Impact of vaccination and non-pharmaceutical interventions on SARS-CoV-2 dynamics in Switzerland

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Abstract

As countries increase vaccination coverage against SARS-CoV-2, amidst the emergence and spread of more infectious and potentially more deadly variants of concern, they need to make decisions on the timing and extent of relaxing effective, but unsustainable, non-pharmaceutical interventions (NPIs). We used a mathematical model to compare the impact of various vaccination and NPI strategies on the SARS-CoV-2 epidemic in Switzerland.

We developed a new individual-based model of SARS-CoV-2 dynamics, OpenCOVID, that captures key biological and epidemiological dynamics, population demographic and network structures, seroprevalence levels, and the impact of vaccines and NPIs; as well as new viral variants, seasonal patterns of transmission, and age and risk-group dependent disease progression and severity. Using a Bayesian optimization approach with model emulators, we calibrated the model to data on confirmed cases, hospitalisations, ICU occupancy, and mortality in Switzerland between February 2020 and early March 2021. We simulated various scenarios that captured different vaccination rollouts and relaxation schedules, while considering uncertainty in the transmissibility of new variants, mortality of new variants, vaccine properties and vaccine hesitancy. We analysed the impact of the vaccination and relaxation strategies on confirmed cases, hospitalisations, ICU admissions, and deaths between March and September 2021.

Results suggest that under reference scenarios of increased transmissibility of new variants, any relaxation of NPIs in March 2021 will lead to an increase in cases and consequently more hospitalisations and deaths. Scenarios involving quicker relaxation of NPIs are likely to lead to more person-to-person contact, increased transmission, and hence a larger “third” wave of infections, high ICU occupancy, and deaths in spring and into summer 2021. Faster vaccine rollout can mitigate this third wave to some extent but cannot completely prevent it if relaxation is too fast. Sensitivity analyses suggest that the largest driver of impact of vaccination and NPI relaxation on mortality is the level of increased transmissibility of new variants. Further analysis indicates the recently reported 50% increased mortality of variants of concern will lead to 41-44% extra deaths in the third wave depending on the relaxation and vaccination scenario.

Our model simulations provide scenario outcomes comparing the relative impact of SARS-CoV-2 control strategies over the coming months and should not be considered as future predictions. In the current situation with high uncertainty in the transmissibility of new variants, even with a vaccination rollout that is as fast as possible, a slower and more phased relaxation is more likely to mitigate a potential third wave with high numbers of cases, ICU occupancy, and deaths.

Introduction

Since the emergence of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in Switzerland over 12-months ago, approximately 8,725 deaths were reported by the end of January 2021[1]. The SARS-CoV-2 pandemic has caused a public health and economic crisis worldwide. In response to the first steep increase in cases (the 'first wave') in the spring of 2020, a variety of non-pharmaceutical interventions (NPIs) were introduced, such as physical distancing, facemasks, contact tracing, isolation of contacts, quarantining of confirmed cases, and closure or limited openings of shops and schools. As a result, COVID-19 case numbers, ICU admissions, and deaths decreased prior to the summer of 2020, which led to a relaxation of some NPIs. In October 2020 however, a second wave hit Switzerland, like the rest of Europe, and NPIs were again strengthened[2]. The associated economic and social consequences of NPIs make them unsustainable in the long-term while, at the same time, the emergence of more transmissible SARS-CoV-2 variants has presented new challenges. However, approval and rollout of safe and efficacious COVID-19 vaccines in December 2020 and early 2021 will likely contribute to a substantial reduction in the burden of the pandemic and thus raises possibilities of relaxing current NPIs while protecting the health and wealth of the population. Rollout of these new vaccines in Switzerland raises several questions, including when and how to relax NPIs to best protect its population, while vaccination campaigns proceed?

Mathematical transmission models provide insights to support decision-making regarding various control strategies and public health objectives[3-5]. In this study, we present an individual-based model 'OpenCOVID' which captures SARS-CoV-2 transmission dynamics, including an age-structured population network structure, seasonal patterns, and risk-groups (e.g., elderly and healthcare workers). The model has been calibrated to the SARS-CoV-2 epidemic in Switzerland from 1st February 2020 to 5th March 2021 and captures the introduction and transmission of new variants, and different effects of COVID-19 vaccines.

Using OpenCOVID, we compared multiple vaccine rollout scenarios with several phased NPI relaxation strategies to explore the potential impact and interaction on the future dynamics of SARS-CoV-2 in Switzerland. This present analysis was undertaken in mid-March prior to Federal decisions of a potential relaxation of measures planned on 22nd March. The model was applied at the national level, analysing scenarios over all of Switzerland and it therefore does not model the substantial heterogeneity in/or between cantons. In this study, we stress that the model is not intended to provide future predictions, but rather to allow for the relative comparison of public health outcomes for various vaccine rollout strategies alongside different levels of NPIs. We explored when and how NPIs could be relaxed during different levels of vaccine rollout to prevent or limit a potential 'third wave' surge in confirmed cases, hospitalisations, ICU admissions, and deaths. Importantly, there are other factors in addition to the control measures that can strongly influence the course of the epidemic. Therefore, we also analysed the potential impact on outcomes via sensitivity analysis of 1) the spread of new variants of concern (VOC), for example B.1.1.7 or other VOC with varying assumptions on their transmission advantage and potential increased mortality, 2) different vaccine property profiles with respect to protection from infection or symptom reduction, and 3) levels of vaccine uptake by the population. Future changes or potential developments in the clinical care and the general health of the population were not considered here; nor were potential changes in mass testing or in rates of effective testing, tracing, isolating, and quarantining, or the introduction of new, as of now, unknown interventions.

Results

We developed a new individual-based model of SARS-CoV-2 dynamics, OpenCOVID, that captures key biological and epidemiological dynamics, population demographics and network structures, along with viral variants, seasonal patterns of transmission, disease severity progression by age and risk-group, vaccines, and various NPIs. We calibrated our model to historical national trends in Switzerland of hospital admissions, ICU occupancy, and mortality, up to the 5th of March 2021 (Supplementary Figures S1 and S2, Table S1 for parameter values). Our model accurately captured the past dynamics in Switzerland well, including the first and second wave. Model dynamics estimated that 18-26% of the

Swiss population have been previously exposed by the end of February 2021. Supplementary Figure S3 shows the model calibration for the B.1.1.7 variant[6-8], which we assumed to have increased baseline transmissibility of 60% over the original variant D614G (chosen to fit available data on prevalence in Switzerland[6, 7, 9, 10].). This translates to a relative transmission advantage over January–February 2021 of 1.3–1.4 under existing control measures and existing prevalence in Switzerland.

We used our calibrated model to simulate SARS-CoV-2 dynamics under several vaccination and NPI relaxation scenarios for Switzerland, and compared relative trends in multiple epidemiological outcomes. Specifically, we estimated numbers of daily confirmed cases, ICU occupancy, hospitalisations, and mortality until the end of September 2021. We did not simulate beyond this date due to substantial uncertainty on the duration of natural and vaccine-induced immunity, the role of additional new variants, and changes in NPIs, in adherence, and testing policies. The impact of NPIs was modelled as a reduction in effective contacts, to a level scaled by the Oxford Containment and Health Index[11]. Increase in vaccine coverage was modelled according to priority groups defined by the Swiss Federal Office of Public Health (FOPH), and by comparing faster and slower vaccination rollouts (Figures 2-3). Details of all vaccine scenarios are given in Tables 1 and 2, along with vaccine assumptions.

Our results suggest that under our reference scenarios of increased VOC transmission levels (60%), any relaxation of NPIs in March 2021 (Figures 2 and 3) or April (Figures 4 and 5), whether phased or otherwise, will lead to an increase in infections and hence more hospitalisations and deaths. This is due to a combination of 1) increased rates of human contacts due to relaxed NPIs, 2) the majority of the population being immunologically naïve (i.e., no previous infection or no vaccination), and 3) higher transmissibility of the VOC, leading to an increase of cases. The size of the resulting third wave is strongly dependent on the timing and strength of the relaxations, with faster and stronger relaxations of measures leading to larger third waves. We observed that slower relaxation of NPI measures results in a smaller, but also delayed third wave peak, compared with faster relaxation (Figure 2). If relaxation is too rapid, either in large steps or via quick successive relaxations, then ICU occupancy could become overwhelmed. The size of a potential third wave however can be substantially reduced with faster vaccination by increasing the number of individuals vaccinated per day. We found that increasing vaccination rates from 50,000 to 100,000 per day results in a halved and slightly earlier third wave peak. Furthermore, for the more gradual phased relaxation scenario, this increased vaccination rate results in a 35% reduction in ICU occupancy and deaths until September 2021.

Our results indicate that even if current NPI measures in place in early March are maintained, increased prevalence of VOC, such as B.1.1.7 (assuming increased transmissibility of 60%), are likely to result in an increase in cases, hospitalization, and mortality, even with vaccination (Figures 2 and 3). Even in a relatively unrealistic scenario of no relaxation of NPI through summer 2021, the predicted increase in cases highlights the critical role of VOC currently being transmitted in the community in Switzerland on health outcomes. We stress here that these findings may be sensitive to uncertainties quantities relating to VOCs and vaccinations (this is explored in sensitivity analyses).

