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Additional Information

Effect of the early use of antivirals on the COVID-19 pandemic. A computational network modeling approach

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Abstract

It seems that we are far from controlling COVID-19 pandemics, and, consequently, returning to a fully normal life. Until an effective vaccine is found, safety measures as the use of face masks, social distancing, washing hands regularly, etc., have to be taken. Also, the use of appropriate antivirals in order to alleviate the symptoms, to control the severity of the illness and to prevent the transmission, could be a good option that we study in this work. In this paper, we propose a computational random network model to study the transmission dynamics of COVID-19 in Spain. Once the model has been calibrated and validated, we use it to simulate several scenarios where effective antivirals are available. The results show how the early use of antivirals may significantly reduce the incidence of COVID-19 and may avoid a new collapse of the health system.

1 Introduction and motivation

COVID-19 pandemic has already caused more than 430.000 deaths [1] around the world and it still remains uncontrolled in several continents, mainly in America, Africa and parts of Asia.

Widespread vaccination is probably the only way to restore a fully normal life, as we knew it before the appearance of COVID-19 pandemic, if we do not want to wait until herd immunity is achieved which would also imply a great number

of additional human losses. Even though Europe has been one of the continents most affected by COVID till now, recent seroprevalence studies [2] conclude that European countries are probably very far from herd immunity.

Unfortunately, although more than a hundred research groups around the world are developing a vaccine, and healthy volunteers are speeding up the clinical trial process, fabrication of a large quantity for the world population and its widespread distribution, will not be possible at least before the end of Autumn 2020. In the best scenario, some vaccines might be distributed to the most vulnerable population by the end of this year.

Therefore, the research for alternative treatments should be pursued not only for the current situation of the pandemic in America and Africa but also in prevision of a second large wave after the summer season in the northern hemisphere.

One fast way to achieve a successful treatment in the next few months is the repurposing of current approved drugs for its use as antivirals. Unfortunately, there is only one antiviral drug approved for the treatment of COVID that has shown some efficiency against COVID-19 in clinical trials: Remdesivir [3]. However, even though Remdesivir was shown to be superior to placebo in shortening the recovery time in adults hospitalized with COVID-19 and has also shown evidence of lower respiratory tract infection, this drug has not proved to reduce COVID-19 mortality rate as of today. Moreover, this drug needs to be administered at a hospital setting, hampering a more efficient antiviral action if it was delivered at the first symptoms.

This study is based on the hope of the appearance in the clinic of a new antiviral drug approved for the COVID-19 treatment that should be inexpensive, available at the drug stores for a large part of the population, with no significant secondary effects and with some efficacy against the virus. We call these, the *democratic conditions*.

Fortunately, there are many candidates identified by several research groups around the world that might potentially fulfill those democratic conditions. Some of them have been found using an automatic platform to test an *in vitro* library with a large quantity of approved drugs for their action against SARS-2 virus in cell cultures and simultaneously testing its toxicity on those cells [4, 5]. Both quantities, antiviral activity and toxicity, determine a therapeutic window for each drug, and the drugs in the library are ordered according to that window. For instance, Azithromycin has been selected in such a way [6] and clinical trials are being performed with this drug in COVID-19 patients. **In a different *in vitro* screening study [7], Niclosamide and Ciclosonide have been selected as antivirals against SARS-CoV-2 with low toxicity at the required doses. A new formulation of Niclosamide, an anthelmintic drug, to enhance absorption, might be used as a very potent antiviral against SARS- CoV-2. Ciclesonide is a corticosteroid used to treat asthma and allergic rhinitis through inhalation and therefore, even less potent than Niclosamide, is high bio-available at the respiratory tract.**

Other drugs have been found through *in silico* (computing programs) studies and then tried its action against the virus in cell cultures. Ivermectin, an anti-parasitic drug, has been identified with that method [8]. Furthermore, a recent clinical trial [9] has shown that Ivermectin might reduce COVID-19 mortality

by 40%. Even though, the study had some limitations.

Furthermore, new orally available antivirals have shown potent activity in human epithelial lung cells in vitro (see for instance [10]). Therefore, there are many SARS-CoV-2 antiviral candidates currently under clinical trials.

In this paper we propose a computational network model to assess the effect of the use of an antiviral in democratic conditions and administered early on in the course of the disease, on the COVID-19 transmission dynamics. To do so, we build a random network model, estimate the model parameter values that explain the dynamics of the COVID-19 in Spain, and we simulate possible future scenarios where an accessible and cheap antiviral is available and can be considered as an effective treatment.

The paper is organized as follows. In Section 2, the computational random network model is built and the model parameter values estimated. In Section 3, the model is validated, that is, we check that reproduces accurately the situation in Spain since the beginning of the pandemics. In Section 4, we describe and simulate scenarios to assess the use of antivirals, which may be an additional tool to fight against COVID-19. Finally, in Section 5 we present our conclusions.

