Assessment of the risk of SARS-CoV-2 reinfection in an intense re-exposure setting

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Summary: In a cohort of 133,266 laboratory-confirmed cases, SARS-CoV-2 risk of reinfection was 0.02% and incidence rate of reinfection was 0.36 per 10,000 person-weeks. Reinfection occurs but rarely indicating protective immunity for at least a few months post primary infection.
ABSTRACT

**Background:** Risk of reinfection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is unknown. We assessed risk and incidence rate of documented SARS-CoV-2 reinfection in a cohort of laboratory-confirmed cases in Qatar.

**Methods:** All SARS-CoV-2 laboratory-confirmed cases with at least one PCR positive swab that is ≥45 days after a first-positive swab were individually investigated for evidence of reinfection, and classified as showing strong, good, some, or weak/no evidence for reinfection. Viral genome sequencing of the paired first-positive and reinfection viral specimens was conducted to confirm reinfection. Risk and incidence rate of reinfection were estimated.

**Results:** Out of 133,266 laboratory-confirmed SARS-CoV-2 cases, 243 persons (0.18%) had at least one subsequent positive swab ≥45 days after the first-positive swab. Of these, 54 cases (22.2%) had strong or good evidence for reinfection. Median time between first and reinfection swab was 64.5 days (range: 45-129). Twenty-three of the 54 cases (42.6%) were diagnosed at a health facility suggesting presence of symptoms, while 31 (57.4%) were identified incidentally through random testing campaigns/surveys or contact tracing. Only one person was hospitalized at time of reinfection, but was discharged the next day. No deaths were recorded. Viral genome sequencing confirmed four reinfections out of 12 cases with available genetic evidence. Reinfection risk was estimated at 0.02% (95% CI: 0.01-0.02%) and reinfection incidence rate at 0.36 (95% CI: 0.28-0.47) per 10,000 person-weeks.

**Conclusions:** SARS-CoV-2 reinfection can occur but is a rare phenomenon suggestive of protective immunity against reinfection that lasts for at least a few months post primary infection.

**Keywords:** SARS-CoV-2; epidemiology; reinfection; immunity; genetics
INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been spreading around the globe causing severe disruptions to social and economic activities [1-3]. Qatar, a peninsula in the Arabian Gulf region with a diverse population of 2.8 million [4, 5], has experienced a large epidemic with one of the highest laboratory-confirmed rates of infection at >60,000 infections per million population [6-8]. Antibody testing and mathematical modeling indicated that about half of the population has already been infected [6, 8-12].

The intensity of the epidemic with a high risk of re-exposure to the infection, as well as the availability of a centralized data-capture system of all laboratory-confirmed infections, provided an opportunity to epidemiologically assess the presence and incidence of reinfections; a poorly-understood feature of SARS-CoV-2 epidemiology whose elucidation is critical to inform global response, timing and intensity of future cycles, and impact and durability of potential vaccines [13-16].

Our aim was to assess the risk and incidence rate of documented reinfection in a cohort of 133,266 SARS-CoV-2 laboratory-confirmed infected persons. Since the relevant underlying question is whether risk of reinfection is appreciable or not, we implemented a conservative epidemiological approach for assessing documented reinfections, that is prone to overestimate rather than underestimate risk of reinfection. However, we also conducted sensitivity analyses implementing more stringent criteria for assessing reinfection. We further performed viral genome sequencing to confirm the reinfections.
METHODS

Sources of data

We analyzed the centralized and standardized national SARS-CoV-2 testing and hospitalization database compiled at Hamad Medical Corporation (HMC), the main public healthcare provider and nationally-designated provider for Coronavirus Disease 2019 (COVID-19) healthcare needs. The database covers all SARS-CoV-2 cases in Qatar and encompasses data on all polymerase chain reaction (PCR) testing conducted from February 28-August 12, 2020, including testing of suspected SARS-CoV-2 cases and traced contacts and infection surveillance testing. The database further includes data on hospital admission of COVID-19 patients and the World Health Organization (WHO) severity classification for each infection [17], which is assessed through individual chart reviews by trained medical personnel. Recently, data on serological testing for antibody on residual blood specimens collected for routine clinical care from attendees at HMC were also incorporated [6, 10].

