Reproductive number of the COVID-19 epidemic in Switzerland with a focus on the Cantons of Basel-Stadt and Basel-Landschaft

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Summary

The WHO declared the COVID-19 outbreak a "Public Health Emergency of International Concern" on January 30, 2020, after rapid spread from a few initial cases to thousands of cases across China and introductions to several other countries. On March 11, 2020, the WHO classified the outbreak as a pandemic. The first cases in Switzerland, Basel-Stadt, and Basel-Landschaft were confirmed on February 25, February 27, and February 28, 2020. As of March 31, 2020, there are 17097 confirmed cases in Switzerland, including 657 and 561 in the Cantons of Basel-Stadt and Basel-Landschaft, respectively. The rapid increase of confirmed cases over the past month reveals considerable community transmission.

Here, we estimate the reproductive number through time for the whole of Switzerland and its cantons for which sufficient data is available. For the estimation of the reproductive number, we use publicly available data on the number of confirmed cases through time, as well as additional data directly obtained from the University Hospital of Basel and the Health Department of Basel-Landschaft. If the reproductive number is below 1, the epidemic in the particular location is under control, with the number of new infections per day and the incidence decreasing through time. If this number is above 1, the epidemic is exponentially increasing in size.

We find that the reproductive number in some Swiss cantons may have been above 2 during the first third of March, and has consistently decreased to around 1. Since the initiation of strict measures to contain SARS-CoV-2 transmission in mid-March 2020, the reproductive number stabilized around 1. These results are confirmed in sensitivity analyses using data for the Cantons of Basel-Stadt and Basel-Landschaft. The sensitivity analyses were designed to address the concern of a decreasing reproductive number being merely an artifact of less intense testing through time. We note that estimates of the reproductive number lag 10 days behind the last date of data collection since confirmation usually occurs with a delay of 10 days after infection. In summary, our results suggest a decline of transmission in mid-March. Going forward, we will provide daily estimates for the reproductive number on our webpage.

Introduction

The SARS-CoV-2 virus was first identified in China in December 2019 (1). Switzerland recorded its first case on February 25, 2020. As of March 31, 2020, there were 17097, 657, and 561 (2) documented cases in Switzerland, Basel-Stadt, and Basel-Landschaft, respectively. Initial COVID-19 cases had travel links to Italy (3), indicating an import of infections from other locations. These imports seeded the initial COVID-19 epidemic in Switzerland. The rapid increase in the number of newly confirmed cases through time reveals that infection occurs mainly through so-called community transmission, i.e., transmission within a location.

The reproductive number (4) quantifies the expected number of secondary infections caused by a single infected individual. In particular, the basic reproductive number quantifies the number of secondary infections in a completely susceptible population, while the effective reproductive number quantifies the number of secondary infections at a particular time point of an epidemic. The basic reproductive number has been estimated to be between 2 and 3.5 for China based on the initial number of confirmed cases through time. For an overview of papers estimating the basic reproductive number, see (5). Estimating the basic reproductive number based on confirmed cases in locations different from China is not straightforward due to early dynamics being driven by imports seeding the epidemic outbreaks. Using genomic sequences of SARS-CoV-2, we confirmed the basic reproductive number to be between 2 and 3.5 for China, as well as for Italy and Washington State (U.S.A.) (6). The effective reproductive number in different countries and regions is estimated in (7).

Here, we aim at quantifying the effective reproductive number for the epidemic in Switzerland and in 10 out of the 26 cantons forming the Swiss Confederation. The cantons for which we present analyses are among the most-affected cantons by COVID-19 measured in absolute case numbers. We further perform sensitivity analyses for the epidemic in Switzerland and the epidemics in the Cantons of Basel-Stadt and Basel-Landschaft. Hereafter, we refer to the effective reproductive number as the reproductive number or as R(t) with t denoting the time point for which we determine the reproductive number. We will update estimates for R(t) as the epidemic unfolds in the future.

Materials and methods

Datasets

For 92 patients in Basel-Landschaft, we obtained the time of symptom onset and the time of COVID-19 case confirmation (data from the Health Department of the canton). We calculated the mean and standard deviation for the time between symptom-onset and confirmation.

