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The Sooner Strict Public Health Strategies are Applied the Lower the Peak of the Epidemic: the SARS-CoV-2 Case

J. G. VILLAVICENCIO-PULIDO[1*], I. BARRADAS[2], F. SALDAÑA[3] and C. NILA LUÉVANO[4]

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ABSTRACT. An epidemiological model is proposed to analyze the COVID-19 epidemics when control interventions are being applied to reduce the speed of the disease. The analyzed model includes parameters that describe control strategies such as behavioral changes of susceptible individuals to reduce the transmission of the disease, rates of diagnosis of the infectious individuals, and other control measures as cleaning and disinfection of contaminated environments. The proposed model is calibrated using Bayesian statistics and the official cumulative confirmed cases for COVID-19 in Mexico. We show which public health strategies contribute the most to the variation of R_0. A central result is the fact that the peak of the epidemics can drastically be changed depending on the time when the control strategies are introduced.

Keywords: SARS-CoV-2, COVID-19, epidemic model, public health strategies, parameter estimation.

1 INTRODUCTION

The COVID-19 pandemic has been the centre of intense epidemiological research in the last months. The infectious agent COVID-19 is the coronavirus SARS-CoV-2 that causes the severe acute respiratory syndrome. The COVID-19 infected at least 9.3 million of people in the world, and there have been at least 497,000 deaths from December, 2019 to June 26, 2020. Since the beginning of the epidemic in Wuhan, China, the Surveillances Epidemiological Systems of all countries have been alerted and have taken control measures against the disease. Despite this, there have been abundance COVID-19 cases in many countries. In this sense, the COVID-19 disease was declared, by the WHO, an international emergency on January 30, 2020, and it was declared a pandemic in March 11, 2020; see [25]. Since the WHO emitted the COVID-19 alert,

*Corresponding author: José Geiser Villavicencio Pulido – E-mail: j.villavicencio@correo.ler.uam.mx
[1]Departamento de Ciencias Ambientales, Universidad Autónoma Metropolitana, Av. de las Garzas No. 10, C.P. 52005, Lerma de Villada, Estado de México, México – E-mail: j.villavicencio@correo.ler.uam.mx https://orcid.org/0000-0003-1085-8556
[2]CIMAT. A.C., México – E-mail: barradas@cimat.mx https://orcid.org/0000-0002-5973-9200
[3]UNAM, México – E-mail: fernando.saldana@cimat.mx https://orcid.org/0000-0003-0558-1169
[4]Independent researcher, México – E-mail: claudia.nila@gmail.com https://orcid.org/0000-0002-9695-089X

the interventions for controlling the spread of COVID-19 have differed from one country to another. Those public health strategies differ from each other not only in the kind of intervention for controlling the epidemic outbreak but also in the time when they are applied to the population.

The transmission of COVID-19 may occur by different routes. Some of them are human-to-human contacts while others are humans-to-contaminated environments. In the former case, an effective infectious contact occurs when someone inhales respiratory droplets that are produced by an infectious individual, who can show symptoms or not; see [2]. In the second case, an effective infectious contact may occur if one susceptible individual touches a contaminated surface, and then he touches his own mouth, nose, or eyes. It has been suggested by different researches [8, 24] and by the WHO that COVID-19 virus is spreading more efficiently than influenza; however, it is spreading less efficiently than measles. The value of the basic reproduction number associated to measles ranges from $12 - 18$ [8]; while the basic reproduction number for H1N1 influenza ranges from 1.2 to 1.3 and the basic reproduction number for SARS-CoV-2 ranges from 2.5 to 3.2 [24].

On the other hand, the COVID-19 has revealed gaps in the health systems in many countries because almost all intensive care beds are being taken. This saturation of the healhtcare systems occurs because symptoms related to COVID-19 can cause from mild or moderate respiratory illness to severe respiratory illness, septic shock, or other characteristic that require intensive care as mechanical ventilation; see [15].

These reasons make us think of the importance of analyzing how control interventions can smooth the epidemic curve for the healthcare systems not to be saturated. The control interventions range from travel restriction, social distancing, including banning public gatherings, to hand hygiene; see [23, 26].

In this race against the spread of the coronavirus SARS-CoV-2, the epidemiological models have been used to understand and forecast the horizon of the epidemics [11, 13, 14, 22, 27]. Compartmental epidemiological models are frequently used as basic structure to model the spread of an infectious disease; see [4, 10]. These models are used for calculating some epidemiological parameters such as infectiousness rates and the basic reproduction number that is denoted by R_0.

In this work, the spread of COVID-19 is analyzed through one compartmental epidemic model that shows how the number of infectious individuals changes due to the application of control strategies into a population. Epidemiological parameters are estimated for the cases of COVID-19 in Mexico, which occurred from March 09, 2020 to May 07, 2020; see [16]. With this parameters, plausible scenarios are shown as function of the control interventions at an specific time. We will use Sobol method which is a variance-based global sensitivity analysis that decomposes the variance of the output of the model into fractions which can be attributed to sets of inputs using a sensitivity index. Also, Sobol's indices are calculated to find which model parameters must be chosen such that their election allows to reduce R_0 below 1, so that the epidemic outbreak will be controlled.

For this purpose, in Section 2, the epidemic model with adjusted-incidence is constructed to analyze the COVID-19 spread in a totally susceptible population; also, the basic reproduction number is calculated. In Section 3, epidemiological parameters are estimated using Bayesian statistics for COVID-19 cases in Mexico. In Section 4, Sobol's indices for basic reproduction number of the proposed model are calculated. In Section 5, plausible scenarios are shown as function of one specific time when the public health intervention strategies to control the coronavirus disease are applied. Finally, Section 6 presents a discussion of the obtained results.

2 MODEL CONSTRUCTION AND R_0

In this section, a compartmental epidemic model with adjusted-incidence is proposed to describe the evolution of an infectious disease when the total population is divided in epidemiological classes and there is one compartment to describe free-virus in the environment. For this purpose, the model proposed in [18] is extended.

