

Biomaths in times of Coronavirus

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Since the outbreak of the coronavirus disease 19 (COVID-19), many mathematical models have been proposed, various of which several governments had used to implement their policy to lockdown the population. In particular, Mexico City has posed for an ordinary differential equations model to keep the spread of the virus under control. But, no optimal span of the lockdown was proposed, and therefore, the city is in an indefinite quarantine, affecting the economy of the whole country. Here we assess different aspects of the coronavirus epidemic in Mexico City, studying the dynamics in response to different spans and intensities of the lockdown, performing simulations using the ODE model proposed by the government of Mexico City, and a new individual agent-based model that takes into account hygiene measures of individuals.

1. INTRODUCTION

We are living in strange times, the ongoing coronavirus disease 19 (COVID-19) outbreak, emerged in Wuhan, China at the end of 2019, has claimed more than 8500 lives as to 27 May 2020 in Mexico [1], and the cumulative cases rise to 78,023 infected. In particular, Mexico City is the most affected by this epidemic, reporting 20,999 cases of coronavirus and 1963 deaths [2]. In response to this catastrophic scenario, since march 19 the government of Mexico City has implemented strategies of containment followed by quarantine, these responses to the COVID-19 epidemic, were made principally based on epidemic spreading models [3].

Mathematical models are descriptions of systems using mathematical concepts and language [4]. They are used extensively in many areas including science and engineering. A model may help study the effects of different components, and to make predictions about the behavior of a system [4]. There are many types of models, but, in this scenario, we are only revising ordinary differential equations (ODE) and individual agent-based (ABM) models. An ODE model is a set of differential equations involving functions of only one independent variable and one or more of their derivatives [5]. On the other hand, the ABM models consist of a set of agents that encapsulate the behaviors of various individuals that make up the system [6].

In this study, we recreate the differential equation model proposed by the government of Mexico City, and developed a novel individual agent-based model, to characterize the coronavirus epidemic in Mexico City.

2. METHODS

We employ two different modeling strategies designed to capture the main ingredients characterizing the propagation of

SARS-CoV-2 and the clinical characteristics reported for the cases of COVID-19. These two strategies are the ordinary differential equation (ODE) modeling and agent-based modeling (ABM).

A. ODE overview

For the ODE model, we used the epidemiological model of the Government of Mexico City which was proposed to take into account some characteristics of the dynamics of COVID-19, such as the important effect of asymptomatic (or with mild symptoms) infectious individuals [3]. This model also considers the fraction of individuals which require hospitalization to ICU, since their saturation constitutes one of the major political and health problems of COVID-19 outbreak. The resulting model is composed of nine compartments as seen in figure 1, and can be written:

$$\begin{aligned}
 \frac{dS}{dt} &= - \left(\frac{R_0}{d_{infect}} \right) IS \\
 \frac{dE}{dt} &= \left(\frac{R_0}{d_{infect}} \right) IS - \left(\frac{1}{d_{incb}} \right) E \\
 \frac{dI}{dt} &= \left(\frac{1}{d_{incb}} \right) E - \left(\frac{1}{d_{infect}} \right) I \\
 \frac{dM}{dt} &= (1 - p_{severe}) \left(\frac{1}{d_{infect}} \right) I - \left(\frac{1}{d_{RL}} \right) M \\
 \frac{dA}{dt} &= p_{severe} \left(\frac{1}{d_{infect}} \right) I - \left(\frac{1}{d_{hosp}} \right) A \\
 \frac{dH}{dt} &= \left(\frac{1}{d_{hosp}} \right) A - (1 - p_{ICU}) \left(\frac{1}{d_{RH}} \right) H - p_{ICU} \left(\frac{1}{d_{ICU}} \right) H \\
 \frac{dICU}{dt} &= p_{ICU} \left(\frac{1}{d_{ICU}} \right) H - (1 - p_M) \left(\frac{1}{d_{RICU}} \right) ICU - p_M \left(\frac{1}{d_M} \right) ICU \\
 \frac{dR}{dt} &= \left(\frac{1}{d_{RL}} \right) M + (1 - p_{ICU}) \left(\frac{1}{d_{RH}} \right) H + (1 - p_M) \left(\frac{1}{d_{RICU}} \right) ICU \\
 \frac{dD}{dt} &= p_M \left(\frac{1}{d_M} \right) ICU \\
 S + E + I + M + A + H + ICU + R + D &= 1
 \end{aligned}$$

