



Mahalul Azam &lt;mahalul.azam@mail.unnes.ac.id&gt;

**Invitation to Review for BMJ Open bmjopen-2021-049180**

1 message

BMJ Open &lt;onbehalf@manuscriptcentral.com&gt;

Fri, Jan 22, 2021 at 12:52 AM

Reply-To: info.bmjopen@bmj.com

To: mahalul.azam@mail.unnes.ac.id

---

COVID-19: A message from BMJ: <https://authors.bmj.com/policies/covid-19>

---

21-Jan-2021

Dear Dr. Azam:

BMJ Open is an open access journal from BMJ, a sister journal to The BMJ but with different editorial priorities. The journal is published here: <http://bmjopen.bmj.com>.

Manuscript ID bmjopen-2021-049180 entitled "SARS-CoV-2 reinfection: A new challenge for the effectiveness of global vaccination campaign. A systematic review." with Prof. Lo Muzio as contact author has been submitted to BMJ Open.

I invite you to review this manuscript. The abstract appears at the end of this letter, along with the names of the authors. Please let me know as soon as possible if you will be able to accept this invitation. We ask reviewers to return their reviews within 14 days of agreeing to review.

The Journal is located at <https://mc.manuscriptcentral.com/bmjopen>.

PLEASE NOTE: BMJ Open uses compulsory fully open peer review. You will be asked to sign your review and declare any competing interests. The authors will be aware of who reviewed their manuscript and your review will be published alongside the author's original versions and responses to your review if the article is accepted. If you do not sign your review the editorial office will complete this section on your behalf.

BMJ Open has partnered with Publons, a free service for reviewers, to help reviewers gain credit for their work. To take advantage of this service, you will first need to create a profile on Publons. When you submit your review via ScholarOne you will then be asked whether you would like to be credited for your review on Publons. In addition, Publons has partnered with ORCID so that reviewers can opt to have their verified review history automatically added to their ORCID profile.

If you are unable to review at this time, I would greatly appreciate your recommendations for other expert reviewers. You may e-mail me with your reply or click the appropriate link at the bottom of the page to automatically register your reply with our online manuscript submission and review system, ScholarOne Manuscripts.

In recognition of reviewers' support, any reviewer that returns a full review, on time, can receive a 25% discount on Article Processing Charges for a paper for which they are the corresponding author, if submitted within 12 months of completing the review.

We ask reviewers to help ensure studies are scientifically credible and were conducted ethically and in accordance with appropriate reporting guidelines. We do not require a judgement on priority or breadth of appeal.

Once you accept the invitation to review, you will be notified via e-mail about how to access ScholarOne Manuscripts. You will then have access to the manuscript and reviewer instructions in your Reviewer Center.

BMJ Open's success will rely heavily on the thoroughness of reviews submitted and I thank you for your present and/or future support.

Sincerely,

BMJ Open Editorial Office

[info.bmjopen@bmj.com](mailto:info.bmjopen@bmj.com)

We are constantly trying to find ways of improving the peer review system and have an ongoing programme of research. If you do not wish your review entered into a study please let us know by emailing [info.bmjopen@bmj.com](mailto:info.bmjopen@bmj.com) as soon as possible.

\*\*\* PLEASE NOTE: This is a two-step process. After clicking on the link, you will be directed to a webpage to confirm.  
\*\*\*

Decline - Conflict of Interest: [https://mc.manuscriptcentral.com/bmjopen?URL\\_MASK=8d3f6a96b3f14684ae459b5fcb47cc1f](https://mc.manuscriptcentral.com/bmjopen?URL_MASK=8d3f6a96b3f14684ae459b5fcb47cc1f)

Agreed: [https://mc.manuscriptcentral.com/bmjopen?URL\\_MASK=45d20dcf0cd945bcaed6504ddf12c7c0](https://mc.manuscriptcentral.com/bmjopen?URL_MASK=45d20dcf0cd945bcaed6504ddf12c7c0)

Declined: [https://mc.manuscriptcentral.com/bmjopen?URL\\_MASK=2927daecdbf944bf9c8896037449634b](https://mc.manuscriptcentral.com/bmjopen?URL_MASK=2927daecdbf944bf9c8896037449634b)

Unavailable: [https://mc.manuscriptcentral.com/bmjopen?URL\\_MASK=87305ce8807b424fa54fd412ad38bbb2](https://mc.manuscriptcentral.com/bmjopen?URL_MASK=87305ce8807b424fa54fd412ad38bbb2)

## MANUSCRIPT DETAILS

TITLE: SARS-CoV-2 reinfection: A new challenge for the effectiveness of global vaccination campaign. A systematic review.