2 Model building

2.1 Random networks

Networks have become a paradigm of paramount importance in the analysis of many complex systems. In the field of epidemiology, networks have been used to describe the transmission dynamics of several diseases [11, 12, 13, 14].

A network is a set of nodes representing individuals. Labels or properties may be assigned to each node, such as age, sex, and state respect to the disease (susceptibility, infection, recovery, latency, etc.). Nodes are connected by edges that represent disease transmission paths. Once the network model and the disease evolution rules are stated, it is possible to simulate the evolution of the disease on the network nodes over time and to study its spread on the population.

The already developed of networks provide several standard alternatives for implementing the network substrate. The most traditional one is based upon the pioneering work of Bollobas [15], employing the so-called *random graphs*, where connections among the pairs of subjects are created with the same probability. The most natural sparse generalization of the complete graph in mathematics is provided by the so-called Erdős-Rényi graphs [15], which in the fifties of the past century defined the concept of a random graph. In modern times, this idea has been redefined as a random network and it has become an important paradigm with many applications.

The spread of infectious diseases is determined by random encounters among people around the same location: meeting at the bus stops, crossing in the streets, gathering at shop centers, etc. COVID-19 is known to be transmitted person to person, mainly through respiratory droplets produced when an in-

ected person coughs or sneezes [16]. As other respiratory viruses, it induces coughing and sneezing in infected subjects, which also favors the transmission of the disease.

For these reasons, we have chosen the Erdős-Rényi random network as the most appropriate for the modeling of the transmission of COVID-19 and infectious diseases in general. Random networks are characterized by the number of sites or nodes N and the average number of contacts of every individual k . Consequently, the number of links in the network is given by $N \times k/2$. These links are randomly assigned to pairs of nodes with the obvious rule that, at most, only a link can connect two nodes. We will say that two nodes are neighbors if they are connected. An example of a random network can be seen in Figure 1.

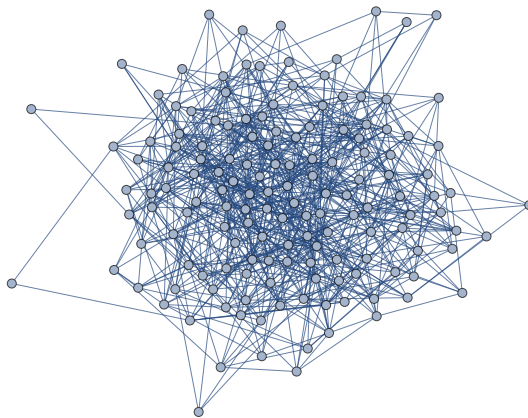


Figure 1: Random network with $N = 150$ and $k = 10$. The small circles are the nodes representing individuals and the lines between nodes are the links describing the contacts among individuals with possible transmission of the virus. The links describe the transmission paths of the disease.

2.2 Model compartments

The network is the substrate that determines how people relate and what the transmission paths are. However, to study the transmission dynamics of diseases, we have to build a compartmental model and determine how individuals transit from one state to another as time goes on. The compartments are the following:

- Susceptible (S) when the individual is healthy;
- Latent or Exposed (L) when the individual has been infected but he/she still is not infectious;
- Infectious (I) when the individual can infect others;
- Recovered (R) when the individual recovers from the disease being asymptomatic or having mild symptoms;

- Hospitalized (H) when the individual has severe symptoms and needs to be hospitalized;
- Deceased (F) when the individual dies because of the virus;
- Discharged (A) when the individual gets better and is discharged from the hospital.

Also, the nodes have a label determining if they are in Quarantine (Q), that is, when the individual is at home to avoid the spread of the virus. This label can be assigned to all individuals except people in H (hospitalized) and F (deceased).

In the proposed model, we consider that people who decease as a consequence of COVID-19, pass away at the hospital. The data regarding people who die outside the hospital in Spain is scarce and inconclusive. Also, we do not consider re-infection. The total population in Spain will be given by the term $P_T = 47\,100\,396$ [17].

2.3 Transmission dynamics

In this section we are going to define the transmission dynamics of COVID-19 on the network. The time step is set in 1 day.

1. A susceptible (S) node may transit to latent (L) state if it gets infected through a successful contact with an infectious (I) node with a transmission rate $\beta > 0$.

Within the dynamics of the network, this transition is going to be simulated as follows: if a node is susceptible (S), we collect all the infectious (I) neighboring (connected) nodes. In turn, for each of the infectious neighbors, we generate a random number $r \in [0, 1]$ and if $r < \beta$ we consider that this neighboring node transmits COVID-19 to the node and the node is then labeled as latent (L) and changes its state.

2. A latent (L) node becomes infectious (I) at rate $l_i > 0$ after some days, and it is able to infect other nodes.

Within the simulation, a latent node needs a number of days to become infectious (3 days as we shall see later).

