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COVID-19 SUPPRESSION USING A TESTING/QUARANTINE STRATEGY: A MULTI-PARADIGM SIMULATION APPROACH BASED ON A SEIRTQ COMPARTMENTAL MODEL

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ABSTRACT

During the current COVID-19 pandemic, non-pharmaceutical interventions represent the first-line of defense to tackle the dispersion of the disease. One of the main non-pharmaceutical interventions is testing, which consists on the application of clinical tests aiming to detect and quarantine infected people. Here, we extended the SEIR compartmental model into a SEIRTQ model, adding new states representing the testing (T) and quarantine (Q) dynamics. In doing so, we have characterized the effects of a set of testing and quarantine strategies using a multi-paradigm approach, based on ordinary differential equations and agent based modelling. Our simulations suggest that iterative testing over 10% of the population could effectively suppress the spread of COVID-19 when testing results are delivered within 1 day. Under these conditions, a reduction of at least 95% of the infected individuals can be achieved, along with a drastic reduction in the number of super-spreaders.

1 INTRODUCTION

Despite the impressive biotechnological development promoted since the launch of the Human Genome Project in 1990 (Watson 1990), leading to novel pharmaceutical approaches such as personalized medicine (Lesko 2007) and genetic editing (Jiang and Doudna 2017), the spread of infectious diseases still remains a major issue. In fact, some scholars argue that infectious diseases are one of the most significant obstacles to surpass along the development path of modern societies (Sanders et al. 2008). Since 2019, due to the spread of the SARS-CoV-2, the etiological agent of the Coronavirus associated disease 19 (COVID-19), not only developing societies but the entire world has become aware of this burden. According to the COVID-19 Cumulative Infection Collaborators, as of November 2021, more than 3.8 billion (95% uncertainty interval 3.44 – 4.08) people worldwide have being infected with SARS-CoV-2 (COVID-19 Cumulative Infection Collaborators et al. 2022). When pharmaceutical strategies, such as vaccines (Ndwandwe and Wiysonge 2021) and antivirals (Frediansyah et al. 2021), are not available, as was the case of the COVID-19 pandemic since its beginnings and up to the first part of 2021 (U.S. Centers for Disease Control and Prevention 2021), authorities around the world relied heavily on non-pharmaceutical interventions to tackle the pandemic. Thus, during most part of 2020 and 2021, the world experienced quarantines (Ashcroft et al. 2021), mask use (Wang et al. 2021), different communication strategies (Bernardin et al. 2021), and contact tracing

(Barrat et al. 2021), among others. On top of that, testing strategies has demonstrated to be crucial to understand the actual impact of the pandemic (nowcasting), allowing to detect infected people, either symptomatic and asymptomatic cases, so to isolate them before they can infect susceptible people. The COVID-19 pandemic has led to the development of new technologies and strategies to improve testing efforts, creating new public health policies (Mercer and Salit 2021). Hence, a deeper knowledge on the effects of different testing strategies on the dispersion of SARS-CoV-2 is crucial to improve public health policies and to provide evidence to decision makers and the authorities. Moreover, an efficient testing strategy combined with individual isolation and quarantines, could be key to suppress the emergence of super-spreading events, a phenomenon characterizing the COVID-19 pandemic. In fact, a significantly high number of COVID-19 infection events is produced by infected individuals acting as super-spreaders (Cave 2020; Lloyd-Smith et al. 2005). In other words, infected individuals who are able to infect a higher number of individuals, compared to the average, leading sometimes to hundreds of secondary cases. This is the case of the so-called 'patient-31' in South Korea whom, apart from directly infecting more than 40 individuals, her interactions resulted in one of the largest infection clusters documented to date (Shim et al. 2020).

To better understand the impact of testing and quarantine strategies during the dispersion of an infectious disease such as COVID-19, in this work, we have implemented a multi-paradigm simulation approach based on both ordinary differential equations (ODEs), and agent-based models (ABM), using the SEIRTQ compartmental model. Using this model, we evaluated a series of simulations to search for strategies combining testing and quarantines able to decrease the impact of the pandemic and, if possible, to suppress it entirely. Our models suggest that iterative testing over 10% of the population could effectively suppress the spread of COVID-19 when testing results are delivered within 1 day. Under these conditions, a reduction of at least 95% of the infected individuals can be achieved, along with a drastic reduction in the number of super-spreaders.

2 METHODS

2.1 General Compartmental Model

A simple general compartmental model can be used as a base to study the propagation dynamics of different systems. In a compartmental model, a population is categorized as to belong to different compartments in which they interact, having flux between them (Figure 1). To define a compartmental model, the modeler has to specify the compartments, the nature of the interaction and the mechanics of the population fluxes. All these dynamics are determined by parameters that can be time dependent.

