

Impact of cross-border-associated cases on the SARS-CoV-2 epidemic in Switzerland from June to September 2020

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Abstract

Introduction: In Switzerland, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) epidemic grew from a few dozen confirmed cases to several hundred cases per day during summer 2020. During this time, travelling to higher incidence countries might lead to more SARS-CoV-2 cases. Holiday travel without quarantine or having tested negative for SARS-CoV-2 was largely allowed. The impact of potential cross-border-associated cases (imports) on the national epidemic dynamics remained unclear. Our objective was to assess the impact of imports on the SARS-CoV-2 epidemic in Switzerland during summer 2020.

Method: We analysed individual data on confirmed SARS-CoV-2 cases reported by the Swiss Federal Office of Public Health (FOPH) from 1 June to 30 September 2020. We used a stochastic branching process model that accounts for super-spreading of SARS-CoV-2 to simulate epidemic trajectories in absence and presence of cross-border-associated cases.

Results: From June to September 2020, a total of 23,199 SARS-CoV-2 cases were reported in Switzerland. For 12,259 (53%) of these cases, the most likely country of exposure was available and 3,304 (27%) declared that exposure was most likely abroad. Assuming that all cases were infected locally (no imports), we estimated the effective reproduction number \mathcal{R}_e above the critical threshold of one (1.08, 95%-credible interval, CrI: 1.05-1.11). In contrast, we estimated \mathcal{R}_e to 0.84 (95%-CrI: 0.81-0.87) if imports were taken into account.

Discussion: In Switzerland, imports have had a considerable impact on the national dynamics and can explain the growth of the SARS-CoV-2 epidemic during summer 2020.

1 Introduction

In this study we would like to focus on the impact of human behaviour on SARS-CoV-2 incidence. In early 2020 SARS-CoV-2 spread around the world through business and holiday travel.[1] This resulted in many new introductions through cross-border-associated cases that were most likely responsible for local outbreaks.[2] It is known that the local effective reproductive number \mathcal{R}_e is likely to be overestimated when the number of introductions from cross-border associated cases is high.[3] The \mathcal{R}_e represents the average number of secondary cases per infectious case in a population with a given susceptibility state and certain prevention and control measures without new introductions. Thus, cross-border-associated cases should be taken into account when trying to estimate the local \mathcal{R}_e . However, the estimates of \mathcal{R}_e did not generally exclude cross-border associated cases. After all the impact of cross-border-associated cases on the increased SARS-CoV-2 incidence in Switzerland in summer 2020 remained largely unknown.

After unprecedented measures - closure of public institutions, leisure facilities, schools and universities, mandatory home office and closing of borders - in April and May 2020, Switzerland and other European countries reopened their borders allowing for travel. Switzerland reopened borders on 15 June 2020 to countries of the Schengen area.[4] With 8,5 millions citizens Switzerland is a relatively small country in the heart of Europe with borders to Germany, France, Italy, Austria and Liechtenstein. Moreover, Swiss like travelling and many countries were easily visited by the Swiss and conversely, many citizens from other countries might visited Switzerland. Around 80% of Swiss said that traveling is part of their holidays.[5] Before the SARS-CoV-2 pandemic, around 49% planned to travel abroad, this reduced to 15% in June 2020.[6] For many Swiss, the SARS-CoV-2 incidence of holiday destinations was crucial for their decision.[6] A survey in June showed that around 4% were planning to go to Germany, 3% to France and 2% to Italy or Austria.[6] More distant holiday destinations like Spain or Greece was planned to visit by less than 1%.[6]

In the absence of travel restrictions, cross-border-associated cases are to be expected.[2] In order to come to Switzerland in the summer of 2020, tests were neither mandatory nor were quarantine restrictions widespread. A phylogenetic analysis assessed the occurrence of

cross-border-associated cases in summer 2020.[7] The SARS-CoV-2 variant, 20E (EU1), that most likely originated in Spain spread multiple times to several other countries including Switzerland.[7] No evidence was found that 20E (EU1) spread rapidly across Europe due to viral changes, rather through increased mobility.[7] Multiple introduction in many countries was preferred due to loosening of restrictions, increased travel and lack of traceability.[7] Variant 20E (EU1) revealed failures in travel control during the pandemic, e.g. there were travels to higher incidence countries without adequate contact tracing and containment.[7] In contrast to 20E (EU1), the spread of variants of concern (VOC) like alpha, gamma, beta, and delta were not only accelerated by increased mobility but preferred due to higher transmissibility, longer generation time or immune evasion.[8, 9, 10, 11, 12] These findings highlighted the need of global collaboration in combating the pandemic and importance of large genomic surveillance. First to stop introductions of VOC and second to control the spread of VOCs.

Previously, stochastic branching process models were used to find trajectories that were consistent with surveillance data.[13, 14] It helped to determine epidemiological parameters such as the \mathcal{R}_e or the over-dispersion parameter.[13, 14] In this study, we aimed to quantify the impact of cross-border-associated cases on \mathcal{R}_e in Switzerland between June and September 2020. During this time the Swiss Federal Office of Public Health (SFOPH) reported a slow increase in the number of confirmed SARS-CoV-2 cases from a few dozen per day to several hundreds. Additionally, we analysed the reported most likely country of their exposure, i.e., where cases had been the last 14 days before they got tested or began to have symptoms. We used a stochastic branching process model with different cross-border-associated scenarios to find the most plausible trajectories of the summer 2020 epidemic in Switzerland.

2 Method

2.1 Data

For the purpose of this study, we analysed surveillance data of the SARS-CoV-2 epidemic in Switzerland from 1 June to 30 September 2020. We used individual data on positive cases re-

ported by the SFOPH. Data included for each case: age, sex, date of diagnosis or registration, place of residence, and the most likely country of exposure, i.e., a country where they had been within the last 14 days before they got tested or began to have symptoms. We considered the 23 most frequently reported countries of exposure including Switzerland (Table 2). Other countries (mentioned less than ten times) were grouped to 'others'. We performed a linear regression to estimate the differences in age (in 1 years steps) between individuals that had been exposed in different countries. Further, we grouped individuals into three categories based on their age: <21 years, 21-64 years and >64 years. 'Our World in Data' was used to present incidence for all 23 countries (variable: 'new_cases_smoothed_per_million'; Supplementary Figure 1).[15] Additionally, we calculated the incidence for Switzerland. Therefore, we calculated incidence of confirmed cases for each day including one week, i.e. mean of three days before and after the date of interest. The estimated mean of incidence was divided by 8,697,905 (number of Swiss citizens see here) and multiplied by 100,000.

