Optimizing testing policies for detecting COVID-19 outbreaks

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Abstract

The COVID-19 pandemic poses challenges for continuing economic activity while reducing health risk to individuals and preventing uncontrolled outbreaks. These challenges can be mitigated by extensive testing. We study testing policies that optimize a fixed budget of tests within a single institution (e.g., business, school, nursing home, etc.) by varying the number of batches that the tests are split into.

We prove that, in an exponential spread model and for reasonable parameter values, the expected size of an outbreak at initial detection is smaller when random subgroups of the population are tested frequently, as opposed to periodic testing of the entire population.

We also simulate the effect of different policies in a network SEIR model taking into account factors such as variable connectivity between individuals, incubation period, and inaccurate testing results. We show that under a broad set of early-outbreak scenarios, given a certain budget of tests, increasing testing frequency of random samples of the population will reduce the societal risk, defined as the number of infection opportunities until first detection. For example, testing a quarter of the institution members every week is generally better than testing the entire institution every month. In fact, in many settings, sufficiently frequent testing (combined with mitigation once an outbreak is detected) can decrease the risk even compared to the baseline when the institution is closed and testing is not conducted.

The bottom-line is a simple policy prescription for institutions: distribute the total tests over several batches instead of using them all at once.

1 Introduction

As many countries begin the process of easing restrictions during the COVID-19 epidemic, the role of *testing* and *tracing* is crucial in monitoring and controlling the viral spread,

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and a key factor in policy adjustments [1]. Here we focus on a specific aspect of this challenge: how should institutions, including businesses, schools, hospitals, prisons, and nursing homes, use a limited budget of tests for outbreak detection and mitigation. As a running example, consider a company of a 1000 employees that is allocated 1000 tests per month. A straightforward strategy is to test all employees at the first day of each month. Here we argue that under a broad set of scenarios, this is sub-optimal, and that testing subgroups of the employees more frequently (e.g. ≈ 250 employees per week) will yield better outcomes. While detailed knowledge of institution members roles, connections within the institution, preexisting conditions, and other characteristics could be leveraged to optimize a testing protocol, in this work we aim to offer a simple and general strategy, and therefore consider testing schedules that are independent of individual characteristics. Such randomized testing policies, which are oblivious to symptoms, can also be crucial in the discovery of asymptomatic or pre-symptomatic individuals.

We demonstrate the benefit of frequent testing of subsamples of the population in a simple model of exponential infection spread, as well as a network SEIR model. The SIR epidemic model [2] and its variations such as SEIR (e.g. [3]) were recently shown to be useful as a modeling framework for COVID-19 analysis [4]. We also find that, perhaps surprisingly, in many scenarios, randomized testing can *completely offset the excess risk* to society from opening a workplace. That is, the total number of infection opportunities can be *lower* in the setting when a workplace is open with (sufficiently frequent) randomized testing as opposed to the baseline where the workplace is closed and hence workers have no chance to infect one another, but undergo no routine testing. For example, in several realistic settings of the overall prevalence of COVID-19 and the internal connectivity of the workplace, keeping the business open but testing a quarter of employees every week will reduce the number of infectious days compared to the baseline scenario where the business is closed but no randomized testing takes place (Figure 1a).

2 Results

Our main result is that it is generally beneficial to distribute tests in batches by randomly sub-sampling the population, relative to administering all tests at once. We focus on analyzing the period until the first detection of an outbreak within an institution. Once an outbreak is detected, a variety of mitigation techniques can be implemented (e.g., quarantine, contact tracing, temporary distancing, etc.) that are outside the scope of our model. We analyze the cost in two models: a simple (and analytically tractable) *exponential spread* model, and a more realistic network-based *SEIR model*.

2.1 Analysis of exponential spread model

We consider an exponential spread model [5, 6], where the infection grows by a factor of R per time unit. We show that given a budget enabling testing of a p fraction of individuals

per time period, if the tests are split into large number of batches then the expected number of infected individuals at the time of the first detection scales logarithmically with \bar{R} and equals $1 + \frac{\ln \bar{R}}{p}$ (methods). In contrast, if the same budget is used to periodically test the entire population, the number of infected individuals at the time of the first detection scales nearly *linearly* with \bar{R} . While there can be some cases where the expected cost for frequent sub-population testing is higher than periodic population-wide testing, this difference is bounded, and for many setting of \bar{R} frequent testing performs much better. See the Methods section for the derivation and more details.

2.2 Simulations of network SEIR model

We examine the effect of increasing testing frequency in a stochastic network-based model of SEIR (susceptible-exposed-infected-recovered) dynamics with a non-homogenous population, based on [7, 8] (*Methods*). We show that in most parameter settings, frequent testing of random sub-samples is superior to infrequent testing of the entire population (Figure 1, Figure 2b). We also show that under several (though not all) realistic parameters, testing a quarter of the population per week is not just superior to testing all the population every 28 days, but even improves on the baseline of keeping a business closed where workers can get infected only from an external source (Figures 1a, 2a). That is, the total number of infection opportunities will be *lower* in the setting that an institution is open (with increased intra-institution infections) but its members are tested periodically (with isolation and widespread testing once an outbreak is detected), compared to the baseline where the institution is closed but no random testing takes place.

Specifically, we assume an institution of N members is given a budget of N tests per time T (and hence larger T corresponds to lower budget). We compare different testing strategies, where in each strategy the total number of tests is divided into k batches that are equally allocated over time. For example, in an institution of 1000 members, if we get 1000 tests every 28 days, then the "28/1" strategy correspond to testing all members once per 28 days, while the "28/4" strategy corresponds to randomly dividing the members to four groups of 250 people each, and testing a different group every week. Here we do not assume any additional prior knowledge that distinguishes between different individuals (e.g. their role in the company, relationships to other people in the community, risk factors, etc.). To couple between the institution dynamics and the disease spread in the society, we assume that there is a constant external infection rate P_{ex} (e.g., value of 0.001 day⁻¹ means that every day there is 1/1000 probability for each community member to be infected by an external source).

We define the *societal risk* as the mean number of infectious community members per day up to the point of outbreak detection (*Methods*). We find that in general, consistent with our results for the exponential model, more frequent testing of subsamples of the population lowers the societal cost (see Figure 1). This holds broadly (though not always) across variations in the overall testing budget (Figure 1a), different values for the external



Figure 1: Societal risk as a function of testing policy, external and internal infection rates. (a) Social risk for different testing policies. The internal reproductive number is $R_0^I = 2.1$ (except for the "business closed" baseline where $R_0^I = 0$). The external infection rate is ($P_{ex} = 0.0005 \text{ day}^{-1}$). (b,c) Comparison between different testing frequency given a testing budget of 1000 tests every T = 28 days. Different colors represent different number of batches: k = 1 – blue, k = 2 – orange, k = 3 – green, k = 28 – red). Results are shown for (b) different external infection rate (and constant internal reproductive number of 2.1), where $\rightarrow 0$ represents one external infection which is drawn form a uniform distribution between day 1 and day 28. and (c) Comparison between different testing policy was simulated using 500 realizations, and all realizations were executed for 56 days or until first detection. In each violin plot the lines show the mean, minimum and maximum values of all simulations of each case, and the gray dashed line shows the mean social risk of the baseline simulation.



Figure 2: Risk (mean infectious individuals per day until first detection) of testing quarter of the population per week (i.e., 28/4 testing policy). Panel (a) measures the 28/4 policy as percentage of the baseline when business is closed but no testing takes place, panel (b) compares it to testing all population once every 28 days, and panel (c) compares it to opening the business with no testing at all. Values less than 100% correspond to cases where the risk in the 28/4 policy is better than the comparators. The "business closed" baseline risk is calculated as $N \cdot P_{\text{ex}}/\gamma$ where P_{ex} is the external infection probability, N is the total number of individuals, and $1/\gamma$ is the mean length of the infectious period. The "no testing" risk is obtained by running a simulation for 56 days with no testing, and measuring the average number of infected individuals.

infection rate (Figure 1b), and internal reproductive rate (Figure 1c, where the internal reproductive rate refers to the expected number of cases directly generated by one case within the institution where all individuals are susceptible to infection). The relative improvement of frequent testing increases when external infection rate is higher or internal reproductive rate is higher (Figure 2). In most regimes, testing in batches improves even over the baseline where the business is closed (and no testing policy is used), with relative improvement increasing when the external infection probability increases or internal reproduction rate *decreases* (Figure 2a).

3 Discussion

Our work suggests *frequent randomized testing* as a way to enable safe re-opening of businesses and institutions. Significantly, increasing the *frequency* of testing can yield much better outcomes for the same overall budget. We show this both via simulations of realistic scenarios, and analytically for the exponential spread model. Specifically, our analytic formula for the exponential-spread cost shows that frequent sub-population testing enables the cost to grow at most *logarithmically* in the growth-factor of the infection, as opposed to nearly linearly in periodic full-population testing. Our simulation results for the network SEIR model demonstrate that in many settings, frequent subsample testing can be used to control outbreaks and the cost of keeping a business, school, or institution open. The parameters we use, including the length of incubation period, the probabilities of infection, and the false negative rates, are taken from the literature, but could be refined with further knowledge. However, these should not change any of the qualitative conclusions. We remark that a complete re-opening strategy will involve many factors beyond testing, including re-organization, screening for symptoms, and changing testing frequencies based on business role or risk factors. We do not model such strategies in this paper, beyond their effect on the internal reproductive number.

