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Rapid Review: What is known on the potential for COVID-19 re-infection, including new transmission after recovery?



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Executive Summary

Background

The potential for COVID-19 re-infection is an important public health issue, as potential for re-infection will significantly impact future infection prevention and control measures, particularly related to vaccine development and immunization efforts.

This rapid review was produced to support public health decision makers' response to the coronavirus disease (COVID-19) pandemic. This review seeks to identify, appraise, and summarize emerging research evidence to support evidence-informed decision making.

This rapid review includes evidence available up to May 29, 2020. Information newly added or updated in this version is included in maroon text.

In this rapid review, we provide the most recent research evidence to answer the question: **what is known on the potential for COVID-19 re-infection, including new transmission after recovery?**

Key Points

- There is very limited evidence on the occurrence of COVID-19 re-infection. Evidence quality is low; findings are inconsistent.
- Two recent syntheses found the percentage of patients discharged from hospital following a negative RT-PCR test who subsequently tested positive during routine follow-up, usually in self-isolation or quarantine, to range from 2-21%; study quality is low and findings are inconsistent.
- Most patients who test positive following a previous negative test are asymptomatic; study quality is low and findings are consistent.
- A variety of tests have been used, which raises the question as to whether any noted re-infections are false positives at the initial or follow-up test, or a false negative indicated that the virus had cleared, study quality is low and findings are inconsistent.
- There is no evidence to date that addresses the question as to whether those who may have been re-infected may be able to transmit the virus.

Overview of Evidence and Knowledge Gaps

- Evidence specific to COVID-19 is lacking and this question should be reviewed again as more information is available from higher quality prospective studies around the world.
- The majority of current evidence comes from China where patients enter a 14-day quarantine following discharge from hospital. Because of this some researchers believe it is highly unlikely that subsequent detection of COVID-19 is due to a re-infection and is more likely due to testing inaccuracies; there is insufficient data to fully support this claim.
- Longer follow-up of patients following COVID-19 disease is needed to answer the question about long term immunity and ability to transmit the virus to others.

Methods

Research Question

What is known on the potential for COVID-19 re-infection, including new transmission after recovery?

Search

The following databases were searched on May 11, 2020, and again on May 25 and 26, 2020, for evidence for reinfection with COVID-19.

- Pubmed's curated COVID-19 literature hub: [LitCovid](#)
- [Trip Medical Database](#)
- World Health Organization's [Global literature on coronavirus disease](#)
- Joanna Briggs Institute [COVID-19 Special Collection](#)
- [COVID-19 Evidence Alerts](#) from McMaster PLUS™
- [Public Health +](#)
- [COVID-19 Living Overview of the Evidence \(L-OVE\)](#)
- Cochrane Rapid Reviews [Question Bank](#)
- [Prospero Registry of Systematic Reviews](#)
- NCCMT [COVID-19 Rapid Evidence Reviews](#)
- [MedRxiv preprint server](#)

A copy of the search strategy is available on request.

Study Selection Criteria

The search first included recent, high-quality syntheses. If no syntheses were found, single studies were included. English-language, peer-reviewed sources and sources published ahead-of-print before peer review were included. Grey literature and surveillance sources were excluded.

	Inclusion Criteria	Exclusion Criteria
Population	Individuals with cases of COVID-19 confirmed by RT-PCR test	Presumptive cases of COVID-19
Intervention		
Comparisons		
Outcomes	Subsequent COVID-19 infection following recovery	

When available, findings from syntheses are presented first as these take in to account the available body of evidence and therefore can be applied broadly to populations and settings. Single studies were included if no syntheses were available, or if single studies were published since the search in the synthesis was conducted.

Data on study design, setting, location, population characteristics, interventions or exposure and outcomes were extracted when reported.

Data Extraction and Synthesis

Data on study design, setting, location, population characteristics, interventions or exposure and outcomes were extracted when reported. We synthesized the results narratively due to the variation in methodology and outcomes for the included studies.

We evaluated the quality of included evidence using critical appraisal tools as indicated by the study design below. Quality assessment was completed by one reviewer and verified by a second reviewer. Conflicts were resolved through discussion.

Study Design	Critical Appraisal Tool
Synthesis	Health Evidence™ Quality Appraisal Tool
Case Series	Joanna Briggs Institute (JBI) Checklist for Case Series

Completed quality assessments for each included study are available on request.

