Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

	Bamlanivimab	Bebtelovimab	Casirivimab	Cilgavimab	Etesevimab	Imdevimab	Sotrovimab	Tixagevimab	Casirivimab plus imdevimab (Ronapreve)	Etesevimab plus bamlanivimab	Cilgavimab plus tixagevimab (Evusheld)
B.1.1 (parental)	12·8	8·1	9·9	21	12	79	94	6·7	6·2	6·7	4·1
BA.2	>3700	3·8	>50 417	19	>6050	>50 000	2190	>2750	>2400	>3700	33
BA.2.11	>3700	2·3	>50 417	71	>6050	>50 000	540	>2750	>2400	>3700	154
BA.2.12.1	>3700	5·5	>50 417	75	>6050	>50 000	629	>2750	>2400	>3700	135
BA.4/5	>3700	6·3	>50 417	443	>6050	>50 000	1261	>2750	>2400	>3700	609
BA.2 L452Q	>3700	5·0	>50 417	26	>6050	>50 000	2443	>2750	>2400	>3700	82
BA.2 S704L	>3700	1·1	>50 417	28	>6050	>50 000	1213	>2750	>2400	>3700	27
BA.2 HV69-70del	>3700	2·2	>50 417	19	>6050	>50 000	774	>2750	>2400	>3700	34
BA.2 F486V	>3700	1·1	>50 417	18	>6050	>50 000	1575	>2750	>2400	>3700	23
BA.2 R493Q	>3700	4·2	3697	22	>6050	>50 000	1791	101	431	>3700	31

Representative neutralisation curves are shown in appendix pp 4–5.

Table: **50% neutralisation concentration (ng/mL)**

the L452R/Q substitution rendered approximately 2–5-fold resistance. Notably, BA.4/5 exhibited about 20-fold more resistance to cilgavimab and Evusheld than BA.2 (table). Recently, Cao and colleagues showed that the neutralising activity of cilgavimab against BA.4/5 is approximately 4-fold lower than that against BA.2.[6] Here, we used lentivirus-based pseudoviruses, whereas Cao and colleagues used vesicular stomatitis virus-based pseudoviruses.[6] Therefore, the disparity between our results and those of Cao and colleagues might be due to the difference in the type of pseudoviruses used in the neutralisation assay.

Since mutations are accumulated in the spike proteins of newly emerging SARS-CoV-2 variants, we suggest the importance of rapid evaluation of the efficiency of therapeutic monoclonal antibodies against novel SARS-CoV-2 variants.

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Daichi Yamasoba, Yusuke Kosugi, Izumi Kimura, Shigeru Fujita, Keiya Uriu, Jumpei Ito, Kei Sato, for the Genotype to Phenotype Japan (G2P-Japan) Consortium
keisato@g.ecc.u-tokyo.ac.jp

Division of Systems Virology, Department of Microbiology and Immunology (DY, YK, IK, SF, KU, JI, KS), International Research Center for Infectious Diseases (KS), and International Vaccine Design Center (KS), The Institute of Medical Science, The University of Tokyo, Minato-ku, Tokyo, Japan; School of Medicine, Kobe University, Kobe, Hyogo, Japan (DY); CREST, Kawaguchi, Saitama, Japan (KS)

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Immune responses after omicron infection in triple-vaccinated health-care workers with and without previous SARS-CoV-2 infection

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The SARS-CoV-2 omicron variant (B.1.1.529) is less sensitive to neutralising antibody responses induced by vaccination and prior infection than previous variants.[1,2] Less is known regarding omicron-induced serological and T-cell responses after breakthrough infection of vaccinated individuals with and without prior infection.

In this prospective cohort study, we analysed serological and T-cell responses following omicron infection in 56 triple-vaccinated health-care workers in Sweden with and without prior SARS-CoV-2 infection. A surrogate virus neutralisation test (sVNT) was used to assess neutralisation of SARS-CoV-2 variants. Immune responses of all participants had been

regularly assessed since April, 2020, in the ongoing Swedish COMMUNITY study.[3,4] For this sub-study, participants were screened with qPCR twice a week for 4 weeks,[5] with additional qPCR tests every other day for 14 days if positive. Blood samples were collected 1 week, 2 weeks, 3 weeks, 5 weeks, and 7 weeks after the first positive qPCR sample. For information on study design, demographic characteristics of the study population, and vaccination histories see appendix pp 4–5.

See Online for appendix

Overall, we observed a two-fold increase in anti-spike IgG and sVNT titres against wildtype, delta (B.1.617.2), BA.1, and BA.2 variants 2–5 weeks after omicron breakthrough infection (appendix pp 6–7). Strikingly, however, post-omicron serological responses were significantly higher in previously non-infected (triple-vaccinated with no history of SARS-CoV-2 infection; n=40) than in previously SARS-CoV-2-infected (triple-vaccinated with a confirmed SARS-CoV-2 wildtype infection before primary vaccination; n=16) participants (figure A,C; appendix pp 8–9). The magnitude of serological responses correlated with nadir cycle threshold (Ct) values (appendix pp 8–9). Notably, nadir Ct value and symptomatology[5] were similar in participants with and without previous SARS-CoV-2 infection (appendix pp 8–9). The magnitude of serological responses correlated inversely with pre-infection titres in both previously non-infected and previously infected participants (appendix pp 10–11).