Laboratory methods

All PCR testing was conducted at HMC Central Laboratory or at Sidra Medicine Laboratory, following standardized protocols. Nasopharyngeal and/or oropharyngeal swabs (Huachenyang Technology, China) were collected and placed in Universal Transport Medium (UTM). Aliquots of UTM were: extracted on the QIAsymphony platform (QIAGEN, USA) and tested with real-time reverse-transcription PCR (RT-qPCR) using TaqPath™ COVID-19 Combo Kit (100% sensitivity and specificity [18]; Thermo Fisher Scientific, USA) on ABI 7500 FAST (Thermo Fisher, USA); extracted using a custom protocol [19] on Hamilton Microlab STAR (Hamilton, USA) and tested using AccuPower SARS-CoV-2 Real-Time RT-PCR Kit (100% sensitivity and specificity [20]; Bioneer, Korea) on ABI 7500 FAST; or loaded directly to Roche cobas® 6800 system and
assayed with cobas® SARS-CoV-2 Test (95% sensitivity, 100% specificity [21]; Roche, Switzerland). The first assay targets the virus’ S, N, and ORF1ab regions; the second targets the virus’ RdRp and E-gene regions; and the third targets the ORF1ab and E-gene regions.

Serological testing was performed using Roche Elecsys® Anti-SARS-CoV-2 (99.5% sensitivity [22], 99.8% specificity [22, 23]; Roche, Switzerland), an electrochemiluminescence immunoassay that uses a recombinant protein representing the nucleocapsid (N) antigen for determination of antibodies against SARS-CoV-2. Qualitative anti-SARS-CoV-2 results were generated following the manufacturer’s instructions (reactive: cutoff index for optical density ≥1.0 vs. non-reactive: cutoff index <1.0).

**Inclusion criteria**

All SARS-CoV-2 laboratory-confirmed cases with at least one PCR positive swab that is ≥45 days after a first-positive swab were considered as suspected cases of reinfection. The 45-day cutoff was informed by data from observational cohorts of SARS-CoV-2 infected persons [24, 25], and was set to account for the duration of prolonged PCR positivity of several weeks in these patients. Cutoff determination was further informed by the distribution of the time difference between the first-positive swab and subsequent positive swabs among SARS-CoV-2 cases with multiple swabs (Figure 1). The tail of this distribution indicates that a cutoff of 45 days (at the 99th percentile) provides an appropriate mark for defining the end of prolonged PCR positivity: a subsequent positive swab within 45 days of the first-positive swab is likely to reflect prolonged PCR positivity (due to non-viable virus fragments) rather than reinfection, and thus should not be included in analysis.
**Suspected reinfection case classification**

Suspected cases of reinfection, that is cases fitting above indicated inclusion criteria, were classified as showing either strong evidence, good evidence, some evidence, or weak (or no) evidence for reinfection (Box 1). Classification was based on holistic quantitative and qualitative criteria applied to each investigated case. Criteria included the pattern and magnitude of the change in PCR cycle threshold (Ct) value across repeated swabs, time interval between subsequent swabs, PCR testing site (such as outpatients at primary care, hospital emergency, or inpatient hospitalization), purpose of PCR testing (such as appearance of symptoms, contact tracing, or survey/testing campaign), age, history of COVID-19-related hospital admission, and case severity per WHO classification [17].

Overall, swabs with Ct <30 (suggestive of recent active infection) at least 45 days after the first-positive swab were considered as showing strong evidence for reinfection. Swabs with Ct ≥30 at least 45 days after the first-positive swab were considered as showing good evidence for reinfection if PCR positivity was associated with contextual evidence supporting the status of “reinfection” including appearance of symptoms (often as proxied by being diagnosed at a health facility), if the infection was diagnosed through contact tracing (indicating recent exposure to an infected person), if the change in Ct value from the last swab was to a lower Ct value (indicating increasing viral load), and/or if the repeated swabbing did not follow a regular pattern and time interval between repeated swabs was not short (to exclude cases under clinical management that are indicative of poor control of first infection).

