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Testing of asymptomatic individuals for fast feedback-control of COVID-19 pandemic

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Abstract

We argue that frequent sampling of the fraction of *a priori* non-symptomatic but infectious humans (either by random or cohort testing) significantly improves the management of the COVID-19 pandemic, when compared to intervention strategies relying on data from symptomatic cases only. This is because such sampling measures the incidence of the disease, the key variable controlled by restrictive measures, and thus anticipates the load on the healthcare system due to progression of the disease. The frequent testing of non-symptomatic infectiousness will (i) significantly improve the predictability of the pandemic, (ii) allow informed and optimized decisions on how to modify restrictive measures, with shorter delay times than the present ones, and (iii) enable the real-time assessment of the efficiency of new means to reduce transmission rates. These advantages are quantified by considering a feedback and control model of mitigation where the feedback is derived from the evolution of the daily measured prevalence. While the basic model we propose aggregates data for the entire population of a country such as Switzerland, we point out generalizations which account for hot spots which are analogous to Anderson-localized regions in the theory of diffusion in random media.

1. Introduction

The COVID-19 pandemic has led to a worldwide shutdown of a major part of our economic and social activities. This political measure was strongly suggested by epidemiologic studies assessing the cost in human lives depending on different possible policies (doing nothing, mitigation, suppression) [1–4]. Mitigation can be achieved by combinations of different measures, including physical distancing, contact tracing, restricting public gatherings, and the closing of schools, but also the testing for infections.

The quantitative impact of very frequent testing of the entire population for infectiousness has been studied in references [5, 6]. We will estimate in section 3 that to fully suppress the COVID-19 pandemic by widespread testing for infectiousness, one needs a capacity to test millions of people per day in Switzerland. This should be compared to the modest number of 7000 tests per day performed across Switzerland during April 2020. Here, we suggest that, when the daily incidence of symptomatic COVID-19 infections is of the order of one per 10 000, the daily testing for (*a priori* non-symptomatic) infectiousness of 15 000 persons chosen randomly every day, or the weekly screening of a cohort of the order of 100 000 persons (preferentially essential workers with high exposure), delivers important quantitative information on the rates of transmission. This information allows the adjustment of restrictive measures with significantly shorter delay than is possible presently. The higher the daily testing rate the shorter the reaction time in the case of an undesired increase of incidence, and accordingly the lower the damage to public health and the economy. We point out that such testing is entirely realistic for small central European countries: in order to secure the country's success as a post-corona holiday destination, the government of Austria has announced the weekly testing of nearly this number in its hospitality sector [7].

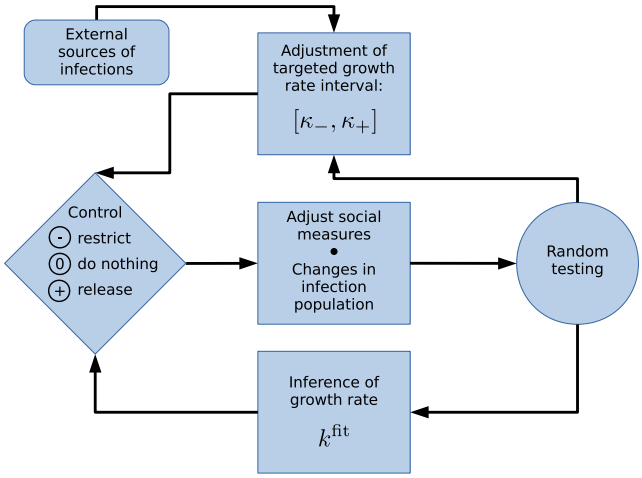

Figure 1. Feedback and control loop that allows stabilization of the pandemic. The key quantity measured by sufficiently frequent non-symptomatic testing is the growth rate k of infection numbers with a time delay (T) shorter than the one (T_{D}) obtained by symptomatic testing. If k exceeds a tolerable upper threshold κ_+, restrictions are imposed. For k below a lower threshold κ_-, and if infection numbers are below critical, restrictions are released. In the absence of a substantial influx of infected people from outside the country, and provided infection numbers are below a critical value, the optimal target of the growth rate is $k = 0$, corresponding to a marginally stable state, where the prevalence neither grows nor decreases exponentially with time. If higher testing rates are available, the measured observables and control strategies can be geographically refined, particularly to avoid hotspots.

Figure 1 summarizes the key concept of the paper, namely a feedback and control model for the pandemic [8]. The idea is to collect a time series of daily detected infectious people (our primary indicator), either obtained directly from testing *a priori* non-symptomatic people, or from waste water analysis [9, 10].[6] Its essential output is the growth rate of the number of persons who became infectious T days in the past. Hereby, the delay T can in principle be very short, being strictly bounded from below only by the latency time for COVID-19 provided the daily testing rate is sufficiently large. This (delayed) growth rate and the incidence are then regulated by measures such as those enforcing physical distance between persons, their tolerable values being fixed by the capacity of the health-care system. A feedback and control approach [12, 13], familiar from everyday implementations such as thermostats regulating heaters and air conditioners, should allow policy makers to damp out oscillations in disease incidence which could lead to peaks in stress on the health-care system as well as the wider economy.

An important benefit of our feedback and control scheme is that it allows a faster and safer reboot of the economy than would be possible only with the feedback from the time sequence of daily numbers of positively tested symptomatic persons [14, 15], hospitalizations, or deaths [4, 14]. Indeed, these secondary indicators measure the growth rate of the pandemic with a delay T_{D} that is necessarily bounded from below by a minimal time of order 8–12 days, whatever the testing rate for COVID-19, as we shall explain. Hence, testing for the primary indicator and increasing the non-symptomatic testing rate can reduce the time delay T below the delay T_{D} inherent to the secondary indicators. Figure 2 illustrates the resulting difference in the ability to control the disease.

Without the feedback and control informed by the primary indicator, there is a larger lapse in time between policy changes and the observable changes in the daily numbers of infectiousness measured by secondary indicators. To relax restrictions safely when using secondary indicators, the prevalence (defined as the fraction of presently infectious persons), must decrease to a level i^{**} (that is smaller than i^{*} when using the primary indicator) such that a subsequent undetected growth during $T_{\mathrm{D}} = 8$–12 days will not move it above the critical fraction i_{c} manageable by the health-care system. Monitoring the time evolution of the COVID-19 pandemic by only relying on secondary indicators is comparable to driving a car from the back seat with knowledge only of the damage caused by previous collisions. To minimize harm to the occupants of the vehicle, driving very slowly is essential, and oscillations from a straight course are likely to be large. Making use of the shortened time delay $T < T_{\mathrm{D}}$ based on the primary indicator allows a reboot to be attempted at higher levels of prevalence, $i^{*} > i^{**}$, which implies a shorter time in lockdown. In turn, if a long lockdown has already resulted in a low level of prevalence, as is currently the case in many European countries, a fast reaction time allows to keep the case numbers low by reacting quickly to a potential new onset of exponential growth. In figure 3

[6] Any other measurement of the fraction of infectious people can replace direct testing of individuals. For example there are proposals to estimate this fraction from analysis of sewage water with PCR tests [9–11].

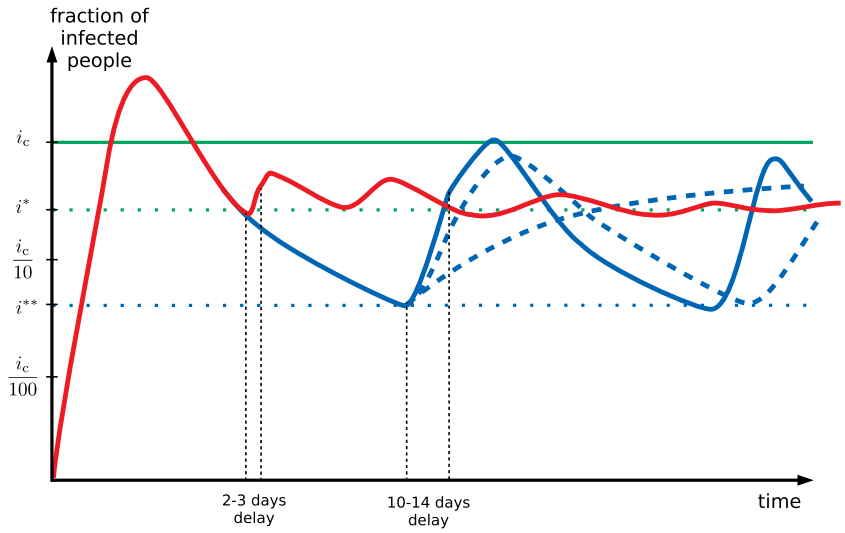

Figure 2. Dynamics of the pandemic with and without a feedback and control scheme in place, as measured by the prevalence i, i.e. the fraction of currently infected people (logarithmic scale). After the limit of the health system, i_c, has been reached, a lockdown brings i down again. The exponential rate of decrease is expected to be very slow, unless extreme measures are imposed. The release of measures upon a reboot is likely to re-induce exponential growth, but with a rate difficult to predict. Three possible outcomes are shown in blue curves in the scenario without testing feedback, where the effect of the new measures becomes visible only after a delay of 10–14 days. In the worst case, i grows by a multiplicative factor of order 20 before the growth is detected. A reboot can thus be risked only once $i \leqslant i^{**} \equiv i_c/20$, implying a very long time in lockdown after the initial peak. Due to the long delay until policy changes show observable effects, the fluctuations of i will be large. Random testing (the red curve) has a major advantage. It measures i directly and detects its growth rate within a few days, whereby the higher the testing rate the faster the detection. Policy adjustments can thus be made faster, with smaller oscillations of i. A safe reboot is then possible earlier, at the level of $i \leqslant i^* \approx i_c/4$.

we estimate quantitatively the benefits of frequent non-symptomatic testing.

We point out before proceeding further that this is a contribution from physicists that makes simplifying assumptions inconsistent with details of medical and epidemiological reality to obtain some key estimates and illustrate the basic principles of feedback and control as applied to the current pandemic. When reduced to practice, special attention will need to be paid to all aspects of the testing methodology, from the underlying molecular engineering paradigm (e.g., PCR) and associated cost/performance trade offs, to population sample selection consistent with societal norms and statistical needs, and safe operation of testing sites that does not risk further infections. Furthermore, in preparation for the day when more is known about the immune response to COVID-19 and possible vaccines, we plan to revise our models for feedback derived from a reliable immunoassay with well-specified performance parameters, such as lag times with respect to infection.

The paper is organized as follows. We summarize our key findings in section 2. In section 3, we discuss the use of massive testing as a direct means to contain the pandemic, showing that it requires a 100-fold increase of the current testing frequency. In section 4, we define the main challenge to be addressed: to measure the quantitative effect of restrictive measures on the transmission rate. Section 5 explains the difference between using primary or secondary indicators to monitor the time evolution of the COVID-19 pandemic. Section 6 constitutes the central part of the paper, showing how data from sparse sampling tests can be used to infer essentially instantaneous growth rates, and their regional dependence. We define a model of policy interventions informed by feedback from random testing and analyze it theoretically. The model is also analyzed numerically in section 7. In section 8, we generalize the model for regionally refined analysis of the epidemic growth pattern which becomes the preferred choice if higher testing rates become available. We conclude with section 9 by summarizing our results and their implication for a safe reboot after the current lockdown. In the appendix A, we present the algorithm used for our numerical results.