Consider the $S_1, S_2, ..., S_i$ compartments of a model. The value of the $S_i(t)$ represents the population on each of the compartment through time t. The population flux on the state S_i can be described as:

$$\dot{S}_i = \sum_j F_{ji} - \sum_j F_{ij} + \phi_i$$

where F_{ji} represent the population flux from compartment j to i, and ϕ_i represents the external flux. This flux function can be characterized by any of the following shapes:

Decay: Exponential decay depending on the people belonging to the compartment. In a classical SEIR model (subsection 2.2), this kind of transitions represent people belonging to Exposed (E) or Infectious states (I).

$$F_{ij} = \frac{\rho_{ij}}{\tau_{ij}} S_i$$

where ρ_{ij} is the population proportion subject to this transition and τ_{ij} the expected transition time.

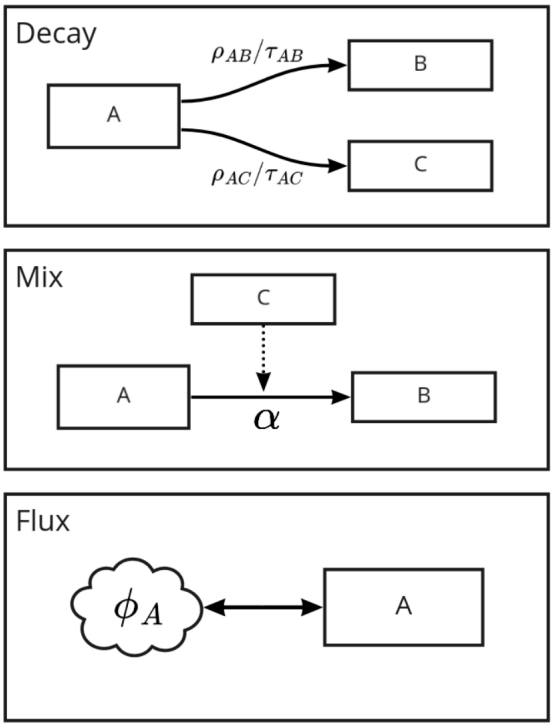

Figure 1: Transition dynamics for compartmental models. A general compartmental model is driven by at least three coupled dynamics, namely; decay, mix and flux. See parameter description in section 2.1.

Mix: Population flux due to the mixing of two states. In a classical SEIR model, this represents the flux from Susceptible (S) to Exposed (E) due to the interaction between S and I.

$$F_{ij} = \alpha \frac{S_i S_k}{N}$$

where α is the product between the expected contact rate per person and the expected probability of an effective mixture event during a contact, and N stands for the total system's population. S_k represents the compartment that causes the mix dynamic, but whose population doesn't necessarily take part in that compartment transition. E.g., I causes the flux from S to E in a SEIR model.

Flux: Exogenous flux of people, non-dependent on the system's dynamics. Depending on the model, this can represent dynamics such as migration and travel, among others.

$$F_i = \phi(t)$$

where ϕ is the exogenous flux dynamic function.

2.2 SEIR Model

One of the most simple and classical epidemiological model is the SEIR compartmental model (Kermack and McKendrick 1927) (Figure 2), where the population is divided into 4 compartments: Susceptible (S), individuals that are susceptible of being infected; Exposed (E), individuals incubating the illness which are still not transmitting it; Infectious (I), individuals that are spreading the infectious disease and; Removed (R), individuals that recovered or died from the infection. In a SEIR model, the transitions from S to E is characterized by a mix between S and I, and the transitions from E to I, I to R, and R to S are characterized

by a decay process. Our model also accounts for the exogenous flux of people representing migrations. These relations can be represented by the following differential equations.

$$\frac{dS}{dt} = -\beta\frac{SI}{N} + \frac{\rho_{RS}}{\tau_{RS}}R + \phi_S$$

$$\frac{dE}{dt} = \beta\frac{SI}{N} - \frac{1}{\tau_{EI}}E + \phi_E$$

$$\frac{dI}{dt} = \frac{1}{\tau_{EI}}E - \frac{1}{\tau_{IR}}I + \phi_I$$

$$\frac{dR}{dt} = \frac{1}{\tau_{IR}}I - \frac{\rho_{RS}}{\tau_{RS}}R + \phi_R$$

$$\frac{dN}{dt} = \sum_i \phi_i$$

$$E_0 = \mu I_0$$

$$N_0 = S_0 + E_0 + I_0 + R_0$$

where β (effective transmission rate) is the product between the average number of contacts per person per time and the probability of disease transmission in a contact between S and I, τ_{EI} is the incubation time, τ_{IR} is the recovery time, ρ_{RS} is a binary parameter representing the existence of immunity loss, τ_{RS} is the immunity loss time, ϕ_i is the external flux of people belonging to compartment i, N is the total Population, and μ is the initial relation between I and E, commonly related with the basic reproduction number (R_0) at the beginning of the epidemic.

