THE IMPORTANCE OF MATHEMATICAL MODELING IN THE BATTLE AGAINST COVID-19.

Fernández Naranjo Raúl [1], *Feijoo Javier* [2], *Ortiz Prado Esteban*[*1]

OPEN ACCESS

Este artículo está bajo una licencia de Creative Commons de tipo *Reconocimiento – No comercial – Sin obras derivadas* 4.0 International.

1. Universidad de Las Americas, Faculty of Health Science, One Health Research Group. Quito Ecuador
2. Universidad Nacional de la Plata, Instituto de Física La Plata, La Plata, Argentina

ORCID ID:
Fernández Naranjo Raúl
https://orcid.org/0000-0002-4875-9652
Feijoo Javier
https://orcid.org/0000-0002-0917-909X
Ortiz Prado Esteban
https://orcid.org/0000-0002-1895-7498

***Corresponding author:** Ortiz-Prado Esteban
E-mail: e.ortizprado@gmail.com

Article history

Received: 17 – May - 2020
Accepted: 28 – May - 2020
Publish: 1 – Jul – 2020

Conflict of interest: All authors declared that there are no conflicts of interest

Financial disclosure: The authors have no financial relationships relevant to this article to disclose

Authors' contribution: All the authors contributed in the search, selection of articles and writing. All the authors reviewed and approved the final manuscript.

Forma de citar este artículo:
Fernández-Naranjo R, Feijoo J, Ortiz-Prado E. THE IMPORTANCE OF MATHEMATICAL MODELING IN THE BATTLE AGAINST COVID-19. Rev Med Vozandes. 2020; 31 (1): 7-9

Since the very beginning of modern epidemiology, disease estimates and understanding of transmission dynamics have been an important pillar* in understanding future outbreaks and predicting possible disease outbreaks. Ronald Ross, a medical doctor in 1902 won his first Nobel Prize for his studies in the origins of the transmission of malaria, years later, his SIR Model (Susceptible, Infected and Recovered) was perfected by William Kermack and Anderson Mckendrik and since then it has been used to calculate the progression of multiple diseases in which we can include, malaria, Chagas, influenza or Zika[1].

With the arrival of multiple outbreaks, epidemics and pandemics scenarios, the usefulness of mathematical models has been challenged. During 2002 with the arrival of the recently discovered SARS-CoV virus, the microorganism responsible for the Severe Acute Respiratory Syndrome (SARS), in 2009 the H1N1 (swine flu), the MERS-CoV (Middle East Respiratory Syndrome) in 2012 and the most recently discovered SARS-CoV2 (COVID-19) in 2020 have put the use of mathematical calculations and Bayesian estimates to the limit[2].

During the current situation, the COVID-19 pandemic has constituted an enormous challenge for governments and societies to handle one of the biggest public health challenges, especially in those countries with weaker health systems[3].

In order to counteract the global challenges of a pandemic, scientists all over the world have relied on data in order to use advanced modelling for disease transmission estimation and to sketch possible outcomes about the behavior of pandemic in their countries[4].

The initial case of application of data analytics tools during the current COVID-19 pandemic, was tested in China, where statistical models were used in order to forecast the number of cases in days after the beginning of the disease, as well as, the basic reproduction number R0 [5,6]. Zhang et al. [2020] and Zhao et al. [2020], who modeled the expansion of COVID19 in their country using mathematical models based on Poisson and gamma distributions to replicate the evolution of daily cases. As a result, they computed reproduction factors and levels of new cases [5,6].

Mathematical Stochastic models and probabilistic distributions to explain epidemiology phenomena have been improved since the origin of SARS diseases in Hong Kong and China in early 2000's, when new formulations to the SIR model appeared[7]. This classic method is based in differential equations in order to obtain parameters that define the specific situation of a pandemic related to susceptible (S), infectious (I) and recovered (R), nevertheless, more variables can be added to the population analysis. Despite showing solid estimations about the evolution of pandemics, such as, AH1N1, the quality of this kind of model depends on the volume of the data. Many variables are necessary to explain the four components that derive in a series of estimated parameters. These values can be highly sensible to changes and can present correlation between them, sometimes conducting to wrong conclusions if something was not considered in the data sources.

