# Reinfection rates among patients previously infected by SARS-CoV-2: systematic review and meta-analysis

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**Abstract**

**Background:** Asymptomatic or symptomatic infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can be followed by reinfection. The protection conferred by prior infection among coronavirus disease 2019 (COVID-19) patients is unclear. We assessed the incidence of SARS-CoV-2 reinfection and the protection effect of previous infection against reinfection.

**Methods:** We searched PubMed, EMBASE, Cochrane, Scopus, Web of Science, and ClinicalTrials.gov for publications up until the end date of May 1, 2021. The reinfection rate of recovered patients and the protection against reinfection were analyzed using meta-analysis.

**Results:** Overall, 19 studies of 1096 reinfection patients were included. The pooled reinfection rate was 0.65% (95% confidence interval [CI] 0.39–0.98%). The symptomatic reinfection rate was a bit lower (0.37% [95% CI 0.11–0.78%], $I^2 = 99\%$). The reinfection rate was much higher in high-risk populations (1.59% [95% CI 0.30–3.88%], $I^2 = 90\%$). The protection against reinfection and symptomatic reinfection was similar (87.02% [95% CI 83.22–89.96%] and 87.17% [95% CI 83.09–90.26%], respectively).

**Conclusions:** The rate of reinfection with SARS-CoV-2 is relatively low. The protection against SARS-CoV-2 after natural infection is comparable to that estimated for vaccine efficacy. These data may help guide public health measures and vaccination strategies in response to the COVID-19 pandemic. High-quality clinical studies are needed to establish the relevant risk factors in recovered patients.

**Keywords:** COVID-19; Reinfection; SARS-COV-2; Rate

## Introduction

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has had profound implications, not only on human health but also on collective mental health, the economy, and the social structure of global communities.[1,2] At the time of this writing (June 10, 2021), SARS-CoV-2 has caused >174 million cases of COVID-19, which have led to >3.7 million deaths worldwide.[3] Furthermore, reinfection may occur, which is of great importance to public health.

On August 25, 2020, the first case of reinfection was reported in the medical literature; a total of 24 nucleotide differences existed between the viruses identified in the two infections;[4] this was followed by the establishment of other cases of reinfection around the world.[5-7] One of the largest studies in the UK reported 304 reinfections in 36,509 recovered patients, or a reinfection rate of 0.8%.[8] These cases have aroused widespread concern. Several questions are still unclear. For instance, what is the incidence of reinfection? Are there any differences in incidence by sex or region? How long after initial infection can reinfection be expected?

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Vaccines have now been licensed in various countries that show efficacies ranging from 62% to 95%.[9,10] Because there is an urgent need for immunity from SARS-CoV-2, a more comprehensive understanding of the degree of protection provided against SARS-CoV-2 reinfection is critical for guiding the ongoing development of vaccines and the creation and implementation of appropriate interventional strategies. However, to date, evidence for protective efficacy against reinfection has been lacking. To address this gap in the research, we performed a systematic review and meta-analysis in patients previously infected with SARS-CoV-2 using a wide range of pertinent studies.

## Methods

This meta-analysis was conducted and reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) standards.[11] The PRISMA checklist is given in [Supplementary Table 1, http://links.lww.com/CM9/A856]. The study protocol was pre-registered on International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY) with the registration number INPLASY202160104.

### Search strategy

A comprehensive search was conducted using searches on PubMed, EMBASE, Cochrane Library, Scopus, Web of Science, and ClinicalTrials.gov up to May 1, 2021. An extensive search strategy was used, intended to retrieve all relevant articles, using both Medical Subject Headings terminology and relevant keywords "coronavirus," "COVID-19," "reinfection," "SARS-COV-2," "coronavirus disease 2019," and "severe acute respiratory" [Supplementary Table 2, http://links.lww.com/CM9/A856]. In addition, a manual search of World Health Organization reporting and references in the retrieved articles ensured the identification of studies that were not found in the initial literature search. This selection was limited to publications in English.

### Study outcomes

According to the definition of the US Centers for Disease Control and Prevention (CDC),[12] reinfection is defined as occurring ≥90 days after initial positive testing or ≥45 days with background information supporting contact with confirmed cases or the reappearance of COVID-19–like symptoms. The reinfection rate was determined by dividing the number of reinfected patients by the total number of initially positive patients. Furthermore, the symptomatic reinfection rate was defined by including only symptomatic reinfection patients in the numerator. A high-risk population (HRP) was defined as one that faced a higher burden of virus exposure (e.g., front-line healthcare workers, the residents and staff of care homes and skilled nursing facilities, and older patients with comorbidities), and the reinfection rate in this group was determined by dividing the number of HRP reinfection patients by the total number of initially positive HRP patients. The protection provided by previous infection was measured as one minus risk ratio with a 95% confidence interval (CI) (computed as the infection rate of the initially positive patients *vs.* the infection rate of the initially negative patients). The comparison between the number of initially positive infections and the number of initially negative infections for each study are shown in [Supplementary Table 3, http://links.lww.com/CM9/A856].

### Study selection

The studies were chosen using the following inclusion criteria: (1) studies reporting the number of COVID-19 reinfection that met US CDC criteria and (2) original research including cohort, ecological, and cross-sectional studies. The exclusion criteria were (1) studies with patients with Middle East respiratory syndrome coronavirus or other serotypes of SARS-CoV infection and (2) reviews, commentaries, case reports, case series, and non-human studies.