Findings

Quality of Evidence

We have identified three new syntheses and three new single studies since the previous version of this report released May 19, 2020. This document includes a total of four completed and two in-progress syntheses and four single studies, for a total of 10 publications included in this rapid review. All new publications added to this list since the May 19, 2020 report are indicated by maroon font. The quality of the evidence included in this review is as follows:

		Total	Quality of Evidence
Syntheses	Completed Reviews	4	4 Moderate
	In Progress Reviews	2	-
Single Studies	Completed	4	4 Low

Warning

Given the need to make emerging COVID-19 evidence quickly available, many emerging studies have not been peer reviewed. As such, we advise caution when using and interpreting the evidence included in this rapid review. We have provided a summary of the quality of the evidence as low, moderate or high to support the process of decision making. Where possible, make decisions using the highest quality evidence available.

A number of mathematical modelling studies are emerging related to COVID-19. While these studies may provide important estimates, their ultimate usefulness depends on the quality of the data that is entered into the model. Given the constantly evolving nature and changing understanding of COVID-19 around the world, a high degree of caution is warranted when interpreting these studies, and when presented, include the range of confidence intervals rather than single effect estimates.

Table 1: Syntheses

Reference	Date Released	Description of Included Studies	Summary of Findings	Quality Rating: Synthesis	Quality Rating: Included Studies
Health Information and Quality Authority. (2020, May 13). Evidence summary of the immune response following infection with SARS-CoV-2 or other human coronaviruses.	May 13, 2020 (Search to May 1, 2020)	Relevant to this question, 10 studies were identified that report positive tests for COVID-19 following recovery. Most are from China, with 2 reports from South Korea <ul style="list-style-type: none"> • 7 case series • 2 case reports • 1 cohort 	All studies report cases of COVID-19 detected following recovery, but a variety of testing methodologies, timing of testing and definition of 'recovery' were used making comparisons difficult. Across all studies it is not clear whether these are new infections, or re-detection of prior infection. Across included case series and case reports, rates of re-detection ranged from 2% to 21%. In all studies, re-detected cases were asymptomatic.	High	Low
Health Information and Quality Authority. (2020, May 13). Evidence summary of the infectiousness of individuals reinfected with SARS-CoV-2 or other human coronaviruses	May 13, 2020 (Search to Apr 23, 2020)	No studies were found that examined whether re-detected cases were infectious to other humans. <ul style="list-style-type: none"> • Four studies were included which followed detected cases of COVID-19 over time. 	No evidence of onward transmission was noted, however little to no information was given as to how this was determined, and in most cases, patients were under quarantine or self-isolation so potential for spread was limited.	High	Low
Alberta Health Services: COVID-19 Scientific Advisory Group. (2020, May 12). Can people with previous COVID-19 infection become re-infected by the SARS-CoV-2 virus?	May 12, 2020 (Search to May 4, 2020)	Relevant to this question, 5 publications and 2 pre-prints specific to COVID-19 in humans were included. All were case series or single group observational studies.	To date there is no evidence to answer the question as to whether re-infection is possible or long term immunity may exist, given the short time frame since the virus was first seen in humans. Within the studies available, it is not possible to determine whether a positive test for COVID-19 following a negative test is confirmation of re-infection or simply re-detection due to a prior false negative. Several news reports were included; however, accuracy of these reports are unknown.	Moderate	Low
Previously Reported Evidence					

<p>Flodgren, G.M. (2020, April). Immunity after SARS-CoV-2 infection, 1st update - a rapid review. Oslo: Norwegian Institute of Public Health.</p>	<p>Apr 2020 (Search to Apr 23, 2020)</p>	<p>This rapid review included 3 studies published from 2019 to 23 April 2020, relevant to this question, one of which was a pre-print. Two of the studies were conducted in China and the third is unknown. Study designs included modelling, and cohort.</p> <p>No studies were found for COVID-19 reinfection in humans, but one animal modelling study was found.</p> <p>Two studies examined reinfection from SARS in 2003 in healthcare workers and patients.</p>	<p>No studies of reinfection with COVID-19 conducted in humans were found.</p> <p>One animal modelling study of reinfection with COVID-19 suggested there could be immunity, but this study provides no insight into the duration of potential immunity.</p> <p>In a study of 34 healthcare workers infected with SARS in 2003 whose antibody levels were followed up for 13 years, high levels of IgG were not sustained after one year.</p> <p>Similarly, among 173 patients infected with SARS in 2003 whose antibody levels were followed up for three years, high levels of IgG decreased after two years. Even if sustained levels of antibodies are related to some protection against reinfection, it is not known if this would ensure full protection against reinfection or may result in less severe infection in the future. The extent to which these findings apply to COVID-19 are unknown.</p>	<p>Low</p>	<p>Not reported</p>
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Table 2: In-progress Syntheses

