Estimation of time-varying reproduction numbers of COVID-19 in American countries with regards to non-pharmacological interventions [version 1; peer review: 1 approved with reservations]

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Abstract
This study aimed to estimate the basic reproduction number and the time-varying estimate of effective reproductive number of COVID-19 in American countries as they implemented non-pharmacological strategies for the containment of the SARS-CoV-2 virus. Data sources included COVID-19 epidemic data from Johns Hopkins University data repository and official websites of countries with a relatively high incidence of COVID-19. The maximum likelihood method was used to estimate the and . The results showed that El Salvador, the Dominican Republic, Panama, and Peru have the lowest, while the USA and Canada have the highest. Other American countries have an around 1.4. Countries could be divided into three groups based on the varied behavior of over time. The first group (Mexico, USA, Colombia and Brazil) started with a high, which decreased post-intervention. In the second group, the intervention was performed at the moment when the, is high and it decreased slowly post-intervention (Canada, Argentina, Chile Peru, Panama and Dominican Republic). In the third group (Bolivia, Peru and Guatemala), the, was erratic and could not be attributable to the intervention.

Keywords
Reproduction number, effective reproductive number, COVID-19, American countries
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Introduction
On January 21, the first case of COVID-19 in the United States\textsuperscript{3} was announced in a traveler who had arrived in the country from China 5 days earlier. Wuhan, China is where the health emergency originated\textsuperscript{1} in December 2019. From late January, the North American continent started to see case reports in different states, with cases arriving in South America on February 26 through Brazil after passing through Central America and the Caribbean\textsuperscript{7}. Today, America is the epicentre of the pandemic, with the USA and Brazil being the two largest countries with the most cases. In addition, Peru, Chile, Mexico, Canada, Colombia and Ecuador are among the top 25 countries with the highest incidence worldwide.

Since then, governments across the region have implemented a series of non-pharmacological measures to protect their citizens and contain the spread of COVID-19. All South American countries, including the French overseas region of French Guiana and the Falkland Islands, have reported the presence of coronavirus within their borders, and all took measures at different times of the outbreak.

Non-pharmacological measures of containment (mitigation and suppression) have been implemented from the index case on different dates in each country\textsuperscript{2,4-6}. This is based on projections of contagion and lethality resulting from SIR epidemiological models (susceptible, infected and recovered)\textsuperscript{7} with data taken from the behavior of the virus in Asia and Europe especially, and with approximations to the basic reproduction number ($R_0$),\textsuperscript{8,9}, effective reproduction number ($R_t$), and variable time estimation of $R_t$ ($R_s$), among others. $R_s$ estimates the speed with which a disease can spread in a population and plays a crucial role in predicting the prevalence of infectious disease, in addition to better understanding an epidemic outbreak and preparing the corresponding public health response. $R_t$ is the reproduction number at time $t$, which reveals the actual transmission rate of the virus at a given moment. This number will vary depending on the control protocols established in each country.

Mitigation measures are aimed at slowing down the spread of infection by progressively reducing $R_0$\textsuperscript{10}. Suppression measures aim to reduce $R_s$ below 1, to progressively decrease the number of cases until they disappear. The greatest challenge that this strategy entails is that it needs to be maintained until the pandemic has disappeared or an effective treatment or vaccine is available\textsuperscript{8,10,11}. The estimation of $R_0$ and $R_s$ in different scenarios allows a better prognosis of the trends of the global epidemic\textsuperscript{12}, in addition to evaluating the effectiveness in reducing transmission with the measures taken by the different countries to contain COVID-19\textsuperscript{13-15}.

While this article was being prepared, the $R_0$ and $R_s$ values of some countries were published and modeled in three intervention scenarios; however, they only included the United States and Argentina from the American continent, limiting the comparative analysis for the characteristics of America\textsuperscript{16}. Previous work has calculated $R_t$ and $R_s$ using the maximum likelihood method and sequential Bayesian method, and found that European and North American countries possessed a higher $R_0$ and unsteady $R_s$ fluctuations, whereas some heavily affected Asian countries showed a relatively low $R_0$ and declining $R_t$, with a small number of patients in Africa and Latin America, yet with the potential risk of large outbreaks. Xu \textit{et al.}\textsuperscript{17} who determined $R_s$ as an indicator to measure the transmission of SARS-CoV-2 before and after interventions, showed that the change in the rate of transmission of SARS-CoV-2 is associated with reducing social interactions.