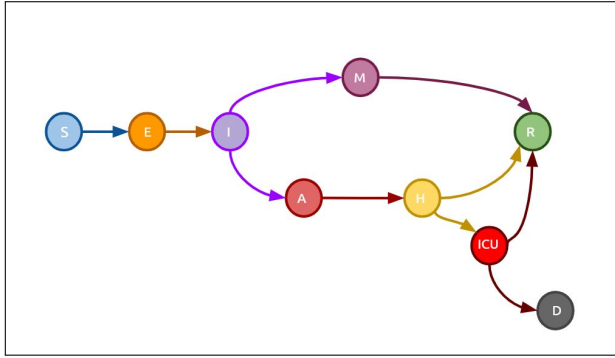


Fig. 1. Compartmental epidemic model proposed by the Government of Mexico City. The acronyms are susceptible (S), exposed (E), infected (I), mild symptomatic infections (and asymptomatic ones) (M), severe symptomatic infections (A), hospitalized (H), hospitalized to ICU (ICU), recovered (R), and deceased (D).

As the government mentioned [3], because of the lack of ‘local parameters’ they used the parameters reported in various sources of the international scientific literature on COVID-19. These parameters and their sources are described in Table 1.

In our implementation we decided to add the parameters $Reff$ and vector τ , which refer to the effective reproduction number that replaces R_0 when the population is during the lockdown period (also reflects social distancing), which is defined by vector τ . This strategy allows modeling the possible impact of different interventions and/or changes in the contact rate for different dates, as suggested by the Government of Mexico City [3], Michael E. Hochberg (2020) [16] and Thomas House in his blog “Modeling Herd Immunity” [17].

B. ABM overview

First of all, let’s decide what we want to simulate. The contagious spreading caused by the circulation and the effects of social isolation are our primary goals.

Contagious Spreading

Following the SIRV model, each agent must be in one of these situations: *Susceptible*, *Infected*, *Recovered* and *Vaccinated*. Each simulation has an initial percentage of infected people, and the remaining population is composed of susceptible individuals. The status also contains the *Death* status, for those agents who develop severe symptoms of the SARS-COVID-2 and did not resist.

The *main assumption* of the contagious spreading is the interaction of the agents by proximity or contact. So, as higher is the mobility of a person, greater is the probability that he approaches an infected person and gets also infected. Each simulation will have a *Contagion Distance*, the minimal distance that two agents have to be to occur the viral transmit. In addition, for viral transmission to occur each individual has a probability of transmission β uniformly distributed variate on $[\beta_{min}, \beta_{max}]$, this reflects the level of hygiene of an individual. β was chosen as an agent parameter instead of a model parameter since in a realistic scenario, the actual virus transmission would depend on the β value of both agents. However, only the β value of the infected individual was considered here for simplicity.

After a period of infection τ an individual may recover or die. However, upon recovery, the individual is still not safe. A

Table 1. Parameters used in the differential equation model

Parameter	Value	Source
Time the patient is infectious: d_{infect}	2.9	[7]
Incubation time (days): d_{incub}	5.2	[8]
Hospitalization rate: ρ_{severe}	13.80%	[9]
Recovery time of mild cases (days): d_{RL}	14	[10]
Time between presence of symptoms and hospitalization in severe cases (days): d_{hosp}	4	[11]
ICU rate: ρ_{ICU}	5%	[12]
Time between hospitalization of severe non-ICU cases and recovery (days): d_{RH}	12	[13]
Case fatality rate compared to the general population: ρ_M	9% or x2 (when ICU capacity is overloaded)	Mention in Lopez-Gatell Conference
Time between hospitalization of severe cases and admission to ICU (days): d_{ICU}	1	[11]
Time between ICU admission and recovery (days): d_{RICU}	7	[13]
Time between admission to ICU and death (days): d_M	8	[13]
Susceptible population (millions): N	22	[14]
R_0	2.83 or 0.95 (when quarantine is very effective ($Reff$))	Inferred, but consistent with [15]

probability of reinfection is defined. Although this is still under debate, the model allows evaluating the possibility of future scenarios given these rules.

