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Finding and explaining optimal screening strategies with limited tests during the COVID-19 epidemics

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ABSTRACT

The COVID-19 epidemics has now lasted for 2 years. A vaccine has been found, but other complementary measures are still required, in particular testing, tracing contacts, isolating infected individuals, and respecting sanitary measures (physical distancing, masks). However these measures are not always well accepted and many fake news circulate about the virus or the vaccine. We believe that explaining the mechanisms behind the epidemics and the reasons for the sanitary measures is key to protect the general population from disinformation. To this end, we have developed a simple agent-based epidemic simulator that includes various screening strategies. We show that it can be used to compare the efficiency of various targeting strategies, starting date, and number of daily tests. We also ran an optimisation algorithm that proves that the best strategies consist in testing widely and early. Our simulator is already available to play online, to raise awareness in the general population.

Keywords

Agent-based simulation, screening strategies, epidemics modelling, COVID-19

INTRODUCTION

When lifting the lockdown after the first COVID-19 wave in spring 2020, the main goals of many countries around the world were to get back to a less restricted way of living while still maintaining the epidemic under control to avoid a "second wave". Indeed, due to the low circulation of the virus during lockdown, herd immunity was still insufficient to prevent a rebound. For instance, it was estimated¹ that only 3 to 7 % of the French population had been exposed to the virus (and was therefore immunised) when exiting the first French lockdown in May 2020. And as time has since proved, not only a second wave, but several more epidemics waves appeared, pushing some countries to enforce other lockdowns.

A key strategy to try to keep the epidemic under control while loosening the restrictions on the population, is to run large scale **screening campaigns**. The strategy recommended very early on by WHO was to test any suspicious case to identify infected individuals, trace their contacts, and isolate only (potentially) infectious people. But testing kits were rare at the start of the epidemics, forcing governments to prioritise who should be tested first to optimise the impact of the testing campaign. Even nowadays, when testing kits are widely available, and as the Delta and Omicron variants of the virus circulate very fast, the number of daily tests has exploded, posing a new issue of financing those tests. Some countries therefore again choose to restrict tests to some categories of people, for instance, the elderly who are more at risk of serious forms, or people with symptoms. Other countries require non vaccinated people to pay for the tests, also in order to limit the number of tests performed.

Screening tests actually pursue two main (partly contradictory) goals. The first one, as mentioned above, is to **control** the epidemics, by spotting infected people and isolating them to break contamination chains. The second

*<https://membres-lig.imag.fr/cadam>

¹by the Pasteur Institute: <https://www.pasteur.fr/fr/espace-presse/documents-presse/modelisation-indique-qu-entre-3-7-francais-ont-ete-infectes>

one is to **know** the epidemic, *i.e.* evaluate the total number of people infected at a given time, in order to deduce the actual case fatality rate of the virus, and to adapt sanitary measures to the actual circulation of the virus. These goals imply different screening strategies: in order to best control the epidemics, one should test in priority people who are more likely to carry the virus, but this leads to an over-estimation of the global circulation; to best know the epidemics, one should randomly test a representative sample of the global population, but this will lead to a large number of negative tests, failing to isolate many infected people. The best screening strategy is therefore not intuitive, and we claim that simulation can help compare different strategies in order to draw interesting insight. Indeed, simulation allows to run the exact same scenario with only the parameters of the screening campaign varying, which is impossible in reality, and to compare estimations with the "real" epidemic curve, which can be known only in a simulation.

Besides, with the epidemics lasting longer than expected and its end being hard to predict, people are tiring out, sanitary measures are not always well accepted, trust goes down (Strandberg 2020) and fake news circulate with deadly consequences (Nieves-Cuervo et al. 2021), such as refusing or hesitating to get the vaccine (Daly et al. 2021; Jennings et al. 2021). We therefore believe that it is very important to inform the population and explain the mechanisms of the epidemics and the reasons behind all the measures (OECD 2020). Indeed, understanding constraints will improve their acceptability. We claim that an interactive simulator is also a good tool to explain mechanisms by letting users play with it and learn by exploring what-if scenarios.

We have therefore designed an agent-based model whose goal is twofold. First, it allows to **simulate** various screening strategies on a virtual population, and to **compare** these strategies in order to discover insight about optimal parameters for future screening campaigns. Secondly, it is simple and interactive, and users from the general population can play with it in order to **understand** the complex mechanisms behind the epidemics and the reasons for the various sanitary measures. This work is part of a larger initiative aiming at answering questions from the general public about the COVID-19 epidemics, through interactive simulators along with explaining texts written by researchers from various disciplines (CovPrehension 2020).

This paper is structured as follows. The next section discusses some useful background about screening and its challenges; we then survey some existing agent-based models and identifies gaps. The following section then introduces our agent-based model. We then present our experiments and results comparing different strategies, and the results of an optimisation algorithm to find the best strategy. Finally, we conclude the paper and discuss future prospects of this work.

SCREENING AND ITS CHALLENGES

This section introduces some useful background about screening, quality features of tests, the possible prioritisation strategies for allocating a limited number of tests, and the goal of this work.

Importance of screening

In order to release the general lockdown, that is hard to maintain on the longterm for both psychological and economic reasons (Atalan 2020), one solution is to selectively isolate only sick individuals. However, this solution is hard to run efficiently. Indeed, the COVID-19 incubation time is long (a week on average, but sometimes up to 20 days), so infected people have time to infect their contacts before they are detected and quarantined. Besides, the share of asymptomatic cases was still mostly unknown, but estimated to be around 30% (Treibel et al. 2020), meaning many infected people could unknowingly spread the virus among their contacts. This implies that governments could not rely entirely on symptomatic displays to isolate infected people, but needed to test their population broadly to confirm any suspicious case, and to trace contacts to identify chains of contamination. This was the strategy recommended by the World Health Organisation (WHO), as early as the 16 March 2020². However, time was needed to develop reliable quality tests and increase testing capacity.

