Higher SARS-CoV-2 Spike Antibody Levels are Associated with Reduced Risk of Subsequent Symptomatic and Severe COVID-19: A Real-World Data Study

Poster number: MT10

Jin, Yue[1]; Yang, Fei[2*]; Rank, Christopher[3]; Letovsky, Stanley[4]; Ramge, Peter[5] and Jochum, Simon[3]

[1]Roche Information Solutions, Roche Molecular Systems Inc, Santa Clara, California, USA; [2]Roche Information Solutions, F. Hoffman-La Roche Ltd, Basel, Switzerland*;
[3]Roche Diagnostics GmbH, Penzberg, Germany; [4]Labcorp, Westborough, Massachusetts, USA; [5]Roche Diagnostics Solutions, Roche Diagnostics International Ltd, Rotkreuz, Switzerland
*FY was an employee of F. Hoffman-La Roche Ltd. at the time the study was conducted

Please scan the above QR code or click the following link to download this poster
https://tei.li/2xpfb6

Introduction

- The global morbidity associated with the SARS-CoV-2 virus and the rapid spread of new variants of concern suggest that it remains critical to understand the general efficacy of COVID-19 vaccines in clinical practice, their long-term effectiveness and the durability of the immune response in the real-world setting.[1]
- Antibodies can be assessed in high throughput with reasonable technical effort, appear to be associated with protection against symptomatic SARS-CoV-2 infection[2,3] and could be used as a surrogate measure for the strength of an individual's immune response against COVID-19.[3–6]
- The Elecsys® Anti-SARS-CoV-2 S (ACOV2S) assay quantifies antibodies for the receptor binding domain of the SARS-CoV-2 spike (S) protein in human serum and plasma.[7]
- An antibody response to the receptor binding domain is elicited by both vaccines and natural infection; quantifying meaningful thresholds of response to predict the risk of severe disease may inform future public health strategies for immunization.

Objective

This study aimed to use real-world data to assess the association between SARS-CoV-2 S antibody levels and risk of COVID-19 related outcomes (symptomatic and severe infections).

Methods

- This was a retrospective cohort study of subjects who tested with the ACOV2S assay at least 14 days after prior COVID diagnoses and/or vaccinations (**Figures 1, 2 & 3**).
- Two real-world data sources were linked via data tokenization:
  - Antibody data from the ACOV2S assay obtained from routine clinical testing by Labcorp laboratories in the US between 2021-04-01 and 2022-06-30.
  - Infection and vaccination records of the same subjects captured from the PurpleLab Open and Closed claims repository.

Figure 1: Use of fit-for-purpose real-world data to address research question

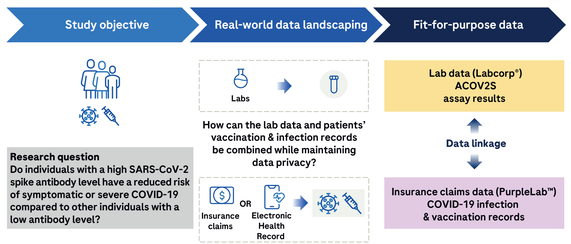
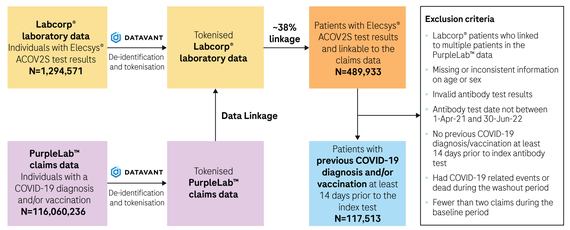
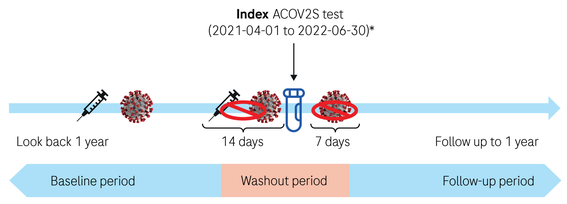


Figure 2: Study data sources and cohort definition



- The study outcomes of interest were:
  1. Symptomatic infection, confirmed by a COVID-19 diagnosis code in the claims database at least 7 days after the index antibody test.
  2. Severe infection, confirmed by a COVID-19 diagnosis code in the claims database and defined as infection leading to hospitalization, admission to the intensive care unit, intubation and/or mechanical ventilation and/or death within 30 days of the infection.

Figure 3: Study design



Patients with **previous COVID-19 diagnosis and/or vaccination at least 14 days prior** to the ACOV2S test performed

Endpoints
- **First symptomatic** SARS-CoV-2 infection
- **First severe** SARS-CoV-2 infection

*Patients with a record of COVID-19 vaccination after the index ACOV2S antibody test were excluded from the study.