The cumulative number of confirmed COVID-19 cases and deaths for Switzerland and the cumulative number of confirmed cases for the Swiss cantons is from the Specialist Unit for Open Government Data of Canton of Zurich (2). We retrieve this data via an online data repository (8). Additionally, we obtained the number of new hospitalizations due to COVID-19 per day (i) for the University Hospital Basel (USB) in Basel-Stadt, and (ii) for the Bruderholzspital in Basel-Landschaft with the patients being Basel-Landschaft residents (the Bruderholzspital is the only hospital in Basel-Landschaft admitting COVID-19 patients). All case and hospitalization data spans until March 31st, 2020; the death data spans until April 5th 2020.

Finally, we obtained the absolute number of tests performed per day as well as the number of positive tests per day from the two testing centers exclusively performing tests in Basel-Landschaft (Münchenstein and Lausen; open since March 18, 2020 (9)) as well as from the University Hospital in Basel-Stadt (about half of the performed tests are on all samples from a major cantonal testing center which is in its current form open since March 9, 2020 (10)).

Data cleaning

For some days after March 12, 2020, confirmed case data was not reported. We allocated half of the cases from the next day to the day on which data was not reported.

Multiple cantons have missing data for some of the early days in the epidemic. We interpolate data for these missing days from the existing data of individual cantons linearly. Note that this interpolation hardly affects our R(t) estimates since we truncate the beginning of the epidemics for R(t). Truncation is done for two reasons: before March 9, 2020, testing policy was different from later time points (see below) and early cases may be imports rather than infections due to community transmission.

Analysis of confirmed case data, the number of deaths, and the number of hospitalizations. We estimate the reproductive number R(t) as a function of time based on the cumulative number of confirmed cases through time. As sensitivity analyses, we estimate R(t) based on the number of deaths per day for Switzerland and the number of new hospitalizations per day for the cantons. R(t) is the expected number of secondary cases caused by an infected individual at a time point t. R(t) is estimated employing the method from (11) using the implementation in the R package EpiEstim on CRAN (12). It is assumed that an individual who has had a COVID-19 infection for s days has an infection intensity w_s . Then the expected number of infected individuals at time t is $E[I(t)] = R(t) \sum_{s=1}^{t} w_s I(t-s)$. To estimate R(t), we can fit this equation with I(t) being the number of newly infected people on day t. We do not know I(t), but we can measure quantities which are closely related to I(t). Here we use the number of confirmed cases on day t+10 as a proxy being proportional to I(t). Second we use the number of newly admitted COVID-19 patients to a hospital on day t+8 as a proxy being proportional to I(t). See below for the rational of the chosen delay (10, 20, and 8 days).

For the distribution of w_s , we use the serial interval estimated for COVID-19 infections from (13), with a mean of 4.8 and a standard deviation of 2.3. Based on this assumption, >90% of onwards transmissions happen within 8 days upon infection of an individual.

We calculate a posterior distribution for R(t) using Bayesian methodology provided in (12). To reduce the influence of stochastic outliers, we smooth the resulting R(t). The smoothed R(t) is calculated based on assessing E[I(t)], E[I(t-1)], and E[(I(t-2)] (i.e., for a 3-day window assuming R is constant during that time).

In addition to the sensitivity analysis regarding the data set mentioned above (i.e., analyses based on cases, deaths, and hospitalizations), we perform a separate analysis assessing the sensitivity of the results to the statistical method. Specifically, we estimate the case reproductive number $R_c(t)$. $R_c(t)$ is defined as the expected number of individuals which an individual becoming infected at time t causes over the period of its infection (14). Thus, $R_c(t)$ takes into account future events. In contrast, R(t) is based on past events; it was defined as the number of secondary infections caused by the individuals which transmit at time t. As a consequence, when calculating $R_c(t)$, a proxy for the number of infections after time t is needed. In fact, since individuals will transmit within 8 days of infection with >90% probability (based on our serial interval assumption), we require data on the number of infections on the interval [t, t+ 8 days] in order to estimate $R_c(t)$. We use the implementation within EpiEstim (12) for calculating $R_c(t)$.

Results

The mean time between symptom onset and a case being confirmed is estimated to be 5.3 days (standard deviation 3.9 days), see Fig. 1. Based on an incubation period of around 5 days (15), we assume a time of 10 days between infection and confirmation. Thus, as a case is only confirmed about 10 days after being infected, we can only quantify the reproductive number R(t) until 10 days prior to today.