We further investigated the impact of delaying relaxation steps by comparing a relaxation on the 22nd of March with the same relaxation step delayed by 3, 6 or 9 weeks (Figure 4). Delaying NPI relaxation can lead to less cases, less morbidity, and less mortality. However, similar gains can also be achieved through a faster vaccination campaign. Scaling up the vaccination in these scenarios allows more flexibility for a faster exit strategy.

For many scenarios, we observe a peak in cases and ICU occupancy in summer followed by a decrease. The initial rise in cases occurs through infections of people who were not previously infected or vaccinated rather than re-infections of previously infected individuals or due to imperfect vaccine efficacy (Supplementary Figure S5). Scenarios involving quicker relaxation of NPIs (Figure 2) lead to more person-to-person contact, increased transmission, and faster population immunity, which along with vaccination, build-up incrementally until the summer of 2021 (Figures 2-3). This also results in a

large wave of infections, high ICU occupancy, and deaths in spring and into summer 2021 (Figures 2-3). The peak in cases occurs when sufficient individuals have vaccine-induced or natural immunity due to infection, such that transmission is largely decreased under NPI measures in place. The subsequent decay in new numbers of daily cases occurs because fewer individuals are susceptible, and the NPI measures in force result in an effective reproductive less than one. It is important to note that when projected estimates increase towards Switzerland's maximum ICU capacity or to the level of death rates as high as observed in previous waves, the predicted trajectories become highly unlikely since alternative measures would most likely be implemented.

We further explored assumptions around increased transmission of VOC, mortality of new variants, vaccine properties, and vaccine hesitancy (Figures 6-7). Over the parameter ranges explored, the largest driver of impact of vaccination and NPI relaxation on mortality was found to be the level of increased transmission of VOC. If new variants are significantly more transmissible than the assumptions explored here, then there is a considerable risk of overwhelming the capacity of the health system. Furthermore, we found that if the new variants have an increased mortality of 50% compared D614G[12, 13], that between 41%-44% more deaths (from March 2021-September 2021) may occur depending on the NPI relaxation strategy and the speed of the vaccination campaign. In the presence of partial onward transmission from individuals who are vaccinated but then become infected (i.e., under a 65% transmission blocking assumption), an even slower relaxation of NPI measures is needed to avoid future restrengthening of measures. This is the case even for the faster vaccination rate. With more vaccine acceptability (90%) among groups P2-P5, more cases are predicted during the third peak of the epidemic, regardless of the speed of vaccination compared with a lower acceptability of 60% (Figure 6). As a result of increased VOC (with increased transmissibility of 60%), more deaths are predicted, even if NPI measures implemented in early March are maintained and vaccines are administered.

Discussion

In this study we demonstrated the use of a new individual-based model, OpenCOVID, to capture national SARS-CoV-2 dynamics in Switzerland between 1st February 2020 and 5th March 2021. We evaluated various vaccine and NPI strategies over the six- to seven-month period from March to September 2021. We analysed the impact of those strategies on confirmed cases, ICU admissions, and deaths, as well as the sensitivity of these epidemiological outcomes to assumptions on the relative transmission advantage or increased mortality of new variants, vaccine properties, and vaccine hesitancy. Our model demonstrated its ability to calibrate and capture past epidemic trends, and to compare potential future scenarios under a range of NPI relaxation strategies, vaccination strategies and efficacy, and transmission dynamics of new variants.

Even accounting for the current uncertainty around the relative transmission advantage of new variants, all simulated scenarios indicated that faster vaccination and more cautious, gradual, NPI relaxation leads to better outcomes in terms of mortality and numbers of cases. This in turn leads to reduced risk of overwhelming the health system and hence to a reduced risk of a need to re-strengthen measures in spring or summer 2021.

We found that significant delays exist between changes in NPI strategies and a measurable effect on cases, hospitalizations, and ICU admissions. Specifically, the consequence of a relaxation is not seen on ICU admissions until at least four- to seven-weeks later. Given these delays, decisions to relax NPI measures made more frequently than every four- to six- weeks[14] run the risk of causing undesirable knock-on effects, including cumulative pressure on the ICU and later needs for restrengthening measures. Furthermore, if too frequent or too large relaxation of NPI measures occur in the period before a maximum ICU capacity trigger is reached, a larger peak in ICU occupancy will occur and a stronger reactive strengthening of NPIs may be required. Decisions on trigger points for changes in NPI measures must take this delay into account to effectively control ICU occupancy.

Vaccination alone will not be sufficient to control mortality in the coming months. Crucially, given the increased transmissibility of the new variants, even without any further NPI relaxation after the 1st of March 2021, a third wave is expected, and, at the time of writing, cases were continuing to increase across Europe. Relaxation of NPIs is likely to lead to a wave of infection, however higher and quicker vaccine uptake, alongside more gradual relaxation will minimise this wave and mortality. Our phased relaxation scenarios indicate if NPIs are relaxed too soon or too fast, the resulting larger third wave has the potential to overload the Swiss health system, and thus prompt re-strengthen of more restrictive NPIs.

Our results suggest that to ensure that a significant third wave does not occur or that the health system and ICU capacity is not challenged, rigorous monitoring of the new variants, cases, effective reproduction number, hospitalization, and vaccination uptake is required to inform careful consideration of the pace and strength of NPI relaxation decisions. While vaccination is ongoing, it is critical to continuously assess the impact of each NPI relaxation before committing to additional relaxations. Effective communication will be key to ensure uptake of the vaccine, and to maintain physical distancing regulations and adherence to NPI measures that protect unvaccinated individuals and individuals who cannot be vaccinated. It is the combination of both vaccination update and ongoing NPIs that dictates the peak and reduction of any third wave. Following vaccination, masks and some level of physical distancing will be required[15] and for this reason we modelled the lowest level of NPI to be roughly equivalent to measures in Switzerland in September 2020.

Although evidence is being accrued on vaccine efficacy beyond clinical studies, e.g., in Israel and the UK, our results are still dependent on our assumed vaccine efficacy, and the assumed uptake and speed of vaccination. Over the simulated time span, we also conservatively assumed no loss of natural or vaccine-induced immunity. It will be crucial to monitor real vaccine coverage and the uptake rate, as well as vaccine efficacy on new variants, and waning immunity over the coming 6- to 12-months. We modelled two scenarios of vaccination, a faster (100,000 doses per day) and slower (50,000 doses per day) rollout, however the feasibility and capacity to vaccinate this number of individuals per day was not explored. We also did not explore the impact of increasing vaccination coverage in the key risk group P1, with coverages over 75% likely to have an impact on mortality in the third wave. Increased vaccine hesitancy in the less vulnerable groups is not expected to lead to increased mortality in the short term. Vaccination of individuals under 18 years of age, or the delaying of second doses of vaccines to increase coverage of first dose, was not explored.

In this model we have considered only current variants of concern (i.e., B.1.1.7, the most prevalent VOC in Switzerland[7]) for which current vaccines appear to be efficacious. We did not consider B.1.351 and P.1, for which vaccines may be less efficacious[16, 17]. Further analysis is required to model and compare scenarios including the effects of new variants as more information about these variants becomes available. We did not consider potential changes in behaviour in vaccinated individuals post vaccination. We also did not consider changes to vaccination strategies, such as deferring the second dose in the face of constrained dose availability.

We used the Oxford Containment and Health Index (OCHI) to measure the strength of NPIs in place. This index incorporates 13 different measures taken to curb the spread of SARS-CoV-2 into one value. Equal levels of OCHI can thus be reached by very different sets of individual NPI. This means that the scenarios modelled are not specific to a certain defined opening or relaxation scenario, but rather treat the effect of a certain total amount of relaxations as measured by the OCHI. The set of relaxation scenarios modelled in this study were chosen to explore interactions of vaccines with different speeds and delays of relaxation, and do not represent explicit measures in Switzerland. A further simplifying assumption is made on the seasonality of force of SARS-CoV-2 infection. While seasonality has been suggested in a recent study[18], the exact mechanism remains unclear. We approximate this by using maximum daily temperature to calibrate our seasonality effect.

While we have quantified short-term consequences of COVID-19 such as hospitalizations and mortality, we did not quantify any long-term sequelae associated with severe and non-severe cases. While

COVID-19 lasts around 2 weeks[19] on average, an estimated one in ten individuals[20] suffer with symptoms for more than 12 weeks, which has been defined as 'long Covid'. Currently, long Covid and disability associated with severe cases are not considered in the model; however, its future impact could be as substantial as the symptoms, including fatigue, anxiety, joint or muscle pain, and more[21] could have a massive impact on the physical and mental health of the affected individual, as well as on their ability to participate in the workforce. Our results are therefore more optimistic compared with outcomes if the impact of long Covid would have been taken into account. We also did not include the economic consequences and the secondary health impacts of relaxing measures and potentially restrengthening of measures. These need to be considered in any policy decisions, alongside additional economic and analysis, and should be a priority for future modelling analysis.