3. An infectious (I) node may be asymptomatic or have mild symptoms and recover (R) without being admitted in the hospital at rate $i_r > 0$; or it may have severe symptoms and be admitted in the hospital (H) at rate $i_h > 0$.
4. A node in the hospital (H) may get better and finally be discharged (A) at rate $h_a > 0$, or get worse and eventually decease at rate $h_f > 0$.
5. Also, a susceptible (S), latent (L), infectious (I), recovered (R) and discharged (A) node can be labeled as in quarantine, during the quarantine periods, if it remains at home to avoid contagion. In this case, the node cannot infect nor be infected.

Points 3 and 4 correspond to a bifurcation, that is, there are two possible ways to change the state.

In the first case (point 3), the parameters involved in the transition from infectious (I) are i_h (to H) and i_r (to R). These model parameters, as we will see later, have two parts: the first one is the probability p to take the way to H or the probability $1 - p$ to take the way to R, and the second is the time to reach the new state, H or R (may be different). Hence, to simulate the transition of a node from I to H or R, we generate a random number $r \in [0, 1]$ and if $r < p$ its destiny will be H. Otherwise R. Then, after some determined number of time steps, the node becomes hospitalized/recovered.

For the second case (point 4), that is, the transition from H to A or F with the model parameters h_a and h_f , we proceed analogously.

Figure 2 shows a flow diagram about how an individual may move around respect to the disease, following the paths described above.

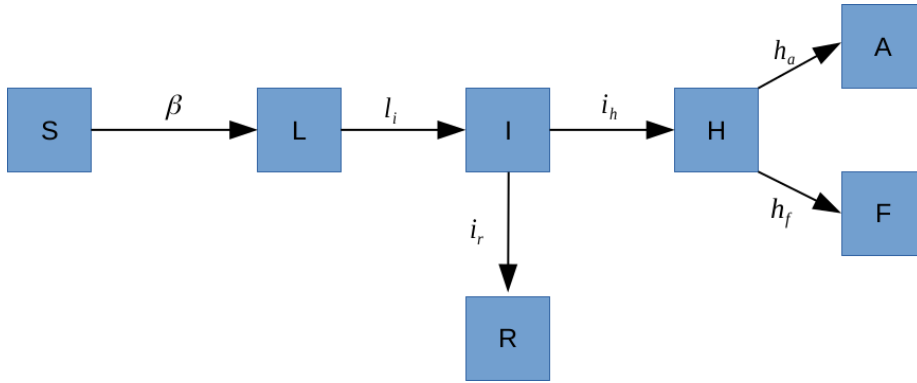


Figure 2: Flow diagram of the COVID-19 transmission dynamics. The boxes represent the states of the individuals respect to the disease and the letters next to the arrows, the transition rates between the states.

2.4 Model parameters

The goal of this section is to quantify the model parameters in order to determine the transmission dynamics of the COVID-19. In Figure 3 we can see the time line of COVID-19.

1. **Average degree k of the network.** The average degree k of a network is the average number of contacts of the nodes. For infectious diseases as the respiratory syncytial virus (RSV) whose contagion mechanisms are similar to COVID-19, k is in the range 48 – 54 [13, 18] contacts per day with possible contagion. Recent unpublished network model studies for influenza, returns values for k around 48 – 49. Hence, we are going to assume in our study

$$k = 50.$$

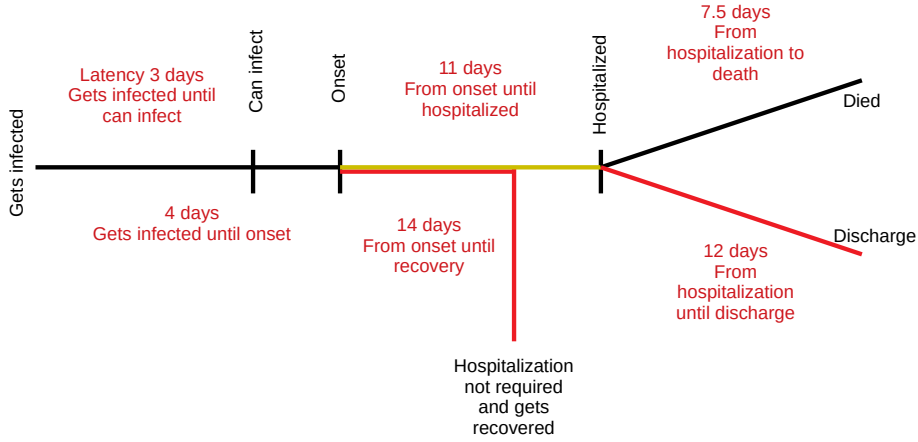


Figure 3: Time line of COVID-19, from an individual gets infected until gets recovered, dies or is discharged.