2.1 The model

In the model are considered two possible ways of infection: human-to-human and human-vector-human contagion. The former occurs when a susceptible individual has contact with one infectious individual. The latter occurs when susceptible individuals are living in one contaminated environment [7], and they touch a surface with SARS-CoV-2 coronavirus. The model captures certain phenomenology related to some public health strategies which are being applied into a susceptible population to control the COVID-19 outbreak. Some examples of such phenomenology are the fact that all susceptible individuals reduce their probability of infection by a factor $1-\theta \in (0,1)$), by taking appropriate measures such as self-imposed home quarantine, social distancing, hand washing, mask-wearing and disinfection of dirty surfaces. For the rest of this work, the susceptible individuals applying preventive measures will be called cautious susceptible individuals.

In the formulation of the model, natural vital rates (birth and death rates) are not considered since the model dynamics is of interest only in the short-term as the life cycle of the coronavirus has been associated with a short time period. A model without vital rates is simpler but still allows to describe the evolution of the disease, particularly, the model analysis allows to find parameter conditions for an epidemic outbreak to occur.

The human population is divided as follows. $N(t) = S(t) + S_c(t) + E(t) + A(t) + I(t) + D(t) + R(t)$. We are interested mainly in the effects of two epidemiological classes, $S_c(t)$ and $D(t)$, the parameter related with these classes, and the public health strategies related to them. $S_c(t)$ denotes the cautious susceptible individuals, that is, the susceptible individuals who changed their behavior and became prudent susceptible individuals. $D(t)$ denotes diagnosed individuals who are isolated and treated. For the description of all the variables and parameters of the model see Tables 1 and 2. Because there are isolated individuals, new human-to-human infections are described by the term $\frac{\beta_A A+\beta_I I}{N-D-\delta S_c}S$, where $0<\delta<1$. The term $\frac{A+I}{N-D-\delta S_c} = \frac{A+I}{S(t)+(1-\delta)S_c(t)+E(t)+A(t)+I(t)+R(t)}$ describes the infectious fraction of the circulating population. This term is called adjusted-incidence

and it is used to describe the effect in the evolution of the disease due to the isolation of individuals. Notice that, when the incidence is modeled using adjusted-incidence, the number of contacts is maintained. This kind of incidence describes scenarios where some individual are forced to stay in quarantine but they are replaced by other individuals. For example, during the COVID-19 contingency, people belonging to risk classes were put into quarantine, and they were replaced by individuals without comorbidities. In particular, medical professionals were hired to help during the contingency; however, even though the number of contacts are maintained, there are more contacts between susceptible and infectious individuals; see [10]. The term δS_c in the adjusted-incidence can be interpreted as certain invisibility degree of cautious susceptible individuals. That is, they are not noted by infectious individuals because they follow in a strict way, for example, the instructions of social distancing. Being more specific, cautious susceptible individuals reduce the infectiousness rate by implementing social distancing strategies, staying at home during contingency, using mouth covers, cleansing and disinfecting, etc.

Table 1: Variables for model (3.1).

Variable	Variable description
$S(t)$	Susceptible individuals
$S_c(t)$	Cautious susceptible individuals
$E(t)$	Exposed/latent individuals
$A(t)$	Asymptomatic individuals
$I(t)$	Symptomatic individuals
$D(t)$	Diagnosed individuals being isolated and treated
$R(t)$	Recovered individuals
$V(t)$	SARS-CoV-2 in circulation in contaminated environments

Table 2: Model parameters for model (2.1).

Parameter	Parameter description
β_A	Asymptomatic infection rate
β_I	Symptomatic infection rate
β_V	Infection rate of hosts in a contaminated environment
σ	Transfer out rate of the exposed class
γ_A	Recovery rate of asymptomatic individuals
γ_I	Recovery rate of symptomatic individuals
μ	Induced-death rate of the disease
p	probability of one exposed individual becoming symptomatic
c_1	Virus reproduction rate by asymptomatic individuals
c_2	Virus reproduction rate by symptomatic individuals
μ_V	Natural mortality rate of virus circulating in the environment
α	Rate in which susceptible individuals become cautious susceptible individuals
θ	$\theta \in (0,1)$ reduction factor of the infectious rate
d_1	Diagnosis rate of exposed and asymptomatic individuals
d_2	Diagnosis rate of symptomatic individuals
γ_D	Recovery rate of diagnosed individuals
m	Induced-death rate of virus due to cleaning measures in the environment
δ	$\delta \in (0,1)$ fraction of susceptible individuals applying strict control strategies

With these assumptions the model is

$$\begin{aligned}
\dot{S} &= -\tfrac{(\beta_A A+\beta_I I)}{N-D-\delta S_c} S - \beta_V V S - \alpha S,\\
\dot{S}_c &= -\tfrac{(\beta_A A+\beta_I I)}{N-D-\delta S_c} \theta S_c - \beta_V \theta V S_c + \alpha S,\\
\dot{E} &= \tfrac{(\beta_A A+\beta_I I)}{N-D-\delta S_c} (S+\theta S_c) + \beta_V V S + \beta_V \theta V S_c - \sigma E - d_1 E,\\
\dot{A} &= (1-p)\sigma E - d_1 A - \gamma_A A,\\
\dot{I} &= p\sigma E - d_2 I - \gamma_I I - \mu I,\\
\dot{D} &= d_1(E+A) + d_2 I - \gamma_D D - \mu D,\\
\dot{R} &= \gamma_A A + \gamma_I I + \gamma_D D,\\
\dot{V} &= c_1 A + c_2 I - (\mu_V + m) V.
\end{aligned} \tag{2.1}$$

The most common term for describing infections is the mass action law (βSI). The term describes the number of new infections per unit of time that occur due to encounters between susceptible and infectious individuals. A mass action law term describes the cases for which the infectious load is reached by a single contact with an infectious individual. Therefore, the mass action law term models the assumption that given a contact, only a factor describing the probability of such contact turning into an actual infection is needed for the infection to occur. Then, the rates β_A and β_I are the product of the average number of single contacts between asymptomatic infectious or symptomatic infectious individuals and susceptible individuals per unit of time, and the probability that those encounters result in new infections. In analogous way, β_V is the average number of single contacts between susceptible individuals and contaminated surfaces, multiplied by the probability that those encounters result in new infections. Also, in the last equation in (2.1) parameter c_1 and c_2 are the contribution rates of coronavirus to the contaminated environment by asymptomatic infectious and symptomatic infectious individuals respectively; see [27]. In the model, a mortality rate m is considered for the circulating virus in the contaminated environment.