Shorter durations bordering the 45-day cutoff with Ct values ≥30 and no contextual evidence supporting the status of “reinfection” were indicative of some evidence for reinfection, but not strong nor good evidence for reinfection, as they are more likely to reflect the long tail of the prolonged PCR positivity distribution (Figure 1) [24, 25]. Age ≥70 years, repeated swabs
on hospitalized patients, and severe or critical WHO disease classifications were considered as contextual factors indicative of poor control of the first infection rather than reinfection. Cases that had such contextual factors (and implicitly did not fit the criteria of strong, good, or some evidence for reinfection) were considered to have weak (or no) evidence for reinfection.

Of note that hospitalized COVID-19 cases often had multiple subsequent swabs administered to them as part of clinical care, and repeated swabbing was standard earlier in the epidemic, as the criteria for discharge from an isolation facility required at least two subsequent PCR negative swabs. This was changed later to a time-based criteria per updated WHO recommendation [26].

**Reinfection risk and rate**

Documented reinfection risk was assessed by quantifying the proportion of cases with strong or good evidence for reinfection out of all laboratory-confirmed SARS-CoV-2 cases that were diagnosed ≥45 days from end-of-study censoring. Incidence rate of documented reinfection was calculated by dividing the number of cases with strong or good evidence by the number of person-weeks contributed by all laboratory-confirmed cases who had their first-positive swab ≥45 days before day of analysis. The follow-up person-time was calculated starting from 45 days after the first-positive swab and up to the reinfection swab, all-cause death, or end-of-study censoring.

**Sensitivity analyses**

Since we implemented a conservative approach prone to overestimate risk of documented reinfection, several sensitivity analyses were conducted implementing more stringent criteria for assessing reinfection: 1) exclusion of cases where the Ct value for the first and/or subsequent positive swab was unknown or with a value ≥35 (to exclude potential PCR false-
positive cases), 2) changing the ≥45-day cutoff to a ≥60-day cutoff to further exclude potential cases of long-term prolonged PCR positivity, and (most stringent) 3) setting definition of recent active infection at Ct cutoff value of <25 (instead of <30) and excluding any suspected reinfection case with Ct >25.

**Viral genome sequencing and analysis**

Viral genome sequencing was conducted on retrieved paired samples of the first-positive swab and reinfection swab for patients with strong or good evidence for reinfection as confirmatory analysis. Further details about the viral genome sequencing methods can be found in Supplementary Text S1.

**Ethical approval**

Study was approved by HMC and Weill Cornell Medicine-Qatar Institutional Review Boards.

**RESULTS**

**Epidemiological analysis**

Figure 2 illustrates the selection process of SARS-CoV-2 eligible cases and summarizes the results of their reinfection status' evaluation. Out of 133,266 laboratory-confirmed cases, 117,458 had only one single positive swab and thus were excluded from further analysis. Of the remaining 15,808 cases with multiple swabs, only 243 persons had at least one subsequent positive swab that is ≥45 days from the first-positive swab, and thus qualified for inclusion in analysis.

There were 299 positive swabs collected ≥45 days after the first-positive swab for these 243 persons. Individual investigation of each of these swabs yielded 54 cases with strong or good evidence for reinfection. Of these, 35 had strong evidence for reinfection (Ct <30) while the remaining 19 had good evidence for reinfection (Ct ≥30). An additional 26 cases showed some evidence for reinfection, while evidence was weak for the remaining 163 cases.
Table 1 shows the characteristics of the 54 cases classified as showing strong or good evidence for reinfection. Almost all cases were males, but this reflects the focus of the epidemic in craft and manual workers [6]. Median age was 33 years (range: 16-57) and median time between the first swab and the reinfection swab was 64.5 days (range: 45-129). Median Ct value was 28 (range: 14-37); it was 22 (range 14-29) for the 35 swabs classified with strong evidence (Ct <30) and 32 (range: 30-37) for the remaining swabs (Ct ≥30).