Mobility Patterns

The simulation is performed in a continuous bi-dimensional *environment* shared by all the agents. Each agent is randomly initialized inside this environment such as $(x, y) \sim U(0, 1)$ and with a velocity assigned through a function $f(s) = \text{sincos}(2\pi \cdot v) \cdot s$, such that $v \sim U(0, 1)$ and s is a speed constant between all agents.

The proximity between two agents a_1 and a_2 is computed using the CityBlock distance, such as

$$2dist(a_1, a_2) = |x_{a_1} - x_{a_2}| + |y_{a_1} - y_{a_2}|$$

To simulate the contacts, an *elastic collision* function is resolved between the agents a_1 and a_2 . They are assumed to be disks of equal size touching tangentially. Their velocities are adjusted for an elastic collision happening between them. Collision only happens if both disks face each other, to avoid collision-after-collision.

One of the two agents can have infinite “mass”, and then acts as an immovable object (isolated individuals) that specularly reflects the other agent. In this case of course momentum is not conserved, but kinetic energy is still conserved. Automatically all dead agents are removed from the environment.

Interventions

Social isolation

To simulate the impact of social distancing, different types of emergency closings were proposed: i) for an indefinite period, ii) with a defined period and, finally, iii) with periodic repetitions. For all cases, given a percentage of isolation from the population, their corresponding individuals are chosen at random. In the case of periodic repetitions of isolation, new individuals are chosen in each period.

Vaccination

Society hopes that, at some point, a vaccine will be developed in order to contend with the virus; providing immunity to its population. However, this may take time. To make an approximation of how the pandemic would evolve given the invention of a vaccine, the possibility of being a vaccinated agent was added. It is known that, in principle, not all vaccines are equally effective in the population. However, it was considered a complete effectiveness for simplicity, that is, once vaccinated, the individual cannot be infected again.

Economics impacts

A secondary goal is to simulate the impact caused in the economy — especially in each agent’s *income* and *wealth* — by the mobility restrictions. The basic *assumption* of the economical dynamics of this simulation is: the *income* of the agents is a function of its mobility. In the real world, there are many cases where this condition is not true, and people still working at home. But unfortunately, this is not always the case.

3. RESULTS

A. ODE

Once we have added the parameters $Reff$ and vector τ , we can explore which intervention would be able to reduce the cases that are hospitalized to the ICU, as we can see in figure 2. It seems that the best combinations are those whose duration of lockdown is greater than 30 days, being the best those whose duration is up to 180 days, however, in a real case we cannot apply a quarantine for so long due to the economic limitations that it imposes.

It’s also noteworthy, that the best interventions are those carried out after 45 days of the first reported cases of infected; this is several days after the start of the exponential phase (after 15 days) if we take into account the dynamics of the system without intervention under the same parameters; and in fact, such interventions are also before the maximum points of exposed and infected individuals (between days 59-60 and 62-63 respectively).

With the previous exploration, we decided to choose five different prolonged interventions that correspond to those that start on day 30 after the first case and end on days 90 and 120 post-infection, those that start on day 50 and end on days 110 and 140, and the last one that begins on day 55 but ends on day 115. But in addition, we decided to incorporate periodic

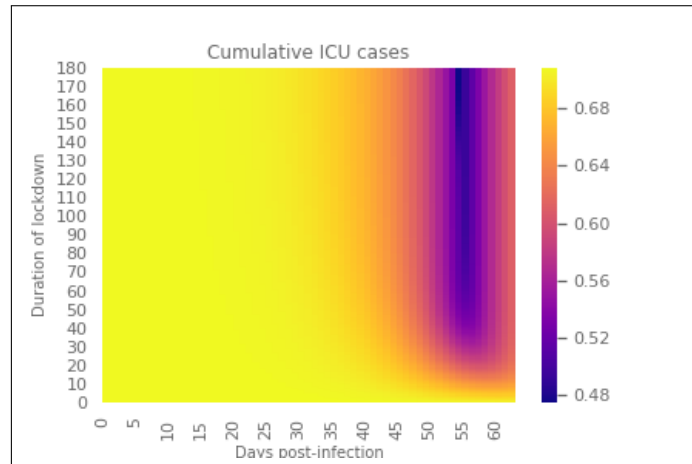


Fig. 2. Cumulative ICU cases from different quarantines with different starts and durations

quarantines of different weekly durations, from every week to every six weeks. We can see in figure 3 the dynamics of the system under the different suggested interventions.