To analyze the behavior of an epidemic at the beginning of the disease, we need to calculate the disease-free equilibrium of model (2.1), which will be denoted by E_0. To compute the coordinates of E_0, we set the rates of changes of all state variables in model (2.1) equal to zero. Solving the nonlinear system of algebraic equations we obtain that $E_0 = (0, N_0, 0, 0, 0, 0, 0, 0)$. This equilibrium point can be explained as follows. In model (2.1) the susceptible population is always a non increasing function of time, and it is strictly decreasing if $\alpha > 0$. $\alpha = 0$ would mean that there is no baseline campaign to educate susceptible. $\alpha > 0$ would mean continuous social efforts to teach individuals to be cautious. In case $\alpha = 0$, the equilibrium point for the system is $(N_0, 0, 0, 0, 0, 0, 0, 0)$. In case $\alpha > 0$, the equilibrium point of the system is $(0, N_0, 0, 0, 0, 0, 0, 0)$. This corresponds to the fact that we are assuming that a cautious susceptible individual maintains the cautiousness all time. In other words, cautious susceptible individuals cannot return to the class of susceptible individuals.

In the following, we show a stability result for the disease-free equilbrium E_0.

Theorem 1. *For model* (2.1) *with* $R_0^A = \frac{\sigma}{(d_1+\gamma_A)(\sigma+d_1)}\left(\frac{\beta_A}{(1-\delta)} + \frac{c_1\beta_V N_0}{\mu_V+m}\right)\theta$,
$R_0^I = \frac{\sigma}{(d_2+\gamma_I+\mu)(\sigma+d_1)}\left(\frac{\beta_I}{(1-\delta)} + \frac{c_2\beta_V N_0}{\mu_V+m}\right)\theta$ *and* $R_0 = (1-p)R_0^A + pR_0^I$.
The disease-free equilibrium, E_0*, for system (2.1) is locally asymptotically stable if and only if* $R_0 < 1$.

Proof. To calculate the basic reproduction number we use the next generation matrix; see [4, 5]. For model (2.1), we calculate the matrix F and V that are defined in [4] which are given by

$$F = \begin{bmatrix} 0 & \frac{\beta_A\theta}{1-\delta} & \frac{\beta_I\theta}{1-\delta} & \theta\beta_V N_0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{2.2}$$

and

$$V = \begin{bmatrix} \sigma+d_1 & 0 & 0 & 0 \\ -(1-p)\sigma & \gamma_A+d_1 & 0 & 0 \\ -p\sigma & 0 & d_2+\gamma_I+\mu & 0 \\ 0 & -c_1 & -c_2 & \mu_V+m \end{bmatrix}. \tag{2.3}$$

Calculating the spectral radius of the next generation matrix FV^{-1}, the basic reproduction number is obtained. It is given by

$$R_0 = (1-p)R_0^A + pR_0^I. \tag{2.4}$$

Where

$$R_0^A = \frac{\sigma}{(d_1+\gamma_A)(\sigma+d_1)}\left(\frac{\beta_A}{(1-\delta)} + \frac{c_1\beta_V N_0}{\mu_V+m}\right)\theta \tag{2.5}$$

and

$$R_0^I = \frac{\sigma}{(d_2+\gamma_I+\mu)(\sigma+d_1)}\left(\frac{\beta_I}{(1-\delta)} + \frac{c_2\beta_V N_0}{\mu_V+m}\right)\theta \tag{2.6}$$

As a consequence of Theorem 2 in [4], the disease-free equilibrium point, E_0, is locally asymptotically stable. □

Therefore, if the number of secondary infections that an infectious individual produces during his infectious period, in a completely susceptible population, is less than 1 ($R_0 < 1$), then the infection cannot grow. In contrast, if the number of secondary infections produced by an infected individual is greater than 1 ($R_0 > 1$), then, an epidemic outbreak occurs [4, 5]. Then, for initial conditions close to E_0, if $R_0 < 1$ there are not an epidemic outbreak. In contrast, if $R_0 > 1$, the disease can persist in the population.

Note that R_0 is independent of the rates γ_D and α. Independence of the parameter γ_D can be explained using the argument that people in the diagnosed class is isolated during the mean period $\frac{1}{\gamma_D}$. During this period, new infections do not occur due to isolated individuals; also, after people are moved out the diagnosed class, they are no longer infectious individuals. Even though the basic reproduction number does not depend on α, its effects are included in the factor θ, which is a reduction factor of the infectiousness rate.

The decomposition of R_0 in the components R_0^A and R_0^I allows to measure the contributions of the asymptomatic and symptomatic class to the progression of infected individuals. So, R_0 is a function of the new transmissions due to the asymptomatic and symptomatic individuals. That is, R_0 for model 2.1 is the weighted sum of the new infections associated to the two infectious classes; asymptomatic and symptomatic individuals. Each components of the basic reproduction number takes into account the contributions of human-to-human contagions and the human-to-contaminated environment contagions as a function of the class, that is, R_0^A measures the contribution of the asymptomatic individuals to R_0 while R_0^I measures the contribution of the symptomatic individuals to R_0. Observe that, R_0 increases with δ. That is, δ increases the effect of the infectiousness rates β_A and β_I in R_0. In other words, δ compensates the effects of the adjusted-incidence.

3 PARAMETER ESTIMATES

In this section, some parameters of the model without intervention control are estimated. In the evolution of the COVID-19 epidemic there are epidemiological and demographic parameters involved that can be known; however, parameters related to the transmission rates are so difficult to estimate because there are many social and environmental drivers involved. In this sense, model (2.1) without control interventions will be used to estimate some parameters. This is shown here.

$$\begin{aligned}
\dot{S} &= -\tfrac{\beta_A SA+\beta_I SI}{N} - \beta_V SV,\\
\dot{E} &= \tfrac{\beta_A SA+\beta_I SI}{N} + \beta_V SV - \sigma E,\\
\dot{A} &= (1-p)\sigma E - \gamma_A A,\\
\dot{I} &= p\sigma E - \gamma_I I - \mu I,\\
\dot{R} &= \gamma_A A + \gamma_I I,\\
\dot{V} &= c_1 A + c_2 I - \mu_V V.
\end{aligned} \tag{3.1}$$

In this case, the population is given by $N(t) = S(t)+E(t)+A(t)+I(t)+R(t)$, and the parameters $\alpha, \delta, \theta, d_1, d_2, \gamma_D$ for model (2.1) are zero.