### Data extraction and quality assessment

Two independent reviewers (M-YJ and W-WW) extracted data from each eligible study and then cross-checked the results. Any disagreements between reviewers on data extraction were resolved through discussions involving and requiring the consensus of the third reviewer (W-SS). The following information was extracted: first author, publication year, country, study design, interval between two infections, age and sex of the initial infection and reinfection patients, reinfection severity (cycle threshold [CT] value), reinfection clinical manifestation, and hospitalization for reinfection. The Newcastle–Ottawa Scale for cohort study was used to evaluate the risk for bias in cohort studies,[13] and the Joanna Briggs Institute critical appraisal tool was used to evaluate the risk for bias for cross-sectional and ecological studies.[14]

### Statistical analyses

Because heterogeneity among the included studies was relatively large due to the various clinical and methodological perspectives in the rate study, we adopted a random-effects model,[15] which was used to obtain a pooled estimate and 95% CI for reinfection rate after recovery from COVID-19, and an arcsine transformation was conducted to stabilize the variance.[16] Heterogeneity was assessed using Cochran $I^2$ and $Q$. The heterogeneity test was truncated at significant Cochran $Q$ values ($P < 0.1$) and $I^2 > 50\%$, because an $I^2$ of 30% to 50% has been recommended as a truncation value for moderate heterogeneity.[17] A prediction interval for the proportion in a new study is calculated if the arguments prediction and "comb.random" are TRUE.[18] The protection provided by previous infection was calculated using a combined Mantel–Hanzsel method with the random-effects model. We used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) to evaluate the quality of evidence for each study outcome.[19]

Cumulative meta-analyses were carried out to determine whether the reinfection rate tended to stabilize as the sample size increased. Sensitivity analyses were also performed with the exclusion of each study at each time to test the reliability of the reinfection rate. In addition,

subgroup analyses were conducted according to sex (male or female), study design (prospective cohort, retrospective cohort, ecological, or cross-sectional study), continent (Europe, North America, or Asia), and infection interval (≥90 days or ≥45 days).

All statistical analyses were conducted with the statistical software R version 4.0.3 (package "meta").

## Results

### Search results and study characteristics

The PRISMA flow chart for the literature selection is shown in Figure 1. Ultimately, 19 of 925 studies with a total of 325,225 COVID-19 patients with initially positive infections were included in the meta-analysis.

The studies[8,20-37] were published between 2020 and 2021 and included 17 cohort studies (3 prospective,[21,32,34] 14 retrospective[20,22-31,33,35,37]), 1 ecological study,[8] and 1 cross-sectional study.[36] The characteristics of the included studies are summarized in Table 1. Reinfections occurred across three continents in our study. Among the nine studies reporting age, the reinfection patients ranged from <1 to 99 years old.[21,23,25,27,33-37] Eight studies mentioned cases of reinfection in HRP, including 30 health care workers and five skilled nursing residents.[20-22,25,28,32,36,37] Thirteen studies reported reinfections of 253 asymptomatic and 447 symptomatic patients.[8,20,21,23,25,28-32,34,36,37] Six studies reported on 13 hospitalized patients who were reinfected.[23,25,26,28,35,37] Among the six studies describing CT values,[21,23,33,34,36,37] one had mean CT values of 32.9,[33] and five had CT values of <30.[21,23,34,36,37]