2. Summary of key results

2.1. Reducing delay by non-symptomatic testing

To shorten the reaction time, we propose to use the time series obtained from daily tests for infectiousness in groups of persons who are *a priori* non-symptomatic. This time series is our primary indicator, in contrast to the secondary indicator that makes use of the time series obtained from testing for the daily numbers of persons who are either symptomatic, hospitalized, or even dead because of COVID-19. The sample to be tested can be random or consist of a pre-selected group that is tested regularly and systematically, e.g., on a weekly basis. The

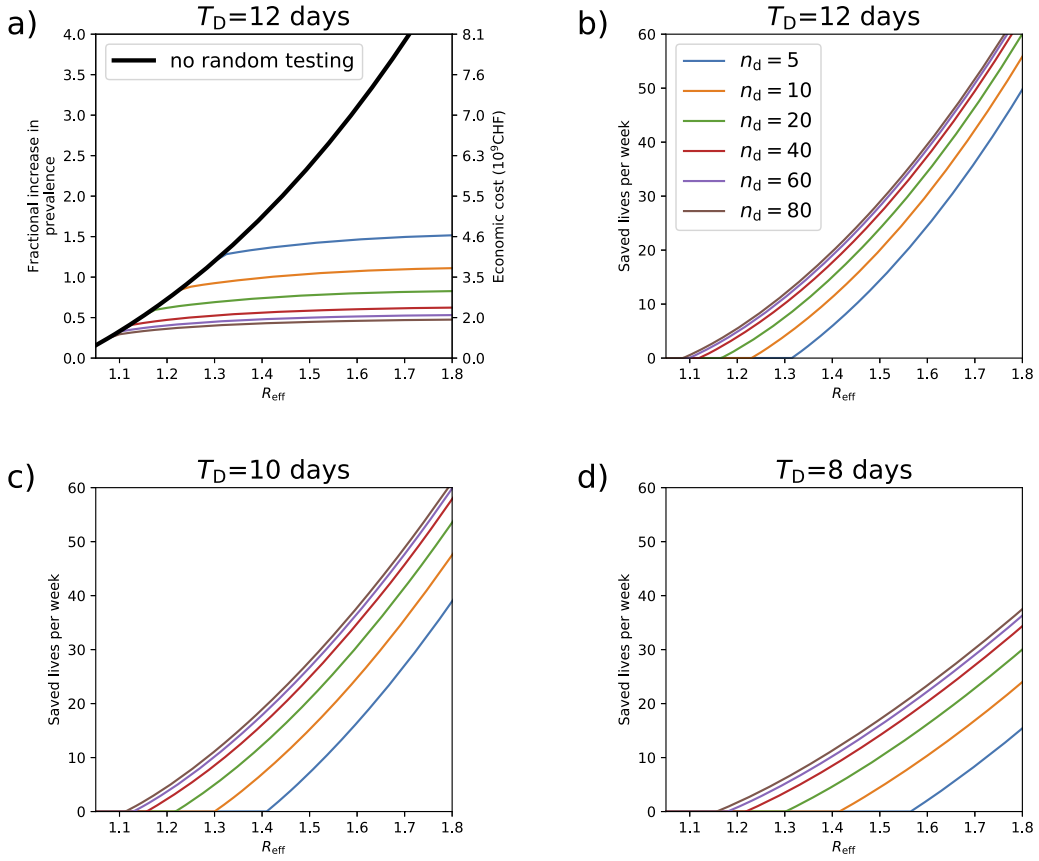

Figure 3. A shorter reaction time allows to take countermeasures earlier if R_{eff} jumps above 1 after a release of restrictions. The results are plotted for interventions being taken when an 85% confidence level is reached for $R_{\text{eff}} > 1$. For a 95% confidence level one would need to test 2.6 times more frequently. In (a) we plot the relative increase of prevalence and incidence without non-symptomatic testing (assuming a time delay $T_D = 12$ associated with symptomatic case data), and show how it is reduced as one tests non-symptomatically for infectiousness, with increasing frequency. The expected number $n_d = r\, i_0$ of positively tested people per day is proportional to the number r of tests per day and the prevalence i_0 in the tested subgroup. The estimate of economic costs is described in the main text. Panels (b)–(d) translate the avoided increase of incidence into the number of saved lives per week in Switzerland, assuming an initial incidence of 300 daily new infections (both symptomatic and asymptomatic) and a mortality of 0.5%.

lower time line of figure 4, illustrates the method. It builds on the fact that the latency time, after which PCR tests return positive results following exposure, is only about 2 days [16–20]. Effects of an increased infection rate can thus be seen even before the onset of symptoms. This non-symptomatic testing allows to obtain direct and model-independent information on $R_{\text{eff}}(t)$, (the number of infections transmitted by a person who was infectious at any time t no less than T days in the past). Let us assume a daily incidence of COVID-19 is of the order of one per 10 000. Then, by testing a few thousand people per day, we find that over a testing time T shorter than the minimal delay time T_D for the symptomatic secondary indicators, it becomes possible to detect a sudden dangerous increase in R_{eff} with reasonable confidence. This shorter response time may potentially save tens of lives per week at the national level, see figures 3(b)–(d), and reduce costs for the health care system as well as for the economy, see figure 3(a). Moreover such monitoring provides greater stability and diminishes the danger of a second wave of the epidemic. Also, by monitoring the fraction of infected people with weak or no symptoms, non-symptomatic testing allows to better determine some of the parameters entering epidemiologic modeling.

2.2. Estimating the intervention time

We are going to estimate the time T after a release, until which one will know with reasonable certainty that a new state with exponential growth has been reached. We then estimate how much damage can be prevented by the more rapid intervention made possible with systematic, but non-symptomatic testing.

Assume that we test r people daily over a period T after the release. We also assume that tests can distinguish persons that are both infected and still infectious. This can be ensured, e.g., by following a large cohort of people (e.g., medical or nursing staff) who are tested on a weekly basis. We denote with i_0 the initial prevalence of acute infections in the population being sampled. The expected number of positive tests per day is $n_d = i_0\, r$. In the first half $(T/2)$ of the measuring period T, one detects

$$N_1 \approx n_d\, T/2 \qquad (1)$$

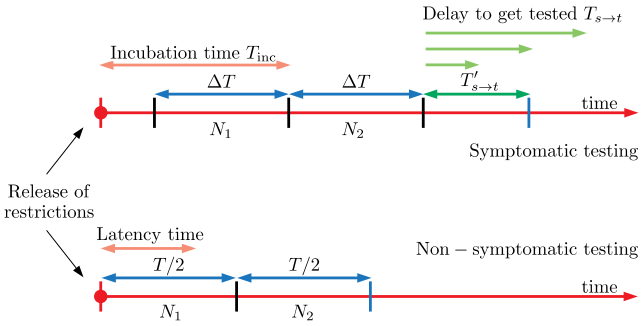

Figure 4. Timing of case counting after a release, up to the first time where a reliable estimate of the new reproduction number $R_{\rm eff}$ can be made. For symptomatic testing (upper time line), the incubation time and the natural delays between symptoms and testing incur a delay $T_{\rm D}$. This delay cannot be less than 9 days, the value of $T_{\rm D}$ for COVID-19 when the observation window ΔT is chosen to be a single day. In the case of non-symptomatic testing (lower time line), the window of time T must be sufficiently large so as to accumulate enough statistics, but with sufficiently frequent testing one still gains precious time as compared to $T_{\rm D}$.

cases. In the second half we expect

$$N_2 = N_1\ \exp(k\,T/2) \equiv N_1\,(R_{\rm eff})^{T/8} \qquad (2)$$

cases, with $k \equiv \ln(R_{\rm eff})/4$ being the growth rate of infections. The relation between the rate k and the effective reproduction number follows if one assumes a 'generation time' of 4 days[7] until an infected person has transmitted the disease to a next generation. Above, we anticipated that $T/2$ will be larger than the short latency time. If so, the simple exponential law (2) should hold to a good approximation, until a further intervention is taken.

We can tell with reasonable certainty that the growth rate is positive once the difference

$$N_2 - N_1 = N_1\,\left((R_{\rm eff})^{T/8} - 1\right) \qquad (3a)$$

is larger by a factor α than its statistical uncertainty $\sqrt{N_1 + N_2} \approx \sqrt{2N_1}$. The latter expression follows from the law of large numbers. An intervention is thus taken when

$$N_1\,\left((R_{\rm eff})^{T/8} - 1\right) = \alpha\,\sqrt{2\,N_1}. \qquad (3b)$$

For our plots we choose $\alpha = 1$, corresponding to a confidence level of 85% that $R_{\rm eff} > 1$, while for $\alpha = 1.6$ it reaches 95%. If we replace N_1 by the right-hand side of equation (1) on both sides of equation (3b), we find the relation

$$n_d \approx \frac{4}{T}\left(\frac{\alpha}{(R_{\rm eff})^{T/8} - 1}\right)^2. \qquad (4)$$

If $R_{\rm eff}$ is not too far from 1, we find the relations

$$n_d(T, \alpha, R_{\rm eff}) \equiv \left[\frac{16\alpha}{\ln(R_{\rm eff})}\right]^2 T^{-3}, \qquad (5a)$$

or, equivalently,

$$T(n_d, \alpha, R_{\rm eff}) \equiv \left[\frac{16\,\alpha}{\ln(R_{\rm eff})}\right]^{2/3} n_d^{-1/3}. \qquad (5b)$$

[7] The number of 12 days is the delay time used by the Robert Koch Institute when performing nowcasting [21], [22].

Non-symptomatic testing becomes beneficial as compared to symptomatic testing as soon as n_d exceeds the right-hand side of equation (5a) evaluated with T replaced by the delay time $T_{\rm D}$ of symptomatic testing, or, equivalently, if $T_{\rm D}$ exceeds the right-hand side of equation (5b).

By the reaction time T, the prevalence and the infection numbers will have increased by the fraction

$$\frac{i(T) - i_0}{i_0} = (R_{\rm eff})^{T/4} - 1 \approx \left(4\,\alpha^2\,\frac{\ln(R_{\rm eff})}{n_d}\right)^{1/3}, \qquad (6)$$

which is to be compared to $(R_{\rm eff})^{T_{\rm D}/4} - 1$ for methods based on fitting symptomatic case numbers, with an inherent delay $T_{\rm D}$. These two relative increases are shown in figure 3(a) for $T_{\rm D} = 12$ days as a function of the effective reproduction number $R_{\rm eff}$ that prevails after the release of restrictions. Sufficiently frequent non-symptomatic tests result in a smaller relative increase of the prevalence. Therefore, less of the achievements of the preceding lockdown will be undone at the shorter intervention time $T < T_{\rm D}$. Since the reproduction number had lowered to $R_{\rm LD} \approx 0.7$ during the final phase of the Swiss lockdown [23, 24] and a loss of $P \approx 500$ million CHF in generated economic added value accrued during every day of lockdown, we can associate an effective price tag to the additional increase of the prevalence if no intervention were taken until the later time $T_{\rm D} > T$. Per day of exponential growth with $R_{\rm eff} > 1$, one undoes the effect of a preceding lockdown effort that had cost $P\,\ln(R_{\rm eff})/\ln(1/R_{\rm LD})$. This cost is indicated in figure 3(a). Even more importantly, the increase in prevalence implies an increase of daily incidence and thus, ultimately, of the death rate. With an estimated low rate of daily $n \sim 300$ new infections (reported and unreported) in Switzerland and assuming a COVID-19 mortality rate of $m = 0.5\%$, the diminished increase of incidence (i.e., equation (6) saves $n\,m\,[i(T_{\rm D}) - i(T)]/i_0$ lives per day in the country. The actual numbers are plotted in figures 3(b)–(d) for different delays $T_{\rm D}$. They

demonstrate that frequent non-symptomatic testing can save a significant number of lives by enabling a more rapid response to an increasing prevalence due to a release of restrictions.