Statistics

- Associations between index antibody levels in ACOV2S and future risk of symptomatic and severe SARS-CoV-2 infections were estimated using Cox regression. To adjust for potential confounding, the model was weighted based on propensity score with inverse probability weighting.

Results

- Of 1.3 million subjects with available assay data, 489,933 could be linked to the claims database and 117,513 met the inclusion criteria. Baseline demographic data of these subjects are shown in **Table 1**. Included subjects had an infection profile comparable to that of the general US population (**Table 2**).
- Baseline antibody level correlates with previous COVID-19 vaccinations or infections (**Figure 4**).

Table 1: Baseline characteristics

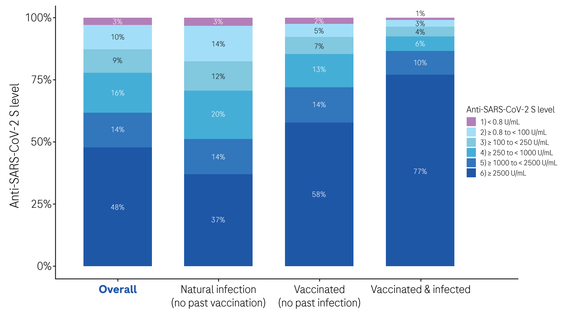
N	Sex & age	Race	Ethnicity
Eligible patients **N=117,513**	**61%** female **39%** male Median age=**55** IQR=[**42, 65**]	**55%** White **5%** Black **3%** Asian **37%** Other/Not specified	**10%** Hispanic **47%** Non-Hispanic **43%** Not specified

US region	Insurance	Prior infection & vaccination	Health conditions
39% Northeast **40%** South **12%** West **9%** Midwest	**28%** Commercial insurance **10%** Medicare/ Medicaid **61%** Claims through point-of-care	**41%** vaccinated (no prior infection) **53%** natural infection (no vaccination) **5%** infected & vaccinated	**29%** immunocompromised **25%** mild comorbidities **11%** moderate-to-severe comorbidities

Table 2: Infection rates compared with the general US population[8–10]

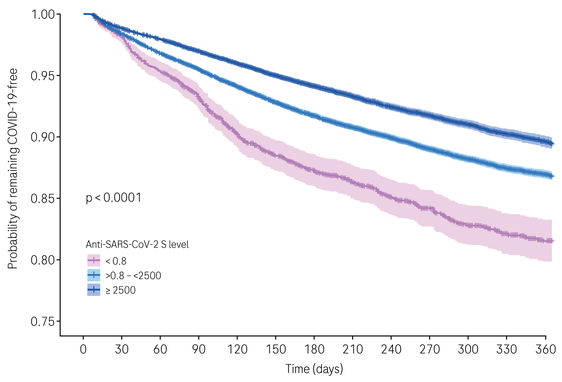
	In the US	Our study data	
SARS-CoV-2 infection rate	**44%** all infection **37%** symptomatic infection	**41%** among linked patients (without study-specific criteria)	
SARS-CoV-2 re-infection rate	**2.7%** in Delta variant period **10%~20%** in Omicron variant period	**11%** among prior- infected patients	**Combined study endpoints (including re-infection & breakthrough infection):** **8.8%** symptomatic infection **1.5%** severe infection
Vaccination breakthrough infection rate	**~1%** in Delta variant period **More common** in Omicron variant period	**5%** among vaccinated patients	

Figure 4: Baseline SARS-CoV-2 S antibody distribution



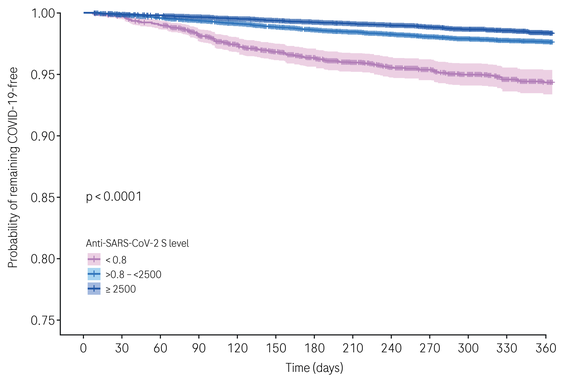
- Individuals with antibody levels of 0.8–2499 U/mL and ≥2500 U/mL, respectively, had 34% and 51% reduced risk of symptomatic infection within 12 months (hazard ratio [HR]=0.66, 95% confidence interval [CI] [0.60, 0.73] and 0.49 [0.44, 0.55]) vs those who tested negative (<0.8 U/mL; **Figure 5** and **Table 3**).
- The risk of severe infection was also reduced, respectively, by 60% and 76% (0.40 [0.33, 0.48] and 0.24 [0.20, 0.30]) vs those with a negative test (**Figure 6** and **Table 4**).