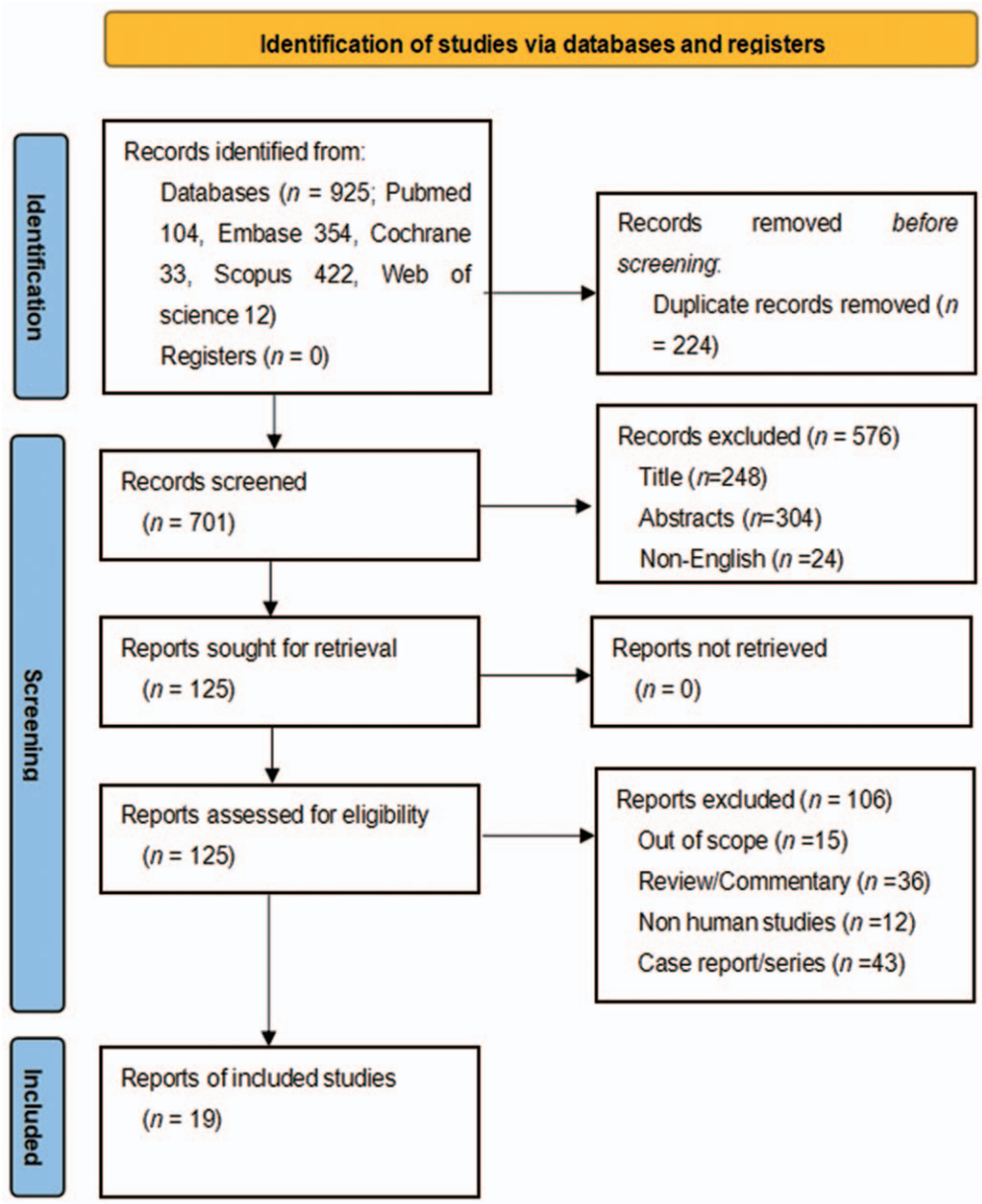


**Figure 1:** PRISMA flow chart illustrating study selection process. PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses.

**Table 1: Baseline characteristics of the included trials.**

| Study (years) | Country | Study design | Interval between two infections, days | Reinfection/Initial positive infection | Initial positive infection | | Reinfection | | Clinical manifestation | | Hospitalization for reinfection, *n* (%) | CT value (average) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Age, years | Female (%) | Age, years | Female (%) | Symptomatic | Asymptomatic | | |
| Jeffery-Smith *et al*[20] (2021) | UK | Retrospective cohort | >90 | 1/88 | NA | NA | NA | NA | 0 | 1 | NA | NA |
| Lumley *et al*[21] (2021) | UK | Prospective cohort | 160–199* | 3/1265 | 17–69* | 77 | 25–59* | 100 | 1 | 2 | NA | 24.6 |
| Hansen *et al*[22] (2021) | Denmark | Retrospective cohort | >90 | 72/11,068 | NA | NA | NA | NA | NA | NA | NA | NA |
| Abu-Raddad *et al*[23] (2020) | Qatar | Retrospective cohort | 45–129* | 54/133,266 | NA | NA | 16–57* | 13 | 23 | 31 | 1 (1.9) | 28 |
| Harvey *et al*[24] (2021) | USA | Retrospective cohort | >90 | 125/41,587 | 44 ± 18 | 54.1 | NA | NA | NA | NA | NA | NA |
| Graham *et al*[8] (2021) | UK | Ecological study | >90 | 304/36,509 | NA | NA | NA | NA | 249 | 55 | NA | NA |
| Soriano *et al*[26] (2021) | Spain | Retrospective cohort | >90 | 2/122 | NA | NA | NA | NA | NA | NA | 1 (50)§ | NA |
| Breathnach *et al*[27] (2021) | UK | Retrospective cohort | >90 | 8/10,727 | 53† | 60 | 55† | 100 | NA | NA | NA | NA |
| Zare *et al*[25] (2021) | Iran | Retrospective cohort | 107–234* | 9/4039 | 64 ± 28 | 49.8 | 13–90* | 44.4 | 9 | 0 | 5 (55.6) | NA |
| Hanrath *et al*[28] (2021) | UK | Retrospective cohort | 162–229‡ | 0/1038 | 30–49‡ | 82.5 | NA | 0 | 0 | 0 | 0 (0) | NA |
| Sheehan *et al*[29] (2021) | USA | Retrospective cohort | 90–295* | 62/8845 | 52 ± 22 | 52.1 | NA | NA | 31 | 31 | NA | NA |
| Qureshi *et al*[30] (2021) | USA | Retrospective cohort | 116 ± 21 | 63/9119 | NA | NA | NA | 55.6 | 19 | 44 | NA | NA |
| Dubelbeiss *et al*[31] (2021) | USA | Retrospective cohort | 106–151* | 3/45 | NA | 100 | NA | 100 | 0 | 3 | NA | NA |
| Sanchez-Montalva *et al*[32] (2021) | Spain | Prospective cohort | >90 | 3/20 | 26–37‡ | 60 | NA | NA | 0 | 3 | NA | NA |
| Abu-Raddad *et al*[33] (2021) | Qatar | Retrospective cohort | >45 | 129/43,044 | 28–47‡ | 20.8 | <1–72* | 28.7 | NA | NA | NA | 32.9 |
| Hall *et al*[34] (2021) | UK | Prospective cohort | 95–297* | 155/8278 | 19–78* | 82.6 | 20–68* | 80 | 78 | 77 | NA | 28 |
| Pilz *et al*[35] (2021) | Austria | Retrospective cohort | 212 ± 25 | 40/14,840 | NA | NA | 26–55‡ | 62.5 | NA | NA | 5 (12.5)‖ | NA |
| Mukherjee *et al*[36] (2021) | India | Cross-sectional study | >102 | 58/1300 | NA | NA | 34 ± 11 | 76.3 | 32 | 6 | NA | 25.1 |
| Cavanaugh *et al*[37] (2021) | USA | Retrospective cohort | 101–110* | 5/25 | NA | NA | 67–99* | 80 | 5 | 0 | 1 (20) | <30 |

Data are shown as *range, †mean, or ‡lower quartile–upper quartile. §The study by Soriano *et al*[26] reported two cases of reinfection, but only described the first case as a 42-year-old obesity male who suffered pneumonia during the two episodes and required hospitalization. ‖Five patients were hospitalized during the second infection, and four of them were also hospitalized during the first infection.CT: Cycle threshold; NA: Not available.