As for all pandemic models, considerable uncertainty exists for projecting further into the future. The current pandemic will not end in September 2021. We ended our simulations at that time point due to increasing uncertainty of predictions beyond this date. In particular, optimistic assumptions about no waning immunity, as well as beneficial climatic effects should be monitored carefully in late summer 2021. We optimistically assumed that the seasonal effect of reduced transmission seen in summer 2020 will apply equally to the new variants of concern. It is important to highlight that the numbers of predicted cases are thus influenced by this phenomenon and that the opposite effect will take place in autumn and winter, also arguing for both high vaccination rates before autumn and effective monitoring beyond summer 2021. Precise quantification of transmission under new variants of concern is also not yet known, which would directly affect measured the effective reproductive number in Switzerland. Likewise, the effectiveness of the various COVID-19 vaccines on existing and possible new variants is not yet accurately known. Changes in testing (including mass testing), changes in NPI measures, and adherence to those measures may result in different future trends than seen in 2020. Furthermore, communication of expected epidemic trends may lead to behavioural changes that make these trends less likely (such as the population becoming more careful and reducing contacts if cases are expected to increase, and vice versa). Such potential behavioural changes were not captured in the model. Although we have undertaken best efforts to update our model with available data and expert-based assumptions, this analysis should not be considered as a future prediction. Instead, our findings provide scenario outcomes comparing the relative impact of SARS-CoV-2 control strategies over the coming months at the national level and do not capture substantial heterogeneity within and between cantons.

Disease models allow us to explore counterfactual scenarios, and to counterbalance the human tendency to underestimate exponential growth. In particular, the interplay between new arising variants and NPI control measures, alongside vaccine rollout, which leads to complex interactions, is intuitively difficult to grasp without using a model. Models offer a snapshot of several possible futures, evaluated at a given point in time. They cannot automatically react to policy changes; these changes will make the model assumptions unfounded. Instead, models provide a tool to compare the relative impact of decisions made now on the future course of the pandemic. With this study, we have addressed these policy-related considerations for the Swiss population from a public health point of view. However, these insights can be applied more broadly to countries or regions that are experiencing similar SARS-CoV-2 dynamics, which we hope will aid in global control of COVID-19.

Methods

Simulation model

SARS-CoV-2 transmission and COVID-19 disease

To represent the impact of vaccines and non-pharmaceutical interventions on the SARS-CoV-2 epidemic in Switzerland, we developed OpenCOVID; a stochastic, discrete-time, individual-based transmission model of SARS-CoV-2 infection and COVID-19 disease. The model is qualitatively described here, with additional details provided in the Supplement, including model equations and parameter values. The open-source model code is available[22].

OpenCOVID tracks characteristics of individuals such as age (in one-year age bins), risk-group (namely those with comorbidities), SARS-CoV-2 infection status, COVID-19 disease state, level of immunity, and vaccination details. If infected, an individual's viral load is tracked as a function of time since infection (see Figure X in Supplement), along with the viral variant infected with (inherited from the infector). The model captures viral transmission as infectious and susceptible individuals come into contact. The probability of transmission is dependent on the viral load of the infectious individual, the variant of the virus being transmitted, and any partial immunity acquired by the susceptible individual (either through previous infection[23] or vaccination[24, 25]). Further, seasonality affects the probability of transmission - with lower probabilities in warmer periods - reflecting a larger proportion of contacts being outdoors with warmer temperatures. Any contact between an infectious and susceptible individual is assumed to carry the same probability of transmission, all else being equal. Human contacts are represented through an age-structured network (see Figure X in Supplement)[26].

A newly infected individual will, following a latent period, be assigned through stochastic distributions an age-dependent disease prognosis of either asymptomatic, mild, severe, critical, or eventual death (Figure 1). These prognosis probabilities are derived from publicly available age-disaggregated morbidity and mortality data[27, 28]. The viral variant an individual is infected with can alter prognosis probabilities, capturing the ability of certain variants to cause increased morbidity and/or mortality (for example, B.1.1.7[12, 13]). Cases with prognosis of severe, critical, or eventual death may be admitted to hospital following some delay from symptom onset, or may alternatively receive care outside of hospital (for example, in a care home). Critical cases under care in hospital will be admitted to an intensive care unit (ICU), with sufficient capacity assumed in the model. The duration an individual remains in any given disease and/or care state is sampled from either a Poisson or Gaussian distribution (see Table X in Supplement).

Diagnosis and testing

Upon infection, an individual is assigned a date at which they may potentially be diagnosed as a consequence of test seeking behaviour. The delay between symptom onset and a potential diagnosis for each individual is sampled from a Gaussian distribution. We assume all non-severe cases isolate for a 10-day period immediately following diagnosis. For individuals presenting with severe disease that seek hospital care prior to diagnosis, a test (and consequent diagnosis) is assumed to be carried out once they are admitted to hospital.

In this application for Switzerland, we derive numbers of diagnoses over time directly from data of confirmed COVID-19 cases. By definition, all COVID-19 cases that seek hospital care receive a diagnosis. After taking hospitalised diagnoses into account, other individuals with severe disease outside of the hospital setting and individuals with mild disease are randomly selected and assigned a diagnosis in the model. To represent future test-seeking behaviour, the model-calculated proportion of cases diagnosed per infected case over the past 30-days is fixed into the future (see Figure X in Supplement). We note here that this assumption is not robust to major changes in testing policies or behaviours, including, but not limited to, mass testing.

Immunity

Following a period of infection, surviving individuals recover to a state in which viral shedding no longer occurs. These recovered individuals are assumed to be susceptible to reinfection, however they are assumed to retain some level of partial immunity which works to reduce susceptibility to subsequent exposures. OpenCOVID can capture immunity decay, however for this study we conservatively assume no immunity decay following natural infection or vaccination. For naturally acquired immunity due to infection, we assume an 83%[23] transmission blocking effect when/if re-exposed. If a previously infected but recovered individual is later vaccinated, the level of transmission blocking immunity is taken to be the highest of the two independent effects. No synergistic effect is considered.

Non-pharmaceutical interventions

In OpenCOVID. non-pharmaceutical interventions (NPIs) can curb the spread of SARS-CoV-2 in an otherwise unprotected population by reducing the number of potentially transmissible pairwise contacts. In Switzerland the NPI have targeted several aspects of public life, from closing shops and restaurants, over restrictions in sizes of spontaneous gatherings and the cancellation of events to facemask mandates in publicly accessible spaces. The Oxford Health and Containment Index (OCHI) is a measure that is proportional to the amount (or stringency) of such measures that are in place at a moment in time[29]. The level of the OCHI, together with a calibrated multiplicative scaling parameter is used in our model to capture the effect of NPI in reducing the effective daily number of contacts.. The Swiss level of the OCHI is collected on cantonal and federal levels based on publicly available information [30]. This publicly available information is translated into 16 Swiss specific variables, and from there into the 12 variables that together make up the Oxford Containment and Health Index.

Viral variants and transmission advantage

OpenCOVID tracks and models the transmission of multiple viral variants. At the time of writing, B.1.1.7 was the dominant variant in Switzerland, replacing D614G[7, 10]. To a lesser extent 501Y was also present. We modelled three variants in this study: D614G, B.1.1.7 and 501Y. We did not consider P1 and B1351 given their low prevalence in Switzerland at the time of writing. A 60% increase in B.1.1.7 transmissibility relative to D614G best matched variant prevalence data between January and February 2021 [see Figure S2 in Supplement]. In the absence of NPIs and in a fully susceptible population, this equates to a 60% transmission advantage for B.1.1.7 over D614G. However, in January 2021 since some of the population had previously been exposed to this variant and control measures were in place, this 60% increase in transmissibility equated to a model-estimated transmission advantage of 1.3–1.4 in the current Swiss setting (early 2021)[7]. For 501Y, a 10% increase in transmissibility relative to D614G was assumed[6]. For the primary results reported in this study, we assumed no increased probability of morbidity or mortality due to viral variants. However, we assess the impact of this scenario in a sensitivity analysis (see 'modelled scenarios' section).

Vaccination and vaccine properties

Fully susceptible, partially susceptible, and actively infected individuals not in hospital can potentially receive a vaccine. Vaccination is modelled using several properties: first to trigger an immune response that blocks transmission for a proportion of exposure events, and second, can further reduce the probability of developing symptoms if infection does occur. Upon vaccination, there is a time delay until the full efficacy of the vaccine is realised; a sigmoidal curve is used to represent this growth in vaccine effect. Vaccine efficacy, delay to full efficacy, transmission blocking effect, and number of doses required is vaccine specific (see Table X in Supplement). In this study, we consider only mRNA vaccines and assume all vaccinated individuals receive two doses spaced by 3 weeks with vaccination reaching maximum efficacy 28-days after the first dose[24, 25, 31] . We assume the vaccine is 80% transmission blocking, and has a further 75% probability of preventing symptoms leading to the observed 95% vaccine efficacy reported in clinical trials[24, 25]. In this study, we conservatively do not model decay of vaccine efficacy over time or reduction in vaccine efficacy due to variants of concern, however the model is able to capture changes to these assumptions.

Model simulation and outputs

Model simulations were initiated on 18th February 2020, 7-days before the first cases were confirmed for three consecutive days in Switzerland (25th to 28th February 2020). All model processes are computed at time intervals representing one day. A number of initial cases are imported into the population, which are then able to cause onwards infections. A number of infections are also imported into the population at each time step. Further, new virus variants are initiated by importing a number of new cases of each variant at a given time point aligned with when the particular variant was first identified in Switzerland. All three importation rates are found through model calibration (see following section). The number of individuals simulated in the model is capped at a predefined number (one

million individuals for all simulations reported here), with a population scaling factor subsequently applied to all relevant model outputs to represent a one-to-one scale for the population of interest.