4 Methods

4.1 Exponential dynamics

Our exponential infection dynamics model assumes there is an initial infection at time t_0 and the number of infected people at time t is \bar{R}^{t-t_0} , where \bar{R} is the growth rate per time unit. For this model, we consider the cost of detecting the outbreak at time t as the number of infected individuals at this time.¹ If we measure each individual with probability p/kper 1/k time periods, and assume no false negative, then the probability that we fail to detect an outbreak at time $t_0 + t$ is $(1-p/k)^{\bar{R}^t}$. The probability that we detect an outbreak at time $t_0 + \ell k$ is equal to the probability we failed to detect up until this point (which is $\prod_{i=0}^{\ell k-1} (1-p/k)^{\bar{R}^{i/k}} = (1-p/k)^{\sum_{i=0}^{\ell k-1} \bar{R}^{i/k}}$) multiplied by the probability we detect at time n. Since the cost at time n is \bar{R}^n we get that the expected cost of the k batch strategy is $S_k(\bar{R},p) = \sum_{n=0}^{\infty} (1-\frac{p}{k})^{\frac{\bar{R}^{n/k}-1}{\bar{R}^{1/k}-1}} \cdot \left(1-(1-\frac{p}{k})^{\bar{R}^{n/k}}\right) \cdot \bar{R}^{n/k}$. When $k \to \infty$ then $(1-p/k)^k \to \exp(-p)$, while $k(R^{1/k}-1) \to \ln R$ and $1-(1-p/k)^{R^{n/k}} \approx pR^t dt$ (where dt = 1/k and t = n/k). Hence the total expected cost converges to the integral $\int_{t=0}^{\infty} \exp(-\frac{p(\bar{R}^t-1)}{\ln \bar{R}})p \cdot \bar{R}^{2t} dt$ which can be verified to be $-\exp\left(\frac{p\cdot(1-\bar{R}^t)}{\ln \bar{R}}\right) \left(\frac{\ln \bar{R}}{p} + R^t\right) \Big|_{t=0}^{t=\infty} = 1 + \frac{\ln \bar{R}}{p}$.

In the particular case of p = 1, this cost is $1 + \ln \overline{R}$. In contrast, if we test the entire population once per time unit, if the infection begins at a random time then at the time of detection, the expected number of infected individuals is $\int_0^1 \overline{R}^t dt = (\overline{R} - 1)/\ln \overline{R}$. For large \overline{R} , this cost grows nearly *linearly* with \overline{R} while the cost for the frequent testing grows only logarithmically. While for small \overline{R} , the cost (i.e., expected number of infected individuals at detection) for the one batch strategy can be lower than the frequent testing cost, this difference can never be more than $\max(1 + \ln x - (x-1)/\ln x) = 3 - e \approx 0.28$ (which occurs when $\overline{R} = e$). However, using frequent testing could lead to a significantly better result compared to a single batch. For example, consider a budget which allows testing everyone once per month, and an exponential increase is by a factor of 20 per month, then the cost of a single batch strategy is ≈ 6.3 , while testing with large number of batches would result

¹We do not use the number of infected days since, unlike the SIR and SEIR models, the exponential spread model does not model "infectious period", but the two costs will be roughly proportional.

in cost of ≈ 3.9 , which is significantly lower. Moreover, frequent testing also reduces the tail probabilities of missing a large outbreak.

4.2 SEIR dynamics

All our code for the SEIR dynamics is available on the GitHub repository https://github. com/boazbk/seirsplus. We use the following parameters: $\sigma = 1/5.2$ (probability of exposed to become infected per day [9]), $\gamma = 1/14$ (probability of infected to recover per day [10]), $\psi_E = 0.33$ (67% false negative rate for exposed [11]), $\psi_I = 0.8$ (20% false negative rate for infected [11]). We inherit all other parameters from the package [8] on which our code is based. The internal reproductive number R_0^I is estimated as $R_0^I = \frac{\beta}{\gamma}$, where β is the mean probability to be infected per day and $\frac{1}{\gamma}$ is the mean infection period in days. We ran 500 realization for each setting of parameters, varying testing policies, external infection probability $P_{\rm ex}$, and probability of internal infection β . The societal risk over a period of time is the mean number of infected and undetected individuals per day during this period. This definition captures the number of opportunities that institution members have on average to infect either other members or people in the external society. If the probability of a member to be infected each day from an external source is $P_{\rm ex}$ then the baseline societal risk is approximately $N \cdot P_{\rm ex}/\gamma$ where N is the number of institution members and $1/\gamma$ is the mean infection period. The baseline societal risk captures the mean number of infection opportunities that are expected to occur per day among institution members if the business is closed. In our simulations we measured the societal risk from the beginning of the simulation until the point of first detection of an outbreak.

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