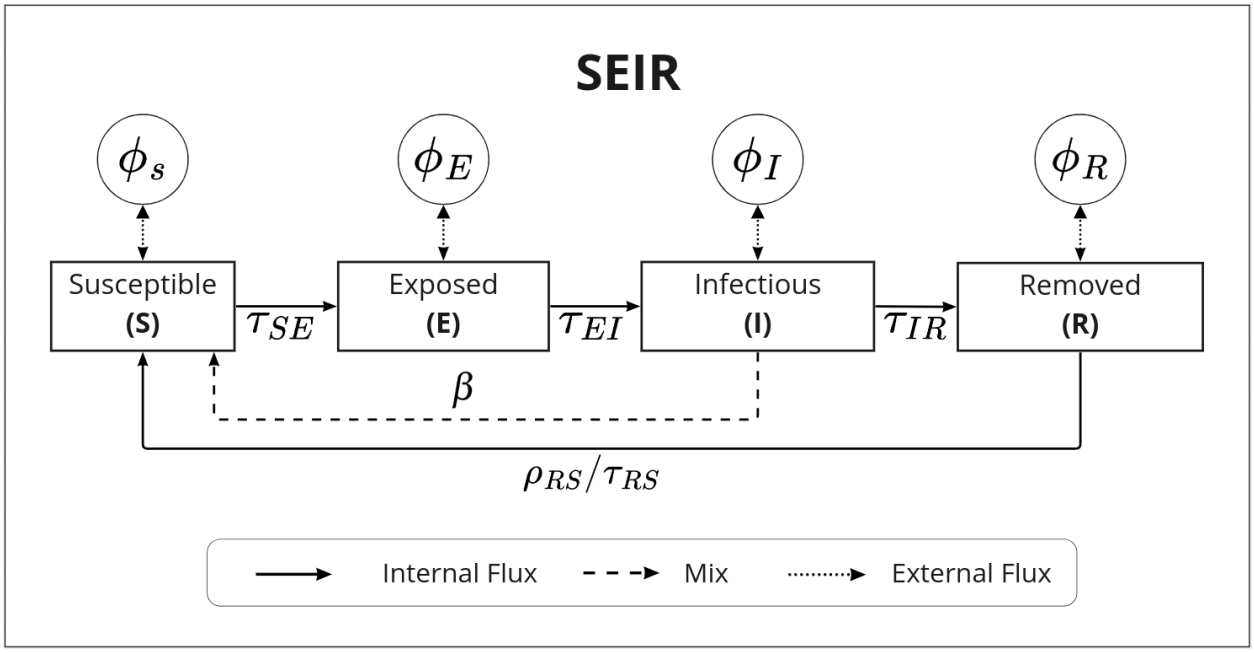

Figure 2: SEIR compartmental model.

2.3 SEIRTQ Model

In order to study the effect of different strategies combining testing and quarantines to reduce the pandemic effects, we propose a model considering the effects of random active testing together with quarantining of infected individuals. To do so, we extended the standard SEIR model into a SEIRTQ model, with new states representing the testing and quarantine dynamics. We added 2 new states: infected individuals that have been tested and are waiting for results (T), and quarantined individuals (Q), representing infected and tested individuals undergoing quarantine. Of note, people at T keep actively infecting during τ_{TQ} days, while waiting for their testing results, being readily quarantined (Q) once they are identified as infected. The quarantined individuals remain in this state during τ_{QR} days, and later become Removed (R).

To model the infection, we used a mass-action law where the contact probability between any two individuals is considered homogeneous along the population, and we assume that there is no exogenous flux. Importantly, we assumed a worst-case scenario in which the infected individuals are homogeneously distributed among the population, and where contact tracing is unachievable. This means that the chance of finding an infected individual per test is $p_D = I/N$. A diagram of the SEIRTQ model can be seen in Figure 3.