Numerous model outputs are captured and reported temporally, including number of infections, diagnosed infections, morbidity, and mortality estimates (for a full list, see Table X in Supplement). Where appropriate, metrics are disaggregated by age, variant of infection, and vaccine priority group. OpenCOVID can be used to assess the SARS-CoV-2 epidemic at the national and subnational level. In this paper, we present outcomes from the model at the national level. All outcomes are reported as mean estimated along with prediction intervals representing parameter uncertainty and stochastic uncertainty.

Data and model calibration

Application of OpenCOVID to the national-level epidemic in Switzerland was informed by publicly available epidemiological and demographic data from the Swiss Federal Office of Public Health (FOPH)[32] and climate data from Meteo Schweiz[28] Data regarding NPI measures which were used to compute national- and cantonal-levels interpretations of the Oxford Health and Containment Index were collected from various publicly available sources, see [30] for details. Model output is matched to six types of observed temporal metrics: 1) daily confirmed COVID-19 cases, 2) daily COVID-19-related deaths, 3) daily hospital admissions, 4) number of COVID-19 patients in hospital, 5) number of COVID-19 patients in ICU, and 6) relative prevalence of virus variants[7, 10]. A log-likelihood objective function captures the overall quality of the model fit, weighted for each data type. A subset of model parameters (see Table X in Supplement) were considered in the calibration process, including contact rates, hospitalisations dynamics, reporting delays, and epidemic initialisation conditions. The effect of NPIs on human contact rates is also subject to the calibration process, where the value of the Oxford Health and Containment Index is proportionally scaled to represent a reduction in contacts.

Model calibration can be a computationally- and time-intensive exercise, particularly for individual based models[33]. We mitigate such issues by using a Bayesian optimisation approach with a model emulator[33, 34]; by training an emulator across the entire parameter-likelihood hyperspace we can more efficiently reach a desirable fit of model output to epidemiological data. The process is as follows: Several thousand parameter sets are drawn, using Latin hypercube sampling, across parameter hyperspace. Each parameter set is simulated multiple times (separate stochastic realisations) using OpenCOVID (capturing stochastic uncertainty). All model simulations are performed simultaneously on a high-performance computing cluster[35]. The log-likelihood for the parameter set given the aforementioned epidemiological data is then calculated. A model emulator is then trained to predict the log-likelihood over all data given a model parameter set. For this analysis, we choose a heteroscedastic Gaussian Process algorithm as the model emulator[8, 36]. Numerous rounds of adaptive sampling are then used to efficiently resample regions of the parameter hyperspace that are good candidates for the global maximum. An expected improvement acquisition function is used to identify these candidate regions, with a filtering function applied to ensure resampled parameters sets are not within a predefined distance of each other (with distance measured in Manhattan space). When resampling iterations no longer identify parameter sets that produce a better log-likelihood, the adaptive sampling process is halted. Following this, an Markov chain Monte Carlo algorithm[37, 38] is applied to the emulated hyperspace to obtain a set of calibrated parameter posteriors. These posteriors are sampled from to produce all future scenarios reported in this analysis.

Modelled scenarios

We used OpenCOVID to predict potential future national-level epidemic trajectories from early March to early September 2021 for different vaccination rollouts and a range of NPI relaxation scenarios. We considered two vaccination campaigns that differ in rollout speed; 1) distributing 50,000 vaccine doses per day from 1st April 2021, and 2) distributing 100,000 vaccine doses per day from 1st April 2021. These vaccine scenarios are referred to as slower vaccine rollout and faster vaccine rollout, respectively. Past vaccine rollout was modelled as per publicly available data[39].

Vaccine eligible individuals are assigned to one of five vaccine priority groups according to age, comorbidities, and profession. Vaccine hesitancy is also considered, whereby vaccines are not given in the model to vaccine hesitant individuals. Priority groups for vaccination are modelled according to the Swiss FOPH[40] (Supplement), and are denoted P1 (highest priority group, adults older than 75 years of age); P2 (Aged between 65 and 75, under 65 with comorbidities, and healthcare workers); P3 (Household members of high-risk people); P4 (Adults aged 18–64 in communal facilities and their caregivers); P5 (adults 18-65 years of age with no comorbidities). As per current Swiss vaccination guidelines, individuals under 18 years of age are not considered eligible for vaccination[40]. We assumed 75% of each priority group were willing to be vaccinated (that is, were not vaccine hesitant). All eligible individuals in a priority group are vaccinated before individuals in the subsequent group begin to receive vaccines. We assumed all vaccinated people receive two doses of an mRNA vaccine.

We first assessed the epidemiological impact of four NPI relaxation scenarios. In these scenarios, an NPI *relaxation step* translates to approximately 5 percent points on the OHCI, reflecting the set of NPI relaxations proposed by the Swiss Federal Council to occur initially on 1st April 2021 (later re-scheduled for 22nd March 2021[27]). This set of NPI relaxations included increasing the limit on indoor private events from 5 to 10, opening professional sporting and cultural events at one-third capacity, and reopening restaurants for outside service[27] amongst other measures (although not all openings have a quantitative effect on the OCHI). We stress here that the specific openings are not modelled explicitly, but rather the abstraction of an equivalent amount of NPI relaxation that is reflected in the OCHI. Moreover, the same amount of opening in terms of OCHI can also be reached with different combinations of openings, so that the OCHI stays agnostic to a specific type of opening, but rather only reflects a certain amount of opening. The modelled NPI relaxations are as follows:

Scenario 1A) Phased relax until May 3 (red scenario, represents 3 relaxation steps over 6 weeks)

Scenario 1B) Phased relax until July 5 (blue scenario, represents 3 relaxation steps over 15 weeks)

Scenario 1C) Relax March 22 (yellow scenario, represents 1 relaxation step)

Scenario 1D) No relax after March 1 (green scenario, no further relaxation step)

We then assessed the impact of a single relaxation step, as modelled in scenario 1C, with varying delays before relaxation:

Scenario 2A) Relax April 12 (tan scenario, represents 1 relaxation step with a 3-week delay)

Scenario 2B) Relax May 3 (bright blue scenario, represents 1 relaxation step with a 6-week delay)

Scenario 2C) Relax May 24 (bright pink scenario, represents 1 relaxation step with a 9-week delay)

In all scenarios we assume adherence to measures is consistent and does not change over time. For each scenario we report the predicted future number of ICU beds in use and the number of COVID-19-related deaths. We further report the number of confirmed cases in each scenario; however, we stress here that these future scenarios assume similar testing behaviours to those observed in Switzerland between early February and early March 2021, and not consider the potential impact of mass testing programs or widespread testing outreach.

Model output and sensitivity analysis

To assess the sensitivity of our findings, we simulated scenarios that independently varied several key model parameters related to vaccine characteristics and currently circulating variants of concern. Namely, we simulated:

Scenario 3A) Vaccine with 60% transmission blocking (dark orange scenario)

Scenario 3B) Vaccine with 95% transmission blocking (light orange scenario)

Scenario 4A) Vaccine acceptability of 60% (increased hesitancy) for priority groups P2–P5 (dark green scenario)

Scenario 4B) Vaccine acceptability of 90% (decreased hesitancy) for priority groups P2–P5 (light green scenario)

Scenario 5A) Variant B.1.1.7 70% more infectious than D614G (dark purple scenario, corresponds to 1.4 relative transmission advantage in Switzerland in early 2021)

Scenario 5B) Variant B.1.1.7 50% more infectious than D614G (light purple scenario, corresponds to 1.2 transmission advantage in Switzerland in early 2021)

Scenario 6A) Variant B.1.1.7 50% higher mortality than D614G (dark pink scenario)

We simulated each of these scenarios using the NPI relaxation steps as described in scenario 1B, and for both vaccination rollout speeds (slower, 50,000 vaccines per day; and faster, 100,000 vaccines per day). We then compared the number of confirmed cases and COVID-19-related deaths to the outcomes associated in scenario 1B (blue scenario). To capture the modelled 95% efficacy of mRNA vaccines in reducing morbidity[24, 25] for the 60% transmission blocking scenario, an additional effect of 87.5% reduction in symptoms for new infections (of fully vaccinated individuals) is used. For the 95% transmission blocking scenario, no further reduction in symptoms is required