Twenty-three cases (42.6%) were diagnosed at a health facility, suggesting presence of symptoms while 31 (57.4%) were identified incidentally either through random testing campaigns/surveys (n=15; 27.8%) or contact tracing (n=16; 29.6%), suggesting minimal symptoms if any.

Nine of the 54 cases showing strong or good evidence for reinfection were hospitalized at any time. However, all but one occurred following the primary infection—only one hospitalization occurred at time of reinfection but the patient was discharged the next day. Most hospitalizations occurred for isolation or initial assessment purposes as cases had no or minimal symptoms. Only one case had sufficient symptoms to warrant an infection severity assessment (during primary infection), but was classified with “mild” severity per WHO classification. No deaths were recorded. Of note that the vast majority of infections in Qatar occurred in young and healthy men and had low severity [6, 12].

Antibody test results were available for 48 out of the 243 assessed individuals (Supplementary Table S1), of whom 30 (62.5%) had detectable antibodies. Of the 13 with strong evidence for reinfection and available antibody results, seven (53.9%) were sero-negative. Meanwhile, both individuals with good evidence for reinfection, three of the four individuals with some evidence for reinfection, and 19 of the 29 individuals with weak evidence for reinfection, were sero-positive.
Risk of documented reinfection was estimated at 0.05% (95% CI: 0.04-0.07)—that is a total of 54 reinfections among 101,349 persons with laboratory-confirmed infection (the cohort of infected persons after excluding persons who were diagnosed within 45 days from end-of-study censoring). Incidence rate of reinfection was estimated at 1.09 (95% CI: 0.84-1.42) per 10,000 person-weeks—that is a total of 54 reinfection events in a follow-up person-time of 495,208.7 person-weeks.

Results of sensitivity analyses can be found in Supplementary Table S2. In these analyses, the estimate for the risk of reinfection ranged between 0.02% (95% CI: 0.01-0.03) and 0.03% (95% CI: 0.02-0.04), while that for the incidence rate of reinfection ranged between 0.38 (95% CI: 0.24-0.60) and 1.06 (95% CI: 0.75-1.50) per 10,000 person-weeks. Although these sensitivity analyses confirmed our results, they suggested overestimation of the already low risk of reinfection.

**Confirmation of reinfection through viral genome sequencing**

Paired specimens of the first-positive and reinfection swabs could be retrieved for 23 out of the 54 cases with strong or good evidence for reinfection. Table 2 summarizes the viral genome sequencing results and Figure 3 and Supplementary Figures S1-S2 show the detailed analysis for each genome pair.

There was insufficient evidence to warrant interpretation for 11 pairs because of low genome quality. For six pairs, there were one to several changes of allele frequency indicative at best of a shifting balance of quasi-species, and thus no evidence for reinfection. For two pairs, remarkably, there was conclusive evidence for no reinfection as both genomes were of high quality yet no differences were found. For both patients, Ct was <25 for the first-positive and reinfection swabs indicating persistent active infection (Table 1). These two cases were also sero-positive (Table 1).
Meanwhile, for two pairs, there was conclusive evidence for reinfection with multiple changes of allele frequency and presence of the D614G mutation (23403bp A>G)—a variant that appeared and expanded replacing the original D614 form [27, 28]. Also for two pairs, and although one of the genomes was of inferior quality, there was sufficient evidence for differences including the presence of the D614G mutation, thereby rendering evidence for reinfection. Three out of these four cases with viral genome sequencing confirmation of reinfection were classified above (epidemiological criteria) as having strong evidence for reinfection, with the fourth classified as having good evidence (Table 1). Antibody test result was available for one case at time of reinfection, and the individual was sero-negative.