Analysis of confirmed case data for Switzerland and 10 cantons

In Fig. 2A, we show the cumulative number of confirmed cases (line) and the daily number of new cases (bars) for Switzerland and 10 out of the 11 cantons with the most confirmed cases on March 31, 2020. Graubünden was among the 11 cantons with the most cases; however, we omitted it due to lack of data.

In Fig. 2B, we show in red the R(t) through time based on the confirmed case data. Values of R(t)>1 correspond to exponential growth of the epidemic, while values of R(t)<1 imply exponential decline. We indicate this threshold of 1 with a dashed horizontal line.

On March 6th, it was announced that the national strategy to fight COVID 19 changed from finding all COVID-19 positive cases and contact tracing to protecting the population at risk, which resulted in not testing every individual with symptoms. The strategy was fully implemented starting March 9th.

We have too little data to reliably estimate R(t) prior to March 6^{th} , and thus all our figures start at March 6^{th} . The same testing policy was in place March $9^{th}-31^{st}$. More than 90% of individuals transmit within 8 days based on our serial interval assumption. Thus, the first day at which we can estimate R using comparable testing data is March 17^{th} (March 9+8 days). Since we have a 10 day reporting delay, this corresponds to R(t) estimates from March 7^{th} onwards. We show a dashed line on March 7^{th} .

In order to compare the R(t) estimates through time to public health policies (16), we highlight changes in policies with dotted vertical lines and a gray area. In particular, we display:

- On March 13th, schools were announced to be closed and on March 16th, non-essential shops, bars, and restaurants were announced to be closed. This "Ausserordentliche Lage" (a lockdown) in Switzerland started on March 17th and the "Notlage" (a lockdown) in Basel-Landschaft on March 15th, (9). The lockdowns are without curfew.
- On March 20th, the Federal Council prohibited gatherings of more than five people in public spaces.

Next, we performed a sensitivity analysis addressing the statistical method. The turquoise lines in Fig. 2B, are the estimates of the case reproductive number $R_c(t)$. We shifted this plot by 5 days compared to the R(t) plot: 4.8 days is the mean serial interval which implies that, at any point in time t, new infections are driven by individuals infected on average 4.8 days before time t. Thus, by shifting $R_c(t)$ by 5 days, the R and R_c curves should roughly align. Indeed, we observe the same overall patterns for R(t) and $R_c(t-5)$, see also (11).

Overall, we observe a decline in R(t) in the first half of March. R(t) stabilized around 1 during the period of the "Ausserordentliche Lage" (lockdown; to the right of the gray box). For Switzerland, R(t) already drops to 1 on March 13 (when additional measures were announced). However, $R_c(t)$ only drops around March 15. Thus, this data does not provide conclusive results as to which interventions resulted in a drop of R(t) to 1. The most recent values for R(t), i.e., for March 21, indicate that the epidemic is under control (R(t)<1).

Analyses with a focus on the epidemic in Switzerland, Basel-Stadt and Basel-Landschaft In Fig. 3 we show detailed results for Switzerland and the cantons of Basel-Stadt and Basel-Landschaft. We again show estimates for R from March 6 onwards. In Basel-Stadt, the main testing center opened on March 9 (10). Their testing policy was not changed until March 31. Thus our R(t) estimates should not be biased due to changes in testing from March 7, onwards (March 9 + 8 - 10 days, see above; dashed line). In Basel-Landschaft, the two testing centers exclusively performing tests in that canton after they opened on March 18 (9). Their testing policies were not changed until March 31, meaning we are confident in our R(t) estimates from March 16 onwards (dashed line).

As of March 19, the criteria for self-isolation in Basel-Stadt became stricter: individuals with COVID-19 symptoms need to self- quarantine for at least 10 days (compared to 24 hours after last symptoms up to March 19). People in the same household as a sick person need to self-quarantine for 10 days (compared to 5 days during March 9 - March 19). This intervention was implemented at almost the same time as the restriction of public gatherings to 5 people, so we only include the dotted line at March 20.