To calculate the disease-free equilibrium associated to model (3.1), we set the right side of equations in model (2.1) equal to zero. Solving the system of algebraic equations we obtain that the disease-free equilibrium for model (3.1) is $E_0 = (N_0, 0, 0, 0, 0, 0)$.

Now, we show a stability result associated to model (3.1).

Theorem 1. *The disease-free equilibrium, E_0, for system (3.1) is locally asymptotically stable if and only if $R_0 < 1$.*

Proof. To prove the result, we calculate the matrix F and V, that are defined in [4], which are given by

$$F = \begin{bmatrix} 0 & \beta_A & \beta_I & \beta_V N_0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \tag{3.2}$$

and

$$V = \begin{bmatrix} \sigma & 0 & 0 & 0 \\ -(1-p) & \gamma_A & 0 & 0 \\ -p\sigma & 0 & \gamma_I + \mu & 0 \\ 0 & -c_1 & -c_2 & \mu_V \end{bmatrix}. \tag{3.3}$$

It is know that the basic reproduction number, R_0, is the spectral radius of the next generation matrix FV^{-1}. Then

$$R_0 = (1-p)R_0^A + pR_0^I, \tag{3.4}$$

with

$$R_0^A = \left(\beta_A + c_1 \frac{\beta_V N_0}{\mu_V}\right) \frac{1}{\gamma_A} \tag{3.5}$$

and

$$R_0^I = \left(\beta_I + c_2 \frac{\beta_V N_0}{\mu_V}\right) \frac{1}{\gamma_I + \mu}. \tag{3.6}$$

As a consequence of Theorem 2 in [4], we establish the following result. The disease-free equilibrium $E_0 = (N_0, 0, 0, 0, 0, 0)$ is locally asymptotically stable. □

To calibrate model (3.1), the unknown parameters $\phi = (\beta_A, \beta_I, \beta_V, c_1, c_2)$ will be estimated using a Bayesian approach based on MCMC (Markov Chain Monte Carlo). This estimation uses the pytwalk implementation on Python; see [3]. For this, some parameter values that appear in the epidemiological literature will be used (see Table 3).

Table 3: Values of some epidemiological parameters for model (3.1).

Parameter	Value	Units	Source
σ	0.15325	day^{-1}	[1]
γ_A	0.13978	day^{-1}	[21]
γ_I	0.33029	day^{-1}	[21]
γ_D	0.1162	day^{-1}	[21]
μ	1.7826×10^{-5}	day^{-1}	[21]
p	0.868343	*dimensionless*	[21]
μ_V	1	day^{-1}	[12]

It is assumed that data $y = (y_0, y_1, ..., y_n)$ consisting on the cumulative daily cases of infected individuals can be modeled as

$$y_t = C(t;\phi) + \eta_t \tag{3.7}$$

where $t = 0, ..., n$, and η_t are independent identically distributed random variables with normal distribution with mean 0 and unknown variance κ^2.

$$C(t;\phi) \quad = \quad \sum_{i=0}^{t} I(i;\phi) \quad = \quad y_0 + \sum_{i=1}^{t} I(i;\phi) \tag{3.8}$$

where $I(i;\phi)$ is the solution of the ODE's system 3.1 for the I compartment given a fixed vector of parameters ϕ with initial values $(S_0, E_0, A_0, I_0, R_0, V_0)$. That is, $I(i;\phi)$ are the infected individuals at time i given ϕ.

The prior distribution for the unknown parameters assumes independence among them. We propose different Gamma distributions for the infection rates and the shedding rates; see (3.10). To take into account the possible asymmetry of the parameter distribution and plausible values concentrated towards zero, we propose gamma distributions for the parameters β_A, β_I and β_V with expected values in agreement with the results presented in [21, 27] to allow the parameters to take values in all positive real numbers. Also, we consider different scales of magnitude for the parameters β_A, β_I and β_V, and for the parameters c_1 and c_2. Therefore:

$$\pi(\phi, \kappa^2) = \pi_1(\beta_A)\pi_2(\beta_I)\pi_3(\beta_V)\pi_4(c_1)\pi_5(c_2)\pi_6(\kappa^2). \tag{3.9}$$

Where

$$\begin{array}{rcl} \beta_A & \sim & \Gamma(1, 10^7) \\ \beta_I & \sim & \Gamma(1, 10^7) \\ \beta_V & \sim & \Gamma(1, 10^7) \\ c_1 & \sim & \Gamma(\frac{121}{24}, \frac{11}{24}) \\ c_2 & \sim & \Gamma(\frac{121}{24}, \frac{11}{24}) \\ \kappa^2 & \sim & \Gamma(1, 10^2) \end{array} \tag{3.10}$$

With a gamma distribution with shape parameter α and inverse scale parameter β, where $z \sim \Gamma(\alpha, \beta)$ means $E(z) = \frac{\alpha}{\beta}$ and $Var(z) = \frac{\alpha}{\beta^2}$.

The pytwalk based on MCMC was simulated in Python for $200,000$ samples with $100,000$ burnin. It returns posterior parameter distributions shown in Figure 1. The maximum a posteriori estimators (MAP), the posterior mean and credible intervals, which were calculated with the library ArviZ, are shown in Table 4.

Table 4: Estimated values of the infectious rates and shedding rates for model (3.1) with its credible intervals.

Parameter	MAP estimate	Posterior mean	95% credible interval
β_A	0.0011449235	0.0011419836	$(4.48\times10^{-5}, 0.071054381)$
β_I	0.020927934	0.107460168	$(0.008764924, 0.290194056)$
β_V	2.70×10^{-6}	2.84×10^{-6}	$(2.63\times10^{-6}, 2.92\times10^{-6})$
c_1	0.000898382	0.00230416	$(0.0001092413, 0.003184447)$
c_2	0.001474126	0.000821253	$(0.000324343, 0.001658102)$

The estimated values of the infection rates β_A, β_I, and β_V seem to be far from the estimated rates that were calculated in [21, 27]; however, β_V is very close to parameter value calculated in [21, 27].