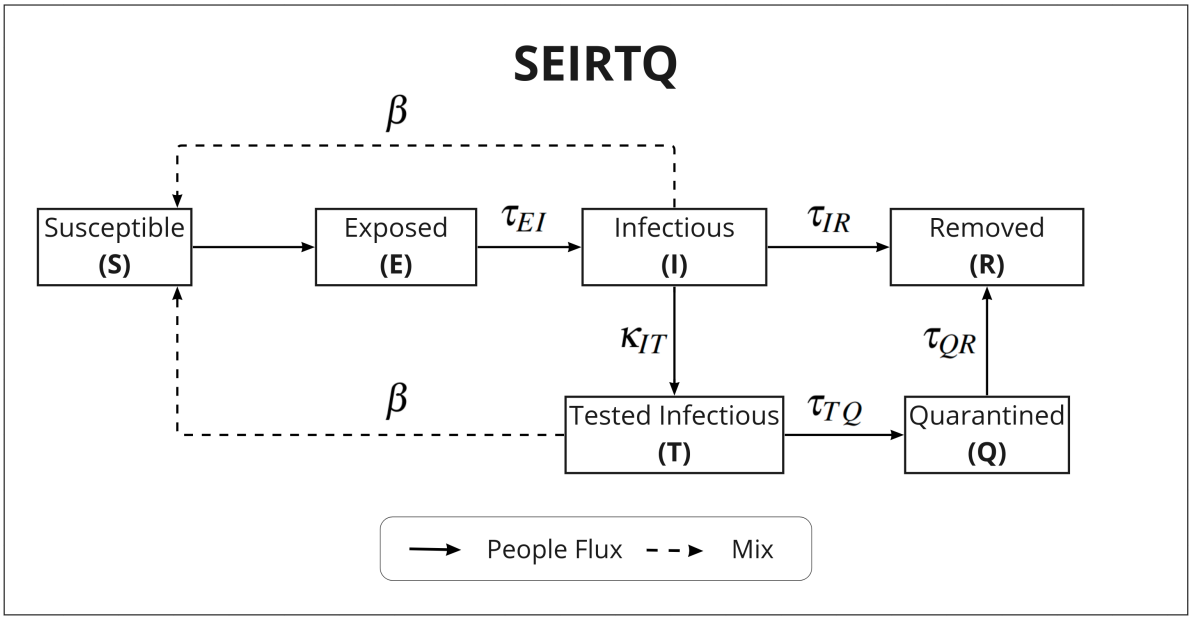

Figure 3: SEIRTQ compartmental model.

Our SEIRTQ model is defined by the set of following ordinary differential equations (ODE) denoting the compartmentalized dynamics occurring between the Susceptible (S) – Exposed (E) – Infected (I) – Recovered (R) – Tested infected (T) – Quarantined (Q):

$$\frac{dS}{dt} = -\beta \frac{S(I+T)}{N}$$

$$\frac{dE}{dt} = \beta \frac{S(I+T)}{N} - \frac{1}{\tau_{EI}} E$$

$$\frac{dI}{dt} = \frac{1}{\tau_{EI}} E - \frac{1}{\tau_{IR}} I - \kappa_{IT} \frac{I}{N}$$

$$\frac{dR}{dt} = \frac{1}{\tau_{IR}} I + \frac{1}{\tau_{QR}} Q$$

$$\frac{dT}{dt} = \kappa_{IT}\frac{I}{N} - \frac{1}{\tau_{TQ}}T$$
$$\frac{dQ}{dt} = \frac{1}{\tau_{TQ}}T - \frac{1}{\tau_{QR}}Q$$

$$\kappa_{IT} = \kappa_E \kappa_{E_{acc}} \kappa_Q$$

where N stands for the total population, β (effective transmission rate) is the product between the average number of contacts per person per time and the probability of disease transmission in a contact between S and I, τ_{EI} is the incubation time, τ_{IR} is the recovery time, τ_{TQ} is the test delivery time, τ_{QR} is the time under quarantine, κ_E is the number of tests performed per day, κ_{Acc} is the accuracy of the tests, and κ_Q is the proportion of infected individuals adopting an effective quarantine. It is important to note that all these parameters can be time dependent, thus they can represent either a change of tendencies due to non-pharmaceutical interventions, a change in people's behavior, or the emergence of new variants affecting the transmission rate, among other phenomena.

2.4 Computer Simulations

To evaluate the efficacy of different combination of testing and quarantine strategies that could be applied to suppress the spread of the COVID-19 pandemic, we developed a set of computer simulations (Ropert 2022a) using two different but complementary paradigms (a multi-paradigm approach) applied to the SEIRTQ epidemiological model: Ordinary Differential Equations (ODE) and Agent-Based Modelling (ABM).

2.4.1 Ordinary Differential Equations

Simulations based in ODE were performed using the cv19gm library (Ropert 2022b), a python library developed by our laboratory, designed as an enabling tool for epidemiological modeling and simulation based on differential equations. The cv19gm library allows the creation of pipelines to conduct scientific research on computational epidemiology, offering capabilities for working with data, embedding it in models, running simulations and performing analysis and projections. It is designed with a mix of simplicity of use, offering a variety of tools, such as data extraction, data fitting heuristics, dynamic parameters for modeling tendency changes like non-pharmaceutical interventions or new variant appearance, integrated function builder, integrated parameter sensitivity analysis, among others.

Our ODE model assumes a 90% testing sensitivity (κ_{Acc}), and 90% of effective quarantine adoption (κ_Q). Once individuals are infected, tested, and their COVID-19 positive results are informed, they will become rapidly quarantined, effectively maintaining their quarantine until they are no longer contagious. As the model depicts (Figure 3), the effect of two important variable parameters should be assessed: the percentage of tested population per day, κ_E, and the delay between the application of the test and the delivery of the COVID-19 positive results, τ_{TQ}. We explored the effect that different testing rates (κ_E) and different delays on the delivery of results (τ_{TQ}), would have during epidemics with different effective transmission rates (β). For the case of the ODE model, we assumed that the testing counter is reset after every day and therefore, some individuals may be tested again the following day. We performed multiple simulations with different combinations of the aforementioned parameters over a 1000 days time period. The values for the simulation parameters are shown in Table 1. Of note, they represent typical parameters characterizing the COVID-19 pandemics during 2020, a time-frame where pharmaceutical interventions were not available.

