to be greater. Thus, in order to perform a more
truthful comparison, we used the cumulative death data and calculated the death rate adjusted by
the population of each country.

Conclusions

We conclude that, in combination, time and GSI have beneficial effects on the decrease of death
rates from COVID-19 in LA countries. Higher strictness of social distancing and isolation, as
measured by the GSI, over time could have flattened mortality curves from COVID-19 from
March to December 2020. Our statistical model explains and substantiates the need for
maintaining social distancing and isolation measures over time during the pandemic.

Acknowledgments

Publication charges for this article were waived due to the ongoing COVID-19 pandemic.

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References

1. Rodriguez-Morales AJ, Gallego V, Escalera-Antezana JP, et al. COVID-19 in Latin America: The implications of the first confirmed case in Brazil. Travel Medicine and Infectious Disease 2020; 35. doi:10.1016/j.tmaid.2020.101613

2. Garcia PJ, Alarcón A, Bayer A, et al. COVID-19 Response in Latin America. American Journal of Tropical Medicine and Hygiene 2020;103(5):1765-1772. doi:10.4269/ajtmh.20-0765

3. Miller MJ, Loaiza JR, Takyar A, et al. Covid-19 in latin america: Novel transmission dynamics for a global pandemic? PLoS Neglected Tropical Diseases 2020;14(5):3-7. doi:10.1371/JOURNAL.PNTD.0008265

4. Pablos-Méndez A, Vega J, Aranguren FP, et al. Covid-19 in Latin America. BMJ 2020;369-370. doi:10.1136/bmj.m2939

5. Burky T. COVID-19 in Latin America Several. The Lancet Infectious Diseases 2020; 20 (5):547-548. doi: 10.1016/S1473-3099(20)30303-0

6. Pacheco-Barrios K, Cardenas-Rojas A, Giannoni-Luza S, et al. COVID-19 pandemic and Farr’s law: A global comparison and prediction of outbreak acceleration and deceleration rates. PLoS ONE 2020;15(9 September):1-25. doi:10.1371/journal.pone.0239175

7. Caicedo-ochoa Y, Rebellón-sánchez DE, Peñaloza-rallón M. Effective Reproductive Number estimation for initial stage of COVID-19 pandemic in Latin American Countries. International Journal of Infectious Diseases 2020; 95(January):316-318. https://doi.org/10.1016/j.ijid.2020.04.069

8. Bermudi PMM, Lorenz C, Aguiar BS de, et al. Spatiotemporal ecological study of COVID-19 mortality in the city of São Paulo, Brazil: Shifting of the high mortality risk from areas with the best to those with the worst socio-economic conditions. Travel Medicine and Infectious Disease 2021;39(October 2020):101945. doi:10.1016/j.tmaid.2020.101945

9. Chen YT, Yen YF, Yu SH, et al. An examination on the transmission of covid-19 and the effect of response strategies: A comparative analysis. International Journal of Environmental Research and Public Health 2020;17(16):1-14. doi:10.3390/ijerph17165687

10. Hale T, Angrist N, Goldszmidt R, et al. A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). Nature Human Behaviour 2021. doi:10.1038/s41562-021-01079-8

11. Bzdok D, Dunbar RIM. The Neurobiology of Social Distance. Trends in Cognitive
12. Sepúlveda-Loyola W, Rodríguez-Sánchez I, Pérez-Rodríguez P, et al. Impact of Social Isolation Due to COVID-19 on Health in Older People: Mental and Physical Effects and Recommendations. *Journal of Nutrition, Health and Aging* 2020;24(9):938-947. doi:10.1007/s12603-020-1469-2

13. Ahmed F, Zviedrite N, Uzicanin A. Effectiveness of workplace social distancing measures in reducing influenza transmission: A systematic review. *BMC Public Health* 2018;18(1):1-13. doi:10.1186/s12889-018-5446-1

14. Paynter S, Ware RS, Shanks GD. Host and environmental factors reducing mortality during the 1918-1919 influenza pandemic. *Epidemiology and Infection* 2011;139(9):1425-1430. doi:10.1017/S0950268811000367