2. **Quarantine.** In March 14, 2020, 70% of people in Spain were isolated at home (quarantine) [19, 20]. After that, in March 31, 2020 there was a strict quarantine isolating at home 85% of people. The strict quarantine was relaxed April 13, 2020 when the percentage of isolated people was reduced again to 70%.
3. **Transition rate from latent to infectious l_i .** The incubation period described in medical literature, refers to the time interval since an individual gets infected until he/she presents symptoms (onset). In [21] the authors affirm that, for COVID-19, the incubation period is 4 days with a range from 2 to 7 days. However, the latency period is the time since one gets infected until he/she is able to infect others, regardless whether symptoms have emerged. Therefore, the incubation period does not correspond exactly to the latency period. There are limited evidences suggesting that the virus may be transmitted one or two days before the onset [22]. Hence, we are going to assume the latency period is going to be less than 4 days, in particular, 3 days, taking

$$l_i = 1/3.$$

In the following, we are going to add 1 day when we have to take into account the time between the end of the latency period and the onset.

4. **Transition rate from infectious to hospitalized i_h .** In Spain, between April 27 to May 11, the preliminary report of the 1st round of the National Sero-epidemiological study for SARS-Cov-2 infection in Spain [23], says that the accumulated infected is 5% of the population. Using data retrieved from [24] in the same time interval as above, the average percentage accumulated hospitalized individuals in Spain is 0.2520%. Then,

$$\frac{100 \times 0.2520}{5} = 5.04\%$$

is an estimation of the percentage of the infected who are hospitalized. Furthermore, the time from onset to get hospitalized is 11 days [25]. We add one day for the end of the latency to the onset. Therefore,

$$i_h = 0.0504/12.$$

5. **Transition rate from infectious to recovered i_r .** From the previous point, we have that $100\% - 5.04\% = 94.96\%$ of the infected are not hospitalized and get recovered after 14 days [26, page 14, 1st paragraph] plus a day for the end of the latency to the onset. Thus,

$$i_r = 0.9496/15.$$

6. **Transmission rate β .** R_0 is the basic reproductive number [27] and it can be interpreted as the number of persons an infectious individual may infect during the time he/she is infectious, in a scenario where almost all the people are susceptible, that is, at the very beginning. For our network model, we have that

$$R_0 = \frac{k \times \beta}{i_h + i_r}.$$

Several papers have treated to estimate the value of R_0 for COVID-19. We are going to use [28] where R_0 is 5.7 CI95% (3.8 – 8.9). This way,

$$5.7 = R_0 = \frac{k \times \beta}{i_h + i_r} = \frac{50 \times \beta}{\frac{0.0504}{12} + \frac{0.9496}{15}},$$

where

$$\beta = 0.00769576.$$

This β will be valid at the beginning of the outbreak. Nevertheless, in Spain, we had periods of quarantine and some measures have been taken to avoid social contacts (teleworking, avoiding meetings, preparing children schools, safe distancing, room ventilation, limiting the capacity of bars, restaurants, hotels and public places), measures of protection (face masks, hand washing), the response of the virus to the summer temperatures, the population immunity, etc. Thus, transmission rate has certainly changed.

7. **Transition rate from hospitalized to death h_f .** Using data retrieved from [24], the average percentage of accumulated hospitalized individuals who died in Spain between March 11 to May 18 is 19.2348%. Also, the time spent in hospital by people who eventually die is 7.5 days on average [25]. Thus,

$$h_f = 0.192348/7.5.$$

8. **Transition rate from hospitalized to discharged h_a .** From the previous point, we have that $100\% - 19.2348\% = 80.7652\%$ of the hospitalized get recovered and are discharged. Also, the time spent in hospital by people who eventually is discharged is 12 days on average [25]. Thus,

$$h_a = 0.807652/12.$$

At this point, we have to establish the initial condition with very little information. First, we take as initial instant January 31 2020. This day was declared the first case in Spain. We are going to consider that this day nobody was in quarantine nor hospitalized nor discharged nor deceased because of COVID-19. However, we have to determine the initial number of latent and infected.

Taking into account that the percentage of infected people between April 27 and May 11 lies in the interval 4.7% – 5.4% [23] and the intrinsic randomness of the network building, we have performed a calibration of the model, where the parameters to be calibrated are the initial number of latent and infected. The process returned 30 model realizations fulfilling the above infected people restriction. The mean and the 95% confidence band of the 30 calibrated realizations can be seen in Figure 4(a). These 30 realizations allow us to say that, initially in January 31, there were in Spain 267 latent IC95% [135, 393] (percentages 0.00057% IC95% [0.00029%, 0.00083%]) and 497 infectious IC95% [371, 628] (percentages 0.00106% IC95% [0.00079%, 0.00133%]). The percentages are calculated respect the total Spanish population.