2.4.2 Agent Based Models

We implemented our SEIRTQ model in Netlogo 6.1.1, an open-source software suitable to implement Agent-Based models (Wilensky 1999). To execute the SEIRTQ model, we defined 10,000 agents in a

Table 1: Parameters for the SEIRTQ model in ODEs.

Parameter	β	τ_{EI}	τ_{IR}	τ_{TQ}	κ_E	κ_{Acc}	κ_Q
Value	0.11-0.2	5	14	0-7	1-20	0.9	0.9

two-dimensional grid of 103 x 103 patches, where each patch represents a square section of the grid. Agents were distributed with a uniform random distribution through the grid, resulting in at least one agent per patch. Importantly, this grid size and distribution of agents (density) allow us to replicate the ODE system. Each agent in the simulation belongs to any of the six different states defined by the SEIRTQ model: Susceptible (S), Exposed (E), Infected (I), Removed (R), Tested (T) and Quarantined (Q). The population that tested COVID-19 positive, become quarantined, so they belong to Q, being subsequently removed from the simulation.

To start our simulation, we defined 10 initial infected agents distributed randomly in the grid, we set the length loop of the testing strategy in 7 days, the percentage of people to be tested daily, and the delay in the delivery of results, according to Table 2. Along the simulation, the contagious process occurs in a stochastic manner, where each infected agent checks the patch where it belongs and infects with a β probability the remaining agents of the patch. After an agent is exposed, the evolution of the exposed time, τ_{EI}, occurs in a deterministic way, which also occurs to transitions from infected to removed, τ_{IR}, and from tested confirmed to quarantined, τ_{TQ}. As seen, τ_{EI} is the time that an individual spends in the E state before becoming I, τ_{IR} the time a person spends in the I state before being R, κ_E denotes the percentage of applied tests, L_S the period loop in which the whole population is tested, κ_{Acc} the accuracy rate of the applied test, κ_Q the rate of quarantine adoption, and τ_{TQ} the test's results delivery time. It is worth noting that in the ABM, τ_{TQ} is the result delivery time which could be interpreted as the time transition from tested confirmed state to quarantined state, because we assume that when a person is detected as infected, she gets immediately quarantined.

Agents are also available to move on the grid, they move one step per day, where each step has length one, in a random direction. Of note, a 7 days length periodic strategy implies that after 7 days, the tested population is reset and the testing process starts again, with the difference that for each loop the number of quarantined agents increases. The set of parameter values used in the simulation appear in Table 2.

Table 2: Parameters for the SEIRTQ model in ABM.

Parameter	β	τ_{EI}	τ_{IR}	τ_{TQ}	κ_E	κ_{Acc}	κ_Q	L_S
Value	0.11-0.2	5	14	0-7	0-20	90	90	7

3 RESULTS

3.1 Testing Effects on Tackling the Pandemic Effects: ODEs Model

We first used our SEIRTQ model to evaluate the percentage of total infected individuals compared to a non-intervened simulation (control) when modifying the amount of people being tested per day, and the delay in the delivery of results (Figure 4). In both cases, we decided to initiate our analyses with a β of 0.13, which was defined based on the data we gathered when modelling the COVID-19 epidemiological status of Chile during 2020 (Chilean Government, www.gob.cl/coronavirus/cifrasoficiales). As expected, when increasing the percentage of people being tested per day, we observe that the peak of infected individuals shifts towards the future and decreases in height, flattening of the curve (Figure 4). Conversely, increasing the delay in the delivery of results, leads to an increase in the number of cases, shifting the peak closer towards the beginning of the simulation and increasing its height. Remarkably, according to our model, the scenario in which daily testing surpasses 10%, and the delay in the delivery of results ranges between 0 (less than 24 hours) and 3 days, may completely suppress the spreading of SARS-CoV-2 (Figure 4). To

further evaluate this observation, we explored the effect that changes in β and the delivery of results would have over the total number of infected individuals (Figure 5).