This study aimed to estimate $R_0$ and $R_s$ in multiple countries of the American continent and evaluate their behavior from the first (index) case in each country, and the time of implementation of the chosen non-pharmacological containment measures.

Methods
Data sources
COVID-19 epidemic data were obtained from the Johns Hopkins University data repository (https://coronavirus.jhu.edu/). This information was verified using official country websites, and these websites were also used to collect data about non-pharmacological interventions (Table 1). We selected countries with a relatively high incidence of COVID-19, as follows: Argentina, Bolivia, Brazil, Canada, Colombia, Chile, the Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Panama, Peru, and the USA. Data were collected from the date on which the first case was reported in the country to June 12, 2020.

Data analysis
We used the COVID-19 daily incidence to estimate the basic reproduction number ($R_0$) and the time-varying reproduction number ($R_t$) with packages $R_0$\textsuperscript{14} and EpiEstim\textsuperscript{15} in R software (version 4.0.1), respectively. $R_t$ was calculated using a serial interval (SI) with a mean of 7.5 and a standard deviation of 3.4\textsuperscript{16}. The incubation period used was 5 days, taking into account the mean incubation period in 16 of 5.0 days (95% CI, 4.2–6.0), the median incubation period estimated in 17 of 5.1 days (95% CI, 4.5–5.8 days), and the mean incubation period in 2 of 5.2 days (95% CI, 4.1–7.0). We used the maximum likelihood method to estimate both $R_0$ and $R_t$.

Results
Basic reproduction number ($R_0$)
El Salvador, the Dominican Republic, Panama, and Peru have the lowest $R_0$; in contrast, the USA and Canada have the highest. Other countries have an $R_0$ around 1.4 (Figure 1).
### Table 1. Data sources by country used for verification of COVID-19 case data from Johns Hopkins University data repository (https://coronavirus.jhu.edu/).

<table>
<thead>
<tr>
<th>Country</th>
<th>Official website used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td><a href="https://www.argentina.gob.ar/coronavirus/informe-diario">https://www.argentina.gob.ar/coronavirus/informe-diario</a></td>
</tr>
<tr>
<td>Bolivia</td>
<td><a href="https://www.minsalud.gob.bo/">https://www.minsalud.gob.bo/</a></td>
</tr>
<tr>
<td>Colombia</td>
<td><a href="https://minsalud.maps.arcgis.com/apps/opsdashboard/index.html#/e18894fa4dd546d094e8267179562413">https://minsalud.maps.arcgis.com/apps/opsdashboard/index.html#/e18894fa4dd546d094e8267179562413</a></td>
</tr>
<tr>
<td>Dominican Republic</td>
<td><a href="https://www.msp.gob.do/web/?page_id=6948">https://www.msp.gob.do/web/?page_id=6948</a></td>
</tr>
<tr>
<td>Ecuador</td>
<td><a href="https://www.salud.gob.ec/coronavirus-covid-19/">https://www.salud.gob.ec/coronavirus-covid-19/</a></td>
</tr>
<tr>
<td>Guatemala</td>
<td><a href="https://tablerocovid.mspas.gob.gt/">https://tablerocovid.mspas.gob.gt/</a></td>
</tr>
<tr>
<td>Honduras</td>
<td><a href="http://www.salud.gob.hn/site/index.php/covid19">http://www.salud.gob.hn/site/index.php/covid19</a></td>
</tr>
<tr>
<td>Panama</td>
<td><a href="http://minsa.gob.pa/destacado/coronavirus-covid-19">http://minsa.gob.pa/destacado/coronavirus-covid-19</a></td>
</tr>
<tr>
<td>Peru</td>
<td><a href="https://covid19.minsa.gob.pe/sala_situacional.asp">https://covid19.minsa.gob.pe/sala_situacional.asp</a></td>
</tr>
<tr>
<td>USA</td>
<td><a href="https://www.hhs.gov/coronavirus/index.html">https://www.hhs.gov/coronavirus/index.html</a></td>
</tr>
</tbody>
</table>

![Figure 1. Basic reproduction number by country.](image-url)
**Time-varying effective reproductive number ($R_t$)**

Countries could be divided into three groups based on the varied behavior of $R_t$ over time (Figure 2–Figure 4). The first group (Mexico, USA, Colombia and Brazil) started with a high $R_t$, which decreased post-intervention. In the second group (Canada, Argentina, Chile Peru, Panama and Dominican Republic), the intervention was performed at the moment when the $R_t$ is high and this then decreased slowly post-intervention. In the third group (Bolivia, Peru and Guatemala), the $R_t$ is erratic and cannot be attributable to the intervention; the $R_t$ increases and decreases without any explanation.