In sum, for the 12 cases where viral genome sequencing evidence was available, four cases were confirmed as reinfections, a confirmation rate of 33.3%. Applying this rate to the above-estimated reinfection metrics yielded risk of documented reinfection of 0.02% (95% CI: 0.01-0.02%) and incidence rate of reinfection of 0.36 (95% CI: 0.28-0.47) per 10,000 person-weeks.

DISCUSSION

Results indicate, employing several analyses and sensitivity analyses, conclusive evidence for presence of reinfections in the SARS-CoV-2 epidemic of Qatar, but the risk for documented reinfection was very rare at about 2 reinfections per 10,000 infected persons. This finding is striking as the epidemic in Qatar has been intense with half of the population estimated to have been infected [6, 8-12]. Considering the strength of the force of infection, estimated at a daily probability of infection exceeding 1% at the epidemic peak around May 20 [6], it is all but certain that a significant proportion of the population has been repeatedly exposed to the infection, but such re-exposures hardly led to any documentable reinfections.
Indeed, of all epidemiologically-identified reinfections, nearly two-thirds (57%) were discovered accidentally, either through random testing campaigns/surveys or through contact tracing. None were severe, critical, or fatal; all reinfections were asymptomatic or with minimal or mild symptoms. These findings may suggest that most infected persons appear to develop immunity against reinfection that lasts for at least few months, and that reinfections (if they occur) are well tolerated and no more symptomatic than primary infections. Further follow up of this cohort of infected persons over time may allow elucidation of potential effects of waning of immunity.

Other lines of evidence for this cohort also support this conclusion. Among 2,559 PCR positive persons where an antibody test outcome was available [6], and where the first-positive PCR test was conducted >3 weeks before the serology test to accommodate for the delay in development of detectable antibodies following onset of infection [24, 25], 91.7% were antibody positive [6]. The high antibody positivity was also stable for over three months [6], as described elsewhere [14, 25]. The epidemic curve in Qatar was further characterized by rapid growth followed by rapid decline [6, 8, 12], at a time when levels of social and physical distancing restrictions were fairly stable. This points to susceptibles-infected-recovered “SIR” epidemic dynamics with most infections eliciting immunity against reinfection.

This assessment has limitations. We assessed risk of only **documented** reinfections, but other reinfections could have occurred but went undocumented, perhaps because of minimal/mild or no symptoms. It is also possible that with the primed immune system following primary infection, reinfections could be milder and shorter [15]. A recent nationwide population-based survey in Qatar estimated that only 9.3% (95% CI: 7.9-11.0%) of those antibody positive had a prior documented laboratory-confirmed infection [9], suggesting that undocumented infections (or reinfections) could possibly be ten-fold higher than documented
infections (or reinfections). This finding indicates that incidence rate of both documented and undocumented reinfections may add up to perhaps ~10 per 10,000 person-weeks. Meanwhile, a recent mathematical modeling study estimated the incidence rate of infection in Qatar at the time of the present study, including both documented and undocumented infections, at ~200 per 10,000 person-weeks [8]. Comparing these incidence rates suggest that the “efficacy” of natural infection against reinfection is around $1 - 10/200 \approx 95\%$.

Viral genome sequencing analysis was possible for only a subset of reinfections. Antibody testing outcomes were also available for only a number of cases, limiting use and inferences of the link between antibody status and risk of reinfection. Of note that for one of the genetically-confirmed reinfections the antibody test result was available but was seronegative (Table 1), just as the Hong Kong reinfected patient [29].

In conclusion, SARS-CoV-2 reinfection appears to be a rare phenomenon. This may suggest that immunity develops after the primary infection and lasts for at least few months, and that immunity may protect against reinfection.
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Author contributions

LJA conceived and co-designed the study and led the statistical analyses. HC co-designed the study, performed the data analyses, and wrote the first draft of the article. JAM led the viral genome sequencing analyses and AAA, YAM, and SY conducted these analyses. All authors contributed to data collection and acquisition, database development, discussion and
interpretation of the results, and to the writing of the manuscript. All authors have read and approved the final manuscript.