Analyzing the MAP estimated rates it turns out the infectiousness rate corresponding to symptomatic infectious individuals is less than the one corresponding to the asymptomatic infectious individuals. This agrees with the fact that asymptomatic infectious individuals are not isolated and symptomatic individuals are isolated when they are diagnosed. On the other hand, comparing the shedding rates we see that $c_2 > c_1$. That is, symptomatic infectious individuals contribute more than asymptomatic ones to the environmental contamination.

The R_0 estimation as well as using the maximum a posteriori (MAP) and the mean posterior estimates are given by $R_0^{MAP} = 1.630414577$ and $R_0^M = 1.566609364$ respectively. These values of R_0 agree with the values calculated in [17, 21, 27].

Using the parameters given in Tables 3 and 4, the cumulative cases of infected individuals $I(t)$ for the MAP and the mean posterior estimates and the data per data are showed in the Figure 2.

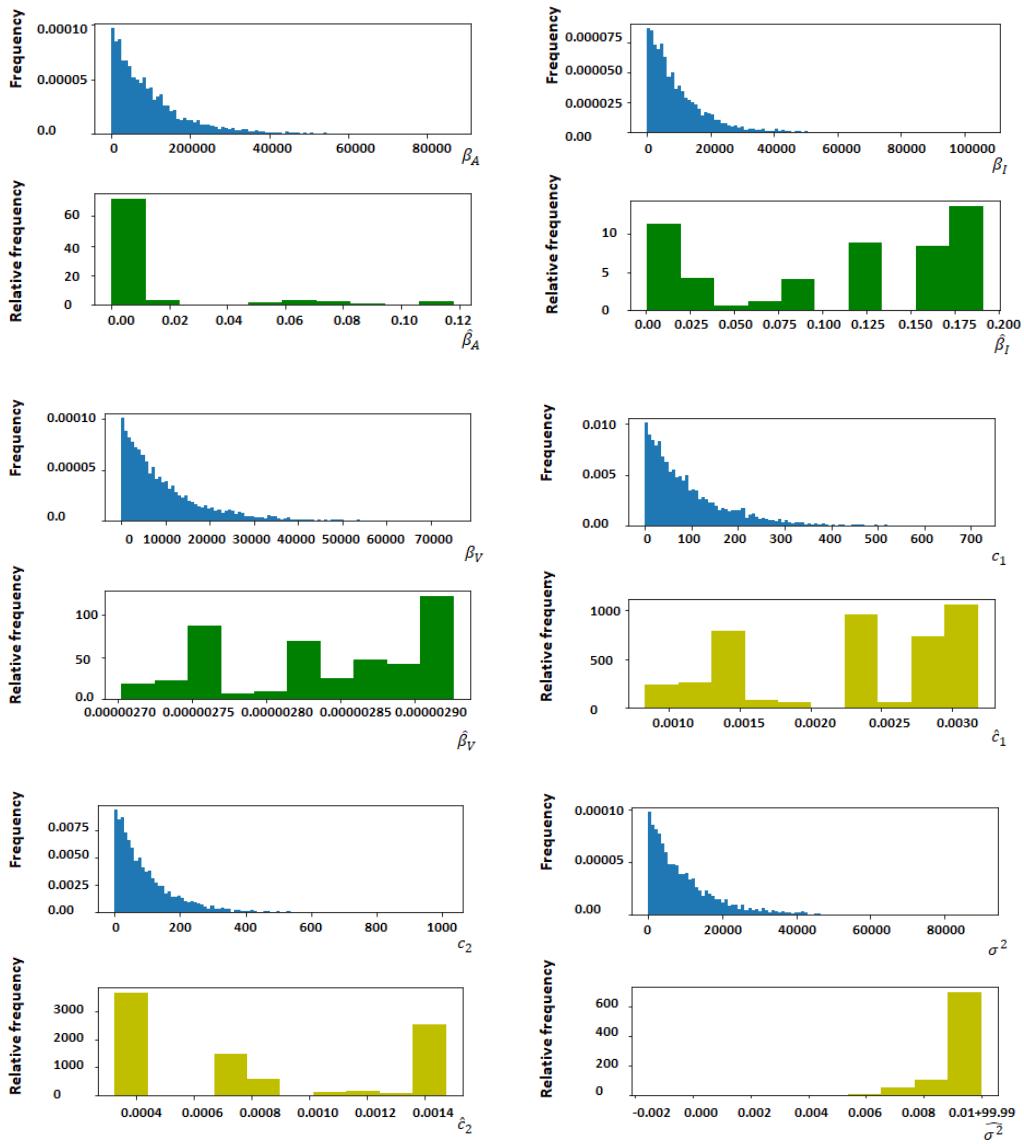

Figure 1: In each case, at the top it shows the prior distribution histogram which shows the values of the parameters that enter into the model while at the botton it shows the posterior distribution histogram which shows the values of the parameters estimated applying the Bayesian model. Observe that the priors frequencies are relative while in posteriors frequencies are absolute.

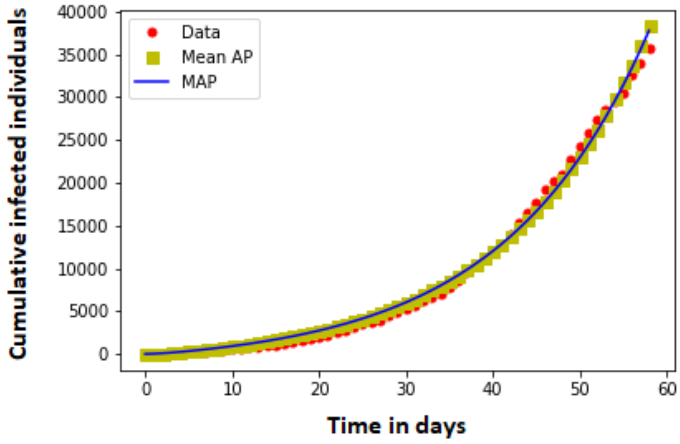

Figure 2: Figure shows the cumulative infections $C(t;\phi)$ for the basic model (3.1) using the estimated MAP (blue), the mean from the posterior distribution for ϕ (yellow), and the confirmed cases for COVID-19 in Mexico from March 09, 2020 to May 07, 2020 (red).

