Prediction of Cumulative Death Cases in Brazil Due to Covid-19 Using Mathematical Models

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ABSTRACT

The novel corona virus (2019-nCoV) infection has spread rapidly to other provinces and neighbouring countries since the emergence of the first cases at Wuhan, China. Estimation of the death cases by mathematical modelling can help to determine the potential and severity of the outbreak and to provide critical information on the type and intensity of disease response. In this paper, we present different growth models such as Von Bertalanffy, Baranyi-Roberts, Morgan-Mercer-Flodin (MMF), modified Richards, modified Gompertz, modified Logistics and Huang in fitting and analyzing the epidemic trend of COVID-19 in the form of total number of death cases of SARS-CoV-2 in Brazil as of 15th of July 2020. The MMF model was found to be the best model with the highest adjusted R^2 value with the lowest RMSE value. The Accuracy and Bias Factors values were close to unity (1.0). The parameters obtained from the MMF model include maximum growth of death rate (log) of 0.03 (95% CI from 0.02 to 0.028), curve constant (δ) that affects the inflection point of 0.7057 (95% CI from 0.68 to 0.73) and maximal total number of death (y_{max}) of 17,619,760 (95% CI from 9,705,100 to 34,994,517). The MMF model predicted that the total number of death cases for Brazil on the coming 15th of August and 15th of September 2020 will be 132,787 (95% CI of 123,422 to 142,863) and 212,166 (95% CI of 192,578 to 233,746), respectively. The predictive ability of the model utilized in this study is a powerful tool for epidemiologist to monitor and assess the severity of COVID-19 in Brazil in months to come. However, as with any other model, these values need to be taken with caution due to the unpredictability of the COVID-19 situation locally and globally.

INTRODUCTION

The world is currently struggling with ongoing corona virus disease outbreaks, namely the 2019 corona virus disease (COVID-19) triggered by the novel corona virus, SARS-COV2, a highly virulent virus that has triggered COVID-19 to become a deadly disease, a disease that affects the human respiratory system [1].

Historically, mathematical models have been used to provide practical insight into the mechanisms of transmission and control of infectious diseases, reminiscent of the groundbreaking work of Sir Ronald Ross and Kermack-McKendrick in the 1900s [2]. Mathematical models have long developed quantitative knowledge in epidemiology and have provided useful guidance for managing outbreaks and designing policies. A variety of modelling studies have been carried out

particularly for COVID-19[3]. Numerous models were introduced to understand the mechanisms for COVID-19 spreading, regulating and mitigating worldwide, SEIR model [4]. A registered value of 3.1 was suggested for the simple early outbreak reproductive number using the assumption of regular time increases distributed by Poisson when fitting their results [5]. Other researchers [6] integrated into their model the clinical progression of the disease, the patient epidemiological status and the intervention measures and found that intervention strategies such as intense contact tracing accompanied by quarantine and isolation would effectively reduce the number of infection replication and the transmission risk.

Another group [7] performed statistical modelling of possible disease trajectories to estimate the scale of the outbreak in Wuhan, China, and their findings suggested that control measures need to block well over 60 per cent of the transmission in order to contain the outbreak effectively. Li et al. [8] applied an SEIR meta-population model and Bayesian inference to infer essential epidemiological characteristics in China, and their results showed that approximately 86 percent of all infections were unidentified before 23 January 2020.

The COVID-19 pandemic began in Brazil on 26 February 2020 and spread rapidly to the world, beginning in the states of Sao Paulo and Rio de Janeiro and spreading a few weeks later to other Brazilian states. Three months after the first COVID-19 outbreak, many Brazilian states are still in precarious condition, with their health systems overwhelmed, most of them occupying or even collapsing more than 80 per cent. Brazil is now considered Latin America's epidemic centre, taking second place in total number of cases and more recently in total deaths [9]. The situation in Brazil is critical and the authorities need a general scenario and the development of the Covid-19 trend. The Use of a basic maths model previously used for microorganism would be described here.