The testing intensity between March 9 and today may have changed throughout the time course of this COVID-19 epidemic in Switzerland, despite official recommendations (including the policies of the testing centres in Basel-Stadt and Basel-Landschaft) not having changed until March 31. For example, a decrease in testing through time due to a shortage of tests and swabs could, in principle, cause the observed decrease in estimated R(t) through time.

In order to address this potential confounding factor, for Switzerland we compare the estimates for R(t) based on the number of confirmed cases through time to the R(t) based on the number of deaths due to COVID-19 through time. We argue that although the chance of a COVID-19 case being confirmed depends on the testing intensity at that time, the chance of a death due to COVID-19 being reported does not change through time. Fig. 3A (bottom) shows the number of confirmed cases and the number of deaths through time (cumulative: lines; per day: bars). We assume a time between infection and death of 20 days (based on 15 days between symptom onset and death (17)). Fig. 3B (bottom) reveals that both data sources indicate a drop of R(t) to around 1 by mid-March, however the dynamics are estimated to be different.

For the cantons of Basel-Stadt and Basel-Landschaft, we compare the number of confirmed cases through time and the number of newly hospitalized COVID-19 patients. Again, until March 31, there have been no changes in the guidelines for when to hospitalize a patient. Thus we have no reason to suspect that the chance of a COVID-19 case being hospitalized changed through time. In Fig. 3A (top and middle), we show the number of confirmed cases and the number of hospitalizations. Fig. 3B (top & middle) shows the estimates of R(t). We assume that the delay between becoming infected and hospitalization is 8 days (compared to a 10-day delay between becoming infected and confirmation). The reason is that the patients may be tested upon hospital entry and the confirmation may take up to two days. Further, severe cases may be confirmed earlier compared to mild cases.

For both cantons, the two different datasets gave very similar estimates for R(t), indicating that potential changes in the testing of cases did not bias R(t). The 95% highest posterior density (HPD) intervals for the hospitalization data are wider, as expected, since the number of hospitalizations is smaller than the number of confirmed cases. The mean R(t) values for the most recent estimate (i.e., March 21) is below 1. The 95% HPD interval of the confirmed case data on this day excludes 1, indicating that the epidemic was on its way to a decline.

Testing intensity

Finally, we looked at the ratio of # positive tests / # total tests per day for the the University Hospital in Basel-Stadt (among others, all the samples from the main cantonal testing center which is open in its current form since March 9 are tested), and for the two testing centers in Basel-Landschaft (open since March 18), see Fig. 4. The correlation between time and ratio was not significant for either canton (p-value for Basel-Stadt: 0.21; for Basel-Landschaft 0.57). We want to highlight that these testing centers do not only test people from the respective canton. Further, some people from the respective canton may be tested elsewhere. Nevertheless, being the major testing centers of the cantons, the relative numbers should indicate the trend of testing intensity for the respective canton.

Discussion

Data on the spread of COVID-19 through time are of utmost importance to control this pandemic. An important measure obtained from the data is the reproductive number through time. Here, we carefully investigated if changes in testing intensity could bias the reported reproductive number, and see no indication for major biases based on comparing confirmed case data and hospitalization data.

By mid-March 2020, the reproductive number has dropped to around 1 across the considered locations. Thus, before or with the start of the strict measures taken between March 13 - March 16, 2020 (school closures, non-essential shop closures), the transmission rate has

decreased. However, after March 16, 2020, our data do not yet show evidence for the reduction of R(t) below 1. An R(t) of 1 only means that the epidemic has stabilized in size, namely the number of new infections per day stays roughly constant. However, the epidemic will not decline and die out with an R(t)=1.

Monitoring of R(t) can help health officials to evaluate the implementation of measures. In response to indications of a growing epidemic (R(t)>1), officials could implement more protective measures in advance to prevent overload of hospital capacity. Conversely, in response to indications of a shrinking epidemic (R(t)<1) officials could carefully relax protective measures in combination with wide-spread testing, contact-tracing, and isolation to avoid a rebound (18).

In (19), the reproductive number through time was estimated for Switzerland based on the number of COVID-19 related deaths through time and based on the effect of interventions on the reproductive number in other countries. The authors report that the reproductive number in Switzerland from March 16, 2020 was still clearly above 1. We obtain a number around 1 for that day based on deaths data and confirmation data. This may indicate that measures implemented in Switzerland have a different effect on R(t) compared to the same measures implemented elsewhere.