From the results shown in figure 3 one readily reads off that the expected number of detected new infections per day, n_d, should be of order 10, and preferably even bigger, to enable an effective monitoring. This implies a relatively large number r of daily tests, $r = n_d/i_0$, especially if the prevalence i_0 is as low as it is currently in many countries in Europe. However, if a sufficiently large group of people, such as medical staff or key workers with high exposure, can be recruited for regular non-symptomatic testing, their test data could be used for the fast feedback system. Moreover, if the prevalence slowly rises again non-symptomatic testing will require accordingly less effort. By autumn 2020, when a second wave of the pandemic becomes more likely, it could act as an early warning system and as a tool for efficient mitigation which is worthy of implementation.

3. Massive testing

If the massive rate of 1.5 million tests per day becomes available in Switzerland, it will be possible to test any Swiss resident every 5 to 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 infections without the need of draconian physical distancing measures. We now explain qualitatively our approach to reach this conclusion (reference [5] gives a more detailed quantitative analysis).

The required testing rate can be estimated as follows. Let ΔT denote the average time until an infected person infects somebody else. The reproduction number R 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 τ_{full}^{-1}, is

$$\tau_{\text{full}}^{-1} = \frac{N_{\text{CH}}}{2\Delta T}, \tag{7a}$$

where

$$N_{\text{CH}} = 8'500'000 \tag{7b}$$

is the number of inhabitants of Switzerland[8]. Without social restrictions, it is estimated that [25]

$$\Delta T \approx 3 \text{ days}, \tag{8a}$$

such that

$$\tau_{\text{full}}^{-1} = 1.4 \times 10^6/\text{days}, \tag{8b}$$

[8] Note that if tests take the nonvanishing time t_{test} to yield a diagnosis, this time needs to be subtracted from the denominator in equation (7a), thereby resulting in an increase of the full testing rate τ_{full}^{-1}.

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

However, even while the Swiss capabilities are still far from reaching 1 million tests per day, testing for infections offers two important benefits in addition to identifying people that need to be quarantined. First, properly randomized testing allows to monitor and study the efficiency of measures that keep the reproduction number R below 1. This ensures that the growth rate k of case numbers and new infections is negative, $k < 0$. Second, frequent testing, even if applied to randomly selected people, helps suppress the reproduction number R_{eff} and thus allows policy to be less restrictive in terms of other measures, such as physical distancing.

To quantify the latter benefit, observe that the effect of massive testing on the growth rate k is proportional to the testing rate [5]. 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 completely suppress the exponential growth in the absence of other measures, a smaller testing rate τ^{-1} decreases the growth rate k_0 by $(\tau^{-1}/\tau_{\text{full}}^{-1}) \times k_0$. 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 trade offs, i.e., a cheaper test with more false negatives could be used for random testing, whereas those displaying symptoms would be subjected to a 'gold standard' (PCR) assay of viral genetic material.

4. Quantifying the effectiveness of restrictions

A central challenge for establishing reliable predictions for the time evolution of a pandemic is the quantification of the effect of social restrictions on the transmission rate [3]. Policymakers and epidemiologists urgently need to know by how much specific restrictive measures reduce the growth rate k. Without that knowledge, it is essentially impossible to take an informed decision on how to optimally combine such measures to achieve a (marginally) stable situation, defined by the condition of a vanishing growth rate

$$k = 0. \tag{9}$$

Indeed, marginal stability is optimal for two reasons. First, it is sustainable in the sense that the burden on the health system does not grow with time. Second, it

is the least economically and socially restrictive state compatible with the stability requirement.

In sections 5 and 6, we suggest how marginal stability can be achieved, while simultaneously measuring the effects of a particular set of restrictions.

5. Time delays: primary versus secondary indicators

The time evolution of the COVID-19 pandemic has been monitored in Europe between March and June 2020 by estimating the time-dependent reproduction number $R_{\text{eff}}(t)$ from the growth rate of confirmed cases over a time window of the generation time of 4 days for COVID-19. An inherent delay time that we denote with T_{D} when estimating $R_{\text{eff}}(t)$ arises as a consequence of (i) the incubation time of about $T_{\text{inc}} \approx 5$ days from the infection until the first symptoms show up, (ii) the time window ΔT ranging from 1 to 4 days over which case numbers are averaged to even out fluctuations throughout the week or uncertainties about the onset of symptoms, and (iii) the time delay $T_{\text{s}\to\text{t}}$ until symptomatic people get tested, see figure 4. Even by using forecasting methods to extrapolate from the number of tests with short delays $T_{\text{s}\to\text{t}}$ to the total expected reports of symptom onsets for a given day, the data accrued for the last $T'_{\text{s}\to\text{t}} \approx 3$ days is usually too incomplete to be incorporated in the analysis. Accordingly, a T_{D} ranging from 9 days to 12 days[7] of delay is unavoidable when using symptomatic testing (secondary indicator) to determine $R_{\text{eff}}(t)$. This is a significant disadvantage when restrictions are released, since one needs to know the resulting new value of $R_{\text{eff}}(t)$ as rapidly as possible, so as to take countermeasures in case the release has caused $R_{\text{eff}}(t)$ to surpass 1, the condition for a stable pandemic.

We claim that an alternative testing can be used so as to keep the dynamics of the pandemic under control as per the feedback loop of figure 1. The idea is either to test on a daily basis a new set of random, *a priori non-symptomatic* people or to choose a cohort of people and test them regularly for infectiousness[9] thereby obtaining a value for $R_{\text{eff}}(t)$ with a shorter time delay than when relying on symptomatic testing.

5.1. Random versus cohort testing

Note that the non-symptomatic testing aims at the early identification of new cases of people who have recently been infected and are still infectious. Standard PCR tests, however, can only tell whether a person has viral material in their body, which is often the case long after symptoms have been resolved [26]. This constitutes a challenge for random testing, where one would have to use additional information (such as viral load, presence of antibodies or specific genetic sequences indicative of active virus) to diagnose infectiousness. Cohort testing with a testing interval of the order of an infectious period (ca. one week), resolves this problem, since the first time a person tests positive, it is highly likely that he or she is still infectious. It has the additional advantage that one may concentrate the non-symptomatic testing preferentially on essential workers with high exposure, where precautionary testing is useful anyway. Moreover the prevalence and incidence in such a cohort is likely to be higher than the average in the population, which reduces the effort needed to detect a dangerous growth dynamics. Note that even if the prevalence and incidence is higher in such a biased cohort, their (relative) growth rate can be expected to be representative of that of the average population. A caveat of cohort testing is, however, that survey participation itself as well as the regular feedback to cohort members about their infectiousness may bias their social behavior.

[9] Note that here we focus on a person being infectious, but *not* on whether the person has developed antibodies. The latter test indicates that the person has been infected any time in the past. Serological tests for antibodies and (potential) immunity have their own virtue, but aim at goals different from those of random testing for infections that we advocate here.

6. National modeling and intervention

We analyze primary, non-symptomatic testing first for the case where we treat the country as a single entity with a population N. This will allow us to understand how testing frequency affects key characteristics of policy strategies.

6.1. Model assumptions

We consider a model with the following idealizing assumptions:

(a) In the case that random testing is used, we assume that a test can actually diagnose infectiousness. Further we assume that an unbiased representative sample of the population is tested.

(b) The rate of false positive tests is much less than the expected frequency of detection of infections.

(c) Tests show whether a person is acutely infected in a short time (on the order of one day).

(d) Policy measures can be applied rapidly, and their effect is immediate. Time delays due to the adaptation of human behavior to new rules is neglected.

(e) The population is homogeneous as far as interactions between its members are concerned, e.g., there are no (semi)-isolated subpopulations. We do not account for large deviations in infectiousness that may lead to superspreading events [27].

As is well known to epidemiologists and the medical profession, the assumptions (a–d) clearly are violated to varying degrees in reality, but they can be taken into account by refinements of our model, whose operating principles and basic behavior will

remain qualitatively the same. On the other hand, violations of assumption (e) can lead to new and dangerous effects, namely hotspots related to Anderson localization [28], which we discuss in section 8.

Let U be the actual number of currently infectious but not yet positively tested persons. (As in reference [5], we assume that positively tested people do not spread the disease since they will be quarantined.) The spreading of infections is assumed to be governed by the inhomogeneous, linear growth equation

$$\left(\frac{\mathrm{d}U}{\mathrm{d}t}\right)(t) = k(t)\,U(t) + \Phi(t), \tag{10}$$

where $k(t)$ is the instantaneous growth rate and $\Phi(t)$ accounts for infections arising from people crossing the national border. For simplicity, we set this influx to zero in this paper, in which case $k(t) = \dot{U}(t)/U(t)$ with the short-hand notation $\dot{U}(t)$ for the time derivative on the left-hand side of (10).

An equation of the form (10) is usually part of a more refined epidemiological model of the SIR (susceptible-infected-recovered) type [29–31] that accounts explicitly for the recovery or death of infected persons. For our purpose, the effect of these is subsummarized in an overall time-dependence of the rate $k(t)$. For example, it evolves as the number of immune people grows, restrictive measures change, mobility is affected, new tracking systems are implemented, hospitals reach their capacity, 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 rate $k(t)$ to be piecewise constant in time[10]. We will exploit this below. The above evolution equation is the simplest model for infection dynamics, as it has no temporal memory and contains the fewest parameters. Generalizations such as SEIR models with a finite latency time (neglected here since it is rather short for COVID-19) [18–20], or discrete evolution models, that are non-local in time, could be considered in further work.

6.2. Modeling intervention strategies

For $t < 0$, we assume a situation that is under control, with a negative growth rate

$$k(t < 0) \equiv k_0 < 0, \tag{11a}$$

as is the case in Switzerland after the lockdown in March, with $k_0 \approx -0.07$ day^{-1}, according to the estimates of reference [4]. Such a stable state needs to be reached before a reboot of the economy can be considered. At $t = 0$ restrictive measures are first relaxed, resulting in an increase of the growth rate k from k_0 to k_1, which we assume positive,

$$k(t = 0) = k_1 > 0. \tag{11b}$$

Hence, compensating countermeasures are required at later times to avoid another exponential growth of the pandemic.

We now want to monitor the performance of policy strategies that relax or re-impose restrictions, step by step. The goal for an optimal policy is to reach a marginally stable state (9) (i.e., with $k = 0$) as smoothly, safely, and rapidly as possible. In other words, marginal stability is to be reached with the least possible damage to health, economy, and society. This expected outcome is to be optimized while controlling the risk of rare fluctuations.

To model the performance of policy strategies, we neglect the contributions to the time evolution of $k(t)$ due to the increasing immunity or the evolution in the age distribution of infected people. We also neglect periodic temporal fluctuations of $k(t)$ (e.g., due to alternation between workdays and weekends), which can be addressed in further elaborations. Instead, 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 made when the sampled testing data indicates that with high likelihood, $k(t)$ exceeds some upper threshold

$$\kappa_+ \geqslant 0. \tag{11c}$$

Likewise, a different intervention is made should $k(t)$ be detected to fall below some negative threshold

$$\kappa_- \leqslant 0. \tag{11d}$$

Note that if there is substantial infection influx $\Phi(t)$ across the national borders, one may want to choose the threshold κ_+ to be negative, to avoid a too large response to the influx. From now on we neglect the influx of infections, and consider a homogeneous growth equation.