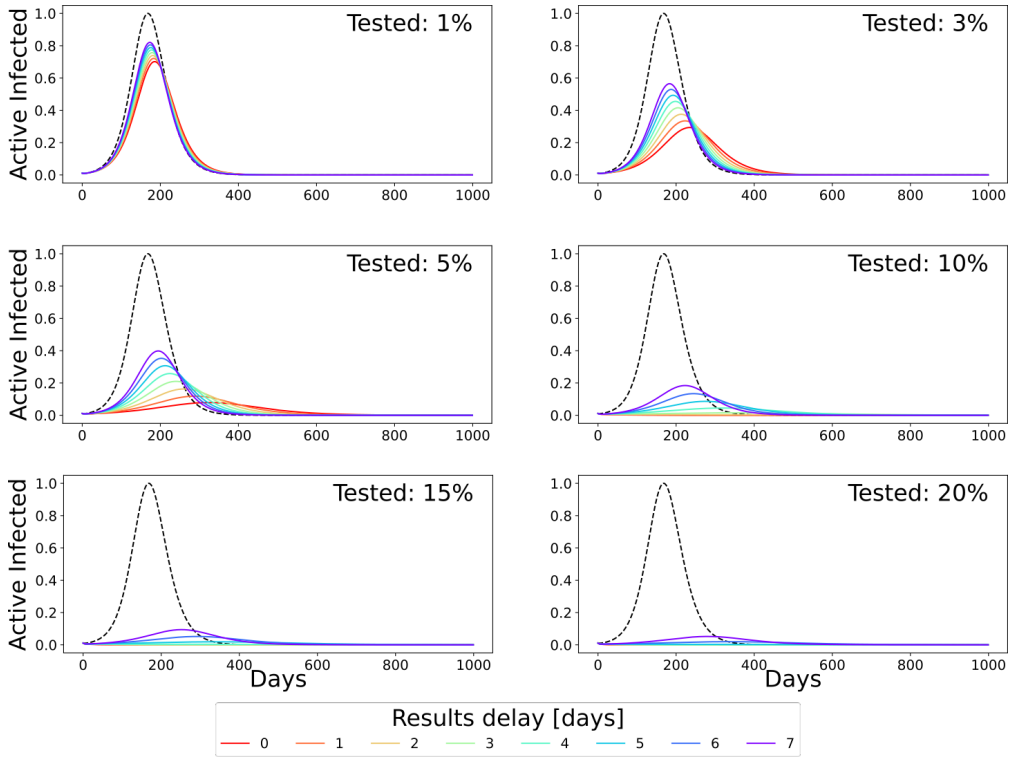

Figure 4: Infected vs time for different examination rates and a unique β. Set of epidemiological curves denoting the number of SARS-CoV-2 infected individuals along the simulation time at specific testing rates and the delay in the delivery of results. Each panel corresponds to a particular percentage of tests daily applied, ranging from 1%, up to 20% of the population. On each plot, we compared the non-intervened (control) simulation (dashed black line) with that of the curves obtained by applying different delays in the delivery of results (colored lines): ranging from 0 (within 24 hours) and up to 7 days of delay.

As the effective transmission rate β increases, the number of daily tests required to maintain the same number of total infected individuals also grows (Figure 5). This relationship is maintained along the set of different contours, becoming evident when considering, for instance, the contour of the 5% of total infected persons in respect to the control scenario. We will refer to this contour as the S_{95} limit where we consider the epidemic is suppressed. An equivalent situation occurs when increasing the delay in the delivery of results: in this scenario, a higher number of tests are required to obtain the same number of infected individuals. Therefore, our model suggests that mass testing strategies could have a clear effect on the total number of infected individuals during the pandemic.

To shed light on the relationship between the effective transmission rate β and the delay in the delivery of results τ_{TQ}, we selected the contour of the 5% of infected population as a suitable goal to achieve and keep the COVID-19 infection rate at bay. Of note, when reaching this goal S_{95}, we will suppress at least the 95% of total infected individuals compared to the control situation. Therefore, we collected the S_{95} contours corresponding to the set of simulations executed with different effective infectivities (Figure 5F), determining the effect that the amount of daily applied tests and the time of results delivery, may produce on the number of total infected individuals. Our results suggest that to maintain the S_{95} contour, for the case of high infectivity rates such as 0.2, we should at least test 15% of the population daily, as long as the results are delivered within 24 hours after testing (Figure 5F). In contrast, when increasing the results delay