### Quality assessment

Of the 17 cohort studies, 7 (41%) were of moderate quality,[20,23,25,26,31,33,37] and the quality of the remainder was high; 53% of the cohort studies did not mention an adjustment of confounders.[20,23,25-27,31,33,35,37] The quality of both the cross-sectional study and the ecological study were high.[8,36] These two studies clearly described their study subjects and the setting, and they measured the exposures and outcomes in a valid and reliable way [Supplementary Table 4, http://links.lww.com/CM9/A856].

### Reinfection rate

Single-study and summary incidences of reinfection are shown in Figure 2. The incidence of reinfection in recovered COVID-19 patients ranged from 0% to 20% across the 19 studies. The pooled reinfection rate was 0.65% (95% CI 0.39–0.98%), with high heterogeneity ($I^2 = 99\%$) [Figure 2]. The symptomatic reinfection rate was a bit lower (0.37% [95% CI 0.11–0.78%], $I^2 = 99\%$; Supplementary Figure 1A, http://links.lww.com/CM9/A856), whereas the reinfection rate was higher in HRP (1.59% [95% CI 0.30–3.88%], $I^2 = 90\%$; Supplementary Figure 1B, http://links.lww.com/CM9/A856).

### Protection against reinfection

Protection against reinfection and symptomatic reinfection was 87.02% (95% CI 83.22–89.96%) [Figure 3A] and 87.17% (95% CI 83.09–90.26%) [Figure 3B], respectively.

### Subgroup analyses of reinfection rate

Table 2 summarizes the results of subgroup analyses for reinfection rate in patients with COVID-19. Only three studies reported reinfection rates, which overall were 0.38% (95% CI 0.27–0.51%) in females and 1.77% (95% CI 0.01–6.75%) in males. Among the study designs, the reinfection rate in cross-sectional studies was higher than in other study designs (4.46% [95% CI 3.41–5.65%]). Similarly, the reinfection rates in both North America and infection intervals >90 days were higher than in the remaining subgroups.

### Cumulative analyses of reinfection rate

Cumulative meta-analyses indicated that with increased sample size, the point estimate gradually stabilized and the CI gradually narrowed, showing that the larger the sample size, the greater the accuracy of the results [Supplementary Figure 2, http://links.lww.com/CM9/A856].

### Sensitivity analyses of reinfection rate

Excluding each study one by one from the analyses, the results of sensitivity analyses (0.51–0.73%) were in good agreement with the reinfection rate, indicating the