Our analysis relies on the assumption of a case being confirmed 10 days post-infection. It has been estimated that the serial interval has a mean of 4.8 days (13). Further, our Basel-Landschaft data suggests a mean time between first symptoms and case confirmation of around 5.3 days (mean). Data for other cantons will allow us to refine these estimates. If the time between infection and confirmation is 10+N days, then the x-axis in all plots showing R(t) need to be shifted by N days. In other words, for day t, we currently report R(t), but we should report R(t+N). The curve for R(t) does not change, however. Importantly, since there is a delay in case reporting (here assumed to be 10 days), we only see new infections with a 10-day delay. Thus, we are only able to calculate the reproductive number and thus transmission dynamics with a 10-day delay.

For estimating the R(t), we use the method presented in (11). We see two main caveats when using this method. First, this method assumes that all infections are included in the analysis. However, in Switzerland, mainly individuals belonging to risk groups are tested for COVID-19. If the proportion of non-reported cases is constant, then the method is still appropriate as the proportion cancels out from the equation given above. Also, in (11), it is shown in a simulation study that the R(t) estimates are robust to underreporting. Second, the method in (11) uses an expectation of the number of infected individuals for a given day (see equation in Methods) and thus ignores the underlying distribution, leading to an underestimation of uncertainty which leads to narrow 95% HPD intervals. We note that in order to present an R(t) which is not too sensitive to stochastic outliers, we smooth the analysis. In particular, R(t) is the reproductive number in a 3-day window ending on day t. By updating this plot daily, we will identify once R(t) is well below 1.

At the start of the Swiss epidemic, new infections were imports from other locations rather than community transmissions (3). The imports can lead to an overestimation of R at the start of the outbreak. Thus we refrain from interpreting the estimated R(t) values at the beginning of March 2020. Future phylodynamic analyses may be able to quantify the reproductive value at these time points based on genomic sequencing data using the concept proposed in (6).

Going forward, we will update R(t) in real-time throughout the course of the epidemic on our website (20). In this way, we intend to provide up-to-date information on the transmission dynamics based on the confirmed case data.

Code and data availability

All code for performing the analyses and all data compiled for this study is available on https://github.com/jscire/Swiss covid Re.

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Disclosure statement

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Author contributions

TS conceived the idea of the study. JS and TS designed and performed the analyses. SN and TV provided feedback on the analysis design. GB assisted in analyses. TS and JS interpreted the results. RM, LM, TG, TE, CQ, MS, STS, MB, RB, WK, KSR, CHN, SB, HHH, AE, RK, AW, CAM, MM, TB, AM designed the testing procedures in their cantons and provided data. SF, KNK, and JS provided data. TS wrote the first draft of the manuscript. All authors critically revised the manuscript and contributed to the final version.

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Figure legends

Figure 1. Histogram of the time between symptom onset and case confirmation for 92 patients from Basel-Landschaft.

Figure 2. A: The line shows the cumulative number of confirmed COVID-19 cases in Switzerland and 10 cantons. The bars show the number of newly confirmed cases for a particular day. Note that the y-axis is on a log scale. **B**: The reproductive number through time estimated based on the confirmed case data. In red, we show the mean R(t) and its 95% HPD interval. In turquoise, we show the estimated values for $R_c(t)$ as a sensitivity analysis. The vertical dotted lines are public health measures. In particular, the right of the gray interval is the time of the "Ausserordentliche Lage" (a lockdown) with non-essential shops and schools being closed. The R(t) values to the right of the dashed line are obtained based on confirmed data collected under the testing policy implemented on March 9^{th} , 2020.

Figure 3. A: The blue line shows the cumulative number of confirmed COVID-19 cases in Switzerland as well as the Cantons of Basel-Stadt and Basel-Landschaft. The blue bars show the number of newly confirmed cases for a particular day. The red line shows the cumulative number of deaths for Switzerland and the green line shows the cumulative number of hospitalizations for the cantons. The bars again show the number of new deaths or hospitalizations for a particular day. Note that the y-axis is on a log scale (thus no bar means 1 case and a bar from 1 down means 0 cases).