Quality of tests

There now exists different types of tests to detect the SARS-COV-2 virus responsible for COVID-19, in particular PCR (polymerase chain reaction) tests, serological tests, antigenic tests, and now even auto-tests that one can realise at home. These tests have different levels of quality, depending on 2 factors:

²<https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---16-march-2020>

- **Sensitivity** of a test indicates the probability that the test is positive when the tested person is really sick. A 100% sensitive test applied to a sick individual will always return positive; therefore a negative test gives absolute certainty that the tested individual is indeed not sick. In other words, there are no false negatives with a 100% sensitive test; so sensitivity is the proportion of true negatives.
- **Specificity** of a test indicates the probability that the test is negative if the tested person is really not sick. A 100% specific test applied to a non sick individual will always return negative; therefore a positive test gives absolute certainty that the tested individual is indeed sick. In other words, there are no false positives with a 100% specific test, so specificity is the proportion of true positives.

However, it is impossible to design tests that are perfect on both criteria (or even on a single one). Screening tests always have an error margin. In particular, screening tests cannot be both highly specific and highly sensitive, so a compromise must be found between two opposites:

- Very **sensitive** tests are more likely to be positive with sick individuals: this reduces the rate of false negatives, so prevents missing infected people who keep moving around instead of being quarantined;
- Very **specific** tests are less likely to be positive when the individual is not sick: this reduces the rate of false positives, to prevent from quarantining healthy people.

The first screening tests designed for COVID-19 were relatively specific (in the range of 95 to 98% of true positives) but still little sensitive (sometimes up to 30 to 40% of false negatives, sick but not detected by the test). As a result, it was sometimes necessary to do a second test to confirm a negative test result.

Screening prioritisation strategies and goal of this work

The **goal** of screening is **twofold**: it allows to **know** as precisely as possible the current state of the epidemic in the country, and to **control** the spread of the virus as well as possible with adapted measures (neither too strong nor too lax).

Under the constraint that testing kits are in limited supply, governments want to prioritise wisely who should be tested, in order to reach both goals with the minimum amount of tests. For instance, France started testing late and slowly³: it took some time to design reliable tests, and the small number of such available tests was thus limited to healthcare workers and people at risk. Nowadays, tests are widely available and are the most cost-effective mitigating measure (Rezapour et al. 2021), but some countries start restricting them again in order to limit the financial cost for society, for instance, by reserving them to elderly people, or by asking non-vaccinated individuals to pay for the tests.

The various possible targeting strategies have different impacts on both goals stated above:

- **Random targeting** consists in choosing randomly people who should be tested. This is a more representative sample of the population, and provides better knowledge of the current state of the epidemics. But when the incidence of the virus is very small (as it was after the first lockdown), the proportion of people infected is very low, so most tests will return negative. There is therefore a risk of "wasting" many tests, *i.e.* the chances of finding infected people to isolate them and control the epidemics are low.
- A solution is to **target suspicious cases** (the symptomatic ones), but this strategy is insufficient to control the epidemics since it ignores all the (also contagious) asymptomatic cases. Besides, the sample is not representative of the general population, and the high proportion of positive tests in the sample might lead to overestimate the global circulation of the virus.
- Another strategy consists in **targeting people who work outside of home**, since they are more likely to get infected and/or infect others. For instance, at the beginning of the epidemic, healthcare workers were tested in priority, since they were the most exposed to the virus; in order to reopen schools, there was also a focus on testing teachers, school workers, and now all the children from the same class as an infected pupil. This strategy focuses on controlling the epidemics while allowing for economic activity, but it ignores contaminations that happen outside of work (shopping, leisure...).

³<https://www.usinenouvelle.com/article/en-retard-la-france-monte-en-puissance-pour-les-tests-de-diagnostic-du-covid-19>. N945261

- Finally a last interesting strategy consists in **targeting high-risk people**. Their profile is now better known, in particular elderly people or people with comorbidities (Jordan et al. 2020). The goal of this strategy is to detect infection soon and treat them early to prevent serious complications. But the results would then not be representative of the global circulation of the epidemic in the general population.

One can see that finding the best strategy on all accounts is not easy by using only our intuition. We claim that simulation can help, by allowing us to compare different strategies and to measure their effects. In particular, simulation will allow us to run the exact same scenario several times, with only the target population or other features of the screening campaign varying, which is impossible in reality. The next section discusses existing work related to simulating the COVID-19 epidemics, mitigating interventions in general, and screening in particular.

AGENT-BASED SIMULATION OF EPIDEMICS

The main measures against COVID-19 have been quarantine, contact tracing, screening, and isolation; there is no consensus on best practices, and countries differ in their approach, but a survey of medical publications (Girum et al. 2020) shows their efficiency, in particular when combined together. It is hard, however, to compare their efficiency in real life, but simulation can help comparing them "in silico".

Advantages of simulation

Computer simulation has many benefits in the context of the crisis management in general, and the current epidemics in particular. Indeed, only simulation allows to compare different intervention strategies, all other things being equal. In the real world, we can only compare between different countries applying different strategies, but they also differ on other regards: climate, culture, etc, that all might influence virus spread, so it is impossible to isolate the precise impact of the strategy being evaluated. But in the simulated world, we control all parameters, and repeat the exact same experiment with only the strategy changing, in order to evaluate its impact independently of all other factors.

Besides, in this work, we are interested in evaluating screening strategies and their efficiency to assess and control virus spread. In the real world, there is no way to access the actual number of infected people (unless we could simultaneously test the entire country), so it is impossible to evaluate how good the curve estimated from the tests is compared to the "real" curve. On the contrary, in a simulation we know the epidemiological status of all agents, so we can access the *real* (simulated) epidemic curve, and compare it with estimations obtained from various screening strategies. Simulation is therefore a great tool to assess screening strategies on a virtual population.

Approaches to epidemics simulation

As a result, a lot of models of the COVID-19 epidemics have been published in the last 2 years. Current epidemic models mainly fall in two approaches.