There were no differences in spike-specific T-cell responses between participants 7 weeks after omicron breakthrough infection and participants without omicron infection, regardless of previous SARS-CoV-2 infection status (figure B,D). A significant increase in specific T-cells against nucleocapsid and membrane proteins was observed in omicron-infected individuals without past SARS-CoV-2 infection, showing that omicron breakthrough infection can prime specific T-cells (appendix p 11). Higher serological responses against both BA.1 and BA.2, but similar T-cell responses, were observed in BA.1-infected compared with BA.2-infected individuals (appendix p 12).

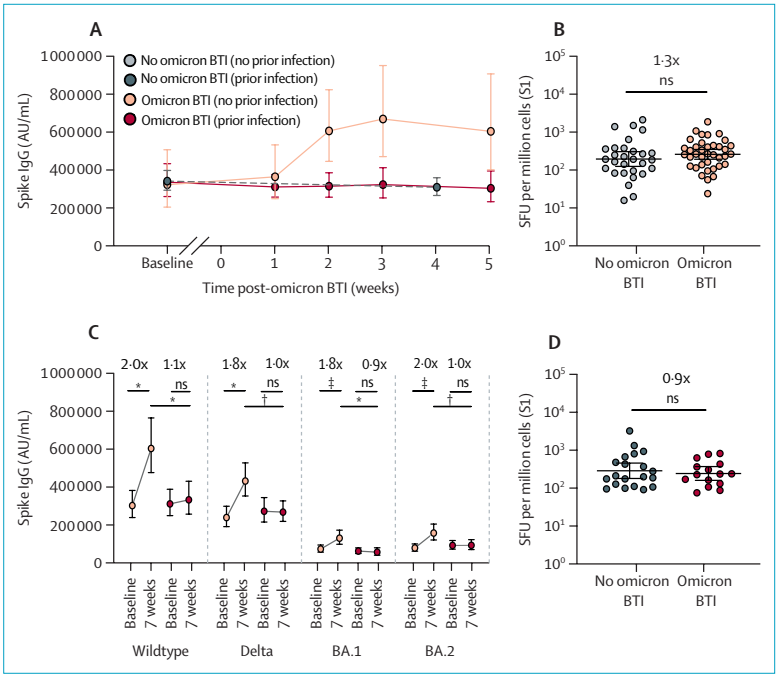

Figure: **Immune responses following omicron BTI in triple-vaccinated health-care workers with and without prior SARS-CoV-2 infection**
(A) GMTs (with 95% CIs) of anti-wildtype spike IgG at baseline and up to 5 weeks post-omicron BTI in participants without (n=20) and with (n=10) previous SARS-CoV-2 infection. The grey dots and dashed line represent participants who remained qPCR negative throughout the study period (n=69). (B) T-cell responses against SARS-CoV-2 S1 protein in participants without omicron BTI and 7 weeks post-infection in participants with omicron BTI; participants had no history of SARS-CoV-2 infection. Individual-participant data (dots) and GMTs (with 95% CIs; lines) are shown. (C) GMTs (with 95% CIs) of anti-spike IgG against wildtype, delta, and omicron BA.1 and BA.2 variants at baseline and 7 weeks after omicron BTI in participants without (n=40) and with (n=16) previous SARS-CoV-2 infection. (D) T-cell responses against SARS-CoV-2 S1 protein in participants without omicron BTI and 7 weeks post-infection in participants with omicron BTI; participants had a history of SARS-CoV-2 infection. Individual-participant data (dots) and GMTs (with 95% CIs; lines) are shown. BTI=breakthrough infection. GMT=geometric mean titre. ns=not significant. SFU=spot-forming units. *p<0·001. †p<0·01. ‡p<0·0001.

This study is limited by the use of sVNT, which is based on the capacity of antibodies to block binding of variant-specific spike protein to ACE2. It is possible that other factors are also involved in neutralisation,[6] which might be better reflected in live microneutralisation assays. However, when analysing a subset of samples we observed a strong correlation between live microneutralising titres and sVNT titres for both wildtype and BA.1 (appendix p 13), mirroring other reports[4,7] suggesting that sVNT can be used as a surrogate method for live virus neutralisation.

These findings suggest that previous SARS-CoV-2 infection, as well as high pre-infection antibody titres, might impact omicron-induced spike-specific serological responses in triple-vaccinated individuals. Close monitoring of immune responses following repeated antigenic exposures through infection or booster doses is needed.