All the above parameters, the initial condition, and the 30 realizations will be used for model validation and further simulation of scenarios. The results and the graphs will be shown in percentages with respect to the total Spanish population in order to facilitate the comparison and the possible extrapolation to other regions or countries.

3 Model validation

We are going to validate the model comparing the model output with the data [24] from January 31 until May 31. The transmission rate β obtained in the previous section, as already mentioned, is valid during the beginning of the outbreak, but later, some measures to avoid the contagion were taken.

Although we initially had data until May 18, during the study new data have been added and they are available until 31 May, which we have included for validation.

In order to simulate these measures we are going to consider that the transmission rate from January 31 (initial condition) to March 14 (starts the quarantine) is $\beta = \beta_1 = 0.00769576$. Then from March 15 until May 31, we consider that, apart from the quarantine, people took measures to prevent the transmission of COVID-19 that we quantify as $\beta_2 = \beta_1 \times 0.5 = 0.00384788$.

Using the model parameter values of Section 2.4 and the β 's defined here, we perform the 30 realizations, calculate the mean and the 95% confidence interval. The similarities between the model output (coloured lines) and the data (black dashed lines) can be seen in Figure 4. The black dashed lines in Figure 4(b) and (c) correspond to accumulated data. As we can see, in the data time series, there are unexpected jumps and drops improper of accumulated data. This is one of the facts that has generated controversy about the quality of the data.

In any case, given that the model reproduces the data quite well, we can expect to make accurate predictions.

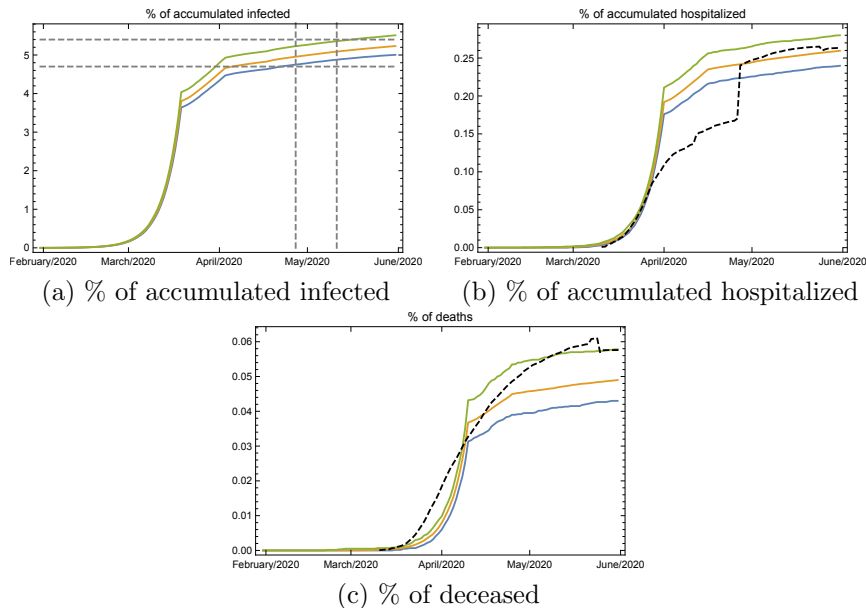


Figure 4: Evolution of the (a) percentage of accumulated infected, (b) percentage of accumulated hospitalized, (c) percentage of deceased, from January 31, 2020 until May 31, 2020. In Figure (a) we can see that the model output between April 27 and May 11 is inside the interval 4.7% – 5.4%, that is, the gray dashed line rectangle. In Figures (b) and (c) we can see the similarities of the model output (coloured lines: orange represents the mean; blue represents the percentile 2.5; green represents the percentile 97.5, every day) and the data (black dashed lines) for accumulated hospitalized and deceased.

4 Simulation of the effect of the antiviral

It is clear that COVID-19 is not going to be controlled until we reach herd immunity, and it will be possible when

$$1 - \frac{1}{R_0} = 1 - \frac{1}{5.7} \approx 82.5\%$$

of the population [27] will be immune. This level of immunity can be achieved if most of the people get infected, effective vaccines or effective antivirals are available.

Since March 14, in Spain, we are under a state of emergency, with restrictions in traveling and many activities. Four stages (0, 1, 2 and 3) have been defined to return to normal life and they have been activated from the middle of May, step by step, in regions satisfying certain public health conditions. In mid-June, most part of Spain is in stages 2 – 3.

For the simulations, we approximate the stage scenarios assuming that people come out of quarantine in steps of 25% in June 1, 8, 15 and 22. Also, we maintain the typical prevention measures as social distancing, the use of face

masks, cleaning the hands regularly, etc. Furthermore, the summer season may difficult the transmission of the virus, at least, because there are a lot of activities performed outdoors. Hence, from June 1 until September 30, the transmission rate considered will be $\beta_3 = \beta_1 \times 0.25 = 0.00192394$. Once the summer ends, during autumn, October 1 2020 until May 31 2021, we increase the transmission rate to $\beta_2 = 0.003847889$. Summarizing:

- from Jan 31 to Mar 14, $\beta_1 = 0.00769576$;
- from March 15 to May 31, $\beta_2 = 0.00384788$;
- from Jun 1 to Sep 31, $\beta_3 = 0.00192394$;
- from Oct 1 to May 31, $\beta_2 = 0.00384788$.

