

The effect of early-stage public health policies on the transmission of COVID-19 in South American countries

AUTHORS

Bryan Valcarcel^a, Jose L. Avilez^b, J. Smith Torres-Roman^c, Julio A. Poterico^d, Janina Bazalar-Palacios^e, Carlo La Vecchia^f

AFFILIATIONS

- a) Milken Institute School of Public Health, The George Washington University, Washington, DC, USA.
- b) Faculty of Mathematics, University of Waterloo, Ontario, Canada
- c) Facultad de Ciencias de la Salud, Medicina Humana, Universidad Científica del Sur, Lima, Perú
- d) Servicio de Genética, Instituto Nacional del Niño San Borja (INSN-SB), Lima, Perú
- e) Universidad Católica los Ángeles de Chimbote, Instituto de Investigación, Chimbote, Perú
- f) Department of Clinical Sciences and Community Health, Università degli Studi di Milano 20133, Milan, Italy

ABSTRACT

Objectives: The analysis of transmission dynamics is crucial to determine whether mitigation or suppression measures reduce the spread of Coronavirus disease 2019 (COVID-19). This study sought to estimate the basic (R_0) and time-varying (R_t) reproduction number of COVID-19 and contrast the public health measures for ten South American countries.

Methods: Data was obtained from the European Centre for Disease Prevention and Control. Country-specific R_0 estimates during the first two weeks of the outbreak and R_t estimates after 90 days were estimated.

Results: Countries used a combination of isolation, physical distancing, quarantine, and community-wide containment measures to staunch the spread of COVID-19 at different points in time. R_0 ranged from 1.52 (95% confidence interval: 1.13-1.99) in Venezuela to 3.83 (3.04-4.75) in Chile, whereas R_t after 90 days ranged from 0.71 (95% credible interval: 0.39-1.05) in Uruguay to 1.20 (1.19-1.20) in Brazil. Different R_0 and R_t values may be related to the testing capacity of each country.

Conclusion: R_0 in the early phase of the outbreak varied across the South American countries. The public health measures adopted in the initial period of the pandemic appear to have reduced R_t over time in each country, albeit to different levels.

Key words: severe acute respiratory syndrome coronavirus 2; Basic Reproduction Number; South America; Communicable Diseases, Emerging; Pandemics; Epidemiology

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an emerging respiratory infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 was first detected in December 2019 in Wuhan, China, and has caused serious public health concerns worldwide (1). Several public health measures—physical isolation; temporary closure of territory borders, academic institutions, and public places; and quarantine—have been used in an effort to reduce the impact of the COVID-19 outbreak. The United Nations highlights that the COVID-19 pandemic, in combination with the profound socioeconomic inequalities in SA, will push over 45 million people into poor conditions and 28 million in extremely poor conditions (2). Compounded with the fragmented and ill-prepared public health systems of South American (SA), COVID-19 could have a comparatively harsher effect in the region, relative to countries with robust health systems (3).

Although the first case of COVID-19 in SA was detected on March 26 in Brazil (4), few SA modeling studies have emerged since (5). Given the rapid spread of SARS-CoV-2 in this region, understanding the dynamics of disease transmission is key to guiding the implementation of necessary prevention and control measures. One parameter, the basic reproduction number (R_0), aids to fulfill this purpose by estimating the number of secondary cases arising from exposure to an infected person in the absence of epidemic or pandemic containment measures (6). Another metric, the time-varying reproduction number (R_t), is useful in monitoring the transmissibility of SARS-CoV-2 over time and to assess the adequacy of current control efforts. R_t estimates the expected number of secondary infections from an infected individual at time t (7, 8). The serial

interval is another key variable to estimate R_0 and R_t ; it measures the time elapsed between symptomatic cases in a chain of transmission. Determining the probability distribution of the serial interval of SARS-CoV-2 and using that distribution to estimate R_0 and R_t is crucial in assessing the rate at which the COVID-19 pandemic expands. Knowing the person-to-person transmission rate helps policymakers understand whether mitigation and suppression measures are effective and when to adopt more or less stringent measures (9, 10).

Given the importance of assessing the public health interventions to monitor their effectiveness, we estimated both reproduction numbers (R_0 and R_t) to identify the impact of the early-stage public health interventions in South America.

MATERIAL AND METHODS

Data sources

We used the COVID-19 database from the European Centre for Disease Prevention and Control (ECDC) (11). The database is publicly available and contains the worldwide geographic distribution of COVID-19 cases. The database is updated daily and provides counts for new cases and deaths by date and country. We extracted the data from the ECDC database for the following ten SA countries: Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Paraguay, Peru, Uruguay, and Venezuela. Early-stage containment and mitigation decrees issued by each country against COVID-19 were found in the corresponding official government webpages.

Variables

The following binary variables were recorded for each country for qualitative analysis: *isolation*, separation of confirmed cases with COVID-19 in a healthcare facility or their home; *quarantine*, social restriction and home containment of persons with suspected or known contact with a patient with COVID-19, or individuals with a travel history to Europe or Asia; *physical distancing*, group of measures related to the prevention of mass gatherings, closure of academic institutions, and cancellation of social and public events; *community-wide containment*, mandatory isolation of every citizen of the country in their home, with permission only to acquire life supplies (i.e. food or water) in restricted hours of the day (12).

Basic reproductive number (R_0) and time-varying reproductive number (R_t)

We estimated R_0 using data for the first two weeks after the first laboratory-confirmed case of SARS-CoV-2 in each country. Since R_0 is the reproductive rate *sans* intervention measures, it should be estimated during the exponential phase of the pandemic; otherwise, R_0 would be underestimated. Thus, the two-week estimation time frame was selected for two reasons: (i) 14 days is regarded as the maximum time after exposure for symptoms to develop, and (ii) it is sensible to assume that the pandemic will be in its exponential phase for the first two weeks after the first case is detected. We specified the SARS-CoV-2 serial interval as a gamma-distributed random variable with a mean serial time of 3.96 days and a standard deviation of 4.75 days, based on a contact tracing study conducted by the Center for Disease Control and Prevention (CDC) (13). R_0 was estimated with the maximum likelihood method described by White and Pagano (14).

We estimated R_t from the time series of daily incidence of SARS-CoV-2 in each country, using the novel methods described by Thompson et al. and setting the same gamma distribution specification for the serial interval as we did for R_0 (15). We chose a five-day moving window to elucidate the time trend exhibited by R_t . A previous study in China used a ten-day moving window to report R_t (16); however, they specified a mean serial time of 7.5 days, a mean higher by a factor of two with respect to the CDC contact tracing study. We selected a narrower window to account for the faster spreading dynamics we specify in our models and estimate R_t after 90 days for each country. The mean difference between R_0 and R_t were estimated to describe the change of both numbers. Sensitivity analysis included the estimation of R_0 up to the first week of the first reported case in each country, based on a follow-up study of 1 000 COVID-19 cases (17).

Data analysis

The statistical analysis was conducted using the R version 3.6.2 software. First, we describe the public health measures taken by SA countries and calculated the cumulative number of cases according to the two periods. Thereafter, the “R0” package was used to compute the basic reproductive number. To estimate both R_0 and R_t , we employed a gamma-distributed serial interval with a mean serial interval of $3.96 \pm$ (standard deviation) 4.75 days. Estimation of R_0 was carried out via the maximum likelihood method, and 95% confidence intervals (95% CI) were computed for the R_0 value of each country. We used the “EpiEstim” package to compute the time-varying reproductive number. Country-wise time series for R_t , with 95% credible

intervals (95% CrI), were plotted. The code is freely available at

https://github.com/jlavileze/covid_sa.

Ethics

The project was revised by the Investigation Review Board of the Scientific University of the South. Given that the investigation is a secondary analysis of a database, it received an exempt category and was approved for its development.

RESULTS

Table 1 shows the public health measures adopted by SA governments against COVID-19. All SA countries adopted isolation, quarantine, and physical distancing measures. However, the period between the first laboratory-confirmed case and the implementation of public health measures differed across SA nations. Seven countries, Argentina, Bolivia, Colombia, Paraguay, Peru, Uruguay, and Venezuela enacted their control policies in ≤ 7 days after their first case detection. Uruguay enacted the public health measures on the day they detected their first case. In Brazil, 19 days elapsed between detection and implementation of control measures.

The time to implement a community-wide containment strategy also varied between SA countries. Two countries, Bolivia and Venezuela, issued their mitigation policies in ≤ 7 days after detecting their first COVID-19 cases; Paraguay and Peru did so between 7-14 days after detection; and Argentina, Chile, Colombia, and Ecuador all took over 14 days (Table 1).

Moreover, Colombia (12 days) and Argentina (10 days) had the longest period between their first measures (isolation, physical distancing, and quarantine) and community-wide containment efforts. Chile implemented a stepwise selective community containment, moving one province at a time.

Table 2 shows R_0 and R_t estimates for each country and the corresponding cumulative number of cases. During the early phase of the pandemic, R_0 ranged from 1.52 to 3.83. An R_0 of 3.83 means that, on average, each infected person will transmit the virus to roughly 4 different individuals. Brazil, Chile, and Ecuador had the highest R_0 ; these three countries enacted their first mitigation measures ≥ 14 days from the initial detection of COVID-19 patients in their territory. For the countries that implemented mitigation measures 5-7 days after detection, the R_0 ranged from 1.60 to 2.95, while for the countries that acted within 3 days, it ranged from 1.52 to 1.74. The sensitivity analysis showed similar results; Brazil was the country with the highest R_0 after seven days of the first case detection. Moreover, the seven-day R_0 estimation ranged from 1.39 to 3.48 for countries with mitigation measures between 5-7 days and from 1.17 to 2.29 in nations that enacted measures in < 3 days after their first COVID-19 case. Furthermore, all SA countries decreased their R_t over time, with a mean difference ranging from 0.61 in Bolivia to 2.80 in Ecuador (Table 2 and Figure 1). At the latest assessment, R_t ranged from 0.99 to 1.13 in all the countries studied. Although the point estimates for R_t were below one in Bolivia and Uruguay, their 95% credible intervals are compatible with a still-growing pandemic (Figure 1 and Table 2).

DISCUSSION

We used two measures to estimate the spread of SARS-CoV-2: R_0 during the early phase of the outbreak, and R_t to measure the changes of transmissibility over time to identify the effectiveness of public health policies in SA countries. The main results identified that R_0 varied across nations, and R_t decreased over time in all countries. The latter, seems to be associated with the timing of implementation of mitigation measures.

Our results differ from previous estimations of R_0 and R_t . Li et al. (18) reported an R_0 of 2.2 (95% CI: 1.4-3.9) calculated during the first 26 days of the outbreak in Wuhan, China. Moreover, Zhao et al. (19) estimated an R_0 between 2.24 (95% CI: 1.96-2.55) and 5.71 (95% CI: 4.24-7.54) withing the first 15 days of the outbreak. We used different parameters to estimate R_0 . First, we chose 14 days based on the maximum incubation period of the virus, providing a reasonable window in which transmission can still be considered exponential. This choice renders our model specification consistent with White and Pagano's method and prevents our R_0 values from being underestimated (14). Second, in the absence of contact tracing data, previous studies used the serial interval of other similar respiratory viruses as a proxy for the serial interval of SARS-CoV-2. Li et al. (18) used a mean of 8.4 ± 3.8 days from SARS, while Zhao et al. (19) employed a mean of 7.6 ± 3.4 days from MERS; with both studies using a gamma distribution. A study from the CDC identified a lower mean serial interval for SARS-Cov-2— 3.96 ± 4.75 days—and proposed a gamma distribution as a plausible model for the serial interval; we adjusted our analysis to this prior.

R_t values from SA countries were lower than those of European nations: R_t estimates by Yuan et al. (20) for Italy, France, Germany, and Spain ranged from 3.10 to 6.56 in an overall 20-day period. In contrast, our study estimated R_t over 90 days after the first case identification; therefore, we stress that the main difference of these outcomes relies on the chosen time interval to estimate R_t . SARS-Cov-2 might have been spreading rapidly during the first 20 days after case detection in Europe, which is reflected in higher R_t values. Another possibility is the longer period that European countries took to implement control measures than SA countries. For example, Italy took over one month to make its first mitigation come into effect (21), which led the virus to spread freely for a longer time in the population.

The reproduction number— R_0 or R_t —is a measure that depends on the population mixing (6). Human behavior play a critical role in the transmission of SARS-CoV-2, as person-to-person contact exposes a susceptible person through respiratory droplets from an infected individual (22). Therefore, mitigation measures, such as social distancing or case isolation, are necessary to stop the spread of SARS-CoV-2. Ideal policies should be country-specific, and the overall objective is to reduce R_0 (mitigation) or to reach an $R_0 < 1$ (suppression). Regardless of the aim, a combination of mitigation and suppression measures is the best strategy to staunch the COVID-19 pandemic (10).

Three countries, Brazil, Chile, and Uruguay opted for a mitigation strategy. Ferguson et al. suggested that the best mitigation strategy is a combination of physical distancing of high-risk groups (elders and patients at risk of severe disease), case isolation, and quarantine (10).

Uruguay implemented these three measures. Brazil and Chile added a stepwise selective population containment, which allows intermittent circulation of SARS-CoV-2, congruent with a mitigation purpose. The remaining SA countries opted for suppression actions. For example, Peru issued a decree to increase the period of the community-wide containment intervention and to fine citizens if they left their home after a specified hour of the day (23). As a result, all nations managed a reduction of R_t .

Here we highlight several explanations for the change between R_0 and R_t . First, the implementation of public health measures by some countries within the first week of the outbreak could have lowered R_0 . These laws aimed to reduce human contact, which, in turn, reduced the spread of the virus in the community. In contrast, the three countries with the highest R_0 in the early phase issued their first mitigation laws ≥ 14 days from their first cases, which gave SARS-CoV-2 a higher chance of transmissibility among the population. Second, the reproduction number is sensitive to the ability of each country to detect COVID-19 cases (24). A shortage of testing impairs the identification of cases within a community and provides limited data to estimate R_0 or R_t , generating unclear information to analyze the effect of mitigation or suppression interventions in a community. In our view, despite international donations of test kits to identify and isolate cases (25, 26), the fragmented healthcare systems and questionable government management of SA countries deter proper development of testing strategy and test distribution for case detection.

Our study has some limitations to address. Although we used national reports of COVID-19 cases, underreporting is likely, and difficult to quantify. True case identification depends on the testing capacity to detect both symptomatic and asymptomatic patients, which is difficult in any country and likely impaired in SA countries. For instance, Venezuela has been under political, socioeconomic, and public health instability before the COVID-19 pandemic, shown through the cessation of publishing of public health statistics since 2016 from their Ministry of Health (27). Moreover, Brazil's president Jair Bolsonaro downplayed COVID-19 regarding it as a benign disease and through avoiding prompt action to address the pandemic (28). These instances may have impaired proper case detection and led to a suppression of information as previous reports suggest (28, 29).

Second, we did not calculate the case-fatality ratio. During the current course of the pandemic in SA countries, the estimation of this metric is biased for underreporting of cases and time lag between the notification of cases and deaths; this analysis is better suited for a post-pandemic period (30, 31). Third, there are issues arising from the model specification for serial interval. For instance, we assumed the same serial interval distribution for all countries at all points in time, even though these should be space- and time-dependent, as serial interval distributions vary throughout an epidemic or pandemic (24). Also, the CDC serial interval model only considers positive serial times, and hence censors all serial interval observations in which a secondary case manifests symptoms before the primary case does. Per their findings, about 12.6% of secondary cases exhibit clinical symptoms before a primary case (e.g. an infected person presenting symptoms before the infector); given how sensitive R_0 estimates are to the serial interval

distribution, our results should be updated as better model specifications of this variable are elucidated.

Our findings suggest a positive, yet insufficient, impact of the mitigation and suppression measures in SA nations to reduce the spread of SARS-CoV-2. Despite the fragmented health system of most of these countries, the different combination of control measures adopted managed to reduce R_t , albeit to different levels. The difference of R_0 in the early phase of the outbreak is probably due to a combination of a shortage of testing and the idiosyncrasies of each country's public health system. However, R_t values above one during the study period suggest that South America is still far from containing the spread of COVID-19.

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Figure 1. Progression of the time-varying reproduction number (R_t) since the first case report in each country

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Table 1. Status of the mitigation and suppression measures of South American countries.

Countries	Isolation, quarantine, and social distancing		Community-wide containment	
	Status	Days after 1 st case	Status	Days after 1 st case
Brazil	Yes	19	Yes ^a	25
Chile	Yes	14	Yes ^a	17
Ecuador	Yes	14	Yes	17
Argentina	Yes	7	Yes	17
Peru	Yes	5	Yes	9
Colombia	Yes	6	Yes	18
Paraguay	Yes	3	Yes	9
Bolivia	Yes	6	Yes	7
Uruguay	Yes	0	No	-
Venezuela ^b	Yes	3	Yes	3

a Chile and Brazil developed a selective community-wide containment with different dates for specific provinces.

b Venezuela started the mitigation measures (isolation, quarantine, social distancing, and community-wide containment) on the same date.

Table 2. The basic and time-varying reproductive numbers in South American countries.

Countries	R_0 after 14 days			R_t after 90 days			Mean difference
	Cumulative cases	R0	95% CI	Cumulative cases	R_t	95% CrI	
Argentina	128	2.05	1.52-2.68	19 255	1.13	1.09-1.16	0.92
Bolivia	39	1.60	0.92-2.55	14 644	0.99	0.95-1.02	0.61
Brazil	25	3.40	1.82-5.70	363 211	1.2	1.19-1.21	2.20
Chile	201	3.83	3.04-4.75	105 159	1.12	1.11-1.14	2.71
Colombia	306	2.05	1.70-2.45	39 236	1.10	1.08-1.12	0.95
Ecuador	168	3.72	2.82-4.80	40 414	0.92	0.88-0.96	2.80
Paraguay	37	1.74	0.96-2.86	1 145	1.06	0.89-1.24	0.68
Peru	263	2.94	2.44-3.51	183 198	1.01	1.00-1.02	1.93
Uruguay	238	1.61	1.34-1.92	847	0.71	0.39-1.13	0.90
Venezuela	119	1.52	1.13-1.99	2 814	1.04	0.97-1.12	0.48

R_0 , basic reproduction number; R_t , time-dependent reproduction number; 95% CI, 95% confidence interval; 95% CrI, 95% credible interval