To reach decisions on policy measures, data are acquired by daily testing of random sets of people for infections, or by periodic cohort testing. We assume that the tests are carried out at a limited rate r (number of tests per day). Let $i(t, \Delta t)$ be the fraction of positive infections detected among the $r\Delta t \gg 1$ tests carried out in the time interval $[t, t + \Delta t]$. By the law of large numbers, it is a Gaussian random variable with mean

$$\langle i(t, \Delta t)\rangle = \frac{\overline{U(t)}}{N}, \quad \overline{U(t)} \equiv \int_t^{t+\Delta t} \frac{\mathrm{d}t'}{\Delta t}\, U(t') \tag{11e}$$

and standard deviation

$$\langle [i(t, \Delta t)]^2\rangle_{\mathrm{c}}^{1/2} = \sqrt{\frac{\langle i(t)\rangle}{r\,\Delta t}} = \sqrt{\frac{\overline{U(t)}}{N\,r\,\Delta t}}. \tag{11f}$$

[10] Replacing the function $k(t)$ by a piecewise constant function is a good approximation provided $k(t)/\dot{k}(t) \gg \Delta t(k)$ where $\dot{k}(t)$ is the time derivative of $k(t)$ (which we assume differentiable between interventions) and $\Delta t(k)$ is given by equation (18a) with the replacement $k_1 \to k(t)$.

The current value of $k(t)$ is estimated as $k^{\mathrm{fit}}(t)$ by fitting these test data to an exponential, *where only data since the last policy change should be used*. The fitting also yields the statistical uncertainty (standard deviation), which we call $\delta k(t)$.

If the instability threshold is surpassed by a certain level, i.e., if

$$k^{\mathrm{fit}}(t) - \kappa_+ > \alpha\, \delta k(t) \tag{11g}$$

a new restrictive intervention is taken. If instead

$$\kappa_- - k^{\mathrm{fit}}(t) > \alpha\, \delta k(t) \tag{11h}$$

a new relaxing intervention is taken. Here, α is a key parameter defining the policy strategy. It determines the confidence level

$$p \equiv [1 + \mathrm{erf}(\alpha)]/2 \tag{11i}$$

that policymakers require, before deciding to declare that a stability threshold has indeed been crossed. This strategy will result in a series of intervention times

$$0 \equiv t_1 < t_2 < t_3 \ldots \tag{11j}$$

starting with the initial step to reboot at $t_1 = 0$. In the time window $[t_\iota, t_{\iota+1}]$, the growth rate $k(t)$ is constant and takes the value

$$k^{(\iota)} = k^{(\iota-1)} - \Delta k^{(\iota)}, \quad \iota = 1, 2, \ldots \tag{11k}$$

where a policy choice with $\Delta k^{(\iota)} > 0$ (corresponding to a restrictive measure) is made to bring back $k(t)$ below the upper threshold κ_+, while a policy choice with $\Delta k^{(\iota)} < 0$ is made to bring back $k(t)$ above the lower threshold κ_-.

The difficulty for policymakers is that so far the quantitative effect of an intervention is not known. We model this uncertainty by assuming $\Delta k^{(\iota)}$ to be random to a certain degree.

If at time t, $k^{\mathrm{fit}}(t)$ crosses the upper threshold κ_+ with confidence level p, we set $t_\iota = t$ and a restrictive measure is taken, i.e., $\Delta k^{(\iota)}$ is chosen positive. We take the associated decrement $\Delta k^{(\iota)}$ to be uniformly distributed on the interval

$$\left[b\, \Delta k^{(\iota)}_{\mathrm{opt},+}, \frac{1}{b} \Delta k^{(\iota)}_{\mathrm{opt},+} \right], \tag{11l}$$

where the optimum choice $\Delta k^{(\iota)}_{\mathrm{opt},+}$ is defined by

$$\Delta k^{(\iota)}_{\mathrm{opt},+} \equiv k^{\mathrm{fit}}\left(t_\iota\right) - \kappa_+ > 0. \tag{11m}$$

The parameter $b < 1$ describes the uncertainty about the effects of the measures taken by policymakers. While the policymakers aim to reset the growth factor k to κ_+, the result of the measure taken may range from having an effect that is too small by a factor of b to overshooting by a factor of $1/b$. A measure with effect $\Delta k^{(\iota)} = \Delta k^{(\iota)}_{\mathrm{opt},+}$ would be optimal according to the best current estimate. The larger $1 - b$, the larger the uncertainty. Unless stated otherwise, we assume $b = 0.5$.

If instead $k^{\mathrm{fit}}(t)$ crosses the lower threshold κ_- with confidence level p at time t, we set $t_\iota = t$ and a relaxing measure is taken, i.e., $\Delta k^{(\iota)}$ is chosen negative. Again, $\Delta k^{(\iota)}$ is uniformly distributed on the interval

$$\left[-\frac{1}{b}\, \Delta k^{(\iota)}_{\mathrm{opt},-}, -b\, \Delta k^{(\iota)}_{\mathrm{opt},-} \right] \tag{11n}$$

with the optimum choice $\Delta k^{(\iota)}_{\mathrm{opt},-}$ defined by

$$\Delta k^{(\iota)}_{\mathrm{opt},-} \equiv \kappa_- - k^{\mathrm{fit}}\left(t_\iota\right) > 0. \tag{11o}$$

The process described above is stochastic for two reasons. First, the sampling comes with the usual uncertainties in the law of large numbers. 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 should be clear that the faster the testing the more rapidly one can respond to a super-critical situation.

A significant simplification of the model occurs when the two thresholds are chosen to vanish,

$$\kappa_\pm = 0, \tag{12a}$$

in which case

$$k^{(\iota)} = k^{(\iota-1)} - \Delta k^{(\iota)}, \quad \iota = 1, 2, \ldots, \tag{12b}$$

with $|\Delta k^{(\iota)}|$ uniformly distributed on the interval

$$\left[b\, |k^{\mathrm{fit}}(t_\iota)|, \frac{1}{b}\, |k^{\mathrm{fit}}(t_\iota)| \right]. \tag{12c}$$

In this case the system will usually tend to a critical steady state with $k(t \to \infty) \to 0$, as we will show explicitly below. In this case the policy strategy can simply be rephrased as follows. As soon as one has sufficient confidence that k has a definite sign, one intervenes, trying to bring k back to zero. The only parameter defining the strategy is α.

6.3. Testing and fitting procedure

Let us now detail the fitting procedure and analyze the typical time scales involved between subsequent policy interventions when choosing the thresholds (12). After a policy change at time t_ι, data is acquired over a time window Δt. We then proceed with the following steps to estimate the time $t_{\iota+1}$ at which the next policy change must be implemented.

Step 1: *Measurement*. We split the time window

$$\Delta T_\iota \equiv [t_\iota, t_\iota + \Delta t] \tag{13a}$$

of length Δt after the policy change into the time interval

$$\Delta T_{\iota,1} \equiv \left[t_\iota, t_\iota + \frac{\Delta t}{2} \right] \tag{13b}$$

and the time interval

$$\Delta T_{\iota,2} \equiv \left[t_\iota + \frac{\Delta t}{2}, t_\iota + \Delta t \right]. \tag{13c}$$

Testing delivers the number of currently infected people

$$N_{\iota,1}(\Delta t) = r\,\Delta t\, i\left(t_\iota, \frac{\Delta t}{2}\right) \tag{13d}$$

for the time interval (13b) and

$$N_{\iota,2}(\Delta t) = r\,\Delta t\, i\left(t_\iota + \frac{\Delta t}{2}, \frac{\Delta t}{2}\right) \tag{13e}$$

for the time interval (13c), where we recall that r denotes the number of people tested per unit time. Given those two measurements over the time window $\Delta t/2$, we obtain the estimate

$$k_\iota^{\mathrm{fit}}(\Delta t) = \frac{2}{\Delta t}\,\ln\left(\frac{N_{\iota,2}(\Delta t)}{N_{\iota,1}(\Delta t)}\right) \tag{13f}$$

with the standard deviation

$$\delta k(\Delta t) = \frac{2}{\Delta t}\sqrt{\frac{1}{N_{\iota,1}(\Delta t)} + \frac{1}{N_{\iota,2}(\Delta t)}}, \tag{13g}$$

as follows from the statistical uncertainty $\sqrt{N_{\iota,\gamma}(\Delta t)}$ of the sampled numbers $N_{\iota,\gamma}(\Delta t)$ and standard error propagation. The above recipe can be replaced by a more sophisticated Levenberg–Marquardt fitting procedure, which yields more accurate estimates for $k(t)$ with a smaller uncertainty $\delta k(t)$. We have confirmed that this uniformly improves the performance of the mitigation strategy.

Step 2: *Condition for new policy intervention*. A new policy intervention is taken once the magnitude $|k_\iota^{\mathrm{fit}}(\Delta t)|$ with $k_\iota^{\mathrm{fit}}(\Delta t)$ given by equation (13f) exceeds $\alpha\delta k(\Delta t)$ with $\delta k(\Delta t)$ given by equation (13g). Here, α controls the accuracy to which the actual k has been estimated at the time of the next intervention. The condition

$$|k_\iota^{\mathrm{fit}}(\Delta t)| = \alpha\,\delta k(\Delta t), \tag{14a}$$

for a new policy intervention thus becomes

$$\left|\ln\left(\frac{N_{\iota,2}(\Delta t)}{N_{\iota,1}(\Delta t)}\right)\right| = \alpha\sqrt{\frac{1}{N_{\iota,1}(\Delta t)} + \frac{1}{N_{\iota,2}(\Delta t)}}. \tag{14b}$$

Step 3: *Comparison with modeling*. We call $i(t) = U(t)/N$ the prevalence of infectious people (in the entire population) that have not yet been detected. According to (10) with $\Phi = 0$, it follows a simple exponential time evolution between two successive policy interventions,

$$i(t_\iota + t') = i(t_\iota)\,\exp(k_\iota\, t'), \tag{15}$$

valid on the interval $t_\iota < t' < t_{\iota+1}$. The expected number of newly detected infected people in the time interval (13b) is

$$\begin{aligned}\langle N_{\iota,1}(\Delta t)\rangle &= r\int_0^{\Delta t/2} \mathrm{d}t'\, i(t_\iota + t') \\ &= r\, i(t_\iota)\,\frac{\mathrm{e}^{k_\iota\,\Delta t/2} - 1}{k_\iota}.\end{aligned} \tag{16a}$$

Similarly, the predicted number of infected people in the time interval (13c) is

$$\begin{aligned}\langle N_{\iota,2}(\Delta t)\rangle &= r\int_{\Delta t/2}^{\Delta t} \mathrm{d}t'\, i(t_\iota + t') \\ &= r\, i(t_\iota)\,\frac{\mathrm{e}^{k_\iota\,\Delta t/2}\left(\mathrm{e}^{k_\iota\,\Delta t/2} - 1\right)}{k_\iota}.\end{aligned} \tag{16b}$$

Step 4: *Estimated time for a new policy intervention*. We now approximate $N_{\iota,1}$ and $N_{\iota,2}$ by replacing them with their expectation value equations (16a) and (16b), respectively, and anticipating the limit

$$k_\iota\,\Delta t/2 \ll 1. \tag{17a}$$

We further anticipate that for safe strategies the fraction of currently infected people $i(t)$ does not vary strongly over time. More precisely, it hovers around the value i^* defined in equations (19b) and (20d) (see figure 2). We thus insert

$$N_{\iota,1} \approx N_{\iota,2} \approx r\, i(t_\iota)\,\Delta t/2 \approx r\, i^*\,\Delta t/2 \tag{17b}$$

into equation (14b) and solve for Δt. The solution is the time until the next intervention

$$\Delta t_\iota \equiv t_{\iota+1} - t_\iota = \frac{(4\,\alpha)^{2/3}}{(k_\iota^2\, r\, i^*)^{1/3}}, \tag{17c}$$

from which we deduce the relative increase

$$\begin{aligned}\frac{i(t_{\iota+1})}{i(t_\iota)} &\equiv \exp\left(k_\iota\,\Delta t_\iota\right) \\ &= \exp\left(\mathrm{sgn}(k_\iota)\,(4\,\alpha)^{2/3}\left(\frac{|k_\iota|}{r\, i^*}\right)^{1/3}\right)\end{aligned} \tag{17d}$$

of the fraction of currently infected people over the time window. This relative increase is close to 1 if the argument of the exponential on the right-hand side is small.