AUTHORS: bizzoca, Maria Eleonora; Ali Quadri, Mir; Lo Muzio, Lorenzo

ABSTRACT: Background: Reinfection with SARS-CoV-2 seem to be a rare phenomenon. It is necessary to know more about the question of acquired immunity versus the possibility of reinfection in order to anticipate future viral spread and to understand the success of the starting vaccine campaigns.

Methods: A systematic search was performed in online databases including PubMed, Scopus, Web of Science, Science Direct, EMBASE, and preprint servers. In order to differentiate prolonged shedding/reactivation and true reinfection, the reported cases were selected according criteria of the Center for Disease Control and Prevention. Specifically, investigative criteria include a positive RT-PCR test more than 90 days after the initial test and the confirmed recover or a positive RT-PCR test more than 45 after the initial test that is accompanied by compatible symptoms or epidemiological exposure, naturally after the confirmed recover.

Results: Only 37 articles met the inclusion criteria and were included in the final review and the cases confirmed according to these parameters were 70. The severity of the reinfection episode itself was more severe in 25 cases with the death only in 1 case. The observation that many reinfection cases were less severe than initial cases is interesting because it may suggest partial protection from disease. Another interesting data is the detection of different clade or lineage by genome sequencing between initial infection and reinfection in 20/70 cases (29%). Discussion: The findings are useful and contribute towards the role of vaccination in response to the COVID-19 infections. Because of the reinfection cases with SARS-CoV-2, it is evident that the level of immunity is not 100% for all individuals. These data highlights how it is necessary to continue to observe all the prescriptions recently indicated in the literature in order to avoid new contagion for all people after healing from COVID-19 or asymptomatic positive.

# BMJ Open

## CERTIFICATE OF APPRECIATION

This certificate is awarded to

**Dr. Mahalul Azam**

in recognition of peer reviewer contributions to

SARS-CoV-2 reinfection: A new challenge for the effectiveness of global vaccination campaign. A systematic review.

bmjopen-2021-049180

for

BMJ Open

Peer review is a fundamental part of publishing. On behalf of the Editorial team, we appreciate the voluntary contribution that each reviewer gives to the Journal. We would like to extend our appreciation and sincere thanks to you for making it possible for us to publish the highest quality content by providing your rigorous clinical, scientific, or methodological expertise. We hope that we may call upon you again to review future manuscripts.

Yours sincerely,



Richard Sands

**Associate Publisher,  
BMJ Open**

2 February 2021



## Thank you for your review - A decision has been made

1 message

**BMJ Open** <onbehalf@manuscriptcentral.com>  
Reply-To: info.bmjopen@bmj.com  
To: info.bmjopen@bmj.com

Wed, Feb 10, 2021 at 6:12 PM

COVID-19: A message from BMJ: <https://authors.bmj.com/policies/covid-19>

10-Feb-2021,

bmjopen-2021-049180

Title: SARS-CoV-2 reinfection: A new challenge for the effectiveness of global vaccination campaign. A systematic review.

Dear Reviewer,

We are very grateful for the time you have generously given to help us ensure that BMJ Open publishes high quality, well-written and accessible research. We could not do this without the advice and expertise of our reviewers.

The decision on the above article was: Reject

Comments to the Author collated during the peer review process are below:

Reviewer(s) Comments to Author:  
Reviewer: 1

Comments to the Author:  
Thank you for the opportunity to review this work

This systematic review has some strength, i.e. clearly determined reinfection as guided by CDC. However, this systematic review involved case reports data, the limitation of this data should be explained in the discussion.

The objective should consider focused on proving the evidence of reinfection without the relevance of vaccine campaign

In the background, previous reports of recurrence SARS-CoV-2 positivity should be informed/referred with the limitation of inability to differ reinfection and reactivation. Authors could refer to this work (<https://doi.org/10.1038/s41598-020-77739-y>).

The current study provides new insight regarding the reinfection of SARS-CoV-2.

We didn't find any systematic review register (Prospero), it is more transparent to provide the protocol in the public register, otherwise, any explanation should be provided in the script.

Study selection (Pg6 Ln31-68)

The theoretical statements of differing prolonged viral shedding or reinfection should be minimized in this section and should be transferred into the background section, on the other hand, detailed inclusion and exclusion criteria of the study selection should be explained instead. It means that the inclusion of study design in this review should be stated, to deliver the understanding to the reader which is there any other design of the study that reported SARS-CoV-2 reinfection (case reports and cross-sectional design was found in this work). As well as the details of the diagnosis methods, investigation confirmation, sampling sites, subjects characteristics & risk factors if provided.

Quality assessment (Pg7 Ln 12-19)

PRISMA checklist is used to check the completeness of the systematic review, in this section authors should apply the check-list or instruments to assess the individual studies' quality by the relevant tool such as GRADE for clinical-trial or maybe in this work could use CARE since reviewed the case reports or STROBE because there is the cross-sectional study of them. Reviewed and preprint studies also should be subject of concern.