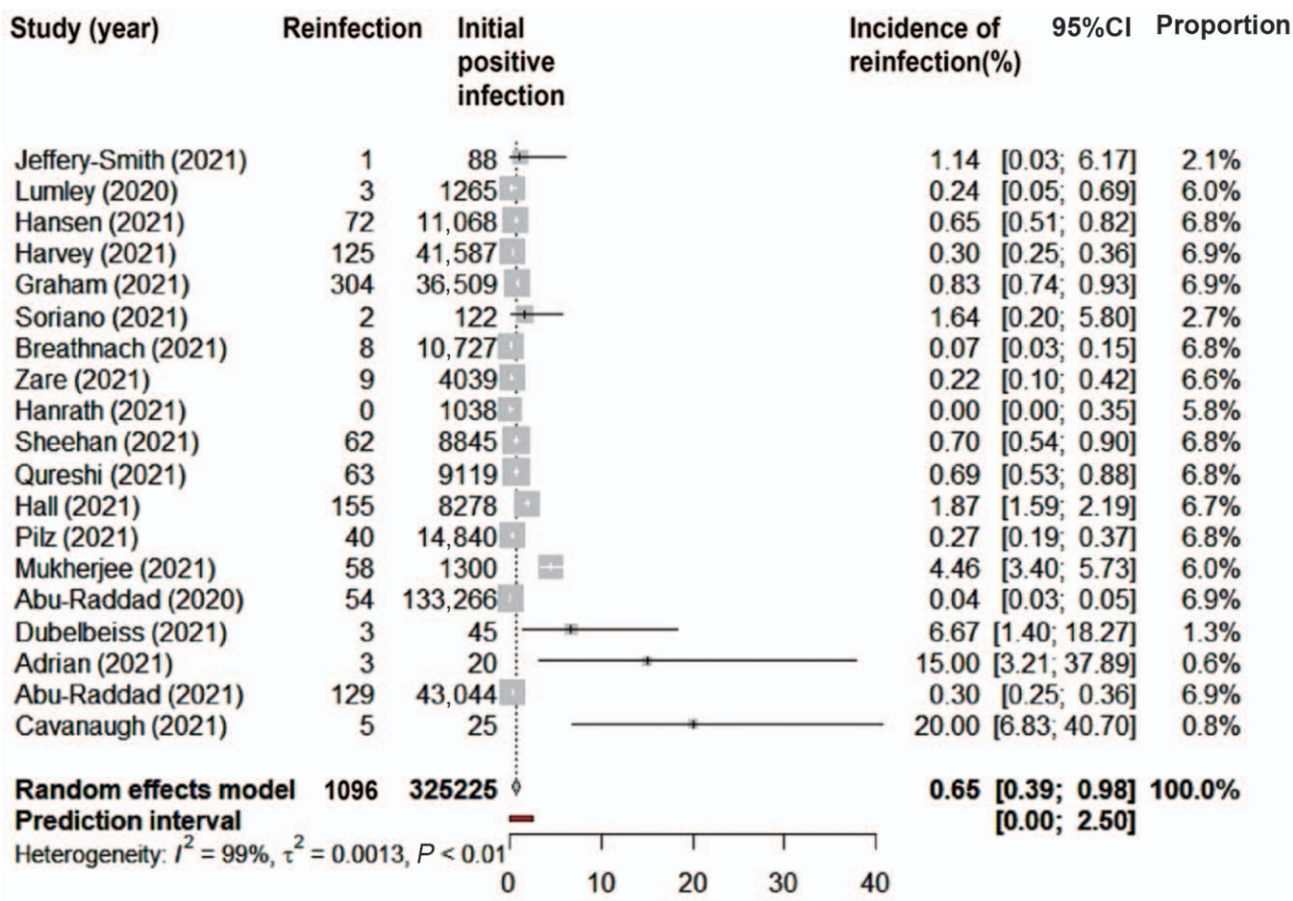


**Figure 2:** Forest plot illustrating the single study and summary incidence of SARS-CoV-2 reinfection. CI: Confidence interval; SARS-CoV-2: Severe acute respiratory syndrome Coronavirus 2.

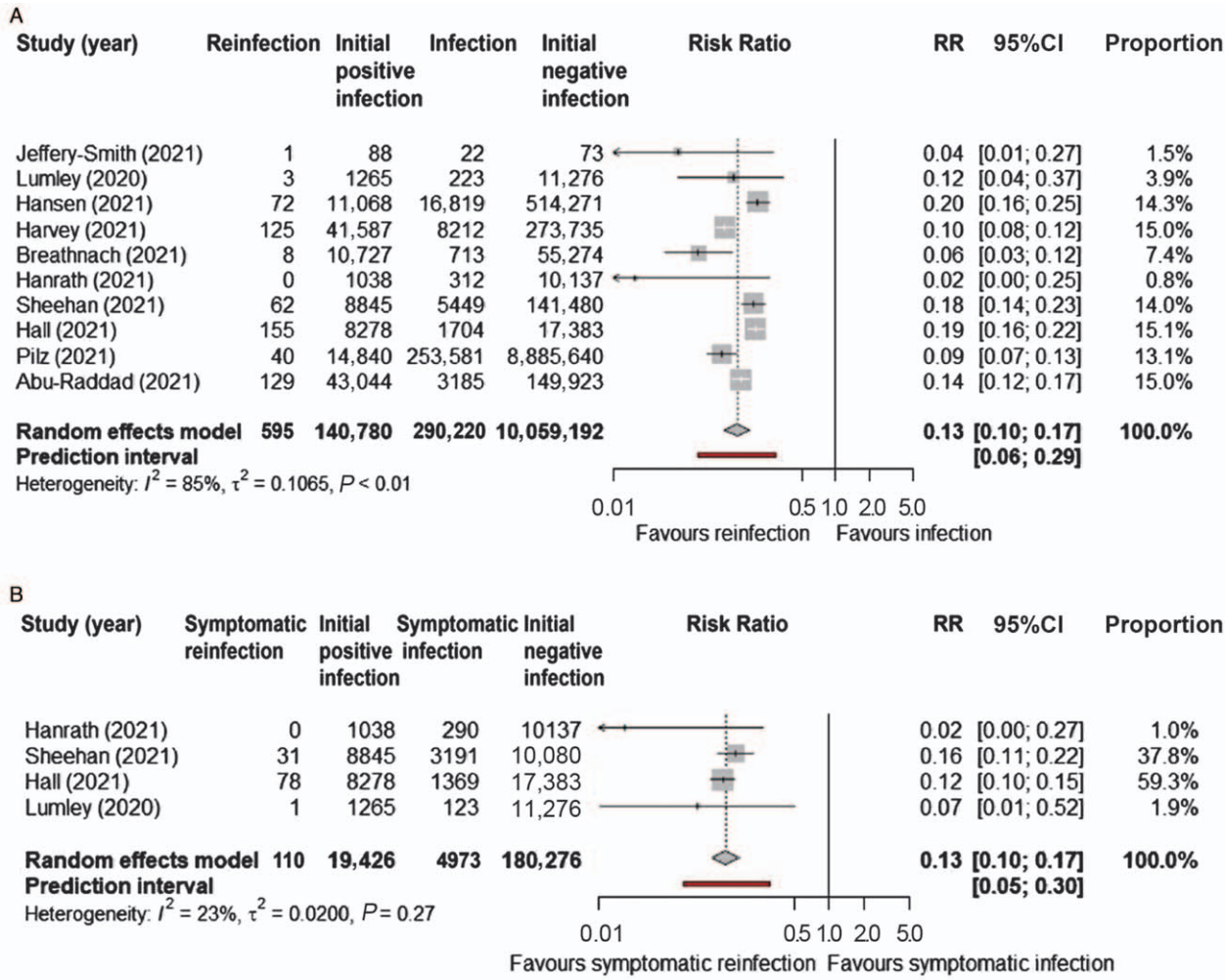


**Figure 3:** Forest plot illustrating the protection afforded from initial SARS-CoV-2 infection (1-RR). (A) Protection against reinfection, (B) Protection against symptomatic reinfection. CI: Confidence interval; RR: Risk ratio; SARS-CoV-2: Severe acute respiratory syndrome Coronavirus 2.