It is important to note that quarantines that start before or at the start of the exponential period, only manage to displace the epidemic in time, regardless of its duration, so they are not a recommended strategy. The reason that this happens is that social distancing measures do not lead to herd immunity, so once they are lifted the epidemic starts again [17].

The latest interventions are those that distribute hospitalized cases over time, and this is what mitigation policies should aim to do: to reach herd immunity with the minimal human cost. This will be extremely difficult, and at every stage we will be dealing with large uncertainties [17], that is why it is important to keep track and forecast the epidemic to make the best decisions at the right times.

With the interventions we chose, we decided to monitor the proportion of economically active population (EAP) over time, which was defined as the set of susceptible, exposed and recovered individuals. This definition will allow us to monitor indirectly the economic activity, adjusting the proportion of EAP to 30% when they are in quarantine period, this 30% is an estimate of the proportion of people who can do home-office and those who have an essential job (Figure 4).

Having these data, we can observe the effectiveness of the interventions by comparing the fraction of the population that dies and by superficially observing its effect in the economy (according to our not very robust indicator), giving greater importance to the interventions that reduce deaths (Figure 4).

Again, the interventions near the peaks of exposed and infected individuals are those that reduce the fraction of people who die, and in fact, if we pay attention to the intervention ‘FromDay55to115’ we will notice that it is the quarantine that reduces the population’s deceased fraction and it is also the one that affects the economy to a lesser extent according to our indicator. It is interesting to note that the two proposals for periodic interventions (every 2 and 4 weeks) also help to reduce the fraction of individuals who die, while too early interventions do not reduce the deceased fraction, nor do those periodic proposals of longer durations (every 5 or 6 weeks). Interventions that start on the same day but with different durations do not seem to drastically modify the proportion of individuals who die, but instead

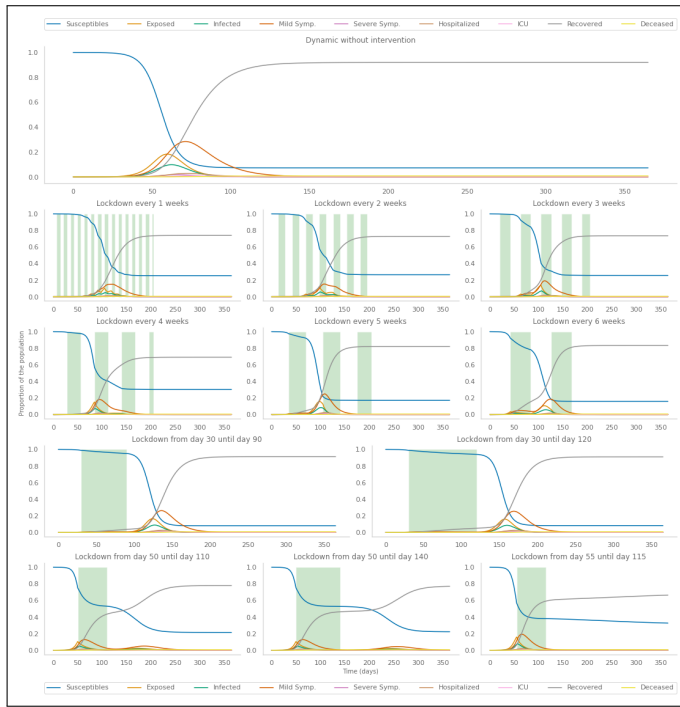


Fig. 3. System dynamics under different time interventions

do affect the economy to a greater extent, as observed in those that begin on days 30 and 50. Also, those post-peak-epidemic interventions (not shown) do not significantly reduce the death fraction, further complicating the choice of the most appropriate time to perform the lockdown.

B. ABM

Individual model

Demonstratively, figure 5 . shows a simulation of the model of individual agents with periodic social isolation with 50% of the population from day 24, with durations of 24 days and intervals between isolations of 14 days. In addition, the invention included a vaccine from day 240.