Pg7Ln54

- Another interesting data is the detection of different clade or lineage detected by genome sequencing between initial infection and reinfection in 20/70 cases (29%). Please clarify 20 were patients that genome sequencing tested and the rest 50- were not DNA sequencing tested. So if want to conclude the percentage/ ratio of different clade total number of different clade divided by the total number that tested by DNA sequencing. ..../20 ?? Please clarify

Pg7In53

Although reinfection is most apparent when viruses are different enough to distinguish by genome sequencing, it remains unclear..... I encourage this part to be transferred into the discussion since this part is not the results of the study but an opinion or statement that strengthens the finding.

In the discussion authors encouraged to give the explanation much more regarding the phenomenon of reinfection providing evidence of molecular data (DNA sequencing) and other relevant facts, instead of iteration of explanation of recurrence and prolonged shedding that previously described in the background.

The term of reinfection based on phylogenetic analysis and disease clinical data as well as time interval category should be described for each individual study (cases) reported in this study.

Pg13In19

Because of the reinfection cases with SARS-CoV-2, it is evident that the level of immunity is not 100% for all individuals.

It is true that evidence shows us the level of immunity is not 100%, but the current study could not provide the percentage/ incidence of reinfection among total covid-19 patients being observed, which could mislead the readers.

Reviewer: 2

Comments to the Author:

Reviewer's comments (bmjopen-2021-049180):

The review article by Bizzoca and collaborators deals with the potential SARS-CoV-2 reinfection with regard to the effectiveness of the global vaccination. For this purpose, the authors undertook a systematic search of relevant data in online databases. The criteria of the CDC were used to distinguish between SARS-CoV-2 reactivation and actual viral reinfection of individuals. Finally, 37 articles were selected and investigated according to the inclusion criteria. From the analyses of data available, it appears that most of the reinfection cases were "milder" than the initial infection, suggesting some partial immune protection of infected persons. Interestingly, reinfection in 20 out of 70 cases (29%) was associated with a different virus clade/lineage, as assessed by genome sequencing.

In my opinion, this is an interesting and scientifically sound analysis. The study clearly provides some important information on the SARS-CoV-2 reactivation versus reinfection of individuals. It is also worth mentioning that the manuscript is clear, well-written and reasonably discussed. However, one may regret the lack of illustration(s).

I have a few concerns to potentially improve the quality of the manuscript, as follows:

1. It would be appropriate and informative to better compare the findings presented in this study with those already reported/published in the literature on the topic (e.g. most recent one being 'Reinfection risk of novel coronavirus (COVID-19): A systematic review of current evidence' by Seyed Alinaghi S et al., World Journal of Virology (2020) Dec 15;9(5):79-90. Doi: 10.5501/wjv.v9.i5.79;
2. What about the differences observed -if any- between males and females, and eventually between adults and children (that are much less infected by SARS-CoV-2)?
3. The manuscript might be revised by a native English speaker for an optimal clarity.

Reviewer: 3

Comments to the Author:

This is a well written review - just a few minor typos that can be corrected using MS Word's Spelling/Grammar check.

The reason for the 'Major' revision is the host of new papers describing antibody responses and their degree of protection - from both natural as well as vaccine-induced immune responses - that that authors need to include and discuss, as the reasons for and the rate of reinfection that we see will clearly be determined by this:

Multiple Phase 1/2 vaccine trials have used various forms of SARS-COV-2 S1/S2 IgG ELISAs and viral neutralisation assays demonstrating similar and measurable vaccine-induced antibody responses - that have gone on to demonstrate correspondingly high vaccine protective efficacy in multiple Phase 3 clinical trials:



• <https://www.thelancet.com/action/showPdf?pii=S0140-6736%2820%2932466-1>  
<https://www.nejm.org/doi/full/10.1056/nejmoa2022483>  
<https://www.nejm.org/doi/10.1056/NEJMoa2027906>  
<https://www.nejm.org/doi/10.1056/NEJMoa2034201>  
<https://www.thelancet.com/action/showPdf?pii=S0140-6736%2821%2900234-8>

- and now we also know from the SIREN and Oxford studies below that recovered/natural immunity with detectable SARS-COV-2 IgG, in healthcare workers also translates to effective protection against reinfection in 80-90% efficacy for at least 5-6 months:

<https://www.nejm.org/doi/10.1056/NEJMoa2034545>  
<https://www.medrxiv.org/content/10.1101/2021.01.13.21249642v1>

If you have any questions or feedback, please do not hesitate to contact the Editorial Office.

Remember that reviewing for BMJ Open entitles you to 25% off publishing charges if you submit a paper as corresponding author to the journal within 12 months of completing your review. Click here to find out more on how to submit: <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

Kind regards,  
BMJ Open editorial office