



AMERICAN  
SOCIETY FOR  
MICROBIOLOGY

# Microbiology Spectrum

## One year follow-up of COVID-19 patients indicates substantial assay-dependent differences in the kinetics of SARS-CoV-2 antibodies

Alexander Egger, Sabina Sahanic, Andreas Gleiss, Franz Ratzinger, Barbara Holzer, Christian Irsara, Nikolaus Binder, Christoph Winkler, Christoph Binder, Wilfried Posch, Lorin Loacker, Boris Harmann, Markus Anliker, Guenter Weiss, Thomas Sonnweber, Ivan Tancevski, Andrea Griesmacher, Judith Löffler-Ragg, and Gregor Hoermann

*Corresponding Author(s): Gregor Hoermann, MLL Munich Leukemia Laboratory*

---

### Review Timeline:

Submission Date:	February 17, 2022
Editorial Decision:	June 2, 2022
Revision Received:	July 10, 2022
Accepted:	September 6, 2022

---

*Editor: William Rawlinson*

*Reviewer(s): Disclosure of reviewer identity is with reference to reviewer comments included in decision letter(s). The following individuals involved in review of your submission have agreed to reveal their identity: Zin Naing (Reviewer #1)*

### Transaction Report:

(Note: With the exception of the correction of typographical or spelling errors that could be a source of ambiguity, letters and reports are not edited. The original formatting of letters and referee reports may not be reflected in this compilation.)

**DOI:** <https://doi.org/10.1128/spectrum.00597-22>

June 2, 2022

Prof. Gregor Hoermann  
MLL Munich Leukemia Laboratory  
Munic  
Germany

Re: Spectrum00597-22 (One year follow-up of COVID-19 patients indicates substantial assay-dependent differences in the kinetics of SARS-CoV-2 antibodies)

Dear Prof. Gregor Hoermann:

The authors study an interesting area, although data are now available from several different studies of a similar nature. The reviewer has raised important issues around whether reinfection occurred, the differences in antibody persistence between patients with single and multiple morbidities, and data on the type of infecting virus (ie what VOC was likely to be infecting these patients).

I agree these are important issues that should be addressed with a resubmitted manuscript, that would then be considered as modifications of the existing manuscript. The authors are encouraged to address these.

Thank you for submitting your manuscript to Microbiology Spectrum. When submitting the revised version of your paper, please provide (1) point-by-point responses to the issues raised by the reviewers as file type "Response to Reviewers," not in your cover letter, and (2) a PDF file that indicates the changes from the original submission (by highlighting or underlining the changes) as file type "Marked Up Manuscript - For Review Only". Please use this link to submit your revised manuscript - we strongly recommend that you submit your paper within the next 60 days or reach out to me. Detailed instructions on submitting your revised paper are below.

Link Not Available

Below you will find instructions from the Microbiology Spectrum editorial office and comments generated during the review.

ASM policy requires that data be available to the public upon online posting of the article, so please verify all links to sequence records, if present, and make sure that each number retrieves the full record of the data. If a new accession number is not linked or a link is broken, provide production staff with the correct URL for the record. If the accession numbers for new data are not publicly accessible before the expected online posting of the article, publication of your article may be delayed; please contact the ASM production staff immediately with the expected release date.

The ASM Journals program strives for constant improvement in our submission and publication process. Please tell us how we can improve your experience by taking this quick [Author Survey](#).

Sincerely,

William Rawlinson

Editor, Microbiology Spectrum

Journals Department  
American Society for Microbiology  
1752 N St., NW  
Washington, DC 20036  
E-mail: [spectrum@asmusa.org](mailto:spectrum@asmusa.org)

Reviewer comments:

Reviewer #1 (Comments for the Author):

This longitudinal study investigated level of humoral immune response in COVID-19 patients for up to one year following SARS-CoV-2 infection, thereby evaluating 8 commercially available anti-spike and anti-nucleocapsid antibody assays, as well as virus neutralisation test. I only have a few minor comments.

- (1) The length of study is relatively long, and re-infection is possible in study participants during one year follow-up. How was re-infection being monitored during the study period?
- (2) Live virus neutralisation test was validated using the WHO reference panel and reference standard for anti-SARS-CoV-2 antibodies. Good correlation was observed between neutralising antibody titres determined by virus neutralisation test and WHO assigned International Units. It would be interesting to determine the performance of 8 commercial SARS-CoV-2 antibody assays (in terms of correlation with WHO assigned International Units), using reference panel and reference standards.
- (3) Clinical data including gender, age, severity of acute COVID-19, polymorbidity, etc. were obtained for each participant. Analysis of antibody levels and COVID-19 disease severity in polymorbidity subgroup could not be found.