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**Competing interests**

We declare no competing interests.
References


Box 1. Classification of suspected cases of SARS-CoV-2 reinfection based on strength of supporting epidemiological evidence.

<table>
<thead>
<tr>
<th>Strength of Reinfection</th>
<th>Definition</th>
<th>Evidence Supporting Reinfection</th>
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<tbody>
<tr>
<td><strong>Suspected cases of SARS-CoV-2 reinfection</strong>: all laboratory-confirmed cases with at least one polymerase chain reaction (PCR) positive swab that is ≥45 days after a first-positive swab.</td>
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<tr>
<td><strong>Strong evidence for reinfection</strong>: individuals having positive swabs with PCR cycle threshold (Ct) value &lt;30 at least 45 days after the first-positive swab. No contextual evidence supporting poor control of first infection such as age ≥70 years, repeated swabs on hospitalized patients, and severe or critical World Health Organization disease classifications.</td>
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<tr>
<td><strong>Good evidence for reinfection</strong>: individuals having positive swabs with PCR Ct value ≥30 at least 45 days after the first-positive swab, but where PCR positivity was associated with contextual evidence supporting the status of reinfection:</td>
<td></td>
<td></td>
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<tr>
<td>- Appearance of symptoms (often as proxied by being diagnosed at a health facility)</td>
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<td>- Infection diagnosis through contact tracing (indicating recent exposure to an infected person)</td>
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<td>- Lower Ct value compared to last positive swab (indicating increasing viral load)</td>
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<tr>
<td>- Irregular and spaced-out pattern for repeated swabbing (to exclude cases under clinical management that are indicative of poor control of first infection).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No contextual evidence supporting poor control of first infection such as age ≥70 years, repeated swabs on hospitalized patients, and severe or critical World Health Organization disease classifications.</td>
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<tr>
<td><strong>Some evidence for reinfection</strong>: individuals having positive swabs with PCR Ct value ≥30 at least 45 days after the first-positive swab, but typically bordering the cutoff of 45 days. PCR positivity was not associated with evidence supporting the status of reinfection (listed above).</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Weak evidence for reinfection</strong>: individuals having swabs with PCR Ct value ≥30 at least 45 days after the first-positive swab, but typically bordering the cutoff of 45 days. PCR positivity was associated with contextual evidence indicative of poor infection control of the first infection rather than reinfection (such as age ≥70 years, repeated swabs on hospitalized patients, and severe or critical World Health Organization disease classifications).</td>
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</table>
FIGURE LEGENDS

**Figure 1.** Distribution of the time difference between the first swab and subsequent swabs among all laboratory-confirmed SARS-CoV-2 cases with more than one positive swab. The cutoff of 45 days was at the 99th percentile, and thus provides an appropriate mark for defining the end of the prolonged polymerase chain reaction (PCR) positivity.

**Figure 2.** Flow chart describing the selection process of SARS-CoV-2 eligible cases and summarizing the results of their reinfection status’ evaluation.

**Figure 3.** Viral genome sequencing analysis of the paired viral specimens of the first-positive and reinfection swabs for the six patients with conclusive or supporting evidence for reinfection or no reinfection.
Table 1. Characteristics of individuals classified as showing strong or good evidence for reinfection.

<table>
<thead>
<tr>
<th>ID#</th>
<th>Socio-demographic</th>
<th>PCR testing</th>
<th>Hospitalization</th>
<th>Ab testing</th>
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<tr>
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<td>Age group</td>
<td>Sample type</td>
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</tr>
<tr>
<td>3</td>
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<td>30-34</td>
<td>Health facility</td>
<td>10 August</td>
</tr>
<tr>
<td>4</td>
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<td>8</td>
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<td>30-34</td>
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<td>20-24</td>
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<td>Female</td>
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**Good evidence for reinfection**

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<th>Outcome</th>
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</table>

Ab, antibody; LOS, length of stay; Reinf, reinfection; PCR, polymerase chain reaction; Pos, positive; Subs, subsequent; Unk, unknown.