2.2 Inferring growth rates and \mathcal{R}_e

We fitted a negative binomial generalised linear model to the daily number of confirmed cases of SARS-CoV-2 infections y starting on 1 June to 30 September 2020:

$$\log(E(y|t)) = a + rt, \quad (1)$$

where a was an intercept, r is a growth rate and t was the time in days. Thus, we estimated a constant growth rate r for the whole study period. Growth rate and reproductive number can be derived from each other taking into account the generation time, i.e. time between the infection of a primary case and one of its secondary cases.[16, 17, 18] This approach assumes that acquired immunity was minimal during the period of interest, and that the reporting rate was stable. We assumed a gamma distributed generation time with shape α and rate β , leading to the relation:

$$\mathcal{R}_e = (1 + \frac{r}{\beta})^\alpha. \quad (2)$$

For SARS-CoV-2, a mean generation time of $\mu = 5.2$ days with a standard deviation of $\sigma = 1.72$ was reported.[19] Parameters α (gamma shape) and β (gamma rate) were given by μ and σ as $\frac{\mu^2}{\sigma^2}$ and $\frac{\mu}{\sigma^2}$, respectively.

2.3 Epidemic simulations

We simulated epidemics for 1 June to 30 September 2020 using a stochastic branching process model that accounted for super-spreading in transmission of SARS-CoV-2.[14] The branching process was based on a negative-binomial distribution for the distribution of secondary cases, with a mean of \mathcal{R}_e and over-dispersion parameter k . The generation time for each transmission event was sampled from a gamma distribution as described in the previous section.

Within our branching process model we considered different values for \mathcal{R}_e , for k and for the seed – the number of infectious individuals during the week preceding the start of the simulation (Table 1). We considered a prior distribution for \mathcal{R}_e from 0.5 to 1.5. For k , we considered values between 0.49 and 0.52 as estimated from contact tracing data in India[20], and in sensitivity analyses we also considered values of 0.1 and 1.[21] For the seed, we used the estimate of the $E(y|t)$ for t_{-7} to t_{-1} in equation (1) with its 95%-predictive interval, resulting in values from 12 to 33 cases per day. For each trajectory seeds for t_{-7} to t_{-1} were randomly selected from a uniform distribution ranging from 12 to 33 cases per day. This resulted in a total of 94 to 222 cases from 25 to 31 May 2020, where the SFOPH reported 126 cases in Switzerland this week.

The simulations proceeded as follows. Firstly, we simulated 10^5 epidemic trajectories with the branching process model, randomly sampling parameter values in each iteration, except for the number of cross-border-associated cases that was fixed to 0. These trajectories only accounted for local transmission and was referred as the baseline scenario. We removed trajectories leading to a cumulative incidence over 10^6 (43 times more than the confirmed cumulative incidence).

Secondly, we accounted for cross-border-associated cases and added these to the baseline scenario. In these scenarios, cross-border-associated cases were added to each trajectory according to the date of test (Figure 1d). Cross-border-associated cases were equally likely to transmit, i.e., initiating new branches of local transmission, as all other cases.

The SFOPH reported 3,304 cross-border-associated cases during the study period, but the information on the country of exposure was missing for 10,940 cases. For 12,259 out of 23,199 (53%, the extrapolation factor) information was available. To capture the uncertainty of missing information we considered three different scenar-

Parameter	Description	Values considered	Sampling strategy
\mathcal{R}_e	Effective reproductive number	0.5 - 1.5	10^5 uniformly distributed
k	Over-dispersion parameter	0.49 - 0.52	10^5 normally distributed
n	Seeds	12 - 32 per day	uniformly distributed
I	Imports	baseline; a); b); c)	four scenarios

Table 1: Prior distributions of the parameters used to simulate the epidemic trajectories.

ios that account for cross-border-associated cases. The most plausible scenario a) considered missing of the country of exposure and the corresponding lack of the exact number of cross-border-associated cases as random by using following calculation: reported cross-border-associated cases per day * extrapolation factor. In the lower limit scenario b) cross-border cases were less likely

among the missing exposure countries by using following calculation: reported cross-border-associated cases per day * extrapolation factor * 2/3. Contrary, in the upper limit scenario c) cross-border cases were more likely among the missing exposure countries by using following calculation: reported cross-border-associated cases per day * extrapolation factor * 3/2.

2.4 Inference

Following the principles of approximate Bayesian computation (ABC), simulated epidemic trajectories were rejected when the cumulative incidence and final incidence fell outside of predefined ranges. Predefined ranges for cumulative incidence and final incidence were constructed using SFOPH reports on confirmed cases. We used (10^4 simulations of) random negative binomial model to obtain 95%-compatibility interval (CI) of (I) the cumulative incidence from 1 June to 30 September 2020, and (II) the final incidence from 24 to 30 September 2020 divided by 7. The random negative binomial model was calibrated with the standard error of equation (1) and (I) the cumulative incidence for the period of interest or (II) the cumulative incidence for the last seven days, respectively.

All analyses were preformed using *R v.4.0* with following packages

`MASS`, `MCMCglmm`, `doParallel`, `foreach`, `lubridate`, `reshape2`, `ggplot2`, `ggpubr`, `grid`, `gridExtra`, `RColorBrewer`.^[22]

3 Results

In total 23,199 cases were confirmed by the SFOPH between 1 June to 30 September 2020 (Table 2). Of them, 13,929 (48%) were female and 14,985 (52%) were male. For nine individuals the gender was not known. For 12,259 (53%) cases the most likely country of exposure was reported. Of them, 3,304 (27%) reported an exposure abroad (Table 2); Figure 1). The peak of reported cross-border-associated was on 6 September 2020 with 105 cases (Figure 1c,d). Of all exposures that were likely to have happened abroad 1,562 (44%) were female and 2,000 (56%) were male.

The study population was 34 (interquartile range (IQR): 24-50) years and individuals that had an exposure abroad were 31 (IQR: 23-48) years (Table 2). Individuals who reported that Switzerland was the only country they had visited within the last 14 days were 35 (IQR: 24-51) years. Different age categories were more likely to visit some countries during summer (Table 2; Supplementary Figure 2). Individuals were significantly younger ($< .05$) if they were exposed to SARS-CoV-2 in France, Croatia, Turkey, Serbia, Greece, Portugal, Albania, Hungary, Poland, Czech Republic, Romania, Slovenia, or the UK compared to individuals that were only in Switzerland. Contrary, individuals were

significantly older ($< .05$) if they were exposed to SARS-CoV-2 in Kosovo, Italy, Germany, Spain, Malta, Austria, North Macedonia, Bosnia and Herzegovina, Netherlands, or in other countries, abroad but unknown, or generally unknown compared to individuals that were only in Switzerland. Tendency of crossing borders was similar regarding residence of Swiss cases (Supplementary Figure 3).