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Figures and Tables

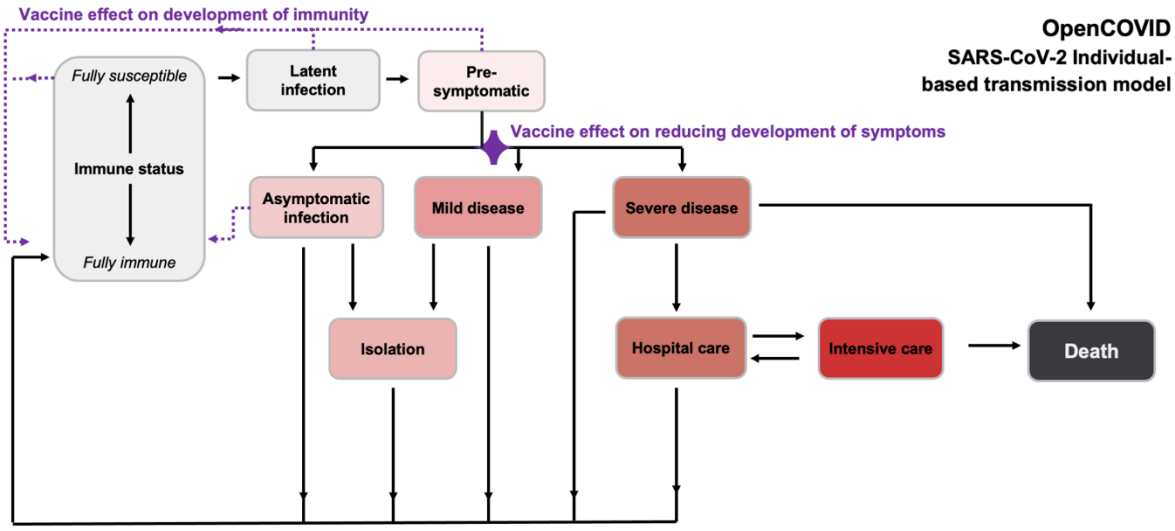

Figure 1: Schematic of OpenCOVID model structure, capturing potential states of individuals in the model, including fully susceptible or immune status (exposure), latent infection, pre-symptomatic state -- for which vaccination may affect immune development (indicated by dotted purple lines). Some remain asymptomatic, while disease progression may occur (mild, severe) -- for which vaccination could reduce symptom development. Isolation or care (hospital care, intensive care) may be required. Recovery (from symptomatic infection, mild or severe disease) or death results. Increasingly darker shading (grey, pink, red, dark grey) indicates increasing severity. Full model details provided in the methods and Supplement.

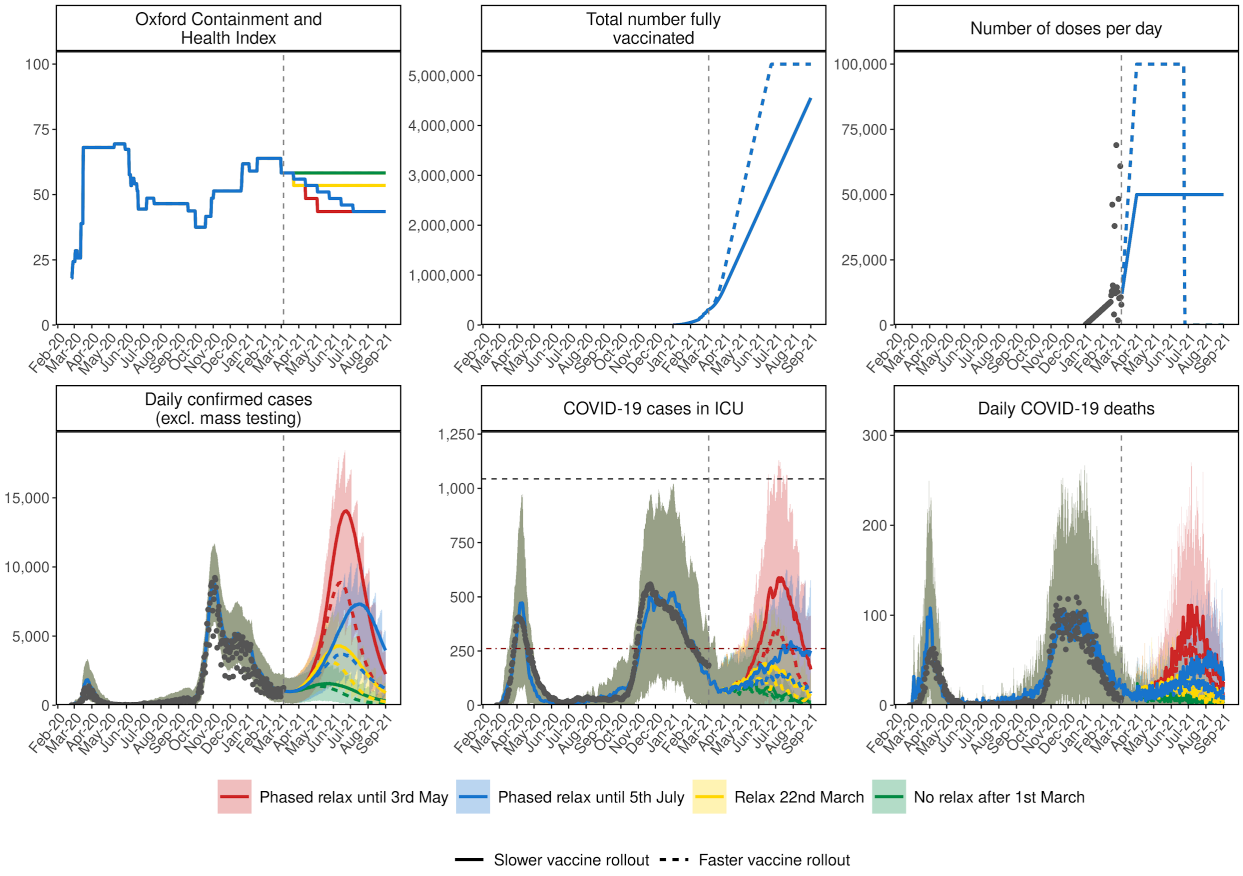

Figure 2: Comparison of the impact of several vaccination and NPI relaxation scenarios on the SARS-CoV-2 dynamics in Switzerland over time. Panels from top left to bottom right: **Oxford Containment and Health Index**: A measure for the severity of NPI measures from 24th February 2020 until 21st March 2021 and for four exemplar relaxation scenarios from 22nd March 2021 (detailed in Table 1 and below). **Total number fully vaccinated**: Cumulative amount of fully vaccinated persons (assuming two doses). **Number of doses per day**: Number of vaccine doses administered per day. **Daily confirmed cases**: Model estimates of the number of confirmed COVID-19 cases per day (not accounting for future testing changes including mass testing). **COVID-19 cases in ICU**: Model estimates of COVID-19 patients in ICU. **Daily COVID-19 deaths**: Model estimates of daily COVID-19-related deaths. In all panels, dark grey dots show data to date. Coloured lines show simulation results of different relaxation scenarios and two vaccine rollout scenarios. **Vaccination scenarios**: **Solid lines** correspond to a vaccination scenario assuming 50,000 vaccines are administered per day, while the **dashed lines** correspond to a faster vaccination scenario of 100,000 vaccines per day. **NPI scenarios** (details Table 1)**: Red** represents an NPI relaxation scenario with opening steps on the 22nd of March, the 12th of April, and the 3rd of May. **Blue** represents a slower NPI relaxation scenario compared with the red scenario, with smaller relaxations, three-weekly steps from the 22nd of March to the 5th of July. **Yellow** represents an NPI relaxation scenario with relaxation only on the 22nd of March and no further openings. **Green** represents a strategy with no further NPI relaxation after the 1st of March (an unrealistic scenario of no relaxations through to the end September 2021, provided as a reference only). The vertical dashed lines on all panels represent the current date at the time of the analysis. The horizontal black dashed line in the “COVID-19 cases in ICU” panel depicts the estimated maximum national capacity of ICU beds; the horizontal red dashed line in this panel depicts a level of 25% of ICU capacity. Predictions of confirmed cases, ICU and mortality are mean estimates and 95% prediction intervals.