4 SENSITIVITY ANALYSIS

Calculating the basic reproduction number for one model is not enough to design control interventions because the effect of each parameter over the threshold parameter R_0 is unknown. In this sense, it would be better for the public health strategies to take into consideration the parameters to which R_0 is more sensitive.

In this section, the Sobol's indices for the basic reproduction number for the model with control interventions (model 2.1) will be calculated; see [17, 19, 20]. We perform the Sobol sensitivity analysis and the graphics of contribution of each parameter on R_0 using the python library Salib [9]. The Sobol's indices will be used to measure the variation of the basic reproduction number given by (2.4) as a function of the relative contribution of the parameters involved in the control interventions. For this, the parameters were ranged in the intervals shown in Table 5.

Figure 3 shows the direct contribution of each parameter on R_0. It also shows the combined contribution of several parameters.

Scenario A) shows that when cautious individuals are extremely cautious, i. e. having a reduction of the infection rate higher than 50%, $0 \leq \theta \leq 0.5$, the parameter θ contributes in 52%. At the same time the parameters associated to the diagnostic rates d_1 and d_2 contribute to the variation of R_0 less than 25%, while cleaning and disinfecting contribute no more in 10% to the variation of R_0. On the opposite scenario case B), i. e. when $0.5 \leq \theta \leq 1$ other contribution prevail. The added contribution of d_1 and d_2 is bigger than 45%, while changes in m contribute less than in 20% to the variation of R_0.

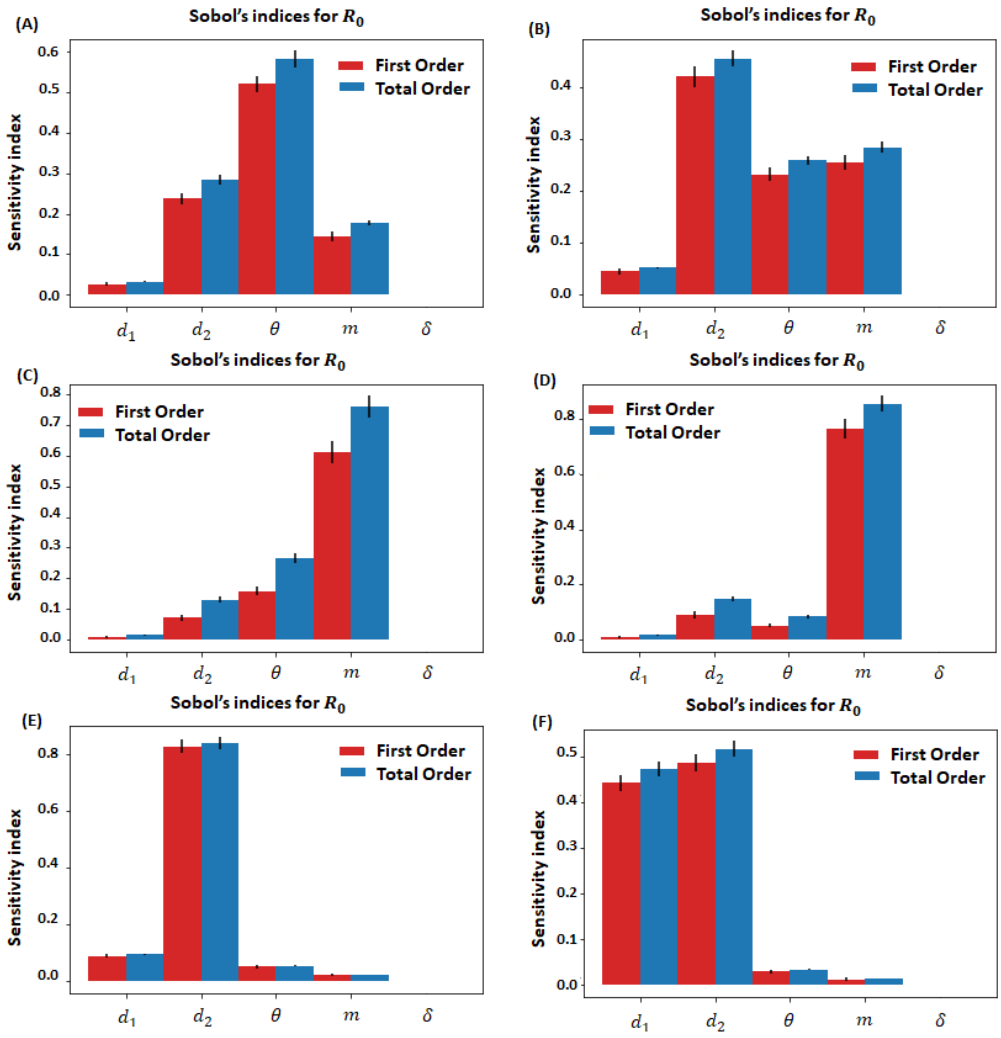

Figure 3: Sobol's indices for the basic reproduction number R_0 associated to model (2.1), for the first and total orders. The Sobol's indices were explored in the ranges showed in Table 5.

Cases C) and D) show scenarios for which the viruses' mortality rate, m is big so that the viruses in the environment degrade rapidly. In particular, scenario C) shows that if the infectiousness rate reduction is less than 50% $(0 \leq \theta \leq 0.5)$, the remaining parameters cannot be neglected, because the sum of their total-order sensibility by Sobol's indices is above 37% which means that still 37% of changes of R_0 can be explained by changes in these parameters. Case D) shows that if $\theta > 0.5$, the contribution of the other parameters to the variation of R_0 is less than 20% in the first as well as in the total orders.

Cases E) and F) show scenarios for which the cautious susceptible individuals do not reduce the infection rate massively (a poor reduction of the infection, $0.8 \leq \theta \leq 1$) and there is a bad cleaning and disinfection of surfaces. In case E), the diagnostic rate of infectious individuals contributes to the variation of R_0 in at least 80% in the first and total order of the Sobol's indices. Notice that, in this scenario, the contribution of the parameters d_1, θ and m to variations in R_0 may be neglected. Case F) shows the scenario of which the asymptomatic individuals are diagnosed with a big rate. Note that, the cases of diagnosed asymptomatic individuals contribute less than 40% to the $R_0's$ variation, and the diagnosed symptomatic individuals contribute less than 45% to the variation of R_0. Observe that, in real world scenarios diagnosing asymptomatic individuals implies a higher effort due to the difficult of finding them.