**Table 2: Results of subgroup analysis of the incidence of reinfection in patients with COVID-19.**

| Items | No. of studies | Reinfection (*n*) | Initial positive infection (*n*) | Incidence, % (95% CI) | $I^2$ (%) | Prediction interval, %(95% CI) |
|---|---|---|---|---|---|---|
| Gender | | | | | | |
| Male* | 3 | 221 | 37,541 | 1.77 (0.00, 6.75) | 99 | 0.00, 100.00 |
| Female | 3 | 71 | 17,807 | 0.38 (0.27, 0.51) | 35 | 0.00, 2.29 |
| Study design | | | | | | |
| Prospective cohort* | 3 | 161 | 9563 | 1.66 (0.18, 4.58) | 95 | 0.00, 82.05 |
| Retrospective cohort | 14 | 573 | 277,853 | 0.35 (0.19, 0.57) | 98 | 0.00, 1.40 |
| Ecological study† | 1 | 304 | 36,509 | 0.83 (0.74, 0.93) | – | – |
| Cross-sectional study† | 1 | 58 | 1300 | 4.46 (3.41, 5.65) | – | – |
| Continent | | | | | | |
| Europe | 10 | 588 | 83,955 | 0.54 (0.22, 0.99) | 97 | 0.00, 2.61 |
| North America | 5 | 258 | 59,621 | 0.73 (0.36, 1.25) | 94 | 0.00, 2.90 |
| Asia | 4 | 250 | 181,649 | 0.63 (0.21, 1.28) | 99 | 0.00, 5.75 |
| Infection interval | | | | | | |
| ≥90 days | 17 | 913 | 148,915 | 0.74 (0.46, 1.08) | 97 | 0.02, 2.48 |
| ≥45 days† | 2 | 183 | 176,310 | 0.14 (0.00, 0.51) | 99 | – |

* Prediction interval was too wide due to severe heterogeneity in very small number of included studies. † Prediction interval could not be calculated due to small number of included studies. CI: Confidence interval; COVID-19: Coronavirus disease 2019.

robustness of the results [Supplementary Figure 3, http://links.lww.com/CM9/A856].

### Evidence quality

The GRADE system showed that the quality of protection against symptomatic reinfection was moderate, while the results of protection against reinfection, reinfection rate, symptomatic reinfection rate, and reinfection rate for HRPs had low quality [Supplementary Table 5, http://links.lww.com/CM9/A856].

## Discussion

To the best of our knowledge, this was the first meta-analysis to investigate the reinfection rate of SARS-CoV-2 in a large population. Our results indicate a relatively low reinfection rate in the general population but a much higher rate in HRPs, and protection against reinfection or symptomatic reinfection was 87%.

Reinfection with the SARS-CoV-2 virus can be attributed to two main causes. The first reason is the decline in immunity over time or the failure of naturally acquired immunity, which results in reinfection with the same virus strain, making people sick or asymptomatic carriers.[38,39] Another reason for this may be viral mutations that can easily lead to reinfection because the previously established naturally acquired immunity may not be effective against the mutant strain.[4,5] Hence, regardless of whether long-term protective immunity is possible for all patients after exposure to COVID-19, it may make them vulnerable to reinfection. It should be recalled that social distancing, the use of masks, hand hygiene, and other preventive measures are very important for recovering patients, particularly those in HRPs who are more exposed to the virus.

Several factors may influence the reinfection rate. First, subjects infected during the first wave of the pandemic did not undergo antibody or polymerase chain reaction testing and were not admitted or hospitalized for treatment (particularly if they had asymptomatic attacks).[40] Thus, it was difficult to accurately identify all reinfected individuals. Second, a recent meta-analysis[41] indicates that some reinfection cases may appear as false-positive results in the first and/or second infection tests, which may produce an overestimated reinfection rate. Additionally, most of the positive cases may simply be protracted first infections rather than true reinfections due to the relatively high positive retest rate (12.0–32.9%) following the convalescent period.[42-46] Thus, the reinfection rate in some included studies might be an overestimate.

As COVID-19 vaccination programs develop, it is important to note that patients who had SARS-CoV-2 antibodies were excluded from some vaccine studies. Nevertheless, previous infections still had an 87% protective effect during the study period. This is equivalent to or better than the protective effect reported in recent vaccine studies. However, due to differences in study design and study populations, direct comparison is not possible.[9,10,47] Based on our findings, we believe that in areas where vaccines are rare, the vaccination of patients previously infected with COVID-19 can be delayed to allow HRPs to be vaccinated first. However, the efficacy of the vaccine for previously immune patients is still unclear and may need to be further examined.

Several limitations should be noted. First, the incidence of reinfection might have been overestimated because most included studies lack the gold standard of confirmation (i.e., genetic lineage or clades between initial infection and reinfection). Second, due to the lack of detailed clinical features in most studies that were examined, cases of reinfection cannot be examined in detail, particularly the immune features, which would be of great assistance to our understanding of the protection of natural immunity and virus escape. Finally, subgroup analyses based on disease severity, age, and comorbidities could not be performed due to the lack of specific data. Thus, the results should be interpreted with caution.

## Conclusion

The reinfection rate of SARS-CoV-2 is relatively low. It has a similar protective effect against SARS-CoV-2 reinfection as vaccine inoculation. These data may help determine public health measures and vaccination strategies in response to the COVID-19 pandemic. Meanwhile, factors affecting reinfection incidence, such as strains of the virus, patient immune status, or other patient-level characteristics, should be evaluated in future studies to help develop strategies to control and prevent their occurrence.

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### Conflicts of interest

None.