15. The Lancet. COVID-19 in Latin America: a humanitarian crisis. *The Lancet* 2020;396(10261):1463. doi:10.1016/S0140-6736(20)32328-X

16. Ferreira LPS, Valente TM, Tiraboschi FA, et al. Description of Covid-19 Cases in Brazil and Italy. *SN Comprehensive Clinical Medicine* 2020: 497–500. doi: 10.1007/s42399-020-00307-y

17. Valente TM, Ferreira LPS, Silva RAD, et al. Brazil Covid-19: Change of hospitalizations and deaths due to burn injury? *Burns* 2020:9-11. doi:10.1016/j.burns.2020.10.009

18. de Souza WM, Buss LF, Candido D da S, et al. Epidemiological and clinical characteristics of the COVID-19 epidemic in Brazil. *Nature Human Behaviour* 2020;4(8):856-865. doi:10.1038/s41562-020-0928-4

19. Zhu D, Mishra SR, Han X, et al. Social distancing in Latin America during the COVID-19 pandemic: an analysis using the Stringency Index and Google Community Mobility Reports. *International Society of Travel Medicine* 2020:1-25. doi: 10.1093/jtm/taaa125

20. Elizondo V, Harkins GW, Mabvakure B, et al. SARS-CoV-2 genomic characterization and clinical manifestation of the COVID-19 outbreak in Uruguay. *Emerging Microbes and Infections* 2021;10(1):51-65. doi:10.1080/22221751.2020.1863747

21. Vannoni M, McKee M, Semenza JC, et al. Using volunteered geographic information to assess mobility in the early phases of the COVID-19 pandemic: A cross-city time series analysis of 41 cities in 22 countries from March 2nd to 26th 2020. *Globalization and Health* 2020;16(1):1-9. doi:10.1186/s12992-020-00598-9

22. Alves THE, de Souza TA, Silva SA, Ramos NA, de Oliveira SV. Underreporting of Death by COVID-19 in Brazil Second Most Populous State. *Frontiers in Public Health*. 2020;8:578645. doi:10.3389/fpubh.2020.578645

23. Karlinsky A, Kobak D. The World Mortality Dataset: Tracking excess mortality across countries during the COVID-19 pandemic. Preprint *medRxiv* 2021;2021.01.27.21250604. doi:10.1101/2021.01.27.21250604
Figure 1. Death rates from COVID-19 and Government Stringency index from March to December 2020 in Latin American countries.

Legend Figure 1a: Death rates adjusted by population size for each country per million inhabitants.
Figure 1b: Mean Government Stringency index reported as percentage.
Figure 2. Analysis of the model fit; a) Q-Q plot envelope. b) Residual analysis.
Table 1. Estimates of the dispersion model and mixed linear model for death rates from COVID-19 in 2020 in Latin American countries.

|                     | Estimate  | Std Error | t Value | p-value |
|---------------------|-----------|-----------|---------|---------|
| **μ**               |           |           |         |         |
| Intercept ($\beta_0$) | 4,91,633.0 | 69,250.3  | 7.099   | <0.005*** |
| Time ($\beta_1$)    | -70,118.5 | 12,794.0  | -5.81   | <0.005*** |
| GSI($\beta_2$)      | -6,721.4  | 984.6     | -6.826  | <0.005*** |
| Time×GSI ($\beta_3$) | 953.6     | 189.2     | 5.041   | <0.005*** |
| **σ**               |           |           |         |         |
| Intercept ($\alpha_0$) | -389      | 0.59      | -6.63   | <0.005*** |
| Time($\alpha_1$)    | 0.72      | 0.04      | 16.67   | <0.005*** |
| GSI ($\alpha_2$)    | 0.05      | 0.01      | 8.00    | <0.005*** |

Legend: GSI - Government stringency index. Significance levels: “***” 0.001, “**” 0.01, “*” 0.05, “.” 0.1. The relationship between the predictors and the original response variable is inversely proportional i.e. a negative sign indicates an increase of death rates while the positive one indicates a decrease.