Compartmental models divide the population in a number of epidemiological classes. The simplest ones (often shortened as SIR models) use only 3 compartments: Susceptible (not yet infected so not immune), Infected (and contagious), Recovered (and immune). The hypothesis is that recovered individuals are then immune and cannot get infected again, which has proven wrong for COVID-19. Compartmental models of COVID-19 have often integrated more compartments, such as Asymptomatic or Hospitalised, in order to more precisely represent the dynamics. These models then rely on the mathematical resolution of differential equations to give a **macroscopic** view of the epidemic dynamics. It is therefore quite fast and scalable.

Agent-based models model each individual as an autonomous agent, in order to give a **microscopic** view of the situation. Agents are heterogeneous, initialised with different values of their attributes, such as age, gender, comorbidities, or social behaviour. This allows to model the influence of individual decisions on the virus spread, such as a refusal to get vaccinated, or not respecting social distancing. These models are more complex to initialise as they require behaviour data that is hard to get, and are less scalable since they require to compute the behaviour of each individual agent. However, they are more precise, in particular to study why a specific individual got infected.

Both approaches have their benefits and drawbacks depending on the goal of the simulator and its scale. Our goal being to explain the complex mechanisms behind the epidemics rather than predicting its spread at the scale of the country, we chose an agent-based approach. We survey various existing agent-based models in the following paragraphs.

Simulations of interventions

A very early report (as soon as March 2020) about the results of an epidemiological modelling informed the first policy-making in the UK and other countries (Ferguson et al. 2020), leading to general lockdown. At that time, in the absence of a vaccine, they assessed other non-pharmaceutical interventions to reduce contacts in the population and therefore transmission of the virus, with 2 main possible strategies: mitigation aiming only at slowing down the epidemic spread, vs suppression that aims at completely stopping that spread. Their results showed that optimal mitigation policies might reduce the pressure on healthcare system by two thirds and deaths by half, but might still result in hundreds of thousands of deaths and an overwhelmed healthcare systems. Therefore, they suggest that where possible, countries should aim at suppressing the epidemics rather than just mitigating it, which would require a combination of several very constraining measures (quarantines, social distancing, school closures) despite their negative side effects. Besides, they predict that such measures would need to be maintained indefinitely (or until a vaccine is found) to prevent a rebound as soon as they are relaxed. Not knowing if such suppression can be maintained on the long-term, or how to reduce their social and economic costs, they also suggest intermittent measures: closely monitoring the epidemic progression to temporarily relax measures but re-instantiate them when needed. This is indeed what has happened all over the world in the past two years.

Other countries have also developed simulators to help policymakers. For instance, COMOKIT (Gaudou et al. 2020) is a framework composed of several realistic spatialised agent-based models of the epidemics and of various interventions, aiming at informing public health decisions made by the Vietnamese government. These models have also been applied to towns in other countries, such as Nice in France (Chapuis et al. 2021). The models run on the GAMA platform. They can be fed from various data sources, provided by the Vietnamese government (census data, epidemiological data) or by private actors (Facebook data, mobile phone data). They have been used to quickly compare potential strategies (lockdown at different scales, quarantines), as well as to suggest optimal timing or combination of multiple strategies. The models offer a precise representation of the population and of contamination in close spaces (shops, schools) although they neglect the role of transportation. They are very complex models aimed at guiding policymakers, but not at informing the general public.

Covasim (Kerr et al. 2021) is an agent-based model of the epidemics that can be tailored to various local contexts (such as age distribution, daily contacts, epidemic progression in number of reported cases and deaths) and has been actually used in a number of countries. It allows to test several types of interventions: physical (*e.g.* lockdown), diagnostic (*e.g.* screening or contact tracing), or pharmaceutical (*e.g.* vaccination). However, it is targeted at researchers and policy makers rather than the general public, and as such is much more complex than our intended simulator. Moreover, testing strategies are expressed in terms of probabilities of testing people with or without symptoms, in/out of quarantine, or over a certain age; it does not include other interesting strategies such as random sampling or prioritising workers.

Testing

Various models have specifically studied different screening strategies. For instance, (Paltiel et al. 2020) modelled several scenarios regarding the measures needed for a safe re-opening of US colleges. They modelled 5000 students, of whom 10 were infected at the start of the semester, and tested several epidemic scenarios (with reproductive numbers values between 1.5 and 3.5, a 0.05% fatality rate, and a 30% probability of showing symptoms when infected). They varied the following parameters of screening: frequency (every 1, 2, 3, or 7 days), sensitivity of tests (between 70 and 99%), specificity of tests (98 to 99.7%), and cost (10 to 50 dollars per test). They conclude that it is best to screen frequently (every 2 days) in addition to strict observance of sanitary measures to keep the reproduction number under 2.5. In order to limit costs, they also show that even a rapid, less expensive but poorly sensitive test (around 70%) is sufficient to control the number of infected students, who are isolated in a dedicated dormitory (within a delay of 8 hours). Of course this strategy is not applicable at the scale of a country (there is not enough medical staff to test the entire population every 2 days). Also the population of a college campus is not representative of the general population, and in particular is younger so less exposed to serious forms of COVID-19.

(Atkeson et al. 2020) focus on the economic benefits of testing. They provide an SIR model of the US population with 5 age groups, working in various economic sectors. Their study shows that the economic benefits of rapid screening programs far exceed their costs, with a ratio between 4 and 15 (excluding the monetised value of lives saved) depending on the parameters of the screening. However, an interesting aspect of their study is that they consider a variable adherence to quarantine measures, depending on the probability to be a false positive: They conclude that tests used must be highly specific, or combined with a confirmatory test, in order to both reduce the cost of having healthy workers in quarantine, and decrease the number of people who break quarantine because they (wrongly) believe they are a false positive.

To conclude, models that include testing as an intervention generally focus only on controlling the epidemics: testing is part of the testing, tracing, isolating strategy recommended by WHO. On the contrary, we want to compare testing strategies with respect to 2 different objectives: not only controlling the epidemics by appropriately isolating infected individuals, but also precisely estimating the current state of the epidemics (total number of cases), which is useful to evaluate the impact of current measures and the necessity to adapt them.

Vaccination

Finally, other models focus on the impact of a vaccination campaign. This is relevant as vaccination poses a similar problem of prioritisation for the allocation of a limited number of doses, but also an additional problem of compliance, or trust: some people might not want to get vaccinated, for various reasons (Hornsey et al. 2018).