Usually, the growth curve of virus and microorganism on substrate such as nutrients or other organisms including human followed a sigmoidal pattern, starting with the lag section just after t = 0, followed by the logarithmic section and then the organism enters the stationary phase and finally moves to death phase or decline growth. In order to describe organism growth curve, there are various sigmoidal functions such as Von Bertalanffy, Baranyi-Roberts, modified Richards, modified Gompertz and modified Logistics [10] including Morgan-Mercer-Flodin (MMF) [11]. The growth curve valuable parameters include the maximum specific growth rate (μ_m), the lag period and the asymptotic values. Analyses of COVID-19 pandemic including theoretical, quantitative and simulation for the total number of death cases and deaths can be carried out using mathematical models. Models such as the modified Gompertz, von Bertalanffy and logistics have been utilized to model COVID-19 pandemic [12] with good predictive ability. The objective of this work is to evaluate several available models such as Logistic [10,13], Gompertz [10,14], Richards [10,15], Morgan-Mercer-Flodin (MMF) [11], Baranyi-Roberts [16], Von Bertalanffy [17,18], Buchanan three-phase [19] and more recently Huang model [20] in fitting and analyzing the epidemic trend of COVID-19 in the form of total death case of SARS-CoV-2 in Brazil as of 15th of July 2020.

MATERIALS AND METHODS

Data for the cumulative or total number of death cases from Brazil as of 15th of July 2020 was acquired from Worldommeter [21]. Data were first converted to logarithmic values and the time after first death was utilized for time zero.

Statistical analysis
Statistical significant difference between the models was calculated through various methods including the adjusted coefficient of determination (R^2), accuracy factor (AF), bias factor (BF), Root-Mean-Square Error (RMSE) and corrected AICc (Akaike Information Criterion) as before [22].

The RMSE was calculated according to Eq. (1), where Pd_i are the values predicted by the model and Ob_i are the experimental data, n is the number of experimental data, and p is the number of parameters of the assessed model.

$$RMSE = \sqrt{\frac{\sum_{i=1}^{n}(Pd_i - Ob_i)^2}{n-p}} \tag{eqn. 1}$$

The adjusted R^2 is used to calculate the quality of nonlinear models according to the formula where RMS is Residual Mean Square and S_y^2 is the total variance of the y-variable ad calculated as follows;

$$Adjusted\,(R^2) = 1 - \frac{RMS}{s_Y^2} \tag{eqn. 2}$$

$$Adjusted\,(R^2) = 1 - \frac{(1-R^2)(n-1)}{(n-p-1)} \tag{eqn. 3}$$

The Akaike information criterion (AIC) [23] was calculated as follows;

$$AICc = 2p + n\ln\left(\frac{RSS}{n}\right) + 2(p+1) + \frac{2(p+1)(p+2)}{n-p-2} \tag{eqn. 4}$$

Where n is the number of data points and p is the number of parameters of the model. The model with the smallest AICc value is highly likely correct [24].

Accuracy Factor (AF) and Bias Factor (BF) as suggested by Ross [25] were calculated as follows;

$$\text{Bias factor} = 10^{\left(\sum_{i=1}^{n}\log\frac{(Pd_i / Ob_i)}{n}\right)} \tag{eqn. 5}$$

$$\text{Accuracy factor} = 10^{\left(\sum_{i=1}^{n}\log\frac{|(Pd_i / Ob_i)|}{n}\right)} \tag{eqn. 6}$$

Fitting of the data

Fitting of the bacterial growth curve using various growth models (Table 1) was carried out using GraphPad Prism (v 8.0 trial version).

Table 1. Models used in this study.

