PSI Research Memorandum: Using random testing to manage a safe exit from the COVID19 lock-down

Markus Müller,[1,*] Peter Derlet,[1] and Christopher Mudry[1]

[1] *Paul Scherrer Institut, CH-5232 Villigen PSI, Switzerland*

(Dated: April 1, 2020)

Summary: This paper argues that random testing is central to controlling the COVID-19 epidemics and to optimizing the response to it. Random testing is crucial to acquire currently lacking quantitative information on how various restrictive measures affect transmission rates. This knowledge will (i) significantly improve the predictability of the epidemics, (ii) allow for informed, optimized decisions on how to modify the set of restrictive measures, and (iii) enable the real-time assessment of the efficiency of new means to reduce transmission rates (such as new tracing strategies).

It is very important to start random testing for COVID-19 infections immediately and to rapidly increase the testing capacity — the more frequently one samples the population the more reliable and geographically refined will be the data. Here we show that for a country with the population of Switzerland, even a few thousand random tests per day suffice to obtain valuable data about the current number of infections and their evolution in time. This is crucial to assess in real time the quantitative effect of restrictive measures. It further allows one to detect geographical differences in spreading rates and thus formulate optimized strategies for a safe reboot of the economy.

In addition to the phenomenology and rough estimates that we outline, we describe simulation strategies for decision support concerning testing, local quarantine regimes, and the safety of a reboot.

The COVID19 pandemic is producing a worldwide shutdown of life as we knew it. This shutdown is a political response informed on epidemiologic studies assessing the cost in human lifes depending on different possible strategies (do nothing, mitigation, suppression). [1–3] Mitigations can be achieved by different strategies such as social distancing or testing. The quantitative impact of very frequent testing has been studied in a recent unpublished work by Jenny et al. in Ref. [4].

Frequent testing far above the currently possible level should soon become available in Switzerland, a substantial increase being forecast on the scale of 1-2 months. What testing frequency can be achieved is not clear yet. To fully control the COVID19 epidemic by widespread testing, we will estimate that the ability to test millions of people per day is required (cf. Sec. I). However, we show that tracking and control of this epidemic is possible by testing a much smaller number of people per day. In fact, we will argue that even with the current testing rate, extremely valuable information on the rates of transmission depending on geographic regions of Switzerland can be obtained.

The paper is organized as follows: In Sec. I we discuss the use of massive testing as a direct means to contain the epidemics, showing that it requires a 100-fold increase of the current testing frequency. In Sec. II we define the main challenge: To measure the quantitative effect of restrictive measures on the transmission rate. Section III is the main part. It shows how data from sparse sampling tests can be used to infer current growth rates and their regional dependence. Section IV comments on the use of contact tracing and argues that it cannot be a substitute for random testing. Section V defines a model whose simulation illustrates the theoretical analysis of Sec. III, and allows to assess the risks and benefits of various control strategies for a reboot of the economy.

I. MASSIVE TESTING

Once the massive frequency of 1.5 million tests per day becomes available, it will be possible to test every person in Switzerland every $5-6$ days. If the infected people that have been detected are kept in strict quarantine (such that they will not infect anybody anymore with high probability), such massive testing could be sufficient to prevent an exponential growth in the number of cumulated infections without the need of draconian social distancing measures. We now explain qualitatively our approach to reach this conclusion.

The required testing rate can be estimated as follows. Let ΔT denote the average time until an infected person infects somebody else. The transmission number R, i.e., the number of infections per sick person, falls below 1 (and thus below the threshold for exponential growth) if non-diagnosed people are tested at time intervals of no more than $2\Delta T$. Thus, the required number of tests over the time $2\Delta T$, the full testing rate $\tau_{\rm full}^{-1}$, is

$$\tau_{\rm full}^{-1} = \frac{N_{\rm CH}}{2\Delta T}, \tag{1a}$$

where

$$N_{\rm CH} = 8'500'000 \tag{1b}$$

* Markus.Mueller@psi.ch

is the number of inhabitants of Switzerland.[1] Without social restrictions, it is estimated that

$$\Delta T \approx 3\,\text{days}, \tag{2a}$$

such that

$$\tau_{\text{full}}^{-1} = 1.4 \times 10^6/\text{days}, \tag{2b}$$

i.e., about **1.4 million tests per day would be required to control the epidemics by testing only.** If additional restrictions such as social distancing etc., are imposed, ΔT may increase by a modest factor and one can get by with indirectly proportionally fewer tests per day. Nevertheless, on the order of 1 million is a minimal requirement for massive testing to contain the epidemics without further measures.

Cost: At the price of 300 CHF per test, massive testing costs about 300'000'000 CHF a week, which is still much less than the economic cost of even a partial lockdown.