For instance, (Li, Giabbanelli, et al. 2021) modelled a nation-wide vaccination campaign in the United States. They varied parameters such as the efficacy of the vaccine, and the population compliance, and tested 6 scenarios combining a vaccination campaign with other interventions (distancing, etc). Their results show that the vaccine significantly reduces infections, even with very low population compliance. However, they also show interesting counter-intuitive results: when compliance is very high, and since the older population is vaccinated first, the delay is longer for younger and more connected individuals to access the vaccine; as a result, the virus spreads more than if the compliance was lower. This also proves that the vaccine alone is not sufficient, and should be combined with other interventions to reduce the spread of the epidemics.

Another study is concerned with prioritising the vaccines. (Tatapudi et al. 2021) simulate different prioritisation strategies with a limited supply of vaccines, in a US urban region of 2.8 million residents. They show a limited impact of vaccination on reducing viral spread, mainly due to exponential contaminations before the start of vaccination, meaning that lots of adults were already immunised. Consequently, they suggest that vaccines should be distributed as fast as possible among all eligible adults after vaccinating the most vulnerable, to improve the speed of the vaccination campaign, rather than strictly respecting a priority schedule. This is consistent with the findings of (Li, Giabbanelli, et al. 2021). Besides, these studies show the interest of simulation to reveal unexpected and unintended consequences of potential sanitary policies, that cannot be tested in real life.

Objective of our work

Not many models specifically focus on comparing various screening strategies to both evaluate and control an epidemic. This can be explained by the now wide availability of testing kits in developed countries, that allow to massively test the entire population. Nevertheless, such work is still important to explore screening strategies in countries where tests are not yet widely available, or to reduce the cost of screening, or for potential future epidemics. Besides, our model also aims at **explaining** the mechanisms to the general public by letting them interact with the simulated population and take on the role of public health deciders to select the parameters of a screening strategy. The originality of our work is to target the general public and focus on explaining a complex phenomenon, unlike most models that are targeted at governments to help them make decisions.

OUR MODEL

As explained above, our agent-based model is quite simple since it is targeted at the general population, and its goal is **not to predict** the evolution of the epidemics, but to explain its mechanisms.

Characteristics of the population

We have modelled a population of 2000 individuals, distributed in several age categories. This influences their sensitivity to the virus (people at-risk) as well as their mobility. For instance, 50% of people aged 20 to 65 have work outside their home ('essential' workers) whereas the rest stay at home (remote work, furloughed workers, family carers, etc.). People aged less than 20 and over 65 are considered homebound (by respectively remote schooling and retirement). Individuals in our population can be in one of five distinct states regarding the virus, as shown in Figure 1 below:

- **Susceptible:** they have never been infected and are therefore not immune either
- **In incubation:** they have been infected but are not yet sick (it lasts 6 days on average)
- **Asymptomatic:** they are sick but display no symptom. Only a test will reveal them (30% of patients below 65 years old, for an average of 21 days)

- **Symptomatic:** they are sick and display symptoms. (70% of patients below 65 years old, and 100% of older patients, for an average of 21 days)
- **Recovered:** they are immune and cannot get infected again (this was a hypothesis of our model, at a time when this was unknown (Roy 2020); we now know that reinfection after recovery or vaccine has a lower risk but is still possible (Cavanaugh et al. 2021))

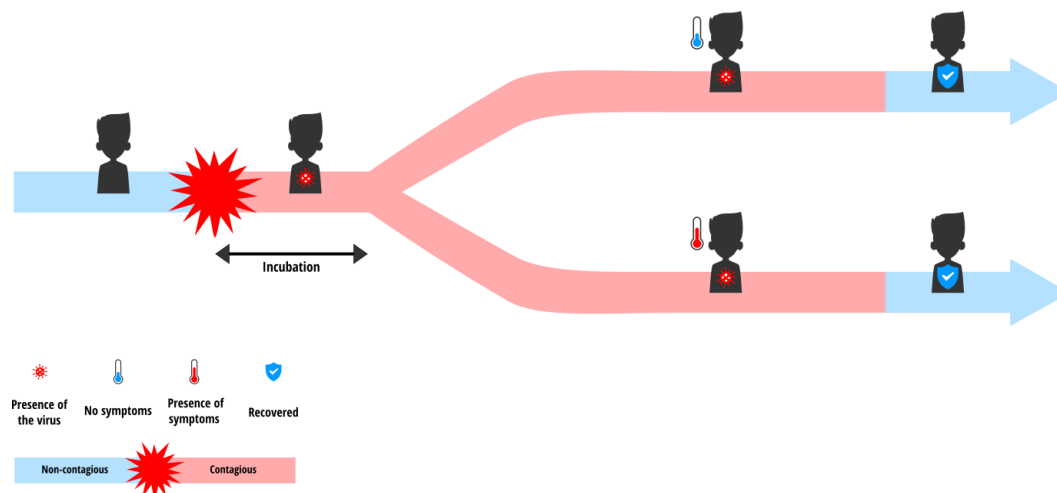


Figure 1. Evolution of epidemiological status of agents

When they move in the simulation world, individuals can come into contact with one another. Infected people (in incubation, asymptomatic and symptomatic) are all contagious and can therefore transmit the virus to susceptible people they are in contact with. Individuals working from home do not move but they can be in contact with people passing by their home (deliveries, postal services, etc.). However, they have less contacts on average than people who have to work outside of home.

In order to reduce the spread of the virus, people who tested positive are put into quarantine and are completely isolated: they cannot transmit the virus any further.

Testing strategies

In our model, we simulate tests with both a sensitivity and specificity of 90%. It would be interesting to vary these 2 parameters in future work, to study their impact on the evaluation of the epidemic curve. Our goal is to find out how we can best use the tests available each day to reach the two main objectives of a massive testing campaign: to monitor the epidemic (optimise fit between estimated and "real" curve) and to control it (minimise the epidemic peak). The screening campaign has the following attributes:

- The **number of tests** available each day. The testing strategy of the French government plans for 500000 to 700000 tests per week, which corresponds to about 2 to 3 tests per day for the reduced population of 2,000 agents in our model;
- The **triggering time**, *i.e.* the moment from which we start testing the population. In the model, it is defined in terms of a threshold X for the proportion of symptomatic people in the population: when more than X% of the population is symptomatic, the testing campaign starts;
- The **target population** being tested, with possible values being: random sampling; symptomatic people; elderly / at-risk people; or people working outside of home.