*Severity classification per WHO guidelines was conducted only on a subset of all cases where it was deemed relevant. Asymptomatic cases or cases with minimal symptoms were not formally assessed for severity.

†It has been common to use hospitalization as a form of isolation especially early in the epidemic.

‡The category “survey” refers to surveillance testing campaigns conducted in workplaces and residential areas.

§Not assessed because of no or minimal symptoms to warrant clinical assessment.

The light blue color highlights reinfection cases that were confirmed by viral genome sequencing.
Table 2. Results of reinfection confirmatory analysis based on viral genome sequencing of the paired viral specimens of the first-positive and reinfection swabs for 23 patients with strong or good epidemiological evidence for reinfection.

<table>
<thead>
<tr>
<th>Viral genome sequencing evidence for reinfection</th>
<th>Indication upon comparing each genome pair</th>
<th>N</th>
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<tbody>
<tr>
<td>Insufficient evidence to warrant interpretation</td>
<td>One or two genomes of low quality</td>
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<tr>
<td>No evidence for reinfection</td>
<td>One change of allele frequency</td>
<td>3</td>
</tr>
<tr>
<td>Shifting balance of quasi-species with no evidence for reinfection</td>
<td>Several changes of allele frequency</td>
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<tr>
<td>Conclusive evidence for no reinfection</td>
<td>Both genomes of high quality yet no differences found</td>
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</tr>
<tr>
<td>Supporting evidence for reinfection</td>
<td>One genome of inferior quality but with D614G mutation</td>
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</tr>
<tr>
<td>Conclusive evidence for reinfection</td>
<td>Multiple changes of allele frequency and D614G mutation</td>
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<tr>
<td>Total</td>
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Figure 1

Proportion of subsequent swabs (%) vs. Time difference between first swab and each of subsequent swabs (days)
Figure 2

133,266 laboratory-confirmed SARS-CoV-2 cases

117,458 SARS-CoV-2 cases with a single positive swab excluded

15,808 SARS-CoV-2 cases with multiple positive swabs

15,565 SARS-CoV-2 cases whose all subsequent positive swabs are within 45 days from the first positive swab excluded

243 SARS-CoV-2 cases with at least one positive swab that is ≥45 days after the first positive swab included in the analysis (299 positive subsequent swabs analyzed)

35 SARS-CoV-2 cases with strong evidence of reinfection (PCR Ct value <30 for the reinfection swab)

19 SARS-CoV-2 cases with good evidence of reinfection (PCR Ct value ≥30 for the reinfection swab)

26 SARS-CoV-2 cases with some evidence of reinfection

163 SARS-CoV-2 cases with weak evidence of reinfection
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<th>Patient 14</th>
<th>Patient 15</th>
<th>Patient 16</th>
<th>Patient 27</th>
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<td>3-Jun</td>
<td>7-Aug</td>
<td>21-Apr</td>
<td>16-Jun</td>
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**Figure 3**

### Description

- **Both genomes of high-quality yield no difference found**
- **Both genomes of high-quality yield multiple changes of allele frequency and D614G mutation**
- **Multiple changes of allele frequency and D614G mutation**
- **One of the genomes of interior quality, but with differences including the D614G mutation**
- **One of the genomes of interior quality, but with differences including the D614G mutation**

### Interpretation

- Conclusive evidence for no reinfecion
- Conclusive evidence for reinfecion
- Supporting evidence for reinfecion
- Supporting evidence for reinfecion

**Letter N denotes unknown.**

Numbers in cells represent the balance of reads for the reference and alternate alleles in that order.

Manual calls are represented by white cells with the nucleotide call.

- Yellow-color-highlighted positions are likely homoplasy.
- Green-color-highlighted positions denote a D614G mutation.
- Light blue color highlights reinfecion cases that were confirmed by viral genome sequencing.
- Light grey color highlights no reinfecion cases that were confirmed by viral genome sequencing.