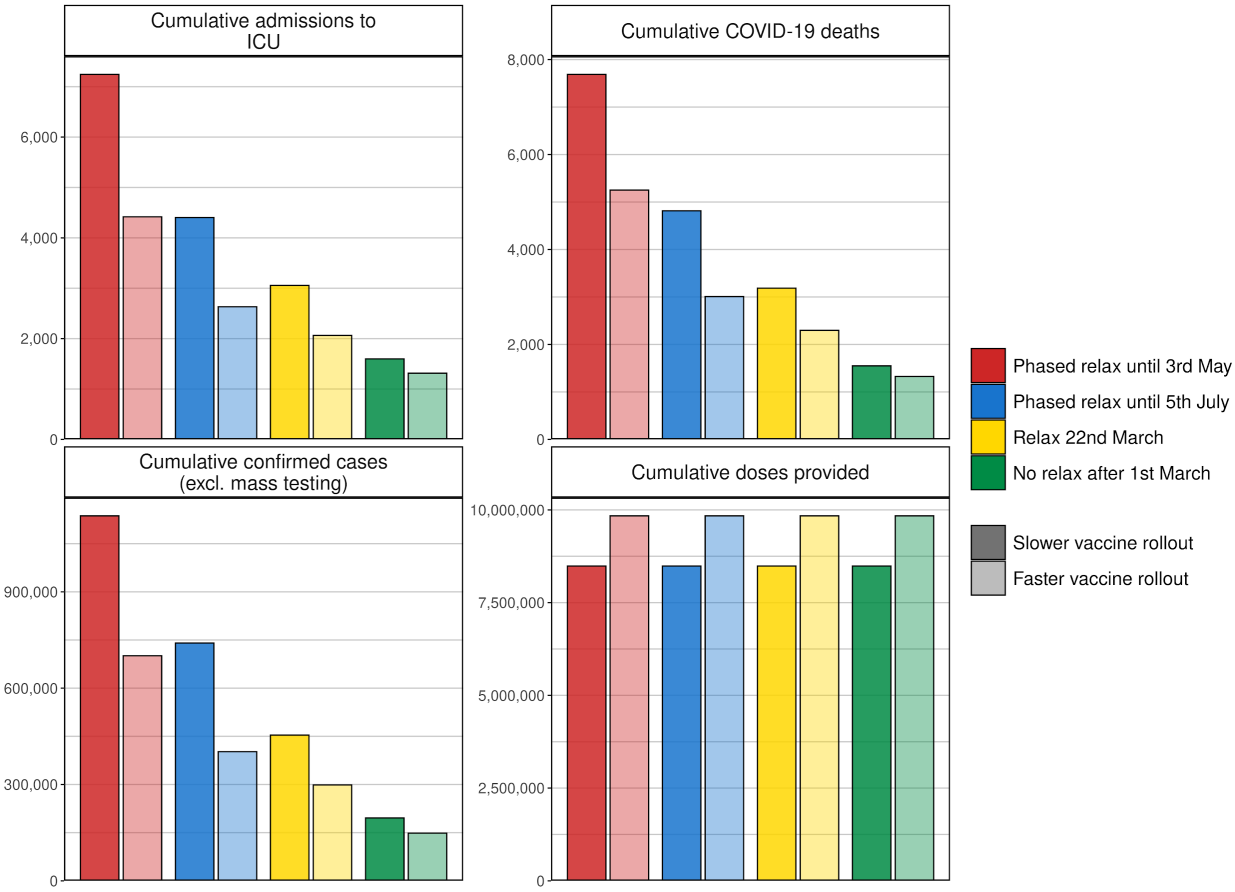

Figure 3: Cumulative estimates of the number of confirmed cases, ICU admissions, COVID-19 deaths, and vaccine doses provided over the time period between the 6th of March 2021 and 5th September 2021 for the scenarios in Figure 2. Panel labels indicate the variable, and the colour of each bar indicates the NPI relaxation and vaccination scenarios as per Figure 2: **Red** represents an NPI relaxation scenario with opening steps on the 22nd of March, the 12th of April, and the 3rd of May. **Blue** represents a slower NPI relaxation scenario compared to the red scenario, with smaller relaxations, three-weekly steps from the 22nd of March to the 5th of July. **Yellow** represents an NPI relaxation scenario with relaxation only on the 22nd of March and no further openings. **Green** represents a strategy with no further NPI relaxation since 1st March (an unrealistic scenario of no relaxations through to end September 2021 and provided for reference only). The shading of each bar corresponds to the vaccination scenario, with the **darker shade** corresponding to the vaccination scenario of 50,000 vaccinations per day, and the **lighter shade** to the faster vaccination scenario of 100,000 vaccinations per day.

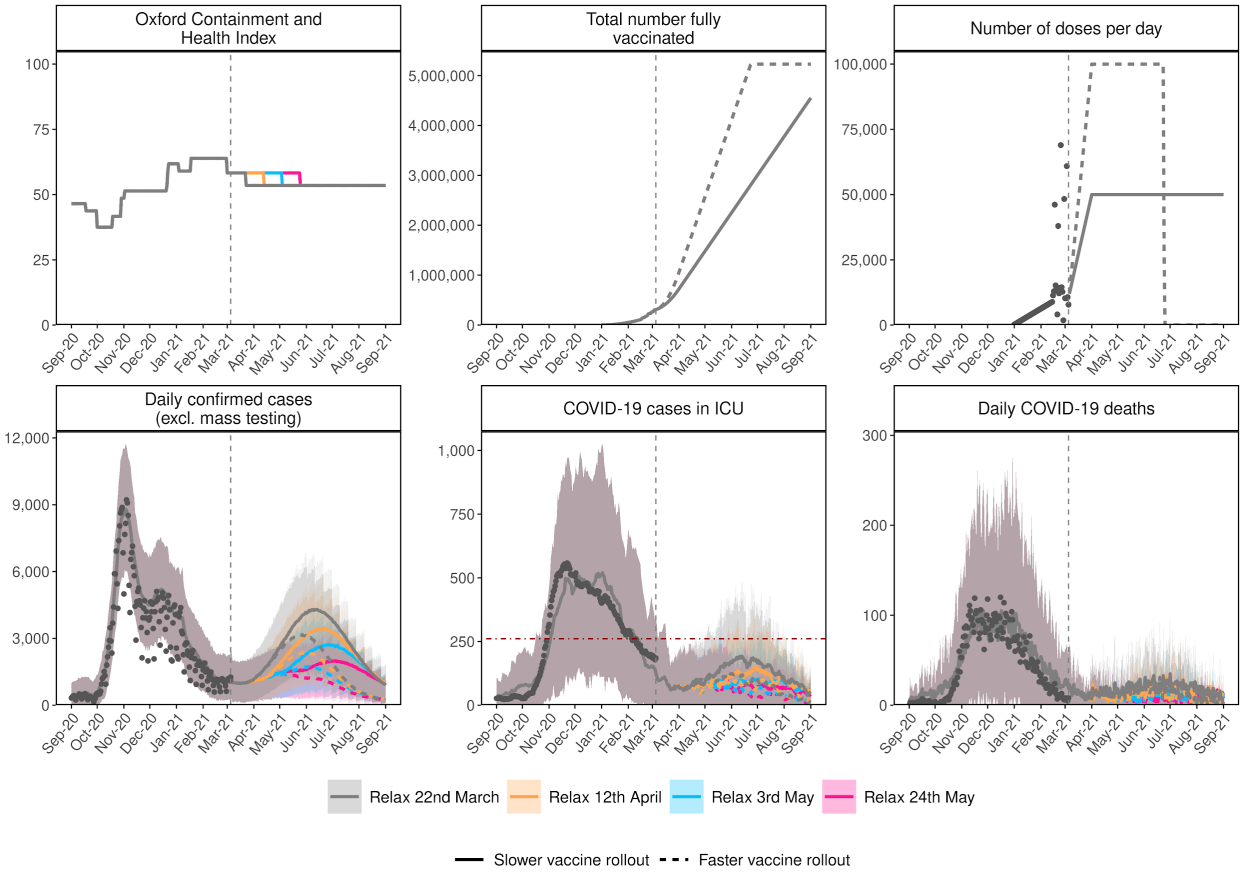

Figure 4: Comparison of the impact of vaccination and NPI relaxation scenarios on the SARS-CoV-2 dynamics in Switzerland over time for delayed single-step relaxation. Panels from top left to bottom right: **Oxford Containment and Health Index**: A measure for the severity of NPI measures from 24th February 2020 until 21st March 2021 and for four exemplar relaxation scenarios with one step relaxation. **NPI scenarios: Grey** represents an NPI relaxation scenario with relaxation only on the 22nd of March with no further openings (also detailed as the yellow scenario in Table 1); **Orange** same relaxation but three weeks later on 12th April; **Blue** same relaxation on 3rd May, and **Pink** same relaxation 24th May. **Total number fully vaccinated**: Cumulative amount of fully vaccinated persons (assuming two doses). **Number of doses per day**: Number of vaccine doses administered per day. **Daily confirmed cases**: Model estimates of the number of confirmed COVID-19 cases per day (not accounting for future testing changes including mass testing). **COVID-19 cases in ICU**: Model estimates of COVID-19 patients in ICU. **Daily COVID-19 deaths**: Model estimates of daily COVID-19-related deaths. In all panels dark grey dots show data to date. The coloured lines show simulation results for the different relaxation scenarios and the two vaccine rollout scenarios. **Vaccination scenarios**: **Solid lines** correspond to a vaccination scenario assuming 50,000 vaccines are administered per day, while **dashed lines** correspond to a faster vaccination scenario of up to 100,000 vaccines per day. The vertical dashed line on all panels represents the current date at the time of the analysis. The horizontal red dashed line in the "COVID-19 cases in ICU" panel depicts the level of 25% of ICU capacity. Predictions of confirmed cases, ICU and mortality are mean estimates and 95% prediction intervals.

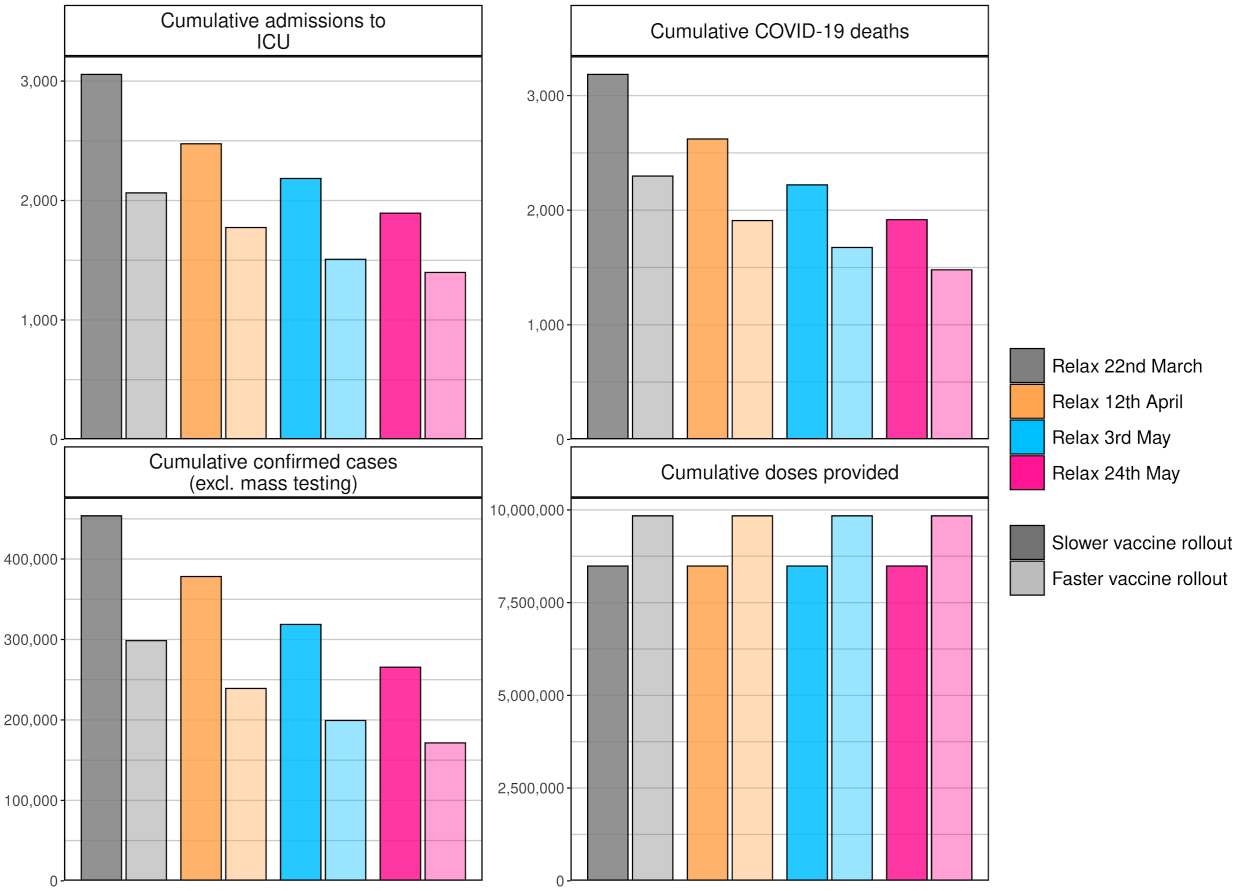

Figure 5: Cumulative estimates of the number of confirmed cases, ICU admissions, COVID-19 deaths, and vaccine doses provided over the time period between the 6th of March 2021 and 1st September 2021 for the scenarios in Figure 4. Panel labels indicate the variable. The colour of each bar indicates the scenarios of NPI relaxation and vaccination as per Figure 4. **Grey** represents an NPI relaxation scenario with relaxation only on the 22nd of March with no further relaxations, orange the same relaxation but three weeks later on the 12th of April, blue the same relaxation on 3rd May, and **pink** the same relaxation on the 24th of May. The shading of each bar corresponds to the vaccination scenario, the **darker shades** correspond to the vaccination scenario of 50,000 vaccinations per day, and the **lighter shades** to the faster vaccination scenario of 100,000 vaccinations per day.

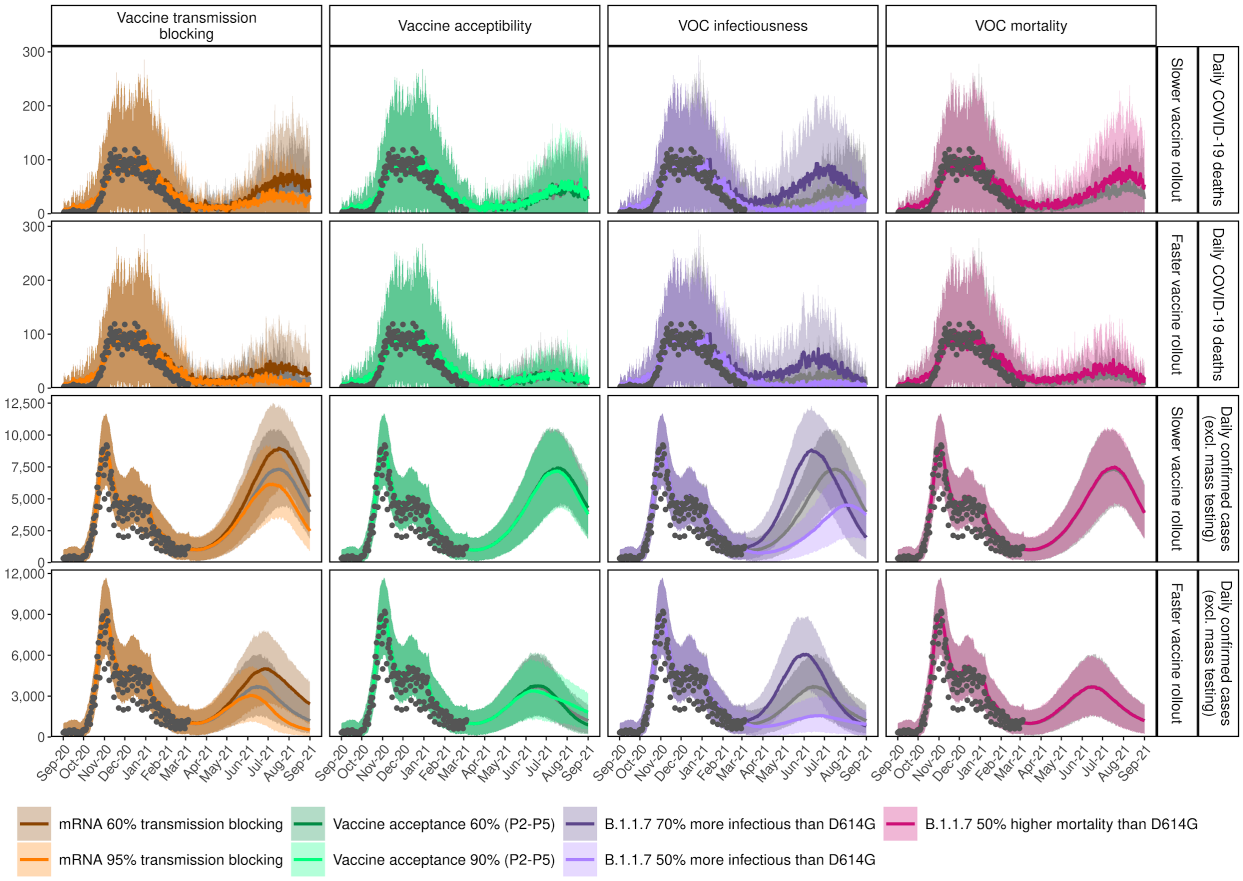

Figure 6: Sensitivity of predictions for daily confirmed cases and COVID-19 deaths given assumptions on vaccine transmission blocking, vaccine acceptability, infectiousness of VOC, and potential increased mortality of VOC. Each panel shows the time series of either daily confirmed cases (excluding testing changes) or daily COVID-19 deaths (indicated by the row labels) between 1st September 2020 and 1st September 2021 for the blue scenario (slower relax until the 5th of July) illustrated in Figure 2 and described in Table 1: slow phased NPI relaxation scenario of three-weekly steps from the 22nd of March to the 5th of July with 50,000 vaccines administered per day (rows 1 and 3) or faster vaccination with 100,000 per day (rows 2 and 4). Results of the blue scenario are represented by grey dots, and colours show the impact of vaccine transmission blocking, vaccine acceptability in terms of coverage, and varying assumptions for VOC. **Vaccine transmission blocking (column 1):** Influence of the assumption on the transmission blocking property of the vaccine. The **dark orange** line represents a vaccine with 60% transmission blocking, the **light orange** line shows 95% transmission blocking, and the **grey** line the best estimate for 80% transmission blocking used in Figures 2 and 3. The transmission blocking property of the vaccine is offset with the symptom blocking property, so that the vaccine always has an efficacy of 95% in reducing symptoms. **Vaccine acceptability (column 2):** The influence of the assumption on vaccine hesitancy, resulting in a change of vaccination coverage. The **dark green** line represents 60% coverage, the **light green** line 90% coverage, and the **grey** line the best estimate of 75% coverage as used in Figures 2 and 3. **VOC infectiousness (column 3):** Influence of the assumed increased transmission for variant B.1.1.7. The **dark purple** line shows a 70% increased transmissibility (corresponding to a transmission advantage of 1.4–1.5), the **light purple** line 50% increased transmissibility (corresponding to a transmission advantage of 1.2–1.3), and the **grey** line the reference scenario of 60% increased transmissibility (corresponding to a transmission advantage of 1.3–1.4) used in Figures 2 and 3. **VOC mortality (column 4):** Influence of the assumed increase in mortality of 50% for variant B.1.1.7 compared with D614G (**dark pink**), and the **grey** line the same mortality assumptions as for variants that emerged in 2020. Predictions of confirmed cases, and mortality are mean estimates and 95% prediction intervals.

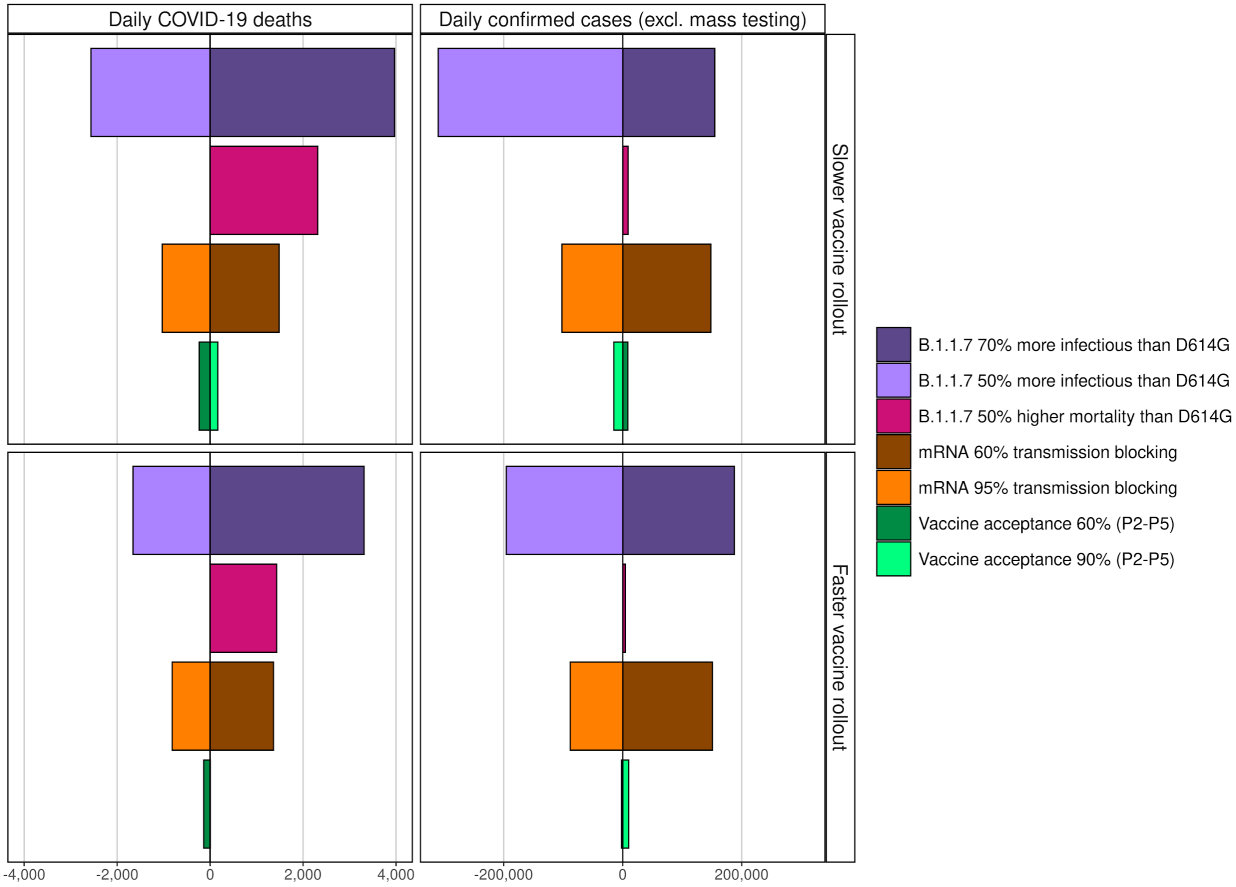

Figure 7: Cumulative mean impact in terms of increase or decrease in number of daily COVID-19 deaths and confirmed cases given the sensitivity analysis of Figure 6 (Table 2) on the blue reference scenario for a slower relaxation until the 5th of July (Table 1, Figure 2). The estimated increase or decrease of cumulative numbers of COVID-19 confirmed cases (excluding test changes) and COVID-19 deaths from 1st September 2020 to 1st September 2021 given the different assumptions on infectiousness of VOC, potential increased mortality of VOC, and vaccine transmission blocking and vaccine acceptability as illustrated in Figure 6. The colour and shading schemes are identical to those in Figure 6. The dividing line at 0 is the reference cumulative mean estimate in Figure 3 for the dark blue scenario bar (50,000 vaccines per day) and light blue scenarios (100,000 vaccines per day): slow phased NPI relaxation scenario of three-weekly steps from the 22nd of March to the 5th of July. Influence of the assumption of the increased transmission of variant B.1.1.7: **dark purple** bars represent an assumed 70% increased transmissibility (corresponding to a transmission advantage of 1.4-1.5), the **light purple** bars, 50% increased transmissibility (corresponding to a transmission advantage of 1.2–1.3), over the reference of 60% transmissibility for D614G. Influence of the assumption of an increased mortality of 50% for variant B.1.1.7 (**dark pink** bars**)**. Influence of the assumption on the transmission blocking property of the vaccine: **dark orange** bars represent a vaccine with 60% transmission blocking, the **light orange** bars represent 95% transmission blocking. The transmission blocking property of the vaccine is offset with the symptom blocking property, so the vaccine has a 95% efficacy for reducing symptoms. The influence of the assumption for vaccine hesitancy, resulting in a change of vaccination coverage: the **dark green** line shows a coverage of 60% (acceptance), the **light green** line a coverage of 90% (compared with the reference 75% coverage). For all bars, the negative values on the left indicate less cases or deaths are predicted compared with the reference scenario, for positive values on the right, more deaths or cases are predicted.

TABLES

Table 1: Summary of model scenarios from Figures 2 and 3. Oxford Containment and Health Index (OCHI) levels are detailed in the methods.

Scenario	NPI relaxation speed	NPI OCHI level on 22nd March	NPI OCHI level on 12th April	NPI OCHI level at 3rd May	NPI OCHI level on 5th July	Vaccination speed	VOC transmission	Vaccine assumptions
1A) RED	Opening steps on the 22nd of March, 12th of April, and 3rd of May 2021	53.5 Similar to levels in early June 2020	48.5 Similar to levels in early July 2020	43.5 Similar to levels at end of September 2020	43.5	50,000 per day (solid line) or 100,000 per day (dashed line)	Baseline – 60% increased transmission	Baseline - 80% transmission blocking
1B) BLUE	Small openings of 3-weekly steps between the 22nd of March and the 5th of July 2021	55.9 Similar to levels in early June 2020	53.5 Similar to levels in early June 2020	51.0 Similar to levels in November 2020 and December 2020	43.5 Similar to levels at end of September 2020	50,000 per day (solid line) or 100,000 per day (dashed line)	Baseline – 60% increased transmission	Baseline – 80% transmission blocking
1C) YELLOW	Opening step on the 22nd of March 2021 and no further openings (this relaxation step is according to relaxations communicated on the 17th of February)	55.9 Similar to levels in early June 2020	55.9	55.9	55.9	50,000 per day (solid line) or 100,000 per day (dashed line)	Baseline – 60% increased transmission	Baseline – 80% transmission blocking
1D) GREEN	No further relaxation after the 1st of March 2021	58.3 Since 1st of March	58.3 Since 1st of March	58.3 Since 1st of March	58.3 Since 1st of March	50,000 per day (solid line) or 100,000 per day (dashed line)	Baseline – 60% increased transmission	Baseline – 80% transmission blocking

Table 2: Summary of model scenarios from Figures 6 and 7

Scenario	**NPI relaxation speed** (blue scenario of Figure 2, Table 2). OCHI level on 22nd March of 55.9, at 12th of April of 53.5, on 3rd May of 51.0 and 5th July of 43.5	**Vaccination speed**	**Variants of concern (VOC)**	**Vaccine assumptions**	**Vaccination coverage (accounts for hesitancy or increased acceptance in groups P2-5)**
3A) DARK ORANGE	Small openings of 3-weekly steps between the 22nd of March and the 5th of July	100,000 per day	Baseline – 60% increased transmission	Lower transmission blocking - 60% transmission blocking	Baseline – 75% coverage
3B) LIGHT ORANGE	Small openings of 3-weekly steps between the 22nd of March and the 5th of July	100,000 per day	Baseline – 60% increased transmission	Higher transmission blocking – 95% transmission blocking	Baseline –75% coverage
4A) DARK GREEN	Small openings of 3-weekly steps between the 22nd of March and the 5th of July	100,000 per day	Baseline – 60% increased transmission	Baseline – 80% transmission blocking	75% coverage for P1 60% coverage for P2-P5 reflecting higher vaccine hesitancy.
4B) LIGHT GREEN	Small openings of 3-weekly steps between the 22nd of March and the 5th of July	100,000 per day	Baseline – 60% increased transmission	Baseline – 80% transmission blocking	75% coverage for P 90% coverage for P2-P5 reflecting lower vaccine hesitancy.
5A) DARK PURPLE	Small openings of 3-weekly steps between the 22nd of March and the 5th of July	100,000 per day	Higher transmission – 70% increased transmission of B1.1.7 relative to D614G	Baseline – 80% transmission blocking	Baseline – 75% coverage
5B) LIGHT PURPLE	Small openings of 3-weekly steps between the 22nd of March and the 5th of July	100,000 per day	Lower transmission – 50% increased transmission of B1.1.7 relative to D614G	Baseline – 80% transmission blocking	Baseline – 75% coverage
6A) DARK PINK	Small openings of 3-weekly steps between the 22nd of March and the 5th of July	100,000 per day	Baseline – 60% increased transmission, and with 50% increased mortality relative to D614G	Lower transmission blocking – 60% transmission blocking	Baseline – 75% coverage

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