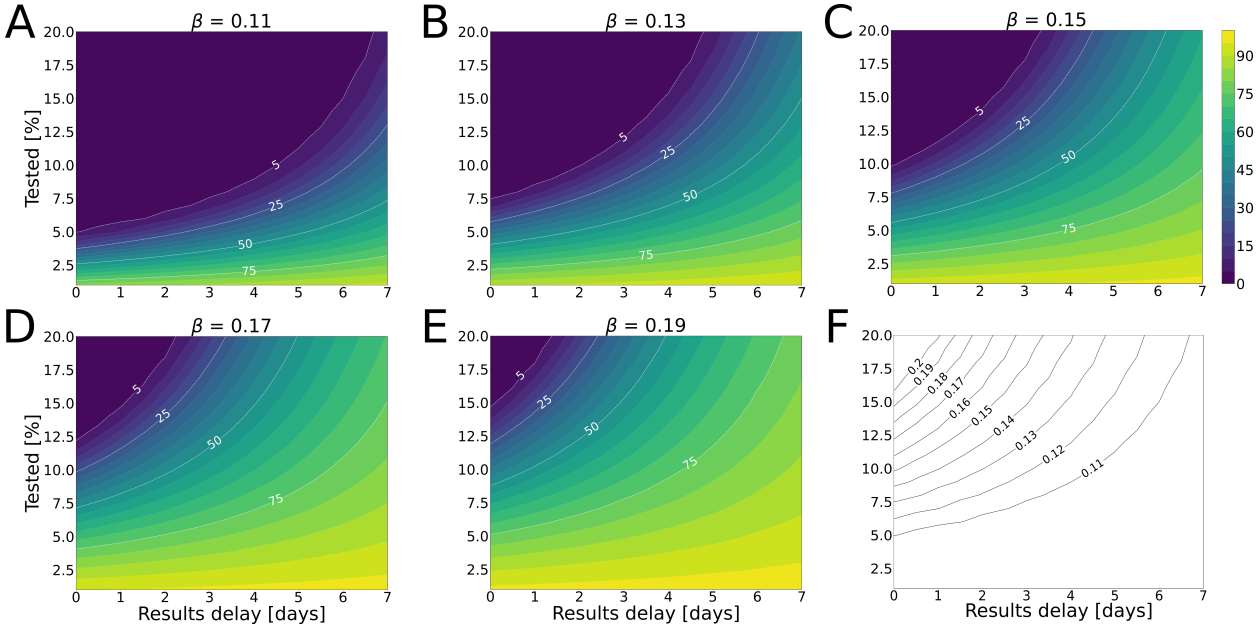

Figure 5: Reducing the time of results delivery while increasing the rate of testing reduces the total number of infected individuals. (Panels A-E) Contour plots show the effect of changing the SARS-CoV-2 effective transmission rate β and the time of the test results over the total number of individuals infected with SARS-CoV-2. We explored the effect of the SARS-CoV-2 infectivity considering the available literature (Toda 2020), starting from 0.11 and up to 0.2, together with the effect of delaying the test results. To evaluate the outcome of the COVID-19 pandemic, each simulation result -i.e., the total number of infected individuals-, was normalized against the control non-intervened simulation. The normalization result appears in the spectrum, where 100% denotes the same number of total infected individuals in the simulation, compared to the control situation. (Panel F) Suppression of total infected individuals according to the percentage of daily test applied and the delay in the delivery of results. Each plotted curve corresponds to the S_{95} contours of the simulations with the infectivity parameters used for panels A to E. As the effective transmission rate and the delay in the delivery of results increase, the percentage of daily tests required to maintain the 95% limit, increases.

to 1.5 days (36 hours), the percentage of the population required to test daily reaches 20%. Conversely, maintaining the S_{95} threshold at lower infectivity rate scenarios, such as 0.11, requires testing around 4.5% of the population -for delay 0-, and more than 20% when the test delivery time reaches 7 days.

3.2 Suppression of Super-spreaders: Agent Based Models

As mentioned before, given the roles of super-spreaders in the spreading of the SARS-CoV-2 virus, we produced an ABM implementation of the SEIRTQ epidemiological model (Figure 3), to determine the abundance of super-spreaders in our simulations. Of note, our ABM implementation uses the same parameters as the ODE model, but contrary to the ODE models that deal with population averages, ABM considers each individual in the population treating them as agents in the simulation. This feature enables following the infection dynamics occurring in the population and identifying the super-spreaders by creating histograms of secondary cases during the course of the simulation. To do so, we quantify the kurtosis, i.e. the fourth statistical moment of the distribution of secondary cases, reflecting how many people are infected by each infected person along the dynamics. Hence, the longest the tail of the distribution, the higher the kurtosis and the higher the number of super-spreaders.

In the case of the ABM models, individuals will not be tested again until the testing loop ends. In agreement with our ODE analyses, we determined the effect of the effective transmission rate β and the percentage of daily tests but, in this case, on the number of super-spreaders. We addressed the effect of the distribution of secondary cases for the range of the evaluated β (Figure 6A-E), and the effect on the mean (mean for β from 0.11 to 0.2) of the kurtosis extracted from this distribution due to the delay in the delivery of results (Figure 6F). Interestingly, at a delay of 0 for results delivery (results delivered in less than 24hrs), we observe a clear and significantly large reduction in the kurtosis of secondary cases when over 10% of the population is tested daily. Of note, an increase in COVID-19 test results delivery time by 1 day, is enough to increase the percentage of daily test required by up to 13.5% to achieve a modest reduction in the number of super-spreaders. Importantly, for delays larger than 1 day, no significant reduction in the kurtosis, i.e., the number of super-spreaders, can be achieved even when testing up to 20% of the entire population daily.