Keys Words: SARS-Cov2, Models, Statistical, Burden of Disease

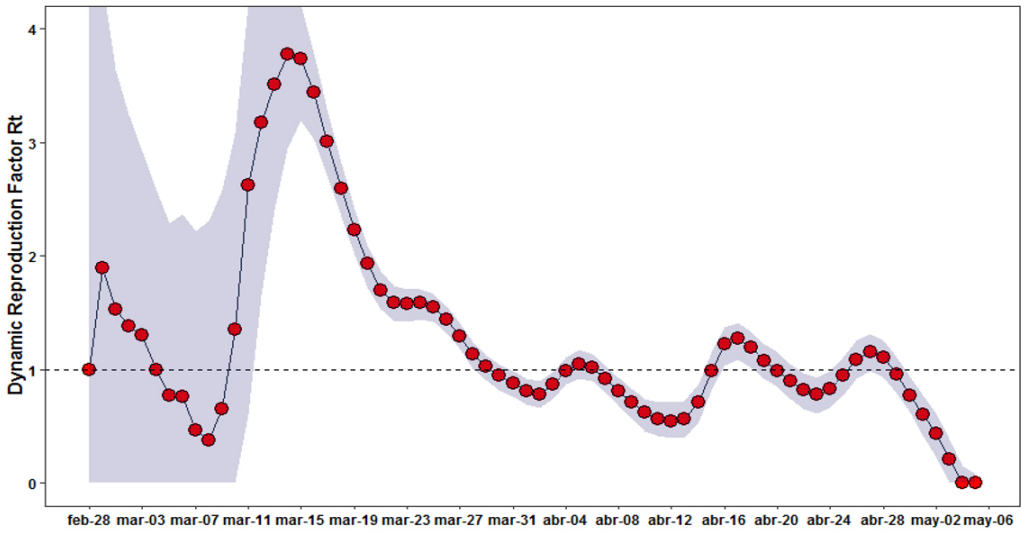

Figure 1. **R_t estimated via Bayesian method.**

Recently, important progress in the field of data science and machine learning, allowed forecasters and big data analysts to compute key indicators about the evolution of COVID-19[8]. These techniques, with large streams of information being produced everyday about confirmed cases or tracing apps interaction, permit the estimation of probability densities for epidemiological parameters, as disease transmissibility, and the prediction of future observations with a degree of confidence[9]. Some models from the machine learning corpus contemplate trajectory matching via least square fitting for cases prediction, probabilistic methods to quantify reproduction factors, and data assimilation methods to infer distributional properties for contagious cases.

The advantage of machine learning methods against classic methods like SIR or SIRS models lies on its capacity of using past information to infer present or future situations[9].

The key to success in the use of predictive models for COVID19 management is composed of two elements: 1) the quality and availability of data being used about the situation of virus spreading cases in the countries and 2) Being able to consider and use all previous evidence to make estimations about a situation in a dynamic way. These two elements even can shape the way how results are understood.

As an example, a method is presented for estimation of reproduction factors in Ecuador, using information from confirmed COVID-19 cases in the country, as well as, frequentist and Bayesian statistical frameworks to compute these quantities. The frequentist method is used to compute the basic reproduction number R_0 and the bayesian method considers a statistical distribution to compute R_t the effective reproduction number in a continuous way by using previous daily information as input for a joint estimation of the future distribution for COVID19 cases based on previous experience. It is ideal that both quantities are below 1 to have signals about the slowing of COVID19 in a country (**Figure 1**).