We will show below that the characteristics

$$\Delta t_1 = \frac{(4\,\alpha)^{2/3}}{(k_1^2\, r\, i^*)^{1/3}}, \tag{18a}$$

and

$$\frac{i(t_2)}{i(t_1)} = \exp\left((4\,\alpha)^{2/3}\left(\frac{k_1}{r\, i^*}\right)^{1/3}\right) \tag{18b}$$

of the first time interval $[t_1, t_2]$ set the relevant scales for the entire process. From equations (17c) and (17d), we infer the following important result. The higher the testing frequency r, the smaller the typical variations in the fraction of currently infected

people, and thus in the case numbers. The band width of fluctuations decreases as $r^{-1/3}$ with the testing rate.

6.3.1. Critical prevalence

As one should expect, it is always the average rate to detect a currently infected person, $r\,i^*$, which enters into the expressions (17c) and (17d). The higher the prevalence i^*, the more reliable is the sampling, the shorter is the time to converge toward the marginal state (9), and the smaller are the fluctuations of the fraction of infected people.

If i^* is too low the statistical fluctuations become too large and little statistically meaningful information can be obtained. On the other hand, if the fraction of infections drops to much lower values, then policy can be considered to have been successful and can be maintained until further tests show otherwise.

We seek an upper bound for a manageable i^*. Here we consider the parameters of Switzerland. However, they can easily be adapted to any other country. We assume that a fraction $p_{\mathrm{ICU}}^{\mathrm{CH}}$ of infected people in Switzerland needs to be in intensive care[11]. Here, we will use the value $p_{\mathrm{ICU}}^{\mathrm{CH}} = 0.05$. Let ρ_{ICU} be the number of ICU beds per inhabitant that shall be allocated to COVID-19 patients. The Swiss national average is about [32]

$$\rho_{\mathrm{ICU}}^{\mathrm{CH}} \approx \frac{1200}{8'500'000} \approx 1.4 \times 10^{-4}. \tag{19a}$$

For the pandemic not to overwhelm the health system, one thus needs to maintain the prevalence safely below

$$i(t) \leqslant i_{\mathrm{c}} = \frac{\rho_{\mathrm{ICU}}^{\mathrm{CH}}}{p_{\mathrm{ICU}}^{\mathrm{CH}}} = 0.0028, \tag{19b}$$

together with similar constraints related to the capacity for hospitalizations, medical care personnel and equipment for specialized treatments. We take the constraint from intensive care units to obtain an order of magnitude for the upper limit admissible for i. A study dated April 10 2020 based on random testing reports that the fraction of people infected with the virus in early April was within the confidence interval $[0.0012, 0.0076]$ in Austria (whereby half of the infected people in the sample were previously undetected) [33]. The estimates in reference [4] suggest that the fraction of acutely infected people was even close to 0.01 before the lock-down of 16 March 2020 in Switzerland. This indicates that our threshold estimate (19b) is conservative. If the actual threshold (which depends on the country, the structure of its population, and its health-care infrastructure) is higher, the testing frequency required to reach a defined accuracy decreases in proportion.

The objective is to mitigate the pandemic so that values of the order of i_{c} or below are achieved. Before that level is reached restrictions cannot be relaxed. It may prove difficult to push the fraction of infected people significantly below i_{c}, since the recent experience in most European countries suggests that it takes a lot of effort to keep growth rates k well below 0. The main aim would then be to reach at least stabilization of the number of currently infected people ($k = 0$).

For the following we thus assume that the prevalence i will stagnate around a value i^* of the order of i_{c}. We will discuss below what ratio i^*/i_{c} can be considered safe.

6.4. Required testing rate

We seek the testing rate needed for a strategy with satisfactory outcome. We assume that after the reboot at $t_1 = 0$, the initial growth rate may turn out to be fairly high, say of the order of the unmitigated growth rate. In many European countries a doubling of cases was observed every 3 days before restrictive measures were introduced. This corresponds to a growth rate of

$$k_0 = \frac{\ln(2)}{3\ \mathrm{days}} \approx 0.23\ \mathrm{day}^{-1}. \tag{20a}$$

We assume an initial growth rate of

$$k_1 = 0.1\ \mathrm{day}^{-1} \tag{20b}$$

just after the reboot, which corresponds to an effective reproduction number of $R_{\mathrm{eff}} = \exp(4\,k_1) \approx 1.49$. For the simulation of a long-term strategy we choose the rather high confidence parameter

$$\alpha = 3. \tag{20c}$$

In section 7, we will find that this choice strikes a good balance between several performance criteria in the longer term (see figure 6). In contrast, when the focus is on preventing damage on short time scales after a release, as discussed in section 2, a smaller value $\alpha \approx 1$ is more appropriate. We further assume that the rate of infections initially stagnates at a level of (for Switzerland)

$$i^* = \frac{i_{\mathrm{c}}}{4} \approx 0.0007. \tag{20d}$$

We estimate that this prevalence level is presumably smaller by a factor of 2–4 than the level that one expects under the incidence conditions for which Germany recommends to take restrictive interventions again[12].

[11] More precisely, $p_{\mathrm{ICU}}^{\mathrm{CH}}$ is the expected time (in Switzerland) for an infected person to spend in an intensive care unit (ICU) divided by the expected time to be sick.

[12] Germany recommends to consider global interventions once 50 confirmed cases per 100 000 residents are recorded weekly. With an infectious time of the order of a week, this corresponds to a prevalence of symptomatic infectious people of $i_{\mathrm{sym}}^D \approx 0.0005$, which is of the same order as the level we assumed in equation (20d) for our simulation. However, since the total number of people that had the disease is known from antibody tests to be a factor of 5–10 higher than the confirmed cases, the threshold value i_{sym}^D of symptomatic incidence will more likely correspond to an actual total prevalence of $i_{\mathrm{sym}}^D = 0.002 - 0.005 > i^*$.

A minimal requirement is that the first relative increase of

$$\frac{i(t_2)}{i(t_1)} = \frac{i(t_2)}{i(0)} \tag{20e}$$

does not exceed a factor of $i_c/i^* = 4$. From equation (18b), we thus obtain the minimal number of daily tests

$$r \geqslant r_{\min} \equiv \frac{(4\,\alpha)^2}{(\ln 4)^3}\,\frac{k_1}{i^*} \approx 7'700 \text{ day}^{-1} \tag{21}$$

for the assumed parameters, including the rather large value of $\alpha = 3$ and k_1. Note in particular the inverse proportionality to the parameter i^*, for which equation (20d) is a conservative estimate. Using this value yields an estimate of the order of magnitude required for Switzerland. In section 7 we simulate a full mitigation strategy and confirm that with additional capacity for just about 15′000 non-symptomatic infection tests per day a nation-wide, safe reboot can be envisioned under such conditions.

We close with two observations. First, this minimal testing frequency is just twice the testing frequency presently available for suspected infections and medical staff in Switzerland. Second, while the latter tests require a high sensitivity with as few false negatives as possible, non-symptomatic testing, whose purpose is statistical analysis, can very well be carried out with tests of lower quality in that respect. Indeed, an increase in false negatives acts as a systematic error in the estimate of the infected fraction of people, which, however, drops out in the determination of its growth rate[13], as long as the prevalence i is not close to 1. However, the success of random testing does rely on a very low probability ($\ll i^*$) of false positives (as is the case of current PCR tests). Otherwise the signal from true positives would rapidly be overwhelmed by the noise from false positives.

6.5. Further intervention steps after the reboot

After the reboot at time $t_1 = 0$ further interventions will be necessary, as we assume that the reboot will have resulted in a positive growth rate k_1. In subsequent interventions, the policymakers try to take measures that aim at reducing the growth rate to zero. Even if they had perfect knowledge of the current growth rate $k(t)$, they would not succeed immediately since they do not know the precise quantitative effect of the measures they will take. Nevertheless, had they complete knowledge of $k(t)$, our model assumes that they would be able to gauge their intervention such that the actual effect on $k(t)$ differs at most by a factor between b and $1/b$ from the targeted value, which would reduce $k(t)$ to 0. This and the assumption $b \geqslant 0.5$ implies that, if α is large, so that $k(t)$ is known with relatively high precision at the time of intervention, the growth rate k_2 is smaller than k_1 in magnitude with high probability (tending rapidly to 1 as $\alpha \to \infty$)[14]. The smaller α however, the more likely it becomes, that $k(t)$ is overestimated, and an exaggerated corrective measure is taken, which may destabilize the system in the longer term. In this context, we observe that the ratio

$$0 < \rho_\iota \equiv \frac{|k_\iota|}{|k_{\iota-1}|} < \infty \tag{22}$$

is a random variable with a distribution that is independent of ι in our model. To proceed, we assume that α is sufficiently large, such that the probability that $\rho_\iota < 1$ is indeed high.

The second policy intervention occurs after a time that can be predicted along the same lines that lead to equation (17c). One finds

$$\Delta t_2 \approx \Delta t_1 \left(\frac{|k_2|}{|k_1|}\right)^{-2/3}, \tag{23}$$

where Δt_1 is given by equation (18a). Since, the growth rate k_3 is likely to be smaller than k_2 in magnitude, the third intervention takes place after yet a longer time span, etc. If we neglect that the fitted value $k_\iota^{\text{fit}}(t)$ differs slightly from k_ι (a difference that is negligible when $\alpha \gg 1$), our model ensures that $k_\iota/k_{\iota-1}$ is uniformly distributed in $[-1/b+1, 1-b]$. After the ιth intervention the growth rate is down in magnitude to

$$|k_\iota| = |k_0| \prod_{\iota'=1}^{\iota} \rho_{\iota'}. \tag{24}$$

To reach a low final growth rate k_{final}, a typical number $n_{\text{int}}(k_{\text{final}})$ of interventions are required after the reboot, where

$$n_{\text{int}}(k_{\text{final}}) \approx \frac{\ln \frac{|k_{\text{final}}|}{|k_1|}}{\langle \ln\, \rho_\iota \rangle} = C(b)\, \ln \frac{|k_1|}{|k_{\text{final}}|}, \tag{25}$$

where the constant $C(b) = -1/\langle \ln\, \rho_\iota \rangle$ depends on the policy uncertainty parameter b.