Let us now focus on the antivirals. The effective antiviral works as follows: when a person has symptoms, he/she can take the treatment with antivirals in such a way that mitigates the symptoms and consequences of the disease, but at the same time, allows him/her to generate antibodies and get protected. If, in addition, this person informs his/her contacts (nodes connected or neighbors) that he/she is infected, his/her contacts can also follow the same treatment and the transmission cut-off effect would be increased, preventing, at least in part, the appearance of possible new outbreaks.

Now, we define the base case simulation. Let us assume that the antiviral is available from October 1, 2020. When a person has symptoms of COVID-19 disease, about 15% of those infected [26, page 12, 3rd paragraph]¹, can take the treatment of this antiviral for 15 days with an effectiveness of p_{ef} %.

When this person takes the treatment, he/she informs the p_c % of his/her contacts who also take the treatment, unless they are recovered, discharged or in hospital.

If one of the contacts is susceptible (S), the treatment will protect him/her for 30 days and afterwards he/she will return to the susceptible state. If one of his/her contacts is latent (L) or infectious (maybe asymptomatic), after 3 days of treatment he/she will move to recovered because the antiviral has relieved him/her (with a probability of p_{ef} %) of the hardest part of the illness and his/her body has had antibodies to successfully defend against possible re-infections.

Under the above conditions and the possibility of having available antivirals, we are going to simulate the following scenarios:

¹In [26, page 12, 3rd paragraph] the authors say that *Most people infected with COVID-19 virus have mild disease and recover. Approximately 80% of laboratory confirmed patients have had mild to moderate disease, which includes non-pneumonia and pneumonia cases, 13.8% have severe disease (dyspnea, respiratory frequency ≥ 30 /minute, blood oxygen saturation $\leq 93\%$, PaO₂/FiO₂ ratio < 300 , and/or lung infiltrates $> 50\%$ of the lung field within 24-48 hours) and 6.1% are critical (respiratory failure, septic shock, and/or multiple organ dysfunction/failure). Asymptomatic infection has been reported, but the majority of the relatively rare cases who are asymptomatic on the date of identification/report went on to develop disease. The proportion of truly asymptomatic infections is unclear but appears to be relatively rare and does not appear to be a major driver of transmission.* In view of this information, taking into account that it is not clear what can be determined as "having symptoms", we decide to consider that 15% of those infected have recognizable symptoms.

- Base case: no antivirals are available;
- Case 1: antivirals are available from October 1 with several percentages of effectiveness and with several percentages of contacts who are informed and take the treatment;
- Case 2: the same as Case 1, where the transmission rate from Oct 1 2020 to May 31 2021 is $\beta_4 = 2 \times \beta_1 = 0.00513051$, higher than the Base Case $\beta_2 = 0.00384788$. This case simulates the scenario where suppression and/or mitigation of the measures may happen and, consequently, the transmission rate may be higher;
- Case 3: the same as Case 1, where antivirals are available later, from December 1.

4.1 Base case

This base case is a situation that would allow us to get out of quarantine while maintaining due precautions in time to avoid contagion that could lead to a new outbreak.

The result of this simulation can be seen in the Figure 5. Under the simulated conditions, the control over the epidemic is maintained until September, when starts a new outbreak that becomes more acute when the transmission rate increases in October (children in schools, colder weather, shorter days, fewer outdoor activities). Note that if the outbreak is not controlled, it could reach a much higher peak in November than the one last March, which corresponds to the peak on the left of the graph.

4.2 Simulation with several percentages of effectiveness

In Cases 1, 2 and 3, we perform simulations to estimate the sensitivity of the antiviral effectiveness with respect to the base case. To do this, we consider that the percentage of contacts to which we inform that we are taking the antiviral is $p_c = 75\%$ and the effectiveness of the antiviral p_{ef} varies by 35%, 50%, 65% and 80%. The comparison with the base case for the average percentage of hospitalized and deaths can be seen in Figure 6. We used hospitalized patients to assess the possibility of the health system becomes overcrowded again.

In Figure 6(a) (Case 1), it is interesting to note that, in the scenario where the percentage of people who have symptoms is low (15%) and effectiveness of the antiviral is also low (35%), there is a significant reduction of more than 50% of hospitalized people at the peak. Also, while the effectiveness of the antiviral significantly reduces the number of hospitalizations, it also delays around 15 days the peak and, consequently, the saturation of the health system.