It can be seen in **Figure 1** the R_t estimates for Ecuador between 2020-02-28 and 2020-05-05 with its highest value of 3.77 at 2020-03-14 and a confidence interval of [2.95,4.42]. Since that day R_t started to fall reaching values below 1 at 2020-03-30 with 0.95 and confidence interval of [0.82,1.05]. In the case of R_0 as static quantity its estimate with exponential growth method is 3.45 with confidence interval of [3.37,3.54] and for maximum likelihood estimation the value of 2.93 with confidence interval of [2.83,3.04]. R_t quantities get a peak and decrease below 1 but R_0 is always over 1. This could be contradictory but in order to succeed with predictive models, it must be aligned data, methodological definitions and technical criteria from medical experts to understand the insights from models and make policies quickly. Based on Yuan et al R naught estimates derived from any analytical method explain how the spreading of a disease will be if no public health policies are adopted. On the contrary, R_t is a pure measure that quantifies in real time how the level of contagious is evolving in pandemic having public health actions. According to this, COVID-19 in Ecuador is being controlled in function of R_t estimates but if no measures were present the scenery would be complex as large R_0 values shown[10].

Light strategy system in Ecuador

Many countries are struggling with the effects of the pandemic, and politics need to take appropriate decisions to balance the economy and public health. The first step is to know specific details and parameters of the virus spread in a population, statistical models used the data available and give accurate parameters that rule the behavior of the pandemic.

One of the countries the pandemic has affected the most is Ecuador, a dramatically high number of unofficial death toll has put this country to the limit[3]. This burden has already stretched not only the health system but the economic engine in

this middle-income country. Ecuador is now facing the challenge to reopen its economy in a controlled manner, so a second wave is prevented. For that purpose, fine-tuned mathematical models can forecast the consequences of a certain decision. The proposed system to reopen the economy in Ecuador is based on a color code as a traffic light (Red: Complete lockdown, Yellow: Reduced lockdown, and Green: Back to the "new normality"). We have used the SIRD (Susceptible, Infected, Recovered, Deaths) model to analyze the light strategy, including parameters such as social distancing, improved hygiene, close borders and collapse of health system policies.

We present the estimation for the light system strategy based on a mathematical model to show the probable scenario when passing from red to yellow to green. When plotted, this strategy seems to impose unnecessary risks when changing from red light (80% lockdown) to yellow light (60% lockdown). **Figure 2** We depict the curve that shows when changing drastically to green light, the health system collapses.

The use of mathematics to study quantitative relationships and biological variables has allowed scientists and epidemiologists to offer new conjectures around disease transmission and populations. Acquiring rigorous deductions is often challenging among life sciences and medicine due to the highly variability among species, nevertheless, the dynamic of infections is well known, and the use of several mathematical models will allow us to predict from several perspectives, opening our view for plenty of possible scenarios. In this sense, we conclude that although the variability in the quantity and quality of the data varies from region to region, multiple modeling will improve the forecast and therefore have safer estimates for policy makers to confront epidemics.