In all analyzed cases, the Sobol indices of δ is null. That is, the number of cautious susceptible individuals who are subtracted from the population $N(t)$ in the adjusted-incidence rate does not affect to the possible values of the basic reproduction number; see Figure 3.

Table 5: Variation ranges for the analysis of the Sobol's indices for the parameters of R_0 for model (3.1).

	d_1	d_2	θ	m	δ
Case A)	[0.0,0.0505]	[0.0,0.505]	[0,0.5]	[0.0,1]	$(0,1)$
Case B)	[0.0,0.0505]	[0.0,0.505]	[0.5,1]	[0.0,1]	$(0,1)$
Case C)	[0.0,0.0505]	[0.0,0.505]	[0,0.5]	[0.0,10]	$(0,1)$
Case D)	[0.0,0.0505]	[0.0,0.505]	[0.5,1]	[0.0,10]	$(0,1)$
Case E)	[0.0,0.0505]	[0.0,0.505]	[0.8,1]	[0.0,0.156]	$(0,1)$
Case F)	[0.0,0.2]	[0.0,0.505]	[0.8,1]	[0.0,0.156]	$(0,1)$

5 NUMERICAL SIMULATIONS

In this section we show numerical solutions of model (2.1). All figures as well as all calculations were produced by the authors via the Python computer program, version 3.8.8 (Python Software Foundation License). The numerical simulations show scenarios for which control interventions are applied at diverse moments after March 09, 2020. In this date, there were recorded 25 diagnosed infectious cases in Mexico City. To simulate scenarios for the epidemic outbreak, we use the values of the parameters given in the Tables 3 and 4 and hypothetical values for the parameters associated with control interventions. In the following, the solution using the estimated values (MAP solution) will be represented in blue color.

Figure 4 shows plausible scenarios when lax control interventions to control the epidemic outbreak are applied with a delay from 1 to 12 weeks after March 09, 2020. The values of the parameter used to describe lax control interventions are $\alpha = 1.0 \times 10^{-12}$, $\theta = 0.999$, $d_1 = 2.0 \times 10^{-5}$, $d_2 = 2.0 \times 10^{-4}$, $m = 1.0 \times^{-6}$, $\delta = 1.0 \times 10^{-9}$. We choose small values for α, m, δ and $(1-\theta)$ to describe that the intervention controls are not strict, and we choose d_1 and d_2 close to zero to describe the scenario for which very few infectious individuals are being diagnosed and treated. In

Mexico, according to some early reports, only 10 percent of mild suspected cases were tested for COVID-19 [6]. On the other hand, for severe cases, 100 percent of patients were tested. Hence, we assume $10d_1 = d_2$.

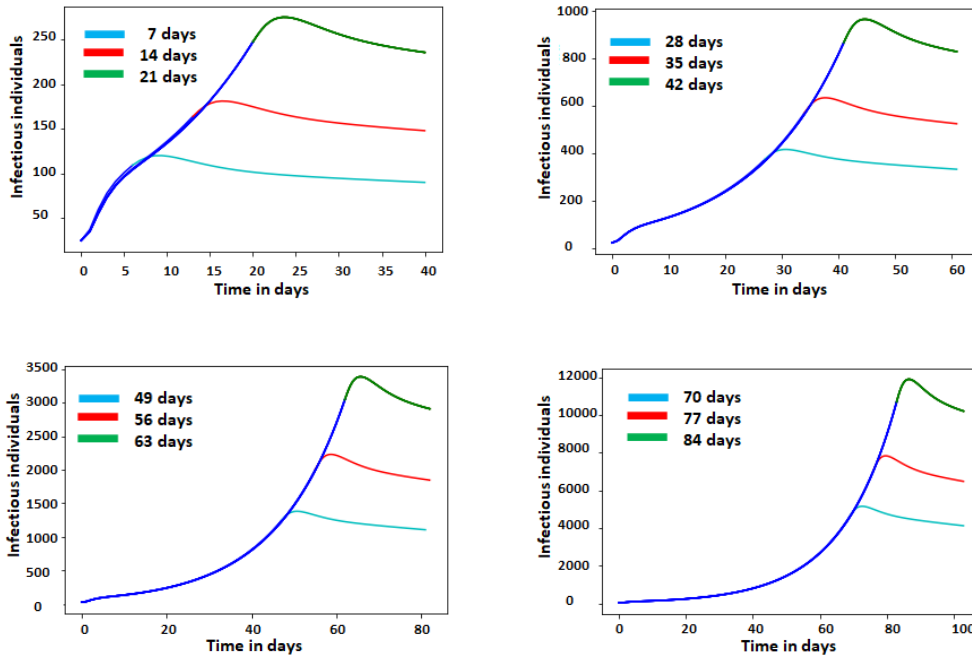

Figure 4: The adjusted solution of model (2.1) at day 7, 14, 21, 28, 35, 42, 49, 56, 63, 70, 77, and 84 is given in color blue. The behavior of solution for future times is given in the other colors. Figures show the effect exerted in the number of infectious individuals when the control interventions are applied in different days after the beginning of the epidemic.

Figure 5 shows two scenarios. In case (a), it is shown the evolution of the number of infected individuals for a scenario in which public health strategies are applied in a population starting day 63 after the beginning of the disease (blue line). The behavior of the solution of model (2.1) for future times is represented with green color. In case (b), it is shown a scenario without control interventions. Figure 6 shows two plausible scenarios: in the first case public health strategies are being strictly applied for cautious susceptible individuals and more infectious individuals are diagnosed (green line). For this scenario, the parameter values are $\alpha = 0.8, \theta = 0.001, d_1 = 0.02, d_2 = 0.2, m = 10, \delta = 0.9$. In this scenario, $m = 10$ describes the case for which the life expectancy of the virus is rapidly reduced to zero because contaminated surfaces were rapidly disinfected. Since $\frac{1}{\mu_V + m}$ describes the mean period that the virus is in the contaminated environment before it is cleaned.

The second scenario describes the case for which the intervention controls are not strict (red line), and the values of the parameters are the same as in the scenarios shown in Figure 4.