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

$$T(k_{\text{final}}) \sim \Delta t_{n_{\text{int}}(k_{\text{final}})} \approx \left(\frac{|k_1|}{|k_{\text{final}}|}\right)^{2/3} \Delta t_1. \tag{26}$$

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

Note, however, that as soon as the expected time interval Δt_ι exceeds the time delay T_D associated with symptomatic testing, one can use the latter to estimate the remaining small growth rate k_ι, since it is based on larger case numbers and might therefore be

[13] If the infected fraction of people is $i(t)$, its growth rate is $\dot{i}(t)/i(t) \equiv k(t)$ with the time derivative of $i(t)$ denoted by $\dot{i}(t)$.

[14] One uses equation (12) to reach this conclusion.

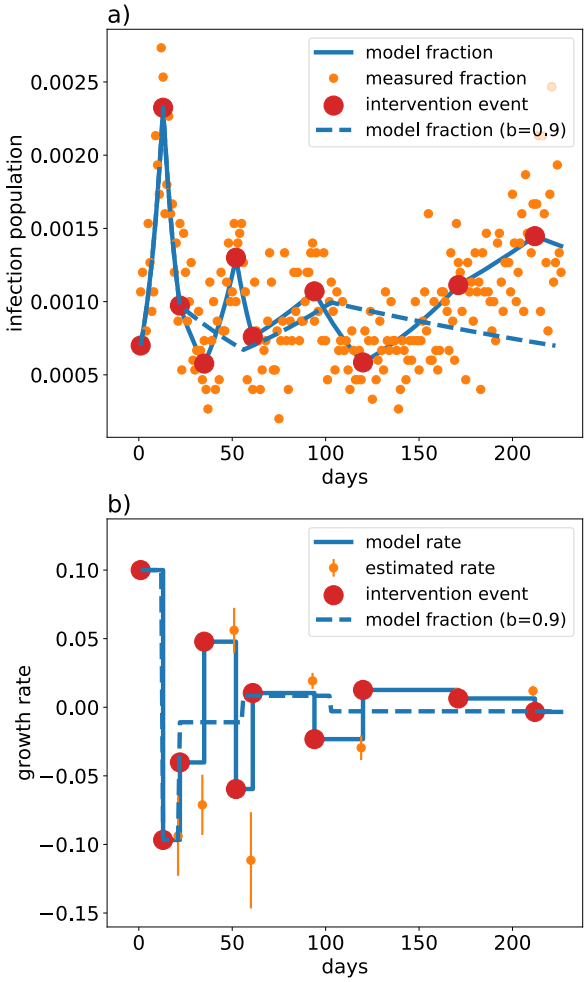

Figure 5. Our algorithm implements policy releases and restrictions aiming at maintaining a vanishing growth rate. It intervenes whenever the estimated slope of the prevalence is found to be non-zero, here with confidence level $\alpha = 3$. We plot the model prevalence $U(t)/N$ and the prevalence $i(t)$ as measured by testing as a function of days in panel (a). The model growth rate $k(t)$ (solid line) and the estimated growth rate k_{est} at times of intervention are shown in panel (b) for the parameters $i(0) = 0.0012$, $k_1 = 0.1$, and a test rate of $r = 15'000\,\text{day}^{-1}$. The dashed blue line corresponds to a history of interventions where we assumed that the effect of policy interventions is better known (described by an uncertainty parameter $b = 0.9$, instead of $b = 0.5$), so that convergence is much faster.

more accurate.[15] Beyond that point, our model, which only assumes non-symptomatic test results as input, merely provides a lower bound on the performance of the mitigation strategy.

6.6. Choosing an optimal intervention strategy

The parameter α encodes the confidence which policymakers need about the present state before they take a decision. Here we discuss various measures that allow choosing an optimal value for α.

As α decreases starting from large values, the time for interventions decreases, being proportional to $\alpha^{2/3}$ according to equation (18a). Likewise the fluctuations of infection numbers will initially decrease. However, the logarithmic average $-\langle \ln \rho_t \rangle$ in the denominator of equation (25) will also decrease, and thus the necessary number of interventions increases. Moreover, when α falls below 1, interventions become more and more ill-informed and erratic. It is not even obvious anymore that the marginally stable state is still approached asymptotically. From these two limiting considerations, we expect

$$\alpha = O(1) \tag{27}$$

to be an optimal choice for α.

Let us now discuss a few quantitative measures of the performance of various strategies, which will allow policymakers to make an optimal choice of confidence parameter for the definition of a mitigation strategy. An optimal strategy might allow α to vary with time, e.g., to take a smaller value of α at the beginning, to prevent potentially large damage, and then increase α later on.

6.6.1. Time scale to approach the marginal state

The time to reach a certain level of quiescence (low growth rates, infrequent interventions) is given by the time (26), and thus by the expectation value of Δt_1.

[15] However, symptomatic case numbers are correlated due to testing carried out due to contact tracing. They also reflect the readiness of people to get tested, as well as the provided testing frequency, which both evolve with time.

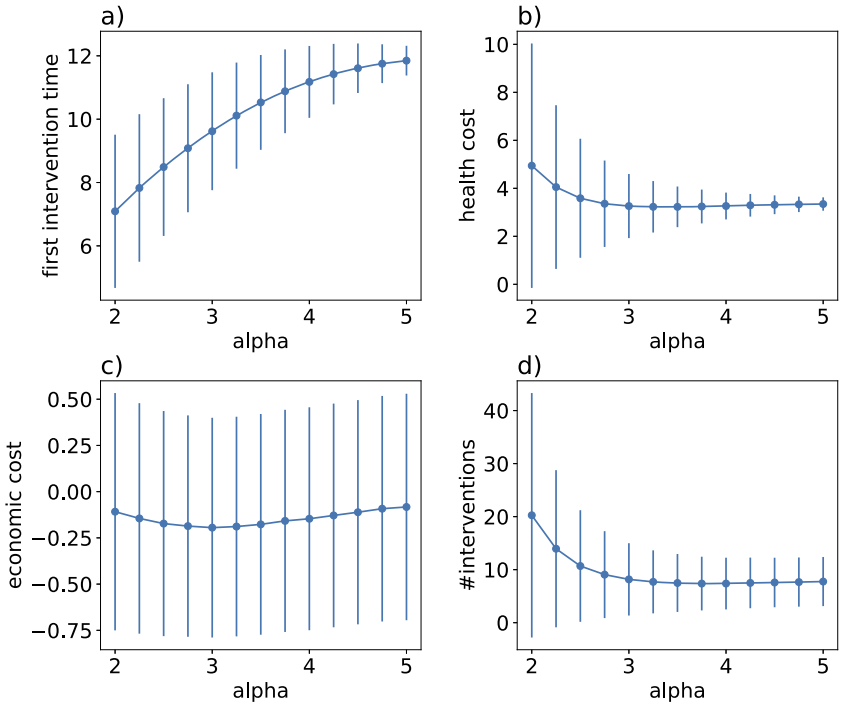

Figure 6. Performance of the mitigation strategy as a function of the confidence parameter α, for a number $r = 15'000$ tests per day and an initial growth rate $k_1 = 0.1$. We plot the time scale Δt_1 (a), and the health (b), economic (c) and political (as measured by numbers of interventions to achieve a steady state) (d) costs (equations (28)–(30)) as measures of performance. The circles are the mean values, the vertical lines indicate the standard deviations of the respective quantities.

6.6.2. Political cost

As a measure for the political cost, C_P, we may consider the number of interventions that have to be taken to reach quiescence. As we saw in equation (25), it scales inversely with the logarithmic average of the ratios of growth rates, ρ, i.e.,

$$C_P \propto \left(\langle -\ln \rho_\iota \rangle\right)^{-1}. \tag{28}$$

6.6.3. Health cost

If restrictions are over-relaxed, the infection numbers will grow with time. The maximal fraction of currently infected people must never be allowed to rise above the manageable threshold of i_c. If one continuously monitors the prevalence by non-symptomatic testing, and given that from the time before the reboot one knows conditions under which the system can be stabilized, the latter could always be re-imposed at a time sufficient to prevent reaching the level of i_c. Beyond this consideration one may want to keep the expected maximal increase of infection numbers low, which we take as a measure of health costs C_H,

$$C_H \equiv \max_t \left\{ \frac{i(t)}{i(0)} \right\}. \tag{29}$$

Note that as defined, C_H is a stochastic number. Its mean and tail distribution (for large R) will be of particular importance.

6.6.4. Economic and social cost

Imposing restrictions such that $k < 0$ imply restrictions beyond what is absolutely necessary to maintain stability. If we assume that the economic cost C_E is proportional to the excess negative growth rate, $-k$ (and a potential gain proportional to k), one possible measure for the economic cost is the summation over time of $-k(t)$,

$$C_E \propto -\int_0^\infty \mathrm{d}t\, k(t), \tag{30}$$

which converges, since $k(t)$ decays as a sufficiently fast power law. Hereto, C_E is a stochastic variable that depends on the testing history and the policy measures taken. However, its mean and standard deviation could be used as indicators of economic performance.

7. Simulation of mitigation strategy by random testing

We introduced in section 6 a feedback and control strategy to tune to a marginal state with vanishing growth rate $k = 0$ after an initial reboot. Interventions were only taken based on the measurement of the growth rate. However, in practice, a more refined strategy will be needed. In case the infection rate drops significantly below i^*, one might (depending on netting out political and economic pressures, something which the authors of this paper are not doing here) benefit from a positive growth rate k. We thus assume that if $i(t)/i^*$ falls below some threshold $i_{low} = 0.2$, we intervene by relaxing some measures,

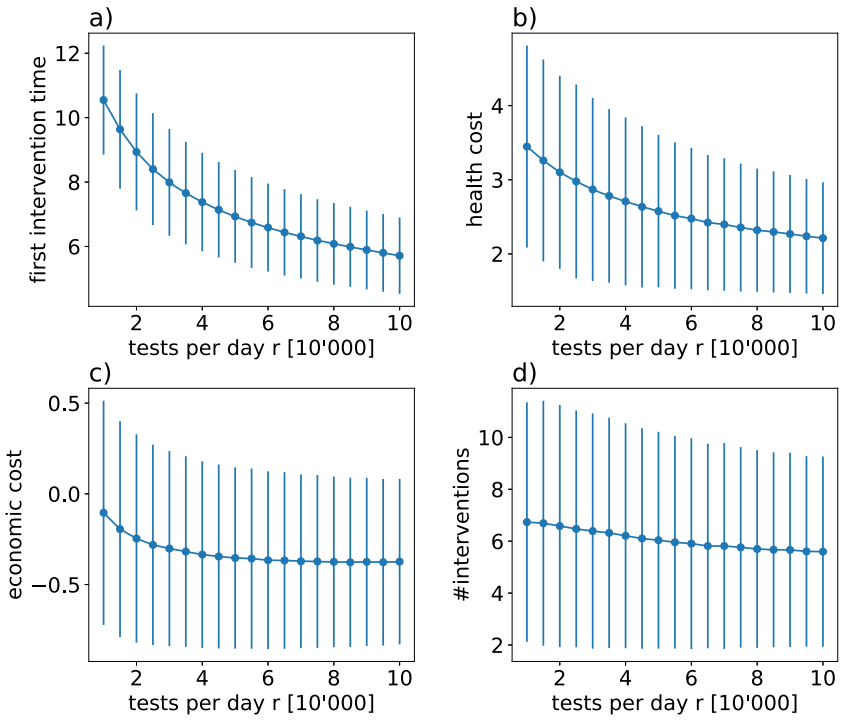

Figure 7. Performance of the mitigation strategy as a function of the number of tests r per day, for a fixed value of $\alpha = 3$ and an initial growth rate $k_1 = 0.1$. We plot the time scale Δt_1 (a), and the health (b), economic (c) and political (as measured by numbers of interventions to achieve a steady state (d) costs (equations (28)–(30)) as measures of performance. The circles are the mean values, the vertical lines indicate the standard deviations of the respective quantities. The large uncertainties in the economic costs, e.g., are a consequence of the relatively large uncertainty in the effect of interventions ($b = 0.5$). If the latter is better known, the standard deviation of the cost functions will decrease accordingly.

that we assume to increase k by an amount uniformly distributed in $[0, k_1]$, but without letting k exceed the maximal value of $k_{\text{high}} = 0.23$. Likewise, one should intervene when the fraction $i(t)$ grows too large. We do so when $i(t)/i^*$ exceeds $i_{\text{high}} = 3$. In such a situation we impose restrictions resulting in a decrease of k by a quantity uniformly drawn from $[k_{\text{high}}/2, k_{\text{high}}]$. The precise algorithm is given in the supplementary information (https://stacks.iop.org/J/00/000000/mmedia).