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Kim Blom, Ulrika Marking, Sebastian Havervall, Nina Greilert Norin,

Max Gordon, Marina García, Teghesti Tecleab, Wanda Christ, Mattias Forsell, Mia Phillipson, Peter Nilsson, Sara Mangsbo, Sophia Hober, Mikael Åberg, Jonas Klingström, Charlotte Thålin
charlotte.thalin@ki.se

Department of Clinical Sciences, Karolinska Institutet Danderyd Hospital, 182 88 Stockholm, Sweden (KB, UM, SHa, NGN, MGo, CT); Public Health Agency of Sweden, Stockholm, Sweden (KB, MGa, TT, JK); Center for Infectious Medicine, Department of Medicine Huddinge, Karolinska Institutet, Stockholm, Sweden (MGa, WC, JK); Department of Clinical Microbiology, Umeå University, Umeå, Sweden (MF); Department of Medical Cell Biology and SciLifeLab (MP), Department of Pharmacy and SciLifeLab (SM), and Department of Medical Sciences, Clinical Chemistry and SciLifeLab (MÅ), Uppsala University, Uppsala, Sweden; Department of Protein Science, KTH Royal Institute of Technology, SciLifeLab, Stockholm, Sweden (PN, SHo)

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Vaccination plus previous infection: protection during the omicron wave in Brazil

As of May 11, 2022, an estimated 519 million individuals have been infected with SARS-CoV-2, and at least 11 billion COVID-19 vaccine doses have been administered worldwide. Therefore, understanding hybrid immunity (ie, immunity derived from infection plus vaccination) is crucial to guide future vaccination policies. We found that vaccination provided additional protection to that induced by past infection during the gamma (P.1) and delta (B.1.617.2) variant waves of the pandemic in Brazil.[1] With the emergence of the omicron (B.1.1.529) variant, vaccine effectiveness appears to decay,[2,3] but protection in individuals who have been previously infected and vaccinated remains unknown. We analysed the effect of hybrid immunity in preventing infection and severe outcomes during circulation of the omicron variant in Brazil.

Using national databases, we did a test-negative case-control study as previously described.[1] Cases were defined as individuals with positive RT-PCR or lateral-flow tests and controls as individuals with negative RT-PCT or lateral-flow tests between Jan 1 and March 22, 2022—a period during which omicron was the predominant variant in Brazil (appendix pp 2–4). Severe outcomes were defined as a positive test obtained from 14 days before to 3 days after hospital admission or death occurring within 28 days after a positive test. We analysed vaccine effectiveness in individuals who had been previously infected using two references groups: unvaccinated with or without previous infection. Individuals could have more than one test included in these analyses, and each test was separately counted as a case or control. Detailed methods, including full inclusion and exclusion criteria, are in the appendix (p 2).

Of 9 266 235 tests from 8 471 561 individuals registered on surveillance databases during the study period, 918 219 tests from 899 050 individuals were eligible for inclusion in our analyses. 476 901 (51·9%) of 918 219 tests from 468 804 (52·1%) of 899 050 individuals were positive and defined as cases, and 441 318 (48·1%) tests from 430 246 (47·9%) individuals were negative and defined as controls; 323 704 (35·2%) tests were from individuals who were unvaccinated (22 935 [2·4%] with and 300 769 [32·8%] without previous infection; appendix pp 6–7). Compared with those who were unvaccinated without previous infection, the effectiveness of past infection in preventing reinfection during the omicron wave was low (28·9% [95% CI 26·9–30·9]), increasing with vaccination with any vaccine type (Ad26.COV2.S [Johnson & Johnson], BNT162b2 [Pfizer–BioNTech], ChAdOx-1 nCoV-19 [Oxford–AstraZeneca], or CoronaVac [Sinovac Biotech]), especially after a booster dose, although this protection waned over time (appendix pp 5, 8). Protection against severe outcomes after a previous infection was relatively high (85·6% [95% CI 82·7–88·0]), increasing with vaccination (vaccine effectiveness ranging from 88·0% to 100%; appendix pp 5, 8). Compared with unvaccinated individuals with a previous infection, vaccination with previous infection showed a moderate increase in protection against symptomatic infection ranging from 7·3% (95% CI 4·0–10·4) to 62·7% (61·0–64·3), once again waning over time, and substantial protection against severe outcomes after the booster (appendix pp 5, 8–9). Similar results were obtained using a matched analysis by date of test (within 10 days), age (5-year bands), municipality of residence, and sex in a ratio of 1:2 (with replacement; appendix pp 10–12).

In summary, during a period when omicron was the dominant SARS-CoV-2 variant in Brazil, robust protection against severe disease was offered by a previous infection, and this was increased with hybrid immunity. However, against symptomatic infection, even boosted

For **COVID-19 case and vaccination data** see https://coronavirus.jhu.edu/map.html

See **Online** for appendix

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