Figure 5: A higher antibody level can provide significantly better protection against symptomatic SARS-CoV-2 infection



Weighted Kaplan–Meier survival curve of SARS-CoV-2 symptomatic infection by anti-SARS-CoV-2 S level.

Figure 6: A higher antibody level can provide significantly stronger protection against severe infection with SARS-CoV-2



Weighted Kaplan–Meier survival curve of severe SARS-CoV-2 infection by anti-SARS-CoV-2 S level.

Table 3: Weighted HRs of symptomatic SARS-CoV-2 infection within 12 months

Anti-SARS-CoV-2 S Titer Level [U/mL]	Weighted Hazard Ratio	95% Confidence Interval	Relative reduced risk of developing endpoints
≥2500	0.49	(0.44, 0.55)	–51%
≥0.8 and <2500	0.66	(0.60, 0.73)	–34%
<0.8	1.00	–	–

Reference antibody level <0.8 U/mL (infection rate=18%).

Table 4: Weighted HRs of severe SARS-CoV-2 infection within 12 months

Anti-SARS-CoV-2 S Titer Level [U/mL]	Weighted Hazard Ratio	95% Confidence Interval	Relative reduced risk of developing endpoints
≥2500	0.24	(0.20, 0.30)	–76%
≥0.8 and <2500	0.40	(0.33, 0.48)	–60%
<0.8	1.00	–	–

Reference antibody level <0.8 U/mL (infection rate=2%).

Strengths and limitations

Strengths	Limitations
• This study leveraged an **innovative approach – data linkage** – to assess the protective effect of antibody titers against SARS-CoV-2 infection • This is **one of the largest real-world data studies** to date in this area of research • Our findings **quantified the level of protection at different antibody thresholds**, which may guide the clinical usage of the antibody assays in offering risk assessment and supporting disease prevention strategies	• This is a convenient sample of patients who tested for ACOV2S assays, which may differ from the general population • COVID-19 cases may also be under-documented or under-reported in the claims database • Categorical reporting of antibody test results at "> 2500 U/mL" impeded our ability to identify protective titers at higher levels (e.g., > 5000 U/mL)

Conclusion

- **Overall, our study demonstrates a strong association between spike antibody levels and the subsequent risk of developing COVID-19.**
- **This evidence contributes to a better understanding of the association between natural immunity and COVID-19 vaccines on the quantitative level of antibodies which may, in turn, inform future public health recommendations.**

This work was supported by Roche Diagnostics International Ltd.

YJ, CR and PR are Roche stock holders; SL participates in employee stock plans at Labcorp; Phillip Morris International has not been involved in the study or publication.

The authors acknowledge the medical writing assistance of Liz Southey, MSc, The Salve Health, UK, funded by Roche Diagnostics Ltd.

References

1. Zheng C, Shao W, Chen X, Zhang B, Wang G, Zhang W. Real-world effectiveness of COVID-19 vaccines: a literature review and meta-analysis. *Int J Infect Dis* 2022;114:252–60.
2. Khoury DS, Cromer D, Reynaldi A, *et al.* Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection. *Nat Med* 2021;27:1205–11.
3. Gilbert PB, Montefiori DC, McDermott AB, *et al.* Immune correlates analysis of the mRNA-1273 COVID-19 vaccine efficacy clinical trial. *Science* 2021;375:43–50.
4. Fleming TR and Powers JH. Biomarkers and surrogate endpoints in clinical trials. *Stat Med* 2012;31:2973–84.
5. Plotkin SA. Correlates of protection induced by vaccination. *Clin Vaccine Immunol* 2010;17:1055–65.
6. Cromer D, Steain M, Reynaldi A, *et al.* Neutralising antibody titres as predictors of protection against SARS-CoV-2 variants and the impact of boosting: a meta-analysis. *Lancet Microbe* 2022;3:e52–61.
7. Roche. Elecsys® Anti-SARS-CoV-2 S [Internet]. 2022 [cited 2022 Aug 10]; Available from: https://diagnostics.roche.com/global/en/products/params/elecsys-anti-sars-cov-2-s.html.
8. Covid-19 infection rate: https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/burden.html [accessed April 2024].
9. Covid-19 re-infection rate: https://www.cdc.gov/mmwr/volumes/72/wr/mm7225a3.htm#:~:text=Reinfections%20represented%202.7%25%20of%20all,10.3%25%20during%20the%20Omicron%20BA. [accessed April 2024].
10. Vaccine breakthrough rate: https://www.hopkinsmedicine.org/health/conditions-and-diseases/coronavirus/breakthrough-infections-coronavirus-after-vaccination; https://coronavirus.health.ny.gov/covid-19-breakthrough-data; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9029338/ [accessed April 2024 for all].