Figure 5 shows how our algorithm implements policy releases and restrictions in response to test data. The initial infected fraction and growth rate are $i(0) = i_c/4 = 0.0007$ and $k_1 = 0.1$, respectively, with a sampling interval of one day. We choose $\alpha = 3$ and a number of $r = 15'000$ tests per day. Figure 5(a) displays the fraction of undetected infectious people, $U(t)/N$, as a function of time, derived using our simple exponential growth model, which is characterized by a single growth rate that changes stochastically at interventions [equation (10) without the source term]. In the absence of intervention, the infected population would grow rapidly representing uncontrolled runaway of a second wave. At each time step (day) the currently infected fraction of the population is sampled. The result is assumed to be normally distributed with mean and standard deviation given by equations (11e) and (11f) to obtain $i(t)$. The former are represented by small circles, the latter by vertical error bars in figure 5. If i/i^* lies outside the range $[i_{\text{low}}, i_{\text{high}}]$, we intervene as described above. Otherwise, on each day $k^{\text{fit}}(t)$ and its standard deviation are estimated using the data since the last intervention. With this, at each time step, equations (11m) to (11o) decide whether or not to intervene. In figure 5, each red circle represents an intervention and therefore either a decrease or increase of the growth rate constant of our model.

Figure 5 shows the evolution of the fraction of currently infectious people (the prevalence). After an initial growth with rate k_1 subsequent interventions reduce the growth rate down to low levels within a few weeks. At the same time the fraction of infectious people stabilizes at a scale similar to i^*. For the given parameter-set this is a general trend independent of realization. Figure 5(b) displays the instantaneous value of the model rate constant and also the estimated value together with its fitting uncertainty. The estimate follows the model value reasonably well. One sees that the interventions occur when the uncertainty in k is sufficiently small.

7.1. Simulation results

We now assume that we have the capacity for $r = 15'000$ per day, and assess the performance of our strategy as a function of the confidence parameter α in

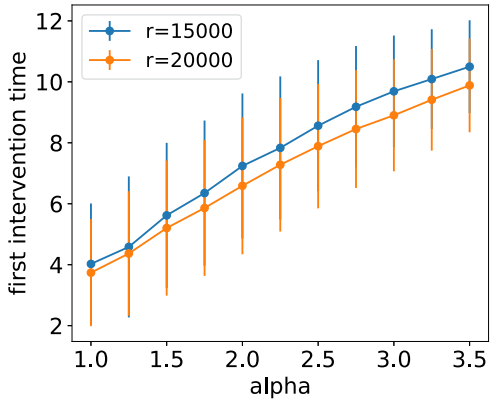

Figure 8. Time after which a significant positive growth rate is confirmed in the worst case scenario for which the growth rate jumps to $k_1 = 0.23$ after reboot. An intervention will be triggered in 3–4 days, since in the case that such a strong growth must be suspected, one should apply a small confidence parameter $\alpha \approx 1$. Results are shown for $r = 15'000$ and $r = 20000$ tests a day. The circles are the mean values, the vertical lines indicate the standard deviations for the first intervention time.

figure 6. Values of $\alpha \leqslant 2$ lead to rapid, but at the same time not very accurate interventions, as is reflected by their rapidly growing number. For larger values of α, the time scale to reach a steady state increases while the economic and health costs remain more or less stable. A reasonable compromise between minimizing the number of interventions, and shortening the time to reach a steady state suggests a choice of $\alpha \approx 2.5$–3.5.

It is intuitive that the higher the number r of tests per day is, the better the mitigation strategy will perform. The characteristic time to reach a final steady state decreases as $r^{-1/3}$, see equation (18a). Other measures for performance improve monotonically upon increasing r. This is confirmed and quantified in figure 7, where we show how the political, health, and economic cost decreases with increasing test rate.

7.1.1. Time delay to detect catastrophic growth rates

After a reboot it is likely that the growth rate k_1 jumps back to positive values, as we have always assumed so far. The time it takes until one can distinguish a genuine growth from intrinsic fluctuations due to the finite number of people sampled depends on the growth rate k_1, see equation (18a).

In the worst case where the reboot brings back the unmitigated value k_0, one will know within 3–4 days with reasonable confidence that the growth rate is well above zero. This is shown in figure 8. In such a catastrophic situation, an early intervention can be taken, while the number of infections has at most tripled at worst. Note that this reaction time is 3–4 times faster than without non-symptomatic testing.

8. Regionally refined reboot and mitigation strategies

We have argued that a daily testing rate r of the order of 10 000 tests per day is sufficient to obtain statistical information on the growth rate k as applied to Switzerland as a whole. This assumes tacitly that the simple growth equation (10) describes the dynamics of infections in the whole country well. That this is not necessarily a good description can be conjectured from data on the rates with which numbers of confirmed infections in the various cantons (states of Switzerland) evolved close to the peak of the first wave, and during the lockdown. These data showed a non-negligible spread suggesting that a spatially resolved approach is preferable, if possible.

If the testing capacity is limited by rates of order $r_{\min}$, the approach can still be used. But caution should be taken to account for spatial fluctuations corresponding to hot spots. One should preferentially test in areas that are likely to show the largest local growth rates so as not to miss locally super-critical growth rates by averaging over the entire country. If however, higher testing frequencies become available, new and better options come into play.

8.1. Partitioning the country for statistical analysis

Valuable information can be gained by analyzing the test data not only for Switzerland as a whole, but by distinguishing different regions.

It might even prove useful not to lift restrictions homogeneously throughout the country, but instead to vary the set of restrictions to be released, or to adapt their rigor. By way of example, consider that after the spring or summer break schools start in different calendar weeks in different cantons. This regional difference could be exploited to probe the relative effect of re-opening schools on the local growth rates k. However, obviously, it might prove politically difficult to go beyond such 'naturally' occurring differences, as it is a complex matter to decide what region releases 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'. Such issues demand careful consideration if regionally varying policies are applied.

Even if policy measures should eventually not be taken in a region-specific manner, it is very useful to study a regionally refined model of epidemic dynamics. Indeed a host of literature exists that studies epidemiological models on lattices and analyzes the spatial heterogeneities [34, 35]. In certain circumstances,

those have been argued to become even extremely strong [36]. In the present paper, we will content ourselves with a few general remarks concerning such refinements. We reserve a more thorough study of regionally refined testing and mitigation strategies to subsequent work.

Let us thus group the population of Switzerland into G sets. The most natural clustering is according to the place where people live, cities or counties[16]. The more we partition the country, the more spatially refined the acquired data will be, and the better tailored mitigation strategies could potentially become. However, this comes at a price. Namely, for a limited national testing rate r_{tot}, an increased partitioning means that the statistical uncertainty to measure local growth rates in each region will increase. This limitation would not apply, however, to statistical testing based on sewage water analysis [9–11]. The latter would become a promising tool once it can be shown to be a sufficiently reliable and stable indicator of the prevalence of infectious people within the area covered by the waste water plant.

The minimal test rate r_{min} such as the estimate of equation (21) still holds, but now for each region, which can only test at a rate $r = r_{\text{tot}}/G$. To refine Switzerland into G regions we thus have the constraint that the total testing capacity exceed $G\,r_{\text{min}}$. If testing at a high daily rate r_{tot} indeed becomes available, the statistical analysis should be refined to $G \approx r_{\text{tot}}/r_{\text{min}}$ to make the best use of available data.

8.2. Spatially resolved growth model

Each of the population groups $m \in \{1, \ldots, G\}$ is assumed to have roughly the same size, containing

$$N_m \approx \frac{N_{\text{CH}}}{G} \tag{31}$$

people, U_m of whom are currently infectious, but yet undetected. The spreading of infections is again assumed to follow a linear growth equation (where we neglect influx from across the borders from the outset)

$$\left(\frac{\mathrm{d}U_m}{\mathrm{d}t}\right)(t) = \sum_{n=1}^{G} K_{mn}(t)\,U_n(t), \quad m = 1, \ldots, G. \tag{32}$$

Here, the growth kernel $K(t)$ is an *a priori* non-symmetric $G \times G$ matrix with matrix elements $K_{mn}(t)$. The matrix $K(t)$ has G (generically distinct, complex valued) eigenvalues λ_n, $n = 1, \ldots, G$. The largest growth rate is given by

$$\kappa(t) \equiv \max_{1 \leqslant n \leqslant G} \left\{\mathrm{Re}\,\lambda_n(t)\right\}. \tag{33}$$

[16] One might also consider other distinguishing characteristics of groups (age or 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.

For the sake of stability criteria, $\kappa(t)$ now essentially takes the role of $k(t)$ in the model with a single region, $G = 1$. We note that the number of infections grows exponentially if $\kappa(t) > 0$, and decreases if $\kappa(t) < 0$.

As in the case of a single region, we assume $K(t)$ to be piecewise constant in time, and to change only upon taking policy interventions.

In the simplest approximation, one assumes no contact between geographically distinct groups, that is, the off-diagonal matrix elements are set to zero $[K_{m\neq n}(t) = 0]$ and the eigenvalues become equal to elements of the diagonal: $k_m(t) \equiv K_{mm}(t)$. As current cantonal data suggests, the local growth rate $k_m(t)$ depends on the region, and thus $k_m(t) \neq k_n(t)$. It is natural to expect that $k_m(t)$ correlates with the population density, the fraction of the population that commutes, the age distribution, etc.

If on top of the heterogeneity of growth rates one adds finite but weak inter-regional couplings $K_{m\neq n}(t) > 0$ (mostly between nearest neighbor regions), one may still expect the eigenvectors of $K(t)$ to be rather localized (a phenomenon well known as Anderson localization [28] in the context of waves propagating in strongly disordered media). By this, one means that the eigenvectors have a lot of weight on few regions only, and little weight everywhere else. That such a phenomenon might occur in the growth pattern of real epidemics is suggested by the significant regional differences in growth rates that we have mentioned above. In such a situation it would seem preferable to adapt restrictive measures to localized regions with strong overlap on unstable eigenvectors of $K(t)$, while minimizing their socio-economic impact in other regions with lower $k_m(t)$.