Staff Comments:

### Preparing Revision Guidelines

To submit your modified manuscript, log onto the eJP submission site at <https://spectrum.msubmit.net/cgi-bin/main.plex>. Go to Author Tasks and click the appropriate manuscript title to begin the revision process. The information that you entered when you first submitted the paper will be displayed. Please update the information as necessary. Here are a few examples of required updates that authors must address:

- Point-by-point responses to the issues raised by the reviewers in a file named "Response to Reviewers," NOT IN YOUR COVER LETTER.
- Upload a compare copy of the manuscript (without figures) as a "Marked-Up Manuscript" file.
- Each figure must be uploaded as a separate file, and any multipanel figures must be assembled into one file.
- Manuscript: A .DOC version of the revised manuscript
- Figures: Editable, high-resolution, individual figure files are required at revision, TIFF or EPS files are preferred

For complete guidelines on revision requirements, please see the journal Submission and Review Process requirements at <https://journals.asm.org/journal/Spectrum/submission-review-process>. **Submissions of a paper that does not conform to Microbiology Spectrum guidelines will delay acceptance of your manuscript. "**

Please return the manuscript within 60 days; if you cannot complete the modification within this time period, please contact me. If you do not wish to modify the manuscript and prefer to submit it to another journal, please notify me of your decision immediately so that the manuscript may be formally withdrawn from consideration by Microbiology Spectrum.

If your manuscript is accepted for publication, you will be contacted separately about payment when the proofs are issued; please follow the instructions in that e-mail. Arrangements for payment must be made before your article is published. For a complete list of **Publication Fees**, including supplemental material costs, please visit our [website](#).

Corresponding authors may [join or renew ASM membership](#) to obtain discounts on publication fees. Need to upgrade your membership level? Please contact Customer Service at [Service@asmusa.org](mailto:Service@asmusa.org).

Thank you for submitting your paper to Microbiology Spectrum.

## **Reply to Reviewers**

### **Reviewer: 1**

**This longitudinal study investigated level of humoral immune response in COVID-19 patients for up to one year following SARS-CoV-2 infection, thereby evaluating 8 commercially available anti-spike and anti-nucleocapsid antibody assays, as well as virus neutralisation test. I only have a few minor comments.**

- 1. The length of study is relatively long, and re-infection is possible in study participants during one year follow-up. How was re-infection being monitored during the study period?**

Reply: We agree that re-infection could have been an issue during the observation period of one year. Participants have been asked for symptoms associated with a re-infection at each study visit. No patient had to be excluded due to a symptomatic re-infection. Asymptomatic re-infections can formally not be excluded as regular PCR test have not been performed for monitoring within the study. However, individual antibody levels did not indicate an immune reaction to a re-infection. A paragraph on this minor limitation has been added to the discussion section of the revised manuscript.

- 2. Live virus neutralisation test was validated using the WHO reference panel and reference standard for anti-SARS-CoV-2 antibodies. Good correlation was observed between neutralising antibody titres determined by virus neutralisation test and WHO assigned International Units. It would be interesting to determine the performance of 8 commercial SARS-CoV-2 antibody assays (in terms of correlation with WHO assigned International Units), using reference panel and reference standards.**

Reply: We thank the reviewer for raising this point. We measured dilutions of the WHO reference standard with all 6 quantitative assays used in our study. Data are shown in Table S6 of the revised manuscript. In brief, the WHO standard showed a good agreement between the assays. A comment that the observed differences in the long-term follow-up samples could not be explained due to differences in the calibration according to the WHO standard has been added in the revised manuscript.

- 3. Clinical data including gender, age, severity of acute COVID-19 , polymorbidity, etc. were obtained for each participant. Analysis of antibody levels and COVID-19 disease severity in polymorbidity subgroup could not be found.**

Reply: We agree that data on multimorbidity had not been analysed in particular. A stratification of antibody levels according to multimorbidity has been added as additional subpanel in Figure S1. The overlap between multimorbidity and COVID-19 disease severity according to WHO has been added as Table S8 in the revised manuscript.

August 29, 2022

Dr. Gregor Hoermann  
MLL Munich Leukemia Laboratory  
Munich  
Germany

Re: Spectrum00597-22R1 (One year follow-up of COVID-19 patients indicates substantial assay-dependent differences in the kinetics of SARS-CoV-2 antibodies)

Dear Dr Hoermann:

The paper is now suitable for publication with responses to the reviewers from the authors.

Your manuscript has been accepted, and I am forwarding it to the ASM Journals Department for publication. You will be notified when your proofs are ready to be viewed.

The ASM Journals program strives for constant improvement in our submission and publication process. Please tell us how we can improve your experience by taking this quick [Author Survey](#).

As an open-access publication, Spectrum receives no financial support from paid subscriptions and depends on authors' prompt payment of publication fees as soon as their articles are accepted. You will be contacted separately about payment when the proofs are issued; please follow the instructions in that e-mail. Arrangements for payment must be made before your article is published. For a complete list of **Publication Fees**, including supplemental material costs, please visit our [website](#).

ASM policy requires that data be available to the public upon online posting of the article, so please verify all links to sequence records, if present, and make sure that each number retrieves the full record of the data. If a new accession number is not linked or a link is broken, provide production staff with the correct URL for the record. If the accession numbers for new data are not publicly accessible before the expected online posting of the article, publication of your article may be delayed; please contact the ASM production staff immediately with the expected release date.

Corresponding authors may [join or renew ASM membership](#) to obtain discounts on publication fees. Need to upgrade your membership level? Please contact Customer Service at [Service@asmusa.org](mailto:Service@asmusa.org).

Thank you for your patience and for submitting your paper to Spectrum.

Sincerely,

William Rawlinson  
Editor, Microbiology Spectrum

Journals Department  
American Society for Microbiology  
1752 N St., NW  
Washington, DC 20036  
E-mail: [spectrum@asmusa.org](mailto:spectrum@asmusa.org)

Supplemental Material: Accept