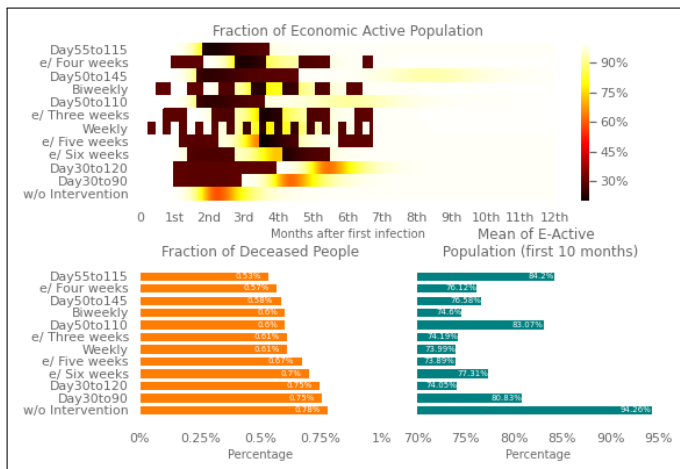


Fig. 4. Effectiveness of proposed interventions.

It is interesting to note how, after a time of beginning periods of social isolation, infected and recovered individuals begin to oscillate; a product of the built-in probability of reinfection and periodic isolations. However, when the vaccine is added to the system, little by little the disease begins to disappear. This behavior could be important, if it is shown that individuals can be reinfected.

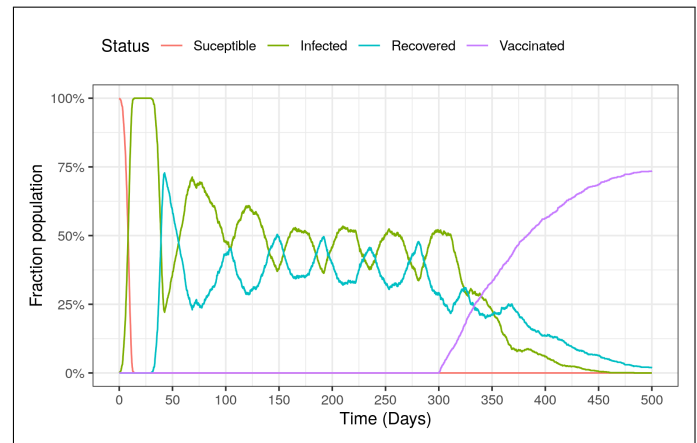


Fig. 5. Dynamics of the individual SIRV agent model.

Effect β amplitude on survival

Unlike models where it is assumed that there is a constant infection rate for all individuals, this model aims to assess the effect of hygiene measures on each individual. If an individual has very poor hygiene measures, they are more likely to infect another person. In a model closer to reality, the probability of infection should depend on the hygiene measures of both individuals, however, for simplicity, only those from the affected individual were considered.

The hygiene measures of a population can determine a high spread of the disease. The transmission probability β , is symbolic of how hygienic a person is; a value of one equals nothing and a value of zero is flawless. Figure 6. shows a combination of different amplitudes of hygiene measures in a population; a range between impeccability and doom.

It was found that, in general, having a narrow range distribution with values between β_{max} and β_{min} of 0.5 is very similar to having a wide distribution bounded by low values of β_{min} . However, when both β values pass values 0.5 (distributions of β narrow) the population decays with greater weight. Therefore, it could be said that, in fact, having good hygiene measures in your population could help to not continue spreading the virus and that, assuming that the hygiene of the population is distributed uniformly, it may not be so bad, but yes upgradeable.

Model performance evaluation

The main objectives of the model are to evaluate the contagious spread caused by circulation and the effects of social isolation. In the previous section, we discussed the effects on the extent of the spread of infection associated with the hygiene measures of each individual. Therefore, the effectiveness of different interventions was evaluated with the objective of reducing the number of deaths.

In order to obtain the different simulations, the Cartesian product of different parameters such as start and end times of

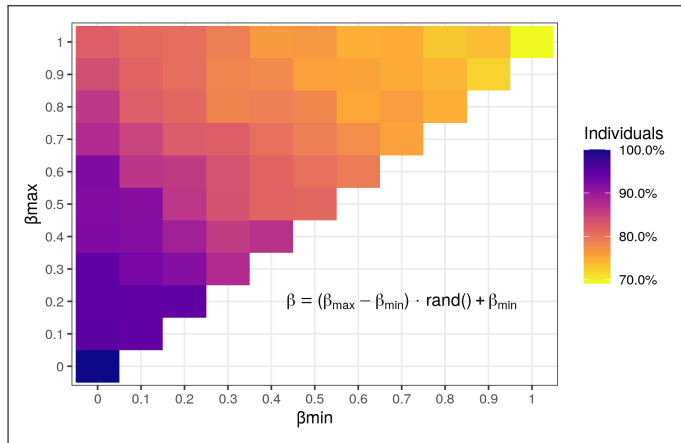


Fig. 6. Effect of the distribution of hygiene measures on the population

isolates, whether they were periodic or not, different proportions of individuals in isolation, the possibility of inventing a vaccine and, finally, different ranges of β es.