The incidence of 22 countries - where Swiss cases were exposed to SARS-CoV-2 - was for 81 (95%-CI 7-122) out of 122 days higher as in Switzerland (Table 2; Supplementary Figure 1). At the beginning of June 2020, none of the 22 countries with at least a dozen returnees

Country	Incidence per 10 ⁶ median (range)	Confirmed cases	Known exposure (in %)	Cases abroad (in %)	Age in years median (IQR)	Mandatory quarantine
All reported cases	-	23199	-	-	34 (24-50)	-
Cross-border-associated	-	3304	26.95	100.00	31 (23-48)	-
Switzerland	17.1 (1.7 - 50.9)	8955	73.05	-	35 (24-51)	-
France	15.4 (4.8 - 181.3)	650	5.30	19.67	29 (23-41)	2020-09-14 - **
Croatia	19.6 (0.0 - 68.2)	419	3.42	12.68	24 (21-28)	2020-09-07 - **
Kosovo	59.9 (3.3 - 122.8)	309	2.52	9.35	49 (31-61)	2020-07-06 - **
Italy	5.0 (2.9 - 29.1)	301	2.46	9.11	32 (24-46)	2020-09-28 - **
Germany	8.0 (2.7 - 23.7)	184	1.50	5.57	37 (26-51)	-
Turkey	14.8 (10.4 - 19.9)	169	1.38	5.12	39 (26-53)	-
Serbia	19.1 (4.8 - 63.6)	153	1.25	4.63	46 (28-60)	2020-07-06 - **
Spain	49.2 (5.4 - 242.0)	136	1.11	4.12	30 (23-42)	2020-08-08 - **
Malta	44.0 (0.0 - 137.5)	125	1.02	3.78	20 (19-24)	2020-08-20 - **
Greece	5.2 (0.5 - 31.6)	116	0.95	3.51	29 (25-37)	-
Portugal	31.7 (16.7 - 71.1)	116	0.95	3.51	36 (25-49)	2020-09-28 - **
Austria	12.8 (2.6 - 81.2)	65	0.53	1.97	35 (28-50)	2020-09-14 - **
North Macedonia	62.6 (21.7 - 77.2)	59	0.48	1.79	61 (50-65)	2020-07-06 - **
Albania	36.9 (5.4 - 55.5)	57	0.46	1.73	38 (27-48)	2020-08-20 - **
Bosnia and Herzegovina	73.9 (4.2 - 110.1)	56	0.46	1.69	46 (30-60)	2020-07-23 - **
Hungary	1.8 (0.3 - 91.0)	38	0.31	1.15	28 (23-34)	2020-09-28 - **
Netherlands	15.8 (3.0 - 172.4)	34	0.28	1.03	30 (23-46)	2020-09-28 - **
Poland	12.4 (6.8 - 37.1)	24	0.20	0.73	32 (31-44)	-
Czech Republic	19.8 (4.0 - 204.2)	22	0.18	0.67	24 (20-33)	2020-09-14 - **
Romania	59.8 (8.0 - 82.9)	13	0.11	0.39	40 (26-52)	2020-07-23 - **
Slovenia	8.7 (0.3 - 68.4)	11	0.09	0.33	30 (18-34)	2020-09-28 - **
UK	14.9 (5.2 - 91.8)	11	0.09	0.33	30 (20-43)	2020-09-28 - **
Others	-	157	1.28	4.75	37 (25-53)	-
Abroad but unknown	-	79	0.64	2.39	33 (26-49)	-
Unknown	-	10940	-	-	35 (25-51)	-

Table 2: Confirmed SARS-CoV-2 cases during summer 2020 regarding age and most likely country of exposure.**Mandatory quarantine did not end on 30 September 2020. Abbreviation: IQR, interquartile range

with a SARS-CoV-2 infection between June and September was on the list where returnees had to do quarantine. In July 2020 the list was including five countries of 22 countries. In August and September 3 respectively 10 additional countries were added to the list. End of September 5 of 22 countries had not been on the list during summer. During this time testing was not mandatory for individuals that crossed borders.

Beginning of June 2020 Switzerland had an incidence of 0.17 per 100,000 citizens (3 cases) and at the end of September 5.36 (540 cases; Figure 2c). The latter was also the maximum value during the time of interest. Accordingly, there was an increase of cases during the summer months. We estimated the 95%-CI of cumulative incidence of 17,019 to 30,533 cases for the period from 1 June to 30 September 2020 (23,199 cases were reported by the SFOPH; Figure 1a). For the final incidence the 95%-CI laid within 93 to 762 cases for the last day. For a day in the last week the mean of the reported cases was 338 cases per day.

Assuming a constant growth, we estimated an epidemic growth rate of 0.03 (95%-CI 0.02-0.03) per day and a \mathcal{R}_e of 1.15 (95%-CI 1.14-1.16) for June to September 2020.

With the baseline scenario and three additional scenarios that accounted for cross-border-associated cases we simulated the Swiss epidemic. Overall, 11,515 of $4 \cdot 10^5$ (2.88%) trajectories were within the 95%-CI of the expected cumulative incidence and final incidence. The baseline scenario assumed no new introductions which was not the case for the Swiss epidemic and thus, \mathcal{R}_e was over-estimated. Accounting for new introductions required to re-evaluate the intensity of local transmission, i.e. the value of \mathcal{R}_e , to match the observed dynamics of SARS-CoV-2 in summer 2020. Assuming no introductions, 40 (0.04%) trajectories were within the 95%-CI of the expected cumulative incidence and final incidence (Figure 3b). The \mathcal{R}_e was 1.08 (95%-CI: 1.05-1.11; which was lower than the \mathcal{R}_e derived from the equation (2) (Figure 2c). The baseline scenario was then extended with three scenarios a), b), and c) that included new introductions of cross-border-associated cases. In extended models, all cases, i.e., cross-border-associated cases and local cases, were equally likely to transmit SARS-CoV-2.

Scenario a) accounted in total for 5,050 cross-border-associated cases resulting from an extrapolation of 3,304 cross-border-associated cases. Overall, 3,690 (3.69%) trajectories were accepted

as they were within the 95%-CI of the cumulative incidence and final incidence (Table 2; Figure 2; Figure 3). These 3,690 trajectories represented a \mathcal{R}_e of 0.84 (95%-CrI: 0.81-0.87) (Figure 2; Figure 3). For scenario b) and c) the number of introductions were extrapolated from the reported cross-border-associated cases and a multiplication with 2/3 and 3/2. In total, 1,241 (1.24%) and 6,543 (6.54%) trajectories were within the 95%-CI of the expected cumulative incidence and final incidence (Table 2; Figure 2). These 1,241 and 6,543 trajectories represented a \mathcal{R}_e of 0.91 (95%-CrI: 0.88-0.93) and \mathcal{R}_e of 0.76 (95%-CI: 0.72-0.80) (Figure 2; Figure 3).

Our results did not depend on the dispersion parameter k . Same \mathcal{R}_e values were estimated for all four scenarios if we set $k = 0.1$ and $k = 1$.

4 Discussion

The SARS-CoV-2 epidemic in Switzerland grew from a few dozen confirmed cases per day in early June 2020 to several hundred by the end of September 2020. Ignoring cross-border-associated cases the \mathcal{R}_e was above one for the time of interest. In summer 2020, however, around a quarter of confirmed cases were cross-border-associated. Using our stochastic branching process model that accounts for cross-border cases, we showed that the Swiss epidemic had a \mathcal{R}_e below the critical threshold of one. Also stabilisation of confirmed cases in September 2020 was captured by scenarios that accounted cross-border-associated cases if \mathcal{R}_e was below one. Thus, cross-border-associated cases and their local spread was one of the leading forces that led to a 100-fold increase of confirmed cases per day within three months despite \mathcal{R}_e below one. Consequently, the impact of cross-border-associated cases cannot be ignored to understand and regulate local epidemics (during a pandemic).

Our stochastic branching process model was calibrated to assess the impact of cross-border-associated cases on an epidemiological, i.e. population-based, level. For simplicity models described only the Swiss epidemic and ignored geographical sub-levels like cantons. Stochastic effects were showed to play an important role in determining parameters in epidemics.[13, 14] Nevertheless, our method has several limitations that need to be addressed. We did not account for variations in growth rates, seasonal effect of the SARS-CoV-2 and contact patterns, different restrictions carried out, or different incidences in

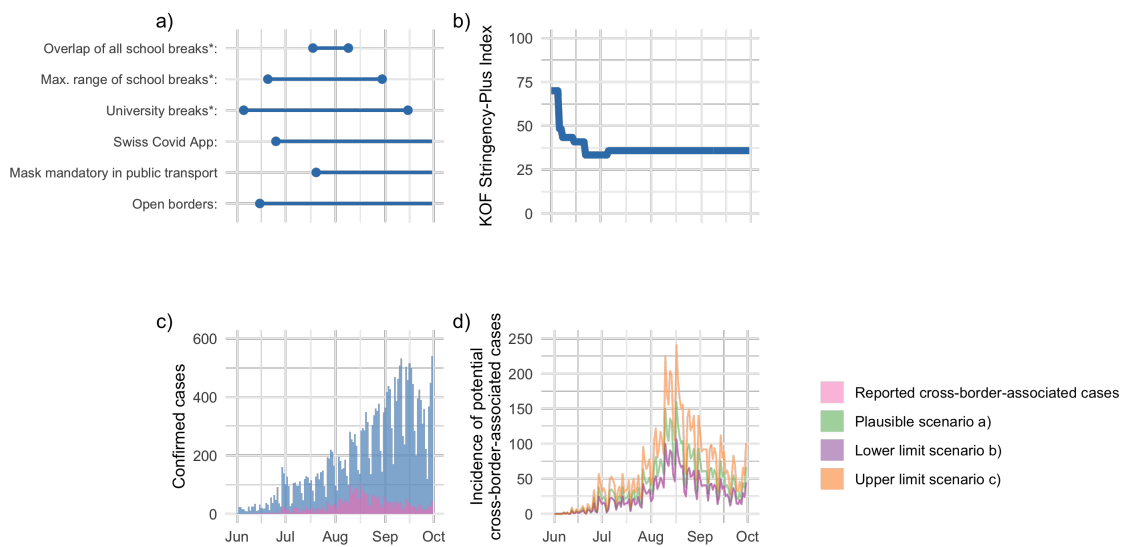


Figure 1: The Swiss SARS-CoV-2 epidemic in summer 2020. a) Five major events that might influenced the Swiss epidemic from 1 June to 30 September 2020. b) The KOF stringency plus index records the stringency of COVID-19 policy measures in Switzerland over time. The values range from 0 (= no measures) to 100 (= full lockdown). c) Daily incidence (blue) and reported cross-border-associated cases (pink). d) Three cross-border-associated scenarios a, b, and c that were processed with a branching process model. *Official breaks of universities and schools might vary for different subjects and between different schools and cantons, respectively. More details on quarantine measures in Table 2 and on www.fedlex.admin.ch. Abbreviations: COVID-19, coronavirus disease 2019.

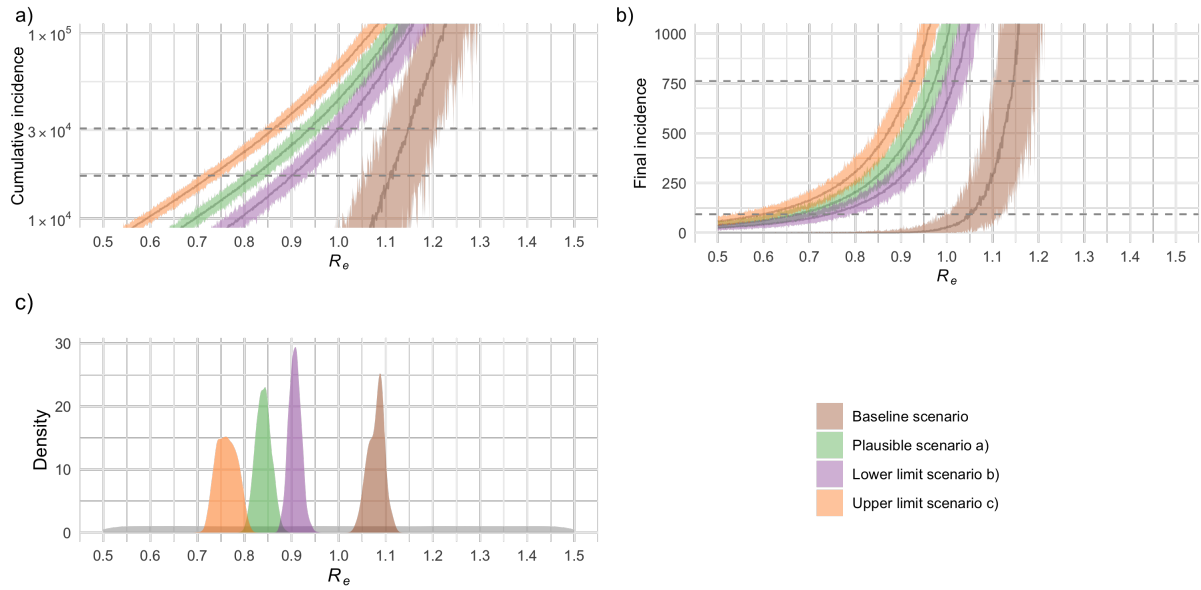


Figure 2: Impact of cross-border-associated cases on the local epidemic. a) Curves represent credible range and median of the cumulative incidence for the baseline scenario and three scenarios that accounted for cross-border-associated cases. Dashed lines represent 95%-CI for the cumulative incidence during 1 June to 30 September 2020. b) Curves represent credible range and median of the final incidence for the baseline and three models that accounted for cross-border-associated cases. Dashed lines represent 95%-CI of the incidence on 30 September 2020. c) Prior and posterior distribution of R_e for the baseline scenario and three scenarios that accounted for cross-border-associated cases. Abbreviations: R_e , the effective reproductive number; CI, compatibility interval.

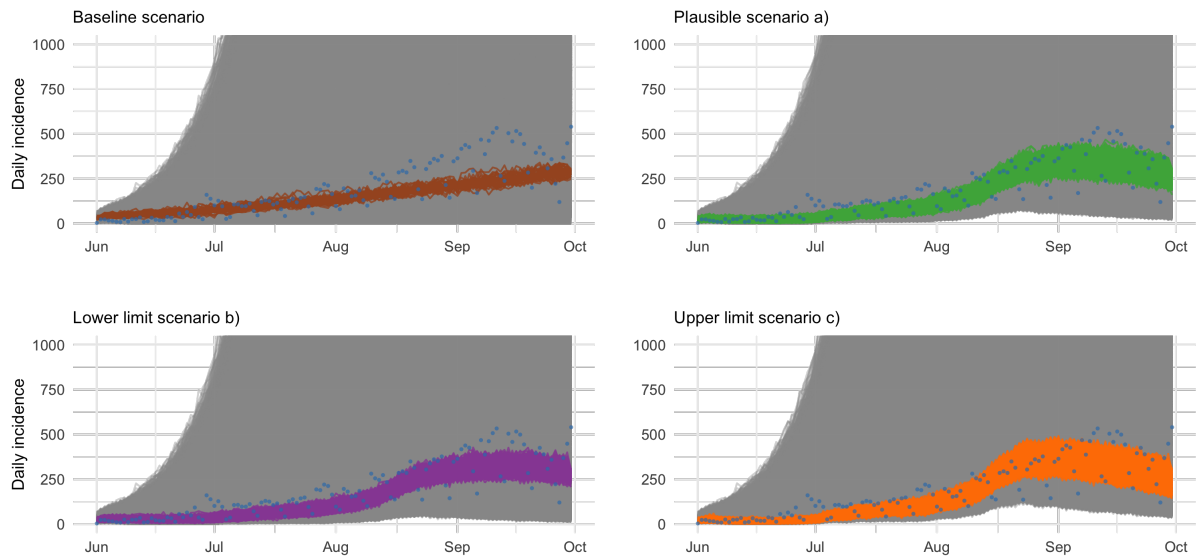


Figure 3: Accepted trajectories (coloured) using the baseline scenario (no cross-border-associated cases) and accounting for cross-border-associated cases within scenarios a-c. Blue dots show confirmed SARS-CoV-2 cases.

groups or countries.

Our approach assumed a constant growth rate and \mathcal{R}_e over the summer and ignored immunity, which was acceptable during low prevalence. The SFOPH reported 30,883 cases before 1 June and 23,199 more until 30 September 2020. Growth rates, can be calculated for different intervals, e.g., weeks, months, or adjusted for different factors. For our study, a constant growth rate and \mathcal{R}_e was more compatible to calculate the overall impact of cross-border-associated cases.

Our study period covered summer months only. The increase in SARS-CoV-2 occurred despite the warm and dry weather in the northern hemisphere, which should have hindered the epidemic from spreading as fast.[23] Also the stringency of policy measures was constant after relaxations in June 2020. However, people were more active during summer compared to winter and probably more optimistic about the pandemic (mostly at the end of summer 2020), which most likely resulted in more physical contacts than before. Tracking contact patterns, i.e., behaviour, can give a fast and good assessment of real physical distancing measures.[24] Unfortunately, contact patterns were missing for this period in Switzerland. By analysing surveillance data, we found that different age groups were exposed to the SARS-CoV-2 in different countries abroad. Further information on age-related mixing patterns like established by the Co-Mix study is needed to better understand the social dynamics.[25] Our study indicated that age-related mixing patterns are important to understand SARS-CoV-2 transmission. However, close contact alone is not responsible for SARS-CoV-2 transmission. Some transmission cluster were linked to crowded indoor spaces which underlines the possibility of aerosol and droplet transmission.[26]

A good balance between travel, tracing, testing, and tracking new variants is needed to reduce new introductions. During summer 2020, in Switzerland testing was free and mandatory for symptomatic cases, but not for asymptomatic cases. If, however, a person had contact with a positive person they were required to do quarantine regardless of test results. The contact tracing was provided either by infectees themselves, through authorities or the Swiss Covid app (launched on 15 June 2020).[27] Testing was not mandatory for individuals that crossed borders. In addition, the quarantine rules in Switzerland differed by time and on the exposed country. If people that crossed borders had to

do quarantine, the level of obedience is uncertain. Thus, hardly all cross-border-associated cases were confirmed and stopped before further transmission. We therefore assumed that cross-border-associated cases were just as likely to transmit as local cases. More sophisticated models adding different probabilities of further transmission inferred by the incidence of different groups, e.g., stratified by behaviour or age, might help to better understand transmission dynamics. To be noted, if cross-border-associated cases were more likely to transmit than local cases due to a higher incidence among travellers, this would be similar to our upper limit scenario.

Studies reported about a two-fold and more underreporting of SARS-CoV-2 cases.[28, 29] For Switzerland, a phylogenetic analysis showed that the degree of under-ascertainment was low during summer 2020.[30] Thus, the Swiss epidemic was represented well by surveillance data.

From our findings travel strategies might be derived, including mandatory quarantine and test strategies for the coming summer 2021. Also in other countries, travel and resulting new introduction had a strong impact on the local epidemic.[1, 2, 7] Most likely (global) herd immunity will not be achieved in the summer 2021, so existing measures such as vaccination, tracing, testing, and physical distancing remain important to keep incidence low. Tracing and testing are also important as there is still uncertainty about asymptomatic cases.[31, 32] Studies found the proportion of asymptomatic cases to be 17% (or 20%) and 1/4 less transmissible.[33, 32, 34] In summer 2020, there was no testing on return from holidays, and quarantine was rarely enforced in most countries. In summer 2021, countries should be more aware of the potential impact of new introductions by travelling and test more broadly. It could be an option to test all that cross borders and give them the option of reduced quarantine if tests are negative.[35] Moreover, mandatory quarantine and testing might reduce the willingness to travel as it includes extra expenses for travellers and keeps awareness of the SARS-CoV-2 pandemic high. Here we need to emphasised that one case might lead to an outbreak thus population based surveillance including reporting of countries of exposure and viral sequence data is crucial for appropriate measures.[1] Worbe et al., highlighted the need to detect new introduction and transmission clusters early through routine, massive, sequence based approaches — not months or years later,

when clinical symptoms have accumulated.[1] Efforts to monitor mutations in pathogens must remain to improve pandemic preparedness and facilitate exchanges between researchers and public health officials in emergencies.

For Switzerland in summer 2020, the incidence was low compared to other countries. Thus, light travel measures introduced a large number of cases into the local epidemic. Ultimately, Switzerland paid a high price through light measures that eventually induced a growing epidemic through cross-border-associated cases. Our results underlined the importance of improved surveillance for (international) travellers in order to better control the spread of SARS-CoV-2.

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6 Author contributions

MLR, EBH, JR, NAR, and CLR conceived the study and contributed to the analysis of the results. MLR performed the analysis and wrote the first draft of the manuscript. NH gave important inputs for the analysis and interpretation. All authors read and approved the final manuscript.

7 Funding

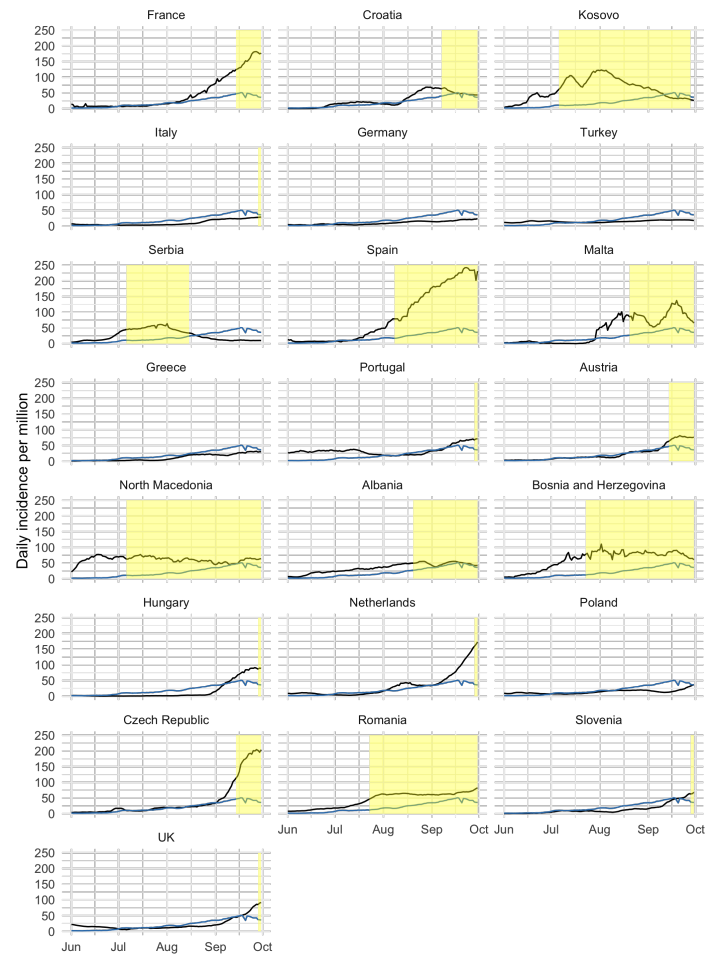
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References

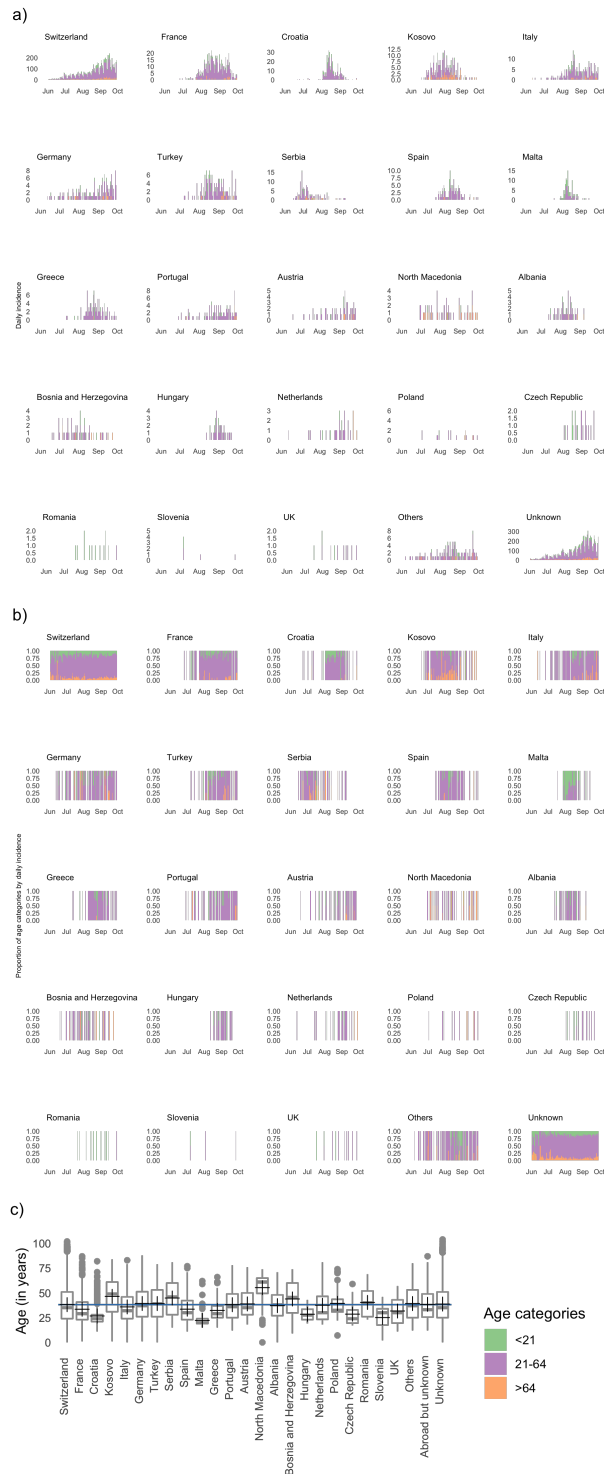
- [1] Worobey M, Pekar J, Larsen BB, Nelson MI, Hill V, Joy JB, et al. The emergence of SARS-CoV-2 in Europe and North America;370(6516):564–570. Available from: <https://www.sciencemag.org/lookup/doi/10.1126/science.abc8169>.
- [2] Russell TW, Wu JT, Clifford S, Edmunds WJ, Kucharski AJ, Jit M. Effect of internationally imported cases on internal spread of COVID-19: a mathematical modelling study;6(1):e12–e20. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S2468266720302632>.
- [3] Roberts MG, Nishiura H. Early Estimation of the Reproduction Number in the Presence of Imported Cases: Pandemic Influenza H1N1-2009 in New Zealand;6(5):e17835. Available from: <https://dx.plos.org/10.1371/journal.pone.0017835>.
- [4] Council F. Coronavirus: Switzerland to reopen its borders with all EU/EFTA states on 15 June;. Bern, Switzerland. Available from: <https://www.admin.ch/gov/en/start/documentation/media-releases.msg-id-79365.html>.
- [5] Heim N. Dreivon vier Reisen werden storniert;. Available from: <https://www.zhaw.ch/storage/hochschule/medien/news/2020/200604-corona-reiseverhalten-medienmitteilung-de.pdf>.
- [6] Bosshardt L, Bühler G, Bütikofer S, Craviolini J, Hermann M, David K, et al. Die Schweiz und die Corona-Krise;. Available from: https://sotomo.ch/site/wp-content/uploads/2020/06/SGR_sotomo_Monitoring_Coronakrise_W4.pdf.
- [7] Hodcroft EB, Zuber M, Nadeau S, Vaughan TG, Crawford KHD, Althaus CL, et al. Spread of a SARS-CoV-2 variant through Europe in the summer of 2020;Available from: <http://www.nature.com/articles/s41586-021-03677-y>.
- [8] Davies NG, Abbott S, Barnard RC, Jarvis CI, Kucharski AJ, Munday JD, et al. Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England;372(6538):eabg3055. Available from: <https://www.sciencemag.org/lookup/doi/10.1126/science.abg3055>.
- [9] Faria NR, Mellan TA, Whittaker C, Claro IM, Candido DdS, Mishra S, et al. Genomics and epidemiology of the P.1 SARS-CoV-2 lineage in Manaus, Brazil;372(6544):815–821. Available from: <https://www.sciencemag.org/lookup/doi/10.1126/science.abh2644>.

- [10] Tegally H, Wilkinson E, Giovanetti M, Iranzadeh A, Fonseca V, Giandhari J, et al. Detection of a SARS-CoV-2 variant of concern in South Africa;592(7854):438–443. Available from: <http://www.nature.com/articles/s41586-021-03402-9>.
- [11] Cherian S, Potdar V, Jadhav S, Yadav P, Gupta N, Das M, et al.. Convergent evolution of SARS-CoV-2 spike mutations, L452R, E484Q and P681R, in the second wave of COVID-19 in Maharashtra, India [preprint];. Available from: <http://biorxiv.org/lookup/doi/10.1101/2021.04.22.440932>.
- [12] World Health Organisation (WHO). Tracking SARS-CoV-2 variants;. Available from: <https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>.
- [13] Althaus CL, Low N, Musa EO, Shuaib F, Gsteiger S. Ebola virus disease outbreak in Nigeria: Transmission dynamics and rapid control;11:80–84. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1755436515000341>.
- [14] Riou J, Althaus CL. Pattern of early human-to-human transmission of Wuhan 2019 novel coronavirus (2019-nCoV), December 2019 to January 2020;25(4). Available from: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.4.2000058>.
- [15] Hasell J, Mathieu E, Beltekian D, Macdonald B, Giattino C, Ortiz-Ospina E, et al. A cross-country database of COVID-19 testing;7(1):345. Available from: <http://www.nature.com/articles/s41597-020-00688-8>.
- [16] Wallinga J, Lipsitch M. How generation intervals shape the relationship between growth rates and reproductive numbers;274(1609):599–604. Available from: <https://royalsocietypublishing.org/doi/10.1098/rspb.2006.3754>.
- [17] Krauer F, Gsteiger S, Low N, Hansen CH, Althaus CL. Heterogeneity in District-Level Transmission of Ebola Virus Disease during the 2013-2015 Epidemic in West Africa;10(7):e0004867. Available from: <https://dx.plos.org/10.1371/journal.pntd.0004867>.
- [18] Svensson A. A note on generation times in epidemic models;208(1):300–311. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0025556406002094>.
- [19] Ganyani T, Kremer C, Chen D, Torneri A, Faes C, Wallinga J, et al. Estimating the generation interval for coronavirus disease (COVID-19) based on symptom onset data, March 2020;25(17). Available from: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.17.2000257>.
- [20] Laxminarayan R, Wahl B, Dudala SR, Gopal K, Mohan B C, Neelima S, et al. Epidemiology and transmission dynamics of COVID-19 in two Indian states;370(6517):691–697. Available from: <https://www.sciencemag.org/lookup/doi/10.1126/science.abd7672>.
- [21] Taube JC, Miller PB, Drake JM. An open-access database of infectious disease transmission trees to explore super-spreader epidemiology [preprint];. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.01.11.21249622>.
- [22] R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing;. Available from: <https://www.R-project.org/>.
- [23] Neher RA, Dyrda R, Druelle V, Hodgecroft EB, Albert J. Potential impact of seasonal forcing on a SARS-CoV-2 pandemic;Available from: <https://doi.emh.ch/smw.2020.20224>.
- [24] Jarvis CI, Van Zandvoort K, CMMID COVID-19 working group, Gimma A, Prem K, Klepac P, et al. Quantifying the impact of physical distance measures on the transmission of COVID-19 in the UK;18(1):124. Available from: <https://bmcmecicine.biomedcentral.com/articles/10.1186/s12916-020-01597-8>.
- [25] Coletti P, Wambua J, Gimma A, Willem L, Vercruysse S, Vanhoutte B, et al. CoMix: comparing mixing patterns in the Belgian population during and after lockdown;10(1):21885. Available from: <http://www.nature.com/articles/s41598-020-78540-7>.

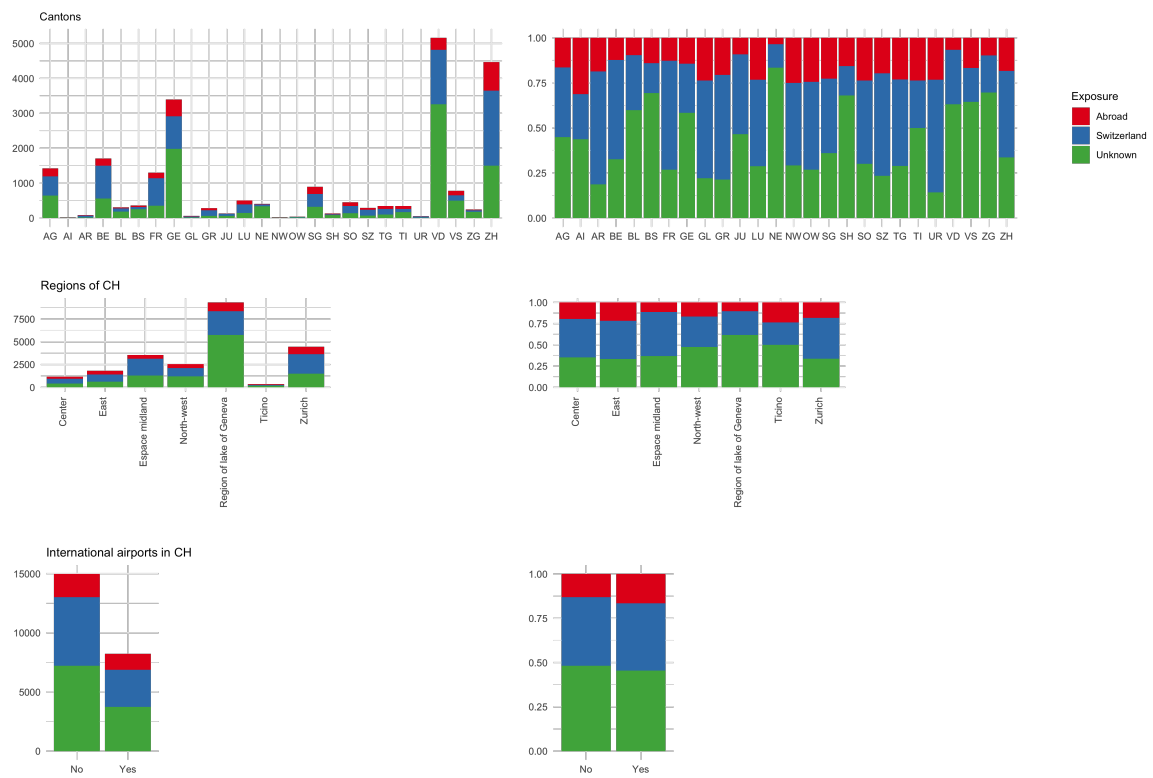
- [26] Tang S, Mao Y, Jones RM, Tan Q, Ji JS, Li N, et al. Aerosol transmission of SARS-CoV-2? Evidence, prevention and control;144:106039. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0160412020319942>.
- [27] Salath M, Althaus C, Anderegg N, Antonioli D, Ballouz T, Bugnon E, et al. Early evidence of effectiveness of digital contact tracing for SARS-CoV-2 in Switzerland; Available from: <https://doi.emh.ch/smw.2020.20457>.
- [28] Li R, Pei S, Chen B, Song Y, Zhang T, Yang W, et al. Substantial undocumented infection facilitates the rapid dissemination of novel coronavirus (SARS-CoV-2);368(6490):489–493. Available from: <https://www.sciencemag.org/lookup/doi/10.1126/science.abb3221>.
- [29] Wu SL, Mertens AN, Crider YS, Nguyen A, Pokpongkiat NN, Djajadi S, et al. Substantial underestimation of SARS-CoV-2 infection in the United States;11(1):4507. Available from: <http://www.nature.com/articles/s41467-020-18272-4>.
- [30] Nadeau S, Beckmann C, Topolsky I, Vaughan T, Hodcroft E, Schär T, et al. Quantifying SARS-CoV-2 spread in Switzerland based on genomic sequencing data [preprint];. Available from: <http://medrxiv.org/lookup/doi/10.1101/2020.10.14.20212621>.
- [31] Nogrady B. What the data say about asymptomatic COVID infections;587(7835):534–535. Available from: <http://www.nature.com/articles/d41586-020-03141-3>.
- [32] Buitrago-Garcia D, Egli-Gany D, Counotte MJ, Hossmann S, Imeri H, Ipekci AM, et al. Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis;17(9):e1003346. Available from: <https://dx.plos.org/10.1371/journal.pmed.1003346>.
- [33] Byambasuren O, Cardona M, Bell K, Clark J, McLaws ML, Glasziou P. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: Systematic review and meta-analysis;5(4):223–234. Available from: <https://jammi.utpjournals.press/doi/10.3138/jammi-2020-0030>.
- [34] Bi Q, Lessler J, Eckerle I, Lauer SA, Kaiser L, Vuilleumier N, et al. Household Transmission of SARS-CoV-2: Insights from a Population-based Serological Survey [preprint];. Available from: <http://medrxiv.org/lookup/doi/10.1101/2020.11.04.20225573>.
- [35] Ashcroft P, Lehtinen S, Angst DC, Low N, Bonhoeffer S. Quantifying the impact of quarantine duration on COVID-19 transmission;10:e63704. Available from: <https://elifesciences.org/articles/63704>.



Supplementary Figure 1: Daily incidence per million compared to Switzerland (in blue). Yellow area represent when country was on the mandatory quarantine list whereby there were regional differences for France, Austria, and Spain.



Supplementary Figure 2: Reported cases and the most likely country of exposure. a) Reported cases and fraction of different age groups. b) Proportion of all cases and fraction of different age groups. c) Age distribution for reported cases according to their reported most likely country of exposure (ordered by number of cases). + represents the mean age; horizontal line is the mean age of individuals that were only exposed in Switzerland.



Supplementary Figure 3: Country of exposure and region of cases' residence.