Model	p	Equation
Modified Logistic	3	$y=\dfrac{A}{\left\{1+\exp\left[\frac{4\mu_m}{A}(\lambda-t)+2\right]\right\}}$
Modified Gompertz	3	$y=A\exp\left\{-\exp\left[\frac{\mu_m e}{A}(\lambda-t)+1\right]\right\}$
Modified Richards	4	$y=A\left\{1+v\exp(1+v)\exp\left[\frac{\mu_m}{A}(1+v)\left(1+\frac{1}{v}\right)(\lambda-t)\right]\right\}^{\left(\frac{-1}{v}\right)}$
Morgan-Mercer-Flodin (MMF)	4	$y=y_{max}-\dfrac{(y_{max}-\beta)}{1+(\mu_m t)^\delta}$
Baranyi-Roberts	4	$y=A+\mu_m x+\frac{1}{\mu_m}\ln\left(e^{-\mu_m x}+e^{-h_0}-e^{-\mu_m x-h_0}\right)$ $-\ln\left(1+\frac{e^{\mu_m x+\frac{1}{\mu_m}\ln\left(e^{-\mu_m x}+e^{-h_0}-e^{-\mu_m x-h_0}\right)}-1}{e^{(y_{max}-A)}}\right)$
Von Bertalanffy	3	$y=K\left[1-\left[1-\left(\frac{A}{K}\right)^{\frac{1}{3}}\right]\exp\left(-\mu_m x/3K^{\frac{1}{3}}\right)\right]^3$
Huang	4	$y=A+y_{max}-\ln\left(e^A+\left(e^{Y_{max}}-e^A\right)e^{-\mu_m B(x)}\right)$ $B(x)=x+\frac{1}{\alpha}\ln\frac{1+e^{-\alpha(x-\lambda)}}{1+e^{\alpha\lambda}}$
Buchanan Three-phase linear model	3	Y = A, IF X < LAG Y=A + K(X−λ), IF λ ≤ X ≥ X_{MAX} Y = Y_{MAX}, IF X ≥ X_{MAX}

Note:
A= maximum no of death cases lower asymptote;
y_{max}= maximum no of death cases upper asymptote;
μ_m= maximum specific growth rate of death;
v= affects near which asymptote maximum no of death cases occurs.
λ=lag time
e = exponent (2.718281828)
t = time after first death case is reported
α,β,δ and k = curve fitting parameters
h_0 = a dimensionless parameter quantifying the initial physiological state of the reduction process. The lag time (h⁻¹) or (d⁻¹) can be calculated as $h_0=\mu_m$
When data at time zero is 0 (Day after 1st death case log 1=0 for COVID-19) the MMF is reduced to a 3-parameter model

RESULTS AND DISCUSSION

Predictive mathematical epidemic models are fundamental for understanding the course of the epidemic and for planning effective control strategies (Giordano et al., 2020).
Figure **1 to 8** represent different models to test and predict the death cases due to covid 19 in Brazil. All of the curves tested show virtually acceptable best fits with the exception of the Buchanan-3-phase model **(Figs 4).** The best performance was the MMF model with the lowest value for RMSE, AICc and the highest value for adjusted R^2. The AF and BF values were also excellent for the model with their values which were closest to 1.0. The poorest performance was the Buchanan-3-phase model (Table 2) with lowest R^2 value. The coefficients for the best analysed model, MMF model are shown in Table 3.

Obviously, a model needs to integrate more variables, at a higher level of complexity, to better represent the (complex) truth. While such a model may theoretically be more beneficial in a practical sense , it is important to note that a model's increased complexity typically results in increased difficulty in evaluating, controlling and executing, thereby sacrificing some or all of the benefits of a simpler model counterpart. It is important to remember, in the meantime, that all mathematical models have underlying assumptions and conditions. No matter its form and sophistication, a model can never be greater than its hypotheses[3].

Prediction intervals were calculated and graphically displayed for each mathematical model of 95% confidence levels. These intervals can predict the behavior of culture in the future. The coefficients of these models are displayed in Tab. I. Their values determine the form of curves. They were found out after fitting experimental data to mathematical model. The coeffi cient A is carrying capacity, N_0 is the population size at time t = 0, r is the intrinsic growth rate and represents growth rate per capita and β by Richards model is the population intrinsic factor. The diff erent values of parameters N_0 and r are given by another form of equations of models. The parameter K is similar by all models, because it determines the maximum population size which should be the same.

Table 2. Statistical tests for the various models utilized in modelling the total number of death due to Covid 19 in Brazil as of 15th of July 2020.

Model	p	RMSE	R^2	adR^2	AF	BF	AICc
Huang	4	0.330	0.970	0.968	1.046	0.99	-95.73
Baranyi-Roberts	4	0.330	0.971	0.968	1.046	0.99	-95.74
modified Gompertz	3	0.279	0.978	0.976	1.062	1.00	-115.73
Buchanan-3-phase	3	0.433	0.948	0.945	1.062	0.99	-72.01
modified Richards	4	0.282	0.978	0.976	1.034	1.00	-111.25
MMF	3	0.116	0.996	0.996	1.013	1.00	-203.74
modified Logistics	3	0.382	0.956	0.953	1.045	0.99	-84.45
von Bertalanffy	3	0.232	0.985	0.984	1.029	1.00	-134.16

Note: p is no of parameter

Table 3. Coefficients as modelled using the MMF model.

Parameters	Value	95% Confidence interval	
μ_m	0.03	0.02	to 0.02837
δ	0.7057	0.68	to 0.73
y_{max}	17,619,760	9,705,100	to 34,994,517

Table 4. Predictions of COVID-19 pandemic for Brazil based on the MMF model.

Prediction	Mean	95% Confidence interval
Maximum number of total cases by the end of COVID-19	17,619,760	9,705,100 to 34,994,517
Maximum number of total cases by 15th of August 2020	132,787	123,422 to 142,863
Maximum number of total cases by 15th of September 2020	212,166	192,578 to 233,746

The parameters obtained from the MMF model include maximum growth of death rate (log) of 0.03 (95% CI from 0.02 to 0.028), curve constant (δ) that affects the inflection point of 0.7057 (95% CI from 0.68 to 0.73) and maximal total number of death (y_{max}) of 17,619,760 (95% CI from 9,705,100 to 34,994,517). The MMF model predicted that COVID-19 deaths will end about 3,027 days (95% CI of 1,866 to 4,188) days from 15th of July 2020 based on the lower bound of the 95% CI from the calculated maximum number of total cases (y_{max}) while the mean and upper 95% CI bound values failed to be predicted by the software for their number of days. The MMF predicted that the total number of death cases for Brazil on the coming 15th of August and 15th of September 2020 will be 132,787 (95% CI of 123,422 to 142,863) and 212,166 (95% CI of 192,578 to 233,746), respectively.

This prediction has to be taken with caution since the model failed to predict the number of days for the mean and upper 95% CI values and the number of days for COVID-19 to end may be much larger. Despite this, without governmental intervention such as imposing strict lockdown, the predicted number of deaths and duration of the pandemic are worrying and deserve further studies. In addition, these data were modelled after intensive Movement Control Order (MCO) measures and little increase to number of cases may appear at the end of the modelling period. If the MCO is lifted as observed in the coming weeks after the sampled data, if cases start to increase then the results of this modelling exercise will have to be validated and another modelling exercise will be carried out using data at the end of the modelling exercise as the baseline.

The MMF model was originally developed to describe a wide variety of nutrient-response relationships in higher organisms [11]. To date the model has found utility in a number of modelling exercise involving animals such as rabbit, sheep, horse, microorganisms [26–30], yield of oil palm [31], ethanol [32] and even in finance [33]. Whether the predicted data is correct or not will depend on a case by case basis and include effectiveness of lockdown, mutation of the virus that increases the infectivity rate of the virus to name a few. Certainly, the models will be revisited every few months to remodel the data so a better prediction can be obtained.
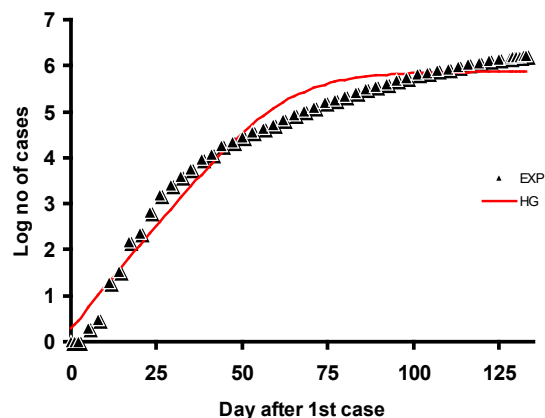

Fig. 1 Total no of SARS-CoV-2 death cases in Brazil as of 15th of July 2020 as modelled using the Huang model
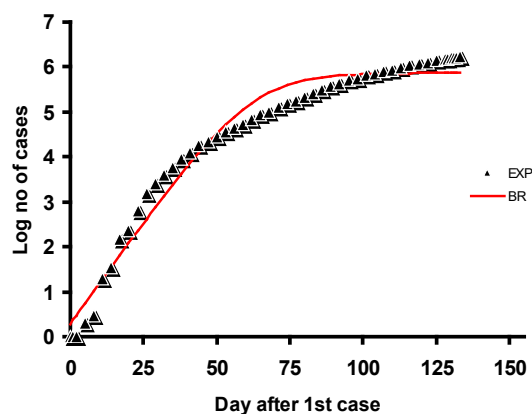

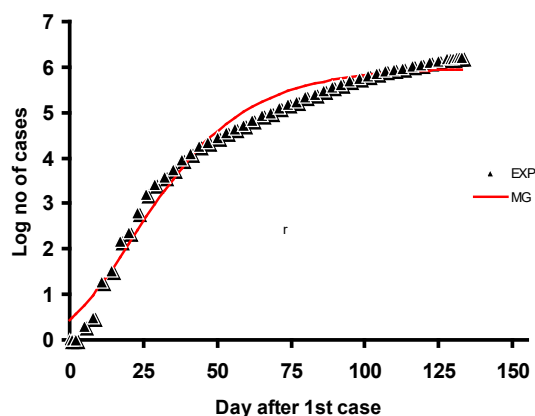**Fig. 2** Total no of SARS-CoV-2 death cases in Brazil as of 15th of July 2020 as modelled using the Baranyi-Roberts model

Fig. 3 Total no of SARS-CoV-2 death cases in Brazil as of 15th of July 2020 as modelled using the modified Gompertz model.
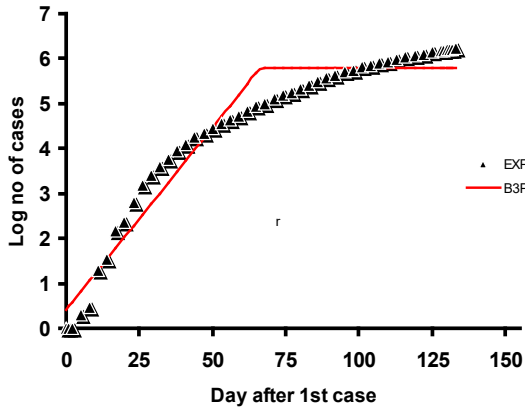
Fig. 4 Total no of SARS-CoV-2 death cases in Brazil as of 15th of July 2020 as modelled using the Buchanan-3-phase model.
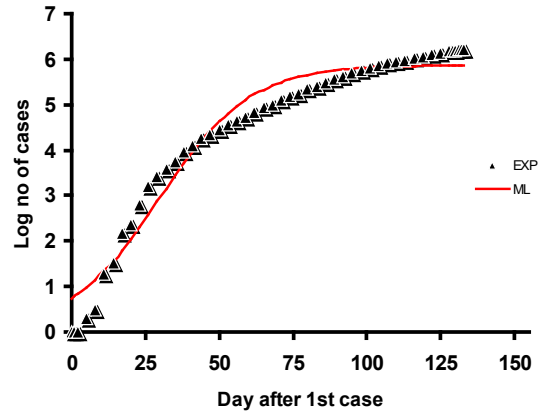

Fig. 7 Total no of SARS-CoV-2 death cases in Brazil as of 15th of July 2020 as modelled using the modified logistics model.
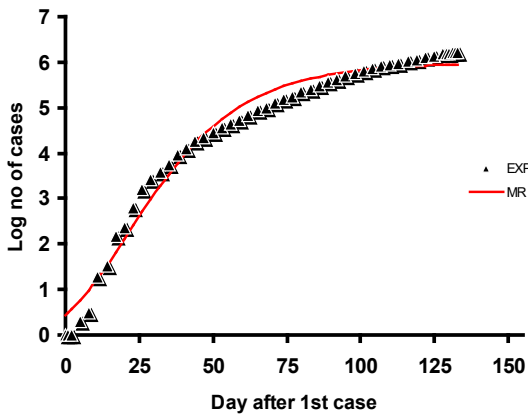