B: The estimates for R(t) based on the confirmed case data for the Cantons of Basel-Landschaft (top, blue), Basel-Stadt (middle, blue), and Switzerland (bottom, blue) and the estimates for R(t) based on the number of COVID-19 related hospitalizations in Basel-Landschaft (top, green), at the University Hospital Basel-Stadt (middle, green), and the number of COVID-19 related deaths in Switzerland (bottom, red). The R(t) values to the right of the dashed line are obtained based on confirmed data collected under the same testing policy. The vertical dotted lines are public health measures. In particular, the right of the gray interval is the time of the "Ausserordentliche Lage" (a lockdown) with non-essential shops and schools being closed.

Figure 4. We show the ratio of # positive tests and # tests per day performed (i) at the University Hospital Basel-Stadt and (ii) the two testing centers in Basel-Landschaft. If testing intensity decreased since the testing centers opened, we would expect an increase in this ratio as we would expect a trend towards testing individuals with stronger symptoms. The correlation between time and ratio is not significant.

Figures

Figure 1:

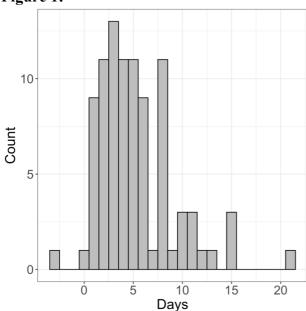
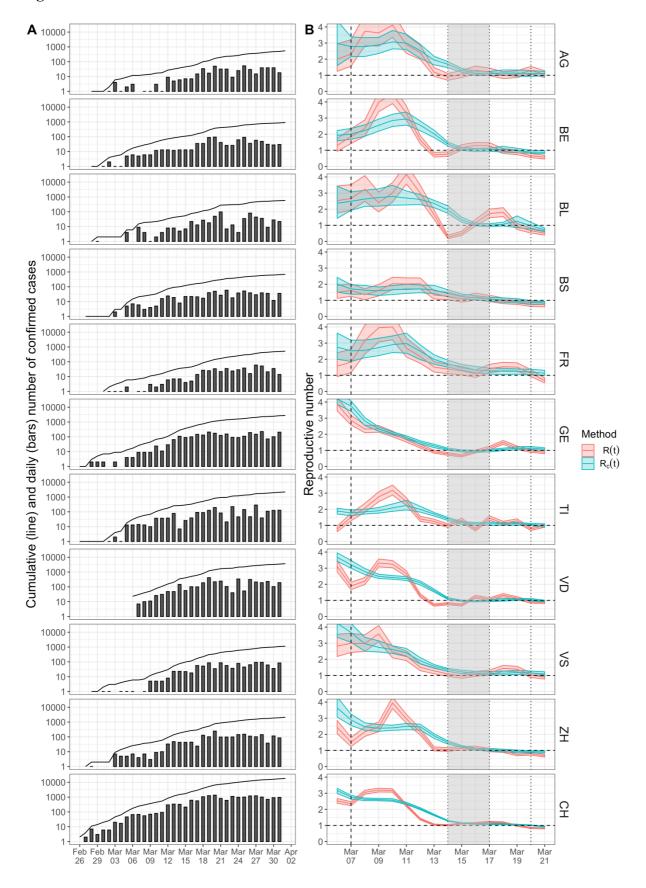


Figure 2:





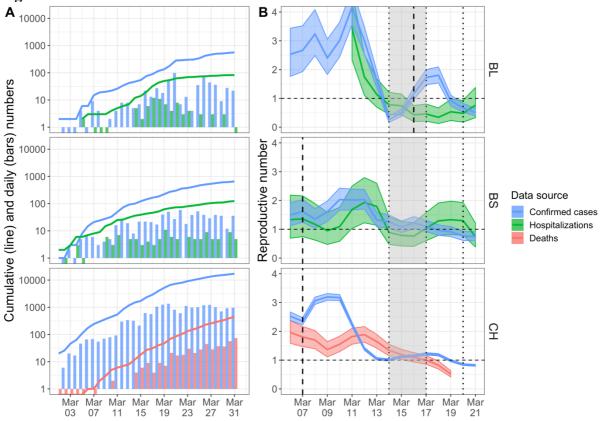


Figure 4:

