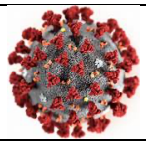
National COVID-19 Science Task Force (NCS-TF)



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Considerations regarding the duration of quarantine for people with possible exposure to SARS-CoV-2 infection

Executive summary:

A quarantine period of 10 days is currently required in Switzerland for two situations: contacts of confirmed COVID-19 cases and travellers returning from high-risk areas. This policy brief assumes that quarantine is in place for these two situations and addresses questions about the duration of quarantine and not about quarantine as a preventive strategy.

Given that the number of COVID-19 cases in Switzerland has been increasing, the priority for SARS-CoV-2 control strategy is to stabilise or reduce case numbers using the full range of public health and individual level prevention measures.

Reducing the duration of quarantine should only be considered if accompanied by measures that compensate for the expected increase in transmission. A nationally coordinated approach is required.

Studies should be commissioned by the cantons or the confederation to assess the effects of the duration of quarantine on SARS-CoV-2 transmission in Switzerland, including in the setting of the current test-trace-isolate-quarantine strategy, and for imported COVID-19.

Contacts of confirmed cases and returning travellers differ in the probability of having been exposed and infected and on the information available about the likely window of exposure.

In the absence of empirical data about the effectiveness of different durations of quarantine, we use mathematical modelling to explore the fraction of onward transmission that can be prevented by different quarantine strategies.

For contacts of confirmed COVID-19 cases,

- A test-and-release strategy can reduce the period of quarantine but the earlier in the quarantine period that the test is done, the lower the fraction of onward transmission that can be prevented.
- We provide estimates of the fraction of transmission prevented for different scenarios.If test-negative individuals strengthen their adherence to preventive measures after leaving quarantine, there is a modest gain in the fraction of transmission prevented for tests done early.

For returning travellers from countries with higher incidence of SARS-CoV-2 than Switzerland,

- Data from Geneva suggest that about 1 in 200 returning travellers is diagnosed with SARS-CoV-2 infection during quarantine, substantially higher than the incidence of diagnosed infection in the general population.
- The effect of quarantine duration differs according to the duration of travel.
- A single test done on arrival in Switzerland can only prevent a small fraction of the transmission, even for longer trips, because of the false-negative rate of RT-PCR early in infection.
- A test-and-release strategy can reduce the duration of quarantine. We provide estimates of the fraction of transmission prevented for different scenarios.

Main text

Background

The exponential increase in numbers of diagnosed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections (411 cases on 30.09.2020), and the increasing proportion of tests with a positive test result (3.3% on 30.09.2020), in Switzerland have put pressure on contact tracing services, particularly in cantons with the highest daily numbers of new cases. At the same time, there are calls from different sectors to relax some control measures, because of prevention fatigue in the general population or because of concerns about damage to businesses and the economy. In addition, some regard the fraction of newly detected SARS-CoV-2 cases among those quarantined as too low to justify the recommendations of the Federal Office of Public Health (FOPH). Shortening the duration of quarantine, with or without the use of virological testing, is now a specific topic of debate in Switzerland and in neighbouring countries. Here the Swiss national COVID-19 science task force (ncs-tf) provides an analysis of the appropriate duration of quarantine for people with possible exposure to SARS-CoV-2 infection.

The primary goal of the SARS-CoV-2 control strategy in Switzerland is to stabilise or decrease case numbers so that the effective reproduction number Re is at or below one. Since early June 2020, the number of confirmed coronavirus disease 2019 (COVID-19) cases in Switzerland has increased exponentially, with an Re greater than one and an average doubling time of around 4 weeks (ncs-tf Re). As of mid-September, the number of new cases has started to decrease.

Quarantine is a non-pharmacological public health intervention that contributes to infectious disease control. Quarantine is defined as the restriction of activities of apparently healthy individuals who have been exposed to cases of a communicable disease to prevent 1 transmission during the incubation period if infection should occur[1]. Quarantine plays a particularly important role in preventing transmission of pathogens, like SARS-CoV-2, that are transmissible before the onset of symptoms.

In Switzerland, the FOPH requires quarantine in two situations: for people who are close contacts of a confirmed case, and people who have returned from travel to countries that the FOPH defines as being at higher risk of SARS-CoV-2 infection than Switzerland. For the contacts of confirmed

COVID-19 cases, quarantine is one part of the test-trace-isolate-quarantine (TTIQ) strategy, which contributes to SARS-CoV-2 combination prevention, including mask-wearing, physical distancing, hand hygiene, and restricted size of social gatherings. The goal of quarantine for returning travellers is to prevent imported SARS-CoV-2 infection, which could cause flare-ups in infection if the imported cases establish new chains of undiagnosed infection. Quarantine of individuals returning from a country with a higher incidence of SARS-CoV-2 than in the home country can prevent the introduction of new sources of infection and break transmission chains[2].
The imposition of quarantine for returning travellers needs to balance the benefits of prevented SARS-CoV-2 transmission against the effects that the restrictions have on the willingness of people to travel, and the economic losses of individuals, their employers and of the overall economy. In a small country such as Switzerland, which depends on international trade, restrictions on international travel have particularly harsh effects on the air travel industry.

From an epidemiological standpoint, any shortening of the quarantine period will lead to an increase in overall transmission per infected individual. This raises the question of how much prevented transmission one deems appropriate for any further day of quarantine. Above a certain duration, there are diminishing returns for further extending quarantine because the amount of onward transmission prevented by an extra day in quarantine decreases with each added day.

The number of people in quarantine depends on the number of new COVID-19 cases. When Re is sustained at or below one, consideration can be given to adapting the duration of quarantine in a way that does not lead to an unacceptable increase in transmission. Any reduction in the quarantine period needs to be compensated by reinforcement of other preventive measures or improved effectiveness of the quarantine procedures, by measures that include better adherence to quarantine rules, strengthened personal prevention measures after the end of quarantine, or more targeted communication. An expansion in the use of virological testing, such as RT-PCR testing during the quarantine period, could reinforce the effectiveness of the TTIQ strategy.
To what extent the expected reduction of transmission depends on the duration of quarantine depends in part on country-specific characteristics, such as disease prevalence, quarantine specificity, and compliance. Addressing this question accurately requires detailed data, specific for Switzerland, from contact tracing and on test positivity at different days during quarantine. We currently do not have these data. **An urgent recommendation of the Science Task Force is that appropriate studies be commissioned and such data be collected by the cantons and the Confederation.**

There are important differences between the two situations of quarantined individuals: they differ in the probability of being infected and on information being available about the time window of exposure. The FOPH recommends a 10-day period of quarantine for both identified contacts of confirmed cases and travel returners. In this document, we deal separately with these two situations.

Methods used to investigate the effects of different durations of quarantine
There are no empirical data that determine the effects of different durations of quarantine,
to our knowledge. We use a mathematical model that is based on empirical data about SARS-CoV-2 transmission to compute the expected effects (Figure 1)[3]. The model includes three key

characteristics of SARS-CoV-2 transmission that are needed to understand how quarantine and its duration affect the prevention of onward transmission of SARS-CoV-2. These are: the generation time (the interval between infection onset in an infected person and the person that they infect), the duration of the infectious period both before and after the onset of symptoms (infectivity profile), and the incubation period (time from infection to the onset of symptoms). The distributions of these characteristics have been calculated from multiple empirical studies of SARS-CoV-2 transmission.[4 5]

The details of the model are available as a preprint.[3] A dashboard shows the model outputs in this policy brief and allows the user to change variables in the model and see how they affect the results.

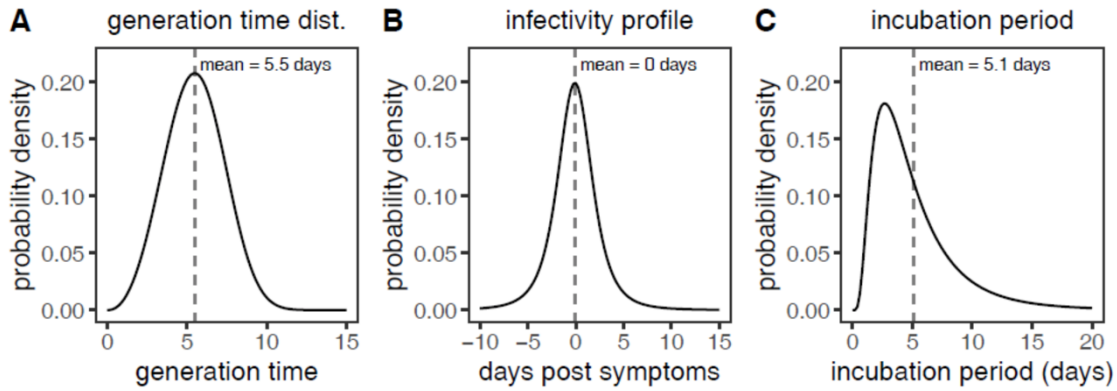

Figure 1. Key characteristics of SARS-CoV-2 transmission. Panel A, generation time distribution (the time interval between the infection of an infected person and the person that they infect); Panel B, infectivity profile (duration of the infectious period both before and after the onset of symptoms); Panel C, incubation period distribution (time from infection to the onset of symptoms). Figure reproduced from Ashcroft et al.[3]

The model incorporates the following features:

- For contacts of confirmed cases, the delay from exposure until quarantine can be varied from zero to 10 days. In the examples in this policy brief, we assume a delay of 3 days;
- For returning travellers, results are shown for trips of varying lengths from 1 to 14 days;
- For both situations, testing can be done and the day of testing can be varied from day zero to day 10. Test performance is based on empirical data about the sensitivity of laboratory-based RT-PCR testing on nasopharyngeal swabs, according to the number of days from exposure to SARS-CoV-2 until the onset of symptoms.[6] Specificity is assumed to be 100%. In the model, people with a negative test result are released from quarantine on the day that the result is received. People with a positive test result become new cases and the status of quarantine changes to isolation, with no onward transmission. The time until receipt of the test result can be varied. We call this strategy test-and-release.

For two separate groups of people in quarantine (contacts of confirmed cases and returning travellers), we use the model to estimate two quantities amongst contacts or returning travellers who have become infected with SARS-CoV-2:

- the fraction of onward transmission of SARS-CoV-2 that is prevented by quarantine, as a function of the duration of quarantine;

- the fraction of onward transmission of SARS-CoV-2 that is prevented if an RT-PCR test is done at different time points during quarantine.

Effects of duration of quarantine of prevention of onward SARS-CoV-2 transmission

1. Contacts of a confirmed case of COVID-19

In contacts of people with confirmed COVID-19, contact tracers establish the period of exposure with the index case. The onset of infection in the contact is assumed to be the last date of their contact with the index case. If there has been prolonged contact between the contact and the index case, infection could have taken place at an earlier time point. In this situation, the model estimate of the fraction of prevented transmission will be overestimated.

1.1 Overall effect of duration of quarantine in contacts of confirmed cases

Figure 2 shows the fraction of SARS-CoV-2 transmission that is prevented for different values of the time delay between the appearance of symptoms in the index case and the start of quarantine of its contacts.[3] A 10-day period of quarantine prevents virtually the same amount of onward transmission as any longer period. Reducing the duration of quarantine below 10 days reduces the fraction of transmission that can be prevented substantially.

When there is no delay between the last exposure of the contact to the index case and going into quarantine, almost all transmission can be prevented (Figure 2). In practice, this scenario does not happen and as the time delay until the contact enters quarantine increases, the maximum efficacy of quarantine is reduced, because the contact may have already transmitted the infection before being quarantined.

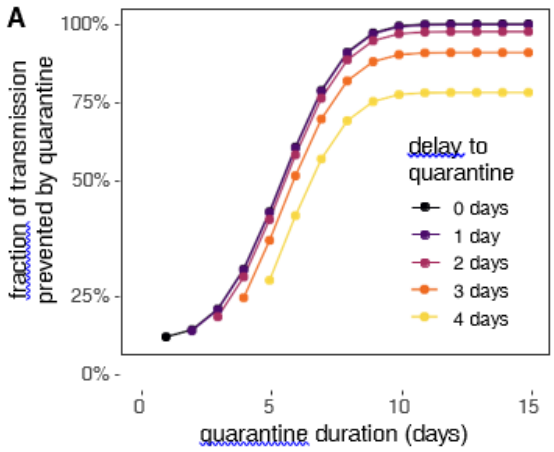

Figure 2. Fraction of total onward transmission, per quarantined infected contact, that is prevented by quarantine.[3]

1.2 Effect of SARS-CoV-2 testing during quarantine on prevention of transmission in contacts

Figure 3 shows the fraction of onward transmission from infected contacts that can be prevented by a test-and-release strategy, with RT-PCR testing on different days during quarantine (with release 2 days later) and the fraction of transmission prevented in the absence of testing. The earlier in the quarantine period that the test is done, the lower the fraction of onward transmission that can be prevented. Tests done 6 days after exposure or later (with release 2 days later) can prevent almost the same fraction of transmission as the 10-day quarantine period. If test-negative individuals

strengthen their adherence to preventive measures after leaving quarantine, there is a modest gain in the fraction of transmission prevented for tests done early.

The fraction of transmission that can be prevented after the start of quarantine is affected by the time until receipt of the negative test result because the sensitivity of RT-PCR is lower earlier in infection (Table 1). For example, a laboratory RT-PCR test on day 6, with a 1- or 2-day delay until the test result (release of those with a negative test at day 7 or 8), could prevent 94 and 98% of transmission that occurs after the start of quarantine.

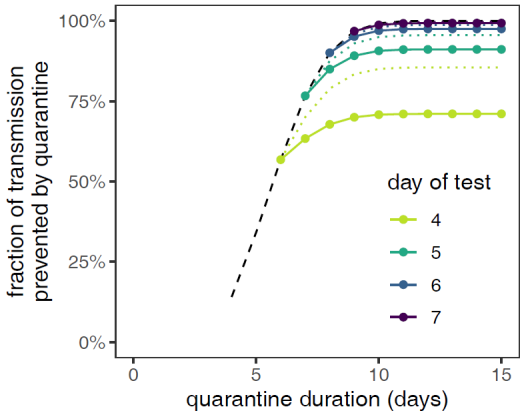

Figure 3. The impact of a test-and-release strategy for quarantined individuals, in terms of the fraction of total onward transmission that can be prevented after an individual is put into quarantine. The dashed line shows the fraction of transmission prevented without testing. The dotted line assumes that individual preventive measures are strengthened and reduce transmission by an additional 50%.

Table 1. Fraction of transmission prevented after the start of quarantine, according to day of test and delay between test and result

	Fraction of transmission prevented, by day of test			
Delay to result*	**4**	**5**	**6**	**7**
2 days	71%	91%	98%	100%
1 day	56%	84%	94%	98%
Same day	42%	75%	89%	95%

* The test characteristics are those of a laboratory-based RT-PCR.[6] A rapid test that gives a same-day result would have to have the same performance characteristics as a laboratory-based RT-PCR to achieve these reductions in transmission.

2. Duration of quarantine for travellers returning from a high-risk country

The situation of quarantine of returning travellers differs from those for contacts of confirmed cases in several ways, resulting in lower certainty about the appropriate duration of quarantine for returning travellers than for known contacts of people with confirmed SARS-CoV-2 infection. The quarantine period should cover the time window in which the returned traveller could transmit SARS-CoV-2, if infected. This period depends on the time spent in the high-risk country, and the time point during the trip at which the traveller became infected. The risk of infection in all countries for which quarantine is required is higher than the average for Switzerland.

The ncs-tf has proposed flow charts for the use of virological testing for SARS-CoV-2 by RT-PCR for quarantine and isolation of returning travellers.[7] The flow charts recommend
testing on arrival and during quarantine, with release of individuals with a negative RT-PCR during quarantine. Here, we examine the effects on SARS-CoV-2 transmission of quarantining returning travellers and of a single virological test at different time points after arrival.

2.1 Imported SARS-CoV-2 infection in Switzerland

Quarantine of returning travellers makes sense if the incidence of SARS-CoV-2 is higher than the average in the population to which the traveller returns. The Canton of Geneva health department has compiled data from 2. July to 22. September 2020. Among 5990 people quarantined on return from travel, 31 people had received a positive test result (0.52%, 95% CI 0.35-0.73%) (Figure 4). Over the period observed, an average of 2-3 cases of SARS-CoV-2 is imported per week (reasons for testing and the numbers of tests not given). For comparison, in the Canton of Geneva, the rate of diagnosis in week 38 was 83.3 per 100,000 inhabitants. The ratio of diagnosed SARS-CoV-2 cases in returning travellers (31/5990) compared with the general population (83.3/100,000) is 6.5. It is possible that returning travellers might be more likely to seek testing during quarantine, in which case the proportion diagnosed might be higher than in contacts of confirmed cases.

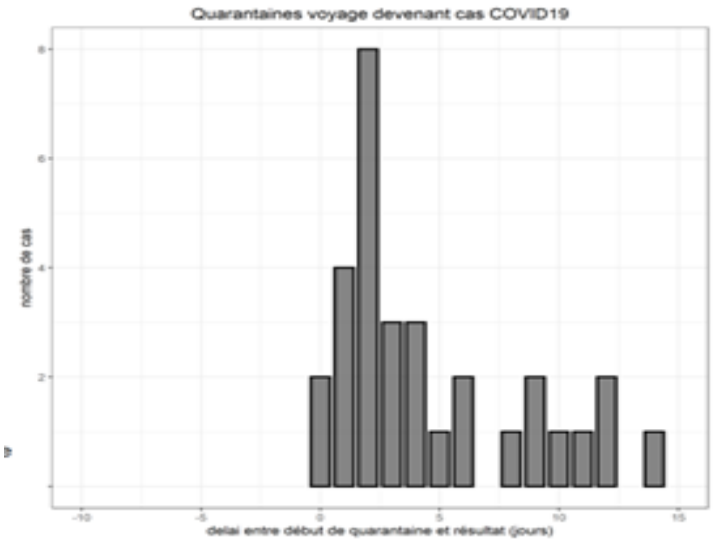

Figure 4. Canton of Geneva, distribution of SARS-CoV-2 positive test results, by day of quarantine (n=31) (Direction générale de la santé, Note de Service, 23.09.2020)

2.2 Overall effect of duration of quarantine for returning travellers

The effect of quarantine duration differs according to the duration of travel. In the model, we assume that the risk of acquiring infection in a high-risk country is the same on each day during the trip. Figure 5 shows the fraction of the transmission that would occur after arrival in Switzerland and that can be prevented by quarantine. For short trips, a longer duration of quarantine is needed to prevent transmission in Switzerland because a person who becomes infected during a short trip will spend almost all of their infectious period in Switzerland. For longer trips, a traveller who becomes infected might already have transmitted infection whilst abroad. The remaining transmission potential after arrival in Switzerland will be spent after a shorter time period.

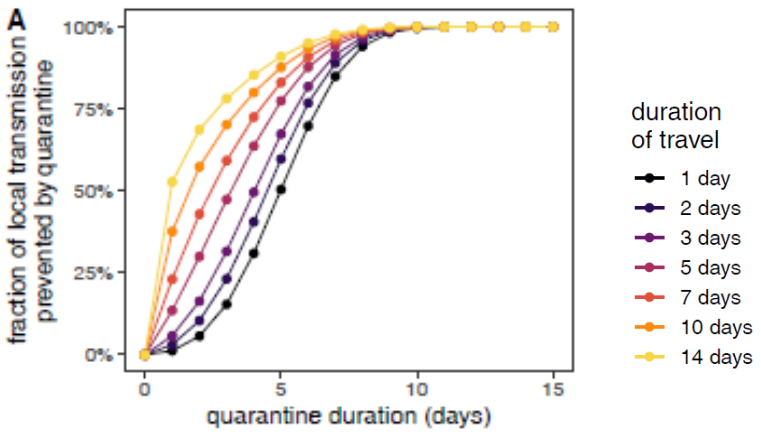

Figure 5. Fraction of onward SARS-CoV-2 transmission after arrival in Switzerland, per infected quarantined traveller, that is prevented by quarantine, according to the duration of travel. We assume that quarantine begins immediately after arrival.

2.3 Effect of SARS-CoV-2 testing during quarantine on prevention of transmission in returning travellers

Figure 6 shows the fraction of onward transmission that occurs after arrival in Switzerland that can be prevented by quarantine for trips of different durations, according to the day on which the test is done. A test done on arrival in Switzerland prevents a small fraction of the transmission, even for longer trips, because of the false-negative rate of RT-PCR early in infection.

The fraction of transmission in Switzerland that can be prevented by testing and releasing travellers with a negative test result is higher for people returning from longer trips because the probability of a false-negative test result is lower. Table 2 shows that almost all transmission for travellers returning from trips of a week or more can be prevented with tests done at 5 days or later, with release 2 days later.

The strengthening of individual preventive measures that reduce transmission after leaving quarantine can increase the fraction of prevented transmission if testing is done soon after arrival, but not to the levels achieved by testing done at 5 days or later.

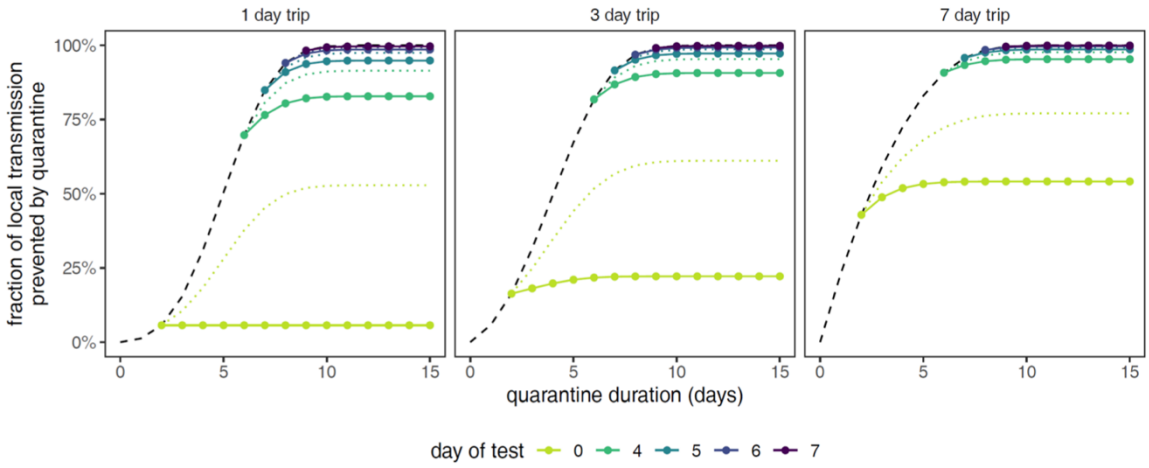

Figure 6. The impact of a test-and-release strategy for quarantined returning travellers, in terms of the fraction of onward transmission prevented by quarantine, assuming a delay of 2 days between the test and result. The dashed line shows the fraction of transmission prevented without testing; at 10 days, 100% of onward transmission is prevented. The dotted line assumes that individual preventive measures are strengthened and reduce transmission by an additional 50%.

Table 2. Fraction of transmission in Switzerland prevented by quarantine of returning travellers, according to day of test and duration of trip. We assume that test results take 2 days to be returned.

	Fraction of transmission prevented, by day of test			
Duration of trip	**4**	**5**	**6**	**7**
1 day	83%	95%	98%	99%
3 days	91%	97%	99%	100%
7 days	95%	99%	100%	100%

Conclusions

Given that the number of COVID-19 cases in Switzerland has been increasing, the priority for SARS-CoV-2 control strategy is to stabilise or reduce case numbers using the full range of public health and individual level prevention measures.

Reducing the duration of quarantine should only be considered if accompanied by measures that compensate for the expected increase in transmission. A coordinated approach on the national level is required.

Studies should be commissioned by the cantons or the confederation to collect data that allow assessment of the effects of the duration of quarantine on SARS-CoV-2 transmission in Switzerland, including the impact of a 10-day quarantine period in the setting of the current TTIQ strategy, and of imported COVID-19 cases.

A quarantine period of 10 days is currently required for two situations: contacts of confirmed COVID-19 cases and travellers returning from high-risk areas. There are important differences between these situations in terms of the probability of having been exposed and infected and on the information available about the likely time window of exposure.

In the absence of empirical data about the effectiveness of different durations of quarantine, mathematical modelling can be used to explore the fraction of onward transmission by infected contacts or returning travellers that can be prevented by different quarantine strategies.

For contacts of confirmed COVID-19 cases,

- delays from exposure until entry into quarantine reduce the maximum efficacy of quarantine, because the contact may have already transmitted infection before being quarantined.
- A test-and-release strategy can reduce the period of quarantine but the earlier in the quarantine period that the test is done, the lower the fraction of onward transmission that can be prevented.
- Tests done at day 6, with release 2 days later, when the test result becomes available can prevent almost the same fraction of transmission as the 10-day quarantine period.
- If test-negative individuals strengthen their adherence to preventive measures after leaving quarantine, there is a modest gain in the fraction of transmission prevented for tests done early.
- The fraction of transmission that can be prevented after the start of quarantine is affected by the time until receipt of the negative test result because the sensitivity of RT-PCR is lower earlier in infection.

For returning travellers from countries with higher incidence of SARS-CoV-2 than Switzerland

- Data from Geneva suggest that about 1 in 200 returning travellers is diagnosed with SARS-CoV-2 infection during quarantine, substantially higher than the incidence of diagnosed infection in the general population.
- The effect of quarantine duration differs according to the duration of travel. For short trips, a longer duration of quarantine prevents a greater fraction of transmission in Switzerland because a person who becomes infected during a short trip will spend almost all of their infectious period in Switzerland.
- A single test done on arrival in Switzerland can only prevent a small fraction of the transmission, even for longer trips, because of the false-negative rate of RT-PCR early in infection.
- A test-and-release strategy can reduce the duration of quarantine. Almost all transmission for travellers returning from trips of a week or more can be prevented with tests done at 5 days or later, with release 2 days later.

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