However, even while the Swiss capabilities are still far from reaching 1 million tests per day, testing offers two important benefits in addition to identifying people that need to be quarantined. First, testing allows to monitor and study the efficiency of measures that keep the number R of transmissions per infected person below 1. This ensures that the growth rate k of case numbers and new infections is negative, $k < 0$. Second, testing helps suppress the transmission number R and thus allows one to be less restrictive in terms of other measures, such as social distancing.

To quantify the latter benefit, observe that the effect of massive testing on the growth rate k is proportional to the testing rate. Let us assume that without testing or social measures one has a growth rate k_0. Then, if the testing rate τ_{full}^{-1} is sufficient to kill the exponential growth in the absence of other measures, a smaller testing rate τ^{-1} decreases the growth rate by $k_0\,\tau^{-1}/\tau_{\text{full}}^{-1}$. The remaining reduction of k to zero must then be achieved by a combination of restrictive social measures and contact tracing.

It is possible to refine the argument above to take account of the possibility of a spectrum of tests with particular cost/performance tradeoffs, i.e., a cheaper test with more false positives and negatives could be used for random testing, whereas those displaying symptoms would be subjected to a "gold standard" (PCR) assay of viral genetic material.

[1] Note that if tests take the nonvanishing time t_{test} to yield a diagnosis, this time needs to be subtracted from the denominator in Eq. (1a), thereby resulting in an enhancement of the full testing rate τ_{full}^{-1}.

II. THE CHALLENGE: QUANTIFYING THE EFFECTIVENESS OF RESTRICTIONS

The main unresolved challenge is the quantification of the effect of social restrictions in reducing the transmission rate. By how much do individual measures reduce the growth rate k? How should they be combined optimally to achieve $k = 0$?

In Section III we show how these effects can be measured. We have the unique opportunity to investigate this in the coming weeks. The earlier one starts with random testing the better.

III. SMART TESTING

We now argue that statistically randomized testing can be used in a smart way, so as to keep the dynamics of the epidemics under control. Moreover, this is possible without the huge time delays of up to 14 days that we currently have.

The idea of smart testing is the following. One regularly tests *randomized* people so as to monitor the fraction of infected people. By following these numbers, one can determine nearly instantaneously the growth rate of infections, and thus assess *and quantify* the effectiveness of socio-economic restrictions. This monitoring can be done in a regionally resolved way, such that measures can be adapted to different regions (urban/rural etc.) in Switzerland.

Note that randomized testing is essential to obtain information on the current number of infections and its evolution with time. It serves an additional and entirely different purpose from testing people with symptoms, medical staff, or people close to somebody infected, which constitute highly biased samples.

The first goal of random testing is to have a firm test/confirmation of whether the current restrictive measures are sufficient to mitigate or suppress the exponential growth of the COVID-19 epidemic. In case they should still be insufficient, we can measure the current rate and monitor the effect of additional restrictive measures.

Suppression of the COVID19 epidemic is achieved if the number of infections decays exponentially with time for a sufficiently long time. Stability of the COVID19 epidemic is achieved when the number of infections is constant in time for a sufficiently long time. Once stability is reached, one may start relaxing the restrictions step by step and monitor the effect on the growth rate k as a function of region.

It might prove useful not to lift restrictions homogeneously throughout the country, but instead to vary the set of restrictions that are released. For example, if Easter holidays end on different dates in different cantons, one may want to see the relative effect on k of re-opening schools. However, to go beyond such natu-

rally occurring differences might prove politically difficult, even if it is just for 1-2 weeks. How to decide which region release which measures first? A further issue is that the effects might be unclear at the borders between regions with different restrictions. There may also be complications with commuters that cross regional borders. Finally, there may be undesired behavioral effects, if regionally varying measures are declared as an "experiment". All these issues need careful consideration.

A. The value of partitioning the country for statistical analysis

We argue that valuable information can be gained by analyzing the test data not for Switzerland as a whole, but by distinguishing different regions. Accordingly the test centers should also be distributed across the whole country with approximately equal density per inhabitant.

Let us group the population of Switzerland into G sets. The most natural clustering is according to the place where people live: cities or counties.[2] The more we partition the country, the more refined the acquired data can be, and the better tailored the measures will be. However, for a fixed national testing rate, increased partitioning means that the statistical uncertainty for each region will grow. In this section we estimate the optimal choice of the number G of groups for the analysis. The choice $G = 1$ means that the whole of Switzerland is treated as one. This is highly sub-optimal, since valuable statistical insight is lost.

Let us take all population groups $m \in \{1, \cdots, G\}$ to have roughly the same size, each one containing

$$N_m \approx \frac{N_{\rm CH}}{G} \tag{3}$$

people. Let U_m be the number of undetected, but infected people in group m. We assume that detected people do not spread the disease. The spreading of infections is also assumed to follow a simple linear growth equation

$$\frac{{\rm d}U_m}{{\rm d}t} = \sum_{n=1}^{G} K_{mn}\, U_n, \qquad m = 1, \cdots, G. \tag{4}$$

Here, the $G \times G$ matrix K has the matrix elements K_{mn}. K has the eigenvalues k_m. The largest growth rate is given by

$$\kappa \equiv \max_m \left\{ {\rm Re}\,(k_m) \right\}. \tag{5}$$

[2] One might also consider other distinguishing characteristics of groups (age/commuting habits, etc.), but we will not do so here, since it is not clear whether the increased complexity of the model can be exploited to reach an improved data analysis. In fact we expect that the number of fitting parameters will very quickly become too large by making such further distinctions.

The number of infections grows exponentially if $\kappa > 0$, and decreases if $\kappa < 0$.

The matrix K will itself evolve with time, as the number of immune people grows, as restrictive measures change, mobility is affected, new tracking systems are implemented, hospitals get overloaded, testing is increased etc. Nevertheless, over a short period of time where such conditions remain constant, and the fraction of immune people does not change significantly, we can assume the effective growth kernel K to be constant in time. We will exploit this below.

In the simplest case, one assumes no contact between geographically distinct groups, that is, the off-diagonal matrix elements are zero ($K_{m\neq n} = 0$) and the eigenvalues become the elements of the diagonal: $k_m \equiv K_{mm}$. In general, the transmission rate depends on the region, and thus $k_m \neq k_n$. It is natural to expect that k_m correlates with the population density, the fraction of the population that commutes, the age distribution etc. **Preliminary fits to the cantonal data of the past month (with the gross assumption that K remained constant over this full period) show that the fitted growth rates are scattered rather strongly. Most eigenvalues k_m lie between 0.1 and 0.3, with a rather substantial spread.**

It is likely that this significant variation of k_m persists in a more careful analysis and after removing the condition $K_{m\neq n} = 0$. **This suggests restrictive measures should be adapted to the regions, so as to minimize their socio-economic impact in the regions with low k_m.**

B. Determining the optimal partition in groups

As we mentioned, it might be desirable to have a considerable geographic refinement, and potentially to have different regions lifting their restrictions in different manners, so that we learn faster about the effect of specific measures. On the other hand, the sampling number in each group decreases with increasing the number G so that statistical uncertainties grow. Here, we determine the maximal number of groups that can be analyzed when a certain precision for the exponential transmission rates k_m is to be achieved.

We assume that each day a constant number of people are tested in each region. If N_t is the number of tests per day in Switzerland, and we assume sampling over a time ${\rm d}t$, the number of tested people in each region is

$$N_{\rm samp} \equiv \frac{{\rm d}t\, N_t}{G}. \tag{6}$$

Let i_m be the fraction of infected people in region m. The instantaneous value of i_m at time t is estimated from the sample. On average one will detect

$$I_m(t) = i_m(t)\, N_{\rm samp} \tag{7}$$

infected people over the sampling time window $\mathrm{d}t$. This comes with random fluctuations whose scale is determined by the standard deviation $\sqrt{I_m(t)}$. In the subsequent test window $\mathrm{d}t$ in time, a similar number $I_m(t+\mathrm{d}t)$ will be measured. The instantaneous growth rate is then defined to be

$$k_m(t) = \frac{1}{\mathrm{d}t}\,\frac{I_m(t+\mathrm{d}t) - I_m(t)}{I_m(t)}, \tag{8}$$

with the standard deviation (statistical uncertainty)

$$\begin{aligned}\Delta k_m(t) &= \frac{1}{\mathrm{d}t}\sqrt{\frac{1}{I_m(t)} + \frac{1}{I_m(t+\mathrm{d}t)}} \\ &\approx \frac{1}{\mathrm{d}t}\sqrt{\frac{2}{I_m(t)}} \\ &= \frac{1}{\mathrm{d}t}\sqrt{\frac{2}{N_{\mathrm{samp}}}}\sqrt{\frac{1}{i_m(t)}}.\end{aligned} \tag{9}$$

The uncertainty is smaller when N_{samp} is larger, i.e., the larger the population groups are. The uncertainty also decreases with the inverse of the square root of the fraction of infected people, i_m — if the fraction is too low the statistical fluctuations become too large and little statistically meaningful information can be obtained. Indeed, for reliable statistical analysis, it is not desirable to reduce the number of infected people to zero, but rather to maintain a level that is well manageable by the health system. In fact, this latter scenario might be more easily achievable.

Let us obtain an upper bound for a manageable i_m. We assume that a fraction $p_{\mathrm{ICU}}^{\mathrm{CH}}$ of infected people in Switzerland needs to be in intensive care. More precisly, $p_{\mathrm{ICU}}^{\mathrm{CH}}$ is the expected time spent in intensive care units (ICU)'s divided by the expected time to be sick in Switzerland. Here, we will use the value $p_{\mathrm{ICU}}^{\mathrm{CH}} = 0.05$. Let $\rho_{\mathrm{ICU},m}$ be the ICU beds per inhabitant that shall be allocated to COVID19 patients in region m. The Swiss national average is about

$$\rho_{\mathrm{ICU}}^{\mathrm{CH}} \approx \frac{1200}{8'500'000} \approx 1.4\cdot 10^{-4}. \tag{10}$$

For the epidemics not to overwhelm the health system, one thus needs to maintain the infected fraction safely (a factor 2 or so) below

$$i_m(t) \le \min\left\{\frac{\rho_{\mathrm{ICU},m}}{p_{\mathrm{ICU}}^{\mathrm{CH}}}, \cdots\right\} \approx \min\left\{i_{\mathrm{ICU}}, \cdots\right\}, \tag{11}$$

where

$$i_{\mathrm{ICU}} \equiv \frac{\rho_{\mathrm{ICU}}^{\mathrm{CH}}}{p_{\mathrm{ICU}}^{\mathrm{CH}}} \approx 0.0028, \tag{12}$$

and the dots stand for further similar constraints.

One should definitely mitigate the epidemics to values of the order of i_{ICU}. Before that level is reached one can certainly not start relaxing restrictions. It may prove difficult to push the fraction of infected people significantly below i_{ICU}, since the recent experience in most European countries shows that it is very hard to ensure that growth rates k fall well below 0. The main aim would then be to reach at least stabilization of the number of infected people ($k = 0$). We thus assume that the i_m's will stagnate at values of the order of i_{ICU}.

Let us proceed, assuming a stable (time-independent) fraction of infected people

$$i_m = i^* \equiv \frac{i_{\mathrm{ICU}}}{2}, \tag{13}$$

where we use the somewhat arbitrary safety buffer of a factor of 2. The accuracy in determining the rates k_m now follows from Eqs. (6), (9), (12), and (13) as

$$\Delta k_m = \sqrt{\frac{2}{i^*\,(\mathrm{d}t)^3\,N_t}}\,\sqrt{G}. \tag{14}$$

The uncertainty increases with the square root of distinct regions, but is inversely proportional to the observation time span $(\mathrm{d}t)^{3/2}$. The optimum number G of distinct regions that remains compatible with an accuracy Δk_m of the rates k_m is

$$G = \frac{i^*\,(\mathrm{d}t)^3\,N_t}{2}\,(\Delta k_m)^2. \tag{15}$$

To assess and adapt the measures on a weekly basis, we choose $\mathrm{d}t = 6-7$ days. (Of course, if releasing certain measures leads to a sudden increase close to the explosive unmitigated growth rate, this will be detected within 2-3 days, and countermeasures can be taken immediately, preventing an explosion.) **With $N_t = 100'000$ tests per day and a targeted accuracy of $\Delta k = 1/(20\,\mathrm{days})$, one can define as many as $G = 60$ different regions!** Note that the growth rate we have had for quite some time has entailed a doubling of cases every 3 days, i.e., a growth rate of

$$k_0 = \ln(2)/(3\,\mathrm{days}) = 0.23\,\mathrm{day}^{-1}. \tag{16}$$

The standard devitation $\Delta k = 0.05\,\mathrm{day}^{-1}$ might be too large a statistical uncertainty to meaningfully assess the actual value of k, which should stay safely away from k_0. A smaller value of $\Delta k = 0.025\,\mathrm{day}^{-1}$ might be more appropriate, corresponding to a growth rate for which doubling occurs every 4 weeks and which leaves ample time to react. This issue will be addressed and resolved by the simulations for various response strategies.

Even with a modest value of $N_t = 8'000$ (in addition to the current 8'000 tests reserved for suspected infections and medial staff) **one can analyze 4-5 different regions with the same accuracy goal.**

We emphasize that such a study will generate valuable socio-epidemiological information for Switzerland and also serve as an important reference for other countries with similar organization.

C. Risk assessment

It is essential to assess and control the risks of releasing restrictions that have brought under control the COVID19 epidemic. In particular, it is crucial to suppress a potential second exponential wave when the economy is rebooted.

Having random testing in place, the risk of a second wave can be kept to a minimum. Additional 8'000 daily tests (on top of the current tests for medical purposes) will allow to detect growth rates as small as $0.025\,\mathrm{day}^{-1}$ (for $G = 1$, that is treating Switzerland as a whole). This corresponds to a slow growth, doubling of infected people in 4 weeks. In the worst case scenario, where releasing certain measures immediately let us jump back to the unmitigated growth rate of $0.23\,\mathrm{day}^{-1}$, this would be detected within 1-2 days from the change coming into effect. One can then take immediate action, at the price of increasing the number of infected people by a certain percentage. A doubling would likely be the worst case scenario, if one immediately reinstates the conditions that had ensured stabilization. Insofar it is rather safe to try the release of certain restrictions. Trying them out first in some regions, or releasing different restrictions in different regions, to learn faster about their respective effects, might also be an option to consider.

These considerations will be underpinned by quantitative modeling, as sketched in Sec. IV.

IV. ASSESSMENT OF CONTACT TRACING AS A MEANS TO CONTROL THE EPIDEMICS

Here we briefly comment on the strategy of contact tracing as a means to contain the epidemics, as has been discussed in the literature [6]. We argue that it is a helpful tool to suppress transmission rates, but is susceptible to fail when no other method of control is used.

Contact tracing means that once an infected person is detected, people in their environment (i.e., known personal contacts, and those identified using mobile-phone based Apps etc) are notified and tested, and quarantined if detected positive. As a complementary measure to push down the transmission rate, it is definitely useful and a low cost measure, since the probability to detect infected people is high. **However, as a sole measure to contain an epidemics contact tracing is impractical and even hazardous.**

The reason is as follows. It is known that a considerable fraction f_{asym} of infected people show only weak or no symptoms, so that they would not get tested under the present testing regime. The value of f_{asym} is not well known, but it might be high (30% or much higher). Such asymptomatic people will go undetected, if they have not been in contact with a person displaying symptoms. If on average they infect R people while being sick, and if $R\,f_{\mathrm{asym}} > 1$, there will be an exponential avalanche of undetected cases. They will produce an exponentially growing number of detectable and medically serious cases. The contact tracing (backward) of those cannot stop this avalanche, ~~and only pushes the threshold value for R slightly above $1/f_{\mathrm{asym}}$.~~ since it can only decrease R to a value slightly above the threshold value $1/f_{\mathrm{asym}}$.

Contact tracing as a main strategy thus only becomes viable once one is reasonably confident about the value of f_{asym} and the ability to control the value of R such that $R\,f_{\mathrm{asym}} < 1$.

V. MODELING POLICY RESPONSE - RISK ASSESSMENT

Let us consider the following model. The evolution in time of the undetected infected population U_m in region m of Switzerland is governed by the forced linear equation

$$\left(\frac{\mathrm{d}U_m}{\mathrm{d}t}\right)(t) = \sum_{n=1}^{G} K_{mn}(t)\,U_n(t) + \Phi_m(t), \tag{17a}$$

where $m = 1, \cdots, G$ and $\Phi_m(t)$ accounts for those infections arising from people crossing the national border. We will mostly set it to zero for the present study.

We assume that the $G \times G$ matrix $K(t)$ is piecewise constant in time and of the form

$$K(t) = \mathrm{diag}\big(k_m(t)\big) + f(t)\,C. \tag{17b}$$

Thus, it is parametrized by the G diagonal elements $\mathrm{diag}\big(k_m(t)\big)$ and a single off-diagonal parameter $f(t)$ that multiplies the connectivity matrix C that we define by

$$C_{mn} = C_{nm} = 1 \tag{17c}$$

when regions m and n are considered connected, and

$$C_{mn} = C_{nm} = 0 \tag{17d}$$

otherwise. We will mainly consider two models. There is the mean-field model, where all regions are connected to each other. There is the nearest-neighbor model for which only regions sgaring borders interact. With these assumptions $K(t)$ is a $G \times G$ symmetric matrix. Thus, $K(t)$ has G real-valued instantaneous eigenvalues

$$\lambda_1(t) \geq \lambda_2(t) \geq \cdots \geq \lambda_G(t), \tag{17e}$$

each of which depends on $G + 1$ time-dependent parameters.

For $t < 0$, we assume stability, with $K(t < 0) \equiv K^{(0)}$ having only negative eigenvalues. This is the state to be reached before a reboot of the economy is considered. For simplicity we take the matrix to be given by

$$k_m^{(0)} = -k_0, \tag{18}$$

and some $f^{(0)}$ small enough to ensure stability. For concreteness, we take $k_0 = 0.05$ and $f^{(0)} = 0.002$.

Our model neglects the contributions to the time evolution of $K(t)$ due to the evolving age distribution of infected people, or increasing immunity. We also neglect its temporal fluctuations (e.g., due to workday/weekend alternation). We assume that $K(t)$ changes only in response to policy measures which are taken at specific times when certain criteria are met, as defined by a policy strategy. An intervention is taken when the sampled testing data indicates that with high likelihood the largest eigenvalue of $K(t)$, $\lambda_1(t)$, is above some upper threshold $\kappa_+ > 0$. Likewise, another intervention is taken once all i_m are below i^*, i.e., $\lambda_1(t)$ is below some negative threshold $\kappa_- < 0$. Note that if one has substantial infection influx Φ_m across the national borders, one may want to choose the threshold κ to be negative, to avoid a too large response to the influx.

To reach these decisions, data is acquired. Every day N_s people (out of all N_m in a group) are tested. The fraction i_m of infections detected by the test is a Gaussian random variable with mean

$$\langle i_m(t)\rangle = U_m(t)/N_m \tag{19a}$$

and standard deviation

$$\langle [i_m(t)]^2 \rangle_c^{1/2} = \sqrt{U_m(t)}/N_m. \tag{19b}$$

The current entries of $K(t)$ are then estimated from fitting data since the last policy change at time t_i. It will take at least 2-3 days to make a fit that is reasonably trustworthy. From the fitted $K(t)$ one obtains $\lambda_1(t)$ with its confidence interval $\delta\lambda_1(t)$. If the instability threshold is surpassed, i.e., if

$$\lambda_1(t) - \kappa_+ > \alpha\, \delta\lambda_1(t) \tag{20a}$$

a new restrictive intervention is taken. If instead

$$\kappa_- - \lambda_1(t) > \alpha\, \delta\lambda_1(t) \text{ and } i_m < i^* \text{ for all } m, \tag{20b}$$

a new relaxing intervention is taken. Here, the parameter α determines the confidence level

$$p \equiv [1 + \mathrm{erf}(\alpha)]/2 \tag{20c}$$

that a stability threshold has indeed been crossed. This results in a series of intervention times

$$0 \equiv t_1 < t_2 < t_3 \cdots . \tag{20d}$$

In the time window $[t_i, t_{i+1}]$, the matrix $K(t)$ is constant and takes the value $K^{(i)} = K^{(i-1)} - \Delta K^{(i)}$ for $i \geq 1$. (A restrictive policy measure will decrease the entries of K by ΔK_{mn}, undoing a measure will increase K_{mn} by the same amount.) The quantitative effect of an intervention is a priori not known to policymakers. For

$$\Delta K^{(i)} \equiv -\left[K^{(i)} - K^{(i-1)}\right], \tag{21a}$$

we thus assume the diagonal elements to be of the form

$$\Delta K^{(i)}_{mm} = \delta k^{(i)}\ (1 + q_m)\,, \tag{21b}$$

where both $\delta k^{(i)}$ and q_m are independent random variables that we choose as follows.

After a new policy measure has been taken at time t_{i-1}, the random testing generates further data. Only the data for $t > t_{i-1}$ should be used to estimate the new growth matrix $K^{(i-1)}$. Let us denote by $\lambda_1^{\rm fit}(t)$ the largest eigenvalue of the matrix $K(t)$, which is extracted from the best fit to the sampled data on the window $[t_{i-1}, t]$.

If at time t, $\lambda_1^{\rm fit}(t)$ crosses the upper threshold κ_+ with confidence level p, we set $t_i = t$ and a restrictive measure is taken. The associated decrement $\delta k^{(i)}$ is uniformly distributed on the interval

$$\left[0, 2\,\delta k^{(i)}_{\rm opt}\right] \tag{21c}$$

with

$$\delta k^{(i)}_{{\rm opt},+} \equiv \lambda_1^{\rm fit}\ (t_i) - \kappa_+. \tag{21d}$$

This describes that, while the policymakers aim to reset the growth factor λ_1 to κ_+, the result of the taken measure may range from having no effect at all to overshooting by a factor of 2.

If instead $\lambda_1^{\rm fit}(t)$ crosses the lower threshold κ_- with confidence level p at time t, we set $t_i = t$. Now, $\delta k^{(i)}$ is chosen to be negative. Again, we take it uniformly distributed on the interval

$$\left[-2\delta k^{(i)}_{{\rm opt},-}, 0\right], \tag{21e}$$

where

$$\delta k^{(i)}_{{\rm opt},-} \equiv \kappa_- - \lambda_1^{\rm fit}\ (t_i)\,. \tag{21f}$$

The random variable q_m is uniformly distributed in

$$[-Q, Q], \tag{21g}$$

where $Q < 1$ is a measure of the regional variability of the response to a certain restrictive measure. The value of f is also changed. For an additional restriction it is decreased to a random quantity in $[0, f]$. For a release of restrictions, f is randomly picked between the current f and some $f_{\rm max}$.

The described process is stochastic for two reasons. First, the sampling comes with uncertainties. Second, the effect of policy measures is not known beforehand (even though it may be learnt in the course of time, which we do not include here). It is clear that the faster the testing the more rapidly one can respond to a supercritical situation.

A significant simplification of the model occurs when the two thresholds are chosen to vanish, $\kappa_\pm = 0$. In this case the system tends to a critical steady state with $\lambda_1(t \to \infty) \to 0$.

1. Assessing performance of strategies

To quantify performance one has to introduce some measures. For example, the time integral

$$\int_0^T \mathrm{d}t \left\{ \kappa_- - \frac{1}{G} \mathrm{Tr}\left[K(t)\right] \right\} \tag{22}$$

is a measure of restrictions in excess of what is absolutely necessary. The number of interventions per unit of time is a further important measure of performance.

A. Treating the country as one region - $G = 1$

It is useful to study the model for a single region, $G = 1$, in which case $Q = f = 0$. This illustrates how temporal fluctuations of the fraction of infected people depend on the testing rate and the imposed upper κ_+ and lower κ_- thresholds.

Here, we theoretically analyze the important case where the thresholds are

$$\kappa_\pm = 0. \tag{23}$$

The only parameters defining the problem are

(i) the initial growth rate k_1 (after the first rebooting step at $t = 0$),

(ii) the testing rate r (number of tested people per unit time),

(iii) the initial fraction of infected people, i_0, which is of the order of i_{ICU}, and

(iv) the parameter α governing the confidence level to take an intervention.

The number of infected people $D(t)$ that are detected in tests after the i'th policy intervention satisfies a stochastic differential equation

$$\frac{1}{r}\left(\frac{\mathrm{d}D}{\mathrm{d}t}\right)(t) = i(t_i)\left[1 + k_i\,(t - t_i) + \cdots\right] + f(t). \tag{24a}$$

Here, $i(t)$ is the fraction of infected people, whose exponential growth was linearized in the square brackets (as will be justified a posteriori). The second term, $f(t)$, becomes a white noise correlated in time in the limit of a sufficiently large number of tests, with the time average (denoted by an oveline)

$$\overline{f(t)\,f(t')} = \frac{1}{r}\,\delta(t - t')\,i(t) \approx \frac{1}{r}\,\delta(t - t')\,i(t_i), \tag{24b}$$

were we neglect the time dependence of the noise level. We will see that the number of infections changes only moderately over the whole time axis, and therefore we simply replace $i(t_i)$ by its initial value

$$i_0 \equiv i(0). \tag{24c}$$

The natural time scale governing the non-linear growth of $D(t)$ is obtained from balancing the second and the third term in Eq. (24a),

$$t_{\mathrm{typ}} = (k_i^2\, r\, i_0)^{-1/3}. \tag{25}$$

For large enough α, the next intervention takes place after a time that scales as

$$\Delta t_i \equiv t_{i+1} - t_i \approx (2\,\alpha)^{2/3}\, t_{\mathrm{typ}}. \tag{26}$$

The exponential growth that can take place in this time interval is rather modest since

$$e^{k_i\,\Delta t_i} \approx 1 + (2\,\alpha)^{2/3}\left(\frac{k_i}{r\,i_0}\right)^{1/3}. \tag{27}$$

Using growth rates of order $k_0 \sim 0.1\,\mathrm{day}^{-1}$ and i_0 of the order of i_{ICU}, the correction term becomes small for testing rates r of the order of a few thousand per day. **This implies that the probability of a substantial increase in infection numbers is very small, and thus the strategy is safe.**

The first intervention occurs at a time

$$\Delta t_1 \approx (2\,\alpha)^{2/3}\,(k_1^2\, r\, i_0)^{-1/3}. \tag{28}$$

In our model, it is very likely that the growth rate k_2 is smaller than k_1 in magnitude so that the second intervention occurs after the time

$$\Delta t_2 \approx \Delta t_1 \left(\frac{|k_2|}{k_1}\right)^{-2/3}. \tag{29}$$

Similarly, the growth rate k_3 is very likely to be smaller than k_2 in magnitude so that the third intervention takes place at yet a longer time. If we neglect that the fitted value $k_i^{\mathrm{fit}}(t)$ differs slightly from k_i (negligibly so when α is large), our model ensures that

$$\rho_i \equiv \frac{|k_{i+1}|}{|k_i|} \tag{30}$$

is uniformly distributed in $[0, 1]$. After the $(n + 1)$-th intervention the growth rate is down in magnitude to

$$|k_{n+1}| = k_1 \prod_{i=1}^{n} \rho_i. \tag{31}$$

To reach a low final growth rate k_{final}, one needs the typical number of interventions $n_{\mathrm{int}}(k_{\mathrm{final}})$ given by

$$n_{\mathrm{int}}(k_{\mathrm{final}}) \approx 1 + \frac{\ln \frac{k_{\mathrm{final}}}{k_1}}{\overline{\ln \rho_i}} = 1 + \ln \frac{k_1}{k_{\mathrm{final}}}. \tag{32}$$