In Figure 6(b) (Case 2), we can see that the increasing of the transmission rate $\beta_4 = 0.00513051$ reduces the effect of the antivirals and the peak delay effect we mentioned before, does not appear.

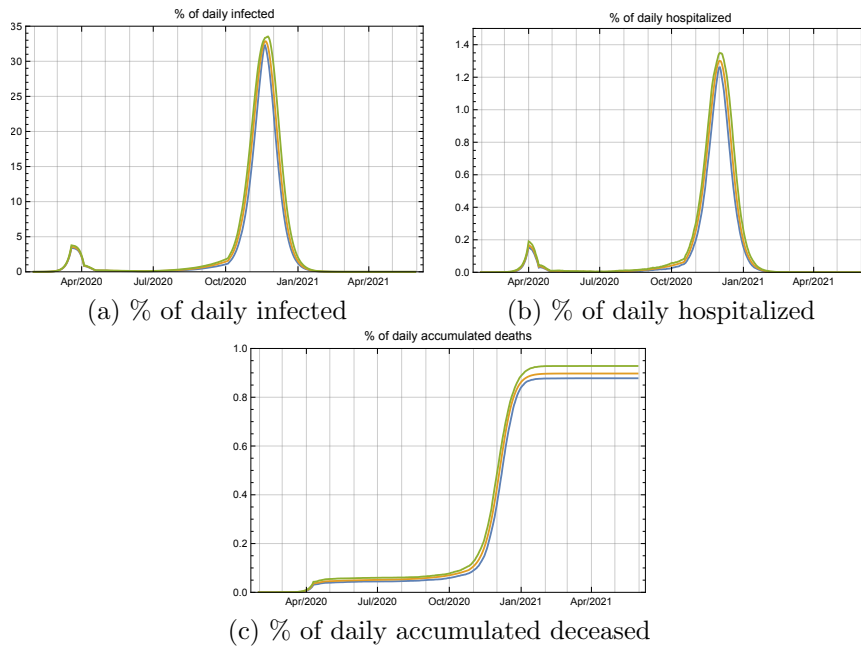


Figure 5: Base case. Evolution of (a) percentage of infected per day, (b) percentage of hospitalized per day and (c) percentage of deaths, from 31 January 2020 to 31 May 2021. The figures show that the pandemic has been under control until September, when there is again an increase in the number of people infected, which grows by the increase in the transmission rate in October. The peak on the left in graphs (a) and (b) corresponds to the peak of March 2020. In all three graphs, the ordinate axis represents a percentage of the total population and the abscissa axis represents time.

In Figure 6(c) (Case 3), the availability of the antivirals is delayed 2 months until December 1. Here, we can see the importance of having accessible antivirals as soon as possible, because any delay may reduce its effect to the point of making it useless.

4.3 Simulation with several percentages of contacts who are informed and take the treatment

In Cases 1, 2 and 3 we assess the effect of informing to a higher or lower percentage of our contacts that we are in treatment for COVID-19 and they take it. We assume $p_{ef} = 80\%$ constant and p_c varying in the 60%, 75% and 90%.

In this case, Figure 7, we can see how the communication to our contacts that we have symptoms may produce a reduction of the hospitalized preventing the collapse of the health system. It is worth mentioning that the simulated scenarios can be considered conservative, if we take into account that our contacts may inform their contacts to take the treatment, expanding the subnetwork of people under treatment and cutting the disease transmission paths.