In figure 7. The behavior of individuals over time is shown in each of the simulations performed, highlighting the top 3 in the number of deaths was minimum (best) and maximum (worst), and those outside the top (others). In turn, the tops are shown for each evaluated β_{min} (0.0 and 0.5) with a β_{max} of 0.8. In general, the best models were characterized by isolates from day thirty and with a duration of one and two months, without repetition and with the invention of a vaccine (see supplemental material, section "plots"). However, it is noteworthy that one of the best models did not need the invention of a vaccine to be the best (id 186), but an isolation of two months in conjunction with a wider range of β es, which as seen in the previous section, helps reduce the number of deaths. For their part, the worst models were noted for doing nothing, not isolating, not vaccinating, and with a narrow β es range skewed to high values.

4. DISCUSSION

As mentioned previously in the ODE model section, choosing the right time for the intervention is difficult since it must be after the start of the exponential phase but before the peak of the epidemic, in addition, within that interval there are interventions that could favor a 'second wave', making effective monitoring and prediction of the epidemic very important. There are strategies that we do not take into account, but that may have favorable results, such as periodic quarantines but with different extensions e.g. periods of 4-day without lockdown with 10 days of lockdown.

Our strategies assume that during the quarantine everyone takes shelter, but this could be directed to vulnerable groups and allow the mobility of the rest of the groups. These and more strategies should be taken into account in subsequent models to expand the spectrum of intervention possibilities.

Given these results, it is interesting to ask what the future will be like without the invention of a vaccine and how, by following sanitary measures together with obeying social distancing, it could help to reduce the number of deaths significantly. In turn, it will be interesting to determine which model is better based on deaths along with the impact on the economy. Not everyone can do home office, only a small fraction of the population

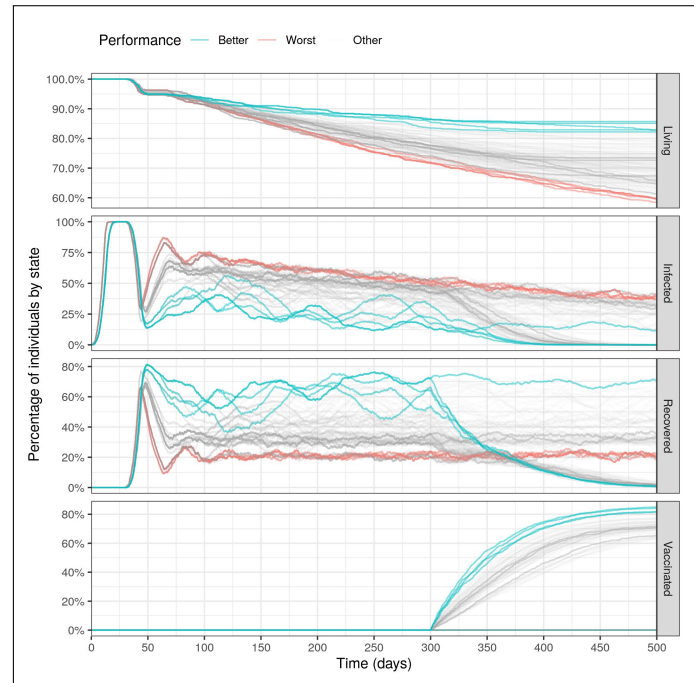


Fig. 7. Model performance evaluation with objective function as number of living individuals.

can afford to do it. At the moment, obeying sanitary measures and social isolation are the best option, washing your hands, wearing face masks, keeping your distance and staying at home should be a momentary lifestyle for those who can afford it and for those who do not, it will be interesting to see the socio-economic plans that are developed to deal with the health and economic problems. Thus concluding that carrying out interventions that minimize the number of deaths while maximizing the economy, they would be adequate to proceed in a country, this is because there are multiple external causes that depend on the economy, including access to food or health. Without access to these primary services, part of the population could suffer collateral damage, including death.

5. SUPPLEMENTAL MATERIAL

The code, and all the data used to make this work can be found here:

- <https://github.com/jvelez-s/biomath>

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