Interactive simulator

The simulator is implemented in Netlogo and available to play online⁴. Fig 2 illustrates its online interface.

The user takes on the role of a public health decider, and must try to reach several goals:

⁴Covprehension question 17: <https://covprehension.org/en/2020/05/12/q17.html>

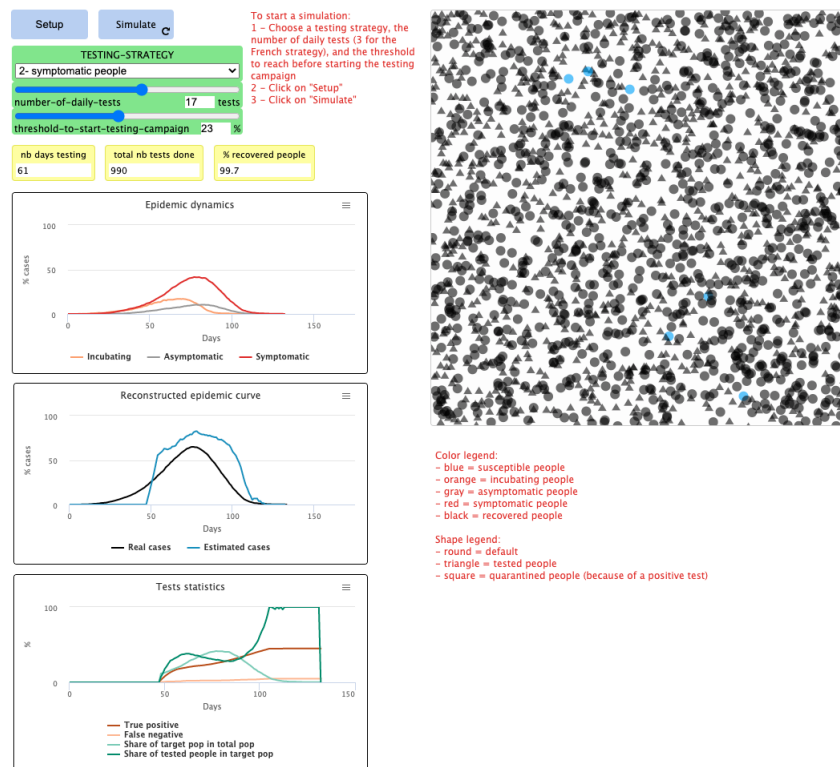


Figure 2. Interface of the online simulator

- To minimize the total number of tests used;
- To minimize the spread of the epidemic, *i.e.* the total number of people infected;
- To minimize the number of people quarantined for no reason, *i.e.* the number of false positive tests;
- To estimate as closely as possible the “true” curve in order to precisely monitor the epidemic over time;

To reach these goals, the user can modify the parameters of the testing campaign as defined above:

- The number of tests available each day (*i.e.* time necessary to test the entire target population);
- The starting date of the testing campaign: immediately from the start of the epidemic, or later on;
- The target population: in-person workers, elderly, random, symptomatic.

The different goals are obviously not always compatible, and the actions can have opposite effects on different goals, improving one at the cost of failing another. For instance, to best know the status of the epidemics, one could test every citizen but that would fail to minimise the number of tests used; or one could randomly test people to get a representative picture of the situation, but would then “waste” many (negative) tests that fail to spot and isolate infected people. Managing the situation therefore requires finding some compromise. We expect that interacting with the simulator will help people understand the stakes behind the sanitary measures, and will make them less subject to blindly believing disinformation. But this will require future experiments with users, to test the actual impact of playing with our simulator.

In the following section, we describe the experiments that we ran by manually varying the different parameters (target population, number of tests per day, and starting date), and we compare how well they estimate the “real” curve, which the simulation allows to know. The next section will then discuss an automated optimisation of the parameters with the goal to best fit the real curve.

EXPERIMENTS

Inference of the epidemic curve

There are several ways to compute the estimated curve from the results of screening tests. The number of confirmed cases communicated every day by the authorities of different countries is a combination of test results and expertise of health professionals. But like any statistical estimation, these figures have error margins and potential biases. We believe that the general public should be aware that the “true” number of infected people is unknown and can only be approximated. It is one goal of our simulator to allow them to observe these variations and errors.

Indeed in our simulator we know the status of all of the agents, so we do know this “true” number of infected agents over time, which is impossible in reality. We can therefore **compare the curve estimated using tests, with the “true” curve**, in order to verify the correctness of the estimations obtained with different strategies. This is a great advantage of agent-based simulation, which will allow us to evaluate how well different computation methods do fit this real curve. We have actually tested two simplified estimation methods, described below: proportionality, and predictive values.

Proportionality rule

First, we could intuitively use a simple cross multiplication: the number of positive tests among the total number of tests provides an estimation of the proportion of cases in the general population, by a proportionality rule. For instance, if we test 700000 people and that 1000 of them are infected, this is a proportion of 0.14%, so we deduce that out of the 70 millions residents of France, 100000 are infected. But this simple **proportionality rule** does not work well in epidemiology, especially when the number of people tested is low, or when the prevalence of the epidemic (*i.e.* the total number of cases at a given time) is too low, as is the case at the beginning and at the end of an epidemic, or when tests are not entirely reliable.

Predictive values

Another method for estimating the total number of infected people is to compute the **predictive values** of the test, which depend on three elements: the prevalence of the epidemic, the rate of false positives (which is equal to $1 - \textit{specificity}$, with specificity being the probability that a positive individual receives a positive test), and the rate of false negatives (equal to $1 - \textit{sensitivity}$, since sensitivity is the probability that a negative individual receives a negative test) obtained with the test. The positive and negative predictive values are not intrinsic to the test (unlike true positive rate and true negative rate), and do not concern a single individual but a population, so they also depend on the prevalence of the epidemics in this population (*i.e.* the probability that an individual is positive).