Fig. 5 Total no of SARS-CoV-2 death cases in Brazil as of 15th of July 2020 as modelled using the modified Richard model.
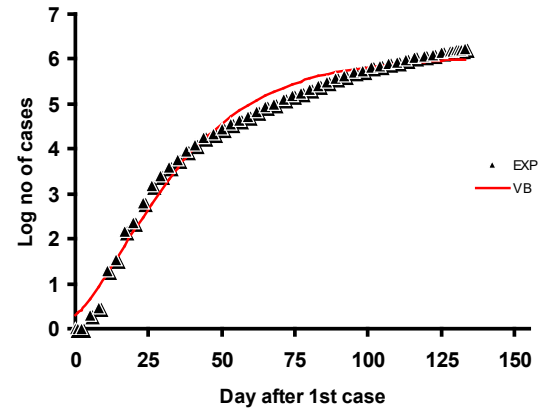

Fig. 8 Total no of SARS-CoV-2 death cases in Brazil as of 15th of July 2020 as modelled using the von Bertalanffy model.
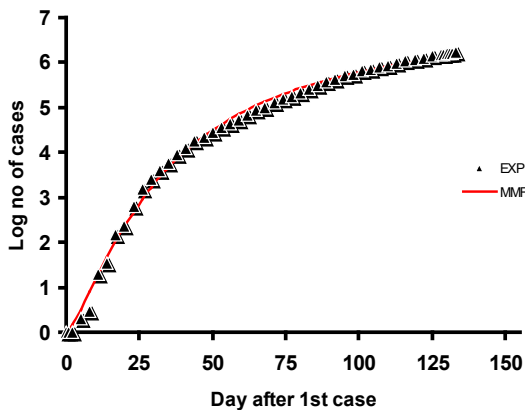

Fig. 6 Total no of SARS-CoV-2 death cases in Brazil as of 15th of July 2020 as modelled using the MMF model.

Masoudi et al. [34] reported that when nonlinear models are fitted to a data set of biological growth statistics, the non-significance of the estimated parameters may imply one of the following:

- One or more parameters in the model may not be useful, or more accurately, a reparameterized model involving fewer parameters might be more appropriate
- The biological growth data used for fitting the model are not adequate for estimating all the parameters; or
- The model assumptions do not conform with the biological system being modelled.

The argument in (ii) was the case with the Buchanan -3-phase model, the reason for not fitting in analyzing the death case of Covid 19 in Brazil.

CONCLUSION

In conclusion, the MMF model was the best model in modelling the cumulative number of death cases in Brazil based on statistical tests such as corrected AICc (Akaike Information Criterion), bias factor (BF), adjusted coefficient of determination (R^2) and root-mean-square error (RMSE). Parameters obtained from the fitting exercise were maximum growth rate (μ_m), the curve constants (δ) and maximal total number of death cases (Y_{max}). The parameters obtained from the MMF model include maximum growth of death rate (log) of 0.03 (95% CI from 0.02 to 0.028), curve constant (δ) that affects the inflection point of 0.7057 (95% CI from 0.68 to 0.73) and maximal total number of death (y_{max}) of 17,619,760 (95% CI from 9,705,100 to 34,994,517). The MMF predicted that the total number of death cases for Brazil on the coming 15th of August and 15th of September 2020 will be 132,787 (95% CI of 123,422 to 142,863) and 212,166 (95% CI of 192,578 to 233,746), respectively. The model allows for prediction of total number of death cases and this prediction will vary according to various number of factors. Despite this, the predictive ability of the model utilized in this study is a powerful tool for epidemiologist to monitor and assess the severity of COVID-19 in Brazil in months to come.

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