8.3. Mitigation strategies with regionally refined analysis

As mentioned above, in the case with several distinct regions, $G > 1$, an intervention becomes necessary when the largest eigenvalue $\kappa(t)$ of $K(t)$ crosses an upper or a lower threshold (with a level of confidence α again to be specified). If the associated eigenvector is delocalized over all regions, one will most likely respond with a global policy measure. However, it may as well happen that the eigenvector corresponding to $\kappa(t)$ is well-localized. In this case one can distinguish two strategies for intervention:

(a) **Global strategy.** One always applies a single policy change to the whole country. This is politically simple to implement, but might incur unnecessary economic cost in regions that are not currently unstable.

(b) **Local strategy.** One applies a policy change only in regions which have significant weight on the unstable eigenvectors. This means that one only adjusts the corresponding diagonal matrix

elements of $K(t)$ and those off-diagonals that share an index with the unstable region.

Likewise, regions that have $i_m < i^*$ and have negligible overlap with eigenvectors whose eigenvalues have real parts above κ_-, could relax some restrictions before others do.

Fitting test data to a regionally refined model will allow us to estimate the off-diagonal terms $K_{mn}(t)$, which are so far poorly characterized parameters. However, the $K_{mn}(t)$ contain valuable information. For instance, if a hot spot emerges [that is, a region overlapping strongly with a localized eigenvector with positive $\mathrm{Re}\,\lambda_n(t)$], this part of the matrix will inform which connections are the most likely to infect neighboring regions. They can then be addressed by appropriate policy measures and will be monitored subsequently, with the aim to contain the hot spot and keep it well localized.

This model allows us to calculate again economic, political, and health impact of various strategies. It is important to assess how the global and the local strategy perform in comparison. Obviously this will depend on the variability between the local growth rates $k_m(t)$, which is currently not well known, but will become a measurable quantity in the future. At that point one will be able to decide whether to select the politically simpler route (a) or the heterogeneous route (b) which is likely to be economically favorable.

9. Summary and conclusion

We have analyzed a feedback and control model for managing a pandemic such as that caused by COVID-19. The crucial output parameters are the infection growth rates in the general population (or in a pre-selected cohort) and spatially localized subpopulations. When planning for an upcoming reboot of the economy, it is essential to assess and mitigate the risks of relaxing some of the restrictions that have brought the COVID-19 epidemic under control. In particular, the policy strategy chosen must suppress a potential second exponential wave when the economy is rebooted, and so avoid a perpetual stop-and-go oscillation between relaxation and lockdown. Feedback and control models are designed with precisely this goal in mind.

Having testing for non-symptomatic but infectious cases in place, the risk of a second wave can be kept to a minimum upon relaxation of restrictions or as the winter season approaches. Additional testing capacity of $r = 15'000\ \mathrm{day}^{-1}$ tests (on top of the current tests for medical purposes) carried out—either with randomly selected people or a large cohort, preferentially of exposed key workers, for whom preventive testing is beneficial anyway—would allow us to follow the course of the pandemic almost in real time, with shorter time delays, and without the danger of increasing the prevalence by more than a modest factor of 3–4, if our intervention strategy is followed.

We recall that our estimate of r assumed a certain level of prevalence, i^*, see equation (19b), which is higher than current levels in many European countries, but smaller than the alarm threshold at which Germany recommends to resume wide-spread interventions. It is even significantly smaller than the manageable prevalence in Switzerland. At those higher prevalences, the required testing rates would even be several times smaller than the estimates we gave.

If testing rates r significantly higher than $r_{\min}$ become available, a regionally refined analysis of the growth dynamics can be carried out, with $G \approx r/r_{\min}$ regions that can be distinguished.

In the worst case scenario, where releasing certain measures immediately makes the country jump back to the unmitigated growth rate of $k_0 = 0.23\ \mathrm{day}^{-1}$, non-symptomatic testing would detect this within 3–4 days from the change coming into effect. This is to be contrasted with the delay of 8–12 days required for symptomatic individuals to emerge in statistically significant numbers. After such a time delay, a prevalence increase by a factor of order 10 may have already occurred. Daily testing for non-symptomatic but infectious cases can significantly diminish such an increase. Thereby the significant reduction of the time delay is absolutely crucial. Note that without daily polling of infections and without knowledge about the quantitative effect of restriction measures, a reboot of the economy is more risky. It thus requires a longer time under lockdown conditions to bring down the prevalence to a level where a reboot will be safe even with a longer reaction time.

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Appendix A. Algorithm to simulate mitigation of reboot

A.1. Definitions

- $t = 1, 2, \ldots$: time in days (integer).
- n_{int}: number of interventions (including the reboot at $t = 1$).
- $t_{\mathrm{int}}(j)$: first day on which the jth rate k_j applies. On day $t_{\mathrm{int}}(1) \equiv 1$ the initial reboot step is taken.
- $\Delta t(j) = t_{\mathrm{int}}(j+1) - t_{\mathrm{int}}(j)$: time span between interventions j and $j+1$.

- t_{first}: first day on which the current rate $k = k(t)$ is applied.
- $i(t)$: fraction of infected people on day t.
- $k(t)$: growth rate on day t.
- r: number of tests per day.
- C_{H}: health cost.
- C_{E}: economic cost.
- $k_{\min} = 0.005$: minimal growth rate targeted.
- $i_{\text{low}} = 0.2$: lower threshold for i/i^*. If $i/i^* < i_{\text{low}}$, a relaxing intervention is made, irrespective of the estimate of k.
- $i_{\text{high}} = 3$: upper threshold for i/i^*. If $i/i^* > i_{\text{high}}$, an intervention is made even if k is still smaller than $\alpha\delta k$.
- $k_{\text{low}} = -0.1$: minimal possible decreasing rate considered.
- $k_{\text{high}} = 0.23$: maximal possible increasing rate considered.
- $T_{\min} = 3$: minimal time to wait since the last intervention, for interventions based on the level of $i(t)$.
- b: parameter defining the possible range of changes Δk due to measures taken after estimating k. $|\Delta k/k_{\text{est}}| \in [b, 1/b]$. Usually we set $b = 0.5$.
- α: confidence parameter.
- $N(t)$: cardinality of random sample of infected people on day t. The number $N(t)$ is obtained by sampling from a Gaussian distribution of mean $i(t)r$ and standard deviation $\sqrt{i(t)\,r}$ and rounding the obtained real number to the next non-negative integer.

A.2. Initialization

- $t_{\text{first}} = t_{\text{int}}(1) = 1$.
- $n_{\text{int}} = 1$.
- $C_{\text{H}} = 1$.
- $C_{\text{E}} = 0$.
- $k(1) = k_1 = 0.1$. (Initial growth rate)
- $i(1) = i^*$. Common choice $i^* = i_{\text{c}}/4 = 0.0007$.
- Draw $N(1)$.
- $k(2) = k(1)$. (No intervention at the end of day 1).
- Set $t = 2$.

A.3. Daily routine for day t

Define $i(t) = i(t-1)\mathrm{e}^{k(t-1)}$,

Define $C_{\text{H}} = \max\{C_{\text{H}}, i(t)/i^*\}$,

Define $C_{\text{E}} = C_{\text{E}} - k(t)$.

Draw $N(t)$.

Determine what will be $k(t+1)$, by assessing whether or not to intervene:

If $t = t_{\text{first}}$, **then** $k(t+1) = k(t)$. (No intervention)

Else Distinguish three intervention cases:

(a) **If** $i(t)/i^* < i_{\text{low}}$ and $t - t_{\text{first}} \geqslant T_{\min}$, **then** $k(t+1) = \min\{k(t) + x\,k_1, k_{\text{high}}\}$ with $x = \text{Unif}[0,1]$.

(b) **ElseIf** $i(t)/i^* > i_{\text{high}}$ and $t - t_{\text{first}} \geqslant T_{\min}$, **then** $k(t+1) = \max\{k(t) - (1+x)/2\,k_{\text{high}}, k_{\text{low}}\}$ with $x = \text{Unif}[0,1]$.

(c) **ElseIf** $i_{\text{low}} < i(t)/i^* < i_{\text{high}}$, **then**

- Set $\Delta t \equiv t - t_{\text{first}} + 1$
- Compute $k_{\text{est}}(t_{\text{first}}, \Delta t)$, and $\delta k_{\text{est}}(t_{\text{first}}, \Delta t)$ using appendix A.4.

If $|k_{\text{est}}| > k_{\min}$
AND
$\left[k_{\text{est}} > \alpha\,\delta k_{\text{est}}\,\textbf{OR}\,k_{\text{est}} < -\alpha\,\delta k_{\text{est}}\right]$,
set
$k(t+1) = k(t) - x\,k_{\text{est}}$
with $x = \text{Unif}[b, 1/b]$.
If $k(t+1) > k_{\text{high}}$, put $k(t+1) = k_{\text{high}}$.
If $k(t+1) < k_{\text{low}}$, put $k(t+1) = k_{\text{low}}$.

(d) **Else** $k(t+1) = k(t)$

$t = t + 1$.

If an intervention was taken above:

- Put $n_{\text{int}} = n_{\text{int}} + 1$.
- Define $t_{\text{int}}(n_{\text{int}}) = t + 1$.
- Define $\Delta t(n_{\text{int}} - 1) = t_{\text{int}}(n_{\text{int}}) - t_{\text{int}}(n_{\text{int}} - 1)$.
- Set $t_{\text{first}} = t + 1$.

If $|k_{\text{est}}| < k_{\min}$ **AND** $k(t) < k_{\min}$ **AND** $t - t_{\text{first}} > 10$, **then** EXIT.

Else return to daily routine for next day.

A.4. Estimate of $k(t, \Delta t)$

Computing $k_{\text{est}}(t_{\text{first}}, \Delta t)$ and $\delta k_{\text{est}}(t_{\text{first}}, \Delta t)$:

If Δt is even:
Define
$N_1 = \sum_{m=0}^{\Delta t/2-1} N(t_{\text{first}} + m)$,
$N_2 = \sum_{m=0}^{\Delta t/2-1} N(t_{\text{first}} + \Delta t/2 + m)$.

- **If** $N_1\,N_2 > 0$, **then**
$k_{\text{est}} = \frac{2}{\Delta t}\ln\left(\frac{N_2}{N_1}\right)$,
$\delta k_{\text{est}} = \frac{2}{\Delta t}\sqrt{\frac{1}{N_2} + \frac{1}{N_1}}$.
- **Else** return
$k_{\text{est}} = 0$,
$\delta k_{\text{est}} = 1000$.

If Δt is odd:
Define
$N_1' = \sum_{m=0}^{(\Delta t-1)/2-1} N(t_{\text{first}} + m)$,
$N_m = N(t_{\text{first}} + (\Delta t - 1)/2)$,
$N_2' = \sum_{m=0}^{(\Delta t-1)/2-1} N(t_{\text{first}} + (\Delta t + 1)/2 + m)$,
$N_1 = N_1' + N_m$,
$N_2 = N_2' + N_m$.

- **If** $N_1\,N_2 > 0$, **then**
$k_{\text{est}} = \frac{2}{(\Delta t-1)}\ln\left(\frac{N_2'+N_m}{N_1'+N_m}\right)$,
$\delta k_{\text{est}} = \frac{2}{(\Delta t-1)}\sqrt{\frac{N_2'}{N_2^2} + \frac{N_1'}{N_1^2} + N_m\left(\frac{1}{N_2} - \frac{1}{N_1}\right)^2}$.
- **Else** return

$k_{est} = 0$,
$\delta k_{est} = 1000$.

A.5. Observables

Time to first intervention: $\Delta t(1)$
Health cost: C_H
Political cost: n_{int}
Economic cost C_E

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