The time to reach this low rate is dominated by the last time interval

$$T(k_{\mathrm{final}}) \sim \Delta t_{n_{\mathrm{int}}(k_{\mathrm{final}})} \approx \Delta t_1 \left(\frac{k_1}{k_{\mathrm{final}}}\right)^{2/3}. \tag{33}$$

Thus, the system asymptotes to the critical state where $k = 0$, but never quite reaches it. At late times T the residual growth rate behaves as $k_{\text{final}} \sim T^{-3/2}$.

By adjusting the confidence parameter α one can finally optimize the expectation value of one the measures of performance that we defined above.

B. Partitioning the country - Several regions

In the case where several regions are distinguished, $G > 1$, an intervention becomes necessary when $\lambda_1(t)$ crosses upper or lower thresholds. However, it may well happen that the eigenvector corresponding to $\lambda_1(t)$ is well-localized, meaning that only some regions really show growth with $\lambda_1(t)$. In this case one can distinguish two strategies for intervention:

(a) **Global strategy** One always applies a policy change to the whole country, as described above.

(b) **Local strategy** One applies a policy change only in regions which have significant weight on the unstable eigenvectors. This means only the corresponding diagonal matrix elements of $K(t)$ are changed. In the mean field model one would also change $f(t)$ as above, whereas for a nearest neighbor model one could instead generalize the model to have different $f_{nm}(t)$ for all nearest neighbor pairs.

Likewise, regions that have $i_m < i^*$ and have negligible overlap with eigenvectors whose eigenvalues are above n, could release some restrictions, before others do.

This model and its generalizations allow us to calculate both economic and health impact. It is important to assess how the global and the local strategy perform in comparison. Obviously this will depend on the variability Q, which is currently not known, but will be a measurable quantity in the future. At that point one will be able to decide whether to go for the politically simpler route (a) or the heterogeneous route (b) which is presumably economically favorable. We are currently engaged in coding the model with the perspective of running it continuously with the best available current data and knowledge and will report on these activities in subsequent memoranda.

[1] Neil M. Ferguson, Derek A. T. Cummings, Christophe Fraser, James C. Cajka, Philip C. Cooley, and Donald S. Burke, *"Strategies for mitigating an influenza pandemic,"* Nature **442**, 448 (2006).

[2] COVID-19 reports from the MRC Centre for Global Infectious Disease Analysis, Imperial College, UK, `https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/`

[3] Neil M Ferguson, Daniel Laydon, Gemma Nedjati-Gilani, Natsuko Imai, Kylie Ainslie, Marc Baguelin, Sangeeta Bhatia, Adhiratha Boonyasiri, Zulma Cucunubá, Gina Cuomo-Dannenburg, Amy Dighe, Ilaria Dorigatti, Han Fu, Katy Gaythorpe, Will Green, Arran Hamlet, Wes Hinsley, Lucy C Okell, Sabine van Elsland, Hayley Thompson, Robert Verity, Erik Volz, Haowei Wang, Yuanrong Wang, Patrick GT Walker, Caroline Walters, Peter Winskill, Charles Whittaker, Christl A Donnelly, Steven Riley, and Azra C Ghani, *"Impact of non-pharmaceutical interventions (NPIs) to reduce COVID- 19 mortality and healthcare demand,"* COVID-19 report numer 9 from the MRC Centre for Global Infectious Disease Analysis, Imperial College, UK, `https://www.imperial.ac.uk/mrc-global-infectious-disease-analysis/covid-19/`

[4] Patrick Jenny, David F. Jenny, Hossein Gorji, Markus Arnoldini, and Wolf-Dietrich Hardt, unpublished.

[5] Ying Liu, Albert A Gayle, Annelies Wilder-Smith, and Joacim Rocklöv, *"The reproductive number of COVID-19 is higher compared to SARS coronavirus,"* Journal of Travel Medicine, **27**, Issue 2, March 2020, taaa021. `https://doi.org/10.1093/jtm/taaa021`

[6] Matt J Keeling, T. Deirdre Hollingsworth, and Jonathan M Read, *"The Efficacy of Contact Tracing for the Containment of the 2019 Novel Coronavirus (COVID-19),"* `https://doi.org/10.1101/2020.02.14.20023036`