Title	Anticipated Release Date	Description of Document
Vancouver Coastal Health. (2020). Possible duration of transmission of COVID-19.	May 6, 2020	The objective of this review is to investigate possible durations of transmission of COVID-19, as measured by viral shedding and contact transmission. <i>[Anticipated release date has passed but no completed review found]</i>
Previously Reported Evidence		
Bobrovitz, N., Arora, R., Boucher, E., Yan, T., Rahim, H., Van Wyk, J., Duarte, N., Atmaja, A., Rocco, S., Jodeph, A., & May, E. A living rapid systematic review of SARS-CoV-2 seroprevalence studies. PROSPERO 2020 CRD42020183634	Jun 22, 2022	The purpose is to provide a rapid up-to-date synthesis of SARS-CoV-2 seroprevalence surveys from around the world.

Table 3: Single Studies

Reference	Date Released	Study Design	Population	Setting	Summary of Findings	Quality Rating:
Kang, Y.K. (2020). South Korea's COVID-19 Infection Status: from the Perspective of Re-Positive after Viral Clearance by Negative Testing. <i>Disaster Medicine and Public Health Preparedness</i> , 1-7.	May 22, 2020	Case series	General population who tested positive from 8 April to 29 April	South Korea	3.3% of patients released from quarantine subsequently tested positive using PCR an average of 13.5 days (range 1-35) days after a negative test. Most were asymptomatic. The authors suggest this is re-detection not re-infection, although there is insufficient data to confirm this.	Low
Cao, H., Ruan, L., Liu, J., & Liao, W. (2020). The clinical characteristic of eight patients of COVID-19 with positive RT-PCR test after discharge. <i>Journal of Medical Virology</i> . Epub ahead of print	May 15, 2020	Case series	General population who tested positive in one hospital in China	Wuhan, China	Of 108 hospitalized cases from Feb 10 to April 13, 8 (7.4%) tested positive within 2 weeks of discharge following a negative RT-PCR test. All were asymptomatic. 2 patients continued to test positive for >90 days, past the end of the follow-up period for this study.	Moderate
Huang, J., Zheng, L., Li, Z., Hao, S., Ye, F., Chen, J., Yao, X., Liao, J., Wang, S., Zeng, M., Qiu, L., Cen, F., Huang, Y., Zhu, T., Xu, Z., Ye, M., Yang, Y., Wang, G., Li, J... Ling, X. B. (2020). Recurrence of	May 10, 2020	Case series	General population who tested positive between 11	Shenzhen, China	Of 414 patients who were discharged from hospital into strict quarantine following a negative RT-PCR test, 16.7% subsequently tested positive	Moderate

SARS-CoV-2 PCR positivity in COVID-19 patients: a single center experience and potential implications. <i>Preprint.</i>			January and 23 April		again, most 5-25 days later. Those who retested positive were younger and most were asymptomatic. A subset of patients had re-detected virus after a second, third and fourth quarantine period.	
Previously Reported Evidence						
Okhue, A.V. (2020). Estimation of the probability of reinfection with COVID-19 coronavirus by the SEIRUS model. <i>JMIR Public Health and Surveillance</i> 6(2): e19097.	May 5, 2020	Modelling study	General population Includes data on diagnosed cases and known recoveries up to 27 March 2020.	Global	The findings from this modelling study found evidence to suggest recovered patients do not become re-infected with COVID-19. However, the data used in the modelling are from 27 March 2020. The hypothesis of zero reinfections was not proven clinically in this study.	Not appraised

References

- Alberta Health Services: COVID-19 Scientific Advisory Group. (2020, May 12). [Can people with previous COVID-19 infection become re-infected by the SARS-CoV-2 virus?](#)
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