## References

1. Nicola M, Alsafi Z, Sohrabi C, Kerwan A, Al-Jabir A, Iosifidis C, *et al*. The socio-economic implications of the coronavirus pandemic (COVID-19): a review. Int J Surg 2020;78:185–193. doi: 10.1016/j.ijsu.2020.04.018.
2. Ioannidis JPA. Global perspective of COVID-19 epidemiology for a full-cycle pandemic. Eur J Clin Invest 2020;50:e13423. doi: 10.1111/eci.13423.
3. WHO Coronavirus (COVID-19) Dashboard. Available from: https://covid19.who.int. [Last accessed on June 10, 2021].
4. To KKW, Hung IFN, Ip JD, Chu AWH, Chan WM, Tam AR, *et al*. COVID-19 re-infection by a phylogenetically distinct SARS-coronavirus-2 strain confirmed by whole genome sequencing. Clin Infect Dis 2020;ciaa1275. doi: 10.1093/cid/ciaa1275.
5. Van Elslande J, Vermeersch P, Vandervoort K, Wawina-Bokalanga T, Vanmechelen B, Wollants E, *et al*. Symptomatic SARS-CoV-2 reinfection by a phylogenetically distinct strain. Clin Infect Dis 2021;73:354–356. doi: 10.1093/cid/ciaa1330.
6. Gupta V, Bhoyar RC, Jain A, Srivastava S, Upadhayay R, Imran M, *et al*. Asymptomatic reinfection in two healthcare workers from India with genetically distinct SARS-CoV-2. Clin Infect Dis 2020;ciaa1451. doi: 10.1093/cid/ciaa1451.
7. Tillett RL, Sevinsky JR, Hartley PD, Kerwin H, Crawford N, Gorzalski A, *et al*. Genomic evidence for reinfection with SARS-CoV-2: a case study. Lancet Infect Dis 2021;21:52–58. doi: 10.1016/S1473-3099(20)30764-7.