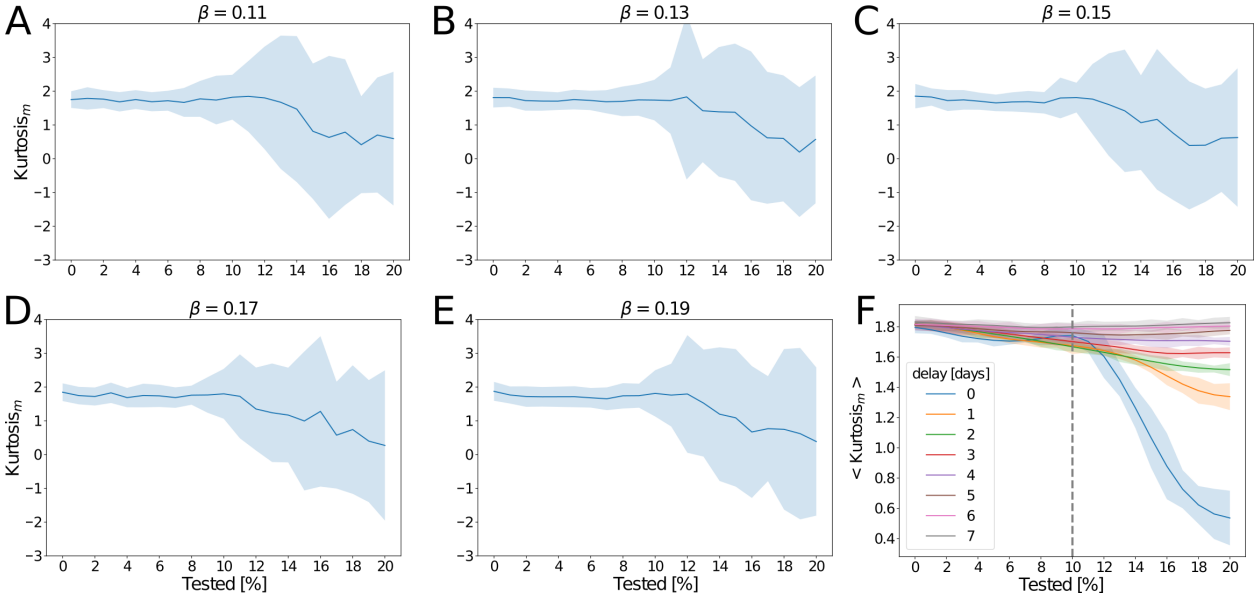

Figure 6: Increasing the rate of testing on the population, while diminishing the time of results delivery, decreases the number of super-spreaders in the population. Each plot shows the distribution of secondary cases due to the percentage of daily tests, considering the range of infectivity and the time of results delivery. (**A**-**E**) Effect on the kurtosis of secondary cases according to the percentage of daily test and the effective transmission rate β of the SARSCoV-2 virus. Each plot denotes the median of the kurtosis and the standard deviation. (**F**) Mean of the medians of the kurtosis of secondary cases for each value of β according to the time of results delivery. The plot denotes the mean of the medians obtained for each β (we calculate the mean for 20 plots with different β), including the standard deviation. Straight dashed gray line in panel **F**) represent the critical value of the percentage of daily applied tests, where the slope of the curve changes significantly for delay 0 (less than 24 hours) and delay 1 day.

4 DISCUSSION

Notably, even though ODE and ABM simulations differ in both their nature and approach, by executing the SEIRTQ model with similar set of parameters we have derived a suitable testing strategy producing a suppression of the 95% of the total infected individuals. Furthermore, under these circumstances we observe a significant decrease in the number of super-spreaders in the infected population, as inferred from studying kurtosis for the distribution of secondary cases. In doing so, our results suggest that to achieve

a 5% level of COVID-19 infections, testing of over 10% of the total population is required daily, when test results are provided within 1 day. Importantly, when the conditions we have identified are fulfilled, our data suggests that we should expect a reduction of at least 95% of the total infected individuals versus a non-intervened situation, together with a drastic reduction in the number of super-spreaders, one of the main players in perpetuating the COVID-19 pandemic. Therefore, simple and straightforward mass testing may help to contain the spreading of airborne contagious diseases and aid avoiding future pandemics by locally containing the propagation of the infection of new viruses and other kind of infections.

When it comes to limitations of the study, we may discuss that this study did not contemplate tracing individuals with close-contact to COVID-19 positive individuals, which could further enhance curbing the spread of the SARS-CoV-2 virus. On the other hand, the infected individuals are homogeneously distributed among the population. However, in reality, infected people are concentrated in clusters, thus tracing efforts should improve the results considerably as each detection would improve the chance of subsequent detections, increasing the detection rate with $p_D >> I/N$. This can be explored in a future work by expanding the SEIRTQ model, taking into account the tracing effects.

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