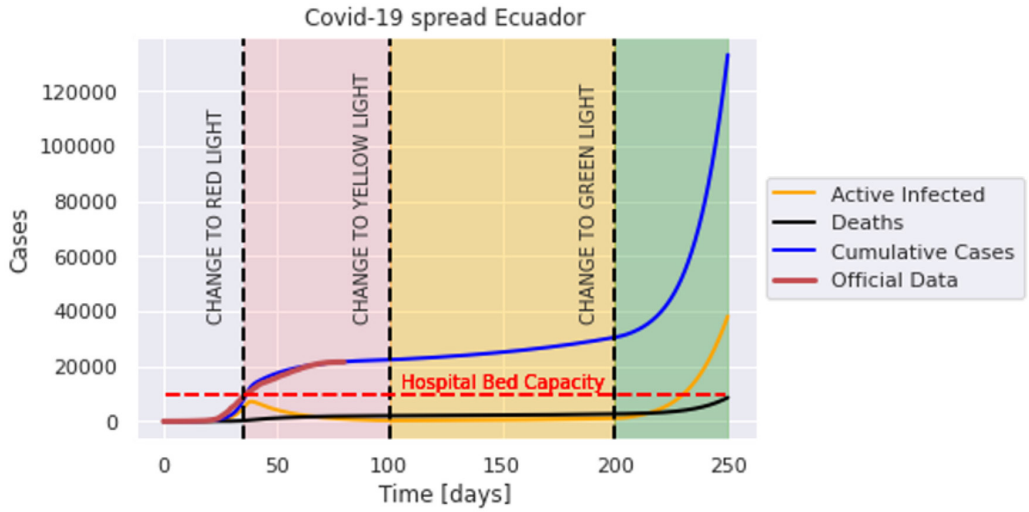

Figure 2. A SIRD model using 4 Dynamic variables, Susceptibles (S), Active infected (I), Recovered (R) and Death (D). with the constraint N=S+I+R+D. with N the population. We also have to define Cumulative cases C=I+R+D.

Referencias

1. Kucharski A. The Rules of Contagion: Why Things Spread-And Why They Stop. 2020.
2. Ortiz-Prado E, Simbaña-Rivera K, Gomez-Barreno L, Rubio-Neira M, Guaman LP, Kyriakidis N, et al. Clinical, Molecular and Epidemiological Characterization of the SARS-CoV2 Virus and the Coronavirus Disease 2019 (COVID-19): A Comprehensive Literature Review. 16 de abril de 2020 [citado 18 de abril de 2020]; Disponible en: https://www.preprints.org/manuscript/202004.0283/v1
3. Simbana-Rivera K, Gomez-Barreno L, Guerrero J, Simbana-Guaycha F, Fernandez R, Lopez-Cortes A, et al. Interim Analysis of Pandemic Coronavirus Disease 2019 (COVID-19) and the SARS-CoV-2 virus in Latin America and the Caribbean: Morbidity, Mortality and Molecular Testing Trends in the Region. medRxiv. 29 de abril de 2020;2020.04.25.20079863.
4. Kucharski AJ, Russell TW, Diamond C, Liu Y, Edmunds J, Funk S, et al. Early dynamics of transmission and control of COVID-19: a mathematical modelling study. Lancet Infect Dis. 2020 May;20(5):553-558
5. Zhang S, Diao M, Yu W, Pei L, Lin Z, Chen D. Estimation of the reproductive number of novel coronavirus (COVID-19) and the probable outbreak size on the Diamond Princess cruise ship: A data-driven analysis. Int J Infect Dis. 2020;93:201□204. doi:10.1016/j.ijid.2020.02.033
6. Zhao S, Lin Q, Ran J, Musa SS, Yang G, Wang W, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven analysis in the early phase of the outbreak. Int J Infect Dis. 2020;92:214–217.
7. Gumel AB, Ruan S, Day T, et al. Modelling strategies for controlling SARS outbreaks. Proc Biol Sci. 2004;271(1554):2223□2232. doi:10.1098/rspb.2004.2800.
8. Alimadadi A, Aryal S, Manandhar I, Munroe PB, Joe B, Cheng X. Artificial intelligence and machine learning to fight COVID-19. Physiol Genomics. 2020;52(4):200□202. doi:10.1152/physiolgenomics.00029.2020
9. Bettencourt LM, Ribeiro RM. Real time bayesian estimation of the epidemic potential of emerging infectious diseases. PLoS One. 2008;3(5):e2185. Published 2008 May 14. doi:10.1371/journal.pone.0002185.
10. Yuan J, Li M, Lv G, Lu ZK. Monitoring transmissibility and mortality of COVID-19 in Europe [published online ahead of print, 2020 Mar 28]. Int J Infect Dis. 2020;95:311□315. doi:10.1016/j.ijid.2020.03.050.