8. Graham MS, Sudre CH, May A, Antonelli M, Murray B, Varsavsky T, *et al*. Changes in symptomatology, reinfection, and transmissibility associated with the SARS-CoV-2 variant B.1.1.7: an ecological study. Lancet Public Health 2021;6:e335–e345. doi: 10.1016/S2468-2667(21)00055-4.
9. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, *et al*. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet 2021;397:99–111. doi: 10.1016/S0140-6736(20)32661-1.
10. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, *et al*. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med 2021;384:403–416. doi: 10.1056/NEJMoa2035389.
11. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al*. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.
12. Investigative Criteria for Suspected Cases of SARS-CoV-2 Reinfection (ICR). Available from: https://www.cdc.gov/coronavirus/2019-ncov/php/invest-criteria.html. [Last accessed on June 21, 2021].
13. NOS-Newcastle-Ottawa Scale. Available from: https://www.abbreviations.com/term/1418908. [Last accessed on June 161.
14. JBI-Joanna Briggs Institute Critical Appraisal Tools. Available from: https://jbi.global/critical-appraisal-tools. [Last accessed on June 16, 2021].
15. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Methods 2010;1:97–111. doi:10.1002/jrsm.12.
16. Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. J Epidemiol Community Health 2013;67:974–978. doi: 10.1136/jech-2013-203104.
17. Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–1558. doi: 10.1002/sim.1186.
18. Higgins JPT, Thompson SG, Spiegelhalter DJ. A re-evaluation of random-effects meta-analysis. J R Stat Soc Ser A Stat Soc 2009;172:137–159. doi: 10.1111/j.1467-985X.2008.00552.x.
19. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, *et al*. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64:383–394. doi: 10.1016/j.jclinepi.2010.04.026.
20. Jeffery-Smith A, Iyanger N, Williams SV, Chow JY, Aiano F, Hoschler K, *et al*. Antibodies to SARS-CoV-2 protect against re-infection during outbreaks in care homes, September and October 2020. Euro Surveill 2021;26:2100092. doi: 10.2807/1560-7917.ES.2021.26.5.2100092.
21. Lumley SF, O'Donnell D, Stoesser NE, Matthews PC, Howarth A, Hatch SB, *et al*. Antibody status and incidence of SARS-CoV-2 infection in health care workers. N Engl J Med 2021;384:533–540. doi: 10.1056/NEJMoa2034545.
22. Hansen CH, Michlmayr D, Gubbels SM, Molbak K, Ethelberg S. Assessment of protection against reinfection with SARS-CoV-2 among 4 million PCR-tested individuals in Denmark in 2020: a population-level observational study. Lancet 2021;397:1204–1212. doi: 10.1016/S0140-6736(21)00575-4.
23. Abu-Raddad LJ, Chemaitelly H, Malek JA, Ahmed AA, Mohamoud YA, Younuskunju S, *et al*. Assessment of the risk of SARS-CoV-2 reinfection in an intense re-exposure setting. Clin Infect Dis 2020;ciaa1846. doi: 10.1093/cid/ciaa1846.
24. Harvey RA, Rassen JA, Kabelac CA, Turenne W, Leonard S, Klesh R, *et al*. Association of SARS-CoV-2 seropositive antibody test with risk of future infection. JAMA Intern Med 2021;181:672–679. doi: 10.1001/jamainternmed.2021.0366.
25. Zare F, Teimouri M, Khosravi A, Rohani-Rasaf M, Chaman R, Hosseinzadeh A, *et al*. COVID-19 reinfection in Shahroud, Iran: a follow up Study. Epidemiol Infect 2021;149:e159. doi: 10.1017/S095026882100087X.
26. Soriano V, Ganado-Pinilla P, Sanchez-Santos M, Gomez-Gallego F, Barreiro P, de Mendoza C, *et al*. Main differences between the first and second waves of COVID-19 in Madrid, Spain. Int J InfectDis 2021;105:374–376. doi: 10.1016/j.ijid.2021.02.115.
27. Breathnach AS, Riley PA, Cotter MP, Houston AC, Habibi MS, Planche TD. Prior COVID-19 significantly reduces the risk of subsequent infection, but reinfections are seen after eight months. J Infect 2021;82:e11–e12. doi: 10.1016/j.jinf.2021.01.005.
28. Hanrath AT, Payne BAI, Duncan CJA. Prior SARS-CoV-2 infection is associated with protection against symptomatic reinfection. J Infect 2021;82:e29–e30. doi: 10.1016/j.jinf.2020.12.023.
29. Sheehan MM, Reddy AJ, Rothberg MB. Reinfection rates among patients who previously tested positive for COVID-19: a Retrospective Cohort Study. Clin Infect Dis 2021;ciab234. doi: 10.1093/cid/ciab234.
30. Qureshi AI, Baskett WI, Huang W, Lobanova I, Naqvi SH, Shyu CR. Re-infection with SARS-CoV-2 in patients undergoing serial laboratory testing. Clin Infect Dis 2021;ciab345. doi: 10.1093/cid/ciab345.
31. Dubelbeiss E, Silverberg M, White C, Jaspan D, Goldberg J, Haines C. Repeat positive severe acute respiratory syndrome coronavirus 2 (coronavirus disease 2019) testing ≥90 days apart in pregnant women. Am J Obstet Gynecol MFM 2021;3:100331. doi: 10.1016/j.ajogmf.2021.100331.
32. Sanchez-Montalva A, Fernandez-Naval C, Anton A, Dura X, Vimes A, Silgado A, *et al*. Risk of SARS-CoV-2 infection in previously infected and non-infected cohorts of health workers at high risk of exposure. J Clin Med 2021;10:1968. doi: 10.3390/jcm10091968.
33. Abu-Raddad LJ, Chemaitelly H, Coyle P, Malek JA, Ahmed AA, Mohamoud YA, *et al*. SARS-CoV-2 antibody-positivity protects against reinfection for at least seven months with 95% efficacy. EClinicalMedicine 2021;35:100861. doi: 10.1016/j.eclinm.2021.100861.
34. Hall VJ, Foulkes S, Charlett A, Atti A, Monk EJM, Simmons R, *et al*. SARS-CoV-2 infection rates of antibody-positive compared with antibody-negative health-care workers in England: a large, multicentre, prospective cohort study (SIREN). Lancet 2021;397:1459–1469. doi: 10.1016/S0140-6736(21)00675-9.
35. Pilz S, Chakeri A, Ioannidis JP, Richter L, Theiler-Schwetz V, Trummer C, *et al*. SARS-CoV-2 re-infection risk in Austria. Eur J Clin Invest 2021;51:e13520. doi: 10.1111/eci.13520.
36. Mukherjee A, Anand T, Agarwal A, Singh H, Chatterjee P, Narayan J, *et al*. SARS-CoV-2 re-infection: development of an epidemiological definition from India. Epidemiol Infect 2021;149:e82. doi: 10.1017/S0950268821000662.
37. Cavanaugh AM, Thoroughman D, Miranda H, Spicer K. Suspected recurrent SARS-CoV-2 infections among residents of a skilled nursing facility during a second COVID-19 outbreak - Kentucky, July-November 2020. MMWR Morb Mortal Wkly Rep 2021;70:273–277. doi: 10.15585/mmwr.mm7008a3.
38. Wajnberg A, Amanat F, Firpo A, Altman DR, Bailey MJ, Mansour M, *et al*. Robust neutralizing antibodies to SARS-CoV-2 infection persist for months. Science 2020;370:1227–1230. doi: 10.1126/science.abd7728.
39. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, *et al*. Antibody responses to SARS-CoV-2 in patients with novel coronavirus disease 2019. Clin Infect Dis 2020;71:2027–2034. doi: 10.1093/cid/ciaa344.
40. Iwasaki A. What reinfections mean for COVID-19. Lancet Infect Dis 2021;21:3–5. doi: 10.1016/S1473-3099(20)30783-0.
41. Hellou MM, Gorska A, Mazzaferri F, Cremonini E, Gentilotti E, De Nardo P, *et al*. Nucleic acid amplification tests on respiratory samples for the diagnosis of coronavirus infections: a systematic review and meta-analysis. Clin Microbiol Infect 2021;27:341–351. doi: 10.1016/j.cmi.2020.11.002.
42. Hoang T. Systematic review and meta-analysis of factors associated with re-positive viral RNA after recovery from COVID-19. J Med Virol 2021;93:2234–2242. doi: 10.1002/jmv.26648.
43. Ulhaq ZS, Soraya GV, Fauziah FA. Recurrent positive SARS-CoV-2 RNA tests in recovered and discharged patients. Rev Clin Esp 2020;220:524–526. doi: 10.1016/j.rce.2020.06.012.
44. Mattiuzzi C, Henry BM, Sanchis-Gomar F, Lippi G. SARS-CoV-2 recurrent RNA positivity after recovering from coronavirus disease 2019 (COVID-19): a meta-analysis. Acta Biomed 2020;91:e2020014. doi: 10.23750/abm.v91i3.10303.
45. Ren X, Ren X, Lou J, Wang Y, Huang Q, Shi Y, *et al*. A systematic review and meta-analysis of discharged COVID-19 patients retesting positive for RT-PCR. EClinicalMedicine 2021;34:100839. doi: 10.1016/j.eclinm.2021.100839.
46. Azam M, Sulistiana R, Ratnawati M, Fibriana AI, Bahrudin U, Widyaningrum D, *et al*. Recurrent SARS-CoV-2 RNA positivity after COVID-19: a systematic review and meta-analysis. Sci Rep 2020;10:20692. doi: 10.1038/s41598-020-77739-y.
47. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, *et al*. Safety and efficacy of the BNT162b2 mRNA covid-19 vaccine. N Engl J Med 2020;383:2603–2615. doi: 10.1056/NEJMoa2034577.


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