The positive predictive value is also called precision. Its complement is the false discovery rate, *i.e.* the rate of false positives among the total of positive tests.

$$PPV = \frac{\textit{sensitivity} * \textit{prevalence}}{\textit{sensitivity} * \textit{prevalence} + (1 - \textit{specificity}) * (1 - \textit{prevalence})} \quad (1)$$

The negative predictive value (the rate of true negatives in the total negative tests) is the complement of the false omission rate, *i.e.* the rate of false negatives upon the total of negative tests.

$$NPV = \frac{\textit{specificity} * (1 - \textit{prevalence})}{\textit{specificity} * (1 - \textit{prevalence}) + (1 - \textit{sensitivity}) * \textit{prevalence}} \quad (2)$$

The following paragraphs describe our experiments on a simulated population of 2000 agents, exploring different scenarios by varying the different parameters of the screening campaign.

Comparison of estimated cases for the different samples of population

Let us look at what happens when we choose a daily number of tests equivalent to that of the French government (*i.e.* 3 tests for 2000 individuals) and when we start testing as soon as the first case appears (which has not been the case in France).

We compare the curves representing the number of cases estimated by the proportionality rule (in red), the number of cases estimated by computing the predictive values (in blue), and the “true” number of cases (in black), for each sampling strategy (testing priority among: random, elderly / at-risk, workers, symptomatic). Figures 3 summarises the results.

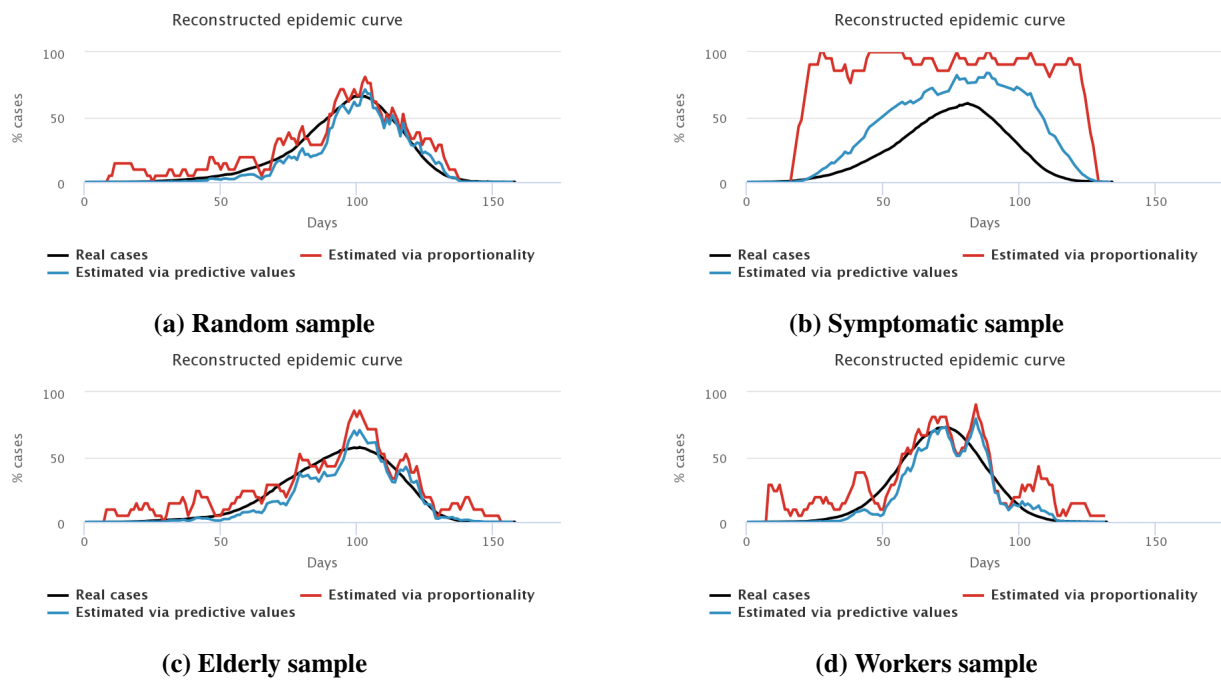


Figure 3. Experiment 1: 3 tests/2000, immediate start, different samples

Firstly, we note that the blue and red curves (the estimated cases) vary a lot more than the black curves (the “true” cases). Indeed, they depend on the number of positive tests each day, which varies greatly depending on who is tested. In general, we choose to “smooth” this estimation by computing the mean result of tests over several days (here, a mean over 7 days), but there is always a larger variability depending on who is tested each week. For example, a lot of negative tests may result in an estimation of a decreasing epidemic which is not necessarily true (maybe we just tested non-infected people, which does not mean that no one is sick anymore).

We also note that the blue curves (with predictive values) are better estimators than the red curves (proportionality rule), especially at the beginning and at the end of the epidemic when the prevalence of the virus is low, and especially for symptomatic people, who are less representative of the total population.

Secondly, we find that the worst estimation happens when we only test symptomatic people (top right figure): since we only test symptomatic people, who therefore have a high probability of being infected by COVID-19, we obtain a high positivity rate of the tests, so we overestimate the “true” number of cases in the general population. Given that the tests we model are diagnostic ones, it is really not sound to extrapolate the number of cases in the general population from the tests performed on symptomatic people. The model confirms this. Such tests allow to control the epidemic by confirming and isolating infected people, but they do not allow to monitor its spread in the population.

Comparison of estimated cases *w.r.t.* the number of daily available tests

Let us now look at what happens when we choose to **increase the number of daily tests**: we start with 3 tests for 2,000 people on the top left corner, then up to 6 tests for 2,000 on the top right corner, then 9 for 2,000 at the bottom. Simulations were done on the random sample only, with a beginning of the testing campaign as soon as the first case appears. The following figures show only the estimation by predictive values since it is better than the proportionality method.