Analysis by regions (North, Central and South America) shows differences between regions and countries. The countries of North America have a low $R_t$, which increased over time. Post-intervention control is achieved by a progressive decrease in all cases in Canada, Mexico and the USA. The behavior of the Dominican Republic and the countries of Central America is similar. Excepting Bolivia, Guatemala and Peru, the countries of South America and Central America show a similar behavior to the first group; the $R_t$ is high at the beginning and decreases suddenly after control measures. However, Peru had a considerable peak after intervention implementation, as did Chile and Panama. This is possibly related to the flexible measures of mass community isolation.

Despite the differences between the first and second group, the $R_t$ is high before the intervention in all countries and its decrease is achieved post-intervention, corroborating the purpose of these interventions in the mitigation and suppression of a pandemic.

**Discussion**

The $R_t$ for the countries selected in this study was 1.2–1.8, which is much lower compared to China where it was reported to be 2.2, 2.6, 3.8, or even 6.47 according to different research. Our study findings agree with Xu et al. in the estimated for the United States and Argentina. The $R_t$ for these countries is also identical to that found by Xu et al.

As in the study by Xu et al., there are some limitations to the current study. First, the variation in depends on the series interval. Here, we assume 7.5 days for the 13 countries due to limited information on the disease in different nations. In addition, we noticed some errors in the John Hopkins University data when we cross referenced these with official country websites. We were able to correct these by searching for cases directly on the official website of each country. Another drawback is the diversity of RT-PCR (real-time reverse transcription polymerase chain reaction) tests used in the diagnostic process and their sensitivity, which may throw up false negatives, perhaps under-estimating the true impact of the pandemic in various countries. Although data were available from other countries, in the case of Ecuador, the report was not included, because cases were not confirmed by RT-PCR, which is a that s technical criteria.
The epidemic trends in different regions around the world are significantly different due to the great difference in the design and implementation of prevention and control measures. Estimates of both $R_t$ and $R_0$ in different countries will enable a better forecast of global epidemic trends.

In conclusions, our study shows that there is a close relationship between $R_t$ and non-pharmacological interventions decreed by countries’ governments for the control of the COVID-19 pandemic. Additionally, we showed that there are immediate changes in the behavior of the $R_t$, and therefore in

Figure 3. Time-varying effective reproductive number by country in South America. The dotted horizontal line shows the target of 1 at $R_t$, and the vertical line represents the start date of the containment measures decreed in each country. Although there is a difference in the days, there is also a difference in the size of the countries, both in surface area and number of inhabitants that would allow mobility and different behavior of virus spread.
the progression of the outbreak, when the interventions are implemented closer to the index case for each country.

Data availability
Underlying data

This project contains the following underlying data:
- Dataset and data dictionary
- R analysis code

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).
References

Open Peer Review

Current Peer Review Status:  

Version 1  

Reviewer Report 11 August 2020  

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1. English grammar is very poor. It impedes adequate understanding of the content. I suggest that the authors use a professional editing service.

2. In the title the term "America" is ambiguous. I suggest changing it by North America, Latin America and the Caribbean.

3. The manuscript is pertinent. However, the discussion needs more depth, contrasting to other authors' views. Please refrain from making value judgements.

4. The manuscript needs major changes before being considered for indexing.

Is the work clearly and accurately presented and does it cite the current literature?
No

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Anesthesiology, critical care, business in healthcare

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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**Author Response 17 Nov 2020**

**Fred Manrique-Abril**, Universidad Nacional de Colombia, Bogotá, Colombia

Thanks for your contributions, in a future article we will make improvements to achieve an outstanding product. The pandemic data is changing daily and other groups may model the updated Rt.

**Competing Interests:** none

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