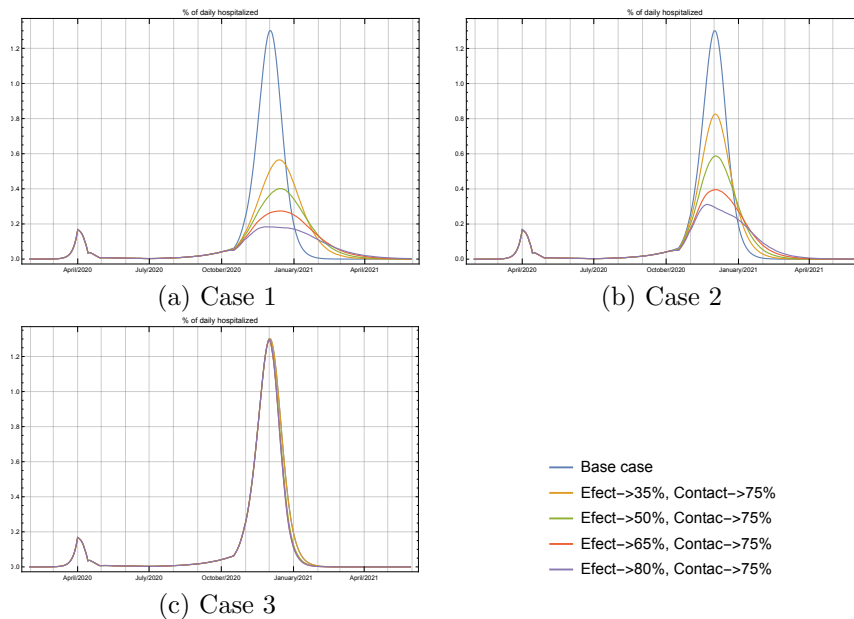


Figure 6: Evolution of the percentage of hospitalized per day, in Case 1 (a), Case 2 (b) and Case 3 (c) from 31 January 2020 to 31 May 2021, compared with the Base Case (blue line). In (a) we can see the reduction effect of the antivirals even with low effectiveness. In (b), the effect of the antivirals is reduced compared to (a) because of the increasing of the transmission rate from Oct 1 to May 31. In (c), we can see that the antiviral do not have any perceptible effect. This shows the importance of the time where the antivirals should be available. The peak on the left in graphs (a), (b) and (c) corresponds to the peak of March 2020. In all three graphs, the ordinate axis represents a percentage of the total population and the abscissa axis represents time.

In the simulated case Figure 7(a) and (b) (Cases 1 and 2), the peak is flatter and appears in mid-November - December. Comparison of graphs in Figure 7 shows again the importance of the accessibility of antivirals in the right moment, that is, before the main outbreak starts.

5 Conclusion

In this paper, we present a computational network model to assess the effect of the antivirals on the COVID-19 pandemic under several scenarios.

As we are far from having COVID-19 controlled and while an effective vaccine is found, antivirals may be a good option that we study in this work. The simulations carried out show us that the use of effective antivirals would help to obtain herd immunity without the cost in health resources and human lives that has taken place until now. In fact, it shows that even using low-effective antivirals and communicating our disease to a low percentage of our contacts, we can achieve a significant reduction in hospitalizations and avoid further saturation

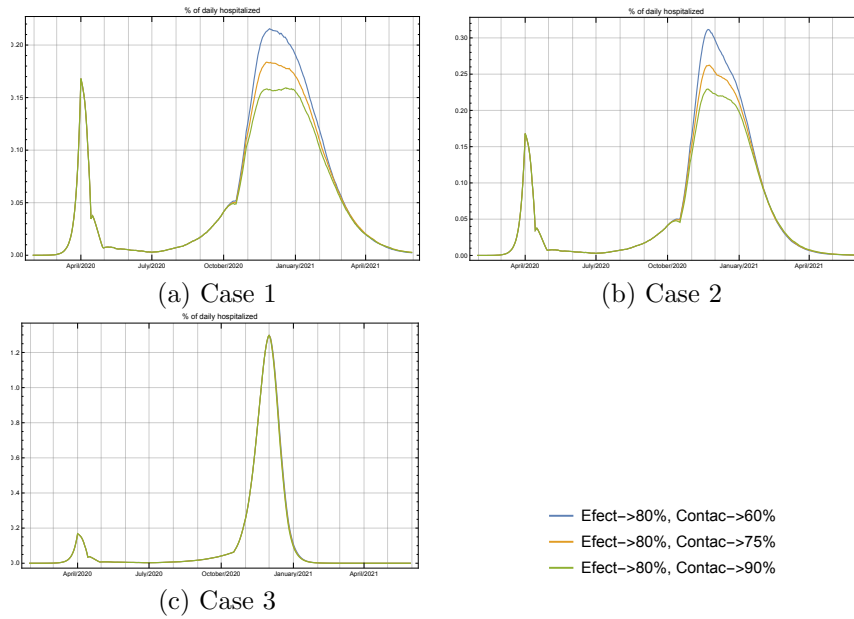


Figure 7: Evolution of the percentage of hospitalized per day, in Case 1 (a), Case 2 (b) and Case 3 (c) from 31 January 2020 to 31 May 2021. In (a) we can see how antivirals may reduce the hospitalized people to levels similar to the last March 2020. It does not happen in (b) because of the increasing of the transmission rate from Oct 1 to May 31. In (c), where the availability of the antiviral is delayed, we do not have any perceptible effect of the antivirals. The peak on the left in graphs (a), (b) and (c) corresponds to the peak of March 2020. In all three graphs, the ordinate axis represents a percentage of the total population and the abscissa axis represents time.

of the public health system **if the antivirals are available before the starting of the new main outbreak.**

The scenarios presented here may be considered as conservative in the sense that we do not consider the likely possibility that, if we have symptoms and communicate it to our contacts, in turn they may also communicate to their contacts and so on, expanding the network of people who can take the antiviral treatment cutting the virus transmission ways and blocking the contagion.

On the other hand, we are assuming that infected people acquire permanent immunity, which it is still under discussion.

Finally, one of the most important conclusion of this simulation is that any action we take against COVID-19 adds up significantly when it comes to fighting it. As already indicated for the masks [29], whatever percentage reduction an antiviral may have on the number of infected/hospitalized/dead, it must be applied.

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