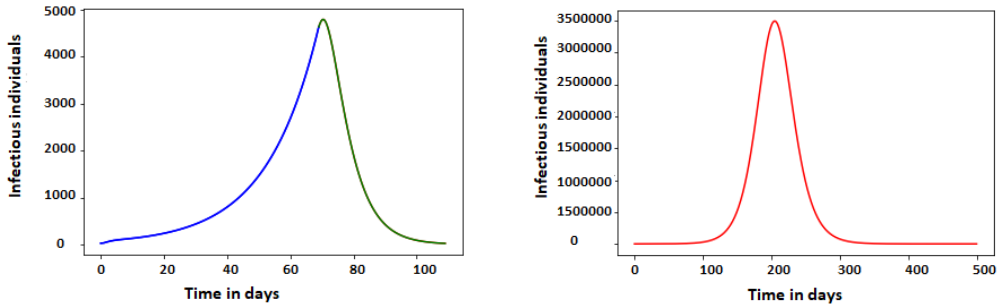

Figure 5: Case a) shows the solution of the combined model (2.1) for an horizon of 175 days. The solution from the beginning of the epidemic to the day 70 (when control strategies were applied) is represented with green color. The solution in color green shows the behavior of the solutions for future times. Case b) shows the solution of the basic model (3.1) for a horizon of 250 days if control strategies were not applied.

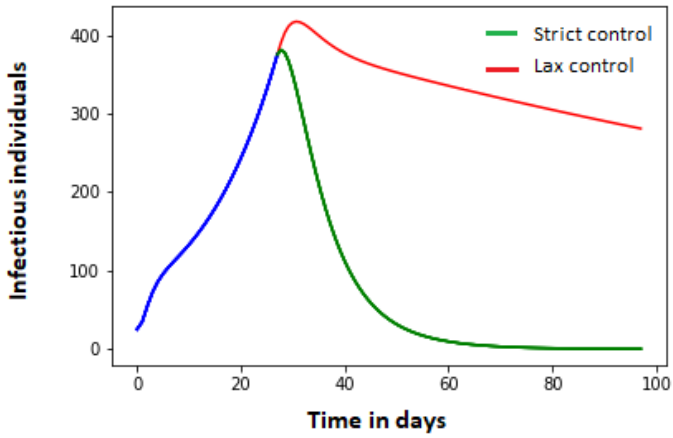

Figure 6: Figure shows the effect in the shape of the epidemic curve given by model (2.1), if control interventions are applied starting day 28 after the beginning of the epidemic (blue line). In particular, the suggested parameters by the Sobol's analysis are changed. For the scenario with strict intervention controls (green line) the parameters are $\alpha = 0.8, \theta = 0.001, d_1 = 0.02, d_2 = 0.2, m = 10, \delta = 0.9$ while, for the lax scenario (red line), the parameters are the same as that the values used for the scenarios shown in Figure 4.

6 DISCUSSION

The implications of the occurrence of epidemic outbreaks such as the Covid-19 have a great social and economic impact. That is why all new knowledge of its dynamics can leads to understanding, controlling, and even forecasting the spread of COVID-19 in future times. In this work, we focus on how the control interventions affect the evolution of the disease. We present a mathematical model for Covid-19 that explicitly incorporates the asymptomatic individuals category and the possibility of a contaminated environment. We also include the role played by behavioral changes of the individual due to external as well as internal decisions. It could include reacting to a large number of cases by staying home, being more cautious in general or just washing hands more often. In a different setting it includes restrictions set by a central authority. In any case it is of great interest to know the effect of each parameter on the outcome of the epidemics. In particular we found that personal care and personal protection together with regular environmental cleansing can strongly reduce the need for regular screening, which is not affordable in some setting or at least may be more expensive than education. We found in the case of lax restrictions or careless behaviour that the screening requirements for controlling the epidemics can dramatically grow.

Since the parameter associated to the cautious individuals, θ, is located in the numerator of R_0, the results suggest that changes in the behavioral conducts have a big impact in the spread of the infectious disease. When susceptible individuals turn cautious, they decrease their chances of being infected which has a big impact in the evolution of the COVID-19 epidemic. This agrees with results of the sensitivity analysis since the Sobol's indexes indicate that the parameters θ and m have a higher contribution to the variation of R_0. In particular, when the efforts are concentrated in increasing θ and m, the contributions of the other parameters such as the diagnostic rates d_1 and d_2 decrease. Notice that increasing θ and m has to do with human behavior more than with economical issues, whereas diagnostic requires not only an economical but a social effort. In particular, the diagnosis of asymptomatic individuals needing to find them before they can be tested. Therefore, it is of paramount importance that susceptible individuals boost their awareness about public health strategies in which they can contribute to decrease the speed of the propagation of the SARS-CoV-2. Those control interventions include, hand hygiene practices, cleaning and disinfection of contaminated surfaces, safe management of health care waste associated with infected individual, environmental cleansing, social distancing, etc. The system is highly sensitive to the moment the control strategies are introduced. The sooner control strategies are applied the lower the epidemic peak will be. Figure 4 shows that the smallest epidemic peak is associated with the shortest reaction time, and this peak is smaller in many orders of magnitude. Figure 5 shows the solutions $I(t)$ for the model when the intervention controls are applied 10 week after the start of the epidemic (March 09, 2020), and without intervention controls. Note that any health care system can collapse if the epidemic follows its natural spread, while it is not the case when there are opportune control interventions and the epidemic outbreak can be administered.

Figure 6 shows that the shape of the solutions $I(t)$ for model (2.1) are drastically changed as a function of the parameters that describe the public health strategies. Note that the epidemic

curve suffers changes in its shape depending whether the intervention controls are lax or strict. In both cases, the number of new infectious individuals decrease until the epidemic outbreak is controlled. Since, the sooner public health strategies are applied the lower number of infectious individuals will be, it follows that the epidemic peak can be drastically decreased further if strict interventions strategies to control the spreading of the SARS-CoV-2 are used. So, the central statement we can share is the fact that the sooner a public health strategy is applied the stronger its effect on the reduction of the peak reached in the outbreak. This means, promt allocation of resources as an early response can save huge amounts later on. This might be of relevance for future waves of Covid-19 or any similar diseases.

Ongoing work, by the authors is looking into the effect of periodical behavioral changes of the susceptible individuals in the evolution of the spread of the infectious disease.

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