We notice that the higher the number of tests, the better the estimation of the number of cases in the general population. After an initial overestimation, when there are very few cases in the population and very little tests performed, the reconstructed curve follows rather precisely the actual epidemic curve, in particular around the peaking time, the key moment of the epidemic.

Comparison of estimated cases *w.r.t.* activation date of testing campaign

In this final experiment, we use the random sample again, and vary the starting date of the campaign as well as its intensity, in terms of the number of daily tests performed. The lower intensity, 3 tests/2000 people, corresponds to

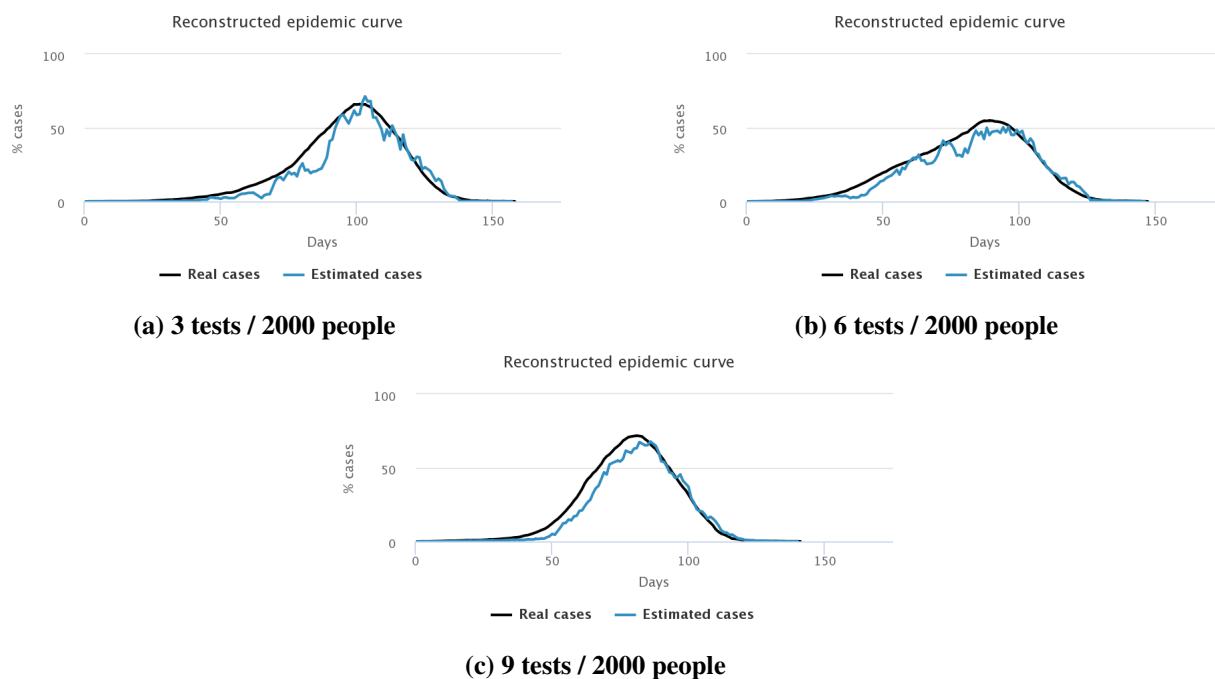


Figure 4. Experiment 2: immediate start, random sample, varying number of daily tests

the initial strategy in France, when the number of available kits was still quite low. The objective of this experiment is to assess how well we can estimate the "real" epidemic curve, by either starting screening very early, or performing it at a very high intensity, or both. Figure 5 shows the results of the 4 different combinations of parameters.

We notice that with a low screening intensity of 3 tests for 2,000 people (first column), the reconstructed curve cannot capture the epidemic peak when screening started late (after 15% of infections, upper left).

Similarly, if the screening campaign starts late (15% people symptomatic, bottom line figures), even increasing the number of tests to 9 for 2,000 people (bottom right), we notice that the peak identification is very uncertain, and cases are strongly overestimated after the peak. When screening starts immediately and intensively, this overestimation only happens when the number of cases is very low (top right). The conclusion is that if we wait too late to activate the testing campaign, the knowledge of the epidemic we get is strongly diminished, even if we ramp up the number of tests available daily.

OPTIMAL STRATEGY

The perfect test does not exist, but there can be an "optimal" one. Similarly, no ideal screening strategy exists, but we can still search for the optimal strategy in a given situation.

Setup

In order to find the strategy that gives the best result, we ran an optimisation algorithm on our model, using the OpenMOLE platform⁵. Through this algorithm, the model is simulated for a wide range of different input parameters combinations, in order to find out which combinations lead to a "successful screening campaign", according to various pre-selected criteria.

We varied the following 3 input parameters:

- Screening sampling strategy (random people, only workers, only the elderly, only symptomatic people);
- Daily number of tests (between 0.5 to 7 times the French strategy);
- Ratio of infected people needed in the population to trigger the start of the screening campaign (between 0% - immediate start - and 50%)

⁵<https://openmole.org/Calibration.html>

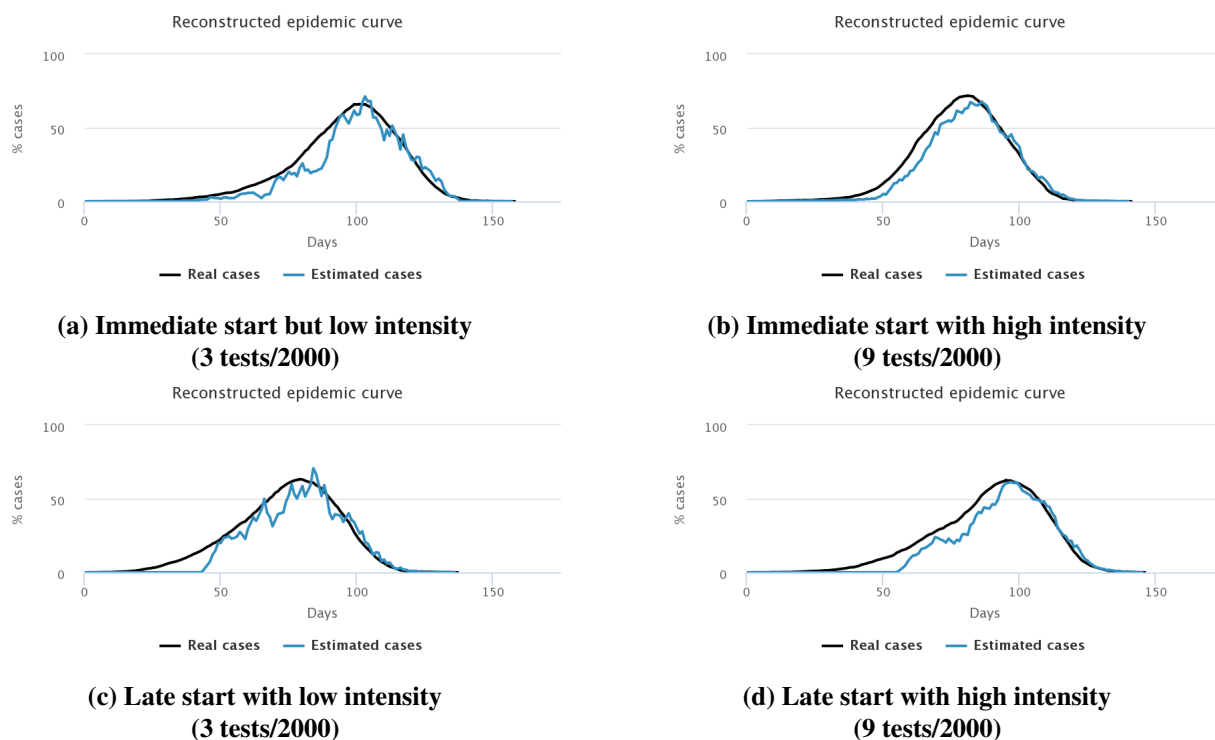


Figure 5. Experiment 3: random sample, varying starting date and intensity of the testing campaign

In order to try and minimise the following output indicators:

- Total number of tests performed (we want to perform the fewest possible tests given that their availability is limited);
- Number of false positive results (people put uselessly in quarantines);
- Number of undetected infected people (who keep spreading the virus unknowingly, whether because they were not tested at all, or because they were a false negative).

Optimisation results

Since we have several output indicators, there is no unique best solution, but several equivalent solutions that better minimise one or the other of these output criteria. This is called a Pareto front.

For a population of 10000 agents, all the best solutions found by the algorithm for our model have two features in common:

- they target symptomatic people;
- and they start screening as soon as the first case appears (as early as possible, exactly as recommended by WHO).

Besides, the best solutions selected by the optimisation algorithm show that the more tests are performed, the more infected people are detected (see Figure 6). This result looks obvious, but it is always reassuring to confirm that the model behaves as expected. It could also reassure the general population that a higher positivity rate in a given country compared to neighbours can simply mean that this country is testing its population more.

The results of our optimisation algorithm therefore also confirm that the strategy to massively test the population as early as possible does work and can avoid a lockdown, on condition of course that enough test kits and medical staff are available. Incidentally, this is the strategy that was adopted in South Korea⁶.

⁶https://www.lemonde.fr/international/article/2020/03/20/en-coree-du-sud-des-tests-massifs-pour-endiguer-le-coronavirus_6033800_3210.html

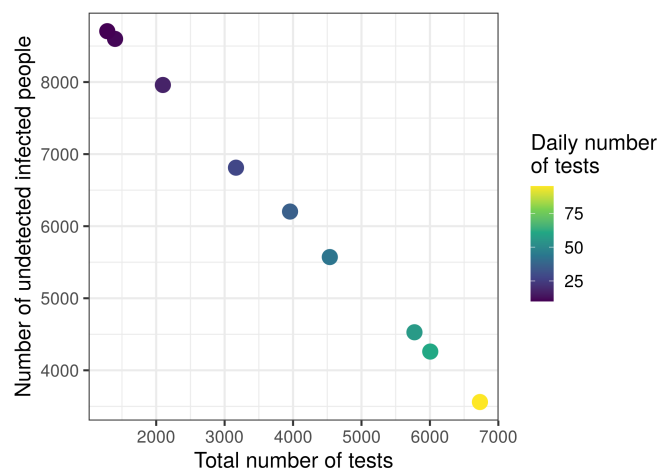


Figure 6. Calibration: number of undetected infected people wrt total number of tests

DISCUSSION AND CONCLUSION

In this work, we have provided a simple model of the propagation of COVID-19 in a population, and of different screening strategies to both control and evaluate the epidemic curve. The model is based on figures available for France but is easily adaptable to other countries. It is willingly simplified, in order to provide an interactive simulator to explain to the general public the mechanisms of the epidemics and how the count of infected people is estimated every day. We believe that providing the population with scientific facts and explanations is key to protect them from fake news and to improve the acceptability of sanitary measures (*e.g.* necessity of regular self-tests for children at school, etc). Besides, we have also used our simulator to compare different computation methods and different screening parameters. An optimisation algorithm proved the required properties of a successful screening campaign, which happens to have actually been successfully used by South Korea at the start of the epidemics.

In future work, we would like to conduct more experiments, evaluating not only how well we can fit the epidemic curve, but also how to control it; in this case the output indicators to optimise would be the total number of infections and the height of the epidemic peak. Another interesting experiment would compare tests of various quality (sensitivity and specificity) to check if it is better to start screening early with low quality tests (as suggested for college reopening in the US (Paltiel et al. 2020)), or to wait that more reliable tests are available, at the risk of not being able to catch up (as suggested by our experiments).

Finally, our simulator has been made available online but we have not yet surveyed the users to assess its impact. Future experiments need to be setup with users of different profiles to prove our claim that changing role (playing the role of a health decider), actually interacting with the parameters to test what-if scenarios, and getting feedback about one's choices, can provide a welcome feeling of control and a better understanding and acceptance of the situation.

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⁷<https://covprehesion.org/en/2020/05/12/q17.html>

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